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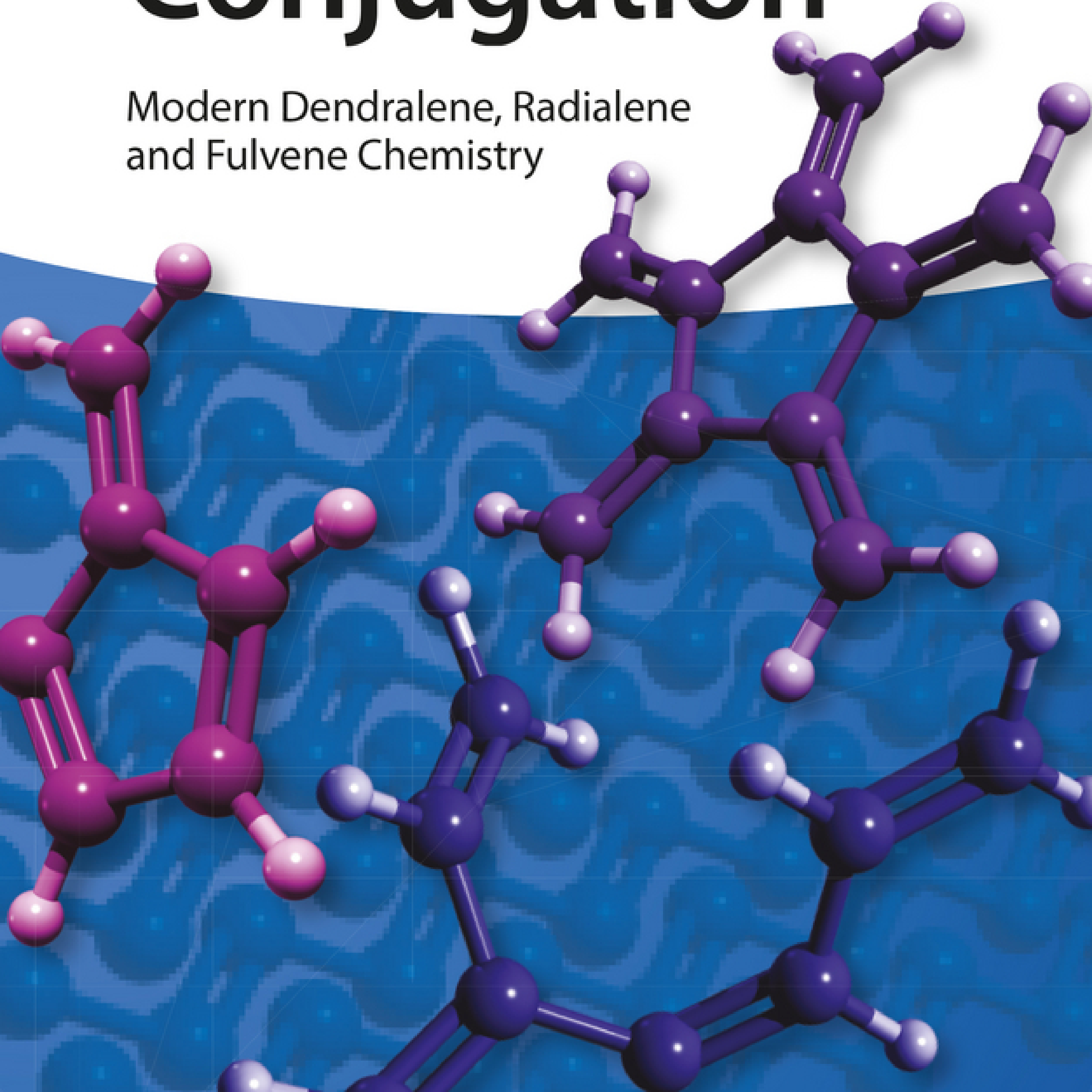
Cross Conjugation

Modern Dendralene, Radialene and Fulvene Chemistry



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Preface

Cross-conjugation has been important since the dawn of organic chemistry. The first compound synthesized, urea, contains a cross-conjugated π-system. Cross-conjugated structures also played a vital role in the early development of industrial organic chemistry in the mid nineteenth century. Synthetic triarylmethane compounds, and specifically the cationic dyes derived therefrom, contain cross-conjugated π-systems. The natural dyestuff indigo, first produced by extraction and later by industrial synthesis, also contains a cross-conjugated π-system.

Yet, compared to the other π-systems, the acyclic linear polyenes, and the cyclic oligoenes (i.e., the annulenes), cross-conjugated molecules have lived in the shadows so far. Acyclic linear polyenes are encountered widely in fatty acid, polyketide, and terpenoid natural product domains and the ultimate polyene, "polyacetylene" is a conductive polymer that was the focus of the 2000 Chemistry Nobel Prize. The annulenes played crucial roles in the development of practical and theoretical organic chemistry (aromatic and antiaromatic compounds), and serve as pivotal bulk chemicals in industry (benzene, toluene, the xylenes, styrene, etc.).

The difference between linear and cross-conjugated systems stems from atom connectivity: taking oligo-olefinic systems as an example, in the linear polyenes, and annulenes, the C=C building unit is connected by bonds extending from both carbons (i.e., vicinal connectivity), whereas cross-conjugated π-systems extend geminally, from one and the same carbon atom of a C=C unit. This geminal substitution represents a bifurcation point and results in branching, a characteristic and defining property of cross-conjugated systems.

Altogether there are three fundamental classes of oligo-olefins that exhibit cross-conjugation: the dendralenes (acyclic and branched), the radialenes (cyclic and branched), and the fulvenes. The fulvenes contain both branched and linear conjugation within the same π-system, and are therefore hybrid systems. As they are widely regarded as cross-conjugated molecules in the chemical literature, we follow this convention here.

Thematically, our book is organized along very simple structural principles. We start with a review of the (carbo-)dendralenes, a class of compounds lying dormant for many years, but receiving growing attention recently. Then we move on to the heterodendralenes, which result by replacing one or more of the sp^2-hybridized carbon atoms of the parent hydrocarbons by heteroatoms, most often oxygen, sulfur, or nitrogen. The systematic investigation of these compounds, which have a high potential for preparative organic chemistry, is in its infancy presently. We next move to the (carbo-)radialenes and heteroradialenes, formally derived from the dendralenes by replacing the two penultimate (methine) protons of their terminal double bonds by an intramolecular C–C σ-bond. Replacement of the terminal methylene group of a radialene by an isovalent moiety leads to the heteroradialenes – an oxocarbon, for example, if every $=CH_2$ – unit of a carboradialene is replaced by oxygen. Finally, in this section we discuss the (carbo-)fulvenes and heterofulvenes, and compounds derived therefrom.

Once the parent molecules and their syntheses have been covered, we show the reader that these π-bond rich systems may be used as starting points for more "extended" cross-conjugated compounds, the extension originating from the insertion of unsaturated moieties – for example, triple bonds, aromatic rings, and so on – into the π-framework of the starting compounds.

The second thematic section of the volume will cover some questions from the more "theoretical" side. In particular, we will be concerned with the (eventual) use of cross-conjugated systems in material science. Compared to linear conjugation, cross-conjugation leads to very different chemical and physical properties, and these should have a strong influence on, for example, the photophysical properties of the respective compounds.

A final section covers the use of cross-conjugated compounds in synthesis. Besides the preparation of metal complexes of these compounds, particular emphasis lies on the use of carbodendralenes for the rapid generation of molecular complexity and – as one typical example for the practical application of heterodendralenes – in Nazarov cyclizations.

The reader will note that there are some overlaps in the different chapters dealing with these classes of compounds. We deliberately did not remove these, because we think it attractive that different authors have a different view on similar aspects of the topic they are dealing with. We want the readers to share these different views with the authors.

Carbodendralenes, which have only come of age very recently, are exciting substrates for the generation of complex natural and nonnatural compounds by highly atom- and step-economic syntheses. We expect a very rapid growth in this area in the near future. Besides the fascinating alternating reactivity of the even- and odd-parent [*n*]dendralenes, the high potential of the dendralenes in synthesis lies in their deployment as multidienes partaking in the most important reaction of organic chemistry, the Diels–Alder cycloaddition.

Our book, the first monograph dedicated to cross-conjugation exclusively, is a multiauthor effort. Not all potential contributors could in the end provide their views on the chemistry of these important classes of compounds. This led to several unforeseeable delays. For these, we want to excuse ourselves emphatically and to thank our authors for their patience.

Specifically we are grateful to Nicholas Green and Samuel Drew for proofreading and correcting, and to the Wiley-VCH company for supporting this project.

2015 *Henning Hopf and Michel Sherburn*
Braunschweig and Canberra, Fall and Spring, respectively

1
Synthesis of Dendralenes

Nicholas J. Green, Mehmet F. Saglam, and Michael S. Sherburn

1.1
Introduction

The synthesis and study of conjugated polyenes has been at the heart of the chemical sciences ever since an appreciation of their structure began to develop. Of the five classes of conjugated alkenes that arise from the different possible modes of connectivity (Figure 1.1), some have received significantly more attention than others. The linear and cyclic classes featuring vicinal connections between alkene units – the linear polyenes **1** and annulenes **2** – are common structural motifs in naturally occurring compounds and contrived structures of industrial, commercial, and academic importance, and have hence been extensively synthesized and studied. Oligoalkenes with geminal connections between alkenes – cyclic radialenes **4** and acyclic dendralenes **5** – are yet to receive such attention, nor are "hybrid" structures featuring both geminal and vicinal connections, the fulvenes **3**. There is, however, undoubtedly a growing interest in the subject of this chapter: the synthesis of dendralenes.

Dendralenes have been the subject of two comprehensive reviews [1, 2]. The first covers research in the area until 1984; and the second covers the period between 1984 and 2011. While it would be impossible to summarize the evolution of dendralene synthesis without some repetition of the key strategies found in each of these reviews, we seek to present the subject differently herein, by summarizing the best methods from both reviews, and placing emphasis on the significant work that has appeared between 2011 and the present. We also present the synthetic strategies in a new way, based on which carbon–carbon bonds of the dendralene are formed in the approach. Newly formed bonds are highlighted in bold, and should not be confused with wedged bonds, used to indicate stereochemistry. A broad measure of the synthetic power of a strategy is the number of bonds formed in the process, and we have therefore first highlighted strategies that form more than one bond per step [3]. This has allowed us insight into the strengths, weaknesses, and gaps present amongst current approaches. Our review covers examples in the literature up until April 2015, and we exclusively deal with the synthesis of the parent and substituted

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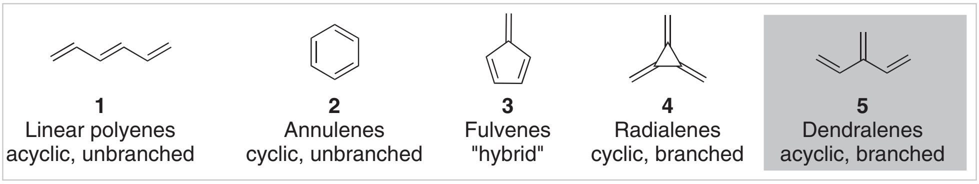


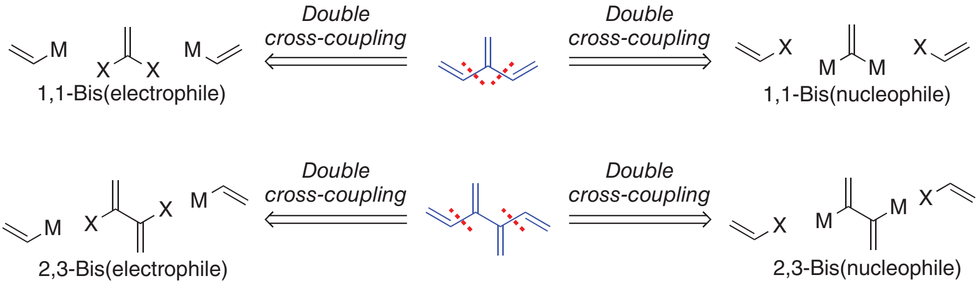
Figure 1.1 Fundamental conjugated hydrocarbons.

dendralenes, directing readers to other reviews or chapters of this book dealing with their closely related, cross-conjugated relatives (fulvenes [4], radialenes [5, 6], quinomethanes [7], etc.). We have not included related compounds that may be generated by substituting a carbon atom in the dendralene backbone with a similar unsaturated moiety, such as an alkyne or aromatic ring. We have also limited our survey to exclude cross-conjugated polymers, which have been reviewed elsewhere [8].

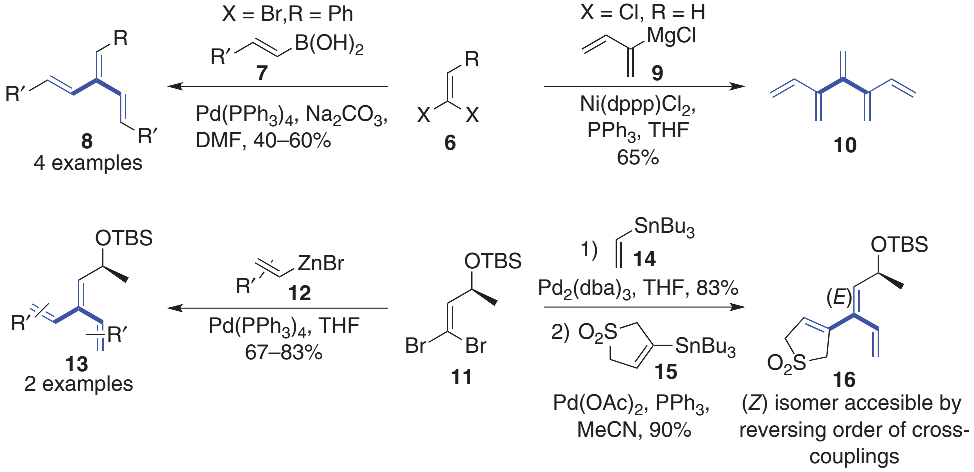
1.2
Multibond Forming Processes

1.2.1
Double Alkenylation Reactions

The double alkenylation approach (Scheme 1.1) has only been exploited relatively recently, most probably because of the rise to prominence of cross-coupling methodologies in recent times. The first double cross-couplings between 1,1-dihaloalkenes and metalloalkenes were isolated examples appearing in 1998 [9] and 2000 [10]. In 2002, Oh and Lim [11] reported a series of double Suzuki–Miyaura reactions between a 1,1-dibromoalkene **6** and alkenyl boronic acids **7** (Scheme 1.2). In 2007 and 2008, the Sherburn research group reported syntheses of substituted [3]dendralenes [12] and the state-of-the-art synthesis of [5]dendralene [13] respectively, transforming a 1,1-dihaloalkene via double



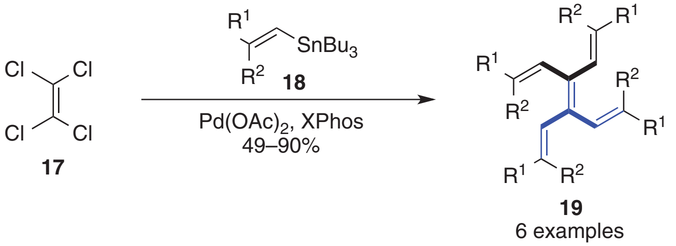
Scheme 1.1 Double alkenylation approaches to [3]- and [4]dendralene, via sp^2–sp^2 cross-coupling.



Scheme 1.2 Examples of double cross-coupling approaches to dendralenes by Oh and Lim [11] and Sherburn and coworkers [12, 13].

Negishi or Kumada cross-couplings to incorporate one alkenyl substituent (**9** or **12**) twice, and also, in the former case, the related stepwise, stereoselective Stille couplings to form unsymmetrically substituted, chiral [3]dendralenes **16** (Scheme 1.2). An application of this stepwise approach *en route* to the natural product triptolide [14] highlighted that when using two different metalloalkene cross-coupling partners, complete control of the stereochemistry of the resulting alkene is sometimes unattainable. Thus, most successful applications of this method incorporate two identical alkenes, so no issues of stereochemistry arise. A recent example is the synthesis by Ichikawa and coworkers [15] of a single tetrafluoro[3]dendralene via double Negishi cross-coupling of 2,2-difluorovinylzinc bromide to a dibromoolefin.

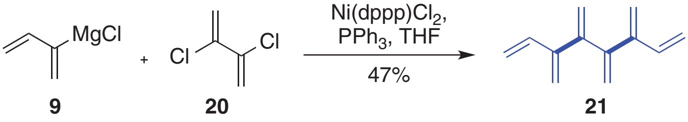
Recently, a new benchmark in alkenyl cross-coupling syntheses was set by the Sherburn group, using an extension of this double cross-coupling strategy. Tetravinylethylene (TVE) and substituted analogs **19**, previously only accessible by longer, lower yielding, sequences [16–18], were generated via a fourfold Stille cross-coupling of alkenyl stannanes **18** and tetrachloroethylene (**17**), a cheap



Scheme 1.3 Synthesis of TVEs via fourfold sp^2–sp^2 cross-coupling reactions [19, 20].

and readily available starting material produced annually on a kiloton scale (Scheme 1.3) [19–21]. TVEs possess an interesting carbon framework composed of two [3]dendralene subunits sharing the same central, tetrasubstituted alkene. The bold, one-step approach was used to generate six different symmetrically substituted TVEs, is unique in its use of a tetrachloroalkene, and cannot be surpassed in terms of step economy [22].

Higher dendralenes are accessible by double cross-coupling by including branched alkenes into the electrophile unit. For example, in their state-of-the-art synthesis of the parent dendralenes [23], Sherburn and coworkers prepared [6]dendralene (**21**) by the reaction between 2,3-dichloro-1,3-butadiene (**20**), and the Grignard reagent (**9**) prepared from chloroprene, another readily available unsaturated halide produced annually on a megaton scale (Scheme 1.4) [24]. The scope of this reaction in the synthesis of substituted higher dendralenes remains unexplored.

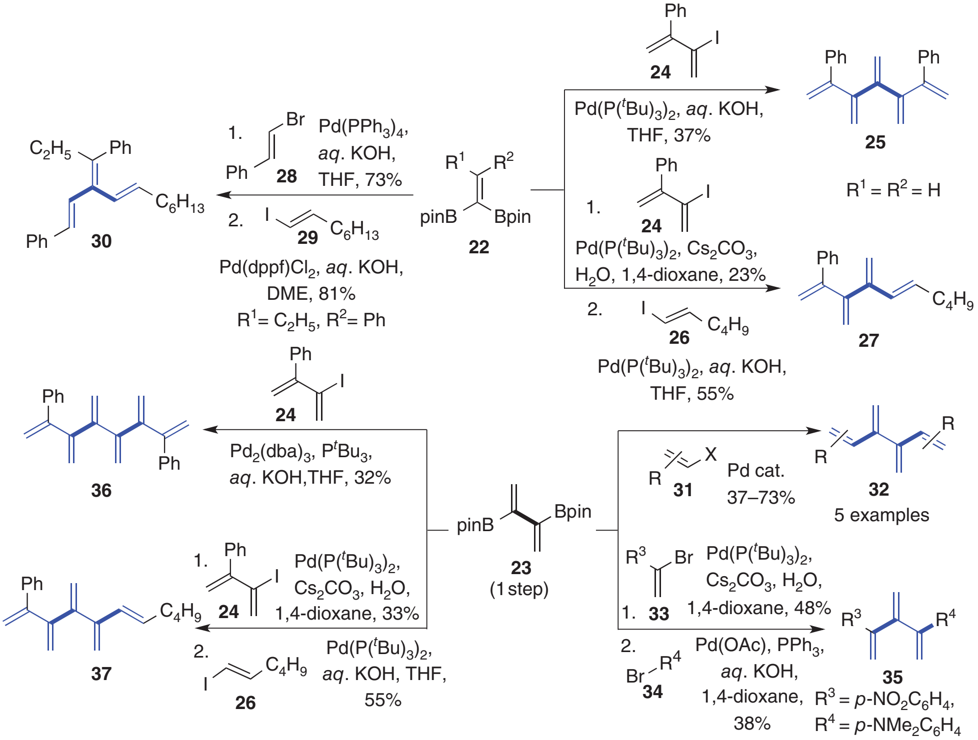


Scheme 1.4 Synthesis of [6]dendralene via a double sp^2–sp^2 cross-coupling reaction [23].

The same double cross-couplings are feasible by swapping the reactivity of components, that is, using a double nucleophilic ethylene or 1,3-butadiene and two alkenyl electrophiles. So far, apart from an isolated example by the Sherburn group using 2,3-bis(trimethylstannyl)-1,3-butadiene [10], the Shimizu group is presently the only one to explore this avenue of dendralene synthesis, and have published a series of papers detailing the use of 1,1-bis(pinacolatoboryl)ethylene (**22**) and 2,3-bis(pinacolatoboryl)-1,3-butadiene (**23**) as nucleophilic components in Suzuki–Miyaura cross-coupling reactions (Scheme 1.5) [25–27]. A double cross-coupling reaction leads to symmetrically substituted [4]-, [5]-, and [6]dendralenes (**32**, **25**, **36**), and a two-step process leads to unsymmetrically substituted [3]-, [4]-, and [5]dendralenes (**30**, **35**, **27**, **37**). While the yields for many of these reactions remain quite low, the potential scope is broad. The two strategies are complementary, and many interesting substituted dendralene frameworks are within rapid, step-economic reach from some very readily available starting materials.

1.2.2
Double Alkenation Reactions

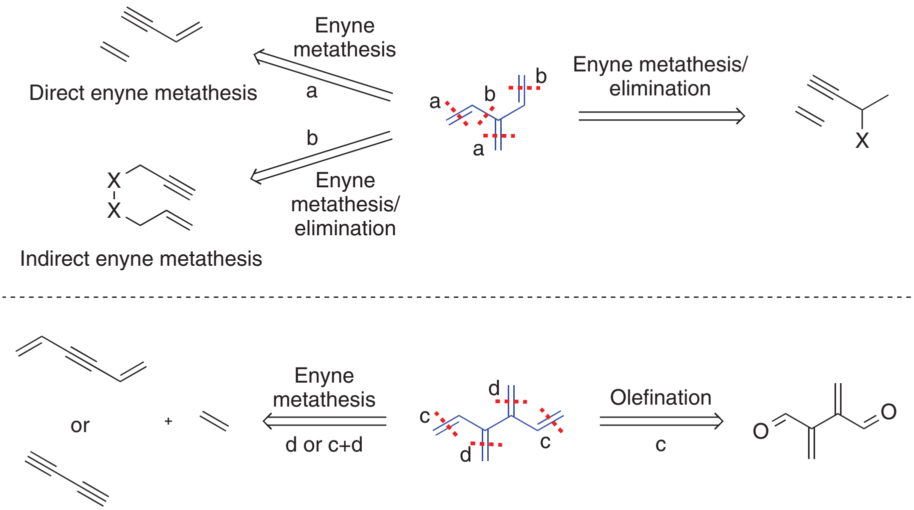
Various approaches that synthesize butadienes by the installation of methylene groups on two adjacent carbon atoms can be classified as the same overall transformation as the enyne metathesis reaction (Scheme 1.6). Unsurprisingly, metal-catalyzed enyne metathesis has proved versatile in this regard, as have



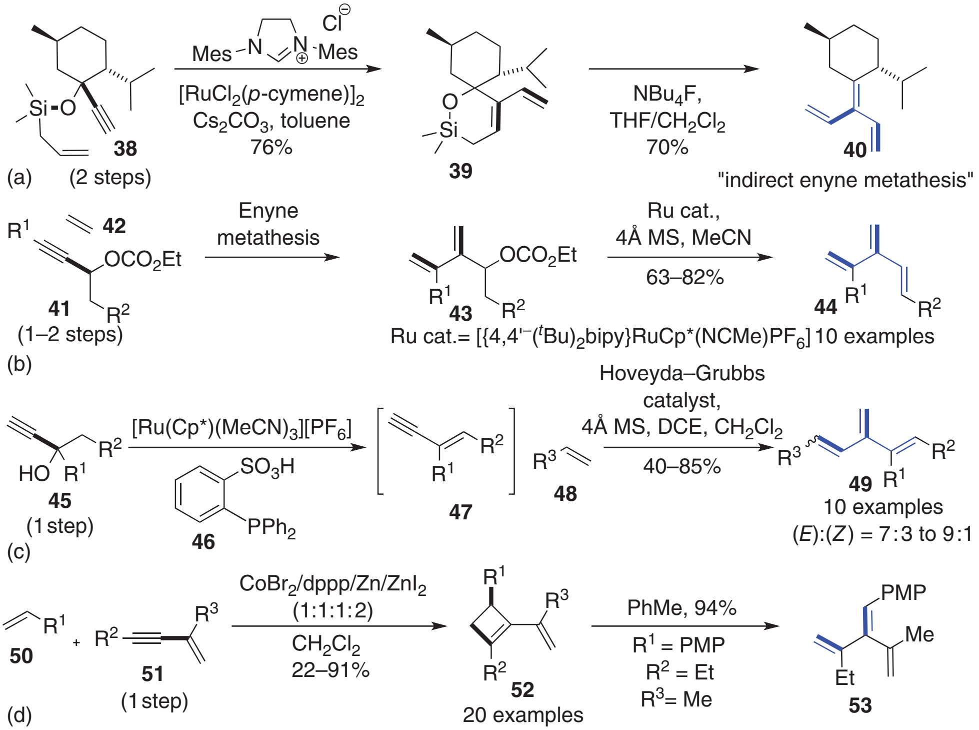
Scheme 1.5 Syntheses of dendralenes utilizing a double nucleophilic cross-coupling building block, from the Shimizu group [25–27].

[2+2] cycloaddition/4π electrocyclic ring-opening sequences (referred to herein as *uncatalyzed enyne metathesis reactions*), but other complementary examples of multibond forming processes that effect the same bond formations have also been developed.

In 2003, Bruneau and coworkers reported the first use of enyne metathesis to synthesize masked dendralenes **39** (Scheme 1.7 (a)) [28]. This work paved the way for a series of related syntheses of dendralenes with a variety of substitution patterns [29, 30], including a remarkable synthesis of a [4]dendralene via a double intramolecular enyne metathesis/double elimination sequence by Park and Lee [29]; however, because the products are masked dendralenes, the carbon–carbon bond disconnections for this strategy are different from the direct metathesis approach, in which the newly formed butadiene unit stays intact (Scheme 1.6). It was Bruneau again who first developed this route, using metathesis between ethylene (**42**) and propargylic carbonates **41** to synthesize 1,3-butadiene **43**, revealing the third alkene via subsequent elimination (Scheme 1.7 (b)) [31]. The same group has now published metathesis reactions that directly furnish intact [3]dendralenes **49** by conducting the elimination first and then performing metathesis on an alkyne **47** already bearing the third alkene (Scheme 1.7 (c)) [32].



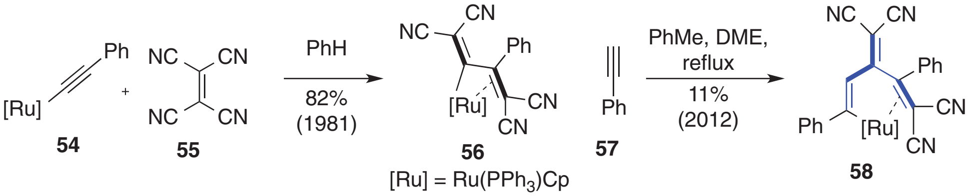
Scheme 1.6 Possibilities for the synthesis of dendralenes via reactions forming two or more alkene groups.



Scheme 1.7 Representative examples of substituted [3]dendralene syntheses involving enyne metathesis or an equivalent transformation [28, 31–33].

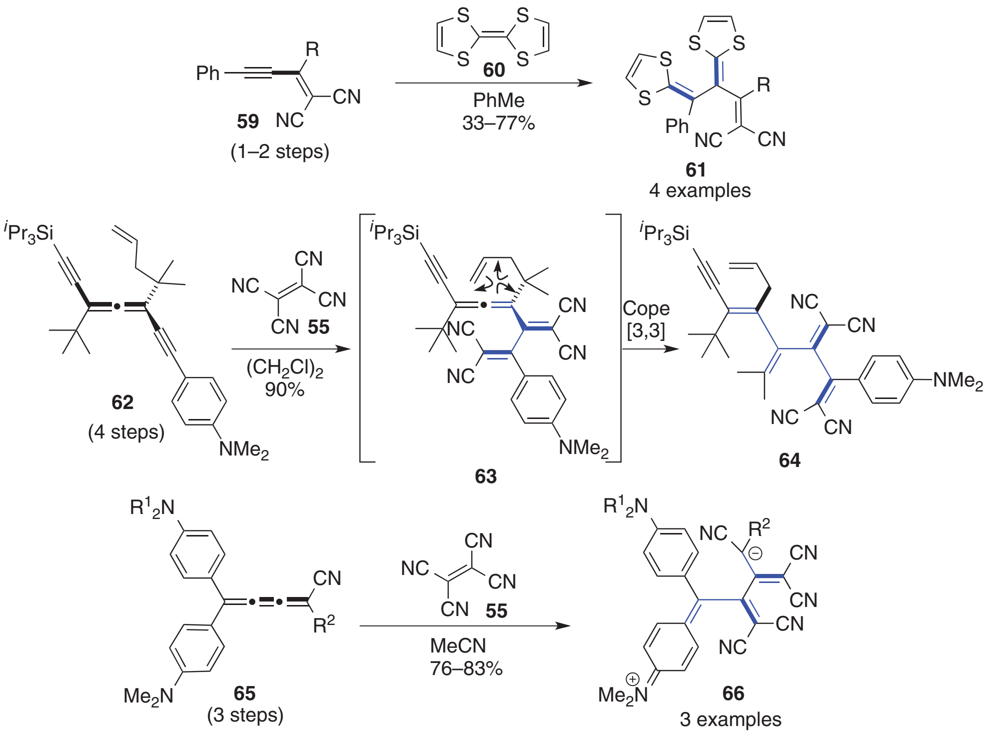
The related, intramolecular ring-closing enyne metathesis had been reported by Chang and coworkers [34]. A promising, if isolated, example of a related metal-catalyzed synthesis of a [3]dendralene **53** was reported by the Ogoshi group in 2014 (Scheme 1.7 (d)) [33]. A cobalt catalyst was used to generate a variety of alkenyl cyclobutenes **52** from the reaction of an alkene **50** and alkyne **51**. One of the cyclobutenes **52** was converted by thermal electrocyclic ring-opening to a substituted [3]dendralene **53**. If this ring-opening proves general, the methodology provides a modern, step-efficient incarnation of older methods that unmasked dendralenes from alkenyl cyclobutenes, derived from lengthy sequences [1]. A couple of isolated examples of dendralene synthesis via Ru(II)-catalyzed double carbene addition to alkynes have also been reported, albeit with only moderate (*E*)/(*Z*) selectivity [35]; and a coupling of an organozirconium reagent and vinyl bromide, equivalent to an enyne metathesis, has also been used to prepare a [3]dendralene [36].

In the 1970s and 1980s, it was discovered that electron-deficient alkenes, such as tetracyanoethylene (TCNE, **55**) reacted with metallated alkynes **54** to furnish a metallated hexasubstituted 1,3-diene unit **56**, an overall transformation akin to enyne metathesis (Scheme 1.8) [37, 39]. In a recent (2012) addition to this work, the Bruce group reported the synthesis of a ruthenated [3]dendralene **58** via insertion of phenylacetylene (**57**) into **56** (Scheme 1.8) [38]. The metallated dendralene synthesis is low yielding and, as yet, an isolated example, but presents an interesting avenue for future investigations.

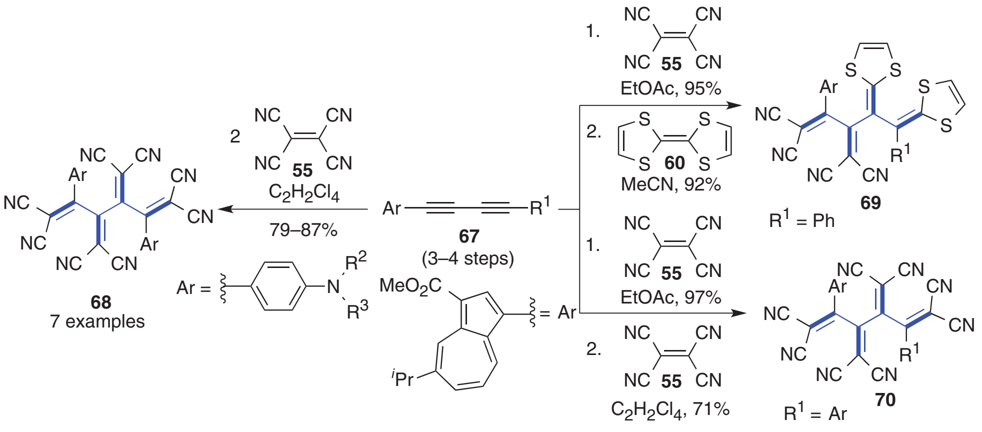


Scheme 1.8 Synthesis of a ruthenated [3]dendralene [37, 38].

Uncatalyzed metathesis has also been performed on systems without metal components. Hopf was the first to show that highly electron-rich olefins such as tetrathiafulvalene (TTF, **60**) undergo a sequence of [2+2] cycloaddition and 4π electrocyclic ring-opening with electron-deficient alkynes **59** to generate a new butadiene unit, which may be part of a dendralene (e.g., **61**) if a neighboring alkene is already in place (Scheme 1.9) [40]. The group of Diederich has made extensive use of the cycloaddition/4π electrocyclic ring-opening pathway to generate butadienes, some of which appear in dendralene frameworks [43–45]. Examples from recent papers demonstrate the versatility of this approach. TCNE (**55**) undergoes the cycloaddition/ring-opening process with alkyne **62** [41]. A preexisting alkene in the alkyne starting material (akin to Hopf's strategy) allows the generation of the [3]dendralene framework in **63**. Finally, the presence of the requisite functionality for a Cope rearrangement allows further downstream functionalization, and the *in situ* generation of [4]dendralene **64**. A similar



Scheme 1.9 Representative dendralene syntheses featuring uncatalyzed metathesis reactions [40–42].

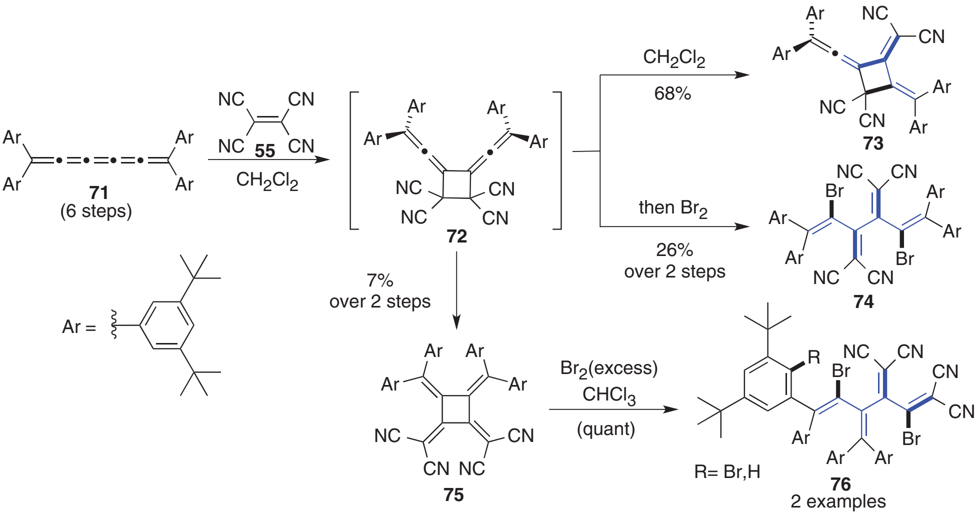


Scheme 1.10 Stepwise or double [2+2]cycloaddition/retro-4π-electrocyclization cascades to synthesize [4]dendralenes [46, 47].

strategy from the same group has also led to interesting zwitterionic dendralene structures **66** derived from the cycloaddition/4π electrocyclic ring-opening sequence between cumulenes **65** and TCNE (**55**) [42].

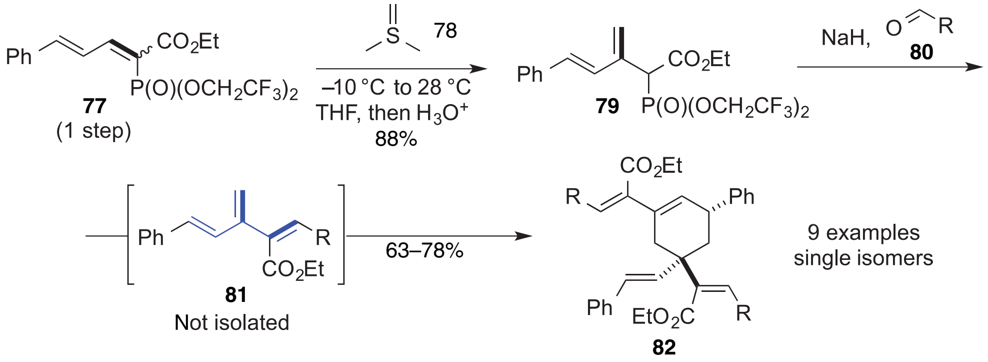
Uncatalyzed metathesis can also be performed on substrates that contain two reactive alkyne sites, for the rapid synthesis of highly substituted [4]dendralenes. Diederich and coworkers recently reported double [2+2] cycloaddition/retro-4π-electrocyclization cascades to yield a number of fully substituted [4]dendralenes **68** featuring push–pull chromophores (Scheme 1.10) [46, 48]. Using a similar double alkyne substrate **67**, Diederich has also used different alkenes to incorporate varied functional groups into the product dendralene, a strategy recently also adopted by Morita and coworkers [47], who in 2012 reported stepwise or one-pot reactions to incorporate both TCNE (**55**) and TTF (**60**) into the structure of [4]dendralenes **69**, via double uncatalyzed metathesis.

Further varied examples of the [2+2] cycloaddition/ring-opening sequence, this time promoted by the addition of bromine, were reported by the group of Tykwinski (Scheme 1.11) [49]. By using a [5]cumulene **71** as starting material, the group generated unsaturated cyclobutanes **72** which formed highly substituted [4]dendralenes **74** when a ring opening was triggered by bromination, or underwent thermal, radical isomerization to yield cyclic [3]dendralene **73**, or [4]radialene **75**. [4]Radialene **75** could itself undergo bromination and ring opening to furnish [4]dendralene **76**.



Scheme 1.11 Cycloaddition/ring-opening sequences by Tykwinski and coworkers to synthesize various dendralenes [49].

A new, complementary approach to enyne metathesis has also emerged in the work of Singh and Ghosh (Scheme 1.12) [50, 51]. A stepwise methylenation (using dimethyl sulfonium methylide ylide **78**) and Stille–Gennari olefination sequence



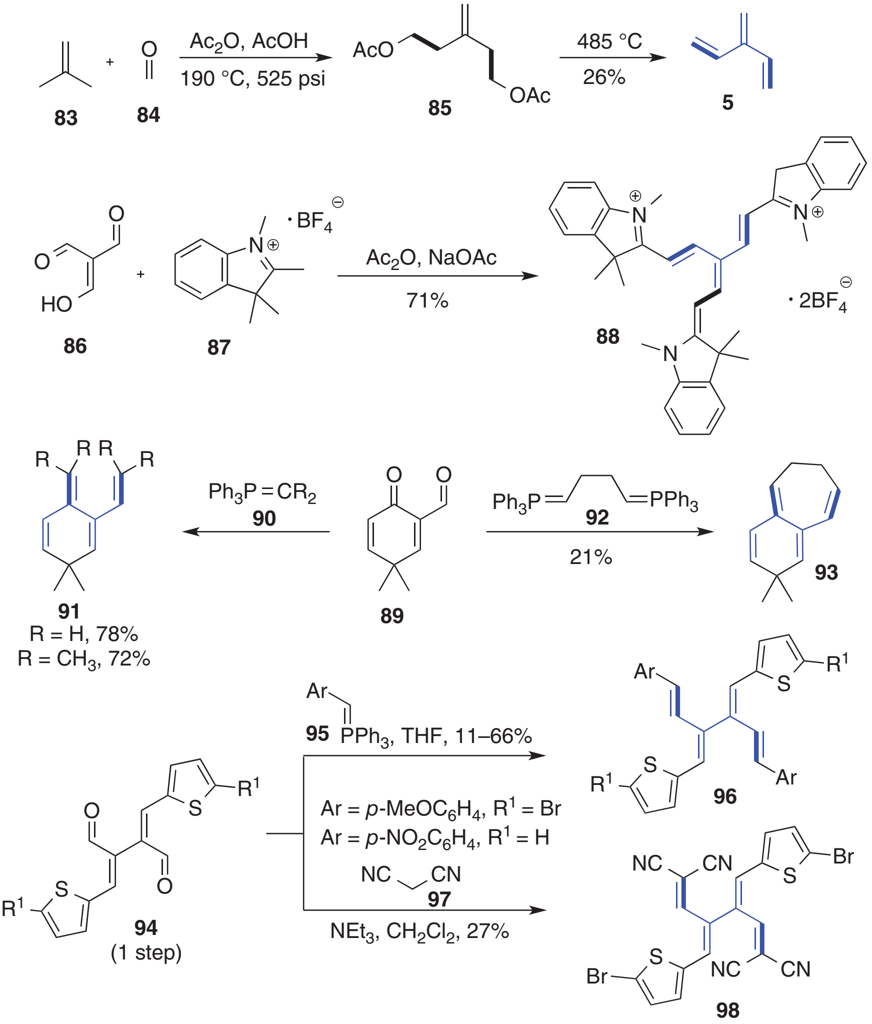
Scheme 1.12 The methylenation/olefination sequence of Singh and Ghosh that forms [3]dendralene prior to *in situ* dimerization [50, 51].

was used to furnish a variety of 1,2,5-trisubstituted [3]dendralenes **81**, which rapidly underwent Diels–Alder (DA) dimerization to yield the isolated DA dimer products **82**. The sequence can be performed in one pot, via the intermediacy of the ylide adduct of **77** and **78**, but was highest yielding when proceeding after quenching this intermediate with water and isolating dienyl phosphonate **79**.

Olefination-type reactions (including addition/elimination sequences) are a reliable method of generating alkenes, and have therefore seen many applications in dendralene synthesis. Their use in multibond forming approaches to dendralenes has also been documented. The landmark first synthesis of [3]dendralene (**5**) by Blomquist in 1955 employed a double Alder–ene reaction between 2-methylpropene (**83**) and two molecules of formaldehyde (**84**), followed by acetylation and elimination to furnish the target hydrocarbon **5** (Scheme 1.13) [52]. Double addition/elimination strategies have also been employed on 1,1-dicarbonylalkenes and 2,3-dicarbonylbutadienes to form [3]- and [4]dendralenes, respectively [56–61]. Another notable and very early example of this approach was used by Reichardt and Mormann to synthesize tri-substituted [3]dendralene **88**, via a triple condensation reaction (Scheme 1.13) [53]. This strategy has found application in a number of related examples [62–65]. Cassens and Lüttke used double Wittig olefinations to form cyclic and bicyclic [4]dendralene structures from 1,3-diketones **89** (Scheme 1.13) [1, 54]. Bryce and coworkers also used the double olefination approach to install the terminal alkenes of a [3]dendralene [66]. Talpur and coworkers [55] have recently used the same double Wittig reaction, and also a double Knoevenagel condensation, to form functionalized [4]dendralenes **96** and **98** (Scheme 1.13).

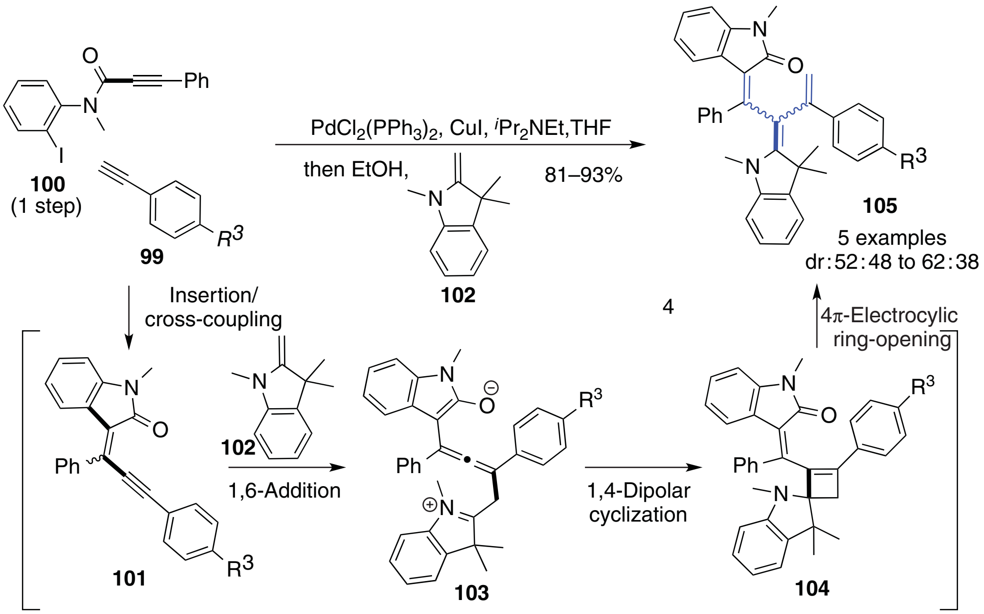
1.2.3
Other Multibond Forming Processes

The Müller group has reported a rapid approach to highly substituted [3]dendralenes via a remarkable, consecutive one-pot palladium(0)-catalyzed sequence

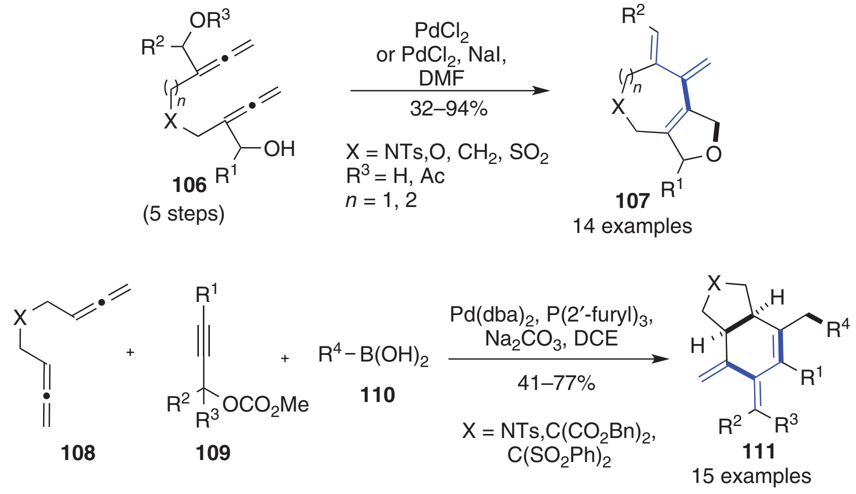


Scheme 1.13 Representative examples of double alkenation syntheses of dendralenes, featuring double addition/elimination sequences or double olefination reactions [1, 52–55].

(Scheme 1.14) [67]. Pd(0)-mediated 5-*exo-dig* cyclization followed by Sonogashira cross-coupling between alkyne **99** and the alkenyl palladium(II) species generated from cyclization yielded intermediate **101**, which underwent 1,6-addition from Fischer's base **102**, followed by Mannich-type 1,4-dipolar cyclization to form cyclobutene intermediate **104**. Ultimately a 4π electrocyclic ring opening furnished [3]dendralenes **105** as the product of this complex mechanism. The methyl substituent on the nitrogen of anilide **100** was found to be crucial to enforce the mechanistic pathway that generates dendralenes, as opposed to other structures. While five examples were cataloged, only the substituent on one aryl



Scheme 1.14 The Pd-catalyzed cascade synthesis of substituted [3]dendralenes by Müller and coworkers [67].

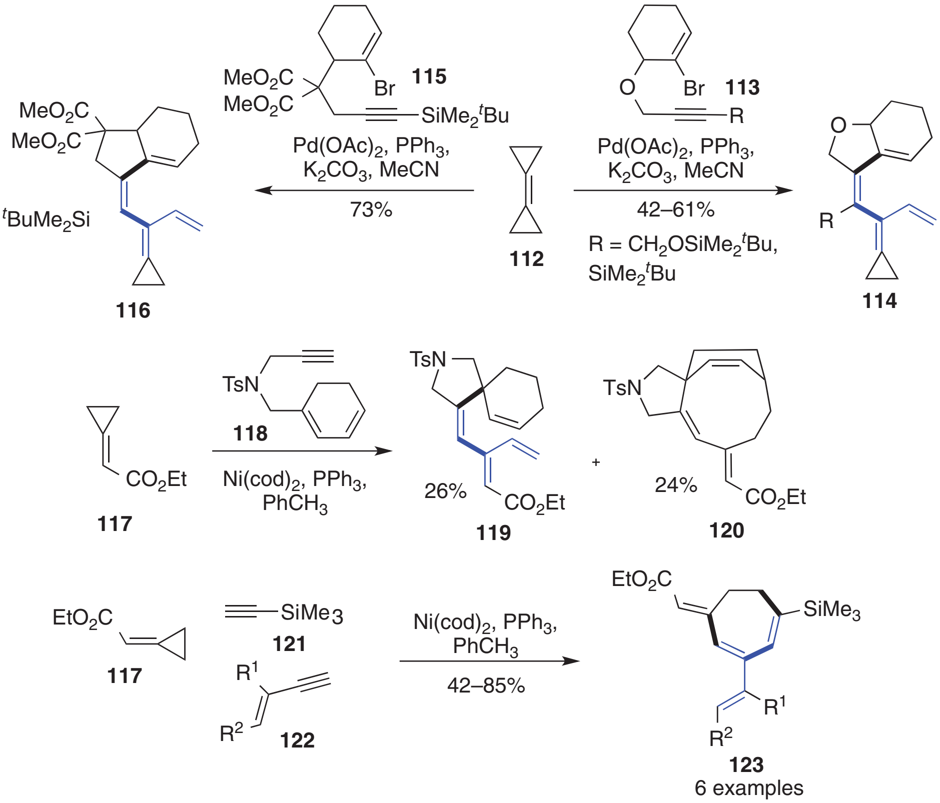


Scheme 1.15 Multi-bond-forming syntheses of [3]dendralenes from the Ma group [68–70].

group was varied; and the dendralenes were formed as mixtures of (*E*) and (*Z*) isomers about the central alkene. Evidently, increased scope and selectivity is worth pursuing in this impressive sequence.

The Ma group has reported some very elegant multibond forming processes to synthesize dendralenes, including both palladium(II)- and rhodium(I)-catalyzed cycloisomerizations of di-allenes **106** to form cyclic dendralenes **107** (Scheme 1.15) [68, 69, 71], and also the remarkable palladium(0)-catalyzed three-component reaction of di-allenes **108**, propargylic carbonates **109**, and boronic acids **110** to form bicyclic [3]dendralenes **111** (Scheme 1.15) [70]. Similar, intermolecular transformations to those used to form dendralenes **107** had been reported earlier by Alcaide, to synthesize dihydrofuran-containing dendralenes [72, 73].

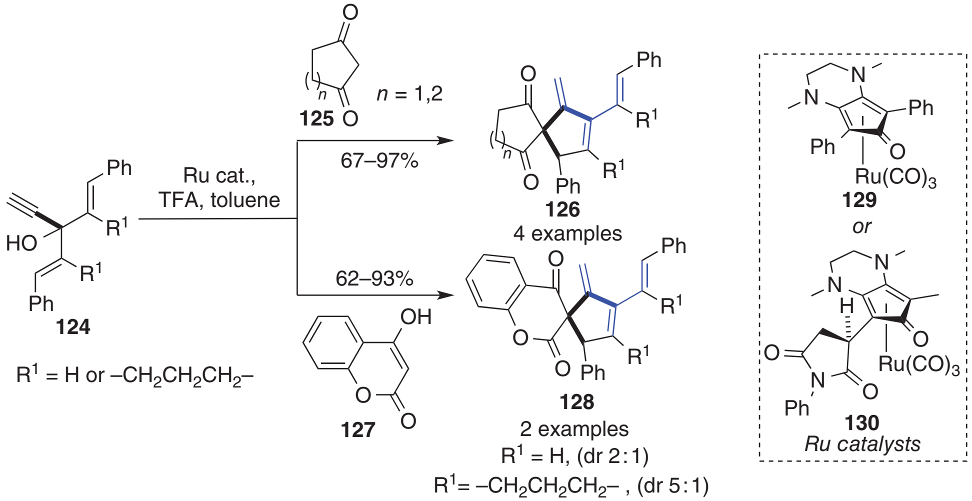
Alkynes are also versatile starting materials to couple with alkenes or allenes in transition-metal-catalyzed processes to form dendralenes. In 2014, building



Scheme 1.16 Transition-metal-catalyzed reactions of alkynes and cyclopropylidenes to form [3]dendralenes [75–77].

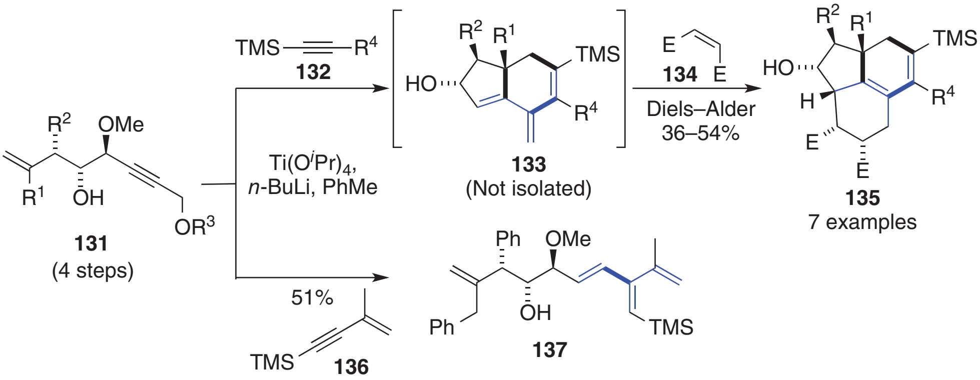
on earlier work from Schelper and de Meijere [74], Demircan reported [75] the synthesis of 3-cyclopropylidene-containing dendralenes using Pd(0)-catalyzed cascade reactions of alkynes and 1,1′-bi(cyclopropylidene) (**112**) (Scheme 1.16). In 2013, Saito and coworkers [76] had reported a related, isolated synthesis of [3]dendralene **119** employing a Ni(0) catalyst, building on their earlier, more general work employing alkynes **121**, ene–ynes **122**, and ethyl cyclopropylideneacetate (**117**) in Ni(0)-catalyzed three-component cycloaddition reactions (Scheme 1.16) [77].

Haak and coworkers in 2015 [78] and 2012 [79] reported monocyclic and bicyclic [3]dendralenes, which were generated via ruthenium-catalyzed cascade transformations. The complex mechanism involves ruthenium(0)-mediated dehydration of the alkyne **124**, addition of the nucleophile to an alkenyl ruthenium allenylidene, and cyclization at a ruthenated alkyne to furnish unusual spirocyclic [3]dendralenes **126** and **128** (Scheme 1.17).



Scheme 1.17 Ru(0)-catalyzed synthesis of cyclic [3]dendralenes by Haak and coworkers [78, 79].

In a very nice titanium-mediated annulation cascade, Cheng and Micalizio [80] synthesized functionalized, bicyclic [3]dendralenes **133** *in situ* as intermediates that were trapped via a subsequent DA reaction (Scheme 1.18). The report includes one example of a DA dimerization product, seven examples of intermolecular metallocycle-mediated annulation followed by intermolecular [4+2]cycloaddition reaction to afford (**135**), and one example of an isolated, acyclic substituted [3]dendralene **137**.

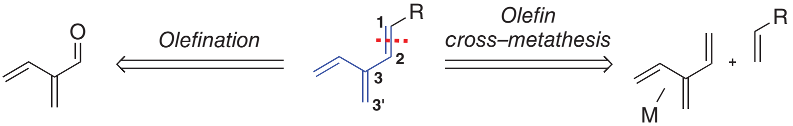


Scheme 1.18 Ti(IV)-mediated cascade syntheses of [3]dendralenes by Cheng and Micalizio [80].

1.3
Solo-Bond-Forming Reactions

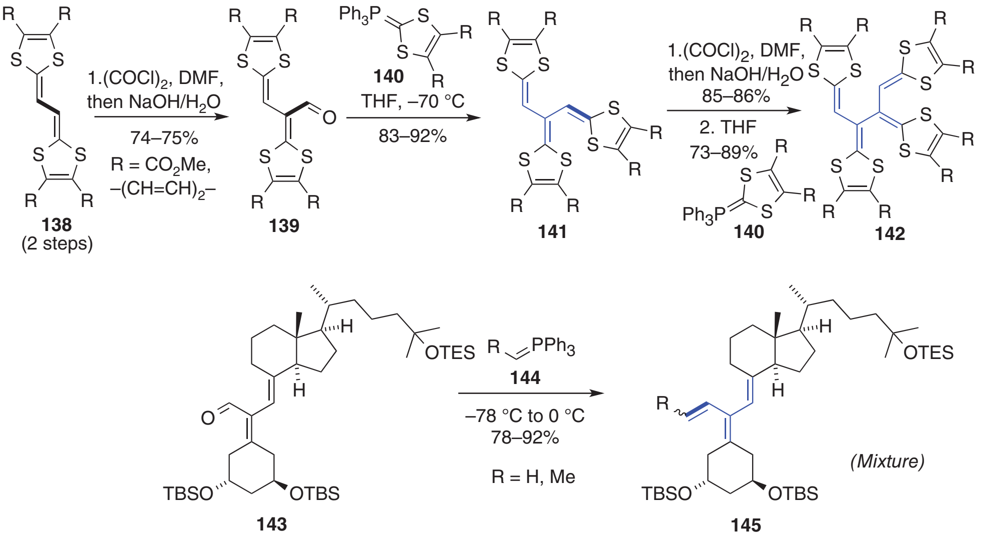
1.3.1
C1–C2 Alkenation Reactions

The most obvious method to install the C1–C2 alkene of a dendralene is an olefination reaction (Scheme 1.19), but it has seen very little use, because of the propensity of 2-carbonyl-1,3-butadiene derivatives to undergo rapid Diels–Alder dimerization [81]. In fact, the only successful uses of 2-carbonyl-1,3-butadienes in such processes feature substrates stabilized by 1,1-disubstitution and a 4*Z* substituent. Such an example is the iterative formylation/olefination sequence reported by Yoshida and coworkers (Scheme 1.20) [82]. A selective, single electrophilic formylation followed by a Wittig reaction gave hexa-substituted [3]dendralenes **141**, which could be further homologated to octa-substituted [4]dendralenes **142** using the same sequence. Related examples have also been reported [84, 85]. A similar iterative formylation/Horner–Wadsworth–Emmons (HWE) sequence was used by Bryce *et al.* to synthesize [3]- and [4]dendralenes containing dithiole and ferrocene functionalities [66]. DeLuca and coworkers [83] recently reported the synthesis of two [3]dendralenes **145** using a Wittig reaction;, however, the stereoselectivities of the reactions were not reported (Scheme 1.20).

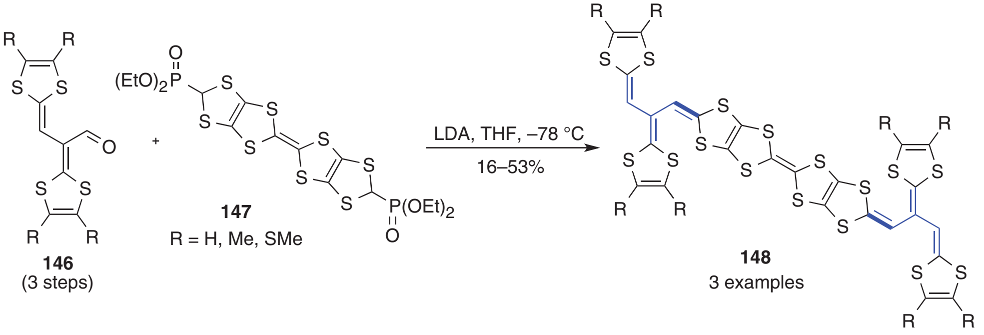


Scheme 1.19 Single alkene (C1–C2) bond disconnections of [3]dendralenes.

In 2012, Misaki and coworkers [86] prepared three examples of compounds containing two hexa-substituted [3]dendralene subunits **148** using a double HWE



Scheme 1.20 Syntheses of dendralenes using Wittig reactions [82, 83].

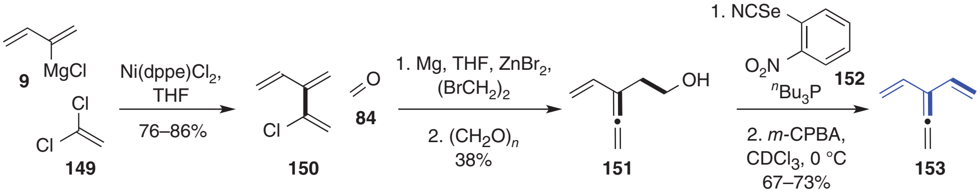


Scheme 1.21 Syntheses of dendralenes using double HWE reactions, by Misaki and coworkers [86].

reaction (Scheme 1.21). The starting materials were synthesized using Yoshida's method via a single electrophilic formylation to give the cross-conjugated diene aldehyde **146**.

Recently, Sherburn and coworkers [87] attempted to use Wittig olefination to synthesize 1-substituted [3]dendralenes, only to determine that [3]dendralenes featuring a 1*E*-conjugating substituent underwent rapid DA dimerization and could not be isolated. The Wittig reaction furnished only an isolated example of a 1*Z*-phenyl substituted [3]dendralene in low yield (20%), along with a mixture of three Diels–Alder dimerization products. This led to the development of a cross-metathesis approach involving tricarbonyl-iron complexed dendralenes, which is discussed in Section 1.4.

1,1-Divinylallene (**153**) is a dendralene prone to decomposition, but it could be isolated and characterized through a cautious approach [88]. The extreme sensitivity of this compound to dimerization and decomposition dictated that a mild elimination method be used to reveal the last alkene, after the C3–C3′ bond was established by Kumada cross-coupling (Scheme 1.22). The isolation of this compound (with a half-life of 43 h at 0.02 M) via this method suggests that similar strategies could be used to obtain and characterize highly reactive dendralenes.

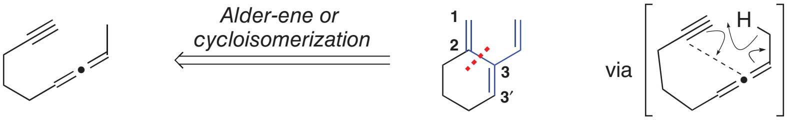


Scheme 1.22 Synthesis of 1,1-divinylallene, by Sherburn and coworkers, using a mild elimination method [88].

Finally, we note the absence of general cross-metathesis routes to functionalize preexisting dendralene frameworks. This is no doubt due to the reduced reactivity of conjugated alkenes in cross-metathesis reactions [87, 89]. A solution to this problem is addressed below, in Section 1.4.

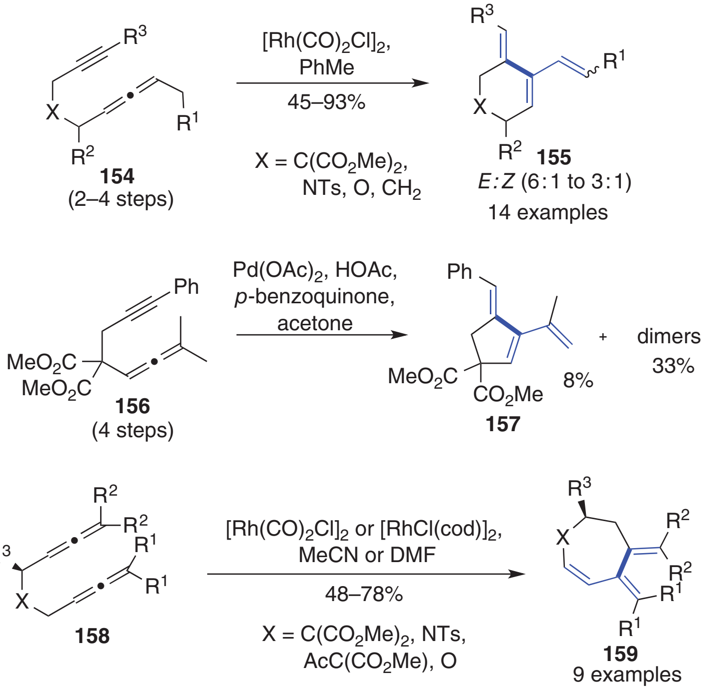
1.3.2
C2–C3 Alkenylation Reactions

Reactions that incorporate a new alkene onto an existing carbon framework, forming the C2–C3 bond, are very common (Scheme 1.23). From the 1970s onwards, a few examples of thermal rearrangements, Alder–ene reactions [90–93], and isomerizations that generally require harsh conditions and show limited scope were published. Hullio and Mastoi also reported an isolated example of a substituted [3]dendralene, prepared by pyridine-catalyzed addition of dimethylacetylene dicarboxylate to *trans*-cinnamyl aldehyde [94]. Developments in transition-metal catalysis have allowed much milder transformations with significantly enhanced scope. Foremost among these are the transition metal-catalyzed cycloisomerizations, which are formal Alder–ene reactions, that provide robust access to a wide variety of cyclic dendralenes, most especially 2,3′-cyclodendralenes [95–105]. For example, Brummond and coworkers reported



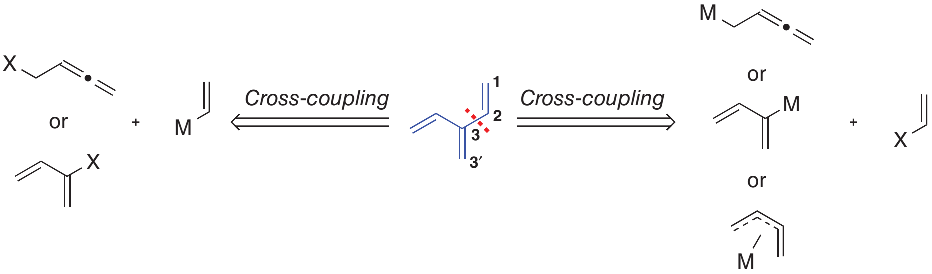
Scheme 1.23 Formation of dendralene via Alder–ene or metal catalyzed cycloisomerization reaction.

the rhodium(I)-catalyzed synthesis of 14 different cyclic [3]dendralenes **155** featuring a variety of different functional groups and heterocycles (Scheme 1.24) [99]. In many cases, mixtures of alkene isomers are observed. Iridium(I) [105], platinum(II) [107, 108], cobalt/rhodium nanoparticles [109], palladium(II) [68], rhodium(I) [69, 110], and gold(I) catalysts [108, 111, 112] have also been used to perform these and related cycloisomerizations, with the mechanism, scope, and limitations varying among catalysts. Recently, Deng and Bäckvall [106] reported another palladium(II)-catalyzed example, but it only formed dendralenes **157** as the unwanted by-products of acetoxylation reactions (Scheme 1.24). Aside from developments in the metal-catalyzed formal Alder–ene reaction, Malacria *et al.* and Mukai and coworkers have revisited the thermal variant, with some promising results [108, 113, 114]. A related reaction, the intermolecular ruthenium(II)-catalyzed coupling of cyclic allenes and alkynes, has also been used to synthesize a variety of 2,4-cyclo-[3]dendralenes [115]. Di-allenes are also useful substrates for similar transition-metal-catalyzed processes [71]. Lu and Ma reported Rh(I)-catalyzed cycloisomerizations of 1,5-diallenes **158**, to provide seven-membered heterocycle-containing [3]dendralenes **159** (Scheme 1.24) [69]. Where chiral, enantioenriched substrates were used, no significant racemization was observed under the reaction conditions.



Scheme 1.24 Representative examples of transition-metal-catalyzed cycloisomerization reactions forming the C2–C3 bond of cyclic [3]dendralenes [69, 99, 106].

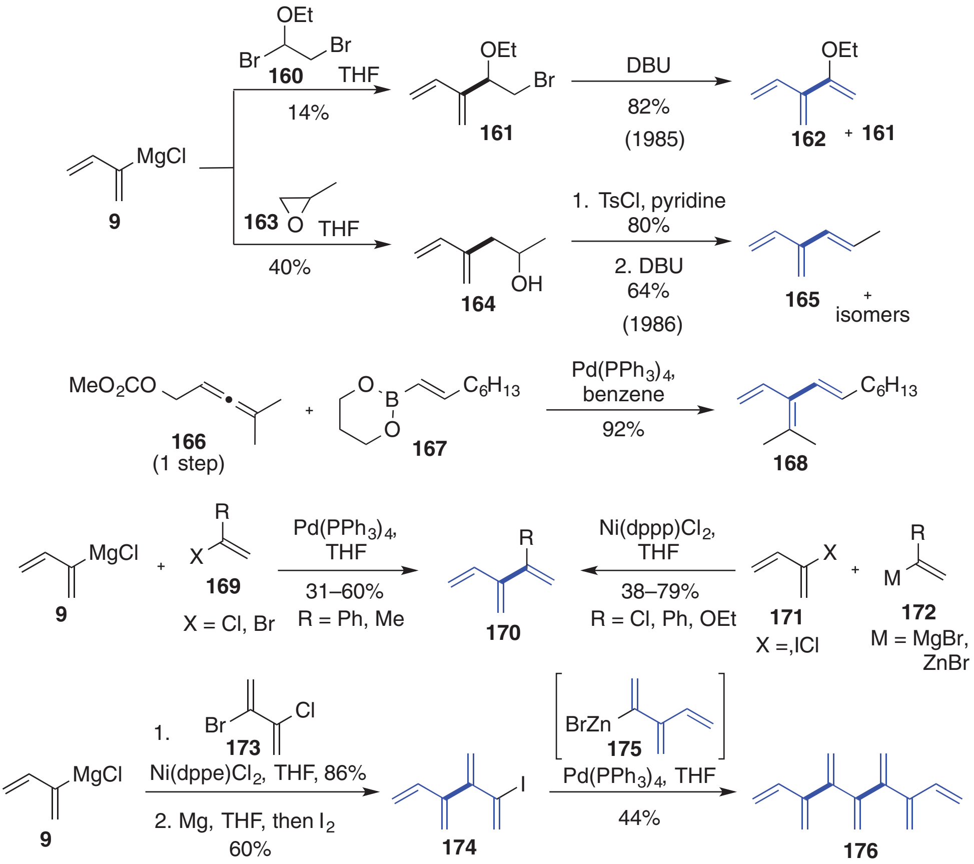
The first syntheses of dendralenes by C2–C3 bond formation (Scheme 1.25) were reported by Tsuge and coworkers in 1985 and 1986, and proceed via substitution at either a bromide **160** or an epoxide **163**, followed by elimination (Scheme 1.26) [116, 117]. Similar addition/elimination sequences to carbonyl groups or epoxides [120], and substitution reactions [121], followed. Such methods have been superseded by cross-coupling techniques that take place between a 2-functionalized 1,3-butadiene and an alkene (each can be either electrophilic or nucleophilic); or a 4-functionalized 1,2-butadiene and alkene, and occur with allylic transposition (Scheme 1.25). No doubt due to the ready availability of alkenyl halides and allenes, and the variety of increasingly mild and selective reaction variants, cross-coupling has provided access to a large number of diversely substituted dendralenes over the past 20 years, some of which have even been part of natural product syntheses [14, 122, 123].



Scheme 1.25 Alkenylation approaches to [3]dendralene via cross-coupling C2–C3 bond formation.

The first reports of cross-coupling routes to dendralenes were isolated examples in 1994 by Suzuki *et al.* (Scheme 1.26, **166** + **167** → **168**) [118] and 1998 by Allain *et al.* [124]. This early work paved the way for a more general approach featuring Kumada, Stille, and Negishi reactions to synthesize mono-substituted [3]dendralenes **170** and the parent dendralenes, developed by the Sherburn group (Scheme 1.26) [119]. Aside from cross-couplings with readily available alkenyl and butadienyl units, including the use of 3-sulfolene building blocks as “masked butadienes” to synthesize higher dendralenes [10, 125], the group also reported bond formations between higher dendralene cross-coupling partners, such as the Negishi cross-coupling of 2-iodo[4]dendralene (**174**) and the organozinc derivative of 2-chloro[3]dendralene (**175**) (Scheme 1.26) [23]. Double cross-coupling reactions that furnish the C2–C3 bond in addition to another bond, have already been discussed (Section 1.2.1).

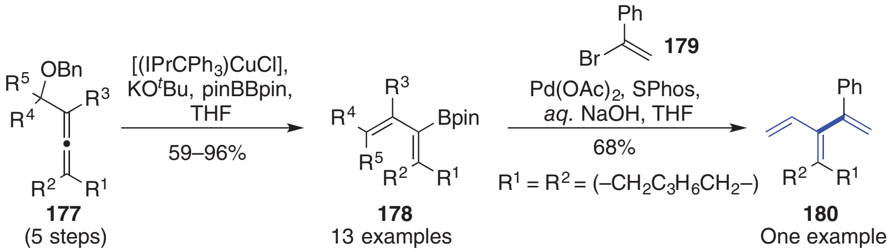
Recently, Tsuji and coworkers reported an isolated synthesis of a [3]dendralene **180** via a Suzuki–Miyaura cross-coupling reaction (Scheme 1.27) [126]. A variety of different 2-boryl-1,3-butadienes **178** were synthesized. While only one was coupled with an alkenyl halide **179**, these butadien-2-yl coupling partners **178**, in



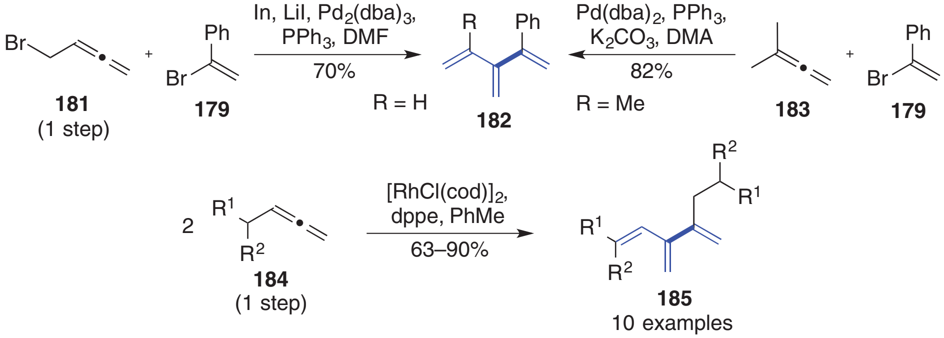
Scheme 1.26 Representative syntheses of dendralenes via C2–C3 bond formation, featuring either classical approaches or transition-metal-catalyzed sp^2–sp^2 cross-coupling [23, 116–119].

principle, offer a variety of building blocks to add to those already available for simple cross-coupling routes to dendralenes. 1,3-Butadien-2-yl cross-coupling partners have also been used in other Stille and Negishi cross-couplings [127–130].

Despite being a less obvious starting material than a 1,3-butadiene-2-yl coupling partner, 1,2-butadien-4-yl precursors (such as **166** in Suzuki's pioneering example in Scheme 1.26) have seen the most use in dendralene synthesis [118, 131–136]. A couple of more recent examples include the palladium-catalyzed cross-coupling reaction of alkenyl bromides **179** with, for example, the organoindium derived from allenyl bromide **181**, or 1,1-dimethyl allene (**183**) (via a Mizoroki–Heck reaction) (Scheme 1.28) [132, 135]. Palladium(0)-catalyzed dimerizations or homocouplings can also furnish the C2–C3 bond [138–142], as can nickel(0)- [143, 144] and rhodium(I)-catalyzed ones [137].

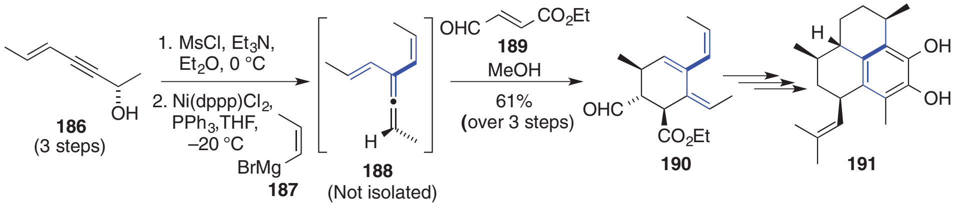


Scheme 1.27 Recent [3]dendralene synthesis by Tsuji and coworkers using a metallated butadiene [126].



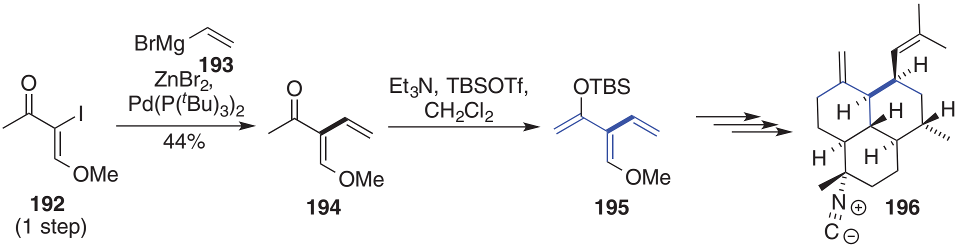
Scheme 1.28 Cross-coupling syntheses of [3]dendralenes using allene starting materials [132, 135, 137].

Two final examples of cross-coupling to furnish [3]dendralenes via C2–C3 bond formation are part of very short and efficient total syntheses, and highlight the versatility and attractiveness of the approach. As an extension of their work on 1,1-divinylallene (**153**) (Scheme 1.22), Sherburn *et al.* [123] synthesized allenic [3]dendralene **188** via Kumada cross-coupling of a metallated alkene **187** and a chiral, propargyl mesylate. A subsequent Diels–Alder reaction produced cyclic [3]dendralene **190** *en route* to a pseudopterosin aglycone **191** (Scheme 1.29). Allenic [3]dendralenes are prone to decomposition [136], so the subsequent DA reaction was carried out *in situ*.



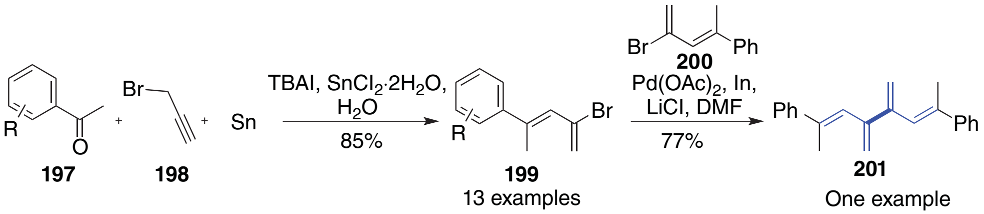
Scheme 1.29 Chiral [3]dendralene synthesis via sp^2–sp cross-coupling as part of a total synthesis by Sherburn and coworkers [123].

In another total synthesis involving a [3]dendralene, Pronin and Shenvi [122] synthesized a “Danishefsky dendralene” **195** using a Negishi cross-coupling reaction with a functionalized alkenyl iodide **192** followed by silyl enol ether formation to generate the dendralene (Scheme 1.30). A subsequent series of transformations, including two DA reactions, led to the total synthesis of amphilectene natural product **196**.



Scheme 1.30 [3]Dendralene synthesis via sp^2–sp^2 cross-coupling as part of a total synthesis by Pronin and Shenvi [122].

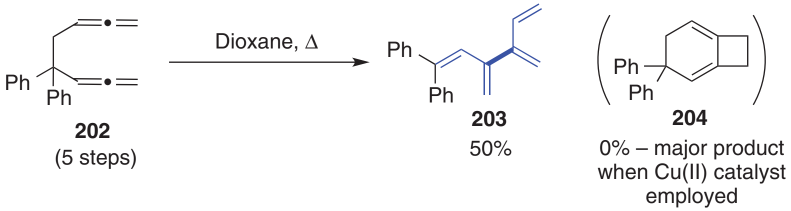
[4]Dendralenes have also been assembled by solo sp^2–sp^2 bond-forming reactions. The most prominently targeted C–C bond has been the central one. This approach is maximally convergent, and especially well suited to symmetrical targets. Li and coworkers [145] recently synthesized a symmetrical, 1,1,6,6-tetrasubstituted [4]dendralene **201** by a palladium(0)-catalyzed homocoupling reaction (Scheme 1.31). While only an isolated example of a [4]dendralene **201** was synthesized in this study, in principle, many different butadienyl halide-coupling partners **199** could be employed in this way. Other palladium-catalyzed homocouplings of functionalized 1,3-butadienes [146], and thermal oxidative homocoupling of highly electron-rich butadienes [147] have also been reported. In fact, the first practical synthesis of the parent [4]dendralene was an oxidative homocoupling of the chloroprene Grignard reagent [148].



Scheme 1.31 Synthesis of 2-bromo-1,3-butadienes and subsequent homocoupling to form a [4]dendralene, by Li and coworkers [145].

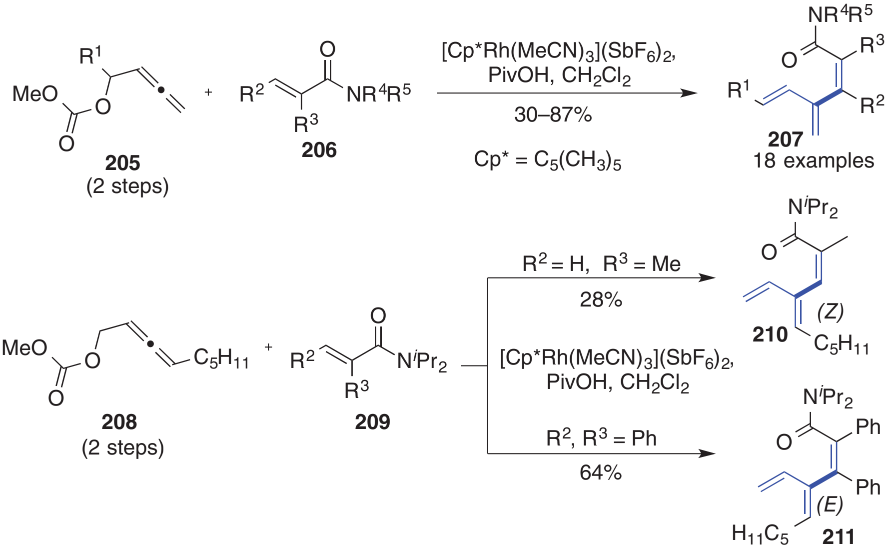
Isomerizations and rearrangements featured heavily in early approaches to [4]dendralene and derivatives [17, 149–155]. An interesting, recent case of unsymmetrical [4]dendralene formation was reported by Mukai and coworkers in

2012 (Scheme 1.32) [156]. Cu(II)-promoted intramolecular [2+2] cycloaddition of 1,4-diallenes **202** yielded bicyclooactadienes **204**; however, under uncatalyzed thermal conditions, the authors noted that the formal [3,3]-sigmatropic rearrangement product, [4]dendralene **203**, was formed in 50% yield. If optimized, this presents a nice method to form unsymmetrical [4]dendralenes, but relies on a lengthy synthesis of starting materials.



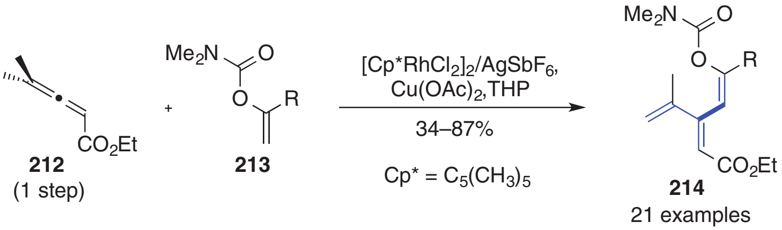
Scheme 1.32 Thermal isomerization synthesis of an unsymmetrical [4]dendralene by Mukai and coworkers [156].

C–H activation is an important and rapidly developing area of dendralene synthesis. In very recent years, several C2–C3 bond forming approaches to dendralenes involving C–H activation have been reported. In 2013, Glorius and coworkers developed a Rh(III)-catalyzed, Heck-type alkenyl C–H activation and coupling reaction with allenyl carbinol carbonates **205** and acrylamides **206** (Scheme 1.33) [157]. This new reaction performs well for the synthesis of highly substituted [3]dendralenes.



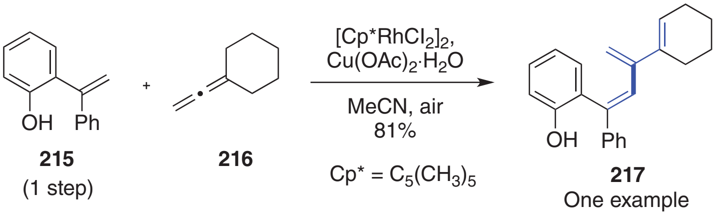
Scheme 1.33 Rh(III)-catalyzed Heck-type C–H activation of carbonates by Glorius and coworkers [157].

A similar transformation was subsequently reported in 2014 by Fu and coworkers, who used allene and carbamate precursors to generate [3]dendralenes via rhodium(III) catalysis (Scheme 1.34) [158]. A variety of different carbamates **213** successfully underwent Rh(III)-catalyzed C–H activation and coupling to generate cyclic and acyclic substituted [3]dendralenes **214**. While the general route works quite well between the tri-substituted allene and acyclic carbamates, the reaction is not high yielding if the enol ester is cyclic or the allene is mono- or tetra-substituted.



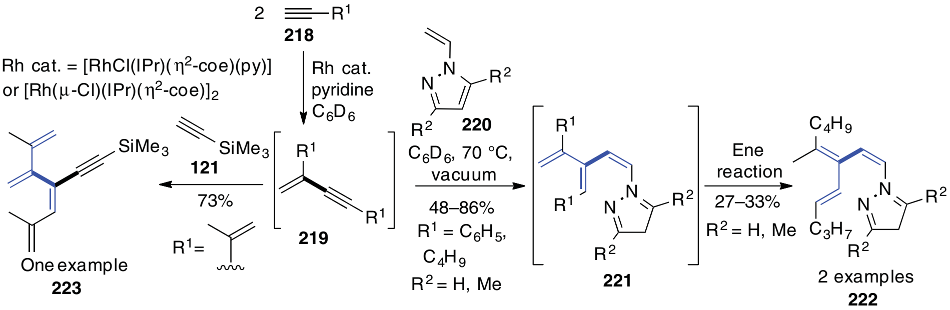
Scheme 1.34 Rh(III)-catalyzed C–H activations of carbamates by Fu and coworkers [158].

Another C–H activation method that has potential in the synthesis of dendralenes was reported by Gulías and coworkers in 2015 (Scheme 1.35) [159]. A stable dendralene intermediate **217** was prepared from substituted phenol **215** and allene **216**, as an intermediate in the Rh(III)-catalyzed synthesis of 2*H*-chromenes. In principle, this method could be adapted to target substituted dendralenes.



Scheme 1.35 Rh(III)-catalyzed allene alkenylation by Gulías and coworkers [159].

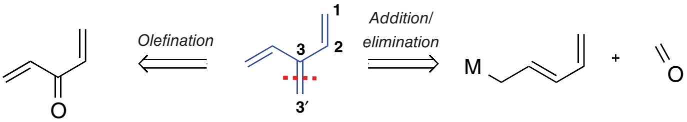
A final recent contribution to C–H activation-based methods is the work by Oro and coworkers, who reported the Rh(I)-catalyzed hydrovinylation of alkynes **218** with *N*-vinylpyrazoles **220** to form pyrazole-containing [3]dendralenes **221** (Scheme 1.36) [160, 161]. Some of these dendralenes could also be subjected to thermal Alder–ene reactions to alter the substitution pattern on the dendralene products.



Scheme 1.36 Rh(I)-catalyzed hydrovinylation of alkynes by Oro and coworkers, and a subsequent ene reaction, to synthesize [3]dendralenes [160, 161].

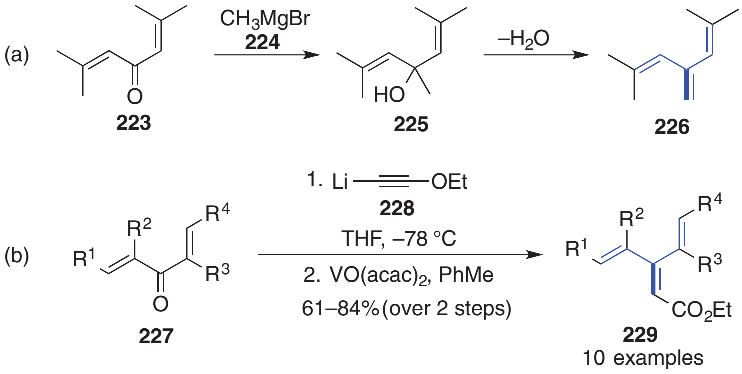
1.3.3
C3–C3′ Alkenation Reactions

The first example of a dendralene synthesis via C3–C3′ bond formation (Scheme 1.37) dates back to 1904, when Fellenberg reported an addition/elimination sequence between methyl magnesium bromide (**224**) and phorone (**223**) (Scheme 1.38 (a)) [162]. Since then, a number of variations leading to different substituents have been reported. In fact, early syntheses of dendralenes prominently feature the C3–C3′ bond disconnection, utilizing classical reactions such as Wittig reactions [165–175], HWE olefination [176–178], ketene additions/decarboxylation sequences [179–183], and Grignard addition/dehydration sequences [162, 184, 185] to transform readily available 1,4-dien-3-ones into dendralenes. Recently, West and coworkers made several cyclic and acyclic derivatives of substituted [3]dendralenes **229** through catalytic Meyer–Schuster rearrangements of propargyl alcohols derived from alkyne **228** addition to dienones **227** (Scheme 1.38 (b)) [163, 164]. It was found for these highly substituted dendralenes that if the dienone **227** was not symmetrical, mixtures of (*E*) and (*Z*) alkene isomers were formed. Despite this limitation, a very noteworthy feature of the work is the use of a less substituted dienone **227** starting material – prior to this, only highly substituted variants had been employed.

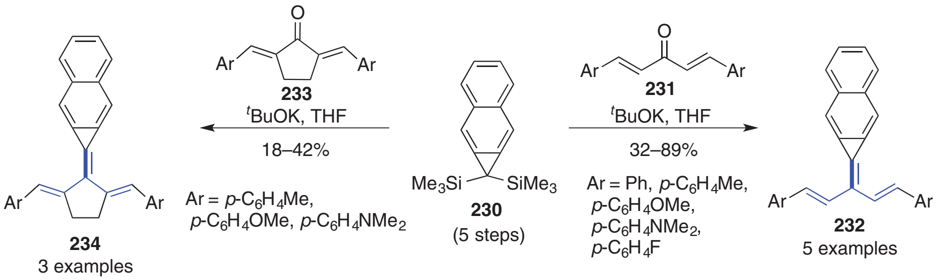


Scheme 1.37 Single alkenation (C3–C3′) bond disconnections of [3]dendralene.

Other variants of olefination have also been applied to dendralene synthesis [186–188]. In 2004, Dixon and Halton [189] prepared a variety of cyclic [3]dendralenes using Peterson-type olefination reactions (Scheme 1.39). These



Scheme 1.38 (a) Addition/elimination sequence by von Fellenberg [162] and (b) Meyer–Schuster rearrangement by West and coworkers [163, 164].

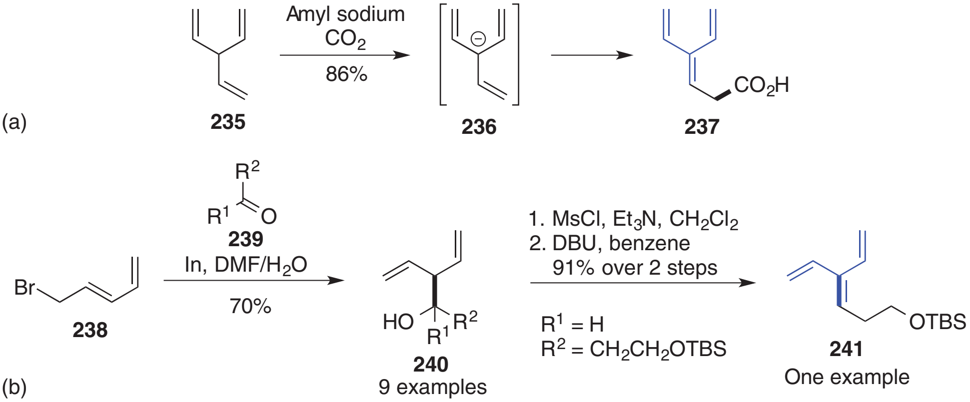


Scheme 1.39 Peterson-type olefination approach to [3]dendralenes by Dixon and Halton [189].

examples feature symmetrical dienone starting materials, so the stereoselectivity of the Peterson olefination approach to dendralenes is yet to be tested.

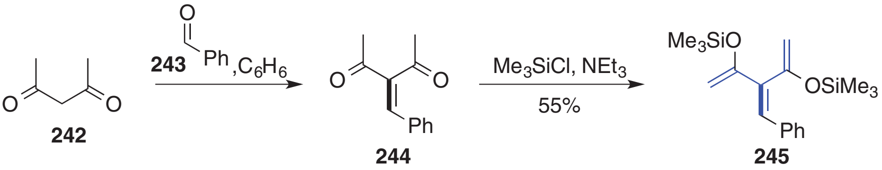
Another way to circumvent the stereoselectivity issues that may arise from olefination or addition/elimination sequences to 1,4-dien-3-ones is to switch the polarity of components and olefinate a carbonyl compound with a symmetrical nucleophilic pentadienyl anion equivalent. A seminal contribution was reported by Paul and Tchelitcheff in 1951, who combined trivinylmethane (**235**) and carbon dioxide to form a [3]dendralene **237** (Scheme 1.40 (a)) [190]. In this instance, the anion of trivinyl methane **236** is indeed a pentadienyl anion, but bond formation occurs with allylic transposition through a vinyl unit.

Fallis and coworkers [191, 192] have synthesized substituted [3]dendralenes using a similar approach, by reacting indium metal with bromodiene **238**, and using the resulting indium pentadienyl species in addition/elimination sequences with a number of functionalized aldehydes or ketones **239** (Scheme 1.40 (b)). This strategy builds on work by the Miginiacs in 1964 [193], and has also seen subsequent use [12, 194–196].



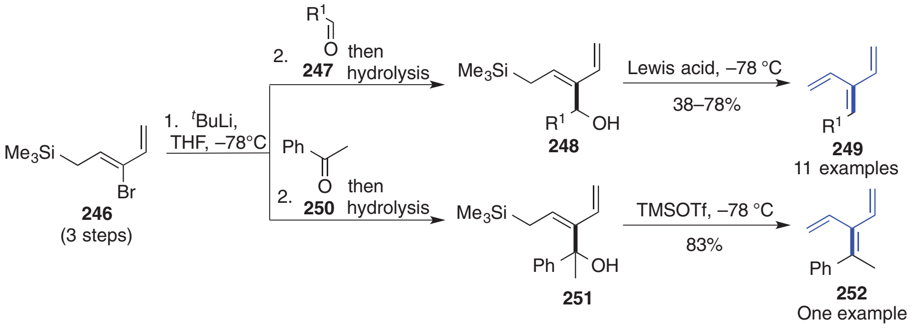
Scheme 1.40 [3]Dendralene synthesis using (a) a trivinyl methide anion [190] and (b) an indium pentadienyl nucleophile [191, 192].

A separate approach to this bond formation is the Knoevenagel condensation of a 1,3-diketone with a carbonyl compound, followed by conversion of the carbonyl groups to alkenes. For example, in 1983 Tsuge and coworkers reported condensation between diketone **242** and benzaldehyde (**243**), followed by double silyl enol ether formation to generate a [3]dendralene **245** (Scheme 1.41) [197–199]. The ready availability of the carbonyl compounds involved suggests that this method could be useful for other substituted dendralenes. Silyl enol ether formation to generate a [3]dendralene was subsequently used to great effect in total synthesis by Pronin and Shenvi (Scheme 1.30, [122]). The Knoevenagel condensation can also be performed with different electrophiles, followed by chlorinative dehydration to reveal a dihalodendralene [200, 201], or hydride reduction/elimination to reveal a terminally unsubstituted [3]dendralene [202].



Scheme 1.41 A Knoevenagel condensation/silyl enol ether formation approach to a [3]dendralene [197].

Recently, a Peterson-type olefination variant of this strategy was explored by Parrain and coworkers [203]. By incorporating a trimethylsilyl group in the pentadienyl anion equivalent **246**, alcohols **248** that readily undergo Lewis-acid-catalyzed γ-elimination were formed as addition products of aldehydes **247** (Scheme 1.42). The one-step, facile elimination is an improvement on the mesylation/elimination approach of Fallis. Interestingly, while alcohols of the type **248** and **251** bearing different, substituted alkenyl substituents have been



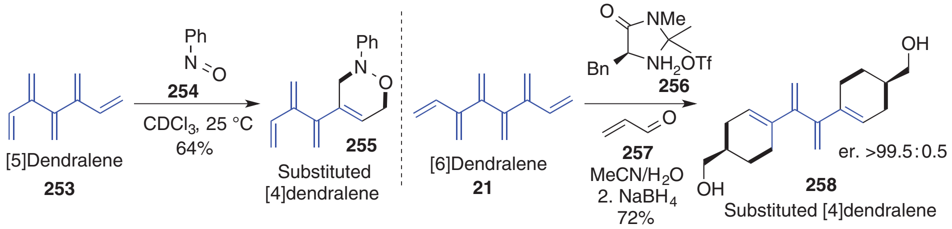
Scheme 1.42 Syntheses of dendralenes via Peterson-type olefination by Parrain and coworkers [203].

prepared [204], the corresponding elimination reactions (now with the possibility of forming mixtures of (*E*) and (*Z*) isomers), do not appear to have been reported. This presents an avenue worthy of further investigation.

1.4
Dendralenes from Dendralenes

Aside from the synthesis of dendralenes from nondendralenic materials, there also exist a variety of transformations that can be applied to a preexisting dendralene framework to add further functionality. Most of these examples form part of exploratory studies to test the reactivity of dendralenes; nevertheless, they show potential for the synthesis of a variety of functionalized dendralenes. Broadly, these can be divided into transformations that reduce the length of the [*n*]dendralene framework (e.g., $n \rightarrow n-1$), ones that functionalize and preserve an existing [*n*]dendralene framework (i.e., $n \rightarrow n$), or ones that add extra branched alkenes to form a higher [*n*]dendralene (e.g., $n \rightarrow n+1$).

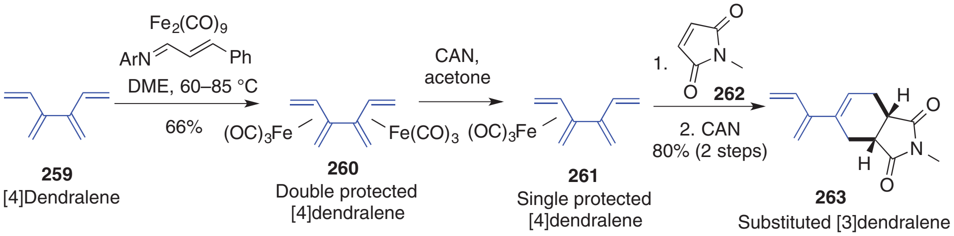
In the first category, the Sherburn group, the first to synthesize the parent family of dendralenes, have documented a number of transformations that result in the conversion of a higher dendralene into a lower one. [5]Dendralene (**253**) and



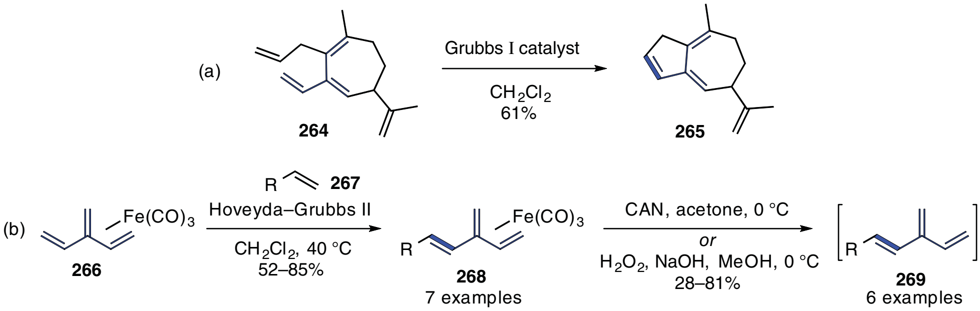
Scheme 1.43 Hetero-DA and enantioselective DA reactions of dendralenes from the Sherburn group [205, 206].

higher [*n*]dendralenes undergo DA reactions to furnish [*n* – 1]dendralenes. Aside from reactions with *N*-methylmaleimide (NMM) (**262**) [19, 20, 23, 89, 148] and SO_2 [10], these include hetero-DA reactions to form heterocycle-containing dendralenes **255** [205], and enantioselective DA reactions to form chiral, enantioenriched dendralenes **258** [206] (Scheme 1.43).

Singly complexed tricarbonyliron-[4]dendralene **261** (prepared from [4]dendralene (**259**)) [89, 207] can be reacted with NMM (**262**) to undergo a single DA reaction at a terminal diene site to produce, after decomplexation, a reactive [3]dendralene **263** (Scheme 1.44), which cannot be isolated by reacting uncomplexed [4]dendralene (**259**) and dienophiles (see Chapter 12). Complexation and reaction, therefore, provides a viable avenue toward dendralenes not isolable from other reaction conditions.



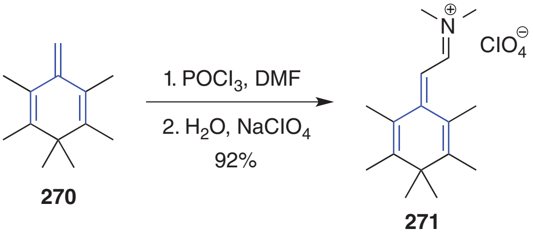
Scheme 1.44 Tricarbonyl iron-complexed dendralenes enabling the synthesis of a formal terminal single DA-adduct of [4]dendralene [89].



Scheme 1.45 Examples of (a) RCM [120] and (b) cross-metathesis using dendralene precursors [87, 89].

Dendralenes may also be functionalized at one of the alkene positions without destroying the alkene. An interesting case is the ring-closing metathesis (RCM) reaction of cyclic dendralene **264**, using Grubbs I catalyst, to form a bicyclic dendralene **265**, maintaining the [3]dendralene framework (Scheme 1.45 (a)) [120]. In contrast to the "naked" parent dendralene, tricarbonyliron-complexed [3]dendralene (**266**) undergoes smooth cross- and homometathesis reactions to furnish a variety of highly reactive, 1*E*-substituted [3]dendralenes **269** (Scheme 1.45 (b)) [87, 89].

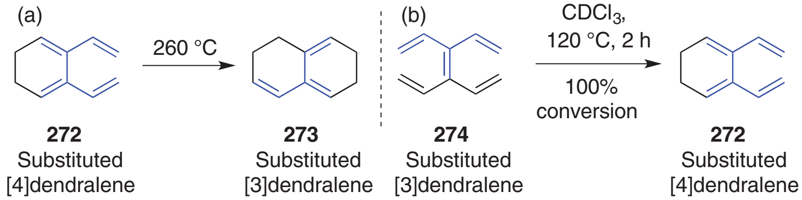
Instances where a dendralenic alkene participates as a nucleophile in an addition or substitution, and the alkene is regenerated by elimination, appear surprisingly rare. One such example is the preparation of the Vilsmeier salt **271** of cyclic [3]dendralene **270** (Scheme 1.46) [208]. Formylation of very electron-rich dendralenes has also been reported, such as part of the iterative formylation/olefination sequence to build higher dendralenes reported by Yoshida *et al.* (Scheme 1.20) [82].



Scheme 1.46 Synthesis of the Vilsmeier salt of a cyclic [3]dendralene [208].

Halodendralenes are valuable substrates for dendralene to dendralene transformations that preserve or extend the dendralene framework. They are intermediates in the synthesis of [7]- and [8]dendralene (Scheme 1.26) [23], as are their nucleophilic relatives, pinacolatoboryldendralenes, in the synthesis of substituted [4]-, [5]-, and [6]dendralenes [25, 27]. (Pseudo)halodendralenes have also been used in Stille [209] and Sonagashira cross-couplings [178, 210]. Dendralene dimers can be obtained via homocoupling of halodendralenes [211]. Dendralene frameworks can also be extended by uncatalyzed metathesis reactions on alkyne-containing dendralenes, and olefination reactions on carbonyl-containing ones [1, 211–214], each of which has been discussed.

Rearrangements and isomerizations can lead to either an extension or a reduction of an existing dendralene framework. For example, the Cope rearrangement shown in Scheme 1.9 converted a [3]dendralene **63** to a [4]dendralene



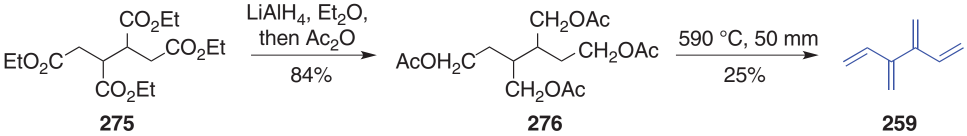
Scheme 1.47 Isomerization reactions that either reduce [215] or extend the dendralene framework [19].

64, while changing the path of the dendralene backbone. In contrast, rearrangement and electrocyclic ring closure of [4]dendralene **272** leads to bicyclic [3]dendralene **273** (Scheme 1.47 (a)) [215]. **272** is itself the product of thermally or photochemically promoted electrocyclic ring closure of TVE (**274**) (a [3]dendralene), (Scheme 1.47 (b)) [19]. The intramolecular Alder–ene reaction of a [3]dendralene reported by Oro and coworkers in Scheme 1.36 provides an example of an isomerization that neither reduces or extends the dendralene framework, but does alter the connectivity [160, 161].

Elimination reactions to reveal masked dendralenes featured prominently in early attempts to synthesize cross-conjugated compounds [1]. Cheletropic extrusion of sulfur dioxide was used to convert lower dendralenes to [5], [6], and [8]dendralene [10], and to make substituted chiral [4]dendralenes [12].

1.5
Functional Group Interconversion Reactions

Our review has focused on syntheses of dendralenes that construct the carbon framework via carbon–carbon bond formation. While almost all strategies ultimately rely on carbon–carbon bond formation, some are better considered as distinct isomerization or functional group interconversion strategies that unmask a hidden dendralene. For example, one of the earliest syntheses of [3]dendralene (**5**) [216], and the very first synthesis of [4]dendralene (**259**) (Scheme 1.48) [217], proceed from commercially available starting materials without any carbon–carbon bond formations. Therefore, while we have taken note in each section of strategies that, while ultimately relying on an elimination or isomerization, have included an earlier key carbon–carbon bond-forming reaction, there are a number of somewhat esoteric strategies that we have not mentioned in this review. These approaches, which typically feature long sequences of steps to form synthetic intermediates primed for a key thermal elimination and/or isomerization, and are therefore limited in their preparative utility, are more prevalent in the early literature, and are very well summarized by Hopf's earliest review [1], with more recent variations being covered by the 2012 review of Hopf and Sherburn [2].



Scheme 1.48 The first synthesis of [4]dendralene, by Bailey and Nielsen, has no C–C bond forming events [217].

1.6
Concluding Remarks

By categorizing syntheses of dendralenes based on the carbon–carbon bonds formed in their approach, it is clear that over the past few decades there has been a massive shift away from lengthy and scope-limited isomerization and elimination-based strategies to unmask dendralenes, toward direct formation of functionalized dendralene frameworks via carbon–carbon bond-forming reactions. A plethora of techniques to directly and rapidly access dendralenes with a wide variety of substitution levels and functionality now exist. Some of these reactions, the most notable example being C–H activation, have only very recently enjoyed intense research focus. Given the number of short and practical preparative methods that now exist for the preparation of dendralenic structures, selective "dendralene to dendralene" functionalization reactions are also likely to see significant growth in the near future. It is therefore likely that the current trend of rapid expansion in synthetic means to dendralenes will continue strongly, driven by research in these areas, and in other reactions that are yet to be realized.

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2
The Diene-Transmissive Hetero-Diels–Alder Reaction

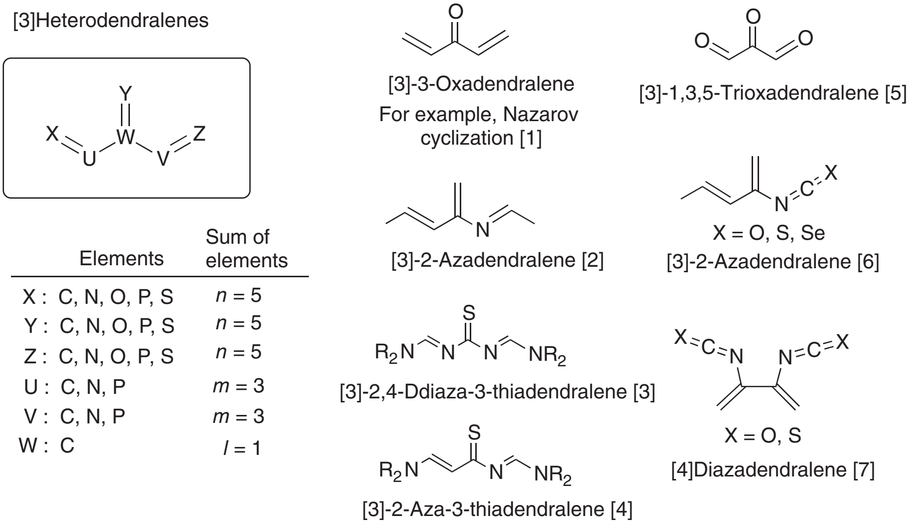
Takao Saito and Noriki Kutsumura

2.1
Introduction

When one or more carbon atoms in the frameworks of parent, all carbon-dendralenes are replaced by heteroatoms, the resulting compounds are called *heterodendralenes*. When heterodendralenes are limited to [3]heterodendralenes and one or more atoms in each position (X, Y, Z, U, V, and W) of the framework are limited to the elements shown in Scheme 2.1, at least 1249 kinds of parent [3]heterodendralenes can formally be considered (by combination of the component elements, omitting substituents and stereochemistry). Even if the elements for X, Y, Z, U, and V are each limited to only two elements ($n, m = 2$), for example, C and N, still 19 kinds of parent [3]heterodendralenes can formally be possible, after excluding one case of all carbon-[3]dendralene. A survey of the literature on SciFinder Scholar for such [3]heterodendralene structures reveals the following outcome:

1) Compounds with certain [3]heterodendralene structures including more complex substructures and substituents such as carbonyls, imines, and ylides are very popular, and hence many reports on their synthesis/generation, application and/or characterization, and so on, were found. However, only a few examples of their diene-transmissive hetero-Diels–Alder (DTHDA) reactions have been reported so far. For instance, although divinyl ketones ([3]-3-oxadendralenes, Scheme 2.1) are well recognized, for example, for their Nazarov cyclization [1] (see Chapter 3), only two reports are known on DTHDA reactions of β,β′-diphenyl- and di-2-thienyl-substituted divinyl ketones (*vide infra*) [8].
2) Some examples of other kinds of [3]- and [4]heterodendralene structures are actually known but are not so common (Scheme 2.1) [2–7]. The one or two of the heterocumulenic double bond can also be incorporated in [3]-2-azadendralene [6] or [4]diazadendralene [7]. Thus, many types of heterodendralene structures are identified, but their DTHDA reactions have not been reported so far.

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

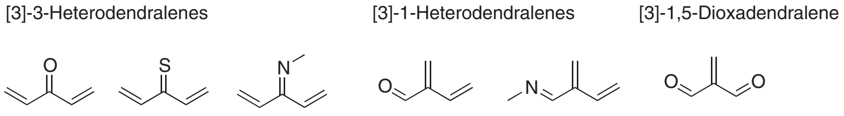


	Elements	Sum of elements
X :	C, N, O, P, S	$n = 5$
Y :	C, N, O, P, S	$n = 5$
Z :	C, N, O, P, S	$n = 5$
U :	C, N, P	$m = 3$
V :	C, N, P	$m = 3$
W :	C	$l = 1$

Scheme 2.1 Formally constructed [3]heterodendralenes and selected examples.

3) Of course, there are many unknown [3]heterodendralene structures and higher ones.

Scheme 2.2 illustrates the known types of [3]heterodendralenes that have been successfully used in DTHDA reactions to date. This chapter introduces the DTHDA reactions of both [3]heterodendralenes (heterotrienes) and of carbon-dendralenes with hetero dienophiles.



Scheme 2.2 [3]Heterodendralenes used in DTHDA reaction.

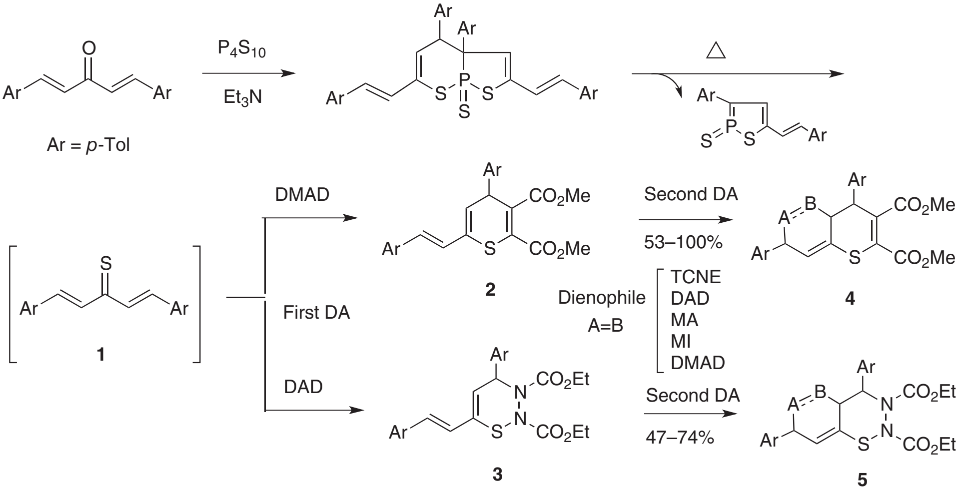
The DTHDA reaction is a special case of the DTDA (diene-transmissive Diels-Alder) reaction in which one or more heteroatoms are contained within a cross-conjugated triene/polyene (heterodendralene) π-system, a dienophile π-system, or both. The DTHDA protocol is an efficient and attractive method for the stereoselective synthesis of a variety of heterocyclic systems.

The merit and potential of the DTHDA methodology for heterocyclic synthesis can be widely extended by structural variations of both diene and dienophile; the kind of heteroatoms, their number, and their positions in either the cross-conjugated triene/polyene ([3/*n*]heterodendralene) or the dienophile framework, as well as the inter- or intramolecular cycloaddition mode, and control of regio- and stereoselectivities.

2.2
DTHDA Reaction of Heterotrienes

2.2.1
DTHDA Reaction of Thiatrienes

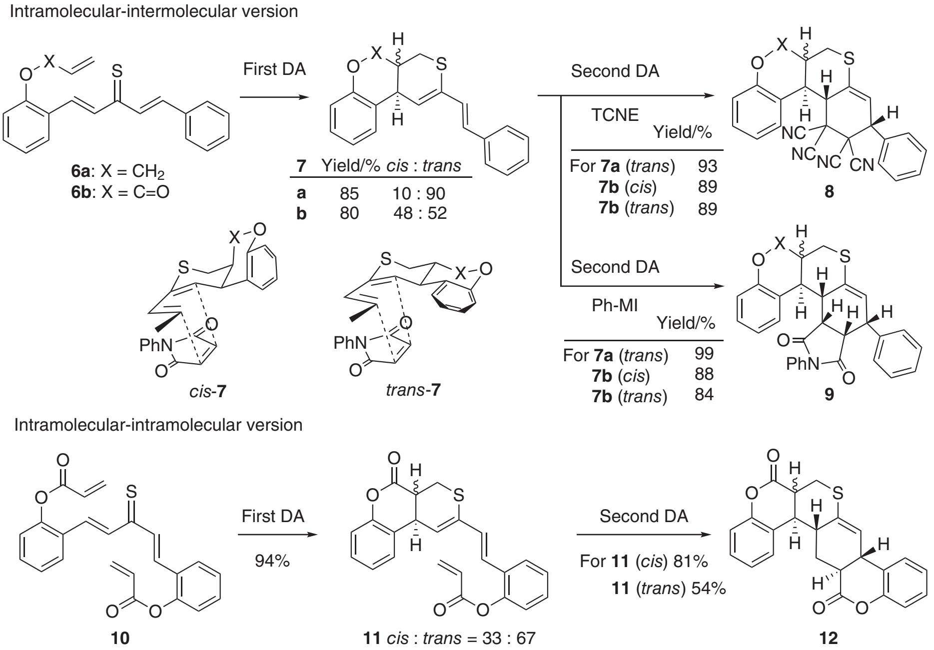
The first example of the DTHDA reaction was disclosed by the Motoki and Saito group using divinyl thioketone as a cross-conjugated thiatriene ([3]-3-thiadendralene) **1** (Scheme 2.3) [9]. The thiatriene **1** was generated by heating its precursor (the formal [4+2] adduct between **1** and 1,2-thiaphosphole), which was obtained by the thionation reaction of the corresponding ketone with P_4S_{10} in the presence of excess amounts of triethylamine. The initial hetero-Diels-Alder (HDA) reaction of **1** with dimethyl acetylenedicarboxylate (DMAD) or diethyl azodicarboxylate (DAD) gives mono-adducts **2** and **3**, respectively. The adducts **2** and **3** undergo the second Diels-Alder (DA) or HDA reaction with a dienophile, tetracyanoethylene (TCNE), maleic anhydride (MA), *N*-(*p*-methoxyphenyl)maleimide (MI), DMAD, or DAD to produce fused thiopyrans **4** and 1,2,3-thiadiazines **5**, respectively.



DMAD: dimethyl acetylenedicarboxylate, DAD: diethyl azodicarboxylate, TCNE: tetracyanoethylene, MA: maleic anhydride, MI: *p*-methoxyphenylmaleimide

Scheme 2.3 DTHDA cycloaddition of cross-conjugated thiatriene, [3]-3-thiadendralene.

The variations of intramolecular–intermolecular and intramolecular–intramolecular DTHDA sequences of this cross-conjugated thiatriene system have been reported (Scheme 2.4) [10]. The thiatrienes **6** generated from the corresponding ketones by thionation with Lawesson's reagent in refluxing benzene were trapped *in situ* by the internal dienophile to give the initial HDA monoadducts **7**. The second DA reaction of each separated stereoisomer **7**

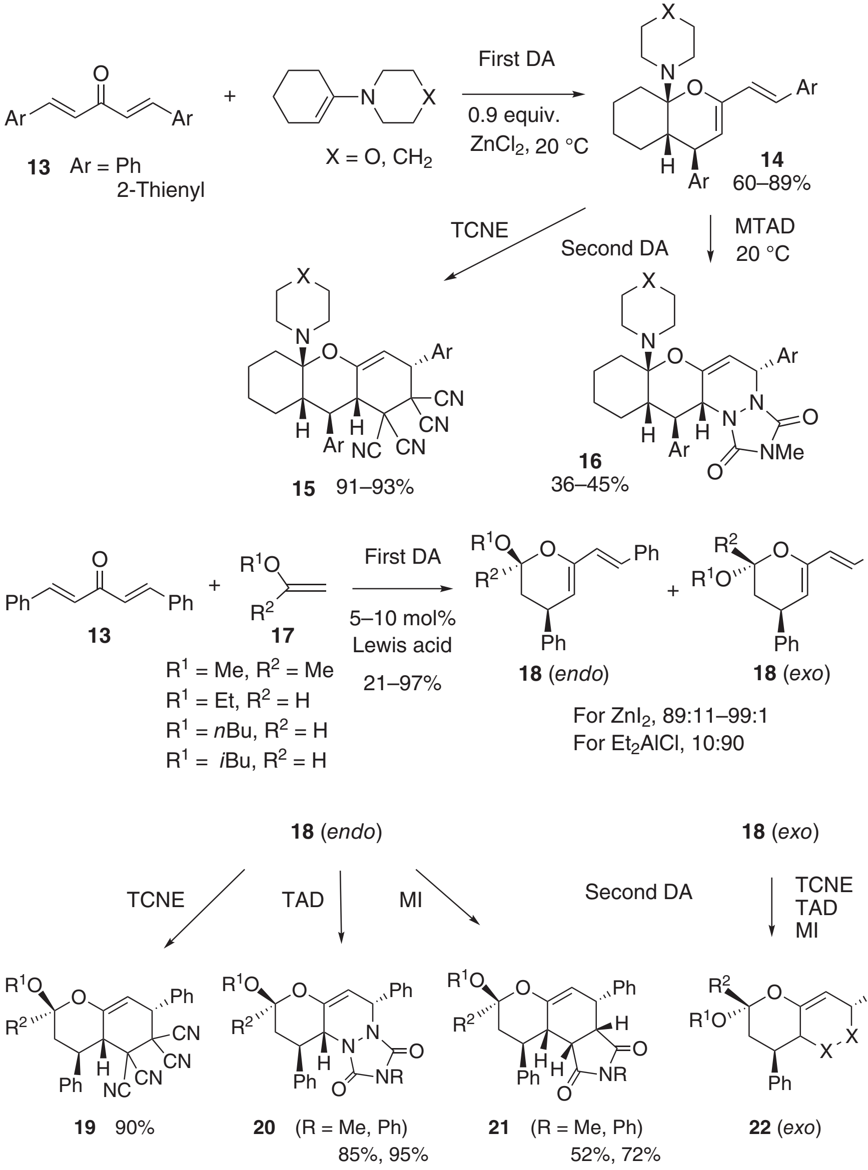


Scheme 2.4 Intramolecular–intermolecular and intramolecular–intramolecular DTHDA cycloaddition of the cross-conjugated thiatriene, [3]-3-thiadendralene.

with TCNE and *N*-phenylmaleimide (Ph-MI) produced bis-adducts **8** and **9**, respectively, in good yields with both high-diastereo-π-facial selectivity and with high-*endo* selectivity for **9**. The postulated transition state models are also in accordance with the observation that *cis*-configured **7** reacted faster than *trans*-**7**. The cross-conjugated thiatriene **10**, produced by the above procedure, gave the initial HDA adduct **11** in (94%) yield with a *cis*/*trans* ratio of 33/67. Upon simply heating at 140 °C, the separated isomers **11** underwent the second intramolecular DA reaction to produce bis-adducts **12** in fair to good yields with excellent diastereo-π-facial and *exo* selectivities.

2.2.2
DTHDA Reaction of Oxatrienes

Tsuge and coworkers [8] reported the DTHDA reaction of divinylketone **13** as a cross-conjugated oxatriene ([3]-3-oxadendralene) (Scheme 2.5). In the initial HDA reaction with enamine [8a], the presence of a nearly stoichiometric amount of a mild Lewis acid such as $ZnCl_2$ was necessary to obtain mono-adduct **14** as a single *endo*-isomer in good yield. The second DA reaction with electron-deficient dienophiles, TCNE, and 4-methyl-1,2,4-triazoline-3,5-dione (MTAD), smoothly preceded to give bis-adducts **15** and **16**, respectively, with high-π-facial selectivity. The initial HDA reaction of **13** with vinyl ethers gave



Scheme 2.5 DTHDA cycloaddition of cross-conjugated oxatriene, [3]-3-oxadendralene, **13**.

monoadducts **18** [8b], in which the *endo*/*exo* diastereoselectivity depends on the Lewis acid used in a benzene or toluene solvent; $ZnCl_2$, ZnI_2, $MgBr_2$, and $Eu(fod)_3$ [fod: tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate)] preferred *endo* selectivity (81 : 19 to 99 : 1), whereas $GaBr_3$, $AlCl_3$, and Et_2AlCl preferred *exo* selectivity (13 : 87 to 9 : 91). The second DA reaction of both *endo*- and *exo*-monoadducts **18** with TCNE, 1,2,4-triazoline-3,5-diones (TADs), and MIs gave bis-adducts **19–22** with again high-diastereo-π-facial selectivity (and *endo* selectivity with MI) in each case.

Elegant and extensive studies on the synthesis of quassinoids have been reported by Spino and coworkers, where a stereoselective DTHDA strategy is a key method for the construction of the tetracyclic quassinoid frameworks [11–15]. In 1993, they first proved the utility of this DTHDA strategy using a model substrate **23** (cyclic [3]-1-oxadendralene) (Scheme 2.6) [11, 13]. The $Yb(fod)_3$-catalyzed initial inverse-electron demand HDA cycloaddition between **23** and ethyl vinyl ether smoothly proceeded to give *endo* adduct **24**, which immediately underwent the intramolecular second DA cycloaddition with good diastereoselectivity (*exo* relative to the tether) to produce the tetracyclic compound **25** in 87% yield in 6 : 1 ratio. After extensive studies, Spino *et al.* developed the DTHDA methodology as key steps for synthesis of important intermediates for highly oxygenated quassinoids such as **28** and **35** [11–15]. Sulfur-bridged oxatriene **26** underwent the $Yb(fod)_3$-catalyzed initial HDA cycloaddition with ethyl vinyl ether to give **27** as a single diastereomer, resulting from the approach at the less-hindered bottom face with an *endo* orientation [14]. The intramolecular second DA reaction of **27** required high temperatures, but the stereochemistry of the cycloadduct **28** was highly controlled. Cross-conjugated oxatriene **29** similarly underwent the initial HDA reaction with vinyl ether to afford cycloadduct **30**, but the newly transformed diene unit was not used for the second DA reaction. Instead, spontaneous decarboxylation occurred to give a new cross-conjugated carbotriene **31**. This compound was used in an extended DTHDA methodology involving the initial HDA cycloaddition with the thioketone dienophile and, after transformation to **34**, the second DA reaction with the inner dienophile to provide cycloadduct **35** with efficient stereocontrol.1)

Recently, the DTHDA cycloaddition of acyclic cross-conjugated oxatrienes **36** ([3]-1-oxadendralene) to give bis-adducts **38** was reported by Carboni *et al.* (Scheme 2.7) [16]. The $Yb(fod)_3$-catalyzed initial HDA cycloaddition with ethyl vinyl ether, followed by the second DA reaction of the mono-adduct **37** with Ph-MI, gave bis-adducts **38** in high yields with both high *endo* and diastereo-π-facial selectivities. This two-step DTHDA cycloaddition with electron-rich dienophiles (first DA) and various electron-deficient dienophiles (second DA) was successfully performed in one pot as a domino process (nine examples). With Ph-MI, the oxatriene **36** reacted as a carbodiene to afford monoadduct **39** as a single *endo*-isomer. The second HDA cycloaddition of **39a** ($R = Me_3Si$) with

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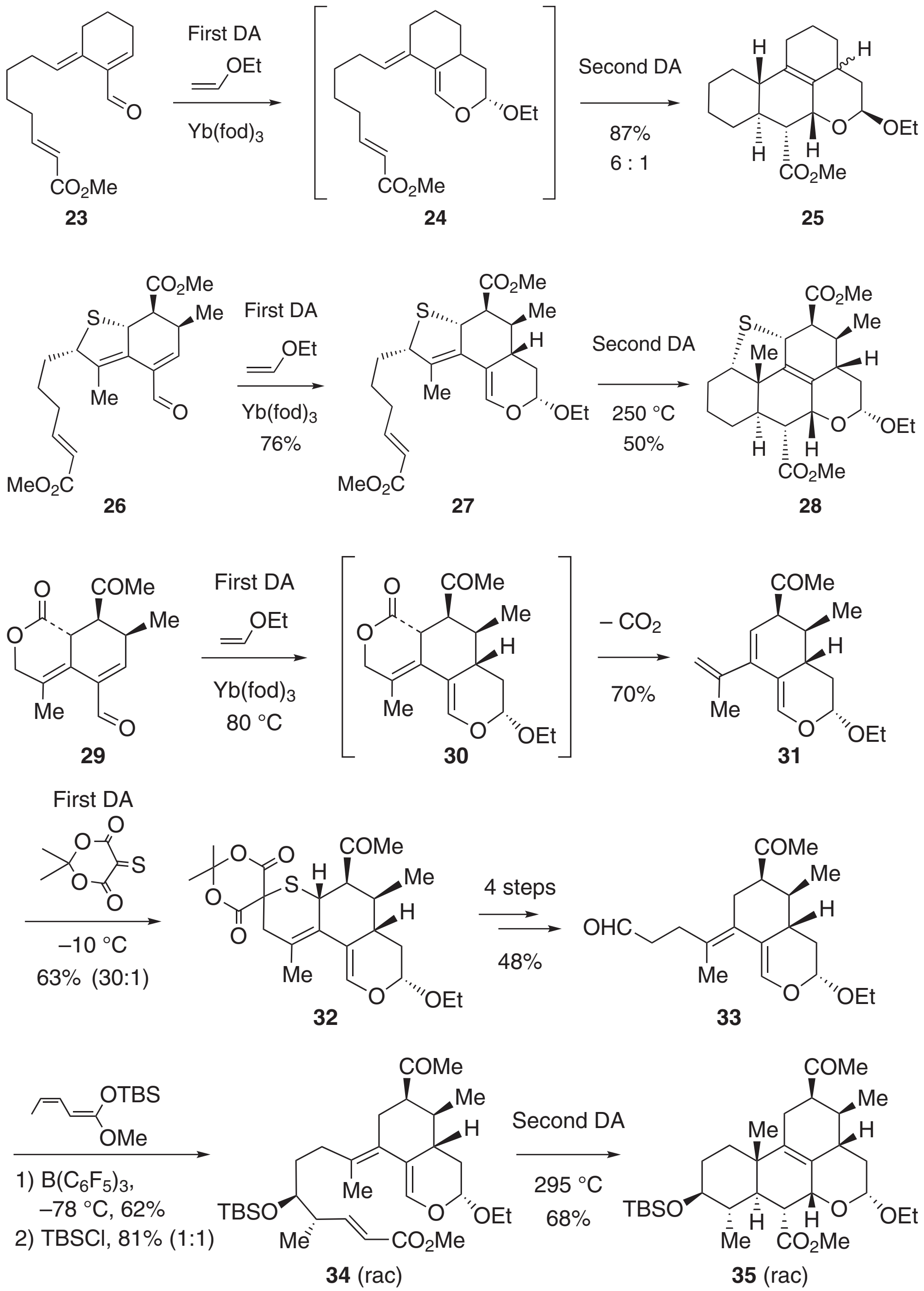
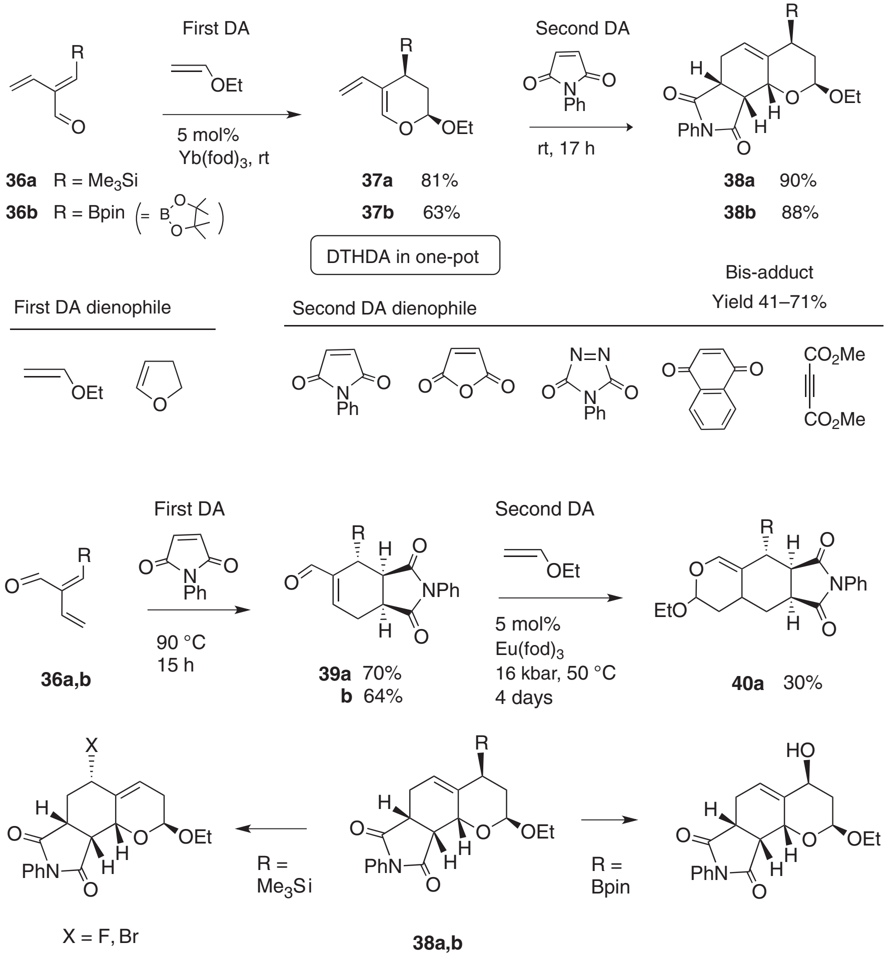
1) This example is a carbotriene DTHDA reaction with thioketone and carbon dienophiles and may be included in Section 2.3.



Scheme 2.6 DTHDA strategy for construction of a quassinoid frameworks.

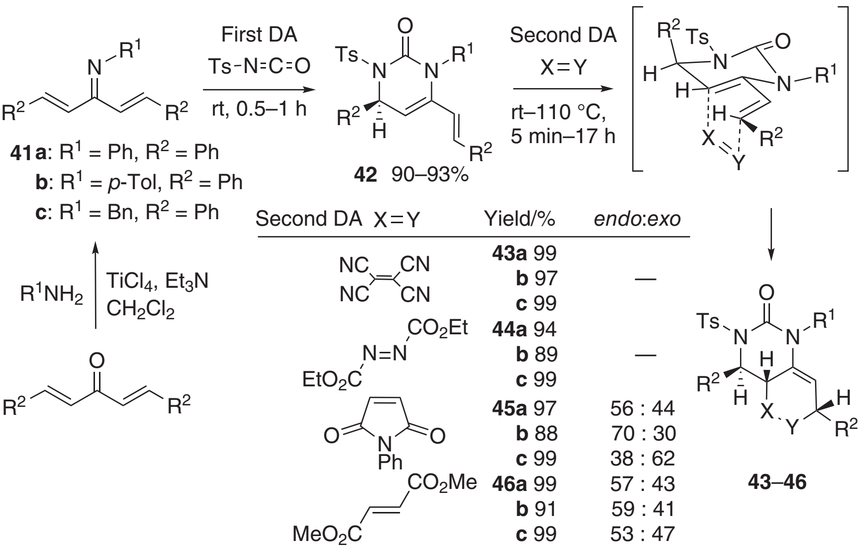


Scheme 2.7 DTHDA cycloaddition of cross-conjugated oxatriene, [3]-1-oxadendralene.

ethyl vinyl ether required rather harsh reaction conditions to provide bis-adduct **40a** (30%) as a mixture of two diastereomers. The trimethylsilyl (TMS)- or boryl auxiliary group R in the bis-adduct **38** was transformed to a hydroxyl group with retention of stereochemistry, or to fluorine or bromine atoms at the allylic position with inversion.

2.2.3
DTHDA Reaction of Azatrienes

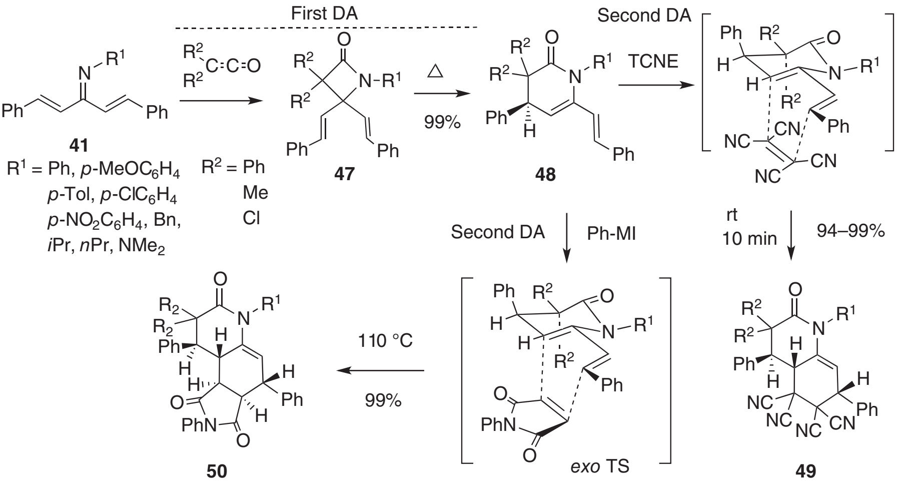
In 1997, the first example of a DTHDA reaction of a cross-conjugated azatriene was reported by Saito's group (Scheme 2.8) [17]. Di(β-styryl)methanimines ([3]-3-azadendralenes) **41**, which were prepared from corresponding ketones,



Scheme 2.8 DTHDA cycloaddition of cross-conjugated azatriene, [3]-3-azadendralene, **41**.

were allowed to react as a 4π-heterodiene with reactive tosyl isocyanate to give the initial HDA cycloadducts **42** in high yields, followed by the second DA reaction with electron-deficient dienophiles such as TCNE, DAD, Ph-MI, and dimethyl fumarate, which provided bis-adducts **43–46** in excellent yields with high-diastereo-π-facial selectivity and moderate *endo/exo* selectivity.

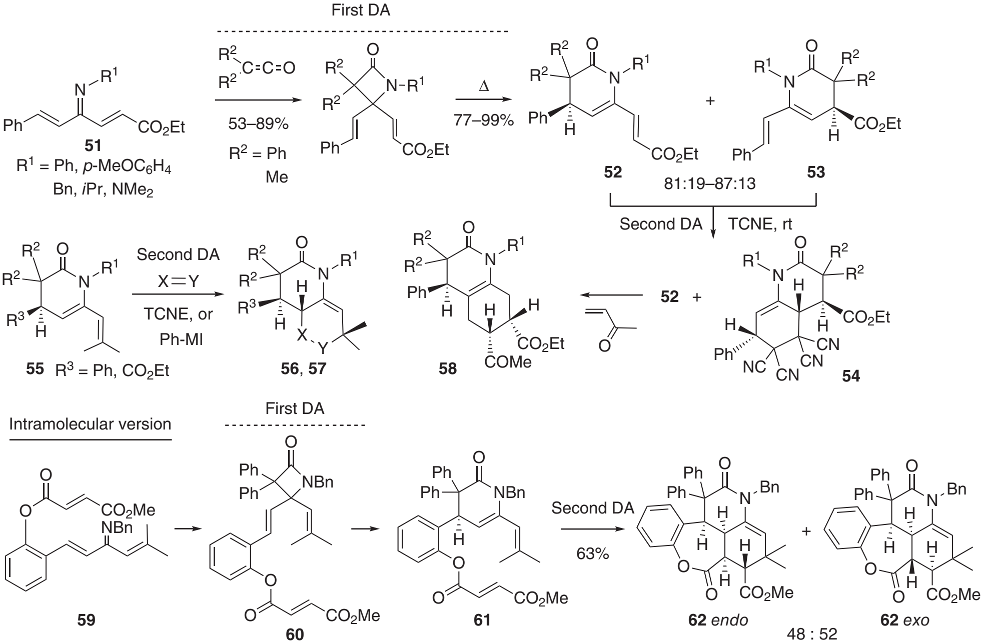
The azatrienes **41** also reacted with ketenes, but [2+2] cycloadducts **47** were initially formed when the reaction was performed at rt (room temperature)



Scheme 2.9 DTHDA cycloaddition of cross-conjugated azatriene, [3]-3-azadendralene, **41**.

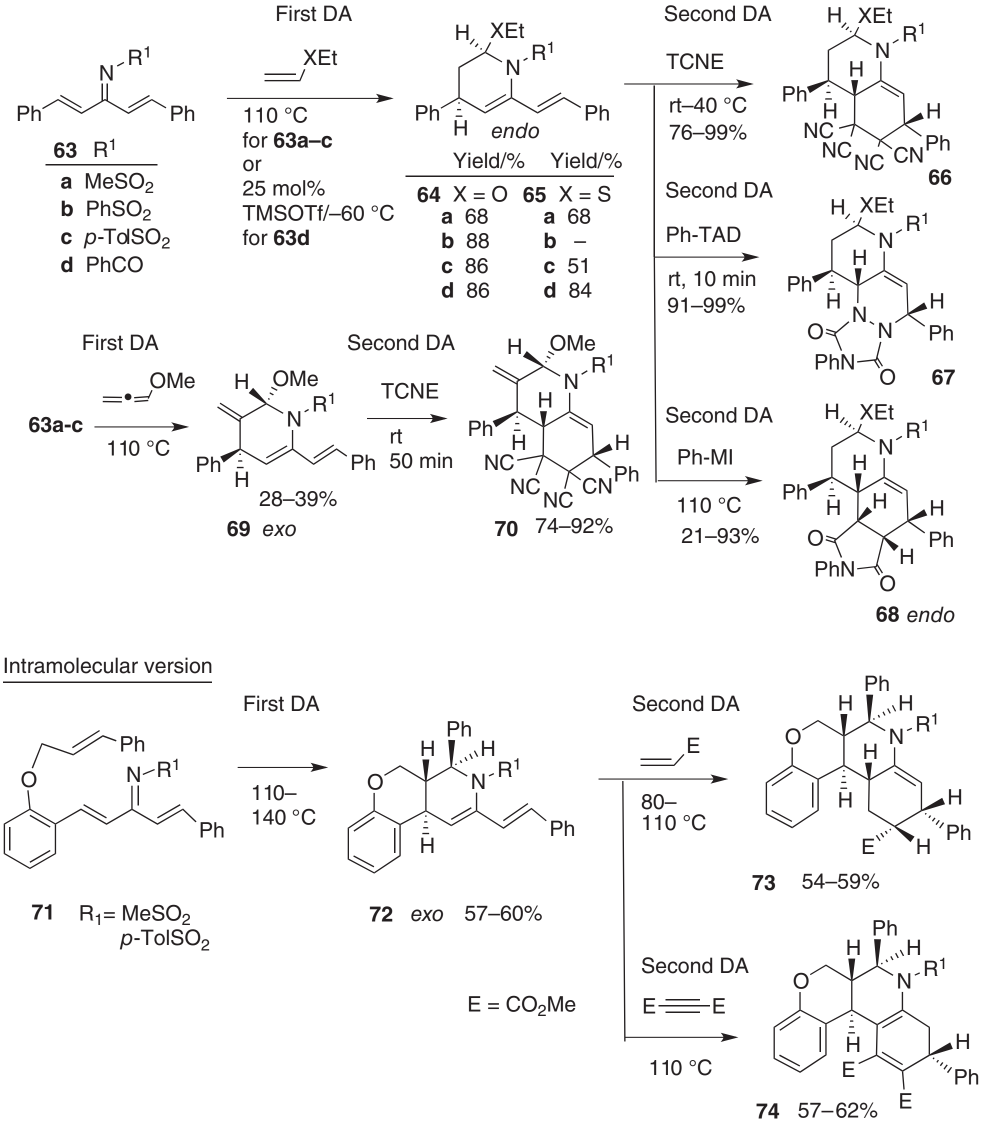
(Scheme 2.9) [18, 19]. These compounds could be isolated (except when $R^1 = NMe_2$ and $R^2 = Cl$) but are readily converted to the formal [4+2] cycloadducts **48** via [1,3]-sigmatropic rearrangement upon heating (115 °C). The second DA reaction of monoadducts **48** with TCNE and Ph-MI gave bis-adducts **49** and **50**, respectively, both with high-diastereo-π-facial selectivity and *exo* selectivity for Ph-MI.

The different vinyl-group-bearing azatrienes **51** similarly reacted with ketenes to produce [4+2]cycloadducts **52** and **53** as a mixture in a ratio of 81 : 19 to 87 : 13 via the [2+2]cycloadducts (Scheme 2.10) [18, 19]. When the mixture of **52** and **53** was treated with TCNE at rt for 10 min, only monoadduct **53** reacted to afford bis-adduct **54** in quantitative yield; the other major monoadduct **52** being unchanged. Upon heating, the recovered **52** underwent the second DA reaction with methyl vinyl ketone to give 1,3-H-migrated compound **58** in good yield together with its preformed *endo*-adduct. The ketene cycloadduct **55** derived from prenyl-group-bearing azatrienes also underwent the second DA reaction with TCNE and Ph-MI to yield nearly quantitatively bis-adducts **56** and **57**, respectively, with high-diastereo-π-facial and *exo* selectivity. The intermolecular–intramolecular version of this DTHDA methodology with azatriene **59** was successfully applied to the synthesis of polycyclic compounds, **62**.



Scheme 2.10 DTHDA cycloaddition of cross-conjugated azatrienes, [3]-3-azadendralenes.

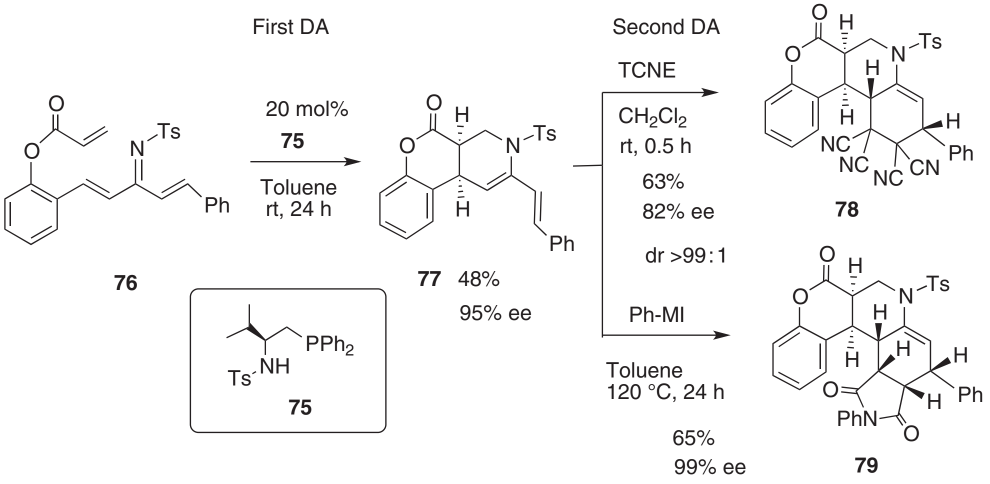
The cross-conjugated azatrienes bearing an electron-withdrawing group on the nitrogen atom **63** underwent, on heating or in the presence of trimethylsilyl triflate, the initial HDA reaction of an inverse-electron demand with electron-rich dienophiles (vinyl ether, vinyl thioether, and allenyl ether) to produce mono-cycloadducts **64**, **65**, and **69**, respectively, (Scheme 2.11) [20, 21]. Noteworthy is that the reaction with vinyl ether and thioether was *endo* selective, whereas the reaction with allenyl ether was *exo* selective. In the second DA reaction of mono-adducts **64** and **65** with TCNE, Ph-TAD, and Ph-MI, the dienophiles reacted on the less-hindered face of the diene in an *endo* manner with Ph-MI to



Scheme 2.11 DTHDA cycloaddition of cross-conjugated azatrienes involving an inverse-electron-demand HDA reaction.

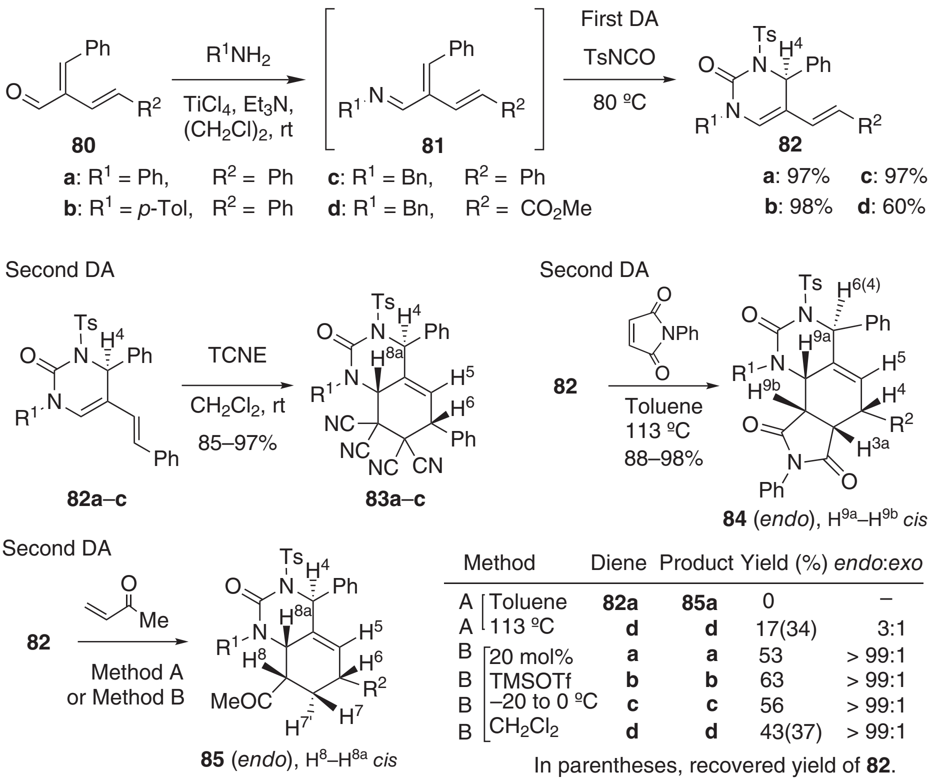
give bis-adducts **66–68**, respectively. Similarly, mono-adduct **69** reacted with TCNE to give bis-adduct **70** with high-diastereo-π-facial selectivity. The cross-conjugated azatrienes bearing a tethered cinnamyl moiety **71** readily underwent, on heating, the initial intramolecular HDA reaction of an inverse-electron demand type via an *exo* orientation with regard to the tether, giving *trans*-fused adducts **72**. On heating, the second DA reaction of **72** with methyl acrylate and DMAD proceeded with high stereoselectivity to provide the polycyclic compounds **73** and **74**, respectively, the latter cycloadduct **74** being formed by 1,3-H-migration from the preformed cycloadduct (see also bis-adduct **58**).

Recently, Chi and coworkers reported the first example of enantioselective DTHDA cycloaddition as an additional transformation of a cycloadduct formed from a chiral phosphine-catalyzed enantioselective 1-azadiene–HDA reaction (Scheme 2.12) [22]. The DTHDA methodology involved a chiral phosphine (**75**)-catalyzed intramolecular initial HDA cycloaddition of cross-conjugated azatriene ([3]-3-azadendralene) **76** to give mono-adduct **77** in 48% yield with 95% ee, followed by the second DA reaction of **77** with TCNE and Ph-MI, to give cycloadducts **78** and **79** as single diastereomers (dr > 99 : 1) in good yields with 82% ee and 99% ee, respectively.



Scheme 2.12 Chiral phosphine-catalyzed enantioselective DTHDA cycloaddition of cross-conjugated azatriene, [3]-3-azadendralene.

In 2014, it was shown that cross-conjugated 1-azatrienes ([3]-1-azadendralenes) **81** could also participate in the DTHDA cycloaddition (Scheme 2.13) [23]. The 1-azatrienes **81** prepared *in situ* from aldehydes **80** and amines underwent the initial HDA reaction with tosyl isocyanate to afford the mono-adduct **82** in high yields. The second DA reactions with TCNE and Ph-MI proceeded smoothly at rt or 113 °C to produce bis-adducts **83** and **84**, respectively, in good yields with high diastereo-π-facial selectivity for both **83** and **84** and with *endo* selectivity for **84**.



Method		Diene	Product	Yield (%)	*endo*:*exo*
A	Toluene 113 ºC	**82a**	**85a**	0	–
A		**d**	**d**	17(34)	3:1
B	20 mol% TMSOTf –20 to 0 ºC CH$_2$Cl$_2$	**a**	**a**	53	> 99:1
B		**b**	**b**	63	> 99:1
B		**c**	**c**	56	> 99:1
B		**d**	**d**	43(37)	> 99:1

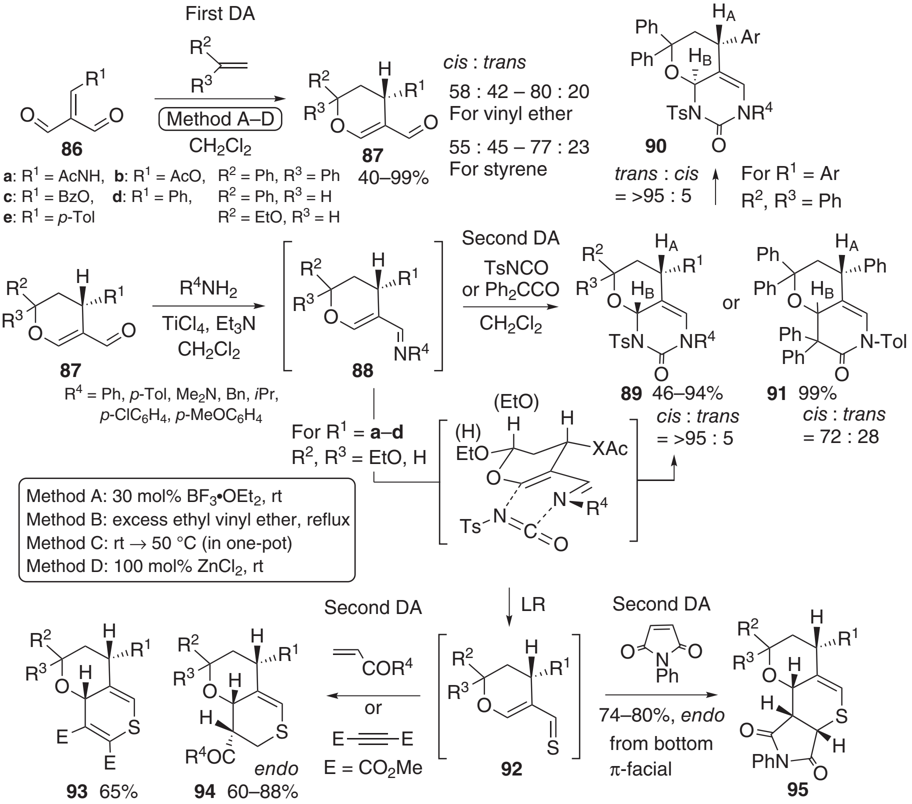
In parentheses, recovered yield of **82**.

Scheme 2.13 DTHDA cycloaddition of cross-conjugated azatriene, [3]-1-azadendralene.

The dienophiles approached the diene from the H^4-side of **82**. The reaction with methyl vinyl ketone in a sealed tube at 113 °C hardly proceeded, but TMSOTf catalyzed the reaction to give bis-adducts **85** in good yields with high diastereo-π-facial and *endo* selectivities.

2.2.4
DTHDA Reaction of Dioxatrienes as Masked Oxathiatrienes and Oxazatrienes

Among a very limited number of examples reported on the DTHDA cycloaddition of heterodendralenes, cross-conjugated dioxatrienes with two heteroatoms were engaged for the first time in the extended DTHDA cycloaddition (Scheme 2.14) [24]. Cross-conjugated dioxatrienes ([3]-1,5-dioxadendralenes) **86** [25] readily underwent the initial inverse-electron demand HDA reaction with 1,1-diphenylethene (Method A or D), styrene (Method A or D), and ethyl vinyl ether (Method B or C) to afford mono-adducts **87** with *cis (endo)*-isomer as major products. The 1-azadienes **88** generated from the separated isomers of 1-oxadienes **87** underwent the second HDA reaction with tosyl isocyanate or diphenyl ketene in one pot to give bis-adducts **89** and **91**, respectively, in good

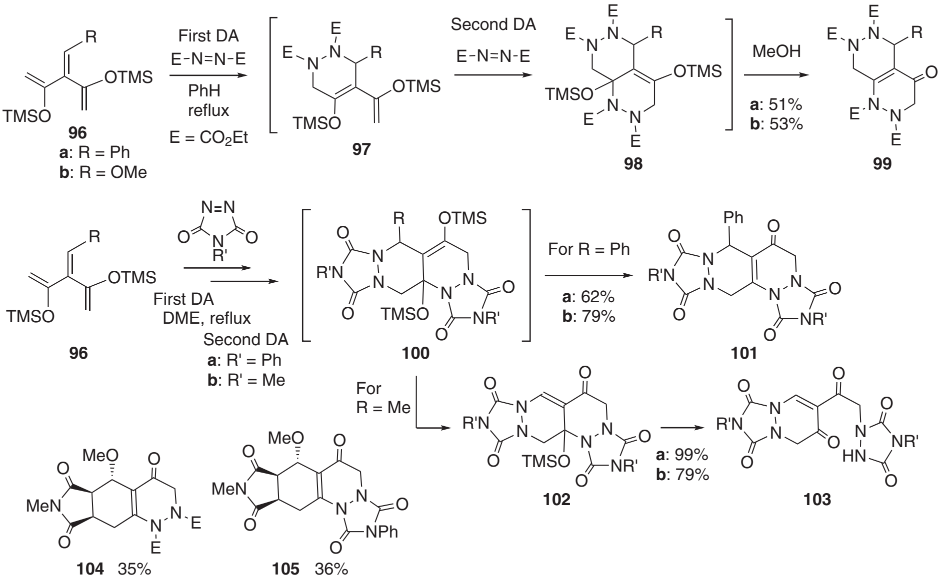


Scheme 2.14 DTHDA cycloaddition of cross-conjugated dioxatriene, [3]-1,5-dioxadendralene.

to excellent yields with high-regio- and π-facial selectivities. The *cis*-isomers **89** (R^1 = Ar, R^2, R^3 = Ph) fully isomerized into their *trans*-isomers **90** in the presence of acidic silica gel in $CDCl_3$. Similarly, sequential reaction **86** → **87** (first DA) → **92** (thionation with Lawesson's reagent) → **93**–**95** (second DA) completed the extended DTHDA methodology. Thus, cross-conjugated dioxatrienes **86** behaved as masked oxazatrienes **88** and as oxathiatrienes **92** to provide pyranopyridines **91**; pyranopyrimidines **89** and **90**; and thiopyranopyrans **93**–**95**.

2.3
DTHDA Reaction with Heterodienophiles

This section focuses on the DTHDA cycloaddition of cross-conjugated carbotrienes with heterodienophiles in either or both DA processes. Tsuge and coworkers demonstrated the DTHDA cycloaddition of cross-conjugated carbotrienes **96** with azodicarbonyl compounds as heterodienophiles (Scheme 2.15) [26]. When the trienes **96** were allowed to react with 2 equiv. of DAD in refluxing

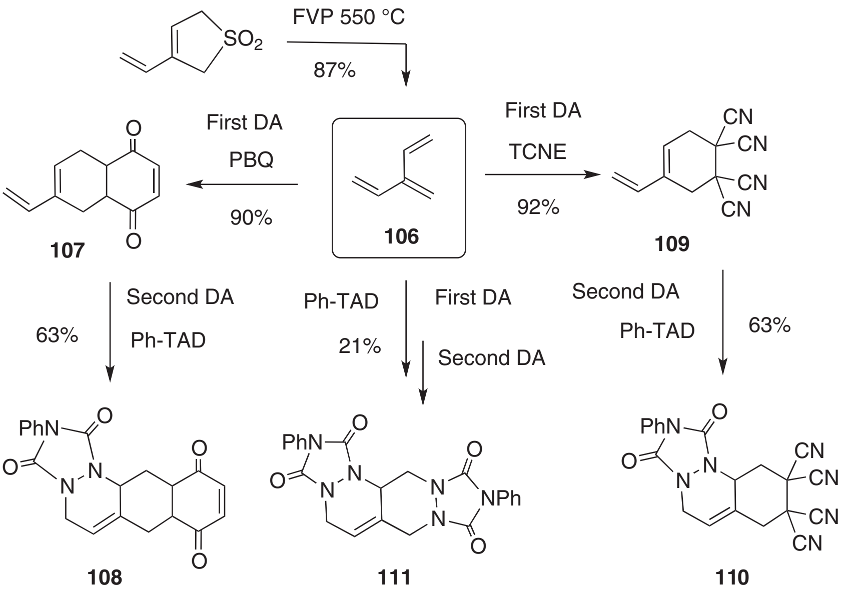


Scheme 2.15 DTHDA cycloaddition of cross-conjugated carbotrienes with heterodienophiles.

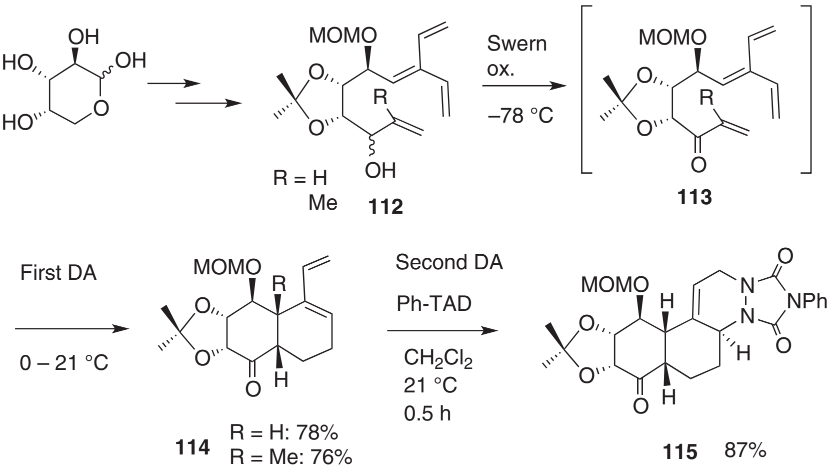
benzene, desilylated bis-adducts **99** were obtained after treatment of labile bis-adducts **98** with methanol. With only 1 equiv. of DAD, under mild conditions, the reaction did not give any mono-adducts. Similarly, the reactions with R′-TAD produced bis-adducts **101** and **103** as the final products. The intermediate **102** was isolated. The initial DA reaction with Me-MI, followed by the second reaction with DAD or Ph-TAD, furnished mixed bis-adduct **104** or **105**, respectively.

Cadogan *et al.* [27] reported the DTHDA cycloaddition of parent cross-conjugated carbotriene ([3]dendralene) **106** with some representative electron-withdrawing dienophiles including heterodienophiles (Scheme 2.16). They applied a flash vacuum pyrolysis technique to synthesize parent carbotriene **106** in pure form from 3-vinyl-3-sulfolene. The initial DA reaction with *p*-benzoquinone (PBQ) at 40 °C afforded mono-adduct **107** (90%), followed by the second HDA reaction with Ph-TAD at 40 °C to provide the mixed bis-adduct **108** (63%). Triene **106** gave mono-adduct **109** in the presence of even an excess amount of TCNE at 40 °C. Ph-TAD was able to react with mono-adduct **109** at 40 °C to provide crossed bis-adduct **110** (63%). Bis-adduct **111** was directly obtained (21%) by reaction of **106** with excess Ph-TAD at 40 °C, as same as the reaction with Ph-MI.

The DTDA cycloaddition strategy for the synthesis of oxygenated norsteroid and triterpenoid skeletons has been disclosed by Fallis *et al.* [28]. Scheme 2.17 illustrates the representative DTHDA cycloaddition strategy involving the initial intramolecular DA and the second HDA reaction with Ph-TAD. l-Arabinose-derived allylic alcohol **112** was oxidized to form **113** *in situ*, which spontaneously cyclized (first DA) at rt or 0 °C to afford *cis*-fused, *endo*-adduct **114** (R = H, 78%;



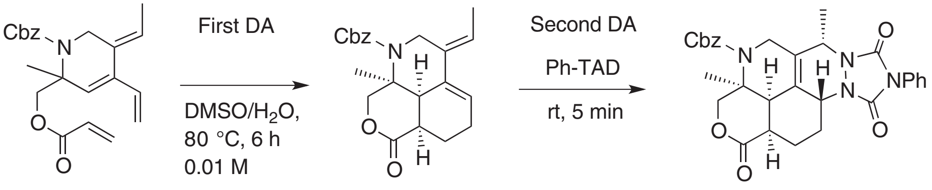
Scheme 2.16 DTHDA cycloaddition of parent cross-conjugated carbotriene **106** ([3]dendralene) with heterodienophiles.



Scheme 2.17 DTHDA strategy for oxygenated norsteroid and triterpenoid skeletons.

R = Me, 76%). The second DA reaction with Ph-TAD gave bis-adduct **115** (R = H, 87%) by approaching from the less-hindered convex π-face.

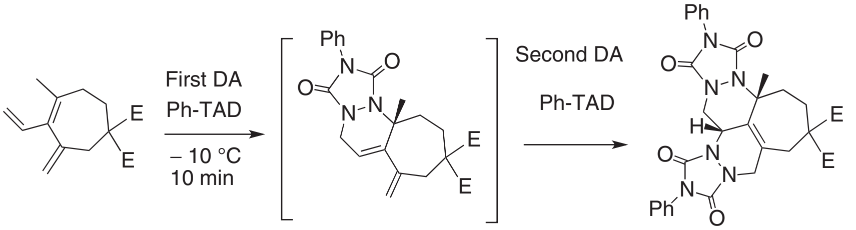
Brummond *et al.* reported that the amino acid-derived cross-conjugated triene bearing an acrylate dienophile **116**, which was synthesized via Rh(I)-catalyzed allene Alder–ene reaction and introduction of the dienophile moiety, underwent the initial intramolecular DA reaction by heating at 80 °C in DMSO/H_2O (2 : 1) with 0.01 M concentration to afford the tricyclic *endo*-adduct **117** (50%) as a single diastereomer (Scheme 2.18) [29]. The second DA reaction with a representative diaza dienophile, Ph-TAD, gave the pentacyclic adduct **118** in 95% yield.



116 **117** 50% **118** 95%

Scheme 2.18 DTHDA cycloaddition of amino acid-derived carbotriene.

A new synthesis of monocyclic cross-conjugated carbotrienes ([3]dendralenes) was presented by de Meijere and coworkers (Scheme 2.19) [30], which included palladium-catalyzed cycloisomerization of 2-bromoalka-1,*n*-dienes with tetra-substituted methylenecyclopropane end groups and the corresponding 1,6- and 1,7-enynes. Carbotriene **119** underwent DTHDA cycloaddition with Ph-TAD in a domino fashion to give a single diastereomer of the pentacyclic aza-heterocycle **121** in 81% yield.

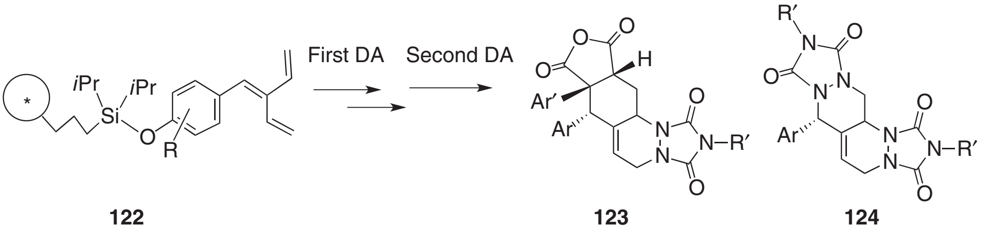


119 E = CO_2Et **120** **121** 81%

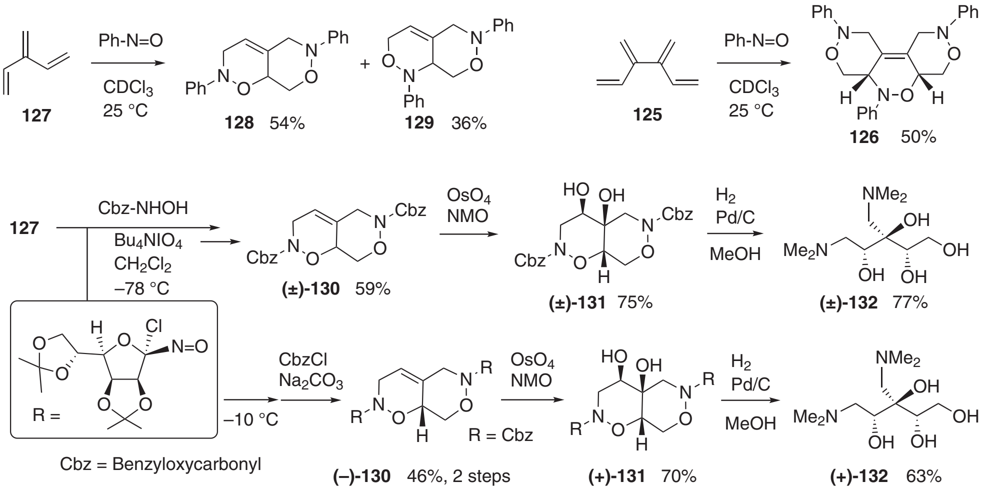
Scheme 2.19 DTHDA cycloaddition of carbotriene with Ph-TAD.

Schreiber and coworkers reported a branching diversity-oriented synthesis applying DTDA methodology that yielded 29 400 discrete compounds comprising 10 distinct polycyclic skeletons [31]. Scheme 2.20 shows only two DTHDA products in the DTDA reactions in which 40 aromatic hydroxyaldehydes, 41 disubstituted dienophiles, and 22 tri- or tetrasubstituted dienophiles were employed as building blocks.

Recently, Sherburn and coworkers reported interesting results on the HDA cycloaddition of parent [3]–[8]dendralenes with nitroso dienophiles and its application to a synthesis of branched aminosugars [32]. Scheme 2.21 depicts selected results of the full sequential DTHDA cycloadditions of parent [3]dendralene, **127** and [4]dendralene, **125**, with nitroso dienophiles. [4]Dendralene **125**



Scheme 2.20 Skeletal diversity-oriented DTHDA cycloaddition methodology.



Scheme 2.21 DTHDA reaction with nitroso dienophiles and synthesis of diaminotetrol.

reacted with 3 equiv. of nitrosobenzene to give tris-adduct **126** (50%) together with a minor regioisomer. The reaction of [3]dendralene **127** in the presence of 3 equiv. of nitrosobenzene afforded a mixture of bis-adducts **128** (54%) and **129** (36%). The reactivity depended upon the parity *n* of the [*n*]dendralene. The racemic and enantiomeric DTHDA reactions with nitroso compounds followed by dihydroxylation provided racemic and homochiral bis-adducts (±)-**131** and (+)-**131**, respectively. These compounds were transformed to branched diaminotetrols, (±)-**132** and (+)-**132**, respectively.

In summary, the DTHDA protocol is an efficient and attractive method for stereoselective synthesis of a variety of complex ring-fused heterocyclic systems.

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3

The Nazarov Cyclization of Cross-Conjugated Ketones

Louis Barriault and Mathieu Morin

3.1

Introduction

Electrocyclization reactions are powerful synthetic tools to prepare compounds of great molecular diversity. These reactions allow for the formation of many substituted cyclic and polycyclic compounds important in medicine, materials science, cosmetics, and so on. The well-established mechanisms and predictable outcomes of electrocyclization reactions permit the elaboration of logical blueprints for the synthesis of important molecules. Among these, the Nazarov cyclization is a salient member of the family. Reported first in 1941 by Ivan Nikolaevich Nazarov [1], this reaction has been studied extensively and many variations and applications have been developed over the years. In this chapter, we will present selected examples highlighting the versatility and synthetic power of this transformation [2]. In its simplest form, the Nazarov employs a divinyl ketone as the starting material, a cross-conjugated compound which can be regarded as a 3′-oxa-[3]dendralene.

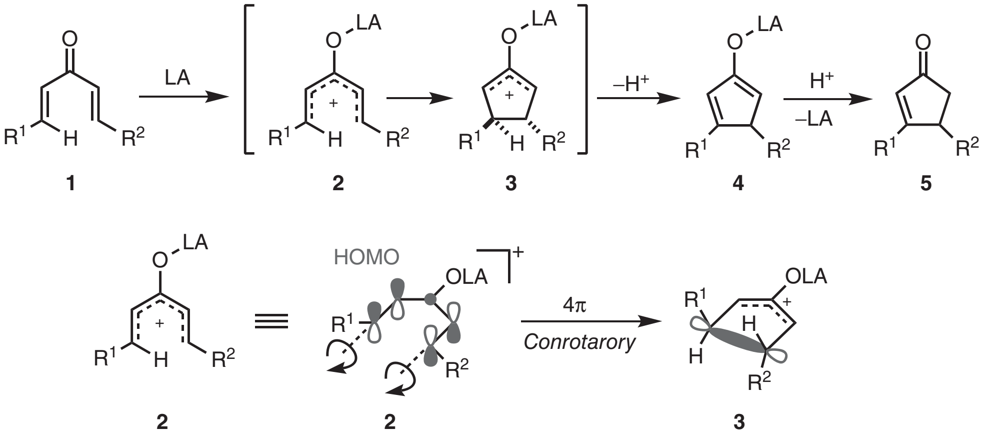
3.2

Mechanism

The Nazarov reaction is a conrotatory [4π]electrocyclization. Overall, the transformation involves conversion of a divinyl ketone **1** into a cyclopentenone **5** (Scheme 3.1). The reaction is triggered by complexation of the ketone with a Lewis acid (LA) or protonation, leading to the formation of the pentadienyl cation **2**. This intermediate undergoes cyclization to yield the oxyallyl cation **3**, which, after deprotonation, affords the cyclic dienol **4**, which tautomerizes to the final cyclopentenone **5**. Owing to the frequent occurrence of five-membered carbocycles in natural products, the usefulness of the Nazarov reaction in total synthesis becomes evident.

The high stereocontrol of the reaction is attributed to the conservation of orbital symmetry. According to frontier molecular orbital (FMO) theory, the

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.



Scheme 3.1 General scheme for the Nazarov reaction.

highest occupied molecular orbital (HOMO) of the pentadienyl cation **2** cyclizes by a conrotatory process to afford the corresponding oxyallyl cation **3**, carrying the substituents R^1 and R^2 in the *trans*-configuration, if the substrate has the *E*,*E*-geometry. Both the subsequent deprotonation and the ensuing tautomerization can be nonselective but, through modifications of the original method, these disadvantages have been overcome.

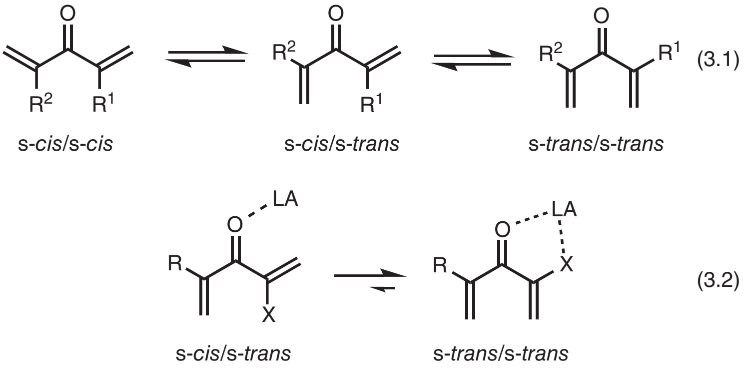
3.3
Substituent Effects

Synthetic applications of the Nazarov reaction require substrates other than an unsubstituted 1,4-pentadien-3-one. Indeed, substituents on the divinyl ketone moiety have a significant impact on reactivity. Steric and electronic effects of substituents play a major role regarding both substrate reactivity and the torquoselectivity (see Section 3.3.3) of the cyclization.

3.3.1
α-Substituents

3.3.1.1 Steric Hindrance

Steric hindrance at the α-position has a considerable impact on the preferred conformation of the 1,4-pentadien-3-one. While the dienone can adopt three in-plane conformations, only one of them is properly aligned for the Nazarov reaction to occur (Scheme 3.2, Eq. (3.1)). If R^1 and R^2 have small *A*-values, the divinyl ketone prefers the unreactive s-*cis*/s-*cis* conformer, it being the most stable by avoiding 1,3-diaxial interactions between the allyl groups. Conversely, α-substituents possessing large *A*-values favor the formation of the reactive s-*trans*/s-*trans* conformer. Thus, the increased prevalence of the reactive conformer

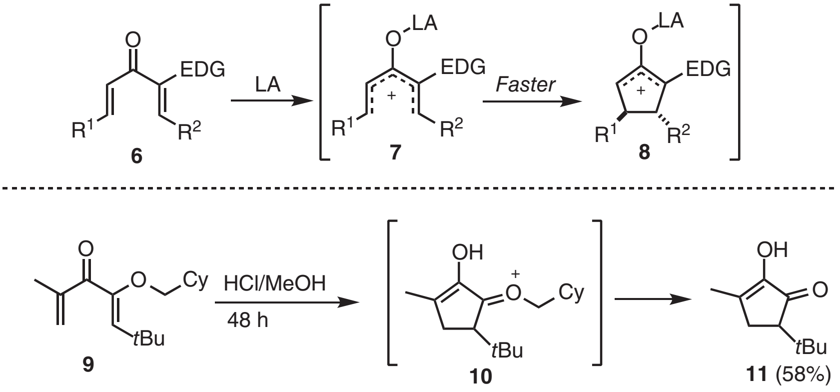


Scheme 3.2 Possible in-plane conformers of 1,4-pentadien-3-one.

in solution augments the reactivity of the compound. It was also found that, with a Lewis basic α-substituent X, certain LAs favor the s-*trans*/s-*trans* conformer by bidentate complexation (Scheme 3.2, Eq. (3.2)).

3.3.1.2 **Electron-Donating Substituents**

It was observed that enones **6**, possessing an electron-donating group (EDG) at the α-position, undergo facile Nazarov cyclization in the presence of an LA or Bronsted acid (Scheme 3.3). To rationalize this peculiar reactivity, one can suggest the EDG increases the electron density at the terminal carbon of the pentadienyl cation **7**. As a result, it lowers the activation barrier for the cyclization. In addition, the EDG stabilizes the oxyallyl cation intermediate **8** and leads to highly regioselective elimination.



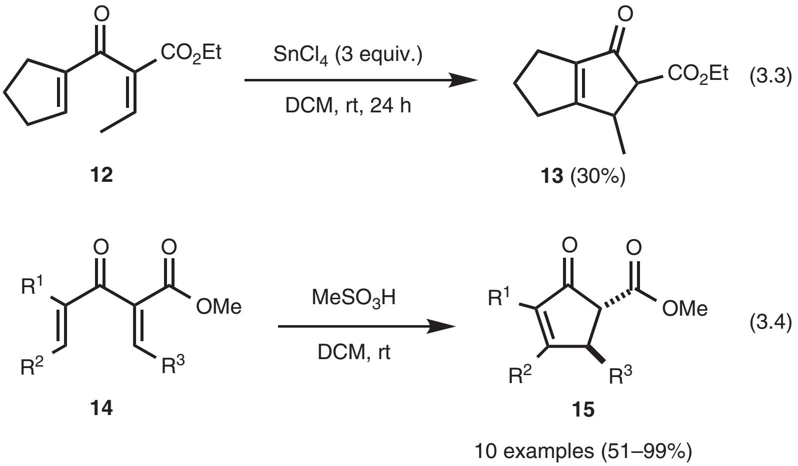
Scheme 3.3 Nazarov cyclization of divinyl ketones having an EDG at the α-position.

In 1994, the Kocieński group reported the formation of a cyclic by-product during an attempt to hydrolyze compound **9** using HCl in MeOH [3]. They isolated compound **11** in 58% yield, which is the result of a Nazarov cyclization.

The mechanism of the reaction can be explained by protonation of **9** followed by cationic cyclization to afford an intermediate of type **7**. After electrocyclization, intermediate **10** is converted by hydrolysis into enone **11**. The ease with which the cationic cyclization occurred (compared to direct enol ether hydrolysis) testifies to the rate-accelerating effect of the electron-rich α-substituent.

3.3.1.3 Electron-Withdrawing Substituents

A synthetically useful variant of the Nazarov reaction involves cyclization of dienones possessing α-electron-withdrawing groups (EWGs, Scheme 3.7). In 1981, Marino and Linderman [4] reported a trimethylsilyl triflate-mediated Nazarov cyclization of dienone **12** to give cyclopentanone **13** in 31% yield (Scheme 3.4, Eq. (3.3)). Although this initial result showed a low yield, Flynn and coworkers [5] subsequently demonstrated that the cyclization of dienones **14** to the corresponding cyclopentenones **15** can be achieved in high yield and diastereoselectivity using 1.1 M equiv. of $MeSO_3H$ or $Cu(OTf)_2$ (Scheme 3.4, Eq. (3.4)).



12

13 (30%)

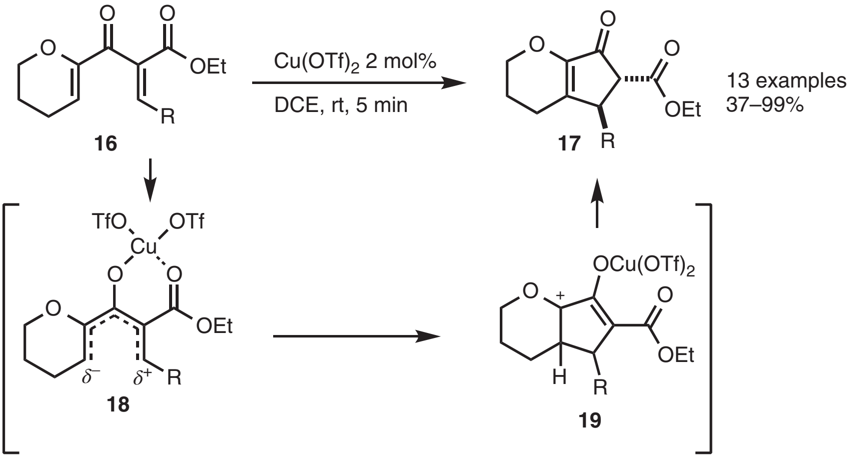
14

15

10 examples (51–99%)

Scheme 3.4 Nazarov cyclization of divinyl ketones having an EWG at the α-position.

Divinyl ketones containing both electron-donating and electron-withdrawing groups have also been studied and have been shown to display a distinct reactivity pattern. In 2003, Frontier and coworkers [6] reported the cyclization of these types of substrates using a polarizing effect to enhance reactivity (Scheme 3.5). The EDG increases the electronic density at one β-carbon and the electron-withdrawing group reduces it at the other, effectively creating a “vinyl nucleophile” and a “vinyl electrophile.” This activation allows the reaction to be promoted by a mild LA. Thus, the use of catalytic amounts of $Cu(OTf)_2$ promotes the cyclization of dienones such as **16** to give the corresponding cyclized product **17** via polarized intermediates **18** in very high yields. The polarization also provides a regioselective elimination step, which results from cation stabilization by the adjacent oxygen atom in the oxyallyl intermediate **19**.



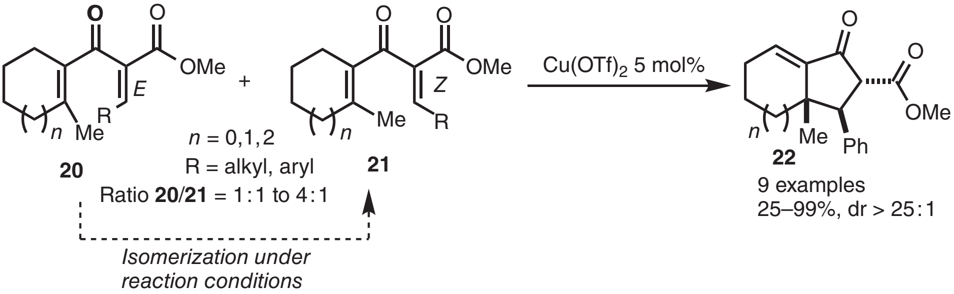
Scheme 3.5 Polarizing effect of EDG and EWG α-subtituents on dienones.

3.3.2
β-Substituents

3.3.2.1 Steric Hindrance

In general, steric hindrance at the β-carbon atom slows down the reaction. Tetra-substituted alkenes cyclize slower than tri-substituted ones, which react slower than di-substituted olefins. One could suggest that steric interactions diminish the stability of the s-*trans*/s-*trans* conformer. We should keep in mind, however, that EDG or EWG groups also have an influence on the ease by which a Nazarov reaction proceeds.

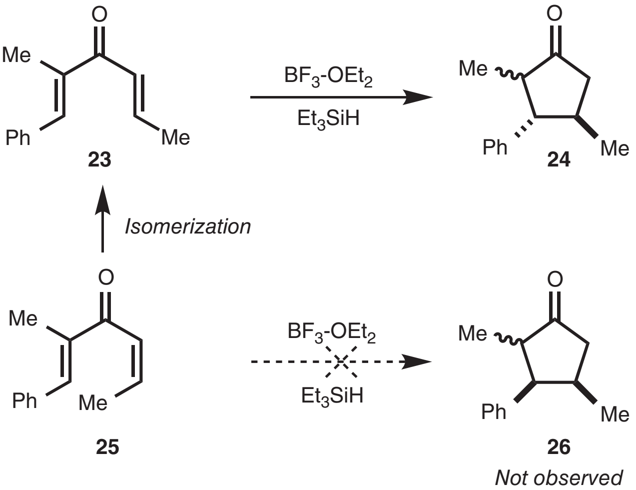
In 2008, Frontier and coworkers [7] reported a stereoselective Nazarov reaction using *inside* β-substituents (Scheme 3.6). Under standard conditions, the cyclization of *E*-configured dienones such as **20** should form the corresponding *anti*-product by a stereospecific conrotatory cyclization. Surprisingly, only *syn*-product **22** was observed. At first glance, one might suggest that the selectivity arose from a disrotatory cyclization; however, according to the rules of



Scheme 3.6 Nazarov reaction of sterically hindered divinyl ketones.

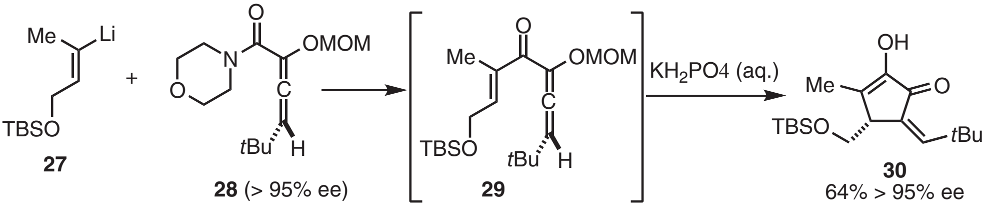
conservation of orbital symmetry, this process is forbidden. As a result, one can postulate that a rapid *E* to *Z* isomerization (**20** → **21**) takes place under the reaction conditions prior to the cyclization.

This isomerization process would not usually be detected, because the elimination step removes one of the stereocenters during most Nazarov reactions. Prior to Frontier's work, West and coworkers [8, 9] reported a reductive Nazarov cyclization. Thus, when both **23** and **25** were submitted to the reductive Nazarov conditions, only product **24** was observed (Scheme 3.7) supporting the isomerization/cyclization hypothesis.



Scheme 3.7 Isomerization of 25 to 23 under reductive Nazarov reaction conditions.

The presence of sp-hybridized β-carbons, in the form of allenes, minimizes steric hindrance, thereby increasing the s-*trans*/s-*trans* population and thus increasing reactivity [10]. Furthermore, the cyclization alleviates allenic strain, which further increases reactivity. In 1999, Tius and coworkers [11] reported a Nazarov cyclization of allenyl vinyl ketones (Scheme 3.8). The combination of substituted vinyllithium **27** with enantiomerically pure allene **28** produced dienone **29** *in situ*, which was converted into cyclopentenone **30** in 65% yield. The enantiomer ratio of the precursor allene (ee >95%) is transcribed without

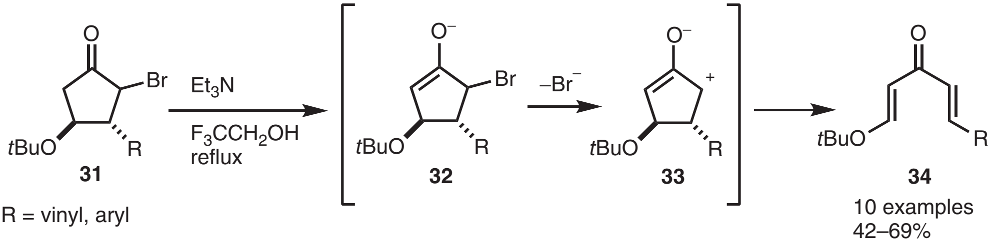


Scheme 3.8 Cyclization of allenyl vinyl ketones with complete transfer of chirality.

loss into the product. This is caused by a steric interaction between the *t*-butyl group and the newly forming bond, making the *t*-butyl substituent rotate away from the ring. One can see this transformation as an example of torquoselectivity, a phenomenon that will be discussed later in the chapter (see Section 3.3.3).

3.3.2.2 **Electron-Donating Substituents**

In comparison with their influence as α-substituents, one would expect an electron-donating β-substituent to stabilize the pentadienyl cation rather than the oxyallyl cation. Thus, the cyclization would be expected to be slower. Aside from retarding the rate of the cyclization, an electron-rich β-substituent facilitates – and sometimes favors – the retro-Nazarov process. In 2002, Harmata and Lee [12] reported a ring-opening reaction of α-bromo-pentanones **31**, to generate divinyl ketones **34** in 42–69% yield, with triethylamine in trifluoroethanol (Scheme 3.9). Under these conditions, enolate **32** would undergo a solvolytic debromination to form an oxyallyl-type intermediate **33**. The latter is poised to undergo a [4π]electrocyclic ring opening to produce a divinyl ketone, namely **34**. Note that the retro-Nazarov process still occurs in an orbital symmetry-controlled, conrotatory manner, allowing reliable prediction of alkene geometry in the final product.

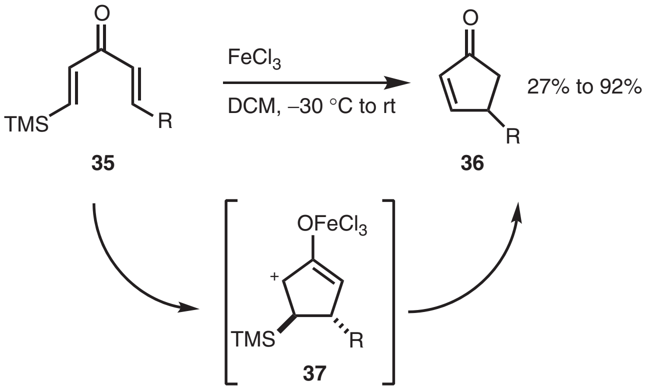


Scheme 3.9 Retro-Nazarov reaction driven by electron-donating β-substituents.

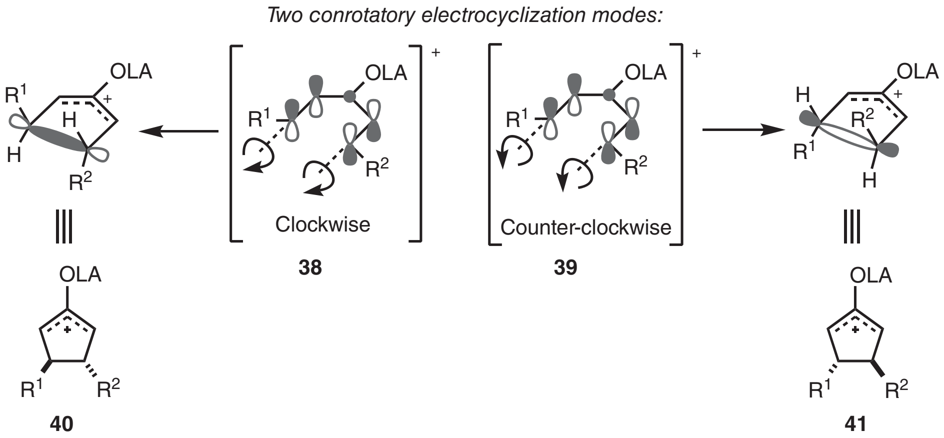
Along similar lines, a trimethylsilyl substituent at the β-position would, like other EDGs, be expected to promote a retro-Nazarov reaction. Trialkylsilyl groups, however, possess unique electron-donating properties, stabilizing a cation at the β-position by hyperconjugation. This β-effect was exploited by Denmark and coworkers [13–15], who reported a highly selective silicon-directed Nazarov reaction of **35** to cyclopentenone **36**. Following the activation of the divinyl ketone **35** with FeCl$_3$, the oxyallyl intermediate **37**, stabilized by the β-trimethylsilyl group, undergoes desilylation to produce the final cyclopentenone **36** (Scheme 3.10).

3.3.3
Torquoselectivity

Torquoselectivity is described as the preference of clockwise (**38**) or counterclockwise (**39**) rotation of substituents in an electrocyclization reaction, giving rise to



Scheme 3.10 Hyperconjugative effect of β-silyl subtituents on Nazarov cyclizations.

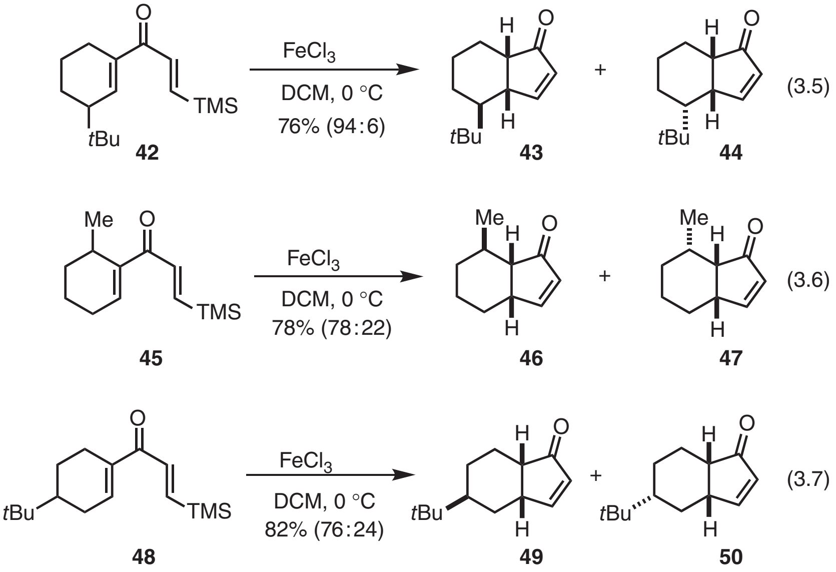


Scheme 3.11 Representation of torquoselectivity in Nazarov reactions.

different products, for example, **40** and **41**, respectively (Scheme 3.11). We next discuss the control elements that lead to torquoselectivity in Nazarov reactions.

3.3.3.1 Silyl Groups as Traceless Substituents

In the Nazarov reaction, silyl substituents are frequently employed as traceless intermediates to enable stereocontrol. Denmark and coworkers [15] demonstrated that a β-silyl substituent can be used in combination with a substituent on a six-membered ring to induce torquoselectivity (Scheme 3.12). The substituent is assumed to adopt an equatorial or pseudoequatorial orientation in the transition state of the reaction. There are two conrotatory pathways, each of which gives rise to one of two diastereomeric products. Owing to better orbital overlap, the new bond is created on the less-hindered face of the six-membered ring favoring one diastereomer over the other. The desilylation process removes all trace of the



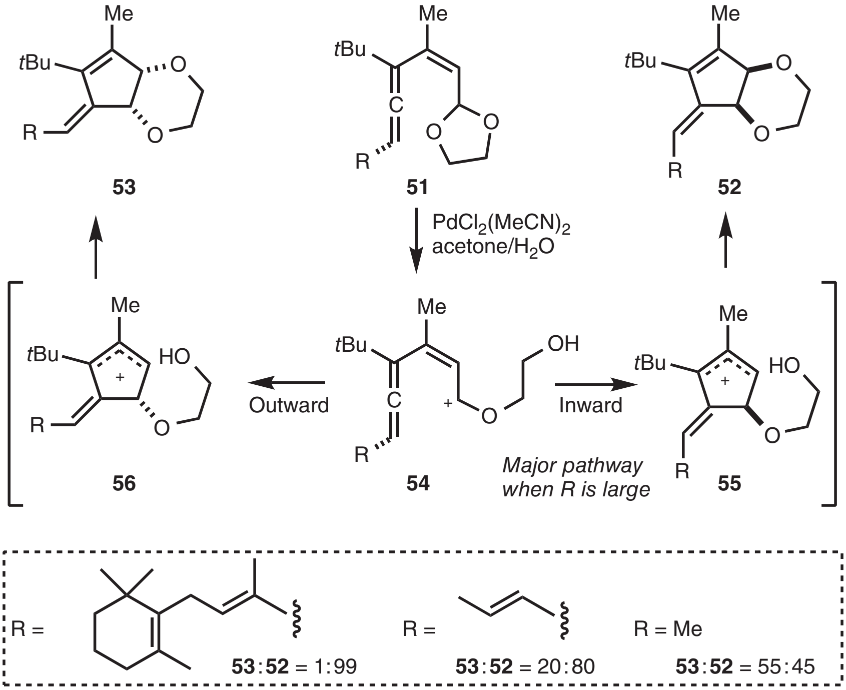
Scheme 3.12 Torquoselective induction via the use of silyl groups in the Nazarov reaction.

silyl group from the final product. On comparing the product ratio described in Eq. (3.5) versus Eqs. (3.6) and (3.7), one can realize that substitutions near the β-carbon have a greater effect on the torquoselectivity.

3.3.3.2 **Allenyl Alkenyl Ketones**

As mentioned in the previous section, the small steric interaction at the β-carbon along with the release of allenic strain favors the conversion of allenyl alkenyl ketones into the desired cyclopentenones. In the example depicted in Scheme 3.8, the axial chirality of the allene enforces the formation of one product, owing to the steric interactions between the newly forming bond and the *t*-butyl group at the allene moiety.

In 2000, de Lera reported the use of an allyl allenyl acetal **51** as a dienone substitute. Under acid conditions, this underwent a Nazarov-type cyclization to produce compounds **52** and **53** (Scheme 3.13) [16]. Here, the acid-mediated acetal ring opening generates the pentadienyl cation **54**, which can cyclize via an inward (**54**–**55**) or outward (**54**–**56**) rotation of the allenyl substituent to give the *Z* and *E* isomers **52** and **53**, respectively. In this system, the oxyallyl cation is trapped by an intramolecular nucleophilic addition to form a 1,4-dioxane ring. This case represents an example of a so-called interrupted Nazarov reaction, which will be discussed subsequently. A cursory inspection of the **52 : 53** ratio reveals that steric interactions are directly involved in the torquoselectivity. Larger R groups favor the formation of *Z* isomers, implying that R rotates inwardly during cyclization to avoid the *tert*-butyl substituent.

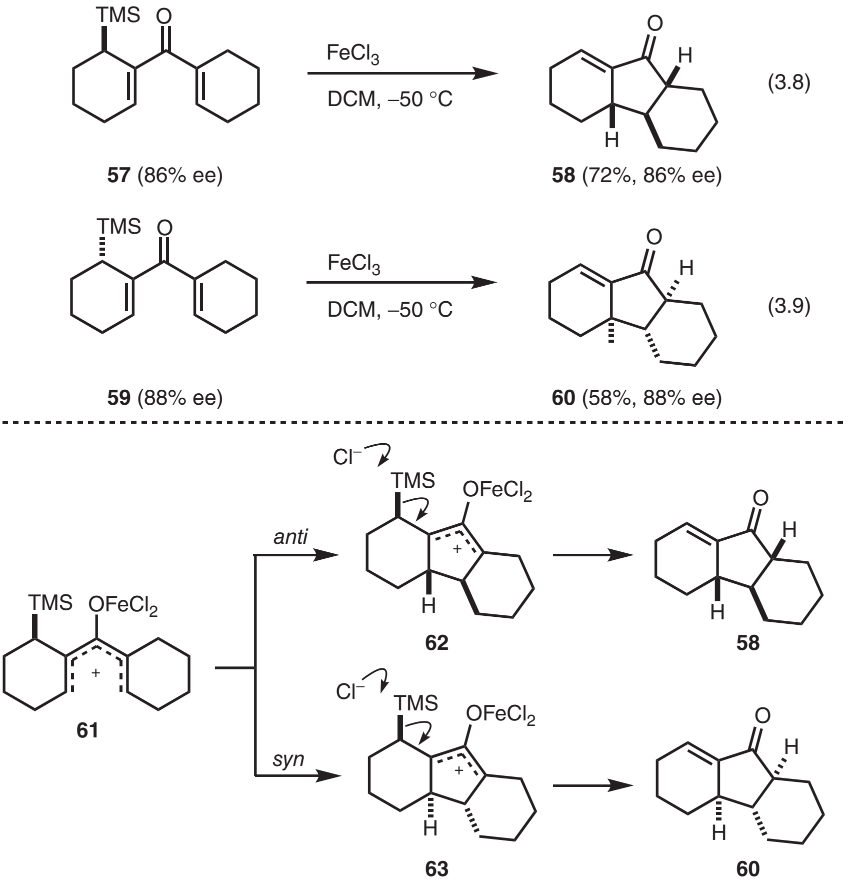


Scheme 3.13 Torquoselectivity in allenyl vinyl ketones during the Nazarov reaction.

3.3.3.3 Chirality Transfer

Torquoselectivity can be induced by a stereocenter located in the precursor, even if it is lost *en route* to the final product. Denmark and coworkers [17] reported a clever utilization of a "traceless functional group" to produce enantiomerically enriched products in Nazarov reactions (Scheme 3.14). The exposure of enantiomerically enriched dienone **57** to $FeCl_3$ gave the corresponding cyclized product **58** in 72% yield with complete transfer of enantiopurity (Eq. (3.8)). As shown in Eqs. (3.8) and (3.9) of Scheme 3.14, both enantiomers are accessible under the same conditions. To rationalize the high transfer of enantiopurity, it has been suggested that, upon the cyclization of **61**, two diastereomeric intermediates **62** and **63** can be generated via *anti*-conrotatory and *syn*-conrotatory pathways, respectively. A close examination of the *anti* and *syn* processes reveals that in the *anti* pathway, the TMS Trimethylsilyl group has a continuous overlap with the cationic system. Thus, stereoelectronic effects account for the preferential formation of **58** over **60**.

A similar type of chirality transfer was exploited by Tius in the total synthesis of roseophilin (**69**) (Scheme 3.15) [18]. A key intermediate in the synthetic pathway consisted of a substituted cyclopentanone, constructed via a Nazarov-type cyclization. The asymmetric cyclopentannulation reaction was initiated by generating the cyclopentenyl intermediate *in situ* using the lithioallene **64** and the amide **65**. The chiral substituent on the delocalized carbocation **66** induced

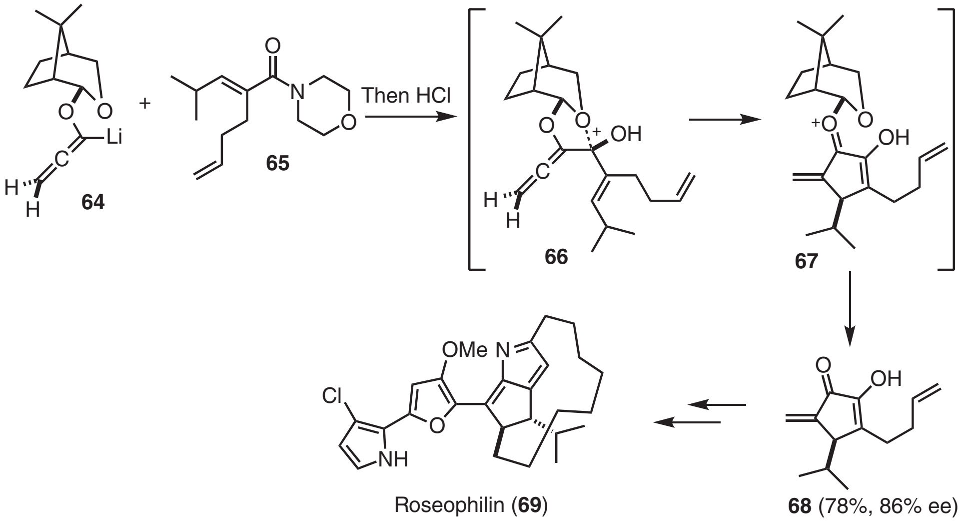


Scheme 3.14 Chirality transfer using traceless functional groups in the Nazarov reaction.

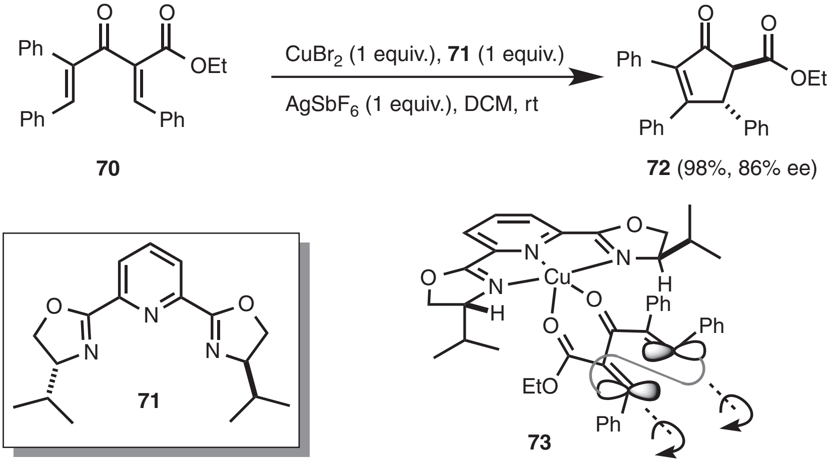
a torquoselective cyclization to **67** by blocking the rotation of the isopropyl toward the back of the newly forming ring, yielding the desired cyclopentenone **68** in 78% yield and 86% ee. As shown on intermediate **66**, the axial lone pair electrons of the pyran oxygen are believed to have a stabilizing effect on the cation derived from the allenyl alkenyl ketone. This interaction reduces conformational mobility, thereby contributing to the stereoselectivity of the reaction.

3.3.3.4 Catalysis of the Nazarov Reaction

Another way to induce torquoselectivity involves the use of chiral catalysts. In 2003, Aggarwal and Belfield disclosed the first asymmetric Nazarov reaction catalyzed by a chiral LA complex (Scheme 3.16) [19]. It was found that a complex formed between copper bromide and tridentate ligand **71** was capable of controlling the conrotation of the cyclization of precursor **70** in good enantioselectivity and yield. With substrate attached, the resulting complex **73**



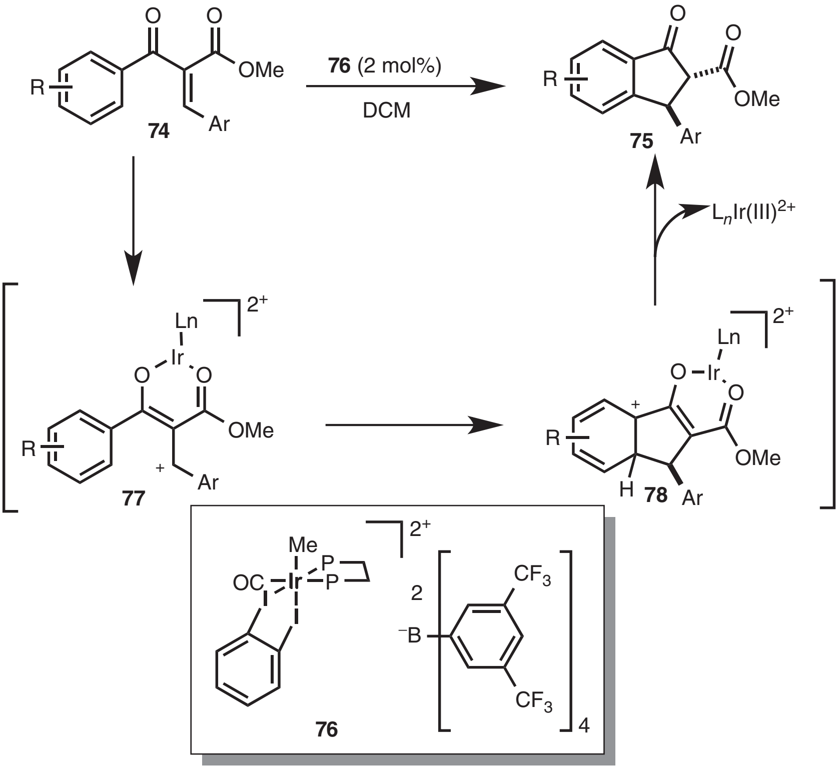
Scheme 3.15 Another example of chirality transfer using traceless functional groups used as a key step in the total synthesis of roseophilin.



Scheme 3.16 Enantioselective Nazarov cyclization catalyzed by chiral copper complex.

adopts a square-based pyramidal geometry in which the alkenes are pushed away from the diisopropyl group of the ligand. As a result, the conrotation proceeds in a clockwise manner to give **72**. Although a noteworthy advance in chiral control of Nazarov reactions, a β-ketoester on the cyclization precursor **70** is required to achieve good selectivity and the reaction needs a stoichiometric amount of the copper complexes; otherwise, lower yields are observed.

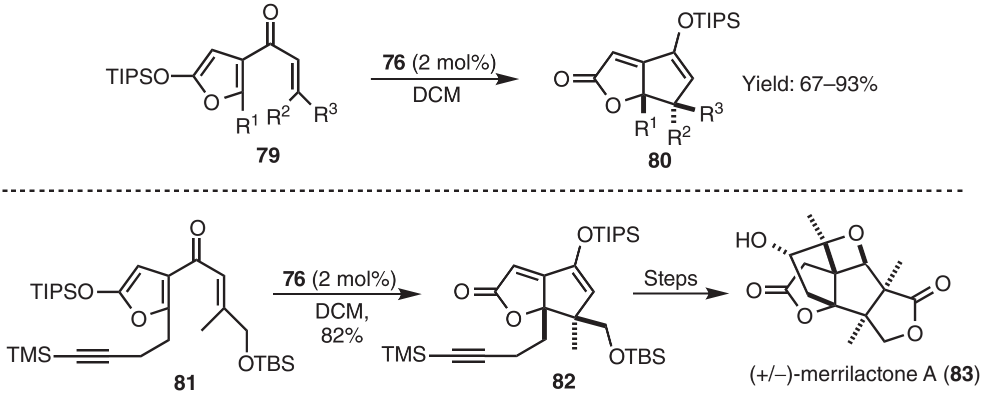
In 2004, the first example of a Nazarov cyclization catalyzed by [IrMe(CO)(dppe)-(DIB)](BARF)$_2$] (**76**) was reported by Frontier and Eisenberg (Scheme 3.17) (dppe = bis(diphenylphosphino)ethane, DIB = *o*-diiodobenzene, and



Scheme 3.17 Enantioselective Nazarov cyclization catalyzed by cationic Iridium complex.

BARF = $^{-}B(3{,}5\text{-}C_6H_3(CF_3)_2)_4$ [20]. A reasonable mechanism would comprise the complexation of the iridium catalyst **76** to the beta-ketoester **74** to generate the oxyallyl cation **77**. This sequence is followed by a Nazarov cyclization to give **78**, with subsequent aromatization and enolate protonation leading to the final product **75**. When compared with the more commonly used LA $Cu(OTf)_2$ over a range of substrates, iridium catalyst **76** possessed better turnover frequency (TOF) and provided higher yields. This enhanced reactivity was attributed to two factors: the enhanced electrophilic character of the metal and the lability of the DIB ligand, which provides an easily accessible *cis* binding site for a 1,3-dicarbonyl substrate.

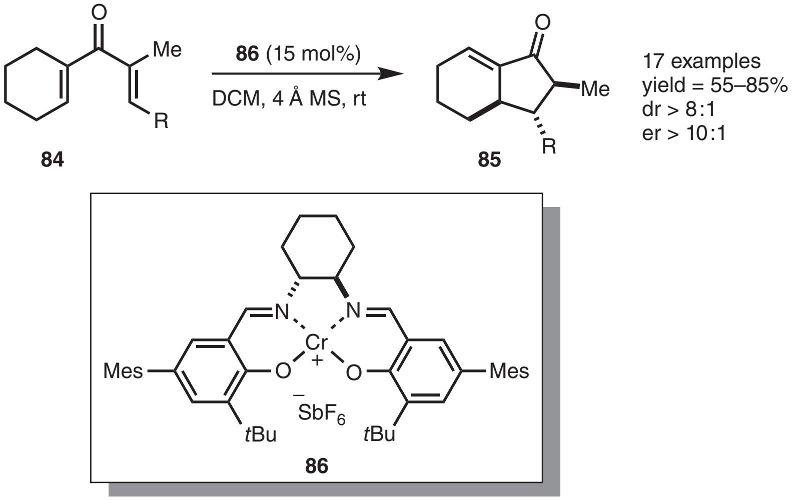
A detailed investigation was later reported by Frontier in which a conrotatory electrocyclization of silyloxyfurans **79** was catalyzed by the same Ir(III) complex (**76**) to produce lactones **80** in good yield. This work culminated in the total synthesis of racemic merrilactone A (**83**) (Scheme 3.18) [21]. Generally, only one diastereoisomer was isolated from the Nazarov reaction. These cyclizations also demonstrated complete transfer of the trialkylsilyl group from the silyloxyfuran to the ketone oxygen. It had been previously demonstrated that trialkylsilyl species can catalyze the Nazarov reaction; further experiments showed that although



Scheme 3.18 Iridium catalyzed Nazarov cyclization in the synthesis of (+/–)-merrilactone A.

TIPSOTf (Triisopropylsilyl trifluoromethanesulfonate) could not promote the reaction effectively, Triisopropylsilyl (TIPS$^+$)BARF$^-$ catalyzed the cyclization. This result reveals that, in this particular reaction, the triisopropylsilylium cation is most likely involved in the activation of the substrate in conjunction with the Ir(III) catalyst.

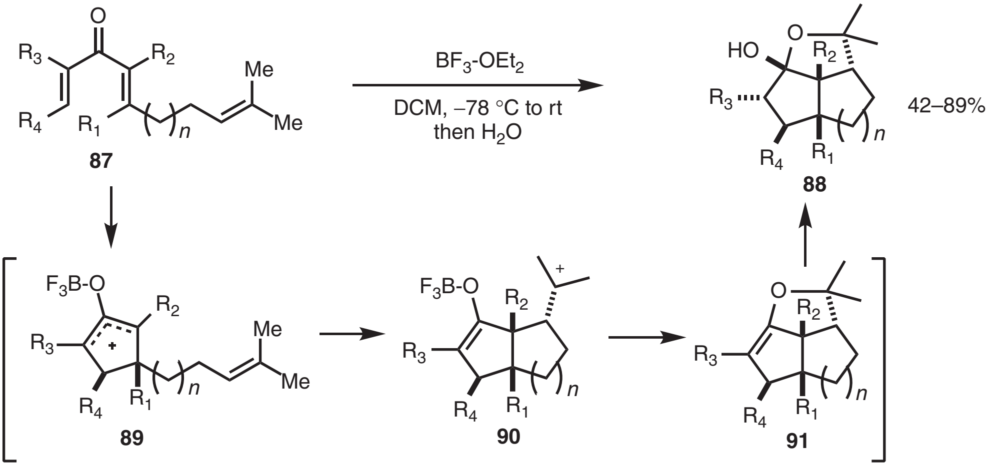
Almost 10 years after Aggarwal's report, Rawal and coworkers [22] reported the use of chiral chromium–salen complexes to catalyze enantioselective Nazarov cyclizations. While other asymmetric Nazarov reactions had been reported since Aggarwal's publication, the chromium–salen complex **86** was the first to catalytically perform the cyclization of unactivated divinyl ketones **84** to give cyclic ketones **85** in high diastereoselectivity and enantioselectivity (Scheme 3.19).



Scheme 3.19 Chromium-salen catalyzed enantioselective Nazarov cyclization.

3.4
Interrupted Nazarov Reactions

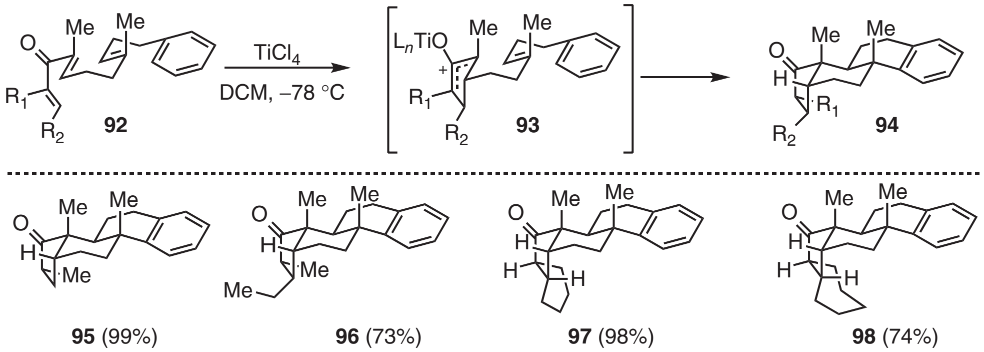
In 1998, the first deliberate attempt to trap the oxyallyl cation with a nucleophile during a thermal Nazarov reaction was reported by West and coworkers [23].Coining the term *interrupted Nazarov reaction*, they described the interception of the oxyallyl intermediate of a Nazarov reaction by a tethered alkene (Scheme 3.20). Upon submission of divinyl ketones **87** to the LA, a conrotatory ring closure generates the oxyallyl cation intermediate **89**. The alkene moiety adds selectively to the oxyallyl cation intermediate to form bicycle **90**. The stabilized tertiary carbocation is then trapped by the enolate oxygen to give intermediate **91**, which, under acidic aqueous conditions, is converted to the final hemiketal product **88**. The reaction provides an efficient and stereoselective method to prepare tricyclic compounds **88** in yields ranging from 42 to 89% [24].



Scheme 3.20 Stereoselective interrupted Nazarov reaction and trapping of the oxyallyl cation intermediate

3.4.1
Cascade Cyclizations

After observing the trapping of the oxyallyl intermediate with a tethered olefin to generate a new ring and new carbocationic intermediate (**90**, Scheme 3.20), West and coworkers [25] imagined an extension to allow the formation of another ring, and a third C–C bond. Several trienes containing a tethered aryl group were prepared and various acids were screened. After significant experimentation, $TiCl_4$ was found to be the best LA to promote the polycyclization in excellent yield and stereocontrol (Scheme 3.21). Upon addition of $TiCl_4$, dienone **92** is converted to the oxyallyl cation intermediate **93**, which undergoes a double cationic cyclization to generate tetracycle **94**. The process proved to be both of

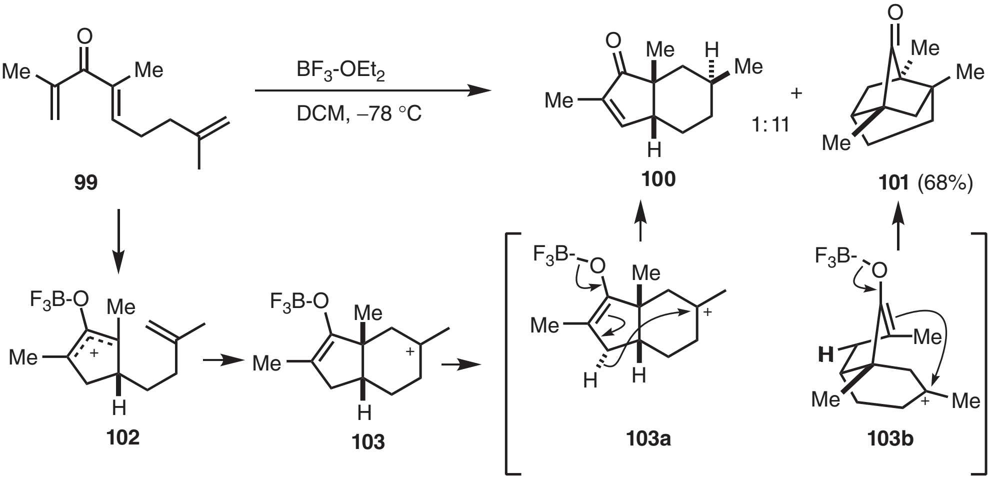


Scheme 3.21 Diastereoselective cationic cyclization cascade.

reasonable scope (generating products **95–98**) and highly diastereoselective, as only one stereoisomeric product was observed in each case.

3.4.2
[3+2]- and [4+3]Cycloadditions of the Oxyallyl Cation

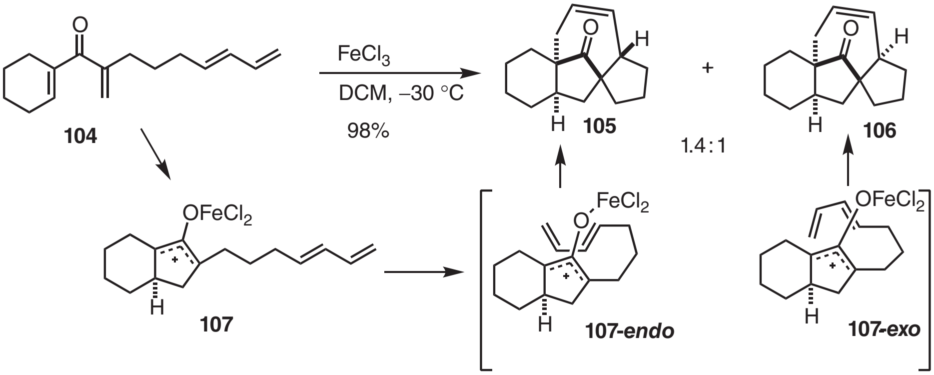
Addition of the oxyallyl intermediate using a tethered alkene can produce new C–C bonds with ease. When short tethers are used, the formation of a second C–C bond can be seen by way of a formal [3+2]cycloaddition onto the oxyallyl cation. West and coworkers [26] were the first to demonstrate this behavior (Scheme 3.22). The Nazarov cyclization of substrate **99** generates the first ring **102** via the standard conrotatory cyclization. The intermediate **102** is poised to undergo an *endo*-mode cationic cyclization to produce bicyclic compound **103**. At this point,



Scheme 3.22 Formal intramolecular [3+2] cycloaddition of the oxyallyl cation intermediate.

two competitive intramolecular processes can be envisaged. A close-proximity hydride shift (**103a**) affords **100** as the minor product, whereas an intramolecular enolate-carbocation trapping **103b** gives the bridgehead ketone **101** (the product of a stepwise, formal [3+2]cycloaddition) in 68% yield.

The trapping of the oxyallyl cation by the alkene in a formal [3+2] fashion is not the only cycloaddition possible by this method. The oxyallyl cation, in the presence of a 1,3-butadiene, undergoes a [4+3]cycloaddition. West and coworkers [27] reported cases of cascade-interrupted Nazarov/intramolecular [4+3]cycloadditions in 1999, a representative example of which is depicted in Scheme 3.23. Thus, tetraenone **104** was subjected to $FeCl_3$ at low temperature to produce a mixture of stereoisomeric tetracyclic products **105** and **106** in 98% yield. The initially formed oxyallyl cation **107** generates these two diastereomeric products by way of putative *endo* and *exo*-mode cycloaddition transition states, **107-*endo*** and **107-*exo***, respectively.

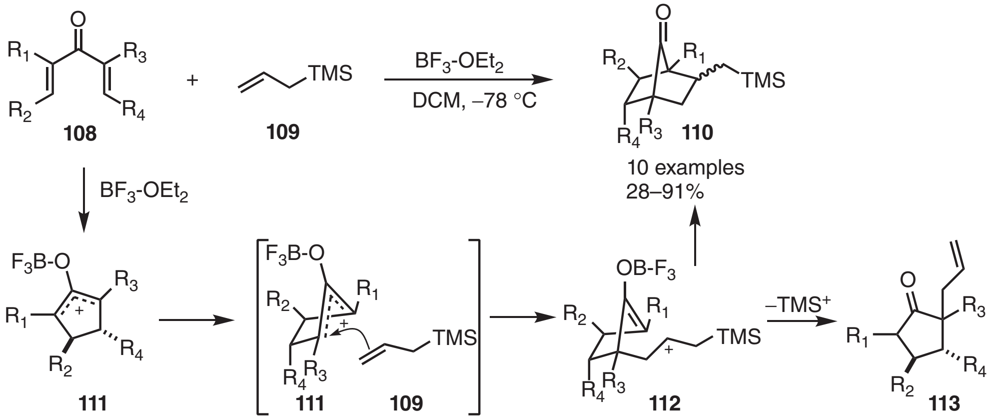


Scheme 3.23 Intramolecular [4+3] cycloaddition of the oxyallyl cation intermediate.

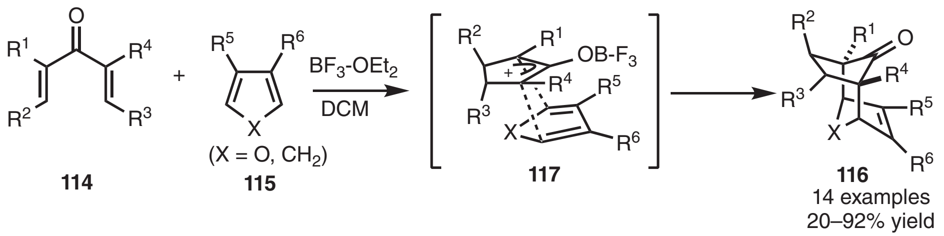
3.4.3
Intermolecular Trapping of the Nazarov Intermediate

West and coworkers [28] reported the efficient formation of bicyclic bridgehead ketones **110** via the electrocyclization/formal intermolecular [3+2]cycloaddition of dienones **108** with allyltrimethylsilane **109** (Scheme 3.24). LA-mediated electrocyclization of **108** provides oxyallyl intermediate **111**, which reacts with allylsilane **109** to give intermediate **112**. At this point, ring closure provides the bridgehead ketone **110**. In some cases, a minor product **113** was observed, the result of the elimination of the TMS group from the same silicon-stabilized carbocation **112**.

The same group showed that certain cyclic and acyclic 1,3-dienes react with the oxyallyl cation via an intermolecular [4+3]cycloaddition (Scheme 3.25) [29]. In this manner, bicyclo[4.2.1]nonenones **116** can be obtained in a single operation



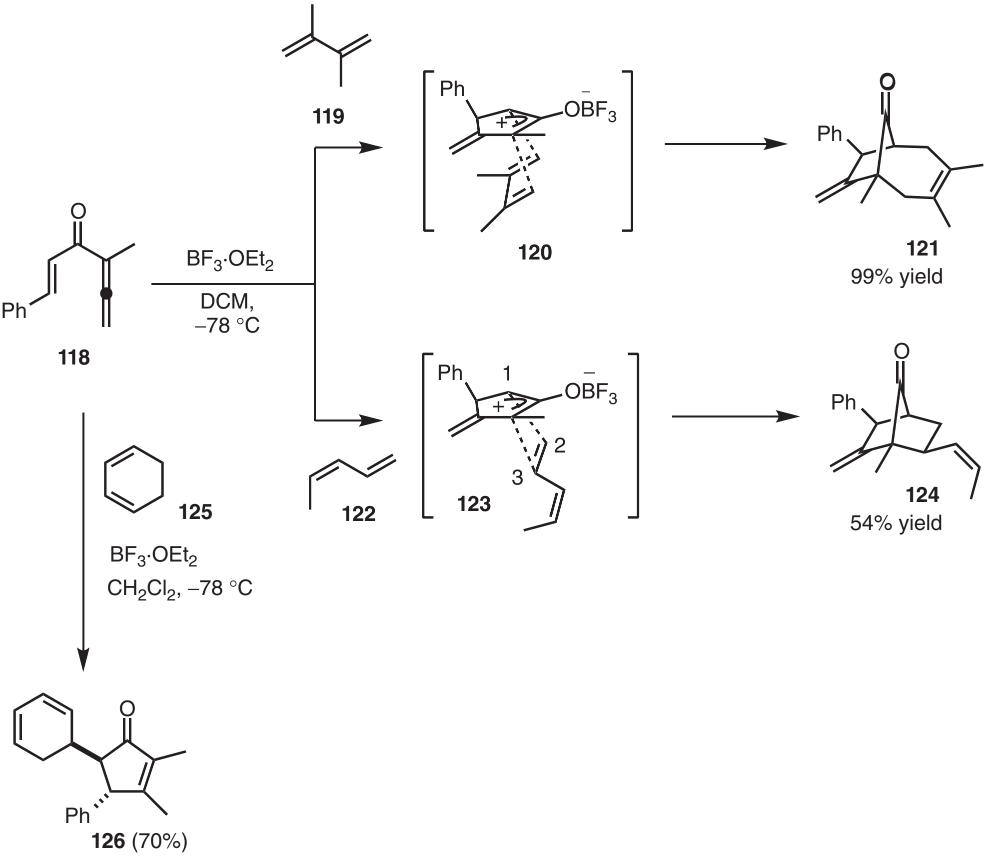
Scheme 3.24 Intermolecular [3+2] cycloaddition of the oxyallyl cation intermediate.



Scheme 3.25 Intermolecular [4+3] cycloaddition of the oxyallyl cation intermediate.

from dienones **114** and dienes **115**. The high diastereoselectivity of the reaction can be rationalized by invoking a compact *endo*-transition state between the diene and oxyallyl cation (**117**).

In 2010, Burnell and Marx [30] reported the deployment of allenyl vinyl ketones (such as **118**) in related interrupted Nazarov reactions. Highly stereoselective intermolecular [3+2]- and [4+3]cycloadditions with 1,3-butadienes were induced with $BF_3{\cdot}OEt_2$ (Scheme 3.26). A range of substituted 1,3-butadienes carrying different numbers of methyl substituents at different positions were examined, and some showed high selectivity for either the [3+2]- or [4+3]-mode of reaction. Representative examples are 2,3-dimethyl-1,3-butadiene **119**, which generates [4+3] adduct **121** exclusively, and 1*Z*-methyl-1,3-butadiene **122**, which forms the [3+2] adduct **124** only. In the former case, steric strain presumably disfavors the [3+2] pathway relative to the [4+3] transition state **120**. The exclusive formation of the [3+2]cycloaddition product in the latter case can be rationalized on the basis that the s-*cis* conformation of the 1,3-butadiene, which is required for a concerted [4+3]cycloaddition, is not accessible. The orientational regioselectivity of the latter case can be rationalized by invoking an asynchronous transition state **123** with an advanced (i.e., shorter) bond between C1 and C2, which would cause partial cationic character to develop at C3, which in turn would benefit from substituted allylic delocalization.



Scheme 3.26 Intermolecular trapping of the oxyallyl cation intermediate.

A noteworthy observation is the lack of [4+3] or [3+2] cycloaddition products when using cyclic dienes to trap the oxyallyl intermediate. Indeed, the use of furan or 1,3-cyclohexadiene **125** gave only alkylation product **126**. One can assume that significant steric hindrance between these dienes and the oxyallyl cation in the [4+3]- and [3+2]cycloaddition transition states would prevent these transformations from occurring and favor the Friedel–Crafts alkylation process.

Since Nazarov's initial discovery over 70 years ago, the reaction that bears this discoverer's name has enjoyed sustained interest by the synthetic community. The originally reported reaction has seen significant development from its original version. Through the efforts of many contributing researchers, the Nazarov reaction has become a method of choice when synthesizing 2-cyclopentanones with multiple contiguous stereocenters. As illustrated in this chapter, various LAs of increasing sophistication and complexity can efficiently catalyze the Nazarov reaction with increasing levels of control. The deployment of the Nazarov reaction and its "interrupted" versions as the key step in a number of recent syntheses of complex polycyclic natural products is a testament to their reliability, efficiency, and selectivity. The recent development of new, more efficient catalysts for the enantioselective Nazarov reaction opens uncharted territories in organic synthesis. Future applications will no doubt continue to refine and generalize the enantioselective catalysis of this important transformation, thereby facilitating its involvement in the efficient and step economical assembly of diterpenes and related natural products.

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4

[*n*]Radialenes

Gerhard Maas

4.1

Introduction

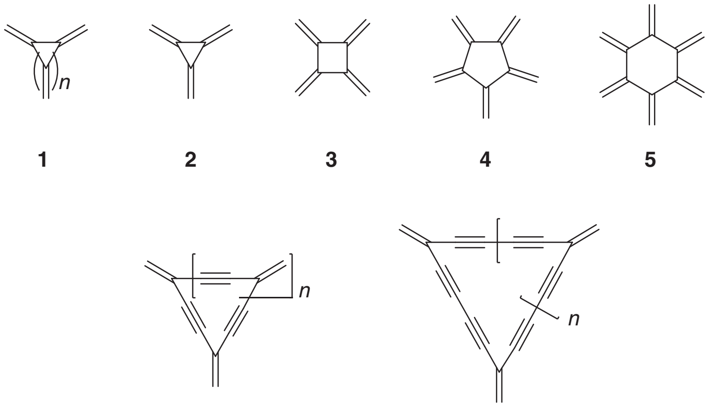
Radialenes are carbocyclic compounds consisting of sp^2-hybridized ring carbon atoms, which carry as many exocyclic double bonds as possible. The general term for these ring systems is [*n*]radialenes with $n \geq 3$, where n stands for both the number of ring atoms and the number of exocyclic double bonds. The general constitutional formula for the parent systems is $C_n(CH_2)_n$ (**1**) or C_nH_n. The systems with $n = 3$, 4, 5, 6 are thus called [3]-, [4]-, [5]-, and [6] radialenes (**2**–**5**) (Figure 4.1). The radialenes are cross-conjugated polyolefinic compounds. From the structural viewpoint, they are formally related to the acyclic [*n*]dendralenes (Chapter 1) by bond formation between the two penultimate sp^2-carbon atoms of the dendralene chain.

The first radialene to be reported was all-(*E*)-7,8,9,10,11,12-hexamethyl[6] radialene [1]. The first syntheses of the parent systems [3]radialene **2** [2], [4]radialene **3** [3], and [6]radialene **5** [4–6] were reported in 1965, 1962 and 1977/1978, respectively, yet unsubstituted [5]radialene **4** (see below, however: note added in proof) as well as monocyclic [*n*]radialenes with $n > 6$ are still unknown. On the other hand, significant research activities have been devoted recently to the so-called expanded radialenes, which have general structural formulae such as **6** and **7** ($n \geq 1$), with ethyne, butadiyne, or benzene spacers being inserted between the corners of the parent [*n*]radialenes; they are covered in Chapter 9 of this book.

The first decades of radialene research were covered in two comprehensive reviews by Hopf and Maas [7, 8] and again in more condensed form in Hopf's book *Classics in Hydrocarbon Chemistry* [9]. A systematic overview on synthetic methods for the preparation of radialenes was compiled by M. Iyoda in 2008 [10].

Radialenes have been and are still objects of study for a variety of reasons. Their particular structures, the high chemical reactivity of the parent systems, and the quest for derivatives with specific functionalization have spurred the interest of synthetically oriented chemists. Molecular properties such as structure, bonding, thermodynamics, and electronic properties have attracted

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.



1 **2** **3** **4** **5**

6 **7**

Figure 4.1 Parent [*n*]radialenes **1**–**5** and expanded radialenes **6** and **7**.

researchers in the fields of structural, physical organic, theoretical, and materials chemistry. Appropriately functionalized radialenes have been studied with the aim of identifying applications based on their electronic and electrochemical properties. Certain charge-transfer complexes of radialenes have also been investigated as potential organic magnets. For these aspects as well as detailed structural and spectroscopic data, readers are advised to consult the existing reviews [7, 8].

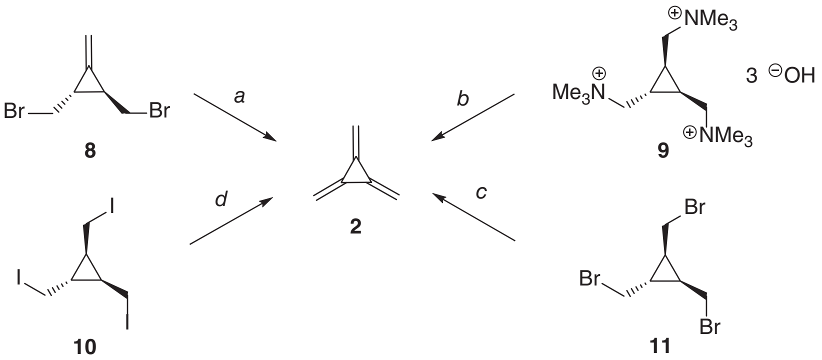
4.2
Syntheses and Reactivity

The following general strategies have been applied with success to the synthesis of radialenes with different ring size: (i) introduction of the exocyclic double bonds by elimination or condensation reactions of appropriately functionalized carbocyclic precursors; (ii) cyclooligomerization of vinylidene building blocks, typically provided as the corresponding carbenoids; and (iii) thermal or transition-metal-mediated cycloaddition reactions of [*n*]cumulenes. Quite often, specialized experimental procedures were required to achieve these transformations, either because the targeted radialenes were difficult to handle (such as the parent systems) or because of chemo- or regioselectivity issues (such as in carbenoid- or cumulene-based reactions). Although several of the syntheses deliver the radialenes with well-defined stereoselectivity at the exocyclic double bonds, it appears difficult at present to control the diastereoselectivity at will. This may be a major reason why many radialene derivatives carry symmetrically disubstituted exocyclic carbon atoms.

The majority of the radialenes synthesized so far have been the ultimate synthetic targets and these have hardly been used for subsequent synthetic transformations. In fact, relatively few reactivity studies on radialenes have been published; the most important results are presented in the following sections. Perhaps the most thoroughly investigated reactivity aspect is the redox chemistry of appropriately substituted electron-rich or electron-deficient radialenes. Another recent aspect to be mentioned is the use of certain substituted radialenes as tectons in supramolecular coordination chemistry.

4.2.1
[3]Radialenes

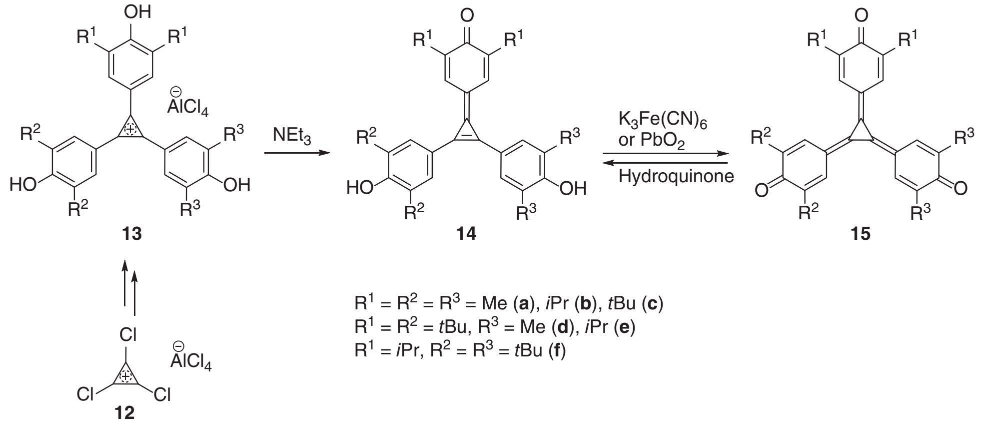
The parent [3]radialene (**2**) has been obtained by 1,2- and 1,4-elimination reactions from cyclopropane derivatives **8** [2, 11], **9** [12], **10** [12], and **11** [13] in very low to moderate yields (Scheme 4.1). Later, a practical large-scale synthesis of triethyl cyclopropane-1α,2α,3β-tricarboxylate [14] has facilitated the synthesis of **2** via 1,2,3-tris(iodomethyl)cyclopropane (**10**). All transformations were performed as gas-phase reactions, and the radialene was condensed in a cold trap. Liquid **2** is stable at −78 °C for some days, but it easily polymerizes under other conditions (in the presence of oxygen, in CCl_4 solution at 0 °C, by bringing the vapor to room temperature).



(*a*) KOH, 150 °C [2], 47% (KOH, CaO, 155 °C, 57% [11]; (*b*) 160–170 °C, 4.5 Torr, 1.5%; (*c*) KOH, 140 °C, ~20%; (*d*) powdered KOH, CaO, 150 °C, 1 Torr (no yield given).

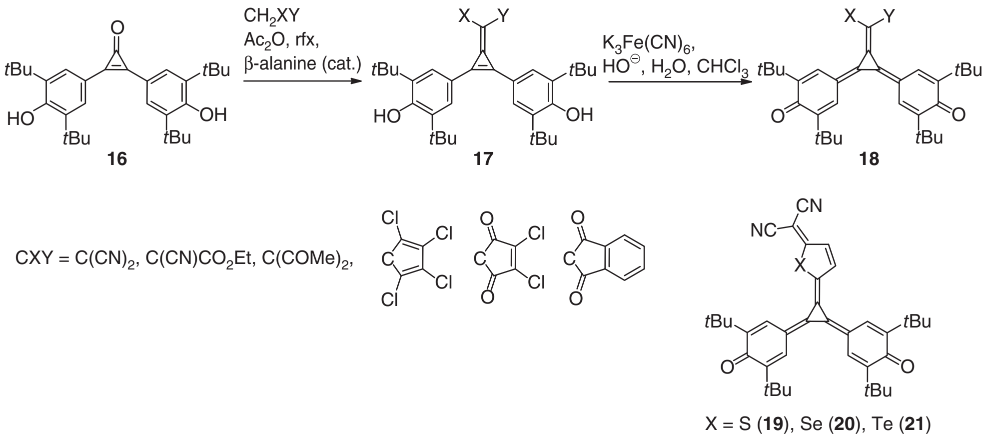
Scheme 4.1

A wide range of substituted [3]radialenes are accessible from perchlorinated cyclopropenylium ion, cyclopropene, and cyclopropane-active methylene compounds through nucleophilic substitution/deprotonation/oxidation sequences. This strategy was pioneered by West and coworkers [15] who used it to obtain an array of [3]radialenes with *p*-quinoid substituents. As the example given in Scheme 4.2 shows, tris(4-hydroxyphenyl)cyclopropenylium salts **13** were obtained from trichlorocyclopropenylium tetrachloroaluminate (**12**) by (eventually stepwise) threefold addition/elimination reactions and were converted into monoquinoid triafulvenes **14** by deprotonation. An oxidation step, which is easily reversible, then furnished the blue-purple trisquinoid [3]radialenes **15** [15]. The (thermal) stability of radialenes **15** depends on the steric demand of the substituents R^1 and R^2. Thus, **15a** could be characterized in solution only, while **15b** and **15c** rapidly decomposed when heated in air at 133 and 280 °C, respectively, thereby being partly reduced to their bisphenolic precursors **14**.



Scheme 4.2

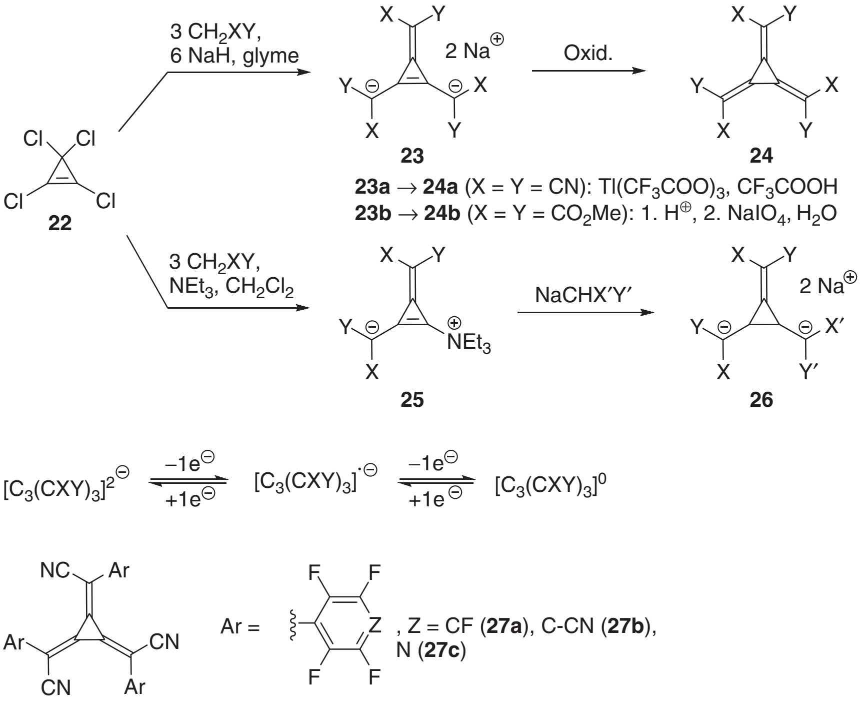
Similar to the reaction sequence shown in Scheme 4.2, 1,2-bis(3,5-di-*tert*-butyl-4-hydroxyphenyl)cyclopropenone (**16**) was converted into [3]radialenes **18** by a Knoevenagel-type condensation followed by oxidation of the triafulvene intermediates **17** (Scheme 4.3) [16]. Other similar compounds, such as the 2-(dicyanomethylene)-substituted 2,5-thienoquino-, 2,5-selenoquino-,



Scheme 4.3

and 2,5-telluroquino-derivatives **19** [17], **20** [18], and **21** [19] were prepared accordingly.

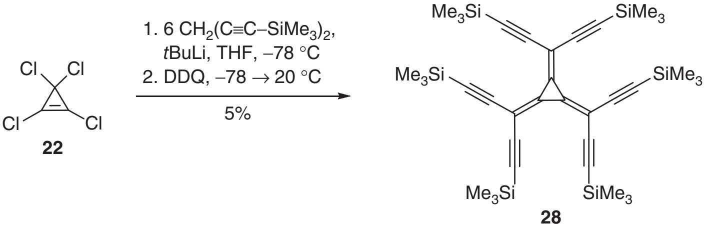
Tetrachlorocyclopropene (**22**) and a variety of active methylene compounds are building blocks for hexasubstituted [3]radialenes, as was first reported by Fukunaga *et al.* Thus, **22** reacted with malononitrile, dimethyl malonate, and methyl cyanoacetate in glyme in the presence of an excess of NaH to give triafulvene dianion salts **23**, which were isolated as tetrabutylammonium salts (Scheme 4.4) [20]. With triethylamine instead of NaH, the triafulvene betaine **25** was formed, where the NEt_3 group could be replaced by another carbanion to give triafulvene dianions **26** containing two kinds of exocyclic CXY moieties [20]. Polarographic studies showed that, in general, two reversible one-electron oxidations via a radical anion intermediate connect the dianions with the neutral [3]radialene. In fact, oxidation of the disodium salt of **23a** with potassium persulfate in water furnished crystalline radical anion salt $K^+[C_6(CN)_6]^{\bullet -}$, but Tl(III) oxidation of **23a** afforded hexacyano[3]radialene (**24a**). Oxidation of the conjugate diacid of **23b** with sodium periodate in water gave hexa(methoxycarbonyl)[3]radialene (**24b**) [21]. Bright yellow radialene **24a** turned brown in contact with air and blue in contact with many solvents and was readily reduced to the radical anion and the dianion on treatment with KBr and NaI, respectively. In contrast, **24b** was obtained as stable yellow crystals; it is also readily reduced to the dianion with LiI, but the radical anion is much less stable than that derived from **24a**.



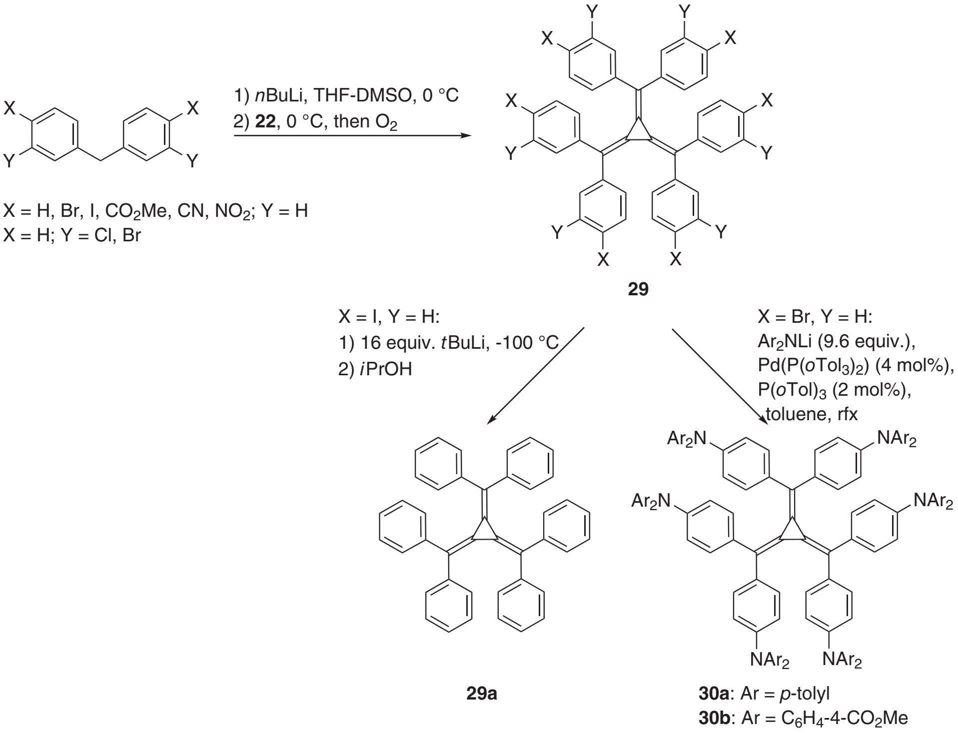
Scheme 4.4

According to a patent, a similar synthetic sequence gives access to [3]radialenes such as **27**, which, besides nitrile groups, carry highly fluorinated phenyl and pyridyl rings as strong electron-accepting substituents; based on the redox behavior according to the general equation shown in Scheme 4.4, they were considered as doping agents for organic semiconductive matrix materials and related applications [22].

Some modifications of the Fukunaga route also allow the combination of tetrachlorocyclopropene (**22**) and anions of methylene compounds less CH-acidic than those just discussed (Schemes 4.5 and 4.6). Thus, **22** was added to



Scheme 4.5



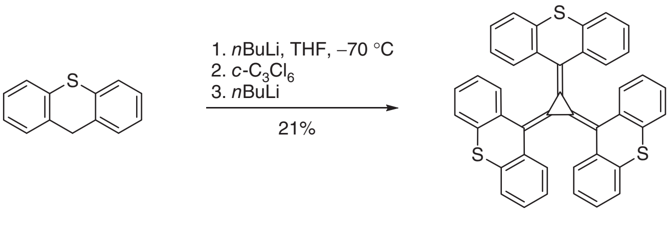
Scheme 4.6

an excess of the anion of 1,5-bis(trimethylsilyl)penta-1,4-diyne, obtained by deprotonation of the methylene compound with *tert*-butyl lithium in THF at −78 °C, and the resulting triafulvene dianion was oxidized *in situ* with DDQ to give hexakis(trimethylsilylethynyl)[3]radialene (**28**) in low yield [23]. This acceptor-substituted radialene shows unusual electronic properties; crystals of **28** are deep red and solutions in hexane are intensely purple-red. Attempts to use **28** as a building block for two-dimensional all-carbon networks were thwarted when desilylation efforts under mild conditions gave instead, an unidentified, unstable product.

Oda and coworkers [24, 25] have developed the synthesis of hexaaryl[3] radialenes **29** from **22** and the anions of diarylmethanes that are more acidic than diphenylmethane (pK_a = 32.3) (Scheme 4.6). Hexaphenyl[3]radialene (**29a**) was not accessible directly by this method, but could be obtained from the iodophenyl derivative by halogen/metal exchange and protonation. Hexa(2-thienyl)[3]radialene [24] and hexakis(3,5-dimethylpyrazolyl)[3]radialene [26] were also obtained by this method. Hexakis(4-cyanophenyl)[3]radialene so obtained is sixfold phenylogous to hexacyano[3]radialene, but it is of course much more difficult to reduce [25, 26]. Hexakis(3,4-dicyanophenyl)[3]radialene, on the other hand, is the most electron-deficient hexaaryl[3]radialene reported so far [26]. Most of the hexaaryl[3]radialenes are orange or red in color, and fluorescence was characterized by large Stokes shifts in some cases [26]. Two fascinating triarylamine/[3]radialene conjugates, **30a** and **30b**, were obtained by a sixfold Hartwig amination of hexakis(4-bromophenyl)[3]radialene; they are multistep redox systems with remarkably low oxidation potentials [27].

Shortly after the hexaaryl[3]radialenes, the analogous syntheses of hexa(2-pyridyl)- and hexa(3-pyridyl)[3]radialene were reported concurrently by the groups of Steel [28] and Oda [29], and hexa(4-pyridyl)[3]radialene followed more recently [30]. These water-soluble radialenes represent a new class of multidentate ligands with applications in metallo-supramolecular coordination chemistry (*vide infra*).

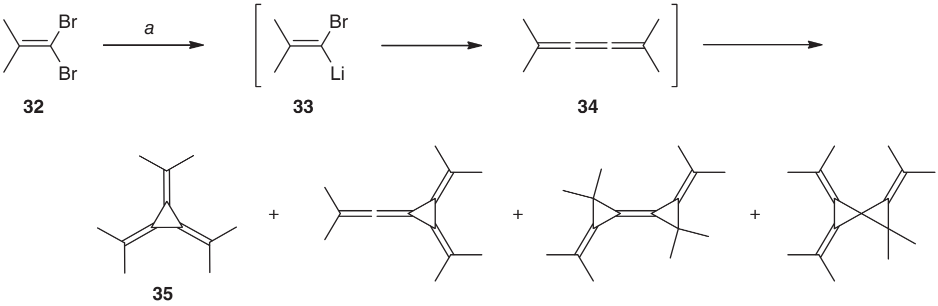
Hexachlorocyclopropane was used as the platform to assemble the electron-rich, blue radialene **31**, which is so far the most electron-rich [3]radialene (Scheme 4.7) [31].



31

Scheme 4.7

Various alkyl- and/or aryl-substituted [3]radialenes could be prepared from 1,1-dihaloalkenes via organometallic intermediates. These transformations, however, often give the radialene in low yield due to competing reaction pathways. The first radialene, hexamethyl[3]radialene (**35**), was obtained from dibromoalkene **32** and *n*-butyl lithium in very low yield, the lithium carbenoid **33** and the [3]cumulene **34** being the likely reaction intermediates (Scheme 4.8) [32]. Preferential cyclopropanation of the outer double bonds of the [3]cumulene by the carbenoid (or carbene) is a major factor for the complexity of the product mixture.

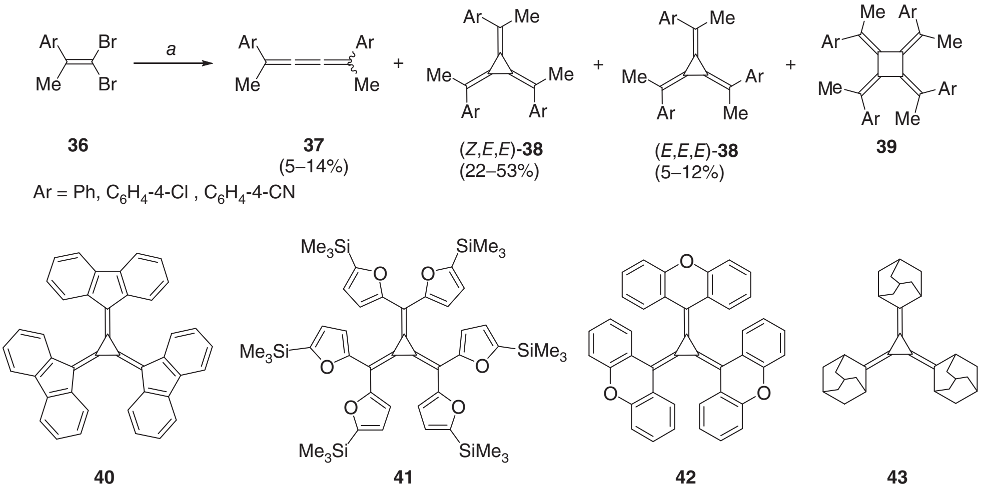


(*a*): 2 equiv. of **32**; 1. *n*BuLi (1.25 equiv.), THF, –110 °C; 2. –110 → –65 °C;
3. *n*BuLi (0.75 equiv.), –65 → 20 °C; yield of **35**: 0.3–2%.

Scheme 4.8

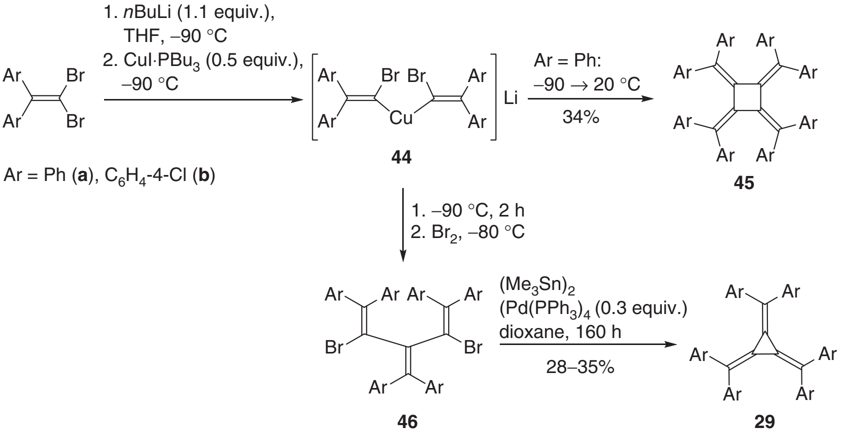
An alternative with enlarged scope is provided by the dehalogenative cyclotrimerization of 1,1-dibromoalkenes or 1,1-dichloroalkenes via copper or nickel carbenoids; these reactions are mechanistically different from those with lithium carbenoids. The olefinic substrates are now converted into organocuprate intermediates (by reaction of the Li-carbenoid with Cu(I)) or treated with chemically activated nickel. As an example, Scheme 4.9 shows the Ni-assisted cyclotrimerization of 1,1-dibromo-2-arylprop-1-enes **36**, which, besides two diastereoisomeric [3]radialenes **38**, yielded the [3]cumulenes **37** and small amounts of stereoisomeric [4]radialenes **39** [33].

Some [3]radialenes obtained by cyclotrimerization of 1,1-dihaloalkenes via either copper (**40** [33], **41** [34]) or nickel carbenoids (**40** [35], **42** [35], **43** [36]) are also shown in Scheme 4.9. In almost all cases, the yield was quite low and a significant amount of the corresponding [3]cumulene was also formed; the highest yield was obtained for tri(adamantan-2-ylidene)[3]radialene (**43**) (54%, when performed with activated nickel prepared from NiI$_2$, Li powder, and 4,4′-di-*tert*-butylbiphenyl in THF with sonication). It appears that the substituents at the other end of the double bond in 1,1-dihaloalkenes must be sufficiently large to have a real chance for the formation of a [3]radialene and to suppress the formation of larger radialene rings. In fact, using the organocuprate pathway with 1,1-dibromoalkene **32** led to the permethylated [4]- and [5]radialenes (Sections 4.2.2 and 4.2.3), and from 1,1-dibromo-2,2-diphenylethene, octaphenyl[4]radialene (**45a**) rather than hexaphenyl[3]radialene (**29a**) was



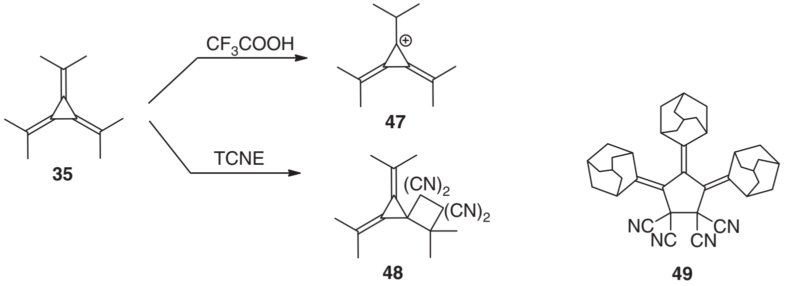
Scheme 4.9

obtained (Scheme 4.10) [37]. Interestingly, however, the organocuprate intermediate **44**, from which octaphenyl[4]radialene (**45a**) is likely to be formed on warming, can be diverted by quenching with bromine to form [3]dendralene **46**; the latter could be transformed into hexaphenyl[3]radialene (**29a**) by an intramolecular Pd-catalyzed C–C coupling reaction in the presence of hexamethylditin (Scheme 4.10). The 4-chlorophenyl derivatives reacted analogously [38].



Scheme 4.10

Reports on transformations of [3]radialenes by classical chemical reactions are scarce (see Chapter 12). Due to the already mentioned difficulties in handling and the ease of polymerization, the parent [3]radialene appears to be not well suited for reactivity studies. Hexamethyl[3]radialene (**35**), on the other hand, is able to accept diverse electrophiles. It is protonated by trifluoroacetic acid to form a delocalized cyclopropyl cation **47**, which was observed in solution (UV/Vis: $\lambda_{max} = 480\,nm$) [39], and its reaction with TCNE was reported to give the [2+2]cycloaddition product **48** (Scheme 4.11) [32b]. With the sterically more congested hexa(adamantan-2-ylidene)[3]radialene (**43**), however, the formal [3+2]-cycloaddition product **49** was generated [36]. With both substrates, these reactions proceed via persistent 1 : 1-charge-transfer complexes, which then are presumably transformed into zwitterionic intermediates resulting from electrophilic attack of TCNE at a radialene double bond. On the other hand, radialene **35** was found not to enter into [4+2] cycloaddition (Diels–Alder) reactions with maleic anhydride, probably because of steric hindrance due to the dimethyl substitution at both ends of the 1,3-diene moiety and their unfavorable distance [32b].



Scheme 4.11

Charge-transfer complexes of variously functionalized, both electron-rich and electron-poor, [3]radialenes have attracted attention because of their magnetic properties [7] and as potential organic metals [17, 18]. Most of the [3]radialenes reported so far have been studied with respect to their oxidation and reduction chemistry (see the reviews [7, 8] and some examples mentioned in this chapter). With appropriate substitution patterns, the range of redox properties extends from the most electron-rich [3]radialene **31** to the very electron-poor radialene **24a**, a strong oxidant [21]. The first one-electron reduction step of **18** (X = Y = CN) [16], **19**, and **20** [17] occurs at potentials similar to TCNQ, and at potentials similar to chloranil for other derivatives of **18** (Scheme 4.3).

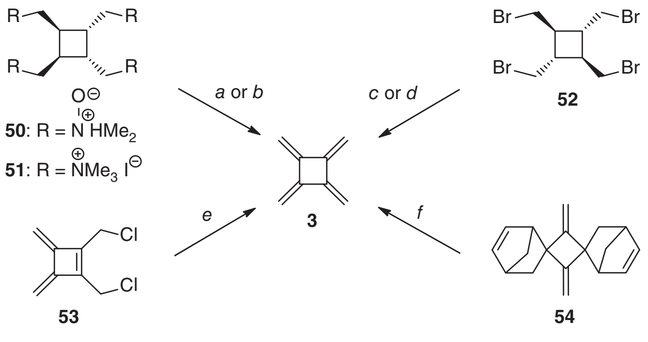
[3]Radialenes with substituents that are able to act as ligands to transition-metal centers have recently been considered as tectons in supramolecular coordination chemistry. Hexakis(4-cyanophenyl)[3]radialene and $AgClO_4$ or $AgPF_6$ form two-dimensional 6,3-coordination polymers in which each radialene molecule coordinates to three Ag^+ ions at cyano nitrogen atoms, leading to a repeating hexagonal ring motif [40]. In addition, it was observed that the anions, PF_6^- or ClO_4^-, sit in close proximity to the radialene core and maintain weak C–H···anion hydrogen bond and π···anion hydrogen bond interactions. Quantum chemical

calculations supported the idea of anion· · ·π interactions between halide ions and electron-deficient hexakis(cyanophenyl)[3]radialenes, and, in fact, the existence of such complexes in the gas phase was confirmed through tandem MS/MS experiments [41].

The ability of hexapyridyl[3]radialenes to act as multidentate ligands through their pyridyl nitrogen atoms has been demonstrated. Hexa(2-pyridyl)[3]radialene was found to give different coordination motifs with Ag^+ ions [42], depending on the silver salt employed, including an Ag_6L_2 cage [28] and a one-dimensional coordination polymer with a 2 : 1 metal/ligand composition [43]. The same radialene formed a dinuclear 1 : 2 complex when combined with the (2,2′-bipyridyl)ruthenium(II) moiety [44]. A three-dimensional coordination polymer with 1 : 1 composition was formed from hexa(4-pyridyl)[3]radialene and $AgClO_4$ in DMSO or methanol [30].

4.2.2
[4]Radialenes

All known routes to the parent [4]radialene (**3**) use elimination reactions of appropriately functionalized cyclobutane derivatives (Scheme 4.12), namely, fourfold Cope elimination or Hofmann degradation of tetra(aminoxide) **50** and tetrakis(trimethylammonium iodide) **51**, respectively [2]; fourfold dehydrobromination of **52** [2, 45, 46], reductive 1,4-dehalogenation of 1,2-bis(chloromethyl)-3,4-dimethylenecyclobutene **53** [47]; and twofold thermal [4+2] cycloreversion of 1,3-dimethylenecyclobutane derivative **54** [48]. In all these preparations, radialene **3** was vacuum transferred into a cold trap. The extremely oxygen-sensitive compound [2] is stable at −78 °C as a solid or in an inert solvent, but it quickly oligo- and polymerizes in a very exothermic reaction at room temperature [47].

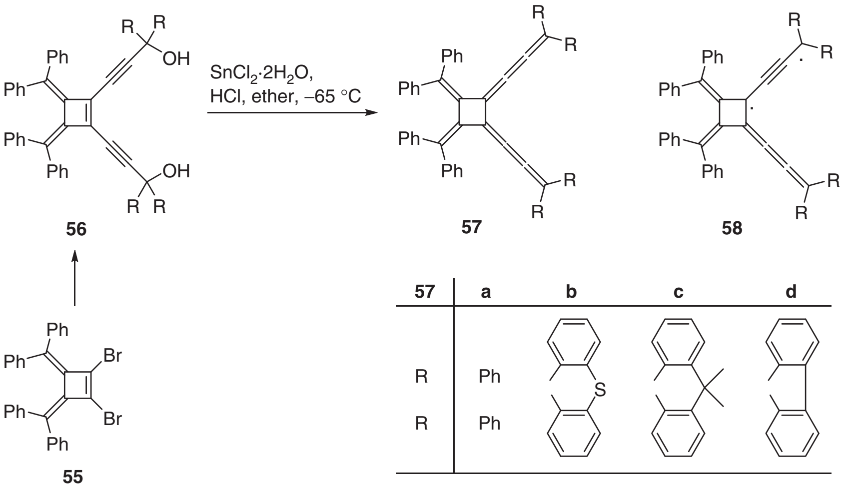


(*a*) 250 °C, 1–5 Torr, 1–2%; (*b*) 115 °C, ~1% (no pure product); (*c*) NaOEt, EtOH, 0 °C, 50%; (*d*) solid KOH, 150 °C; (*e*) Zn, $BuO(CH_2)_2O(CH_2)_2OBu$, 50 °C, 77%; (*f*) 680 °C, 5.10^{-5} Torr, 65%.

Scheme 4.12

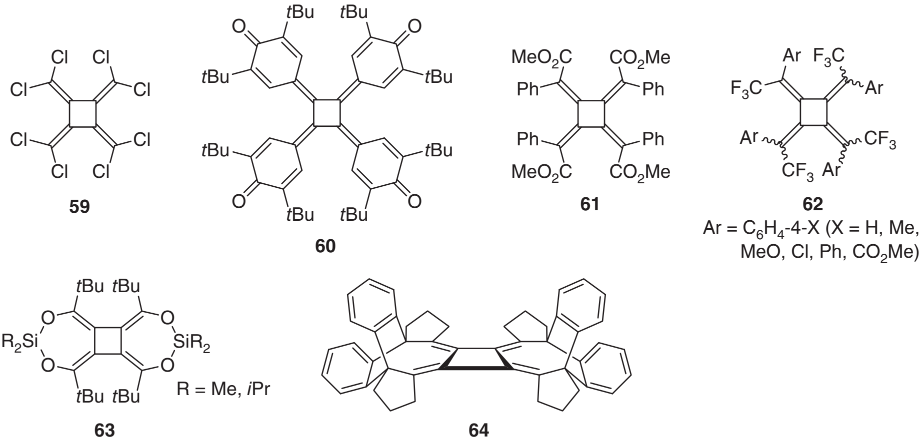
[4]Radialenes bearing four to seven phenyl groups, but not octaphenyl[4]radialene, could be prepared from 3,4-bis(diphenylmethylene)cyclobutane-1,2-dione and 2,3-bis(diphenylmethylene)-4-benzylidenecyclobutan-1-one [49].

A reductive 1,8-didehydroxylation of 1,2-dialkynyl-3,4-bis(diphenylmethylene)-cyclobutenes **56**, which themselves were prepared from 1,2-dibromocyclobut-1-ene **55** and the appropriate terminal alkyne by a Sonogashira coupling reaction, provided the deeply colored [4]radialenes **57a–d** [50, 51]. A remarkable feature of **57** is the fast rotation around the cumulenic bonds at ambient temperature, with $\Delta G^{\neq}$ values of 13.7 (**b**, −20 °C), 14.9 (**c**, 0 °C), and 17.8 (**d**, 27 °C) kcal mol^{-1} in chlorinated solvents. The bond rotation process was explained as proceeding through a diradical intermediate **58**, that is, the geometrical isomerizations at the two cumulenic units occur independently (Scheme 4.13).



Scheme 4.13

The thermal or photochemical [2+2]cyclodimerization of [3]cumulenes (butatrienes) appears to be an obvious approach to the [4]radialene framework, but, in practice, the success of this route is limited. Thermolysis of the parent butatriene yields 1,5-cyclooctadiyne in very low yield besides other products [52]. Tetrafluorobutatriene polymerizes even at −78 °C. Advanced quantum-chemical calculations of the dimerization energies of butatriene and tetrafluorobutatriene have shown that the cyclodimerization leading to the [4]radialene is strongly exothermic and larger than for any other cyclodimer; the failure to detect the radialenes might be attributed to their high reactivity, undergoing fast oligomerization reactions [53]. Alkyl-, silyl-, stannyl-, and germyl-substituted butatrienes have no tendency to dimerize thermally. Tetraphenyl- and tetrakis(4-methoxyphenyl)butatriene also do not cyclodimerize thermally, and exposure to sunlight in the solid state triggers a head-to-tail cyclodimerization at the outer double bond of the cumulene [54]. On the other hand, the substituted



59 **60** **61** **62**

Ar = C_6H_4-4-X (X = H, Me, MeO, Cl, Ph, CO_2Me)

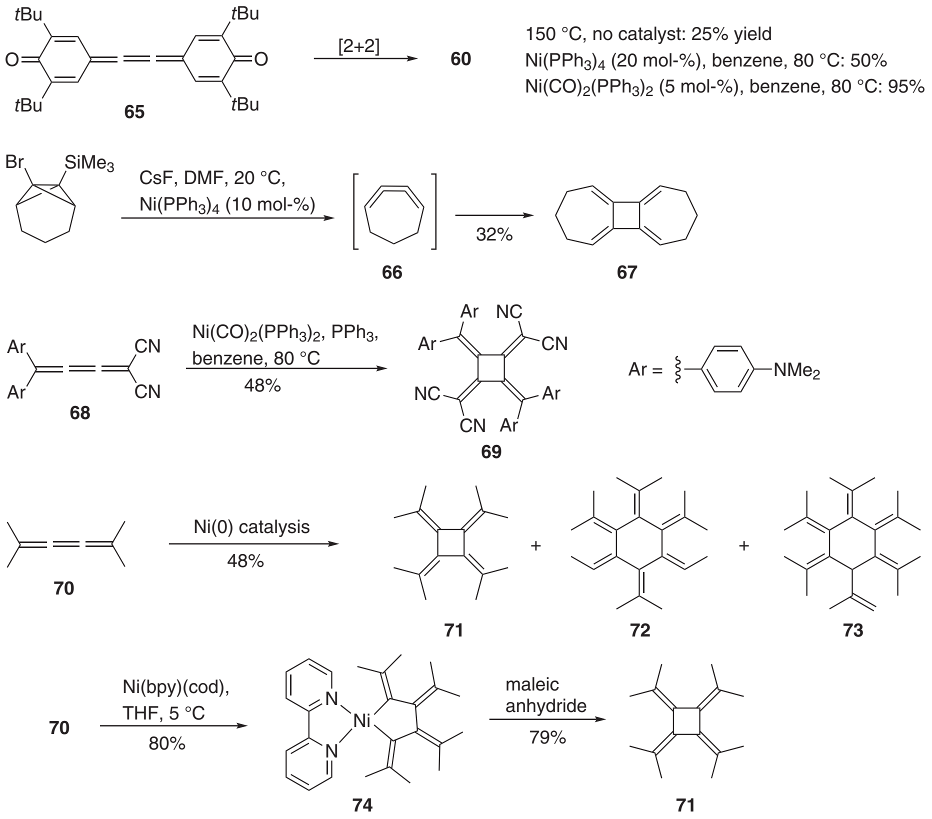
R = Me, *i*Pr

63 **64**

Figure 4.2 [4]Radialenes obtained by cyclodimerization of acyclic and cyclic [3]cumulenes.

[4]radialenes **59** [55], **60** [56], **61** [57], and **62** [58] have been obtained, mostly in good yields, by heating the corresponding [3]cumulenes at 100–200 °C (Figure 4.2). Thus, it appears that only those acyclic butatrienes, which carry sufficiently electron-withdrawing substituents, cyclodimerize across the central double bond. On the other hand, the two [4]radialenes **63** [59] and **64** [60] have been isolated, which are assumed to result from short-lived strained seven- or eight-membered cyclic [3]cumulenes as the immediate precursors. Due to their *in situ* formation, it is not clear, however, whether the radialenes were formed by a purely thermal, transition-metal-catalyzed (**63**), or photochemical (**64**) [2+2] cyclodimerization reaction.

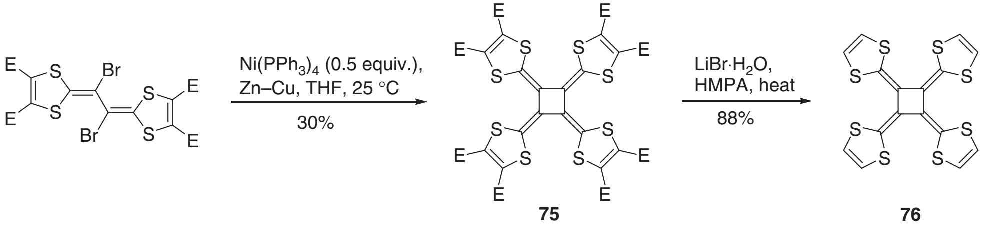
The scope of the synthesis of [4]radialenes from [3]cumulenes is significantly enhanced by nickel(0) catalysis. In some cases, this can improve the yield over that of the uncatalyzed thermal reaction – as was first shown by West and coworkers for the synthesis of **60** from **65** [61] – and in other cases [62, 63] Ni(0) catalysis is required to achieve the [2+2]-cycloaddition. For example, (Scheme 4.14), *in situ* formed 1,2,3-cycloheptatriene (**66**) cyclodimerizes to form the tricyclic [4]radialene **67** in the presence of $Ni(PPh_3)_4$, but not under purely thermal conditions [63]. The donor–acceptor-substituted butatriene **68** underwent a highly regioselective Ni(0)-mediated head-to-tail cyclodimerization, yielding [4]radialene **69** (blue colored in solution) in fair yield [64]. Ni(0)-catalyzed conversion of 2,5-dimethylhexa-2,3,4-triene (**70**) into octamethyl[4]radialene (**71**) is also possible, but the choice of catalyst and solvent is crucial. With $Ni(PPh_3)_4$ or $Ni(CO)_2(PPh_3)_2$ as catalysts in benzene or DMF, **71** is formed in low yield together with larger amounts of permethyl[6]radialene (**72**) and an isomer **73** of the latter [65, 66]. Wilke [67] has reported that exposure of **70** to $Ni(cod)_2$ yields the [4]radialene in toluene but the [6]radialene in DMF (no yields given). The isolation of the 2,2′-bipyridyl nickel(0) complex **74** from [3]cumulene **70**, which can be cleaved with maleic anhydride to give radialene **71** in good yield [68], sheds some light on the mechanism [66] of the cyclodimerization reaction.



Scheme 4.14

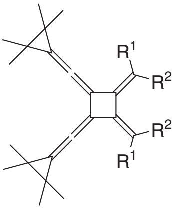
Based on the ability of Ni(0) complexes to induce reductive dehalogenation reactions, [3]cumulenes are accessible from 2,3-diiodo(dibromo)-1,3-butadienes and 1,4-dichloro-2-butynes, respectively, and can be subjected without isolation to the nickel-mediated cyclodimerization reaction. With preformed Ni(0) complexes or a catalytic system generated from $NiBr_2(PPh_3)_2/PPh_3$ (or Et_4NI)/activated Zn (excess), several [4]radialenes could thus be obtained advantageously, including **71** [65, 66] (again, the reaction is strongly affected by the solvent polarity); some other peralkylated [4]radialenes [66], and the functionalized radialene **75**, which was further converted into the very electron-rich tetrakis(1,3-dithiol-2-ylidene)[4]radialene (**76**) (Scheme 4.15) [69, 70].

Thermal or Ni(0)-catalyzed [2+2] cyclodimerization reactions of higher [*n*]cumulenes give access to radialenes bearing cumulenic π-systems ("extended radialenes," compare Scheme 4.13, Section 4.2.2, and Chapter 9). However, the success and the regioselectivity of the cycloaddition event depend strongly on the steric demand of the substituents at both ends of the cumulene [7, 8, 51]. Thus, a thermally induced cyclodimerization of a [4]cumulene furnished radialene **77**



Scheme 4.15

($R^1 = t$Bu, $R^2 = $H [71]) (Scheme 4.16), whereas with $R^1 = R^2 = $Me [72] a head-to-head cycloaddition across the cyclopropylidene=C double bond occurred. Tetra-*tert*-butylhexapentaene, by virtue of its bulky end groups, cyclodimerizes across the central C=C bond and yields the symmetrical, thermally highly stable [4]radialene **78** (no solvent, 200 °C, 15 min, 90% yield) [73, 74].



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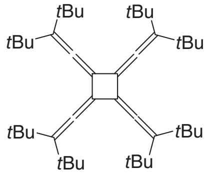

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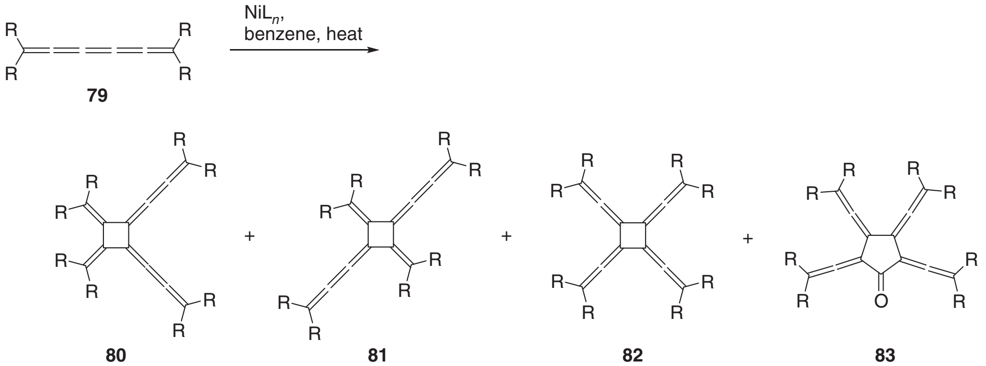


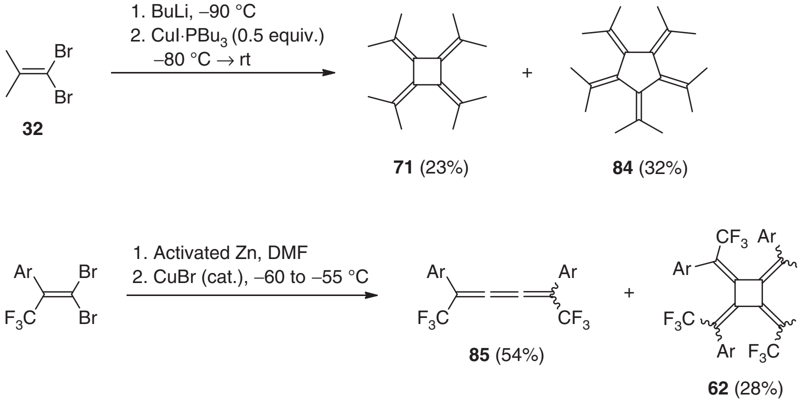
Scheme 4.16

Nickel(0)-mediated [2+2] cyclodimerization reactions of [5]cumulenes **79** have been investigated in detail by Iyoda and coworkers [50a, 51, 75]. Here again, the regioselectivity depends on the steric demand of the substituents and on the reactivity of the double bonds as well. Thus, [4]radialene structures **80**–**82** have been obtained, and in the presence of $Ni(CO)_2(PPh_3)_2$ the [5]radialenone **83** was isolated as a significant by-product in some cases (Scheme 4.16). For example, tetraarylhexapentaenes form extended octaaryl[4]radialenes **80** (see **57**, Scheme 4.13); treatment of tetra-*tert*-butylhexapentaene with $Ni(CO)_2(PPh_3)_2$

(1 equiv.)/PPh_3 (3 equiv.) in refluxing benzene gave a mixture of **82** (see **78**) (6%) and **83** (74%).

The formal cyclooligomerization of vinylidene units via copper or nickel carbenoids represents another route to [4]radialenes. To this end, a 1,1-dibromo(or chloro)-alkene can be converted into a bis(1-halogenovinyl)cuprate at low temperatures, which, on warming, furnishes the [4]radialene, often accompanied by the corresponding dimerization product, the [3]cumulene. This method is so far the only route to octaphenyl[4]radialene (see Scheme 4.10, Section 4.2.1) and other octaaryl[4]radialenes [10, 37]. With 1,1-dibromo-2-methylprop-1-ene (**32**) as the starting material, a mixture of [4]radialene **71** and [5]radialene **84** as the major products is formed [76] (Scheme 4.17). While this method is not the preferred route to the former radialene, it represents the only known way for the preparation of **84**. Treatment of dibromoalkene **32** with a Ni(0) complex [37] or activated nickel [10] does not improve the yield of radialene **71**.

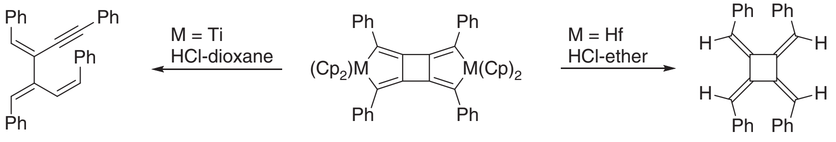
By a related carbenoid approach, tetrakis(aryl, trifluoromethyl)[4]radialenes **62** were obtained as mixtures of four diastereoisomers besides the [3]cumulenes **85** (Scheme 4.17) [58, 77]. The thermal cyclodimerization of **85** to form diastereomeric mixtures of [4]radialenes **62** [58, 77] has already been mentioned.



Scheme 4.17

The unique titanocene- or hafnocene-substituted [4]radialenes **86** [78] and **87** [79] were formed in low yields from diphenylbutadiyne and $Cp_2Ti(\eta^2\text{-}Me_3SiC{\equiv}CSiMe_3)$ or $Cp_2Hf(n\text{-}Bu)_2$, respectively (Scheme 4.18). Other 1,3-diynes did not react analogously. Efforts to liberate the free radialene from these organometallics by acidolysis were only partly successful: treatment of **86** with hydrogen chloride led to the [3]dendralene **88** in high yield, while **87** furnished the tetraphenyl[4]radialene **89** only as an unstable, impure product.

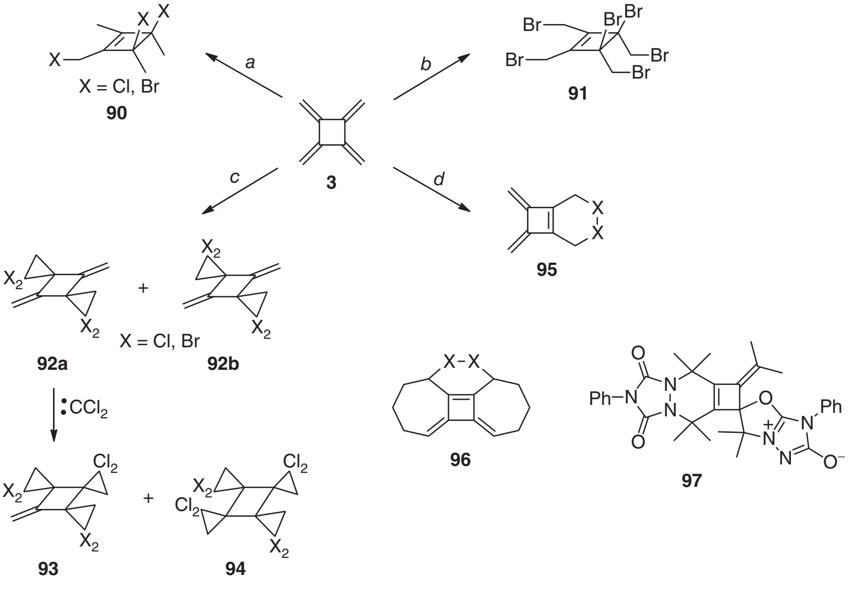
As far as chemical reactivity is concerned, much more is known about [4]radialenes than the other radialene classes, mainly due to the studies of Griffin and Peterson [2], and Hopf *et al.* [47, 80] on the parent [4]radialene and of Wilke *et al.* [67] on the permethyl derivative. In spite of its ease of dimerization



88 M = Ti (**86**), Hf (**87**) **89**

Scheme 4.18

(by a formal [4+4] cycloaddition) and polymerization in the condensed phase and extreme oxygen sensitivity [2] (*vide infra*), [4]radialene (**3**) is extremely stable in the gas phase; flow pyrolysis above 850 °C finally caused a reaction which gave mainly styrene besides small amounts of *o*-xylene, phenylacetylene, toluene, and benzene [47]. It reacts cleanly with various electrophiles and dienophiles (Scheme 4.19). Thus, although it is stable toward dilute mineral acids (and strong bases as well), it adds 3 equiv. of HCl, HBr, and bromine to form cyclobutenes **90** and **91**, respectively [47]. *In situ*-generated dichloro- and dibromocarbene first add to two radialene double bonds, forming the diastereoisomeric dispiro compounds **92a** and **92b**. With **92a** (X = Cl) only, a subsequent third and fourth addition of :CCl_2 could be achieved (**93** and **94**) [80]. Diels–Alder reactions with various electron-deficient dienophiles occur under mild conditions, yielding 1 : 1 adducts **95** [2, 47]. A second Diels–Alder reaction, which would have resulted in a cyclobutadiene



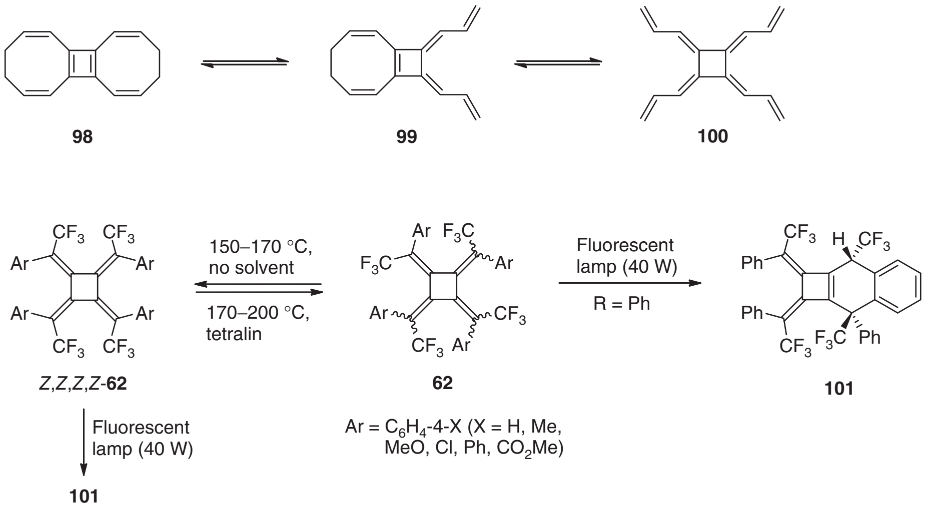
(*a*) HCl or HBr, ether, −78 °C, 50–68% yield; (*b*) Br_2, CCl_4, −20 °C, 68%;
(*c*) $CHCl_3$, aq. NaOH (50%), $[BnEt_3N]Cl$, 20 °C or $CHBr_3$, KO*t*Bu, −20 °C;
(*d*) X=X = *N*-phenylmaleimide, tetracyanoethylene (TCNE), 4-phenyl-3*H*-1,3,4-triazole-3,5(4*H*)-dione (NPTD), diethyl azodicarboxylate.

Scheme 4.19

derivative, has never been achieved. This did not change with the more electron-rich [4]radialenes **67** and **71**. In the former case, once more only the 1 : 1 adduct **96** was obtained [63]. Octamethyl[4]radialene (**71**), on the other hand, gave the 1 : 1 Diels–Alder adduct with TCNE, whereas with the highly reactive dienophile NPTD not only the 1 : 1 adduct but also the 1 : 2 adduct **97** (a formal [3+2] cycloaddition product) was formed [67].

Surprisingly little is known about the coordination chemistry of [4]radialenes. The interaction of octamethyl[4]radialene (**71**) with CpCo(η^2-$CH_2{=}CH_2$)$_2$ may begin with the formation of a diene complex CpCo(η^4-**71**), but it continues as a catalytic rearrangement to finally furnish 1,3-diisopropyl-5-methyl-2-(1-methylvinyl)benzene [81].

Intramolecular thermal reactions have been observed for [4]radialenes with additional conjugated π bonds (Scheme 4.20). Thus, electrocyclic reactions seem to connect the easily polymerizing 5,6,7,8-tetravinyl[4]radialene (**100**) with cyclobutadiene **98** and cyclobutene **99** in a valence-tautomeric equilibrium [82]. (Aryl,trifluoromethyl)-substituted radialenes **62** exhibit a complex isomerization behavior under thermal and photochemical conditions [77]. While thermal activation causes a geometrical isomerization at the exocyclic bonds and converts the original mixture of four diastereomers into isomer *Z,Z,Z,Z*-**62** with good selectivity, irradiation of the latter in diastereomerically pure form with light first leads to diastereomeric scrambling and then to the formation of cyclobuta[*b*]naphthalene derivative **101** and stereoisomers thereof, resulting from a combination of photochemical and thermal reactions (6π-electrocyclization and 1,3-sigmatropic H-shift).



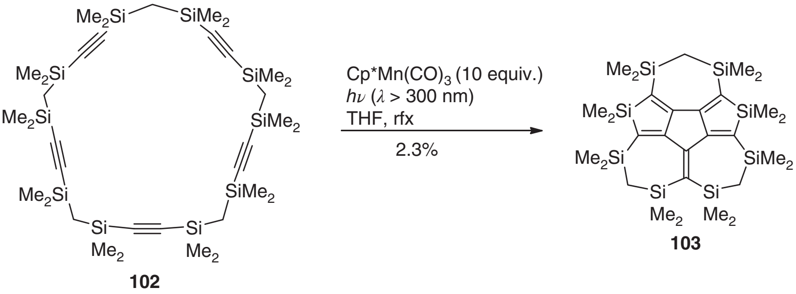
Scheme 4.20

The redox chemistry of substituted [4]radialenes has been reviewed [7]. Depending on the substituents, the charge states range from the dianion to the tetracation.

4.2.3
[5]Radialenes

The parent [5]radialene is still unknown (see below, however: note added in proof). As the simplest substituted derivative, decamethyl[5]radialene (**84**) has been obtained along with [4]radialene **71** by a formal cyclooligomerization of dimethylvinylidene units via copper [76] or nickel [10, 37] carbenoids (see Scheme 4.17, Section 4.2.2). It is unlikely, however, that other [5]radialenes will become accessible by the same method, because increasing steric demand of the substituents favors the formation of the [4]- and [3]radialene as well as the [3]cumulene structures (see Sections 4.2.1 and 4.2.2).

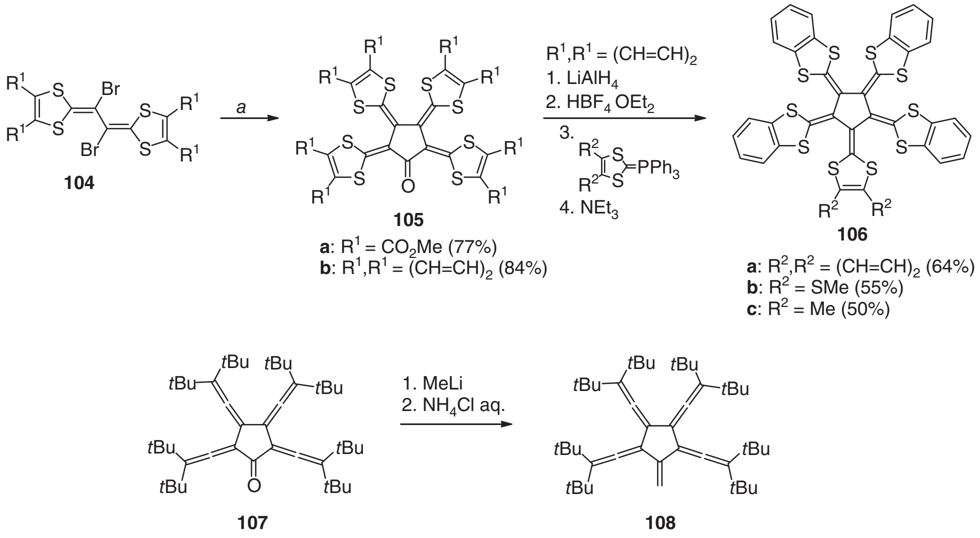
Sekiguchi and coworkers have detected the extraordinary rearrangement of the octasilacyclopentayne **102** into persilylated [5]radialene **103** in the presence of a large excess of Mn(Me–Cp)(CO)$_3$ (Scheme 4.21) [83, 84]. An analogous transformation yielding a pentacyclic persilylated [4]radialene was found by the same research group [85]. In mechanistic terms, these low-yielding, manganese-assisted isomerizations could include a 1,2-silyl shift at each acetylenic bond followed by cyclooligomerization of the so formed vinylidene moieties. Radialene **103** could be reduced with lithium in tetrahydrofuran to form a stable tetraanionic salt, [Li(thf)$_4$)]$^+$**103**$^{4-}$ [84].



Scheme 4.21

[5]Radialenones have the potential to serve as precursors to a range of new [5]radialenes. Thus, 2,3-dibromo-1,3-butadiene derivatives **104** were converted into [4]radialenes in a Ni(0)-catalyzed cyclodimerization reaction (see Section 4.2.2, Scheme 4.15), but in the presence of carbon monoxide, [5]radialenones **105** were formed in good yields (Scheme 4.22) [86]. Subsequent olefination of the keto group furnished the fivefold [5]radialene/1,3-dithiol conjugates **106** [87]. The tetraallenic [5]radialenone **107** (for its formation, see Section 4.2.2, Scheme 4.16) reacted with methyl lithium via the corresponding alcohol to give the radialene **108** in one step [51].

The very electron-rich [4]radialenes **106a–c** could be oxidized with NOBF$_4$ or NOPF$_6$ in acetonitrile to the corresponding tetracations which were isolated as BF$_4$ or PF$_6$ salts. Cyclic voltammetry of **106a** and **106b** indicated a unique single-wave four-electron transfer, which results from 2 × 2 electron transfer steps at the same potential. In **106c**, these two steps are only partly overlapping.



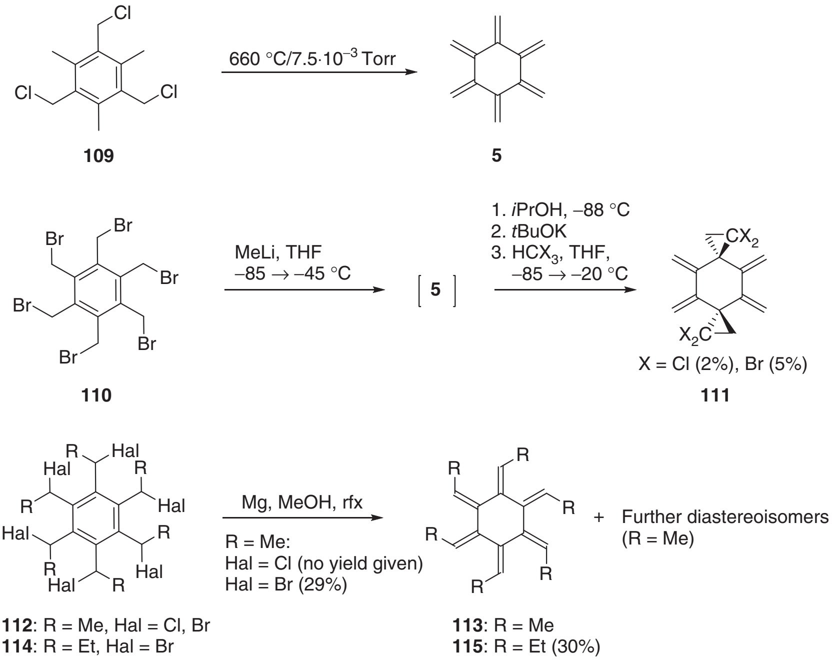
(a) $Ni(PPh_3)_4$ (0.2 equiv.), Zn–Cu (excess), CO (1 atm), THF, 50 °C.

Scheme 4.22

4.2.4
[6]Radialenes

Syntheses of the parent [6]radialene (**5**) were published by three research groups in 1977/1978 4, 5, 6. Among the various gas-phase flash pyrolysis reactions reported, the triple HCl-elimination from 1,3,5-tris(chloromethyl)mesitylene (**109**) is the most practicable one and yields the radialene in 35–48% yield (Scheme 4.23) [5]; other flash pyrolyses were carried out, typically at 900 °C, with cyclododeca-1,5,9-triyne, benzo[1,2:4,5]dicyclobutene derivatives and benzo[1,2-*c*:3,4-*c*′:5,6-*c*″]tris(2,5-dihydrothiophene 1,1-dioxide). The sixfold dehydrobromination of hexa(bromomethyl)benzene (**110**) with methyl lithium at low temperature has been achieved more recently; in this case, **5** has been trapped without isolation by cyclopropanation reactions yielding spiro compounds **111** in very low yield [88]. Radialene **5** is a difficult-to-handle, extremely air-sensitive compound with properties [5] that resemble those described for the parent radialenes **2** and **3**; see Sections 4.2.1 and 4.2.2.

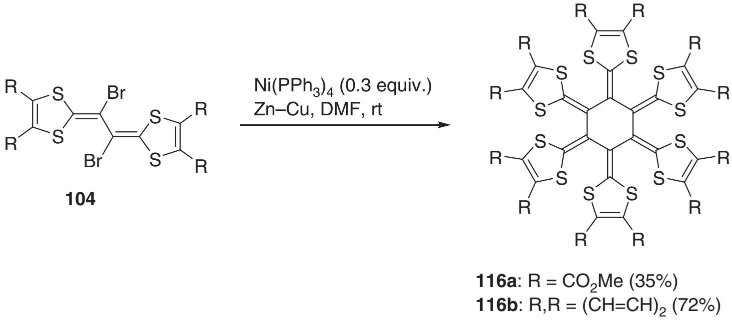
In contrast to the parent [6]radialene, alkyl-substituted derivatives **113** and **115** are quite stable compounds that can even be handled in the presence of oxygen. All-(*E*)-7,8,9,10,11,12-hexamethyl[6]radialene (**113**) was the first radialene ever reported. It was obtained by dehalogenation of hexakis(1-chloroethyl)- [1a] or hexakis(1-bromoethyl)benzene [1b] (**112**) with magnesium in methanol (Scheme 4.23). A recent GC/MS study of the product mixture has revealed the concomitant formation of several diastereoisomers of **113**, which, however, could not be separated completely [88]. Hexaethyl[6]radialene (**115**) was obtained analogously from hexakis(1-bromopropyl)benzene (**114**) [89].



Scheme 4.23

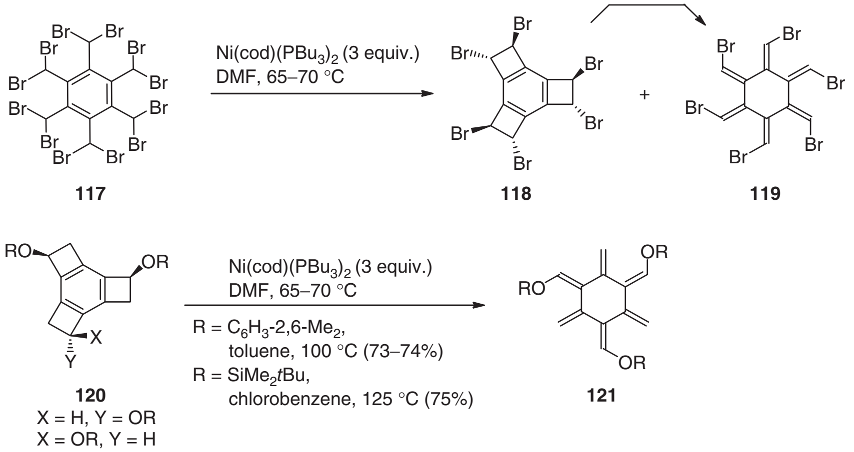
The formation of dodecamethyl[6]radialene (**72**) by a Ni(0)-mediated [2+2+2] cycloaddition of 2,5-dimethylbuta-2,3,4-triene (**70**) has already been mentioned (see Section 4.2.2). Much better yields could be obtained, when 3,4-dibromo(or diiodo)-2,5-dimethylhexa-2,4-diene was exposed to a Ni(0) complex. Here, the [3]cumulene **70** is a likely reaction intermediate, and the product distribution ([4]radialene **71**, [6]radialene **72**, and its isomer **73**; see Scheme 4.14) depends strongly on the solvent, with donor solvents favoring the formation of **72**. With DMF as the solvent and *in situ*-generated Ni(PPh$_3$)$_4$ as a mediator, a yield of 63 and 50% could be achieved for **72** from the dibromo- and the diiododiene, respectively [65, 66].

Similarly, tetrathio-functionalized 2,3-dibromobutadienes **104**, which also serve as precursors to [4]- and [5]radialenes (see Schemes 4.15 and 4.22), can be converted into hexakis(1,3-dithiol-2-ylidene)cyclohexanes **116a,b** when treated with Ni(PPh$_3$)$_4$ and Zn–Cu couple in DMF (Scheme 4.24) [90]. Interestingly, these highly substituted [6]radialenes are initially formed with a twist-boat conformation of the central six-membered ring, which can be converted thermally into the more stable chair conformation (see below).



Scheme 4.24

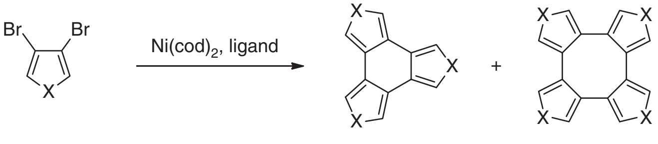
Hexakis(dibromomethyl)benzene (**117**) was converted in a multiple Ni(0)-mediated debromination reaction in DMF as solvent into a mixture of the hexabromotricyclobutabenzene **118**, which has the unsymmetrical *syn*-all-*trans* geometry, and all-*E*-7,8,9,10,11,12-hexabromo[6]radialene (**119**) (Scheme 4.25) [91]. The strained tetracycle **118** rearranges smoothly into **119** on warming. It was suggested that this isomerization has a radical mechanism, because the concerted conrotatory cyclobutane ring opening of **118** would not provide the all-*E* isomer of **119**. Crystal structure analyses of both compounds showed that the rearrangement requires only minor displacements in the carbon skeleton. As all efforts to achieve the reverse reaction failed, the early opinion [4] is confirmed that [6]radialene is thermodynamically more stable than its valence isomers with one, two, or three cyclobutane rings.



Scheme 4.25

A thermal tricyclobutabenzene/[6]radialene isomerization also gave rise to the first alkoxy-substituted [6]radialenes (Scheme 4.25). Both the *syn–anti* and the *syn–syn* diastereoisomers of tricyclobutabenzenes **120**, which were prepared through a multistep route, rearrange stereoselectively to the symmetrical 7,9,11-tris(2,6-dimethylphenyloxy)- or tris(silyloxy)-[6]radialenes **121**. The aryloxy derivatives reacted with dimethyl acetylenedicarboxylate to give the 1 : 1, 1 : 2, and 1 : 3 Diels–Alder adducts, which uncovers that the three cyclobutane rings are opened successively [92].

When the termini of each of the three 1,3-diene moieties in [6]radialene are bridged with a sulfur or selenium atom, benzo[1,2-*c*:3,4-*c*′:5,6-*c*″]trithiophene (**123a**) or -triselenophene (**123b**) result. They were readily obtained by a Ni(0)-mediated cyclotrimerization of 3,4-dibromothiophene (**122a**) and 3,4-dibromoselenophene (**122b**), respectively, together with the corresponding cyclotetramers **124a,b**, the relative yields depending on the added ligand (PPh_3 or 2,2′-bipyridyl) (Scheme 4.26) [93]. The benzotrithiophene had been prepared before from hexakis(bromomethyl)benzene [94]. According to experimental and theoretical results, **123a,b** are properly counted among the [6]radialenes: although the six-membered ring is practically planar, it is nonaromatic and has bond lengths corresponding to $C(sp^2)-C(sp^2)$ single bonds (1.44–1.46 Å) as opposed to exocyclic double bond lengths of 1.36–1.37 Å.

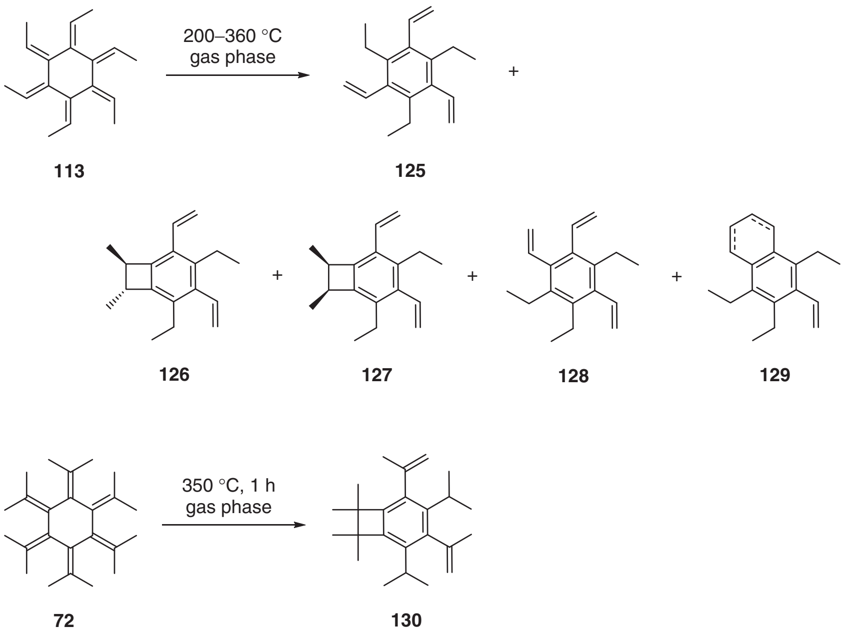


122 X = S (**a**), Se (**b**) **123** **124**

Scheme 4.26

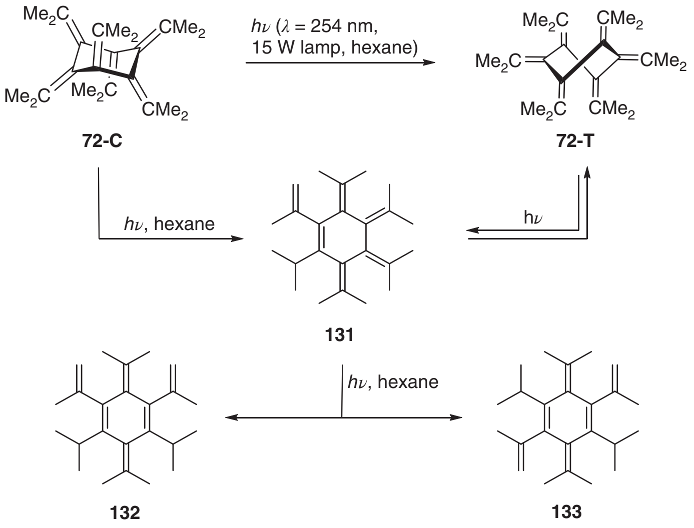
Only a few facts about the chemical reactivity of the parent [6]radialene (**5**) are known – certainly because it is not easy to handle – but they reveal its character as a triple 1,3-diene system (catalytic hydrogenation, triple 1,4-addition of Br_2, [4+2] cycloaddition reactions [5, 6]). Much more is known about the alkyl-substituted radialenes **113** and **72**, in particular due to the detailed investigations of Hopf and coworkers [88]. Because of the presence of three hexa-2,4-diene subunits in the latter radialenes, it is not surprising that isomerization pathways via sigmatropic and electrocyclic reactions exist. Thus, in a gas-phase thermolysis of **113**, products **125–129** were formed in relative yields that depended on the reaction temperature (e.g., **127** was the major product at 260 °C and **129** at 360 °C). The mechanistic scenario includes the isomerization **113** → **125** by three consecutive 1,5-H shifts, and the sequence **127** → **128** → **129** [88]. The permethylated [6]radialene (**72**) is thermally much more stable than **113**; the product mixture obtained from its pyrolysis at 350 °C was dominated by benzocyclobutene **130** (an analog of **127**), which, however, could be isolated in only 17% yield [88] (Scheme 4.27).

UV irradiation of radialene **72**, which in the solid state has the chair conformation **72-C**, unexpectedly led to a conformational change; yielding the twist conformer **72-T** that was unequivocally identified by an X-ray diffraction analysis



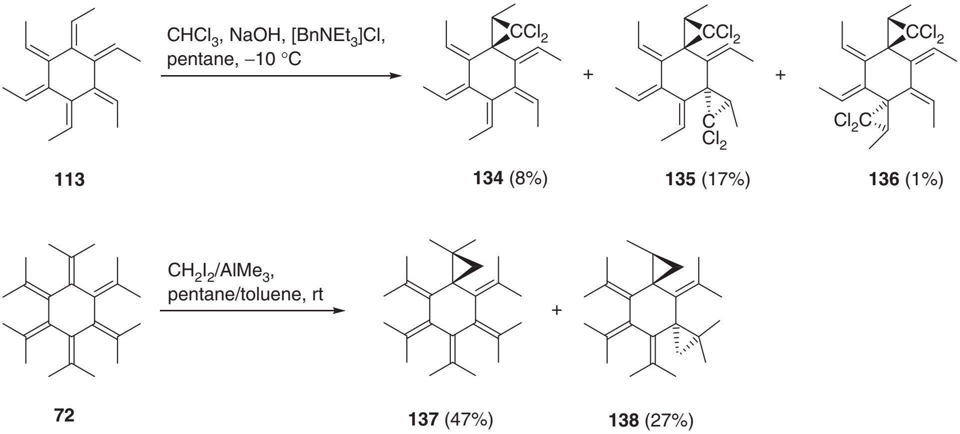
Scheme 4.27

(Scheme 4.28). Photochemical hydrogen shifts account for the formation of polyenes **131**–**133**, all of which could be isolated depending on the duration of the irradiation [88].



Scheme 4.28

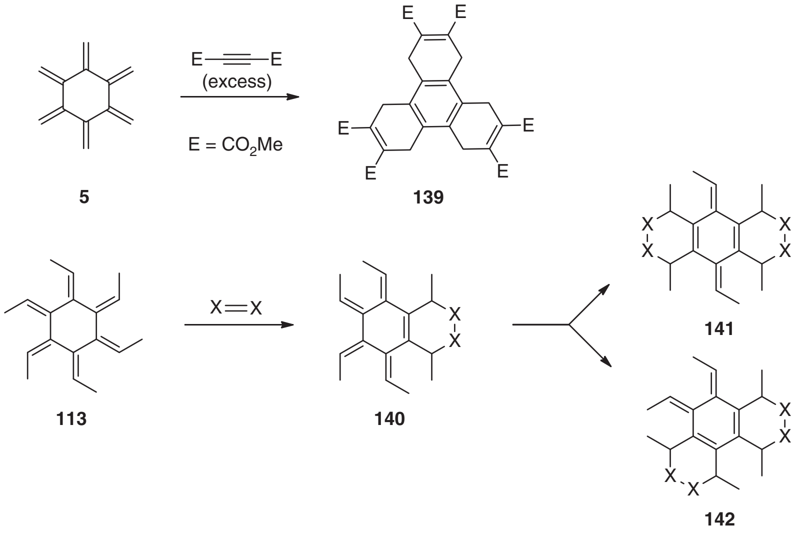
Similar to the parent [6]radialene, the hexamethyl derivative **113** accepts 3 equiv. of H_2, Br_2, and HX (X = Br, Cl) [1b]. According to a GC/MS analysis [88], HCl addition (HCl_g, Et_2O, HOAc, −22 °C) produced a mixture of regioisomers and diastereoisomers. Some [2+1] cycloaddition reactions with electrophilic carbenes could also be achieved (Scheme 4.29). Thus, dichlorocarbene addition to **113** under phase-transfer catalysis conditions yields the monocyclopropanation product **134** and the two regioisomeric bisadducts **135** and **136**. Dibromocarbene addition could, however, not be observed. The permethylated analog **72** reacts neither with dichloro- nor with dibromocarbene, but can be cyclopropanated with the diiodomethane/trimethyl aluminum reagent to give monoadduct **137** and bisadduct **138** [88]. In a similar manner, single and multiple epoxidation reactions of **113** and **72** with *meta*-chloroperbenzoic acid have been achieved [88].



Scheme 4.29

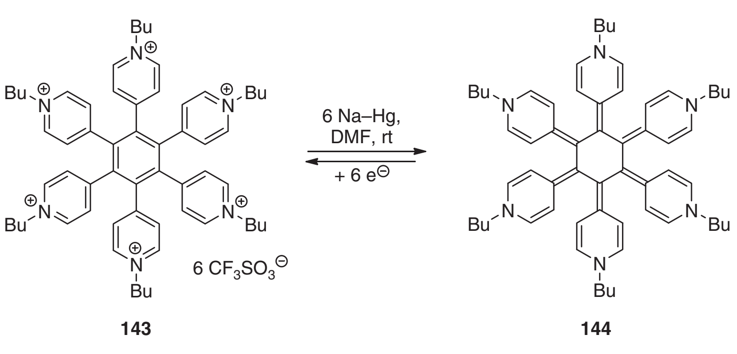
[4+2]Cycloaddition (Diels–Alder) reactions have been reported for [6]radialene (**5**) and its hexaalkyl derivatives **113** and **115**, but not for the permethylated radialene **72**, which was inert even to the reactive dienophiles TCNE and "*N*-phenyltriazolinedione" [67]. The sterically least hindered radialene **5** reacted with acetylenic and olefinic dienophiles in a 1 : 3 ratio to give triphenylene derivatives such as **139** in low yield (Scheme 4.30) [5, 95]. On the other hand, radialenes **113** and **115** gave linear, *p*-quinodimethane-type 1 : 2-adducts, when they were exposed to an excess of various common dienophiles (*inter alia* maleic anhydride, tetracyanoethylene, *p*-benzoquinone, acrolein, ethyl acrylate, acetylenedicarboxylic acid) [89, 96, 97]. The 1 : 1 adduct **140**, which was isolated so far only from the reaction with an equimolar amount of TCNE (92% yield) [97], presumably prefers the second cycloaddition step in the linear (*para*) position (**141**) over that in the angular (*meta*) position (**142**) for steric reasons.

Due to the paucity of existing [6]radialenes with strongly polarizing substituents, not much can be said about the redox properties of this radialene



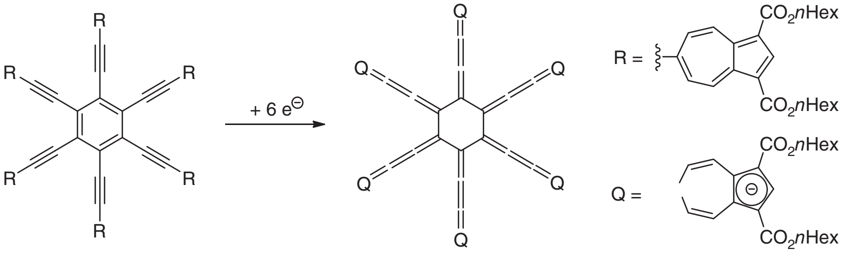
Scheme 4.30

class. For the hexakis(1,3-dithiol-2-ylidene)cyclohexanes **116a,b**, the cyclovoltammograms of the twist-boat modifications showed three oxidation waves leading finally to the dication, of which only the first one (formation of the radical monocation) was reversible [90]. Another electron-rich [6]radialene, hexakis(1-butyl-1,4-dihydropyridin-4-ylidene)cyclohexane (**144**), a homolog of Hünig's tetrakis(1,4-dihydropyridin-4-ylidene)cyclobutanes [98], has been obtained by six-electron reduction of the hexapyridiniobenzene salt **143** with sodium amalgam (Scheme 4.31) [99]. With an oxidation potential of −1.33 V (vs ferrocene$^{0/+}$) for **144**$^{0/2+}$, this radialene is a moderately strong reducing agent. A cyclovoltammogram of **143** in *N*,*N*-dimethyl formamide displayed a reversible reduction/oxidation scenario composed of two steps: **144**$^{6+}$ (= **143**) + 4e$^-$ ⇌ **144**$^{2+}$ and **144**$^{2+}$ + 2e$^-$ ⇌ **144**^{0}.



Scheme 4.31

Ito and coworkers have designed an electrochemical route to the elusive hexaanionic-extended radialene **146** (Scheme 4.32), which was presumably formed in a six-electron reduction of hexakis(6-azulenylethynyl)benzene (**145**). The low chemical stability of the latter (or intermediates in the reduction process), however, meant that a salt of **146** could not be isolated nor identified beyond doubt [100].

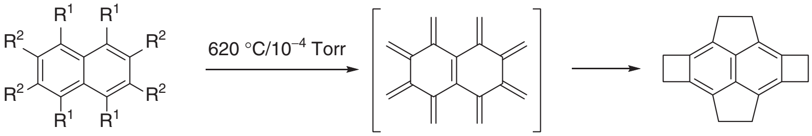


145 **146**

Scheme 4.32

4.2.5
Higher [*n*]Radialenes and Radialene Substructures in Polycyclic Conjugated π-Systems

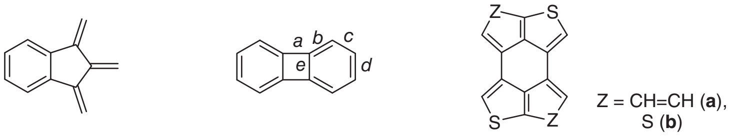
Monocyclic [*n*]radialenes with $n > 6$ are unknown at present. On the other hand, "naphtharadialene" (**148**) would meet the radialene definition (see Section 4.2.1): it consists only of C(sp^2) atoms and has as many exocyclic double bonds as possible. This compound has been postulated as an intermediate in flash pyrolysis reactions of tetramethyl-tetrakis(chloromethyl)naphthalenes **147** leading to polycycle **149**, but was not detected directly (Scheme 4.33) [101].



147a: R^1 = CH$_2$Cl, R^2 = Me
147b: R^1 = Me, R^2 = CH$_2$Cl
148 **149**

Scheme 4.33

In polycyclic aromatic π-systems, one may detect radialene substructures when an appropriate resonance structure is considered. As long as the π-electrons in the aromatic ring(s) are fully delocalized, the question of the radialene character remains a hypothetical one. For example, benzannulated *n*-methylene-cyclo($n + 2$)alkenes, 1,2,3-trimethyleneindane (**150**) do not belong to the [5]radialenes. But how about biphenylene (**151**), for example? Precise

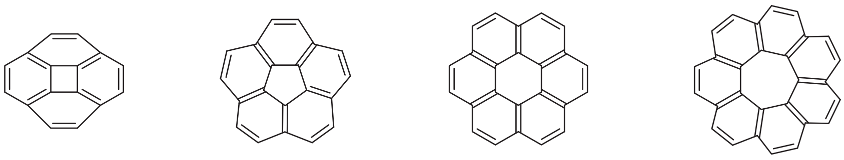


Z = CH=CH (**a**),
S (**b**)

150 **151** **152**

Bond distances (Å) in **151**: *a* 1.5174(13), *b* 1.3750(12), *c* 1.4248(10), *d* 1.3917(10), *e* 1.4283(12).

Figure 4.3 Localized bond structures of **150**, **151** and **152**.



153 **154** **155** **156**

Figure 4.4 The parent [*n*]circulenes **153**–**156**.

bond parameters, obtained from a low-temperature X-ray crystal structure determination, indicate a distinct bond alternation in the two aromatic rings, which corresponds to a [4]radialene-like core of the molecule (Figure 4.3) [102, 103]. Nevertheless, **151** is considered as two aromatic benzene rings connected by two adjacent σ bonds. The bond localization was discussed in terms of a strain-induced Mills–Nixon effect [104]. On the other hand, the completely planar benzo[1,2-*c*:3,4-*c*′:5,6-*c*″]trithiophene (**123a**) and -triselenophene (**123b**) are considered as proper [6]radialenes with no aromaticity in the central six-membered ring [93] (see Section 4.2.4). Benzothiophene and thienothiophene derivatives **152a,b** [105][1] may belong in the same category. It is interesting to note that the prediction of enhanced π-stacking ability of **152a** due to π-depletion in the inner ring has recently led to the development of its sodium 2,2′-disulfonate derivative as a molecular sensor for caffeine [106].

A radialene-type core also appears in the appropriate bond resonance structures of the so-called [*n*]circulenes, where the central *n*-sided ring is surrounded by *n* fused benzenoid rings (Figure 4.4) [107]. As the first members of the homologous series, the parent structures comprise the [3]circulene (probably too strained to be accessible by synthesis), the so far unknown [4]circulene (**153**), [5]circulene or corannulene (**154**) which is a substructure of buckminsterfullerene (C_{60}), the long-known [6]circulene or coronene (**155**), and [7]circulene (**156**).

The first [4]circulene has been obtained only very recently. King and coworkers have prepared **158** in a three-step synthesis starting from the naphthoquinone photodimer **157**, with a cobalt-catalyzed alkyne cyclotrimerization as the key step

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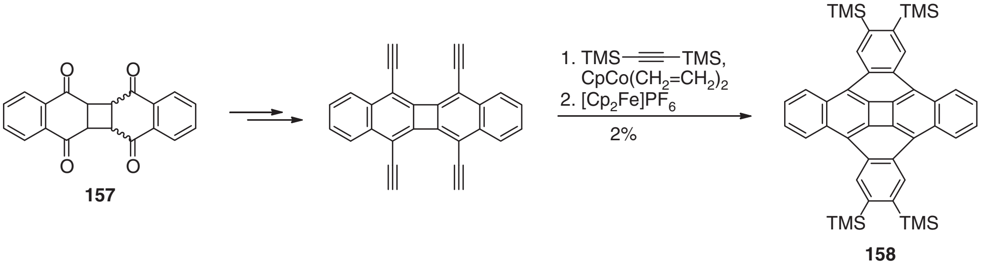
[1] Structural data for **152a** are not available; for **152b**, the experimentally determined bond lengths in the six-membered ring are 1.439–1.452 Å, those of the radiating C–C bonds 1.363–1.376 Å.

(Scheme 4.34) [108]. According to the experimentally determined bond lengths, a natural bond orbital (NBO) bond order analysis and the calculated nucleus-independent chemical shifts (NICSs), the bowl-shaped circulene **158** can be considered as a fourfold benzoannulated [4]radialene, not a fourfold napthoannulated cyclobutadiene.



Scheme 4.34

For a failed attempt to prepare the parent compound **153**, see Ref. [109].

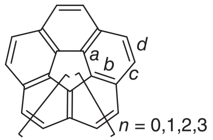
If one takes the bond length pattern (Table 4.1) as a topological criterion for radialene-like character, one may find it to some extent in the geometry of corannulene (**154**). This is supported by calculations of the molecular electrostatic potential, which show five minima at the bonds exocyclic to the central ring and another five at the peripheral double bonds of the six-membered rings [115]. These structural features, with rather localized double bonds, are also reflected in fullerene C_{60}, which consists of three corannulene substructures. Notably, the chemical reactivity of C_{60} is dominated by addition reactions at a 6–6 bond (connecting two six-membered rings) [116], and it fits into this picture that the first addition of dichlorocarbene to corannulene also occurs at a radial (6–6) C=C bond [117].

Coronene (**155**) is a planar, polycyclic benzenoid hydrocarbon with almost complete bond length equalization (Table 4.1); it can be viewed as a substructure of graphite. For [7]circulene (**156**), a flat, saddle-shaped molecule with rapid inversion of the twisted seven-membered ring in solution, the limitation of the bond length criterion becomes obvious: the lengths of bonds *a* and *d* correspond to localized single and double bonds, respectively, but bonds *b* and *c* do not fit into the radialene-type picture, perhaps as a consequence of the out-of-plane deformation of the carbon atom shared by these two bonds. For the three polycyclic conjugated systems **154–156**, *ab initio* calculated density maps show the presence of counter-rotating ring currents: a paratropic current at the inner ring and a diatropic current at the outer rim of the system [112, 114].

4.3
Structural and Bonding Properties

The structural aspects of [*n*]radialenes have been reviewed [7, 118]. Experimental data on molecular symmetry or shape and bond geometry have been collected

Table 4.1 Bond lengths (Å) in [*n*]circulenes.



[*n*]Circulene	Shape, symmetry	Method[a)]	*a*	*b*	*c*	*d*	References
Quadrannulene (**158**)	Bowl-shaped, C_{2v}	B3LYP/6-311G**	1.45	1.36	1.48	1.46[b)]	[108]
Corannulene (**154**)	Bowl-shaped, C_{5v}	experimental (−183 °C)	1.4151(16)	1.3790(14)	1.4464(16)	1.3831(15)	[110]
Coronene (**155**)	Planar, D_{6h}	experimental	1.425(4)	1.433(4)	1.415(4)	1.346(4)	[111]
		MP2/6-31G*	1.424	1.423	1.421	1.377	[112]
[7]Circulene (**156**)	Saddle-shaped, C_2	experimental	1.453–1.467	1.427–1.432	1.417–1.427	1.342–1.345	[113]
		RHF/6-31G**[c)]	1.466	1.411	1.421	1.334	[114]

a) Data were determined experimentally by X-ray diffraction analysis or obtained from quantum chemical calculations.
b) Further bond lengths in the benzene ring: 1.40, 1.38, 1.39 Å.
c) Averaged values are given.

for many radialenes, and most of the radialenes that have been synthesized more recently have also been characterized by single-crystal X-ray structure analysis.

According to experimental evidence and theoretical calculations, the parent systems of [3]- and [4]radialene are planar and have D_{nh} symmetry. For [5]- and [6]radialene, the D_{nh} structures do not represent local minima on the potential energy hypersurface. A slightly twisted planar conformation has been predicted for the still unknown [5]radialene (see below, however: note added in proof), and for [6]radialene both a chair and a slightly less stable twisted-boat conformation represent local energy minima [118, 119]. With increasing number and size of substituents, deviations from these conformations are found, in particular for fully substituted radialenes. Not unexpectedly, steric strain is relieved primarily by changes in the endo- and exocyclic torsion angles [120]. Some interesting structural information, reported since the last reviews were published, is given in the following section.

Hexaaryl- and hexapyridyl[3]radialenes are sterically overcrowded molecules. According to NMR spectra, the (hetero)aryl rings are tilted against the plane of the radialene core and adopt a propeller conformation in solution; several crystal structure analyses [24, 26, 38, 40] reveal the double three-bladed propeller structure with a nearly planar radialene core.

Substituted [4]radialenes can have a planar four-membered ring as in tricyclic radialene **67** [63] or a puckered ring as in octamethyl[4]radialene (**71**) [67]. Notably, the donor–acceptor-substituted [4]radialene **69**, in spite of its four aryl substituents, features a completely planar four-membered ring [64], but steric strain is obviously relieved by pyramidalization of the two dicyanomethylene carbon atoms and their offset from the ring plane.

Benzotrithiophene (**123a**) and benzotriselenophene (**123b**) have joined the untypical [6]radialene **152b** as examples of [6]radialenes with (practically) planar six-membered rings [93]. The solid-state structure of all-(*E*)-7,8,9,10,11,12-hexaethyl[6]radialene (**115**) [121] is similar to the hexamethyl analog (**113**) [122], the ring adopting a chair conformation with effective S_6 ($\bar{3}$) symmetry and absolute torsion angles in the range 45.4–45.8°. Gas-phase electron diffraction studies had shown the cyclohexane ring of the hexamethyl derivative to be more puckered (torsion angles 52.8°) [123]. All-*E*-hexabromo[6]radialene (**119**) also exists in the chair conformation (C_i) [91]. For dodecamethyl[6]radialene (**72**) both a chair conformation (ring torsion angles ±56°) [67] and an almost ideal twist-boat conformation [88] are known. Twist-boat conformations have also been observed for hexakis(1,3-benzothiol-2-ylidene)cyclohexane (**116b**) [90] and 7,9,11-tris(2,6-dimethylphenyloxy)[6]radialene (**121**) [92].

The characterization of radialenes as cyclic cross-conjugated polyolefins with no aromatic stabilization follows from a range of diverse observations and findings, which include the high chemical reactivity of the parent systems, the bond geometry, thermochemical considerations, and the results of theoretical calculations. Characteristic values of bond lengths are given in Table 4.2. As for the bond geometry of the parent systems, only that of [3]radialene has been determined experimentally; for [4]- and [6]radialene, the X-ray diffraction data of **67** and **113**, respectively, should be representative. On the other hand,

Table 4.2 Theoretically calculated[a] and experimental[b] bond lengths (Å) in radialenes.

Bond	[3]Radialene (2)	[4]Radialene (3)	[5]Radialene (4)	[6]Radialene[c] (5)
C=C	1.332[d] (1.330(4)[e])	1.332 (1.326[f])	1.342	1.343 (1.332(3)–1.337(3)[g])
C–C	1.454[d] (1.437(4))	1.488 (1.484(2)–1.492(2))	1.493	1.493 (1.493(3)–1.495(2))

a) B3LYP/6-311G [119].
b) In parentheses.
c) Chair form.
d) For **2**, values of 1.333 and 1.442 Å have been obtained using B3LYP/6-311+G* [124].
e) Determined by electron diffraction in the gas phase [11]; an earlier study gave $d(\text{C=C}) = 1.343 \pm 0.02$ Å and $d(\text{C–C}) = 1.453 \pm 0.02$ Å [125].
f) Data for **67** [63].
g) Data for **115** [122].

a geometry optimization of radialene structures at different levels of theory is an integral part of most of the recently published theoretical papers that deal with radialenes in one way or another ([3]- and [4]-radialene [119, 124, 126–134], hexaethynyl[3]radialene [124, 135, 136], hexacyano[3]radialene [124], [5]- and [6]radialene [119, 133, 137], and perfluororadialenes [53, 138]). The reported exocyclic bond lengths are typical for olefinic double bonds, and the endocyclic bond lengths correspond to $\text{C(sp}^2\text{)–C(sp}^2\text{)}$ single bonds. The smaller values for the ring bonds in **2** and **3** compared to **4** and **5** can be attributed to the particular bond structure and different hybridization of the ring atoms in small rings.

The calculation of molecular energies of [3]radialene and other C_6H_6 isomers including benzene was a part of recent studies, where the reliability of several popular DFT and advanced *ab initio* methods has been evaluated [130, 132, 139, 140] by comparison with the experimentally determined value of $\Delta H_f^{o} = 94.7\ \text{kcal mol}^{-1}$ ($396.12\ \text{kJ mol}^{-1}$) [13a]. Because [3]radialene showed an exceptional deviation from the experimental value compared to the other C_6H_6 isomers with some of the methods, earlier doubts about the correctness of the experimental value, which was not determined calorimetrically, have been recalled, and it has been suggested that the value $\Delta H_f^{o}{}_{(g)} = 104.6\ \text{kcal mol}^{-1}$, obtained with the *ab initio* post-Hartree–Fock method G4MP2, is a better estimate [140]. Recent energy calculations place [3]radialene 84.5–85.4 kcal mol^{-1} above benzene (MP2, CCSD(T) [130]; G3MP2 [141]; and G4MP2 [140]). In a benchmark study on the theoretical calculation of the energy separation of C_8H_8 isomers, [4]radialene was found to be higher in energy by 63.3 kcal mol^{-1} than styrene (W1-F12 thermochemical protocol) [134]. It is clear that for both radialenes angular and torsional strain make the major contribution to the energy separation from the aromatic reference systems. Thermochemical considerations concluded that the stabilization of [3]radialene by exocyclic conjugation, if any, amounts to not more than 5 kcal mol^{-1} [141].

Estimation of resonance energy by spin-coupled valence bond calculations [129] and the application of newly developed aromaticity indices considering the cyclic π-electron delocalization [142, 143] have confirmed that [3]- and [6]radialene are nonaromatic. As far as the magnetic criterion for aromaticity of conjugated π-electron systems is concerned, recent calculations of the NICS(1) value for [4]radialene [144]) and current density maps [133, 145] have confirmed earlier statements that [*n*]radialenes (including their dianions with $n > 3$ [133]) are nonaromatic molecules.

Note added in proof:
Section 4.2.2. A [4]radialene with an unusual substitution pattern, 1,2-bis(diarylmethylene)-3,4-bis(dicyanomethylene)cyclobutane, has been isolated, among other products, from the uncatalyzed reaction of a tetraaryl-[5]cumulene and TCNE [146].

Section 4.2.3. The parent [5]radialene has been synthesized at last [147]. Key to success was a low-temperature decomplexation of a [5]radialene-bis($Fe(CO)_3$) complex, that had been prepared from a 2,6-dichloro-3-oxa-[5]dendralene precursor. A 30 mM solution of the hydrocarbon in acetone had a half-life time of around 16 min at −20 °C. According to G4(MP2) calculations for the gas phase, a Diels-Alder reaction, which leads to dimerization/polymerization, is outstandingly facile.

Misaki and coworkers have pepared several new electron-rich [5]radialenes structurally related to **106**, but containing one or two vinylogous 1,3-dithiole groups, and have studied their redox behavior by cyclic voltammetry [148–150].

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5

Oxocarbons, Pseudo-oxocarbons, and Squaraines

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5.1

Introduction

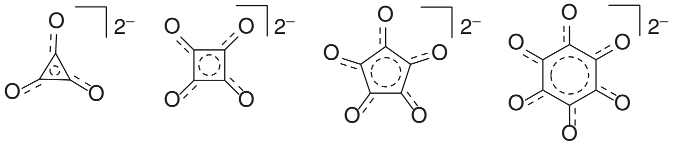
Oxocarbons are organic compounds consisting only of carbon and oxygen; in their neutral state, they exist as diacids, and their anions possess the general formula $C_nO_n{}^{2-}$, where $n > 2$ and generally $= 3 - 6$. Oxocarbons have been the focus of research since the nineteenth century, when the croconate (**3**, $n = 5$) and rhodizonate (**4**, $n = 6$) anions were first synthesized [1]. The squarate anion (**2**, $n = 4$) was later synthesized by Cohen *et al.* in 1959, and the oxocarbon deltate anion (**1**, $n = 3$) was synthesized by Eggerding and West in 1976 (Figure 5.1) [2].

The literature on oxocarbons has been summarized several times, the most comprehensive reviews being the monograph by West and the review by Seitz and others [1, 3], as well one review from 1992 by our group [4]. It has been more than 20 years since the publication of the last review on the subject, despite several brief comments about these compounds in the recent literature [5].

Oxocarbons are not only study objects in their own right but can also serve as model compounds for other, related systems which are obtained by replacing one or all of their carbon atoms by isovalent other atoms (e.g., sulfur) or groups (e.g., imines). Especially in the case of several such replacements, a large variety of derivatives results quickly (see reference to the squaraines, etc., discussed later). Formally, the oxocarbons themselves are "replacement" compounds, of course, because they are radialenes in which methylene groups have been replaced by oxygen atoms (see Chapter 4 on radialenes).

The oxocarbons exhibit numerous interesting properties, including planar cyclic structures, high molecular symmetry, π-delocalized systems, and singular electronic absorption spectra due to the Jahn–Teller effect [6]. Experimental evidence for the delocalized structures of these compounds was obtained by Hirata *et al.* using infrared absorption spectroscopy [7]. These studies verified the absence of the band corresponding to the vibration mode $\nu(C{=}O)$ that normally occurs in the 1850 to 1710 cm^{-1} region. Further studies revealed that variations in ring size cause a modification in the electron delocalization of the respective oxocarbon, with larger rings resulting in less electron delocalization [7, 8]. From

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

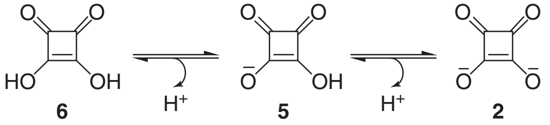


1 **2** **3** **4**

Figure 5.1 Chemical representation of deltate **1**, squarate **2**, croconate **3**, and rhodizonate **4** dianions.

this point of view, the deltate ion **1** is the only oxocarbon considered to be aromatic. It exhibits high stability due to more balanced charge distribution compared with the other oxocarbons; this stability diminishes as the size of the ring increases. The other oxocarbons are considered nonaromatic, conjugated systems. Theoretical calculations have been made for oxocarbon and pseudo-oxocarbon ions for many years [6, 9], including in this category even the neutral $[CO]_n$ species, despite their thermodynamic instability [10].

The conjugate acids, $C_nO_nH_2$, possess high dissociation constants, indicating the increased stability of their corresponding anions $C_nO_nH^-$ and $C_nO_n^{2-}$ (Scheme 5.1).



Scheme 5.1

For example, the pK_1 and pK_2 values are 0.8 and 2.2, respectively, for the $n = 5$; 0.5 and 3.5 for $n = 4$; and 4.3 and 4.7 for $n = 6$ system [3]. Recent work on the squaric acid system **6** demonstrated that the acid strength in DMSO solution is weaker than in water; in this case, pK_1 and pK_2 values were calculated to be 0.80 and 0.84, respectively. In dilute solutions, the squarate dianion form **2** predominates, whereas in concentrated solution the hydrogen-squarate species **5** is the dominant form [11].

The high molecular symmetry of the oxocarbons **1**–**4** is verified by their Raman spectra, in which the spectroscopic profile reveals the Jahn–Teller effect that is characteristic of these species. The observed splitting is due to the double degeneracy of the first excited electronic state of the molecules and affects their respective vibrational spectra [6, 9a]. Raman measurements performed under nonresonance conditions display bands that are attributed to nontotally symmetric modes with equal or higher intensities than the bands of the totally symmetric modes [12]. Of particular note is the carbonyl stretching mode, a totally symmetric mode that appears in the Raman spectrum as a relatively low intensity band compared to the bands from nonsymmetric modes, such as the CC stretching of the ring and ring deformation [13].

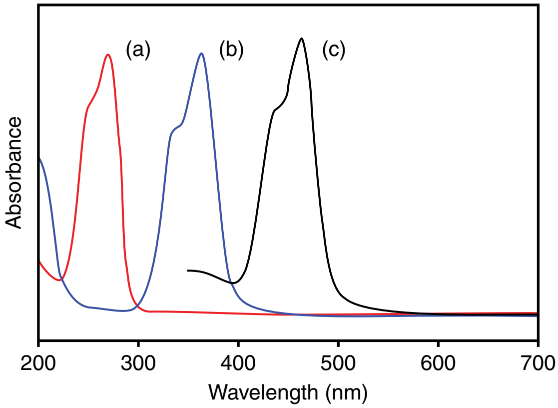


Figure 5.2 Electronic spectra of oxocarbons (a) squarate **2**, (b) croconate **3**, and (c) rhodizonate **4** dianions in aqueous solutions.

The electronic spectra of the potassium salts of squarate **2**, croconate **3**, and rhodizonate (**4**) ions in aqueous solution exhibit bands with high molar absorptivity, in the order of $10^4\,\mathrm{l\,mol^{-1}\,cm^{-1}}$, and a similar profile for all the spectra, with unfolded bands (Figure 5.2).

The absorption maxima in these spectra are always accompanied by a shoulder in the highest energy region that also displays high molar absorptivity. These ions exhibit strong absorption in the visible and ultraviolet regions, with the exception of the deltate derivative **1**, which absorbs at wavelengths below 200 nm. In the case of the rhodizonate salt **4**, the absorption maximum occurs at approximately 500 nm; the croconate **3** absorbs at approximately 350 nm and the squarate **2** absorbs at 250 nm. Studies have demonstrated that the shift of the absorption bands to low energies is directly related to ring size. This electronic behavior explains one of the most important applications of the oxocarbons: their use as spectroscopic probes [1].

The ^{13}C NMR spectra of dianions **1**–**4** (sodium salts) are simple, with one singlet in the low-field region between $\delta = 204$ and 130 ppm. Note that for rhodizonate **4**, the chemical shift is at a lower field (204 ppm) than for croconate **3** (189 ppm), which in turn resonates at lower field than squarate **2** (174 ppm) [14]. This observation suggests that there is more charge localized on the squarate ring than on the croconate ring and, in turn, on the croconate ring than the rhodizonate ring. Because of these singular characteristics, these compounds are valuable spectroscopic molecular markers, because any change in the molecular structure caused by any kind of chemical or physical interaction can also change the spectroscopic properties of such species.

The structural simplicity of species **1**–**4** is further confirmed in the solid state through single crystal X-ray analysis [15]. Based on these studies, it was concluded that the squarate ion **2** exhibits D_{4h} molecular symmetry, the croconate ion **3** exhibits D_{5h} molecular symmetry and the rhodizonate ion **4** exhibits D_{6h} molecular symmetry. Additional spectroscopic studies concluded that deltate

Table 5.1 Number of theoretically expected and observed bands for squarate ion **2** by both Raman and infrared vibrational techniques.

Spectroscopic technique	Squarate ion (theoretical)					Squarate ion (experimental)
	C_{2v}	C_{2h}	C_{4v}	D_{2d}	D_{4h}	
Polarized Raman	7	5	3	4	2	2
Raman total	18	9	13	13	7	7
Infrared	15	9	7	7	4	4

Table 5.2 Theoretically expected and observed bands for croconate ion **3** by both Raman and infrared vibrational techniques.

Spectroscopic technique	Croconate ion (theoretical)	Croconate ion (experimental)
	D_{5h}	
Polarized Raman	2	2
Raman total	7	5
Infrared	4	3 or 4

anion **1** shows D_{3h} symmetry [16]. To determine the point group of the squarate **2** and croconate anions **3**, the theoretical number of infrared and Raman bands for five different point groups (C_{2v}, C_{2h}, C_{4v}, D_{2d}, and D_{4h}) were compared with the total number of bands obtained experimentally (Tables 5.1 and 5.2) [15a,b].

The single-crystal X-ray analysis of potassium squarate monohydrate, determined in 1964, confirmed its D_{4h} symmetry [15c]. The D_{5h} symmetry of the croconate ion **3** was confirmed in the same way at about the same time.

Patton and West studied the electrochemistry of these species. The radical anions of squarate **2**, croconate **3**, and rhodizonate **4** were characterized in dichloromethane using the electron paramagnetic resonance (EPR) technique [17]. Likewise, Carré, Fabre, and collaborators obtained the UV/visible and EPR spectra of these radical dianions, produced electrochemically in dimethylformamide [18]. The oxidation potential of the oxocarbonic acids was determined in perchloric acid solution using platinum electrodes. The oxidative process was proposed to proceed in two stages, beginning with the transfer of charge from substrates at the electrode. Subsequently, the oxidation product is desorbed from the electrode and hydrated [19].

Oxocarbon anions are frequently used as photoreceptors, organic semiconductors, and in nonlinear optical applications [20]. Rhodizonate salts **4** are widely used as analytical reagents for metal salts, typical examples being lead traces in forensics, to analyze radium in drinking water and to identify iron and barium [21]. Rhodozinate **4** is also interesting because of its luminescent properties [21, 22].

Squaric acid **6** is often used as a raw material in products for biochemical and photoconductive processes [22]. The conjugate base of squaric acid (the squarate dianion **2**) is also used in biological systems as an electrostatic mimic of common, negatively charged groups [23].

The potential of oxocarbon anions in coordination chemistry has already been mentioned, and they have also been employed in supramolecular chemistry. Recent research has explored squarate **2** and croconate **3** dianions as ligands for the construction of coordination polymers because these ligands possess many metal coordination sites (see below). The squarate dianion **2** has been frequently used as a poly-functional (μ_1 to μ_6 bridges) ligand that also permits hydrogen bonding and $\pi\cdots\pi$ stacking interactions to form more extended networks [24]. The croconate anion **3** is also a ligand for transition metals [25] and has been investigated in a similar manner [25a,d,l, 26]. Because oxocarbons exhibit supramolecular interactions, they are currently being used to understand the properties of ion–metal interactions, and a thorough understanding of these properties will enable the intelligent incorporation of supramolecular compounds in the development of novel materials.

Recently, Tsoureas and coworkers [27] described the use of a mixed-sandwich U(III)-complex in the reductive coupling of CO. In this work, the authors demonstrate the effect of the steric environment around the uranium center in the reduction process by the complex in formation of oxocarbons, in particular squarate **2** and croconate **3** species.

5.2
Oxocarbons and Coordination Chemistry

The number of studies focusing on metal–ligand interactions of oxocarbons has increased significantly in the past 20 years [12, 21, 24a,b, 28]. The first studies on this topic involved the attempted complexation of these compounds with transition metals to form sandwich compounds [2b, 29]. The aim of these investigations was to study the various coordination geometries and spectroscopic characteristics of the complexes. Most of the work focuses on squarate **2** and croconate **3** dianions. As these anions possess four ($C_4O_4^{2-}$) and five ($C_5O_5^{2-}$) potential oxygen donor atoms, they could interact with a wide variety of transition metal ions and lanthanide ions. Thus, in principle, complexes with very different molecular structures with one-, two-, and three-dimensional architectures might be obtained [28d]. In particular, their potential as bridging ligands offers materials with new spectroscopic, magnetic, and optical properties [24a–c, 30]. Tables 5.3 and 5.4 show the schematic representations of all coordination modes that have been reported for squarate **2** and croconate **3** dianions toward transition metals and lanthanides obtained by X-ray diffraction analysis. The synthesis of these coordination compounds is usually performed by reactions between a metallic precursor, which can be chloride, nitrate, perchlorate, acetate, and so on, and the oxocarbons salts (lithium, potassium, sodium, ammonium, etc.). Three synthetic

Table 5.3 Coordination modes of squarate dianion **2** toward transition metals and lanthanides.

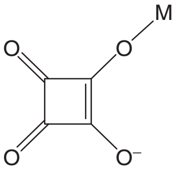
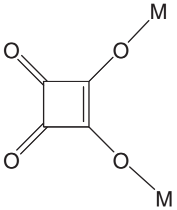
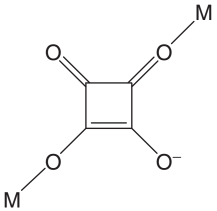
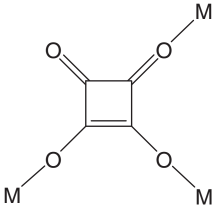
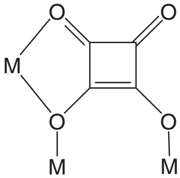
Number of metals	Coordination mode	Structural schematic representation	References
1	Monodentate **(I)**		[28a,b]
2	μ-1,2-Monodentate **(II)**		[24a,b, 28a,c,d]
	μ-1,3-Monodentate **(III)**		[24a,b, 28a,c,d]
3	μ_3-Tris-monodentate **(IV)**		[31]
	μ_3-1-Monodentate-2,3-bidentate-2-μ-oxo **(V)**		[32]

Table 5.3 (*continued*)

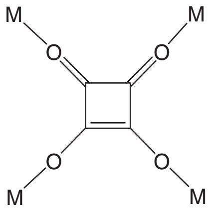
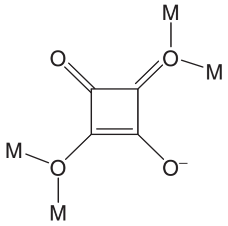
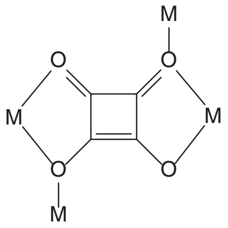
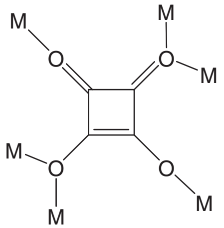
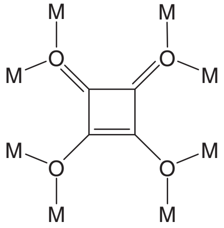
Number of metals	Coordination mode	Structural schematic representation	References
4	μ_4-Tetrakis-monodentate **(VI)**		[28d, 32, 33]
	μ_4-1,3-μ-Oxo **(VII)**		[32]
	μ_4-1,2,3,4-Bis-bidentate-1,3-μ-oxo **(VIII)**		[32]
6	μ_6-1,3-μ-Oxo-2,4-monodentate **(IX)**.		[24b,r]
8	μ_8-1,2,3,4-μ-Oxo **(X)**		[24v, 34]

Table 5.4 Coordination modes of croconate dianion **3** toward transition metals and lanthanides.

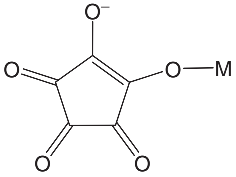
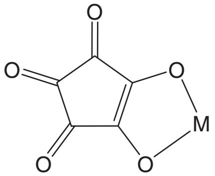
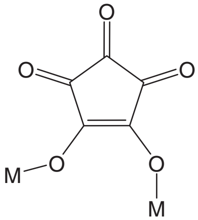
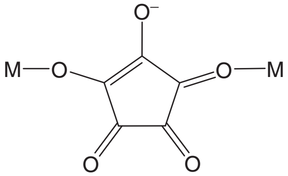
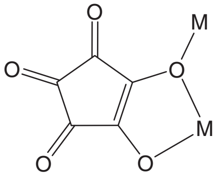
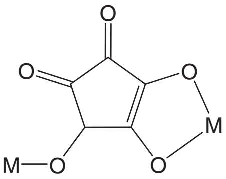
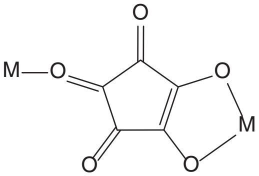
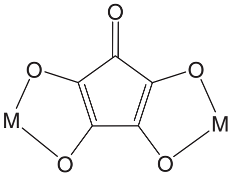
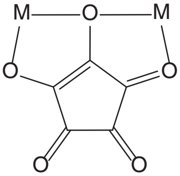
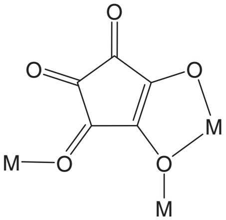
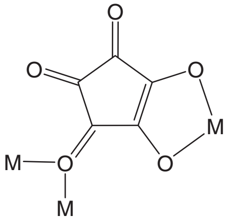
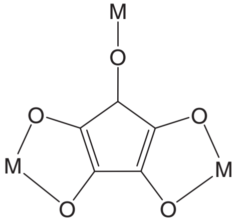
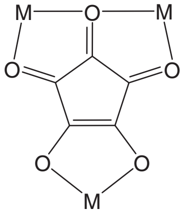
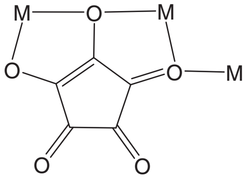
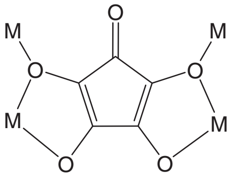
Number of metals	Coordination mode	Structural schematic representation	References
1	Monodentate **(XI)**		[35]
	Bidentate chelate **(XII)**		[28c, 36]
2	μ-1,2-Monodentate **(XIII)**		[37a]
	μ-1,3-Monodentate **(XIV)**		[38]
	μ-1,2-Bidentate-1-μ-oxo **(XV)**		[38]

Table 5.4 (*continued*)

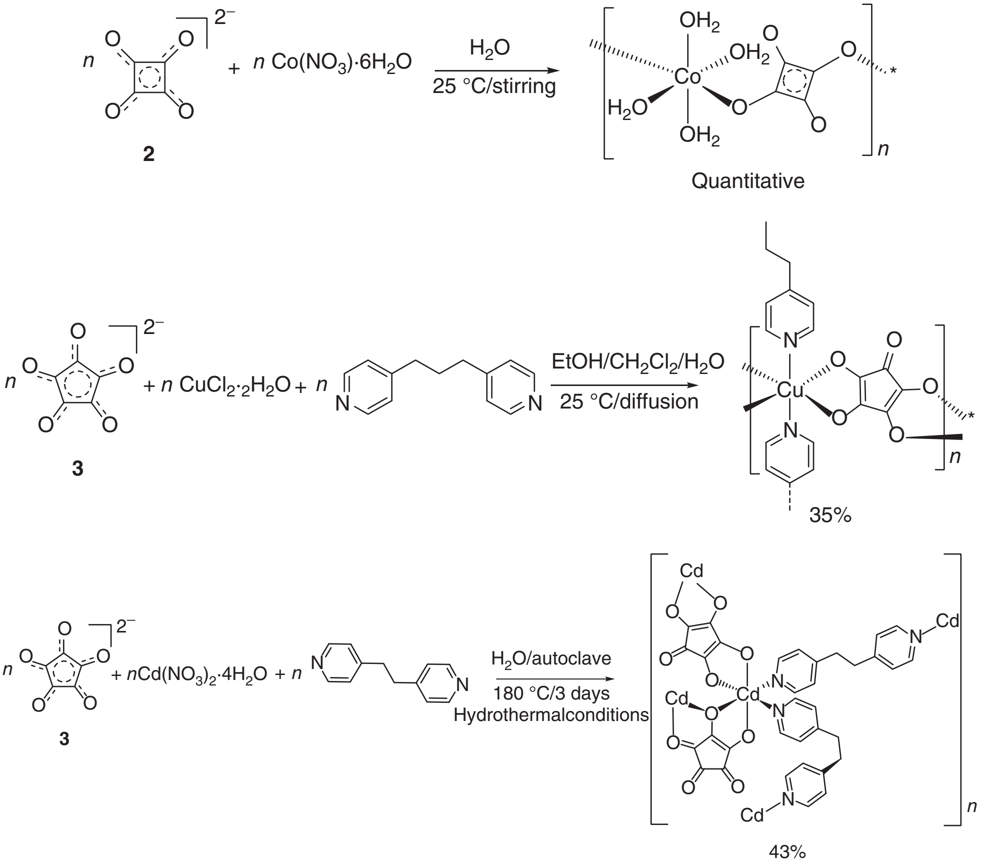
Number of metals	Coordination mode	Structural schematic representation	References
2	μ-1,2-Bidentate-3-monodentate **(XVI)**		[38]
	μ-1,2-Bidentate-4-monodentate **(XVII)**		[31, 38]
	μ-1,2,3,4-Bis-bidentate **(XVIII)**		[37]
2	μ-1,2,3-Bis-bidentate **(XIX)**		[37b]
3	μ3-1,2-Bidentate-2-μ-oxo-3-monodentate **(XX)**		[25g]

(*continued overleaf*)

Table 5.4 (*continued*)

Number of metals	Coordination mode	Structural schematic representation	References
	μ3-1,2-Bidentate-3-μ-oxo **(XXI)**		[25h]
	μ3-1-Monodentate 2,3,4,5-Bis-bidentate **(XXII)**		[39]
3	μ3-1,2,3-bis-bidentate-4,5-bidentate **(XXIII)**		[38, 40]
	μ3-1,2,3-Bis-bidentate-1-μ-oxo **(XXIV)**		[41]
4	μ4-1,2,3,4-Bis-bidentate-1,4-μ-oxo **(XXV)**		[37b]

procedures: stirring, diffusion, and hydro/solvothermal, are currently applied in their preparation. Scheme 5.2 shows some examples of these procedures [28c, 37].



Scheme 5.2

The most common coordination mode for squarate anion **2** is the μ-1,3-monodentate (motif **III**, see Table 5.3) bridging motif [42]. Chelation of a transition metal by squarate anion **2** was originally postulated on the basis of spectroscopic evidence [43]. This probably arose from a misleading analogy with the oxalate ($C_2O_4^{2-}$) anion. In fact, the squarate geometry and the usually measured metal–oxygen bond lengths are such that the chelation can only be achieved by way of a wide deformation of the involved O–C–C angles. Based on the bite angle, it has been established that only the largest cations have a chance to be chelated [28a,b], like trivalent lanthanides and alkali-earth cations [33]. On the other hand, the most common coordination mode of croconate anion **3** is not a bridging mode but a terminal one, the bidentate chelating (motif **XII**, see Table 5.4). The Cambridge Structural Database (CSD), mentions 26 deposited structures of metal complexes in which the croconate anion **3** prefers this coordination mode.

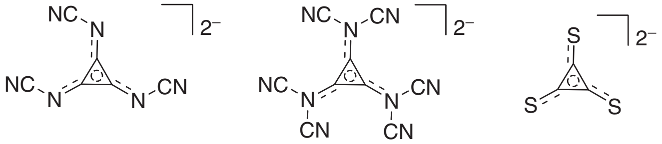
Squarate **2** and croconate **3** oxocarbons have been employed widely in crystal engineering as construction blocks along with transition metal ions because of their magnetic and optical-electronic properties [24a,c, 30, 44]. Squaric acid **6** and its deprotonated forms (hydrogen-squarate **5** and squarate ions **2**) are known as *ligands* capable of propagating magnetic interactions because of their various coordination modes. In addition, compounds with different electronic and vibrational properties can be produced by varying the metal or the synthetic method [15c, 45]. Both dianions **2** and **3** can also be used for the preparation of network topologies in supramolecular chemistry, exploiting the formation of strong hydrogen bonds [46]; these supramolecular species can exhibit properties similar to those of zeolites, including strong luminescence and even magnetism in the case of metallic complexes [47].

5.3
Pseudo-oxocarbons

The reactivity of the oxocarbon ions **1**–**4** has been extensively investigated in the past few decades, resulting in the synthesis of numerous oxocarbon derivatives. Studies have described the reactivity of these derivatives as well as a large number of possible compounds that can be used to substitute the carbon atoms in the precursors [48]. The complete or partial substitution of the carbonyl oxygen atoms leads to the formation of compounds called *pseudo-oxocarbons* [45a]. Each species can be considered to originate from an oxocarbon precursor in which one or more oxygen atoms have been replaced with other atoms or functional groups. However, few of these derivatives have been investigated in detail from a spectroscopic standpoint, such as vibrational (Raman and infrared) or nuclear magnetic resonance.

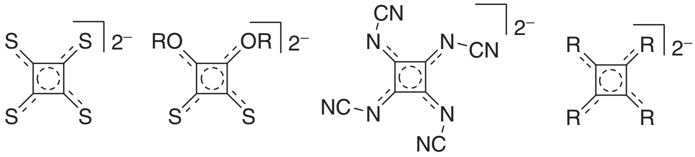
Oxocarbon derivatives either totally or partially substituted by phosphorus and selenium atoms or by nitrogenous groups are examples of the so-called pseudo-oxocarbons [4, 49]. Sulfur derivatives are also among these compounds, with the nature of the substituent group resulting in substantial electron delocalization, which is an interesting feature in the context of optical materials with nonlinear properties [20]. The most studied pseudo-oxocarbons and their respective oxocarbons are depicted in Figures 5.3–5.6.

The most studied pseudo-oxocarbons derived from the croconate dianion **3** are croconate violet [3,5bis(dicyanomethylene)cyclepentane-1,2,4-trionate] **17** and croconate blue [2,4,5-tris(dicyanomethylene)cyclepentane-1,3-dionate] **18** [16b, 17–19]. They can be obtained from the reaction between croconate **3** and malononitrile ($H_2C(CN)_2$), as can be seen in Scheme 5.3. These derivatives are of interest because of their reversible electrochemical character [20, 21], their strong absorption maxima in the visible region, which determine their intense colors (molar absorptivity in the range of $10^5\,l\,mol^{-1}\,cm^{-1}$), their delocalized π-system,



7 **8** **9**

Figure 5.3 The most common pseudo-oxocarbons derived from deltate **1**: tris(cyanoimino)deltate **7**, tris(dicyanomethylene)deltate **8**, and tritiodeltate **9**.



10 **11** **12** **13**

Figure 5.4 The most common pseudo-oxocarbons derived from squarate **2**: tetrathiosquarate **10**, 1,2-dithiosquarate **11**, tetra(cyanoimine)squarate **12**, and carbosquarate **13**.

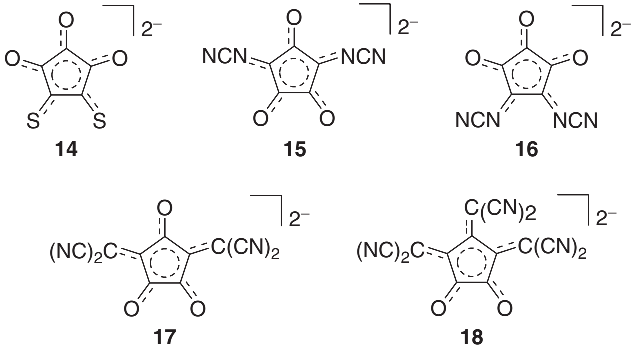
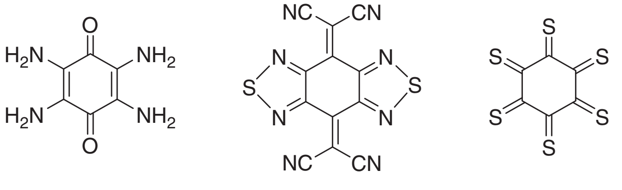


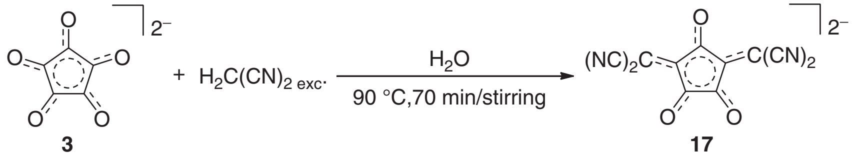
Figure 5.5 The most common pseudo-oxocarbons derived from croconate **3**: 1,2-ditihocroconate **14**, 1,3-bis(cyanoimine) croconate **15**, 1,2-bis(cyanoimine)croconate **16**, 1,2,3-tris(dicyanomethylene) croconate **17**, and 1,2-bis(dicyanomethylene)croconate **18**.



19 **20** **21**

Figure 5.6 The most common pseudo-oxocarbons derived from rhodizonate **4**: tetra(amine)-*p*-benzoquinone **19**, hexathiorhodizonate **20**, and tetracyanoquinodimethane **21**.

and their typical semiconductive properties [22, 23]. Because of these characteristics, the compounds are important for the development of novel materials for photophysical studies, the conversion of solar energy, and electrochromic applications [3, 13].

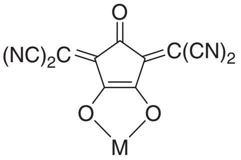
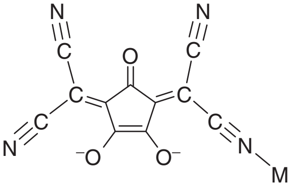
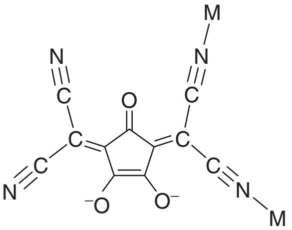
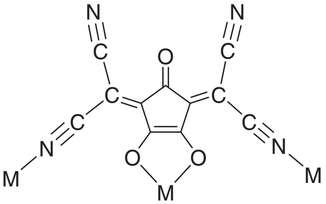


Scheme 5.3

In the literature, the crystal structures of the potassium salt [50] of anion **17** and those of the tetra(*n*-butyl)ammonium N(But)$_4$ [51], rubidium [52], caesium (two structures) [53], ammonium (NH$_4$) [54], and barium [55] croconate violet **17** salts are described. Mixed salts of **17** with rubidium–potassium [52], caesium–potassium [53], and lanthanide–potassium cations [56] are also known. These investigations revealed that the amount of water molecules present is affected by both cation size and crystal packing. In the triclinic salts (K, N(But)$_4$, NH$_4$, CsK, and Cs), the number of water molecules decreases with cation size: K and NH$_4$ salts contain two water molecules, the mixed salt (CsK) has only one water molecule, and, finally, Cs and NBut$_4$ are anhydrous. The Cs salts crystallize in a different system with a unit cell volume ($V = 1393.8(2)$ Å^3); this is bigger than the one observed for the other salts (around 680 Å^3), and allows the inclusion of one water molecule in the asymmetric unit. On the other hand, in mixed potassium–rubidium (RbK) and in rubidium (Rb) salts, the cation exchange (changing potassium for rubidium ion) does not modify the number of included water molecules and the crystal packing. A similar result was observed in lanthanide–potassium salts, where all compounds (La, Nd, Gd, and Ho) crystallize in the same space group (P–1) and contain the same number of water molecules (10 water molecules per croconate violet **17** ion). However, the Ba and MgK salts crystallize in the same space group ($P2_1/n$), but the volume of the unit cell for the Ba salt is bigger than that of the MgK salt (1623.0(3) and 1271.4(2) Å^3): This allows five water molecules in the Ba salt, although the MgK salt presents only two molecules of water per croconate violet **17** unit. In all these compounds, the water molecules are engaged in hydrogen bonds, thus enabling the stability in the solid state. All these results are in total agreement with those observed for croconate **3** compounds, where previous work from Braga and coworkers have pointed out the role of water molecules in the crystal packing [57]. As a general remark, water molecules are needed to fill the crystal voids, if the cation size is not enough to fill out the required spaces.

For these compounds it was verified that the greatest difference in CC bonds (ΔCC) of the pseudo-oxocarbon ring lies in the range of 0.039–0.053 Å, except for Cs salts which showed the largest ΔCC (0.107 Å). These values indicate that

Table 5.5 Schematic representation of the coordination modes exhibited by croconate violet **17** dianion.

Number of metals	Coordination mode	Structural schematic representation	References
1	Bidentate chelate, O,O-bonded **(XXVI)**		[56, 58]
	Terminal, N-bonded **(XXVII)**		[33, 58c]
2	Bridging, N,N-bonded **(XXVIII)**		[33, 58c]
3	**(XXIX)**		[58c]

a degree of electronic delocalization is observed in croconate violet **17**, which is similar to that observed for croconate **3** and squarate **2** oxocarbons. However, π-stacking interaction is not as effective as that observed in croconate **3** salts [57].

Pseudo-oxocarbons coordination chemistry has hardly been described in the chemical literature. Croconate violet **17** exhibits four different coordination modes as can be inferred from Table 5.5.

The most common coordination mode is by way of neighboring oxygen atoms (motif **XXVI**). These function as a chelate and have been observed with the transition metal salts of Co^{2+}, Cu^{2+}, and Zn^{2+} as well as those of La^{3+}, Nd^{3+}, Gd^{3+}, and Ho^{3+}. Another possibility is offered by the nitrogen atoms of dicyanomethylene groups in terminal or bridging modes [44b, 51, 58]. In this case, the terminal binding mode (**XXVII**) has been observed in the isostructural complexes $K_2[M(CV)_2(H_2O)_4]$ where M = Fe^{2+} and Co^{2+} and the bridging mode (**XXVIII**) in the Fe^{2+} binuclear compound $\{[Fe(2,2'\text{-bipy})CV(H_2O)_2]\_H_2O\}_2$ [58c]. The fourth coordination motif is a combination of the chelating and bridging patterns (**XXIX**) involving both the oxygen and nitrogen atoms. This has, for example, been recognized in a Fe^{2+} one-dimensional coordination polymer $\{[FeCV(H_2O)_2]\cdot 2H_2O\}_n$ [58c].

Some complexes with croconate violet **17** display intramolecular interactions in which the metal transmits electronic properties for electrocatalytic or electrochromic applications [44b]. Such intramolecular interactions can be understood as the most important driving forces existing in the solid state for the coordination compound, where the electronic properties are localized over the oxocarbon moieties. Croconate violet **17**, croconate blue **18**, and lithium croconate are highly soluble in water and also in many nonaqueous solvents, thus restricting their practical applications [59]. However, this solubility can be circumvented in the case of croconate violet, for example, by incorporating it in a protonated film of poly(4-vinylpyridine), which, after adequate treatment, exhibits interesting electrocatalytic properties [60].

In addition to the previously mentioned pseudo-oxocarbons, derivatives of the squarate ion **2** (or 1,2-dihydroxycyclebutene-3,4-dione **6** in the acid form) have been prepared with carbon chains, nitrogen, sulfur, and selenium as substituent species [61]. The study of thio-derivatives of pseudo-oxocarbons demonstrates the interest to understand the characteristics and chemical behavior of these derivatives, which could be useful for the preparation of reduced dimension materials with metallic or semiconductive properties [4].

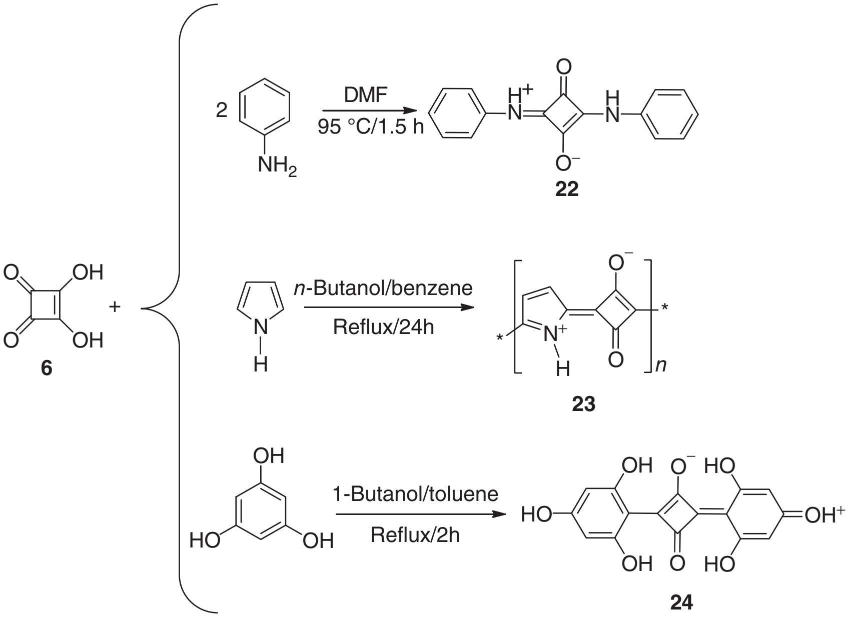
Squaric acid **6** possesses a unique structure that may enable new physicochemical properties as well as enhance other preexisting characteristics, such as its highly delocalized electron density.

5.3.1

Squaraines

Many authors agree that products with one or more *nitrogen groups* as substitutes of the oxygen atoms in the squarate **2** ion should be called rather squaraines. The first of this class of compounds was prepared in 1965 through the reaction of squaric acid **6** and pyrroles, which produced intensely colored condensation products [62]. But the literature also describes the synthesis of a squaraine obtained from resorcinol, which does not possess nitrogen atoms; therefore, there is no consensus on the concept of squaraines in the literature [63].

Squaraines are usually prepared by condensation of electron-rich aromatic or heteroaromatic compounds such as anilines [45a, 50], phenols [64], and pyrroles [65] with squaric acid **6**, as can be seen in Scheme 5.4.



Scheme 5.4

Thus, a huge number of systems has been synthesized by varying the donor system, providing a large number of squaraines with unique characteristics. In the solid state, many of these compounds exhibit an absorption band with a significant absorption coefficient. The self-aggregation that induces the high-absorption coefficients must be controlled in order to improve the efficiency of the device under study [66], if the electronic absorption of light in the visible region is the property to be achieved.

Semi-empirical calculations of the molecular orbitals reveal that both the ground and the excited states of squaraines exhibit donor–acceptor–donor (D–A–D) intramolecular charge transfer [67]. This class of compounds possesses a resonance-stabilized zwitterionic structure. Typical squaraines have a four-membered central electron-deficient ring and two-electron donor groups. As monomers in solution, these compounds strongly absorb at wavelengths above 600 nm with high molar absorptions ($\varepsilon > 10^5\,\mathrm{l\,mol^{-1}\,cm^{-1}}$) and intense fluorescent emission with a small Stokes shift; moreover, squaraines are photostable [66, 67].

In the majority of these studies, 1,3-substituted squaraines were employed, which are bonded by two-electron donor groups with a D–A–D configuration, allowing a high degree of intramolecular charge transfer [68]. Typically, the nitrogen atom is linked directly to the ring-like squaraine **22** [48a, 69]. These di-substituted squaraines exhibit high absorption coefficients (greater than $2 \times 10^5\,\mathrm{l\,mol^{-1}\,cm^{-1}}$), absorbing in the red, and are remarkably photostable [70]. They also exhibit photoconductivity and high absorption bands in the near infrared. Because of these properties, squaraines are used in xerography or in the fabrication of laser diodes. Preliminary studies demonstrate that noncentrosymmetric squaraines could possess nonlinear optical properties [71].

Squaraines with ring substituents which absorb and emit in the red and near-infrared regions have also been developed [72]. When compared to conventional Cy5–NHS systems (open chain), these derivatives have several advantages. For example, these compounds can be excited not only with red lasers but also with blue lasers or with luminescent diodes; being useful compounds, they can be excited all over the visible range of the electromagnetic spectrum. These compounds are particularly useful in biomedical applications due to their favorable spectral and photophysical properties, such as fluorescence [72].

Polysquaraines, also known as *wide absorption spectrum squaraines*, are currently under development. The optical properties of these systems are ideal for a variety of optical-electronic materials, such as squaraine-based near-infrared dyes, low-band gap polymers, and cation sensors; however, these compounds are difficult to solubilize and process [73].

Some squaraines have been synthesized for use in chemical sensors for the selective detection of specific analytes in biological and chemical systems [74], including the selective detection of biologically important cations, such as Na^+, K^+, Mg^{2+}, and Ca^{2+}. The squaraines enable sensitive detection due to their unique optical properties. Various chromophores linked to polyether systems can be utilized for cation capture [75]. Because the intermolecular charge transfer involved in near-infrared transitions of squaraines is highly sensitive to substituent and solvent changes [76], these compounds are ideal for the design of new fluoroionophores. Ionophores that are covalently linked to redox-active ligands have found important applications as metal ion probes as well as in studies involving metal ion transport through membranes [77].

The number of studies on squaraines has grown significantly in recent years, especially for the development of fluorescent materials, photoelectrochemical batteries, photoelectric conversion elements [78], substrates for photovoltaic cells, photoreceptors, and photoconductors [79]. Squaraine derivatives with well-differentiated behavior can be obtained by tailoring the substituent type. As a result of this tuning, a large variety of compounds has been described in the literature [61, 67, 69a, 71, 79]. In our group, we are interested in squaraines [20, 78, 80] which carry anilines and aliphatic groups as substituents.

Modified anilino squaraines have been widely utilized in surface-enhanced Raman resonance scattering (SERRS) spectroscopy. Their molecular structure displays a quadrupole D–A–D system that is characterized by an electron-deficient cyclobutendione (C_4O_2) bridge (Figure 5.7). The total structure can be represented in many ways, with the charge homogenously distributed over the entire molecule. Several theoretical studies have been conducted on this class of materials and their unusual nonlinear optical properties [4, 81].

The synthesis of anionic compounds derived from squaric acid possessing one or more π-delocalized substituents, such as dicyanomethylene groups,

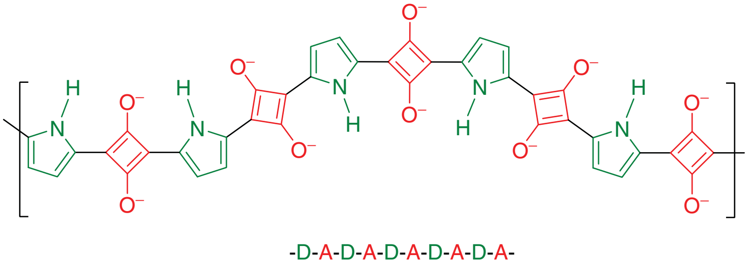


Figure 5.7 General structure of donor–acceptor–donor quadrupolar system of cyclobutendione (C_4O_2) in the bridge with deficient electronic system.

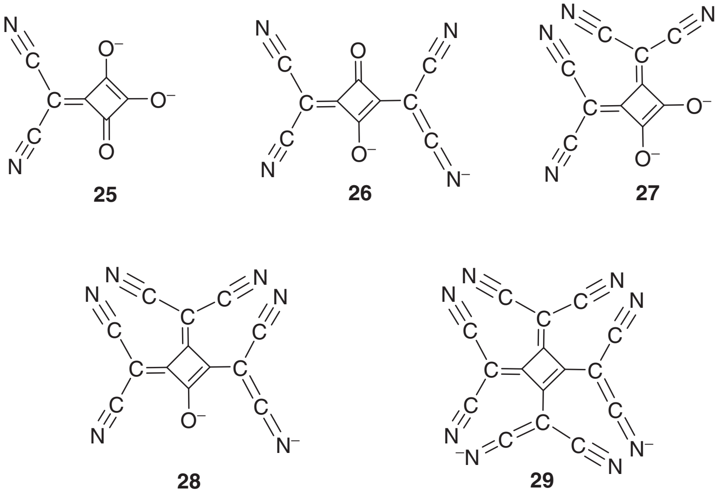
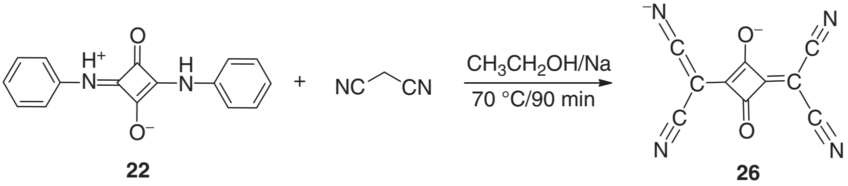


Figure 5.8 Molecular structures of substituted squaraines: mono(dicyanomethylene) squarate **25**; *trans*-bis(dicyanomethylene)squarate **26**; *cis*-bis(dicyanomethylene)squarate **27**; tris(dicyanomethylene)squarate **28**; and tetraquis(dicyanomethylene)squarate **29**.

is particularly interesting because π-electrons extend the preexisting strong electron delocalization in a D–A–D-type electron system, thus producing intensely colored compounds with a characteristic fluorescence [1].

Numerous studies have been conducted on the synthesis of compounds substituted by dicyanomethylene groups, as shown in Figure 5.8 [1, 48b, 82]. Malononitrile is often used in substitution reactions of oxocarbon systems, especially in the croconate and squarate series [83], as shown in Schemes 5.2 and 5.5.

In a previous review article, Gerecht and collaborators summarized the known routes for obtaining these compounds [46]. With the exception of recent studies by our research group, there are, however, few publications in which the results of multiple spectroscopic techniques are discussed in comparison [84].



Scheme 5.5

Lunelli and collaborators described the crystal structure of sodium *trans*-bis(dicyanomethylene)squarate **26** as well as computer calculations of the fundamental vibrational frequencies of the respective dianion [82]. In this study, the crystal structure of the free anion of sodium *trans*-bis(dicyanomethylene)squarate **26** tetrahydrated reveals its D_{2h} symmetry with an essentially planar structure (deviation of approximately 0.05 Å). Water molecules were found to be essential in the crystal architecture because they coordinate with the sodium cations and provide stability to the crystal through strong hydrogen bonds. After determining the bond distances, the study concluded that the structure exhibits the lowest perturbation, as evidenced by the canonical forms with negative charge at the most electronegative atoms of the molecule.

The crystal structure of sodium *cis*-bis(dicyanomethylene)squarate **27** tetrahydrated has also been reported in the literature [85]. The ring was demonstrated to be planar with small deviations, and the bond distances of the carbon atoms in the ring are equivalent to a value of 1.422 Å, suggesting a significant residual double-bond character. Electron spin resonance (ESR) or EPR measurements confirm that *cis*-bis(dicyanomethylene)squarate **27** exhibits extension of its π-electron delocalization [85].

Squarate compounds with transition metal ions are rarely described in the chemical literature. For example, the crystal structure of *cis*-bis(dicyanomethylene) squarate **27** in a complex with Cu(I) has been reported [48b]. Galibert and collaborators synthesized a complex of Cu(II) with *trans*-bis(dicyanomethylene) squarate **26** [86]. The pseudo-oxocarbon ring in this complex was found to be planar. However, a significant deviation of the cyano groups from the best plane formed by the ring contributes to the diminished planarity of the complex, a phenomenon that is also reflected by the loss of π-delocalization in the ring.

The crystal structure of the dianion of the compound of *trans*-bis(dicyano methylene) squarate **26** with two phenylphosphine substituents and two water molecules was characterized by X-ray diffraction [48a].

Two more complexes were obtained with the dianion **26** as a ligand. These complexes were characterized by X-ray diffraction, UV/visible spectroscopy, and electrochemical measurements [69b]. The Cu(II) complex with the dianion plus four coordinated water molecules and two molecules of water of hydration molecules forms a polymeric chain with the copper atoms linked to the two nitrile groups of the ligand. The complex of copper (I) with the *trans*-substituted ligand

26 crystallizes in the $P2_1/n$ spatial monoclinic group [48a]. In this structure, four coordinated and two noncoordinated acetonitrile molecules form a polymeric chain with the copper atoms, which are linked by the four nitrile groups of the ligand. The copper complexes dissociate in an acetonitrile solution. In addition, the Cu(II) is reduced to Cu(I) by the dianion. The electrochemistry in the solid state (polymer that lines the electrode) shows redox transition of the different compounds.

Copper is the only transition metal cited in the literature that has been utilized for the complexation with *trans-* and *cis-*dianions, **26** and **27**, respectively. In a study by our research group, two more crystal structures of new complexes with transition metals have been synthesized. The structures of these new complexes were characterized by various spectroscopic techniques and by single-crystal X-ray diffraction [84]. Figure 5.9 shows the crystal structures of the coordination compounds of *trans*-bis(dicyanemethylene) squarate **26** with the Zn(II) and Co(II) metals, respectively. The zinc complex belongs to the $P2_1/c$ spatial monoclinic group [86, 87]. The zinc complex is isostructural with the

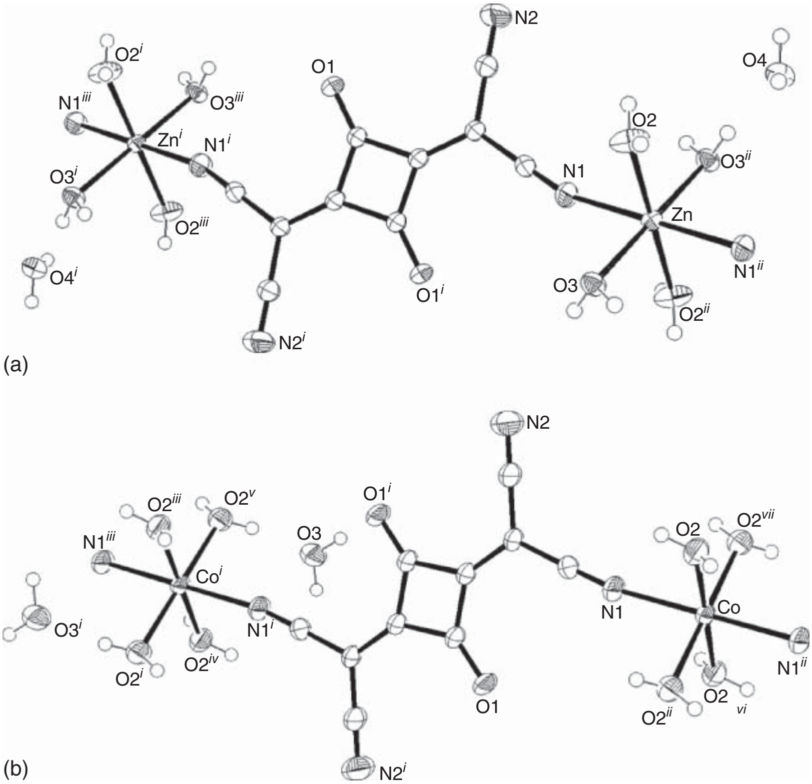


Figure 5.9 Crystal structures of zinc(II) (a) and cobalt(II) (b) ions coordinated to *trans*-bis(dicyanomethylene)squarate **26**.

copper complex, as described previously, and the cobalt complex belongs to the $C2/m$ spatial monoclinic group. Both complexes consist of polymeric chains with the respective metals linked to two nitrogen atoms on different ligands. The molecule extends in a two-dimensional polymeric structure; in one direction, the molecule extends through hydrogen bonds, while in the other its extension takes place by ligand–metal coordination. Both metals are coordinated with the nitrogen atom of the cyan group in a monodentate manner, and, together with molecules of water, exhibit a distorted octahedral geometry. No π-interaction among the ligand rings is observed because the distance between the centroids of the respective rings is greater than 6 Å in both complexes.

In addition to the two crystal structures obtained in this study, six other coordination compounds have been synthesized and characterized [73, 84]. A complete spectroscopic study was performed involving squaraines 1,3- and 1,2-disubstituted with dicyanomethylene groups and four different transition metals: cobalt, manganese, zinc, and nickel. The Raman and infrared spectra of all these complexes with both ligands reveal that the ligands exhibit an inverted symmetry element, meaning that the bands which are seen with one technique are not seen with the other, and vice versa. The complexation did not affect the molecular symmetry (in the case of the *trans* dianion) or the solid-state structure (in the case of the *cis* dianion).

The electronic spectra of the ligands indicate that the substitution of the oxygen atoms by $[CC(CN)_2]$ groups results in a substantial shift of the transition energy $\pi \rightarrow \pi^*$ due to the introduction of a new transition involving the substituent groups. Depending on the size of the oxocarbon ring, and the number of the $[CC(CN)_2]$ groups, the electronic transition can be shifted more than 100 nm, such as the example of croconate violet anion **18**, when compared to the croconate ion **3**.

The synthesis of dicyanomethylene-substituted oxocarbons is interesting because it enables the exploration of the spectral changes caused by symmetry modifications. The spectroscopic study performed using several techniques revealed relevant information from the stability and reactivity standpoints, what can be seen in the work of Seitz and Imming [1]. However, much remains to be learned about the synthesis mechanisms, the spectroscopic properties, and the crystal structures of these ligands with other transition metals. Once these characteristics are understood, further knowledge may be gained about their precursors. In this sense, some research groups are developing studies using spectroscopic or structural information to understand the properties of such systems. Thus, in the near future a more complete set of data will be available to assist in the understanding of these properties.

Summing up, squaraines are important organic substances with useful optical properties and considerable susceptibility to photoelectric stimuli. They are of great interest in the development of a variety of optical-electronic materials. Hence, the chemistry of these compounds and their precursors will continue to be promising and viable in the near future.

5.4
Conclusion and Outlook

Oxocarbons, pseudo-oxocarbons, and squaraines are a very versatile class of compounds, being useful in a wide range of areas, from model compounds to medicinal chemistry. Their role in coordination of metal ions appears to be their most important property. For the coming years, oxocarbons and their derivatives will be very important in crystal engineering. For this application, their impressive ability to provide several different coordination modes is particularly important.

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6

Recent Developments in Fulvene and Heterofulvene Chemistry

Takeshi Kawase and Hiroyuki Kurata

6.1

Introduction

Cyclic conjugated systems involving an *exo*-methylene unit in the ring system are generally termed *fulvenes*. In order to elucidate their aromatic character, fulvenes have received much attention from a large number of chemists for a long time. Pentafulvene (fulvene) **1**, a structural isomer of benzene, triafulvenes **2**, and heptafulvenes **3** are representative examples of the class of compounds (Figure 6.1). While the parent systems **1**–**3** are highly reactive species, appropriately substituted fulvenes, in which the polar structures **1B**–**3B** contribute significantly to the ground state, are stable and isolable compounds [1].

Fulvene derivatives can serve as building blocks for construction of the polycyclic conjugated systems. Polycyclic conjugated systems involving a fulvene moiety such as azulene **4**, pentalene **5**, and indacene **6** have also received much attention from the viewpoint of aromaticity (Figure 6.2), and their synthesis has been developed on the basis of fulvene chemistry. In the well-known Ziegler–Hafner azulene synthesis, a fulvene derivative **7** is employed as an important intermediate (Scheme 6.1) [2].

The conjugated systems constructed by linking two fulvene units through an exocyclic double bond are known as *fulvalenes*. Triapentafulvalene (calicene) **8**, pentafulvalene **9**, sesquifulvalene **10**, and heptafulvalene **11** are representative examples of this class of compounds (Figure 6.3). The first synthesis of a fulvalene derivative, the benzannulated compound **12**, was reported as early as 1915 by Courtot [3]. Benzannulation largely perturbs the electronic properties of the fulvene π-system, but, in general, it enhances the stability of the system. Many experimental results reveal that parent **9** is a highly reactive species; it can be handled only in highly diluted solution (<0.01 M) under inert gas at −60 °C [4]. Hafner found that *tert*-butyl groups can be employed as protective groups to stabilize the highly reactive species without a large electronic perturbation of the π-system. In the course of his study, tetra-*tert*-butylpentafulvalene **13** was synthesized as a thermally stable molecule [5]. On the other hand, although parent **8** and **10** are labile, a number of their derivatives with substituents capable of stabilizing their

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
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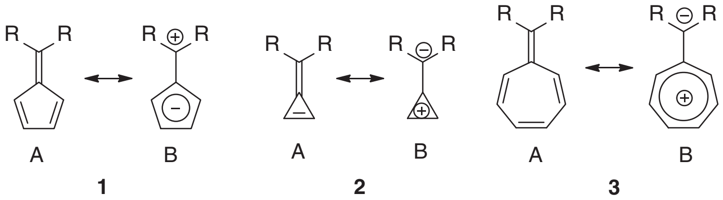


Figure 6.1 Pentafulvene (fulvene) **1**, triafulvene **2**, heptafulvene **3** and their polar structures.

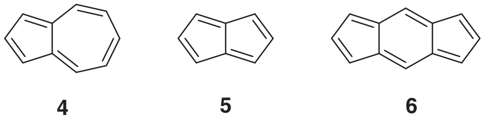
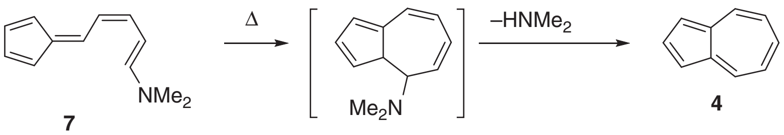


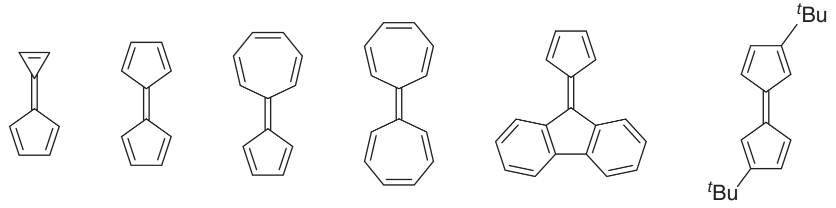
Figure 6.2 Azulene **4**, pentalene **5** and indacene **6**.



Scheme 6.1 Ziegler–Hafner azulene synthesis.

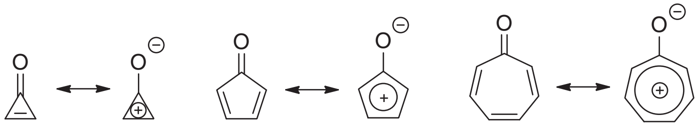
polar structures have been obtained as stable compounds [1, 6]. Heptafulvalene **11**, which has a nonplanar structure, is obtained as a relatively oxygen sensitive, but thermally stable, reddish purple solid. Its chemical and physical properties have been well explored since the 1980s [7].

Heterofulvenes and heterofulvalenes have been explored from the viewpoint of their electronic properties; that is, how the replacement of the skeletal carbon atoms of fulvenes and fulvalenes by heteroatoms affects their properties. Among these derivatives the fully conjugated cyclic ketones cyclopropenone (CPN) **14**, cyclopentadienone (CPDN) **15**, and tropone **16** are categorized as "oxafulvenes" (Figure 6.4). The oxafulvenes have been employed as versatile synthetic building blocks for polycyclic compounds, and their chemistry has a long history of over half a century [1]. Owing to the polar character of the carbonyl group, **14** and **16** are stable compounds, while **15** is highly reactive. Actually, parent **15** easily dimerizes even at low temperatures [8]. The reactivity can be controlled by the substituents. For example, tetraphenylcyclopentadienone (tetracyclone) **17** is a thermally stable compound with moderate reactivity toward dienophiles. Analogous to benzofulvenes, 4-indenone **18** and 9-fluorenone **19** are fairly stable compounds, and they are considered fundamental structures that constitute the central core of a variety of compounds exhibiting extraordinary biological and pharmaceutical activities as well as optical and electronic properties.



8 **9** **10** **11** **12** **13**

Figure 6.3 Representative fulvalenes.

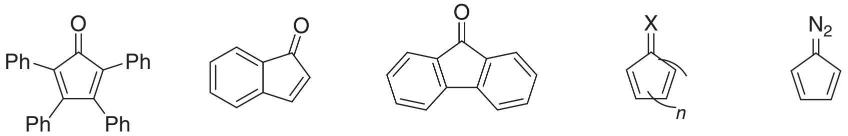


14 **15** **16**

Figure 6.4 Cyclopropenone (CPN) **14**, cyclopentadienone (CPDN) **15**, tropone **16** and their polar structures.

The compounds in which the *exo*-methylene carbon atom of fulvene is replaced by nitrogen, silicon, phosphorous, and sulfur atom are called *azafulvenes*, *silafulvenes*, *phosphafulvenes*, and *thiafulvenes* **20**, respectively. Diazocyclopentadiene **21** as a kind of azafulvene is a stable compound, while the other heterofulvenes are highly reactive materials [9]. Without appropriate substituents on the system, the formation is generally assumed from trapping reactions (Figure 6.5).

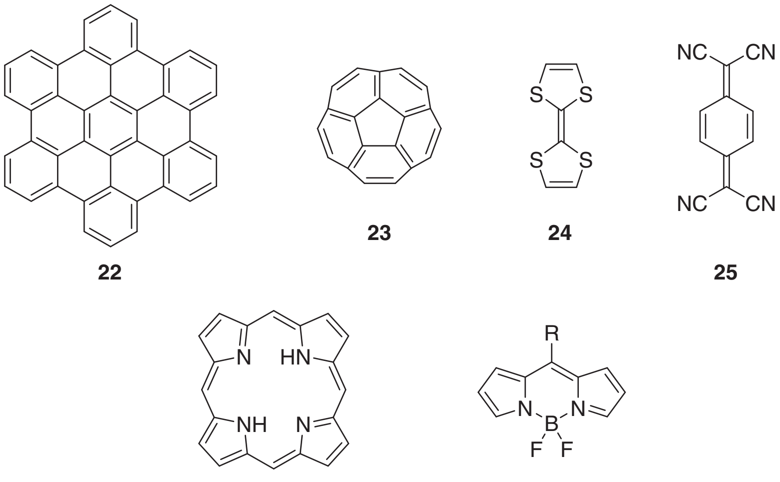
Until 1990, a great variety of fulvenes and heterofulvenes have been synthesized, and their essential properties have been well documented in many books and review articles. Has fulvene chemistry declined or even ceased by now? The answer is a clear 'no'! A number of new synthetic methods and reactions of fulvenes have been recorded in the past two decades, and the developments have progressively proved of great value to fulvene and heterofulvene chemistry. Particularly, knowledge of fulvene chemistry has provided a great advantage to renew and promote the chemistry of carbon-rich compounds after the discovery



17 **18** **19** X = NR, PR, S, SiR_2 **21**
n = 0, 1, 2

20

Figure 6.5 Tetracyclone **17**, indenone **18**, fluorenone **19**, and heterofulvenes **20** and **21**.



22 23 24 25 26 27

Figure 6.6 Hexa-*peri*-hexabenzocoronene (HBC) **22**, corannulene **23**, tetrathiafulvalene (TTF) **24**, tetracyanoquinodimethane (TCNQ) **25**, porphyrin **26** and boron dipyrromethanes (BODIPYs) **27**.

of fullerene [10]. For example, hexa-*peri*-hexabenzocoronene (HBC) **22** and corannulene **23** as representative carbon rich compounds were prepared from CPDN derivatives as important synthetic building blocks [11]. Fulvene (including heterofulvene) chemistry has now widely expanded into materials science (Figure 6.6). This chapter mainly describes the recent development of fulvene and heterofulvene chemistry (see also Chapter 7).

An epoch-making discovery in heterofulvene chemistry was the metallic conductivity in the charge-transfer complex formed from tetrathiafulvalene (TTF) **24** and tetracyanoquinodimethane (TCNQ) **25** in 1973 [12]. Upon this discovery, various functional dyes have been designed and constructed on the basis of electronic character of TTF; however, this chapter only describes the functional dyes involving a fulvene moiety, because TTF chemistry is considerably larger (see Chapter 8) and many good books and reviews have already been published to date [13]. For the same reason, this chapter does not refer to the chemistry of porphyrins **26** and boron dipyrromethenes (BODIPY) **27**, although they formally possess azafulvene moieties in their π-systems [14, 15].

6.2
Triafulvenes

Triafulvene (methylenecyclopropene) **2**, the smallest member of the fulvenes, is of particular interest not only for its aromatic character but also for its highly strained nature. Since the first synthesis of derivatives of **2** about 50 years ago [16],

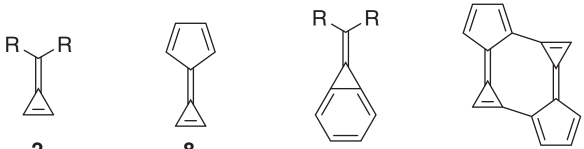


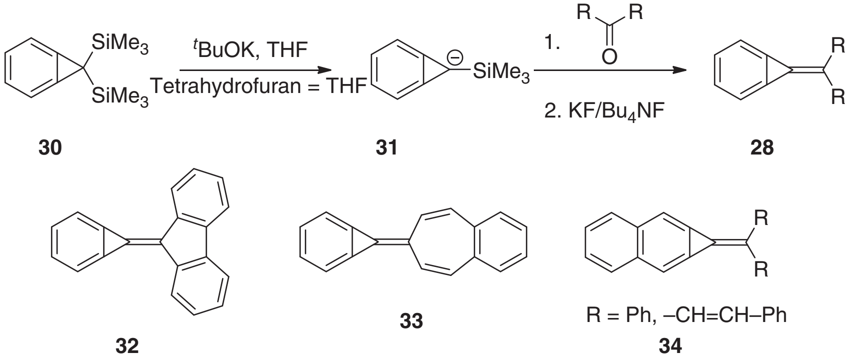
Figure 6.7 Triafulvenes **2**, calicene **8**, benzotriafulvenes **28** and cyclic bicalicene **29**.

many resonance-stabilized triafulvenes involving calicene derivatives **8** have been prepared and characterized [17]. In 1984, the parent hydrocarbon **2** ($R = H$) was synthesized and characterized by two research groups independently [18, 19]. The same year, the first syntheses of benzotriafulvenes **28** and cyclic bicalicene **29** were also reported (Figure 6.7) [20, 21]. This section describes the recent development of the chemistry of triafulvenes after these epoch-making syntheses.

6.2.1
Benzotriafulvene and Related Compounds

6.2.1.1 **Synthesis**

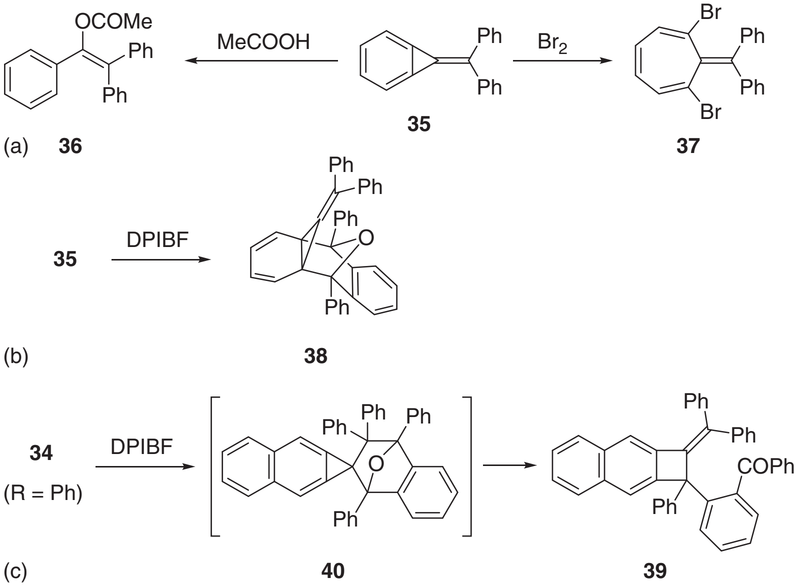
Although benzotriafulvene **28** is isoelectronic to heptafulvene **3**, it shows individual electronic properties, because it incorporates a highly strained cyclopropabenzene and a [3]radialene component in its system (see Chapter 4). The first synthesis, reported by Halton in 1984, has been performed from bis(trimethylsilyl)cyclopropabenzene **30** as the starting material [20]. Peterson olefination of carbonyl compounds with a silyl anion **31** derived from **30** using potassium *tert*-butoxide as desilylating agent led to **28** (Scheme 6.2). The procedure provided various benzo- and naphthotriafulvenes such as **32**–**34** [22].



Scheme 6.2

6.2.1.2 **Reactions of Benzotriafulvenes**

The reactions and physical properties of triafulvenes and related compounds have been summarized in a review by Halton [23]. The diphenyl derivative **35** has remarkable thermal and photochemical stability. Flash vacuum pyrolysis (FVP) leads only to ring-opening products. On the other hand, various electrophiles smoothly open the three-membered ring through cleavage of 1,7-bond to form styrene derivatives such as **36**, and a few electrophiles like bromine lead to the formation of cycloheptatriene derivatives **37** (Scheme 6.3a). Cycloaddition chemistry with dibenzoisobenzofuran (DPIBF) as a diene has been examined. In the case of **35** as a benzotriafulvene, DPIBF is incorporated with addition exclusive to the bridge bond to form the norcaradiene-bridged *endo*-adducts **38** (Scheme 6.3b). In contrast, the reaction of the naphthotriafulvene **34** (R = Ph) with DPIBF affords **39** via an initial cycloaddition at the exocyclic double bond to form intermediate **40** (Scheme 6.3c).



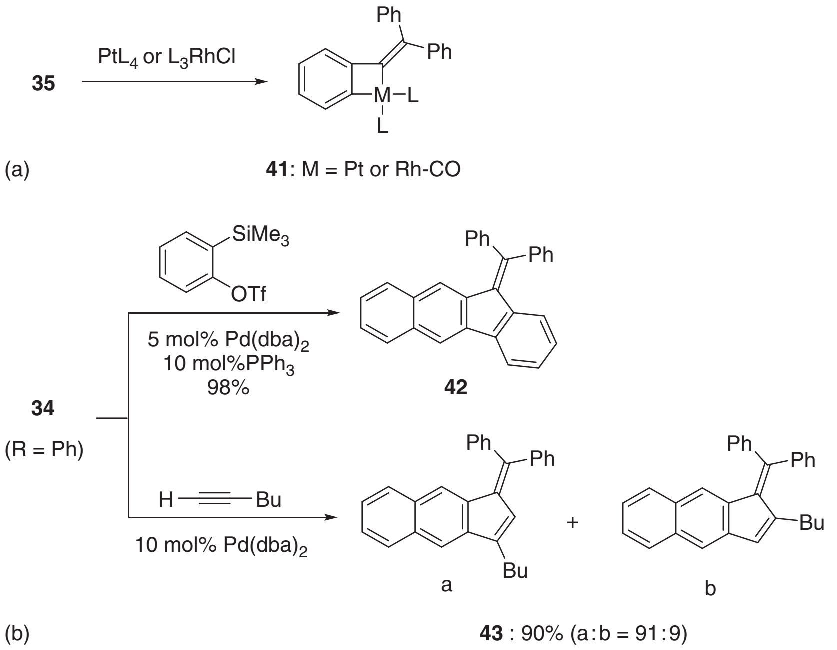
Scheme 6.3

The reactions between benzotriafulvenes and transition metals (Pt and Rh) afford metallacyclobutane derivatives **41** as stable crystalline compounds in good yields. Recently, Huang developed the highly regioselective palladium-catalyzed [3+2] cycloaddition reactions of **34** (R = Ph) with arynes or alkynes to provide fluorene **42** and indene derivatives **43**, respectively (Scheme 6.4) [24].

6.2.2
Triafulvalene and Related Compounds

6.2.2.1 Synthesis of Benzotriafulvalenes

Neidlein showed that *gem*-dichlorocyclopropabenzenes **44** could be converted into their carbene equivalents **45**, which undergo dimerization to provide



Scheme 6.4

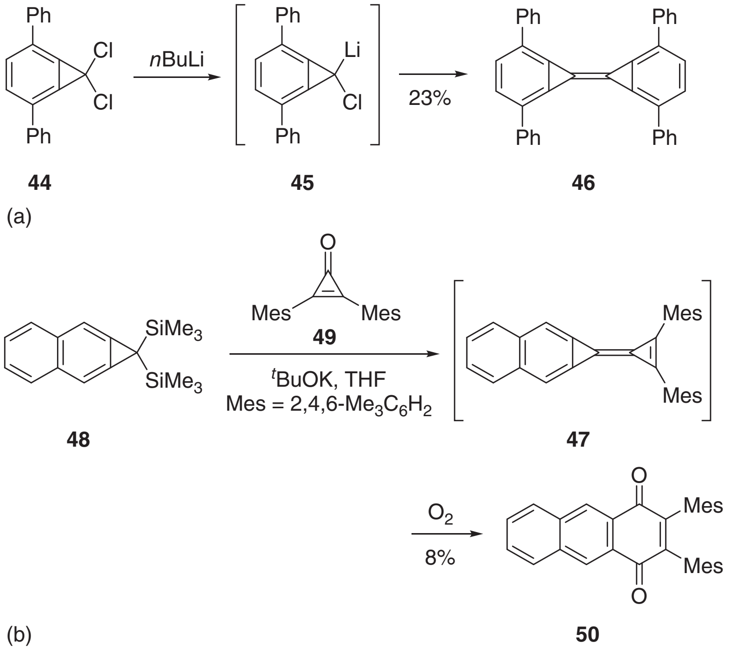
bicycloproparenylidenes **46** as deep-red needles displaying a strong yellow fluorescence in CS_2 (Scheme 6.5a) [25]. On the other hand, synthetic attempts to prepare naphthotriafulvalene **47** from **48** and 2,3-dimesitylcyclopropenone **49** resulted in failure, because of the high reactivity of **47** toward oxygen. Only anthraquinone derivative **50** was obtained in 8% yield (Scheme 6.5b) [26].

6.2.2.2 **Triafulvalenes**

Despite intensive efforts, the isolation and characterization of triafulvalene derivatives **51** was not achieved until quite recently; theoretical calculations predict that triafulvalene **51** (R = H) possesses antiaromatic character. In 2009, Bertrand and coworkers synthesized kinetically protected triafulvalenes **52** as thermally stable compounds, as shown in Scheme 6.6 [27]. Selection of the bulky 2,4,6-triisopropylphenyl (Tip) and mesityl (Mes) groups as protective groups formed the basis of success. An X-ray diffraction analysis of an anti-isomer **52a** shows that the triafulvalene skeleton is almost perfectly planar, and the observed short bond distance (1.303(5) Å) confirms the highly localized nature of the π system.

6.2.2.3 **Cyclic Bicalicenes**

In 1984, Yoshida and coworkers synthesized cyclic bicalicenes **29** as outlined in Scheme 6.7 [21, 28]. Although parent calicene **8** is a highly reactive species, **29** is a



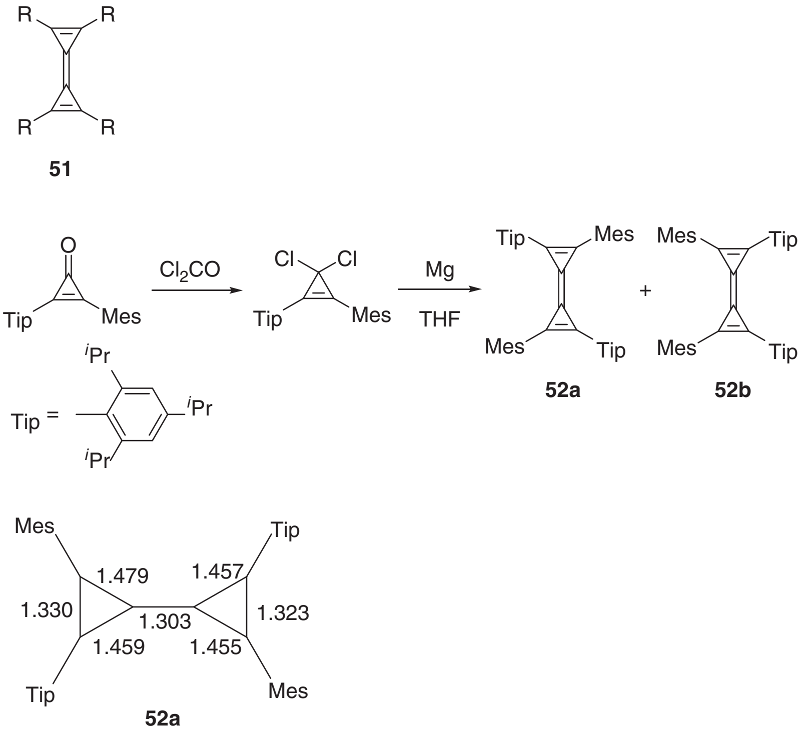
Scheme 6.5

fairly stable, reddish purple compound. The crystallographic analysis reveals that the skeleton is planar and almost no bond alternation is observed, indicating the presence of D_{2h} symmetry. From the ^{1}H NMR data, there is no paramagnetic ring current as expected for a peripheral 16π system. The stability is attributed to the unexpectedly large contribution of the tetrapolar structures **29A** to the ground state. Cyclic tercalicene **53** and quatercalicene **54** were also prepared from **29** by the same group [29]. These compounds have 22π and 28π electron peripheries, respectively; however, ^{1}H NMR analysis provides no significant evidence for ring current effects.

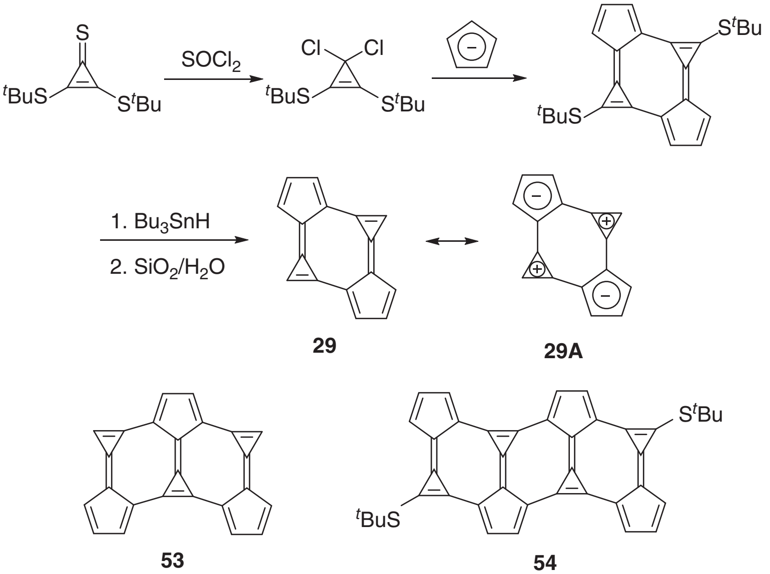
6.2.3
Heterotriafulvenes

6.2.3.1 Cyclopropenones (CPNs)

Since the first synthesis of a CPN derivative, diphenylcyclopropenone **55**, reported independently in 1959 by Breslow and Vol'pin [30, 31], the unique and diverse reactivities of CPNs **56** and cyclopropenone acetals (CPNA) **57** have been extensively explored (Figure 6.8) [17, 32]. Today, **56** and **57** can be regarded as versatile synthetic building blocks. Furthermore, the recent discovery of CPN-containing natural products as well as CPN-based protease inhibitors renewed interest in this class of cyclic ketones [33].



Scheme 6.6



Scheme 6.7

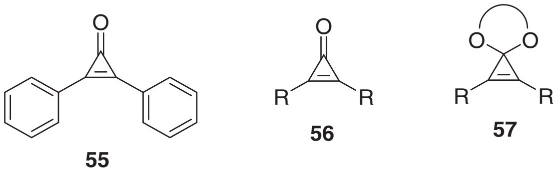


Figure 6.8 Diphenylcyclopropenone **55**, CPNs **56** and CPNAs **57**.

Synthesis

Reliable synthetic methods used to prepare CPNs **56** have been developed during the past two decades, and they are classified as falling into four categories: (i) Friedel–Crafts arylation of trichlorocyclopropenium cation **58** derived from tetrachlorocyclopropene **59** and followed by hydrolysis (Scheme 6.8a) [17, 34], (ii) the cyclopropenation of alkynes using *in situ*-generated dichlorocarbenes followed by hydrolysis (Scheme 6.8b) [35], (iii) introduction of substituents into the 2- and 3-positions of CPNA **57** followed by deprotection of the carbonyl group (Scheme 6.8c) [32], and (iv) modifications of the Favorskii cyclization (Scheme 6.8d) [36].

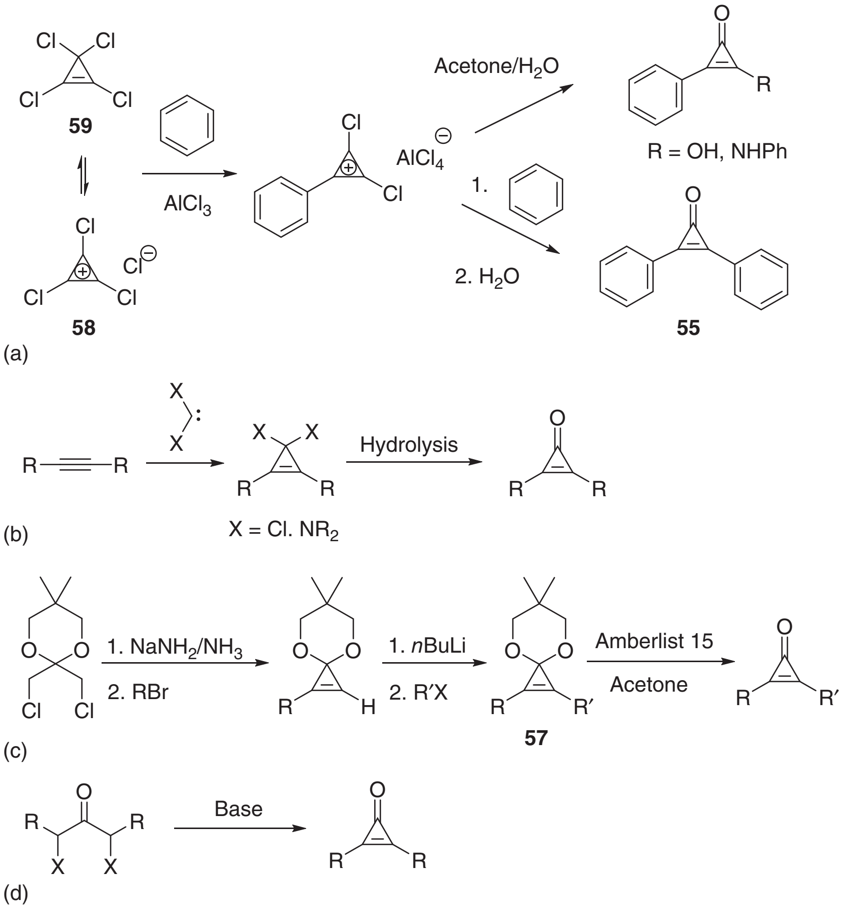
Popik and coworkers [37] prepared various macrocyclic compounds possessing a CPN moiety to investigate the phototriggering of the cycloaromatization reaction by the *in situ* generation of an activated enediyne system. Compound **60** with a 10 membered ring was constructed from CPNA **61** as a starting material (Scheme 6.9a), and macrocycles **62** and **63** were also prepared through cyclopropanation of the relatively stable cyclic and acyclic alkynes, **64** and **65**, with dichlorocarbene and difluorocarbene, respectively (Scheme 6.9b,c) [38]. In these compounds, CPNs act as a protective group for thermally reactive cyclic enediynes such as **66**.

Popik's group also synthesized a masked cyclooctyne **67** by the Friedel–Crafts arylation method as the key step (Scheme 6.10). Irradiation of the CPN **67** results in the efficient and clean regeneration of the corresponding dibenzocyclooctyne **68**, which undergoes facile catalyst-free cycloadditions with azides to give corresponding triazoles **69** under ambient conditions, although **67** does not react with azides in the dark [39].

A CPN-fused dibenzocyclooctyne **70** was prepared by Boons (Scheme 6.11). It undergoes fast strain-promoted cycloadditions with azides under catalyst-free conditions to yield a triazole **71**, displaying more than 1000-fold brighter fluorescence than **70** [40].

6.2.3.2 Reaction of CPNs and Related Compounds

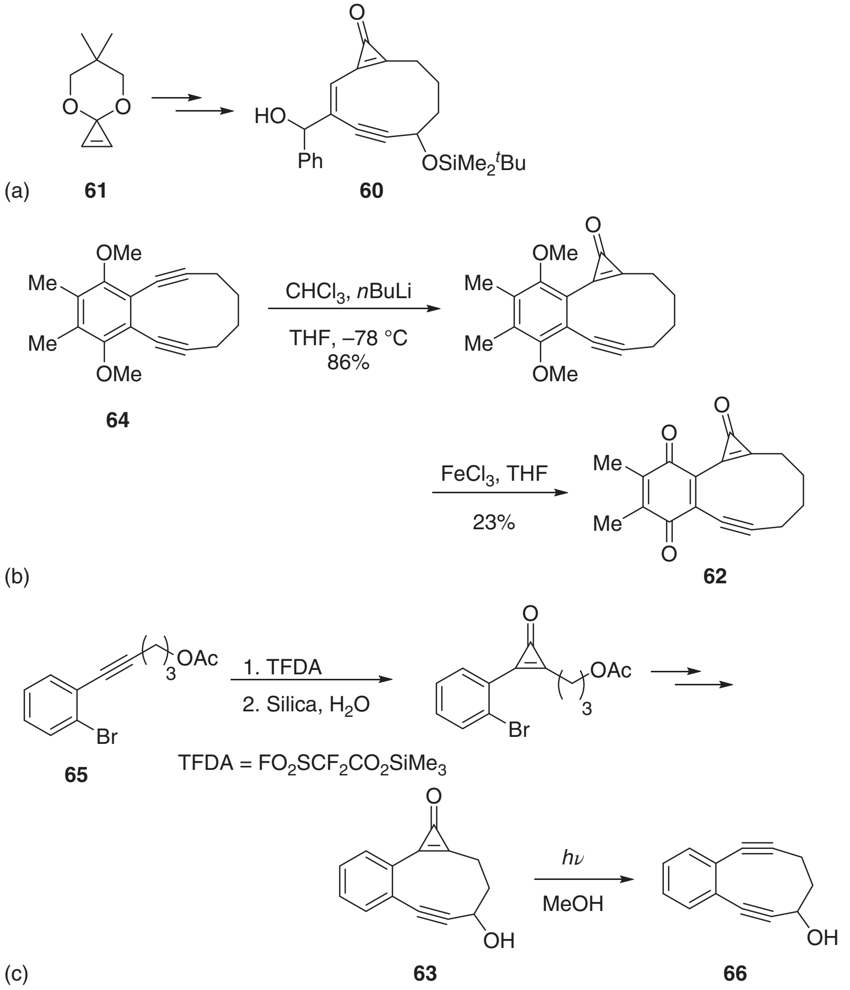
As mentioned, the photochemistry of **55** in solution has been well investigated. The solid-state reaction, however, has not been thoroughly studied. Garcia-Garibay found that **55** undergoes a novel chain reaction to afford diphenylacetylene **72** (tolane) with high quantum yield in the crystalline state (Scheme 6.12) [41].



Scheme 6.8

There have been reports of a number of reactions of CPNA **73** that result in cleavage of the strained C–C σ-bond under thermal conditions. The formed reactive intermediate **74** undergoes insertion and cheletropic [1+2]-, [3+2]-, and [3+4] cycloaddition reactions under thermal conditions (Scheme 6.13a). The reactivity profiles reported to date are consistent with such a σ-delocalized singlet species **74** that can react either as a 1,1- or as a 1,3-dipole. Moreover, the 2-alkylidenecyclopropanone acetal **75** derived from a CPNA **76** is a useful precursor of dialkoxy trimethylenemethane (TMM) **77**. Mild thermolysis of **75** in the presence of an electrophile generates **77**, which undergoes a [3+2] cycloaddition to form cyclopentane derivative **78** (Scheme 6.13b). These results were reviewed by Nakamura and coworkers [32].

In the course of the study, Nakamura and Isobe have developed a new synthetic method for substituted cyclopentadienone acetals (CPDNAs) **79** employing

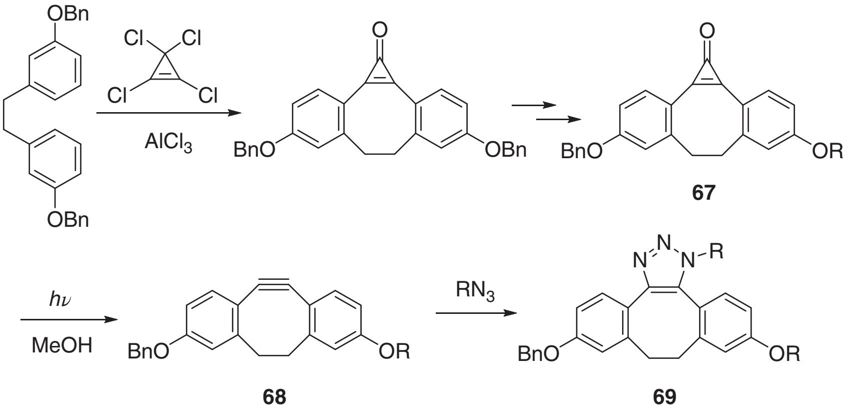


Scheme 6.9

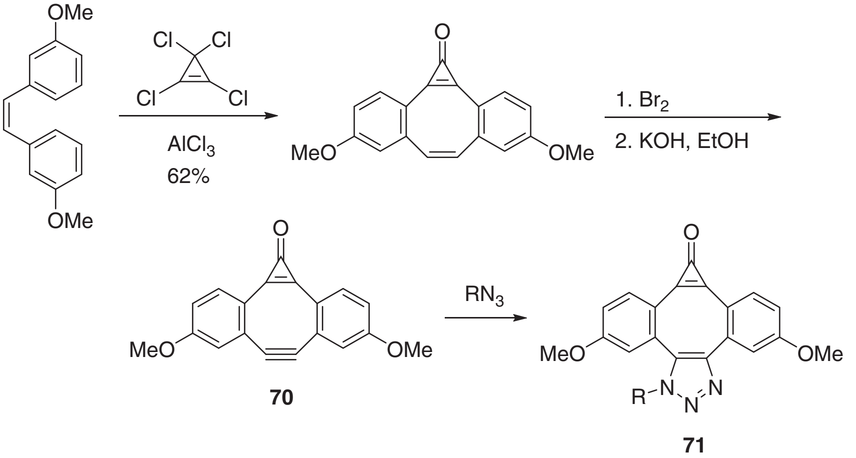
palladium-catalyzed [3+2] cycloadditions of substituted CPNAs such as **80** to an electron-deficient acetylene (Scheme 6.14) [42].

Later, Wender reported that CPN **55** itself can also serve as an excellent three-carbon component in Rh(I)-catalyzed [3+2] cycloadditions with a wide range of alkynes, providing CPDNs **81** selectively and in moderate-to-high yields (Scheme 6.15) [43].

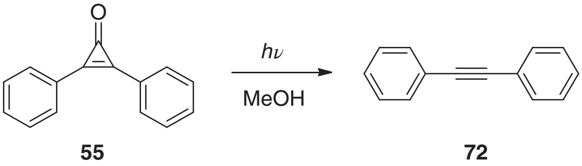
Inspired by the unique reactivity profile of cyclopropenium ions, Lambert and coworkers reasoned that activation of alcohols toward nucleophilic displacement should be possible according the mechanistic design shown in Scheme 6.16. In this reaction, the oxygen atom of the starting materials was transferred into the carbonyl oxygen of **56** [44].



Scheme 6.10

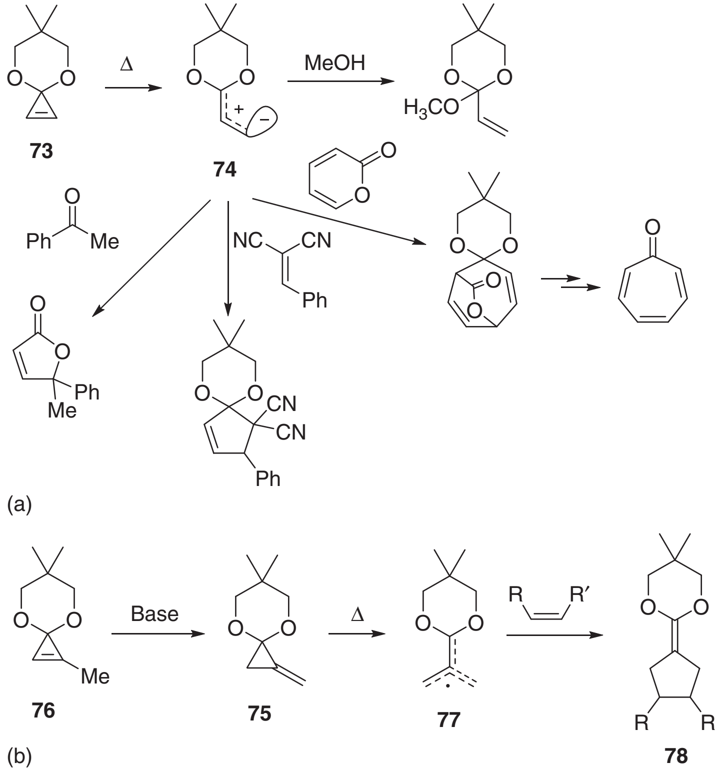


Scheme 6.11

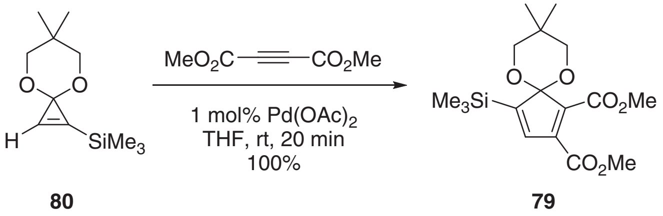


Scheme 6.12

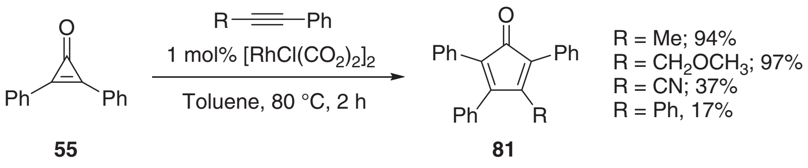
The “cyclopropenium activation” approach has been employed in a number of elimination reactions, such as nucleophilic substitution of alcohol, nucleophilic acyl substitution of carboxylic acid, cyclodehydration of diol, and the Beckmann rearrangement (Scheme 6.17) [45].



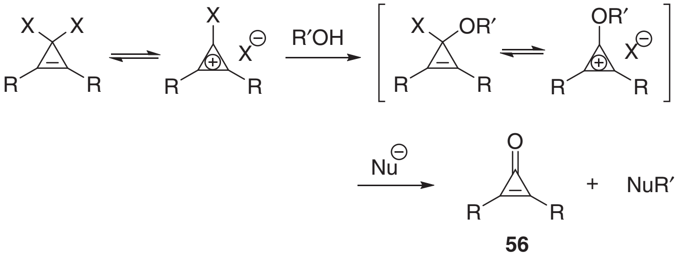
Scheme 6.13



Scheme 6.14

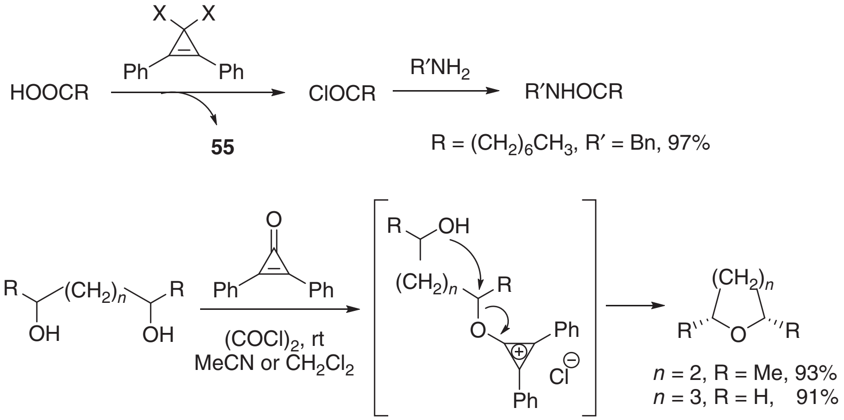


Scheme 6.15



R = Ph, R′ = CH(CH$_3$)Ph, rt, 30 min,in CH$_2$Cl$_2$, 91%

Scheme 6.16



Scheme 6.17

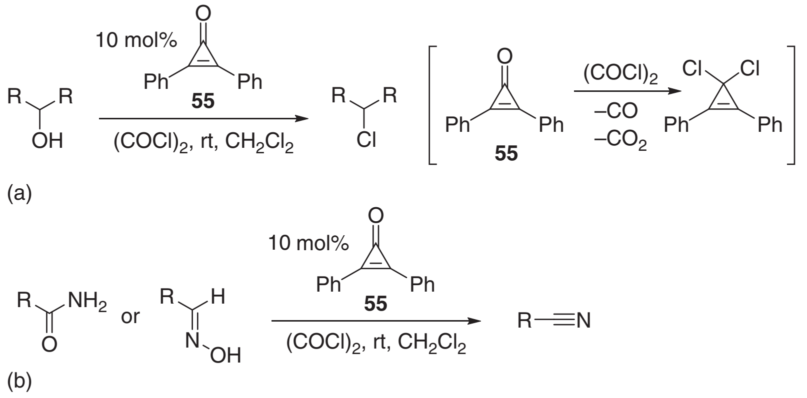
A catalytic route for nucleophilic substitution of alcohols using simple CPN **55** as a catalyst was also developed by Lambert in 2011 (Scheme 6.18a) [46]. In this reaction, oxalyl chloride acts as an activating reagent for **55**. The catalytic system is also employed for the conversion of oximes and primary amides into nitriles (Scheme 6.18b) [47].

6.2.3.3 Cyclopropenone Imides (Azatriafulvenes)

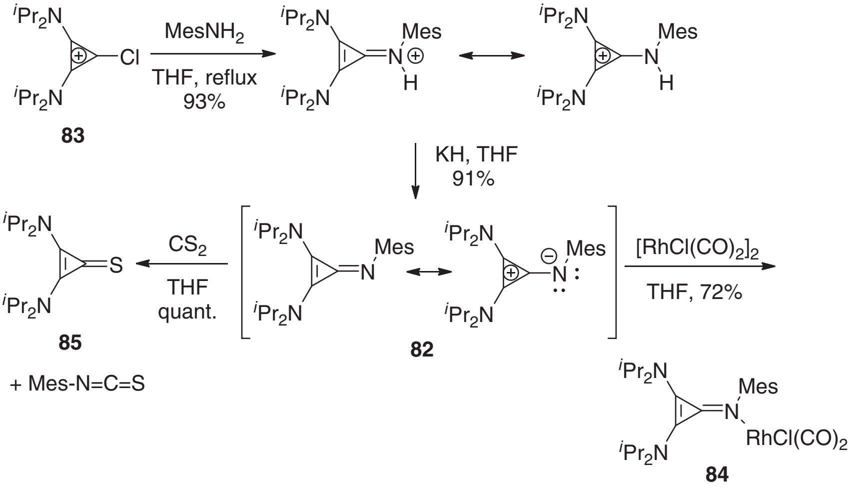
Alcarazo and coworkers prepared cyclopropenylidenimines (azatriafulvene) **82** from cyclopropenium cation **83**. The exocyclic nitrogen atom in **82** exhibits all attributes of a nitrogen atom, namely, the availability of two lone pairs essentially localized on that atom. The azatriafulvene **82** reacts with [RhCl(CO)$_2$] to form a complex **84**; with CS$_2$, it yields thioketone **85** (Scheme 6.19) [48].

6.2.3.4 The Other Heterotriafulvenes

Recent developments in experimental techniques or protective group manipulation have enabled several heterofulvenes to be isolated in pure form.



Scheme 6.18

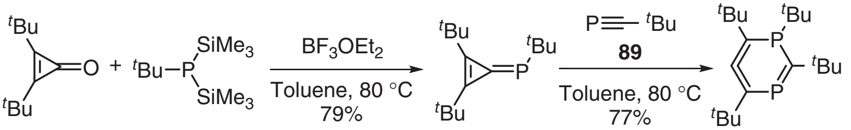


Scheme 6.19

Phosphatriafluvenes

Phosphatriafulvene **86**, the next higher analog of azatriafulvene, was obtained by condensation of di-*tert*-butylcyclopropenone **87** with a silylphosphide **88** as the first all-carbon-substituted phosphaalkenes with inverse electron demand [49]. When **86** is allowed to react with the kinetically stabilized phosphaalkyne **89** at 80 °C, the isobenzene **90** is obtained. The product, demonstrating unexpected thermal stability, was obtained as a red oil in 77% yield (Scheme 6.20) [50].

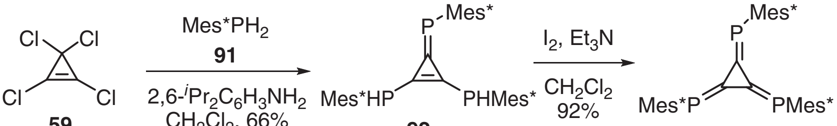
The reaction of tetrachlorocyclopropene **59** with the bulky (2,4,6-tri-*tert*-butylphenyl)phosphine **91** in the presence of 2,6-diisopropylaniline as a base afforded a diastereomeric mixture of 4-phosphatriafulvenes **92** as a stable orange solid in 66% yield. Oxidation of **92** with iodine afforded the first stable



87 **88** **86** **90**

Scheme 6.20

phosphorus-containing [3]radialene **93** as a deep-purple solid in 92% yield (Scheme 6.21) [51].



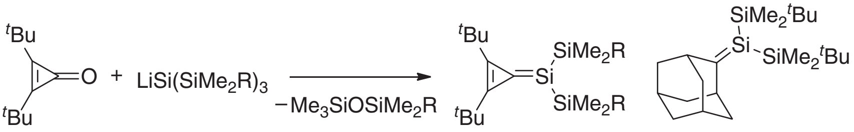
59 **92** **93**

Mes* = 2,4,6-(^{t}Bu)$_3$C$_6$H$_2$

Scheme 6.21

Silatriafluvenes and Related Compounds

The first 4-silatriafulvene derivative **94** (R = Me) was obtained by Kira's group as a reactive intermediate using the sila-Peterson reaction [52]. By use of the bulky *tert*-butyldimethylsilyl groups rather than trimethylsilyl (TMS) substituents in **94**, the first stable 4-silatriafulvene **95** was synthesized by the same group (Scheme 6.22). An X-ray analysis reveals that **95** has an almost planar skeleton with bond alternation; all skeletal carbon and silicon atoms are located almost in a plane and the silicon–carbon double bond length is 1.755 Å, which is close to that of *tert*-butyldimethylsilyl-(trimethylsilyl)adamantylidenesilane **96** (1.741 Å) [53].

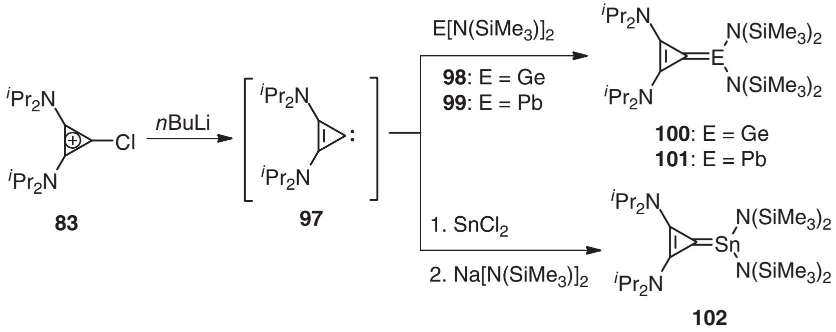


94 (R = Me)
95 (R = ^{t}Bu)

96

Scheme 6.22

Bis(dialky1amino)cyclopropenylidene **97** prepared by the reaction of cyclopropenium ion **83** with *n*-butyllithium was treated with the bisamides **98** and **99** to afford germa- and plumbatriafulvenes **100** and **101**, respectively. The analogous tin compound **102** was also synthesized by reaction of **96** with SnCl$_2$, followed by amidation of the intermediate carbene adduct (Scheme 6.23). Compounds **100–102** are isolated as thermally stable yellow crystals. X-ray analyses reveal that they have a trigonal–pyramidal structure and the distances between the E atom (E = Ge, Sn, and Pb) and the carbene–C atom (Ge–C = 2.085 Å, Sn–C = 2.303 Å, and Pb–C = 2.423 Å) are appreciably longer than those in "true" germaethenes (1.83 Å) and stannaethenes (2.02 Å) and fall in the range expected for single bonds [54].



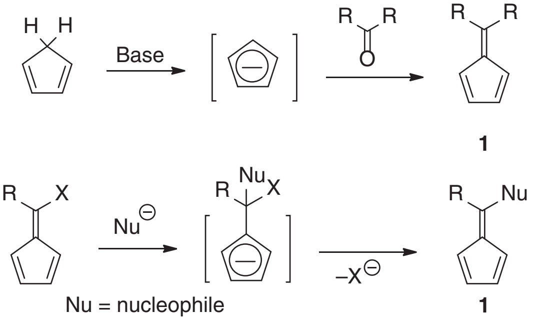
Scheme 6.23

6.3
Pentafulvenes and Related Compounds

6.3.1
Pentafulvenes

6.3.1.1 Synthesis of Pentafulvenes

This section focuses on new developments in the area of pentafulvene synthesis. The traditional methods (condensation between cyclopentadienyl (CP) anion and ketones, and nucleophilic substitution reaction of six-substituted fulvenes) are still often used for the synthesis of pentafulvene derivatives (Scheme 6.24) [1], and some improved procedures for these transformations will be described

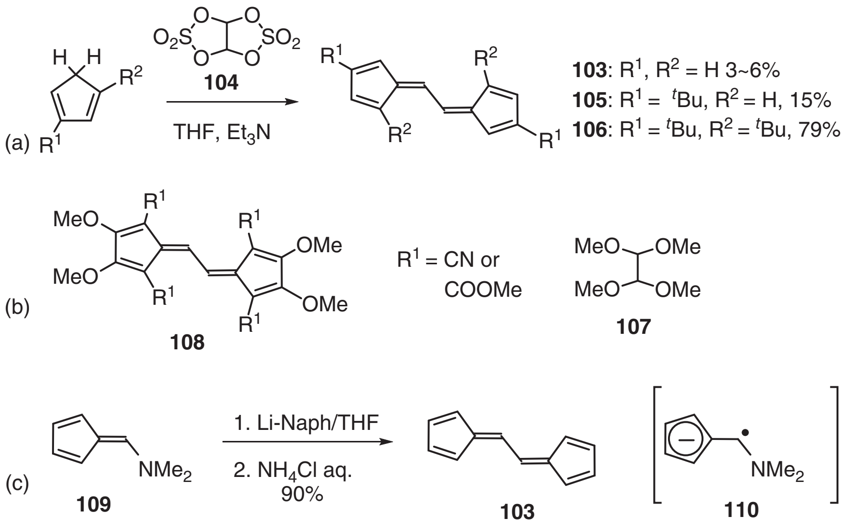


Scheme 6.24

first. Subsequently, a section devoted to ring-closure and ring-construction reactions constitute the main part. The Schmittel cyclization and transition-metal-catalyzed ring-closure reactions have been newly and widely developed in the past two decades.

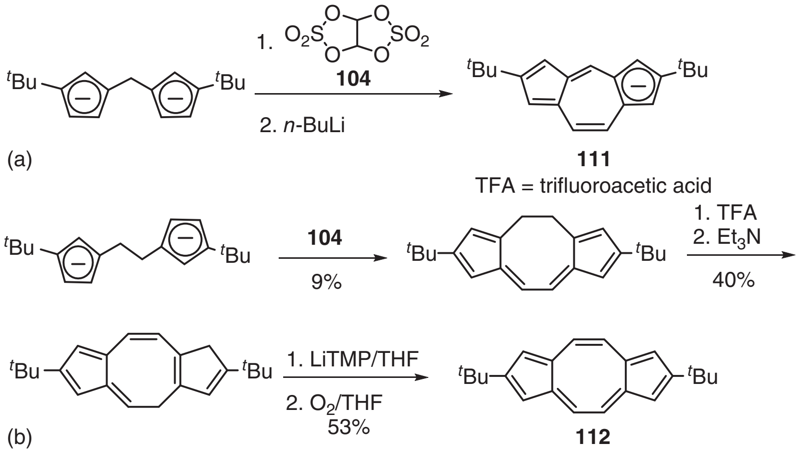
Reactions between CP Anions and Ketones or Ketone Equivalents

Even today, a general synthesis of pentafulvenes **1** employs a condensation reaction between the CP anion and ketones under basic conditions (Thiele reaction). A report in 1901 described that the reaction using acetone as the ketone component afforded 6,6-dimethylfulvene in good yield (Scheme 6.24a). However, the preparation of 6,6-bifulvenyl **103** using this method resulted in failure. To overcome the problem, a new method using glyoxalic sulfate **104** as an oxalaldehyde equivalent was found by Prinzbach [55]. Ten years later, Hafner reported that this method furnished 6,6-bifulveneyl derivatives **105** and **106** bearing *t*-butyl groups in good yields (Scheme 6.25a) [5]. Recently, bisacetal **107** has been employed for the synthesis of bifulvenyls **108** with electron-donating substituents (Scheme 6.25b) [56]. On the other hand, the best method for the synthesis of bifulvenyl **103** has been reported by Kawase *et al.* [57]. Treatment of 6-dimethylaminofulvene **109** with 1 equiv. of lithium naphthalene cleanly affords **103** via the corresponding fulvene radical anion **110** in 90% yield upon acidic workup (Scheme 6.25c).



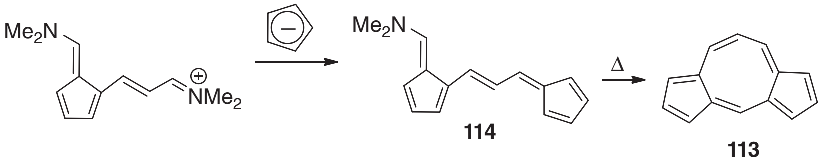
Scheme 6.25

Hafner applied the method using glyoxalic sulfate **104** to the synthesis of tricyclic anion **111** and dicyclopenta[*a,e*]cyclooctene **112** containing 14π electron peripheries, as outlined in Scheme 6.26 [58, 59]. X-ray crystallographic and spectroscopic analyses revealed that **112** has a planar eight-membered ring and an aromatic 14π-electron periphery [59].



Scheme 6.26

Later, the [*a,d*]isomer **113** was synthesized by Oda and Kuroda's group using a modified Hafner azulene approach. A thermal ring-closure reaction of fulvene **114** provides **113** in 2% yield (Scheme 6.27). The ^{1}H-NMR spectrum of **113** indicates the presence of an aromatic 14-π electron ring current [60].

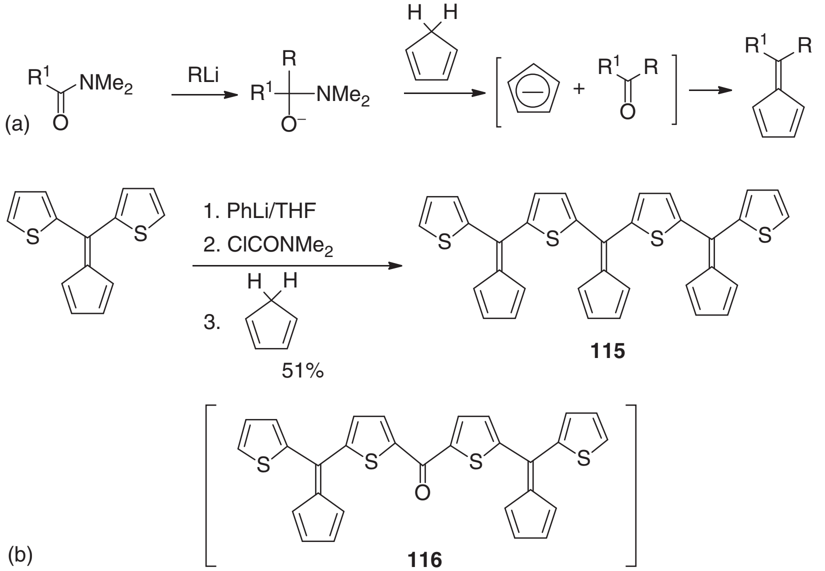


Scheme 6.27

Kurata, Kawase, and Oda's group developed a new one-pot fulvene synthesis; the method uses the reaction of *N*,*N*-dimethylformamide (DMF) or *N*,*N*-dimethyl chlorocarbamate ($ClCONMe_2$) with aryl lithium reagents to provide fulvene derivatives without the isolation of rather unstable precursor ketones (Scheme 6.28a). As shown in Scheme 6.28a, CP anion and the corresponding ketone are generated *in situ* [61]. The procedure provides a fulvene oligomer **115** without isolation of the precursor ketone **116** (Scheme 6.28b) [62].

Synthesis from Fulvenes with Leaving Groups at the 6-Position

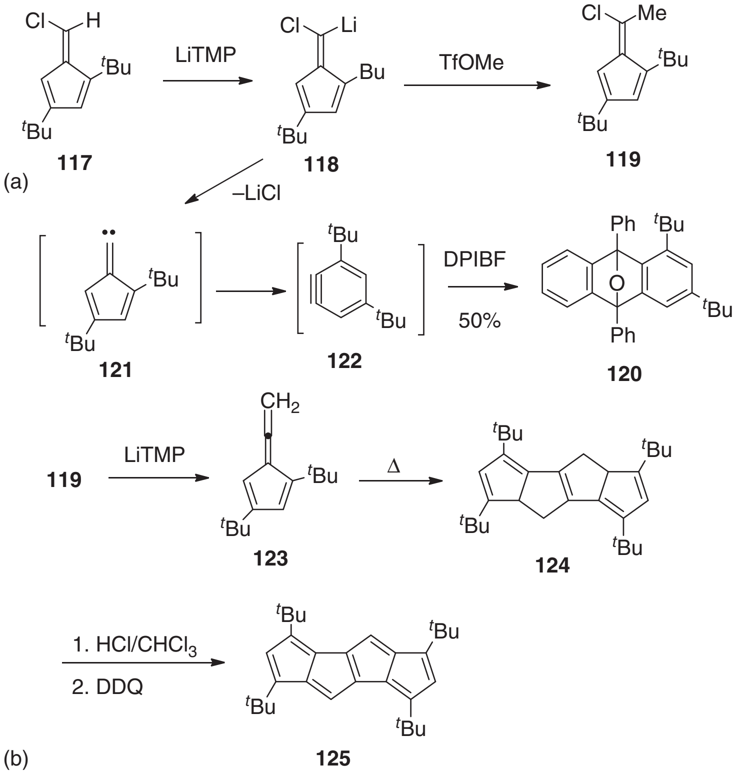
Another versatile synthetic method for pentafulvenes was employed by a formal nucleophilic substitution reaction (addition and subsequent elimination reactions) of fulvenes carrying leaving groups at the 6-position [1]. While



Scheme 6.28

chlorine would be a good leaving group for the formal substitution reaction, 6-chlorofulvene is less suitable for this purpose because of its high reactivity. Hafner found that 6-chloro-2,4-di-*t*-butylfulvene **117** shows high thermal stability and novel reactivity. Treatment of **117** with lithium tetramethylpiperidide (LiTMP) generates the corresponding 6-fulvenyl anion **118** in solution. The generation was proven by the formation of 6-chloro-6-methylfulvene **119** by quenching with methyl triflate. When the reaction was carried out in the presence of DPIBF, it affords adduct **120** in 50% yield, indicating the successive formation of carbene **121** and aryne **122** as reaction intermediates (Scheme 6.29a) [63]. When 6-chloro-6-methylfulvene **119** was subjected to LiTMP treatment, it forms the vinylidenefulvene **123**, which dimerizes to the tetracyclic compound **124**. Subsequent treatments of **124** with hydrogen chloride and dichlorodicyano-*p*-benzoquinone (DDQ) afforded pentalenopentalene **125** (Scheme 6.29b) [64].

A novel 6-fulvenyl anion **126** is also generated by treatment of 6,6-bis(dimethylamino)fulvene **127** with 2 equiv. of lithium naphthalenide (Li-Naph) through the intermediate formation of the corresponding dianion **128** ($R = NMe_2$). Quenching **126** with electrophiles gave several fulvenes **129** functionalized at the 6-position (Scheme 6.30a) [65]. Thermally stable fulvene dianions **130** and **131** are successfully generated from 6-dimethylamino-6-phenylfulvene **132** and 6,6-diphenylfulvene **133** upon alkaline metal reduction (Scheme 6.30b). Formation of **131** is confirmed by NMR experiments, and the dianion **130** reacts with 1,2-dibromoethane to afford dihydropentalene **134** (Scheme 6.30c) [66].



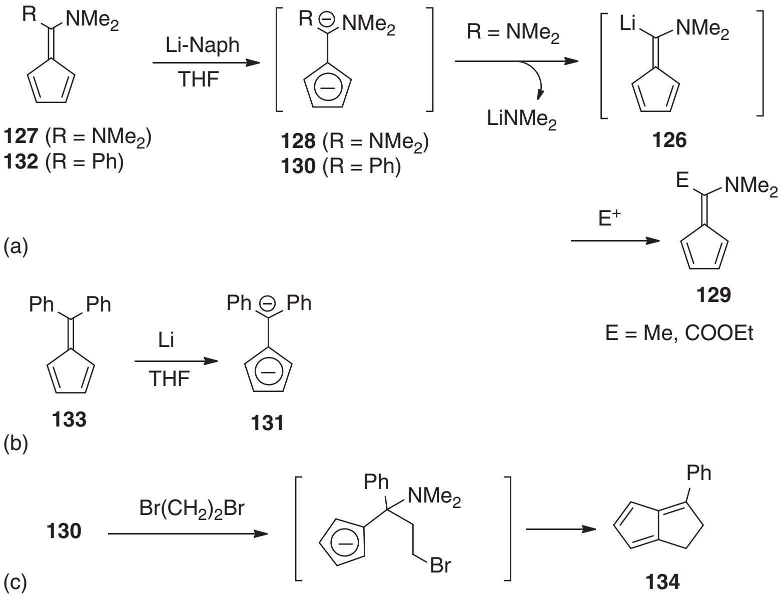
Scheme 6.29

Furthermore, treatment of 6-dimethylamino-6-(2-thienyl)fulvene **135** with lithium naphthalene affords 2-thiafulvalene **136** in 15–20% yield upon aqueous workup [67]. Scheme 6.31 illustrates a proposed reaction mechanism involving ring opening of the 2-thienyl group of the corresponding dianion **137**.

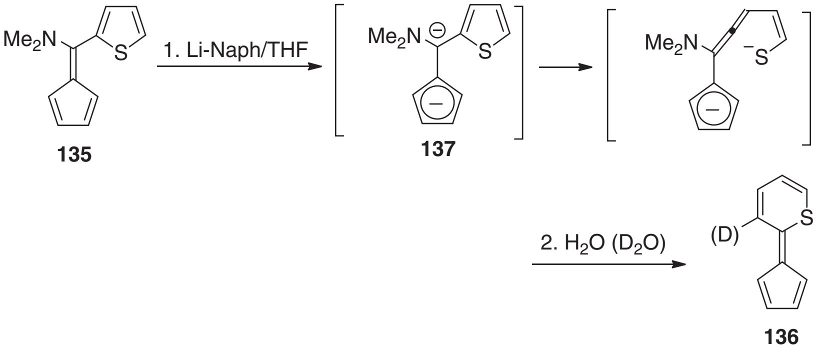
Synthesis Using Ring-Closure Reactions

Schmittel Cyclization The formation of reactive diradical intermediates in the thermal cyclizations of enediynes and enyne–allenes is both mechanistically intriguing and biologically important. The ring-closure reactions to generate benzenoid diradicals **138** and **139** are known as *Bergman* and *Myers–Saito cyclizations*, respectively [68, 69]. The ability of simple reactants to form highly reactive intermediates is usually attributed to the aromaticity gained on cyclization. On the other hand, the cyclization leading to the fulvenoid diradical **140** is known as the *Schmittel cyclization* (Scheme 6.32) [70].

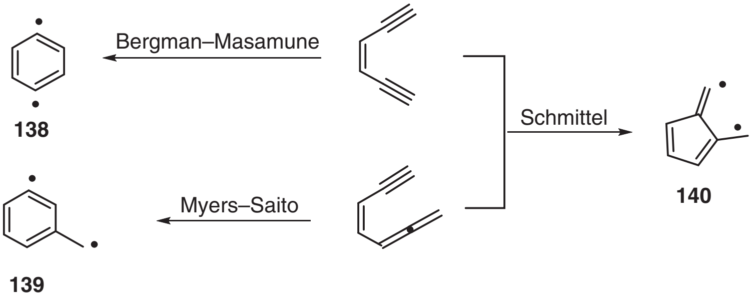
For example, a yne–allene **141** is smoothly converted into a benzofulvene **142** via diradical **143** in good yield (Scheme 6.33a) [71]. Similar regioselective biradical cyclizations from aza-analogous enyneallenes **144** to carbazoles **145** have also



Scheme 6.30

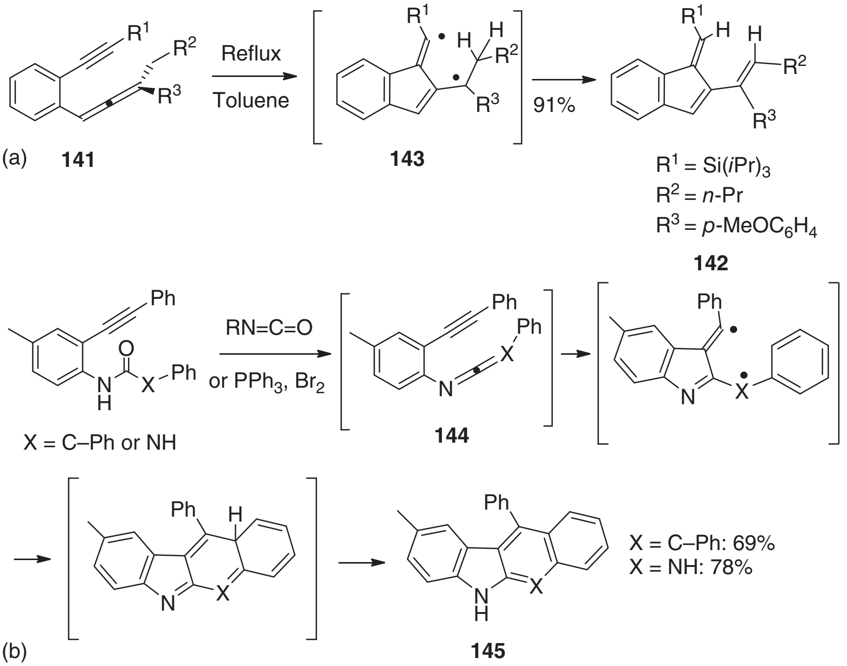


Scheme 6.31



Scheme 6.32

been reported by Schmittel (Scheme 6.33b) [72]. The cyclization gains no aromaticity but is still promoted by the formation of a σ bond from sp-hybridized carbons. Many mechanistic studies of the cyclization have so far been performed from the experimental and theoretical points of view [73].

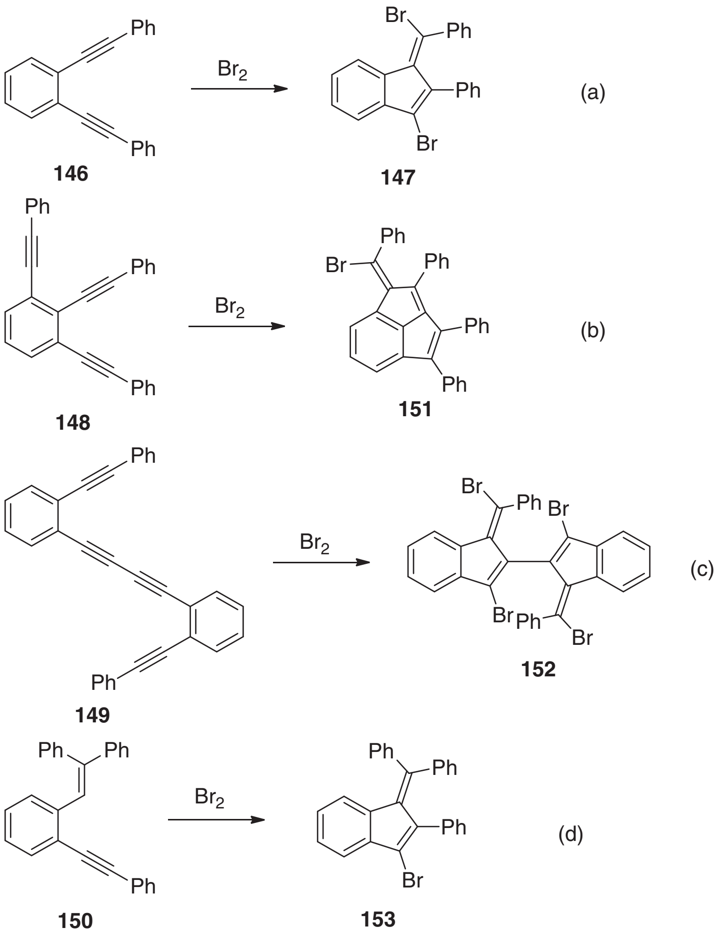


Scheme 6.33

Ring-Closure Reactions from 1,2-Diethynylbenzene Derivatives In 1972, Whitlock reported the reaction of **146** with bromine to afford benzofulvene **147** in good yield (Scheme 6.34a) [74]. Later, Schreiner and coworkers [75] expanded the study; some poly(phenylethynyl)benzenes **148**–**150** lead to novel benzofulvene derivatives **151**–**153** (Scheme 6.34b–d).

Radical cascade transformations using stannyl radical as an initiator efficiently cause analogous ring-closure reactions of oligo-*o*-aryleneeth ynylenes **146** and **154** to benzofulvene derivatives **155** and **156**, respectively (Scheme 6.35) [76].

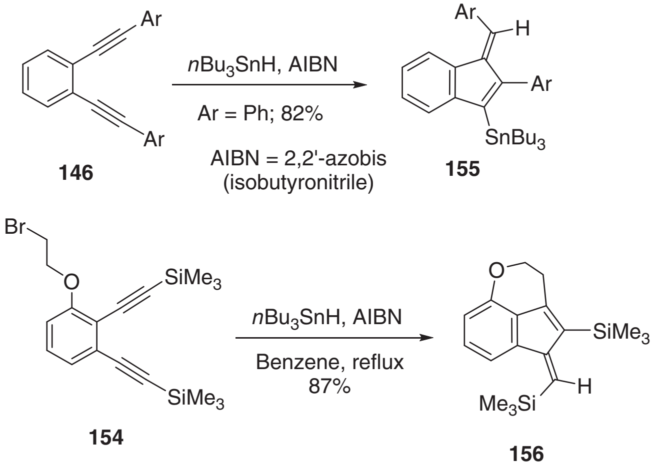
Transition-metal-catalyzed ring-closure reactions of 1,2-diethynylbenzenes have also been investigated. Surprisingly, platinum salts ($PtCl_4$ and H_2PtCl_6) and elemental tellurium catalyzed the ring-closure reaction of **146** to dibenzopentalene derivatives **157** (Scheme 6.36a) [77]. In both cases, the transition metals act as a halogen transfer reagent from halogenated solvents. On the other hand, the reactions of **146** with PdX_2 and CuX_2 (X = Cl or Br) as a catalyst system afforded benzofulvenes **147** in good yields (Scheme 6.36b) [78].



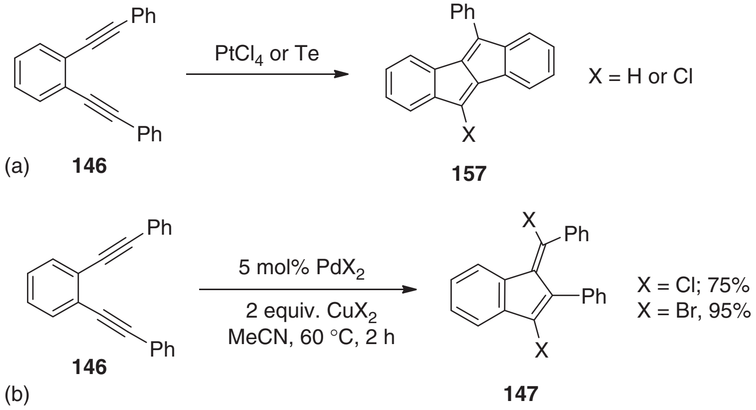
Scheme 6.34

More recently, Au(I)-catalyzed ring-closure reactions of 1,2-diethynylbenzenes **158–160** bearing a terminal acetylene unit afford benzofulvene and dibenzopentalene derivatives **161–163**, as illustrated in Scheme 6.37 [79]. Gold vinylidene complexes are postulated to generate the respective reaction intermediates. These reactions are of importance for the construction of asymmetric polycyclic systems.

Ring-Closure Reactions Using Transition-Metal Catalysts With their mild reaction conditions, wide tolerance of functional groups, ease of scale-up, and transition-metal-mediated intramolecular and intramolecular ring constructions have emerged as an excellent tool for organic synthesis. In the past two decades, synthesis with transition-metal catalysts developed rapidly in the area of fulvene and oxafulvene chemistry [80]. Early studies using transition-metal complexes,



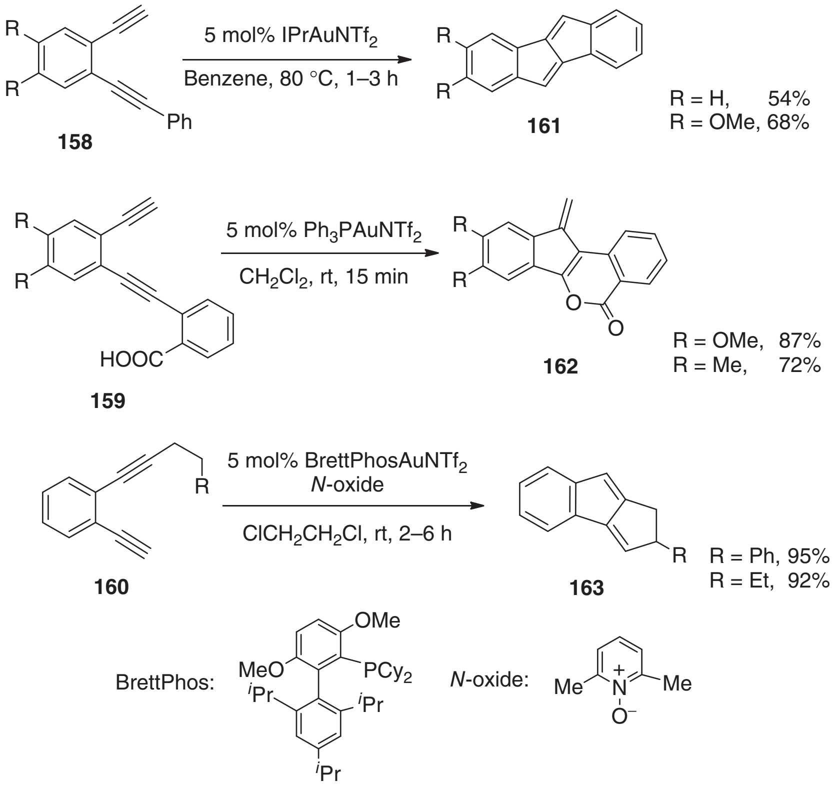
Scheme 6.35



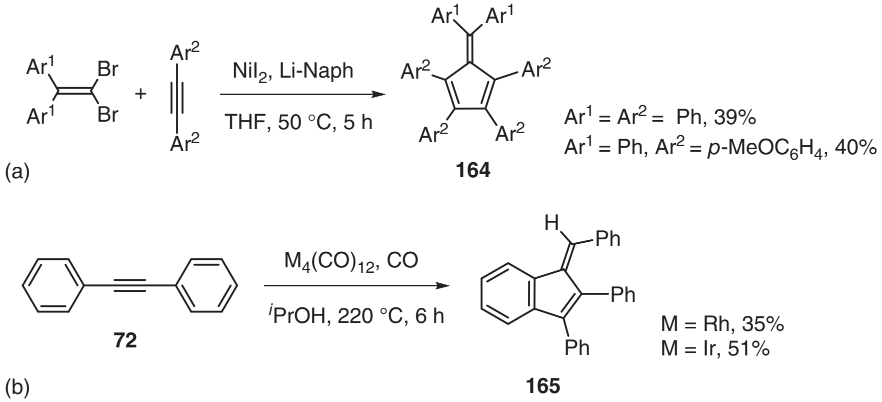
Scheme 6.36

however, often provided fulvenes as a mixture of products. In 1988, Iyoda *et al.* [81] reported that nickel-mediated reaction of 1,1-diaryl-2,2-dibromoethene and diarylacetylene afforded hexaarylpentafulvenes **164** in moderate yields (Scheme 6.38a). Soon afterwards, Yamazaki reported that the reaction of diphenylacetylene **72** and carbon monoxide in the presence of rhodium- or iridium-carbonyl complex leads to benzofulvene derivatives **165**, together with a variety of π-conjugated compounds (Scheme 6.38b) [82]. These reactions used stoichiometric amounts of reagents and were not designed for the synthesis of fulvene derivatives as target molecules.

In 1989, Heck *et al.* [83] first reported the palladium-catalyzed formation of 2,3-diphenyl-l-indenone from *o*-iodobenzaldehyde and diphenylacetylene as a single example (see Section 6.3.5.1). The results stimulated synthetic chemists

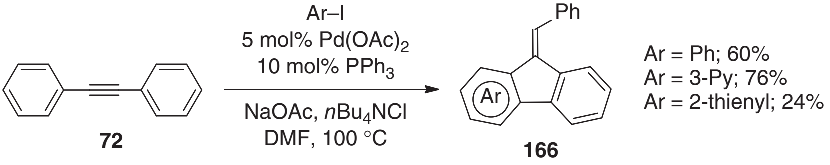


Scheme 6.37



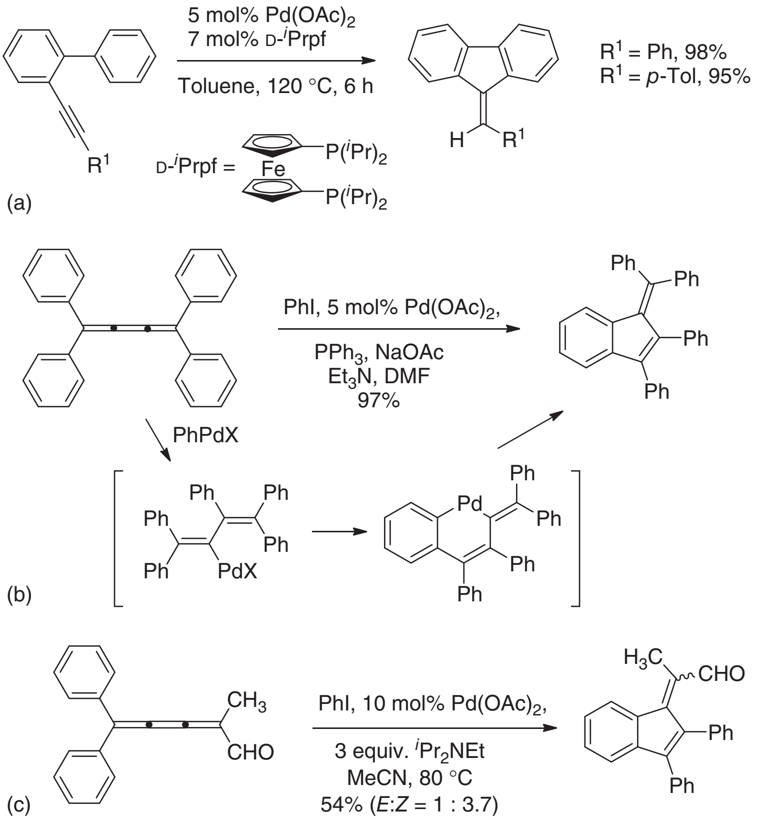
Scheme 6.38

to investigate the construction of polycyclic conjugated systems containing five-membered ring systems. Later, Larock and coworkers observed that Heck type reaction of iodobenzene and diphenylacetylene **72** under standard palladium reaction conditions with NaOAc as base provided 9-benzylidenefluorene **166** (Scheme 6.39) [84].

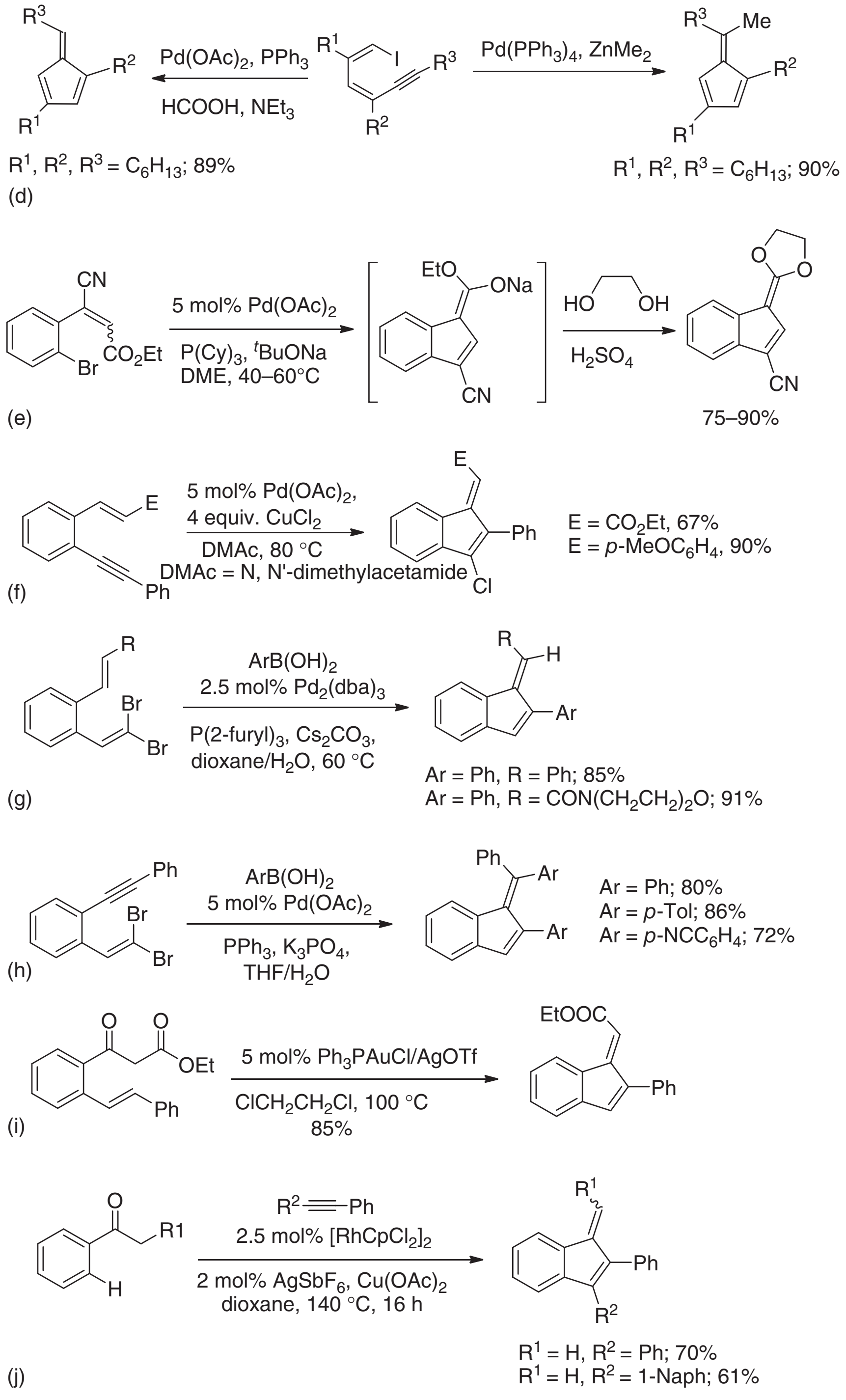


Scheme 6.39

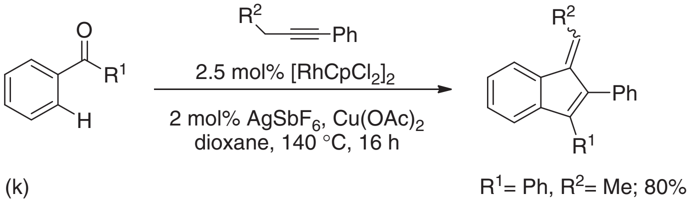
Later, a variety of transition-metal-catalyzed ring-closure reactions leading to fulvene derivatives were reported. These reactions are summarized in Scheme 6.40 [85–96].



Scheme 6.40

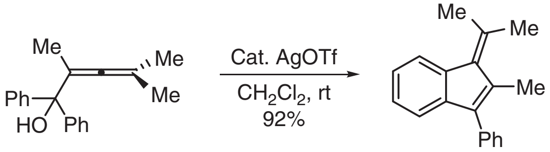


Scheme 6.40 (cont.)



Scheme 6.40 (cont.)

Moreover, a Nazarov-type ring-closure reaction (see Chapter 3) of allenyl alcohols such as **167** to a fulvene, **168**, was shown to be catalyzed by silver triflate (Scheme 6.41) [97].

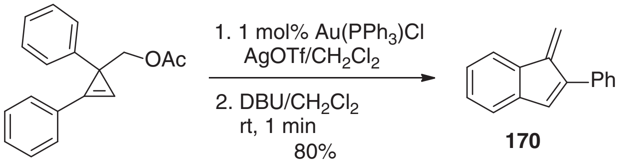


167

168

Scheme 6.41

Ring-Enlargement Reactions Gold catalysis has been known as an efficient method for ring enlargement reactions of cyclopropenes. Cyclopropene **169**, for example, was subjected to Au(PPh_3)Cl to afford a benzofulvene **170** as the major product. A gold vinyl carbenoid has been suggested as the reactive intermediate here (Scheme 6.42) [98].



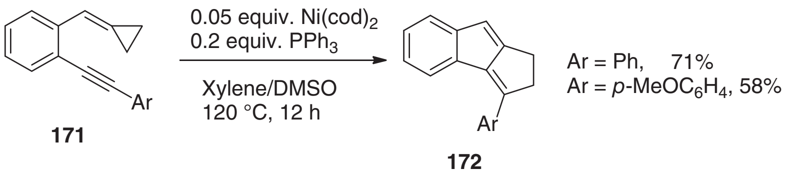
169

170

DBU = diazabicyclo[5.4.0]undecene

Scheme 6.42

A unique Ni(0)-catalyzed intramolecular cycloaddition of methylenecyclopropanes (MCPs) **171** with arylalkynes by cleavage of proximal bonds has been reported by Zhang. An aryl ring moiety was employed as the linker of MCPs and the alkyne, which led to the formation of dihydropentalene derivatives such as **172** (Scheme 6.43) [99].



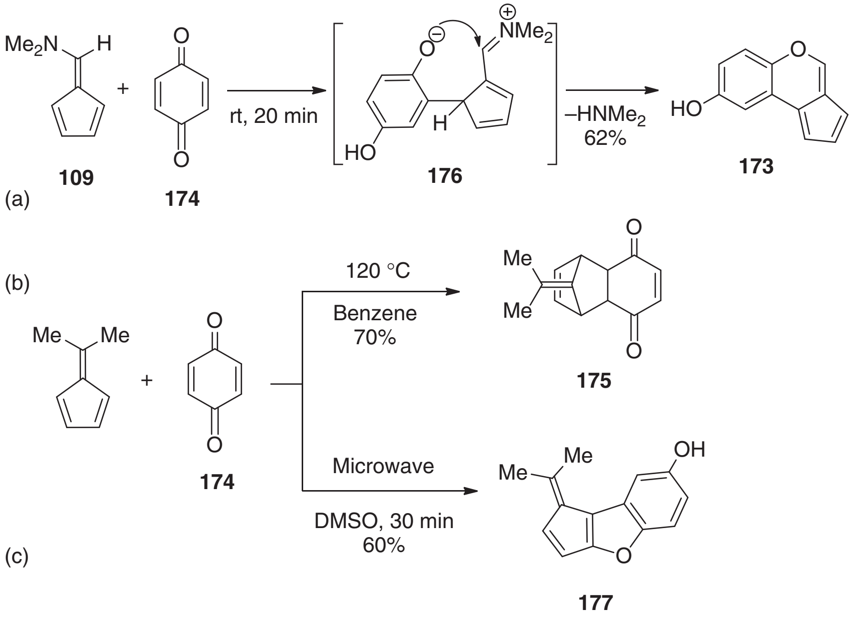
Scheme 6.43

6.3.1.2 Reactions of Pentafulvenes

Cycloaddition Reactions of Pentafulvenes

Due to often easy availability and high reactivity, pentafulvenes can act as versatile synthetic building blocks displaying diverse reaction patterns depending on the reagents, conditions, and substituents. From the viewpoint of the reactants for the cycloaddition process, they can provide three types of π-segments: as the ene, diene, and triene moiety. Actually, cycloaddition reactions of fulvenes constitute general and powerful approaches to polycyclic frameworks. In the past two decades, various types of cycloaddition reactions (e.g., [4+3], [2+2], [2+4], [6+4], [6+3], and [6+2]) were investigated as well as well-known [4+2] cycloaddition process. This section mainly describes the reactions of pentafulvenes as a triene segment.

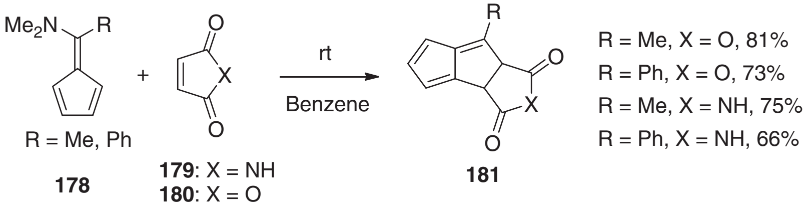
Hong reported an unexpected formation of a cyclopenta[*c*]pyran derivative **173** by the [6+3]-cycloaddition of 6-dimethylaminofulvene **109** and *p*-benzoquinone **174** (Scheme 6.44a); usually, fulvenes react with **174** to give [4+2] cycloadducts



Scheme 6.44

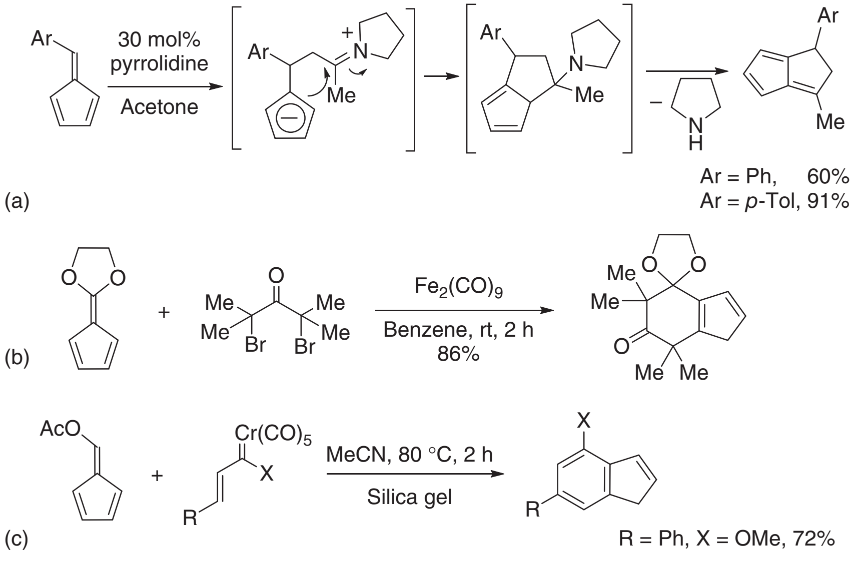
such as **175** (Scheme 6.44b). Formation of the zwitterionic intermediate **176** was postulated in the reaction pathway [100]. Furthermore, the reaction of 6,6-dimethylfulvene and **174** under microwave conditions afforded the hetero-[2+3] adduct **177** in 60% yield (Scheme 6.44c) [101].

Shortly afterwards it was reported that dimethylaminofulvenes **178** adopt the [6+2] cycloaddition modus as a general pathway in reactions with electron deficient olefins; for example, the reactions with maleic anhydride **179** and maleimide **180** gave dihydropentalene derivatives **181** in good yields (Scheme 6.45) [102].

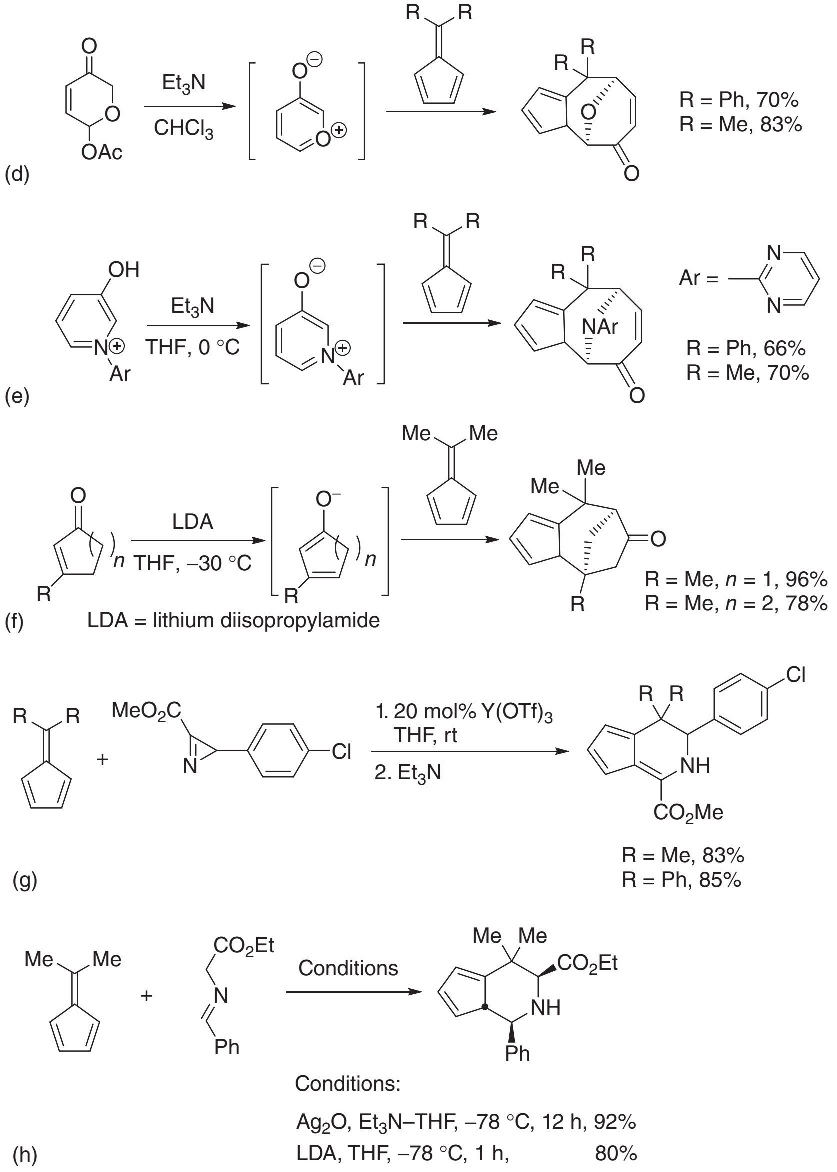


Scheme 6.45

Analogously, fulvene π-systems can act as a triene unit for enamines (Scheme 6.46a) [103], 2-oxyallyl cations (Scheme 6.46b) [104], chromium alkenyl carbene complexes (Scheme 6.46c) [105], 3-oxidopyrylium (Scheme 6.46d) [106], 3-oxidipyridinium betaines (Scheme 6.46e) [107], dienolates (Scheme 6.46f) [108], azirines (Scheme 6.46g) [109], and azomethine ylides (Scheme 6.46h) [110].

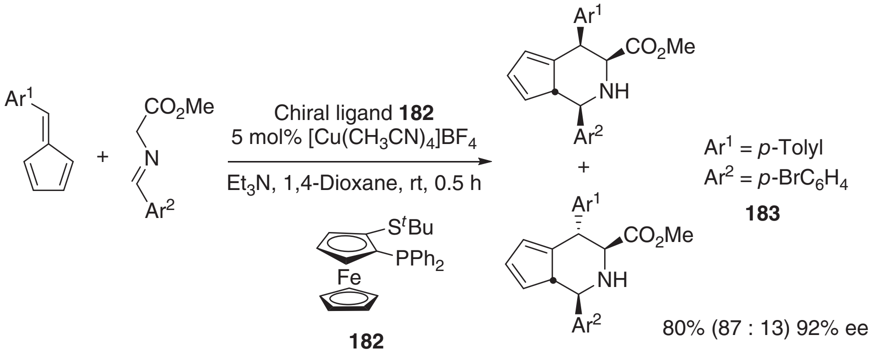


Scheme 6.46



Scheme 6.46 (cont.)

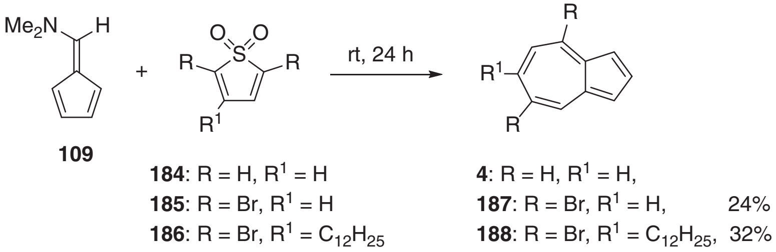
In the last case, the enantioselective cycloaddition of the azomethine ylides was established by Antonchick and Waldmann. Use of substoichiometric amounts of copper(I) salts in the presence of a stereodirecting ligand such as **182** and base led to the formation of two diastereomeric [6+3] cycloaddition products **183** (Scheme 6.47) [111].



Scheme 6.47

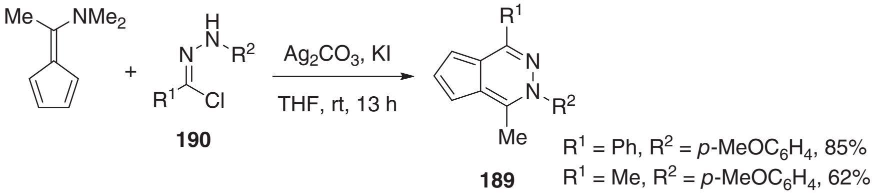
Synthesis of Azulene and Heteroazulene from Pentafulvenes

In 1977, Houk reported a new general synthesis of azulene **4** by using the [6+4] cycloaddition of thiophene-*S*,*S*-dioxides **184** and **109** [112]. This reaction provides the azulene nucleus in a single step. Several azulene derivatives **187** and **188** were prepared; the substituents of the formed azulenes are derived from those of the thiophene-*S*,*S*-dioxides **185** and **186** (Scheme 6.48) [113].



Scheme 6.48

In addition, cyclopenta[*d*]pyridazines **189** as a heteroazulene was prepared by a novel 1,3-dipolar cycloaddition of fulvenes and hydrazonyl chlorides **190** (Scheme 6.49) [114].



Scheme 6.49

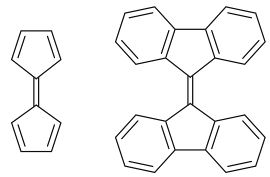


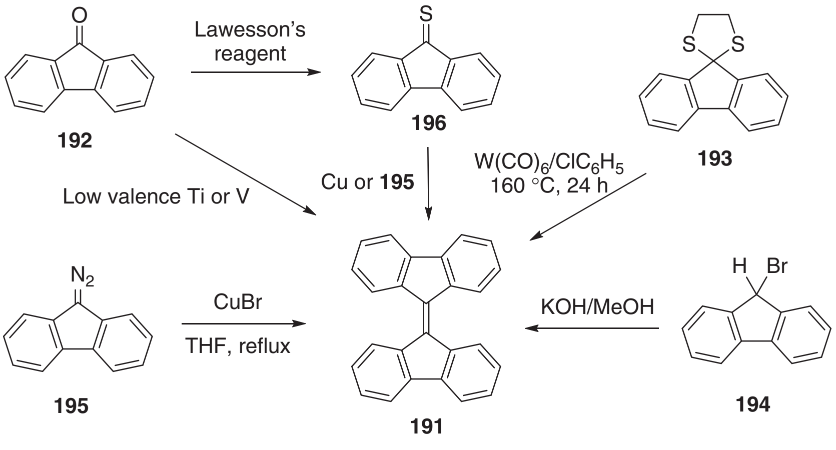
Figure 6.9 Pentafulvalene **9** and 9,9′-bifluorenylidene **191**.

6.3.2
Pentafulvalenes

In contrast to pentafulvalene **9**, benzannulated pentafulvalenes such as 9,9′-bifluorenylidene **191** are thermally fairly stable compounds, because the benzannulation perturbs the electronic properties of the original π-system strongly. Hydrocarbons like **191** have recently attracted much attention from the viewpoints of carbon-rich chemistry and materials science; they can be employed as an electron acceptor with high thermal stability and as a synthetic building block for carbon-rich compounds containing nonplanar conjugated systems as subunits (Figure 6.9).

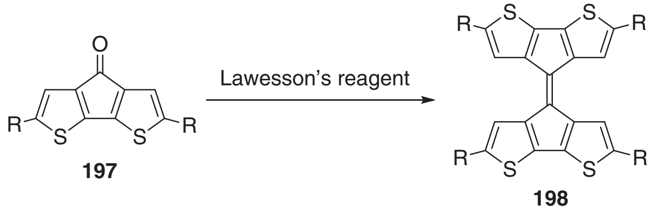
6.3.2.1 Synthesis of Symmetric Benzofulvalenes

Various syntheses of **191** are summarized in Scheme 6.50. Deoxygenative coupling of fluorenone **192** using low-valence titanium [115] and vanadium [116] are efficient methods for preparation of **191**. Similarly, reductive dimerization of a thioacetal **193** with $W(CO)_6$ also affords **191** in good yield [117]. Treatment of 9-bromofluorene **194** with KOH in methanol cleanly gives **191** by an E_2 elimination sequence [118]. Coupling of diazofluorene **195** and thioketone **196**, prepared



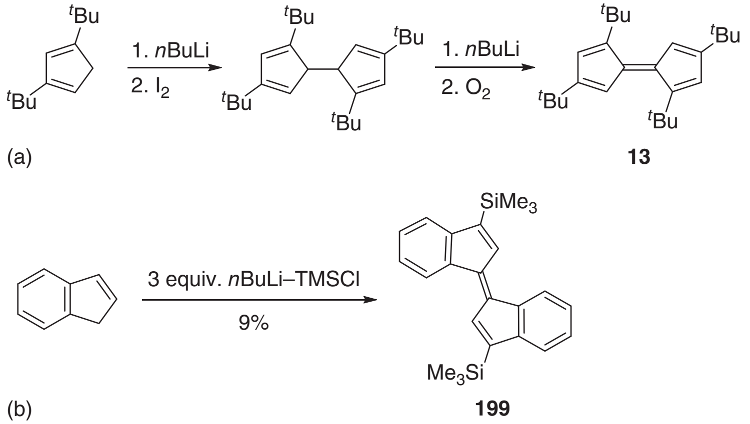
Scheme 6.50

by the reaction of **192** with Lawesson's reagent, in the presence of copper powder affords **191** also [119]. The reaction is known as *Barton's double extrusion diazo–thione coupling method* [120]. Fluorenone analogs like **197** bearing thiophene rings are directly converted into fulvalene derivatives **198** with Lawesson's reagent (Scheme 6.51) [121]. Different from normal oligothiophenes, the derivatives **198** show low band gaps and amphoteric redox behavior due to intramolecular charge transfer [122].



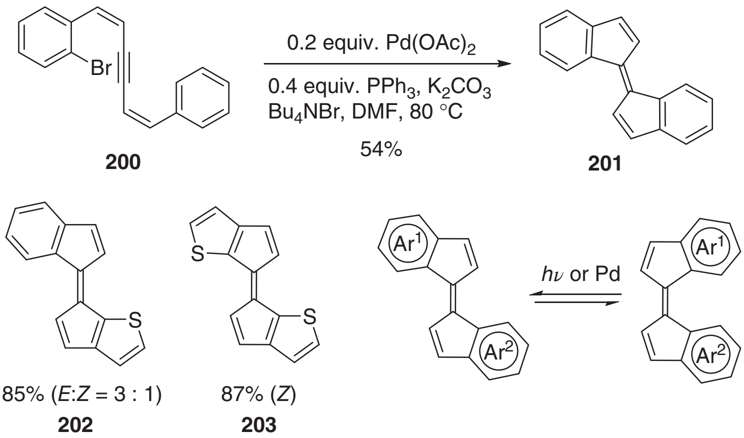
Scheme 6.51

Hafner synthesized tetra-*tert*-butylfulvalene **13** from di-*tert*-butylcyclopenta diene, as shown in Scheme 6.52a [5]. The method involves oxidative coupling of the corresponding CP anion with iodine. Unexpectedly, subsequent treatment of indene with *n*-butyllithium and trimethylsilyl chloride (TMSCl) afford dibenzofulvalene **199** as a stable bright red solid in low yield together with silylated indenes (Scheme 6.52b) [123].



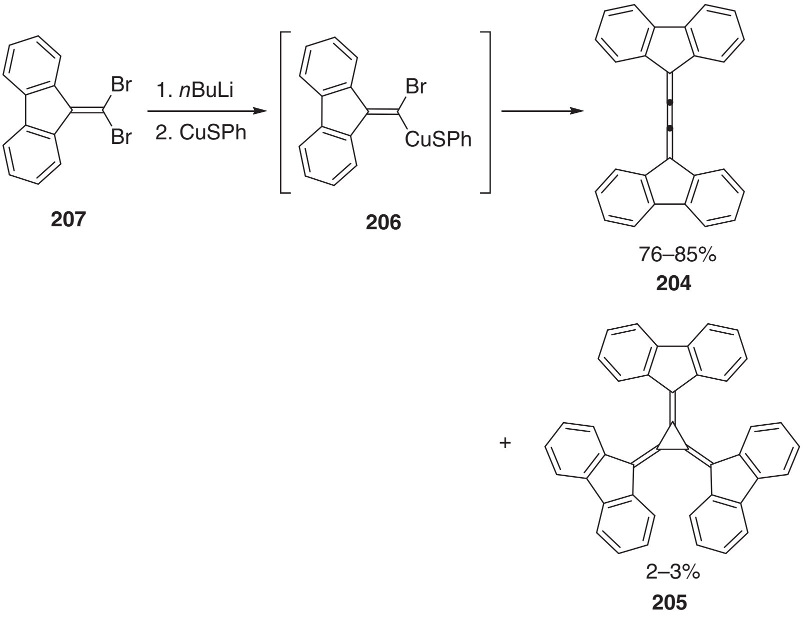
Scheme 6.52

Tobe reported that palladium-catalyzed ring-closure reaction of **200** provides 1,1′-biindenylidene **201** by a domino-Heck-type double cyclization in moderate yields (Scheme 6.53) [124]. The reaction is applicable to the synthesis of fulvalene derivatives involving thiophene ring(s) **202** and **203** [125]. The (*Z*)-isomers of the products are obtained selectively; they can be transformed into the corresponding (*E*)-isomers by Pd-catalyzed *E*/*Z*-isomerization or photoisomerization.



Scheme 6.53

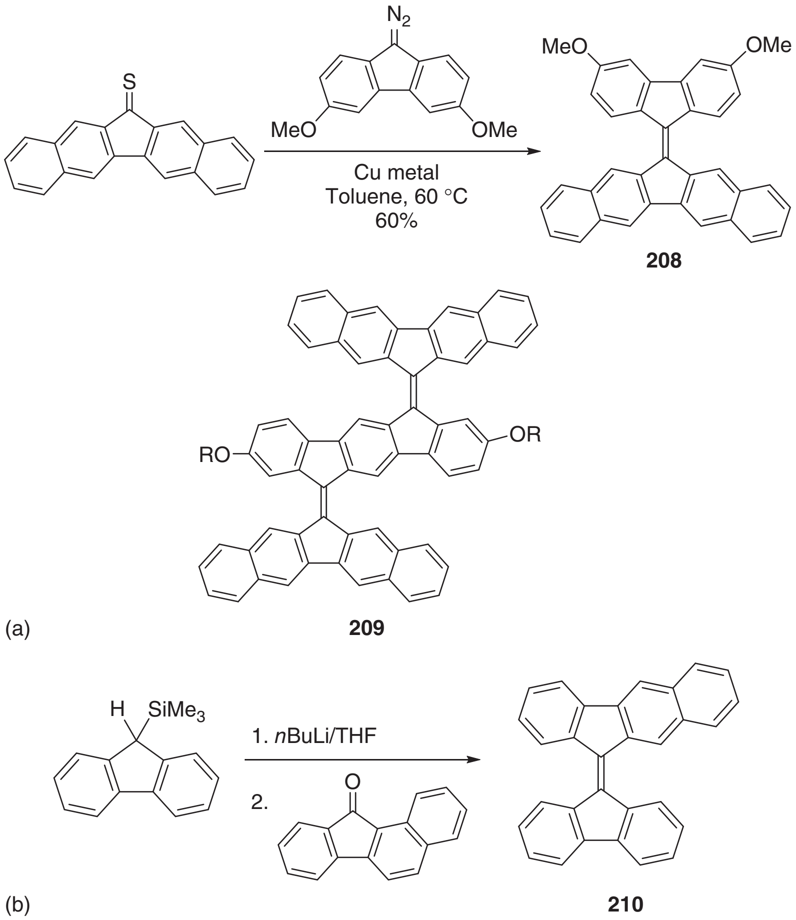
Fulvalene analogs possessing a butatriene moiety **204** together with a [3]radialene **205** (see Chapter 4) were obtained by a reductive oligomerization of the copper carbenoid **206** derived from dibromomethylene **207** by Iyoda and Oda. These compounds are thermally stable and intensely colored (Scheme 6.54) [126].



Scheme 6.54

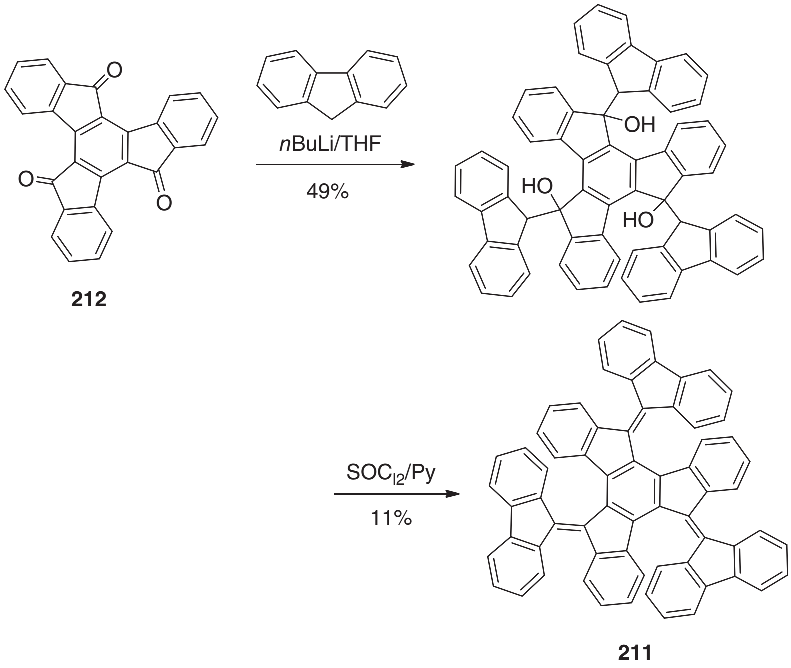
6.3.2.2 Synthesis of Asymmetric Benzofulvalenes

Recently, several groups (Wudl, Brunetti, and Agranat) prepared various symmetric and asymmetric benzofulvalene derivatives such as **208–210** for evaluating their inherent potential as electron acceptors. The Barton method (Scheme 6.55a) and the Peterson olefination (Scheme 6.55b) were employed for the syntheses [119, 127]. Among them, Wudl and Heeger's groups demonstrated that dissymmetric bifluorenylidene **208** is significantly distorted from planarity with a torsional angle of 36.51°; it can be used as an electron acceptor for organic photovoltaic devices (with an open-circuit voltage (V_{OC}) of 1.10 V, a fill factor (*FF*) of 0.40, and a power conversion efficiency (PCE) of 1.7%) [119].



Scheme 6.55

An overcrowded fulvalene derivative **211** based on a truxene core was also prepared by treatment of truxenetrione **212** with fluorenyl lithium and dehydration of the formed alcohol using thionyl chloride (Scheme 6.56) [128].



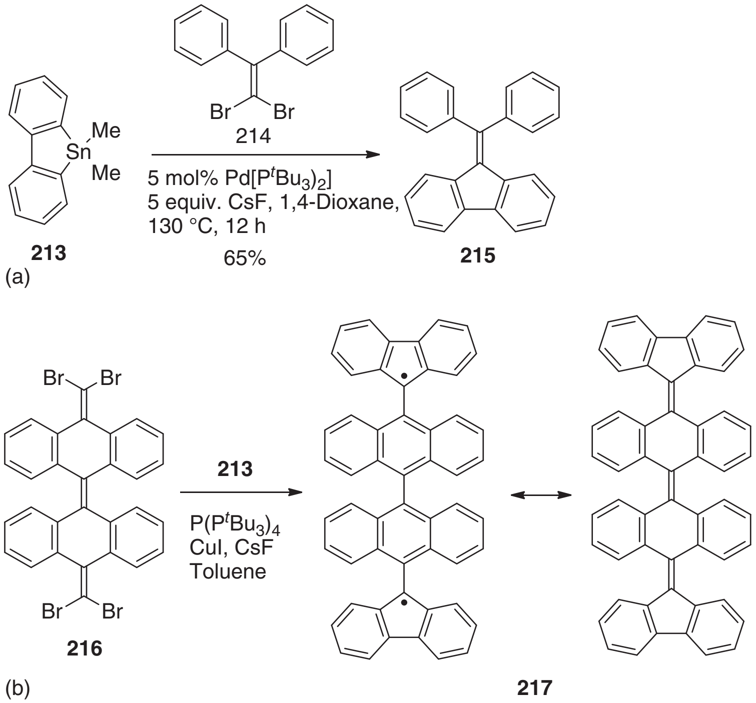
Scheme 6.56

Shimizu and Hiyama [129] reported that the palladium-catalyzed double-cross-coupling reaction of 9-stannafluorenes **213** with 1,1-dihaloethylene **214** yields the dibenzofulvene **215** (Scheme 6.57a). The 9-stannafluorene **213**, an equivalent of a 1,4-dimetalated reagent, is available from the corresponding 2,2′-dihalobiphenyls. The reaction was applied to the synthesis of the π-extended fulvalene derivative **217** from **216**. The former is a stable benzannulated Chichibabin hydrocarbon possessing an open-shell diradical character (Scheme 6.57b) [130].

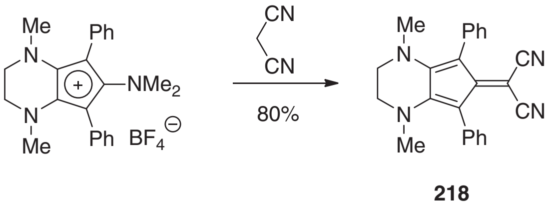
6.3.3
Synthesis of Pentafulvenes as Functional Dyes

6.3.3.1 6,6-Dicyanofulvenes

As mentioned, since the discovery of metallic conductivity in the charge-transfer complex from TTF **24** and TCNQ **25** in 1973, various functional dyes have been designed on the basis of TTF and TCNQ derivatives. Although fulvene derivatives bearing a dicyanomethylene unit would possess strong electron-accepting properties, they have received little attention until quite recently, probably due to expected high instability similar to CPDN. 6,6-Dicyanofulvene derivative **218** was firstly synthesized by Gompper in 1988 (Scheme 6.58). The push–pull electronic structure would enhance the thermal stability of **218** [131]. On the other hand, benzannulation should enhance the stability. Fluorenylidene



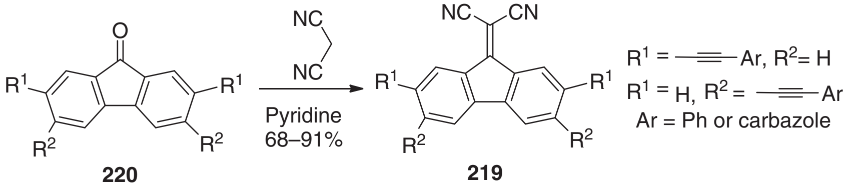
Scheme 6.57



Scheme 6.58

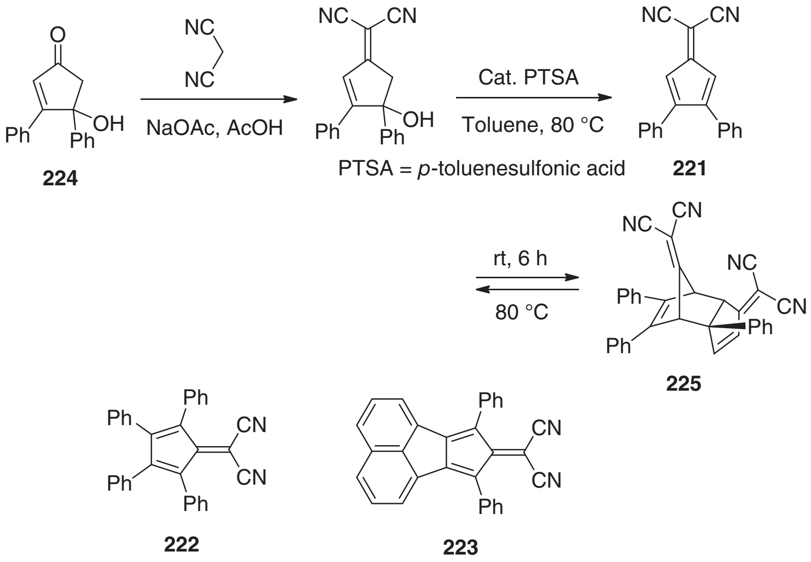
derivatives **219** with arylethynyl groups at 2,7- and 3,6-positions are obtained as stable compounds by Knoevenagel condensation of corresponding fluorenone derivatives **220** (Scheme 6.59). Their optical properties were evaluated by Estrada and Neckers [132].

Swager and coworkers explored the synthesis and electronic properties of 6,6-dicyanofulvenes **221**–**223**. As shown in Scheme 6.60, 2,3-diphenyl-6,6-dicyanofulvene **221** is synthesized in two steps from cyclopentenone **224**. Compound **221** dimerizes even at room temperature to form **225**. The dimerization is reversible: **221** can be recovered by heating **225** at 80 °C. On the other hand, highly substituted dicycanofulvenes **222** and **223** are obtained as stable



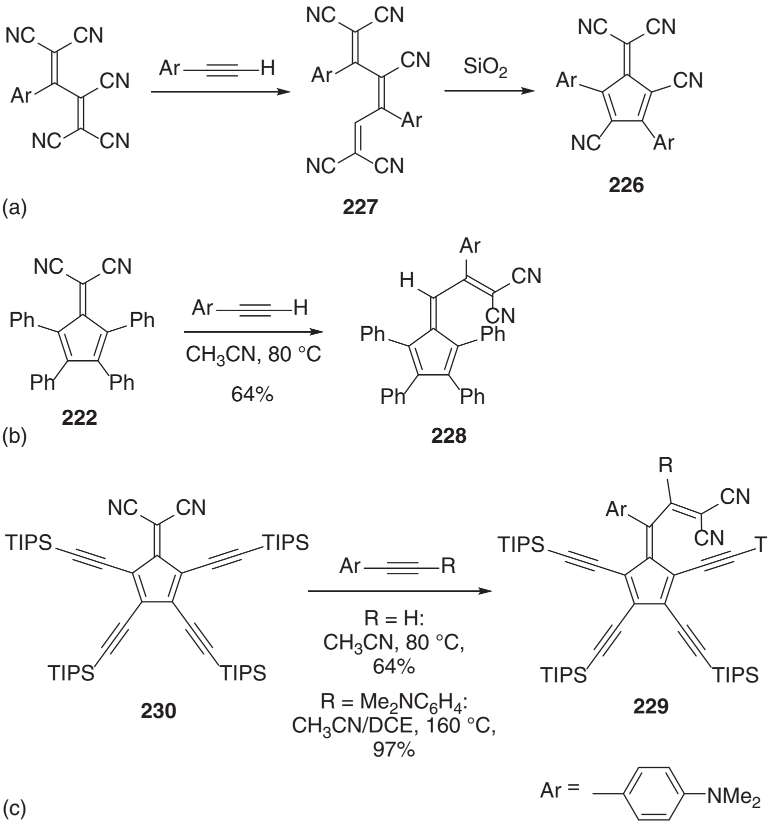
Scheme 6.59

compounds from the corresponding CPDNs straightforwardly. These fulvenes show high electron affinity and display two distinct, reversible one-electron reductions by cyclic voltammetry [133].



Scheme 6.60

Diederich and coworkers have developed a new class of push–pull chromophores resulting from the formal [2+2] cycloaddition–retroelectrocyclization (CA–REC) reaction between electron-rich alkynes and electron-poor olefins such as tetracyanoethylene (TCNE) [134]. A highly functionalized 6,6-dicyanopentafulvene **226** with an intense, low-energy charge-transfer band is obtained by a novel ring-closure reaction of a push–pull chromophore **227** (Scheme 6.61a) [135]. Later, they also reported the synthesis of new fulvene-based push–pull chromophores **228** and **229** via the formal [2+2] CA–REC reaction of dicyanopentafulvenes **222** and **230** with electron-rich alkynes (Scheme 6.61b,c) [136].

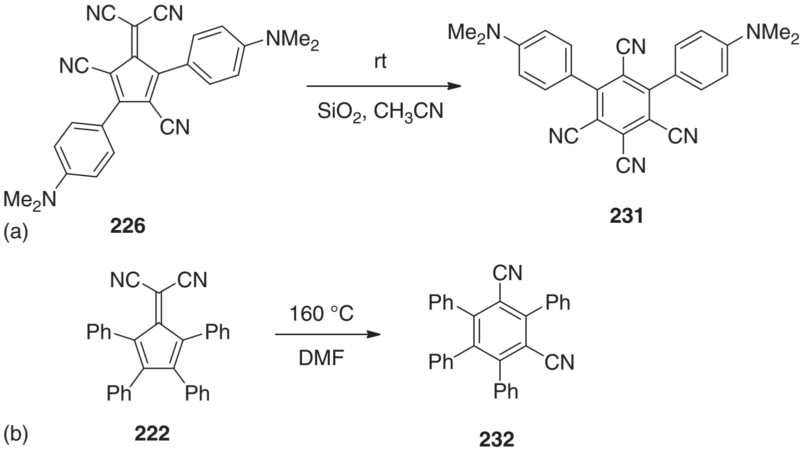


Scheme 6.61

Quite recently, Diederich and coworkers reported a novel thermal rearrangement from 6,6-dicyanofulvenes to 1,3-dicyanobenzenes. A push–pull-substituted 6,6-dicyanofulvene **226** is smoothly converted into 1,3-dicyanobenzene **232** at room temperature in the presence of hydrated acidic SiO_2 in acetonitrile [137]. Surprisingly, when 6,6-dicyano-1,2,3,4-tetraphenylpentafulvenes **222** was heated to 160 °C for 1 h in DMF, it quantitatively rearranged to the 1,3-dicyanobenzene derivative **232** in high yields [138]. Because this reaction requires polar aprotic solvents, the authors proposed a "ring-walk" mechanism involving ionic intermediates (Scheme 6.62).

6.3.3.2 1,3-Dithiafulvalenes

1,3-Dithiafulvalene **233** as a fulvene analog of TTF **24** can be regarded as a conjugated donor–π–acceptor molecule (D–p–A) with strong electronic coupling between the D(onor) and A(cceptor) moieties. These dyes have been of general interest for a number of electronic and optoelectronic applications. The 1,3-dithiol-2-ylidene unit has been widely used as a component of new π-electron donor systems due to the high thermodynamic stability of the derived cation



Scheme 6.62

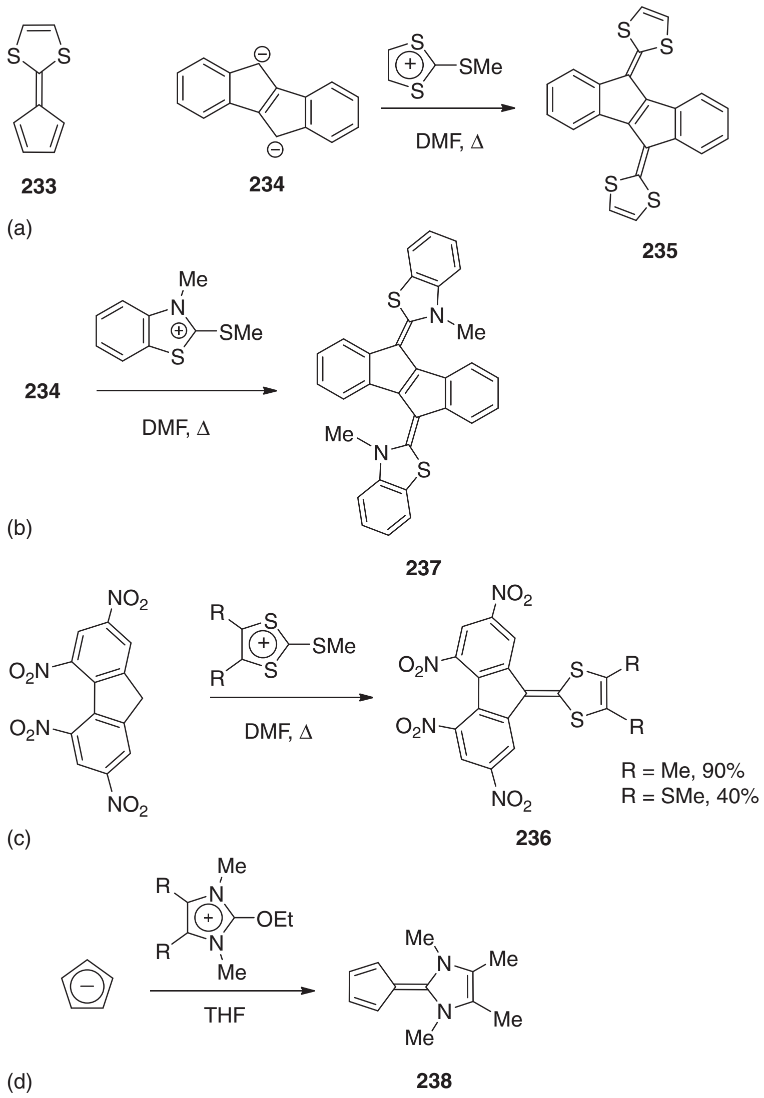
radical species that contains the heteroaromatic 6π-electron dithiolium cation. The reactions of the 1,3-dithiol cation and CP anion derivatives **234** readily afford the corresponding dithiafulvalene derivatives **235** and **236**. Typical examples were reported by Gompper's and Sokolov's groups (Scheme 6.63a,c) [139, 140]. The method is applicable to the construction of the corresponding thiaza- and azafulvalene derivatives **237** and **238** also (Scheme 6.63b,d) [141].

1,3-Dithiafulvalene derivatives **239** fused with aromatic rings are also accessible by olefination of the corresponding fluorenone and its thiophene analogs **240** using 1,3-dithiole Wittig–Horner reagents **241** under basic conditions (Scheme 6.64). The method is widely applicable to the synthesis of π-extended dithiafulvelene derivatives **242** and **243** with high electron-donating properties [142]. Martin and coworkers synthesized truxene-TTF derivatives **243** with multistage redox properties as an electron donor system. A derivative **243** (R = H) exhibits host properties for fullerenes owing to its concave bowl-shaped configuration [143].

Kato and coworkers also synthesized C_3 symmetric, truxene-based TTF and TCNQ derivatives **244** and **245** (Scheme 6.65). These compounds exhibit columnar liquid crystalline (LC) phases, and serve as n- and p-type semiconducting materials with the carrier mobilities on the order of 10^{-4} cm^2 V^{-1} s^{-1}, respectively [144].

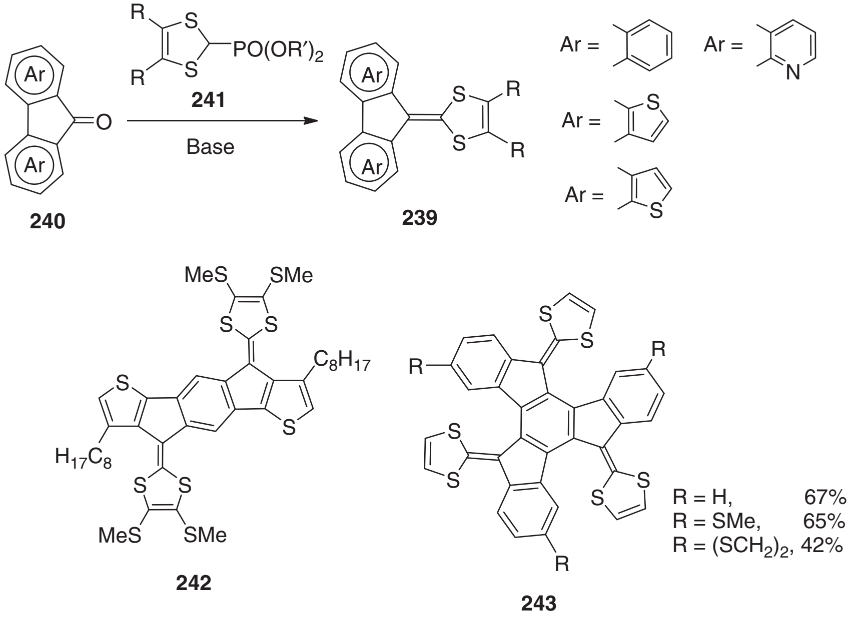
6.3.4
Fused Ring Systems Involving Pentafulvene Moieties

Fully conjugated polycyclic systems involving pentafulvene moieties, such as azulene **4**, pentalene **5**, and indacene **6**, have attracted much attention due to their novel properties. Recently, higher oligoacenes such as rubrene **246** and pentacene

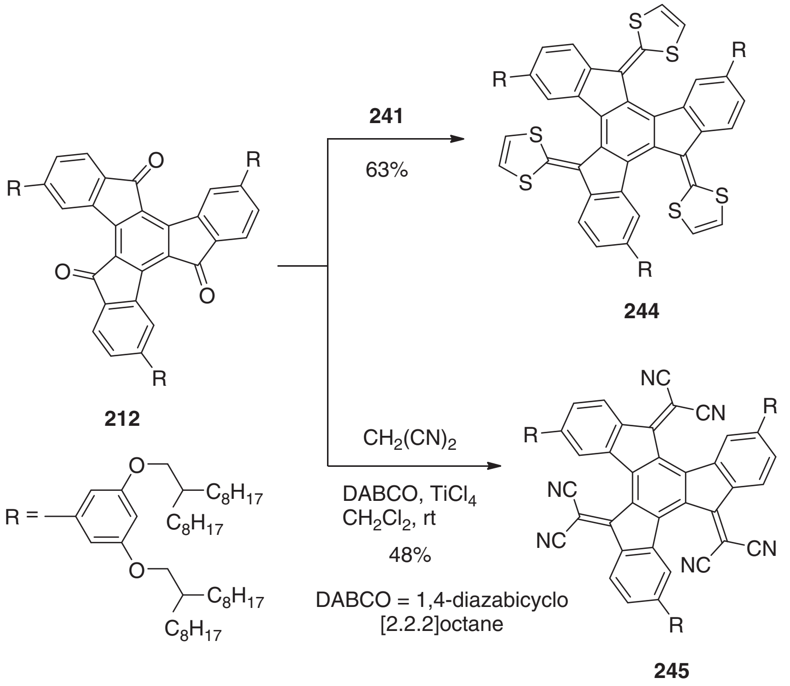


Scheme 6.63

247 have been shown to be essential as the active layer in high-performance organic field effect transistors (OFETs) (Figure 6.10); they are, however, less stable due to their reduced aromaticity [145]. Researchers have thus focused on more stable, but structurally related π-extended, polycyclic compounds as substitutes for acenes. In this context, dibenzopentalene **248** and dibenzoindacene **249** have been explored as a functional dye for potential applications in organic electronics [146]. In contrast to the parent π-systems, pentalene **5** and indacene **6**, they are stable and isolable compounds with a planar π-skeleton.



Scheme 6.64



Scheme 6.65

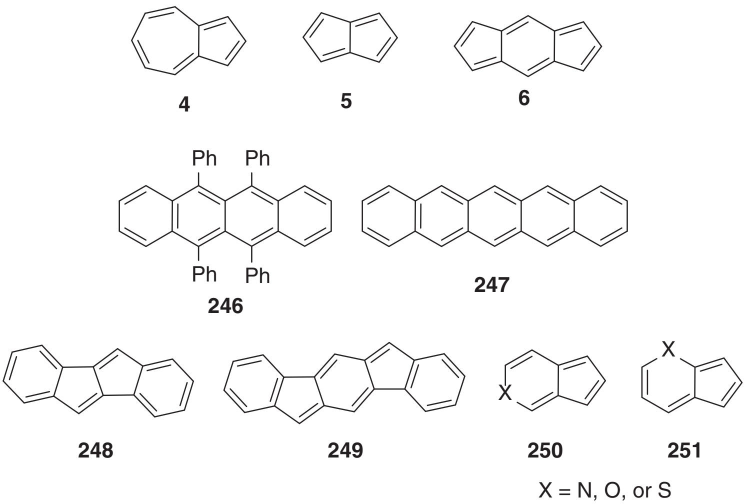
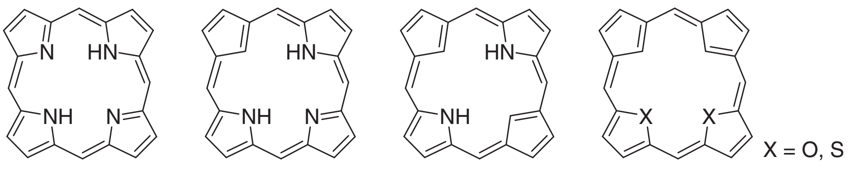


Figure 6.10 Azulene **4**, pentalene **5**, indacene **6**, rubrene **246**, pentacene **247**, dibenzopentalene **248**, dibenzoindacene **249**, and pseudoazulenes **250** and **251**.

Pseudoazulenes **250** and **251** are π-isoelectronic with azulene **4**, where the lone pair of electrons of a heteroatom in the six-membered ring is formally derived from one of double bonds at the seven-membered ring of the azulene skeleton. Therefore, these compounds should exhibit similar but specific properties in relation to azulene. Recently, it has been shown that a 5*H*-cyclopenta[*c*]quinolone derivative displays moderate-to-high inhibitory activity against cancer cells. This possible biological importance renewed interest in this class of compounds. Because some old reviews summarize the synthesis and the chemistry of pseudoazulenes [147], this section describes new synthetic methodologies published in the past two decades only. Because new azulene syntheses published during the past two decades are discussed in Sections 6.3.1.2 and 6.4.1, this section skips the azulene chemistry.

As mentioned in Section 6.1, this chapter does not deal with the chemistry of porphyrin **25** and its analogs. Nevertheless, porphyrin analogs bearing a pentafulvene moiety in the π-system, namely, "carbaporphyrinoids," are described in this section. The nitrogen electrons must have an important influence on the electronic structure of the porphyrin π-system, but it is less obvious how significant the [18]annulene substructure is in relation to the chemical, physical, and spectroscopic properties of the macrocycles. Berlin and Lash have explored the possibility of replacing one or more of the nitrogen atoms in the porphyrin macrocycle by carbon atoms. So far, three carbaporphyrinoid systems **252**–**254** and some related compounds have been synthesized (Figure 6.11).

The last part of this section concentrates on the synthesis of fullerene fragments possessing fulvalene π-systems. Recent advances in fullerene chemistry have attracted much interest in bowl-like polycyclic aromatic hydrocarbons (PAHs)



25 **252** **253** **254**

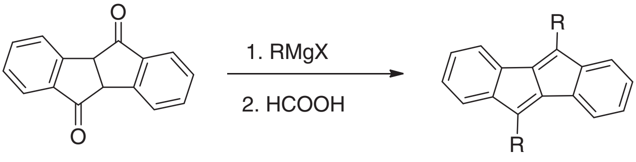
Figure 6.11 Porphyrin **25** and a selection of carbaporphyrinoids **252–254**.

as fullerene fragments [148]. For their synthesis, 9,9′-fluorenylidene **191** and its derivatives as overcrowded fulvalene moieties can be regarded as good starting materials. This section describes pyrolytic and photocatalyzed pericyclic and transition-metal-catalyzed ring-closure reactions as the synthetic key step.

6.3.4.1 Dibenzopentalenes

Pentalene **5** is a bicyclic conjugated system possessing an eight π-electron periphery. Various experimental results indicate that pentalenes without bulky substituents are highly elusive due to their high reactivities [1]. In contrast, dibenzo[*a,e*]pentalene **248** with C_{2h} symmetry is a fairly stable compound despite possessing a 16π-electron periphery and a planar structure [149].

In 1912, Brand reported the first synthesis of dibenzopentalenes **256** from diphenylsucindanedione **255** (Scheme 6.66) [150]. Cava and coworkers applied Brand's method to synthesize various 5,10-diaryldibenzopentalenes including a di(2-thienyl) derivative **257** for application in electronic devices [151].

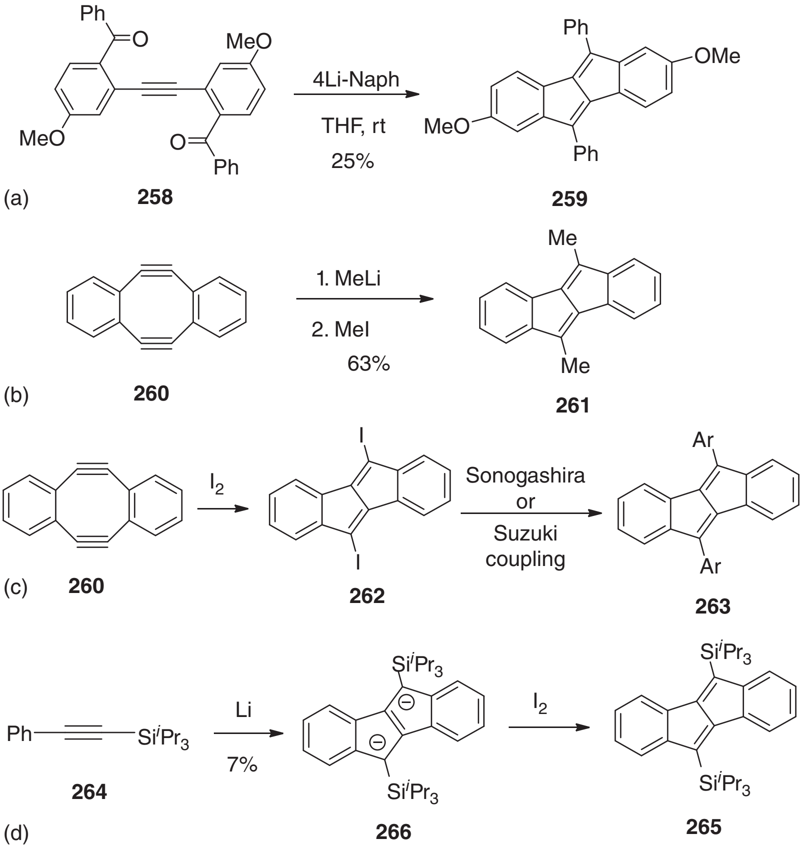


255

256: R = Ph
257: R = 2-Thienyl

Scheme 6.66

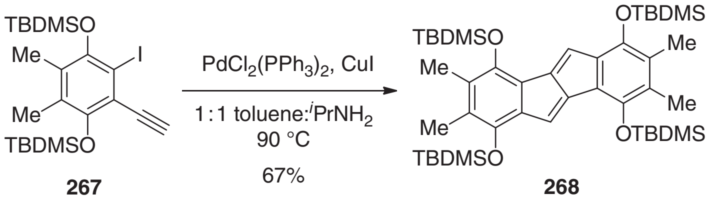
Intramolecular cyclization reactions of *o*-substituted phenylacetylene derivatives are also effective for dibenzopentalene synthesis. Yamaguchi reported that reduction of *o,o*′-bis(aryl-carbonyl)diphenylacetylenes **258** with lithium naphthalenide produces dibenzopentalenes **259** in 8–25% yields (Scheme 6.67a) [152]. Orita and Otera's groups demonstrated that treatment of dibenzocyclooctadiyne **260** with methyllithium followed by iodomethane affords the dimethyl derivative **261** by a transannular reaction (Scheme 6.67b) [153]. 5,10-Diiododibenzopentalene **262** derived from **260** by a similar treatment with iodine can be converted into variety of dibenzopentalene derivatives **263** involving dibenzopentalene oligomers using a combination of Sonogashira and Suzuki couplings from **262** (Scheme 6.67c) [154]. Saito found that the reduction of phenyl(triisopropylsilyl)acetylene **264** with lithium to produce dilithium dibenzopentalenide **265**, which is subjected to oxidation with iodine to afford 5,10-bis(triisopropylsilyl)dibenzopentalene **265** (8%) in a one-pot manner (Scheme 6.67d) [155]. His group has explored the electronic and structural properties of the dianion **266** and of the radical anion of dibenzopentalenes [156].



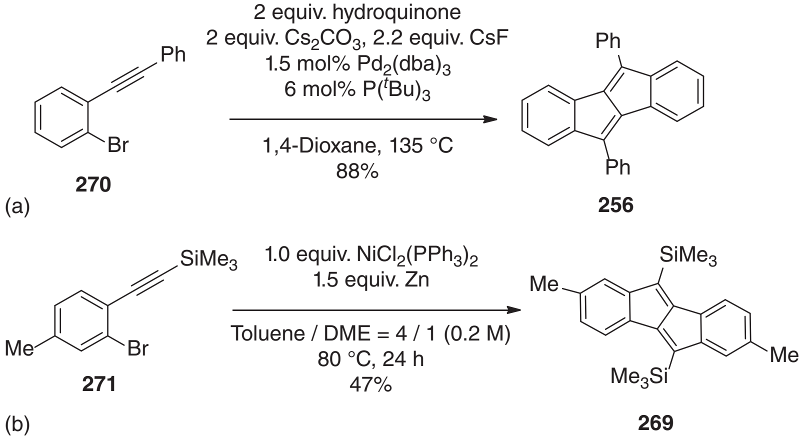
Scheme 6.67

In 1999, Youngs reported the formation of a dibenzopentalene derivative **267** from an *o*-iodoethynylbenzene **268** under Sonogashira coupling conditions (Scheme 6.68) [157]. Unfortunately, this reaction seems to be an exceptional case because the Sonogashira reaction of *o*-iodoethynylbenzenes generally affords phenylene–ethynylene macrocycles [158].

Recently, Tilley's and Kawase's groups independently found a novel reaction yielding dibenzopentalene derivatives **256** and **269** from readily available *o*-bromoethynylbenzenes **270** and **271** using palladium (Scheme 6.69a) and nickel complexes (Scheme 6.69b) [159, 160]. These reactions can provide



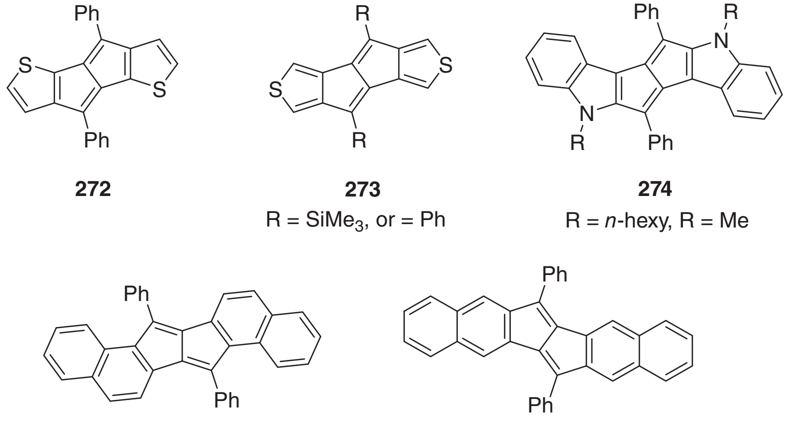
Scheme 6.68



Scheme 6.69

various π-extended pentalene derivatives. Tilley initially synthesized di-(2,3)-thienopentalene **272**; the isomer di-(3,4)-thienopentalenes **273** was prepared by Kawase soon afterwards [159, 161]. Using Tilley's method, Li and Zu's group synthesized pentalene derivative **274**, which contains doubly fused indole rings (Figure 6.12) [162]. Dinaphthopentalenes **275** and **276** are readily accessible by Kawase's method from the corresponding bromoethynylnaphthalenes. Among these derivatives, **276** is the first pentalene system applicable to the construction of an organic thin-film transistor. While **256** and **275** show negligible mobilities under the measurement conditions, **276** has a hole mobility of $1.8 \times 10^{-3}\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$ with current on/off ratio (I_{on}/I_{off}) of 10^5, which is a comparatively high value for an amorphous material. Moreover, **276** has been applied to an electron-donor layer for heterojunction organic thin-film solar cells (PCE = 0.94% and $V_{OC} = 0.96\ \mathrm{V}$) [163]. These results also suggested that π-extended pentalenes should provide a good platform for materials applicable to organic electronics.

Under Heck conditions, bromostilbene derivatives **277** reacted with diphenylacetylene **278** to afford indene **279**. Oxidative cyclodehydrogenation of **279** with $FeCl_3$ (Scholl reaction) affords the pentalene **280** as a dark purple solid in 38% yield (Scheme 6.70) [164]. Tilley and Levi [165] applied the method to the synthesis of a series of extended dibenzopentalene derivatives **281**–**283** (Figure 6.13).



272

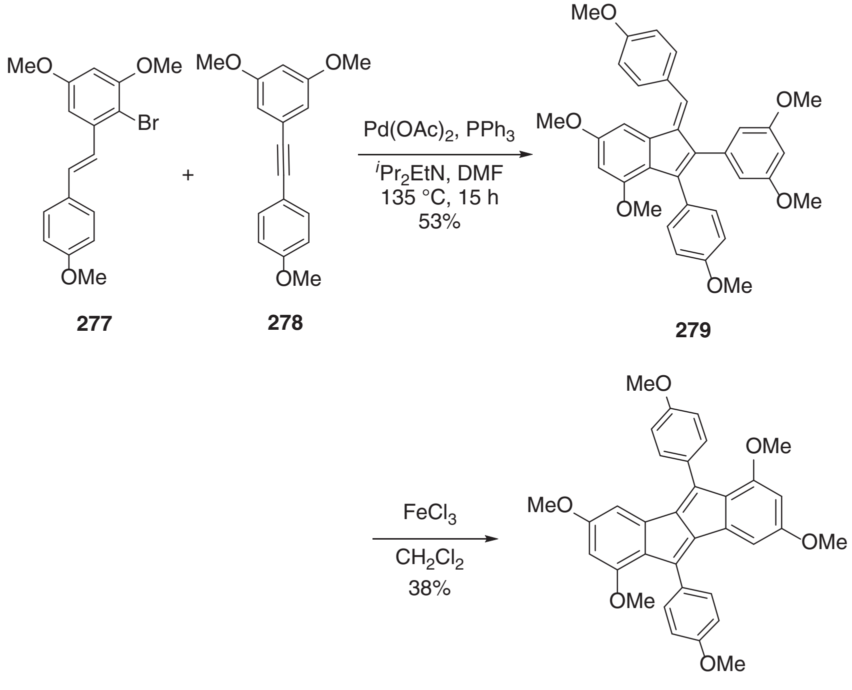
273
R = SiMe$_3$, or = Ph

274
R = *n*-hexy, R = Me

275

276

Figure 6.12 Dibenzopentalene related compounds **272**–**276**.



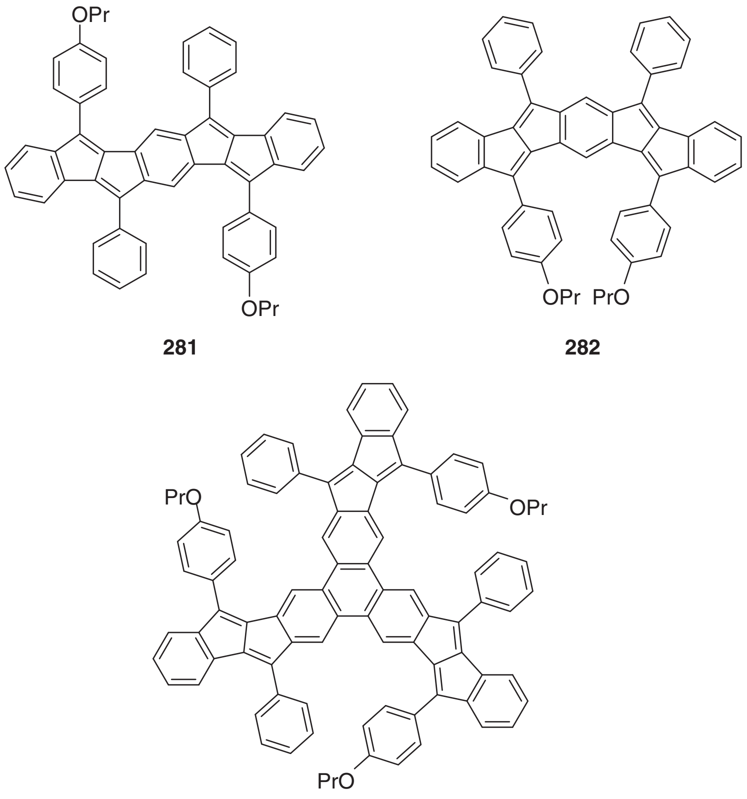
277

278

279

280

Scheme 6.70



281 **282**

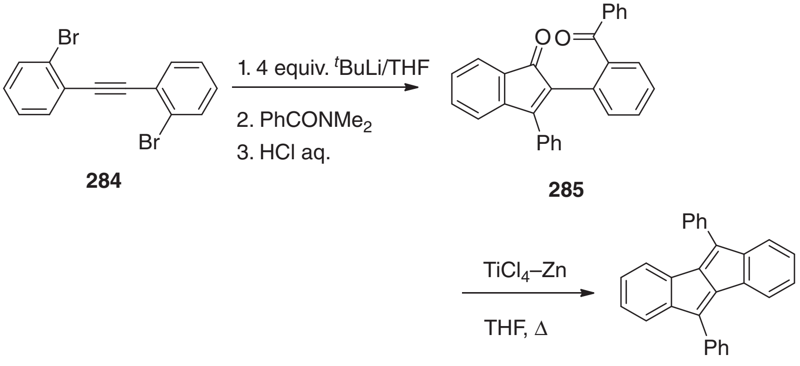
283

Figure 6.13 Fused dibenzopentalenes **281**–**283**.

Recently, Kawase developed a new synthesis for dibenzopentalene from an indenone derivative prepared by a novel amino-migration reaction. The reaction of 2,2′-dilithiotolan, generated from corresponding dibromide **284**, with *N*,*N*-dimethylbenzamide produces 2-(2-benzoylphenyl)-3-phenylindenone **285** in 65% yield, the structure of which was determined by crystallographic analysis. The McMurry reaction of **287** subsequently leads to dibenzopentalene **256** in 58% yield (Scheme 6.71) [166].

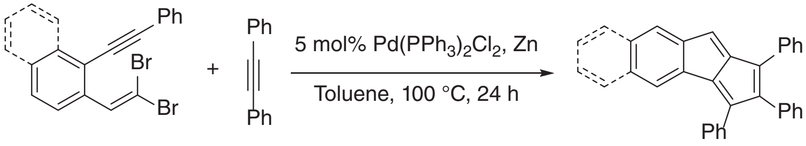
As shown in Scheme 6.37, some transition-metal-assisted ring-closure reactions of 1,2-diethynylbenzenes afford dibenzopentalene derivatives unexpectedly. Diederich's group designed a carbopalladation cascade reaction of easily accessible *gem*-dibromoolefins **286** and alkynes to furnish monobenzo-**287** and mononaphthopentalenes **288** (Scheme 6.72). This successful methodology allows the preparation of asymmetrically substituted pentalene derivatives with only one fused aromatic system [167].

The above area has attracted much attention in recent years. Several new synthetic methods for symmetric and asymmetric π-extended pentalene derivatives



284 **285** **256**

Scheme 6.71



286

287: benzo = 42%
288: naphtho = 23%

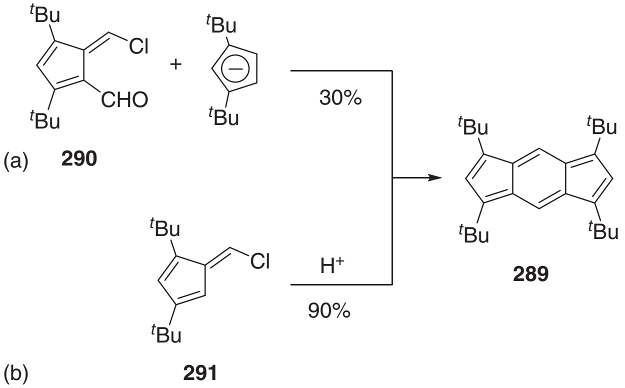
Scheme 6.72

using transition-metal catalysts and boron Lewis acids were reported. The appropriate literature is cited in references [168–170].

6.3.4.2 Indacenes

According to theoretical calculations *s*-indacene **6**, a [12]annulene perturbed by two additional σ-bonds, can be expected to display a strong influence on the bonding situation of the 12π perimeter. 1,3,5,7-Tetra-*tert*-butyl-*s*-indacene **289** was obtained as red needles (yield 30%) by reaction of 2,4-di-*tert*-butyl-6-chloro-1-formylpentafulvene **290** with lithium 1,3-di-*tert*-butylcyclopentadienide (Scheme 6.73a). Moreover, **289** is also obtained by the protic acid-catalyzed condensation of 1,3-di-*tert*-butyl-6-chloropentafulvene **291** in boiling methanol (Scheme 6.73b) [171]. The crystal structure analysis of **289** reveals C–C bond lengths for the perimeter consistent with a delocalized structure.

In 1994, Swager *et al.* reported the formation of a tetraiodide of dibenzo[*a*,*g*]-*s*-indacene **292** from dibenzo[12]annulene **293** ($R = n\text{-}C_{10}H_{21}$). Owing to electronic instability for a 20π-electron periphery, **292** rapidly oxidized to the corresponding diones **294** upon exposure to air (Scheme 6.74) [172]. Recently, Tobe *et al.* [173] reexamined the reaction using tetrabutoxy derivative **295**, and found the formation of *syn*-diiodoindenofluorenedione **296** together with the corresponding *anti*-isomer **292**. Haley and coworkers synthesized tetraethynyl derivative **297**

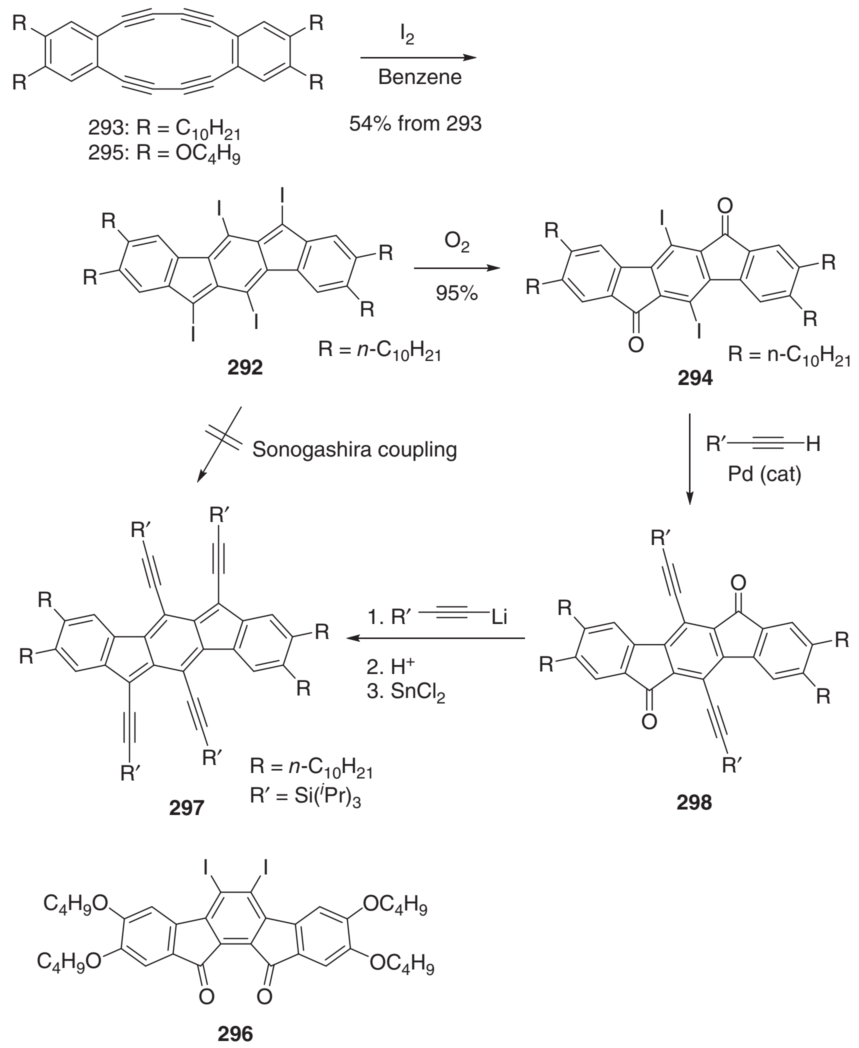


Scheme 6.73

from **292** in a stepwise manner via the *anti*-diketones **294** and **298**, because direct synthesis from tetraiodide **292** using a quadruple Sonogashira coupling resulted in failure (Scheme 6.74). Compound **297** is red in the solid state, while the solutions exhibit a brilliant blue-purple color. X-ray crystal structure confirms the planar structure with a *p*-quinodimethane (*p*-QDM) subunit [174].

Haley's and Yamashita' groups prepared a family of 6,12-diarylindeno[1,2-*b*]fluorenes **299**–**302** and diethynylindeno[1,2-*b*]fluorenes **303** from the corresponding diketones **304** (Scheme 6.75) [175–177]. The aryl and arylethynyl substitution can significantly affect the electronic and the OFET properties of the molecules. While **299** (Ar = Ph) only exhibits p-type semiconducting behavior ($1.6\times10^{-5}\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$), **300** (Ar = 2,6-$F_2$Ph) and **301** (Ar = 9-anthryl) show ambipolar characteristics (**301**: p-type for $8.2\times10^{-5}\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$ and n-type for $1.9\times10^{-5}\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$) [176]. Interestingly, **302** (Ar = C_6F_5) exhibits enhanced carrier and hole mobilities (7×10^{-4} and $3\times10^{-3}\ \mathrm{cm^2\,V^{-1}\,s^{-1}}$) as the active element in a single-crystal OFET [177].

as-Indacene **305** is still elusive and is anticipated to be formed as a reactive intermediate only. Indeno[2,1-*a*]fluorine **306** as a dibenzo[*a,g*]-a*s*-indacene possesses an *o*-quinodimethane (*o*-QDM) structure instead of the *p*-QDM moiety of dibenzo[*a,g*]-*s*-indacene. In 1956, a 11,12-diphenyl derivative **307** was synthesized by Le Berre and coworkers [178]. Because of its high reactivity toward oxygen, however, it has not been characterized so far. Tobe and coworkers synthesized an air-stable derivative, 11,12-dimesitylindeno[2,1-*a*]fluorene **308** (Figure 6.14) [179]. Due to its *o*-QDM structure, **308** displays some singlet biradical character; it is weakly antiaromatic as a result of the *as*-indacene moiety with low-energy absorptions and excellent electrochemical properties. More recently, Tobe's group reported a new topological isomer, the indeno[2,1-*b*]fluorene derivative **309** [180]. The compound has a moderate singlet biradical character, and exhibits extremely low-energy light absorption. A 1,8-dimesitylfluoreno[4,3-*c*]fluorene derivative **310** bearing a 6–5–6–6–5–6 fused ring system, has been synthesized using a similar procedure by Haley's group. In contrast to **308**, the

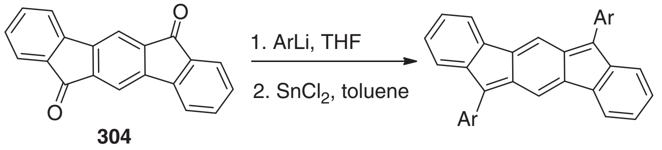


Scheme 6.74

crystal structure establishes the closed-shell ground state possessing a neutral 2,6-naphthoquinone dimethide structure [181].

6.3.4.3 Heterocyclic Systems

The reaction of 1,2-diphenylethanedione with the CP anion unexpectedly affords a novel 2,3,7-triphenyl derivative of the bicyclic cyclopenta[*c*]pyran **311**, which has a planar structure and relatively large bond alternation (Scheme 6.76a) [182]. Babaev reported that oxazolo[1,2-*a*]pyridinium salts **312** react with CP anion, leading to cyclopenta[*a*]quinolizines **313**. Parent pyrindines **250** (X = NR) are



299: Ar = Ph
300: Ar = 2,6-$F_2C_6H_3$
301: Ar = 9-Anthryl
302: Ar = C_6F_5
303: Ar = -CC-Ph

Scheme 6.75

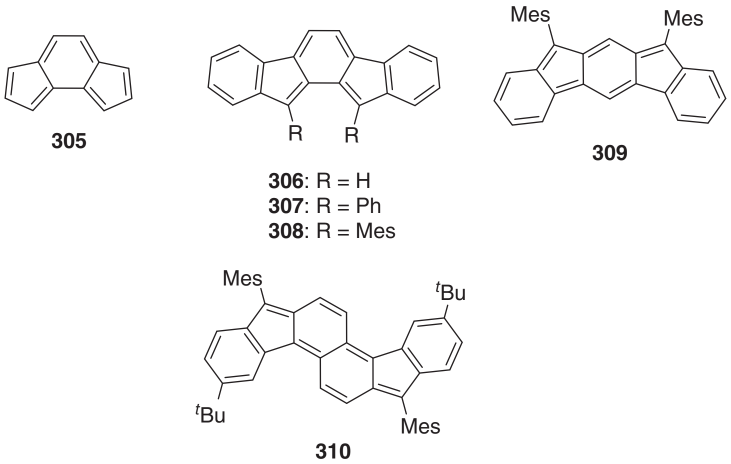
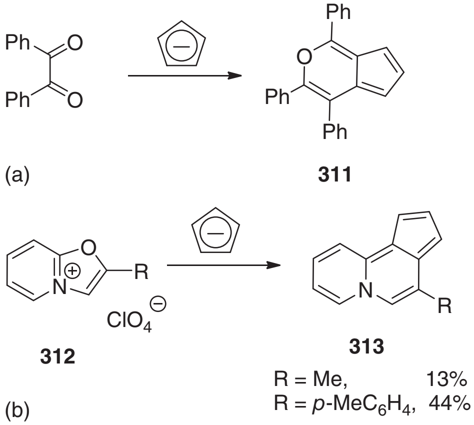


Figure 6.14 *as*-Indacene **305** and dibenzoindacene derivatives **306–310**.

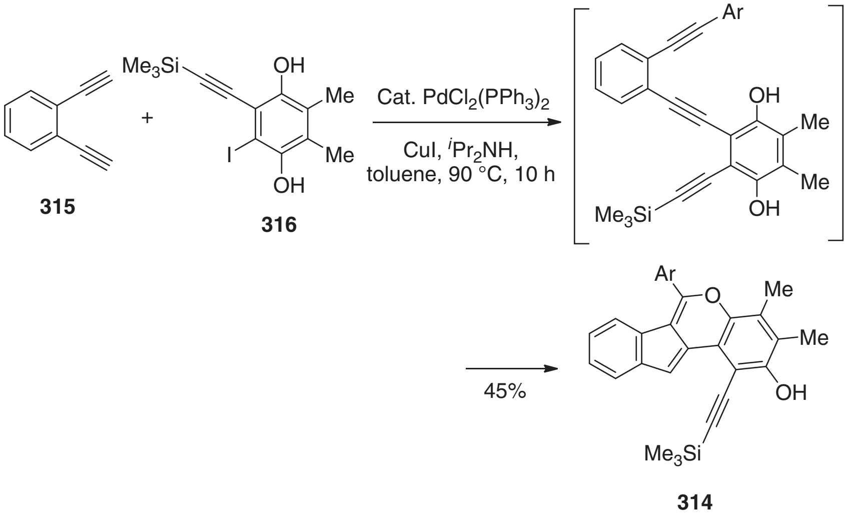
usually unstable compounds, whereas **313** is a quite stable 14π-electron system. No bond alternation is observed in the fulvene fragment, indicating that the negative charge is delocalized at the five-membered ring (Scheme 6.76b) [183].

The unexpected formation of a cyclopenta[*c*]pyran derivative **314** has been reported by Youngs and coworkers. Treatment of 1,2-diethynylbenzene **315**



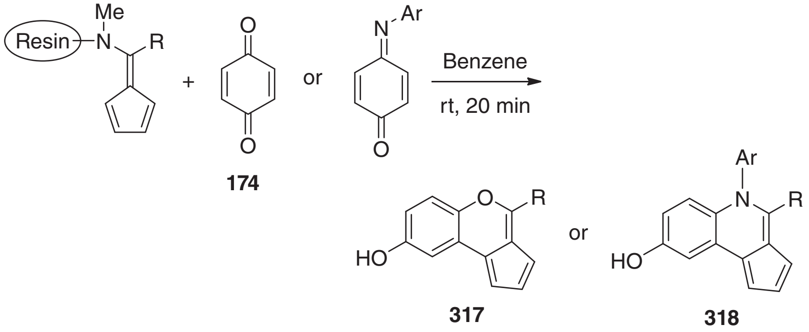
Scheme 6.76

with 2 equiv. of *o*-iodo-ethynylhydroquinone **316** under Sonogashira coupling conditions affords **314** as a yellow solid in 45% isolated yield (Scheme 6.77). The structure was confirmed by X-ray analysis [184].



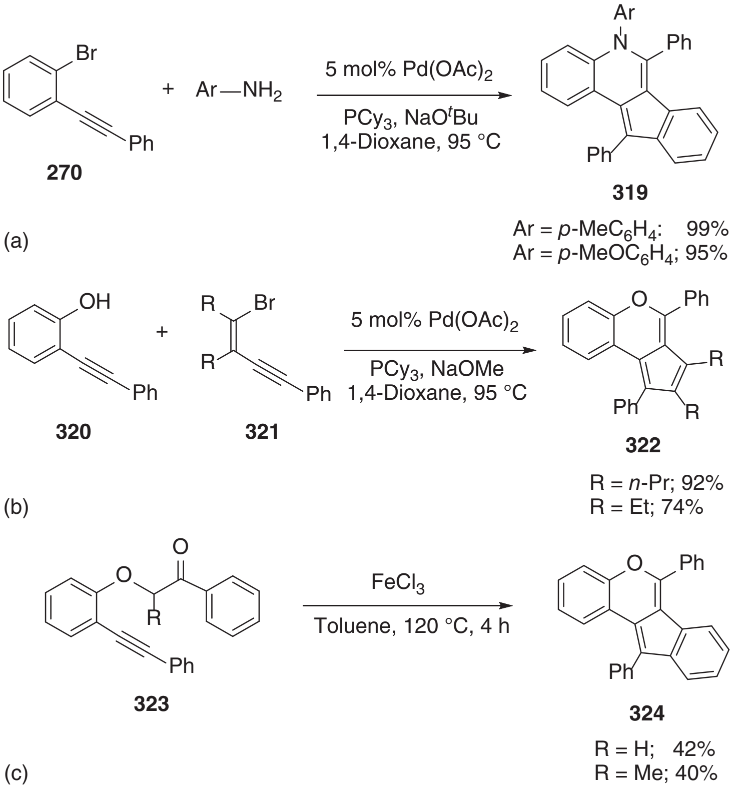
Scheme 6.77

As mentioned in Chapter 7, soon afterwards, Hong reported another unexpected formation of cyclopenta[*c*]pyran derivative **317** by a [6+3] cycloaddition of dimethylaminofulvene **109** and *p*-benzoquinone **174** [108]. He developed a solid-phase synthesis of **317** and cyclopenta[*c*]quinolone derivatives **318** using a resin-bonded fulvene derivative and a hetero [6+3] cycloaddition sequence (Scheme 6.78) [101].



Scheme 6.78

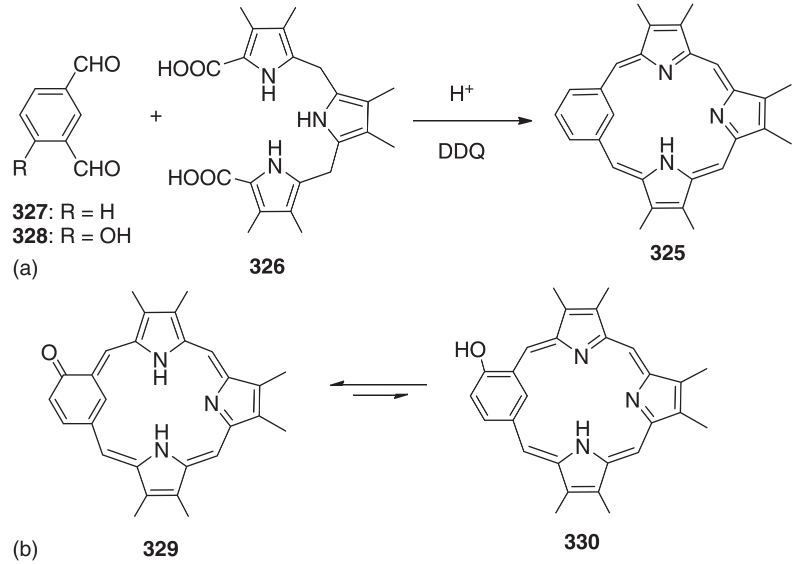
Transition-metal-catalyzed annulation reactions constitute attractive and efficient routes for the construction of heteroaromatic skeletons. The formation of 5*H*-cyclopenta[*c*]quinoline **319** via a palladium-catalyzed domino reaction of *o*-alkynylhalobenzene **270** with an amine was explored by Wu's group (Scheme 6.79a) [185]. They also reported a similar reaction using *o*-alkynylphenols **320** and 2-alkynylvinyl bromide **321** providing cyclopenta[*c*]chromene **322** (Scheme 6.79b) [186]. An iron-mediated intramolecular annulation of 2-ethynylphenol derivatives **323** by intramolecular [3+2] cyclization of an alkyne with a carbonyl group produces indeno[1,2-*c*]chromenes **324**, selectively (Scheme 6.79c) [187].



Scheme 6.79

6.3.4.4 **Carbaporphyrinoids**

Berlin and Breitmaier [188] first synthesized a benzene-containing porphyrin analog **325**. The method exploits the ready availability of tri- or tris-pyrroles **326** and their ability to condense with *m*-phthalaldehyde **327** and related compounds to give the macrocycle **325** (Scheme 6.80a). Owing to the presence of the benzene ring in the ring system, **325** does not exhibit aromatic properties. Soon after, Lash [189] reported that the macrocycle obtained by reaction of **326** with 5-formylsalicylaldehyde **328** exists in the keto form **329** as a fairly stable aromatic compound rather than in the phenolic form **330** (Scheme 6.80b).



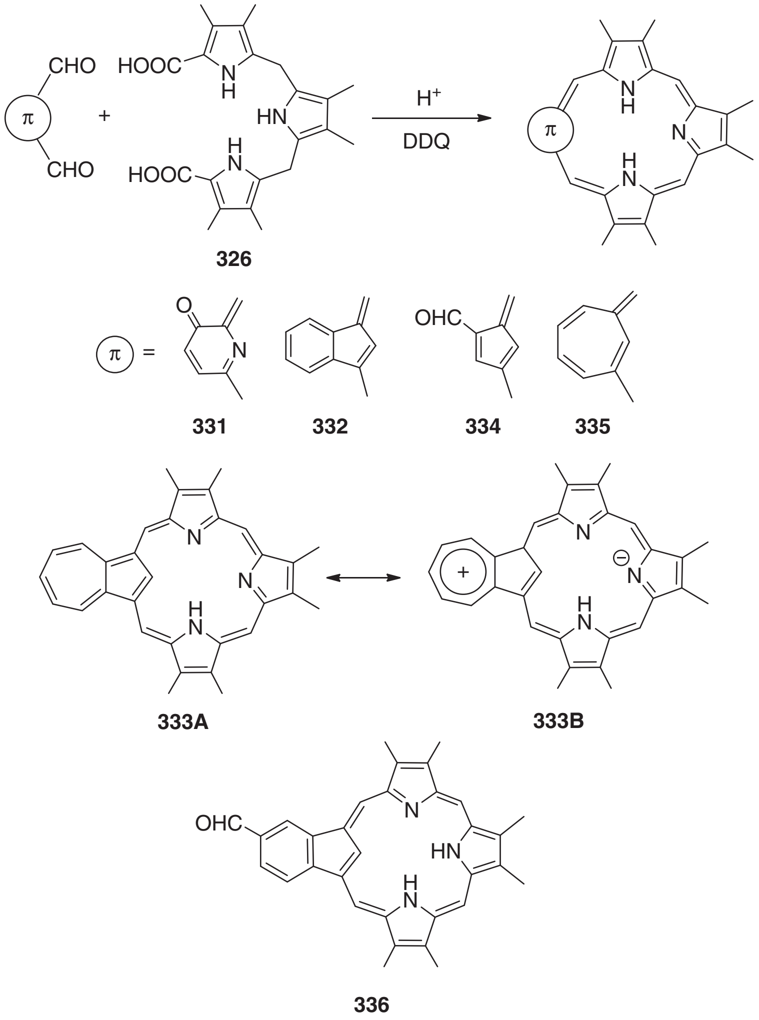
Scheme 6.80

As shown in Scheme 6.81, this synthetic methodology has been successfully applied to the synthesis of various carbaporphyrinoids with pyridine **331** [190], indene **332** [178, 191], azulene **333** [192], and the related subunits **334** [193] and **335** [191] as components of the conjugated macrocycle [194–197]. The azuleneporphyrins **333** was prepared by the reaction of 1,3-diformylazulene as a stable compound by Lash and coworkers. But, under different conditions, **336**, involving an indene moiety, is produced. The authors conclude that **333** shows aromatic character due to zwitterionic canonical forms such as **333B** [192].

In 2002, Lash and coworkers synthesized carbaazuleneporphyrin **337** as the first dicarbaporphyrin by condensation of the azulenetripyrrane **338** with diformylindene **339** in 9.4% yield (Scheme 6.82a) [198]. Compound **337** appears to be weakly diatropic, due to the rather strong aromatic character of an azulene ring. Very recently, the new series of porphyrin analogs **340** incorporating two adjacent indene units was synthesized as outlined in Scheme 6.82b [199]. The ^{1}H NMR spectrum of **340** reveals the macrocycle to be highly diatropic, and X-ray analysis demonstrates that the macrocycle is remarkably planar; the framework bond distances are consistent with a nearly delocalized π-bonding pattern of a [18]annulene core.

6.3.4.5 Reactions of Fulvalenes for the Construction of Fullerene Fragments

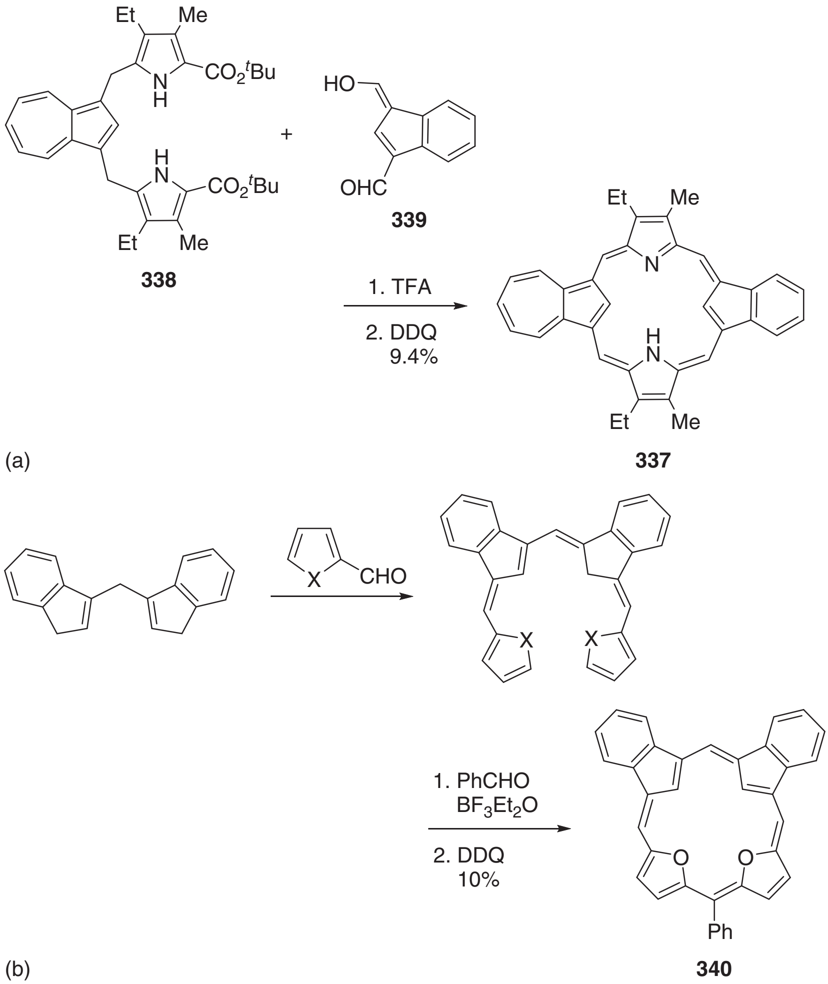
Recent advances in fullerene chemistry have attracted much interest in bowl-like PAHs [148]. In this context, pyrolytic, photocatalyzed pericyclic, and transition-metal-catalyzed ring-closure processes for the preparation of overcrowded fulvalenes such as 9,9′-fluorenylidene **191** have been investigated by several groups. Thermal dehydrocyclization of **191** above 700 °C yields **341**, which can further cyclize to **342** at elevated temperature, but in quite low yields [200].



Scheme 6.81

Agranat reported a facile synthesis of **341** by a reductive cyclodechlorination of dichlorobifluorenylidene **343**, using palladium acetate as a homogenous catalyst [201]. Buckybowl **342** is successfully obtained in 37% yield by FVP of dibromobifluorenylidene **344** at 1050 °C (Scheme 6.83a) [202]. For the synthesis of **342**, the catalytic system ($Pd(Cy_3P)_2Cl_2$/DBU/$CsCO_3$) provides fruitful results: Wu *et al.* [203] reported the palladium-catalyzed cyclization of phenanthrene derivative **345** to **342** in 33% yield (Scheme 6.83b).

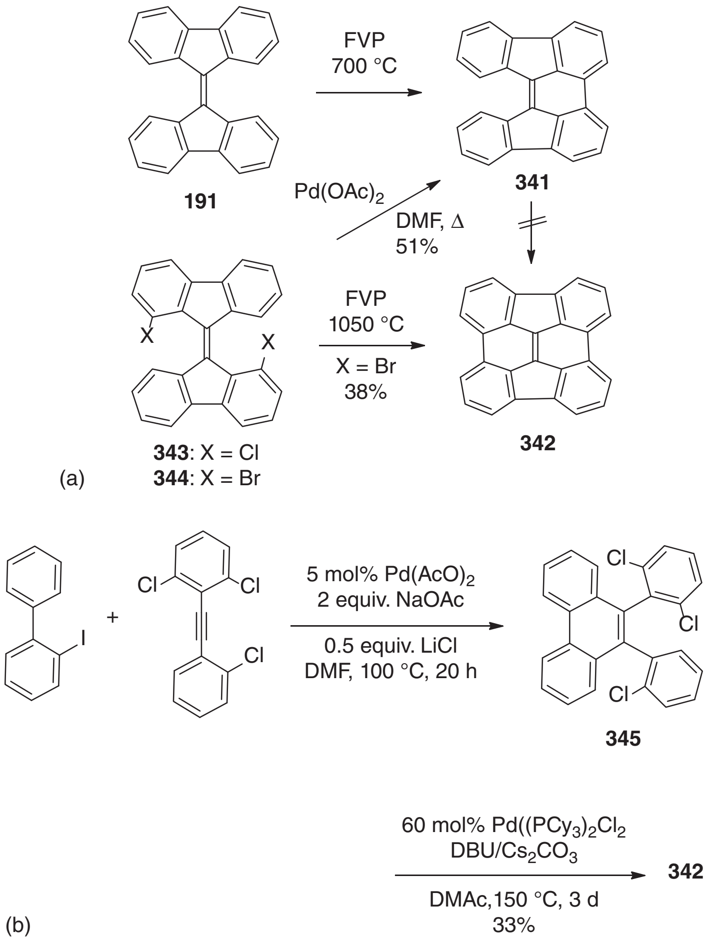
Because of a good precursor for the Buckybowl **346**, a so-called semibuckminsterfullerene, the ring-closure reaction of the highly distorted fulvalene **347** has



Scheme 6.82

also been explored well. The fulvalene **347** was synthesized by Harvey's group as outlined in Scheme 6.84 [204]. Owing to its high molecular strain, **347** easily rearranges into tetrabenzonaphthacene **348** under acidic conditions. While pyrolysis of **347** gives **349** as one of the products in low yield, photocyclization of the 2,2′-tethered fulvalene **350** efficiently affords a ring-closure product **351** in 50% yield (Scheme 6.84b) [205].

Unfortunately, however, the final ring-closure from **349** to **346** resulted in failure. The synthesis of **346** was accomplished using the FVP methods from **353** to **354** by the Rabideau and Hagen and Zimmermann groups, independently (Scheme 6.85) [206, 207].

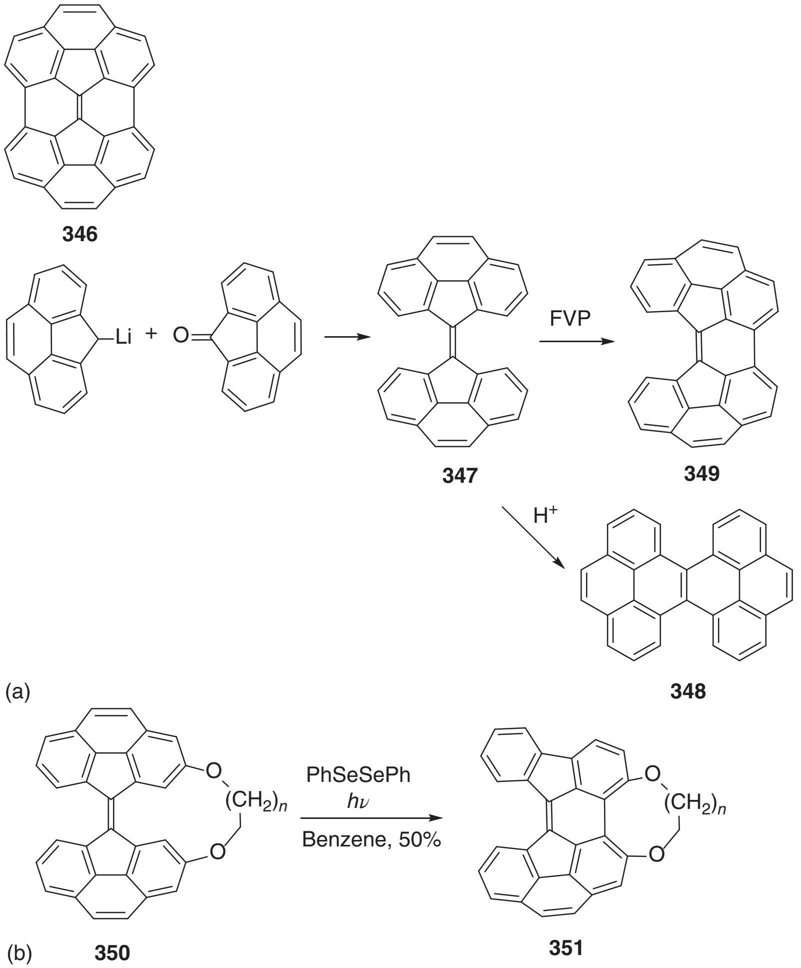


Scheme 6.83

As mentioned, the catalytic system (Pd($Cy_3P)_2Cl_2$/DBU/$CsCO_3$) efficiently provides an alternative route to bowl-shaped molecules. The bowl-shaped molecules **354–357** are synthesized from easily accessible planar precursors by the palladium-mediated five-membered ring formation in good to excellent yields (Scheme 6.86 and Figure 6.15). X-ray analyses of these compounds unambiguously establishes their nonplanar structures [208–211].

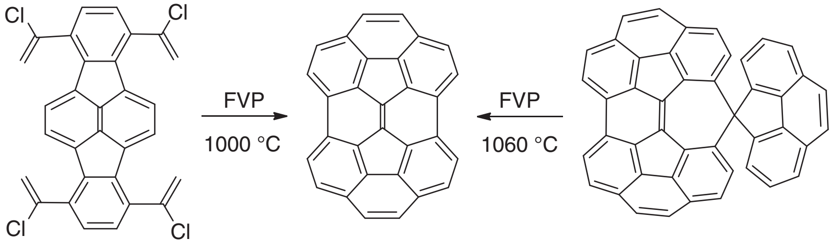
6.3.5
Cyclopentadienones (Oxapentafulvene)

Tetracyclone **17** with moderate reactivity as a diene has been well known as a *versatile synthetic building block* for perphenyl-substituted aromatic compounds.



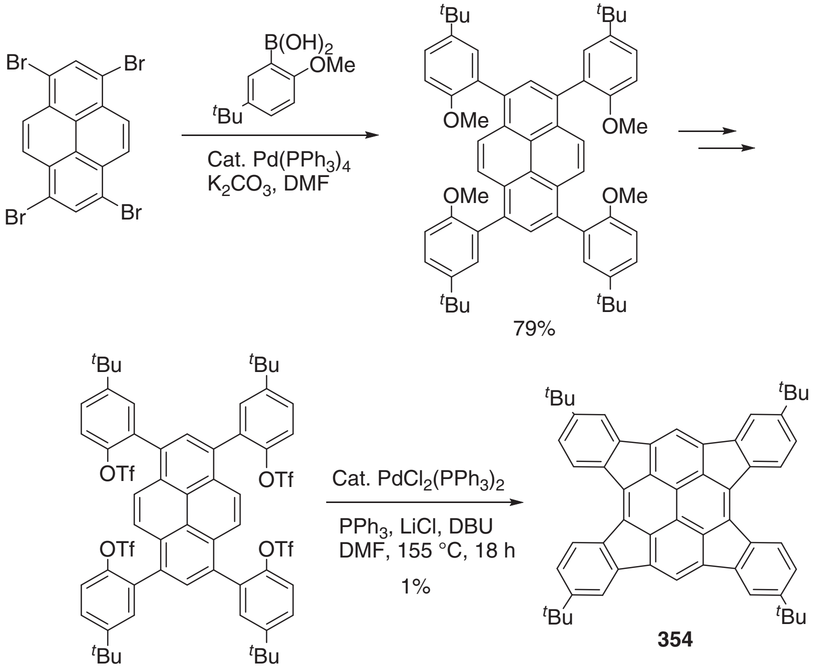
Scheme 6.84

The chemistry has a long history [8]. Recent developments in carbon-rich compounds have renewed the interest in CPDNs, because HBC **22** [10, 11] as a representative carbon-rich compound, can be prepared from **17** and related compounds. Moreover, in the past two decades, CPDN and its benzannulated derivatives (indenone **18** and fluorenone **19**) have received much attention as synthetic targets for five-membered ring-construction reactions using transition-metal catalysts. A variety of new synthetic methods and applications have been published to date. This section mainly describes the chemistry of CPDNs from the viewpoints of synthesis and reactivity.



352 **346** **353**

Scheme 6.85



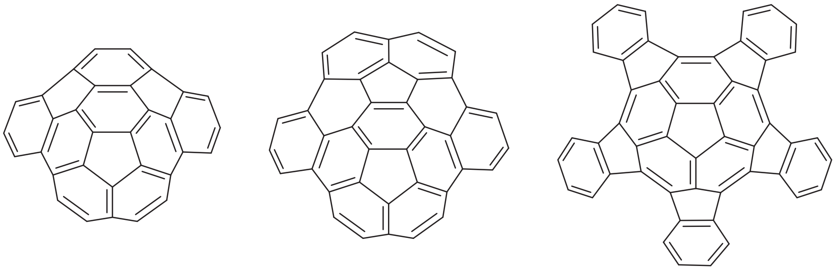
354

Scheme 6.86

6.3.5.1 Synthesis of CPDN

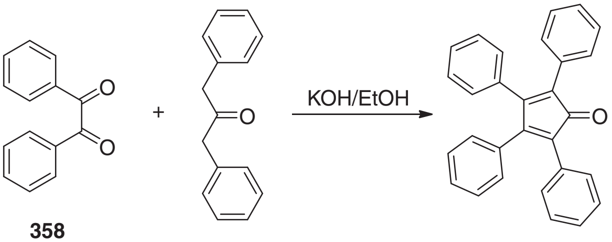
Synthesis of Tetracyclone derivatives

A convenient method of synthesizing **17** involves the ethanolic potassium hydroxide-mediated Knovenagel condensation between benzil **358** and 1,3-diphenyl-2-propanone **359** (Scheme 6.87) [8]. A variety of CPDN derivatives bearing polycyclic conjugated systems **360–364** are synthesized by the method for construction of HBC and the related compounds (Figure 6.16) [11, 212].



355 **356** **357**

Figure 6.15 The bowl-shaped molecules **355**–**357**.



358 **359** **17**

Scheme 6.87

A series of tetracyclone derivatives **365** with various functional groups were synthesized by Hughes' group. A good correlation was observed between the density functional theory (DFT)-computed HOMO (highest occupied molecular orbital)–LUMO (lowest unoccupied molecular orbital) gap and the observed absorptions of **365** [213]. Sambri and coworkers reported that tetracyclone **366** exhibit pronounced aggregation properties in various organic solvents responding to thermal and ultrasound stimuli. It is the first example of a tetracyclone-based low-molecular-weight organogelator [214].

Tetracyclone analogs bearing heteroaromatic rings can also be prepared by this method. Because the green tetra(2-thienyl) derivative **367** prepared by Kawase and Oda, is unstable under extended basic conditions, short time exposure (5 min) in the presence of base gives an optimal yield (Scheme 6.88) [215]. Wudl and coworkers prepared 2,5-di(2-thienyl) derivative **368** as a dark green, almost black solid. Chemical oxidation of **368** with ferric chloride can be carried out to yield corresponding polymer as an intractable black powder [216]. Furthermore, copolymers, comprising electron-donor (oligothiophene) and electron-acceptor (CPDN) units in the backbone, were also synthesized from **368**, and display a substantial field-effect mobility ($\mu_{\text{DDT}} = 2.26 \times 10^{-2}\,\text{cm}^2\,\text{V}^{-1}\,\text{s}^{-1}$ (on/off ratio $\sim 10^6$)) [217]. Tetra(4-pyridyl) derivative **369** was synthesized by Sanders as a stable solid; it is a synthetic building) block for hexapyridylbenzene [218].

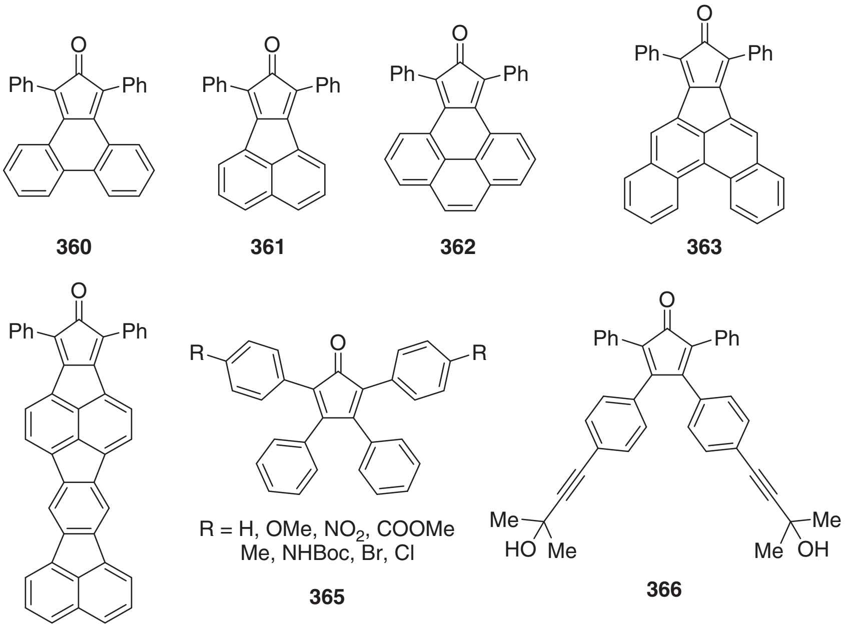
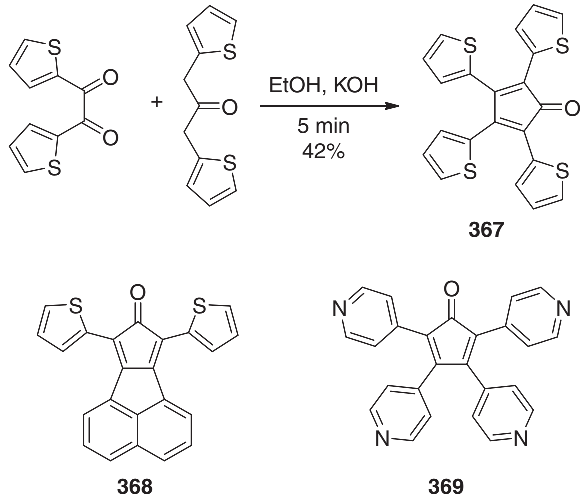


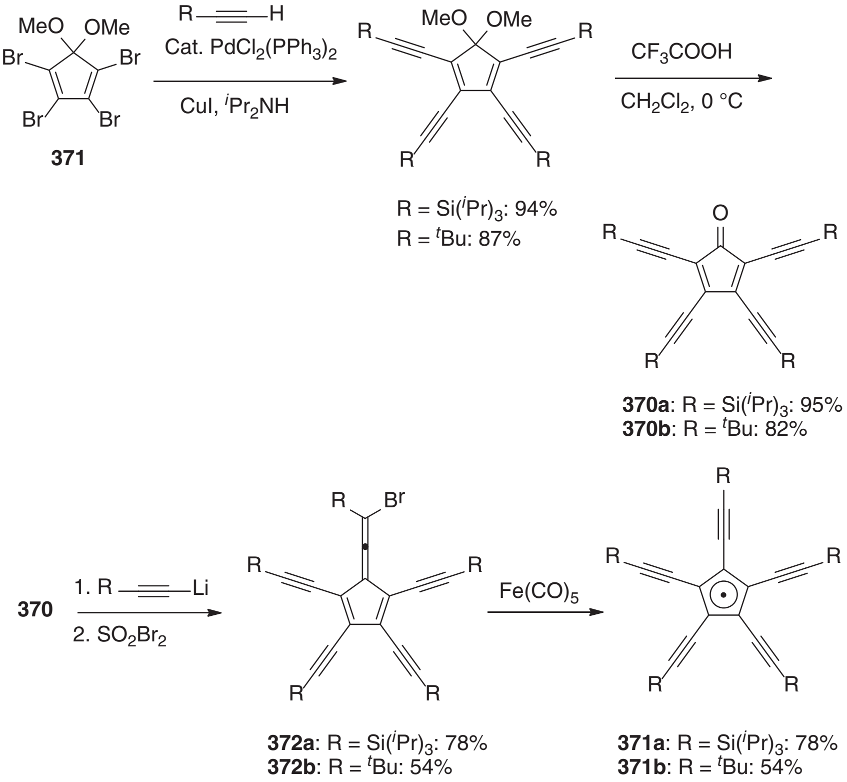
Figure 6.16 p-Extended CPDN derivatives **360**–**366**.



Scheme 6.88

Synthesis of CPDNs with Acetylenic Bonds

Rubin and Tobe's groups prepared tetraethynyl CPDNs **370** from 1, 1-dimethoxytetrabromocyclopentadiene **371** using a modified Sonogashira reaction as a key step, independently (Scheme 6.89). The triisopropylsilyl (TIPS) and *tert*-butyl substituted tetraethynylCPDNs **370a** and **370b** are stable purple



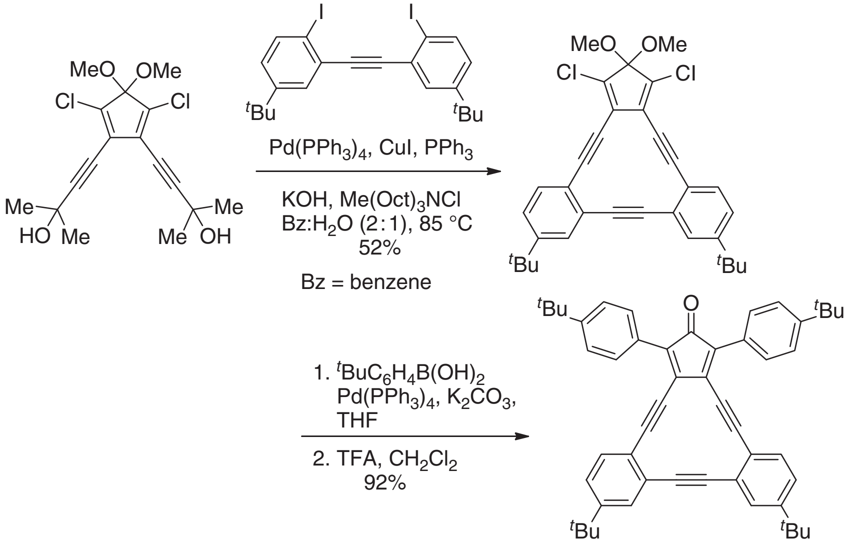
Scheme 6.89

crystalline solids which show no tendency to dimerize. As shown in Scheme 6.89, **370** can be converted into the corresponding CP radical **371** via a vinylidenefulvene **372**. Because **371** is surprisingly stable, it can be purified by column chromatography on silica gel with hexanes in air [219, 220].

Hexadehydrodibenzo[12]annulene annelated by a CPDN moiety **373** was synthesized by Tobe as outlined in Scheme 6.90. Theoretical calculations and experimental NMR and IR spectra indicate that **373** is weakly aromatic owing to the contribution of the diatropic [15]annulenone resonance structure [221].

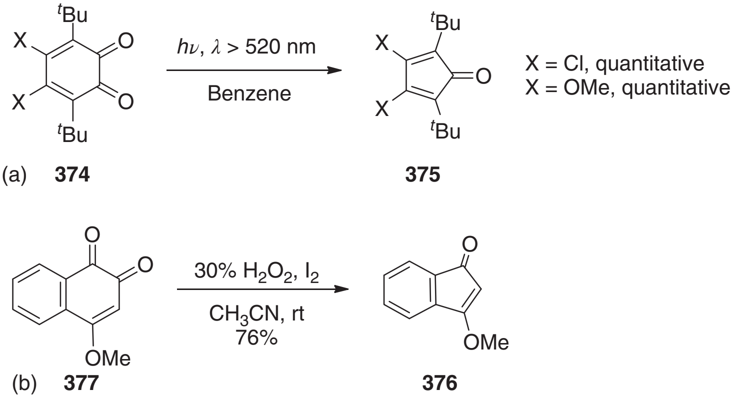
Synthesis of CPDNs Using Decarbonylation

Decarbonylation of *o*-benzoquinones **374** can be considered as a method of synthesis of CPDNs **375**. Photodecarbonylation of *o*-quinones under UV radiation has a long history, and many mechanistic studies have been performed and described in the literature (Scheme 6.91a) [222]. Another ring contraction to an indenone **376** from *o*-naphthoquinone **377** in aqueous H_2O_2 (30%) in the presence of catalytic amount of iodine in acetonitrile has also been reported (Scheme 6.91b) [223].



373

Scheme 6.90



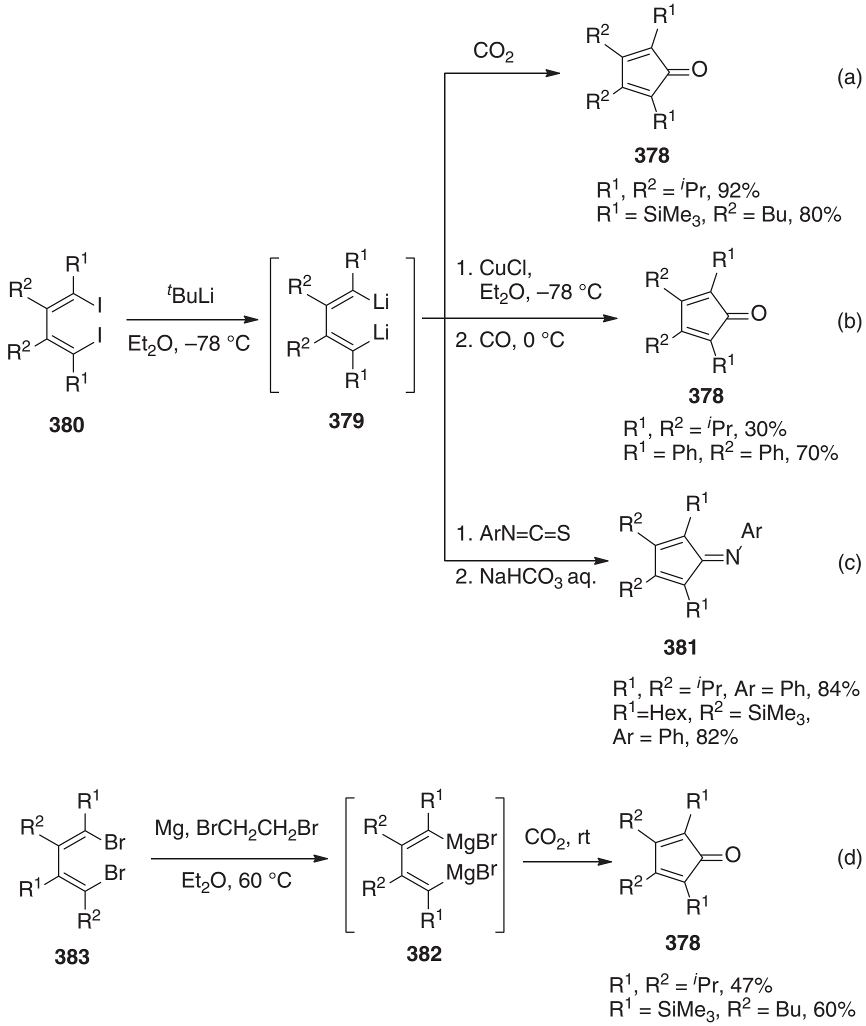
(a) **374** **375**

(b) **377** **376**

Scheme 6.91

Synthesis of CPDNs Using [4+1] Reactions

Xi has developed practical methods for the synthesis of CPDNs **378** by the reaction of 1,4-dilithio-1,3-dienes **379** with carbon dioxide, carbon monoxide, and isothiocyanates (Scheme 6.92a–c) [224]. The dianions **379** are derived from readily available 1,4-diiodo-1,3-dienes **380**. In the reaction in Scheme 6.92b, the presence of CuCl plays an important role in the formation of CPDNs. Moreover, the reaction with isothiocyanates affords iminocyclopentadienes (ICPDs) **381** in good yields, which are easily converted to CPDNs by acidic hydrolysis. 1,4-Bis-Grignard reagents **382**, easily derived from 1,4-dibromobutadiene **383**, react similarly with



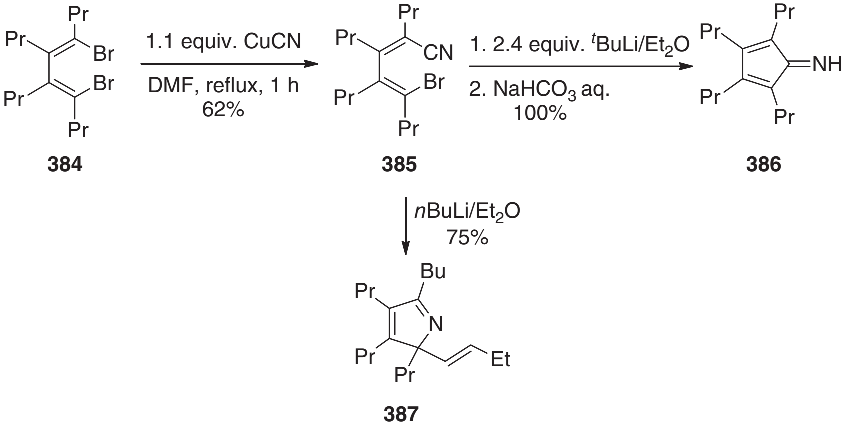
Scheme 6.92

CO$_2$ affording substituted CPDNs **378**, although in lower yields (Scheme 6.92d) [225].

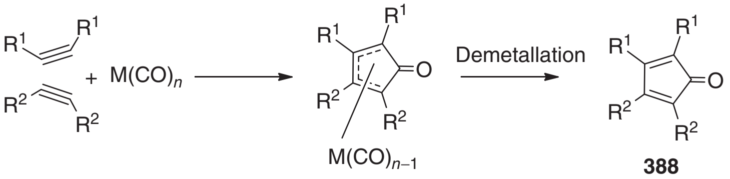
The dibromodiene **384** can be also transferred into the 4-bromodienenitrile **385** with 1.1 equiv. of CuCN in DMF. Treatment of **385** with *t*BuLi affords ICPD **386** quantitatively. On the other hand, when *n*BuLi is used as a base, 2*H*-pyrrole **387** is obtained in good yield as the isolated product (Scheme 6.93) [226].

Synthesis of CPDNs Using [2+2+1] Reactions

Several examples of the [2+2+1] coupling of alkynes and carbon monoxide for the synthesis of CPDNs **388** have been reported for Co, Fe, Ni, Rh, Ru, and Cr



Scheme 6.93

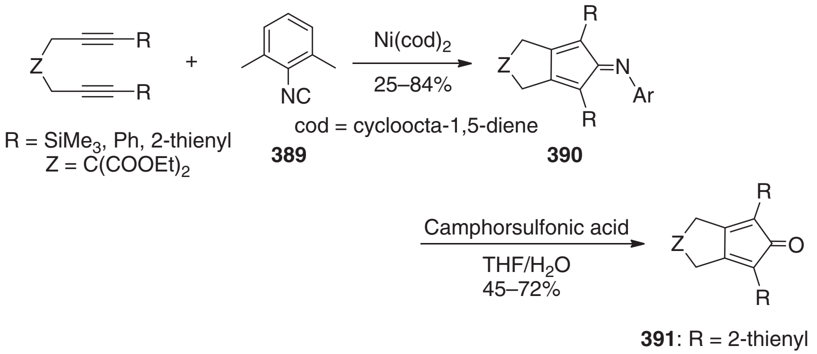


Scheme 6.94

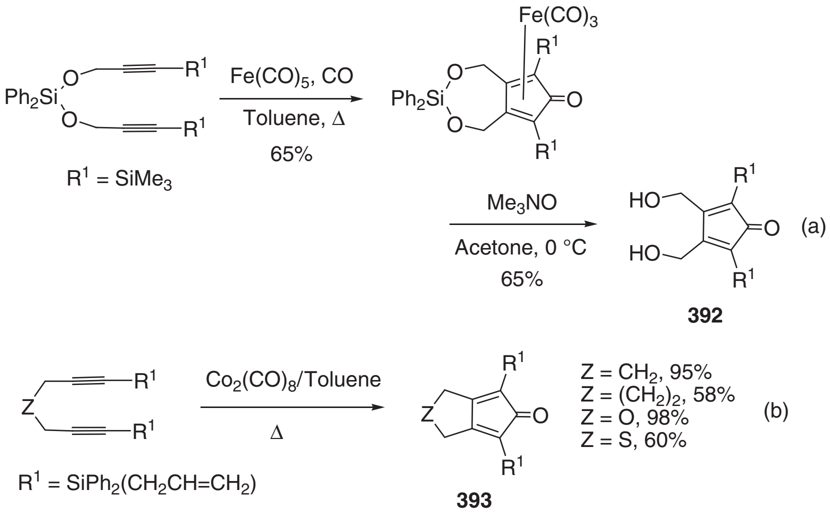
complexes (Scheme 6.94). Yamazaki reported the leading work of synthesis of CPDN by $CpCo(PPh_3)_2$-mediated alkyne–alkyne coupling, following insertion of carbon monoxide and reductive elimination of cobalt [227]. In 1980, Vollhardt and coworkers [228] reported a cobalt-mediated synthesis of new types of bicyclic CPDNs which contain the TMS group or no substituents in 2,5-positions. In most cases, a stoichiometric amount of complex is required, and the formed CPDN tends to remain coordinated onto the metal [229, 230].

Tamao and Ito's groups reported that 1,*n*-diynes bearing alkyl, aryl, and TMS groups as the terminal substituents undergo cyclization with 2,6-dimethylphenyl isocyanide **389** in the presence of a stoichiometric amount of $Ni(cod)_2$ to form bicyclic ICPDs **390** [231]. The reaction can be applied to the synthesis of thiophene–cyclopentadienone cooligomers. As shown in Scheme 6.95, the reaction of 1,7-diyne a having 2-thienyl groups leads to the corresponding CPDNs **391** upon hydrolysis using camphorsulfonic acid [232].

It is known that $Fe(CO)_5$-promoted cyclocarbonylation provides a method for the construction of CPDNs **392** (Scheme 6.96a). In this reaction, a stoichiometric amount of iron carbonyl and demetallation procedure is needed for the synthesis [233]. In 1998, Soai and Shibata's group [234] reported the first direct synthesis of CPDNs **393** by $Co_2(CO)_8$-complex mediated intermolecular carbonylative alkyne–alkyne coupling reaction (Scheme 6.96b).



Scheme 6.95

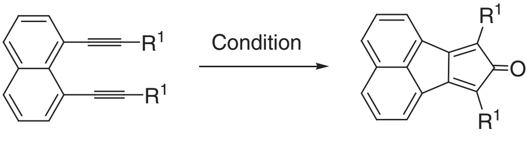


Scheme 6.96

CPDN **394** is an important intermediate for the synthesis of corannulene **23**; it can be prepared by [2+2+1] reaction of 1,8-diethynylnaphthalene **395** using Fe(CO)$_5$ upon demetallation procedure (Scheme 6.97) [235]. Later, Shibata reported the iridium complex-catalyzed carbonylative alkyne–alkyne coupling, which provides **394** in high isolated yields without demetallation procedure. The iridium phosphine complexes, [IrCl(CO)$_2$(PPh$_3$)$_2$] enables the catalytic coupling under carbon monoxide at atmospheric pressure or less (Scheme 6.97) [236].

The Shibata group also achieved a first catalytic synthesis of ICPDs **396** using portion-wise additions of isocyanides to a solution of diynes and [RhCl(cod)]$_2$ (Scheme 6.98) [237].

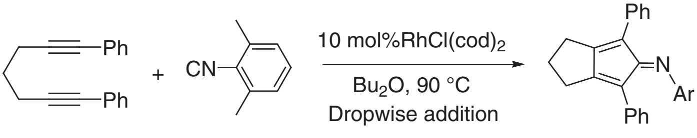
Zirconacyclopentadienes **397**, which are alkyne–alkyne coupling products of zirconocene, have attracted much attention, because they have been shown to be useful synthetic tools; **397**, however, does not react with CO directly. Takahashi



395 **394**

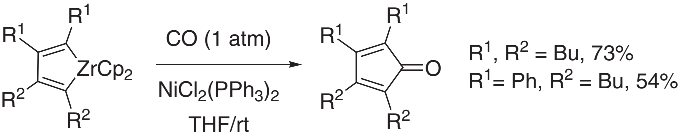
Condition (ref. 235): R^1 = $SiMe_3$, (1) $Fe(CO)_5$, DME, 140 °C, 20 h: 90%, (2) NaOH/THF, (3) $C_5H_{11}I$, (4) H_3PO_4, 89%.
Condition (ref. 236): R^1 = $SiPh_2(CH_2CH{=}CH_2)$, $Co_2(CO)_8$/toluene, 120 °C, 1.5 h: 75%, R^1 = $SiPh_3$, 5 mol% $IrCl(CO)_2(PPh_3)_2$, xylene, CO, 120 °C, 98%, 5 mol% IrCl(cod)(dppp), xylene, CO, 120 °C: 96%.

Scheme 6.97



396

Scheme 6.98



397 **398**

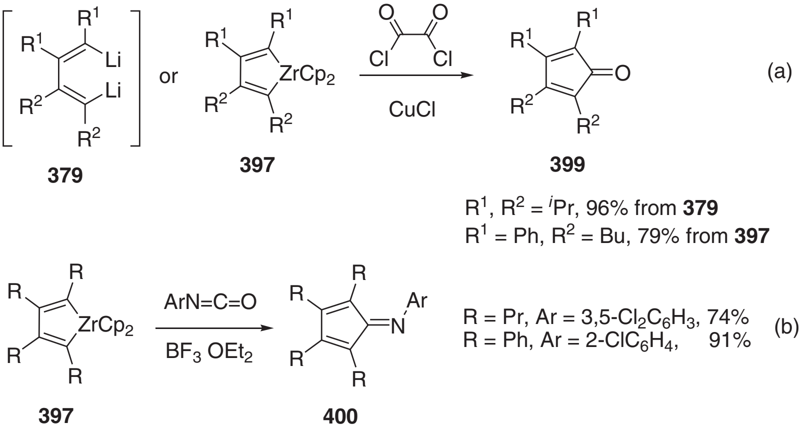
Scheme 6.99

reported that treatment of **397** with CO in the presence of $NiCl_2(PPh_3)_2$ affords CPDNs **398** in moderate yields (Scheme 6.99). The mixture of **397** and isocyanate, when exposed to air in the presence of CuCl, gives the ICPD in 63% yield [238].

In 2005, Xi and coworkers reported that 1,1-cycloaddition of oxalyl chloride with 1,4-dilithio-1,3-dienes **379** or zirconcyclopentadienes **397** afford CPDNs **399** in the presence of CuCl (Scheme 6.100a), in which the carbon–carbon bond of the 1,2-dicarbonyl component cleaves during nucleophilic addition [239]. They also found that no reaction is observed when **397** is treated with isocyanates. However, multiply substituted ICPDs **400** are formed from Lewis acid-promoted reactions ($BF_3{\cdot}Et_2O$) by a one-pot three-component coupling process (Scheme 6.100b) [240].

Synthesis of CPDNs Using [3+2] Reactions

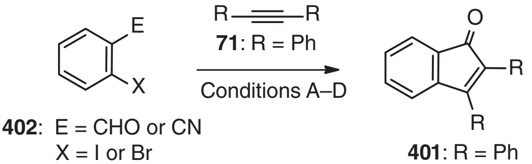
As mentioned in Section 6.3.1.1, Heck first reported the palladium-catalyzed formation of 2,3-diphenyl-l-indenone **401** from *o*-iodobenzaldehyde **402** and diphenylacetylene **71** as a single example in 1989 (Scheme 6.101) [83]. After



R^1, R^2 = ^{i}Pr, 96% from **379**
R^1 = Ph, R^2 = Bu, 79% from **397**

R = Pr, Ar = 3,5-$Cl_2C_6H_3$, 74%
R = Ph, Ar = 2-ClC_6H_4, 91%

Scheme 6.100



Condition A (ref. 241a): 5 mol% $Pd(OAc)_2$, NaOAc, $n$$Bu_4NCl$, DMF 100 °C. E = CHO, R = Ph, X = I, 84%; R = Ph, X = Br, 82%. Condition B (ref. 241b): E = CHO, X = Br: 1% [Pd], K_2CO_3, DMF, at 130 °C, 2 h under Ar. [Pd] = 4,4'-dichlorobenzophenone oxime palladacycles. Condition C (ref.241c): E = CHO, X = I : p-toluidine, $[CoCl_2(dppe)]$, Zn, MeCN/THF, 12 h, 100 °C. Condition D (ref. 242): X = I, E = CN: 10% $[Pd(dba)_2]$, Et_3N, 9 : 1 DMF/H_2O, at 100 °C. under Ar.

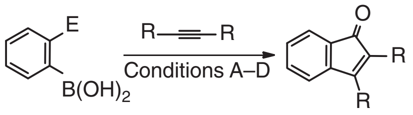
Scheme 6.101

this seminal report, transition-metal-catalyzed approaches to indenone and fluorenone derivatives have been well explored. Among these transformations, several direct annulation reactions between alkyne and *ortho*-functionalized aldehydes [241], nitriles [242, 243], esters [244], boronic acid [245], or ketones [246] have been developed as important synthetic methods (Schemes 6.101–6.103).

Recently, Shi developed a rhodium(III)-catalyzed annulation involving a directed C–H functionalization. The reactions of benzimides **403** or ethyl benzoate **404** with alkynes afford indenones **405** and **402**, respectively (Scheme 6.104) [247].

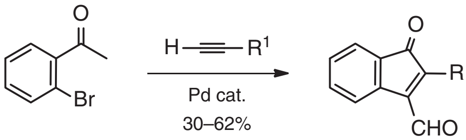
Synthesis of CPDNs and Related Compounds by Ring Closure Reactions

Fluorenones **19** are an interesting class of compounds because of their important applications in organic electronics. Useful syntheses of **19** include Friedel–Crafts ring closures of biarylcarboxylic acids. The method has been widely employed for fluoren-9-one derivatives. For example, isotruxenone **406**, an isomer of



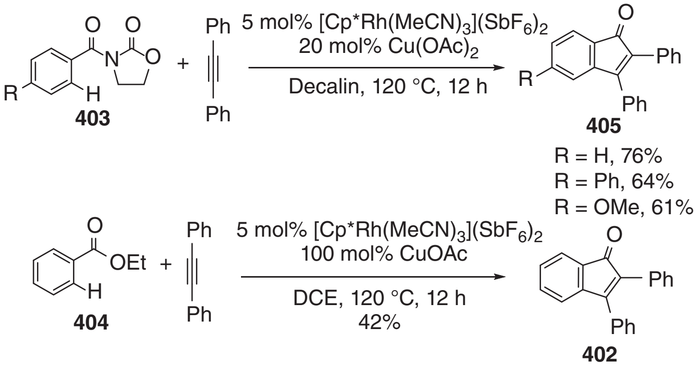
Condition A (ref. 241c): E = CHO: (1) [$CoCl_2$(dppe)] (0.0210 mmol), Zn (0.60mmol), *p*-toluidine at 100 °C for 12 h (2) 1 MTBAF, (3) HCl aq. Condition B (ref. 243): E = CN: $[Rh(OH)(cod)]_2$ (0.1 equiv. in Rh) in dioxane/H_2O (40/1) at 100 °C under Ar. Condition C (ref. 244): E = COOR: [Pd($OCOCF_3$)$_2$(dppe)], MeOH, 80 °C, 2 h under Ar. Condition D (ref. 245): E = Br: $[RhCl(cod)]_2$, Na_2CO_3, in dioxane/H_2O (100/1) at 80 °C under CO (1atm).

Scheme 6.102



Condition (ref. 246): 10mol% Pd[$(PPh)_3$]$_2Cl_2$, CuI, PPh_3, morpholine, 80 °Cunder Air.

Scheme 6.103

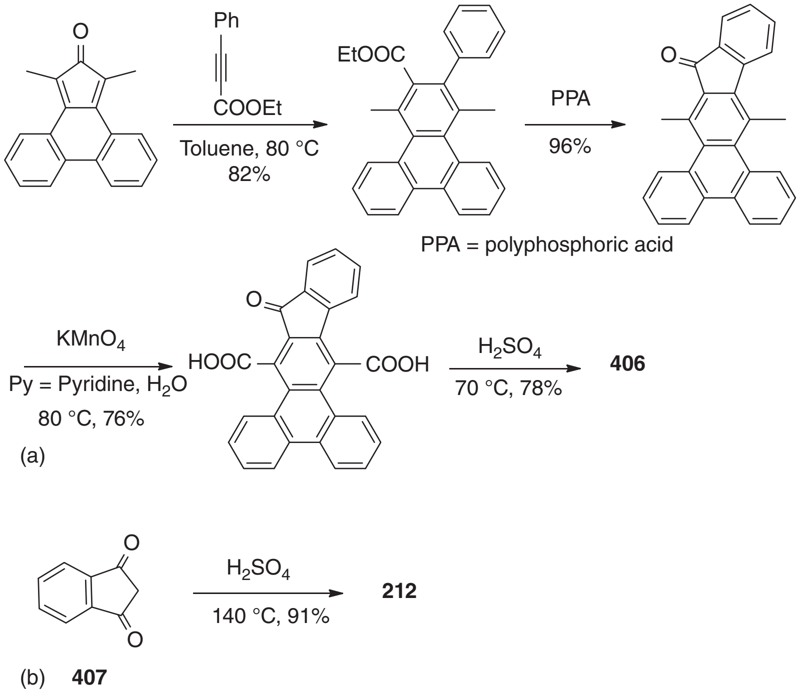


Scheme 6.104

truxenone **212** with a C_3-symmetry, is synthesized by successive Friedel–Crafts acylation (Scheme 6.105a, Figure 6.17) [248]. The triketone **212** is readily prepared by acid-mediated cyclotrimerization of indane-1,3-dione **407** in good yield (Scheme 6.105b) [249].

Recently, a new conversion of arenecarboxaldehydes **408** into benzocyclic ketones **409** in a straightforward one-pot process was reported by Barluenga and coworkers. They found that efficient results are obtained, when HBF_4 and IPy_2BF_4 as an iodinating reagent are used (Scheme 6.106) [250].

A variety of fluoren-9-one syntheses using transition-metal-catalyzed cyclization of 2-haloarylketones **410** and cyclocarbonylation reaction of *o*-halobiaryls



Scheme 6.105

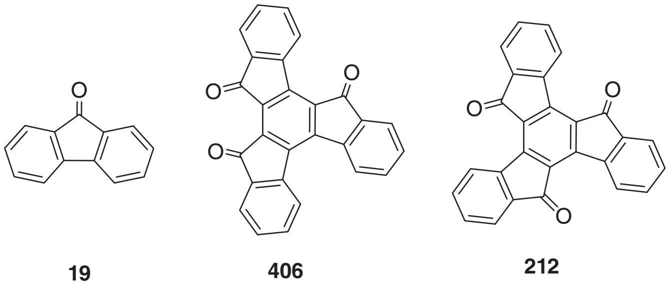
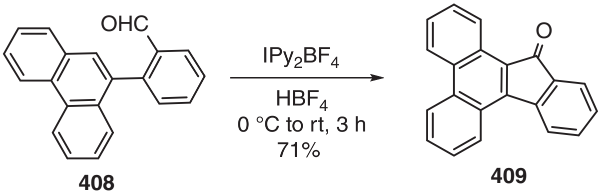


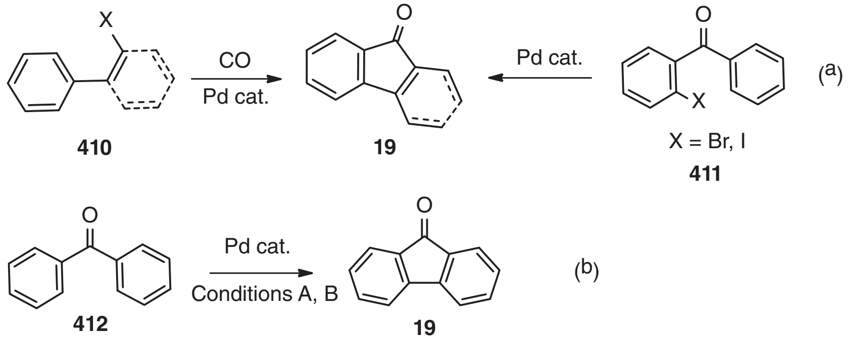
Figure 6.17 Fluorenone **19**, isotruxenone **406** and truxenone **212**.

411, first reported by Larock [251], have been extensively explored to date (Scheme 6.107a) [253]. Recently, Pd-catalyzed oxidative cyclization from simple biaryl ketones **412** was accomplished by Shi's and Cheng's groups, independently (Scheme 6.107b) [252].

Intramolecular [4+2] cycloaddition reactions of conjugated enynes, namely, dehydro-Diels–Alder reactions, afford benzo-fused CPDNs [254]. Thus, 2-propynyldiarylacetylenes **413** undergo thermal intramolecular [4+2] cycloadditions to give benzo[*b*]fluorene derivatives **414** in good yields (Scheme 6.108a). The reactivity of the reactions increases in the order hydrocarbon



Scheme 6.106



Condition A (ref. 252a): 5 mol% $Pd(OAc)_2$, 1.5 equiv. Ag_2O, K_2CO_3, TFA,140 °C, 24 h, Yield = 91%. Condition B (ref. 252b): X = I, Br: 5 mol% $Pd(PCy)_3$, CsPiv, DMF, at 110 °C under Ar. Yield = 94%.

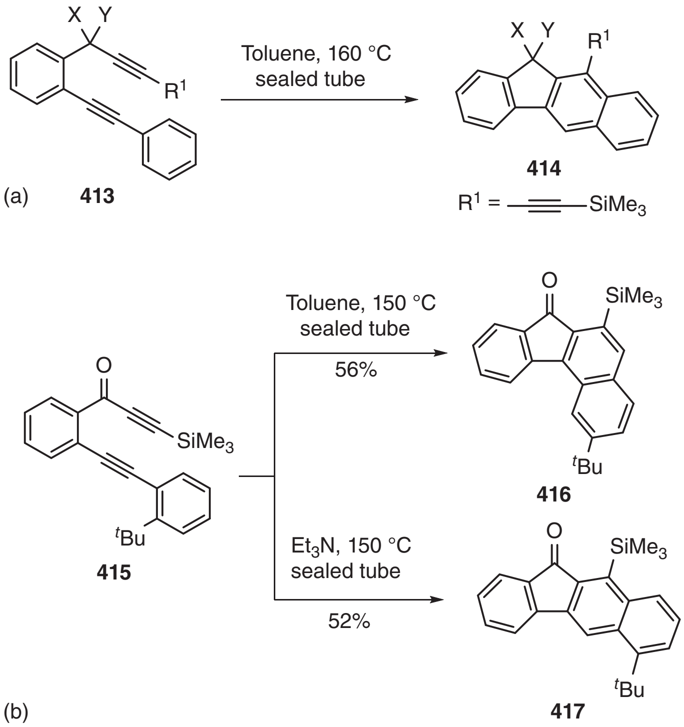
Scheme 6.107

(X,Y = H) < alcohols (X,Y = OH, H) < ketone (X,Y = O). The reaction of **413** (X,Y = O) takes place spontaneously and gives the fluorenone **414** (X,Y = O) in 98% yield. This drastic improvement would be due to the carbonyl group favoring adoption of a conformation in which the p-orbitals of the alkynes interact very easily in the transition state [255]. Thermal cyclization of a propynones **415** generally affords a mixture of benzo[*b*]- and -[*c*]fluorenones, **416** and **417**. The ratio of the two isomers can be efficiently varied between 1 : 0 and 0 : 1 by introducing substituents and using an appropriate solvent (Scheme 6.108b) [256].

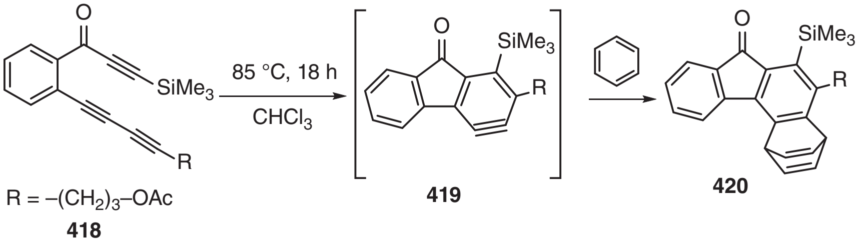
Recently, Hoye and coworkers [257, 258] reported a new fluorenone synthesis by a novel hexadehydro-Diels–Alder (HDA) reaction (Scheme 6.109). In the HDA reaction, a 1,3-diyne **418** is engaged in a [4+2] cycloisomerization with a “diynophile” to produce the highly reactive benzyne intermediate **419**. When trapping reagents are absent, the generated benzyne **419** undergoes a cycloaddition reaction with benzene as the solvent to form adduct **420**.

6.3.5.2 **Reaction of CPDNs**

The discovery of fullerenes has prompted a general interest in bowl-shaped aromatic hydrocarbons. Although corannulene **23** as the first bowl-shaped conjugated system had already been synthesized by Barth and Lawton [259], a simple

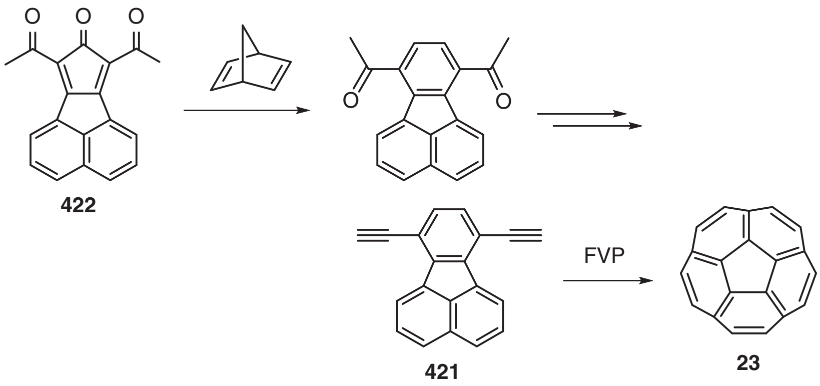


Scheme 6.108

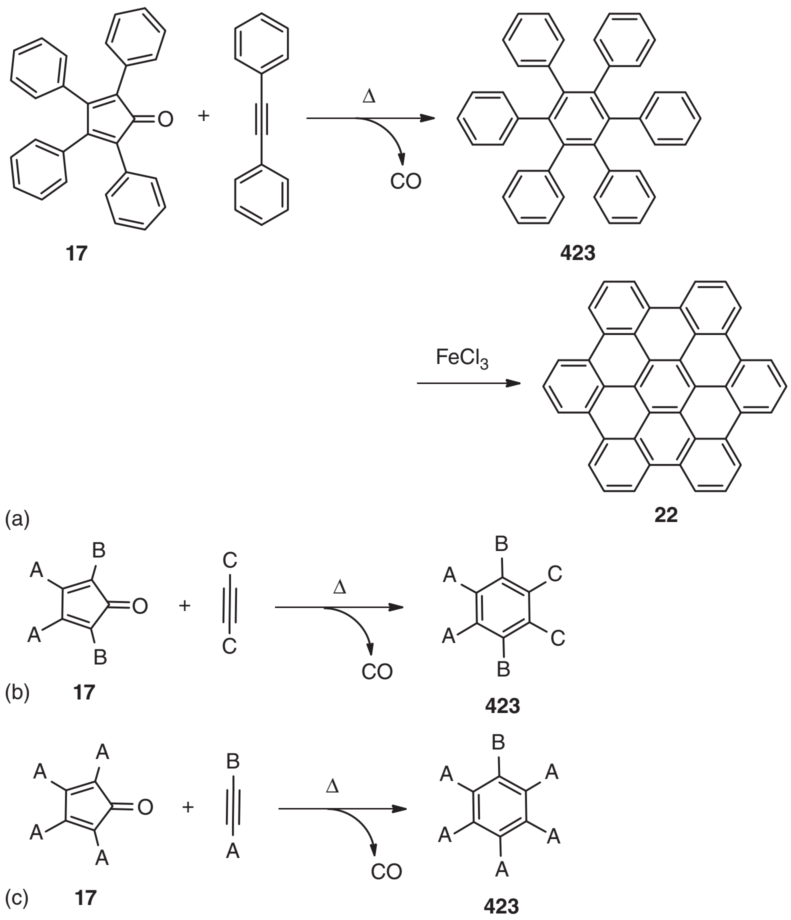


Scheme 6.109

and practical synthesis of **23** was desirable. In 1991, Scott reported a new synthesis of **23** involving FVP of fluoranthene **421** (Scheme 6.110) [260]. In the synthesis, CPDN **422** is employed as an important synthetic building block for the preparation of **421**. Soon afterwards, Siegel's and Rabideau's groups have independently developed other synthetic methods for **23** and related compounds. A variety of polycyclic conjugated systems bearing a curved conjugated system were synthesized from CPDN derivatives [148].



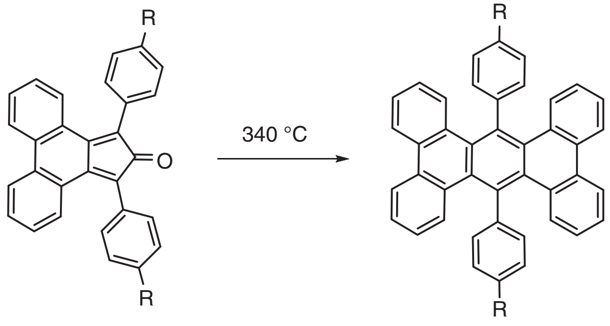
Scheme 6.110



Scheme 6.111

As mentioned, tetracyclone derivatives are important synthetic building blocks for HBC **22**. Müllen's group has developed an efficient way to prepare **22** by intramolecular oxidative cyclodehydrogenation of hexaphenylbenzene **423** with $FeCl_3$ (Scheme 6.111a), and this method (Scholl reaction) has later been extended to the synthesis of more complex PAHs with different shapes and sizes [11]. $Co_2(CO)_8$-catalyzed cyclotrimerization of substituted diphenylacetylenes efficiently affords **423** with C_6 symmetry. On the other hand, HBC derivatives carrying substituents in different regioisomeric patterns are commonly synthesized by Diels–Alder cycloadditions between appropriately functionalized tetracyclone **17** and diphenylacetylenes (Scheme 6.111b,c) [11].

Pascal and coworkers found unexpectedly that pyrolysis of phencyclones **424** forms diaryltetrabenz[*a,c,h,j*]anthracenes **425** (Scheme 6.112) [261]. The compounds **425** possess large twists of the polyacene units (66°, 61°, and 70°, respectively), because benzannulated acenes with phenyl groups positioned to clash with the benzo hydrogens give molecules with the largest end-to-end twists.



424: R = H, Cl, CF_3

425: R = H, Cl, CF_3

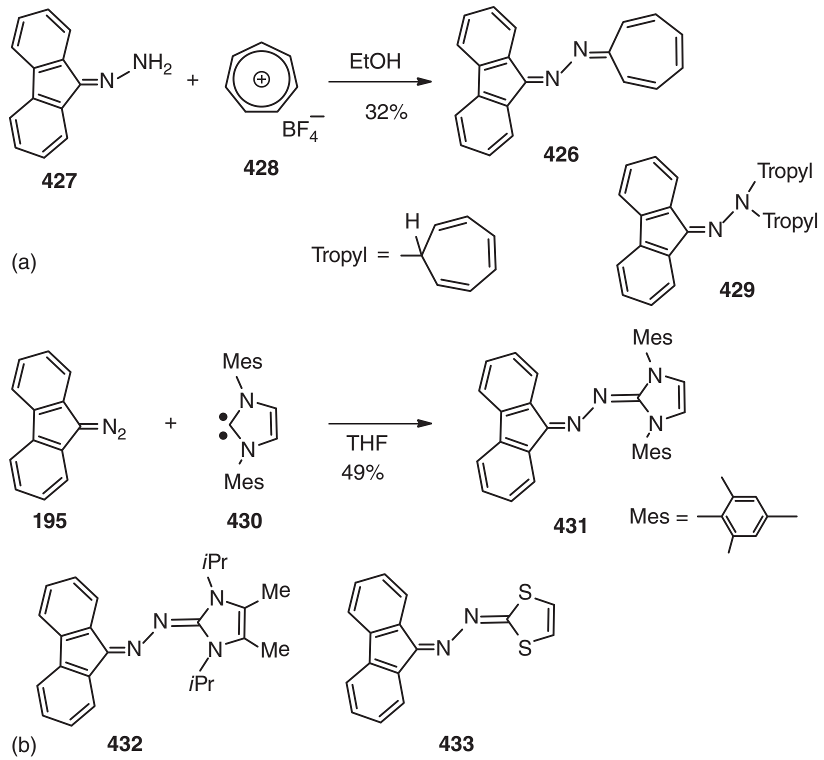
Scheme 6.112

6.3.6
Heterofulvenes

6.3.6.1 Azafulvenes

Because azafulvenes, namely, ICPDs, are readily converted to CPDNs **15** by an acidic hydrolysis, ICPDs can be regarded as a synthetic equivalent for CPDNs. Therefore, new syntheses of these are described together with synthesis of CPDNs in Section 6.3.5.1. This section thus discusses azafulvene derivatives with an azine moiety ($R_2C{=}N{-}N{=}CR_2$) in the molecule. 9-(Tropylidenehydrazono)fluorene **426** is obtained as a stable compound by reaction between 9-fluorenone hydrazine **427** and tropylium ion **428** in 32% yield (Scheme 6.113a). To produce **426**, 2 equiv. of tropylium ion are needed, indicating the formation of the bitropyl compound **429** as an intermediate [262]. Clyburne and coworkers reported that a stable, crystalline nucleophilic (singlet) carbene **430** reacts readily with diazofluorene **195** in

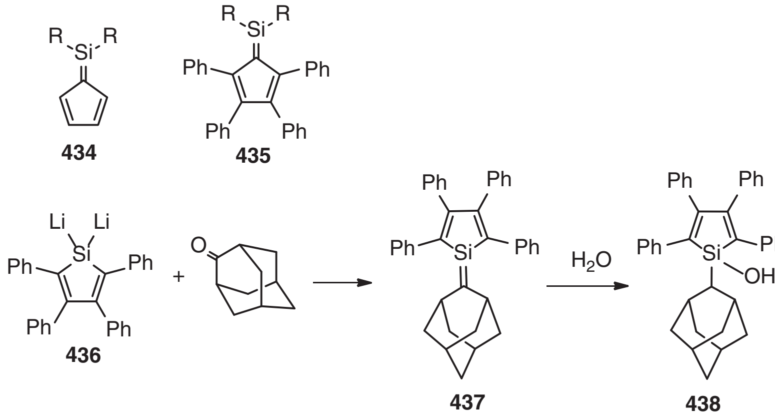
THF solution to produce azine **431** as a dark red, crystalline material (Scheme 6.113b). Crystallographic analysis reveals that there is little evidence for significant changes of the azine unit due to asymmetric electron distribution in the molecule [263]. Later, these authors synthesized several azine derivatives involving **432** and **433**. They are strongly polarized materials with large NLO behavior (β_{tot} 10^{30}/esu = 23.3 for **431**, 37.7 for **432**, and 35.5 for **433**) [264].



Scheme 6.113

6.3.6.2 Silafulvene

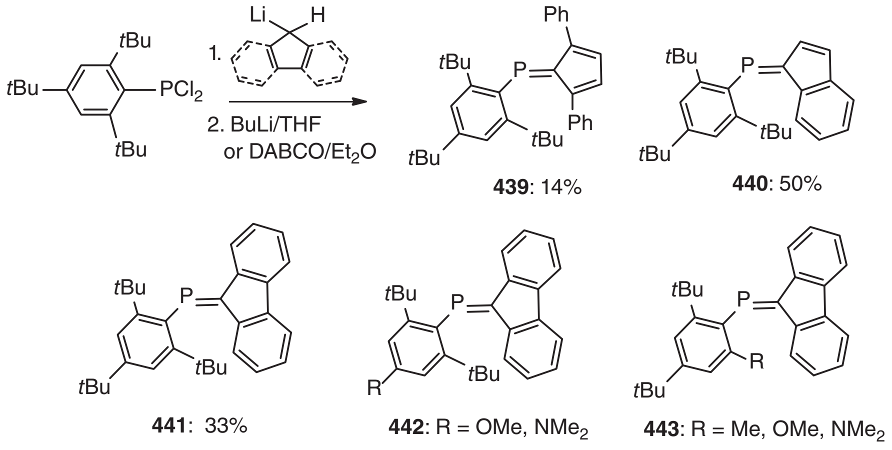
6-Silapentafulvene and the related compounds **434** and **435** are elusive species, and their generation has been proved only by trapping experiments [265]. In 2004, West and coworkers reported a new silene synthesis from 1,1-dilithium-2,3,4,5-tetraphenylsilole **436** and 2-adamantanone, leading to the first 5-silapentafulvene **437**. It was not isolated, though, but hydrolysis of the reaction mixture leads to 1,1-di-adamantanol-2,3,4,5-tetraphenylsilole **438**, the structure of which was confirmed by X-ray crystallography (Scheme 6.114) [266].



Scheme 6.114

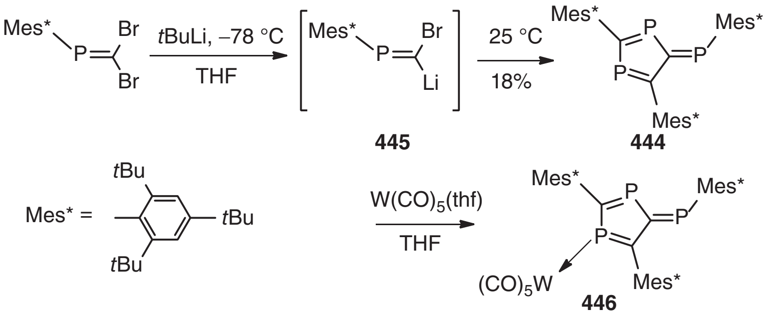
6.3.6.3 **Phosphafulvene**

The 2,4,6-tri-*t*-butylphenyl group is a powerful bulky protecting group, and by utilizing this substituent, Märkl's and Yoshifuji's groups have successfully prepared various types of phosphorus compounds of unusual structures. Stable phosphafulvene derivatives **439–441** were successfully synthesized using the substituent by Märkl as shown in Scheme 6.115 [267]. Later, Yoshifuji and coworkers synthesized a series of fluorenylidene(phenyl)phosphines **442** and **443** with bulky substituents, and they concluded that the *ortho*-functional groups and the corresponding *para*-functional groups seem to exert their influence in a different manner: While the *ortho*-functional groups seem to affect the π*-orbital, the *para*-functional group affects the n-orbital [268, 269].



Scheme 6.115

Furthermore, Yushifuji reported that 2,4,6-tris(2,4,6-tri-*t*-butylphenyl)triphosphafulvene **444** is formed as a deep red solid by the trimerization of lithium phosphaylidene carbenoid **445** (Scheme 6.116). The signal of the exocyclic phosphorus atom ($\delta_P = 313.8$) is downfield compared to ring P atoms ($\delta_P = 291.3, 264.7$), but similar to that of **441** ($\delta_P = 321.5$). Treatment of **444** with [W(CO)$_5$(thf)] afforded the corresponding tungsten complex **446**. The signal for the exocyclic phosphorus atom is shifted significantly to higher magnetic fields ($\delta_P = 268.8$) [270].



Scheme 6.116

6.4 Heptafulvenes

It has been well known that the discovery of natural products containing a tropolone moiety **447**, such as colchicine and hinokitiol, opened the way to the chemistry of nonbenzenoid aromatic compounds. Problems related to the aromaticity of π-conjugated systems bearing a seven-membered ring system have also received much attention. Among them, heptafulvene **3**, tropone (oxaheptafulvene) **16**, and azulene **4** are main subjects of synthetic and physical organic chemists (Figure 6.18). The contributions of Nozoe's group are particularly important in this area [271]. The abundant results were already summarized in many books and reviews [1]. This section hence restricts itself to (i) photoswitching behavior between dihydroazulene (DHA) and vinylheptafulvene (VHF), (ii) efficient azulene synthesis from oxaheptafulvenes, and (iii) functional dyes containing an oxaheptafulene as a subunit. In the past two decades, heptafulvene chemistry has largely developed along these three lines.

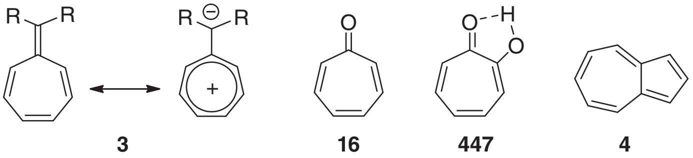
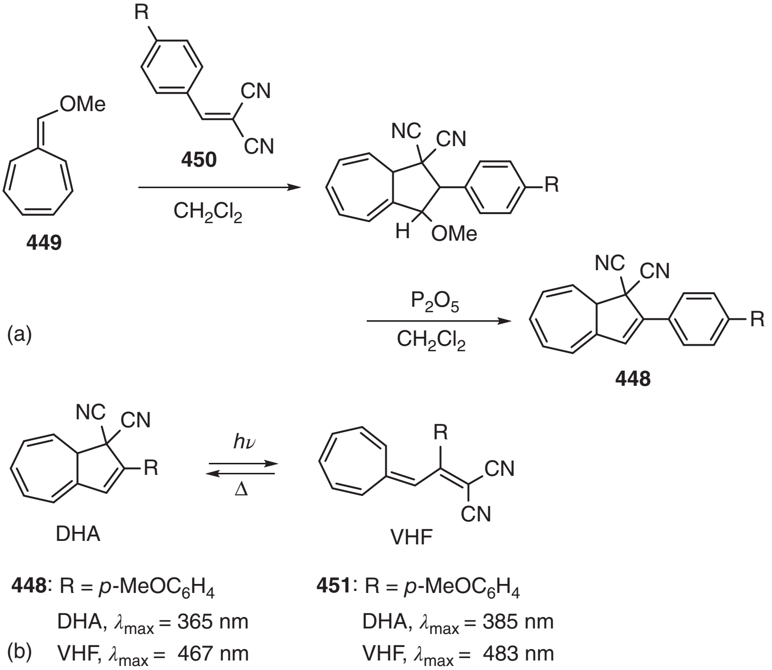


Figure 6.18 Heptafulvene and its polar structure **3**, tropone **16**, tropolone **447** and azulene **4**.

6.4.1
Synthesis of Heptafulvenes

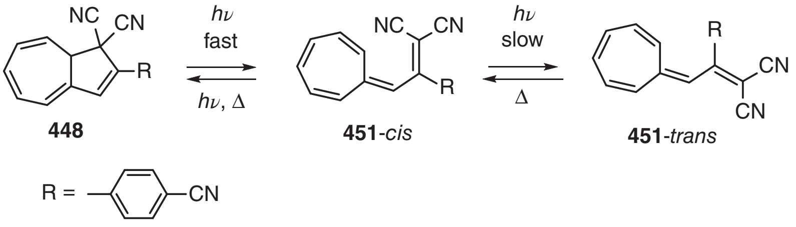
6.4.1.1 Synthesis of Dihydroazulene/Vinylheptafulvene (DHA/VHF) Systems

The dihydroazulene/vinylheptafulvene (DHA/VHF) system, first reported by Daub in 1984, represents such a photochromic system. DHAs such as **448**, a ring-closed system, are prepared by [8+2] cycloaddition of 8-methoxyheptafulvene **449** and dicyanoethylenes **450**. The double bond between C−2 and C−3 is introduced by elimination of methanol with phosphorus pentoxide (Scheme 6.117a). The yellow solutions of **448** turn dark red to **451** (VHF) on exposure to daylight. The thermolabile **451** rearranges quantitatively within 70 h at 25 °C into **448** in the dark (Scheme 6.117b) [272].



Scheme 6.117

This type of system has been intensively studied because it is an example of "one-way" photochromism; the photochemical rearrangement of DHA to VHF cannot be reversed by VHF absorption at a different frequency, but only by heat [273]. The final product of the photoconversion has been identified as a *trans* conformer by X-ray analysis. Therefore, as described in Scheme 6.118, the conversion from **448** to **451** must involve a **451**-*cis* conformer. Femtosecond pump–probe experiments



Scheme 6.118

performed by Daub and Riedle revealed that the internal conversion to the **451**-*cis* ground-state conformer proceeds within 15 ps [274].

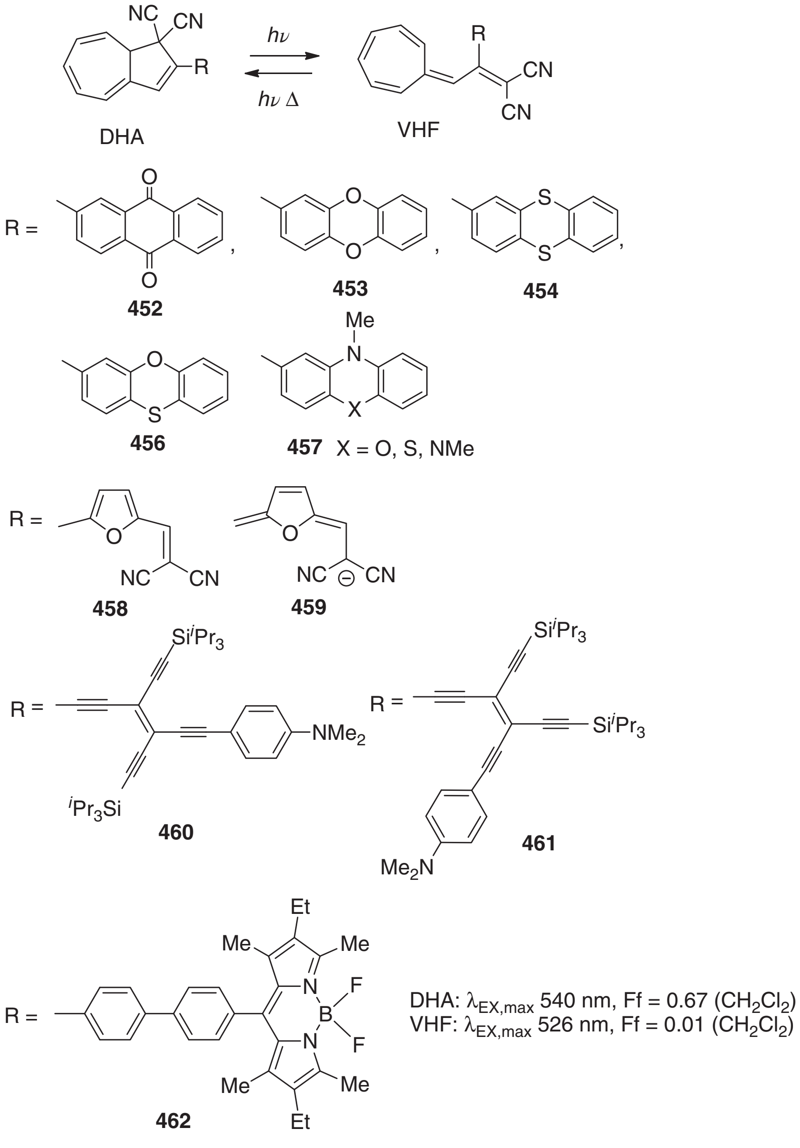
The photochromic conversion of DHA into VHF occurs by means of a 10-electron rearrangement of the carbon framework, which strongly influences the electronic properties of the substituents attached to the photochromic system. Thus, a variety of the DHA/VHF systems **452–462** have been reported so far (Figure 6.19) [275–278]. Daub and coworkers constructed the DHA/VHF system involving a BODIPY fluorophore in dyad **462**. The system shows photogated electrochemiluminescence; light-induced conversion of DHA to VHF is accompanied by a 50-fold decrease of luminescence, defining the system as a true ON/OFF photoswitch (Figure 6.19) [279].

A multimode-photochromic system based on DHA/VHF and diarylethene systems **463** was also constructed by Daub and coworkers. VHF **463A** can be prepared by the reaction of 1,1-dicyanopropene **464** and tropylium cation under basic conditions (Scheme 6.119), and thermal ring closure of **463A** produces **463B**, which is photochemically converted into **463A** and **463C**. The photostationary state of the B → A and B → C is sensitive to the irradiation wavelength [280].

The first synthetic protocol for functionalizing the DHA photoswitch in its seven-membered ring has been developed by Nielsen. DHAs **465** incorporating an arylethynyl-substituent in the seven-membered ring are prepared by palladium-catalyzed Sonogashira cross-coupling reactions employing a suitable bromo-functionalized DHA **466**. The thermal ring closure proceeds most readily in the presence of an electron-donating group on the seven-membered ring [281]. They also synthesized DHAs **467** with an aryl group in the seven-membered ring (Scheme 6.120) [282].

Later, Nielsen presents a new method for the DHA **468** containing a phenyl substituent on the seven-membered ring using the reaction of phenyltropylium ion and 1,1-dicyanopropene **469** under basic conditions (Scheme 6.121). The DHAs are obtained as a mixture of isomers [283].

The synthesis of a new molecular switch **470** incorporating two heptafulvene rings on a dicyanoethylene unit are accomplished by the reaction of 1,1-dicyano-2-methylpropene with 4 equiv. of tropylium ion, followed by subsequent hydride and tropylium ion removals from intermediate **471** (Scheme 6.122) [284].



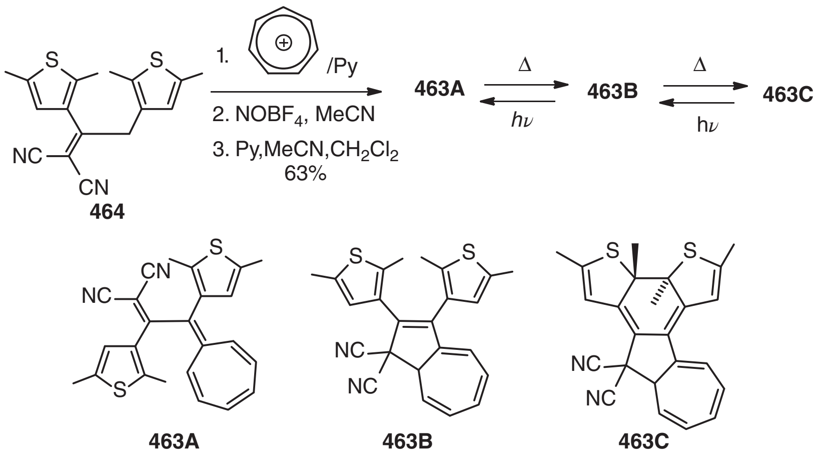
DHA: $\lambda_{\mathrm{EX,max}}$ 540 nm, Ff = 0.67 (CH_2Cl_2)
VHF: $\lambda_{\mathrm{EX,max}}$ 526 nm, Ff = 0.01 (CH_2Cl_2)

Figure 6.19 DHA and VHF systems **452–462**.

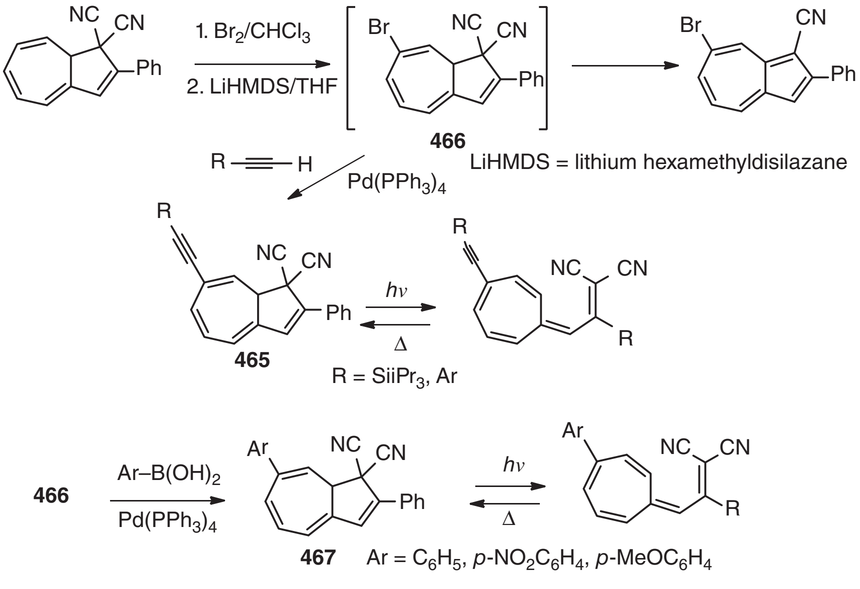
6.4.1.2 Reaction of 2*H*-Cyclohepta[*b*]furan-2-one Derivatives

Azulene Synthesis

2*H*-Cyclohepta[*b*]furan-2-one **472** was prepared by the reaction of 2-tosyloxytropone **473** and dimethyl malonate in the presence of sodium methoxide in ethanol. The heptafulvene **472** is a versatile synthetic building block for azulene



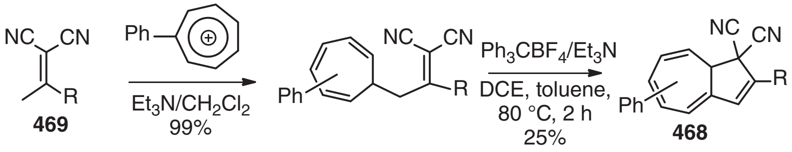
Scheme 6.119



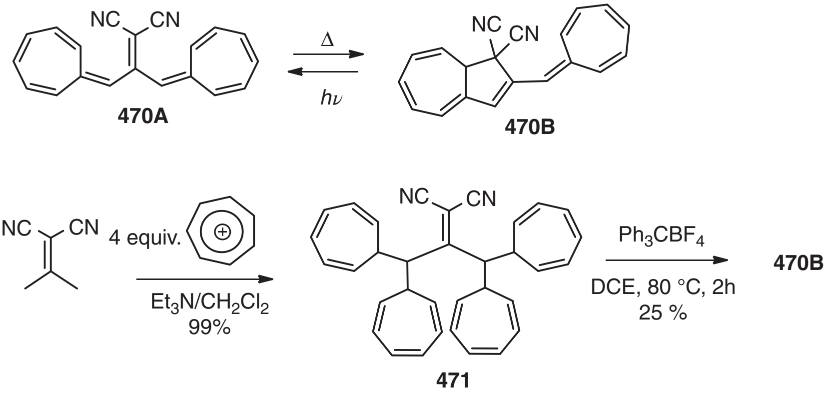
Scheme 6.120

synthesis, by the so-called enamine method (Scheme 6.123) [285]. The route, developed by Takase and coworkers, provides a variety of azulene derivatives **474**; the carboxyl group of **474** is readily removed by treatment with acid.

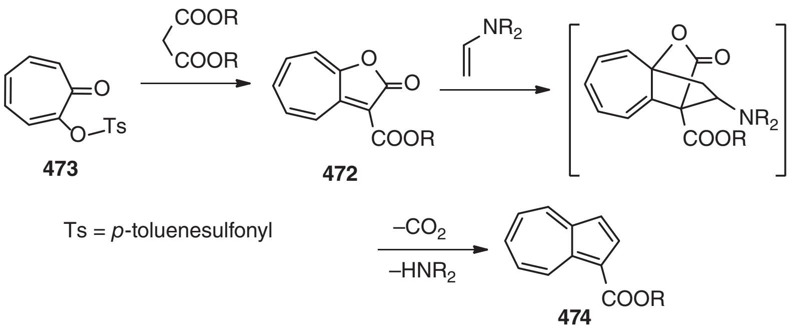
A disadvantage of the enamine method is that the condensation reaction does not work well with alkylated tropolones. Polyalkylated cyclohepta[*b*]furan-2(2*H*)-ones **475** can easily be prepared from polyalkylphenyl propiolates **476** by dynamic gas phase thermoisomerization. The resulting heptafulvenes react thermally with



Scheme 6.121



Scheme 6.122



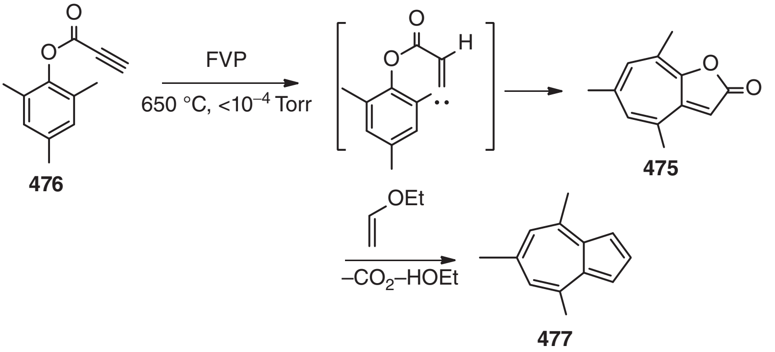
Scheme 6.123

enol ethers or enamines to afford the corresponding azulenes **477** (Scheme 6.124) [286].

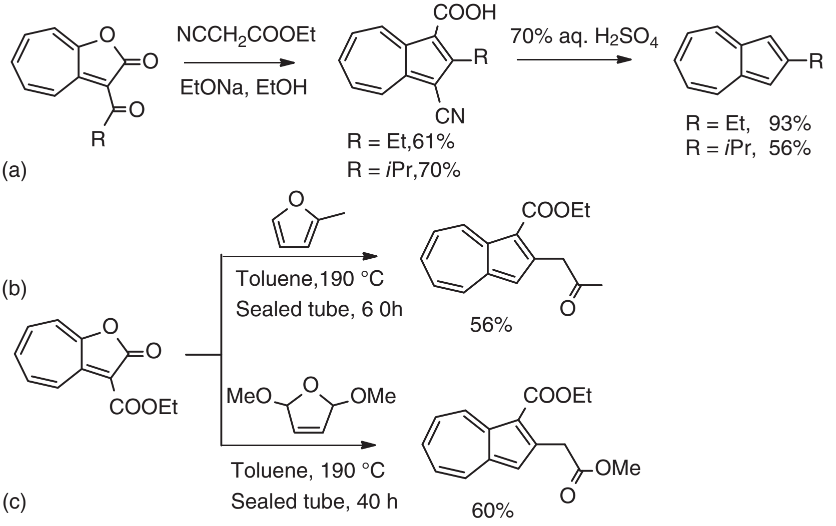
An alternative method using enols in place of enamines has also been developed by several groups, as shown in Scheme 6.125a–c [287].

Reaction with Electrophiles

2*H*-Cyclohepta[*b*]furan-2-one **478** and related compounds undergo electrophilic substitutions at the 8-position of the fulvenes [288]. Heteroazulene-substituted tropylium ions **479** are prepared by the reaction of **478** with tropylium ion (Scheme 6.126a) [288]. Nitta and coworkers [289] synthesized ketones **480**,



Scheme 6.124

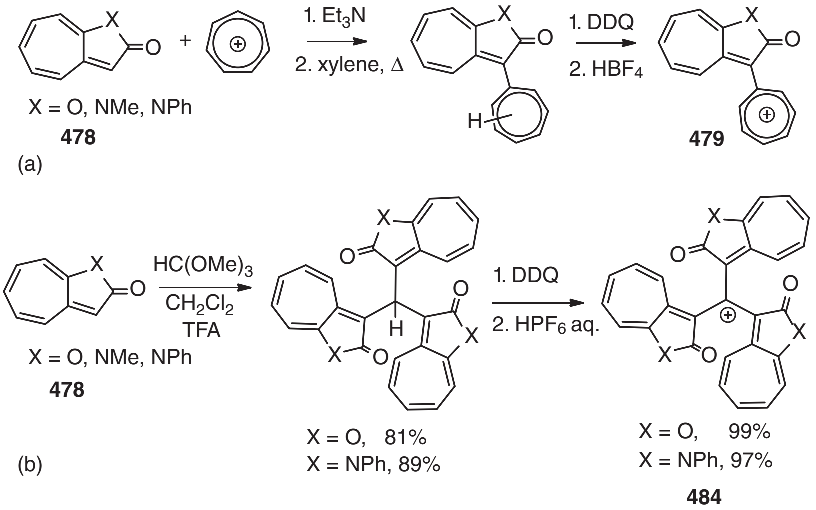


Scheme 6.125

quinone methides **481**, and dicyanoquinodimethane **482** and **483** bearing two heptafulvene π-systems by using similar electrophilic reactions at the 8-position of **478** (Figure 6.20). Analogous to azulene, **478** can be converted into the fairly stable tris(8-heteroazulenyl)methyl cation **484** by condensation with trimethyl orthoformate, followed by hydride abstraction (Scheme 6.126b) [290].

A similar reaction of **478** with 1,3,5-triformylbenzene affords the corresponding trication **485** upon hydride abstraction with DDQ (Scheme 6.127) [291].

Ethynylated 2*H*-cyclohepta[*b*]furan-2-ones **486** are prepared by Pd-catalyzed alkynylation of 3-iodo-5-isopropyl-2*H*-cyclohepta[*b*]furan-2-one **487** with the corresponding ethynylarenes [292]. The compound reacts with tetracyanoethylene (TCNE) **488** and TCNQ **25** to afford highly polarized dicyanoethylene derivatives **489** and **490** respectively (Scheme 6.128) [293].



Scheme 6.126

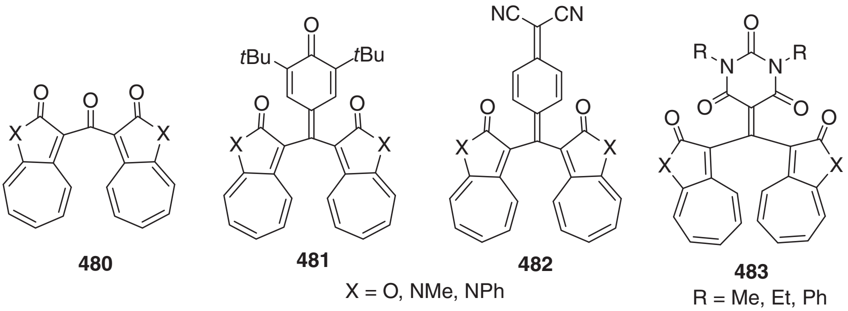
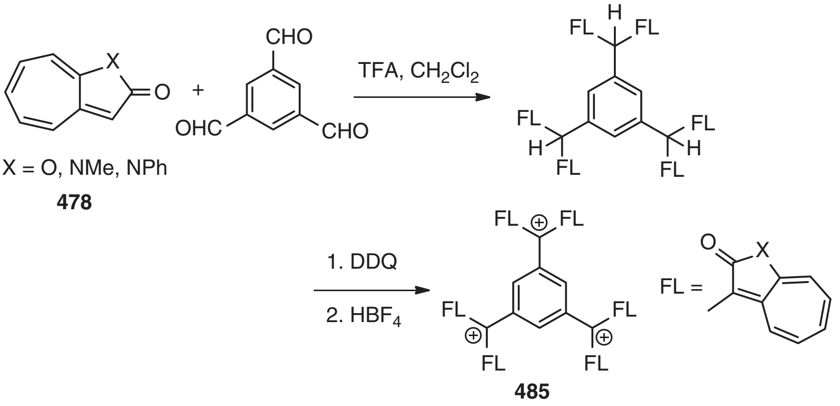
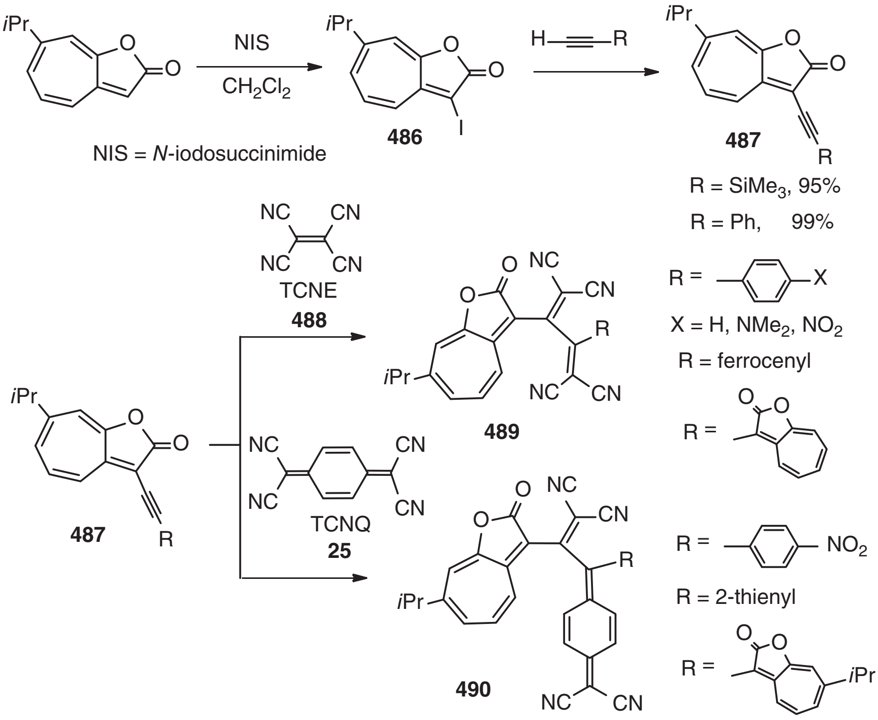


Figure 6.20 Push–pull type of compounds bearing heptafulvene moieties.



Scheme 6.127

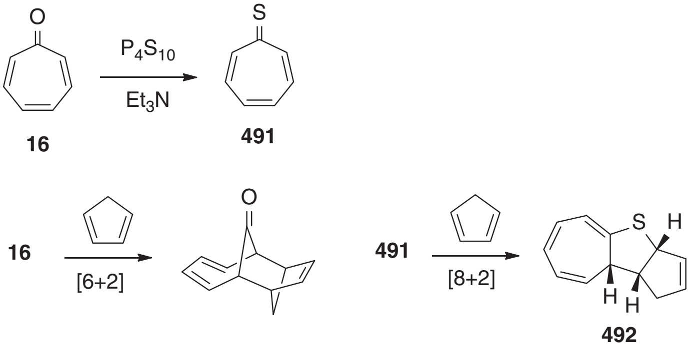


Scheme 6.128

6.4.2
Heteroheptafulvenes

6.4.2.1 Thiatropone (Tropothione)

Machiguchi and coworkers [294] reported the synthesis and isolation of tropothione **491** as thermally labile crystals and described novel properties of related compounds (Scheme 6.129). Fundamental physical and chemical properties of **491** are

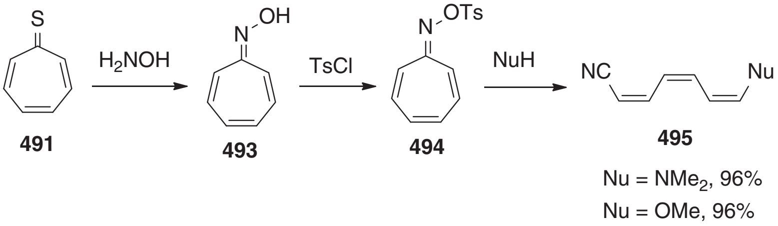


Scheme 6.129

quite different from those of tropone **16**. For example, in contrast to the [6+4] cycloaddition between **16** and cyclopentadiene **491** reacts with it to afford an [8+2] cycloadduct, **492**.

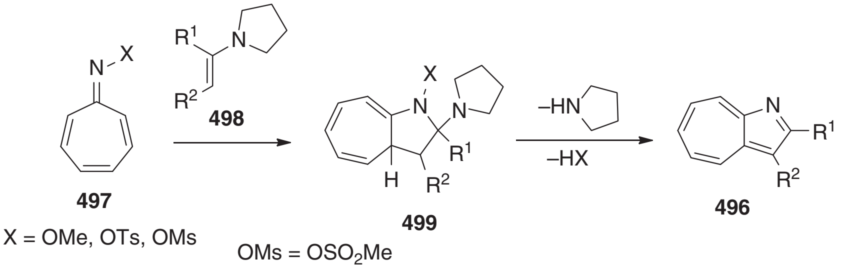
6.4.2.2 **Azaheptafulvenes**

Tropone oxime **493** cannot be efficiently obtained from the reaction between **16** and hydroxylamine, because the reaction gives mainly 2-aminotropone. However, if the reaction employs tropothione **491** as the starting material, **493** is produced in good yield. The contrast of the C−2 attack of **16** and the C−1 attack of **491** is rationalized in terms of frontier orbital theory. The tosylate **494** derived from **493** reacts quite readily with a variety of nucleophilic reagents at low temperatures to give hexatriene derivatives **495** with (*Z,Z,Z*)-configuration in excellent yields (Scheme 6.130) [295].



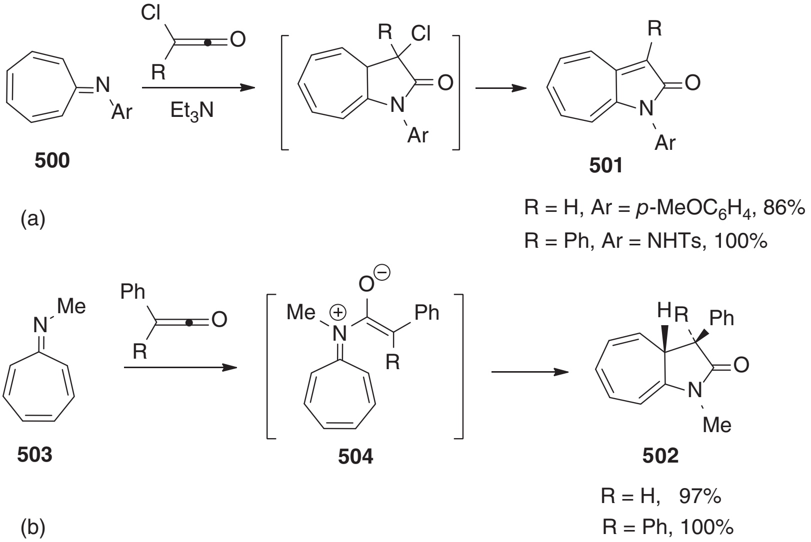
Scheme 6.130

A short new synthesis of 1-azaazulene derivatives **496** consists in the alkylation of troponimines **497** with pyrrolidino enamines **498**, as reported by Nitta's group. The reaction leads to formal [8+2] cycloadducts **499**, and subsequent aromatization takes place under the reaction conditions (Scheme 6.131) [296]. In this transformation, pyrrolidino enamines are required, probably because of ring strain in the [8+2] cycloadduct **499**.



Scheme 6.131

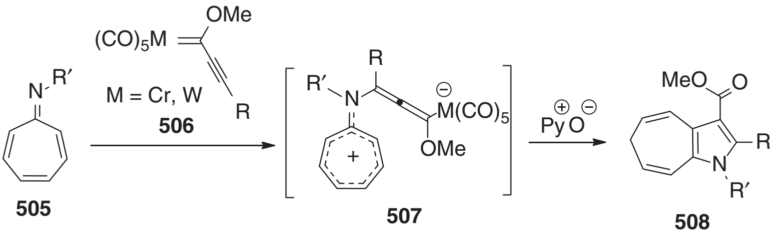
The [8+2] cycloaddition reaction of 8-azaheptafulvenes **500** with 2-chloroketenes constitutes an efficient synthetic method for the preparation of azaazulen-2-ones **501** (Scheme 6.132a) [297, 298]. The reaction with aryl



Scheme 6.132

ketenes leads exclusively to the corresponding *trans*-[8+2] cycloadducts **502**, as has been investigated by Torres and coworkers [299]. According to DFT calculations, the reaction occurs stepwise by initial nucleophilic attack of the nitrogen atom of **503** at the electrophilic carbonyl group of the ketene to form a zwitter ionic intermediate **504** (Scheme 6.132b).

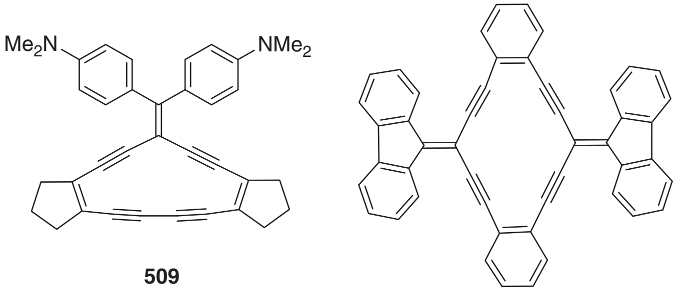
The [8+2] cycloaddition reaction between 8-azaheptafulvenes **505** and ethynyl-Fischer carbene complexes **506** occurs through similar zwitterionic intermediates **507** to afford the cycloheptapyrrole derivatives **508** (Scheme 6.133) [300].



Scheme 6.133

6.5
Other Fulvenes

Several fulvene derivatives bearing a macrocyclic ring system were synthesized by Iyoda’s and Ojima’s groups in the 1980s [301, 302]. During the past two decades,



509

510

Figure 6.21 The macrocyclic fulvene systems **509** and **510**.

numerous macrocyclic systems were synthesized [303]. The number of reports dealing with new fulvene syntheses in this category, however, is quite limited. Here, the macrocyclic fulvene systems **509** and **510**, prepared by Tykwinski's and Diederich's groups (Figure 6.21) [304, 305], may suffice to illustrate this group of compounds.

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7

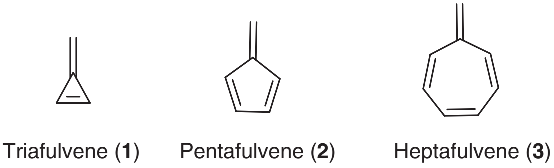
Constructing Molecular Complexity and Diversity by Cycloaddition Reactions of Fulvenes

Bor-Cherng Hong

7.1

Introduction

Fulvenes, cyclic molecules with odd number of carbon atoms in the ring, represent one of the fundamental categories of cross-conjugated systems (see Chapters 1 and 6). According to the ring size of these molecules, the compounds are classified as triafulvenes **1**, pentafulvenes **2**, heptafulvenes **3**, and so on (Scheme 7.1). Owing to their dipole moments, fulvenes possess unique reactivity, different from that of open-chain polyolefins and aromatic compounds. In 1989, Neuenschwander [1] reported a thorough review of fulvene chemistry. Recently, Nair and Abhilash [2] published a review on [8+2]-cycloaddition reactions, which included some reactions of fulvenes. A very brief review of progress in the synthesis and applications of fulvenes was reported in 2008 [3]. Nevertheless, a comprehensive review of cycloadditions of fulvenes has not appeared since 1989. This chapter covers the cycloaddition reactions of pentafulvenes published after 1989, along with the cycloaddition reactions of triafulvenes and heptafulvenes, with particular focus on the synthesis of polycyclic systems. For the synthesis of numerous other fulvenoid compounds, see Chapter 6.

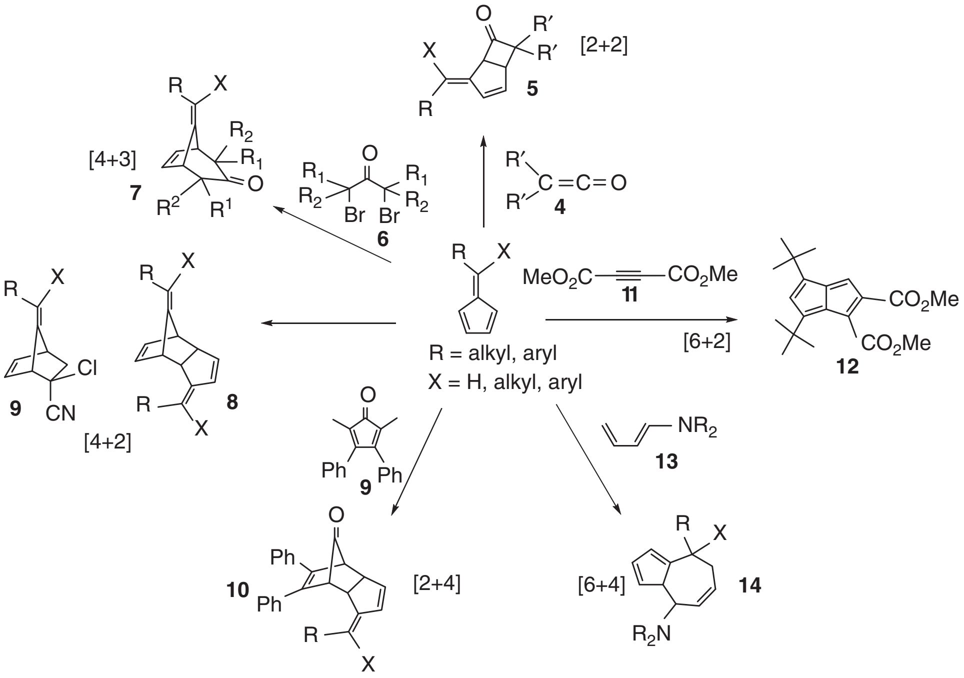


Scheme 7.1

Among the various types of fulvenes, pentafulvenes stand out as the most widely studied. They serve as 2π-, 4π-, 6π-, or even three-carbon components in annulation processes, depending on the reaction partners. The periselectivity of these reactions depends upon both reaction partners. For decades, pentafulvenes have

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

served as excellent building blocks for the synthesis of polycyclic compounds. Representative examples are shown in Scheme 7.2.



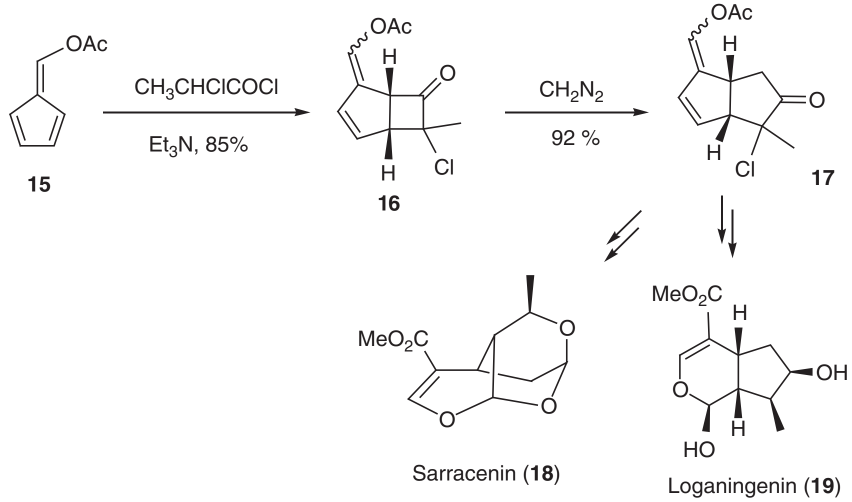
Scheme 7.2

7.2
Reactions of Pentafulvenes

7.2.1
[2+2]Cycloadditions

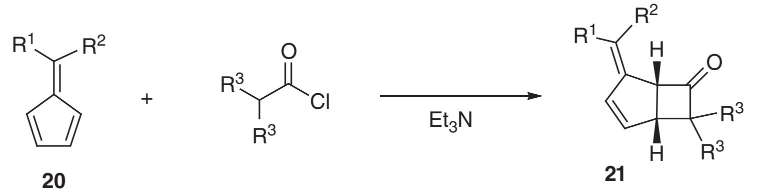
The [2+2]-cycloadduct **16** of 6-acetoxypentafulvene, **25**, and methyl chloroketene (generated *in situ* from α-chloropropionyl chloride and triethylamine) was prepared by Chang and coworkers. This product was used in the synthesis of the iridoids, loganin, and sarracenin (Scheme 7.3, **18**, **19**) [4].

[2+2]Cycloadditions of α-chloroketenes to fulvenes are well documented; and the adducts have also been applied to the synthesis of other natural products, including ophiobolin, filifolone, and chrysanthemic acid (Scheme 7.4) [5]. Nevertheless, Hong and coworkers [6] reported a new mode of reaction between α-halo acyl halides and 6,6-dialkoxyfulvene **20.** Under standard conditions of *in situ* generation of α-chloroketenes, nucleophilic acyl substitution of the acyl chloride by



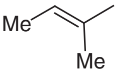
Scheme 7.3

the fulvenic ketene acetal gave products **21** (Scheme 7.5). The product **21** was transformed into carbocyclic analogs of captopril by two subsequent steps.



R^1, R^2 = H, CH_3, Ph, OTBDMS, OAc, OEt, NMe_2, $-(CH_2)_4-$, $-S(CH_2)_4S-$

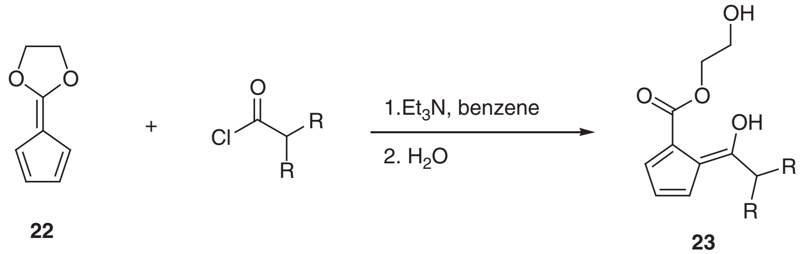
R^3 = Me, Cl,



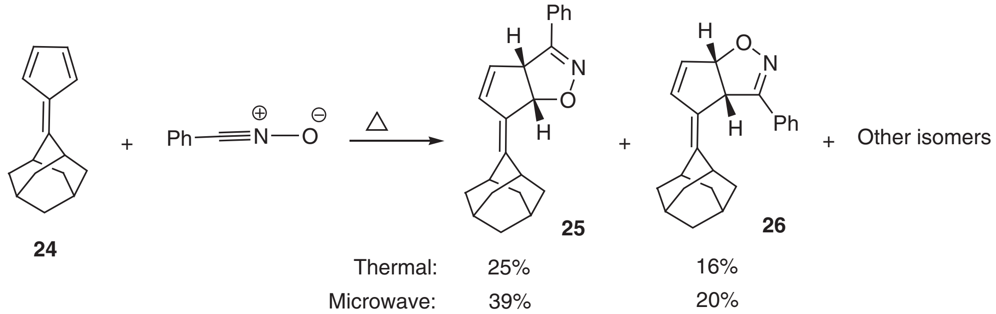
Scheme 7.4

7.2.2
[2+3]Cycloadditions

Chung and coworkers [7] reported a 1,3-dipolar cycloaddition of adamantylidenefulvene **24** with 2 M equiv. of alkyl nitrile oxides under thermal and microwave conditions providing a about 1 : 1-ratio of the [2+3]-cycloadducts **25** and **26** as the major products, and four minor cycloadducts (Scheme 7.6). The regioselectivity of these [2+3]cycloadditions was enhanced by carrying them out in the presence of β-cyclodextrin.

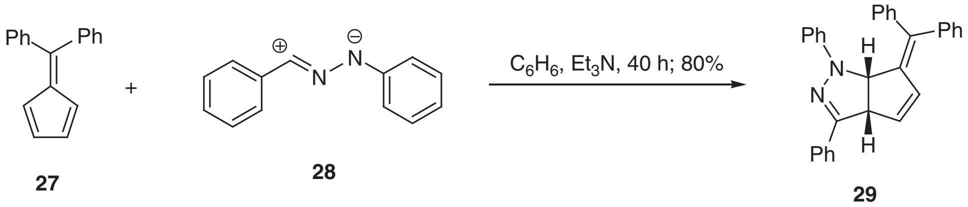


Scheme 7.5



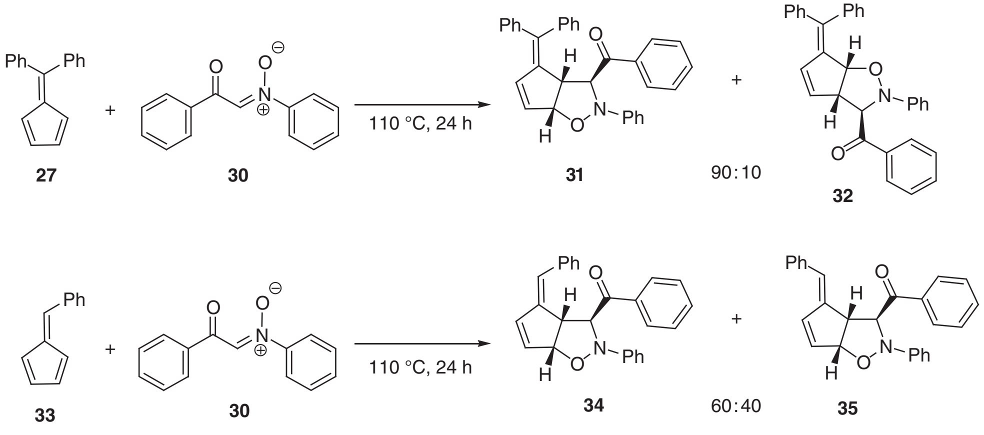
Scheme 7.6

1,3-Dipolar cycloadditions of 1,3-diphenylnitrilimine with various fulvenes, for example, 2,3,4,5-tetraphenylfulvene, 9-benzalfluorene, and 6,6-diphenylfulvene, providing a series of spiro-pyrazolines, were studied by Dhar and Ragunathan (Scheme 7.7) [8]. Most of these 1,3-dipolar cycloadditions took place across the *exo*-cyclic double bond to give the spiro-pyrazoline derivatives, the exception being 6,6-diphenylfulvene **27**, which underwent reaction at the *endo*-cyclic site to afford the fused pyrazoline derivative **29**.

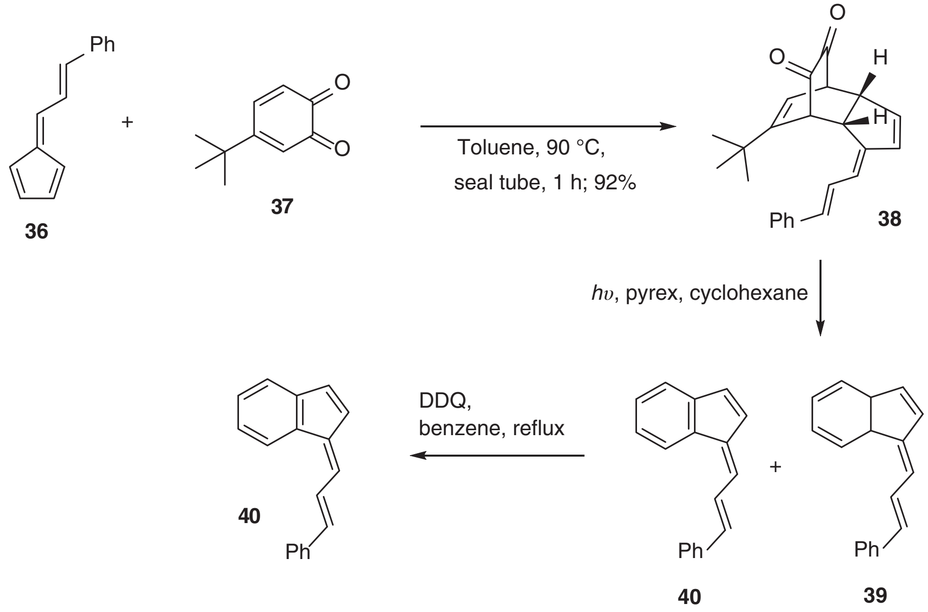


Scheme 7.7

Ciamala *et al.* reported the [2+3]cycloadditions of a series of mono- and disubstituted pentafulvenes with acylnitrones to afford the corresponding fused bicyclic monoadducts (Scheme 7.8) [9]. The regioselectivity of this reaction was rationalized by theoretical calculations.



Scheme 7.8

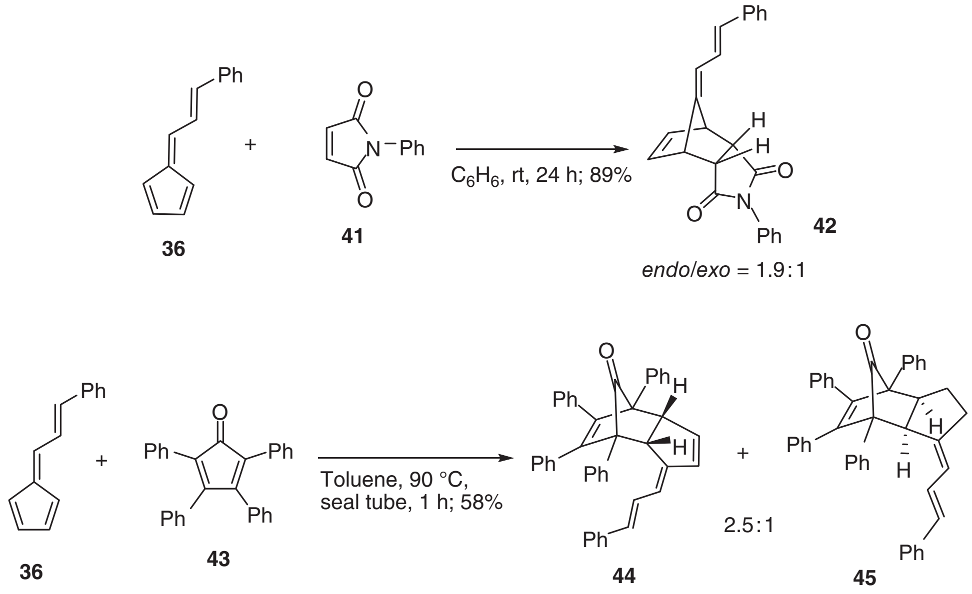


Scheme 7.9

7.2.3
[2+4]Cycloadditions

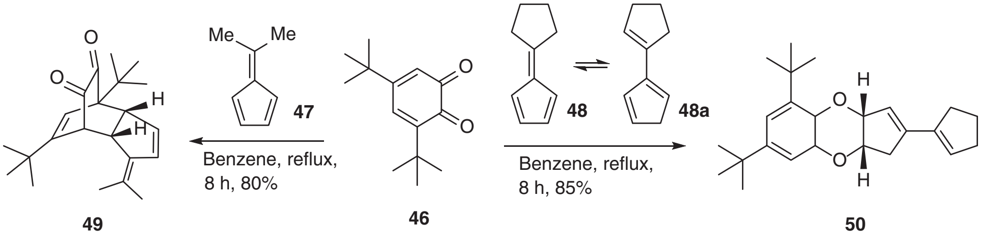
Nair and coworkers [10] reported the Diels–Alder reactions of a 6-arenyl fulvene with dienes and dienophiles (Scheme 7.9). Thus, 6-(2-phenyl ethenyl) fulvene **36**, with 4-*t*-butyl-*o*-benzoquinone **37** on heating in a sealed tube (at 90 °C for 1 h), afforded the [2+4]adduct **38** with *endo*-selectivity. Subsequently, facile photochemical transformation of the formed bicyclo[2.2.2]octenediones **38** in cyclohexane led to the formation of decarbonylated products **39** and **40**. Treatment of the inseparable mixtures with DDQ in refluxing benzene afforded the vinylogous benzofulvenes **40**.

It was observed that when the same 6-(2-phenyl ethenyl) fulvene **36** acted as a 4π-component in a [4+2]cycloaddition with electron-deficient dienophiles (such as *N*-phenyl maleimide **41** (Scheme 7.10) [11], whereas fulvene **36** reacted as a 2π-component with electron deficient dienes, for example, **43**.

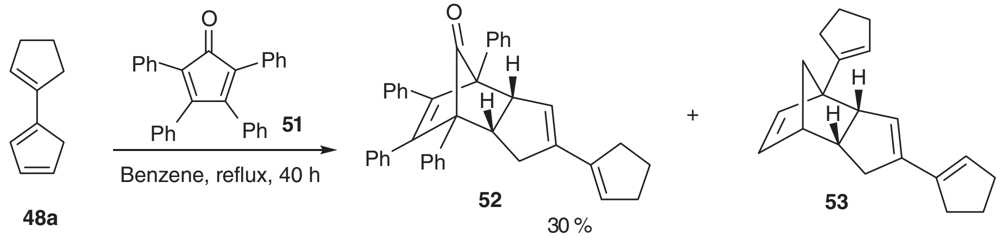


Scheme 7.10

Nair and Kumar [12] reported a [2+4]cycloaddition of *o*-benzoquinones **46** with symmetrical 6,6-dialkylfulvenes **47** and cycloalkylfulvenes **48** to give bicyclo[2.2.2]octanediones **49** and cyclopenta[*b*][1,4]benzodioxins **50**, respectively (Scheme 7.11). The latter product arises by way of a hetero-Diels–Alder reaction between the *ortho*-quinone (the 4π-component) with the isomerized fulvene (the 2π-component, a cyclo-[3]dendralene; see Chapters 1 and 12) [13]. 5-Cyclopentylidenecyclopenta-1,3-diene **48** was prepared from the pyrrolidine-catalyzed condensation of cyclopentanone and cyclopentadiene at 0 °C. The group was able to isolate cyclopent-1-enylcyclopentadiene **48a** by treatment of the *in situ* prepared **48a** with a slight excess of acetic acid at zero degree Celsius, followed by the regular isolation and chromatographic separation [14]. Reaction of cyclopent-1-enylcyclopentadiene **48a** with tetracyclone **51** in refluxing benzene gave a 30% yield of the [2+4]adduct **52**, along with a considerable amount of the [3]dendralene Diels–Alder dimerization product **53** (Scheme 7.12).



Scheme 7.11

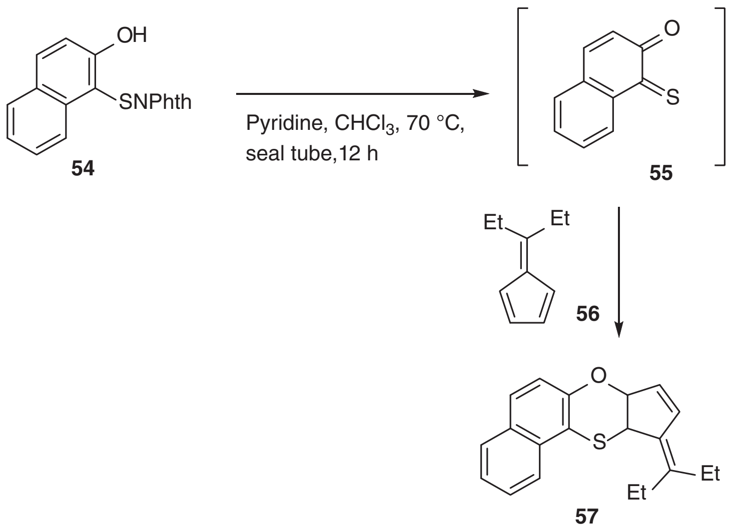


Scheme 7.12

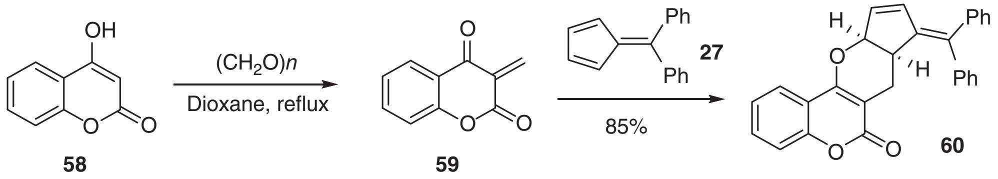
A [2+4]cycloaddition of *o*-thioquinones **55** with pentafulvenes **56** constitutes an efficient protocol for the synthesis of benzoxathiins **57** (Scheme 7.13) [15].

Nair and coworkers reported a [2+4]cycloaddition reaction of coumarin quinone methide **59** (generated *in situ* by Knoevenagel condensation between formaldehyde and 4-hydroxycoumarin **58**) with pentafulvenes such as **27**, providing a facile synthesis of pyranocoumarins **60** (Scheme 7.14) [16]. A computational study was performed to shed light on the process.

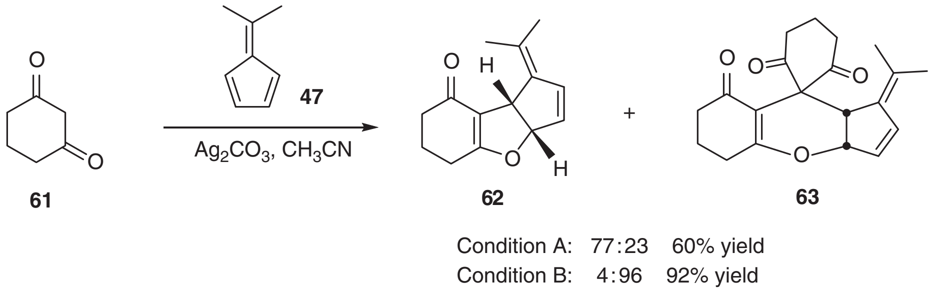
Hong and coworkers [17] described a sequence involving oxidative dimerization 1,3-diketones **61**, then cycloaddition with fulvenes **47**. The methodology allows a facile synthesis of cyclopenta[*b*]chromenes 1,3-diketones **63** (Scheme 7.15). For example, a CH_3CN solution of 6,6-dimethylfulvene **47**, cyclohexane-1,3-dione **61**, and Ag_2CO_3 was heated to reflux for 5 h and provided a 46% yield of 1-oxacyclopenta[*a*]indene **62** (a formal [3+2]adduct) along with 14% of cyclopenta[*b*]chromene **63.** Alternatively, a mixture of cyclohexane-1,3-dione **61** and Ag_2CO_3 was heated to reflux for 12 h in CH_3CN, followed by addition of 6,6-dimethyl fulvene **47**, to give cyclopenta[*b*]chromene **63** as a major product (92% yield). Possible mechanisms to rationalize the formation of the [4+2]adduct are depicted in Scheme 7.16. Initially, dimerization of radical **61R**, generated from **61** and Ag_2CO_3 in refluxing CH_3CN, afforded tetraone **64**. Three possible



Scheme 7.13

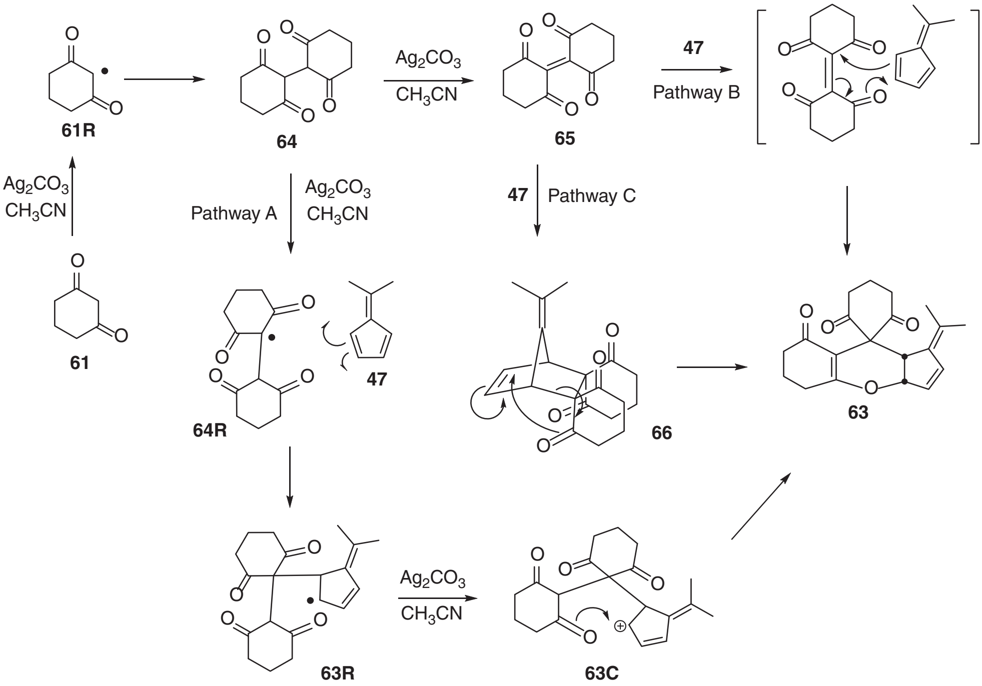


Scheme 7.14



Condition A: ketone, fulvene and Ag_2CO_3 were heated to reflux for 5 h in CH_3CN.
Condition B: ketone and Ag_2CO_3 was heated to reflux for 12 h in CH_3CN, followed by addition of fulvene.

Scheme 7.15

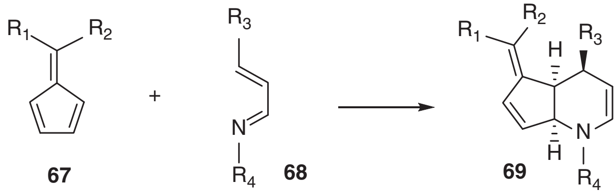


Scheme 7.16

pathways were proposed toward **63**. Pathway A arises from the attack of the 1,3-diketoalkyl radical **64R** at the endocyclic double bond of fulvene **47**, generating an allyl radical **63R**, followed by oxidation to give an allyl cation **63C** and cyclization to provide the pyran product **63**. Alternatively, Pathway B involved a hetero-Diels–Alder reaction of tetraone **65**, generated *in situ* from **64** in the reaction media, with fulvene **47** to give **63**. Furthermore, Pathway C engages Diels–Alder reaction of **65** with fulvene **47**, providing the adduct **66**, followed by a [3.3]sigmatropic rearrangement to afford cyclopenta[*b*]chromene **63**.

Hong and coworkers [18] also reported an azadiene Diels–Alder cycloaddition involving fulvenes (Scheme 7.17). Pentafulvenes **67** was reacted with *N*-sulfonyl-1-aza-1,3-butadiene **68** to give the tetrahydro-[1]pyridine system **69** efficiently. The reactions provided **69** in moderate yields at room temperature; the yields could be improved by high-pressure reactions and microwave conditions. Formally, this reaction involves a regio- and diastereoselective inverse electron-demand Diels–Alder reaction.

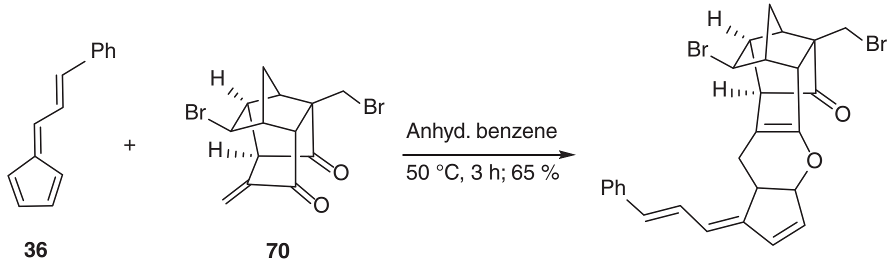
Nair and coworkers [19] reported a hetero-Diels–Alder reaction of pentafulvene **36** (acting as a 2π component) with tetracyclic enone **70** (the 4π-heterodiene), to give the polycyclic cage compound **71** containing a pyran moiety (Scheme 7.18).



67 **68** **69**

R_1 = Me, Et, Pr, Ph, p-ClC_6H_4, $-(CH_2)_5-$;
R_2 = H, Me, Et, Pr, Ph, p-ClC_6H_4, $-(CH_2)_5-$;
R_3 = CO_2Et, Ph; R_4 = Ts, SO_2Ph

Scheme 7.17



36 **70** **71**

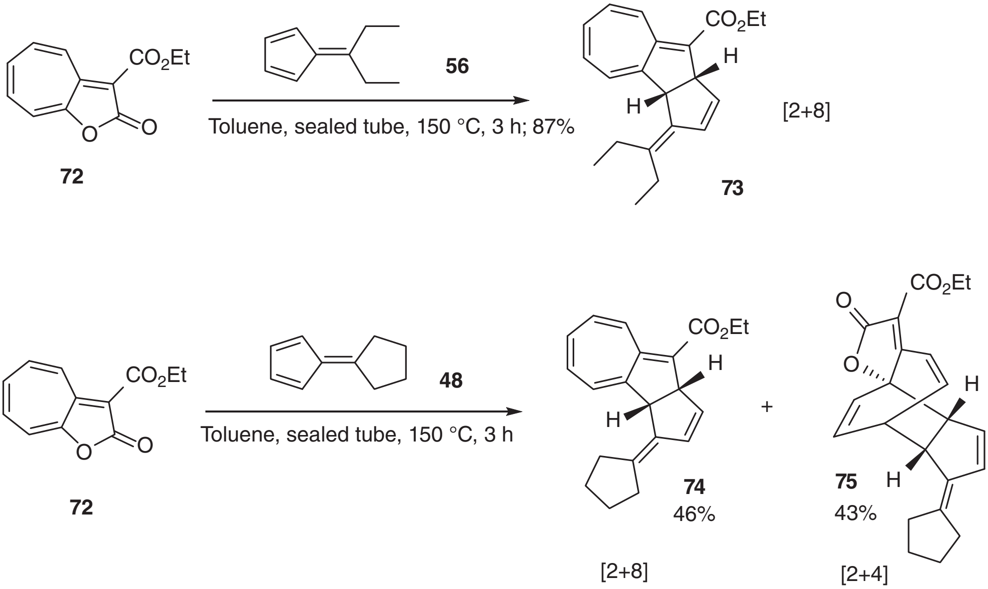
Scheme 7.18

7.2.4
[2+8]Cycloadditions

Competing [2+8]- and [2+4] modes of cycloaddition between pentafulvenes **2** and 2*H*-cyclohepta[*b*]furan-2-one **72** were reported by Nair and coworkers (Scheme 7.19) [20]. The pericyclic reaction of diethylfulvene **56** and **72** in toluene in a Schlenk tube at 150–170 °C predominantly gave tricycle **73** as the major product, with trace amounts of the [4+2]adduct. The formation of **73** resulted from a [2+8]cycloaddition of **56** and **72** followed by decarboxylation. The reaction between **72** with 6,6-cycloalkyl pentafulvene **48**, however, gave about 1 : 1-mixture of [2+8]- and [2+4]adducts, **74** and **75**, respectively. The outcomes of these inverse electron-demand cycloadditions are probably governed by steric factors.

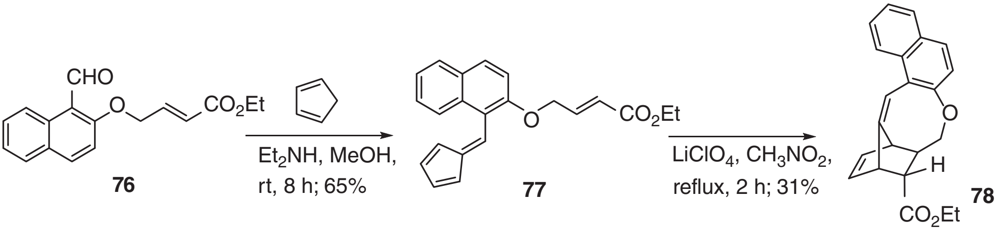
7.2.5
[4+2]Cycloadditions

An intramolecular [4+2]cycloaddition involving a fulvene moiety as the 4π component provided the 6-oxatricyclo[6.4.0.0^{2,10}]dodeca-2,11-diene ring system **78** was reported by Shanmugasundaram and Raghunathan (Scheme 7.20) [21]. The



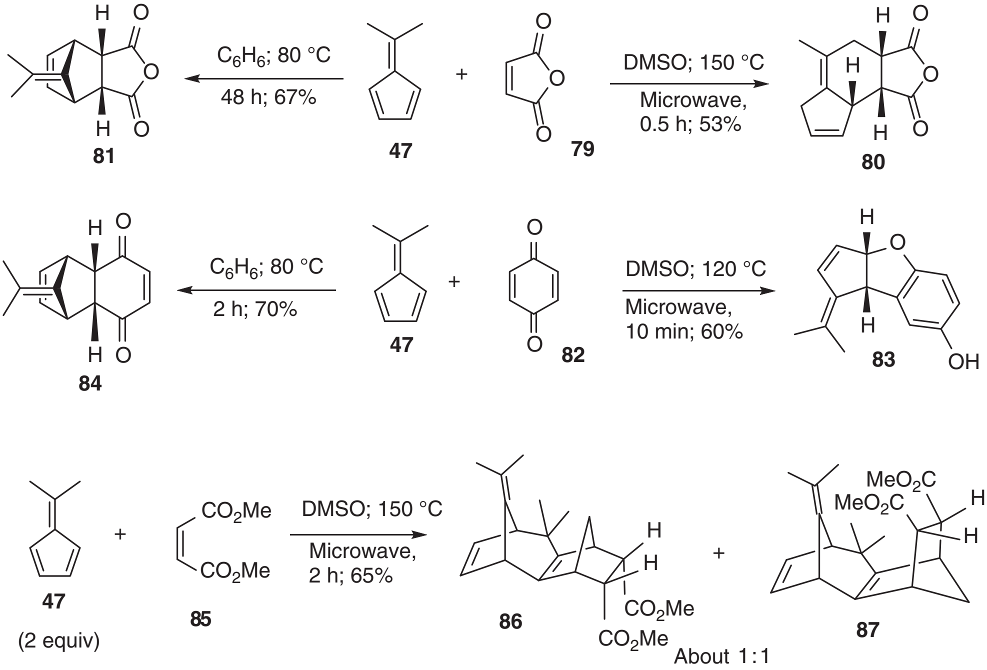
Scheme 7.19

steric buttressing effect of the naphthyl group was subsequently found to be the significant factor in promoting the reaction [22].



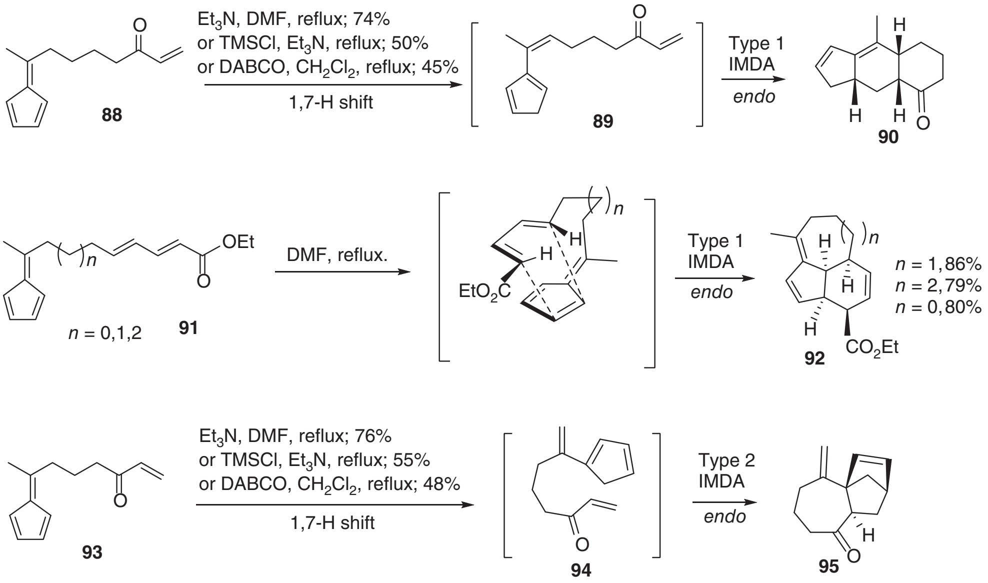
Scheme 7.20

Hong and coworkers [23] have discovered a novel microwave effect on cycloadditions of pentafulvenes (Scheme 7.21). Reaction of 6,6-dimethylfulvene **47** with maleic anhydride **79** in DMSO under microwave condition for 30 min gave a unique hydrindane [4+2]cycloadduct **80**, where maleic anhydride **79** adds across the C-1 methyl and C-6 atom of the fulvene **47**, arising from a 1,7-sigmatropic H shift. In contrast, reaction of maleic anhydride **79** with 6,6-dimethylfulvene **47** under conventional heating in refluxing benzene for 48 h gave the regular Diels–Alder adduct **81**, where fulvene **79** acted as the 4π-donor. The same reaction of **47** and **79** in DMSO under conventional heating at 150 °C for 30 min afforded complicated mixtures, with no observation of the expected products. The study demonstrates that microwave irradiation can effect reactions by giving rise to products that do not form under conventional thermal conditions. Moreover, reaction of 6,6-dimethylfulvene **47** and benzoquinone **82** under microwave conditions afforded the formal [2+3]adduct **83**; the result from the microwave experiments differs completely from the well-known thermal [4+2]cycloaddition of fulvenes **47** and benzoquinone **82**. In addition, reaction of 6,6-dimethylfulvene **47** with dimethyl maleate **85** in DMSO under microwave conditions afforded the [6+4]–[4+2]cycloaddition products **86** and **87**. Product **86** was further transformed to a tricyclo[5.3.0.1^{2,5}]alkane with an isobarbatene skeleton after a sequence of reactions.

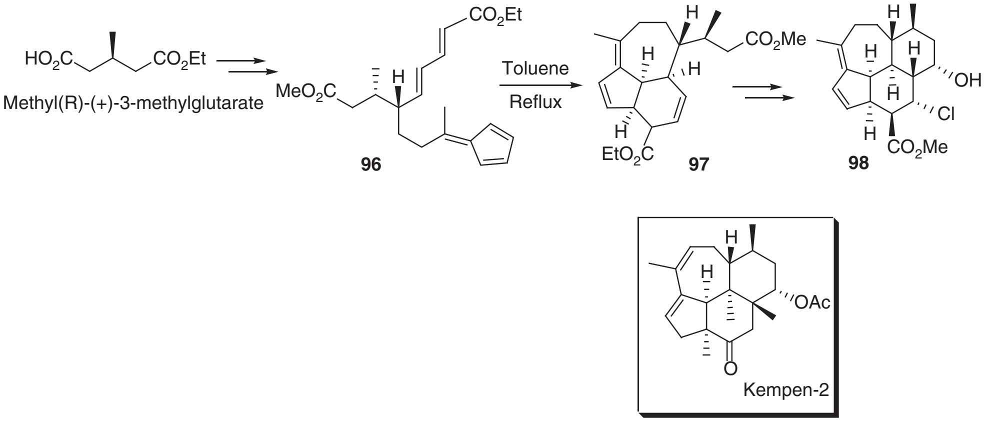


Scheme 7.21

Intramolecular Diels–Alder (IMDA) cycloadditions of pentafulvenes have been investigated comprehensively by Hong and coworkers (Scheme 7.22) [24]. The length of the tether and the nature of substituents on the fulvene core dictate the outcome of the IMDA reaction. The strategy was applied in the efficient synthesis of a variety of polycyclic ring skeletons (e.g., kigelinol, neoamphilectane, and kempene systems). In these examples, some of the pentafulvenes acted as a 4π-donor (diene) and a few examples acted as the 2π-donor (dienophile) in type 1 and type 2 IMDA reactions. In addition, the tetracyclic core of kempene **98** was prepared in nine steps via the key step of this IMDA reaction of pentafulvene **96** from commercially available methyl (*R*)-(+)-3-methylglutarate in 12% overall yield (Scheme 7.23).

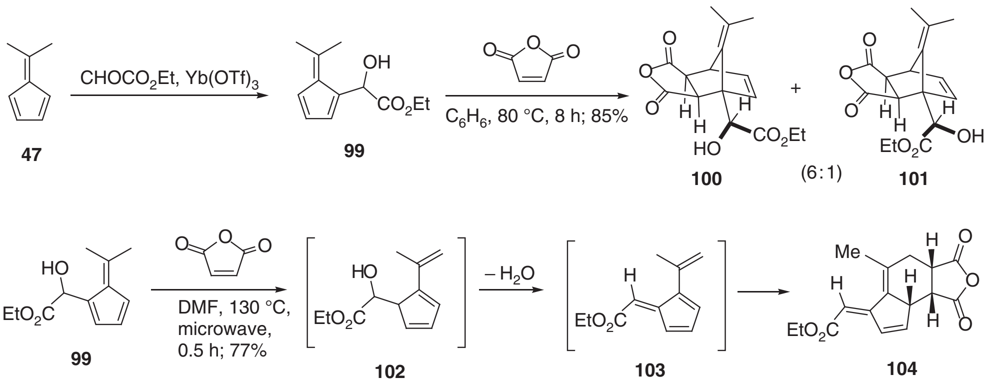


Scheme 7.22



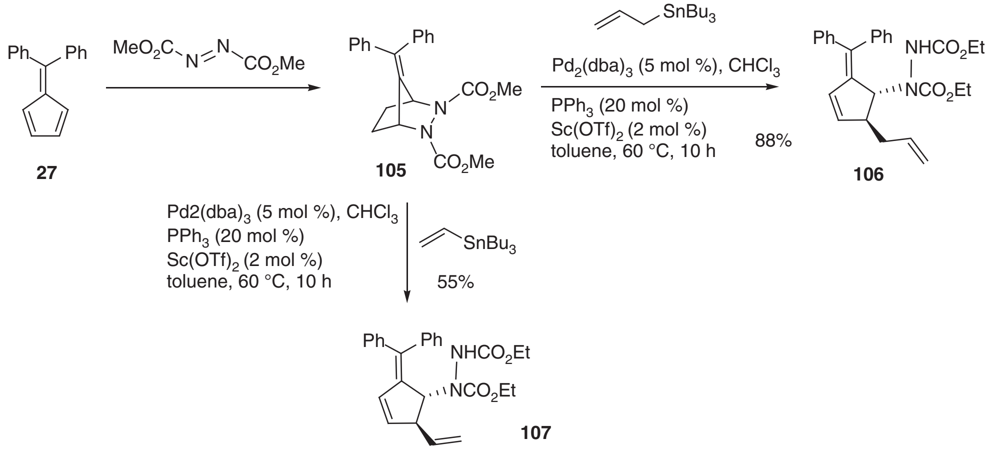
Scheme 7.23

Hong and coworkers reported a highly regioselective electrophilic substitutions of fulvene **47** with ethyl glyoxylate, catalyzed by $EtAlCl_2$ or $Yb(OTf)_3$ to give the hydroxyfulvene **99**. Reaction of **99** with maleic anhydride in refluxing benzene provided the [4+2]adducts **100** and **101**. Alternatively, reaction of **99** with maleic anhydride in DMF under microwave condition at 130 °C resulted in the 1,7-H shift of the fulvene **99** to give **102**, followed by dehydration to generate **103**; the subsequent Diels–Alder reaction of **103** with maleic anhydride then gave the highly functionalized indane **104** (Scheme 7.24) [25].



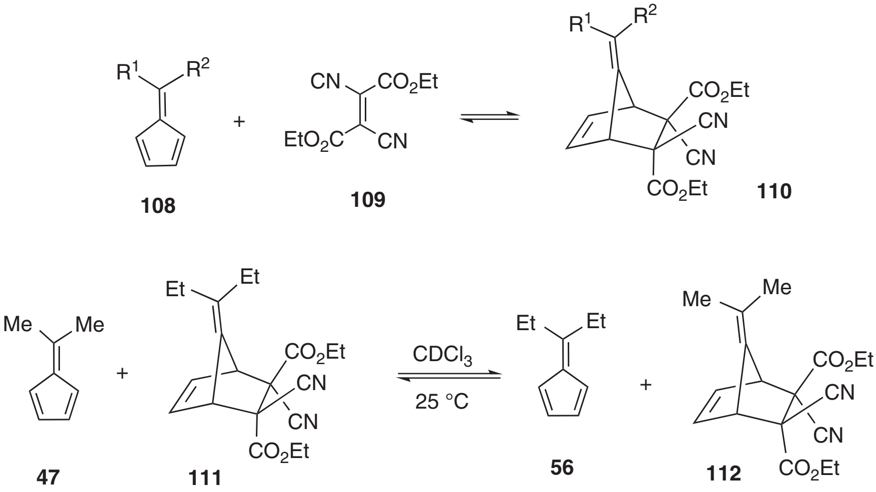
Scheme 7.24

Radhakrishnan and coworkers reported desymmetrization of bicyclic hydrazines, derived from the [4+2]cycloaddition of fulvene **27** with diethylazodicarboxylate, followed by a palladium/Lewis acid-catalyzed reaction with allyl and vinyl stannane to provide the alkylidene cyclopentenes **106** and **107**, respectively (Scheme 7.25) [26].

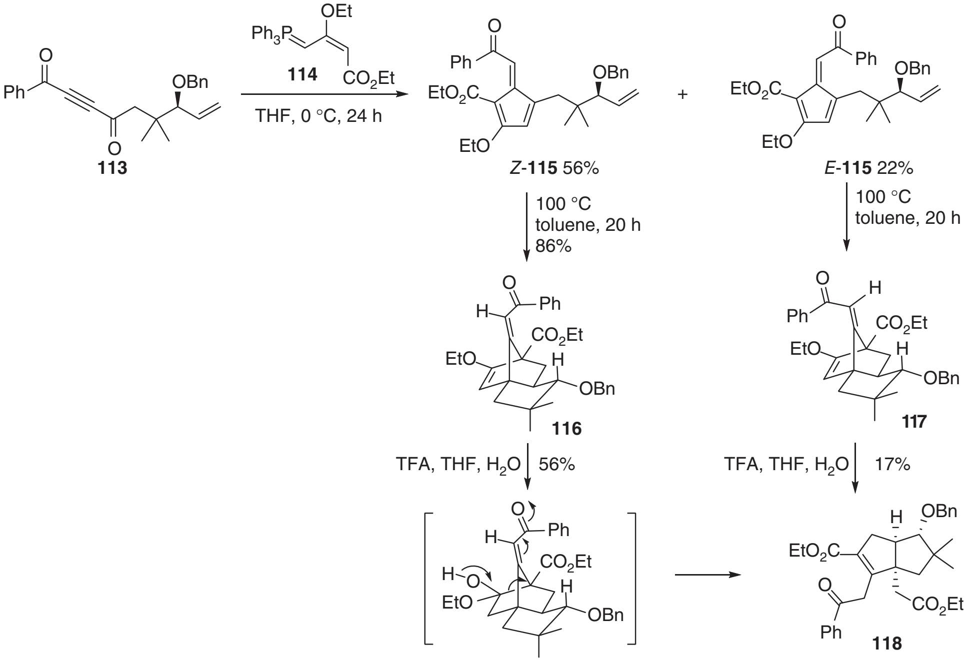


Scheme 7.25

Lehn and coworkers reported a series of reactive diene and pentafulvenes involving reversible Diels–Alder reactions at ambient temperature. The results provide a foundation for the implementation of the reversible Diels–Alder reaction in constitutional dynamic chemistry (Scheme 7.26) [27]. With variation of the functionalized substituted fulvenes **108** and cyanoolefin esters **109**, the methodology may be applied for the preparation of dynamic combinatorial libraries and provides an entry to reversible dynamic polymers and the discovery of biologically active substances.



Scheme 7.26 Fulvene exchange Diels–Alder reaction.

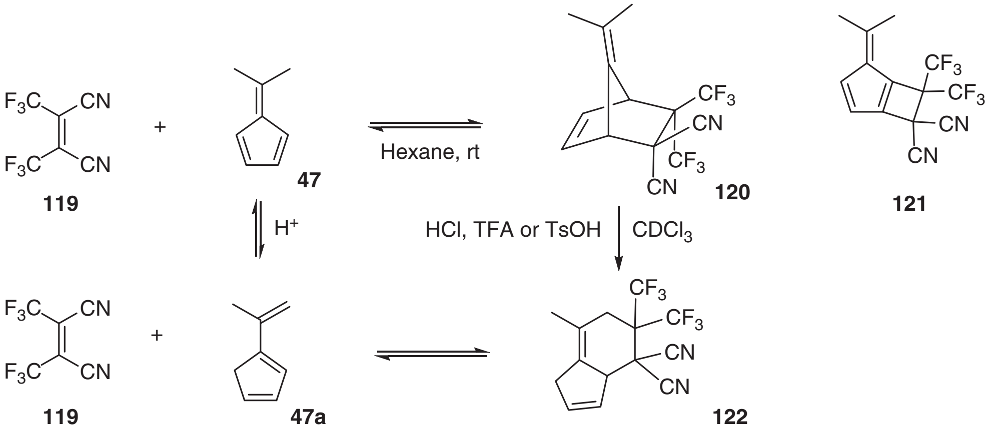


Scheme 7.27

Hatanaka and coworkers [28] developed an intramolecular cycloaddition route of 4-alkenylfulvene **115** to give the bicyclo[3.3.0]octene derivative **118** (Scheme 7.27). Treatment of the ynone **113** with 2-ethoxyallylidenetriphenylphosphorane **114** in THF afforded a mixture of *Z*-fulvene and *E*-fulvene isomers **115**. The fulvenes are formed via initial conjugate addition of the phosphorane to the

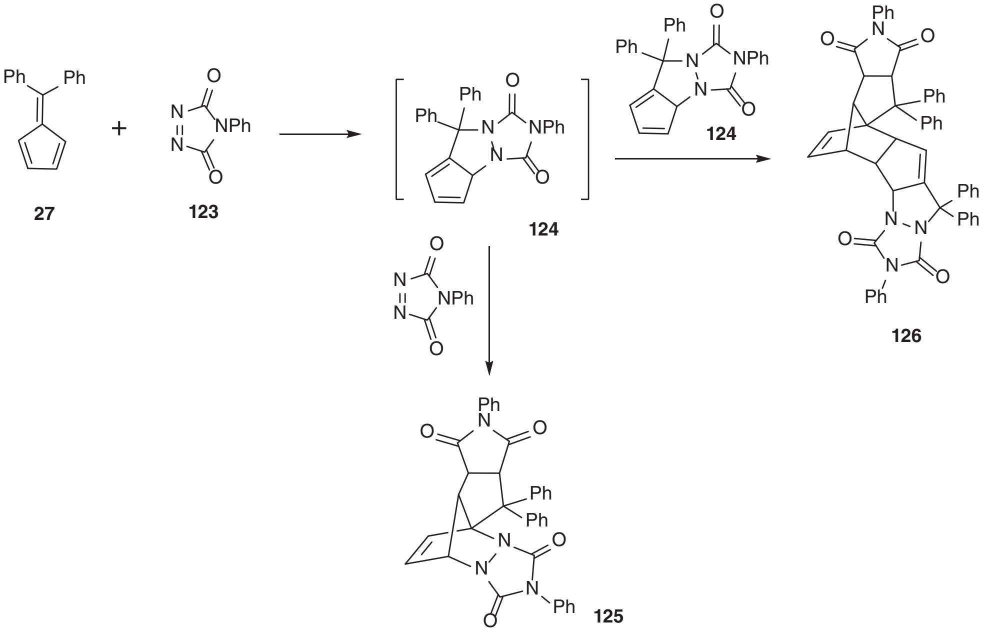
1,4-ynedinone followed by intramolecular Wittig reaction with the 4-keto group. Heating the solution of *Z*-fulvene **115** in toluene at 100 °C for 20 h afforded the [4+2]adduct in 86% yield with a 96 : 4 diastereomeric ratio of isomers. Treatment of the Z-[4+2]adduct **116** with TFA gave the bicyclo[3.3.0]octane **118**. On the other hand, *E*-fulvene **115** was treated under the same reaction conditions; however, much lower yields of the [4+2]adduct **117** were obtained along with other reaction products.

Howard and coworkers reported a cycloaddition reaction of 6,6-dimethylfulvene **47** with 2,2-bis(trifluoromethyl)-1,1-dicyanoethylene **119** and noted a subsequent retro-Diels–Alder reaction and rearrangement (Scheme 7.28) [29]. The 2,2-bis(trifluoromethyl)-1,1-dicyanoethylene (BTF) **119** reacted with 6,6-dimethylfulvene **47** to give the [4+2]cycloaddition product **120**. The cycloadduct exists in equilibrium with the starting materials in certain solvents. On standing in polar solvent such as DMSO and CH_3CN or on contact with silica gel or alumina, the [4+2]adduct **120** existed in a stable equilibrium with its precursors **119** and **47** and then was converted to the formal [2+2]adduct **121**. Later, the authors found that the faster and highest yielding method for converting **120** to **121** is passing the adduct **120** through a silica gel or alumina column. Compound **121** is stable and does not revert to **120** upon heating. The mechanism may involve a radical or a zwitterionic intermediate. On the other hand, treatment of **120** with HCl, trifluoroacetic acid, or *p*-toluenesulfonic resulted in conversion of **120** to the alternative [4+2]adduct **122**. The mechanism could involve an acid-catalyzed isomerization of the cross-conjugated **47**, arising from the retro Diels–Alder reaction of **120**, to give the fully conjugated 1-isopropenyl-1,3-cyclopentadiene **47a**, followed by the [4+2]cycloaddition with BTF to furnish the indene **122**.



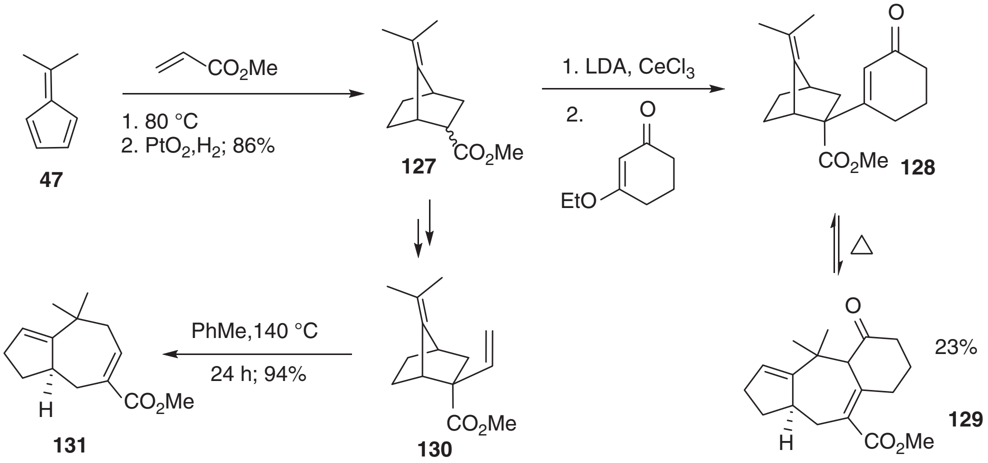
Scheme 7.28

Suresh and coworkers [30] noted an interplay of dual reactivity ([4+2] cycloaddition and formal [3+2]cycloaddition) in the reaction of pentafulvenes **27** with *N*-substituted 1,2,4-triazoline-3,5-dione **123** to give five- and seven-membered azapolycycles (Scheme 7.29). The pentacyclic compound was formed from the [4+2]cycloaddition of the cyclopentadiene unit in the initial [3+2]adduct **125**, which was produced from pentafulvene **27** and 1,2,4-triazoline-3,5-dione **123**, and the N=N double bond of another triazoline molecule. The heptacyclic product **126** was formed by the [4+2]cycloaddition between the two molecules of the initially generated [3+2]adduct at their cyclopentadiene unit.

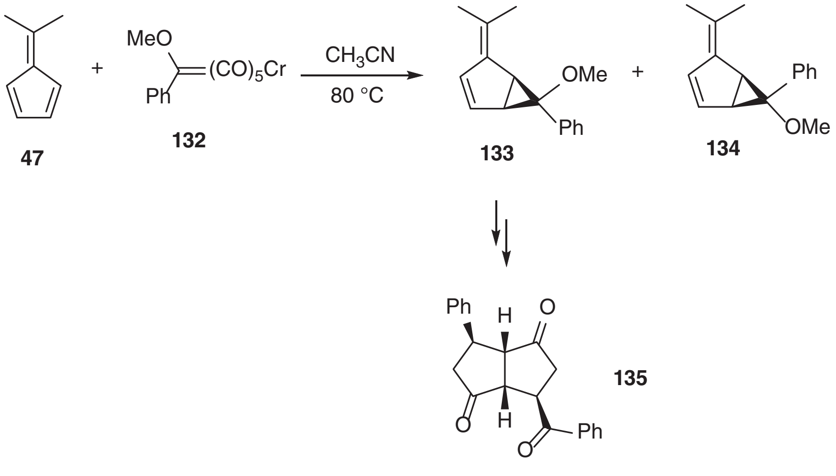


Scheme 7.29

Birman and coworkers [31] reported a Cope rearrangement of 2-*exo*-vinyl-7-alkylidenenorbornane **130**, prepared from the Diels–Alder reaction of pentafulvene **47** with methyl acrylate and subsequent alkylation, to give hexahydroazulenes derivative **131** (Scheme 7.30). Later, the group applied the methodology to the Stork–Danheiser-like variant for the synthesis of the desired Cope rearrangement precursors. The aldol reaction between the lithium enolate of (3-ethoxy)-2-cyclohexenone and **127** was achieved in the presence of anhydrous $CeCl_3$ in THF at −78 °C and furnished the desired precursor **128** in 84% yield. Heating the diene **128** at elevate temperature resulted in the formation of an equilibrium Cope adduct **129**.



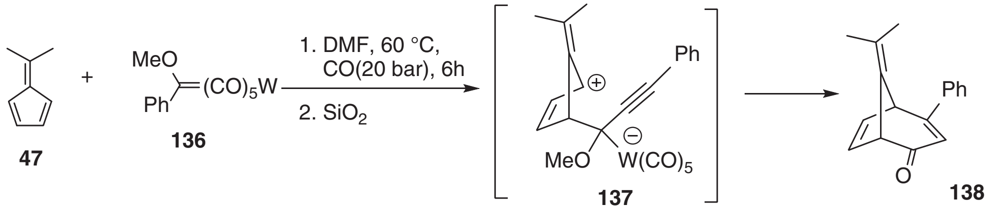
Scheme 7.30



Scheme 7.31

7.2.6
[4+3]Cycloadditions

Barluenga and coworkers [32] reported on [2+1]- and [4+3]cyclization reactions of alkyl-, aryl-, and acetoxyfulvenes with Fischer carbene complexes (Scheme 7.31). Unlike the previous cyclopropanation reactions of dienes with Fischer carbene complexes, the cyclopropanation reactions of fulvenes therein displayed complete diastereoselectivity here. The adduct **133** obtained from 6,6-dimethylfulvene **47** and chromium alkoxycarbenes **132** was transformed to the functionalized diquinane **135** and demonstrated the application in the synthesis of a masked cyclopentadienone. On the other hand, the cyclopropanation reaction was inhibited in the presence of CO, and the [4+3]cyclization of alkynylcarbene was dominating, especially in the reactions with $W(CO)_6$ (Scheme 7.32). The formation of [4+3]adducts could be via a two-step process: initial 1,2-addition of fulvene to the carbene complex, generating the zwitterionic intermediate **137**, followed by regioselective cyclization with the promotion of a 1,2-[$W(CO)_5$] shift.



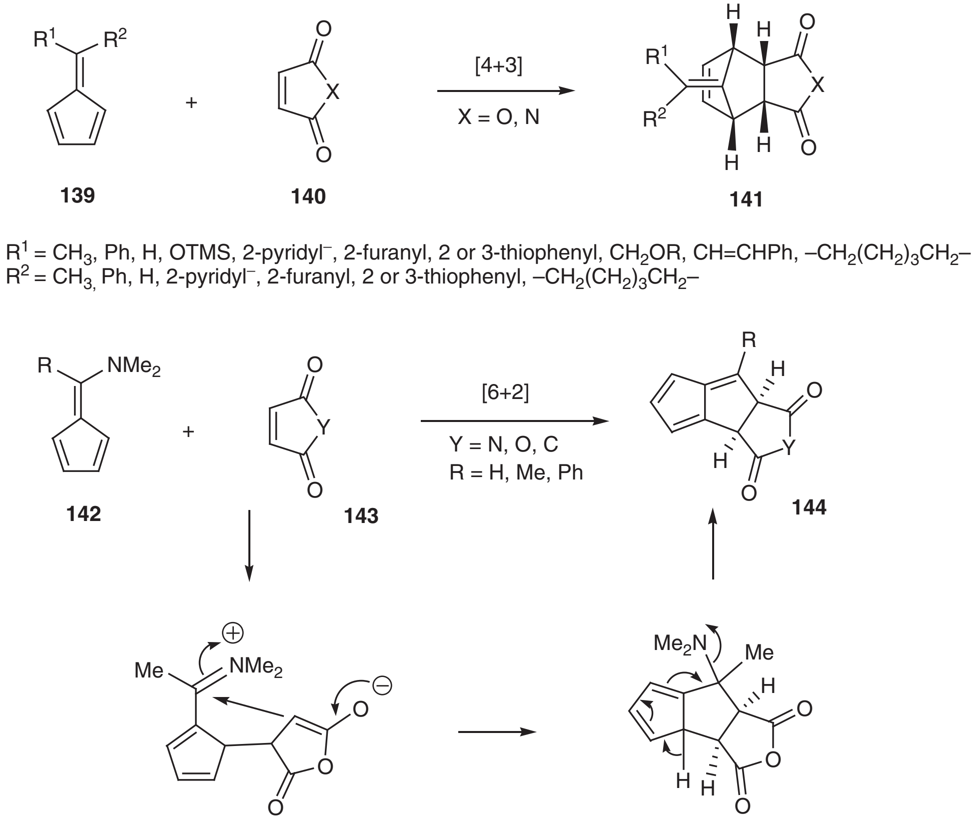
Scheme 7.32

7.2.7
[6+2]Cycloadditions

In contrast to the Diels–Alder reaction of pentafulvenes **139** and various alkenes, for example, **140**, the electron-enriched 6-aminofulvenes **142** was found by Hong and coworkers to react with maleic anhydride (or maleimide) **143** to provide [6+2]cycloaddition adducts **144** (Scheme 7.33) [33]. The methodology constitutes an efficient route to pentaleno[1,2-*c*]furans with anislactone and merrilactone skeletons, pentaleno[1,2-*c*]pyrroles, and cyclopenta[*a*]-pentalenes with a hirsutane framework.

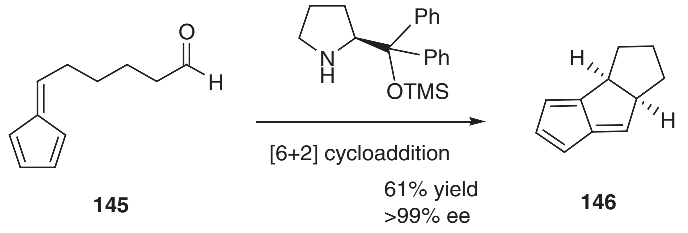
Recently, Hayashi and coworkers [34] reported an organocatalytic enantioselective intramolecular [6+2]cycloaddition reaction of pentafulvene **145** for the formation of tricyclopentanoids **146** (Scheme 7.34). Reaction of the pentafulvene bearing a δ-formylalkyl group at the exocyclic 6-position gave the linear *cis*-fused triquinane derivatives with excellent enantioselectivity. The mechanism involved initial formation of an enamine from the formyl group in the substrates, followed by a [6+2]cycloaddition of the fulvene moiety and the enamine part to provide the tricyclic product **146**. A detailed mechanistic study and computational investigations were also presented.

Erden and coworkers [35] reported a [6+2]cycloadditions of fulvenes **147** with *in situ*-generated acetone pyrrolidine enamine to give 1,2-dihydropentalenes **148**



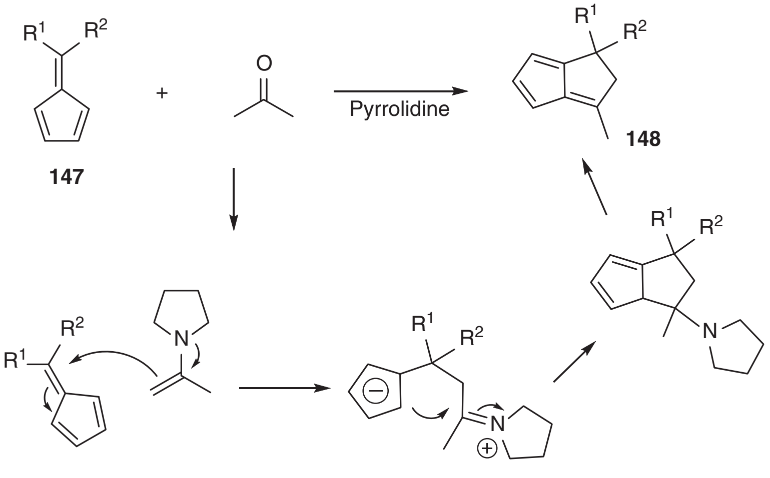
R^1 = CH_3, Ph, H, OTMS, 2-pyridyl$^-$, 2-furanyl, 2 or 3-thiophenyl, CH_2OR, CH=CHPh, $-CH_2(CH_2)_3CH_2-$
R^2 = CH_3, Ph, H, 2-pyridyl$^-$, 2-furanyl, 2 or 3-thiophenyl, $-CH_2(CH_2)_3CH_2-$

Scheme 7.33



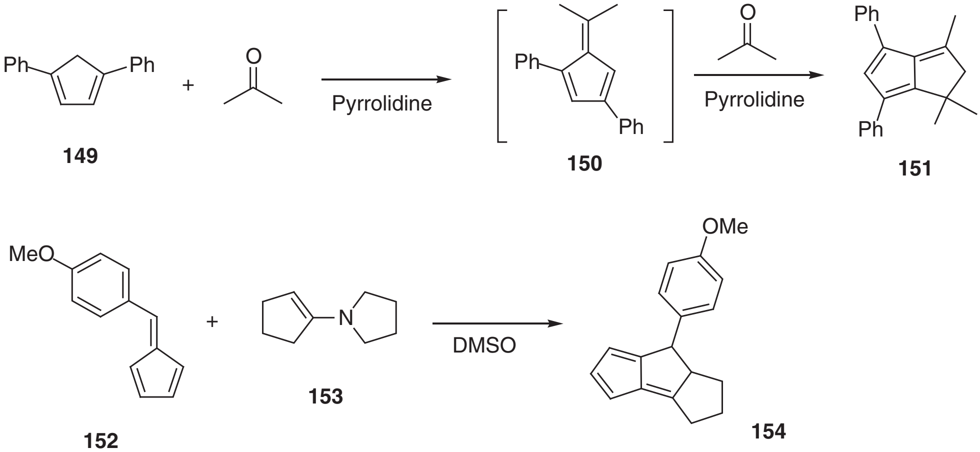
Scheme 7.34

(Scheme 7.35). A plausible mechanism proposed for the transformation involves nucleophilic attack of the 1-isopropenylpyrrolidine, formed *in situ* from acetone and pyrrolidine, at C-6 of the fulvene to afford a zwitterionic intermediate. This then undergoes cyclization and elimination steps to regenerate the catalysts and deliver the 1,2-dihydropentalenes. Interestingly, reaction of diphenylcyclopentadiene **149** with acetone in the presence of pyrrolidine underwent a tandem reaction with fulvene **150**, a sequence of condensation and [6+2]cycloaddition, to give



R^1 = Me, Et, *i*-Pr, Ph, *p*-tolyl, anisyl, ClPh
R^2 = H, Me, Et

Scheme 7.35

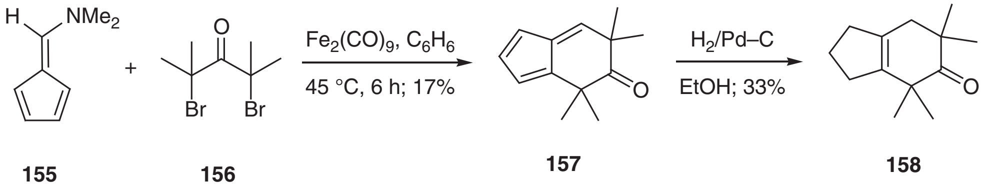


Scheme 7.36

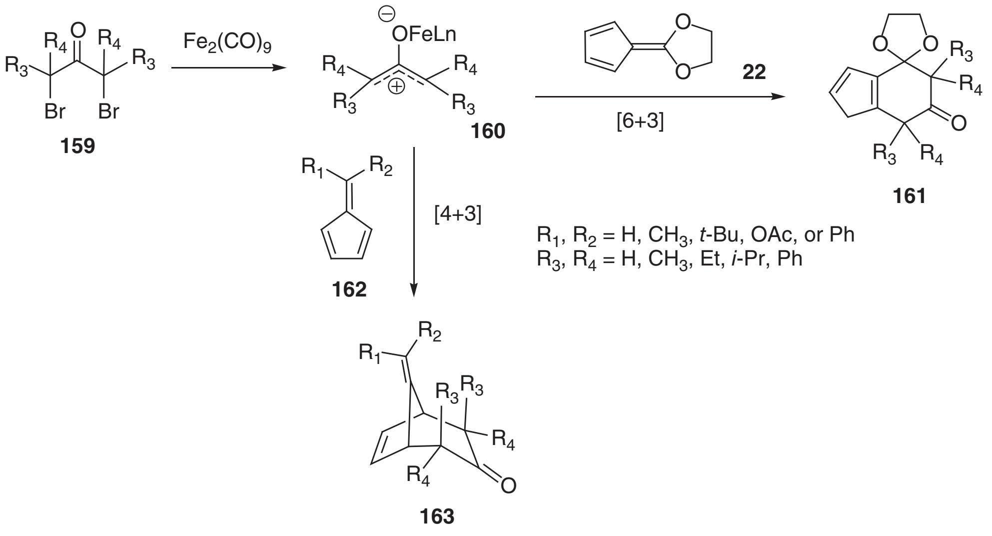
the dihydropentalene product **151** (Scheme 7.36). Extension of this work to other tricyclic 1,2-dihydropentalene **154** has also been achieved.

7.2.8
[6+3]Cycloadditions

The first [6+3]cycloaddition of pentafulvene was reported by Kanematsu *et al.* [36] by the reaction of 2-oxyallyl action and 6-(dimethylamino)fulvene **155**, although it proceeded in relatively low yield (17%) (Scheme 7.37). Usually, reactions of 2-oxyllyl actions with 6-mono and 6,6-dialkyl pentafulvenes exclusively afforded [4+3]adducts in good yield. It was suspected that formation of the [6+3]adducts involved a stepwise mechanism: initial addition of the electrophilic cation to C-1 of the aminofulvene followed by cyclization and elimination. It can be envisioned that the yield in this type of [6+3]pathway could be enhanced by further increasing the electron density on the fulvene. As a result, Hong *et al.* reported a [6+3]cycloaddition of fuleveneketene acetal **22**, 2-cyclopentadienyliden-1,3-dioxolane, with 2-oxyallyl-Fe(II) cations **160** to give the [6+3]adducts **161** in good yields (Scheme 7.38) [37]. The methodology provides rapid access to highly substituted indane ring systems.



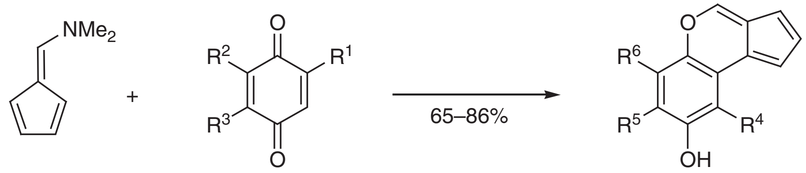
Scheme 7.37



R_1, R_2 = H, CH_3, *t*-Bu, OAc, or Ph
R_3, R_4 = H, CH_3, Et, *i*-Pr, Ph

Scheme 7.38

In contrast to the regular [4+2]cycloaddition of pentafulvenes and benzoquinone, Hong and coworkers [38] observed a hetero [6+3]annulations of 6-dimethylaminofulvene **164** and benzoquinones **165** (Scheme 7.39). The methodology constitutes an efficient route to the 3-oxabicyclo[4.3.0]nonanes and cyclopenta[*c*]chromenes **166**, including 11-oxasteroids. The striking difference in the chemoselectivity of aminopentafulvene with regular alkyl pentafulvene may be attributed to an increase in the electron density of 6-aminopentafulvene system. The reaction was proposed to occur by a stepwise mechanism.



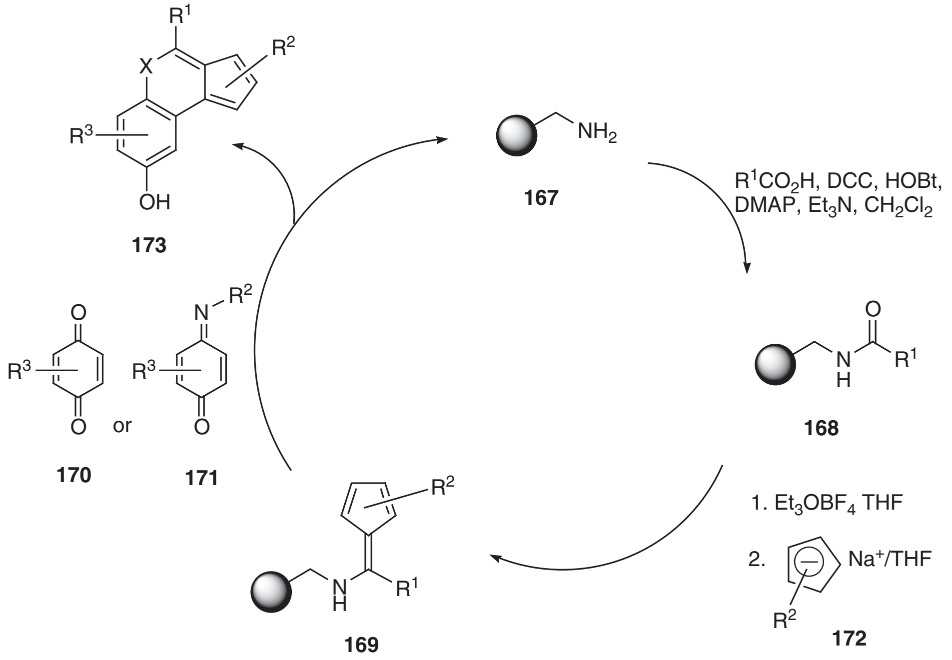
164 **165** **166**

R^1 = H, Me, Cl, Br
R^2 = H, Me, Cl, –CH=CHCH=CH– , –CH=CHC(OH)=CH–
R^3 = H, Me, Cl, Br, –CH=CHCH=CH– , –CH=CHC(OH)=CH–
R^4 = H, Me, Cl, Br
R^5 = H, Me, Cl, –CH=CHCH=CH– , –CH=CHC(OH)=CH–
R^6 = H, Me, Cl, Br, –CH=CHCH=CH– , –CH=CHC(OH)=CH–

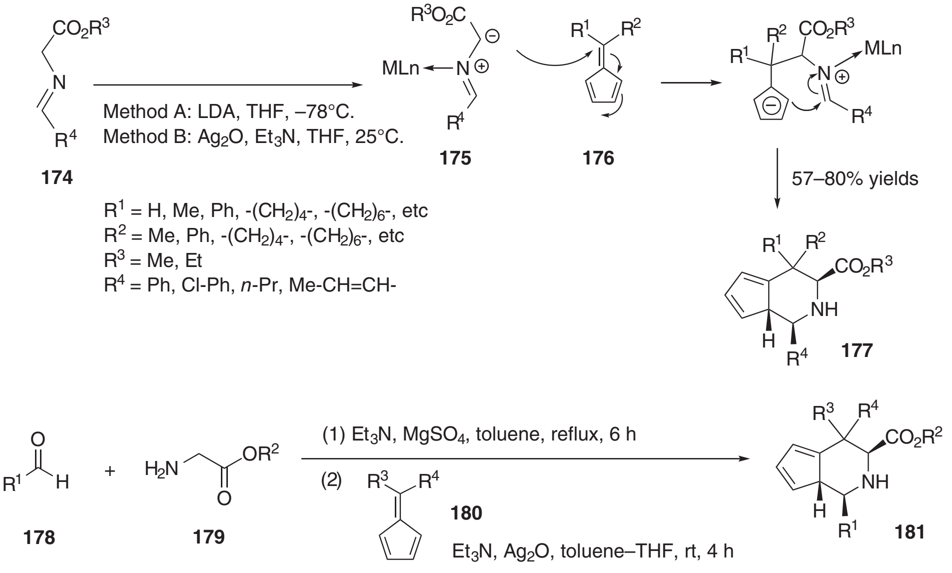
Scheme 7.39

Later, Hong and coworkers [39] reported the traceless solid-phase synthesis of cyclopenta[*c*]quinolines and cyclopenta[*c*]chromenes **173** by hetero [6+3]cycloadditions of polystyrene amino resin linked fulvene **169** with benzoquinones **170** and 4-iminocyclohexa-2,5-dienone **171** (Scheme 7.40). The traceless linker strategy provides a facile approach to the 11-heterosteroid framework, and a small library consisting of 110 examples, was synthesized by reacting benzoquinones or iodoanilines with the amino fulvene resin [40]. Some compounds prepared showed antiproliferative activity against a number of carcinogenic cell lines (e.g., $GI_{50} = 3.9 \times 10^{-7}$ M and 3.0×10^{-7} M against MCF7 and T-47D breast cancer lines, respectively). The structure of the cyclopenta[*c*]chromene skeleton was confirmed by X-ray analysis of the appropriate derivatives.

Hong and coworkers [41] also reported a hetero [6+3]cycloaddition of fulvenes **176** with *N*-alkylidene glycine esters **174**; the methodology provides a facile synthesis of the [2]-pyrindine derivatives **177** with the delavayine and incarvillateine framework (Scheme 7.41).The two-step reaction can be carried out in one pot by heating a solution of aldehyde **178**, glycine ethyl ester hydrochloride **179**, Et_3N (5 equiv.), and $MgSO_4$ in toluene to reflux for 6 h, followed by addition of a THF solution of various fulvenes, Et_3N, and Ag_2O at ambient temperature and stirring for 4 h. This process yields adduct without the need for isolation of the *N*-alkylidene glycine ester **174**, and a 30-membered [2]pyridine library **181**, selected from the reaction of three fulvenes, two glycine esters, and five aldehydes, was prepared on the basis of the above methodology. A mechanism for the formation of [2]pyrindine was proposed. Initial addition of the metalloazomethine ylide to the C-6 position of fulvene generates the zwitterionic intermediate, followed by cyclization through a chairlike transition state with the alkyl substituents at the equatorial positions to give the [2]pyrindine.



Scheme 7.40

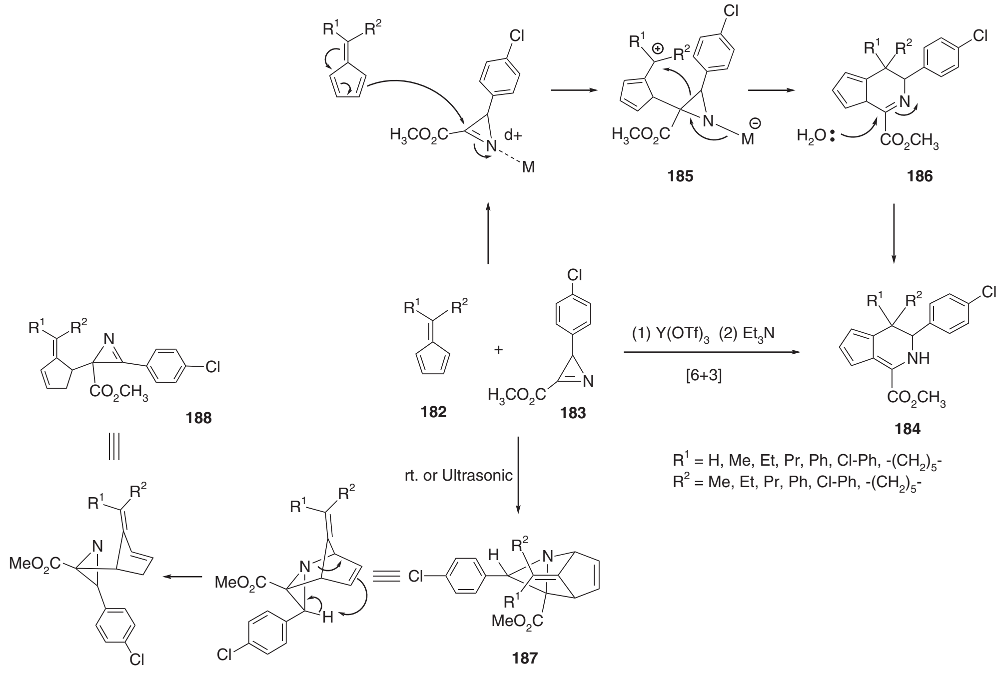


R^1 = H, Me, Ph, -$(CH_2)_4$-, -$(CH_2)_6$-, etc
R^2 = Me, Ph, -$(CH_2)_4$-, -$(CH_2)_6$-, etc
R^3 = Me, Et
R^4 = Ph, Cl-Ph, *n*-Pr, Me-CH=CH-

R^1 = C_6H_6, *p*-ClC_6H_6, *p*-OMeC_6H, C_3H_7, *c*-C_6H_{11};
R^2 = Me, Et; R^3 = Me, -$(CH_2)_5$-, Ph; R^4= -$(CH_2)_5$-, H

Scheme 7.41

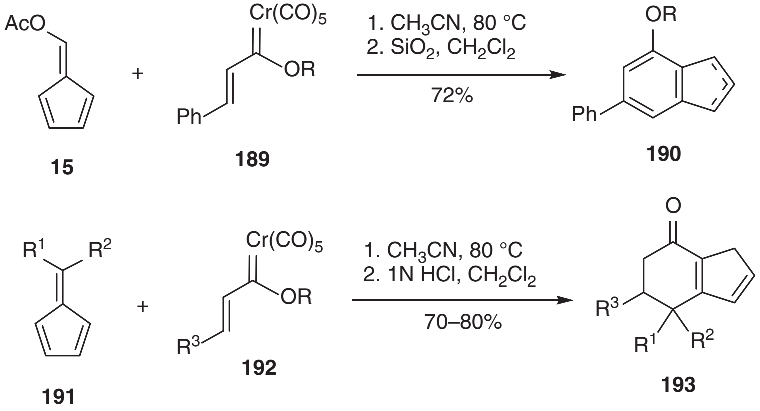
Hong and coworkers [42] further revealed a formal [6+3]cycloaddition of fulvenes **182** with 2*H*-azirine **183**, catalyzed by Y(OTf)$_3$, and the methodology constitutes a facile approach to the [2]pyrindines **184** (Scheme 7.42). The initially formed hydroxy[2]pyrindine adduct **186** proved unstable and gradually converted to fulvenelike [2]pyrindines **184** after a few days in the refrigerator. This isomerization was accelerated in the presence of Et_3N in CH_2Cl_2 at ambient temperature. The formation of the [2]pyrindines **184** may be rationalized by the stepwise mechanism shown in Scheme 7.42. Initial addition of the fulvene to the activated 2*H*-azirine generates the zwitterionic intermediate **185** followed by cyclization to give [2]pyrindine **186**. On the other hand, reaction of fulvene **182** and azirine **183** under ultrasonic conditions provided the alkylation product **188**. Mechanistically, it is possible that the initial Diels–Alder adduct of fulvene and azirine rearranges to give the alkylation product as depicted in the following scheme.



Scheme 7.42

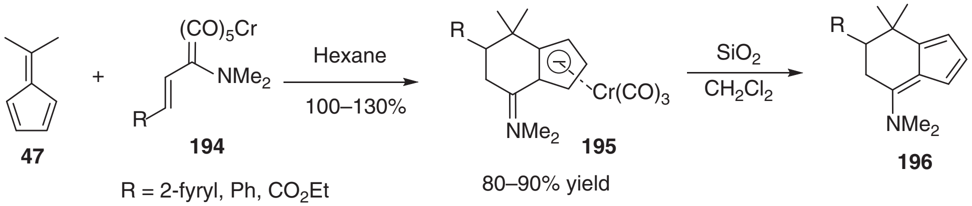
In 2001, Barluenga and coworkers [43] developed the [6+3]cycloaddition of chromium alkenyl carbene complexes **189** with pentafulvenes **15**, involving nucleophilic 1,2-addition and the subsequent cyclization prompted by [1,2]-M(CO)$_5$ shift, to afford a number of indenes **190** and indanones **193** (Scheme 7.43).

Later, in 2005, the group reported the [6+3]cycloaddition of Fischer aminocarbene complexes **194** to pentafulvenes **47** by the 1,2-addition/[1,2]-M(CO)$_5$ shift mechanistic model affording aminoindene derivatives **196** (Scheme 7.44) [44].



R^1 = Me, *i*-Pr, CH=CH–Ph–, $CH_2CH_2CO_2Me$
R^2 = H, Me
R^3 = 2-fyryl, Ph

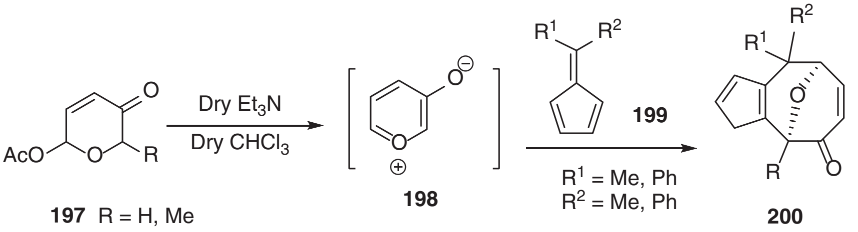
Scheme 7.43 [6+3]Cycloaddition of chromium alkenyl carbene with pentafulvene.



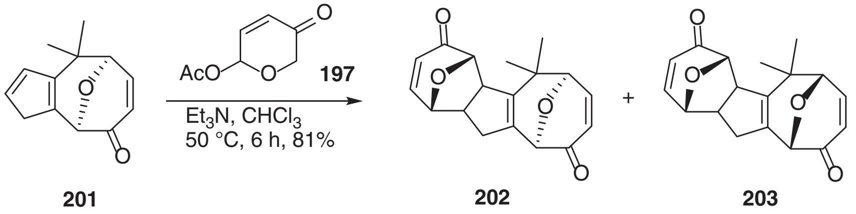
Scheme 7.44

Radhakrishnan and coworkers [45] revealed a [6+3]cycloaddition of fulvenes **199** with 3-oxidopyrylium betaine **198**, generated from the corresponding pyranulose acetate **197**, providing a methodology for the synthesis of 5-8 fused oxabridged cyclooctanoid natural products **200** (Scheme 7.45). A consecutive [6+3]- and [4+3]cycloaddition of pentafulvenes **197** with 3-oxidopyrylium betaines leading to the 7-5-8-fused oxabridged tricyclic molecules **202** and **203** was reported by the same group (Scheme 7.46) [46]. Later, the authors reported a strategy toward 11-membered carbocycles through a two-step reaction sequence of the [6+3]adduct. The transformation was performed by the selective hydrogenation of the two disubstituted double bonds in the [6+3]adduct **204**, followed by oxidative cleavage of the tetrasubstituted double bond of **205** by $RuCl_3-NaIO_4$ to give the 11-membered carbocycle **206** (Scheme 7.47) [47].

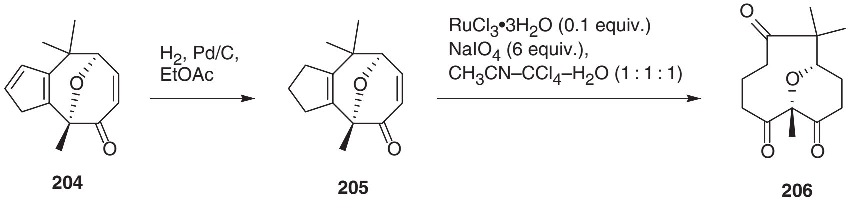
More recently, the group utilized the [6+3]adduct **201** in the Diels–Alder reaction of *N*-phenyl maleimide **207** to give the fused ring cyclooctanoids **208** and **209** (Scheme 7.48) [48]. In addition, the [6+3]adduct **201** underwent dipolar cycloaddition of the azomethine ylide generated *in situ* from *N*-methoxy methyl *N*-(trimethylsilylmethyl)benzylamine **210** in the presence of CF_3CO_2H to give a 74% yield of the 5-8-5 fused adduct **211**. Similar reactions were observed for



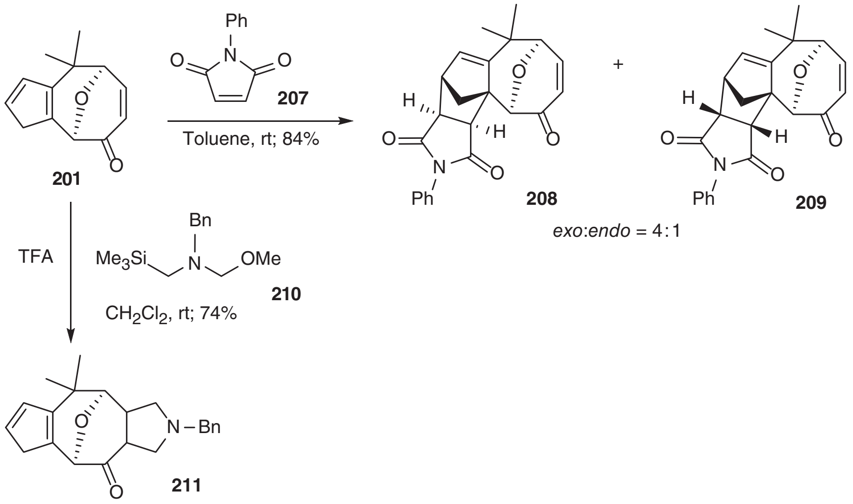
Scheme 7.45



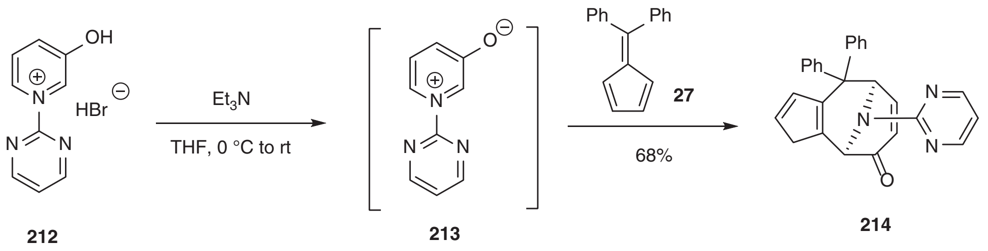
Scheme 7.46



Scheme 7.47



Scheme 7.48

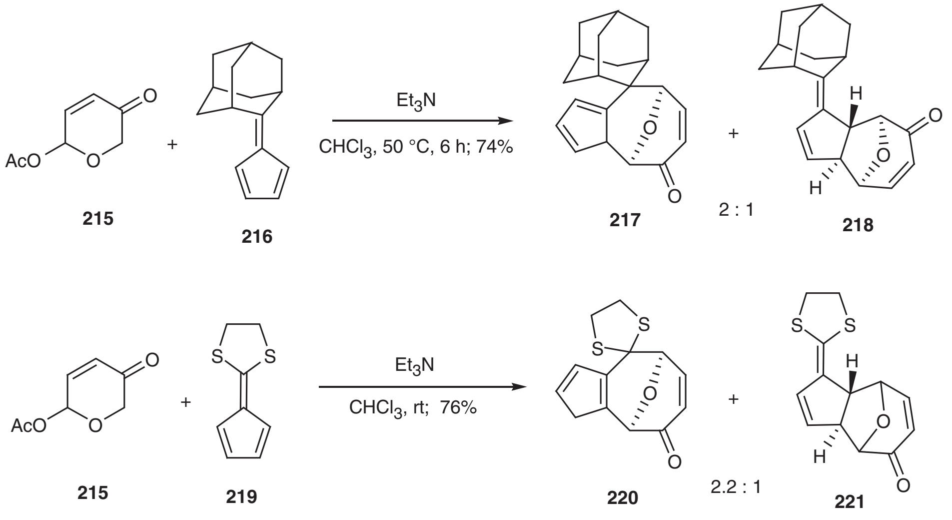


Scheme 7.49

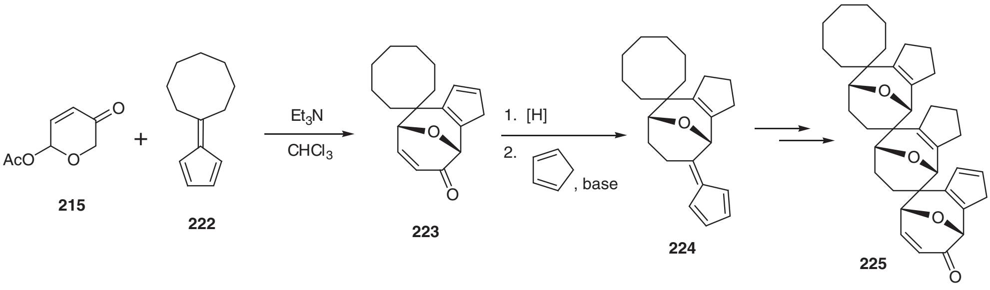
the [6+3]cycloadditions of pentafulvene **27** with 3-oxidopyridinium betaine **213**, generated either by the action of a base on the pyridinium salt **212** or thermally from pyridinium betaine dimer, to give the *N*-bridged heterocycle **214** (Scheme 7.49) [49].

Krishnan and coworkers [50] treated 6,6-adamantylidenefulvene **216** with various two-substituted 3-oxidopyrylium betaines, for example, **215**, providing a mixtures of [6+3]- and [3+2]adducts **217** and **218** in the ratio of 2 : 1 to 4 : 1 (Scheme 7.50). Similarly, reaction of 6,6-dithiodimethylenefulvene **219** with oxidopyrylium betain at room temperature gave 76% of a mixture of [6+3]- and [3+2]adducts **220** and **221**. The formation [3+2]adducts, in addition to the [6+3]adducts, which is different from the predominant formation of the [6+3]adduct in the reaction with fulveneketene acetal **22**, was traced back to a decrease in the electron density of 6,6-dithiodimethylenefulvene **219**, arising from the hyperconjugation of the d-orbital of sulfur and the fulvene π-electrons.

In addition, the group has applied this protocol to the synthesis of spirocyclic oxa-bridged cyclooctanoids **225** (Scheme 7.51) [51].

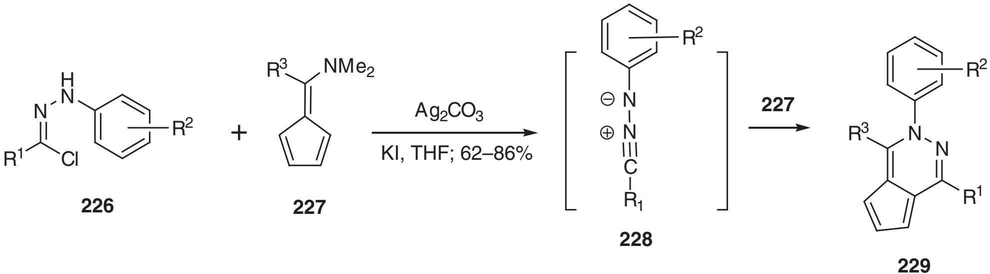


Scheme 7.50



Scheme 7.51

Cho and coworkers report a 1,3-dipolar cycloaddition [52] of aminofulvenes **227** to aliphatic or aromatic hydrazonyl chlorides **226** in the presence of silver carbonate, a method which provides a facile synthesis of the cyclopenta[*d*]pyridazines **228** (Scheme 7.52) [53]. A plausible intermediate, nitrile imine **228**, was found to react with **227** in the presence of KI and silver carbonate and yield the cyclopenta[*d*]pyridazines **229**.



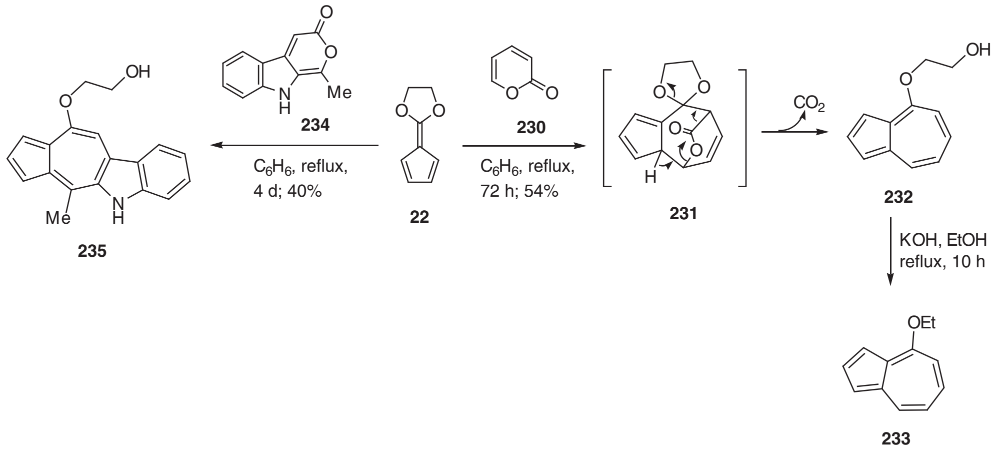
R^1 = Ph, CH$_3$, *i*-Pr, *i*-Bu, cyclohexyl, 3-OMePh,
R^2 = H, 3-OMe, 4-OMe, 4-Me, 4-F, 2-Cl, 3-Br, 2,3-diCl, 2,5-diCl, 3,4-diCl,
R^3 = Ph, CH$_3$, *i*-Pr, *i*-Bu, cyclohexyl, 3-OMePh.

Scheme 7.52

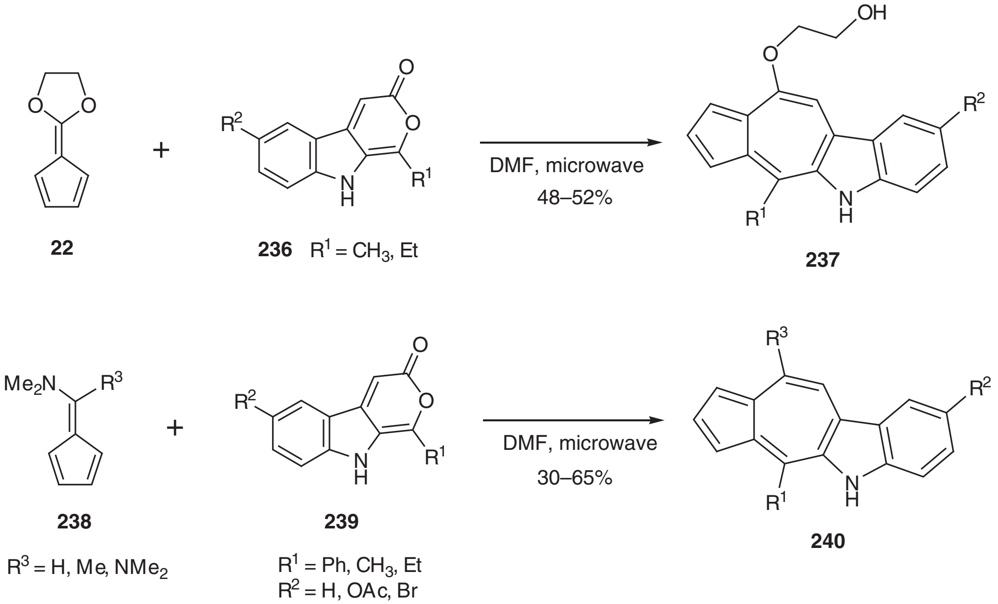
7.2.9
[6+4]Cycloadditions

A pioneering study on [6+4]reactions of diazomethane to dimethylfulvene was reported by Houk [54]. Other advances include the double [6+4]cycloaddition of tropone to dimethylfulvene [55], intramolecular [6+4]cycloadditions of fulvenes [56], selective intramolecular [6+4]cycloadditions of aminodienylfulvenes [57], and the [6+4]cycloadditions of diethylaminobutadiene to fulvenes for the synthesis of azulenes [58].

In contrast to the well-known Diels–Alder reaction of fulvene and α-pyrones, Hong and Sun reported a [6+4]cycloaddition of α-pyrones with the electron-rich fulveneketene acetals to give azulenols. In their study, a solution of fulveneketene acetal **22** and α-pyrones **230** was heated at reflux for 72 h in the dark to afford 54% yield of the purple azulenol **232** (Scheme 7.53) [59]. The azulenol arises from the addition of the α-pyrones across C-1 and C-6 of the fulvene affording the [6+4]adduct followed by cheletropic extrusion of CO_2. Alternatively, a benzene solution of **22** with **234** was heated to reflux for 4 days to give the [6+4]adduct **235**.



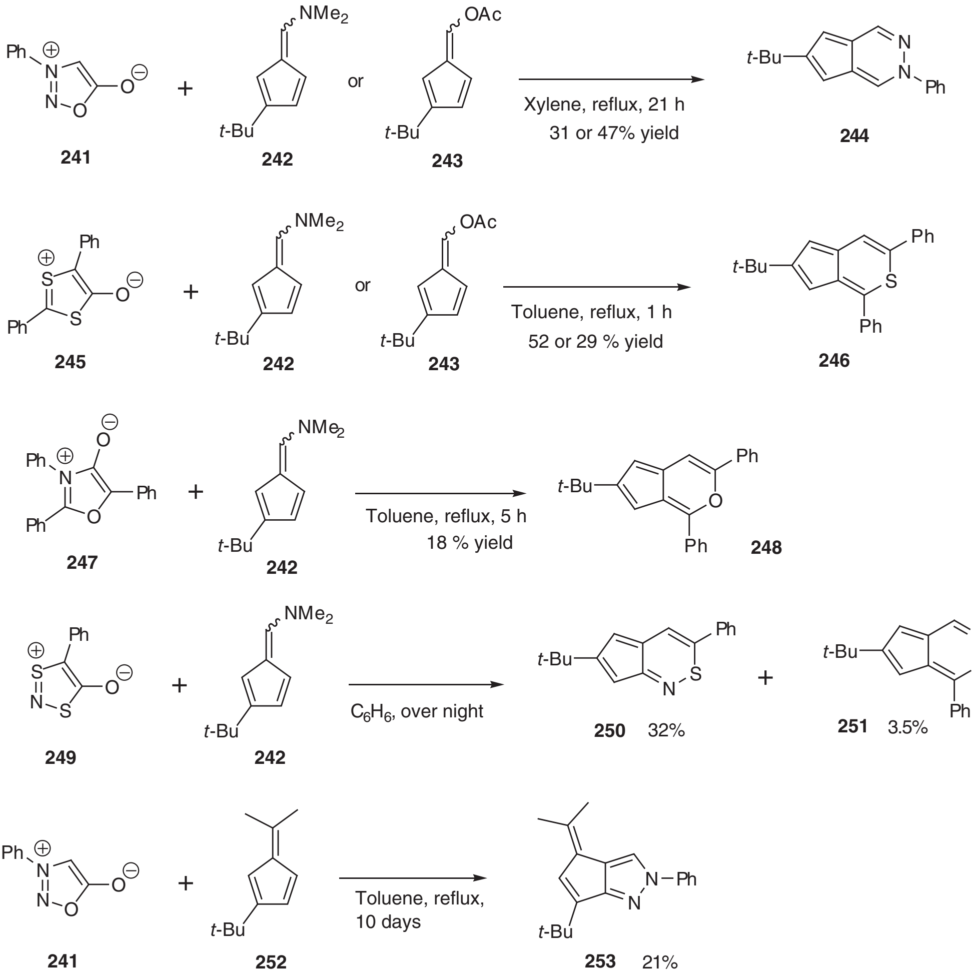
Scheme 7.53 Synthesis of azulenols via the [6+4]cycloaddition of fulveneketene acetal **22**.



Scheme 7.54 Synthesis of various azuleneindoles.

Later, a series of azuleneindoles **237** and **240** were synthesized by Hong and coworkers [60] by the microwave-assisted [6+4]cycloaddition of fulvenes **22** and **238** with various α-pyrones (**236** and **239**). Some of the azuleneindoles display potent antineoplastic activities (Scheme 7.54). For example, an azuleneindol was found to be a potent and selective growth inhibitor of the K-562 leukemia cell line with IC_{50} of 0.51 mM.

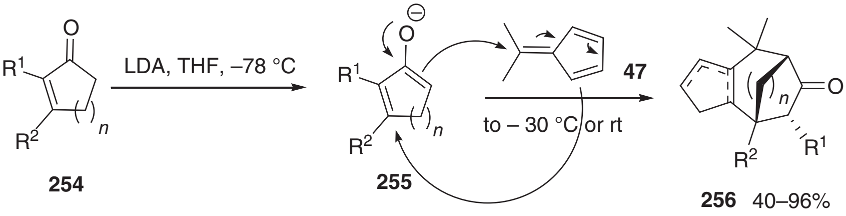
Kato and coworkers [61] reported that a sterically assisted [6+4]cycloaddition of 2-*tert*-butylfulvenes and to mesoionic compounds provides a route to pseudo-heteroazulenes (Scheme 7.55). The [6+4]adduct underwent further fragmentation, elimination or isomerization to yield a series of heterocycles isoelectronic with azulene.



Scheme 7.55

7.2.10
Miscellaneous Reactions

Hong and coworkers [62] reported a sequential "double-Michael" addition of lithium dienolates **255** to pentafulvene **47** (Scheme 7.56). The reaction provides an efficient route to the tricyclo[5.3.0.$n^{2,5}$]alkane ring systems **256**. In addition, the reaction is attractive as two bonds and three stereocenters are formed in one step with high stereoselectivity.

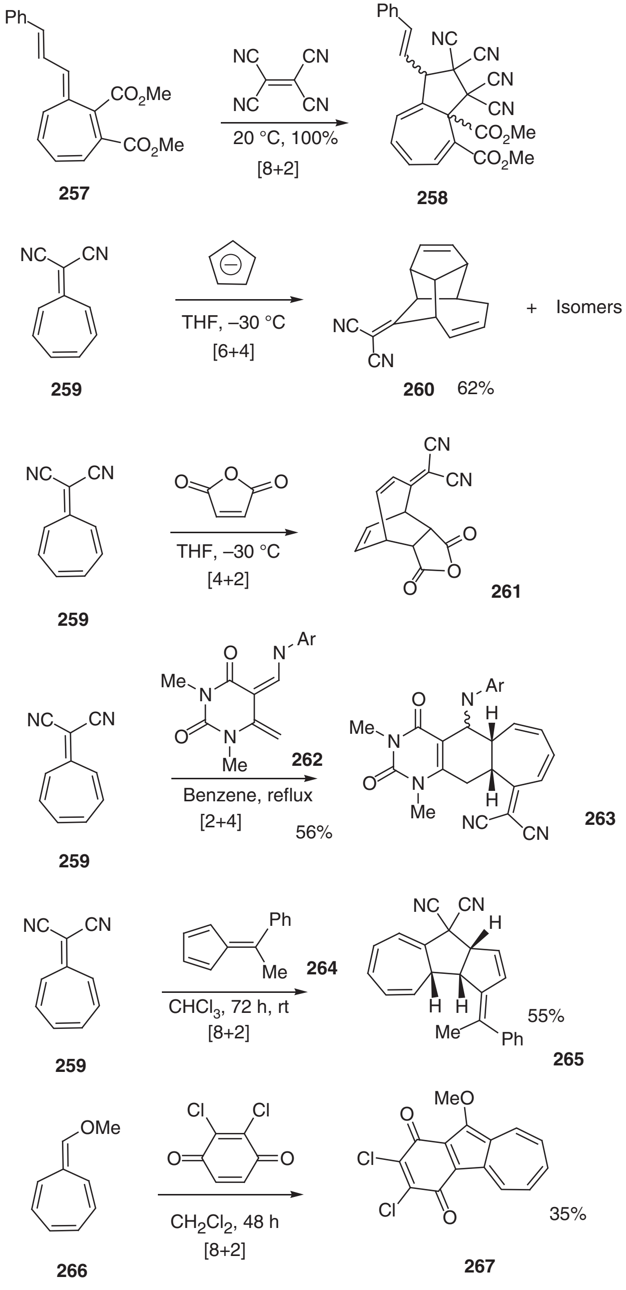


Scheme 7.56

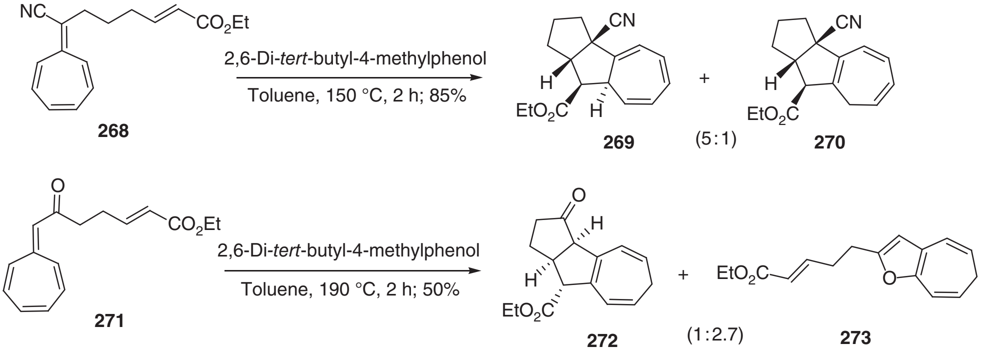
7.3
Reactions of Heptafulvenes

Heptafulvene, **3**, a cross-conjugated eight-π-electron system with a seven-membered carbocycle, has been of theoretical and synthetic interest for decades [63]. For example, a computational method for the analysis of heptafulvene has been reported by Aumüller and coworkers [64]. Heptafulvenes have shown to undergo cycloadditions by various modes, acting as a 2π-, 4π-, 6π-, or 8π-component [65]. An overview of the cycloadditions of heptafulvenes was reported by Nair and coworkers [66]. Typical reactions of heptafulvene are shown in Scheme 7.57. Houk and coworkers [67] have reported the intramolecular cycloadditions of heptafulvene **268** and **271** with enonate to give polycyclic products (Scheme 7.58). On the other hand, Neuenschwander and coworkers [68] have reported on a new general pathway to the parent hydrocarbons heptafulvene **274**, heptapentafulvalene **275**, and heptafulvalene **276** (Scheme 7.59). Several mono- and bis-exocyclically substituted heptafulvene derivatives have been studied by theoretical calculations on the B3LYP/6−311+G** level of theory [69]. Later, Nair and coworkers [2] have published a review on [8+2]cycloaddition reactions in organic synthesis, which describes several [8+2]cycloaddition reactions with heptafulvene. Therefore, the examples summarized in this section are mainly focusing on the literature published after 1997 along with some important preceding examples.

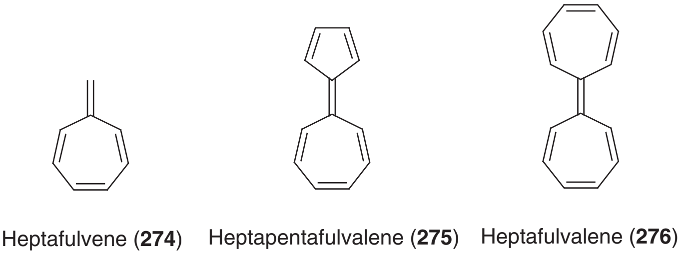
Nair and coworkers [70] reported a [8+2]cycloaddition of 8,8-dicyanoheptafulvene **259** and cycloahexadiene **277** as well as a [6+4]cycloaddition


257
258
20 °C, 100%
[8+2]
259
260 62%
+ Isomers
THF, –30 °C
[6+4]
259
261
THF, –30 °C
[4+2]
259
262
263
Benzene, reflux
[2+4]
56%
259
264
265
CHCl$_3$, 72 h, rt
[8+2]
55%
266
267
CH$_2$Cl$_2$, 48 h
[8+2]
35%

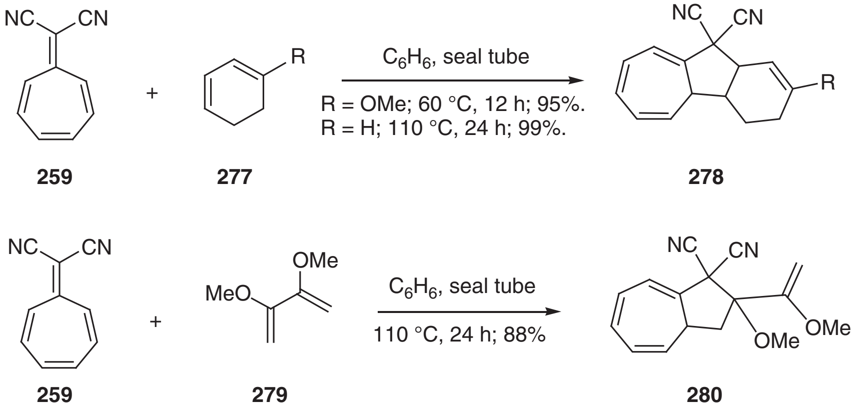
Scheme 7.57



Scheme 7.58



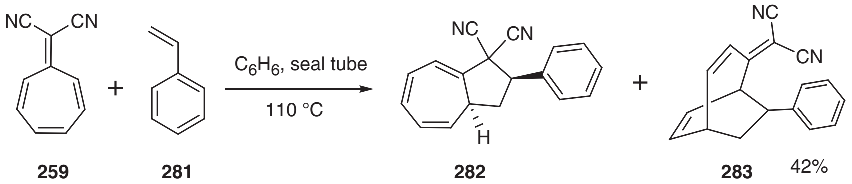
Scheme 7.59



Scheme 7.60

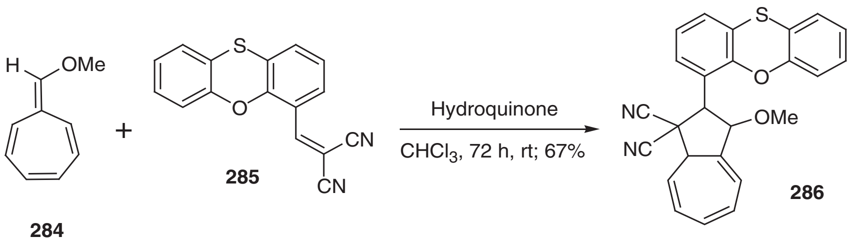
of **259** and 2,3-dimethoxybuta-1,3-diene **279** (Scheme 7.60). In their study, the formation of the [8+2] or the [6+4]adducts are exclusive, depending on the different substituents of the dienes.

Nair and coworkers [71] also described a facile cycloaddition reaction of **259** with styrenes **281**, providing the corresponding [8+2]- and [4+2]-adducts **282** and **283** in about 1 : 1 ratio (Scheme 7.61).



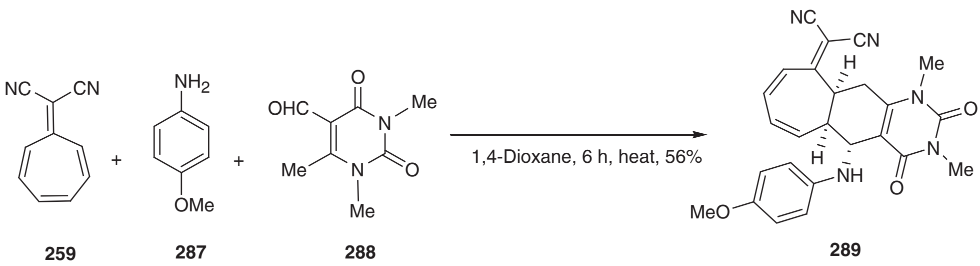
Scheme 7.61

In a study of multimode switching based on dihydroazulene/vinylheptafulvene photochromism, Spreitzer and Daub [72] reported a [8+2]cycloaddition reaction of 8-methoxyheptafulvene **284** and dicyanovinylene compound **285** in chloroform to give the tetrahydroazulene **286** (Scheme 7.62).



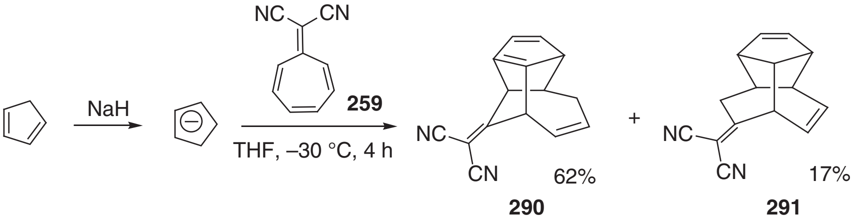
Scheme 7.62

Ikuno and coworkers [73] studied the reaction of 4-methoxybenzenamine **287** and 1,2,3,4-tetrahydro-1,3,6-trimethyl-2,4-dioxopyrimidine-5-carbaldehyde **288** with 8,8-dicyanoheptafulvene **259**, which yields tetrahydrocyclohepta[*g*]quinazoline **289** (Scheme 7.63).



Scheme 7.63

Machiguchi and coworkers [74] reported the reaction of **259** and sodium cyclopentadienide to give two tetracyclic cage molecules **290** and **291** with (dicyanomethylene)tetracyclo[7.2.1.0.0]dodecadiene structures. The products are formed by a nucleophilic addition, followed by protonation and an IMDA reaction (Scheme 7.64).



Scheme 7.64

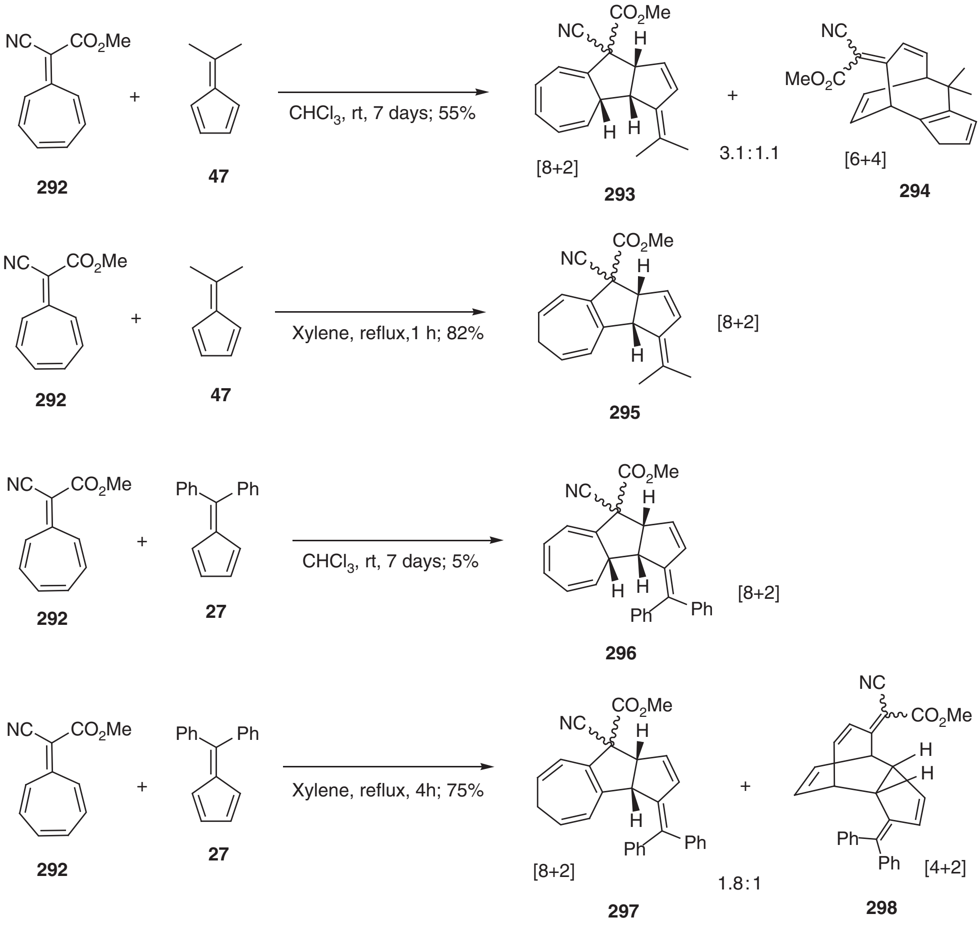
Liu and coworkers [75] reported that the reaction of 8-cyano-8-(methoxycarbonyl)heptafulvene **292** with 6,6-dimethylfulvene **47** in $CHCl_3$ at ambient temperature for 7 days affords the [8+2]adduct **293** and the [6+4]adduct **294** in a ratio of 2.1 to 1.1. The same reaction in refluxing xylene for 1 h afforded an 82% yield of the isomeric [8+2]adduct **295**, produced by a 1,5-H shift of **293**. Different periselectivity was observed for the same reaction of **292** with 6,6-diphenylfulvene **27** (Scheme 7.65).

Morita and coworkers [76] described a [8+2]cycloaddition of 8-oxoheptafulvene **299**, a heptafulvene ketene, with cycloheptatriene iron carbonyl **300** to give tricyclo[8.5.0.0^{3,9}]pentadeca-3,5,7,11,13-pentaene-2-one $Fe(CO)_3$ **301** (Scheme 7.66). Usually, ketenes undergo [2+2]cycloaddition reactions (see above), and the observation mentioned here is a special case.

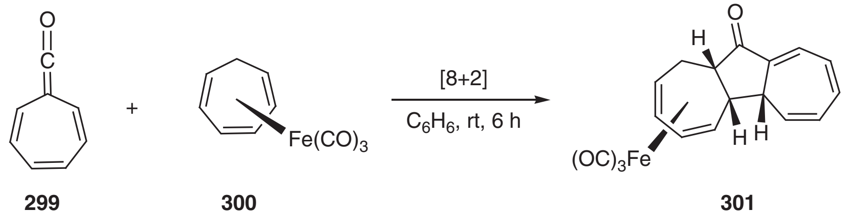
Liu and coworkers [77] studied intramolecular [8+6]- and [4+2]cycloadditions of electron-deficient 8-cyanoheptafulvenes with pentafulvenes at various temperatures (Scheme 7.67). The stereoselectivity and periselectivity of these intramolecular cycloaddition depend on the side chain and the substituents at the fulvene systems.

7.4
Reactions of Triafulvenes

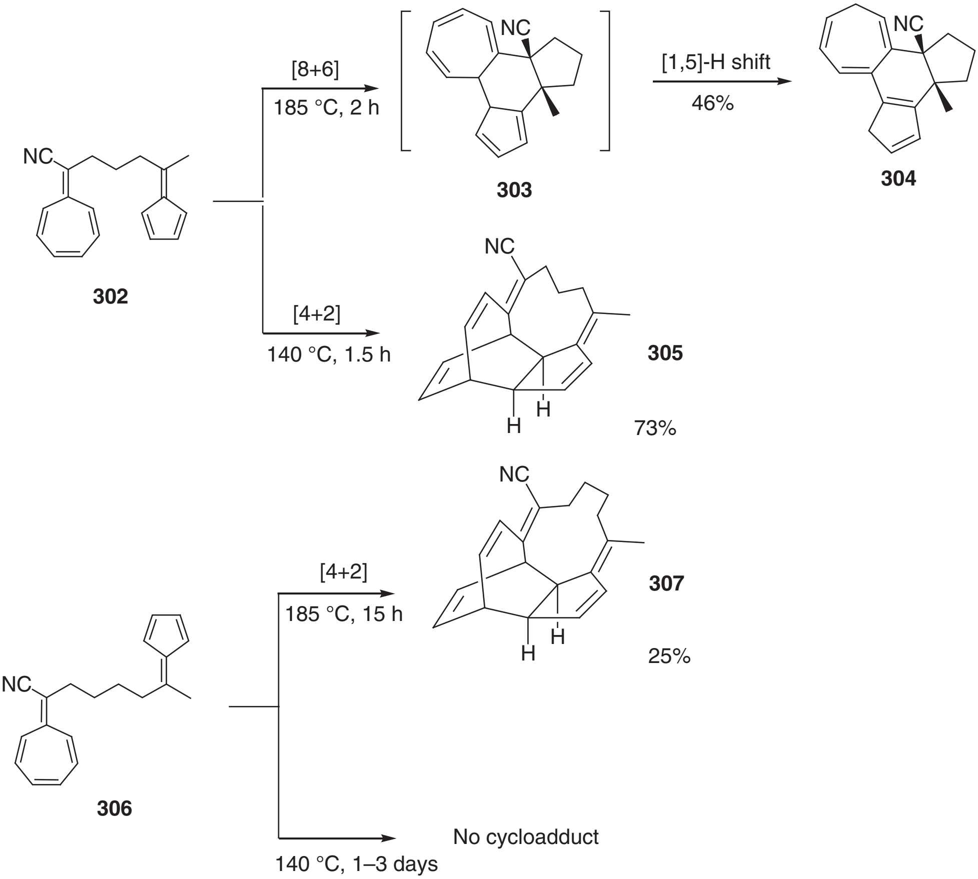
The reactions of triafulvene and its derivatives have scarcely been studied, and most of the reports were published before 1980. A review on the synthesis and the reactive behavior of triafulvene was reported by Eicher and coworkers [78]. Most of the triafulvenes undergo [2+2]-, [4+2]-, and [3+2]cycloaddition and subsequently suffer fragmentation processes to give the corresponding cycloadducts. The cycloaddition reactions of triafulvenes are summarized in this section.



Scheme 7.65



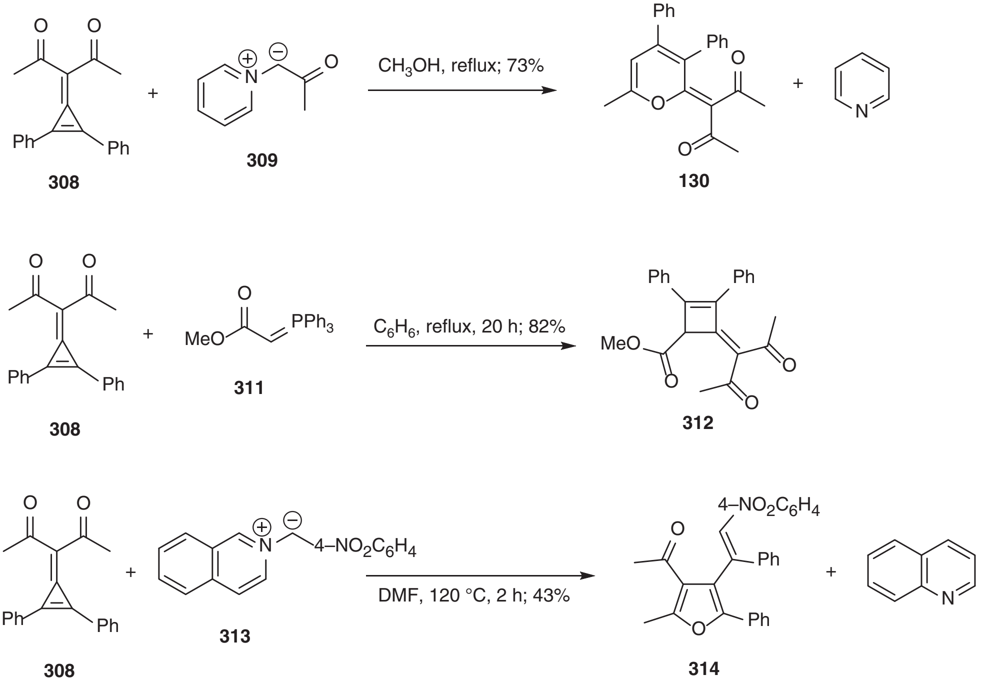
Scheme 7.66



Scheme 7.67

For decades, it has been well known that triafulvene reacts with various 1,3-dipoles, and the modes of the reaction depend on the nature of the 1,3-dipole as well as the substituents on the triafulvenes. For example, triafulvene **308** treated with pyridium ylide **309** to give pyran derivative **310** was reported by Eicher *et al.* The same reaction with methyl (triphenylphosphoranylidene)acetate **311** gave the cyclobutene derivative **312** (Scheme 7.68) [79]. Alternatively, treatment of triafulvene **308** with isoquinolinium ylide **313** afforded furan derivative **314**. The mechanism of these reactions, proposed by the authors, is depicted in Scheme 7.69.

Tsuge and coworkers reported on a [3+2]cycloaddition of benzothiazolium *N*-phenacylide **316** and triafulvene **315** to give the corresponding [3+2]adduct **317** (Scheme 7.70) [80].

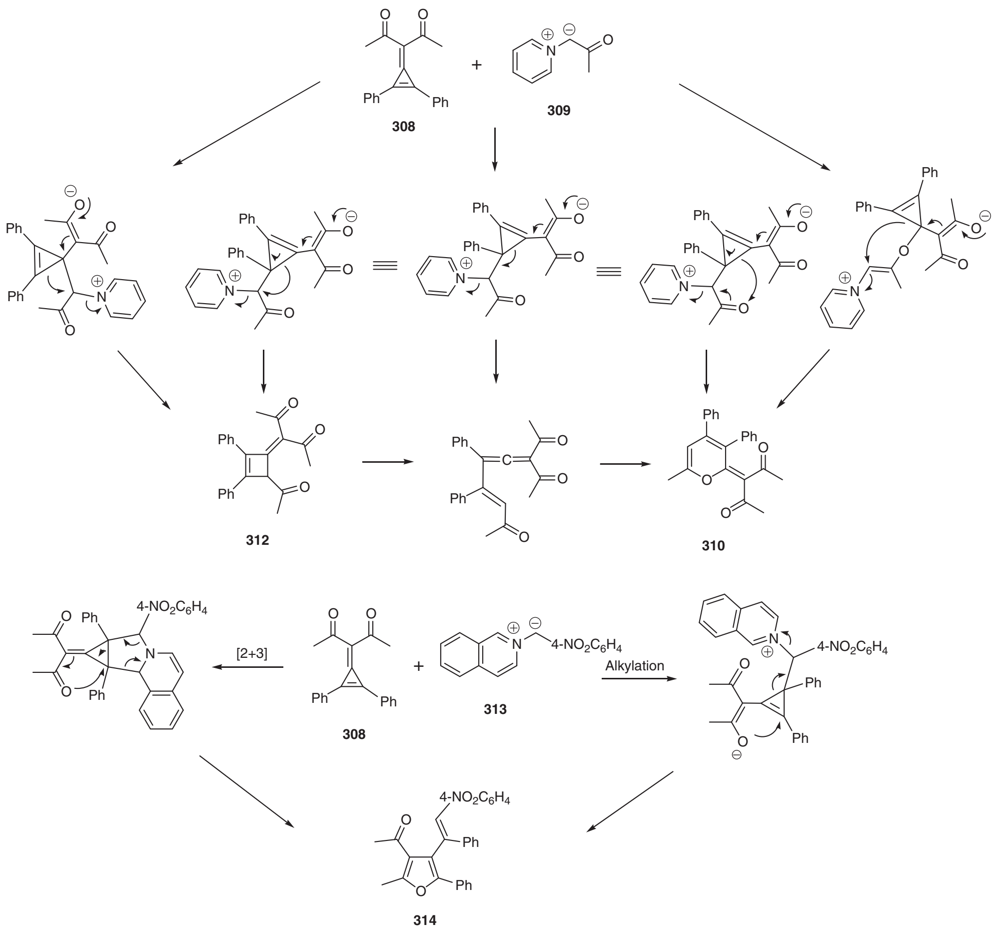


Scheme 7.68

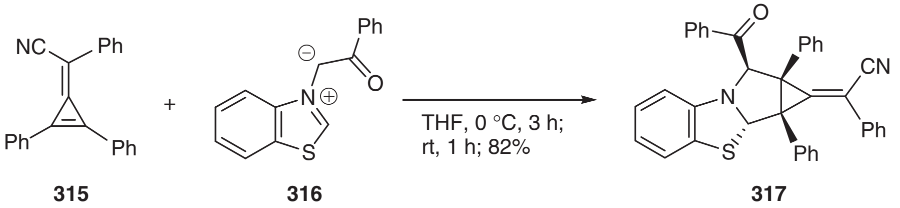
In addition, these authors reported on a reaction of benzothiazolium *N*-phenacylide **316** with triafulvene **308** to give 3*a*,11*a*-dihydro-5*aH*-furo[3′,2′:2,3]pyrido[6,1-*b*]-benzothiazole derivatives **317** and **318** in 55 and 31% yield, respectively (Scheme 7.71) [81]. In the proposed mechanism, the benzothiazolium **316** initially attacks **308** and generates the betaine **319**. This step is followed by dissociation of **319** to afford benzothiazole and allene **320**. Subsequent recombination of these two intermediates provides **321**, followed by stepwise cyclization via **322** to **323** and elimination to give the final product **317** and **318**.

Similarly, Tsuge *et al.* reported the reaction of triafulvene **315** with thiazolium *N*-phenacylide **325** in THF at room temperature for 4 days to give the cage compounds, 6,8-thiazapentacyclo[6.3.1.$0^{1,10}$.$0^{5,12}$.$0^{7,11}$]dodecenes **326** and **327** in 51% and 36% yield, respectively (Scheme 7.72) [82]. The polycycles **326** and **327** were produced by a pericyclic reaction of the initially formed *endo*[3+2]cycloadduct **328**, followed by a 1,3-hydrogen shift of **329**.

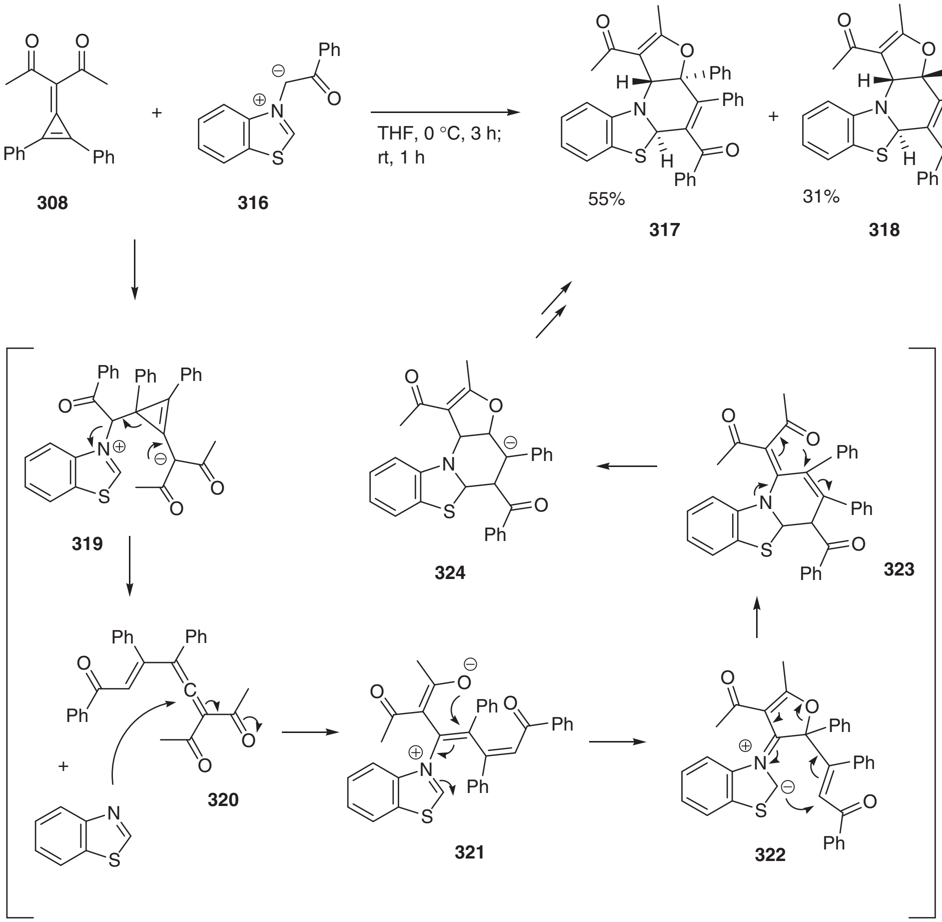
Moreover, Tsuge and coworkers [83] revealed a double cycloaddition of pyridinium *N*-methylide **328** to methylenecyclopropene **315** to provide the cage



Scheme 7.69



Scheme 7.70

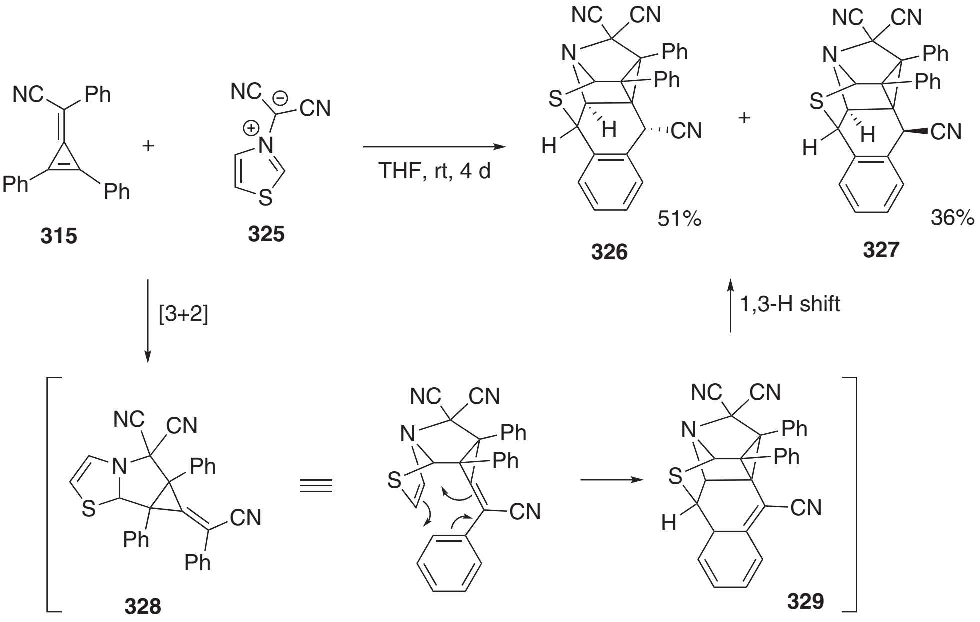


Scheme 7.71

compound **329** (Scheme 7.73). Alternatively, Tsuge *et al.* reported on the reaction of thiazolium *N*-methylide **325** with triafulvene **308** to give the cage compound **332** in 94% yield, which presumably arises from an intramolecular cyclization of the initially formed *endo*[3+2]cycloadduct [84].

Furthermore, Tsuge and coworkers reported the intermolecular 1,3-dipolar and IMDA cycloaddition reactions of imidazolium **334** or **337** and triafulvene **333** or **315** to give the cage compound **336** or **340**, respectively (Scheme 7.74) [85].

In 1967, Ciabattoni and Nathan [86] described a cycloaddition of triafulvene **315** with enamines (e.g., **341** and **344**), followed by ring opening to yield the dendralene products **343** and **346** (Scheme 7.75) (see Chapter 1).



Scheme 7.72

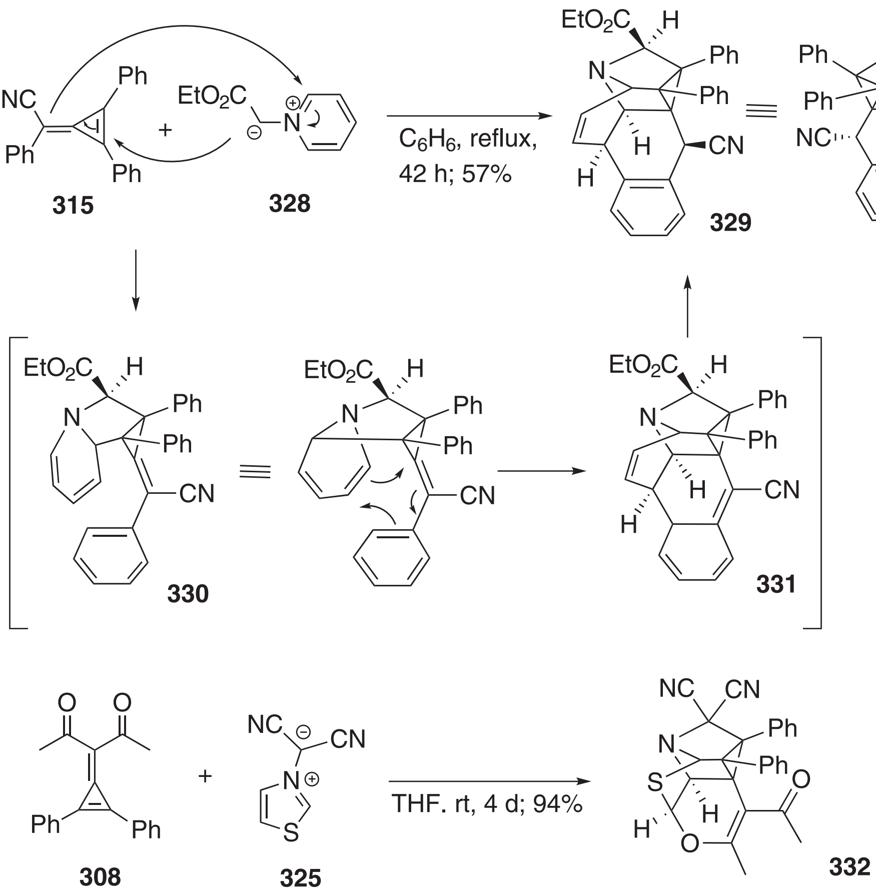
Eicher and coworkers [87] have reported on a reaction of triafulvene **347** with enamine **348** to afford the 6,6*a*-dihydro-5*H*-cyclopenta[*b*]furan **349** (Scheme 7.76).

As noted by Tsuge and coworkers [88], the reactions of cyclic enamines (e.g., **350**) with triafulvene **315** yields the medium ring compounds **351** (Scheme 7.77).

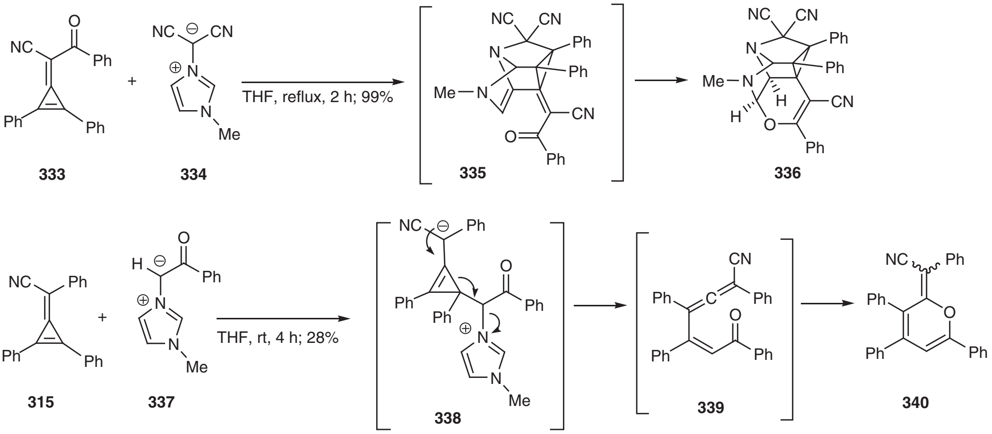
Moreover, Tsuge and coworkers reported the reaction of **315** with 1-(1-pyrrolidinyl)acenaphthylene **352** which furnishes tetrahydroindeno[1′,2′]cyclopenta[4,5-*a*]acenaphthelenes **353** and **354** in 57% and 30% yield, respectively. The reaction mechanism of the formation of **353** and **354** was proposed to proceed by a regioselective Cope rearrangement of the initially formed [2+2]cycloadduct **355**, which subsequently isomerizes by a 1,3-hydrogen shift of **356** (Scheme 7.78) [89].

Eicher and coworkers [90] investigated the reaction of a series of cyanotriafulvenes (e.g., **357**) with cyclic imines (e.g., **358** and **360**); it leads to the formation of polyheterocyclic derivatives of 2-methylenetetrahydropyridine **359** and 4-methylene tetrahydroazocine **361** (Scheme 7.79).

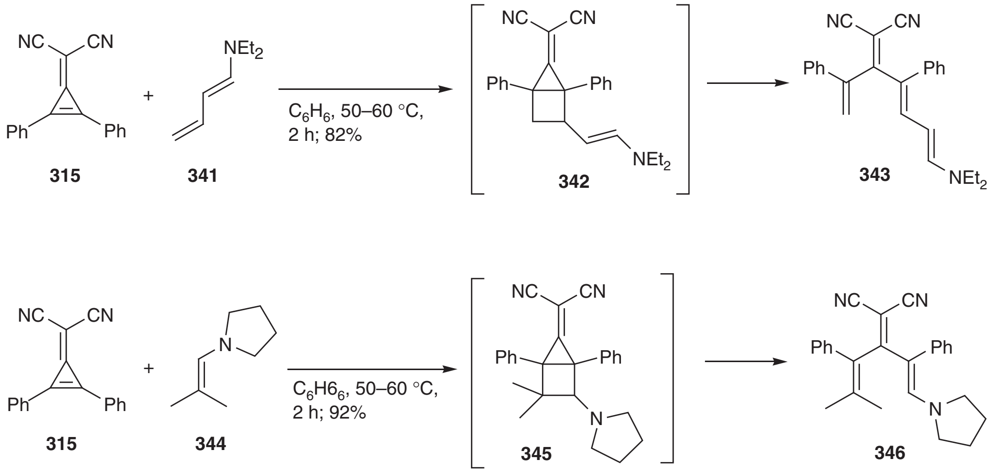
In addition, the same group reported on a synthesis of heptafulvenes and related seven-membered ring systems (e.g., **363**) from triafulvene **357** (Scheme 7.80) [91]. A series of donor-substituted 1,3-dienes, when reacted with triafulvenes by a Diels–Alder addition, yielded bicyclic methylene cyclopropanes, which were subsequently transformed to 1,6-diphenyl-substituted heptafulvenes or seven-membered ring derivatives.



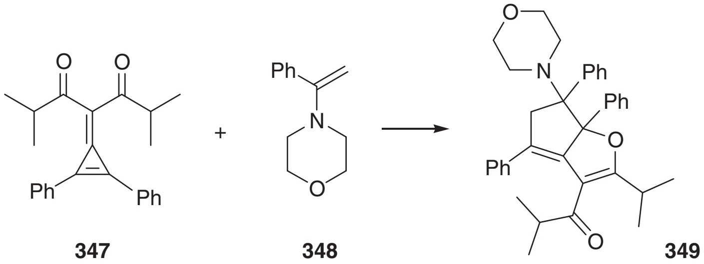
Scheme 7.73



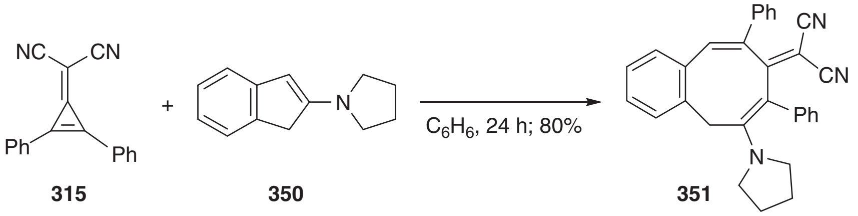
Scheme 7.74



Scheme 7.75



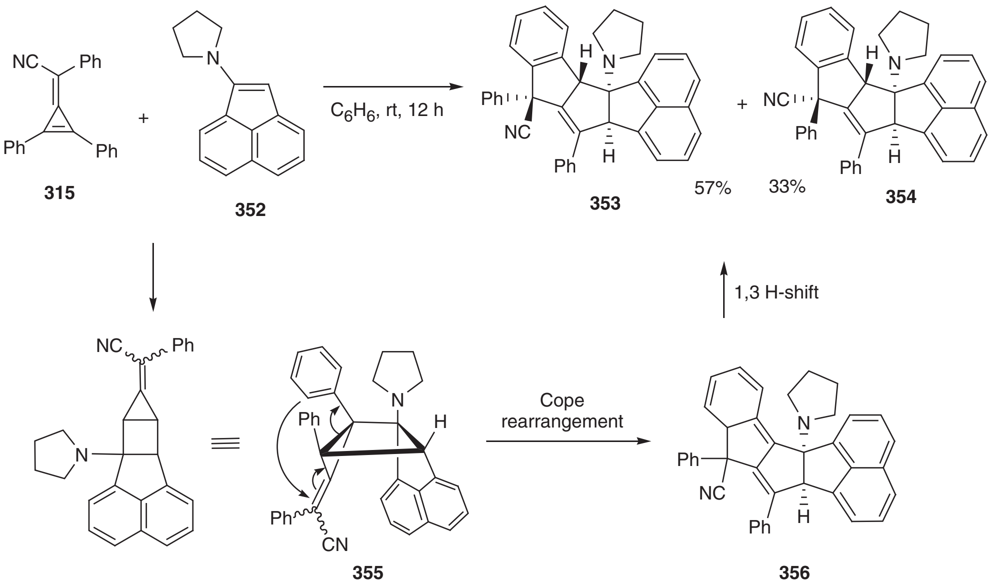
Scheme 7.76



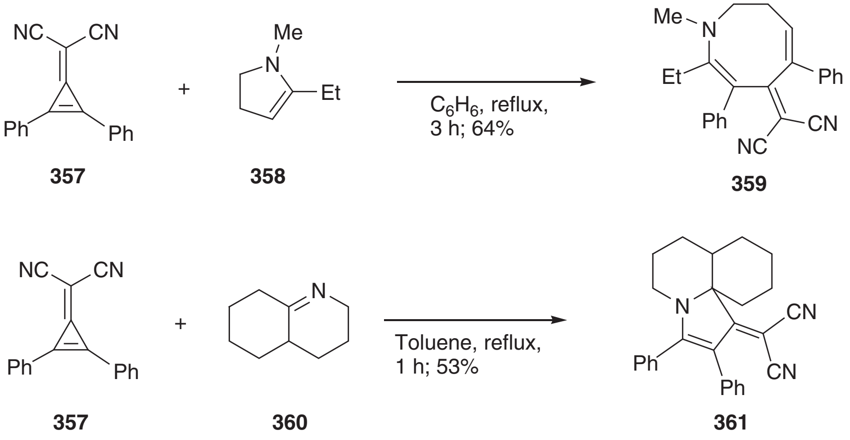
Scheme 7.77

Similarly, when triafulvene **357** reacted with ynamine **364**, the aminofulvene **365** was produced, which, by ring expansion with dimethyl but-2-ynedioate furnished heptafulvene **366** (Scheme 7.81) [92].

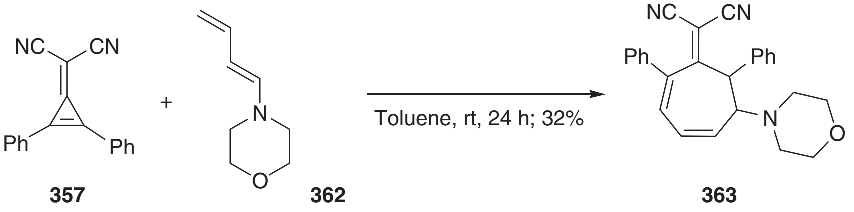
Interestingly, the triafulvene exhibits ambiguous behavior toward ynamines. Reactions of triafulvene derivative **357** with ynamine **367** by [2+2]cycloaddition and subsequent fragmentation gave the fulvene derivative **370**. In contrast, reaction of calicene **371** with ynamine **367** yielded the naphthalene derivative **374** by



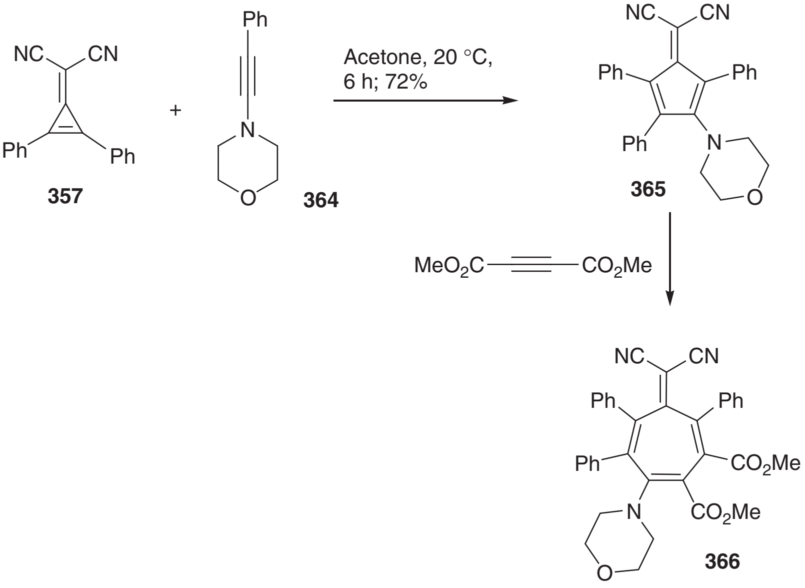
Scheme 7.78



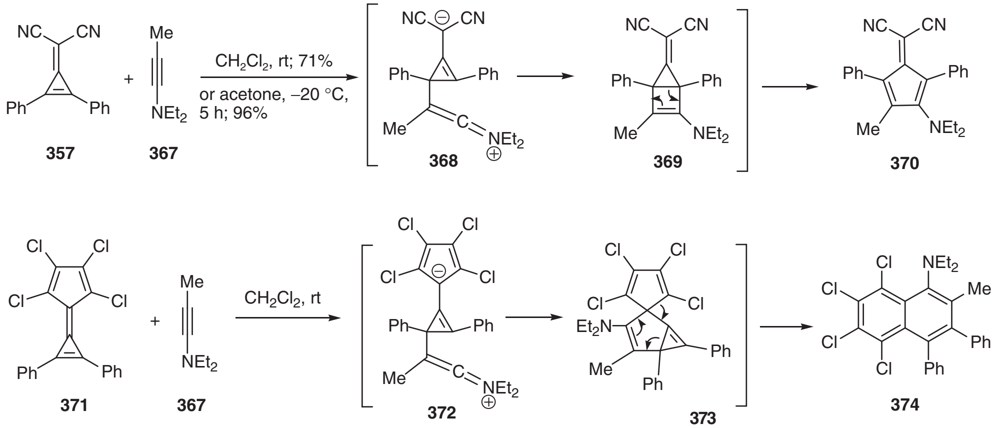
Scheme 7.79



Scheme 7.80



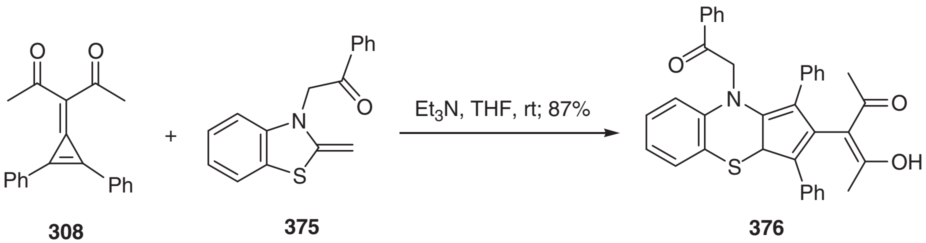
Scheme 7.81



Scheme 7.82

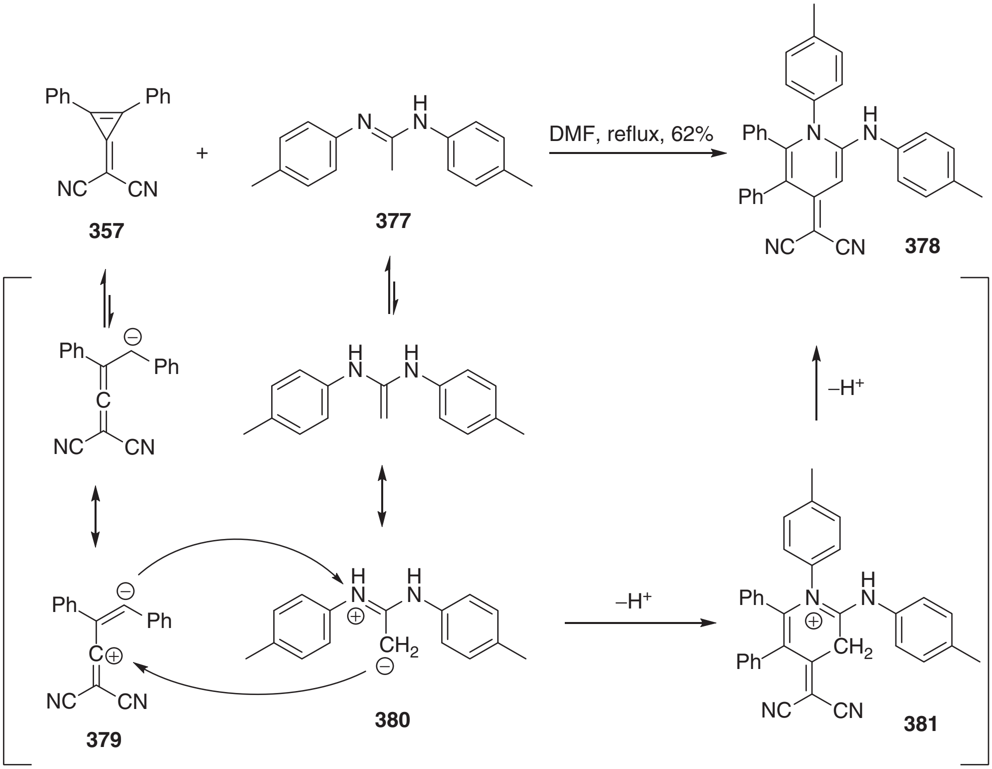
way of another type of cycloaddition and fragmentation cascade (Scheme 7.82) [92a, 93].

Tsuge and coworkers [94] studied the reaction of triafulvene **308** with 2-methylenebenzothiazoline **375**, generated *in situ* from the corresponding 2-methylbenzothiazolium bromide and triethylamine, to give the cyclopentabenzothiazine **376** (Scheme 7.83).



Scheme 7.83

Finally, Gomaa and Döpp reported on a synthesis of [2-arylamino-4(1*H*)-pyridinylidene]propanedinitrile **378** by reaction of *N*,*N*-diarylamidines **377** and triafulvene **357** (Scheme 7.84) [95]. The mechanism of the reaction, proposed by authors, involves a formal [3+3]cycloaddition reaction of ylidene **379**, arising from ring-opening of triafulvene **357**, and the ketene aminal **380** (tautomer of amidine **377**), followed by a sequence of thermal dehydrogenation steps.



Scheme 7.84

7.5
Conclusions

The efficient generation of molecular complexity and diversity by cycloaddition reactions of fulvenes, summarized in this review, are noteworthy. Nevertheless, many efforts still need to be explored to develop more sophisticated cycloaddition reactions with elaborate multibond formation in a cascade fashion with high enantioselectivity. With the thriving advances in the past decades, it is safe to assume that the subject of fulvene reactions will continue to evolve for years to come.

Acknowledgments

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8

Cross-Conjugation and Electronic Structure in TTF Analogs

Masashi Hasegawa and Yohji Misaki

8.1

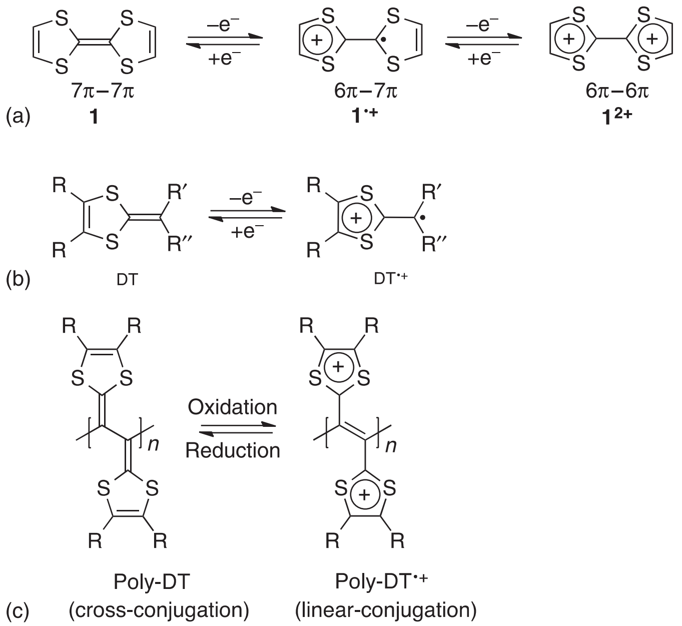
Introduction

To date, tremendous advances have been witnessed in the chemistry and physics of molecular conductors for organic electronic materials with scientific and commercial motivation [1, 2].

Versatile π-electron systems with interesting electronic properties have been synthesized as potential candidates. Since the seminal discovery of the electrical conductivity of charge-transfer (CT) complexes of tetrathiafulvalene (TTF) **1** and 1,3-dithiol-2-ylidene derivatives (Scheme 8.1), many materials scientists have been fascinated by these compounds as typical donor components for molecular-based organic conductors [3, 4]. An enormous number of studies have been devoted during the past four decades to improve the conductivity and T_c of organic conductors and superconductors. Among them, a series of cross-conjugated compounds such as radialenes (Chapter 4), dendralenes (Chapter 1), tetraethynylethane (TEE), radiaannulene (Chapter 9), and so on, containing TTF or 1,3-dithiole (DT) moieties have been prepared [5–7]. Classically, these cross-conjugated compounds have been developed to act as a superior electronic donor with a reduced on-site Coulomb repulsion and an increasing dimensionality of the intermolecular interactions. Coulomb repulsion is one of the largest impediments to electronic transportation in a conduction pathway of the molecular conductors, and multi-redox systems extended by π-frameworks can effectively reduce it. More intriguing issues of cross-conjugated frameworks are their unusual electronic properties and topological features [8–11]. Contrary to linear conjugation, the electronic structure of a cross-conjugated system is very elaborate (see Chapters 1 and 11). Topological and conformational factors usually confine the electron delocalization to the conjugated region (see Chapter 11). Hence, the redox properties of cross-conjugated multi-redox systems strongly depend on their unique conjugation patterns as well as the nature of the substituents.

Once an electron oxidation/reduction occurs, the electronic structure of the cross-conjugated systems is changed drastically (Scheme 8.1). For example, TTF, which is also one of the simplest cross-conjugated systems, changes its

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.



Scheme 8.1 Redox of (a) TTF, (b) 1,3-dithiol-2-ylidene compounds, and (c) a dendralene-type polymer with DT rings.

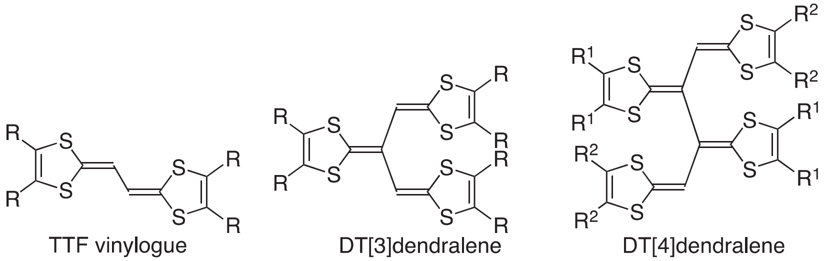
electronic structure upon one-electron oxidation into a stable heteroaromatic 6π-configuration, in which the valence electrons can delocalize over the whole framework. The redox behavior of multi-DT compounds installed into cross-conjugation also brings about the switch of the conjugation pattern. The alternate linear conjugation strongly contributes to the stabilization of the resulting cationic species. Such a unique property of controlling the conjugation envisaged for us the potential application of the bifurcation area as a soliton valve or switching unit in conjugated systems of molecular-scale electronics [12].

This chapter provides an overview of recent syntheses, redox properties, and electronic structures of the multi-redox system of TTF or DT rings in cross-conjugation.

8.2
Dendralene-Type TTF Analogs and Related Compounds

8.2.1
[*n*]Dendralenes (*n* = 3,4) with DT Units

Dendralenes, acyclic cross-conjugated polyenes having a nonplanar structure, containing DT rings (DT[*n*]dendralenes) have received considerable attention as novel multistage redox systems. The [3]- and [4]-dendralenes containing



TTF vinylogue

2a: R = Me
2c: R = CO_2Me

DT[3]dendralene

3a: R = Me
3b: R = SMe
3c: R = CO_2Me
3d: R = H

DT[4]dendralene

4a: $R_1 = R_2 =$ Me
4c: $R_1 = R_2 = CO_2Me$
4d: $R_1 = R_2 =$ H
5ab: R_1 = Me, R_2 = SMe

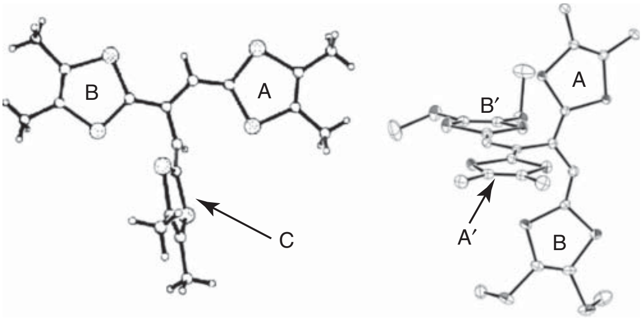
Figure 8.1 Molecular structures of TTF vinylog **2**, DT[3]dendralene **3**, and DT[4]dendralene **4**.

DT rings, **3**–**5**, were first reported in 1989 (Figure 8.1) [13]. They are considered as a π-extended model of vinylogous TTF **2** [14–17] to reduce the on-site Coulomb repulsion and increase in dimensionality.

Generally, the dendralene skeleton cannot adopt a planar structure [18]. Thus, DT[*n*] dendralenes, where "*n*" is an odd number, adopt a skew conformation composed of vinylog TTF moieties and the remaining isolated DT unit. In contrast, DT[*n*]dendralenes, where *n* is an even number, tend to adopt a combination of the distorted tetrathiafulvalene vinylogs (TTFVs). Indeed, the X-ray structure of DT[3]dendralene **3a**, reported by Bryce and coworkers, reveals that the three DT rings (A, B, and C) are not coplanar (Figure 8.2a) [19, 20]. Ring C is almost perpendicular to the mean planes of rings A and C, forming a nearly coplanar arrangement.

On the other hand, the molecular structure of a [4]dendralene derivative, determined by X-ray diffraction analysis, showed a different picture. [4]Dendralene **5ab** formally consists of a σ-bonded pair of independent TTFVs and they are orthogonal to each other at the center of [4]dendralene (M. Ueda, T. Shirahata, and Y. Misaki, unpublished result). Two DT rings, A and B, are almost coplanar, whereas the mean planes of A and A′ are perpendicular to each other (Figure 8.2b).

The redox potentials of selected [3]- and [4]-dendralenes measured by cyclic voltammetry (CV) are summarized in Table 8.1. All [3]dendralenes show two pairs of one-electron-reversible redox waves and a quasi-reversible wave, arising from the subsequent formation of cation radical, dication, and trication, respectively. The lower $E_1^{1/2}$ values of **3a** and **3c**, compared with those of **2a** and **2c**, suggest increase of the electron-donating ability by attachment of the additional DT ring. In addition, the significant lowering of the $E_2^{1/2}$ values indicates the decrease in the on-site Coulomb repulsion in [3]dendralenes. The considerably higher E_3 value suggests the existence of an isolated DT ring, so that the conformation of [3]dendralene and its cationic species in solution may be similar to that of **3a** in the solid state. The CV of [4]dendralenes **4a** and **4d** exhibited two pairs of single-electron waves and one pair of a two-electron wave. The $E_1^{1/2}$ and $E_2^{1/2}$ values are similar



(a) **3a** (b) **5ab**

Figure 8.2 X-ray structures of (a) **3a** and (b) **5ab**. Reproduced with permission from Ref. [20] © 2000 Wiley-VCH Verlag GmbH & Co. KGaA.

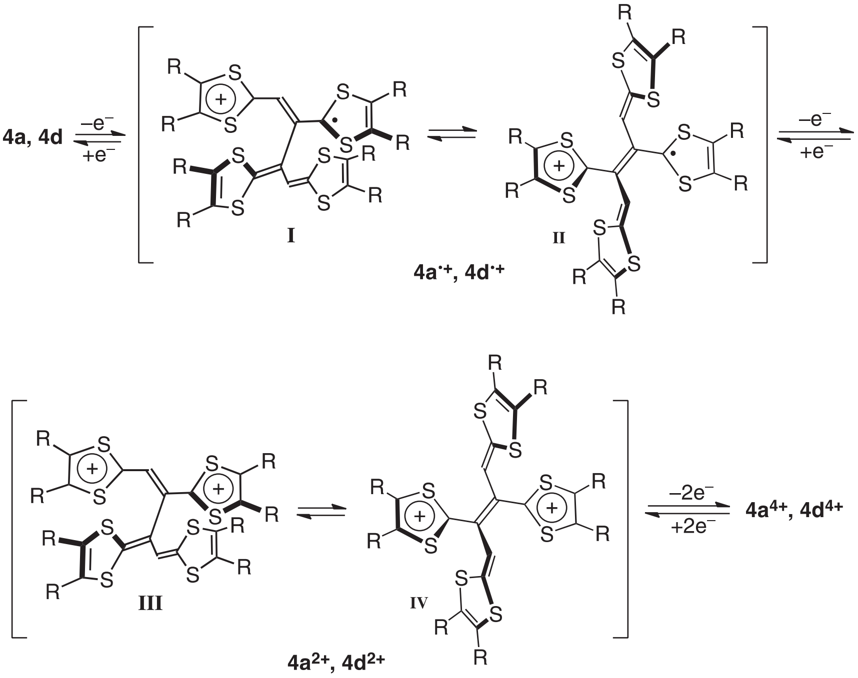
Table 8.1 Redox potentials of DT[3]- and [4]-dendralenes (**3** and **4**), and corresponding TTF vinylogs **2**[a].

Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$
3a (R = Me)	−0.31	−0.13	0.78[b]
3c (R = CO_2Me)	0.24	0.33	1.29[b]
3d (R = H)	−0.20	−0.06	0.86[b]
4a (R = Me)	−0.32	−0.18	0.24 ($2e^-$)
4c (R = CO_2Me)	0.27 ($2e^-$)		0.68 ($2e^-$)
4d (R = H)	−0.21	−0.09	0.26 ($2e^-$)
2a (R = Me)	−0.26	−0.01	—
2c (R = CO_2Me)	−0.16	0.05	—

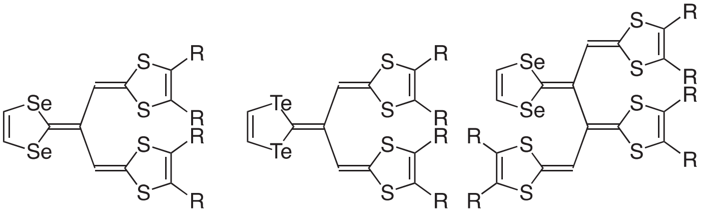
a) In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.
b) Quasi-reversible.

to those of [3]dendralene **3a** and **3d**, respectively. However, the third redox potentials, corresponding to the simultaneous redox of $\mathbf{4}^{2+}/\mathbf{4}^{4+}$, are drastically decreased compared with those of **3a** and **3d**. These facts indicate that the cation radical actually forms a vinylog moiety (**I** in Scheme 8.2) in $\mathbf{4}^{\bullet+}$, and it may transform to a vinylog cation radical having two independent uncharged DT-rings (**II**). In addition, dication $\mathbf{4}^{2+}$ also can exist as the mixture of **III** and **IV**. In contrast, the CV of **4c** displayed only two redox waves. Both contain simultaneous two-electron redox processes, because the electron-withdrawing ester groups prevent the formation of a stable cation radical of $\mathbf{4c}^{\bullet+}$.

The [3]- and [4]-dendralene analogs, the sulfur atoms of which are replaced by selenium or tellurium atoms, have been reported by Cava and coworkers (Figure 8.3) [21, 22]. The CV of compounds **6c**,**d** and **7c**,**d** indicate similar redox processes to **3c** and **3d**. The oxidation potentials of **6c** and **6d**, however, are higher than those of **3c** and **3d**, owing to the replacement of a DT unit by a 1,3-diselenium ring reflecting the higher polarizability of Se atoms. A similar trend was observed



Scheme 8.2 Plausible redox process of the DT[4]dendralene **4**.



6c (R = CO_2Me)
6d (R = H)

7c (R = CO_2Me)
7d (R = H)

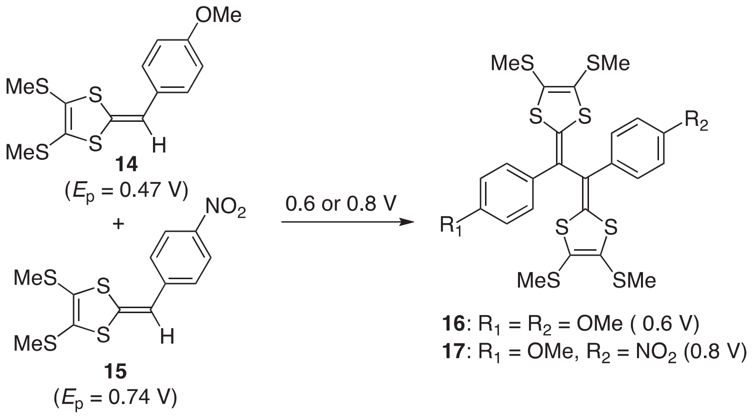
8c (R = CO_2Me)

Figure 8.3 Chalcogen analogs of the DT[*n*]dendralenes **6–8**.

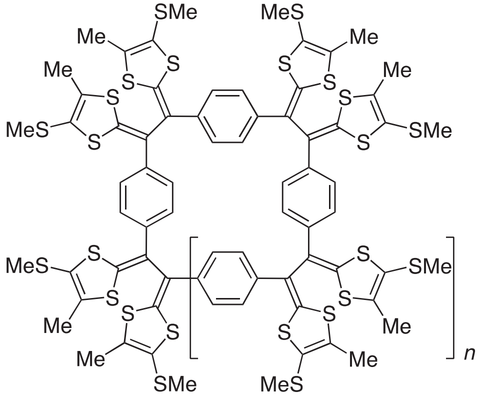
in **8c**. Meanwhile, lower potentials than for the parent [3]dendralenes were found in **7c** and **7d**.

8.2.2
Analogs of DT [*n*]Dendralenes

Lorcy and coworkers [23, 24] employed the electrochemical oxidative dimerization of half units to form a series of TTFVs extended by electron-donating/accepting moieties **14**,**15** (Scheme 8.3). Interestingly, when the oxidation starting from a mixture of **14** and **15** was performed at sufficiently positive potential



Scheme 8.3 Oxidative coupling of 1,4-dithiafulvene **14, 15**.

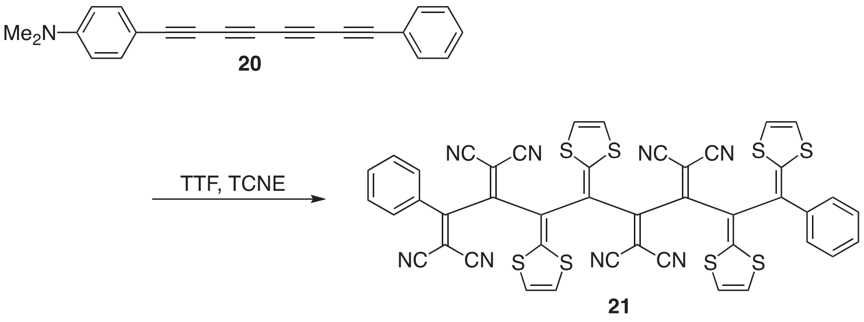


18: (n = 1), **19**: (n = 2)

Figure 8.4 Phenylene-inserted radialene **18, 19**.

to allow for the formation of two cation-radicals, unsymmetrical dimers **17** were obtained in addition to symmetrical dimers. Such a dimerization of the dithiafulvene units is a versatile tool for further expansion, and hence a variety of extended cross-conjugated systems including macrocycles **18**, **19** (Figure 8.4) [25], which are also classified as Ar-inserted radialenes (see Chapter 9), and polymeric structures have been prepared [26, 27].

Recently, Diederich and coworkers synthesized a novel D–A system **21** containing a dendralene backbone, which might be a promising candidate for third-order nonlinear optical materials [28]. The D–A chromophores are introduced by the one-pot cascade of successive [2+2]Tetracyanoethylene (TCNE)/TTF cycloadditions to the tetrayne **20** (Scheme 8.4). This synthetic protocol might have great potential for a new class of cross-conjugated system with multivalent CT chromophores [29].



Scheme 8.4 Cascade reaction of **20**.

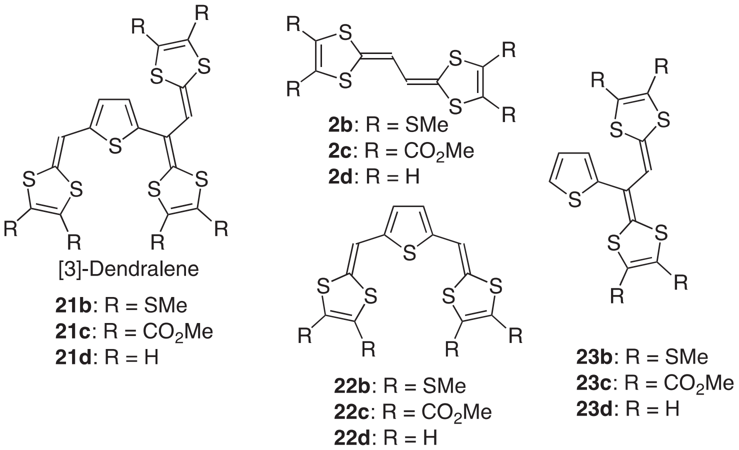
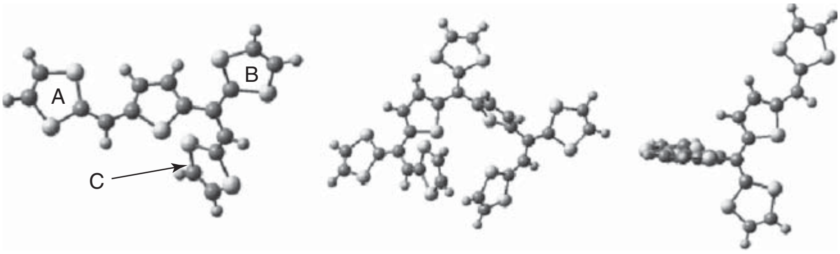


Figure 8.5 Thienylene-inserted DT[*n*]dendralene and related compounds.

8.2.3
Thienylene-Inserted DT[*n*] Dendralenes and Related Compounds

As described in the earlier section, DT[*n*]dendralenes show an unusual conjugation and redox behavior. To control the conjugation pathway and modulate its strength in the cross-conjugation, DT[*n*]dendralenes containing thienylene spacer units have been prepared (Figure 8.5).

Hasegawa, Misaki, and coworkers prepared the thienylene-inserted DT[3]dendralenes **21b–d** [30]. Molecular orbital (MO) calculation of **21d** suggests that a local minimum geometry adopts a twisted structure composed of the DT-thiophene part (A) and the transoid vinylog part (Figure 8.6a, rings B and C). This structure suggests that **21d** has basically a cross-conjugated nature between the building blocks of **22d** and **23d**, and the conjugation derived from **21d** would be stronger than that from DT[3]dendralene **3c**. The redox properties of **21** and **22** and related compounds are summarized in Table 8.2.



(a) **21d** (b) **25d** (c) **26d**

Figure 8.6 Calculated molecular structures of (a) **21d**, (b) **25d**, and (c) **26d**.

Table 8.2 Redox potentials of **21b,d**, and related compounds[a].

Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$
21b (R = SMe)	−0.03	0.09	0.42[b]
21d (R = H)	−0.12	0.02	0.50[b]
3d (R = H)	−0.20	−0.06	0.86[b]
2d (R = H)	−0.17	0.05	—
22d (R = H)	−0.11	0.00	—

[a] In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.
[b] Quasi-reversible.

The dendralenes **21b,d** exhibit two reversible redox waves and an additional quasi-reversible one. The first and second redox potentials of **21d** are similar to those of **22d**, while the first redox potential of **2d** is very close to that of **3d**. These results imply that the charges of oxidized species are distributed on the moiety of **22d** rather than **2d** upon oxidation in CV.

The solution-phase electronic spectra of **21b, 22b**, and their cationic species, generated by electrochemical oxidation under constant voltage conditions, are depicted in Figure 8.7. The spectrum of $\mathbf{21b}^{\bullet+}$ showed mainly three absorption maxima, and a further broad absorption tailing up to 2000 nm (Figure 8.7). As the electronic spectrum of the building block $\mathbf{22b}^{\bullet+}$ exhibits an absorption maximum at 1202 nm, as the result of a mixed-valence (MV) band due to electronic delocalization over the whole extended TTF system being observed under identical conditions [31–33], the existence of the broad absorption at the near-IR region in $\mathbf{21}^{\bullet+}$ suggests a certain contribution of a delocalized electronic structure (Figure 8.8).

On the other hand, DT[*n*]dendralenes containing two or three thienylene groups have been synthesized (Figure 8.9). Yamashita and Ohta [34] prepared the DT[3]dendralene with two thiophene spacers **24** ($n = 3$) for the purpose of reduction of the Coulomb repulsion in the dicationic state. More recently, Misaki and coworkers [35, 36] reported on a series of DT[5]- and [4]-dendralenes having two thiophene moieties **25–26**.

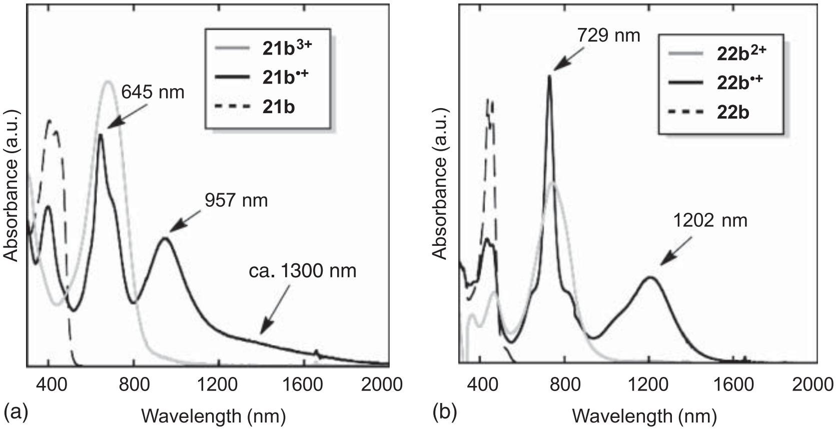
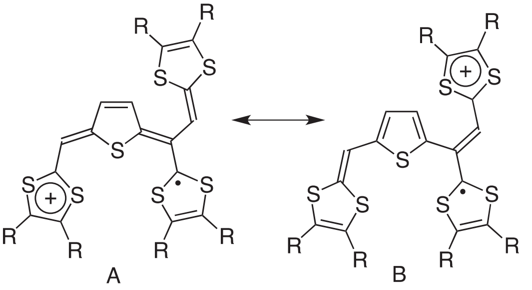


Figure 8.7 Electronic spectra of oxidative species of (a) **21b** and (b) **22b**.

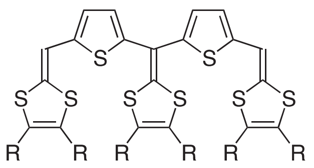


$21^{\cdot+}$

Figure 8.8 Resonance structure of **$21^{\cdot+}$**.

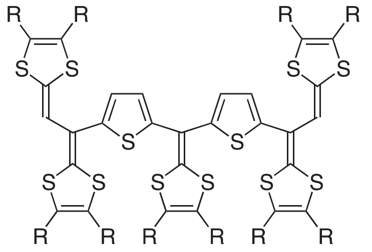
MO calculations of **25d** suggest a skewed structure composed of the central DT ring, two thiophenes, and the terminal vinylogs as the structure at the energy minimum (Figure 8.6b). In sharp contrast, the MO-optimized structure of **26d** (R = H) suggests that both symmetrical two-thiophene-extended TTF moieties are almost planar, indicating effective π-conjugation of two DT rings through the thienylene unit. They are almost perpendicular to each other due to steric hindrance (Figure 8.6c).

Redox potentials of **24**–**26** and related compounds of **2**, **22,** and **27** (Figure 8.10) are summarized in Table 8.3. In their CVs, the donors of **24a**–**c** exhibit two and three pairs of redox waves, respectively. The first redox waves are assigned to simultaneous two-electron redox processes, and the second redox waves are assigned to one-electron redox steps to form a trication radical species. The CVs of **25a,b**, measured in benzonitrile show four pairs of reversible redox waves, involving two two-electron transfer and two one-electron transfer waves. The relatively low redox potentials of $E_1^{1/2}$ and $E_2^{1/2}$ in **25a**, compared to those of the [3]dendralene derivative **24a**, are due to a certain contribution of two kinds of



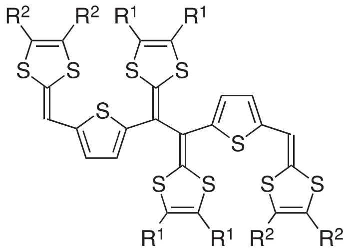
[3]Dendralene

24a: R = Me
24b: R = SMe
24e: R = –SCH$_2$CH$_2$S–



[5]Dendralene

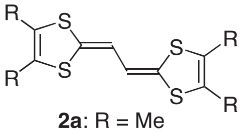
25a: R = Me
25b: R = SMe
25d: R = H



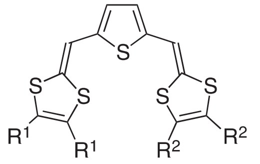
[4]Dendralene

26aa: R^1=R^2= Me
26ab: R^1=Me, R^2= SMe
26ac: R^1=Me, R^2= CO$_2$Me
26ba: R^1=SMe, R^2= Me
26d: R^1=R^2= H

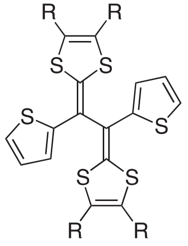
Figure 8.9 Thienylene-inserted DT[*n*]dendralene derivatives of **24–26**.



2a: R = Me



22ab: R^1 = Me, R^2 = SMe
22ac: R^1 = Me, R^2 = CO$_2$Me



27a: R = Me
27b: R = SMe

Figure 8.10 Molecular structures of **2**, **22**, and **27**.

conjugation patterns in the cationic species. Moreover, the fourth redox waves, observed at 0.78 or 0.83 V, is attributed to the formation of pentacation radical of **25**$^{6+}$, which can be stabilized by effective linear conjugation with two thiophene rings (Figure 8.11a).

In contrast, the redox potentials and redox processes of **26** are remarkably affected by its substituents. The CV of **26aa** and **26ba** exhibit four reversible redox waves corresponding to the four steps of oxidation/reduction, whereas the CV of **26ab** shows two one-electron redox waves and the additional broad two-electron redox waves. The $E_1^{1/2}$ values of **26aa**, **26ab**, and **26ba** are comparable to those of their building components, **2a**, **22ab**, and **22ac**, although the $E_1^{1/2}$ values of **26aa**, **26ab**, and **26ba** are significantly lower (by 0.14–0.17 V) compared with those

Table 8.3 Redox potentials of **24–26** and related compounds[a].

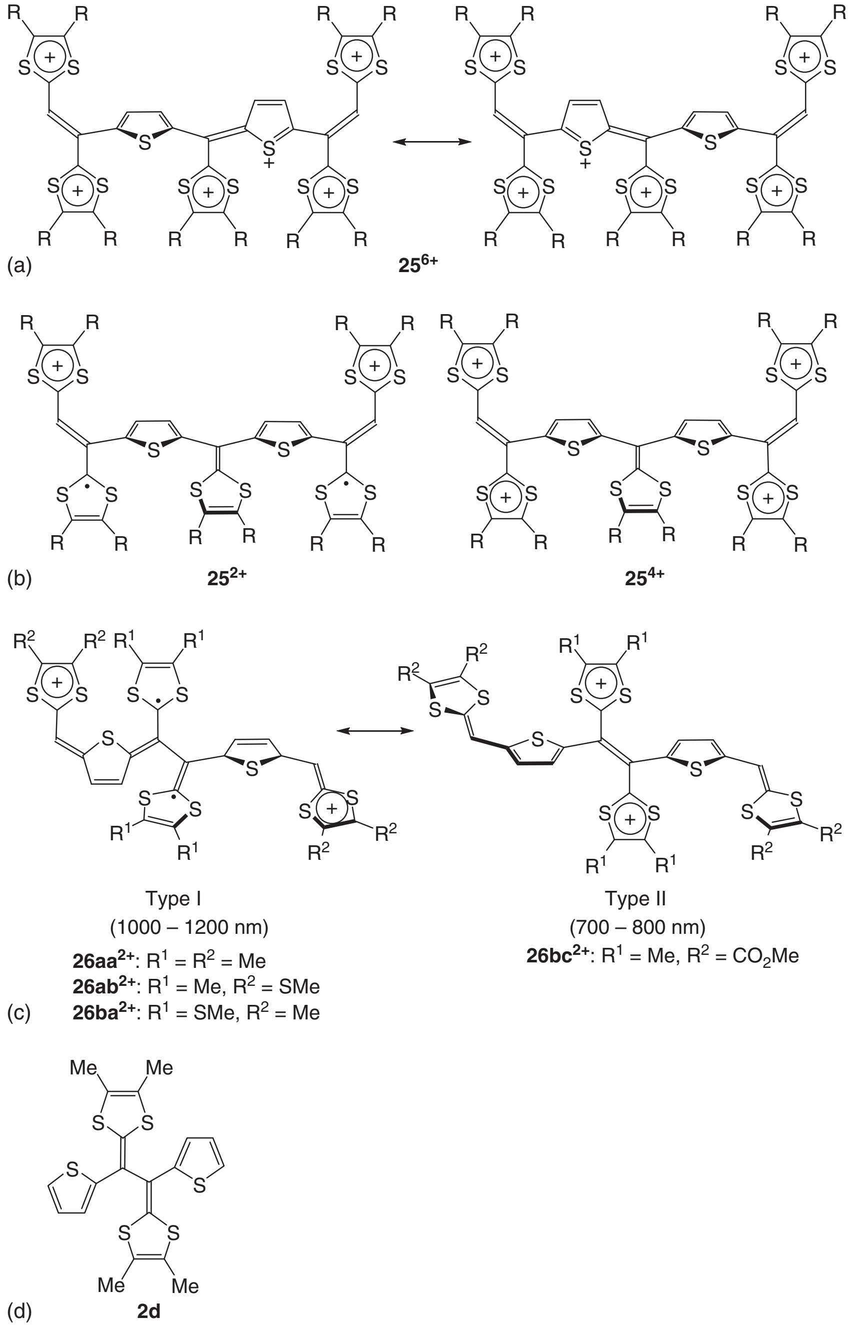
Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$	$E_4^{1/2}$
24a ($R^1 = Me$)	0.04 ($2e^-$)	0.35[b]	—	—
24b ($R^1 = SMe$)	0.12 ($2e^-$)	0.46[b]	—	—
24e ($R^1 = SCH_2CH_2S$)	0.12 ($2e^-$)	0.45	—	—
25a ($R = Me$)	−0.21 ($2e^-$)	0.01 ($2e^-$)	0.50	0.78
25b ($R = SMe$)	−0.02 ($2e^-$)	0.12 ($2e^-$)	0.47	0.83
26aa ($R^1 = R^2 = Me$)	−0.16	−0.04	0.03	0.11
26ab ($R^1 = Me$, $R^2 = SMe$)	−0.07	0.03	0.16 ($2e^-$)	—
26 ac ($R^1 = Me$, $R^2 = CO_2Me$)	0.01 ($2e^-$)	0.35 ($2e^-$)	—	—
26ba ($R^1 = SMe$, $R^2 = Me$)	−0.07	0.02	0.10	0.18
27a ($R = Me$)	0.01 ($2e^-$)	—	—	—
27b ($R = SMe$)	0.14 ($2e^-$)	—	—	—
2a ($R = Me$)	−0.18	−0.06	—	—
22ab ($R^1 = Me$, $R^2 = SMe$)	−0.11	0.02	—	—
22 ac ($R^1 = Me$, $R^2 = CO_2Me$)	−0.03	0.15	—	—

a) In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc$^+$.
b) Quasi-reversible.

of **27a** and **27b**. In addition, there are a few differences of the redox potentials $E_1^{1/2}$ and $E_2^{1/2}$ between **26ab** and **26ba**. These results indicate that the dimeric thiophene-quinoidal structure may be dominant in mono- and dicationic state of **26aa**, **26ab**, and **26ba**. In sharp contrast, two pairs of two-electron redox waves were clearly observed for **26ac**. The $E_1^{1/2}$ value of **26ac** (0.01 V) is higher than that of **22ac** (−0.03 V) and is identical with that of **27a** (0.01 V). Thus, the first redox process may proceed at the central TTFV part, giving vinylogous TTF dications (Figure 8.11c).

As for electronic spectra, the spectrum of **25b**$^{2+}$ shows a remarkable resemblance to **23b**$^{\bullet+}$ (642 and 962 nm) rather than to **22b**$^{\bullet+}$ (729 and 1202 nm, Figure 8.7) under identical conditions. It is clearly indicated that two positive charges in **25b**$^{2+}$ are largely located at the outer two TTF moieties. Likewise, the absorption maximum of **32b**$^{4+}$ exhibits strong similarity to **23b**$^{2+}$ (716 nm) compared with **22b**$^{2+}$ (744 nm), suggesting that **25b**$^{4+}$ can be regarded as a dimeric vinylogous TTF with a dithienylmethylidene spacer (Figure 8.11b).

Like the CV results, the electronic spectra of **26ab**$^{2+}$ and **26 ac**$^{2+}$ also support a clear difference of the electronic structures. The spectrum of **26ab**$^{2+}$ displays absorption maxima at 450, 475, 721, and 1153 nm. It has remarkable resemblance to **22ab**$^{\bullet+}$ ($\lambda_{max} = 729$ and 1201 nm under identical conditions), suggesting a significant contribution of thiophene-quinoidal cationic species (Type I in Figure 8.11c). On the other hand, lack of a strong absorption maximum at 1000–1200 nm in **26ac**$^{2+}$ strongly indicates little contribution of the quinoidal structure. The dication **26ac**$^{2+}$ exhibited absorption resembling that of **2d**$^{2+}$. These differences of the electronic structures can be understood by considering the stability of their dicationic states, depending on the nature of the substituents.



(a) **25^{6+}**

(b) **25^{2+}** **25^{4+}**

Type I
(1000 – 1200 nm)
$26aa^{2+}$: $R^1 = R^2 = Me$
$26ab^{2+}$: $R^1 = Me$, $R^2 = SMe$
(c) **$26ba^{2+}$**: $R^1 = SMe$, $R^2 = Me$

Type II
(700 – 800 nm)
$26bc^{2+}$: $R^1 = Me$, $R^2 = CO_2Me$

(d) **2d**

Figure 8.11 Plausible electronic structures of (a) **25^{6+}**, (b) **25^{2+}** and **25^{4+}**, (c) **26^{2+}**, and (d) structure of **2d**.

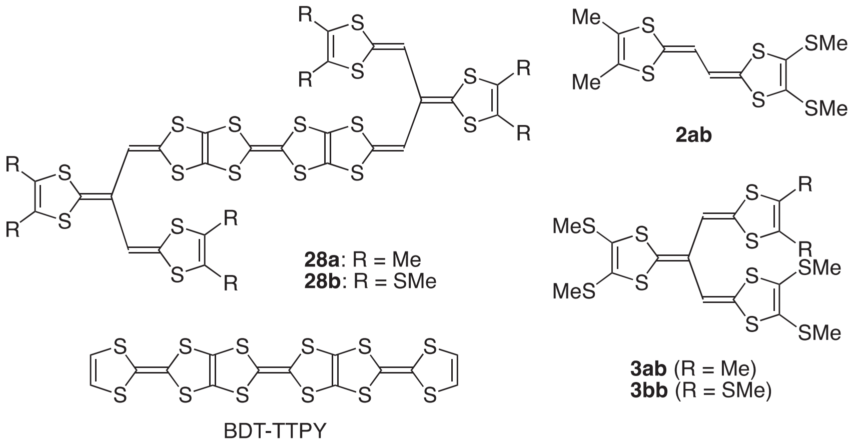


Figure 8.12 Molecular structures of **2ab**, **3ab**, **3bb**, **28a**, **28b**, and BDT-TTPY.

8.2.4
Tris-Fused TTF Analogs Possessing [3]Dendralene Moieties

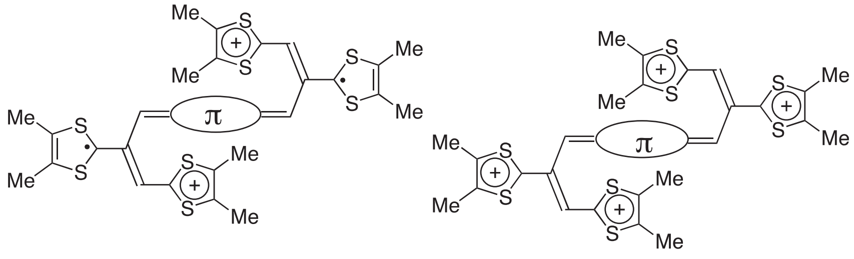
Tris-fused TTF analogs , in which the outer two TTF moieties are replaced by DT[3]dendralenes **28a** and **28b** [37], have been synthesized as analogs of cross-conjugated 2,2′-bi[5-(1,3-dithiol-2-ylidene)-1,3,4,6-tetrathiapentanylidene] (BDT-TTPY), whose nonplanar structure derived from cross-conjugation topology might be in favor of reducing the bandwidth in the metallic state (Figure 8.12) [38]. In addition, 2,5-bis(1,3-dithiole-2-ylidene)-1,3,4,6-tetrathiapentalene (BDT-TTP), TTPY, and their derivatives are, recently, anticipated to be a promising candidate for positive electrode materials for secondary batteries because of their poor solubility in ordinary organic solvents and because of the presence of multiple DT sites [39]. The geometry optimization by density functional theory (DFT) calculation gave a local minimum for a tub-shaped conformation. Branching DT rings at the terminal positions are almost perpendicular to the central core.

The CV of **28a** and **28b** exhibit four and five pairs of reversible redox waves, respectively (Table 8.4). The five waves in **28b** involving three pairs of simultaneous two-electron transfer waves, and in total all eight DT rings in **28b**, are fully oxidized under the CV conditions. The $E_1^{1/2}$ and $E_2^{1/2}$ values of **28a** are close to those of DT[3]dendralene **3ab**, and slightly lower than those of **2ab**. Similarly, the first and second redox potentials of **28b** are comparable to those of **3bb** (Figure 8.12). These facts clearly suggest that the oxidation of **28b** proceeds from the outer [3]dendralene moieties. Furthermore, the electronic spectra of $\mathbf{28a}^{2+}$ and $\mathbf{3bb}^{\bullet+}$ are quite similar. The dication of **28a** exhibits four absorption maxima at 594, 708, 834, and 1184(sh) nm, whereas the cation radical derived from **3bb** possesses bands at 604, 712, 834, and 1078(sh) nm. The broad absorption in the 1000–1100 nm range, observed in both $\mathbf{28a}^{2+}$ and $\mathbf{3bb}^{\bullet+}$, is assigned to

Table 8.4 Redox potentials of **28** and related compounds[a].

Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$	$E_4^{1/2}$	$E_5^{1/2}$
28a (R = Me)	−0.21 (2e$^-$)	−0.04 (2e$^-$)	0.33	0.50	—
28b (R = SMe)	−0.03 (2e$^-$)	0.06 (2e$^-$)	0.37	0.48	1.14 (2e$^-$)
3ab (R = Me)	−0.20	−0.02	0.76	—	—
3bb (R = SMe)	−0.04	0.03	0.71	—	—
2ab (R^1 = Me, R^2 = SMe)	−0.26	−0.01	—	—	—

a) In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc$^+$.



28a^{2+} **28a**$^{4+}$

Figure 8.13 Electronic structure of **28**$^{2+}$ and **28**$^{4+}$.

MV absorption in the near-IR region arising from the charge delocalization at the DT[3]dendralene unit (Figure 8.13).

CT complexes of **28b,c** with TCNQ-F_4 were successfully prepared. The ratio of the donor to TCNQ-F_4 in the CT complexes is 1 : 1. The amounts of CT in the complexes were estimated to be 1.2 by comparison of the CN stretching shift. The electric conductivities of the compressed pellet of these CT complexes measured by the four-probe technique gave moderate electrical conductivities of $\sigma_{rt} = 3 \times 10^{-3}\ \mathrm{S\,cm^{-1}}$. Temperature dependence of their resistivity exhibited semiconducting properties, with activation energies of 0.10–0.13 eV.

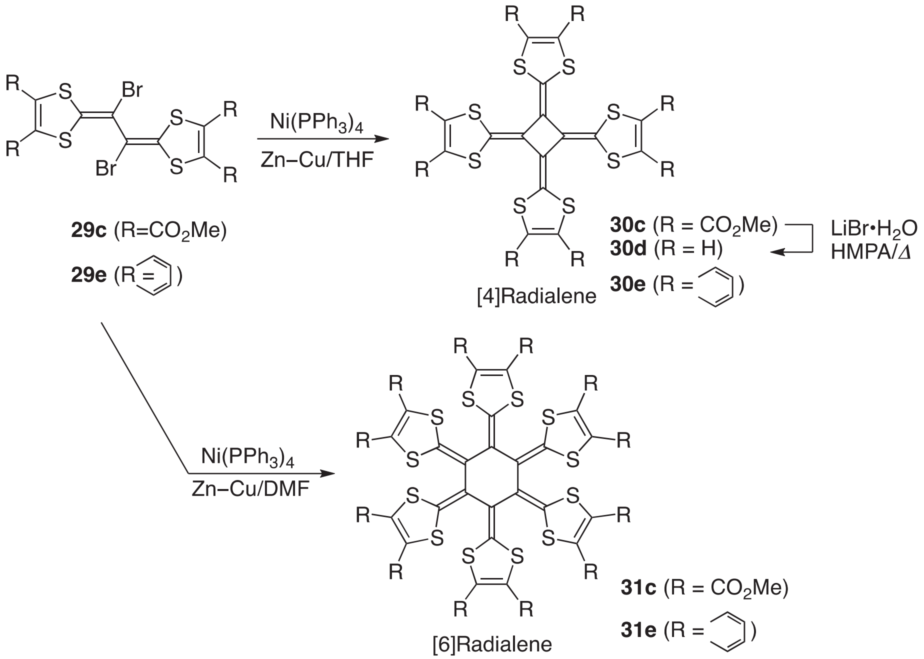
8.3
Radialene-Type TTF Analogs (DT-Substituted Radialenes)

[*n*]Radialenes are cyclic dendralenes; they are formally composed of the *n*-membered ring and *n* exocyclic double bonds (see Chapter 4). Because of the attractive molecular and electronic structures originating from the high D_{nh} symmetry, a wealth of [*n*]radialene derivatives have been prepared [5, 6]. [*n*]Radialenes substituted with DT rings are regarded as multistep redox systems, and on-site Coulomb repulsion in their dicationic states is considerably reduced by delocalization of two positive charges over the whole multi-DT units. Furthermore, the reversible oxidation/reduction from DT rings can lead

to crucial changes in the electronic structure of the radialene core, featuring an aromatic/antiaromatic characteristic. For instance, DT[6]radialene will offer an aromatic center in the cationic state after the oxidation of the DT rings. On the other hand, odd-numbered [*n*]radialenes received interest as possible candidates for CT-type organic ferromagnets, because they can possess a pair of degenerate highest occupied molecular orbitals (HOMOs), assuming a molecular symmetry of C_n or higher [40].

8.3.1
[4]- and [6]Radialenes with DT Rings

Misaki *et al.* [41] synthesized the first [4]radialene derivatives having DT groups **30** in 1985. One synthesis of radialenes has been accomplished by cyclo-oligomerization of cumulene framework by a transition-metal complex catalyst [42]. Synthesis of [4]radialene **30c,e** was carried out by Ni(0)-catalyzed reductive cyclo-dimerization of **29c,e** in THF in the presence of Zn–Cu couple (Scheme 8.5). Interestingly, when the reductive coupling reaction was performed in DMF as a medium of the reaction in place of THF, the cyclotrimerization proceeded preferentially to afford [6]radialene **31c,e** together with a small amount of the corresponding [4]radialene derivatives [43]. The unsubstituted [4]radialene **30d** was obtained by demethoxycarboxylation of **30c** with LiBr·H_2O in HMPA.



Scheme 8.5 Synthesis of DT-substituted [4]- and [6]-radialenes.

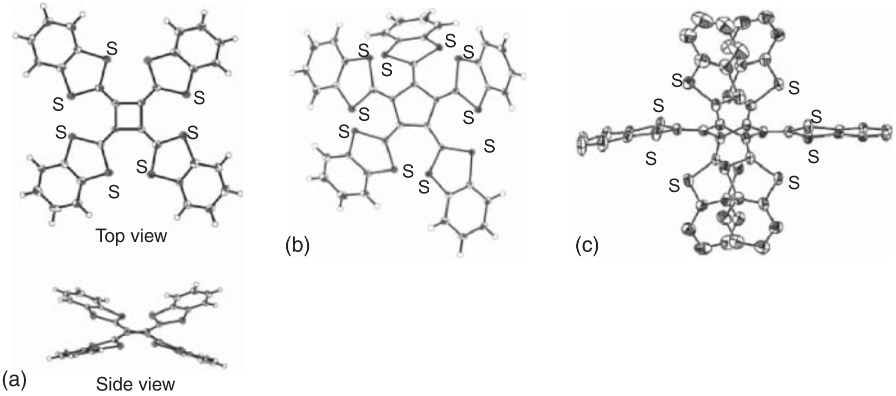


Figure 8.14 X-ray structures of (a) **30e**, (b) **33e**, and (c) **31e**. Reproduced with permission from Ref. [41, 43, and 44] © 1985, 1987, 1989 American Chemical Society.

The molecular structures of the [*n*]dendralenes **30e** and **31e** were determined X-ray analysis. The radialene core and four DT rings of **30c** possess approximate D_{2d} symmetry with a puckered structure (Figure 8.14). As for the [6]dendralene, a twisted-boat conformation of the central six-membered ring in **31d** was found. It is particularly worth noting that the central core of **31d** adopts a twisted-boat conformation, because such a twisted structure in a six-membered ring is rarely determined by X-ray structure analysis (see p. 102, above). The observed twisted conformation would seem to be a metastable structure that might be derived from kinetic formation in Ni(0)-catalyzed cylcotrimerization. Indeed, heating of **31d** in an appropriate solvent induces a quantitative conformational change to give another conformer **31d′**, whose spectra suggest a more stable chair conformation.

The redox potentials of several [4]- and [6]-radialenes are summarized in Table 8.5. The CVs of [4]radialene **30a–c** exhibit three redox peaks containing one two-electron transfer and two one-electron transfer processes. In contrast, the CVs of the vinylogous TTF **2a–c**, which have structures equivalent to halves of [4]dendralene, show two successive one-electron transfer processes. The redox potentials of $\mathbf{30c{-}e}/\mathbf{30c{-}e}^{2+}$ ($E_1{}^{1/2}$-values of −0.23 to 0.23 V), are much lower than the corresponding potentials of $\mathbf{2}^{\bullet +}/\mathbf{2}^{2+}$ (−0.04 to 0.36 V). These results indicate a remarkable decrease on the on-site Coulomb repulsion in **30c–e** by the efficient delocalization of two positive charges over the central radialene core. Concerning [6]radialene, the first oxidation potentials of **31c** and **31e** are comparable or slightly higher than those of **2c** and **2e**. However, the $E_1{}^{1/2}$ values are considerably lower (about 0.4 V) than those of the other conformer of **31c′** and **31e′**, suggesting a more effective conjugation between the adjacent outer DT rings. These facts are consistent with the observation of bathochromic shifts in the electronic spectra of **31c**,**e** compared with **31c′**,**e′** under identical conditions. Interestingly, multicycle scanning voltammetry indicates that conformational conversion of **31c,e** to **31c′**,**e′** in the dicationic state occurs even at room temperature.

Table 8.5 Redox potentials of DT[4]- and DT[6]-radialenes and related compounds$^{a)}$.

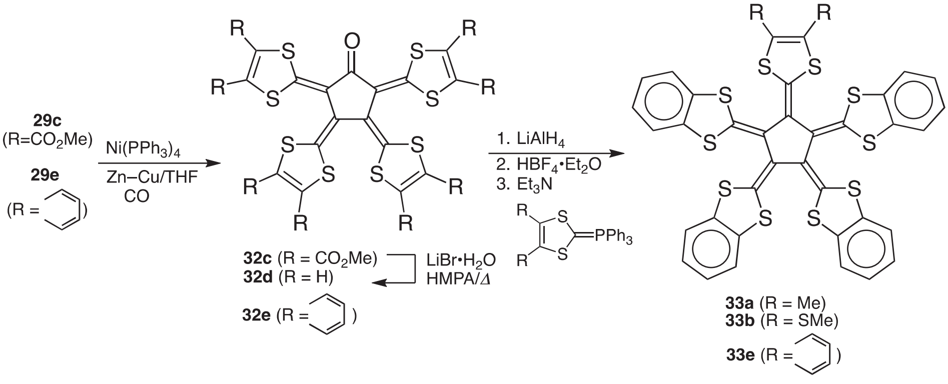
Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$
30c (R = CO_2Me)	0.23 ($2e^-$)	$0.83^{b)}$	$1.32^{b)}$
30d (R = H)	−0.23 ($2e^-$)	$0.54^{b)}$	$0.97^{b)}$
30e (2R = $(CH{=}CH)_2$)	0.00 ($2e^-$)	$0.63^{b)}$	$1.13^{b)}$
31c^{c} (R = CO_2Me)	0.27	$0.43^{b)}$	—
31c′^{d} (R = CO_2Me)	$0.68^{b)}$($2e^-$)	—	—
31e^{c} (2R = $(CH{=}CH)_2$)	−0.03	$0.19^{b)}$	—
31e′^{d} (2R = $(CH{=}CH)_2$)	$0.36^{b)}$($2e^-$)	—	—
2c (R = CO_2Me)	0.15	0.36	—
2d (R = H)	−0.23	−0.04	—
2e (2R = $(CH{=}CH)_2$)	0.00	0.18	—

a) In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.
b) Irreversible redox.
c) Twisted-boat conformation.
d) Chair conformation.

8.3.2
[5]Radialene with DT Rings

The synthesis of DT[5]radialene is depicted in Scheme 8.6 [44, 45]. Ni(0)-catalyzed reductive cyclodimerization from **29c,e** in THF under carbon monoxide atmosphere gave the cyclopentanone analogs of **32c,e**, respectively. Hydrolysis and subsequent decarboxylation from **32c** gave **32d** in good yield. The reduction of **32e** by $LiAlH_4$ and treatment with $HBF_4{\cdot}Et_2O$, followed by Wittig reaction in the presence of Et_3N gave DT[5]radialene **33a,b**, and **33e**.

The cyclopentanone analogs **32c–e** show two pairs of two-electron redox waves corresponding to the redox processes of the four DT groups in the CV (Table 8.6). The first redox potentials of **32c–e** are found to be lower than those of the corresponding [4]radialenes **30c–e** (Table 8.5) despite the insertion of



Scheme 8.6 Synthesis of DT[5]radialene **33a,b,e**.

Table 8.6 Redox potentials of DT[5] radialenes[a)].

Compound	$E_1^{1/2}$	$E_2^{1/2}$
32c (R = CO_2Me)	0.18 ($2e^-$)	0.89 ($2e^-$)
32d (R = H)	−0.29 ($2e^-$)	0.68 ($2e^-$)
32e (R = CH═CH–CH═CH)	−0.05 ($2e^-$)	0.76 ($2e^-$)
33a (R = Me)	−0.16 ($2e^-$)	−0.04 ($2e^-$)
33b (R = SMe)	−0.04 ($4e^-$)	—
33e (R = CH═CH–CH═CH)	−0.01 ($4e^-$)	—

a) In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.

an electron-withdrawing C═O group into the central ring. The second redox potentials are also lower by about 0.3–0.4 V than the third redox step ($E_3^{1/2}$) of **30c–e**. Taking into account of the fact that antiaromaticity of cyclopentadienone and cyclobutadiene of the central ring contribute to the teracationic species of **30**$^{4+}$ and **32**$^{4+}$, respectively, the lowering of the redox potentials of **41** can be attributed to the lower antiaromaticity of cyclopentadienenone compared to that of cyclobutadiene.

In contrast to this behavior, [5]radialenes **33b** and **33e** exhibit notable redox processes, that is, a four-electron transfer occurring simultaneously. Detailed digital simulation analysis assuming Nernstian response in **33e** led to the conclusion that the apparent one-step four-electron redox wave involved two redox couples of **33e**/**33e**$^{2+}$ and **33e**$^{2+}$/**33e**$^{4+}$ estimated at −0.074 and −0.066 V (vs Fc/Fc^+), respectively. In fact, the CV of **33a** having two electron-donating methyl groups clearly exhibits two pairs of two-electron-reversible redox waves. These results suggest that [5]radialenes are subject to a two-step two-electron transfer and sequentially converted into the dication **33**$^{2+}$ and subsequently into the tetracation **33**$^{4+}$.

When the tetracation salt **33e**$^{4+}$ was prepared by chemical oxidation with $NOBF_4$, it showed five signals reflecting an apparent C_5 structure in its ^{13}C NMR chemical shifts. In addition, the chemical shifts of DT rings correspond to DT rings in the tetracationic species and are quite similar to those of 4,5-benzo-1,3-dithiolium salt **34e**$^{+}\cdot BF_4^-$. Thus, the simultaneous four-electron transfer process in **33e** is attributed to a particular stabilization of **33e**$^{4+}$, whose central five-membered ring strongly contributes to the aromatic cyclopentadienide characteristic (Figure 8.15). The same interpretation can be applied to the redox behavior of **33a** and **33b**.

The detailed electronic structure was elucidated by spectroelectrochemistry. The absorption bands in electronic spectra of **33a**$^{2+}$ and **33e**$^{2+}$ are basically similar. The absorption of **33a**$^{2+}$ at longer wavelength ($\lambda_{max} = 993$ nm), however, appears more clearly than that in **33e**$^{2+}$ ($\lambda_{max} = 883$ nm). The spectrum of **33a**$^{4+}$ exhibits the longest absorption maximum at 528 nm, while the corresponding

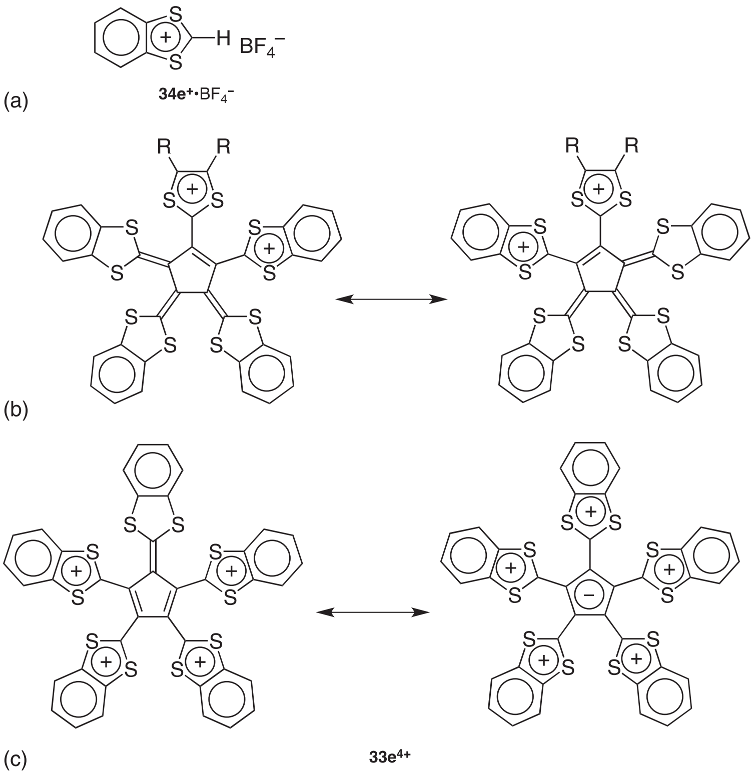


Figure 8.15 (a) Molecular structure of **34e**$^{+}$·BF$_4$$^{-}$, and possible electronic structure of (b) **33e**$^{2+}$ and (c) **33e**$^{4+}$.

absorption maximum of **33a**$^{4+}$ was found at 525 nm. Comparing the difference between dication and tetracation in **33a** and **33e**, a large redshift of the longest absorption band in **33a** by about 470 nm, compared to that of **33e**$^{2+}$, was observed. Considering the highly hindered structure of DT[5]radialene, **33**$^{2+}$ presumably adopts a conformation with a delocalized positive charge over the two DT units that are effectively conjugated with each other, as shown in Figure 8.15b,c.

Very recently, oxidative species other than cation radicals have been found while growing single crystals of the tetracationic species of **33e** [46]. The ion-exchange reaction of (**33e**$^{4+}$)·($BF_4{}^{-}$)$_4$ with excess amounts of $^{n}Bu_4N^{+}\cdot PF_6{}^{-}$ gave single crystals of the oxygen adduct of **35** with $AsF_6{}^{-}$ in addition to a large quantity of powdered precipitates (Figure 8.16). A plausible mechanism for the formation of **35** might begin with a nucleophilic addition of water, originating from an impurity in the solvent, followed by nucleophilic cyclization. The unit cell contains unique molecules of (**35**$^{2+}$)·($AsF_6{}^{-}$)$_2$(PhCl)$_{1.5}$. The central rings A and B are almost planar, and the DT rings of E and F are almost perpendicular. The mean deviation of the C–C bond length in the ring A is found to be 0.01(1) Å, suggesting that ring A possesses an aromatic cyclopentadienyl structure.

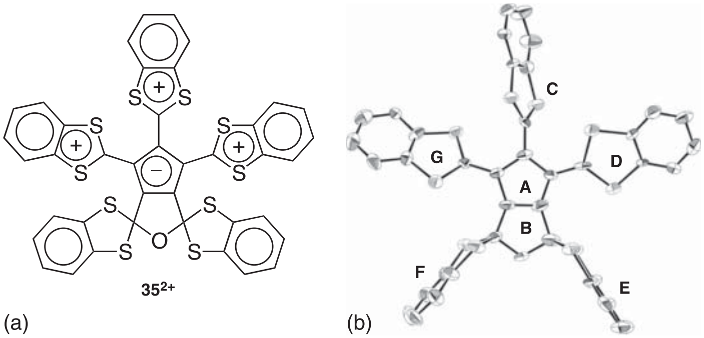
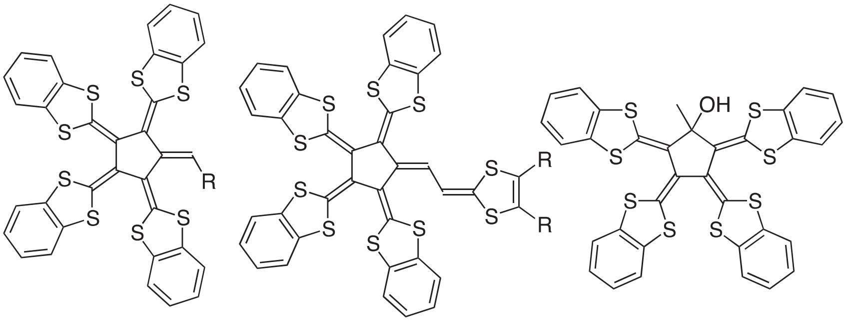


Figure 8.16 (a) Molecular structure of **35** and (b) X-ray crystal structure of **35^{2+}**. Reproduced with permission from Ref. [46] © 2016 The Chemical Society of Japan.



36: R = 2-Thienyl
37: R = Ph

38a (R=Me)
38b (R=SMe)

39

Figure 8.17 Molecular structures of **36**–**39**.

8.3.3
Extended [5]radialenes

One of the authors and his coworkers have reported a series of further π-extended DT[*n*]radialenes (see Chapter 9) of **36**, **37**, and **38a,b** (Figure 8.17) [47]. These radialene derivatives were designed to elucidate the electronic structure of [5]radialenes with different conjugation modes.

The redox potentials are summarized in Table 8.7. The CV of **36**, **37**, and **38a** exhibited two two-electron redox waves, whereas the CV of **38b** showed one simultaneous four-electron transfer process. The shape of CV chart in **36** and **37** depend remarkably on the scan rate. It is suggested that the oxidation of **36**/**36^{2+}** or **37**/**37^{2+}** could occur in association with structural or conformational changes. Although the $E_2^{1/2}$ values of **36** and **37** were found to be lower by 0.12–0.15 V than that of **39**, they were higher by 0.24–0.32 V than that of DT[5]radialene **33a,b** and **33e** (Table 8.6). This result indicates that a cyclopentadienide structure contributes to **36^{4+}** or **37^{4+}** to some extent, in addition to a fulvalene structure (Figure 8.17). Interestingly, the redox potentials of **$38a^{2+}$**/**$38a^{4+}$** and **38b**/**$38b^{4+}$**,

Table 8.7 Redox potentials of DT[5] radialenes [a].

Compound	$E_1^{1/2}$	$E_2^{1/2}$
36	0.05 ($2e^-$)	0.25 ($2e^-$)
37	0.05 ($2e^-$)	0.28 ($2e^-$)
38a (R = Me)	−0.12 ($2e^-$)	−0.04 ($2e^-$)
38b (R = SMe)	−0.04 ($4e^-$)	—
39	0.05 ($2e^-$)	0.40

[a] In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.

Table 8.8 Redox potentials of **40–42** and related compounds[a].

Compound	$E_1^{1/2}$	$E_2^{1/2}$	$E_3^{1/2}$	$E_4^{1/2}$
40	−0.04 ($4e^-$)	0.40	0.63	—
41	−0.03 ($4e^-$)	0.16	0.41	0.87 ($2e^-$)
42	0.01 ($8e^-$)	0.86	1.07	—
43	0.04	0.36	—	—
44	0.07	0.28	0.56	0.70

[a] In PhCN containing 0.1 M Bu_4PF_6, V versus Fc/Fc^+.

which are $E_2^{1/2}$ in **38a** and $E_2^{1/2}$ in **38b**, respectively, are identical at −0.04 V. In addition, this redox potential is also the same as those of DT[5]radialenes **33a**/**33a**$^{4+}$ and **33b**/**33b**$^{4+}$ (−0.04 V). Therefore, the electronic structure of **38**$^{4+}$ might adopt a cyclopentadienide structure similar to that of **33**$^{4+}$. The elucidation by electrospectroscopic analysis is also consistent with these results.

Quite recently, fused TTF analogs having one or two [5]radialene unit(s) **40–42** have also been prepared (Figure 8.18), because the extended TTF moieties are of interest as multi-redox systems, components for molecular conductors, positive electrode materials for rechargeable batteries, and so on [48].

The electrochemical properties of these fused [5]radialenes were investigated by CV and Differential Pulse Voltammetry (DPV) (Table 8.8). The TTP-fused donor **40** and **41** possess three or four pairs of reversible redox waves in the CV, whereas the CV of [5]dendralene **33b** exhibits only one four-electron transfer process. The first redox process of **40** and **41** contains simultaneous four-electron redox processes. As for **41**, the highest redox wave $E_4^{1/2}$ corresponds to a two-electron transfer process. On the other hand, the CV of **42** exhibits three pairs of redox waves similarly to **40**. Interestingly, the peak current of the first redox wave is about 10 times larger than those of the others. This strongly indicates that the first redox wave involves a simultaneous eight-electron transfer process. Presently, this is the only example of a simultaneous eight-electron process in π-conjugated systems.

Spectroelectrochemistry of **42**, applying constant voltage at 0.19 V, provided a spectrum corresponding to octacationic species of **42**$^{8+}$, exhibiting absorption maxima of 402, 514, and 682 nm (Figure 8.19). The spectrum resembles that of

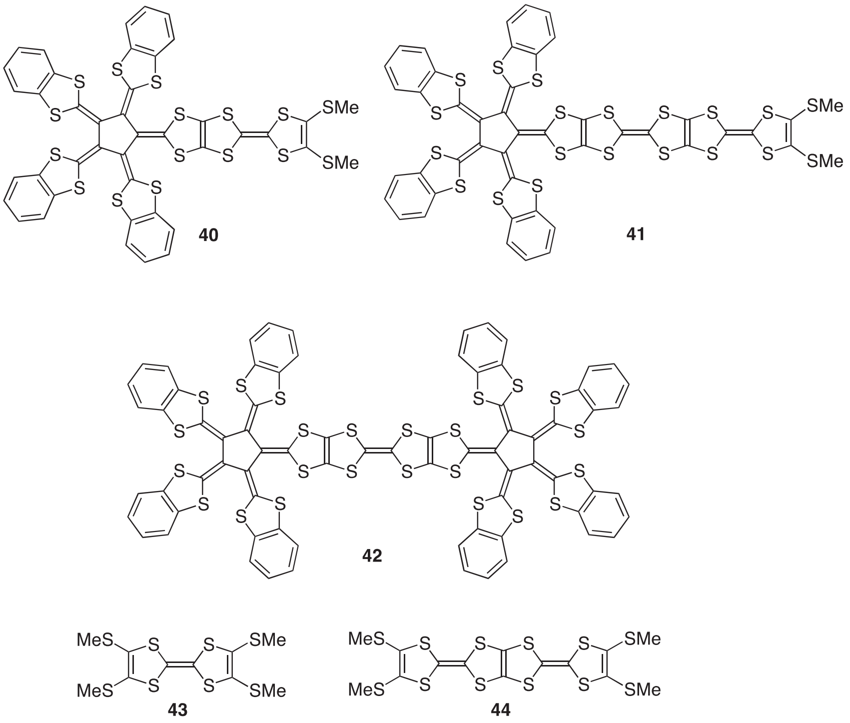


Figure 8.18 Molecular structure of **40–44**.

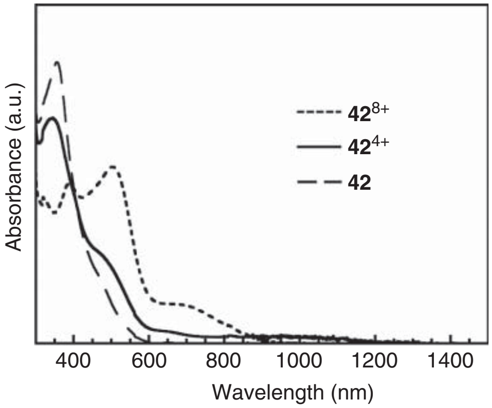


Figure 8.19 Electronic spectra of **42** and its oxidative species. Reproduced with permission from Ref. [48] © 2013 American Chemical Society.

DT[5]radialene tetracation $\mathbf{33}^{4+}$ (397 and 519 nm) except for the absorption at 682 nm. This implies that four positive charges are mainly localized at the radialene moieties. The observed band at 682 nm can be attributed to intramolecular CT from the central TTP core to the radialene units.

8.4
Cross-Conjugated TTFs and Related Compounds Linked by π-Systems

8.4.1
TTFs in Cross-Conjugated Systems

TTF dimer and higher oligomers connected by a cross-conjugated system are expected to provide a stable high-spin system. Fukumoto and coworkers [49] predicted that the radical cationic species of **45** would show a high-spin ground state. In this connection, TTF dimers linked by a carbonyl function, as in **46**, and ethylene **47a–e**, **48**, have been synthesized (Figure 8.20) [50, 51]. In the CV, all donors show reversible two-redox waves corresponding to the formation of TTF/TTF$^{\bullet+}$ and TTF$^{\bullet+}$/TTF^{2+}, respectively, in spite of the number of TTF units. Although dicationic species of **45–48** are expected to show a stable triplet ground state, the dication **46**$^{2+}$ in the CT complex reveals a singlet biradical nature, presumably because it is fairly well stabilized [52]. In contrast, the cation radical salt of **47a** with iodine shows interesting magnetic and electrical behavior. Thus, the ESR spectrum of the salt at low temperature involves a broad signal at the center and a fine structure along with $\Delta m_s = 2$ signals arising from triplet species. These results pave the path for the synthesis of polymeric analogs with high-spin state as represented by **45**.

Iyoda and coworkers [53] have synthesized cross-conjugated dimeric TTF bridged by 1,3-phenylene **49** and trimeric TTFs **50** by using palladium-catalyzed cross-coupling reaction of corresponding iodobenzene and trimethylstannyl-TTF in good yields. Their dication **49**$^{2+}$ and trication **50**$^{3+}$ can be expected to show a ferromagnetic interaction between TTF$^{\bullet+}$ units (Figure 8.21). In the case of **50**$^{3+}$, both doublet and quartet ground states should exhibit ferromagnetic interactions.

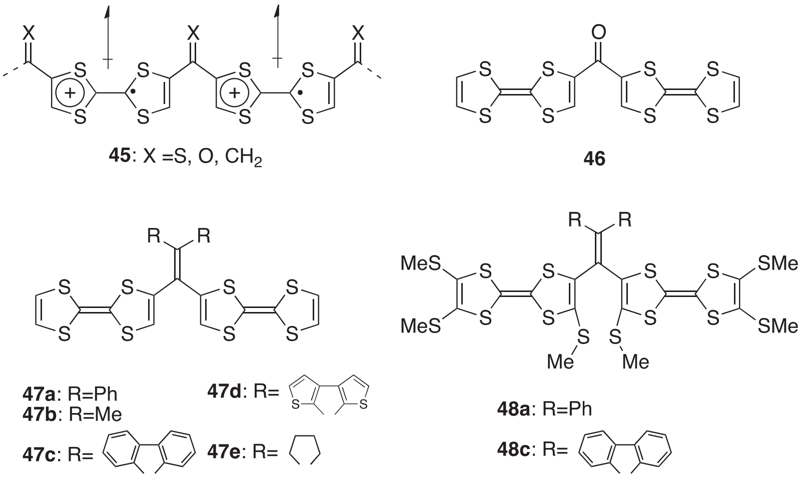


Figure 8.20 Cross-conjugated dimeric and polymeric TTFs.

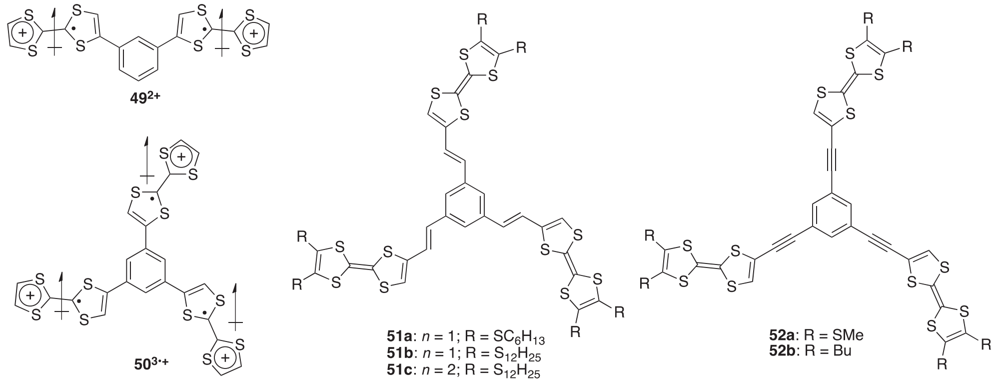
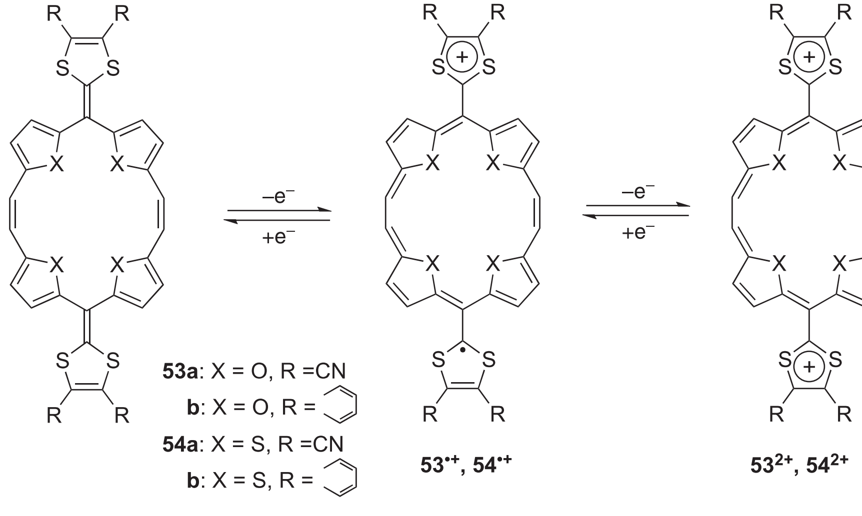


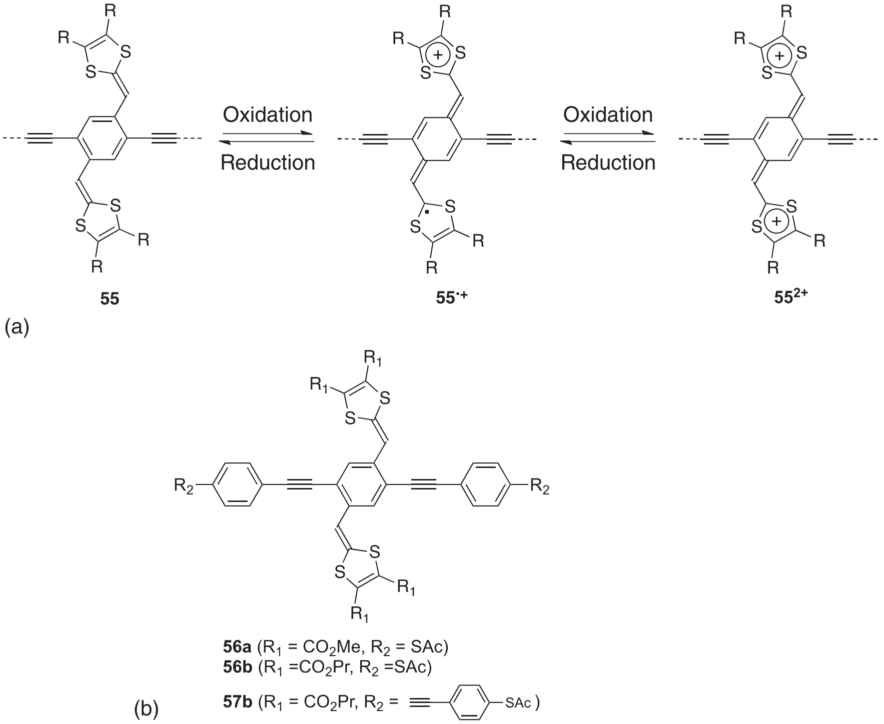
Figure 8.21 Cross-conjugated TTFs having a benzene core.

However, the through-bond interaction in the cross-conjugation is very weak in the ground state, and hence there is almost no spin–spin interaction. A few other examples of cross-conjugation systems with a 1,3,5-tri-substituted benzene core, **51** [54] **52** [55], were also synthesized. Although they could be cross-conjugated systems with C_3 symmetry, their detailed spin states have not been investigated yet. As for compound **52**, a strong self-association behavior though π–π and S· · ·S interactions was observed both in the solid and in solution.

Annulenoid TTF of **53**, **54** were reported by Märkl and coworkers [56]. Two terminal DT rings fix the central annulene rings, whose electronic structures can be tuned by redox reactions of its DT rings via the cross-conjugated system (Scheme 8.7). Cyclization reactions by titanium-catalyzed McMurry coupling of the aldehyde precursors leads to a mixture of several stereoisomers.



Scheme 8.7 Possible redox process of annulenoid TTFs of **53** and **54**.



55 **$55^{\cdot+}$** **55^{2+}**

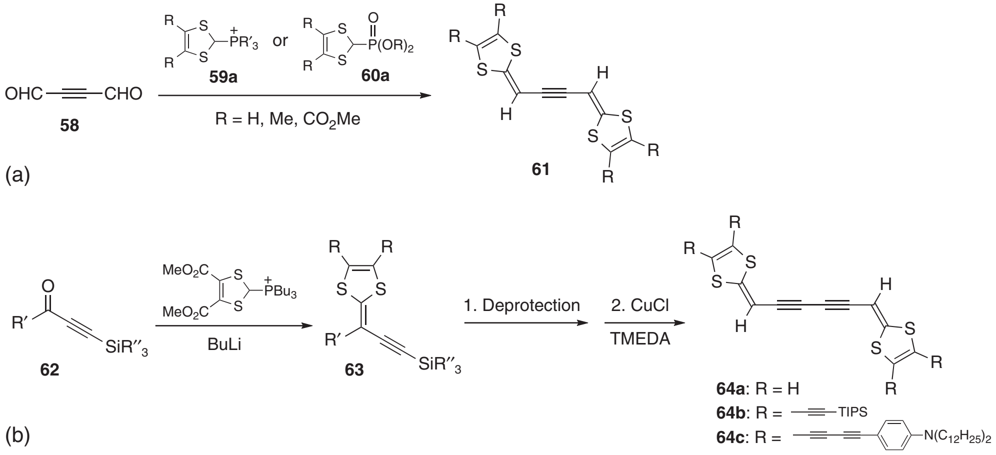
(a)

56a (R_1 = CO_2Me, R_2 = SAc)
56b (R_1 =CO_2Pr, R_2 =SAc)
57b (R_1 = CO_2Pr, R_2 =)

(b)

Figure 8.22 (a) Redox process of OPE-TTF cruciform **55**. (b) Molecular structure of OPE-TTF cruciform **56**, **57** for SAMs.

Nielsen and coworkers [57, 58] have reported further interesting studies toward molecular electronics based on cross-conjugated cruciform molecules of **56** containing DT rings (Figure 8.22). Oligo(phenyleneethynylene) (OPE)-TTF cruciform molecules wedged between two thiole end groups can be considered as molecular junctions when they are utilized as self-assembled monolayers (SAMs) on a substrate. The simplest redox process of the cruciform **55** is depicted in Figure 8.22a. Two-electron oxidation on the two DT ring units at the lateral position of the OPE can change the π-electron delocalization along the OPE backbone from linear- to the cross-conjugated pattern. This idea can be applied to redox-triggered switches for molecular electronics. Recently, Laursen and Nørgaard, together with Nielsen and coworkers, evaluated the electrical properties of the SAMs by using conducting probe-atomic force microscopy (CP-AFM) on a gold substrate [59]. The conductance of SAMs prepared from the treatments of **56b** and **57b** with Et_3N was much higher than that of SAMs from the corresponding normal OPE chain by a factor of 10. Together with quantum calculations, these results demonstrated that the effect of “through-bond” interactions dominates the transport in these molecular junctions.



Scheme 8.8 Syntheses of TTF analogs with acetylenic, **61**, and diacetylenic spacers, **64**.

8.4.2
Acetylene-Extended Tetrathiafulvalenes in Cross-Conjugated Systems

In 1990, Gorgues and coworkers [60, 61] reported the earliest studies of extended TTFs by acetylene scaffolding **61**, in order to decrease on-site Coulomb repulsion. The symmetrically substituted acetylenic analog **61** was prepared from a very reactive aldehyde (**58**) [62] by Wittig or Horner–Wadsworth–Emmons reactions (Scheme 8.8). The CV of **61** exhibited reversible one two-electron redox pair corresponding to **61**/$\mathbf{61}^{2+}$. This behavior is different from the TTFVs series of **2**, which is linked by an ethylene spacer, due to lack of electronic communication through the acetylenic bond in $\mathbf{61}^{\bullet +}$.

Apart from this study, there has been growing interest in cross-conjugated systems containing diethynylethene (DEE) with several DT rings because of potential applications for various optical properties as well as two-dimensional π-conjugation network [63–65]. There is a wealth of research publications about diacetylene-extended cross-conjugated systems; we briefly summarize selected examples in this section [66–70].

Deiderich and coworkers have extensively explored the versatility of the TTF analogs inserted into acetylenic scaffolds (**64**–**68**), and they investigated the substitution and conjugation effects on the electronic and chromophoric properties [66]. Wittig-type reaction of α-acetylenic ketone with **62** under basic condition gave acetylenic analog of **63** as the key building unit for acetylenic scaffolds (Scheme 8.8b). Oxidative coupling after desilylation gave diethynyl-inserted TTF analog of **64**. The repetition of oxidative coupling reactions of ethynyl fragments gave other extended TTFs with, for example, diyne spacers **65**–**68** (Figure 8.23). Further examination of the nonlinear optical responses by using third-harmonic generation (THG) measurements was also performed, and the second-order hyperpolarizabilities' values γ were determined. Incorporation

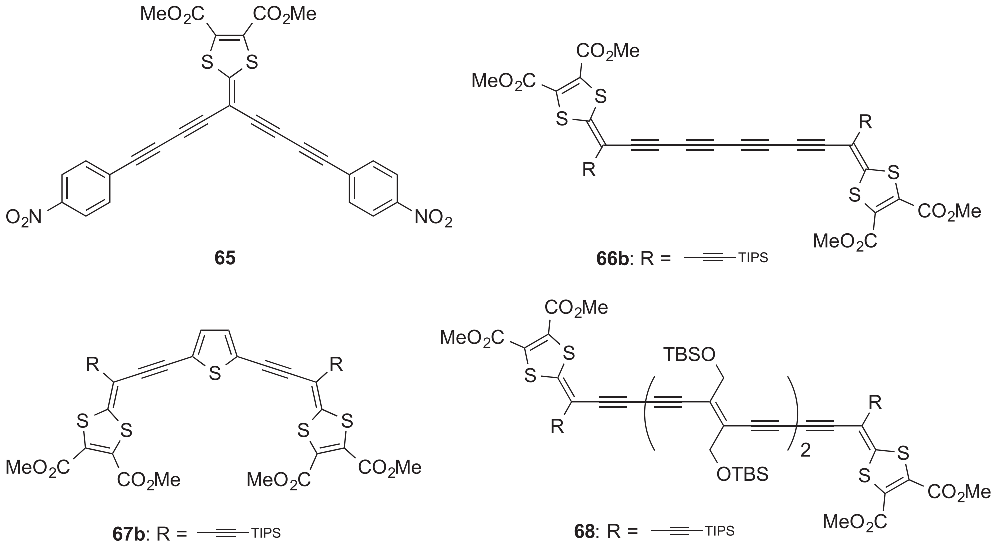
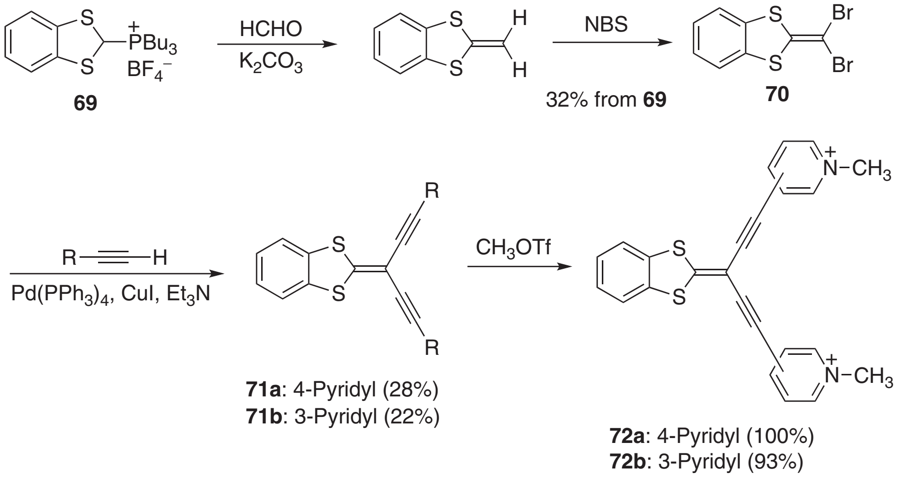


Figure 8.23 A series of extended TTFs linked with acetylene and diyne spacers.

of donor/acceptor substituents enhances the γ values that are promising for future nonlinear optics (NLO) application. Nielsen and coworkers have prepared cross-conjugated donor–acceptor chromophores based on the phenylene group with two redox-active DT ring units.

The Y-shaped 1,3-dithiole-2-ylidene unit, inserted into an acetylene scaffold, was also utilized as a building block for a two-dimensional network in crystals. Yamashita and coworkers [71] have constructed the cross-conjugated system **71**



Scheme 8.9 Synthesis of **71** and **72**.

with anchored by bis(ethynylpyridine) units (Scheme 8.9). Sonogashira coupling was employed for the introduction of ethynylpyridine units from dibromo precursor **70**. The terminal pyridyl groups possess many opportunities to form hydrogen bonds, and can also methylated to give the dication **72** which shows intramolecular CT bands.

8.4.3
Acetylene-Extended Radialenes and Dendralenes

Expanded radialenes (see Chapter 4), produced by insertion of acetylene or diacetylene units into the radialene core, have been also prepared. They have attracted increasing attention for interesting optoelectronic properties as well as their intriguing macrocyclic cross-conjugation [72–74]. Acetylene-extended radialenes with DT-rings **73–75** can be viewed as a new class of expanded cross-conjugated systems bearing redox units (Figure 8.24a). Despite possible fascinating redox properties and the cross-conjugated nature of the homologous series of extended DT[*n*]radialene, their syntheses have not been achieved on a comprehensive scale so far.

Zhang and coworkers [75] reported the only example of a heteroatom-substituted expanded radialene **77**, a 1,3-dithiolan[5]radialene (Figure 8.24b). This

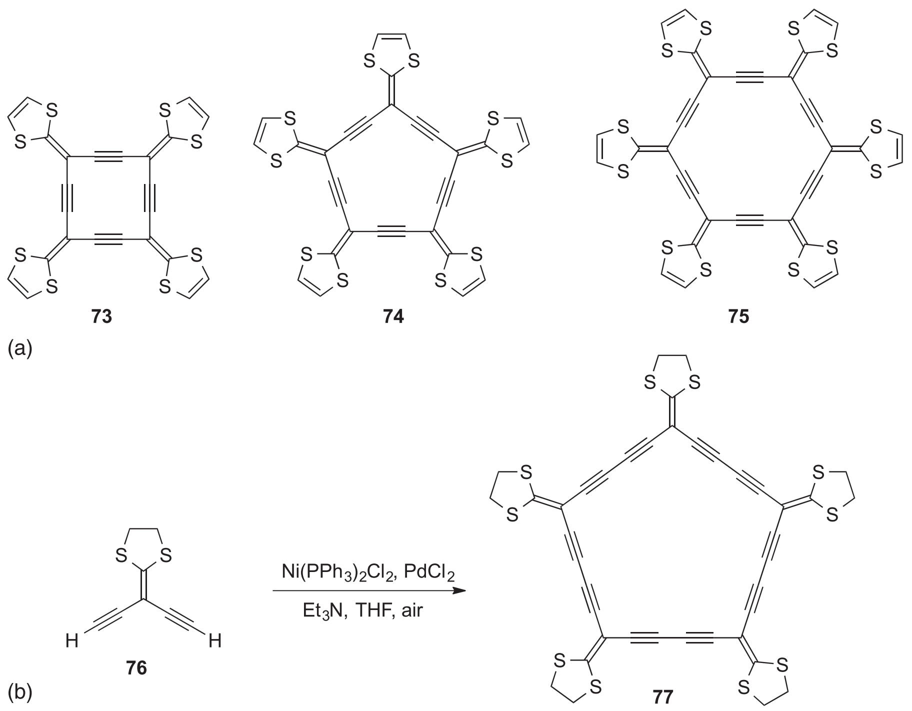


Figure 8.24 (a) Acetylene-extended DT[*n*]radialene series. (b) Synthesis of **77**.

expanded radialene was prepared in a one-pot protocol by an oxidative coupling reaction of α-enediyne **76** with a catalytic amount of $[\mathrm{Ni(PPh_3)_2Cl_2}]-\mathrm{PdCl_2}-\mathrm{CuI}$ (Figure 8.24b). X-ray crystallographic analysis of **77** revealed a nonplanar, envelope-like conformation and the formation of an inclusion complex by insertion of a DMSO molecule into its cavity. Furthermore, the introduction of a polar alkylthio group results in strong intramolecular push–pull interactions and enhanced macrocyclic cross-conjugation.

Zhao and coworkers [76] have synthesized an extended shape-persistent macrocycle **80**, which is associated with an π-extended DT[6]radialene composed of acetylene extended TTFV. The key unit of TTFV **79** was prepared by oxidative coupling reaction of the acetylenic precursor **78** (Scheme 8.10). As the TTFV moieties adopt wedge-like conformation, the oxidative coupling of **72** easily afforded the cyclic structures of **80**. The CV of the macrocyclic compounds showed a reversible redox wave corresponding to TTFV units, implying the absence of the interaction through the acetylenic spacer. A different coupling sequence from the vinylog **81** gave a linear polymer of **82**. From comparison of the electronic spectra, the polymer of **82** would adopt a helical orientation resulting from a *cisoid* conformation of the cross-conjugated TTFV moieties. These could change into the linear structure **83** upon oxidation reactions.

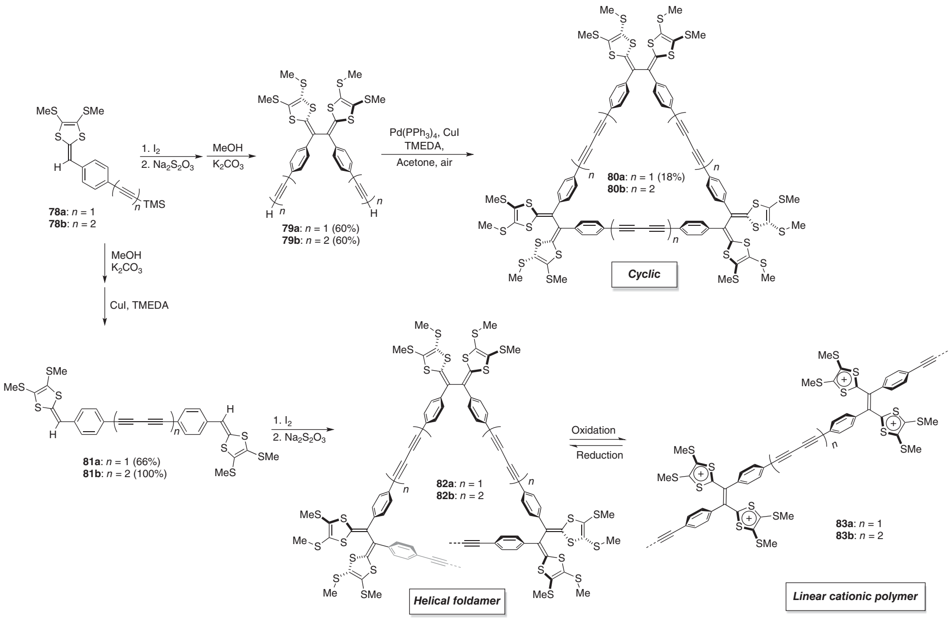
Very recently, Adronov and coworkers [77] reported on a conformational switchable copolymer **77** based on TTFV and fluorene (Scheme 8.11). When this polymer is mixed with single-walled carbon nanotubes (SWNTs), a stable supramolecular complex is obtained. The strong surface interactions between cross-conjugated TTFV and SWNT allow the formation of their homogeneous dispersion in various solvents. The desorption of the copolymer from the SWNT proceeds upon addition of trifluoroacetic acid (TFA) that leads to rapid conformational changes of the cross-conjugated parts of TTFV from a *cisoid* to a *transoid* structure. Interestingly, the purity of the SWNTs after their release from the complex is higher than in the initial dispersion.

8.4.4

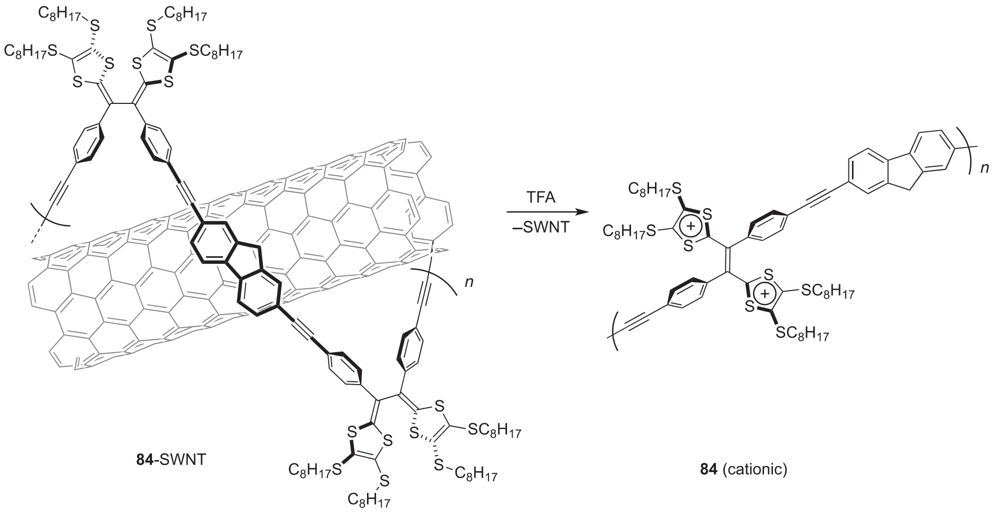
Cross-Conjugated Systems in Acetylene-Extended Radiaannulene Frameworks

In recent years, several groups have reported on a series of radiaannulenes incorporating TTF or DT rings. Radiaannulenes are hybrid frameworks composed of a cross-conjugated radialene and a linearly conjugated dehydroannulene [78–81]. These compounds possess a so-called prearomaticity; that is, the ability of the compound to form aromatized mesomeric 14π-electron system as the result of oxidation or reduction (Scheme 8.12).

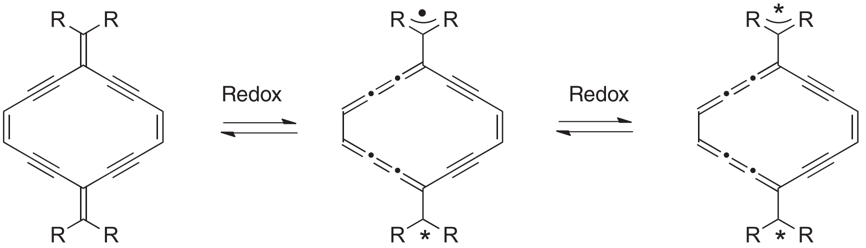
Zhao and coworkers [82, 83] have also reported on the dibenzo-annulated radiaannulene compounds **87** and **88** containing DT rings at their terminal positions (Figure 8.25). From the X-ray crystallographic analyses, the central radiaannulenes units in both **87** and **88** adopt almost planar structures. In addition, the bond length alternation (BLA) indexes of **87** and **88** are found to be 0.165 and 0.155 Å, respectively, owing to a moderate π-delocalization of the central cyclic



Scheme 8.10 Synthesis of **80** and **82**.



Scheme 8.11 Supramolecular complexation of copolymer of TTFV-fluorene **84** with SWNT.



85: R,R = EDG
86: R,R = EWG

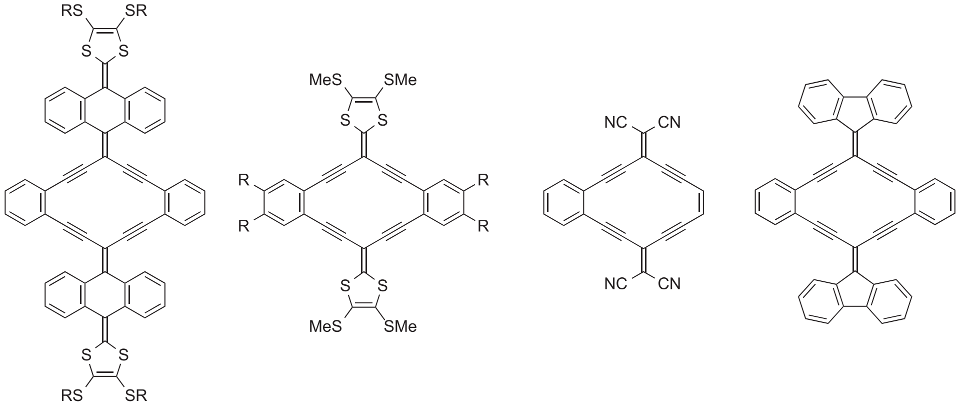
$85^{\bullet+}$: R,R = EDG, * = +
$86^{\bullet-}$: R,R = EWG, * = –

85^{2+}: R,R = EDG, * = +
86^{2-}: R,R = EWG, * = –

Scheme 8.12 Redox process of radiaannulene frameworks containing redox-active substituents.

radiaannulene segment. Although an electronic communication can be anticipated between two DT rings in this system, only irreversible redox patterns were obtained in CV measurements. The authors concluded that the lack of reversibility in the CV is presumably due to electrochemically promoted reactions of the formed cationic species (Figure 8.25).

In sharp contrast, other related radiaannulenes (**89**) terminated with dicyano methylene units – which are strong electron-withdrawing groups – possess a fairly high electron affinity, and its CV exhibits good reversibility upon reduction [84]. Similar high reversibility in redox processes was also observed in another electron-accepting system, **90** [85]. In addition, anionic species of **$89^{\bullet-}$** and **89^{2-}** are smoothly generated by electrochemical reduction without decomposition. The generated anion radical of **$89^{\bullet-}$** exhibits a pronounced charge resonance (CR) band at 1292 nm in the electronic absorption spectra together with an



87a: R = CH_3
87b: R = $C_{10}H_{21}$

88a: R = CH_3
88b: R = $C_{10}H_{21}$

89

90

Figure 8.25 Molecular structures of radiaannulenes **87–90**.

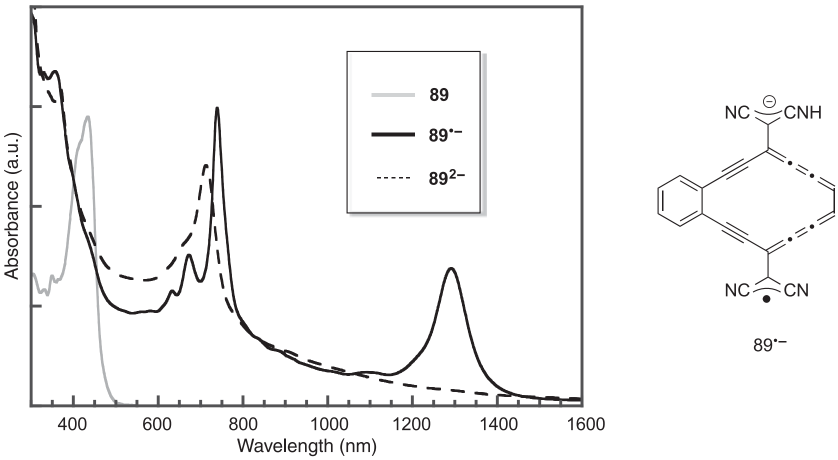


Figure 8.26 Electronic spectra of **89** and its reduced species. Reproduced with permission from Ref. [84] © 2012 Elsevier.

intrinsic absorption band (Figure 8.26). It clearly indicates that a strong electronic interaction of an MV state is present in the anionic radiaannulene framework, in contrast to the situation prevailing in the corresponding cation.

Recently, a hybrid radiaannulene **90** containing electron-donating TTFs and electron-accepting TEE moieties has been prepared by Nielsen and coworkers [86]. This system can be considered as a two-stage Weitz-type redox system, which leads to the aromatic 14π-annulene structure by either oxidation or reduction. Thus, CV analysis clearly showed three reversible oxidation waves corresponding to the formation of three redox states (+1/+2/+4) and showed two reversible reduction waves corresponding to two redox states (−1/−2). From the

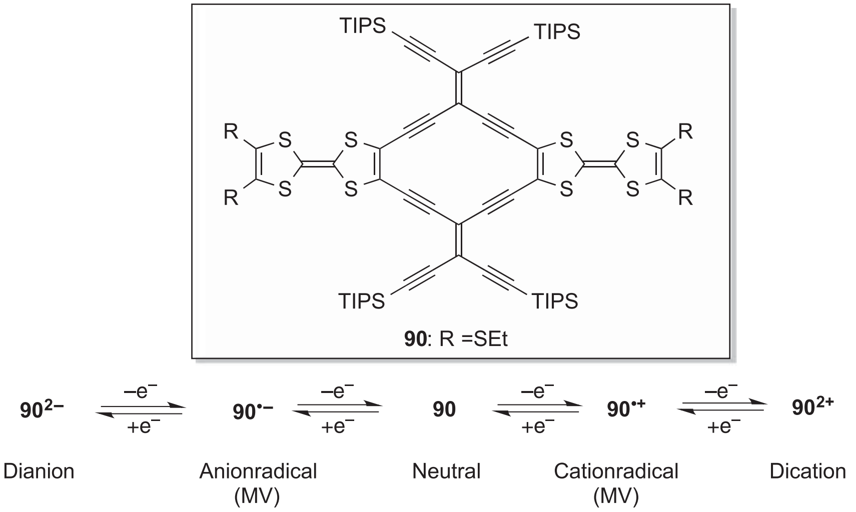


Figure 8.27 Molecular structure of **90** and its redox behavior.

electronic spectra of **90**$^{\bullet +}$, the radiaannulene (RA) core allows a mixed valence state of TTF-RA-TTF$^{\bullet +}$. This was characterized by a CR band in the IR spectrum (Figure 8.27).

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9
Cross-Conjugation in Expanded Systems

Christian Richard Parker and Mogens Brøndsted Nielsen

9.1
Introduction

Tuning of redox and optical properties by inserting a π-conjugated bridge between two redox-active or chromophoric units has been widely exploited in the quest for advanced optical or conducting materials. In this chapter we shall examine how cross-conjugated bridges alter the electronic communication between such units in comparison to linearly conjugated bridges (Figure 9.1). We shall highlight redox-active end groups (X and Y) that are either of organic or organometallic nature. As π-conjugated spacers, oligoenes, oligoynes, oligoenynes, aromatics, and larger macrocycles are of particular interest. It is worth noting that a *meta*-substituted aromatic compound corresponds to a cross-conjugated system, while *ortho*- and *para*-substituted aromatic compounds are linearly conjugated, and comparing the properties of regioisomeric benzene derivatives therefore also provides information on cross-conjugation. We will also examine how single-molecule conductances are influenced by the conjugation pathway. Thus, recent advances in "molecular electronics" have established structure–property relationships and we are now starting to be able to compare optical and electrochemical properties with conductance measurements on single molecules adhered via suitable end groups between two electrodes in a nanojunction. From illustrative examples, our goal is to answer the fundamental question: *How is electronic communication between two groups, X and Y, conveyed by a cross-conjugated spacer in comparison to a linearly conjugated one?* This chapter is not a comprehensive review on all expanded cross-conjugated systems, but instead is focused on a selection of molecules with special emphasis on extended tetrathiafulvalenes (TTFs). For more comprehensive treatments of expanded systems, we refer the reader to a number of reviews [1].

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

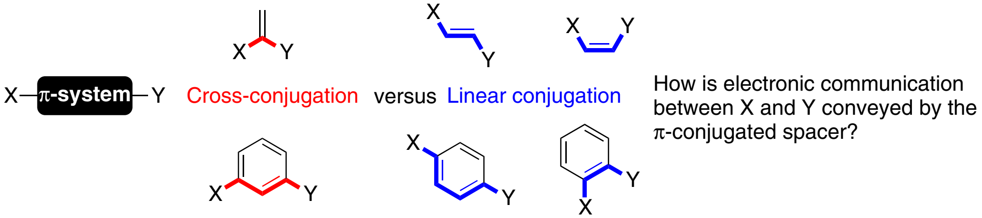


Figure 9.1 Cross-conjugation and linear conjugation in substituted alkenes and benzenes.

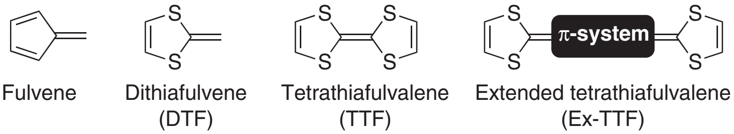
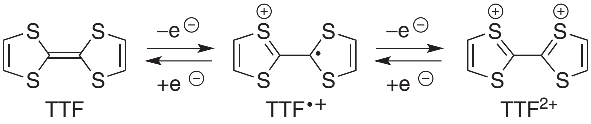


Figure 9.2 Fulvene, dithiafulvene, and tetrathiafulvalenes.

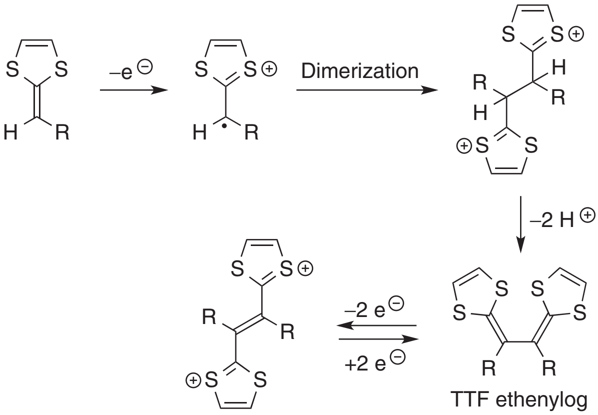
9.2
Tetrathiafulvalene and Dithiafulvene

TTF (Figure 9.2) is a redox-active molecule, which, like its dithiafulvene (DTF) "half-unit," is derived from fulvene (see Chapter 6). TTF is oxidized stepwise in two one-electron oxidations (Scheme 9.1) and has, due to these properties, been extensively employed in materials and supramolecular chemistry [2]. It can be classified as a Weitz-type [3] redox system, which, upon oxidation, gains aromaticity as each cross-conjugated DTF ring is converted into a 1,3-dithiolium ring. These oxidations are reversible and the neutral TTF is generated by stepwise reductions of the TTF dication (see Chapter 8). Separating the two DTF rings by a π-system generates *extended TTFs* with altered properties (*vide infra*) [4].



Scheme 9.1

In contrast, oxidation of monosubstituted DTFs occurs irreversibly as the radical cation generated upon oxidation dimerizes with another radical cation (Scheme 9.2) [5]. By loss of two protons from the resulting dication, a neutral TTF ethenylog is obtained. This molecule undergoes a reversible two-electron oxidation to furnish a dicationic *trans*-alkene. The two-electron oxidation is rather unusual in view of the fact that the two DTFs are so closely situated. From the X-ray crystal structure of one derivative [5b], it transpires, however, that the two DTFs are not coplanar, but almost perpendicular to each other due to steric crowding.



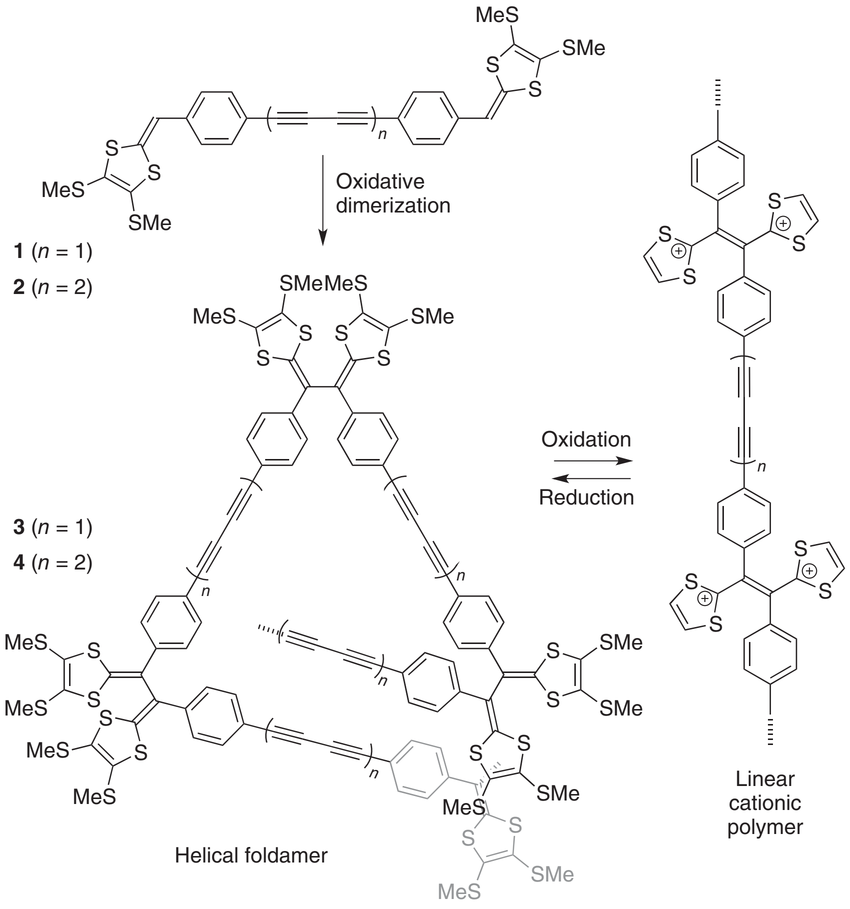
Scheme 9.2

9.2.1
Oligomers by Dithiafulvene Oxidation

The oxidative dimerization of DTFs has been employed to construct conjugated helical foldamers as shown in Scheme 9.3 [6]. Treatment of the extended TTFs **1** or **2** with I_2 as chemical oxidizing agent gave the neutral oligomers **3** (two to eight repeat units) and **4** (two to four repeat units), respectively, which were soluble in organic solvents. The neutral oligomers adopt a "helical foldamer" conformation on account of the preferred s-*cis* conformation of each TTF ethenylog unit. However, upon oxidation, a linear cationic polymer is formed with the central alkene in an *E* configuration. Electrochemical oxidation of the same compounds **1** and **2** by electrodeposition on conductive substrates gave polymers of longer lengths, which were insoluble in common organic solvents. The polymer films showed good conductance; and by redox control, the color could be switched in the ultraviolet to the near-infrared region, giving these polymers potential in electrochromic devices.

9.2.2
Anthraquinone-Extended Tetrathiafulvalenes

Anthraquinone-extended TTFs present a class of compounds with a cyclic, conjugated, π-framework between the 1,3-dithiole rings. These compounds undergo, as the TTF ethenylogs, a two-electron oxidation in one step as shown for the

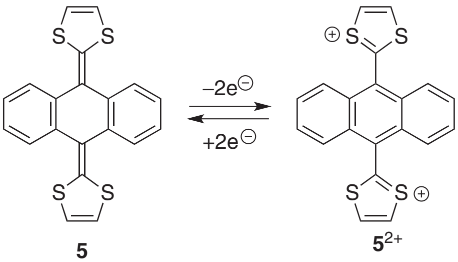


Scheme 9.3

parent compound **5** [7] in Scheme 9.4. This facile oxidation does not only generate two aromatic 1,3-dithiolium rings but also a central anthracene core. In terms of cross-conjugation, both the cross-conjugated DTF units and the cross-conjugated anthraquinone core are accordingly converted into linearly conjugated units by this event. Moreover, the tranformation is accompanied by a significant geometrical change from a butterfly-shaped neutral state to a planar anthracene core.

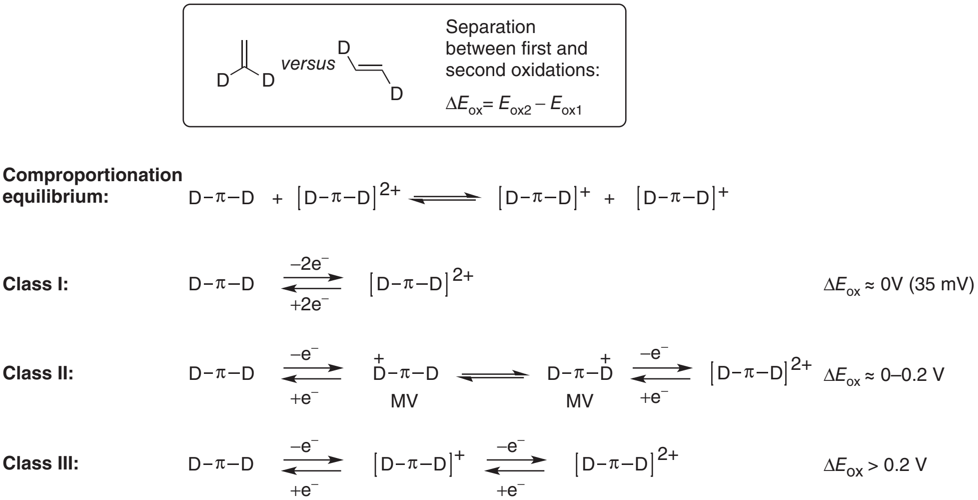
9.3
Communication between Two Identical Redox Centers

We shall now look a little deeper into systems containing two identical redox centers and how properties can be tuned by the connecting bridge. The extent



Scheme 9.4

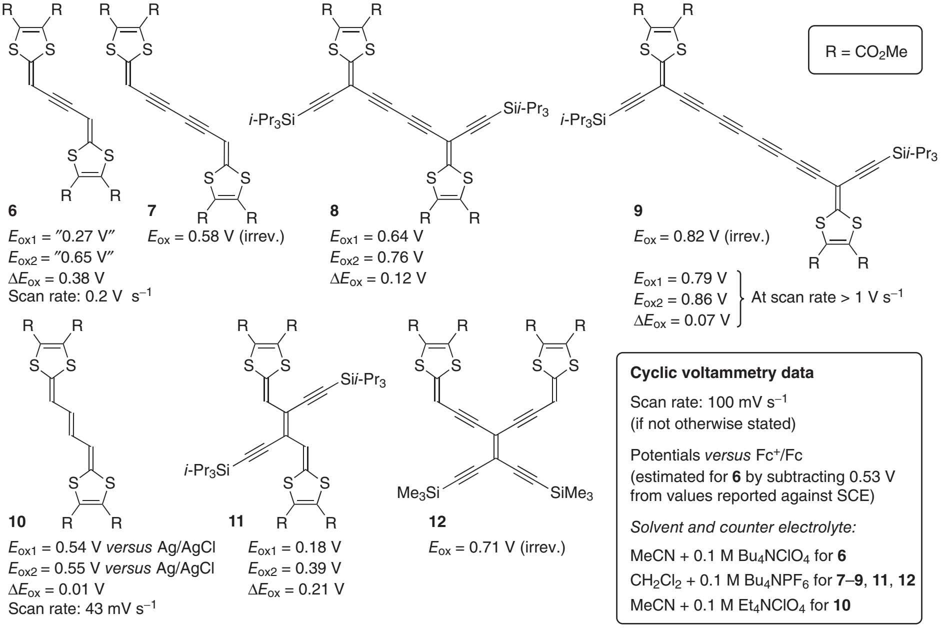
of the electronic communication, determined by electrochemistry, between two identical redox-active groups in a molecule, has been classified by Robin and Day (for metal centers) [8]. Scheme 9.5 shows systems with two identical electron-donating redox-active groups (D), between which a bridge (π) has been placed, which can hence be oxidized and take three overall charge states, 0, +1, +2. The scheme first shows a comproportionation equilibrium where a monocationic species is in equilibrium with the neutral and dicationic species. The more this equilibrium is pushed toward the cationic species, the larger is the separation between the first and second oxidation potentials (ΔE_{ox}). If no communication exists between the two redox centers, they will act as independent redox centers that are oxidized (or reduced for acceptor groups) in an apparent two-electron event, that is, close to two simultaneous one-electron events (Class I, ΔE_{ox} close to 0 V), so the bridge acts as an insulator. To be strictly correct, the separation between the two oxidation potentials will correspond to the statistical limit of 35 mV [9], but this small separation will often be masked as a broadened wave (lack of proper IR-compensation or contributions from sluggish electron transfer). On the other hand, an apparent two-electron oxidation may not always imply that the centers do not interact; as there is also the possibility that the second oxidation becomes easier after removal of the first electron. Thus, the second oxidation occurs at lower potential than the first oxidation ($\Delta E < 0$), but this potential is already passed in the cyclic voltammogram and a single two-electron wave will therefore be observed. The electrochemistry of the anthraquinone-TTF **5** presents an example of this *potential inversion* behavior [9]. If minor electronic communication exists, two poorly separated stepwise one-electron transfers can be observed. For the mono-oxidized species, the charge is localized on one redox-active group according to at least one spectroscopic technique (Class II, $\Delta E_{\mathrm{ox}} \approx 0{-}0.2$ V); this species is called a mixed valence (MV) species. When the electronic interaction is even stronger, there is good separation between the two redox waves (Class III, $\Delta E > 0.2$ V). The charge on the mono-oxidized species is then fully delocalized across the entire molecule, and no spectroscopic technique can differentiate between the two redox centers. Technically, the term *valence-averaged species* would be more appropriate to use than MV species in this case. Caution should be exercised when comparing results performed under different conditions (solvent, electrolyte, scan rate, reference, and type of electrode) and setups as they can give different results. Also, care should be taken when using only the difference between the first two redox potentials to determine electronic interaction [10]; other techniques should be used to validate this assignment (like spectroelectrochemistry, magnetic measurements, theoretical calculations, IR, nuclear magnetic resonance (NMR), and single-crystal X-ray diffraction studies). Therefore, recently, a fourth class (II–III) between Class II and III has been proposed [8b]. Class II, III, and II–III species usually exhibit an intervalence charge-transfer (IVCT) band in the near-infrared (NIR) region, which was first described by Hush [11]. If the mono-oxidized or reduced species is stable enough, the compound can be isolated and analyzed in the UV-NIR region to see this IVCT band or it can be measured spectroelectrochemically. Care should, however, be taken as there can also be other bands observed in the NIR. If this IVCT band can be identified, it can be used to determine the degree of interaction between the two redox-active groups. For literature on this topic, see the cited references [8b, 9–12]. Thus, by comparing the redox properties of identical redox systems containing either linearly or cross-conjugated bridges of similar lengths, one can gain knowledge on the influence of cross-conjugation.



Scheme 9.5

9.3.1
Organic Redox Centers

Figure 9.3 shows a variety of extended TTFs, including a series of alkyne-extended derivatives (**6–9** [13]), two alkene-extended ones (**10** [14] and **11** [15]), and one with a cross-conjugated tetraethynylethylene (TEE) spacer (**12** [15]). The first



Cyclic voltammetry data

Scan rate: 100 mV s^{-1}
(if not otherwise stated)

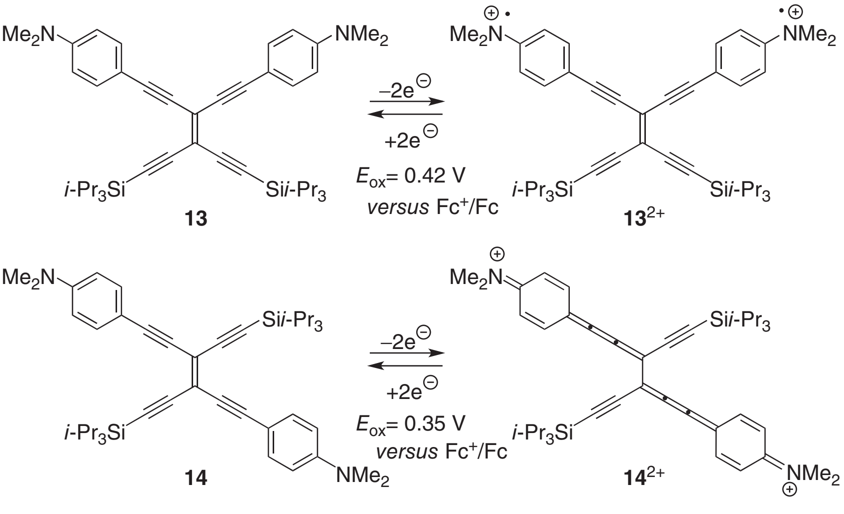
Potentials *versus* Fc$^+$/Fc
(estimated for **6** by subtracting 0.53 V from values reported against SCE)

Solvent and counter electrolyte:
MeCN + 0.1 M Bu$_4$NClO$_4$ for **6**
CH$_2$Cl$_2$ + 0.1 M Bu$_4$NPF$_6$ for **7**–**9**, **11**, **12**
MeCN + 0.1 M Et$_4$NClO$_4$ for **10**

Figure 9.3 First and second oxidation potentials of extended TTFs obtained by cyclic voltammetry.

and second oxidation potentials found by cyclic voltammetry and the separation (ΔE_{ox}) between these potentials are also listed in the figure. First of all, it is noteworthy to mention that the donor strength decreases when expanding the alkyne spacer (cf. **6** vs **7** and **8** vs **9**). This behavior is opposite to that observed for alkene-extended TTFs for which the donor strength increases upon extending the π-system [14]. With regard to the separation between the oxidation events, the alkyne-extended TTFs follow, however, the trend as observed for alkene-extended TTFs [14], that is, ΔE_{ox} decreases with the length of the extended TTF. Thus, while this separation is 0.12 V for **8**, the oxidation of **9** occurred as an irreversible two-electron oxidation, but was split into two reversible oxidations separated by only 0.07 V at a higher scan rate. Enhanced reversibility is, to some extent, observed when the DTF has an ethynyl substituent at the exocyclic fulvene, thereby possibly preventing the oxidative dimerization of the two DTFs described earlier (Scheme 9.2). Incorporating ethynyl substituents at the central ethene unit results in a remarkable increase in ΔE_{ox} from 0.01 V (**10**) to 0.21 V (**11**) and hence makes the formation of the dicationic species harder. The cross-conjugated compound **12** is significantly more difficult to oxidize than the butadiyne-extended TTF **11** (both potentials listed are peak potentials for irreversible electron transfers), but the presence of the additional electron-withdrawing ethynyl substituents could be the major reason for this. Thus, while the studies on this series of acetylenic scaffolds do show how the two DTFs seem to become independent redox centers when placed more remotely relative to each other, it is more difficult to directly deduce the influence of cross-conjugation. This shall, however, be more apparent from some of the following examples.

Aniline presents another redox-active organic molecule, and several TEE derivatives containing anilino substituents at different positions have been prepared and investigated [1b]. Compounds **13** and **14** shown in Scheme 9.6 are typical examples. Cyclic voltammetry of these molecules showed for each a single two-electron oxidation of the two aniline units. The two-electron oxidation occurred more readily for the linearly conjugated **14** (0.35 V vs Fc^+/Fc in $CH_2Cl_2 + 0.1\,M\ Bu_4NPF_6$) than for the cross-conjugated **13** (0.42 V vs Fc^+/Fc). This observation signals a more efficient electron delocalization in the dication through the *trans*-diethynylethene spacer and a cumulenic/quinoid resonance formula can be drawn as shown in Scheme 9.6. A single two-electron oxidation is, in this case, most likely a result of potential inversion ($\Delta E < 0$), and the redox centers should therefore not be considered as being independent.

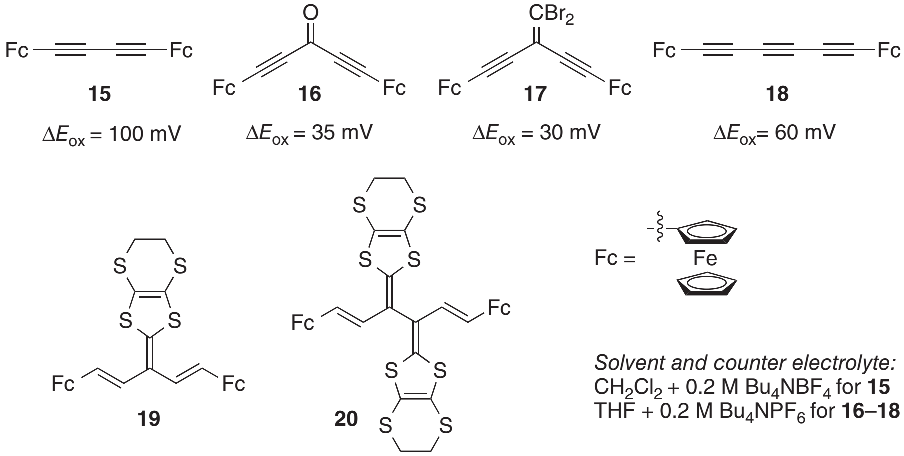


Solvent and counter electrolyte: CH_2Cl_2+ 0.1 M Bu_4NPF_6

Scheme 9.6

9.3.2
Organometallic Redox Centers

Figure 9.4 shows a series of bis-ferrocene (bis-Fc) complexes **15–18** [12c, 16]. Electrochemistry revealed poor separation of the pseudo-two-electron oxidation, but it was possible to estimate the separation of the first and second oxidation potentials as listed in Figure 9.4. Comparing the two linearly conjugated systems

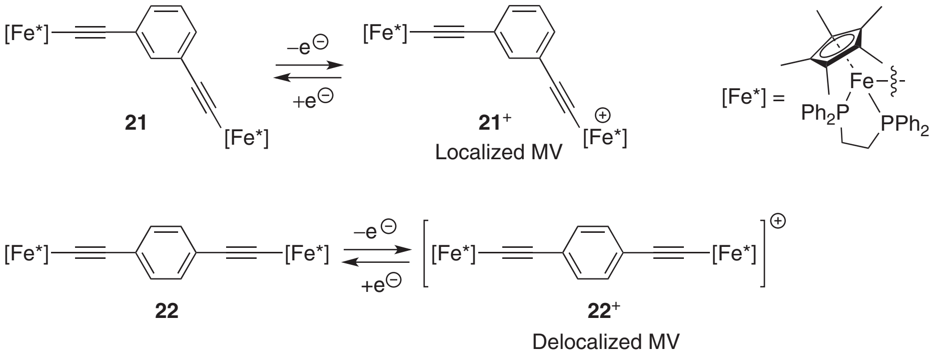


Solvent and counter electrolyte:
CH_2Cl_2 + 0.2 M Bu_4NBF_4 for **15**
THF + 0.2 M Bu_4NPF_6 for **16–18**

Figure 9.4 Molecules containing two separated ferrocene (Fc) units.

15 and **18** shows how the interaction between Fc units decreases as the distance between them increases from 4C-atom bridges to 6C-atom bridges. Nevertheless, the cross-conjugated complexes **16** and **17**, with 5C-atom separation along the backbone of the bridge, have the lowest ΔE_{ox} values; and the interaction between the two Fc units is hence weakest in these two complexes. Systems like **19** and **20** containing more than one type of redox-active group have also been prepared, but here interpretation of electrochemical data is more complicated [17].

Scheme 9.7 shows the oxidations of two organometallic iron complexes **21** [10, 18] and **22** [10, 18b, 19] having two Fe(II) alkynyl moieties connected via *meta*- and *para*-phenylene rings, respectively. Cyclic voltammetry reveals the stronger communication conveyed by the *para*-complex **22**, reflected in a larger separation between the first and second oxidation potentials ($\Delta E_{ox} = 0.26$ V) than in the *meta*-complex **21** ($\Delta E_{ox} = 0.13$ V). The monocation $\mathbf{22}^{+}$ can be characterized as a strongly coupled MV species on account of a strong IVCT band in the NIR region and it belongs to the borderline Class II/III (Robin–Day classification) as two C≡C stretching bands were observed in the IR spectrum. Instead, the monocation $\mathbf{21}^{+}$ has a much weaker IVCT band and two spectroscopically different metal centers, corresponding to localized Fe(II) and Fe(III) metal centers (Class II MV species). A crystal structure of this monocation also revealed that the two Fe metal centers were slightly different [18a]. The second-order nonlinear optical (NLO) responses of compounds **21** and **22** and of their mono- and dications were also investigated [18b]. The first-order hyperpolarizabilities were about the same for the neutral and dicationic states of both **21** and **22**. The monocation $\mathbf{21}^{+}$ exhibited a slightly smaller NLO response, while the value for $\mathbf{22}^{+}$ was about twice that of **22** or $\mathbf{22}^{2+}$. Thus, the NLO properties can be reversibly switched for **22** by changing the oxidation state of the complex. Recently, the complexes **21** and **22** were imaged on a gold (111) surface using scanning tunneling microscopy (STM) [20]. A symmetrical "dumbbell" appearance was observed for both the neutral complexes as well as for the strongly coupled delocalized MV species **22**$^+$. However, MV species **21**$^+$ showed an unsymmetrical appearance because of charge localization.

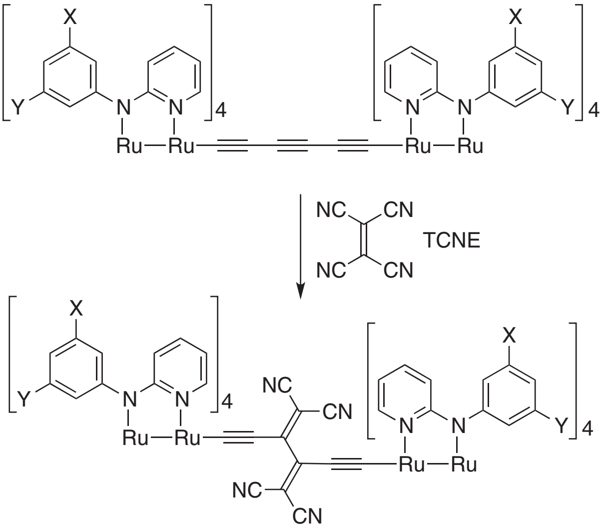


Scheme 9.7

Complexes allowing for studies of communication between ruthenium centers coordinated to substituted 2-anilinopyridinates have also been prepared (Scheme 9.8) [21]. Treatment of the hexatriyndiyl-bridged complexes **23**–**25** with tetracyanoethylene (TCNE) generated the cycloaddition/insertion products **26**–**28** now containing a cross-conjugated backbone. The reactions took place on the central triple bond, possibly because of the steric shielding of the ligands protecting the triple bonds closest to the metal centers. Later on, we shall see that TCNE usually reacts, instead, with the most electron-rich triple bond, that is, the one closest to the donor group. It was important that these complexes (**26**–**28**) were symmetrical for interpretation of the electrochemical measurements. Voltammetry and spectroelectrochemical studies showed that the two Ru_2 termini in **23**–**25** are coupled; the singly reduced monoanions of these complexes had an IVCT band and could be characterized as Robin–Day Class II/III MV species. Interestingly, the coupling was found to be completely absent in the cross-conjugated TCNE adduct.

9.3.3
Expanded Radiaannulenes and Radialenes

Cyclic cross-conjugated bridges can result in electronic communication not conveyed by related acyclic bridges. Thus, the first oxidation of each TTF unit in the cyclic compound **29** (Figure 9.5) was split by 0.09 V, while the TTF units in compound **30**, incorporating a TEE spacer, acted as independent redox centers and were oxidized at the same potential [22]. The singly oxidized species of **29** showed a characteristic MV absorption at 2257 nm. The cyclic core of **29** is called a *radiaannulene* as it has both endocyclic double bonds (as in annulenes) and

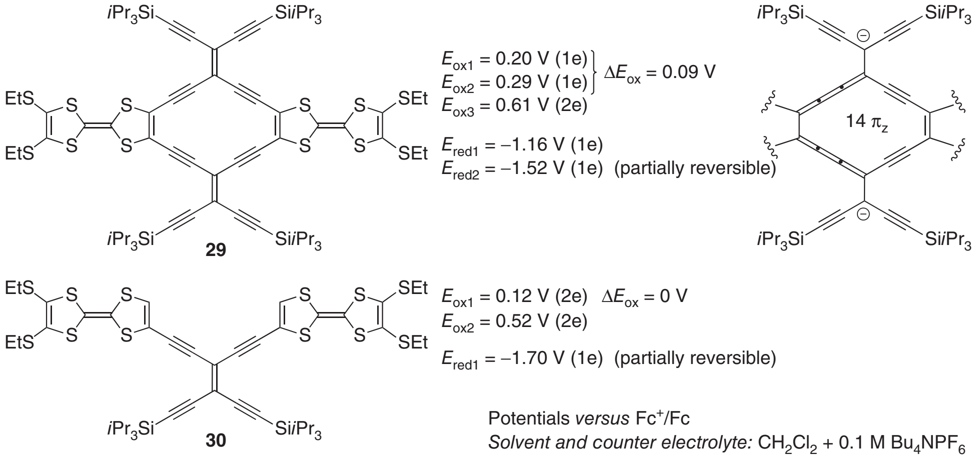


23 (X = Y = H)
24 (X = Y = OMe)
25 (X = H, Y = O*i*Bu)

26 (X = Y = H)
27 (X = Y = OMe)
28 (X = H, Y = O*i*Bu)

Scheme 9.8

exocyclic double bonds (as in radialenes). Interestingly, this cyclic core behaves as a Wurster-type redox system [3] and readily accepts two electrons, despite being fused to two electron-rich TTFs, in two step-wise one-electron reductions, the first reversible and the second partially reversible. It thereby gains a 14π-aromatic core, as illustrated in Figure 9.5. In all, the compound had five reversible and one partially reversible oxidation states, all of which had different colors. A gain in aromaticity upon reduction was supported by nucleus independent



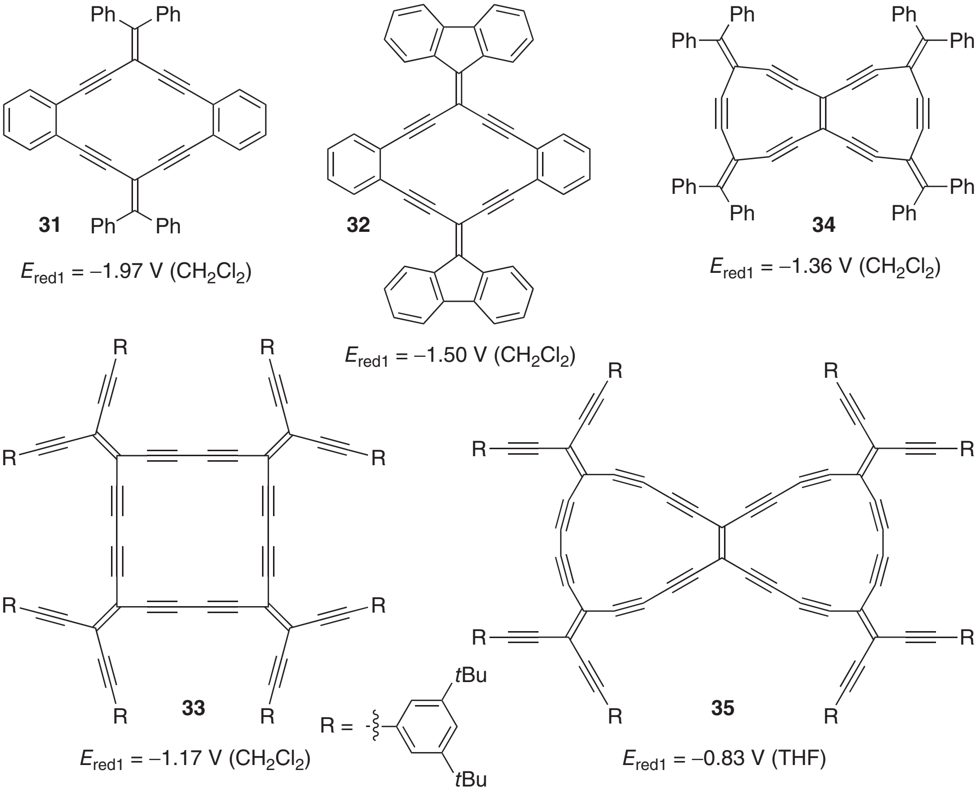
E_{ox1} = 0.20 V (1e)
E_{ox2} = 0.29 V (1e) } ΔE_{ox} = 0.09 V
E_{ox3} = 0.61 V (2e)
E_{red1} = −1.16 V (1e)
E_{red2} = −1.52 V (1e) (partially reversible)

E_{ox1} = 0.12 V (2e) ΔE_{ox} = 0 V
E_{ox2} = 0.52 V (2e)
E_{red1} = −1.70 V (1e) (partially reversible)

Potentials *versus* Fc^+/Fc
Solvent and counter electrolyte: CH_2Cl_2 + 0.1 M Bu_4NPF_6

Figure 9.5 TTF-radiaannulene and a related TEE with two TTF groups.

chemical shift (NICS) calculations. In this regard, it is also interesting to compare the first reduction of the two related radiaannulenes **31** and **32** [23] shown in Figure 9.6. The first reduction occurred much more readily for **32** than for **31**, presumably due to more efficient delocalization of the negative charges into the fluorenyl groups. We note that extended TTFs with a radiaannulene core have also been prepared [24]; these can be seen as an expansion of the quinoid systems shown in Scheme 9.4. In general, expanded radialenes and radiaannulenes are remarkably strong electron acceptors [1]. The first reduction potentials of some additional structures (**33** [25], **34** [26], **35** [27]) are shown in Figure 9.6. The perethynylated bicyclic radiaannulene **35** ($E_{\text{red1}} = -0.83$ V vs Fc^+/Fc) is an even stronger electron acceptor than C_{60} ($E_{\text{red1}} = -1.02$ V under comparable conditions [28]).



$E_{\text{red1}} = -1.97$ V (CH_2Cl_2)

$E_{\text{red1}} = -1.50$ V (CH_2Cl_2)

$E_{\text{red1}} = -1.36$ V (CH_2Cl_2)

$E_{\text{red1}} = -1.17$ V (CH_2Cl_2)

$E_{\text{red1}} = -0.83$ V (THF)

Potentials *versus* Fc^+/Fc
Counter electrolyte: 0.1 M Bu_4NPF_6

Figure 9.6 First reduction potentials of cross-conjugated macrocycles.

9.4
Cross-Conjugation and Optical Properties

Several UV-Vis absorption studies on dendralenes and expanded dendralenes have revealed that π-electron delocalization by cross-conjugation is significantly less efficient than in the related linearly conjugated oligomers [1]. For example, the longest-wavelength absorption maxima of the series of expanded dendralenes **36–39** shown in Figure 9.7 only change slightly with increasing length of the dendralene [29]. We shall examine how this inefficient electron delocalization influences the optical properties of donor–bridge–acceptor systems and in general of multiple chromophore systems.

First of all, however, care should be taken when using UV-Vis absorption spectroscopy to evaluate conjugation effectiveness in donor–acceptor systems. Solvent perturbations can change the positions of charge-transfer (CT) absorptions significantly [30] and a CT absorption can be so weak that it may not actually be observed in the spectrum; in such cases, one has to be careful not to assign a higher energy absorption to the actual CT absorption. In simple terms, a CT transition of low energy (long wavelength) can result from two opposing conjugation effects [1e, g, 30]: (i) by an increase in the HOMO energy of the donor and a decrease in the LUMO energy of the acceptor on account of extended conjugation of each of these individual units and (ii) by a poor mixing of the HOMO of the donor unit and the LUMO of the acceptor unit in the donor–acceptor chromophore via the conjugated bridge (i.e., inefficient conjugation between the

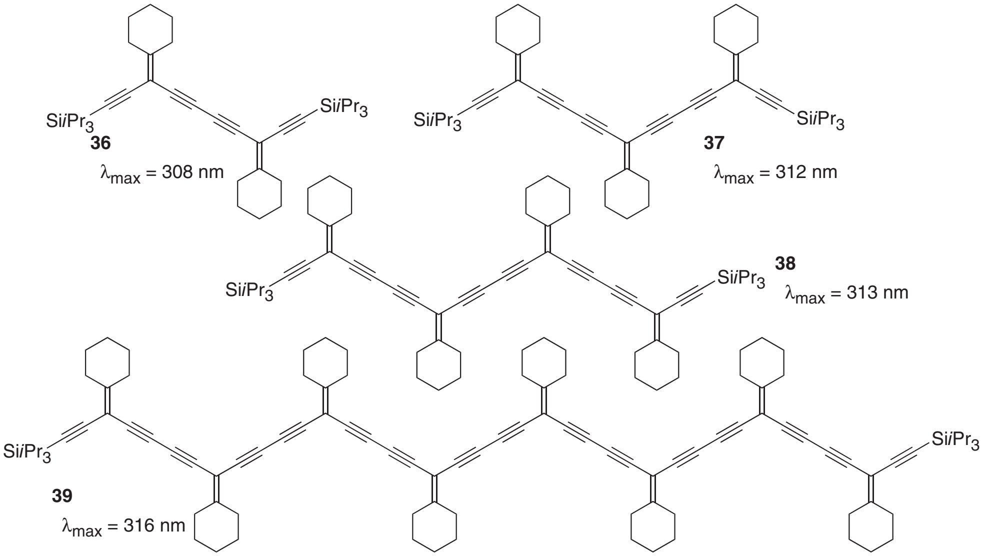


Figure 9.7 Longest-wavelength absorption maxima of a series of expanded dendralenes.

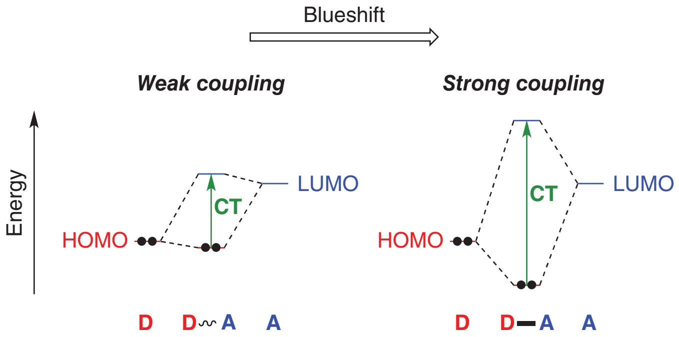
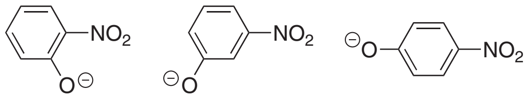


Figure 9.8 Schematic illustration of how the energy of a charge-transfer (CT) absorption depends on the coupling between donor (D) and acceptor (A) groups.

donor and acceptor units). Thus, for donor–acceptor systems, decoupling of the electronic communication between donor and acceptor groups should lead to absorption maxima of lower energies (and intensities, i.e., lower oscillator strengths). This may be counterintuitive to the common perception of the influence of conjugation effectiveness but can be simply illustrated as shown in Figure 9.8. Absorption tuning by solvent interactions or by ion pairing when the chromophore is charged may, in some cases, mask this behavior [30]. It is for this reason interesting to compare results from both solution and gas phases.

9.4.1
Nitrophenolates

The absorption properties of the *o*-, *m*-, and *p*-nitrophenolates were recently studied in both solution and gas phases [31]. As expected, the individual absorption values in solution (with Na^+ as counter ion) and gas phases differ for each compound owing to solvent perturbations, but a nice agreement was obtained with regard to which compound has the lowest energy absorption (Figure 9.9): the *meta*-compound exhibits a CT absorption at the longest wavelength in both phases. The absorption of the *meta*-isomer was very weak and had to be determined experimentally in the gas phase by another method than that



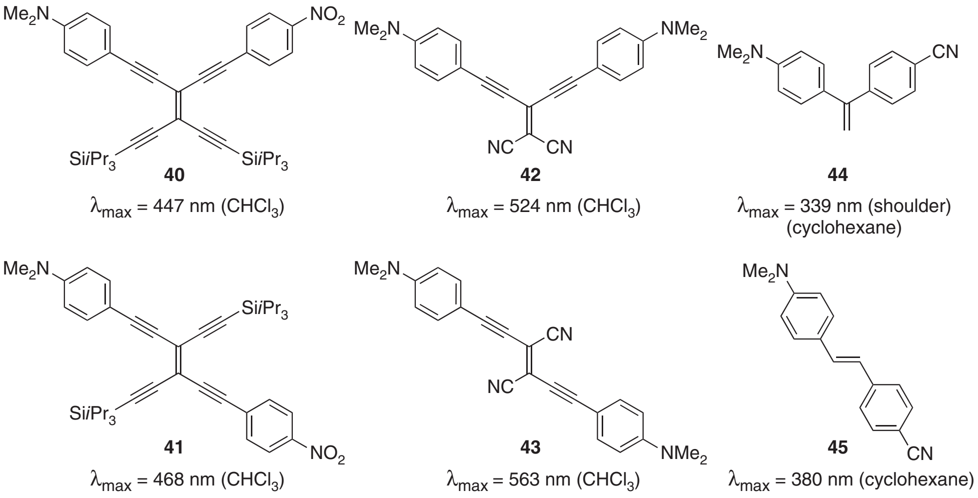
λ_{max} (nm)			
Solution (MeCN):	443	473	430
Gas phase:	399	532	393

Figure 9.9 Longest-wavelength absorption maxima of nitrophenolates. In the solution studies, the counter ion was Na^+.

used for the other two isomers. The redshifted absorption of this chromophore is explained by the inefficient coupling conveyed by the cross-conjugated *meta*-phenylene bridge. Yet, as the following donor–acceptor examples reveal, contradictory interpretations of UV-Vis absorption data can result if one does not consider both of the two opposing effects listed above.

9.4.2
Other Donor–Acceptor Systems

Figure 9.10 shows a comparison of the longest wavelength absorption maxima of different donor–acceptor systems, TEEs **40** versus **41** [32], diethynylethenes **42** versus **43** [33], ethenes **44** versus **45** [34]. It is clearly more difficult to directly correlate effectiveness of conjugation from the absorption maxima of these compounds. The simple picture in Figure 9.8 only takes into account the coupling between donor and acceptor ends, but, as mentioned, raising of HOMO energy by extended conjugation, and/or lowering of LUMO energy, also plays a determining role in the actual position of the absorption and, in that regard, also distortions from planarity as expected for a geminally substituted ethene like **44**. For several anilino-/nitrophenyl-substituted TEEs, electrochemical studies reveal that the potentials of aniline oxidation and nitrophenyl reduction are usually hardly affected by the presence of other aryl substituents (with the exception of compound **14** shown earlier) [1a, e] and donor–acceptor conjugation across the central TEE scaffold can generally be considered inefficient. It is worth noting that anilino-substituted TEEs **13** and **14**, not containing nitrophenyl acceptor groups, also exhibit CT



40 λ_{max} = 447 nm ($CHCl_3$)

42 λ_{max} = 524 nm ($CHCl_3$)

44 λ_{max} = 339 nm (shoulder) (cyclohexane)

41 λ_{max} = 468 nm ($CHCl_3$)

43 λ_{max} = 563 nm ($CHCl_3$)

45 λ_{max} = 380 nm (cyclohexane)

Figure 9.10 Longest-wavelength absorption maxima of donor-acceptor chromophores.

absorptions, at 428 nm (**13**) and 459 nm (**14**) in $CHCl_3$ [32], as the TEE itself has an electron–acceptor character. This interpretation is supported by the fact that the absorption disappears upon protonation of the anilino groups. *Trans–cis* isomerization of **41** can be accomplished by irradiation at 366 nm; the corresponding *cis*-compound has a similar absorption maximum (471 nm), but its intensity is almost halved relative to that of **41**. Compound **42** has two *cis* and two *trans* D–π–A pathways, while **43** has two geminal and two *cis* D–π–A pathways. In agreement with the more efficient linear conjugation pathways, the anilino rings in compound **42** have a 2% higher degree of quinoid character (bond length alternation) than those in compound **43** according to calculations [33b]. The calculated quinoid character was in good agreement with X-ray crystallographic analysis of compound **43** [33a], and it is significantly stronger than observed in any donor–acceptor-substituted TEEs. Calculations also reveal that the HOMO of **43** is 0.41 eV higher in energy than that of **42**, in agreement with the lower transition energy of **43**. Orbital plots show that the HOMO of **43** is not delocalized onto the cyano groups, which is instead the case for **42**. Altogether, the studies on **42** and **43** support the concept that the smallest degree of donor–acceptor coupling in the ground-state (as a result of cross-conjugation) provides the most redshifted CT absorption in the UV-Vis absorption spectrum.

Extensive studies on the third-order NLO properties of arylated TEEs have been carried out, and one important result from these studies is that the arrangement of an anilino donor and *p*-nitrophenyl acceptor in linear conjugation (as in **41**) provides a much higher value of the second hyperpolarizability than when placed in cross-conjugation (as in **40**) [35]. Strong two-photon absorption properties of sublimable donor-substituted cyanoethylenes indicate good potential for optoelectronic applications [33].

9.4.3
Extended Tetrathiafulvalenes and Dithiafulvene-Dendralenes

Absorption maxima of different extended TTFs (**46–52**) are summarized in Figure 9.11. Compound **47** can be seen as an expanded [3]dendralene; and inefficient π-electron delocalization across the central cross-conjugated DTF unit is reflected in the fact that it has the longest wavelength absorption maximum almost identical to that of **46** [36]. Usually alkene-extended TTFs exhibit redshifted absorption maxima as evident when proceeding in the progression TTF – **48–49** [14]. However, when the DTF units are connected in a cross-conjugated dendralene manner, they only show very small redshifts, as revealed by comparing the absorption of the extended TTF **50** [37] with those of the [3]dendralene **51** and [4]dendralene **52** [17]. Along the same line, the cross-conjugated (*meta*-substituted) tris-DTF **53** has a blueshifted absorption maximum relative to that of the *p*-phenylene-extended TTF **54**, despite **53** being a larger π-system (Figure 9.12) [38].

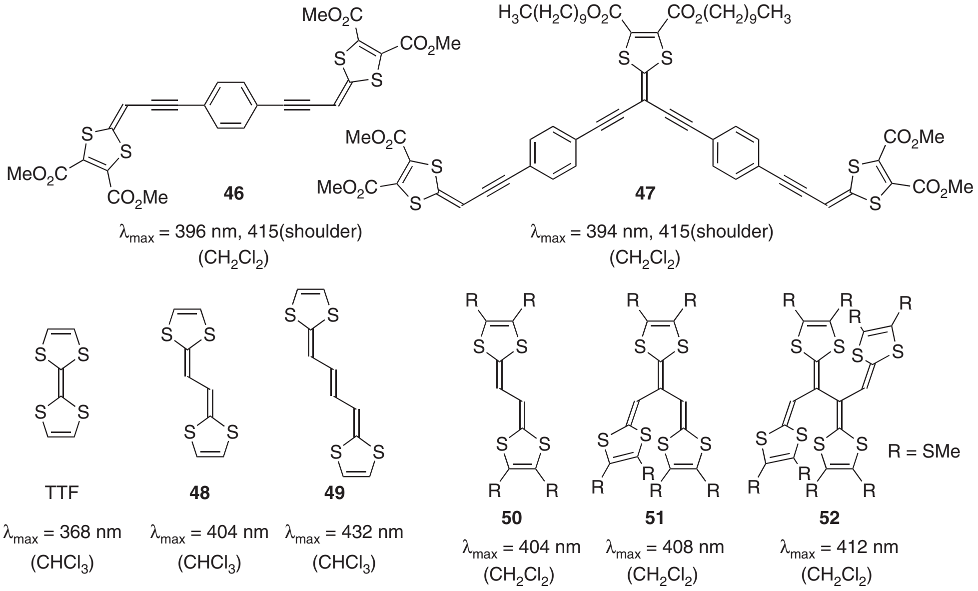


Figure 9.11 Longest-wavelength absorption maxima of extended tetrathiafulvalenes/dendralenes.

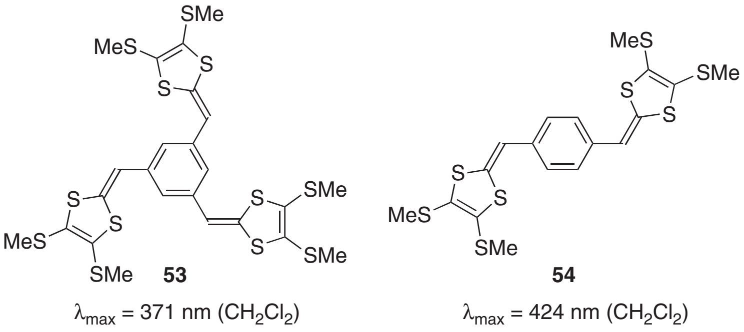
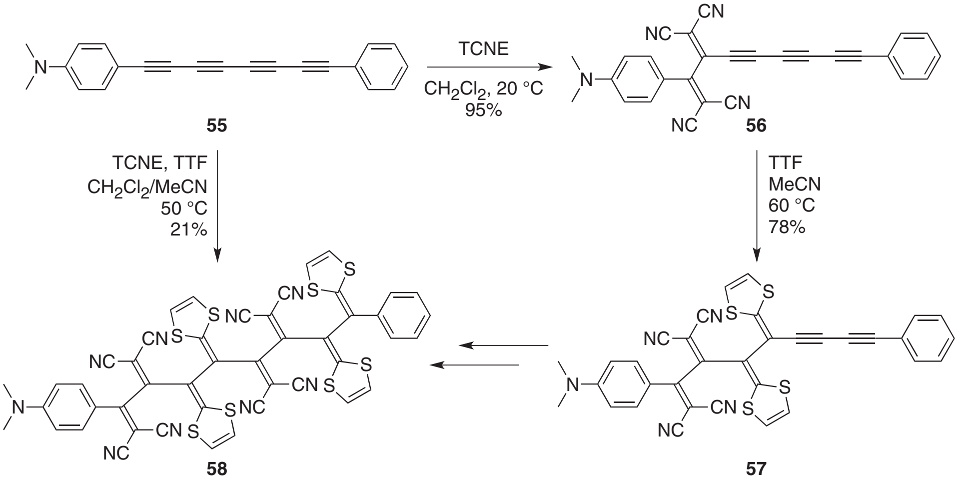


Figure 9.12 Longest-wavelength absorptions of benzene-extended TTFs.

9.4.4
Synthesis of Dithiafulvene-Dendralene Oligomers by Cascade Reactions

The focus of this chapter has so far not been so much on synthesis, but one very nice cascade reaction to dendralenes incorporating DTF donor groups and dicyanomethylene acceptor groups deserves mention. While TCNE can undergo a thermal [2+2] cycloaddition with electron-rich alkynes followed by electrocyclic ring opening [21, 39], TTF can undergo a similar reaction with electron-poor alkynes [40]. These observations were employed to construct a dendralene-type backbone by a cascade of sequential TCNE/TTF additions to the dimethylaniline end-capped polyyne **55** (Scheme 9.9) [41]. After addition of TCNE, furnishing the product **56**, the next triple bond becomes sufficiently electron poor to react with TTF, furnishing **57**; this is followed by TCNE adding to the next, now electron-rich, triple bond, and so on. The sequence of reactions can also be done in a one-pot cascade reaction (Scheme 9.9) to give the dendralene **58**. This reaction turns the linearly conjugated polyalkynyl compound **55** into a cross-conjugated compound with alternating donor and acceptor units. The dendralene **58** was isolated as a thermally stable, black metallic solid. This protocol paves the way for easy access to multivalent D–A chromophores.



Scheme 9.9

9.4.5
Photoinduced Charge Separation in a Donor–Acceptor System

The influence of the electronic nature of the spacer on photoinduced charge separation by local excitation of a donor moiety was investigated for compounds **59**–**62** (Figure 9.13) [42]. These molecules contain 3,5-dimethyl-4-(9-anthracenyl)julodinine as the donor and naphthalene-1,8:4,5-bis(dicarboximide) as the acceptor. Photoinitiated charge separation through the cross-conjugated 1,1-diphenylethene bridge (**59**) was found to be 30 times slower than through the linearly conjugated *trans*-stilbene bridge (**60**) and was comparable to that observed through the diphenylmethane bridge (**62**) with broken conjugation. This means that the σ-system is most likely the primary charge separation pathway in the cross-conjugated compound. Instead, the rate of charge separation through

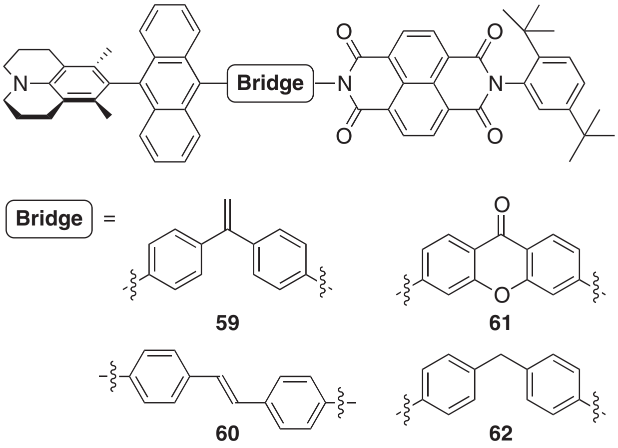


Figure 9.13 Compounds studied for ability to undergo photoinduced electron transfer (charge separation).

the xanthone bridge (compound **61**) was found to be comparable to that of the linearly conjugated bridge.

The next part shall focus on another way of studying electron transfer through different bridges, namely, by conductance measurements.

9.5
Conjugation and Molecular Electronics

The differences in conjugation effectiveness between linear and cross-conjugated systems have been explored in the development of functional molecules for molecular electronics. In particular, it is interesting if changes in conjugation pathways, and hence conductances, can be induced by an external stimulus. Thiols are commonly used as anchoring groups (“alligator clips”) for adhering a molecule between two electrodes [43]; usually, the molecules are prepared as acetyl-protected thiolates. In the following section, we shall summarize a few theoretical and experimental results, which illustrate the influence of cross-conjugation (see also Chapters 8 and 11).

9.5.1
Theoretical Comparison of Conduction Pathways

Electron transport along different pathways between two sulfur end groups in compound **63** (Figure 9.14) was subjected to a theoretical study [44]. These calculations revealed that the linearly conjugated pathway was significantly better at transmitting charge than the cross-conjugated one despite the fact that the linearly conjugated pathway is longer (eight carbon

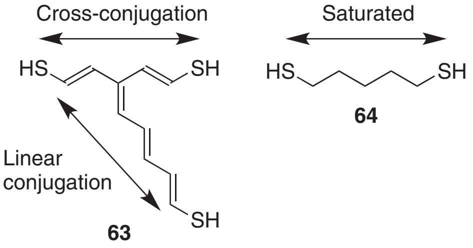


Figure 9.14 Molecules subjected to electron transport calculations between different end-groups.

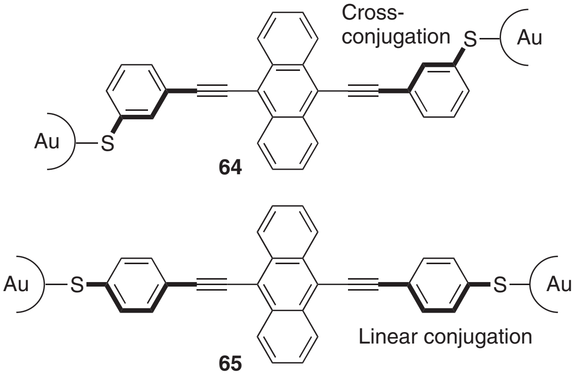


Figure 9.15 The conductance of **65** is almost two orders of magnitude higher than that of **64**.

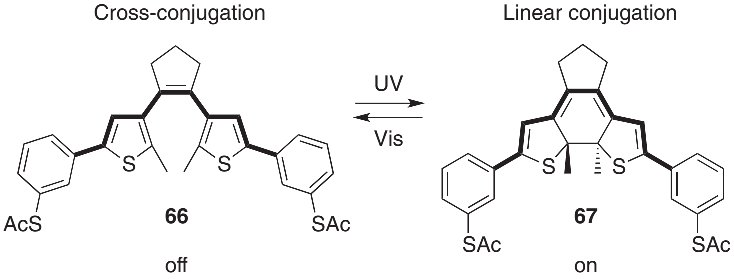
atoms) than the cross-conjugated one (five carbon atoms). In addition, calculations showed that the cross-conjugated pathway conducted only slightly better than the completely saturated pentane-1,5-dithiol **64**. The bad conductance of the cross-conjugated pathway was ascribed to quantum interference.

9.5.2
Meta- versus *Para*-Anchoring

The poorer conductance of cross-conjugated molecular wires has also been demonstrated experimentally. For example, the two molecules **64** and **65** with the same conjugated core were positioned via thiol anchoring groups in *para*- or *meta*-positions between two electrodes (Figure 9.15) [45]. The distance between the two thiols and hence, in theory, between the two gold electrodes is slightly longer on the linearly conjugated *para*-substituted molecule **65**, but the conductance is almost 2 orders of magnitude higher than that of the cross-conjugated *meta*-substituted wire **64**.

9.5.3
The Dithienylethene Photoswitch

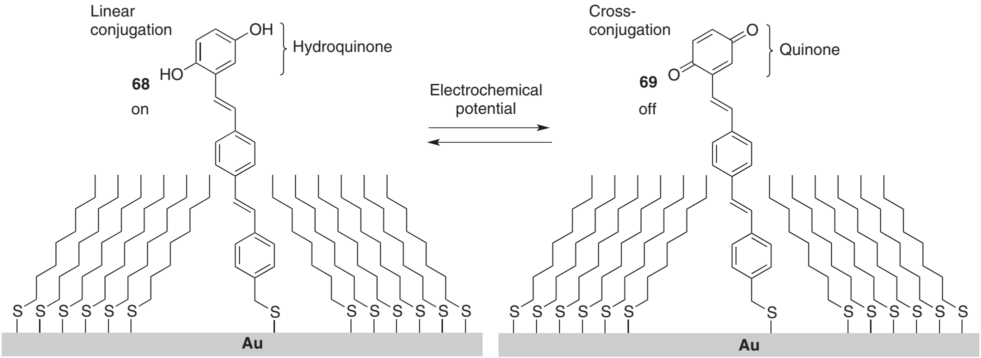
The dithienylethene photoswitch **66**, shown in Scheme 9.10, upon irradiation with UV light, undergoes a conrotatory [6π]-electrocyclization to form the closed dihydrodithienobenzene isomer **67**. This compound exhibits a red-shifted absorption due to the extended linear conjugation; and by irradiation with visible light, it is returned to the original isomer. This photoswitch was incorporated between both electrodes and nanoparticles in different devices via its two protected thiolate groups [46]. The junctions showed clear and reversible conductance switchings upon irradiation. Thus, the open form (**66**) was found to be the low-conducting state (off), while the closed form (**67**) was the high-conducting state (on). This difference is explained by the presence of a cross-conjugated pathway along the dithienylethene unit in **66**, which changes to a linearly conjugated pathway in **67**. The concept of cross-conjugation was also important in another regard for this system. Thus, the thiolate anchoring groups were placed at *meta*-positions rather than at *para*-positions in order to decrease electronic coupling to the electrodes and thereby to prevent quenching of photoactivity of the dithienylethene moiety by strong orbital overlap with the electrodes.



Scheme 9.10

9.5.4
Hydroquinone–Quinone Redox Switch

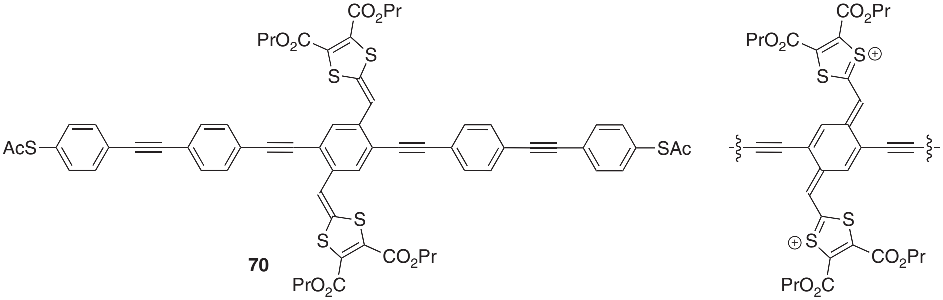
The hydroquinone–quinone redox couple was used in a device to electrochemically switch between linear conjugation and cross-conjugation in the oligo(phenylenevinylene) (OPV) molecular wires **68** and **69**, respectively (Scheme 9.11) [47]. After inserting the molecule in an octanethiolate self-assembled monolayer (SAM) on gold, an electrochemical potential was employed to switch between the quinone and hydroquinone. Electrochemical STM was used to control the oxidation state and to measure the electrical conductivity of the molecule. The linearly conjugated hydroquinone (**68**) was determined to be the high-conducting state, while the cross-conjugated quinone (**69**) was the low-conducting state.



Scheme 9.11

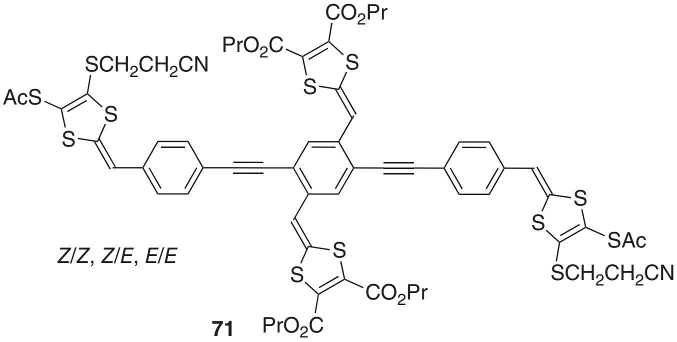
9.5.5
Oligo(phenyleneethynylene)-Tetrathiafulvalene Cruciform Redox Switch

This chapter started with an introduction to TTF and DTF and in our final example we shall show how an extended TTF has been used as a molecular transistor. The oligo(phenyleneethynylene) (OPE5) wire **70** (Figure 9.16) incorporates two orthogonally situated DTF units and is accordingly termed an OPE5-TTF cruciform [48]. Conducting-probe atomic force microscopy (AFM) studies of a SAM of this molecule on gold showed that the DTF functional groups increased the conductivity by about a factor of nine relative to a simple OPE5 without these groups [49]. To exploit its redox-active DTF units, the molecule was recently incorporated in a three-terminal device [50]. In this device, the molecule is spanned between two electrodes (source and drain). The charge state of the molecule could be controlled via the potential of a third electrode (gate). The original idea was that two-electron oxidation could convert the central extended TTF unit to a quinoid structure (Figure 9.16) [51], thereby changing the conjugation along the OPE wire from linearly conjugated to cross-conjugated. However, a detailed theoretical analysis of the obtained conductance data revealed that instead of a cross-conjugated quinoid structure, unpaired spins were formed in the device, even for the neutral species. Three charge states (−1, 0, +1) could be achieved as illustrated in Scheme 9.12. The radical anion exhibited a strong zero-bias Kondo effect, which was split in the presence of a magnetic field. Detailed analysis showed that the neutral species had two ferromagnetically coupled spins (triplet ground state). The single-positively charged species had two ferromagnetically coupled spins, which were both antiferromagnetically coupled to a third spin. In short, the molecule could be switched between polyradical states by changing



70

Figure 9.16 OPE5-TTF cruciform and a possible quinoid structure of the oxidized, central dicationic cruciform unit.



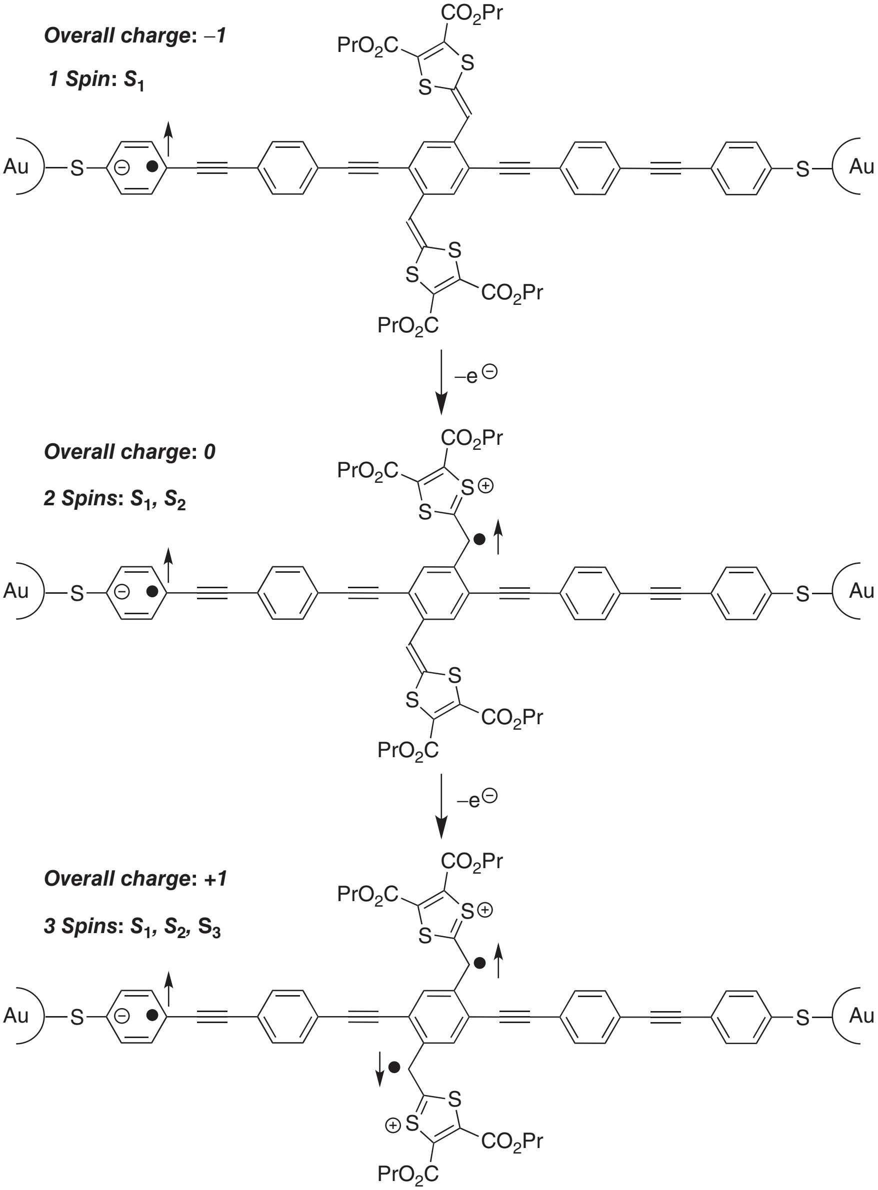
71

Figure 9.17 Cruciform end-capped with DTF anchoring groups.

the gate potential and the further manipulation by an external magnetic field enabled advanced control of quantum spin in this single organic molecule. The diradical description of the extended TTF moiety in this example preserves the aromatic benzene core instead of turning it into a cross-conjugated quinoid structure and thereby presents another implication of cross-conjugation. In a new iteration, a DTF group was incorporated at each end of an OPE3-TTF cruciform and this molecule (**71**, Figure 9.17), containing a total of four DTF units, was successfully anchored in a break-junction device via the SAc groups on the DTF end groups [52]. Gate-controlled studies in a three-terminal device are pending, but hopefully, charging near the electrodes will be controlled by virtue of the neighboring redox-active groups.

9.6
Conclusions

We have shown how communication across cross-conjugated bridges differ significantly from that conveyed by linearly conjugated counterparts. As illustrated


Overall charge: −1
1 Spin: S1
Overall charge: 0
2 Spins: S1, S2
Overall charge: +1
3 Spins: S1, S2, S3
CO2Pr
PrO2C
S
Au
−e⊖

Scheme 9.12

in the last part, the inefficient π-electron delocalization by cross-conjugation has been recognized as a particularly important design element in the field of molecular electronics. Indeed, changing the conjugation along a molecular wire by external stimuli, such as light or a gate potential, also alters single-molecule conductivity, and thereby an important function, namely, conductance switching, has been built into the molecule. It is interesting to see how recent structure–property relationships established within this relatively new field converge with those established from spectroscopy, electrochemistry, as well as our general knowledge of reactivity in synthetic organic chemistry.

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10

Transition Metal Complexes of Cross-Conjugated π Systems

Holger Butenschön

10.1

Introduction

Transition metal complexes of alkenes and alkynes with isolated or linearly conjugated double or triple bonds have been investigated in depth and have found many important applications, particularly in catalytic reactions [1]. In contrast, transition metal complexes of cross-conjugated π systems have been in the focus to a much lesser extent. However, this class of compounds deserves interest: just as antiaromatic compounds such as cyclobutadiene can be stabilized as ligands in transition metal complexes [2–4], there are a number of cross-conjugated π systems that are unstable as such but can be stabilized as ligands. Early concepts such as Y aromaticity [5, 6] or metalloaromaticity [7] show interesting parallels between cross-conjugated and antiaromatic compounds with cyclic conjugation. In addition to their stabilization as ligands of transition metal complexes, some of these species undergo reactions impossible with the uncomplexed ligands and thereby open new ways for synthesis.

This chapter takes a deeper look at the chemistry of transition metal complexes with cross-conjugated hydrocarbon ligands. In each section, issues of their synthesis and structure will be discussed first, followed by some representative reactions.

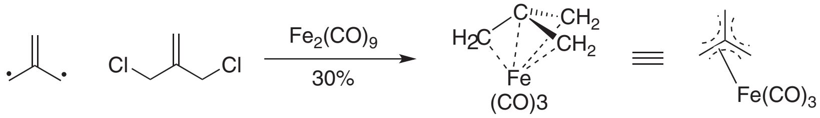
10.2

Trimethylenemethane Complexes

Trimethylenemethane (**1**) is a cross-conjugated π system with a diradical ground state. Its chemistry has been reviewed as early as 1972 by Dowd [8]. The Hückel molecular orbital (MO) scheme resembles that of cyclobutadiene, and accordingly trimethylenemethane can be stabilized as a ligand in transition metal complexes. Trimethylenemethane complexes can generally be obtained by treatment of a trimethylenemethane dianion with a metal halide or by treatment of organic halides with low-valent metal complexes. In addition to these general methods, there are some more specialized procedures.

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

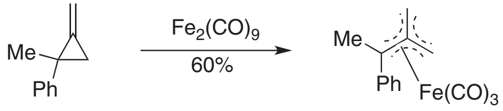
Similar to the first syntheses of cyclobutadiene complexes [2, 9], the first synthesis of a trimethylenemethane complex started from dichloride **2**, which was treated with diironenneacarbonyl to give tricarbonyl(trimethylenemethane) iron(0) (**3**) in 30% yield in addition to iron(II) chloride (Scheme 10.1) [10]. The η^4-coordination has been confirmed by crystal structure analyses [11, 12]. Very recently, Frenking *et al.* published a detailed theoretical bonding analysis of some late transition metal sandwich trimethylenemethane complexes [13].



1 **2** **3**

Scheme 10.1

A short time after the first synthesis of a trimethylenemethane complex, Noyori *et al.* reported a new access to the class of compounds starting from methylenecyclopropane derivatives. While treatment of methylenecyclopropane with diironenneacarbonyl afforded **3** only in very poor yield in addition to (1,3-butadiene)tricarbonyliron, substituted systems such as 2-methyl-2-phenylmethylenecyclopropane (**4**) gave trimethylenemethane complexes such as **5** in up to 60% yield (Scheme 10.2) [14]. These results reflect the tendency of strained small rings to undergo ring-opening reactions in the presence of transition metal complexes. However, few stable complexes of methylenecyclopropane have been described [15].

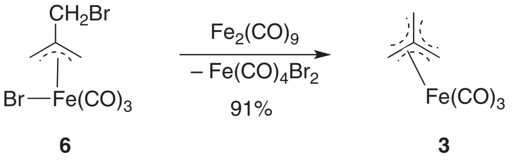


4 **5**

Scheme 10.2

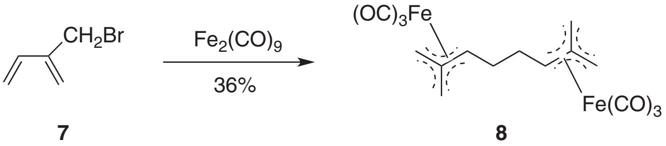
In addition to dihalides such as **2**, other organohalides can serve as precursors for the synthesis of trimethylenemethane complexes by dehalogenation. This dehalogenation can be afforded not only by iron carbonyls but also by disodium tetracarbonylferrate(−II). For example, the reaction of 2-(bromomethyl)allyliron halide **6** with $Fe_2(CO)_9$ afforded trimethylenemethane complex **3** in 91% yield (Scheme 10.3) [16].

Another dehalogenative formation of a trimethylenemethane complex, which involves a dimerization, starts from 2-(bromomethyl)-1,1-butadiene (**7**), which gave dinuclear complex **8** in 36% yield by stirring with $Fe_2(CO)_9$ in hexane for 24 h (Scheme 10.4) [16]. Lillya *et al.* pointed out that the allylic cation derived from **7**



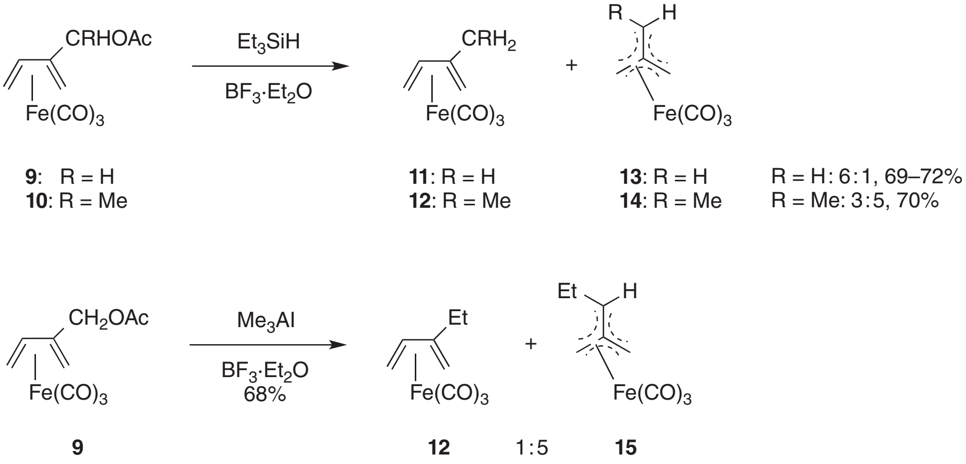
Scheme 10.3

may also be represented by a resonance formula with a trimethylenemethane substructure [17].



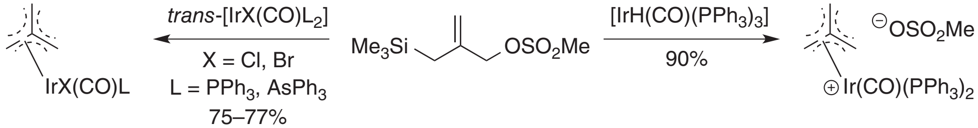
Scheme 10.4

Donaldson reported the reaction of acetates **9** or **10** with triethylsilane and boron trifluoride etherate to give the reduced diene complexes **11** and **12** in addition to trimethylenemethane complexes **13** and **14** in good yield with varying selectivity. Obviously, the cross-conjugated pentadienyl cation complexes derived from the starting materials were reduced by the hydrosilane. Equally interesting is the observation that the intermediate cation derived from **9** can be methylated to give **12** and ethyltrimethylenemethane complex **15** (Scheme 10.5) [18, 19].



Scheme 10.5

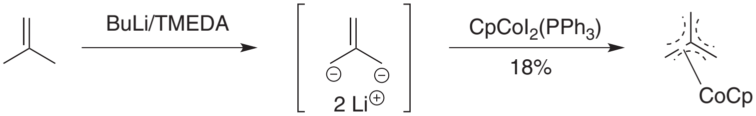
Kemmitt *et al.* used 2-(trimethylsilylmethyl) substituted allylic acetate, chloride, or mesylate as precursors for the formation of trimethylenemethane complexes of ruthenium, osmium, or iridium, with the mesylate performing best. For example, treatment of **16** with *trans*-[IrX(CO)(L)$_2$] (X = Cl, Br, L = PPh$_3$, AsPh$_3$) afforded trimethylenemethane iridium complexes **17** in 75–77% yield; remarkably, the cationic trimethylenemethane complex **18** was obtained in 90% yield by treatment of **16** with [IrH(CO)(PPh$_3$)$_3$] (Scheme 10.6). In a similar way, trimethylenemethane complexes of osmium and ruthenium were prepared, however, in significantly lower yields (20–35%). In these reactions, the 16*e*-iridium(I) complex is thought to undergo an oxidative addition to the C–OSO$_2$Me or C–X (X = Cl, Br) bond with formation of intermediate η^1 and then η^3-allyl complexes followed by an elimination of Me$_3$SiX or Me$_3$SiOSO$_2$Me [20, 21].



17 **16** **18**

Scheme 10.6

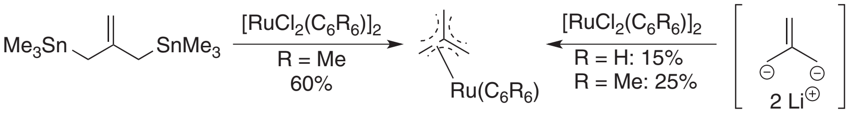
Another general way to prepare trimethylenemethane complexes is the reaction of trimethylenmethane dianions with metal halides. By this way, Mills *et al.* obtained (cyclopentadienyl)(trimethylenemethane)cobalt (**21**) in 18% yield by dilithiation of isobutene (**19**) with butyllithium/tetramethylethylenediamine (TMEDA) to dianion **20** [22, 23] followed by treatment with 1 equiv. of (cyclopentadienyl)diiodo(triphenylphosphane)cobalt (Scheme 10.7). The crystal structure analysis shows a highly symmetric molecule with a slight pyramidalization of the trimethylenemethane ligand away from the cyclopentadienylcobalt unit.



19 **20** **21**

Scheme 10.7

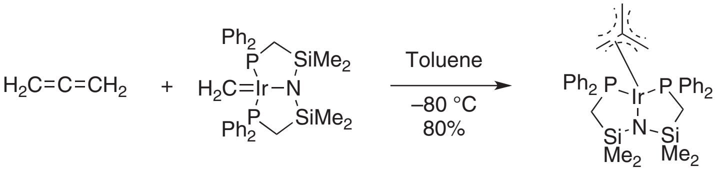
The first ruthenium trimethylenemethane complexes were obtained by Herberich *et al.* by treatment of **20** with [RuCl$_2$(C$_6$H$_6$)] or with [RuCl$_2$(C$_6$Me$_6$)] giving the ruthenium complexes **23** in 15% and 25% yield, respectively. Derivative **23** was also obtained in 60% yield by reaction of **22** with [RuCl$_2$(C$_6$Me$_6$)] (Scheme 10.8) [24]. A rhodium trimethylenemethane complex has been reported by the same group [25]. Some years later, Bursten *et al.* reported the related synthesis of some tantalum trimethylenemethane complexes by treatment of **20** or the triphenyl substituted analog with respective tantalum halides [26].



22 **23** **20**

Scheme 10.8

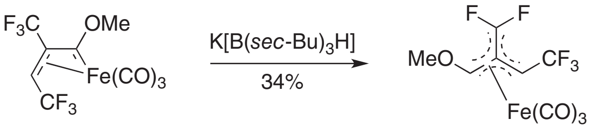
More specialized approaches include the reaction of allene (**24**) with the methylidene iridium complex **25** at −80 °C, which gave trimethylenemethane complex **26** in 80% yield (Scheme 10.9) [27].



24 **25** **26**

Scheme 10.9

Mitsudo reported the synthesis of the fluoro-substituted trimethylenemethane complex **28** by treatment of the trifluoromethyl-substituted vinylcarbene iron complex **27** with K[B(*sec*-Bu)$_3$H] in 34% yield (Scheme 10.10) [28].

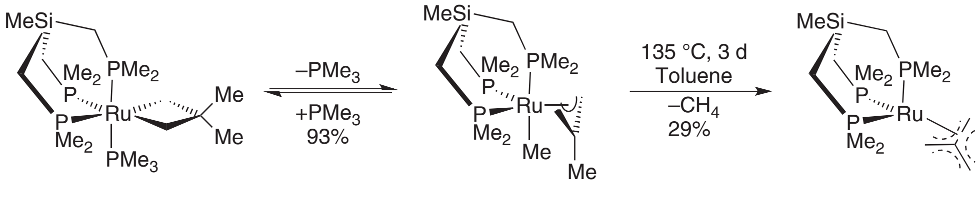


27 **28**

Scheme 10.10

Bergman *et al.* presented a reaction sequence, in which a neopentyl ligand at a tripod ruthenium(II) complex degraded stepwise to a trimethylenemethane ligand. The reaction sequence from **29** via **30** to **31** involves C,C- and C,H-activation steps (Scheme 10.11) [29].

While the η^4-bonding mode in the iron complex **3** has earlier been established crystallographically [11, 12], it is remarkable that this coordination mode is observed in a 17 electron iron(III) complex as well. Dixneuf *et al.* treated iron(III) chloride with magnesium and dichloride **2** in the presence of phosphane ligands and obtained the respective trimethylenemethane iron(II) complexes, which were then oxidized with silver triflate resulting in the formation of cationic trimethylenemethane complexes with the ligand still being η^4-coordinated [30]. Bazan *et al.* reported a distorted η^4 coordination to zirconium [31], and

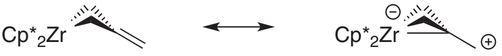


29 **30** **31**

Major (*endo*)

Scheme 10.11

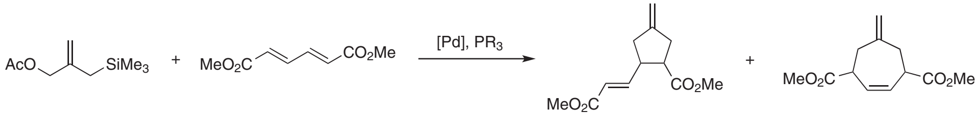
Herberich *et al.* published the structure of bis(pentemethylcyclopentadienyl)(η^3-trimethylenemethane)zirconium (**32**, Cp* = C_5Me_5), for which two resonance formulas were proposed on the basis of the crystal structure analysis (Scheme 10.12) [32].



32

Scheme 10.12

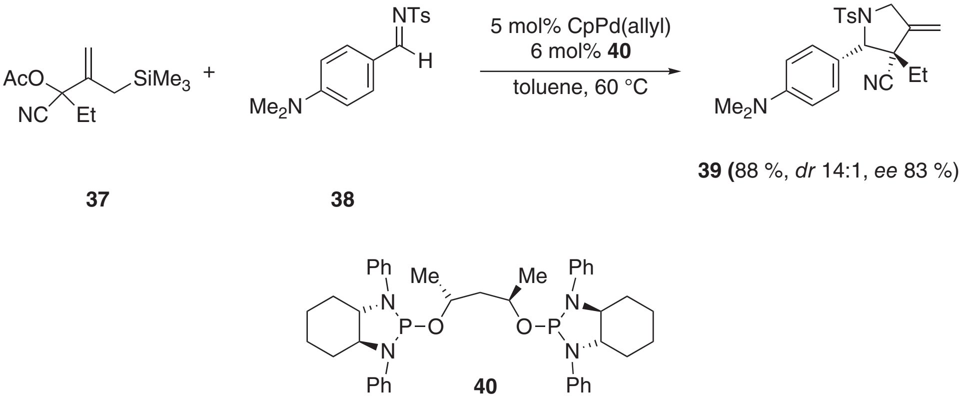
The reactivity of trimethylenemethane complexes has not been studied extensively. There are, however, a number of catalytic reactions, for which the intermediacy of trimethylenemethane complexes is plausible; albeit not proved in all cases, stepwise processes might also be considered [33]. The most prominent examples in this context are palladium-catalyzed trimethylenemethane cycloadditions [34, 35] in the presence of a phosphane or phosphite, starting from 2-acetoxymethyl-3-allyltrimethsilane (**33**), which have been explored in great depth by Trost *et al.* [36, 37]. **33** undergoes [3+2]- as well as [3+4]cyclizations with electron-poor alkenes or dienes such as **34**, respectively, leading to **35** and **36** (Scheme 10.13).



33 **34** **35** **36**

Scheme 10.13

This chemistry has been applied to the synthesis of intermediates to muconic esters [38], hydrazulene derivatives [39], and a number of other cyclopentanoid or cycloheptanoid compounds [40]. The chemoselectivity of the reaction could be improved by the presence of a phenylsulfanyl substituent at the double bond in **33** [41], and the diastereoselectivity has been investigated in the context of intramolecular reactions of tethered starting materials in the syntheses of (−)-isoclavukerin A [42], Most recently, Trost *et al.* [43] developed a regio- and enantioselective synthesis of pyrrolidines bearing a quaternary center making use of the palladium-catalyzed [3+2]-cycloaddition of substituted trimethylenemethanes. The reaction was carried out with **37** as the trimethylenemethane precursor and an aromatic tosyl imine as the cycloaddition partner. (Allyl)(cyclopentadienyl)palladium was used as the palladium source, and the chiral information was introduced by addition of the enantiopure diamidophosphite ligand **40** in the optimized case. As a representative example, **37** reacted with the tosyl amine **38** with formation of the 3-methylenepyrrolidine **39** in 88% yield and 83% ee (Scheme 10.14) [43].



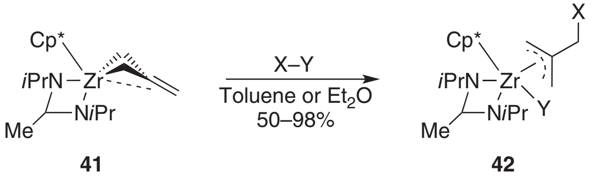
Scheme 10.14

Palladium-catalyzed intramolecular [3+2] cycloadditions starting from alkenylidenecyclopropanes have been reported by Mascareñas *et al.* [44]. For related nickel-catalyzed reactions, the intermediacy of trimethylenemethane complexes has not been invoked [45].

In another reaction of a trimethylenemethane complex, Sita *et al.* identified the unanticipated nucleophilic reactivity of the ligand in an electroneutral zirconium(IV) complex **41**. Nucleophilic addition of methyl, ethyl, or trimethylsilyl triflate, benzyl bromie, or trimethylsilyl chloride afforded adducts **42** in 50–98% yield (Scheme 10.15). The authors rationalized the unexpected behavior on the basis of density functional theory (DFT) calculations [46].

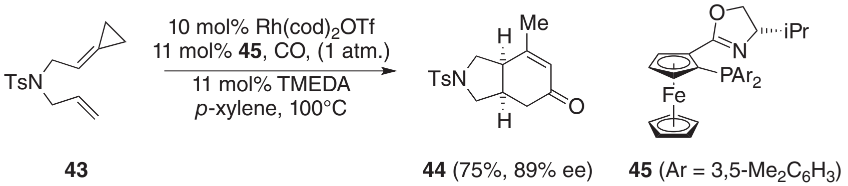
Evans *et al.* recently published an exciting new rhodium-catalyzed [3+2+1] carbocyclization of alkylidenecyclopropanes such as **43** with an alkenyl tether and CO resulting in the formation of cyclohexenones such as **44**. The authors managed to run the reaction enantioselectively in the presence of the chiral ferrocenylphosphane ligand **45** (Scheme 10.16). Extensive DFT calculations make a catalytic cycle with rhodium trimethylenemethane intermediates most likely [47, 48].

Leitner *et al.* very recently published a catalytic application of a trimethylenemethane ruthenium complex. Complex **46** was formed by the reaction



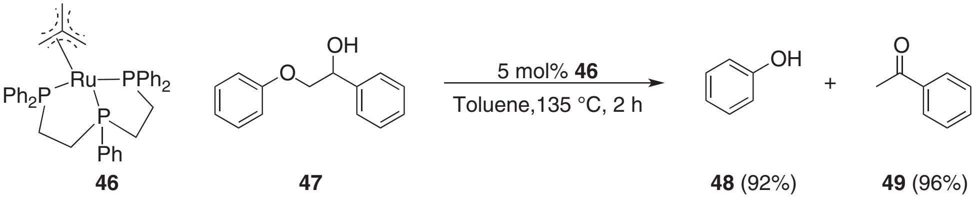
X–Y = MeOTf, EtOTf, BnBr, Me_3SiCl, Me_3SiOTf

Scheme 10.15



Scheme 10.16

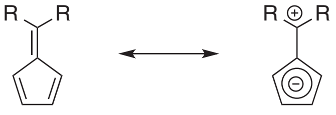
of (1,5-cyclooctadiene)di(methallyl)ruthenium [Ru(cod)(methallyl)$_2$] with bis(diphenylphosphinoethyl)phenylphosphine and came out to be a highly efficient catalyst for the cleavage of C–O bonds, when **47** was used as the model compound. Phenol (**48**) and acetophenone (**49**) were obtained in very high yields (Scheme 10.17) [49]. The proposed mechanism is in accord with a similar reaction disclosed by Bergman *et al.* [50].



Scheme 10.17

10.3
Fulvene Complexes

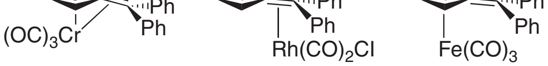
While complexes of triafulvene (methylenecyclopropane; see Chapter 6) have not been reported in the literature, complexes bearing pentafulvene ligands have been investigated for some time. The first review articles about transition metal complexes of fulvenes appeared as early as 1970 by Kerber and Ehntholt [51] and in 1982 by Zdanovich *et al.* [52]. In 2004, Kreindlin and Rybinbskaya [53] published a review article focusing on cationic and neutral transition metal complexes with a tetramethylfulvene or trimethylallyldiene ligand. In many cases fulvenes react



50 **51** Scheme 10.18

with transition metal compounds with formation of a cyclopentadienyl system and a functionalized side chain as a consequence of the formal resonance relation between **50** and **51** (Scheme 10.18). The stabilization of the positive charge in **51** depends on the nature of the substituents R; if one of these bears a lone electron pair, stabilization can be achieved, for example, by formation of an iminium ion. In addition, reactions of fulvenes with reactive metals often result in reductive coupling reactions with formation of the respective metallocenophanes. This chemistry deserves interest with respect to the formation of titanocene-based anti-cancer drugs and has recently been reviewed by Strohfeldt and Tacke [54]. However, there are also complexes, in which one or both of the double bonds of the cyclopentadiene ring are coordinated at a metal.

The modes of complexation of fulvenes include those represented by examples **52**–**54**. Tricarbonylchromium complex **52**, the first fulvene complex, was reported in 1961 by Fischer *et al.* [55] On the basis of its infrared (IR) spectrum, the constitution was originally erroneously assigned with $Cr(CO)_3$ complexation of one of the phenyl substituents. Later, nuclear magnetic resonance (NMR) and crystallographic measurements revealed the true coordination mode shown in **52** as η^6, with the three double bonds of the fulvene system being coordinated to $Cr(CO)_3$ [56, 57]. Wilkinson and Altman [58] published complex **53**, in which only the exocyclic fulvene double bond is coordinated to the transition metal. **54** is an example, in which the fulvene ligand acts as a diene ligand with the two endocyclic double bonds coordinated (Scheme 10.19) [59]. In addition to these mononuclear complexes, some dinuclear fulvene complexes have been reported [60, 61].



52 **53** **54**

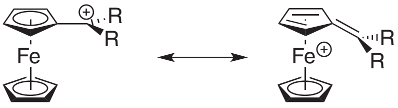
Scheme 10.19

Fulvenes are more or less stable compounds, and their complexes can be obtained by reactions of the ligands with usual complexation reagents. However, the resonance between **50** and **51** allows an alternative route to fulvene complexes: One might envisage the formation of a cyclopentadienyl complex followed by a dissociation of a negatively charged leaving group from the quasi-benzylic position. This route has indeed been pursued and is also used to explain the structural characteristics of, for example, ferrocenylmethyl cations [62].

Tricarbonyl(6,6-diphenylfulvene)chromium(0) (**52**) was obtained by reaction of 6,6-diphenylfulvene with hexacarbonylchromium in 64% yield [56]. Later it was shown that almost quantitative yields can be obtained under photochemical reaction conditions starting from (benzene)$Cr(CO)_3$ or from (mesitylene)$Cr(CO)_3$ as the complexation reagent [63]. The corresponding molybdenum and tungsten complexes were prepared by treatment of the ligands with tris(acetonitrile)$M(CO)_3$ (M = Mo, W) [64]. Olefin complex **53** was obtained by Wilkinson and Altman in 51% yield from 6,6-diphenylfulvene and bis(dicarbonylchlororhodium). Similar complexes were prepared with other rhodium reagents [58]. Hübel and Weiss [59] prepared the diene tricarbonyliron complex **54** (11–30%) in addition to the dinuclear complex, in which either one of the endocyclic double bonds is coordinated at $Fe(CO)_4$ (49–66%).

The η^6-coordination mode in **52** implies a significant bending of the fulvene ligand, which has been verified by the crystal structure analysis. While the bonding distances between the carbon atoms of the five-membered ring and chromium range from 210 to 223 pm, the exocyclic fulvene carbon atom is 253 pm away from the chromium atom. The exocyclic double bond is reported to be bent to the chromium atom by 31° [57].

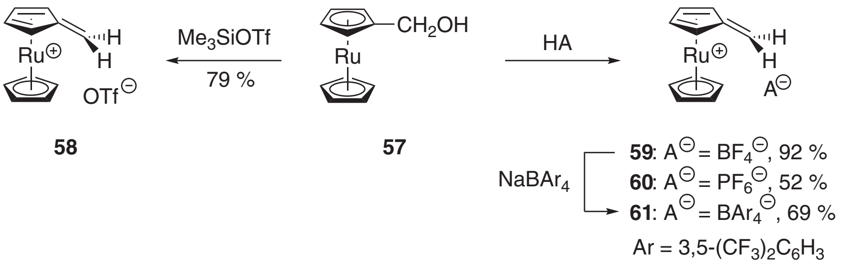
The resonance between **55** and **56** (R = H, alkyl, aryl, ferrocenyl) in ferrocenylmethyl cations including the diferrocenylmethyl cation has been used by Cais to explain the similar bending of the exocyclic C,C bonds toward the iron atom (Scheme 10.20) [65]. The field has recently been reviewed by Gleiter *et al.* [62], who included related isoelectronic boryl substituted systems. Wagner *et al.* [66] have prepared compounds of this type, and the authors proposed attractive interactions between the iron and boron atoms, because the C–B bonds are bent toward the iron atom. The analogy does not only apply to ferrocenes but also to isoelectronic (cyclobutadiene)(cyclopentadienyl)cobalt complexes and other related compounds [62].



55 **56**

Scheme 10.20

Barlow *et al.* reported the synthesis of cationic (η^5-cyclopentadienyl)(η^6-fulvene)ruthenium(II) salts from ruthenocenylmethanol (**57**) either by treatment with trimethylsilyl triflate to achieve **58** in 79% yield. Alternatively, the reaction of **57** with tetrafluoroboric acid or with hexafluorophosphoric acid gave the tetrafluoroborate or hexafluorophosphate salts in **59** and **60** in 92% and 52% yield, respectively. Treatment of **59** with sodium tetrakis[3,5-bis(trifluoromethyl)]borate afforded the tetraarylborate salt **61** in 69% yield, which was, in addition to **60**, crystallographically characterized, confirming the η^6-coordination mode (Scheme 10.21) [67].



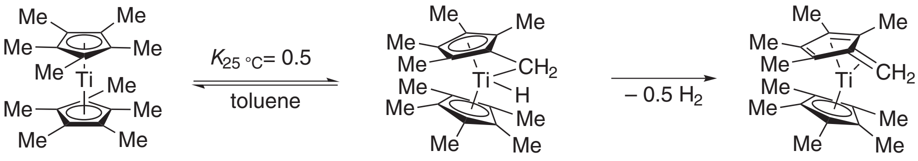
58 **57**

59: $A^{\ominus} = BF_4^{\ominus}$, 92 %
60: $A^{\ominus} = PF_6^{\ominus}$, 52 %
61: $A^{\ominus} = BAr_4^{\ominus}$, 69 %

Scheme 10.21

Recently, Heinekey *et al.* [68] reported the synthesis and structural characterization of a tetramethylfulvene complex of iridium bearing an Arduengo carbene ligand.

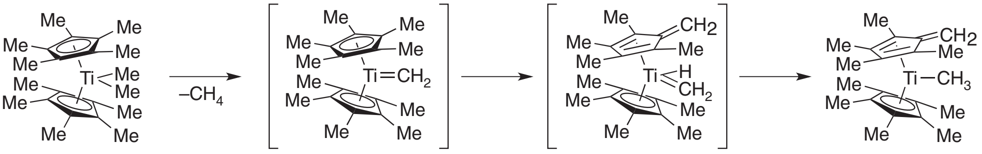
In contrast to reactions of fulvenes with transition metal compounds and the dissociation of methylcyclopentadienyl complexes with a leaving group at the methyl group, the synthesis of titanium fulvene complexes is different in that intramolecular C,H activation processes are involved. As early as 1972, Brintzinger *et al.* [69] prepared the yellow bis(pentamethylcyclopentadienyl) titanium(II) (**62**). This compound was reported to undergo tautomerization to a Ti(IV) species when heated at 35 °C for 10 h. It was not clear at that time if the product was the green fulvene complex **63** with a σ-bound methylene group or a similar species with a coordinated exocyclic double bond. Two years later, Bercaw published a detailed study of the properties of **62** and identified the reaction as a slow, reversible tautomeric process ($K_{25°C} = 0.5$), in which one of the 30 C,H bonds oxidatively adds to the low-valent titanium atom. These assignments are based on detailed analytical studies based on detailed NMR, IR, and mass spectrometry (MS) studies and a variety of other analytical methods. Decamethyltitanocene is reported to be not exceedingly stable. Decomposition occurs upon standing for longer periods of time or by warming above 60 °C with formation of fulvene complex **64** as the main product (Scheme 10.22) [70].



62 (yellow) **63** (green) **64**

Scheme 10.22

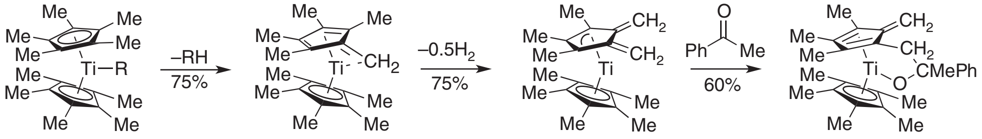
Interestingly, a similar process is observed for the thermal decomposition of dimethylbis(pentamethylcyclopentadienyl)titanium(IV) (**65**). The decomposition takes place at elevated temperatures around about 110 °C and results in the formation of fulvene complex **68** and methane. Extensive labeling experiments and kinetic measurements resulted in two reaction pathways compatible with the experimental observations. Either one involves a titanium methylene species **66** as the key intermediate. The next step is an intramolecular C,H-activation leading to fulvene complex **67**, similar to the formation of **63**. Finally, a hydrogen shift accounts for the final product, fulvene complex **68** (Scheme 10.23) [71].



65 **66** **67** **68**

Scheme 10.23

Teuben *et al.* reported a related reaction, in which the thermolysis of alkylbis(pentamethylcyclopentadienyl)titanium(III) caused a dissociation of alkane with formation of **64**. Further heating at 150 °C resulted in hydrogen dissociation and formation of **70** as a diamagnetic material. Subsequent reaction with acetophenone gave chelate complex **71** in 60% yield, which was fully characterized spectroscopically as well as by an X-ray structure analysis (Scheme 10.24). Interestingly, the authors do not mention the presence of two diasteromers, although the alkyl chain bears an asymmetric carbon atom in addition to the planar chirality of the metallocene. Similar reactions were observed with pyridine derivatives [72].



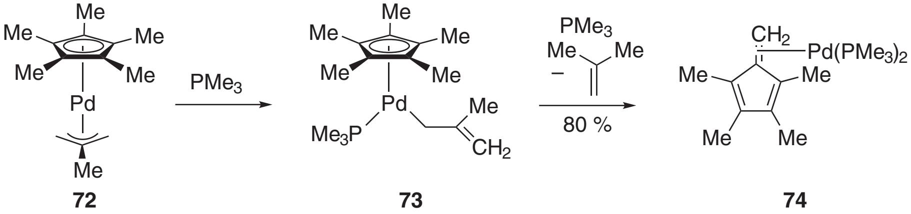
69 **64** **70** **71**

R = Me, Et, Pr

Scheme 10.24

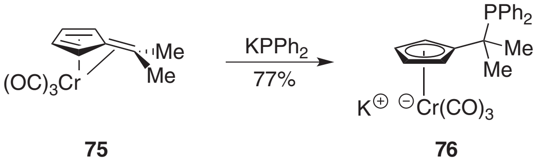
Mach *et al.* [73] showed that similar reactions are possible with less highly methylated titanocene derivatives, and Vondrák *et al.* [74] provided some insight on the basis of respective photoelectron spectra and extended Hückel calculations. Related chemistry has been reported for yttrium complexes [75]. The conversion of a pentamethylcyclopentadienyl ligand to a tetramethylfulvene ligand in a palladium complex was reported by Werner *et al.* [76], who treated

η^3-methallyl complex **72** with trimethylphosphane and observed that a reaction to η^1-methallyl complex **73** followed elimination of isobutene with formation of fulvene complex **74** in 80–90% overall yield (Scheme 10.25).



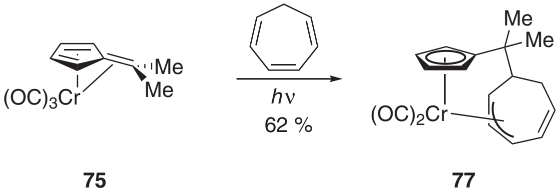
Scheme 10.25

The reactions of transition metal fulvene complexes are dominated by a nucleophilic attack at the exocyclic methylene group with formation of cyclopentadienyl complexes. As an example, Behrens *et al.* treated tricarbonyl(6,6-dimethylfulvene)chromium(0) (**75**) with potassium diphenylphosphide resulting in the formation of the ionic complex **76** in 77% yield (Scheme 10.26). There are many similar reactions with fulvene complexes known [52, 77, 78].



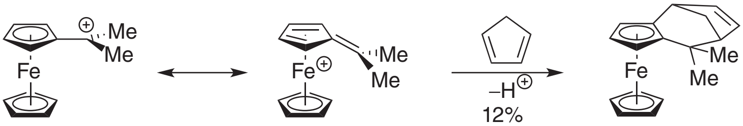
Scheme 10.26

Only a few other types of reactivity of fulvene complexes have been reported. These include the photochemical reaction of **75** with cycloheptatriene, giving chelate **77** in 62% yield [79] (Scheme 10.27).



Scheme 10.27

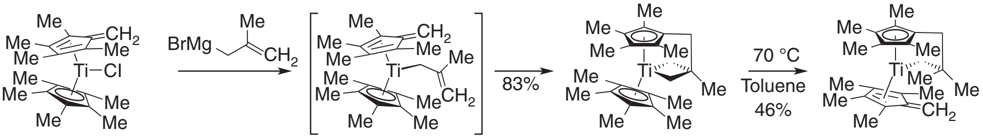
There are some rare reports of cycloaddition reactions involving fulvene complexes. As early as 1971, Watts *et al.* reported the reaction of the ferrocenyldimethylcarbenium ion (**78**) – which is regarded as a 6,6-dimethylfulvene complex **79** by resonance – with cyclopentadiene, resulting in a formal [4+3]cycloadduct **80** in 12% yield, which was characterized spectroscopically (Scheme 10.28). The authors mention that **80** might exist as two diastereomers but do not present experimental evidence [80].



78 **79** **80**

Scheme 10.28

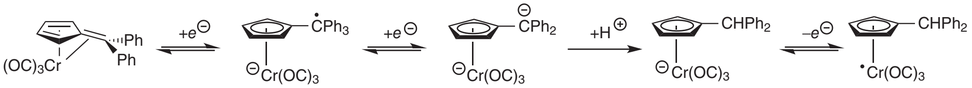
An interesting intramolecular reaction of titanium fulvene complex **81** has been reported by Luinstra *et al.* [81]. Treatment of **81** with methallylmagnesium bromide presumably afforded the unstable η^1-methallyl intermediate **82**, which rapidly rearranged with formation of the tethered titanacycle **83**, which was isolated in 88% yield (from **81**), and which has structurally been characterized. Upon heating at 70 °C in toluene, the remaining pentamethylcyclopentadienyl ligand is transformed into a fulvene ligand, giving **84** in 46% yield (Scheme 10.29).



81 **82** **83** **84**

Scheme 10.29

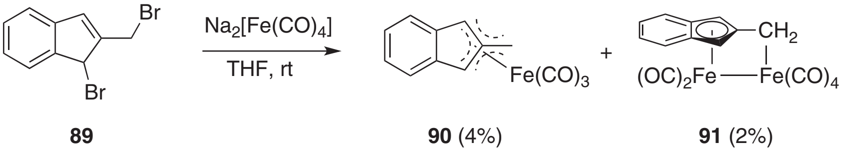
Electrochemical reduction has been applied to a number of transition metal complexes. Geiger *et al.* investigated the electrochemical reduction of the first fulvene complex **52**. They found that the reduction via **85**–**86** involves a haptotropic rearrangement as a result of two single-electron reduction steps. Subsequent protonation to **87** and oxidation accounts for the formation of **88** as the persistent product (Scheme 10.30) [82].



52 **85** **86** **87** **88**

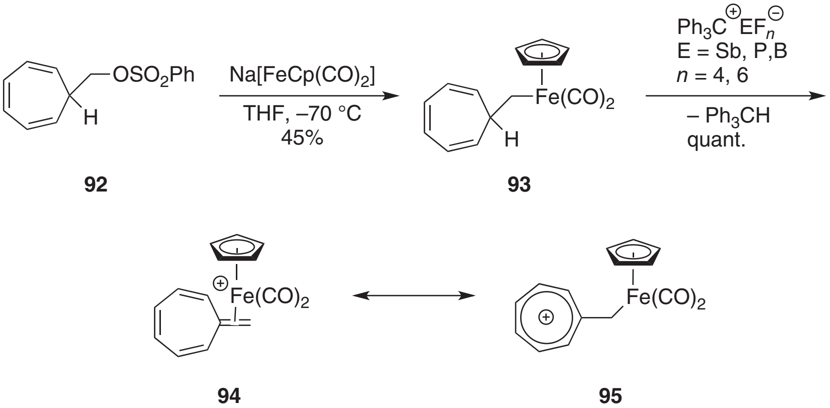
Scheme 10.30

Kerber *et al.* succeeded in the synthesis of the first iron complexes of isobenzofulvene. Reaction of the dibromide **89** with Collman's reagent (disodiumtetracarbonylferrate) afforded isobenzofulvene complexes **90** and **91** in 4 and 2% yield, respectively. **90** is a trimethylenemethane system anellated to an intact benzene ring (Scheme 10.31) [83].



Scheme 10.31

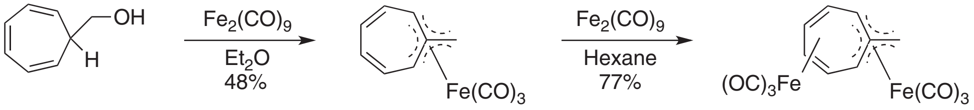
Although pentafulvenes are the by far most common fulvenes, there are some publications describing the synthesis of heptafulvene complexes. The reaction of (cycloheptatrienyl-7-methyl) phenylsulfonate (**92**) with sodium [cyclopentadienyldicarbonylferrate(II)] afforded complex **93** in 45% yield, from which hydride was abstracted quantitatively by treatment with triphenylcarbenium ions. The heptafulvene complex formed was described by resonance formulas **94** and **95**, the latter with an intact aromatic cycloheptatrienylium substructure (Scheme 10.32) [84, 85].



Scheme 10.32

In a similar way, the reaction of carbinol **96** with diironenneacarbonyl afforded heptafulvene complex **97** in 48% yield, showing a trimethylenemethane complex substructure. Further reaction with the iron reagent gave dinuclear complex **98** in 77% yield (Scheme 10.33). The products were characterized by IR, MS, and ^1H NMR analysis.

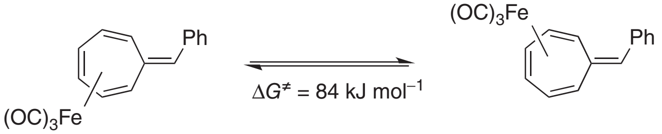
As complexes with more double bonds than necessary for a simple complexation, heptafulvene complexes are of interest in the context of haptotropic



96 **97** **98**

Scheme 10.33

rearrangements. Haptotropic rearrangements are fluxional processes, in which a metal fragment changes its position on an extended π ligand system [86]. Brookhart *et al.* [87] investigated haptotropic rearrangements in cycloheptatriene tricarbonyliron complexes by ^{1}H NMR spin saturation transfer experiments and found a free enthalpy of activation $\Delta G^{\neq} = 84\,\text{kJ mol}^{-1}$ for the reaction between 8-phenylheptafulvene complexes **99** and **100** (Scheme 10.34). Substituent effects in reactions of this kind have later been investigated by Goldschmidt *et al.* [88].



99 (major) **100** (minor)

Scheme 10.34

10.4
Fulvalene Complexes

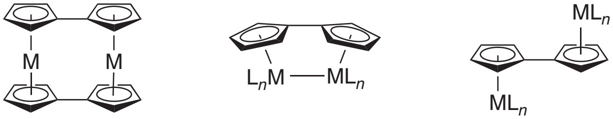
The fulvalenes constitute a class of cross-conjugated hydrocarbons, in which two unsaturated uneven carbocycles are connected by a double bond. Halton showed in a review article that there is a large variety of fulvalenes, which is clearly dominated by pentafulvalene (**101**) and its derivatives (Scheme 10.35) [89].

The pentafulvalenes have a rich organometallic chemistry, which is the result of the redox relation between pentafulvalene (**101**) and its reduction product, the bi(cyclopentadienyl) dianion (**102**). The latter can also be regarded as the product of a double deprotonation of a dihydrofulvalene. In many aspects, this chemistry resembles that of cyclopentadienyl complexes. However, there are a number of features unique to the system of two coupled cyclopentadienyl systems, in particular the chemistry of bimetallic complexes with and without intermetallic bonding and their redox processes [90]. A number of review articles have appeared [91–97]; here, only the key aspects and actual developments are summarized.

101 **102**

Scheme 10.35

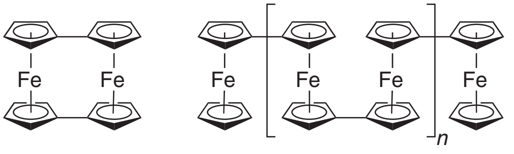
The organometallic chemistry of fulvalene complexes relies on the synthesis of the fulvalene dianion (**102**). This has been achieved by Smart *et al.* [98, 99] by oxidative coupling of the cyclopentadienyl anion with iodine. Later Vollhardt *et al.* [100, 101] published a synthesis of dihydrofulvalene, which the authors described as relatively stable. Most fulvalene complexes are represented by the general formulas **103**–**105**. While **105** is conformationally flexible, this is not the case for **103** and **104**. **103** is a metallocene-derived bis(fulvalene)dimetal complex, a [0.0]ferrocenophane, whereas **104** represents complexes, in which the cyclopentadienyl rings are bent relative to one another, an interplanar angle of 151.5° was observed for a ruthenium example (Scheme 10.36) [101]. The strain caused by this bending might be regarded as a driving force for reactions involving a fission of the metal–metal bond.



103 **104** **105**

Scheme 10.36

The first complex of type **103** was biferrocenylene (**106**), which was first prepared by coupling of ferrocene derivatives in 1969 independently by two groups [102, 103]. A more efficient synthesis was published by Mueller-Westerhoff *et al.*, who treated the fulvalene dianion (**102**) with $FeCl_2$ and obtained **106** in 20–40% yield based on sodium cyclopentadienide in addition to oligomers **107**, some of which were separated [104, 105]. In these oligomers, the fulvalene ligand acts as a bridging ligand between the monomer units. Such complexes deserve interest because of the possible oxidation of Fe(II) to Fe(III), allowing the formation of mixed valence complexes from **106** or **107** (Scheme 10.37).

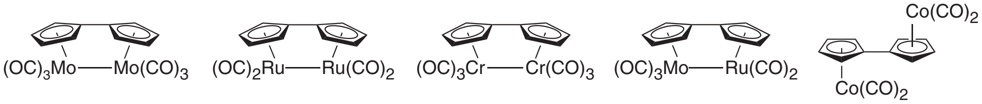


106 **107**

Scheme 10.37

Alternatively, fulvalene complexes have been prepared from alkynylferrocenes by Pauson Khand reactions [106]. Although numerous complexes **103** with metals different from iron and also chiral indenyl-derived dibenzofulvalene complexes are known [107], **106** has remained the most prominent representative of its class. As an example, recent research in the field involves the work of Schmittel *et al.*, who report a higher redox stability for **106** in water at pH = 0–12 as compared to ferrocene, and who incorporated the unit into redox-stable self-assembled monolayers (SAMs) in water [108, 109].

While metallocene-derived complexes **103** deserve interest mainly because of their redox properties and applications resulting therefrom, half-sandwich complexes **104** and **105** show more diverse chemical reactions. Based on their synthesis of the fulvalene dianion **102**, Smart *et al.* [99] prepared some molybdenum complexes such as **108** [62% yield based on Na(DME)Cp] by treatment of **102** with molybdenum hexacarbonyl followed by oxidation with bromine. Vollhardt reported the synthesis of a variety of homo- and heterodinuclear fulvalene complexes such as **109**–**112** by treatment of dihydrofulvalene and respective metal carbonyls. The dichromium complex **110** has some catalytic activity in the hydrogenation of conjugated dienes [110]. The authors report the reaction with iron carbonyls being unsuccessful, whereas the reaction with dicobaltoctacarbonyl resulted in the formation of fulvalene complex **112** lacking a metal–metal bond in 80% yield (Scheme 10.38) [100, 101]. Later, the diiron complex corresponding to **109** was reported [111]. Hermann *et al.* and Cuenca *et al.* prepared zirconium(IV) and zirconium(III) fulvalene complexes [112, 113].



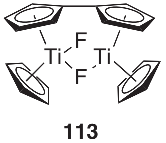
108 **109** **110** **111** **112**

Scheme 10.38

The titanium fulvalene complex **113** was prepared by Roesky *et al.* from bis(cyclopentadienyl)difluorotitanium(IV) by treatment with 1.5 equiv. of potassium at elevated temperature (Scheme 10.39). Although there is no Ti–Ti bond, the fulvalene ligand is bent by 15.3° [114]. Other dinuclear titanium fulvalene complexes were reported by Thewalt *et al.* [115].

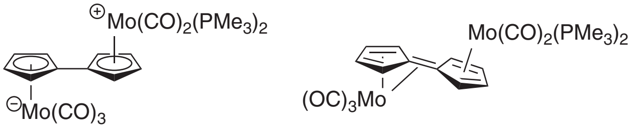
In an interesting reaction with basic phosphines such as PMe_3, the molybdenum complex **108** as well as its tungsten analog reacted with the formation of a zwitterionic complex **114** (63%). In this context, the fulvalene complex **115** has been discussed as an 18-electron complex without charge separation, which was not observed, presumably because **114** allows for a planar fulvalene ligand system (Scheme 10.40) [116].

The reaction of **108** with alkynes (R = CO_2Me, Ph, H) under photochemical reaction conditions afforded complexes **116** with a tetrahedral coordination of the alkyne at the dimetallic unit. Remarkably, these complexes show fluxional



113

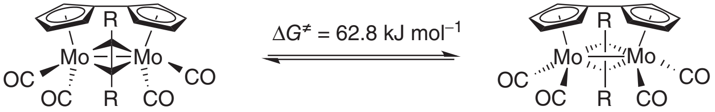
Scheme 10.39



114 **115**

Scheme 10.40

behavior as indicated by variable temperature NMR measurements. The process was identified as the equilibrium between the degenerate structures **116** and **117**, and the free enthalpy of activation $\Delta G^{\neq}$ was determined as 62.8 kJ mol^{-1} (Scheme 10.41) [117, 118].



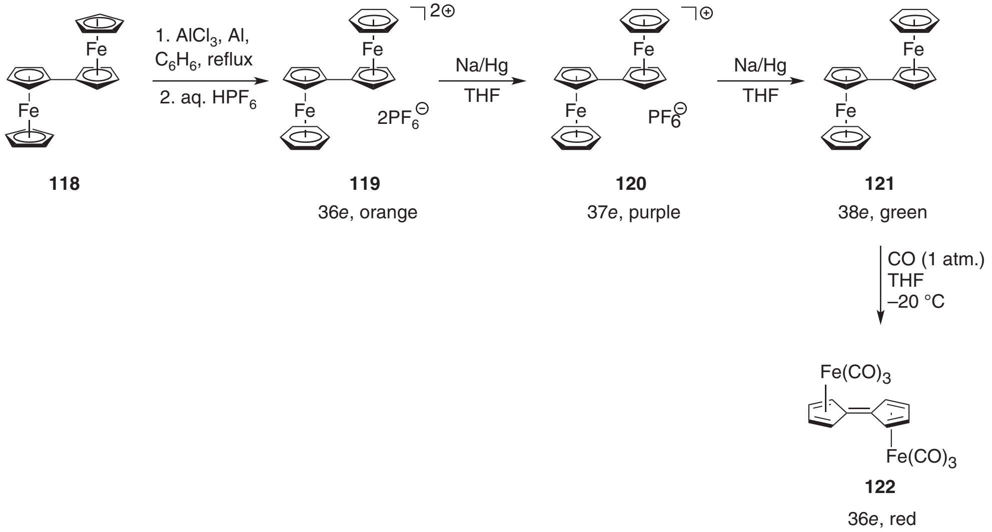
116 **117**

Scheme 10.41

The connection of two metal atoms via a fulvalene ligand has generated interest in the redox chemistry of this type of compounds, which is often investigated by cyclovoltammetry [119, 120]. (Arene)(cyclopentadienyl)iron(I) complexes have been described as the so-called electron reservoir complexes, which have been defined as having at least two stable oxidation states [121]. They have extensively been used by Astruc *et al.* for the design of electrocatalytic processes [122, 123]. In the context of fulvalene complexes, such electron reservoir complexes have been used for the detailed investigation of their redox chemistry by cyclovoltammetry [121]. As (arene)(cyclopentadienyl)iron(I) complexes can be obtained by treatment of ferrocene with aluminum trichloride and aluminum in the presence of the arene, Astruc *et al.* applied this technique to biferrocene (**118**) and obtained after workup with aqueous HPF_6 the dicationic fulvalene complex **119**, which is a 36-electron Fe(II),Fe(II) complex. One electron reduction with sodium amalgam afforded the mixed valence Fe(II),Fe(I) complex **120** and the Fe(I),Fe(I) complex **121**; the latter reacted with carbon monoxide to give the unstable fulvalene Fe(0),Fe(0) complex **122** (Scheme 10.42). These and related complexes were investigated by cyclovoltammetry and Mössbauer spectroscopy, indicating electronic communication (see Chapter 9) between the two iron atoms, presumably via the fulvalene ligand [124].

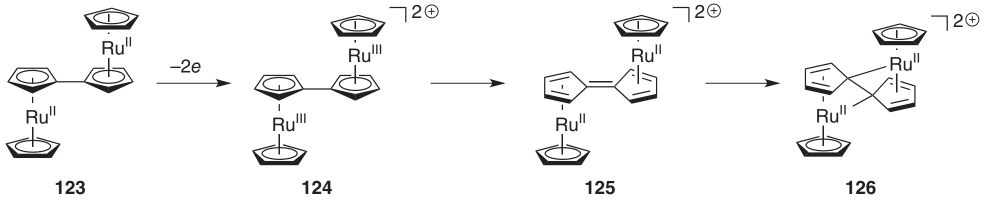
Some fulvalene complexes have served as the backbone of chiral bidendate ligands for asymmetric synthesis [125–127].

Watanabe *et al.* reported an interesting coordination mode of the fulvalene ligand when investigating oxidation reactions of biruthenocene (**123**). Biruthenocene (**123**) was oxidized with *para*-benzoquinone. The reaction is



Scheme 10.42

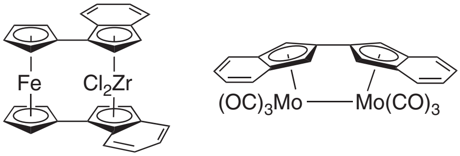
considered to give the biradical intermediate **124** first, which then isomerizes to the fulvalene complex **125**. Finally, reaction to **126**, which has crystallographically been characterized, accounts for an 18-electron configuration (Scheme 10.43) [128].



Scheme 10.43

Vollhardt *et al.* [129] reported the synthesis of some 2,2′,3,3′-tetramethyl- and 2,2′,3,3′-tetra-*tert*-butyl substituted fulvalene complexes of iron, ruthenium osmium, and molybdenum. Some homo- or heterobimetallic fulvalene complexes with anellated benzene rings have been prepared by treatment of the respective dilithium salts with metal halides. Representative examples are the chiral, heteronuclear **127** and the dimolybdenum complex **128**, which have been reported by Brintzinger *et al.* [130] and by Kerber *et al.* [131], respectively (Scheme 10.44).

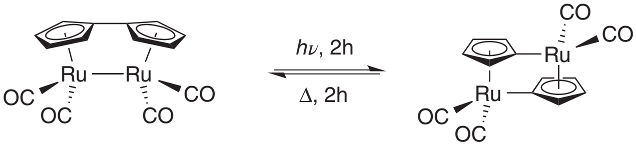
Baird *et al.* [132] observed homolysis of the metal–metal bond in a chromium fulvalene complex derived from **110** by symmetrical disubstitution of two carbonyl ligands by phosphanes with formation of the respective diradical. A remarkable photoisomerization of some fulvalene complexes, which has been found by Vollhardt *et al.* [101, 133], has recently attracted interest in the context



127 **128**

Scheme 10.44

of solar energy storage: Yellow (fulvalene)tetracarbonyldiruthenium (**129**) undergoes a photoisomerization to the colorless **130**, which stores 125 kJ mol^{-1} and can thermally be reversed as indicated by differential scanning calorimetry (DSC) measurements (Scheme 10.45). Labeling experiments involving *tert*-butyl-substituted ligands showed no scrambling, indicating an intramolecular process. A recent picosecond X-ray and IR spectroscopic study combined with DFT calculations has disclosed that the first step of the mechanism is the formation of singlet and triplett *syn*-biradicals, the latter reacting to **130** via a triplet–singlet crossing point toward an *anti*-biradical [134]. The reaction was also realized with ligand exchange products of **129** bearing phosphine or phosphite ligands. Reactions of **129** with alkynes resulted in an interesting ruthenacyclopentadiene, which is intramolecularly coordinated at the second ruthenium atom [135].



129 **130**

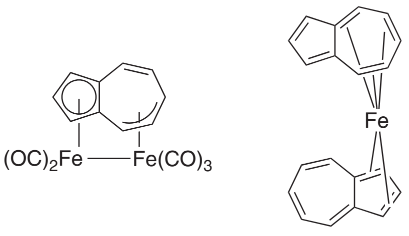
Scheme 10.45

Recently, an IR spectroscopic study showed that the diiron system [111] corresponding to **128** does not undergo such photoisomerization, because this system under irradiation only generates the respective *syn*-biradical and not a triplet species necessary for the formation of a photoproduct corresponding to **130** [136]. Actual publications report on the application of the system for solar energy storage [137].

Higher fulvalene complexes are rarely mentioned in the literature [90]. Higher metallocene oligomers are part of a review by O'Hare *et al.* [95].

10.5
Azulene Complexes

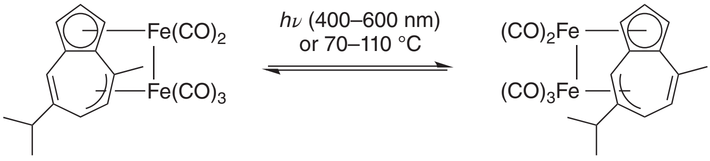
Azulene is an isomer of pentafulvalene and consists of a cyclopentadienyl and a cycloheptatrienyl unit, which are anellated resulting in a fulvene substructure.



131 **132** Scheme 10.46

Formally there are five nonequivalent double bonds; and, as a consequence, a number of different coordination modes have been reported [51]. The complexes are usually obtained by reaction of the ligand with metal complexes such as iron carbonyls. For example, the constitution of the dinuclear iron azulene complex **131** has been identified on the basis of its crystal structure analysis [138]. The interesting complex **132** with two azulene moeties was obtained by the reaction of triisopropyliron (from isopropylmagnesium bromide and $FeCl_3$) and azulene (Scheme 10.46) [139].

Like many complexes of polyolefinic ligands azulene complexes undergo haptotropic rearrangements. Such rearrangements can be detected by variable temperature NMR spectroscopy in cases of symmetric compounds. In asymmetric cases, such processes are detected more easily by normal NMR spectroscopy. Recently, Nagashima *et al.* investigated the haptotropic rearrangement between two isomers of (guaiazulene)$Fe_2(CO)_5$ **133** and **134** (Scheme 10.47). The authors observed the rearrangement between 70 and 105 °C with a 55 : 45 distribution, indicating **133** to be thermodynamically more stable. Based on kinetic studies, the free enthalpy of activation was calculated to be $\Delta G^{\neq}_{373} = 117.2 \pm 4.2\,\mathrm{kJ\,mol^{-1}}$. Interestingly, photochemical irradiation of the compounds also gave the rearrangement, giving an isomeric ratio 35 : 65 [140].



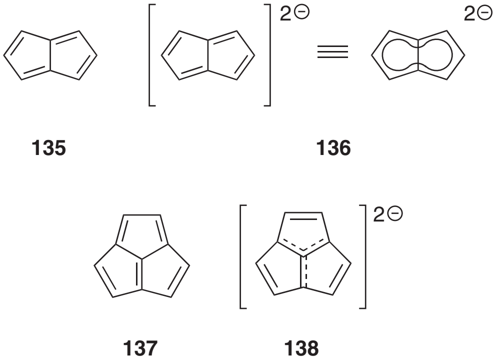
133 **134**

Scheme 10.47

Multinuclear ruthenium complexes with azulene ligands were reported by Nagashima *et al.* [141], who investigated their catalytic behavior in hydrosilylation reactions.

10.6
Pentalene and Acepentalene Complexes

Pentalene (**135**) and acepentalene (**137**) are antiaromatic cross-conjugated compounds with two or three fulvene subunits. According to theoretical calculations [142–147], **135** and **137** are unstable species [147, 148] but can be ligands in transition metal complexes. The respective anions, the planar **136** [149, 150] and the slightly bowl-shaped **138** [151, 152], can be generated by deprotonation of a dihydropentalene or by treatment of 4,7-bis(trimethylstannyl)-4,7-dihydroacepentalene with methyllithium at −60 °C (Scheme 10.48).



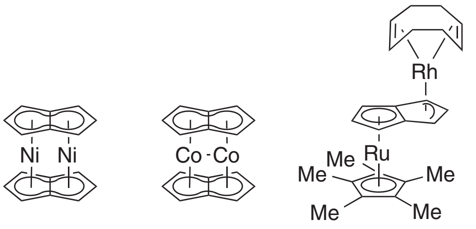
135 **136**

137 **138**

Scheme 10.48

The organometallic chemistry of pentalene has been reviewed; here, only representative examples of this chemistry are presented [95, 153–156].

Remarkably, the dianion **136** has been known for longer than the electroneutral **135**, and some metallocene like complexes such as **139** and **140** have been prepared from **136** by reaction with nickel(II) or cobalt(II) chlorides [157, 158]. Complexes of this kind have recently been the subject of extensive theoretical calculations [159–161]. There are also complexes with the metal atoms on either side of the pentalene ligand, for example, the heterobimetallic complex **141** (Scheme 10.49) [162]. Furthermore, such bimetallic and related pentalene

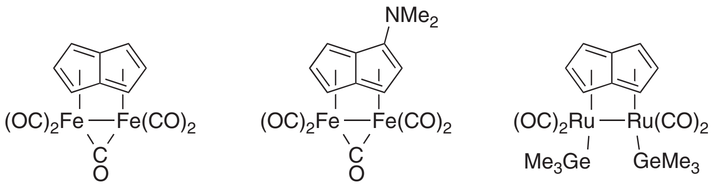


139 **140** **141**

Scheme 10.49

complexes deserve interest with respect to an interaction between the two metal atoms [95, 163, 164].

Hafner succeeded in the synthesis of the unsubstituted pentalene complex **142** as early as 1973 by irradiation of a [2+2] dimer in the presence of $Fe_2(CO)_9$, and substituted complexes such as **143** were obtained by treatment of the respective dihydropentalenes with pentacarbonyliron [165, 166]. In a remarkable reaction, ruthenium complex **144** was obtained by treatment of 1,3,5,7-cyclooctatetraene with *cis*-$Ru(CO)_4(GeMe_3)_2$ (Scheme 10.50) [167].

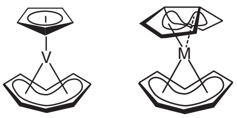


142 **143** **144**

Scheme 10.50

In addition to the complexes mentioned, there are some in which the pentalene ligand is separated into a cyclopentadienyl and an allyl part, comparable to ring slippage chemistry and the so-called indenyl effect [162, 168].

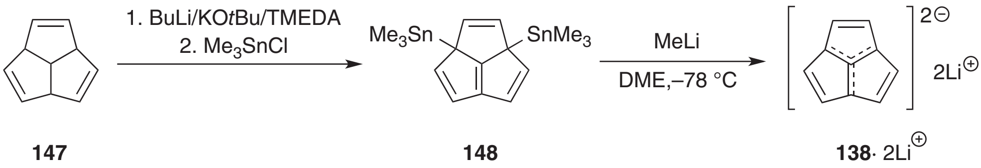
In 1997, Jonas *et al.* reported a new bonding mode of the pentalene ligand, in which all eight carbon atoms are bonded to *one* metal atom. This η^8 bonding mode requires a considerable bending of the pentalene ligand. The first complex of this kind was the vanadium complex **145**. Then the authors presented early transition metal complexes such as **146** (M = Ti, Zr, Hf) with *two* pentalene ligands adopting a perpendicular conformation (Scheme 10.51). Complexes **146** are described as diamagnetic 20*e* complexes [169, 170]. Later, more complexes with this coordination mode have been described [171–173]; for example, an interesting uranium complex, which was obtained starting from 1,3,5,7-cyclooctatetraene via the pentalene dianion (**136**), double silylation, and subsequent deprotonation with potassium amide to give a silylated pentalene dianion, which was finally treated with $U(C_5Me_5)I_2(thf)_3$ [154]. The bent η^8-pentalene ligand and its complexes with early transition metals have been compared with the two cyclopentadienyl ligands and their complexes, the so-called bent metallocenes. Recently, O'Hare reported interesting permethylated derivatives that correspond to the pentamethylcyclopentadienyl ligand system [174–177].



145 **146**

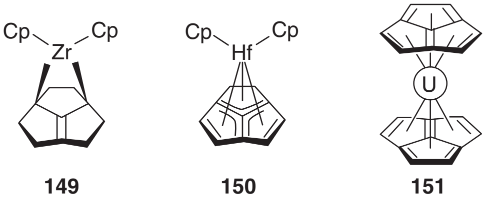
Scheme 10.51

While some complexes of dihydroacepentalene derivatives have been reported some time ago [178–180], metal complexes of the unstable acepentalene (**137**), although they were the subject of DFT calculations [181], are still elusive. The acepentalene dianion (**138**) was obtained as its lithium salt in pure form by treatment of triquinacene (**147**) with BuLi/KO*t*Bu/TMEDA giving **138** as its impure potassium salt, which was trapped with Me_3SnCl. The 1,7-bis(trimethylstannyl)-4,7-dihydroacepentalene (**148**) obtained was then treated with methyllithium, affording pure dilithium acepentalenediide (**138**·$2Li^+$) (Scheme 10.52) [152].



Scheme 10.52

Treatment of **138**·$2Li^+$ with zirconocene dichloride, hafnocene dichloride, and uranium tetrachloride gave acepentalene complexes **149–151** (Cp = cyclopentadienyl), as indicated by NMR spectroscopy. Interestingly, the hafnium complex was described as a tris-etheno-bridged trimethylenemethane complex (Scheme 10.53) [182, 183].

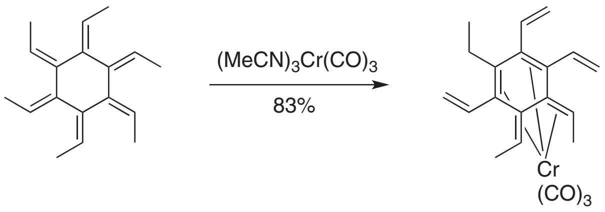


Scheme 10.53

10.7
Various Complexes

This section collects some examples of complexes with cross-conjugated ligand systems, which were not covered in the preceding chapters.

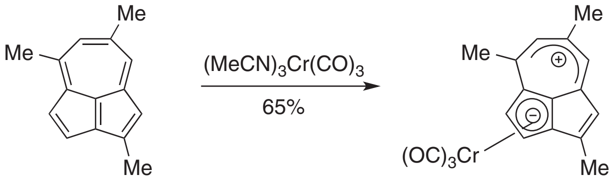
Wilke *et al.* [184] treated the [6]radialene **152** with $(MeCN)_3Cr(CO)_3$ and did not obtain a radialene complex or the desired tricyclobutabenzene derivative. Instead, the *ortho*-quinodimethane complex **153** was obtained in 83% yield (Scheme 10.54). A related complex was later proposed by Kündig as an intermediate of a ring-opening reaction of a benzocyclobutene complex [185].



152 **153**

Scheme 10.54

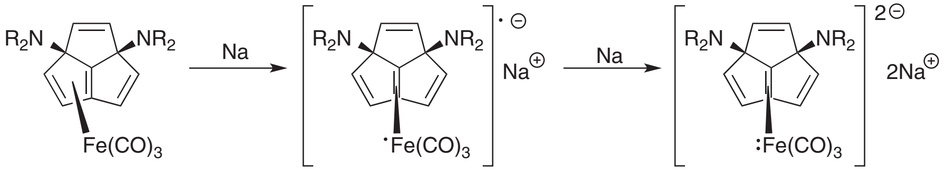
Behrens reported the synthesis of complex **155**, which was obtained in 65% by complexation of the ligand **154** with $(MeCN)_3Cr(CO)_3$ (Scheme 10.55) [186] Note that the ligand **154** is a higher vinylogue of acepentalene.



154 **155**

Scheme 10.55

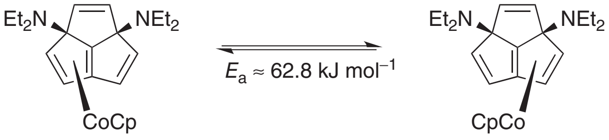
Cross-conjugated dihydroacepentalene complexes **156** ($NR_2 = NEt_2$, piperidino, 3,5-dimethylpiperidino, morpholino) and **159** were prepared by de Meijere and Butenschön [179, 180] by treatment of the ligands with either $Fe_2(CO)_9$ or $CpCo(H_2CCH_2)_2$ in yields up to 70%. When complex **156** was reduced with sodium, the persistent radical anion was detected with spin density on the iron atom as indicated by electron spin resonance (ESR) spectroscopy. Further reduction with sodium afforded the ferrate(-2) **158**, which is diamagnetic and could be characterized by NMR investigations (Scheme 10.56).



156 **157** **158**

Scheme 10.56

The cyclopentadienylcobalt complex **159** was shown to bear the CpCo moiety on the exo surface of the ligand system as shown by normalized one-dimensional nuclear Overhauser effect (NOE) measurements. Interestingly, the complex undergoes a degenerate haptotropic rearrangement, as was shown by variable temperature ^{1}H NMR measurements. This process includes a racemization of the complex (Scheme 10.57) [180].



159 **159**

Scheme 10.57

Note added in proof: Since the submission of this contribution some additional publications have appeared [187, 188].

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11

Cross-Conjugation and Quantum Interference

Gemma C. Solomon

11.1

Introduction

As nanoscience develops, so do the physical measurements we perform, and the types of environments under which we consider molecular properties. One consequence of this development is that classes of systems that are well known and studied in one field can suddenly ignite interest in another. While the result might not surprise in retrospect, it certainly could not have been predicted. This has certainly been the case for cross-conjugated molecules in molecular electronics. This monograph testifies the breadth of this class of compounds and the wide range of their applicability. But it is unlikely that any synthetic chemist, no matter how expert, would have predicted that these systems would become the poster children for quantum interference in electron transport.

The interest in interference effects in cross-conjugated molecules arose from molecular electronics. The chemist's vision of molecular electronics consists of chemically tailored circuits, where the electronic function is controlled by carefully designed substituents. This requires more than "molecular wires"; it requires functions such as memory elements, switches, logic elements, and gate dielectrics. In short, it requires polarizable but nonconducting elements. In many of these cases, an "off" state is required in addition to the "on" state. Sometimes there is a requirement for fast switching between these states, and at other times long-term stability of either the "on" or "off" state is needed.

Cross-conjugation makes this possible as it results in interference effects that deliver an "off" state in fully conjugated systems.

This chapter begins with an introduction to electron transport in organic molecules and how to understand the measurements/calculations. Next, we explore how to understand and predict interference effects; and, finally, we go beyond topology and explain how interference effects can be controlled chemically.

Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.

11.2
Molecular Electron Transport

Molecular electronics has grown from the proposal by Aviram and Ratner in 1974 for a unimolecular rectifier [1] to a field with ongoing theoretical and experimental efforts around the world. While it is relatively simple to imagine a molecule bound between two conducting electrodes (or three in the case of a gated device), practically realizing such a device has been significantly more challenging. It has required heroic experimental efforts to develop methods for reproducibly contacting molecules in these junctions, and even today the work is anything but finished. As with all single-molecule measurements, the variation from measurement to measurement means that the conductance of a single molecule can only be determined from an ensemble of measurements (as opposed to the ensemble of molecules usually studied in bulk measurements).

Traditional studies in chemistry or physics do not prepare us well for dealing with these kinds of junctions. Chemists are used to dealing with molecules in solution, in the gas phase, or possibly in the solid state, not bound between large metallic electrodes. Similarly, physicists are used to dealing with materials or quantum dots. But the chemical details in organic molecules present different challenges. Before we can really use chemistry to control the transport properties, we have to discuss the complexity of the system. Figure 11.1 illustrates some of the factors that may influence the transport properties. In (a) it is illustrated that the binding site may be a decisive factor. But the binding orientation (b), functional groups used to bind the molecule to the surface (c), other substituents (d) including those introduced for solubility, conformational flexibility (e), thermal fluctuations (f), and intermolecular interactions (g) may also be crucial. Clearly, if we want real chemical control of the conduction properties, the changes we induce with functionalization should dominate over the level of variation that might exist from, for example, the variability in how a molecule binds to an electrode surface.

While conductance measurements on single molecules have only been performed over the past 15 years, charge-*transfer* (as opposed to *transport*) measurements have been carried out much longer. Charge-transfer measurements are most often performed in solution with the so-called donor–acceptor or donor–bridge–acceptor systems. The conjugated molecules in Figure 11.1 could be examples of bridges and these could be bound between donor and acceptor moieties. Figure 11.2a illustrates a cross-conjugated bridge bound between a donor and acceptor and in (b) we show the same bridge with binding groups between metallic electrodes.

To the extent that the bridging molecule controls the properties in both instances, these two measurements are indisputably related; however, the difference between molecular donors and acceptors and large electrodes leads to very different observables. Of particular importance for our discussion here, electron transfer measurements are controlled by the electronic coupling at one particular energy, which is set by the nature of the donor and the acceptor. Charge-transport measurements, on the other hand, are mediated by the electronic coupling

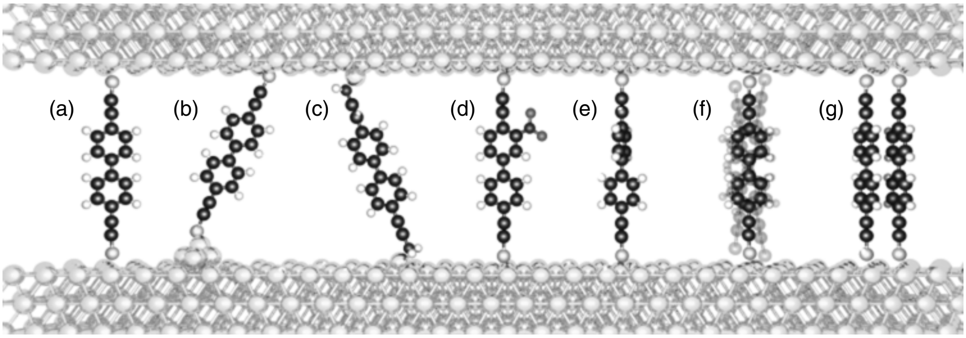


Figure 11.1 Some of the details of a junction that may impact transport properties: (a) the binding site, (b) binding orientation and electrode structure, (c) binding groups, (d) substituent effects, (e) conformational flexibility, (f) thermal fluctuations, and (g) intermolecular interactions.

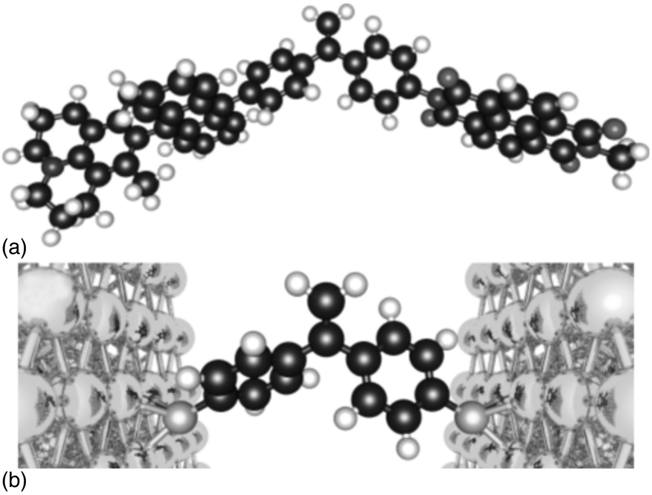


Figure 11.2 (a) An example of a donor–bridge–acceptor system with a cross-conjugated bridge and (b) the same cross-conjugated bridge with binding groups between gold electrodes.

over a range of energies, with the bias window controlling the energy range. We will show that the transport properties through cross-conjugated molecules are extremely energy dependent and, as a consequence, care needs to be taken when comparing these two classes of measurements. At the same time, the charge-transfer and charge-transport properties are sufficiently closely related that inspiration for one area can surely come from the other.

In this chapter, we focus on electron transport through molecules bound between gold electrodes, and even more specifically, we will focus on the theoretical description of the transport properties of cross-conjugated molecules.

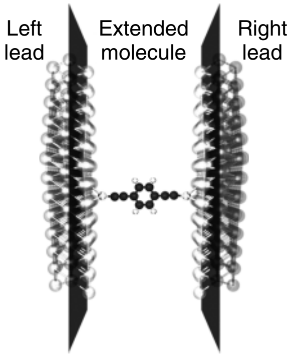


Figure 11.3 The partitioning of the junction into three regions: two leads (electrodes) and an extended molecule.

To this end, we will first give a brief introduction to transport theory and how the properties we calculate – and will discuss throughout this chapter – relate to experimental observables.

Before we detail the formal aspects of the approach, it is important to understand the partitioning of the system in a physical sense. The junction is divided into three regions, illustrated in Figure 11.3, two leads and an extended molecule region that may or may not include some number of lead atoms. In Figure 11.3, the extended molecule includes a whole layer of the electrode, but this need not be the case and the partitioning may simply include some number of atoms that form part of one or several layers.

We calculate the current through the system by calculating the current through the extended molecule with integration over the transmission, $T(E,V)$:

$$I(V) = \int_{-\infty}^{\infty} \mathrm{d}E[f_{\mathrm{L}}(E) - f_{\mathrm{R}}(E)]T(E, V)$$

The bias enters the formalism in two ways. Firstly, through the bias dependence of the electronic structure, that is: the way the molecule polarizes or changes under an applied electric field, and this is wrapped into the transmission. Secondly, through the effective window of integration given by the difference in the Fermi functions of the two leads (f_{L} and f_{R}), that is: the range of energies incident electrons travel (or attempt to travel) through the system. The electronic structure of some molecular systems is relatively invariant to small changes in the bias and in these cases the current–voltage characteristics of the junction may be reasonably approximated by integrating the zero-bias transmission over a varying window.

The transmission is, exactly as the name suggests, the probability (per channel) that an electron incident on the extended molecule with energy E will pass through the system. In the case of a single conduction channel, the transmission maximum will be 1; however, most molecular systems have more than one channel and, while it is not common, the transmission can exceed 1. For the purpose of this chapter, we omit the details of how the transmission is calculated; these can be found elsewhere [2]. The essential point for our present discussion is that high transmission will lead to high levels of current, while low transmission will lead to low levels of current.

Throughout this chapter we will also refer to the conductance of the junction, which is properly the differential conductance and is defined as:

$$g(V) = \frac{dI(V)}{dV}.$$

11.3
The Transport Properties of Cross-Conjugated Molecules

In an interdisciplinary field like molecular electronics, one cannot afford to assume that a concept like cross-conjugation will always be understood. We use the definition provided by Phelan and Orchin [3] "*A cross-conjugated compound may be defined as a compound possessing three unsaturated groups, two of which, although conjugated to a third unsaturated center, are not conjugated to each other. The word "conjugated" is defined here in the classical sense of denoting a system of alternating single and double bonds.*" For our purposes, however, it is not significant whether the molecule as a whole is cross-conjugated, but rather whether the path through the molecule from one electrode to the other is cross-conjugated.

Consider, for example, the system shown in Figure 11.4. We can take a single molecule (which is cross-conjugated according to the Phelan and Orchin definition) and define two paths, a short path that is the cross-conjugated path and a long path that is conjugated in the classical sense, that is, linearly conjugated. Normally, electronic coupling and electron transport decrease exponentially with the length of the system. Thus, relying on this assumption alone, we would predict that the short path should have significantly higher levels of transport/current than the long path. The difference in the conjugation, however, means that the short path has dramatically lower levels of transport than the long path, as shown in Figure 11.5. In fact, just above the Fermi energy (E_F), the transmission through

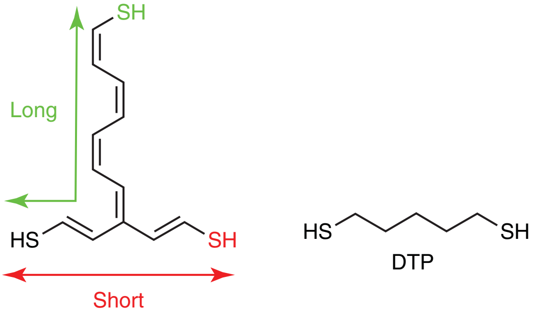


Figure 11.4 The *long* and *short* systems are defined as two different methods of attaching the molecule on the left to two gold electrodes. In both cases, one electrode is attached to the thiol group shown in black; the long system utilizes the thiol shown in light grey, and the short system uses the thiol shown in dark grey. These are compared with DTP (pentane-1,5-dithiol, right). (Reproduced from [4].)

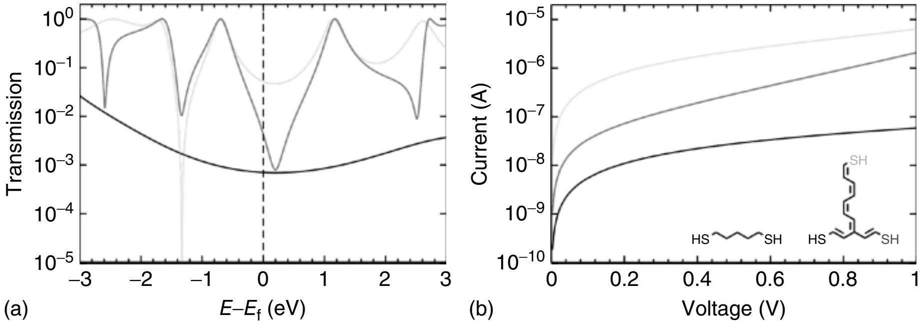


Figure 11.5 The (a) transmission and (b) current through the long system (light grey), short system (dark grey), and dtp (black). The dramatic differences between the long system and the short system cannot be predicted from the conventional understanding of molecular electron transfer. (Reproduced from [4].)

the short path approaches the low levels seen through a fully saturated system of the same length (DTP).

It is tempting to explain transport properties in terms of the molecular orbitals of the molecule, but this example shows why this is perilous. When we compare the short and long systems here, we are not comparing two different molecules, only two different paths. The orbitals for the two systems are therefore identical. Figure 11.6 illustrates the molecular orbital properties of the systems. The long/short system has a relatively small HOMO−LUMO gap with π-type orbitals for the HOMO and the LUMO. These two orbitals are also illustrated in Figure 11.6 and it is not obvious – from the orbital viewpoint, why there is a reduced level of transport through the short path. Both orbitals are delocalized across the entire molecule, illustrating that delocalization is not a simple proxy for electronic coupling. We will show later that it is actually possible to see from the orbitals that there are interference effects reducing the transport. This, however, is something we see from the pattern of nodes in the orbital; it is certainly not obvious at first glance.

As mentioned in the introduction, the reduced transport through the short path is, in fact, an effect of quantum interference. It is common for molecules with cross-conjugated paths spanning the two electrodes. In fact, many molecules exhibit interference effects, but they are not always in an energy range that would make the effect observable experimentally.

Let us take another example to understand what characterizes the interference effects seen in cross-conjugated molecules. Consider the three model systems shown in Figure 11.7. In all cases, there are two thiol groups, which we use to bind the molecule to our gold electrodes with the terminal hydrogen atoms removed, and two triple bond "linkers," used to space the central unit out from the electrodes. These are model systems in the sense that they are unknown in the literature; however, the linking groups can be substituted with any linearly conjugated moiety and the binding group changed as appropriate for the electrode and the trends in the transport will be unchanged.

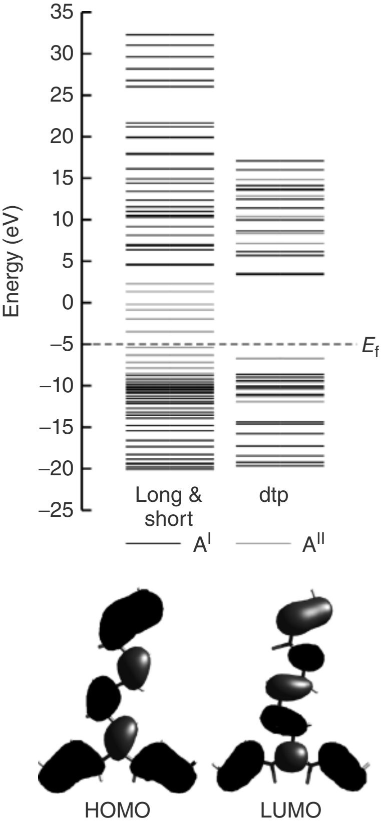


Figure 11.6 The molecular orbital eigenenergies for the isolated molecules (left) show the large band gap typical in the saturated system and the much smaller gap in the conjugated systems. The gold Fermi energy is shown for comparison. The HOMO and LUMO of the short/long system (right) show delocalization across all three arms, giving no indication that there should be any difference between the different paths beyond their differing length.(Reproduced from [4].)

The critical component for our purpose here is the central double bond. When we have both binding groups attached to the same carbon atom of the double bond, we have our cross-conjugated path between the electrodes. The transmission for these three molecules is shown separated into symmetry (σ and π) components. That is, we can isolate the contributions to the total transmission that are carried by the σ and π systems within the molecule. In all cases, the black line is the symmetry component and the black line is the total transmission, which is simply a sum of the two components.

In the two linearly conjugated systems, the π component dominates across the entire energy range; this effect is so strong that we cannot see the black line below the black line. The σ component is significantly lower. This is the "usual" behavior for conjugated molecules: The π-system dominates the transport near the Fermi energy (low bias); the π-orbitals result in nearby transport resonances and much higher levels of transport than those seen in saturated systems.

In the cross-conjugated system, the situation changes. The π-transmission has a sharp dip very close to the Fermi energy; this is a signature of destructive interference. As the π-transport is suppressed, the total transmission is actually dominated by the underlying σ-transport near the Fermi energy. This is why the

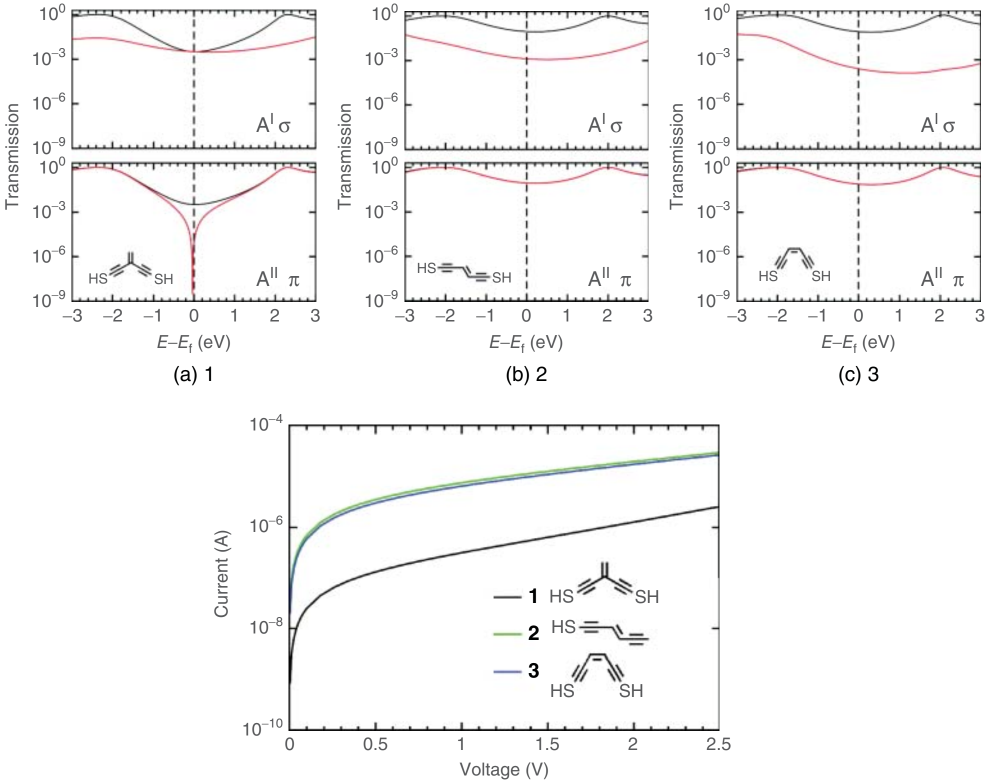


Figure 11.7 (a–c) The electronic transmission as a function of energy (relative to a common electrode Fermi energy) for a series of small molecules bound between Au electrodes using gDFTB. In each case, the grey curve illustrates the individual σ or π components of the transmission and the black curve is the total transmission. In the cross-conjugated species (1), there is an interference feature evident in the π-transmission, meaning that the σ-transmission dominates at the Fermi energy. The interference effect results in a dramatic reduction of the current through the system as shown below. (Reproduced from [5].)

transmission through the short system approaches the low level calculated for DTP. Close to the interference feature, a cross-conjugated molecule will only carry current through the σ-system, and thus resembles a saturated molecule of the same length.

This is perhaps a somewhat surprising result. We normally consider that fully conjugated molecules will be dominated by the π system. Of course, if the π-transport approaches zero, this cannot be the case. As soon as we move away from the interference feature (in energy), the π-system again dominates the transport and a cross-conjugated molecule simply resembles any other conjugated molecule.

Molecules **1**–**3** and our "short" path are cross-conjugated in the sense of the Phelan and Orchin definition. However, one can see exactly the same effect if the

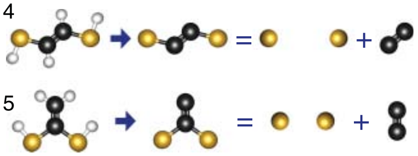


Figure 11.8 The molecules **4** and **5** considered (left) can be reduced to a Hückel model for the π-system (center) and partitioned into the binding groups and central conjugated unit (right).

two triple bond linkers are removed. In these systems, for example, those shown in Figure 11.8, we no longer have three unsaturated centers, but it is the path between the two sulfur atoms or more generally the two electrodes that is not conjugated in the classical sense. In a simple hydrocarbon (no heteroatoms and no electron-donating or electron-withdrawing substituents), the nature of the conjugation is a good predictor for interference. As we will show later, however, substituents can change the situation.

11.4
Understanding and Predicting Interference

The next question that arises is how to understand and predict this interference. In terms of understanding, we can ask the question "What is interfering with what?" In cyclic systems, such as meta-substituted phenyl rings, it is tempting to attribute the interference to the two paths with different lengths around the ring. In our acyclic cross-conjugated molecules, however, we would have to argue that we had perfect cancelation between a pathway going straight through the system and a path that came in, went up on an excursion into the double bond, and headed out the other side. This is one way to interpret these effects, but we never found it to be particularly intuitive or convincing.

Instead, we understand these effects to arise from canceling contributions to the transport from the occupied and virtual molecular orbitals. We will illustrate this idea with the two molecules **4** and **5** shown in Figure 11.8. Following Hoffmann, it is clear that whether the electronic coupling is "through space" or "through bond," the splitting of orbitals is the definitive signature for electronic coupling [6]. As the interference effect is a feature of the π-system transport, we can first reduce the molecules to a model for the π-orbitals only, as shown in the center of Figure 11.8. Secondly, we can split the system into a pair of sulfur atoms and the two carbon atoms that form the double bond. Then, we can ask the question whether the sulfur p_π-orbitals are split by the interaction with the molecule.

In the absence of coupling to the bridge, the bonding and antibonding combination of the two sulfur orbitals will be degenerate (Figure 11.9, left). The bonding and antibonding combination of the p_π orbitals on the carbon atom (Figure 11.9, right) are split significantly due to the interaction across the double bond. By symmetry, the bonding (symmetric) combination of the carbon orbitals will interact with the bonding combination of the sulfur orbitals, the orbitals "repel" each other and lead to two orbitals in the combined system: a lower energy orbital with dominant carbon character and a higher energy orbital with dominant sulfur character.

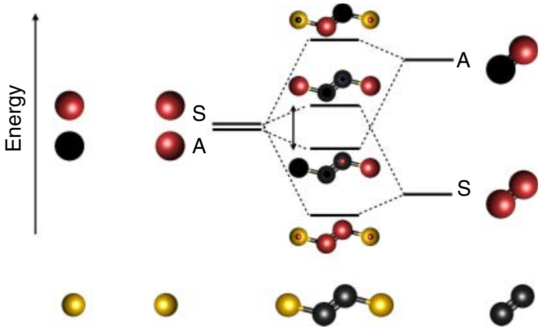


Figure 11.9 The orbital splitting diagram for **4**, showing the interaction between the two S orbitals and two A orbitals of the fragments, lifting the degeneracy of the sulfur dominated orbitals of the combined system (center). Note: *y* axis not to scale.

In the same way, the antibonding (asymmetric) combination of the orbitals will interact and form two combined orbitals; however, this time the sulfur-dominated orbital is the lower energy orbital.

When we look at the final orbital spectrum (Figure 11.9, center), we see that the two sulfur-dominated orbitals are effectively split by the interaction with the bridge. This splitting constitutes the molecular orbital signature of electronic coupling through the molecule.

In the same way, we can construct a molecular orbital diagram for the π-system of our cross-conjugated molecule, as shown in Figure 11.10. The process is identical, but now the symmetry of the system has changed. The antibonding combination of the sulfur orbitals does not interact with either the bonding or antibonding orbital on the bridge because the symmetry of the orbitals is not the same. This

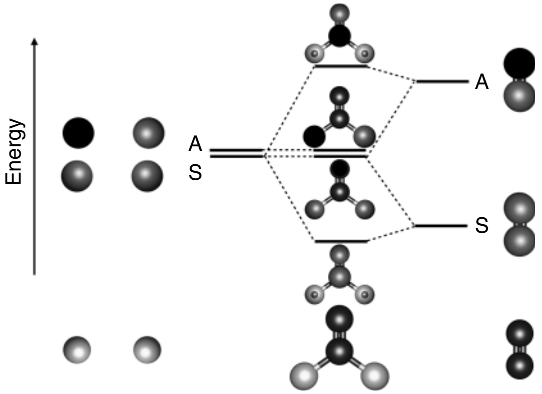


Figure 11.10 The orbital splitting diagram for system **5**, showing the interaction between both the S and A carbon fragment orbitals and the S sulfur fragment orbital. If the site energies for the sulfur pπ orbitals are the same as the carbon pπ orbitals, the sulfur-dominated orbitals of the combined system are degenerate (center), irrespective of coupling between the atoms. Note: *y* axis not to scale.

means that the sulfur-dominated antibonding orbital remains unperturbed in the final orbital diagram. The bonding combination of the sulfur orbitals interacts both with the bonding and the antibonding combination of the carbon atoms. Again, the orbitals "repel" each other so the carbon-dominated orbitals are pushed away from their initial positions. The sulfur-dominated bonding orbital is, however, pushed up and down by equal amounts by the interaction with the two bridge orbitals and, as a consequence, remains unperturbed.

In the final structure, the two sulfur-dominated orbitals are still degenerate; in some sense, this appears as an accidental degeneracy. The sulfur orbitals interact strongly with the bridge but in a way that results in no splitting of the bonding and antibonding combination of the orbitals. This degeneracy is the signature of no electronic coupling and the signature of the interference effect we see as the sharp dip in the transmission.

This picture of the interference effect hints at what we can look for in molecular orbitals as the signature of interference effects. *If we have a "non-spanning node" in the wave function, that is when the extra node that we gain as we move up in energy from one orbital to the next does not introduce a node in the path between the electrodes, we will have the type of cancelation that we saw in our cross-conjugated system.* This criterion for interference was first suggested not for molecules but for quantum dots [7]. While it is straightforward to understand this in connection with acyclic systems – as we have shown here – it is less obvious how to apply the rule to cyclic systems where one can travel over any part of the molecule in a direct path between the electrodes. In that case, we can, instead, specify that the number of nodes should increase in the shortest path between the electrodes, although this rule sounds somewhat complicated.

Another formulation of this rule looks at the phase of the coefficients on the terminal sulfur atoms. *When the coefficients on the two terminal atoms have the same sign between consecutive orbitals (with both orbitals either having the same phase on the terminal atoms or opposite phase), we predict an interference effect* [8–10]. One caveat is that this method can fail for even numbers of units with interference features connected in series, for example, two *meta*-substituted benzene rings together. In this case, the HOMO and LUMO may not indicate that there is interference, when in fact there is. Similarly, method 2 describes well the cyclic systems without side groups, but it may fail to correctly predict interference effects when a cyclic system has side groups that form part of the conjugated system.

Figure 11.11 shows the HOMO and the LUMO for our simple cross-conjugated system **5**. The number of nodes in the wave function increases from two to three, but the additional node appears in the carbon–carbon double bond. Thus, we have a nonspanning node, as this node is not in the shortest path between the electrodes, and the sign of the coefficients on the sulfur atoms is the same in both orbitals. Both formulations predict interference, which is observed in calculations.

The problem with all these explanations/predictions based on molecular orbitals is that most of us cannot "calculate" orbitals in our heads. If we have to perform the calculation, it is not so much additional work to calculate the

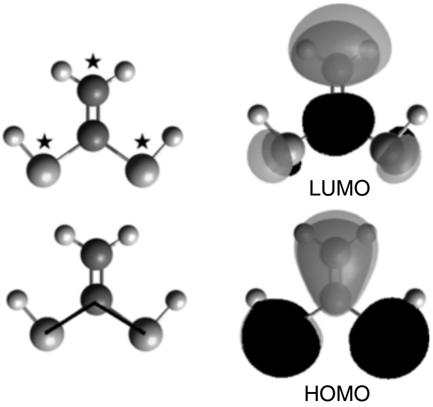


Figure 11.11 Some of the strategies applied to our simple cross-conjugated system **5** (left) and a selection of the molecular orbitals (right). Irrespective of the method used, we can predict that interference effects will dominate.

transport; thus, our predictive method does not save much time. It is more convenient to have methods where we can simply examine a chemical structure and be able to predict interference, without resorting to calculations. Fortunately, there are two methods that fall into this category.

In the case where we have an even alternant hydrocarbon (an even number of carbon atoms in the π-system, no odd-membered rings, no heteroatoms), we can predict interference on the basis of a "starring" rule: *If, when a star is placed on every second atom in a bipartite system, the electrodes bind to two atoms of the same type (either starred or unstarred), we predict that there will be destructive interference* [5] (N.S. Hush, private communication, 2007). This heuristic approach is also illustrated in Figure 11.11, when stars are placed on every second atom: the two terminal sulfur atoms are both starred and we predict interference. If we generalize this rule to larger systems, it turns out that when we have alike coupling (both atoms starred or unstarred) we have an odd number of interference features (1, 3, 5, etc.). When we have disjoint coupling (one atom starred the other unstarred), we have an even number, including 0 (0, 2, 4, etc.) [11].

This rule is still limited by the restriction that we must have both an even number of atoms in the π-system and no odd-membered rings. Fortunately, there is another option. This rule states: *If, after removing all atoms in the shortest path between the electrodes, the atoms that remain cannot be grouped into neighboring pairs we predict interference* [12]. Again this rule is illustrated in Figure 11.11. The shortest path between the electrodes takes the two sulfur atoms and one of the carbon atoms in the double bond; however, one carbon atom remains without a neighboring pair. For a detailed discussion of how this rule relates to our understanding of conjugation and how they should be applied in polycyclic systems, see [13].

This final predictive method is clearly the more versatile; it does not require calculation and odd-membered rings pose no challenge. If one were to remember only one method, this is certainly the method of choice and will provide a good starting point for predicting interference effects in cross-conjugated molecules.

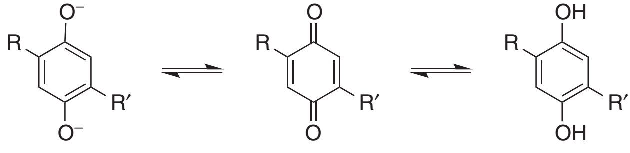
11.5
More than Topology

Earlier, we have defined cross-conjugation in terms of topology (Phelan and Orchin), but energetics matter for transport. The interference effects we have illustrated earlier resulted in a significant suppression of the current through the system, because the interference feature was very close to the Fermi energy. One of the interesting aspects of interference effects is that it allows us to turn electron transport on and off. To do this, we need to understand how to control and perturb interference effects chemically.

Obviously, if we chemically modify a cross-conjugated molecule and change the conjugation through the system, we can remove interference altogether. An example of a modification that will achieve this result is shown in Figure 11.12, where a system exhibiting interference (**6**) can be converted to a linearly conjugated system either by reduction (**7**) or protonation (**8**).

Physical organic chemistry has taught us that we can tune many physical properties by the introduction of electron-donating and/or electron-withdrawing groups. Interference effects are no exception. Figure 11.13 illustrates how the interference feature can be tuned across a wide energy range by the introduction of substituents. In the examples shown, we illustrate the effect with the use of a single substituent. The induced shift will be amplified if two or more substituents were included. This is clearly a design advantage as the extent to which current passes through a molecule can be controlled by appropriate substituents. It can, however, also be a disadvantage if an interference effect is desired, but substituents are required for solubility, reactivity, or stability reasons that inadvertently perturb the interference feature.

As a final point, we note that what can be a small perturbation with an appropriate electron-donating or electron-withdrawing substituent can be an extreme perturbation when heteroatoms are part of the π-system. It is tempting to apply these rules, for heteroatom-containing systems also. Typical examples would



7 **6** **8**

Figure 11.12 When **6** is connected to two electrodes through the R and R′ substituents, it can be easily modified from a system with interference near the Fermi energy to a system without (**7** or **8**), allowing switching from "off" to "on" in this process.

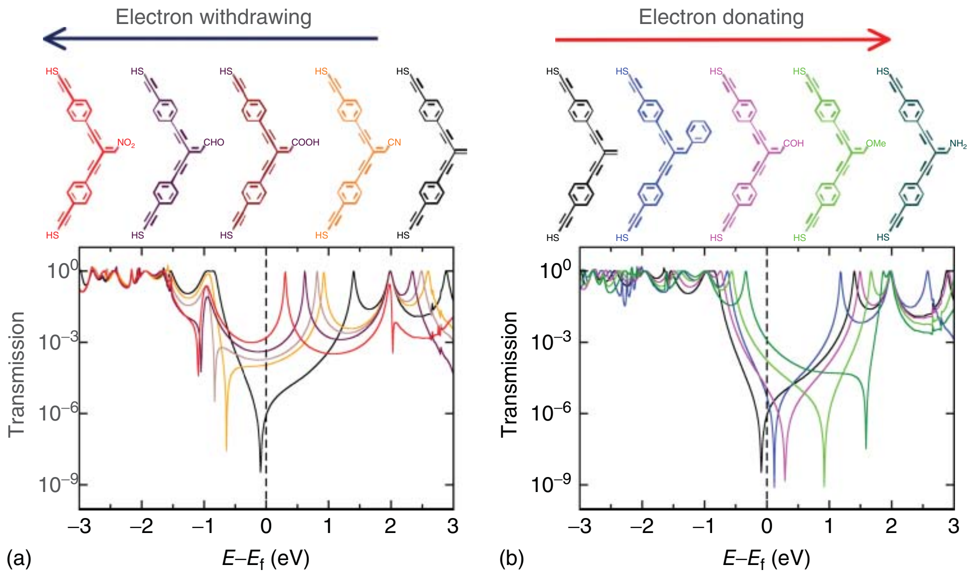


Figure 11.13 Electron-withdrawing or electron-donating substituents can both shift the position of the interference feature in a cross-conjugated molecule. With a careful choice of substituent, the interference feature can be tuned across a large (over 2 eV) range.(Reproduced from [14].)

be the cyclic cross-conjugated systems such as the quinone (**6**) shown above or the extended anthraquinones; however, these are the exceptions rather than the rule. Certainly, for acyclic cross-conjugated systems such as the dendralenes, heteroatoms could have a huge effect.

11.6
Conclusions

Quantum interference effects have captured the imagination of many researchers in molecular electronics, and cross-conjugated molecules are prime candidates for this purpose. The systems can be extended with linearly conjugated units and perturbed with substituents. The systems can be cyclic or acyclic, with odd-membered rings and even cyclophanes. Figure 11.14 illustrates a range of the subunits that will result in interference effects. Cyclophanes do not fit our definition of a cross-conjugated molecule, but with a pseudo-*para* substitution the same interference patterns will be observed (interestingly, there is no interference for pseudo-*meta* substitution) [15].

It remains to be seen whether useful electronic devices will be synthesized on the basis of these principles; but, in the meantime, these systems provide a wonderful playground for chemists interested in molecular electronic design.

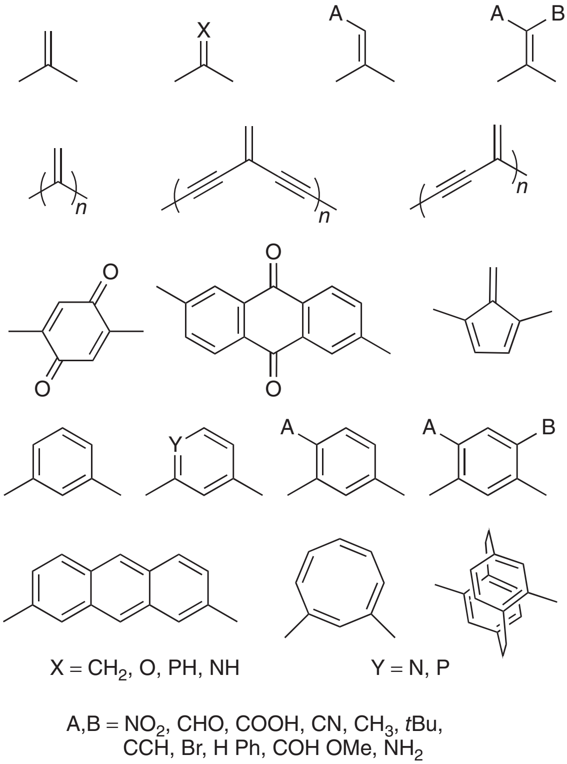


Figure 11.14 Some examples of molecular subunits that will result in interference effects in the transmission. In all cases, there are two bonds without terminal substituents, indicating the positions at which the molecule should be connected (either directly or indirectly) to the electrodes.

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12
Cross-Conjugation in Synthesis

Christopher G. Newton and Michael S. Sherburn

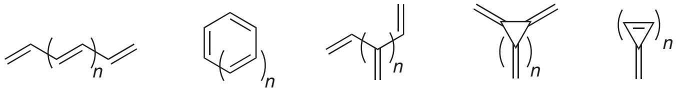
12.1
The Rapid Generation of Structural Complexity

In Chapter 1, aspects of dendralene synthesis and structure were discussed. It is the aim of this final chapter to present their diene-transmissive Diels–Alder (DTDA) chemistry with a focus toward those examples that best demonstrate the rapid generation of structural complexity. As a result of the subjective nature of such a survey, we have comprehensively reviewed the area and systematically classified each transformation. We present here what we believe to be the most important examples from each category, while highlighting modes of reactivity that have yet to be realized. We begin with an analysis of [3]dendralenes, and then progress through the higher homologs. This is followed by the application of dendralene DTDA chemistry in target-orientated synthesis, before we conclude with the Diels–Alder (DA) chemistry of the radialenes. We have elected not to include examples of "heterodendralenes" (see Chapter 2), hetero-DA reactions, or cross-conjugated molecules where one of the terminal double bonds is replaced with an alkyne, or is part of an aromatic system.

12.2
Diene-Transmissive Diels–Alder Reactions

Polyalkenic conjugated hydrocarbons can be classified on the basis of the connectivity of their ethylene units. The linear polyenes **1** and annulenes **2** are comprised of vicinal linked units, whereas the dendralenes **3**, and their cyclic counterparts the radialenes **4**, contain geminal linkages (Figure 12.1). In addition to these four principal classes, "hybrid" molecules that exhibit both vicinal and geminal connectivity are possible, as illustrated by the fulvenes **5**.

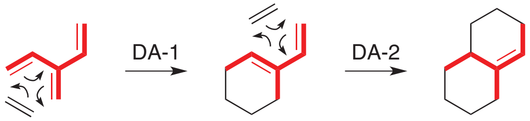
Cross Conjugation: Dendralene, Radialene and Fulvene Chemistry, First Edition.
Edited by Henning Hopf and Michael S. Sherburn.



1 Linear polyenes **2** Annulenes **3** Dendralenes **4** Radialenes **5** Fulvenes

Figure 12.1 Classes of polyene hydrocarbons.

As a consequence of the alkene arrangement present in both the dendralenes and radialenes, these cross-conjugated polyenes are, in principle, able to participate in DTDA reactions. In its most basic form, a DTDA reaction involves the addition of a dienophile to [3]dendralene (**6**) (Scheme 12.1). This reaction generates an alkene that is in conjugation with the originally nonparticipating vinyl group, thus transmitting the diene character to a new location. The product of the first cycloaddition, exocyclic diene **7**, can react in a second DA reaction to provide decalin **8**. Overall this sequence generates four covalent bonds, up to eight stereocenters, two rings, and combines three molecules, making this process extremely efficient in terms of both atom [1] and step [2] economy.

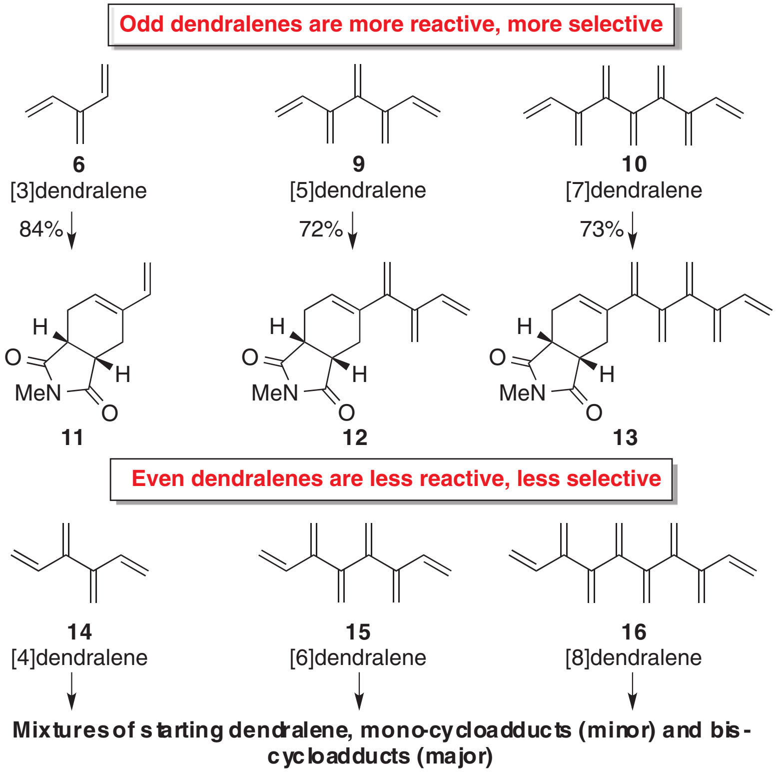


6
[3]Dendralene
7
8

Scheme 12.1 The prototypical DTDA sequence.

The dendralenes exhibit an interesting pattern of DA reactivity that governs much of their DTDA chemistry. In 2011, the Sherburn group reported that the “odd” dendralenes ([3], [5], and [7]) react cleanly with 1 M equiv. of *N*-methylmaleimide (NMM), to provide mono-cycloadducts **11–13** in good yield (Scheme 12.2) [3]. In contrast, when the “even” dendralenes ([4], [6], and [8]) are reacted under the same conditions, a complex mixture of starting material, mono- and bis-adducts, is observed.

These experimental findings were rationalized by density functional theory calculations, and were attributed to differences in populations of reactive conformers [3]. Specifically, the lowest energy conformations of the dendralenes are comprised of unreactive orthogonal s-*trans* 1,3-butadienyl units (Figure 12.2). As a result of their odd number of alkenes, [3], [5], and [7]dendralenes contain at least one quasi s-*cis* unit, which is predisposed to react in a DA reaction. In both series, the first DA reaction occurs preferentially at the less sterically encumbered terminal diene sites; hence, an even dendralene generates a more reactive odd dendralene, and vice versa.



Scheme 12.2 Alternating DA reactivity of the dendralenes.

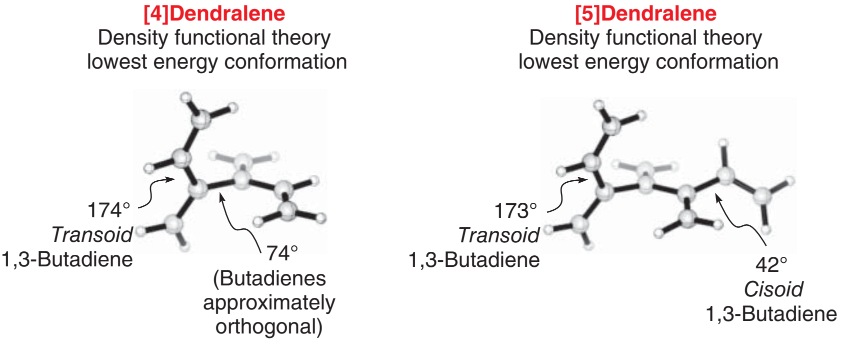


Figure 12.2 The calculated lowest energy conformations of [4]- and [5]dendralene.

12.3
[3]Dendralenes

12.3.1
Classification

Unsurprisingly, the majority of DTDA studies have been conducted on the simplest analogs, the [3]dendralenes [4]. We have classified these reactions, or sequences of reactions, into examples that incorporate either an *acyclic* or *cyclic* [3]dendralene. With regard to monocyclic [3]dendralenes, we find it useful to classify further. Using six-membered rings as an illustrative example, eight different structures are possible, and we have arranged these into four categories based on their DTDA reactivity (Figure 12.3). We consider the first group, comprised of 1,1- and 3,3-cyclo[3]dendralenes **17** and **18**, as pseudo-acyclic. In both of these molecules, the dendralene moiety is “semicyclic,” and consequently their reactivity is akin to the acyclic dendralenes. Of the remaining structures, 1,4- and 2,3-cyclo[3]dendralenes **19** and **20** both contain one diene locked in the s-*trans* conformation; thus, only one DTDA pathway is possible. In comparison, the DTDA sequences of 1,2- and 1,3-cyclo[3]dendralenes **21** and **22** are more complex, as each can adopt two distinct s-*cis* diene conformations. Finally, 1,5- and 2,4-cyclo[3]dendralenes **23** and **24** are not discussed as they are unable to participate in DTDA cascades. The former does not contain a diene in the requisite s-*cis* conformation, whereas the latter can only undergo a single DA reaction as it generates a diene locked in the s-*trans* configuration.

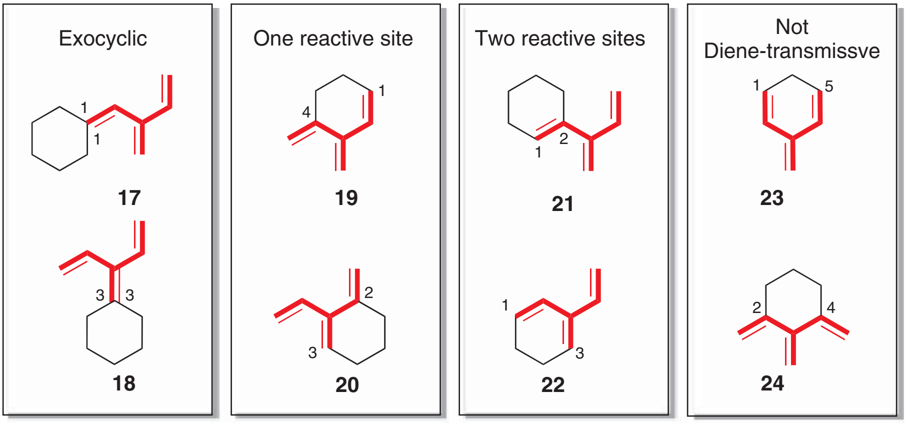


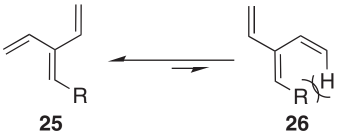
Figure 12.3 The eight possible monocyclic [3]dendralenes.

12.3.2
Acyclic [3]Dendralenes

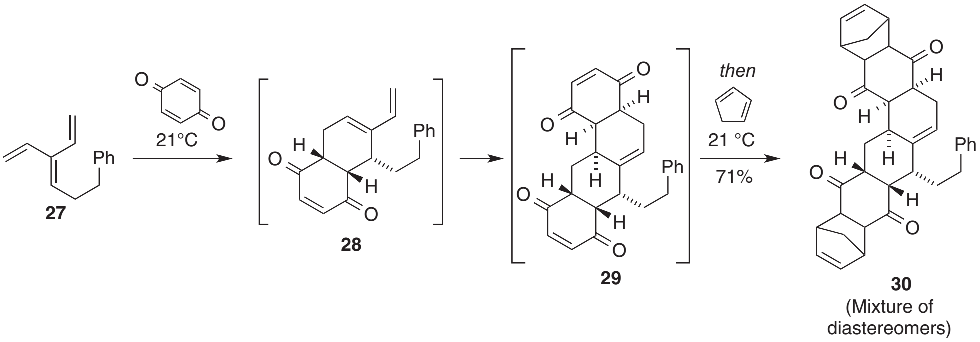
We begin by considering the most conceptually simple case: intermolecular DTDA reactions of acyclic [3]dendralenes. To date, the majority of studies have been conducted on 3-substituted systems as a consequence of their accessibility [4], and the control they offer over DA site selectivity. In the generalized example illustrated in Scheme 12.3, the [3]dendralene conformation **26** is disfavored due to the steric interaction between the terminal *Z*-hydrogen atom shown, and the inside substituent R. Thus, assuming the activation barrier for each DA reaction is approximately equal, the reaction should preferably occur at the s-*cis* diene site depicted in **25** as a result of its increased population.

Our first example of such a sequence comes from the research group of Fallis. In many of their contributions to the DTDA chemistry of [3]dendralenes, they illustrated the ease with which multicyclic frameworks can be generated via repetitive cycloadditions. In one of their most striking examples, four rings are generated in a one-pot operation through the combination of five molecules. This DTDA sequence begins with a completely diastereoselective double DA reaction between [3]dendralene **27** and *p*-benzoquinone, yielding tetracycle **29** (Scheme 12.4) [5].This compound was not isolated, and the subsequent addition of cyclopentadiene to the same reaction vessel allowed for two more DA reactions, generating the octacyclic skeleton **30** as a mixture of diastereomers.

Recognizing the potential of Fallis' methodology, Schreiber and coworkers set about applying solid-supported [3]dendralenes in diversity-oriented synthesis [6]. A collection of 40 3-aryl-substititued [3]dendralenes were reacted with a library

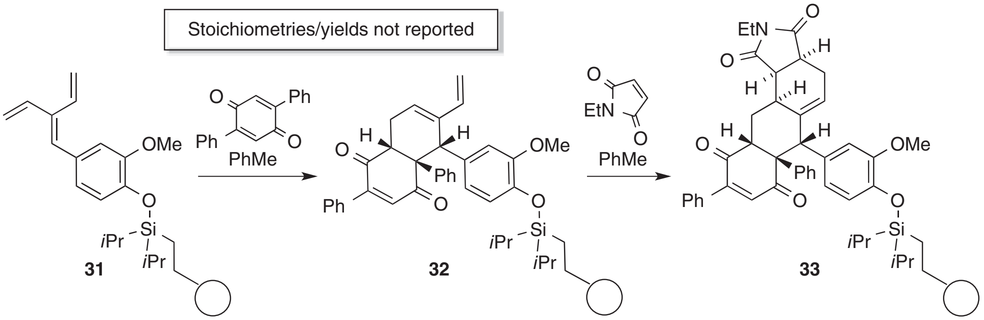


Scheme 12.3 DA site selectivity in 3-substituted [3]dendralenes.



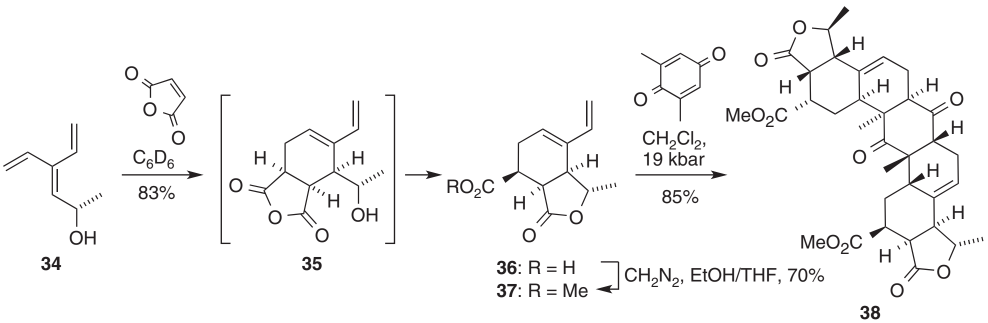
Scheme 12.4 DTDA reaction sequence of 3-substituted [3]dendralene **27** by Fallis *et al.*

of 63 different quinones and maleimides. It was observed that when tri- or tetra-substituted dienophiles were used in the first DA reaction, as is the case in the representative example presented in Scheme 12.5, the mono-DA adduct could be isolated and reacted with a different dienophile. This branching DTDA pathway enabled the synthesis of 29 400 discrete compounds, comprising 10 distinct polycyclic skeletons.



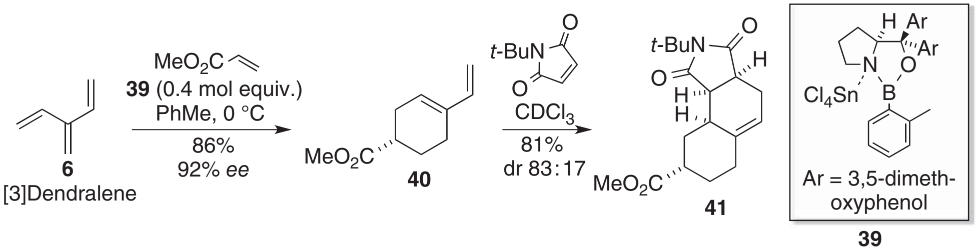
Scheme 12.5 Schreiber and coworkers' application of substituted [3]dendralenes in diversity-oriented synthesis.

Both of the previous examples describe the use of achiral dendralenes to synthesize racemic products. In 2007, the Sherburn group illustrated that chiral 3-substituted [3]dendralene **34** allowed for the preparation of enantiomerically pure cycloadducts (Scheme 12.6) [7]. DA addition of maleic anhydride, followed by *in situ* lactonization, yielded carboxylic acid **36**. This was esterified with diazomethane to improve solubility, and then subjected to a high-pressure double DA sequence using 2,6-dimethyl-*p*-benzoquinone, forming the C_2 symmetric heptacycle **38** in 85% yield.



Scheme 12.6 A DTDA sequence of chiral [3]substituted [3]dendralene **34** by the Sherburn research group.

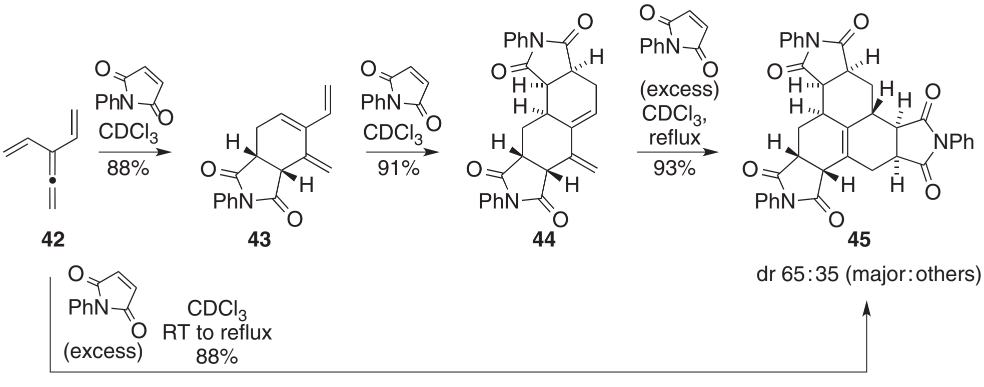
The first example of an enantioselective DA reaction of the parent [3]dendralene (**6**) was conducted by the Sherburn group in 2010 [8]. They demonstrated that



Scheme 12.7 The first enantioselective DTDA sequence of [3]dendralene (**6**).

the addition of methyl acrylate to [3]dendralene, in the presence of a modified version of Corey's oxazaborolidinium catalyst **39**, gave cyclohexene **40** in 86% yield and 92% ee (Scheme 12.7). This was subsequently reacted in a second DA reaction with *N*-*tert*-butylmaleimide, proceeding predominantly through the *endo*-mode, with dienophile approach from the opposite face of the ester. This DTDA sequence is notable for its high control of all aspects of stereoselectivity, namely, the orientational and enantioselectivity of the first cycloaddition, as well as the π-diastereofacial and *endo*/*exo* selectivity of the second.

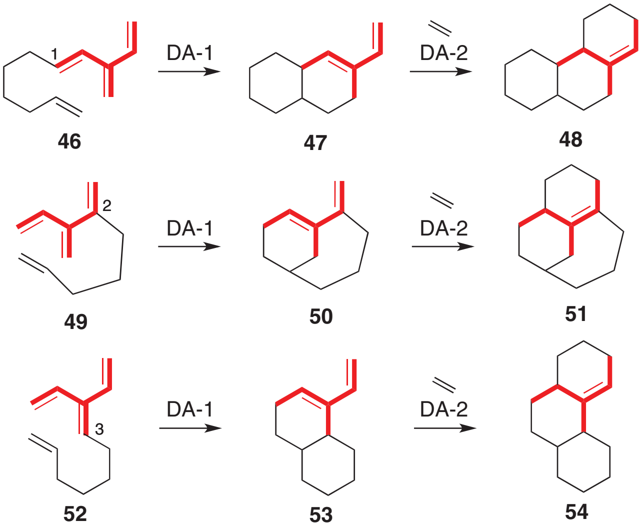
In a rather unique example disclosed by the Sherburn group in 2011, 1,1-divinylallene (**42**), a molecule that can be considered a [3]dendralene derivative where the central alkene has been replaced with an allene, was subjected to a DA study with *N*-phenylmaleimide (NPhM) [9] (Scheme 12.8). Addition of 1 of the reactive dienophile provided 2,3-cyclo[3]dendralene **43** in high yield (additional examples of DTDA sequences of 2,3-cyclo[3]dendralenes are presented in section 12.3.3). This was subjected to a second DA reaction with NPhM, proceeding through the *endo*-mode, and *anti* with respect to the succinimide ring already present. A final DA reaction, this time predominately though the *exo*-mode, and from the same π-diastereoface as the first dienophile, provided hexacycle **45**. This sequence could also be conducted in one pot using an excess of NPhM, generating six C–C bonds, eight stereocenters, and three rings. Thus,



Scheme 12.8 A DTDA cascade of 1,1-divinylallene (**42**) by Sherburn and coworkers.

with the addition of only one extra carbon atom, the already impressive DTDA cascade of [3]dendralene was significantly enhanced.

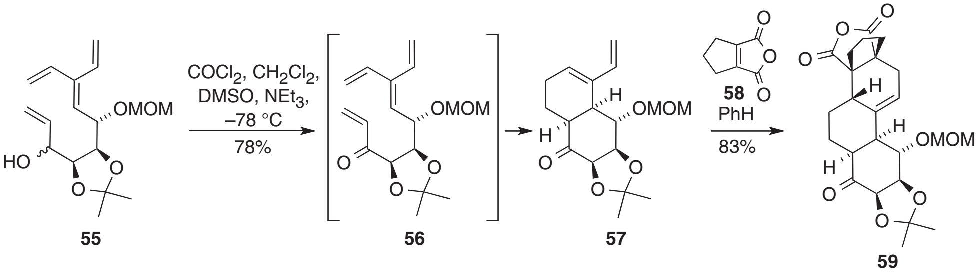
The number of multicyclic frameworks that can be generated from acyclic [3]dendralenes is greatly increased when intramolecular DA reactions are considered. We present here the three most conceptually simple cases, all proceeding via an intramolecular DA reaction with a four-carbon-tethered dienophile, followed by an intermolecular reaction with ethylene (Scheme 12.9). Notably, when the position of the tether is at C1 (as in **46**) or C3 (as in **52**), the same carbon framework can be accessed. However, these approaches are complementary as the location of both the alkene generated in the last DA reaction and any functionality present on the dienophiles are not equivalent. In comparison, when the tether is at C2 (as in **49**), bridged systems become accessible. In these simplified examples, we have intentionally ignored the orientation and site selectivity of each DA reaction, which, if controlled, could lead to more structural variation. This could also be achieved by a number of other means, including varying the length of the dienophile tether, incorporating sequences of two intramolecular reactions instead of just one, and reversing the order of cycloaddition.



Scheme 12.9 The DTDA chemistry of C1, C2, and C3-tethered acyclic [3]dendralenes.

Interestingly, there has yet to be a DTDA sequence involving a dienophile tethered at C1 or C2. Most incorporate a tether at C3 [10–12], but at least one separate example, involving an inter- and then intramolecular DA sequence of an acyclic [3]dendralene where the second dienophile is tethered to the first, has been reported (discussed in section 12.5) [13].

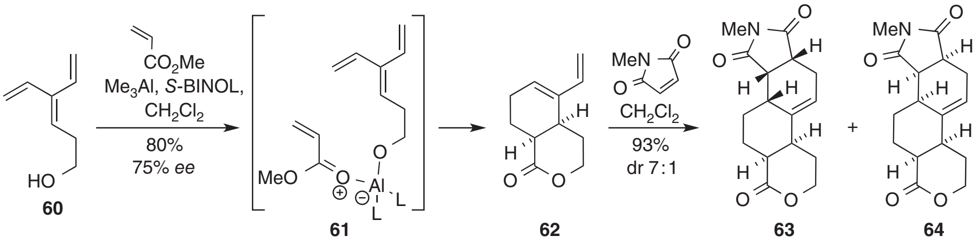
The first example of an intra/intermolecular DTDA sequence of a [3]dendralene was reported by Fallis in 1999 [10]. Enantiopure 3-substituted [3]dendralenes **55**



Scheme 12.10 An intra/intermolecular DTDA cascade of 3-substituted [3]dendralenes **56**.

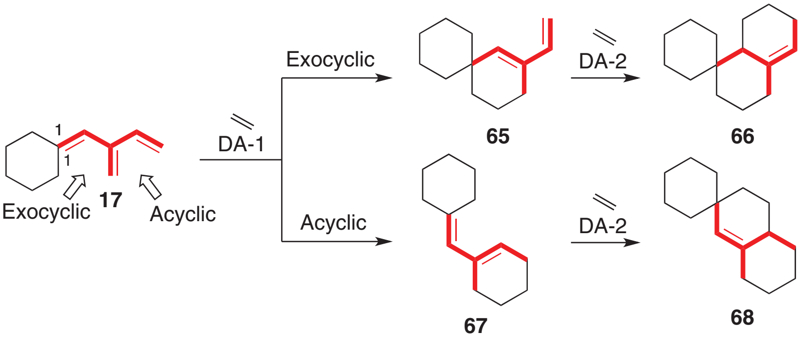
were subjected to a Swern oxidation to generate ketone **56**, which subsequently underwent an *in situ endo*-selective intramolecular DA reaction to provide *cis*-fused bicycle **57** (Scheme 12.10). This was submitted to an intermolecular DA reaction with dienophile **58**, proceeding exclusively through the *endo*-mode and from the convex face, to give the steroid-like structure **59**.

In studies directed toward the isolation of mono-DA adducts of [3]dendralenes, the Fallis research group developed an intramolecular DA procedure that proceeded via a temporary dienophile tether [14]. Thus, when substituted [3]dendralene **60** was mixed with methyl acrylate and stoichiometric amounts of trimethyl aluminum and (*S*)-BINOL (as per the method of Ward *et al.*) [15, 16], mono-adduct **62** was isolated in 80% yield and 75% *ee* (Scheme 12.11). This reaction presumably proceeds via the intermediacy of **61**, and it was observed that no reaction occurred in the absence of Lewis acid. Exposure of **62** to NMM provided *endo*-cycloadducts **63** and **64** in excellent yield.



Scheme 12.11 The application of a temporary tether to facilitate an intra/intermolecular DTDA cascade of 3-substituted [3]dendralene **60**.

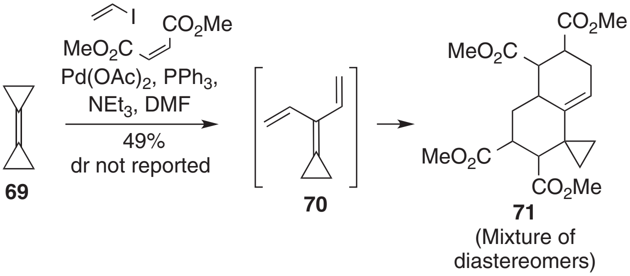
Only one study detailing DTDA reactions of the pseudo-acyclic 1,1- or 3,3-cyclo[3]dendralenes has been reported, most likely owing to the difficulties associated with DA reactions of such highly substituted dienes. The prototypical, and not yet realized, DTDA cascade of 1,1-cyclo[3]dendralene **17** is presented in Scheme 12.12. If the first DA reaction occurs at the more sterically demanding exocyclic diene site, spiro-bicycle **65** is produced, which could react further to generate the



Scheme 12.12 The DTDA sequence of 1,1-cyclo[3]dendralenes.

tricyclic framework **66**. Alternatively, if the first DA reaction occurs at the more accessible acyclic site, then a second DA reaction would provide spiro-cycle **68**.

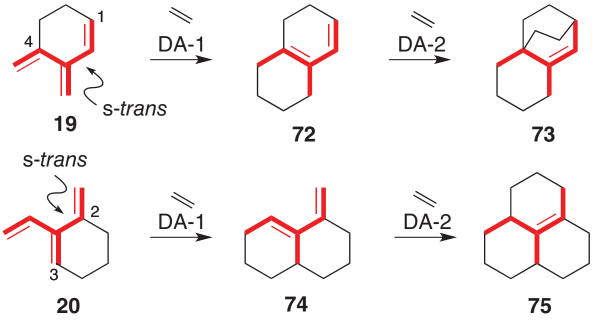
The DTDA chemistry of 3,3-cyclo[3]dendralenes is less complex owing to their inherent symmetry. While pursuing domino Mizoroki–Heck/DA reactions, de Meijere *et al.* developed a route to [3]dendralenes via the nucleophilic ring-opening/β-hydride elimination of methylenecyclopropanes [17]. Although the majority of examples involved intramolecular Heck reactions to provide 2,3-cyclo[3]dendralenes, a single example describing an intermolecular route to a 3,3-cyclo[3]dendralene was disclosed. Thus, a Mizoroki–Heck reaction of bicyclopropylidene (**69**) with vinyl iodide in the presence of dimethyl maleate generated [3]dendralene derivative **70** (Scheme 12.13). This underwent an *in situ* double DA reaction sequence to provide **71** as a mixture of all four possible diastereomers.



Scheme 12.13 One-pot Mizoroki–Heck/DTDA sequence reported by de Meijere *et al.*

12.3.3
Cyclic [3]Dendralenes

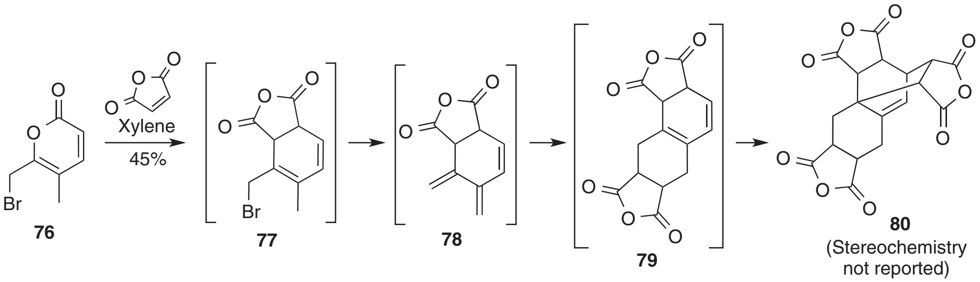
In terms of DTDA chemistry, 1,4- and 2,3-cyclo[3]dendralenes **19** and **20** are particularly attractive substrates. Both contain a single diene that can adopt the



Scheme 12.14 DTDA sequences of 1,4- and 2,3-cyclo[3]dendralene.

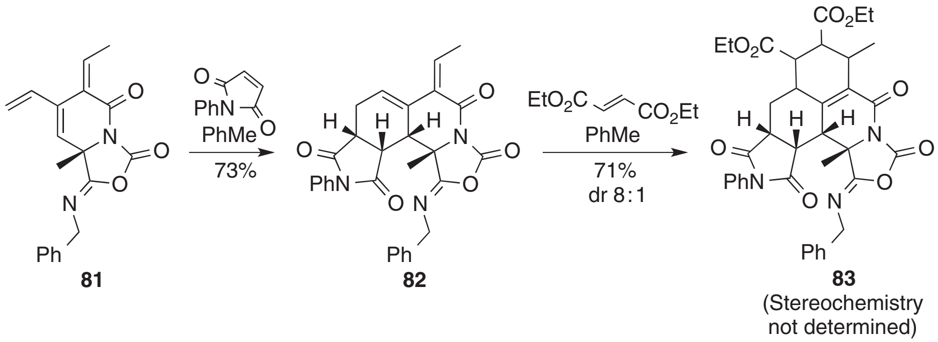
reactive s-*cis* conformation, thus offering complete control over DA site selectivity. The first DA reaction, in both cases, generates a new s-*cis* diene site that can react further to provide tricyclic frameworks of the type **73** and **75** (Scheme 12.14).

Ignoring examples of *o*-quinone dimethides (a special class of molecules that are both linear and cross-conjugated, and thus outside the scope of this review), only two reports detailing DTDA sequences of 1,4-cyclo[3]dendralenes have been disclosed. However, the more recent example is not discussed as it utilizes only hetero-DA reactions [18]. In 1965, Shusherina and coworkers described the stunning cascade of reactions illustrated in Scheme 12.15 [19]. Pyrone **76** was first subjected to a DA reaction with maleic anhydride, which, following a retro-DA reaction to expel carbon dioxide, yielded diene **77**. 1,4-Elimination of HBr generated the 1,4-cyclo[3]dendralene **78**, which subsequently reacted with two more molecules of maleic anhydride, to provide the bridged hexacycle **80**. Overall, six C–C bonds and three new rings are generated in this domino sequence that combines four molecules in just one pot.



Scheme 12.15 *In situ* generation of a 1,4-cyclo[3]dendralene **76** and its DTDA cascade.

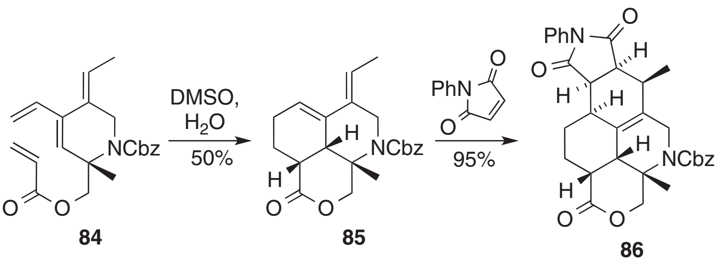
Owing to their availability through cyclo-isomerization reactions, a number of studies describing DTDA reactions of 2,3-cyclo[3]dendralenes have been disclosed [20–22]. One example that perhaps best demonstrates the high levels of stereo- and chemoselectivity possible in such reaction sequences was published by Brummond and coworkers in 2006 (Scheme 12.16) [23]. In this



Scheme 12.16 A DTDA sequence of 2,3-cyclo[3]dendralene **81** developed by Brummond and coworkers.

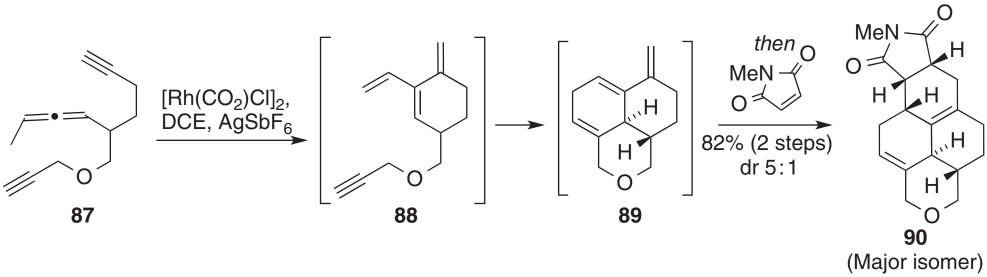
account, hetero-bicycle **81** was reacted with NPhM to provide *endo*-cycloadduct **82** as a single diastereomer. The complete control of π-diastereofacial selectivity presumably arises from the methyl substituent adjacent to the reactive diene, as was observed in the related example disclosed by Sherburn and coworkers in 2007 (described in Scheme 12.6) [7]. Succinimide **82** was then reacted in a highly diastereoselective DA reaction with diethyl fumarate, although the stereochemistry of the major diastereomer was not determined. Notably, in similar examples lacking the carbonyl adjacent to the diene in **82**, the second DA reaction was faster than the first, precluding isolation of mono-DA adducts.

The Brummond research group also illustrated that the stereoselectivity of these reactions can be controlled by tethering the first dienophile to the dendralene [22, 23]. In one such example, ester **84** underwent an *endo*-selective intramolecular DA reaction to provide the tricyclic diene **85** (Scheme 12.17). In this reaction, the dienophile is constrained to the bottom face of the molecule, thus controlling the π-diastereofacial selectivity of the cycloaddition. Piperidine **85** was then subjected to an *endo*-selective intermolecular DA reaction with NPhM to provide the pentacycle **86** in excellent yield.



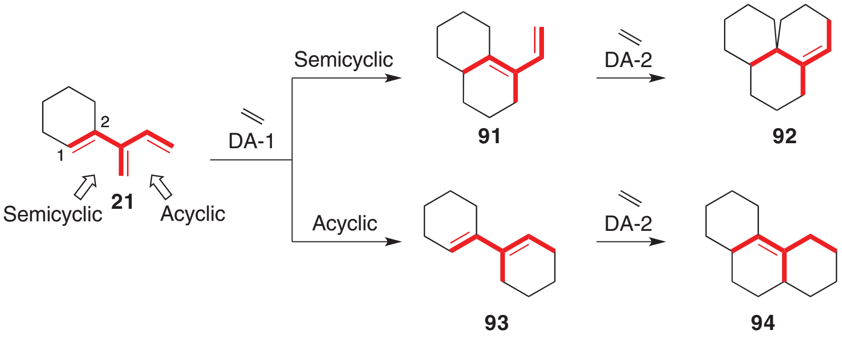
Scheme 12.17 An intra/intermolecular DTDA sequence of 2,3-cyclo[3]dendralene **84** by Brummond *et al.*

In a second example, again from the Brummond group, acyclic allene **87** was converted into pentacycle **90** in just one pot (Scheme 12.18) [22]. This impressive sequence began with a rhodium-catalyzed ene-type cycloisomerization, followed by an *in situ* rhodium-catalyzed intramolecular [4+2], concluding with an *endo*-selective intermolecular DA reaction with NMM to the bottom face of **89**.



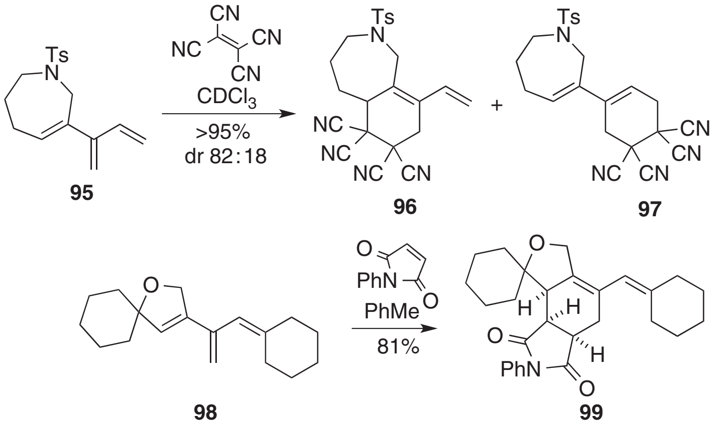
Scheme 12.18 Cycloisomerization/formal DA/DA sequence of allene **87** by Brummond *et al.*

1,2-Cyclo[3]dendralenes contain both a semicyclic and acyclic diene site, and, in principle, either of the two tricyclic frameworks **92** or **94** can be accessed through alternative DTDA sequences (Scheme 12.19).

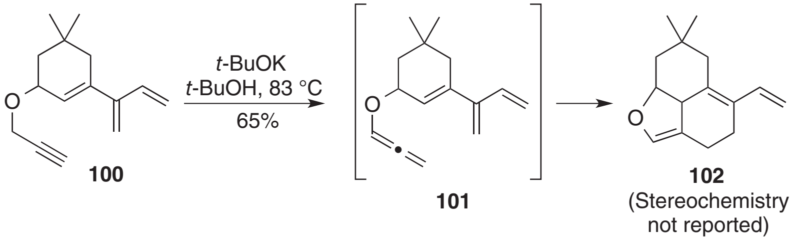


Scheme 12.19 The DTDA sequence of 1,2-cyclo[3]dendralene.

1,2-Cyclo[3]dendralenes can be synthesized via a DA reaction at the terminal site of a [4]dendralene. Consequently, the majority of reports involving DTDA sequences of these compounds are actually part of larger [4]dendralene sequences, and will be discussed later in this chapter. However, two other examples were recently reported by the research groups of Chang [24] and Ma [25]. Interestingly both Chang's amine derivative **95** and Ma's spiro-fused [3]dendralene **98** exhibit a preference for reaction at their semi-cyclic sites, to provide mono-adducts **96**, **97**, and **99** (Scheme 12.20). Although a second DA reaction is possible in both cases, neither report describes multiple additions.



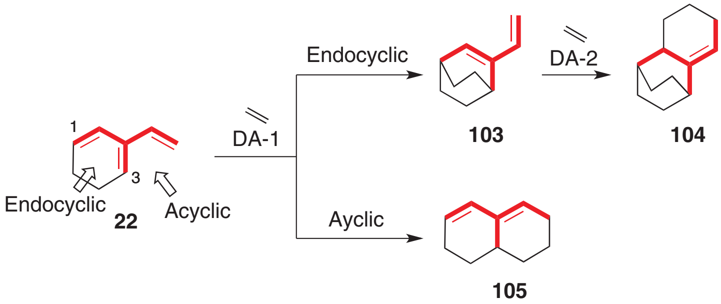
Scheme 12.20 Intermolecular DA reaction of 1,2-cyclo[3]dendralenes.



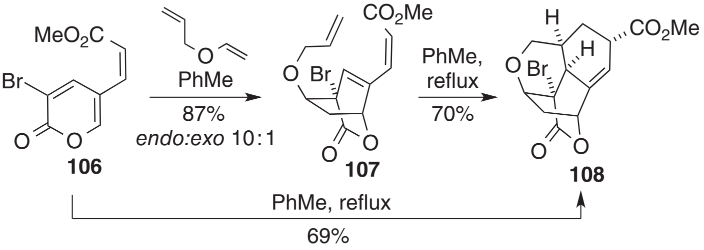
Scheme 12.21 Kanematsu and coworkers' intramolecular DA reaction of 1,2-cyclo[3]dendralene **101.**

Similarly, a single DA reaction of a 1,2-cyclo[3]dendralene was reported by Kanematsu and coworkers in 1986. In this case, a base promoted isomerization of alkyne **100**-generated [3]dendralene **101**, which subsequently reacted in an intramolecular DA reaction to yield tricycle **102** (Scheme 12.21) [26].

The final class of monocyclic [3]dendralenes, the 1,3-analogs **22**, can undergo DA reactions at either their endocyclic position (in a diene-transmissive sense)



Scheme 12.22 The DTDA sequence of 1,3-cyclo[3]dendralenes.

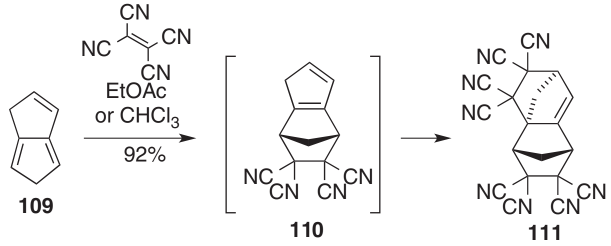


Scheme 12.23 A DTDA sequence of a 1,3-cyclo[3]dendralene.

to access the bridging tricyclic framework **104** or, alternatively, at their acyclic position to provide decalin **105** (Scheme 12.22).

The site selectivity can be controlled by the nature of the ring. For instance, reaction is favored at the cyclic position in 2-alkenyl cyclopentadienes [27, 28], whereas in six- [29–31] and seven-membered [32] rings, this selectivity is usually reversed. Substitution at the acyclic diene can also influence site selectivity, as illustrated by Cho and coworkers in 2006 [33]. Pyrone **106** (and its *E*-isomer), were shown to undergo highly stereo- and regioselective DTDA reaction sequences with allyl vinyl ethers (Scheme 12.23). In a representative example, the first DA reaction occurred at the endocyclic site of **106** and with the vinyl group of the dienophile. The intermediate triene **107** was isolated; and upon warming in toluene, an intramolecular DA reaction ensued to yield bridged tetracycle **108**. This sequence could also be conducted in one pot, avoiding the isolation of **107**.

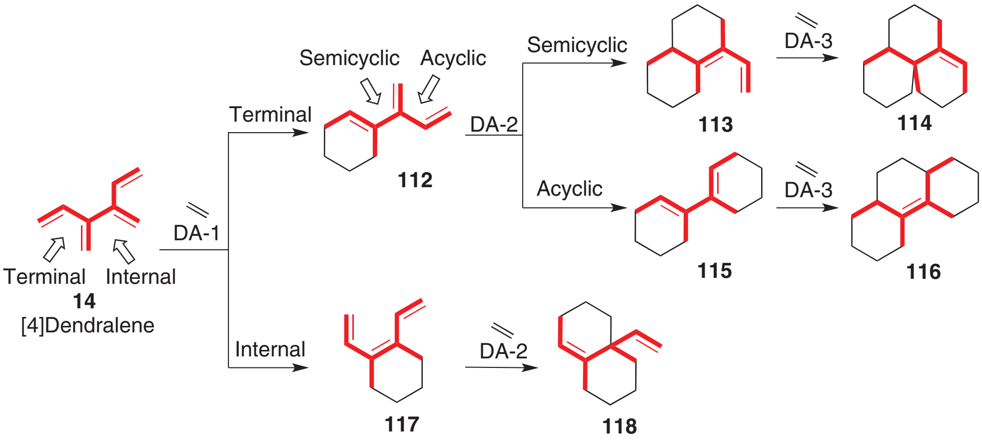
We conclude our section on cyclic [3]dendralenes with Meier and coworkers' DTDA cascade of 1,5-dihydropentalene (**109**) [34] (Scheme 12.24). The sequence began with the addition of tetracyanoethylene (TCNE) to triene **109**, providing the bridging tricycle **110**. This was followed by a second (*in situ*) DA reaction, to the less sterically encumbered bottom face of the diene, yielding **111** in excellent yield. To the best of our knowledge this is the only report of a bicyclic [3]dendralene undergoing multiple DA reactions.



Scheme 12.24 A DTDA sequence of 1,5-dihydropentalene (**109**).

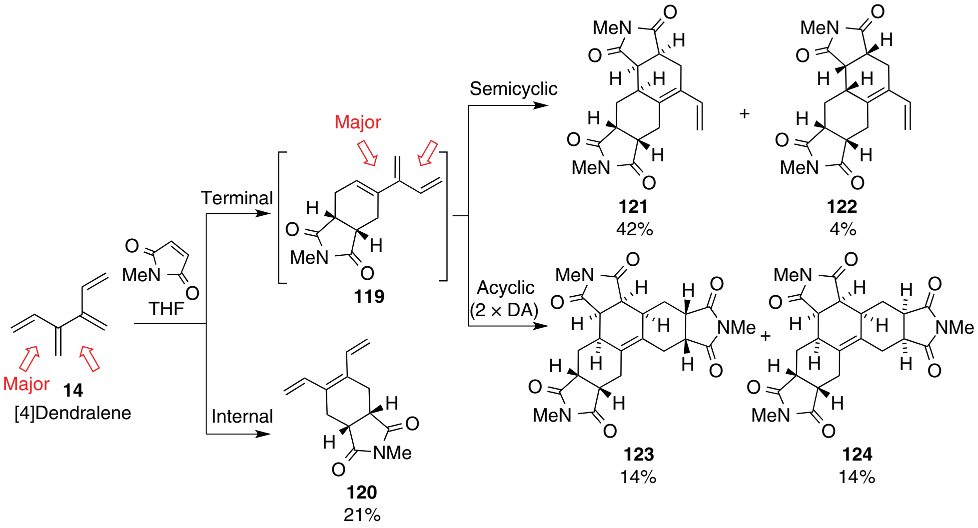
12.4
Higher Dendralenes

The DTDA chemistry of the higher dendralene homologs is significantly more complex than [3]dendralene. In fact, as a general rule, [*n*]dendralene can undergo a sequence of $\leq(n-1)$ DA reactions. For example, the parent [4]dendralene (**14**) can react in three distinct DTDA pathways, two of which are comprised of three DA reactions (Scheme 12.25). In the prototypical example, the first cycloaddition can occur at either the terminal or internal dienes sites to generate cycloadduct **112** or **117,** respectively. The former constitutes a 1,2-monocyclic[3]dendralene, which again contains two diene sites, thus generating a second bifurcation. Continuing along this pathway, exhaustive addition provides the tricyclic frameworks **114** or **116**. Alternatively, if the first DA reaction occurs at the internal diene site of [4]dendralene, only one DTDA pathway is possible, leading to the formation of bicycle **118**.



Scheme 12.25 The prototypical DTDA chemistry of [4]dendralene (**14**).

The first (and only) detailed DTDA study of parent [4]dendralene (**14**) was reported by the Sherburn group in 2005 [35]. Upon addition of an excess of NMM, at ambient pressure and temperature, a mixture of five products was obtained in excellent overall yield (Scheme 12.26). The first DA reaction occurred primarily at the terminal diene site to provide 1,2-monocyclic[3]dendralene **119**, as well as 21% of the internal adduct **120**. Triene **119** could not be isolated, and a second cycloaddition, predominately at the internal site, afforded the two *endo*-DA adducts **121** and **122**. The major diastereomer arises via approach of the dienophile *anti* with respect to the succinimide ring in compound **119**. The tris-adducts **123** and **124** originate from reaction at the acyclic diene site of **119**, and from the less hindered top face (as drawn). The two intermediates generated

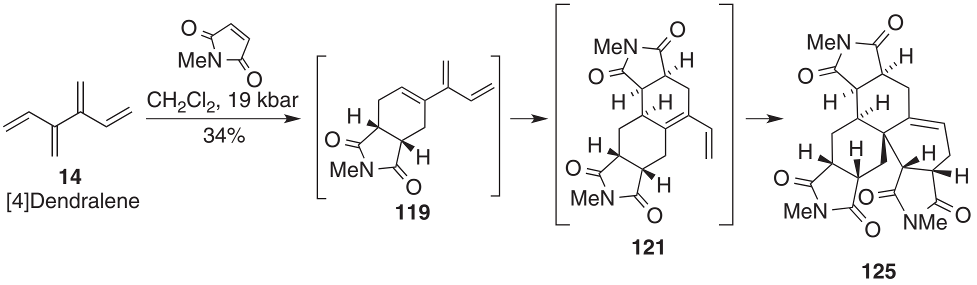


Scheme 12.26 The DTDA cascade of [4]dendralene (**14**) and NMM at ambient pressure and temperature.

(not shown) react again, both from the top face and through the *endo*-mode, delivering **123** and **124** in 28% combined yield.

While the selectivity of this DTDA cascade is relatively poor, preliminary studies under Lewis acid conditions exhibit essentially complete control over site selectivity [35]. These reactions were conducted by pre-complexing NMM with stoichiometric amounts of $MeAlCl_2$ at low temperature. When a 1 : 1 M ratio of NMM:$MeAlCl_2$ was employed, a 77% yield of internal DA adduct **120** was obtained. Interestingly, with a 1 : 2 ratio, exclusive formation of the tris-DA adducts **123** and **124** was observed. At present, the origin of this selectivity remains unclear.

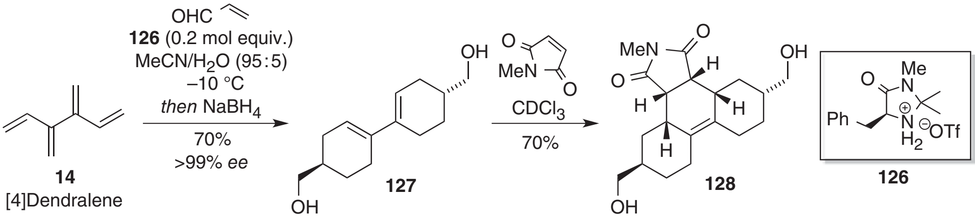
In addition, the Sherburn group demonstrated the selectivity of this sequence is improved under high-pressure conditions [35]. [4]Dendralene was compressed at 19 kbar with an excess of NMM, and tris-adduct **125** was isolated as the major



Scheme 12.27 The DTDA cascade of [4]dendralene (**14**) and NMM at 19 kbar.

product in 34% yield (Scheme 12.27). The compound forms via the intermediates **119** and **121**, and represents the first *double* DTDA sequence.

The synthetic utility of [4]dendralene was dramatically improved by the Sherburn research group in 2013 [36]. Using MacMillan's imidazolidinone organocatalyst **126**, a double DA reaction between acrolein and [4]dendralene (**14**), followed by an *in situ* reduction (to prevent epimerization of the sensitive α-carbonyl site), provided diol **127** in exquisite enantioselectivity (Scheme 12.28). The high enantiomeric ratio was a result of both cycloadditions proceeding with catalyst control, and a preference for the minor enantiomer from the first cycloaddition to form the meso stereoisomer in the second addition. A third DA reaction could be conducted with reactive dienophiles (i.e., NMM, dimethyl acetylenedicarboxylate, or benzoquinone) under noncatalyzed conditions, as illustrated by the representative example **128**. This methodology was applied to [3], [6], and [8]dendralene, as well as a handful of other α,β-unsaturated carbonyl dienophiles.



Scheme 12.28 Organocatalyzed DTDA sequence of [4]dendralene (**14**).

Using six-membered rings as an illustrative example, 11 monocyclic [4]dendralenes are possible, and these have been arranged in Figure 12.4 based on ring connectivity. To date, only the DTDA chemistry of 1,2- (as part of a larger

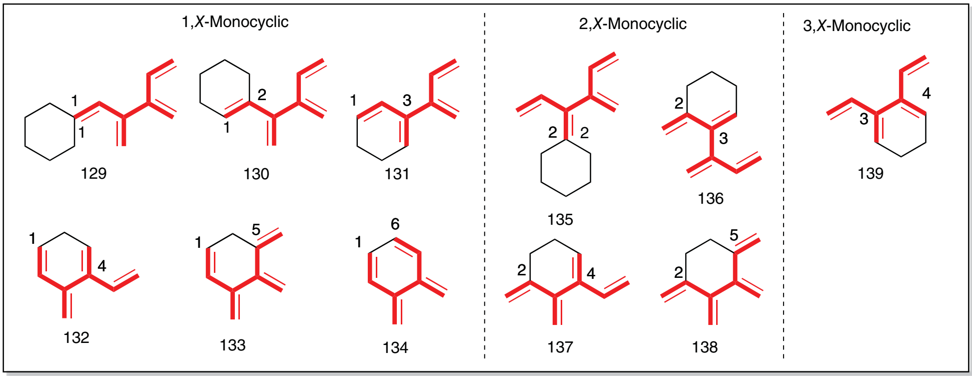
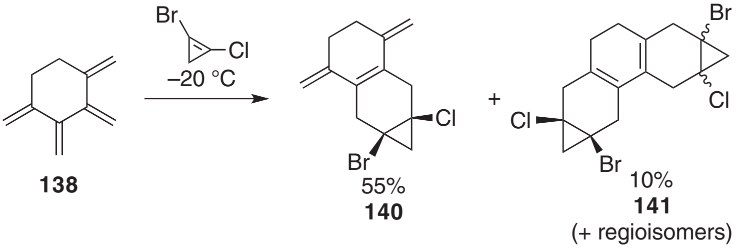


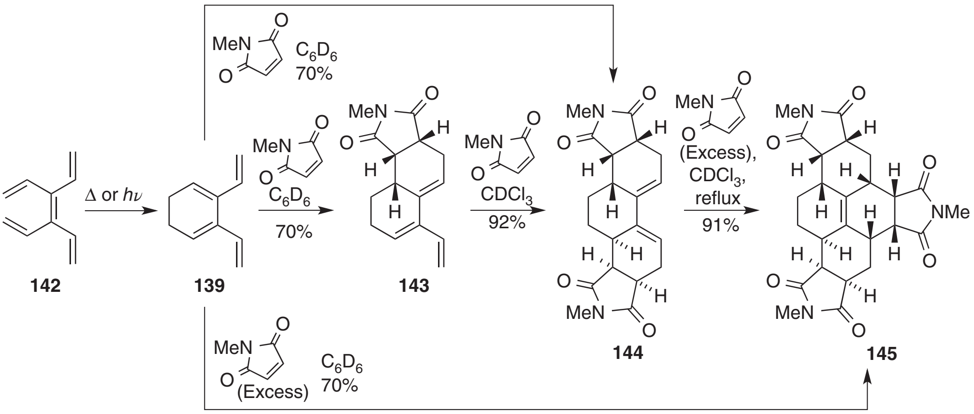
Figure 12.4 The 11 possible monocyclic [4]dendralenes.

[5]dendralene sequence), 1,6-,1) 2,5-, and 3,4- analogs have been studied. As a result, rather than consider every possible dendralene reaction mode, we will instead present only those that have already been realized.

In 1991, Billups *et al.* reported the DA reactivity 2,5-cyclo[4]dendralene **138**, a compound that closely resembles the radialenes (see Chapter 4), both in structure and reactivity (Scheme 12.29) [37]. Unsurprisingly, when treated with an excess of 1-bromo-2-chlorocyclopropene, a preference for addition at the more electronically activated internal diene site was observed, and a mixture of the mono and bis-adducts **140** and **141** was isolated in 65% overall yield.



Scheme 12.29 DTDA reactivity of monocyclic[4]dendralene **138.**



Scheme 12.30 DTDA reactivity of DVC (**139**).

Skattebøl and coworkers reported the first synthesis of 2,4-monocyclic[4]dendralene **139** (dubbed DVC after its IUPAC name: 2,3-divinyl-1,3-cyclohexadiene) over three publications between 1963 and 1965 [38–40]. Its synthesis was recently revisited, and DTDA chemistry studied by Sherburn and coworkers (Scheme 12.30) [41]. In stark contrast to the parent [4]dendralene (**14**), DVC

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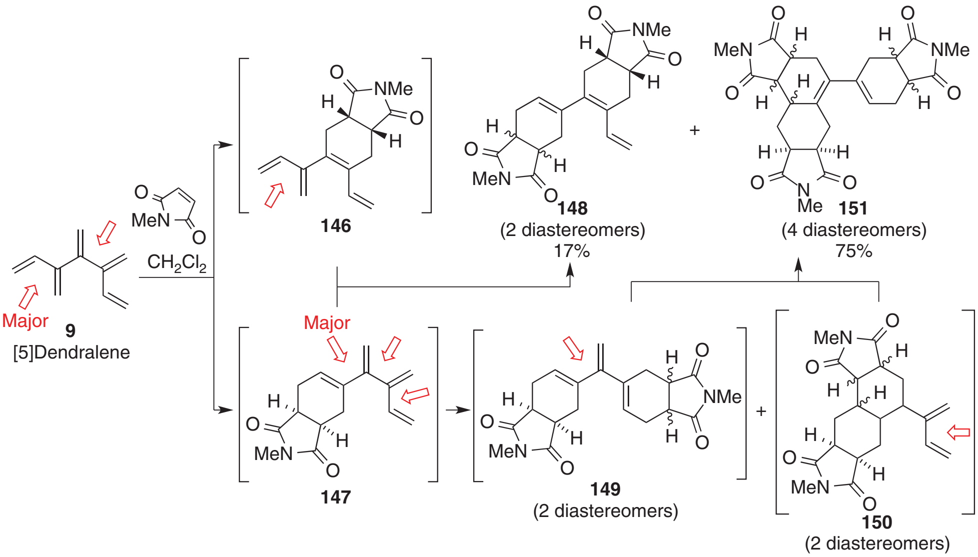
1) As mentioned earlier, *o*-quinone dimethides such as 1,6-monocyclic[4]dendralene **134** are both linear and cross-conjugated, and thus fall outside the scope of this review. In our view, this connectivity pattern only corresponds to a dendralene when the ring system contains more than six carbon atoms.

was observed to react in a highly regio- and diastereoselective DTDA cascade with NMM. This sequence was most conveniently conducted via the thermal or photochemical conversion of tetravinylethylene (**142**) into the unstable DVC, with subsequent addition of NMM. The first two DA reactions occur at the two semicyclic diene sites (presumably for steric reasons), via the *endo*-mode and from opposite π-diastereofaces, to yield C_2-symmetric pentacycle **144**. The third DA reaction, again through the *endo*-mode, provided compound **145** as a single diastereomer. These reactions can be carried out in a stepwise manner, or in one pot when an excess of NMM is employed, in the process forming seven new C–C bonds, four rings, and 10 stereocenters.

The highest dendralene homolog that has been subjected to a comprehensive DTDA study is [5]dendralene (**9**), and a summary of this work (involving an excess of NMM at ambient temperature and pressure) is presented in Scheme 12.31 [42]. Of the two possible diene sites of [5]dendralene (**9**), addition at the terminal site is favored (about 80 : 20), to form mono-adduct **147**. The less favored internal mono-adduct **146** undergoes a second and final DA reaction at the less sterically encumbered diene site to give bis-adduct **148**. The major mono-addition product, **147**, can be considered as a 1,2-monocyclic[4]dendralene, and, interestingly, cycloaddition at the more substituted semicyclic diene site is favored, forming bis-adduct **150**. In addition, the two other bis-adducts **148** and **149** are also formed. Bis-adducts **149** and **150** can both react to provide tris-adducts **151**, which do not



Scheme 12.31 The DTDA cascade of [5]dendralene (**9**) and NMM at ambient pressure and temperature.

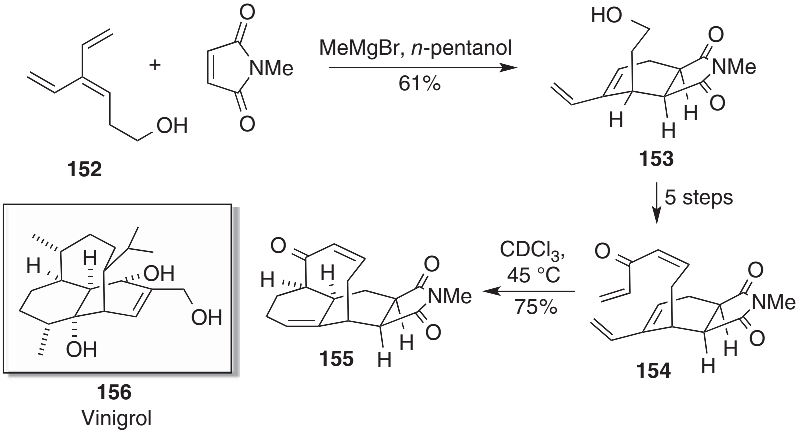
react further, even when resubmitted to a range of common reactive dienophiles under forcing conditions.[2)]

As was observed with [4]dendralene, the selectivity of this sequence is greatly improved under Lewis acid-promoted conditions [42]. A single addition of NMM to [5]dendralene (**9**) in the presence of methylaluminum dichloride enhances the selectivity for the terminal over the internal site to 96 : 4. Furthermore, when [5]dendralene is submitted to a double addition under the same conditions, formation of the terminal/terminal addition products **149** in 70% yield are observed.

12.5
Applications

We complete our analysis of the DTDA chemistry of the dendralenes with a summary of their application in target-orientated synthesis. Only two reports describe a strictly DTDA sequence of a dendralene (as defined earlier); however, we have extended our discussion to include two additional, but closely related, examples.

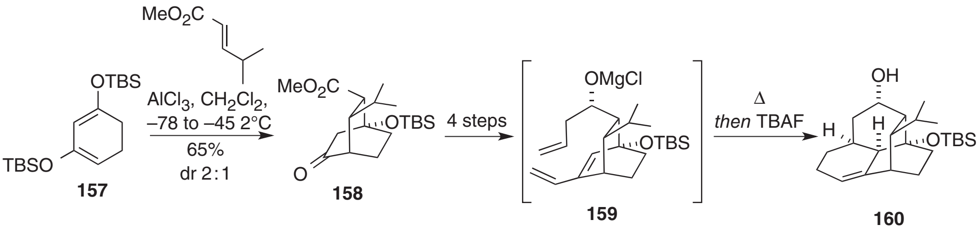
In 2007, the Fallis research group published an approach toward the tricyclic core of vinigrol (**156**) utilizing a DTDA sequence of trieneol **152** (Scheme 12.32) [43]. The first DA reaction proceeded under Lewis acid-promoted conditions, involving the formation of a temporary tether between **152** and NMM, to yield *endo*-DA adduct **153** in 61% yield. After elaboration to enone **154**, an intramolecular DA reaction proceeding under mild conditions provided tetracycle **155**, thus completing the vinigrol carbocyclic core.



Scheme 12.32 Fallis and coworkers' DTDA approach to the framework of vinigrol.

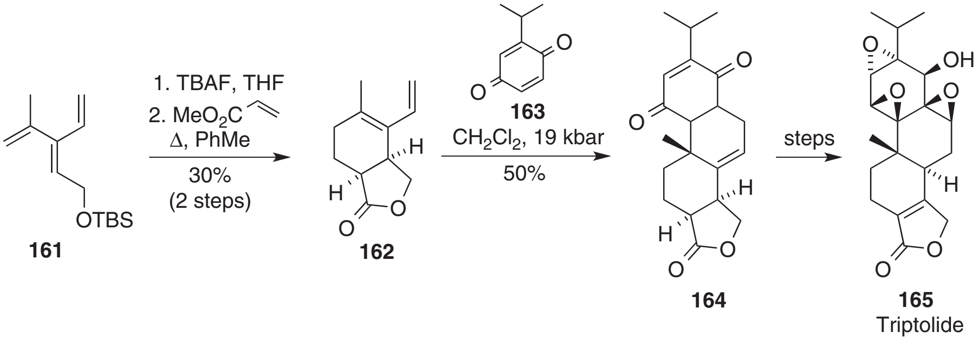
[2)] The pathway from [5]dendralene (**9**) to the six DA adducts was elucidated by a series of reactions involving the addition of 1 equiv. of NMM to each diene.

In an independent but related study, Baran *et al.* completed the first total synthesis of vinigrol via a DTDA strategy, beginning with a DA reaction employing Danishefsky-type diene **157** and methyl (*E*)-4-methylpent-2-enoate (Scheme 12.33) [44, 45]. In preparation for the second cycloaddition, the cyclic ketone was elaborated into semicyclic diene **159**; the dienophile was incorporated through nucleophilic addition of allyl magnesium chloride to an aldehyde. An interesting "proximity-induced" intramolecular cycloaddition involving the unactivated dienophile ensued to yield **160**. The strategy employed in this ultimately successful approach to the natural product is one formally involving a DTDA sequence of a 1,3-cyclo[3]dendralene, with an initial addition at the endocyclic diene site and a second at the resulting semicyclic diene site.



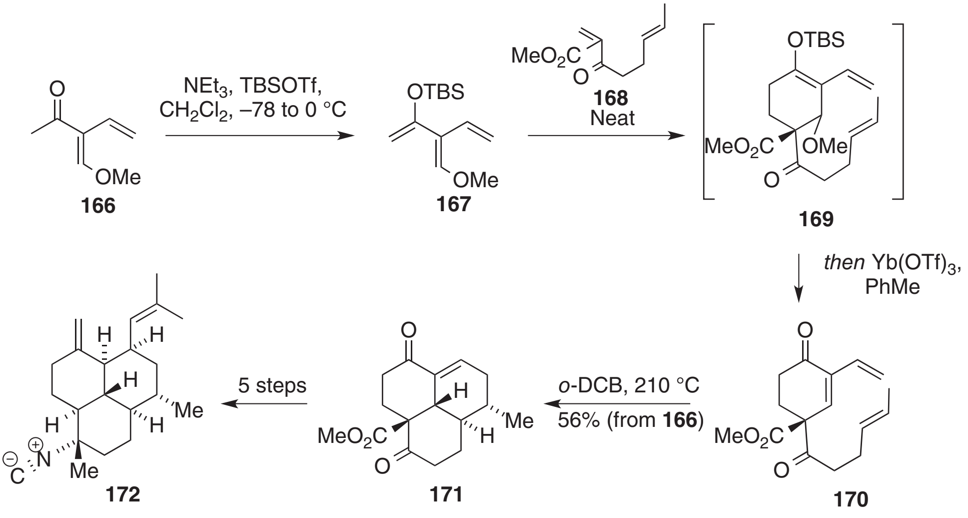
Scheme 12.33 Key steps in Baran's total synthesis of (±)-vinigrol.

The first successful natural product synthesis incorporating a DTDA reaction sequence was published by Sherburn and coworkers in 2008, and constitutes a formal synthesis of triptolide (**165**) (Scheme 12.34) [46]. The carbon framework of this natural product was rapidly assembled from silyl protected [3]dendralene **161**, beginning with a DA reaction between the free alcohol and methyl acrylate. *In situ* lactonization provided semicyclic diene **162**, which was subjected to a high-pressure DA reaction with quinone **163**. Tetracycle **164** was functionalized further to intercept an intermediate from Berchtold's 1982 total synthesis of triptolide [47].



Scheme 12.34 Sherburn and coworkers' formal synthesis of triptolide.

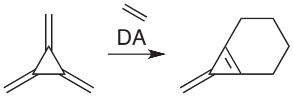
The final, and most recent example, was published by Shenvi and Pronin in 2012 [13]. Although not technically a DTDA sequence (as defined earlier), their synthesis of the potent antimalarial amphilectene **172** represents an exceptionally elegant application of a dendralene in synthesis (Scheme 12.35). Shenvi's synthesis centers around the DA reactivity of "Danishefsky [3]dendralene" **167**. This triene was prepared via the silylation of ketone **166**, and submitted without purification to a DA reaction with bis-activated dienophile **168**. The transmitted diene generated from this reaction migrates upon addition of ytterbium(III) trifluoromethanesulfonate, yielding cross-conjugated enone **170**. Upon heating in *o*-dichlorobenzene, an intramolecular DA reaction occurred, generating tricycle **171**. Five steps were then required to access the amphilectene **172**.



Scheme 12.35 Shenvi and Pronin's synthesis of amphilectene **172**.

12.6 The Radialenes

Despite great advances in the DA chemistry of the dendralenes, their cyclic counterparts, the radialenes (see Chapter 4), remain comparatively neglected. The simplest family member, [3]radialene (**173**), can, in principle, undergo a DA reaction to generate the bicyclic triafulvene **174** (Scheme 12.36). Although this



173
[3]Radialene

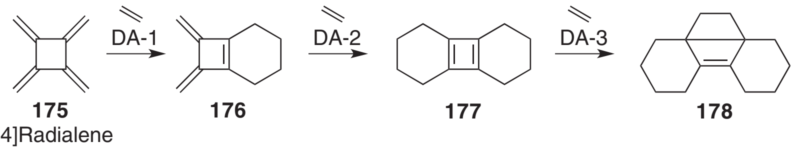
174

Scheme 12.36 The prototypical DA reaction of [3]radialene (**173**).

technically represents a diene-transmissive transformation, the newly generated diene, containing both an endo- and exocyclic alkene, cannot adopt the requisite s-*cis* conformation for a second DA reaction. Furthermore, the distance between the respective carbon atoms required for a successful Diels–Alder addition in **173** might be too large, and **174** should be a highly strained product.

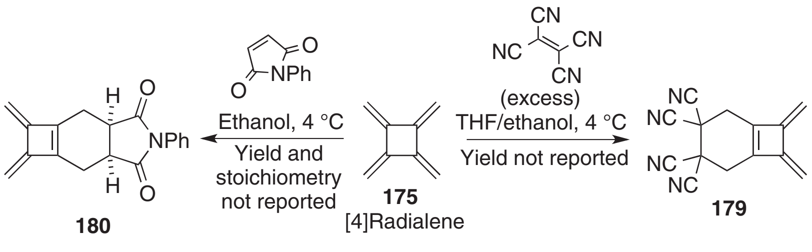
As yet there are no examples of a [3]radialene participating in a DA reaction. Only a small number of experiments exploring the chemical reactivity of the parent [3]radialene have been conducted, most likely on account of its pronounced instability [48–50]. However, a number of substituted and more stable derivatives have been synthesized [51–57], but all reported attempts at DA reactions using these analogs were unsuccessful [52, 56].

In contrast, a handful of successful studies describing DA reactions of [4]radialenes have been disclosed [58–61]. Although only single additions are known, in theory multiple additions are possible. Consider, for example, the DA reactions of [4]radialene (**175**) and ethylene (Scheme 12.37). The first reaction, at any of the 4 equivalent diene sites, affords cyclobutene **176**. If a second DA reaction were to occur, the antiaromatic cyclobutadiene **177** would be generated. Although this class of compounds is reported to be highly unstable, the compounds are not inaccessible [62, 63]. Cyclobutadiene **177** carries a diene locked in the s-*cis* conformation that could react in a third DA reaction to yield the spiro-fused tetracycle **178**, a reaction that is not without precedence [62, 63].



Scheme 12.37 The prototypical DA reaction of [4]radialene (**175**)

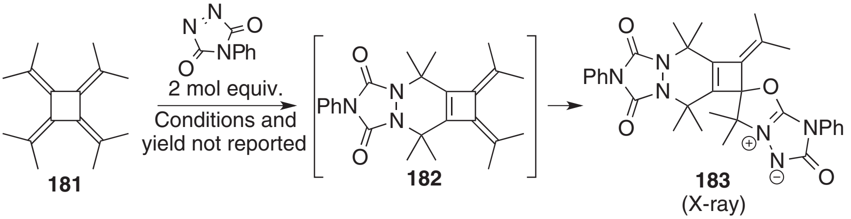
The first example of parent [4]radialene engaging in a DA reaction was published in conjunction with its first ever synthesis by Griffin and Peterson in 1963 [58]. They reported single DA additions of TCNE and NPhM, to provide cyclobutenes **179** and **180**, respectively (Scheme 12.38). The same outcome was observed when the DA chemistry of [4]radialene was later reinvestigated by Hopf



Scheme 12.38 The DA reactions of [4]radialene (**175**) with TCNE and NPhM.

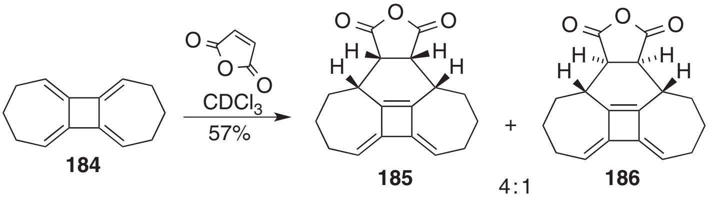
and Trabert in 1980, when it was reacted with 4-phenyl-1,2,4-triazole-3,5-dione and diethyl azodicarboxylate [59].

Only one account of a [4]radialene reacting with more than one molecule of a dienophile has been described, and, despite involving a hetero-DA reaction, we believe it important enough to warrant inclusion. When Wilke and coworkers reacted octamethyl[4]radialene (**181)** with 1 M equiv. of 4-phenyl-1,2,4-triazole-3,5-dione, the expected cycloadduct **182** was obtained (Scheme 12.39) [60]. When 2 M equiv. were employed, a second DA reaction was not observed; instead, the [3+2] cycloaddition product **183** was isolated (confirmed by X-ray analysis).



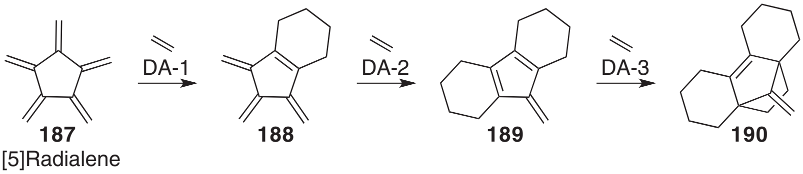
Scheme 12.39 A double addition of 4-phenyl-1,2,4-triazole-3,5-dione to octamethyl[4]radialene (**181**).

In the case of unsymmetrically substituted [4]radialenes, the four diene sites are no longer equivalent, and competing DA pathways become possible. The only study using a differentially substituted [4]radialene was published by Szeimies *et al.* in 1992 [61]. Tricyclic [4]radialene **184** was reacted with maleic anhydride, NPhM, benzyne, dimethyl acetylenedicarboxylate, TCNE, and 4-phenyl-1,2,4-triazole-3,5-dione. The only observed products resulted from reaction at the less sterically encumbered diene site, as illustrated by the representative example in Scheme 12.40 in which *endo*-adduct **185** and *exo*-adduct **186** were isolated in a combined yield of 57%.



Scheme 12.40 The DA reaction of tricyclic [4]radialene **184** with maleic anhydride.

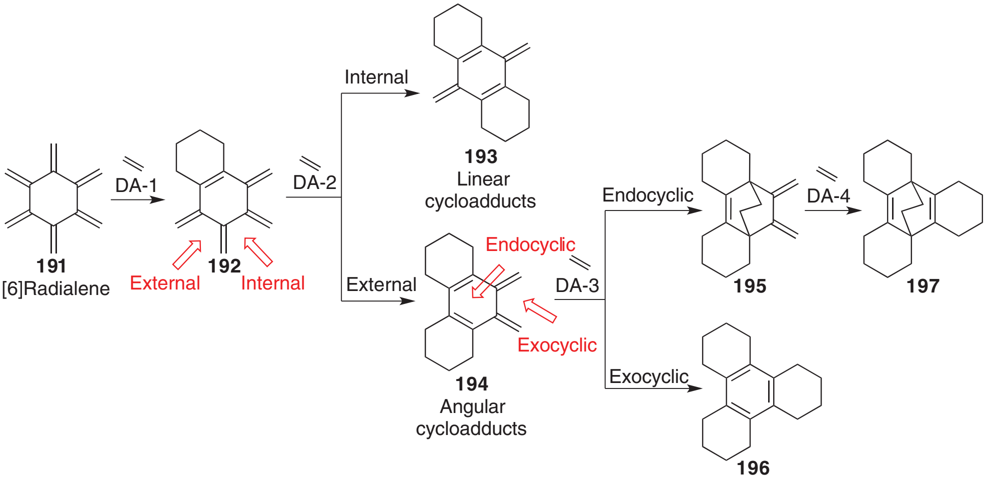
Very little is known about the chemical reactivity of [5]radialenes. The parent compound has yet to surrender to synthesis (see, however, p. 111, note added in proof), and no DA studies have been conducted using the few substituted analogs that have been prepared [55, 64–66]. However, for the sake of completeness



Scheme 12.41 The prototypical DA reaction of [5]radialene (**187**).

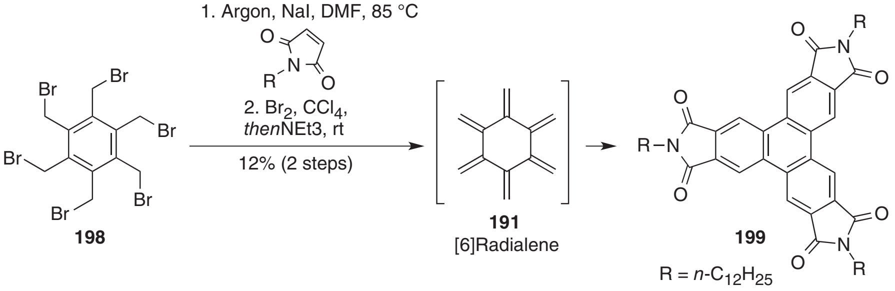
we feel it worthwhile to consider its potential DA reactivity (Scheme 12.41). Using ethylene as dienophile, the first DA reaction would generate tetraene **188**, a molecule containing 2 equivalent dienes locked in the s-*cis* conformation. A second DA reaction would yield pentafulvene **189**, a class of compounds that are known to readily participate as dienes in the DA reaction [67–69] (see Chapters 6 and 7), thus leading to tetracycle **190**.

We conclude with the DA chemistry of the highest known homologs, the [6]radialenes. As with the previous examples, this is most simply presented by considering the DA reactions of [6]radialene (**191**) and ethylene (Scheme 12.42). The product of the first cycloaddition, bicyclic pentaene **192**, contains an internal, and 2 equivalent external diene sites. If the second DA reaction occurs at the internal site, the so-called linear cycloadducts **193** are produced, and no additional DA reactions are possible. Alternatively, the angular cycloadducts are accessed if the second DA reaction occurs (this time in a diene-transmissive sense) at one of the two external diene sites of **192**. *o*-Xylylene **194** contains both an endo and exocyclic diene site, and can lead to either the pentacyclic framework **197** through a double DA sequence beginning with reaction at the endocyclic position of **194** or, alternatively, to arene **196** through a single DA reaction at the exocyclic diene site.



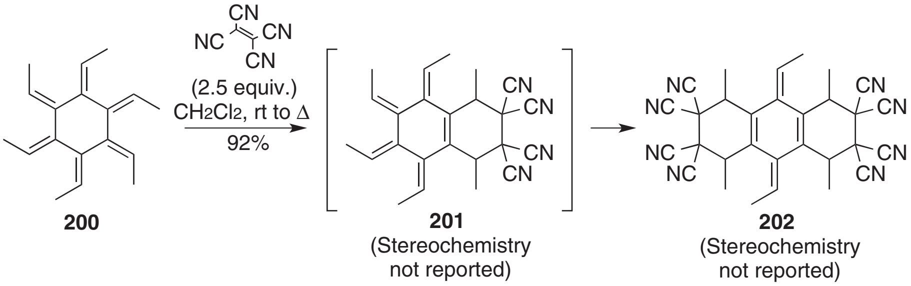
Scheme 12.42 The prototypical DA chemistry of [6]radialene (**191**).

In all three publications describing DA studies of parent [6]radialene, only aromatic compounds of the general structure **196** were isolated [70–72]. Although this appears to suggest a preference for the angular over linear cycloadducts, the yields of these reactions (when reported) were always low, and the remaining mass balance never identified. These studies were conducted using dienophiles that do not create any stereocenters (e.g., dimethyl acetylenedicarboxylate and benzyne), or via DA/aromatization sequences to destroy all generated stereochemistry. The most recently reported study was conducted by Chi, Wu, and coworkers in 2009 [72]. In one example from this investigation, [6]radialene was generated via the sixfold elimination of hexabromide **198** (according to the procedure of Schiess) [70, 73], in the presence of an excess of *N*-*n*-dodecylmaleimide (Scheme 12.43). Following a triple DA cascade, aromatization of the presumed mixture of diastereomers via a bromination/elimination sequence provided triphenylene **199** in 12% yield over two steps.



Scheme 12.43 A triple DA cascade/aromatization sequence of [6]radialene and *N*-*n*-dodecylmaleimide.

The only other DA studies of [6]radialenes were conducted with hexamethyl derivative **200** (Scheme 12.44), and its hexaethyl analog [74]. In contrast to the examples described for the parent [6]radialene, only linear cycloadducts were observed. For example, when Saur, Sustmann, and coworkers reacted hexamethyl [6]radialene (**200**) with an excess of TCNE, *p*-xylylene **202** was isolated in 92%



Scheme 12.44 The DA reactions of hexamethyl [6]radialene **200** and TCNE.

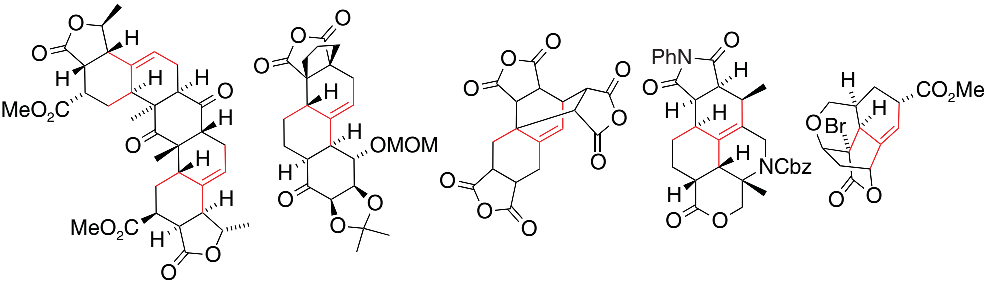
yield. This trend also held true for Hopff and coworkers, who reacted **200** with maleic anhydride, benzoquinone, 1,4-napthoquinone, acrolein, and methyl acrylate as dienophiles, although in these cases no yields were reported [75, 76].

12.7
Concluding Remarks

The examples highlighted in this review demonstrate the enormous power of cross-conjugated polyenes to rapidly generate complex multicyclic frameworks through DTDA sequences. One of the most significant challenges in this area of research is the control of stereo-, regio-, site-, and chemoselectivity. With respect to [3]dendralene, this has been successfully addressed as we have gained an understanding of the inherent reactivity and stability of this class of compounds. This has resulted in the development and application of new methodologies and strategies, for example, employing temporary or permanent dienophile tethers, or reducing the [3]dendralene conformational freedom through appropriate substitution. These advancements have allowed for the synthesis of a diverse array of polycyclic systems, many of which would be difficult to access by other means (Figure 12.5).

At present, the higher dendralenes remain comparatively unexplored, owing partly to the complexity of their DTDA chemistry. However, recent promising results suggest that control over their DTDA chemistry is possible. In particular, the organocatalyzed DA reactions of [4]dendralene (**11**), and the remarkable increase in DA selectivity (with respect to [4]dendralene) observed for the exhaustive addition of NMM to DVC (**139**), both reported by Sherburn *et al.* (Scheme 12.45).

In comparison, the field of radialene chemistry is still in its infancy. We cannot yet synthesize [5]radialene, nor analogs higher than [6], and the DA chemistry of those we can access has not been explored in a complete or systematic manner.



38
Sherburn

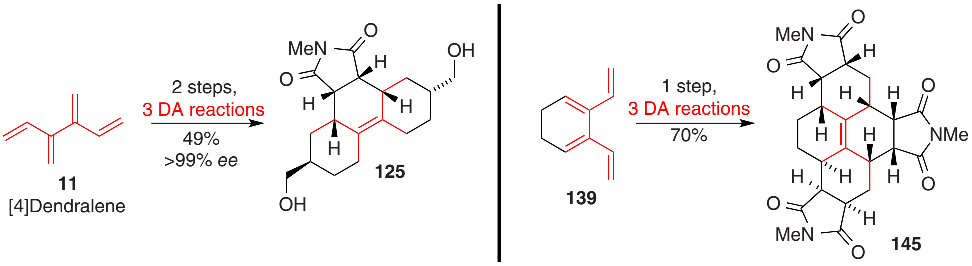
55
Fallis

80
Shusherina

86
Brummond

108
Cho

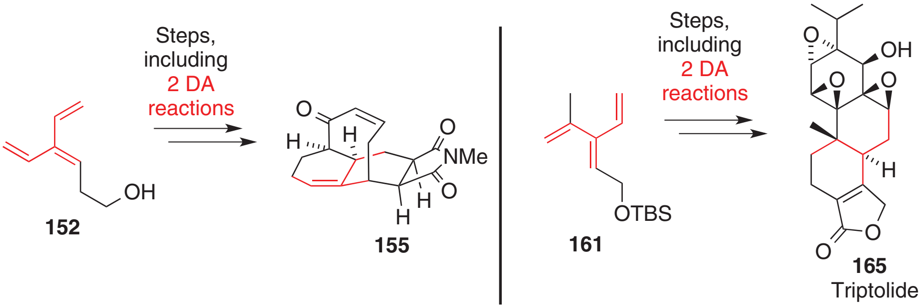
Figure 12.5 Polycyclic frameworks accessed from [3]dendralene DTDA sequences (carbons arising from [3]dendralene component highlighted).



Scheme 12.45 Highly selective DTDA cascades of [4]dendralenes.

This can be partly attributed to their apparent instability, but likely their lack of synthetic utility is also an important factor.

For many, the true measure of DTDA sequences of cross-conjugated polyenes lies with their application in target-orientated synthesis. At present, only four examples have been reported in this area, each featuring a substituted [3]dendralene (or “masked” [3]dendralene) (Scheme 12.46). No doubt, as we advance our understanding and control of DTDA chemistry, many more examples will follow.



Scheme 12.46 Representative examples of DTDA sequences in target-orientated synthesis.

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