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Shaoguang Zhang

The Chemistry of Zirconacycles and 2,6-Diazasemibullvalenes

Synthesis, Structures, Reactions, and Applications in the Synthesis of Novel *N*-Heterocycles

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The Chemistry of Zirconacycles and 2,6-Diazasemibullvalenes

Synthesis, Structures, Reactions, and Applications in the Synthesis of Novel *N*-Heterocycles

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2. Oxidation of C-H bonds to C=O bonds by O_2 only or *N*-oxides and DMSO: Synthesis of Δ^1-bipyrrolinones and pyrrolino[3,2-*b*]pyrrolinones from 2,6-diazasemibullvalenes.
   Shaoguang Zhang, Ming Zhan, Qian Luo, Wen-Xiong Zhang and Zhenfeng Xi*. *Chem. Commun.* **2013**, *49*, 6146–6148.
3. Lewis Acid-Catalyzed Site-Selective Cycloadditions of 2,6-Diazasemibullvalenes with Isocyanides, Azides and Diazo Compounds: Novel Reaction Patterns Leading to Diaza- and Triaza-Brexadiene Derivatives.
   Shaoguang Zhang, Wen-Xiong Zhang and Zhenfeng Xi*. *Angew. Chem. Int. Ed.* **2013**, *52*, 3485–3489.
4. 2,6-Diazasemibullvalenes: Synthesis, Structural Characterization, Theoretical Analysis and Reaction Chemistry.
   Shaoguang Zhang, Junnian Wei, Ming Zhan, Qian Luo, Chao Wang, Wen-Xiong Zhang and Zhenfeng Xi*. *J. Am. Chem. Soc.* **2012**, *134*, 11964–11967. **(Selected as JACS Spotlight:** *J. Am. Chem. Soc*. **2012**, *134*, 13533–13534)
5. One-pot Synthesis of Pyrrolo[3,2-*d*]pyridazines and Pyrrole-2,3-diones via Zirconocene-mediated Four-component Coupling of Si-tethered Diyne, Nitriles and Azide.
   Shaoguang Zhang, Jing Zhao, Wen-Xiong Zhang and Zhenfeng Xi*. *Org. Lett.* **2011**, *13*, 1626–1629.
6. One-Pot Selective Syntheses of 5-Azaindoles through Zirconocene-Mediated Multicomponent Reactions with Three Different Nitrile Components and One Alkyne Component.
   Shaoguang Zhang, Wen-Xiong Zhang, Jing Zhao and Zhenfeng Xi*. *Chem. Eur. J.* **2011**, *17,* 2442–2449.
7. Cleavage and Reorganization of Zr−C/Si−C Bonds Leading to Zr/Si−N Organometallic and Heterocyclic Compounds.
   Shaoguang Zhang, Wen-Xiong Zhang, Jing Zhao and Zhenfeng Xi*. *J. Am. Chem. Soc.* **2010**, *132*, 14042–14045.
8. Efficient One-Pot Synthesis of N-Containing Heterocycles by Multicomponent Coupling of Silicon-Tethered Diynes, Nitriles, and Isocyanides through Intramolecular Cyclization of Iminoacyl-Zr Intermediates.
   Shaoguang Zhang, Wen-Xiong Zhang, and Zhenfeng Xi*. *Chem. Eur. J.* **2010**, *16*, 8419–8426. **(VIP Paper)**

9. One-pot Multi-Component Synthesis of Azaindoles and Pyrroles from One Molecule of silicon-Tethered Diyne and Three or Two Molecules of Organonitriles Mediated by Zirconocence.
   Shaoguang Zhang, Xiaohua Sun, Wen-Xiong Zhang, and Zhenfeng Xi*. *Chem. Eur. J.* **2009**, *15*, 12608–12617.
10. Zirconium- and Silicon-Containing Intermediates with Three Fused Rings in a Zirconocene-Mediated Intermolecular Coupling Reaction.
    Wen-Xiong Zhang, **Shaoguang Zhang**, Xiaohua Sun, Masayoshi Nishiura, Zhaomin Hou,* and Zhenfeng Xi*. *Angew. Chem. Int. Ed.* **2009**, *48*, 7227–7231.
11. Zirconocene & Si-tethered Diynes: A Happy Match Directed towards Organometallic Chemistry and Organic Synthesis.
    Wen-Xiong Zhang, **Shaoguang Zhang**, and Zhenfeng Xi*. *Acc. Chem. Res.* **2011**, *44*, 541–551.

Supervisor's Foreword

This thesis describes the scientific achievements of Dr. Shaoguang Zhang, which were made during his doctoral program at the College of Chemistry and Molecular Engineering, Peking University. Shaoguang joined my research group as a graduate student in 2008 and spent 5 years in this group. He had achieved great progress in research projects on zirconocene chemistry, azasemibullvalene chemistry, and the development of new synthetic methodology. As Shaoguang's Ph.D. supervisor, I would like to introduce two important findings of his research. One is isolation, characterization, and synthetic application of Zr/Si-containing reactive organometallic intermediates in zirconocene-mediated multi-component synthesis of *N*-heterocycles. The other is the synthesis, characterization, theoretical/computational study, and reaction chemistry of 2,6-diazasemibullvalenes (NSBVs), including the first example of an X-ray single crystal structure.

It is of great importance to develop straightforward, efficient synthetic methods toward *N*-heterocycles. However, there are few reports on the synthesis of *N*-heterocycles via isolable metallacycles. Shaoguang's research disclosed that zirconacyclobutene–silacyclobutene fused compound (**A**), resulting from zirconocene and bis(alkynyl)silanes, is highly reactive toward many substrates. Based on the study on coordination-induced skeleton rearrangement and synthetic application of **A**, he developed mechanism-based synthesis of various kinds of *N*-heterocycles via multi-component one-pot coupling of **A** with nitriles and other unsaturated substrates. Several types of diversified *N*-heterocycles such as 5-azaindole, pyrrolo[3,2-*d*]pyridazine, and dihydropyrroloazepine could be synthesized, which were all difficult to synthesize by other means. The key three-fused-ring Zr/Si-containing intermediates were isolated and characterized. His research on reactive organometallic intermediates demonstrated that the isolation and characterization of reactive organometallic intermediates are of great importance for understanding the mechanistic aspects of metal-mediated organic reactions.

On the other hand, 2,6-diazasemibullvalene (NSBV) features an aziridine ring and unique polycyclic strained skeleton, which is expected to show unique properties and reactions toward the synthesis of *N*-heterocycles. NSBV is also

considered as one of the best candidates to approach neutral homoaromaticity, however, little is known experimentally. Shaoguang developed efficient synthesis and isolation of a series of NSBVs. He determined X-ray crystal structure of a substituted NSBV for the first time. He found the aza-Cope rearrangement of NSBVs was extremely rapid in solution, but "frozen" in the solid state. Shaoguang also collaborated with his labmate on theoretical analysis and showed that the localized structure was the predominant form, and the homoaromatic delocalized structure existed as a minor component in the equilibrium. Thus, this work gave solid results and answers to this controversial topic. His exploration into reaction chemistry of NSBV showed its reactive nature and usefulness in the synthesis of diverse and interesting "bowl-shape" or "cage-shape" *N*-containing polycyclic skeletons.

I hope the readers will gain deep insight into the mechanism of zirconocene-based chemistry as well as a full story of our journey on the fascinating NSBVs from this book.

Beijing, China, September 2014 Prof. Zhenfeng Xi

Contents

Chapter 1
Introduction to Zirconacycle Chemistry

In this chapter, the scope, mechanism, and recent progress of zirconocene (II)-mediated cyclization reactions are introduced. Zirconocene(II) is a very important reagent for organometallic chemistry, synthetic chemistry, and polymer chemistry. Zirconocene(II) is capable of coordinating with unsaturated compounds. Further reactions could lead to zirconocene(IV) species, zirconacycles, C–C bond formation, C–X bond formation, and synthesis of carbocycles and heterocycles. Zirconocene(II)-mediated cyclization of bis(alkynyl)silane gives zirconacyclobutene–silacyclobutene complexes, which could react with alkyne, bis(alkynyl)silane, ketone, nitrile, and isocyanate and could be applied in the synthesis of various valuable products.

1.1 *N*-Heterocyclic Compounds

In organic chemistry, *N*-heterocyclic compounds are cyclic compounds containing one or more nitrogen atoms. *N*-Heterocyclic compounds include aromatic *N*-heterocycles such as pyrrole, pyridine, and imidazole, as well as saturated *N*-heterocycles such as aziridine, piperidine [1]. *N*-heterocyclic compounds are very important motifs in biochemical compounds such as nitrogenous bases, as well as pharmaceuticals and materials (Fig. 1.1). Significant synthetic efforts had been made toward *N*-heterocycles with different structures and substitutents [1]; however, it is still demanding to develop new synthetic methods toward *N*-heterocyclic compounds, especially via metallacycles such as zirconacycles.

1.2 Zirconocene Chemistry

The divalent $Cp_2Zr(II)$ species (zirconocene, Cp = η^5-C_5H_5) has been proved to be synthetically very useful for organometallic chemistry, synthetic chemistry, and polymer chemistry [2–14]. Zirconocene species include the Negishi reagent

S. Zhang, *The Chemistry of Zirconacycles and 2,6-Diazasemibullvalenes*,
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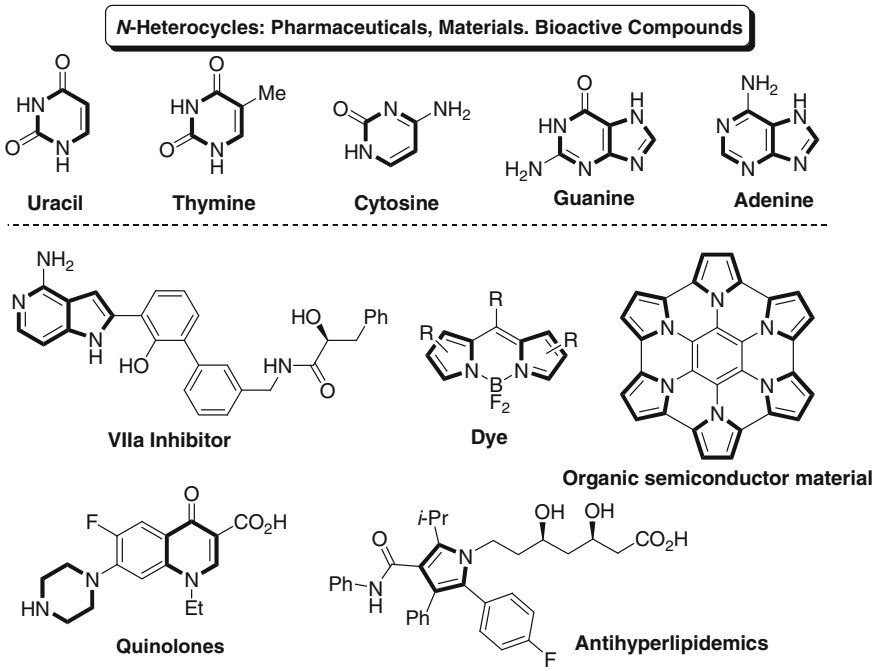


Fig. 1.1 *N*-heterocyclic compounds

Cp_2ZrBu_2 [9], the Takahashi reagent Cp_2ZrEt_2 [10], the Rosenthal complexes $Cp_2Zr(L)(\eta^2\text{-}Me_3SiCCSiMe_3)$, (L = THF [11], L = Py [12]), and the Cp_2ZrCl_2/Mg system [13]. Such species are all precursors of divalent $Cp_2Zr(II)$ species and can be readily generated in situ from several synthetic methods. The 14-electron $Cp_2Zr(II)$ species has a d^2 configuration with one lone-electron pair and two vacant valence orbitals. Therefore, zirconocene species readily coordinate with unsaturated organic substrates and undergo further reactions including the oxidative addition as the major to form $Cp_2Zr(IV)$ species. These transformations could be further applied to C–C or C–X bond formation and construction of functional group or heterocyclic compounds. Among many reactions mediated by low-valence $Cp_2Zr(II)$ species, the reaction with alkynes has been widely reported and is particularly interesting and synthetically useful [9–12].

1.3 Zirconocene-Mediated Cyclization Reactions and Application in the Synthesis of *N*-Heterocycles

Zirconocene(II) is isolobal with CH_2. Based on the analysis of the Dewar-Chatt-Duncanson model (Fig. 1.2), the filled bonding orbitals of the "carbenoidal" zirconocene interact with the empty non-bonding orbitals of alkene or alkyne, while

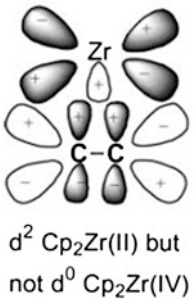
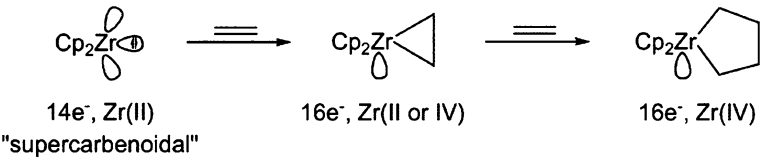


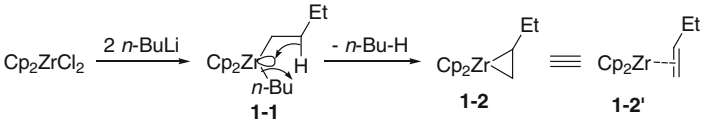
Fig. 1.2 Frontier molecular orbital interaction of zirconocene–alkene π-complexation. Reproduced from Ref. [5] by permission of the Royal Society of Chemistry

the empty non-bonding orbitals of zirconocene accept π-backbonding from alkene or alkyne. Thus, oxidative cyclization leads to the corresponding three-membered zirconacycle (Scheme 1.1). The resulting three-membered zirconacycle is still a coordinatively unsaturated 16-electron species and could further react with alkynes, nitriles, and ketones to give products of migratory insertion [5]. Thus, the two valence-shell empty orbitals and one filled non-bonding orbital are necessary for the complexation–carbozirconation process and the rich redox chemistry of $Cp_2Zr(II)$ species.

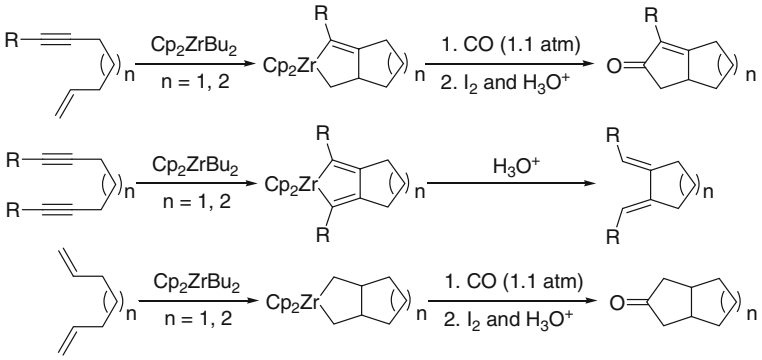
Reaction of zirconocene(IV) dichloride with two equivalents of *n*-butyl lithium gives Cp_2ZrBu_2 (Negishi reagent, **1-1**, Scheme 1.2). Cp_2ZrBu_2 could be formed at lower temperature. Upon warming up, it decomposes via *β*-H elimination and reductive elimination to afford zirconocene(II)–butene complex **1-2′**. Zirconocene-mediated intramolecular cyclization of enyne, diyne, and diene leads to bicyclic zirconacyclopentene, zirconacyclopentadiene, and zirconacyclopentane, respectively, in good regioselectivity and diastereoselectivity (Scheme 1.3) [15, 16].



Scheme 1.1 Coordination and carbometallation reaction of zirconocene with alkenes



Scheme 1.2 Formation and decomposition of Cp_2ZrBu_2

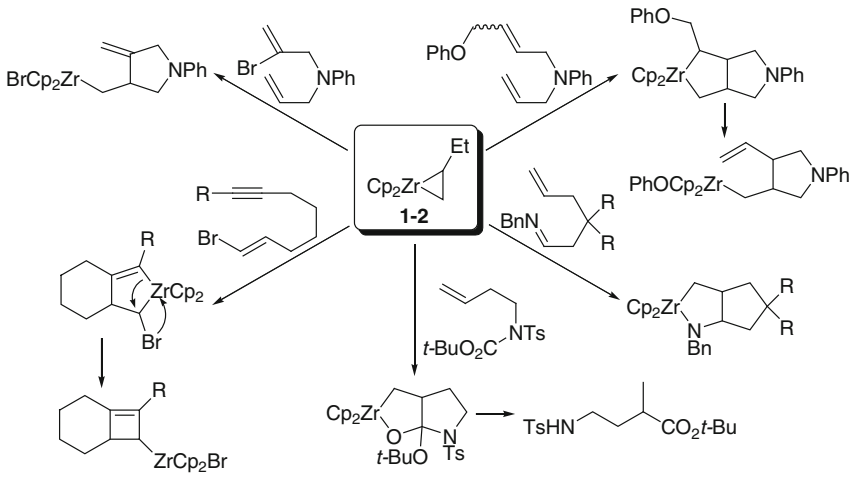


Scheme 1.3 Zirconocene-mediated cyclization of enyne, diyne, or diene

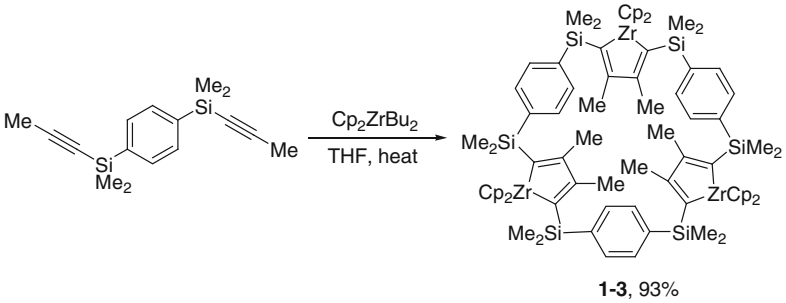
These bicyclic zirconacycles have been used in the synthesis of complicated natural products [17–19].

These substrates could be also applied in the zirconocene-mediated cyclization reaction: halogen-substituted dienes or enynes, dienes with aryloxy or alkoxy substituents at allylic position, ω-alkenyl imine, ω-alkynyl imine, or ω-alkenyl carbamate. The presence of heteroatoms allows further β-X elimination and thus leads to various useful transformations (Scheme 1.4) [20–24].

Tilley et al. reported zirconocene-mediated cyclization and polymerization of structurally rigid diynes to afford polymers, which could be further transformed into cyclic trimer **1-3** in high yield. The macrocyclic structure of **1-3** has been confirmed by X-ray crystal structure (Scheme 1.5) [25].

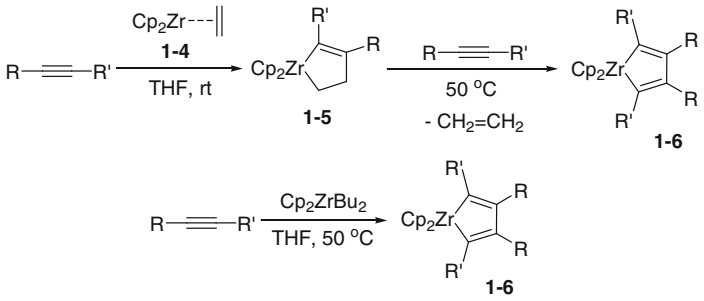


Scheme 1.4 Zirconocene-mediated cyclization of diene, enyne, ω-alkenyl imine, or ω-alkenyl carbamate



1-3, 93%

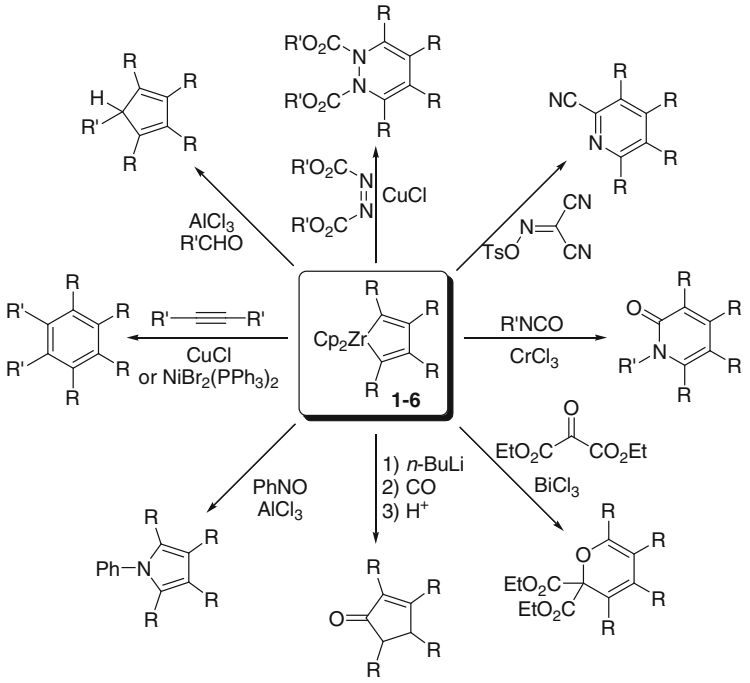
Scheme 1.5 Zirconocene-mediated cyclotrimerization of alkynyl silanes to form macrocycles featuring zirconacyclopentadienes



Scheme 1.6 Zirconocene-mediated intermolecular coupling of alkyne with ethylene or two molecules of alkynes

Takahashi et al. developed another important reagent, Cp_2ZrEt_2, as Cp_2Zr(II) equivalent. Reaction of zirconocene(IV) dichloride with two equivalents of ethyl magnesium chloride gives Cp_2ZrEt_2 (Takahashi reagent), which could decompose in similar pathway with Cp_2ZrBu_2 (Negishi reagent) and afford zirconocene(II)–ethylene complex **1-4**. Under the atmosphere of ethylene gas, **1-4** promotes cyclization of alkyne with ethylene to give zirconacyclopentene **1-5** in high regioselectivity. When R' equals to trimethylsilyl group, R' is selectively located at α-position of Cp_2Zr moiety. Further reaction of **1-5** with another molecule of alkyne leads to β-β' C–C bond cleavage. The second molecule of alkyne replaces ethylene and gives zirconacyclopentadiene **1-6** also in high regioselectivity [26]. Besides, Cp_2ZrBu_2 **1-1** (Negishi reagent) could promote intermolecular coupling of two alkynes to form zirconacyclopentadiene in one-pot, one step (Scheme 1.6).

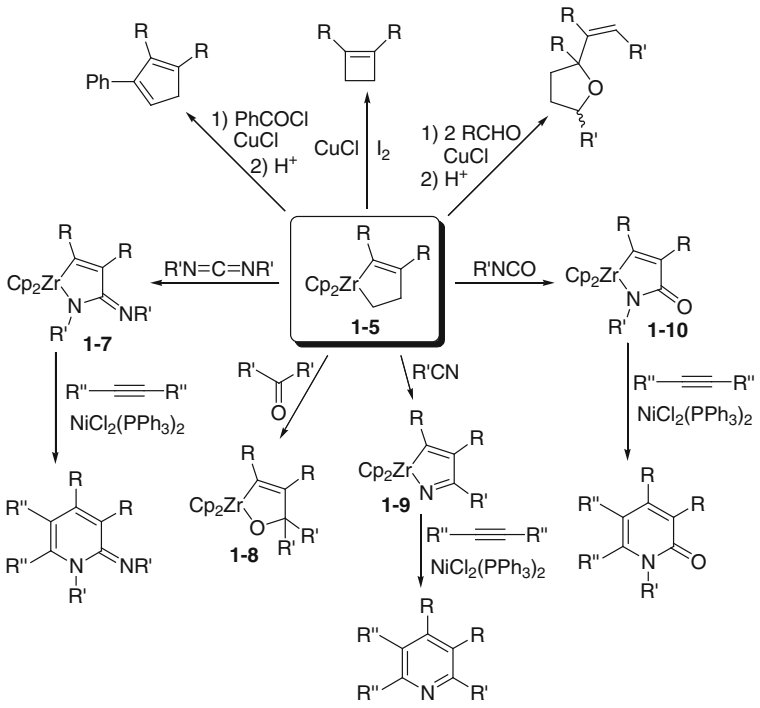
Several research groups have contributed to developing chemistry of zirconacyclopentadienes and disclosed that zirconacyclopentadiene **1-6** is highly synthetically useful and has been used in the construction of various carbocycles and heterocycles (Scheme 1.7). For example, treatment of **1-6** with dicyanide compounds bearing leaving group results in the formation of 2-cyanopyridine derivatives [27].



Scheme 1.7 Construction of carbocycles or *N*-heterocycles from reactions of zirconacyclopentadienes

Transmetallation of **1-6** or treatment of **1-6** with Lewis acid further broadens the scope of its reaction chemistry. In the presence of CuCl, the reaction of **1-6** with diazo dicarboxylate affords pyridazine derivatives [27]. In the presence of CuCl or nickel complexes, the reaction of **1-6** with alkynes leads to benzene derivatives [28, 29]. Transmetallation of **1-6** with $BiCl_3$ allows further reaction with 2-oxo malonate to give 2*H*-pyran derivatives [27]. Transmetallation of **1-6** with $CrCl_3$ followed by reaction with isocyanates affords pyridine derivatives [30]. Transmetallation of **1-6** with $AlCl_3$ followed by reaction with aldehydes affords pentasubstituted cyclopentadiene derivatives [31]. Under the similar condition, **1-6** reacts with nitroso compounds to form pyrrole derivatives [32]. Addition of *n*-butyl lithium activates **1-6** and allows further reaction with carbon monoxide, which leads to carbonylation and affords 2-cyclopentenone upon hydrolysis [33].

Zirconacyclopentene **1-5** could also be applied in synthetic reaction (Scheme 1.8). For example, in the presence of CuCl and iodine, oxidative demetallation of **1-5** gives cyclobutene derivatives [34]. Reaction of **1-5** with acid chloride gives tri-substituted cyclopentadiene derivatives [35]. This research group also reported zirconocene-mediated cyclization of alkyne, ethylene, and two molecules of aldehyde toward synthesis of 2-alkenyl tetrahydrofuran [36].



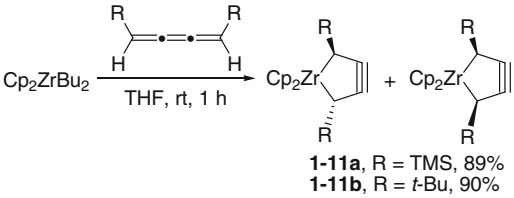
Scheme 1.8 Reaction chemistry of zirconacyclopentene and zirconocene-mediated cyclization of alkyne with aldehyde, ketone, nitrile, isocyanate, or carbodiimide

The reaction chemistry of **1-5** could also be useful for construction of *N*-heterocycles. The reactions of **1-5** with ketone, nitrile, isocyanate, and carbodiimide all lead to *β*-*β*′ C–C bond cleavage and eliminate ethylene. Various *N*-heterocycles or *O*-heterocycles **1-7–1-10** could be thus synthesized. Transmetallation of **1-7–1-10** with nickel complexes followed by treatment with alkyne readily affords pyridine, pyridine, or 2-iminopyridine derivatives [37–39].

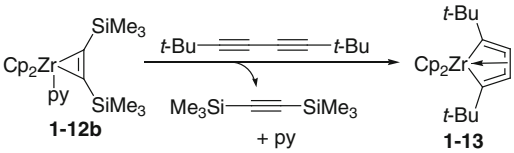
Suzuki et al. reported in 2002 on zirconocene-mediated cyclization of 1,2,3-butatriene to afford highly strained zirconacyclopentyne **1-11** in high yield. This is the first reported example of metallacyclopentyne (Scheme 1.9) [40].

Similarly, the reaction of Rosenthal reagent **1-12** with 1,4-di-*tert*-butyl-1,3-butadiyne gave zirconacyclopentatriene **1-13** as product of intramolecular cyclization. Zirconacyclopentatriene **1-13** have been considered as "bent" allene, and both zirconacyclopentyne **1-11** and zirconacyclopentyne **1-13** feature ring strain and are structurally interesting molecules (Scheme 1.10) [41].

Based on the zirconocene-mediated cyclization of 1,3-butadiyne to form zirconacyclopentatriene, Yuanhong Liu et al. developed zirconocene-mediated cyclization of 1,3-butadiyne with two molecules of acyl nitrile to form azazirconacycle **1-15**.



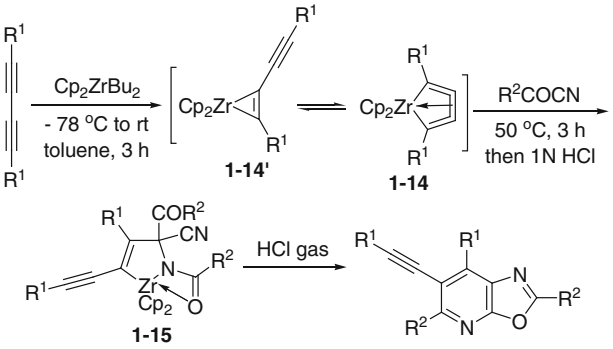
Scheme 1.9 Zirconocene-mediated cyclization of 1,2,3-butatriene to form zirconacyclopentyne



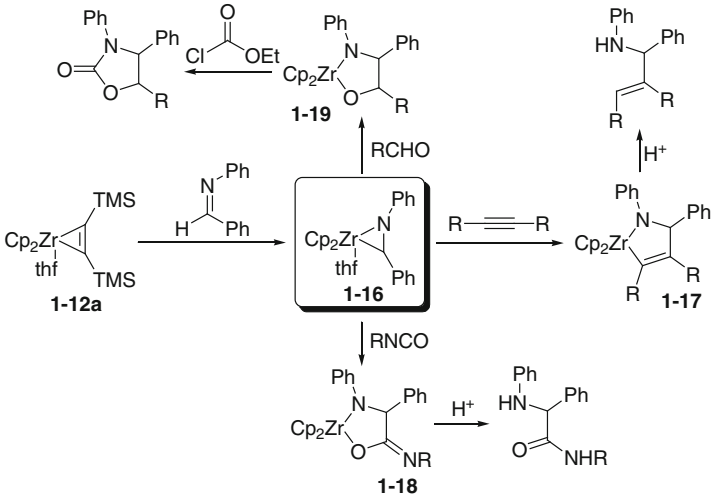
Scheme 1.10 Zirconocene-mediated cyclization of 1,3-butadiyne to form zirconacyclopentatriene

Upon hydrolysis, oxazolo [5,4-*b*]pyridine derivatives were isolated, which could be hardly synthesized by other means (Scheme 1.11) [42].

Norton et al. investigated cyclization of zirconocene and imine to form several types of zirconaaziridine **1-16**. The rich reaction chemistry of **1-16** includes cyclization with alkene or alkyne to afford azazirconacyclopentene **1-17** and cyclization with isocyanate or aldehyde to form azaoxazirconacycle **1-18** and **1-19**. These functionalized zirconacycles could be further transformed into zirconaoxazolidione, allylic amine, and α-amino amide (Scheme 1.12) [43, 44].



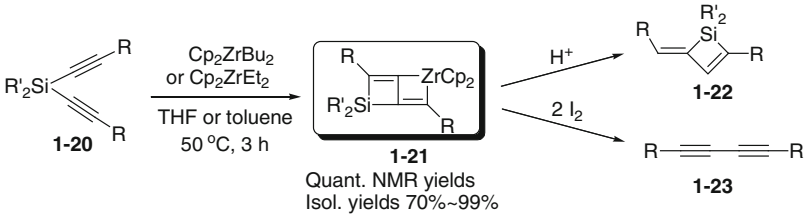
Scheme 1.11 Zirconocene-mediated cyclization of 1,3-butadiyne with acyl nitrile to form oxazolo [5,4-*b*]pyridine



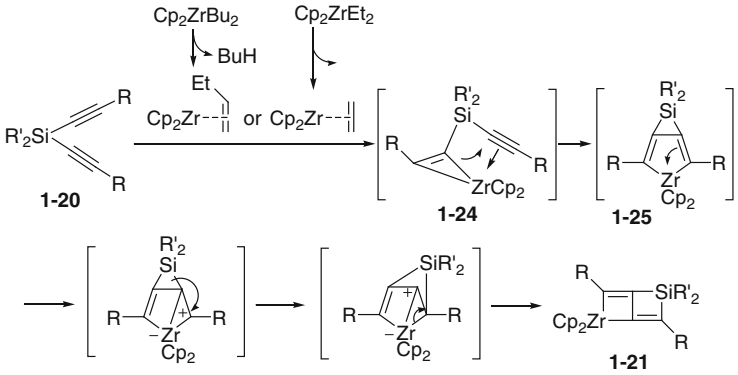
Scheme 1.12 Zirconocene-mediated cyclization of imine with alkyne, isocyanate, or aldehyde and reaction chemistry of zirconaaziridines

1.4 Zirconocene-Mediated Intramolecular Cyclization of Bis(Alkynyl)Silanes

Zirconacyclobutene–silacyclobutene complex **1-20** features the concomitance of two Zr–C bonds and two Si–C bonds as well as two fused 4-membered metallacycles, which are useful for further reaction chemistry and synthetic application [45–52]. In 1995, Takahashi and coworkers reported the reaction of bis(alkynyl) silanes with Cp_2Zr(II) species (Scheme 1.13). When the bis(alkynyl)silane **1-20** was treated with in situ-generated low-valence Cp_2Zr(II) species, such as Cp_2ZrBu_2 (Negishi reagent) or Cp_2ZrEt_2 (Takahashi reagent), a skeletal rearrangement led to formation of a zirconacyclobutene–silacyclobutene complex **1-21**, whose structure was unambiguously confirmed by X-ray single-crystal structural analysis [45, 46].



Scheme 1.13 Zirconocene-mediated intramolecular cyclization of bis(alkynyl)silanes to give zirconacyclobutene–silacyclobutene **1-21**



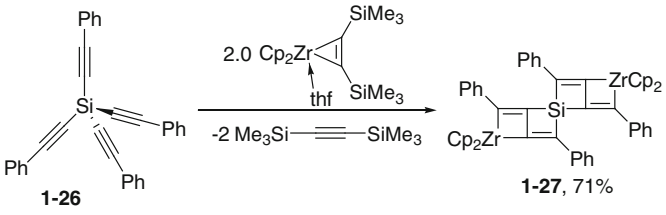
Scheme 1.14 Proposed mechanism of zirconocene-mediated intramolecular cyclization of bis (alkynyl)silanes

Hydrolysis of **1-21** with water affords their corresponding silacyclobutene derivatives **1-22** in high yields. Reaction of **1-21** with iodine results in demetallation and affords 1,3-butadiyne **1-23**.

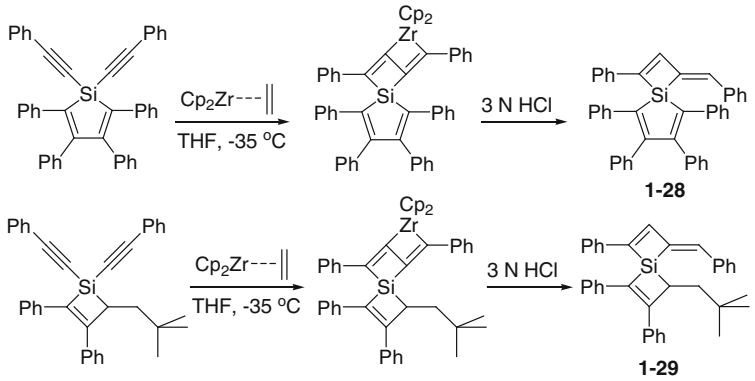
The mechanism is proposed as follows: intramolecular elimination of butane or ethane from Cp_2ZrBu_2 (Negishi reagent) or Cp_2ZrEt_2 (Takahashi reagent) gives zirconocene–butene or zirconocene–ethylene complex, respectively. Elimination of alkene and coordination of one C≡C bond of bis(alkynyl)silane affords zirconacyclopropane **1-24**. Migratory insertion of the second C≡C bond with **1-24** gives zirconacyclopentadiene–silacyclopropane **1-25**. Probably due to the ring strain, **1-25** is unstable and further rearranges intramolecularly via 1,2-silyl migration to afford **1-21** (Scheme 1.14) [45, 46].

In 2000, Rosenthal and coworkers reported the zirconocene-mediated cyclization of tetraalkynylsilane (Scheme 1.15). A spirocompound containing silacyclobutene **1-27** was obtained when tetraalkynylsilane $(RC{\equiv}C)_4Si$ was treated with $Cp_2Zr(thf)(Me_3SiCCSiMe_3)$ (**1-12a**) [52].

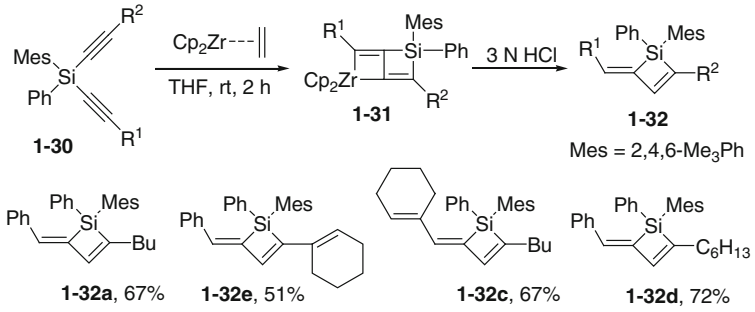
In 2007, Auner et al. successfully synthesized a series of new organosilicon-based spirocompounds **1-28** and **1-29** featuring silacyclobutene moiety, based on zirconocene-mediated cyclization of bis(alkynyl)silanes (Scheme 1.16). The optoelectronic



Scheme 1.15 Zirconocene-mediated intramolecular cyclization of tetra(alkynyl)silanes



Scheme 1.16 Zirconocene-mediated intramolecular cyclization of bis(alkynyl)silanes to give spiro-silacycles

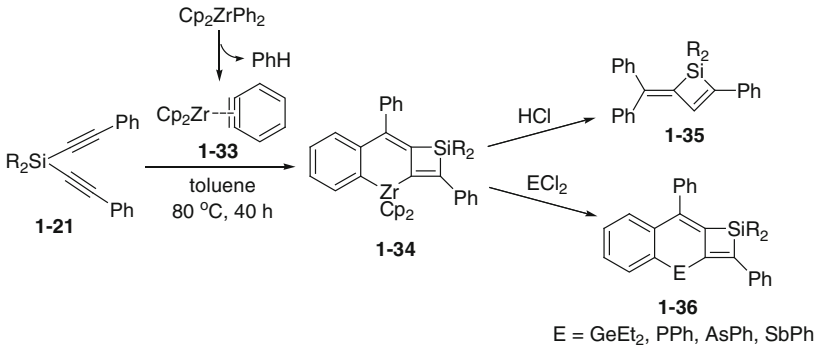


Scheme 1.17 Zirconocene-mediated intramolecular cyclization of bis(alkynyl)silanes bearing bulky substituents

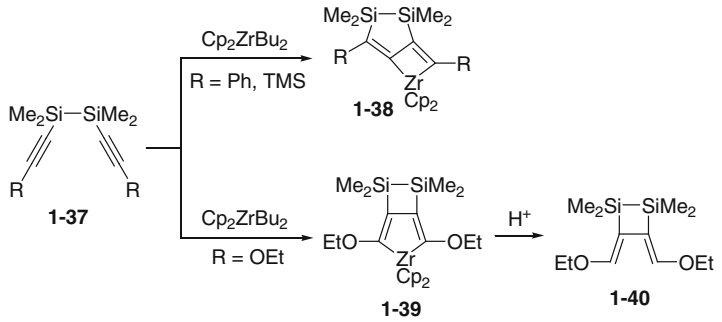
properties of these compounds might be useful for the design of sensitive sensor materials and optical switches [53].

Nagao et al. studied the zirconocene-mediated coupling of unsymmetrical bis (alkynyl)silanes with bulky substituents on silicon atom. When unsymmetrical bis (alkynyl)silanes **1-30** was applied, upon hydrolysis, the silacyclobutene derivatives **1-32** could be synthesized regioselectively (Scheme 1.17); alkyl or alkenyl group was selectively located at α-position of silacyclobutene, while aryl group was selectively located at α-position of zirconacyclobutene [54].

Zirconocene could also promote cyclization of bis(alkynyl)silanes with benzynes. Meunier et al. reported the intramolecular elimination of benzene from Cp_2ZrPh_2 to afford zirconocene–benzyne complex **1-33**. The reaction of **1-33** with bis(alkynyl) silanes **1-21** gives benzozirconacyclohexadiene–silacyclobutene three-ring fused complexes **1-34**. Upon hydrolysis, silacyclobutene **1-35** were isolated. (Scheme 1.18) [55].



Scheme 1.18 Zirconocene-mediated cyclization of bis(alkynyl)silanes with benzyne



Scheme 1.19 Zirconocene-mediated intramolecular cyclization of bis(alkynyl)disilanes

Ando et al. studied zirconocene-mediated intramolecular cyclization of bis (alkynyl)disilanes **1-37**. When the terminal substituents are phenyl group or silyl group, intramolecular coupling and rearrangement give zirconacyclobutene–disilacyclobutene **1-38**. When the terminal substituents are ethoxy group, intramolecular coupling of alkynyl group gives zirconacyclopentadiene–disilacyclobutane **1-39** (Scheme 1.19) [56].

1.5 Reaction Chemistry of Zirconacyclobutene–Silacyclobutene Complexes

Zirconacyclobutene–silacyclobutene complex **1-21** features two fused 4-membered metallacycles as well as two Zr–C bonds and two Si–C bonds. Moreover, **1-21** could be generated in situ via zirconocene-mediated cyclization of bis(alkynyl) silane, or isolated in pure form as a metallacyclic reagent. **1-21** is an isolable and stable compound under inert atmosphere; however, it is highly reactive and is

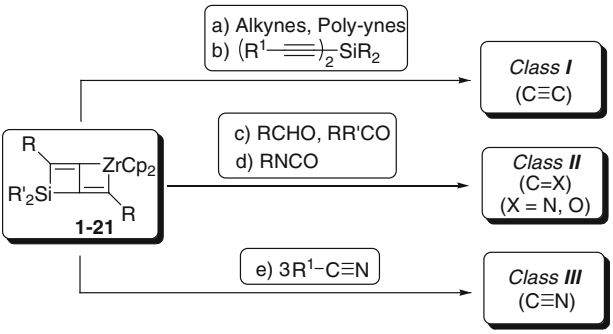


Fig. 1.3 Reaction modes of zirconacyclobutene–silacyclobutene complexes. Reprinted with the permission from Ref. [57]. Copyright 2011 American Chemical Society

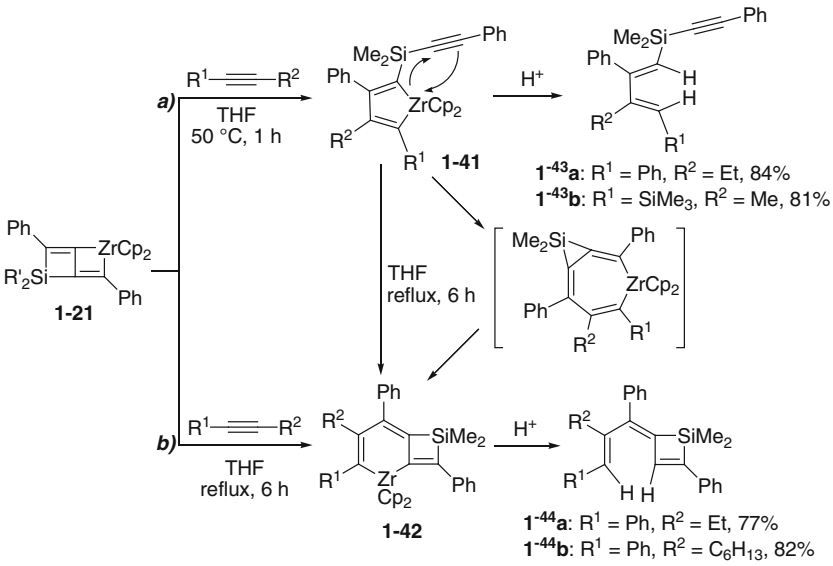
readily transformed when a coordinating ligand/substrate approaches. Three major classes of reaction are summarized in Fig. 1.3: reactions with alkynes, reactions with C=X bond, and reactions with nitriles (Fig. 1.3) [47–51].

1.5.1 Reaction of Zirconacyclobutene–Silacyclobutene Complexes with Alkynes (Class I)

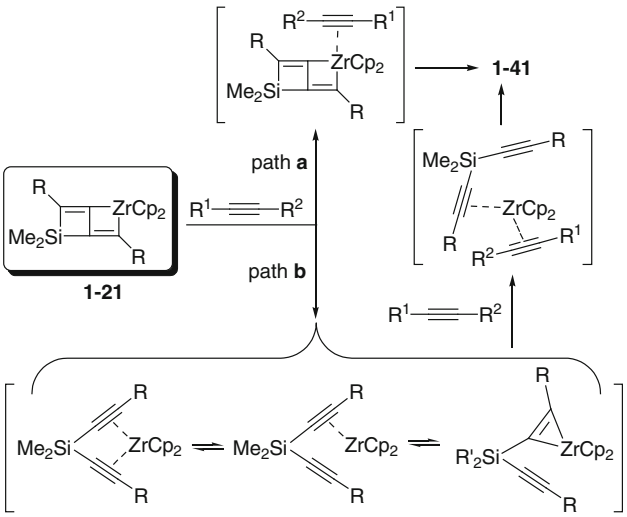
The reaction of **1-21** with alkyne generates the six-membered zirconacycle **1-41** as the result of insertion of alkyne into one of the Zr–C bonds in excellent yields under reflux condition. However, further mechanistic study demonstrated that **1-41** was not formed through direct insertion pathway. When the reaction of **1-21a** with an alkyne was monitored at 50 °C, zirconacyclopentadiene **1-41** was formed as kinetic-favored product. Further reaction at higher temperature results in thermo-rearrangement of **1-41** to give zirconacyclohexadiene–silacyclobutene **1-42** as thermodynamically favored product (Scheme 1.20). Two pathways might be considered for the formation of **1-41** from **1 to 21**: the associative path (path a) and the dissociative path (path b).

The reaction of **1-21** with alkynes is regioselective. When unsymmetrical alkynes such as 1-phenyl-1-butyne was used, **1-43a** and **1-44a** both as single regioisomers were isolated upon hydrolysis of reaction mixture at 50 °C and 90 °C respectively. The Ph group was selectively located at α-position of Cp_2Zr moiety. The substituents on alkynes also have an effect on the chemoselectivity of the reaction. When 1-trimethylsilyl-1-propyne was used, only zirconacyclopentadiene **1-43b** was isolated regioselectively, and the corresponding zirconacyclohexadiene complex was not isolated (Scheme 1.21) [47, 48].

The reaction of **1-21** with poly-ynes are similar to the reaction with mono-ynes. Under similar condition, benzene-based π-conjugated systems containing two or

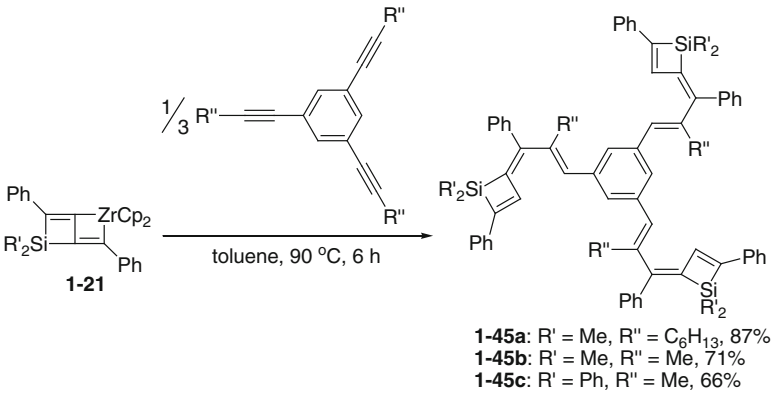


Scheme 1.20 Reaction of zirconacyclobutene–silacyclobutene complexes with alkynes



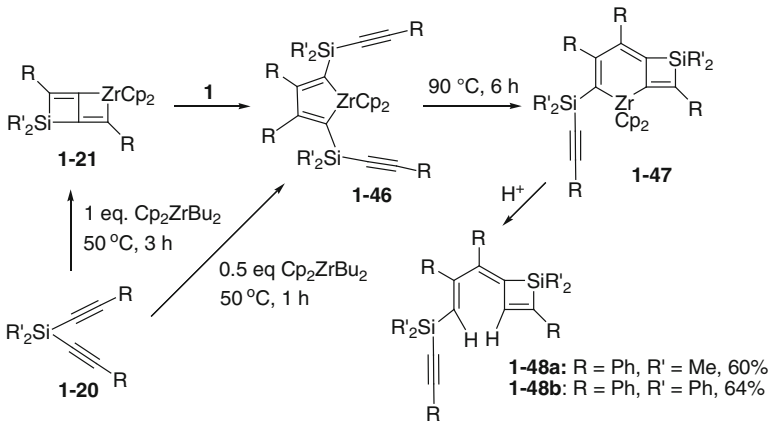
Scheme 1.21 Proposed mechanism of reaction of zirconacyclobutene–silacyclobutene complexes with alkynes

three silacyclobutene units were synthesized in good yields via reaction of **1-21** with poly(alkynyl)benzenes in toluene at 90 °C for 6 h followed by hydrolysis (Scheme 1.22). Preliminary optical properties show that the increase in silacyclobutene units brings about an increase in the extinction coefficient [49].

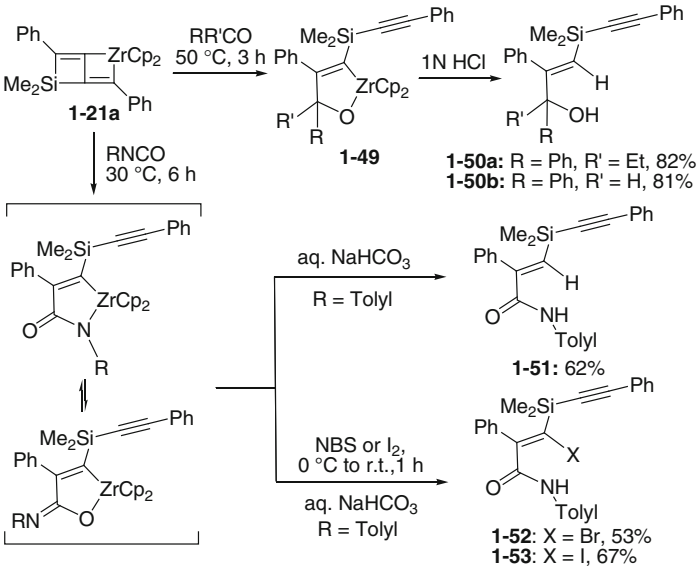


Scheme 1.22 Reaction of zirconacyclobutene–silacyclobutene complexes with poly(alkynyl) benzene to form star-shaped conjugated molecules

The metal-to-diyne ratio also played a key role in the reaction of zirconocene with bis(alkynyl)silanes. When the amount of the Si-tethered diyne **l** was increased from 1 equiv to 2 equiv relative to Cp_2ZrBu_2, the 2,5-bis(alkynylsilyl)zirconacyclopentadiene **1-46** was isolated with high regio- and chemoselectivity (Scheme 1.23). Both aromatic and aliphatic substituents on the Si and the terminal alkynyl carbon atoms could be used. When **1-46** was further heated at elevated temperatures, it changed completely to the zirconacyclohexadiene–silacyclobutene fused compound **1-47**. Further skeletal rearrangement of **1-47** via insertion of the remaining triple bond into the Zr–C bond was not detected even after prolonged reaction time at even higher temperatures [50].



Scheme 1.23 Reaction of zirconacyclobutene–silacyclobutene complexes with bis(alkynyl) alkynes



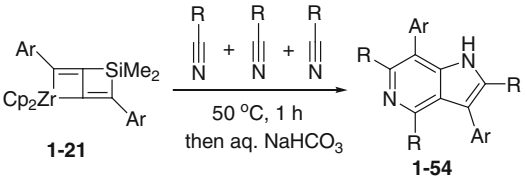
Scheme 1.24 Reaction of zirconacyclobutene–silacyclobutene complexes with aldehydes, ketones or isocyanates

1.5.2 Reaction of Zirconacyclobutene–Silacyclobutene Complexes with C=X Bond (Class II)

Unsaturated substrates containing C=O and C=N bonds, such as ketones, aldehydes, and isocyanides, were also found to be able to react with **1-21** (Scheme 1.24). When the complex **1-21** was treated with ketones or aldehydes, the five-membered oxazirconacyclopentene **1-49** was formed as the intermediate. Hydrolysis of **1-49** affords allylic alcohols **1-50** in good yields. When the complex **1-21** was treated with isocyanides, alkynylsilyl amides **1-51–1-52** were obtained upon hydrolysis or halogenation of the reaction mixture with I_2 or NBS [48].

1.5.3 Reaction of Zirconacyclobutene–Silacyclobutene Complexes with Nitriles (Class III)

In 2004, our research group reported a coupling reaction of **1-21** with three organonitriles in toluene. Along with coupling, cleavage of two Si–C bonds and one of the three C≡N triple bonds took place, affording 5-azaindole **1-54** after hydrolysis (Scheme 1.25). Five components of bis(alkynyl)silanes, zirconocene, and



Scheme 1.25 Reaction of zirconacyclobutene–silacyclobutene complexes with nitriles

three nitriles are integrated in one-pot reaction in perfect chemo- and regioselectivity. However, the reaction mechanism and reactive organometallic intermediates were still unclear [51].

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Chapter 2
Zirconocene-Mediated Cyclization of Bis(alkynyl)silanes and Nitriles: Synthesis of *N*-Heterocycles and Isolation, Characterization, and Synthetic Application of Zr/Si-Containing Reactive Intermediates

2.1 Introduction

The isolation and reactivity investigation of important intermediates in transition-metal-mediated or metal-catalyzed reactions are of general interest in both organometallic chemistry and synthetic organic chemistry. The research into organometallic reactive intermediates focuses on its structures, reaction patterns, and the relationship. On the one hand, these researches play an important role in the in-depth understanding of seemingly complicated reaction mechanisms. On the other hand, it can also lead to discovery of new synthetically useful reactions, such as new types of C–C and C–X bond formation or heterocycle synthesis (Fig. 2.1). However, generally the organometallic reactive intermediates are very reactive toward air, oxygen, and moisture and thus difficult to isolate and characterize.

Azaindoles are a class of heterocycles of considerable biological and pharmaceutical importance and have been frequently applied in natural product synthesis and as indole bioisosteres in the design of biologically active compounds [1, 2]. However, synthesis of azaindoles has remained a challenge for synthetic chemists both in academy and in pharmaceutical industry, since classical methods for synthesis of indole derivatives and related *N*-containing heterocycles do not work well on the synthesis of azaindole analogues, or at least work but not efficiently [1, 2]. In 2004, our research group reported a zirconocene-mediated intermolecular coupling reaction of one molecule of bis(alkynyl)silane with three molecules of organonitrile, which afforded 5-azaindoles upon hydrolysis of the reaction mixture (Scheme 2.1) [3].

In this one-pot reaction, five components are involved and integrated in a selective manner via an unknown pathway, involving cleavage of C≡N triple bonds and Si–C bonds [4–6]. We anticipated that novel and important reaction patterns might be involved. Thus, we expect to isolate and characterize the reactive intermediates ahead of hydrolysis process. Fortunately, we managed to isolate the intermediate in this process and illustrate the interesting and surprising mechanism which puts all the five

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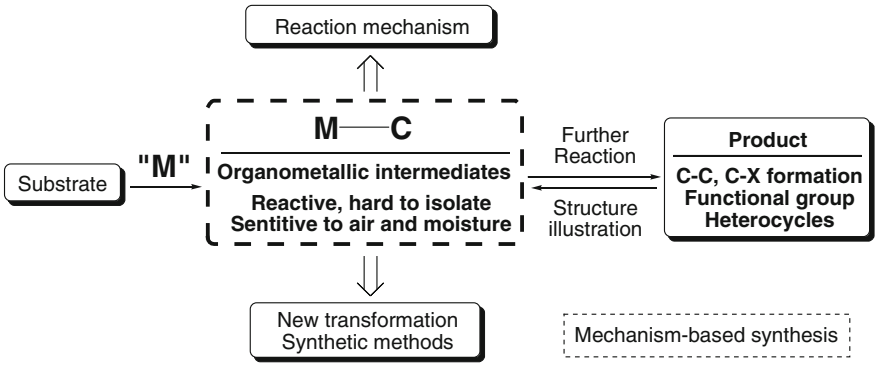
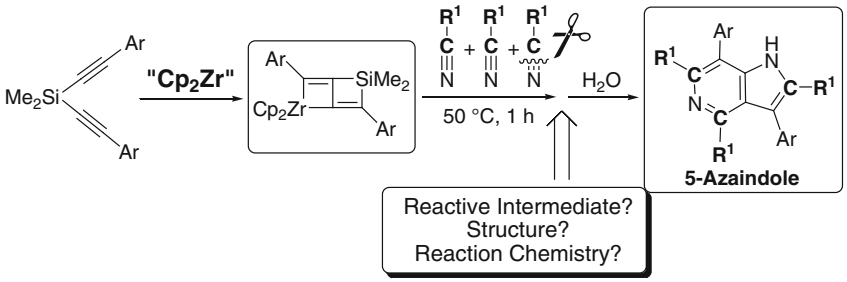


Fig. 2.1 Mechanism investigation and synthesis application based on chemistry of organometallic reactive intermediates



Scheme 2.1 Zirconocene-mediated intermolecular coupling reaction of bis(alkynyl)silane with three molecules of organonitriles affording 5-azaindoles

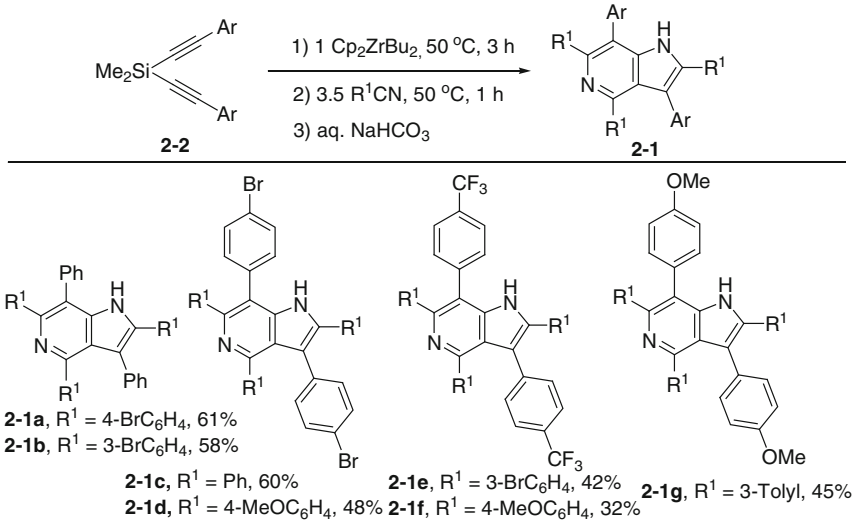
components together. In this chapter, the following researches are disclosed: (1) the scope of synthesis of 5-azaindoles and the further derivation; (2) isolation and characterization of Zr/Si-containing organometallic reactive intermediates; and (3) synthetically useful applications of these reactive intermediates toward synthesis of *N*-heterocycles.

2.2 Results and Discussion

2.2.1 Formation of 5-Azaindoles from One Molecule of Bis (alkynyl)silane with Three Molecules of the Same Organonitrile

Cp_2ZrBu_2 (Negishi reagent), as a very useful zirconocene (II) species, can be easily generated in situ from Cp_2ZrCl_2 and two equivalents of *n*-butyl lithium in toluene at −78 °C for 1 h [7]. Zirconocene (II) species promoted intermolecular coupling of

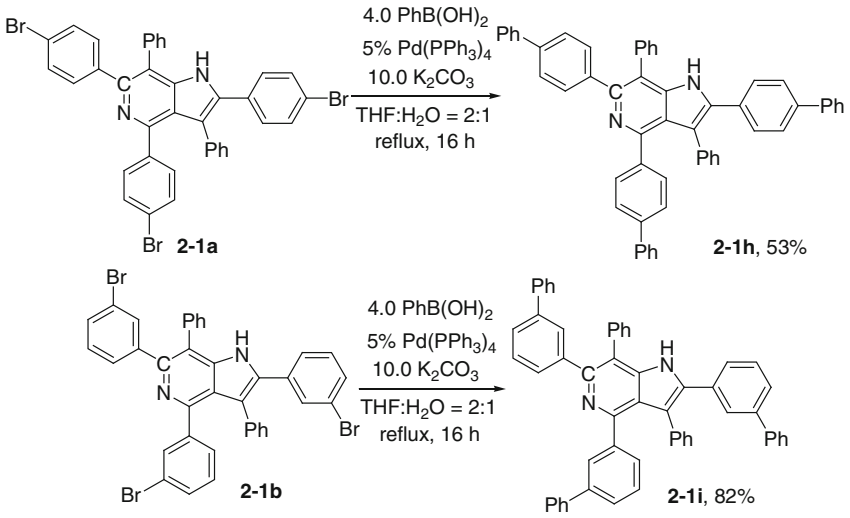
Table 2.1 Formation of 5-azaindoles from one molecule of bis(alkynyl)silane with three molecules of the same organonitrile (R^1CN)



bis(alkynyl)silane with three molecules of the same organonitriles [8, 9], to afford a 5-azaindole derivative upon hydrolysis (Table 2.1) [3]. Further investigation reveals that a wide variety of the bis(alkynyl)silane and organonitriles, especially those functionalized ones, can be applied in this procedure to afford 5-azaindole derivatives with diversified substitution patterns.

A variety of bis(arylalkynyl)silanes **2-2** could act as a suitable component as given in Table 2.1. In addition to Ph-substituted alkynes (**2-2a**), we also investigated substituted or functionalized bis(arylalkynyl)silanes, such as 4-Br (**2-2b**), 4-CF_3 (**2-2c**), and 4-OMe (**2-2d**). Bis(alkynyl)silanes with functional substituents (**2-2b**–**2-2d**) lead to the formation of azaindoles bearing various functional groups, however in lower yields. Electron-donating OMe group and electron-withdrawing CF_3 group on the aryl moiety of **2-2** could also be applied to afford their corresponding multi-functionalized azaindoles (**2-1e**–**2-1g**) in moderate to good yields, respectively. It should be noted that Br in **2-2b** survived this zirconocene-mediated conditions to give the azaindoles **2-1c**–**2-1d** in good yields.

A wide variety of organonitriles, either aliphatic or (hetero)aromatic with both electron-withdrawing groups and electron-donating groups, could be applied to afford 5-azaindoles in good isolated yields. Functionalized groups on the aromatic nitriles were tolerated in this process, albeit slightly lower yields were gained in comparison with PhCN. The 4-OMe- and 3-Br-substituted benzonitriles all gave good results to the corresponding azaindoles. However, as far as other functionalized or steric-hindered nitriles, such as 2-cyanopyridine, 9-cyanophenathracene, and 2-bromobenzonitrile, were concerned, only trace amount of azaindoles were observed.

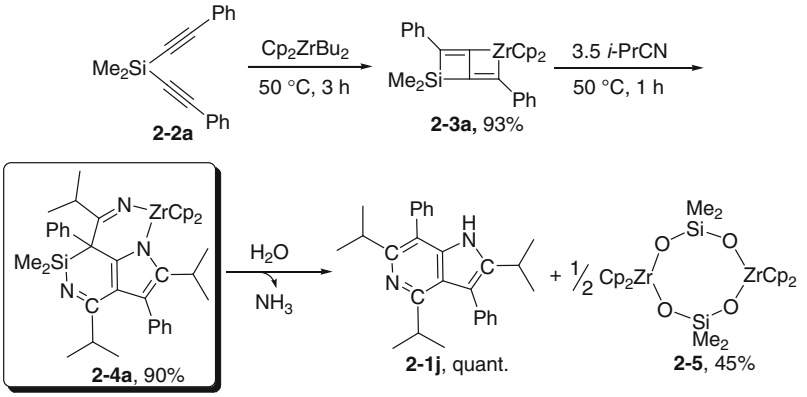


Scheme 2.2 Further application of 5-azaindoles: Suzuki coupling

The functionalized azaindoles with Br group could be further transformed to more complicated and diversified azaindoles. Thus, subjecting the Br-bearing azaindole **2-1a** or **2-1b** to Suzuki coupling condition with benzeneboronic acid gave their corresponding arylated azaindoles **2-1h** and **2-1i** in the respective 53 and 82 % isolated yield [10] (Scheme 2.2).

2.2.2 Isolation and Characterization of Zr/Si-Containing Organometallic Reactive Intermediates

In order to investigate the reaction mechanism in a pure and controllable system and get rid of LiCl generated in situ, we prepared and isolated the intermediate **2-3a** in 93 % yield. 3.5 Equivalents of *i*-PrCN were added to a toluene solution of **2-3a**. After the reaction mixture was stirred at 50 °C for 1 h, a red powder was isolated in 90 % yield, which was confirmed to be a very interesting and totally unexpected complex **2-4a** (Scheme 2.3). Single crystals of **2-4a** suitable for X-ray analysis were grown in benzene at room temperature. X-ray analysis of **2-4a** (Fig. 2.2) reveals its three-ring-fused structure composed of one 6-membered ring containing silicon and nitrogen, one 5-membered pyrrolo ring, and one 6-membered zirconacycle. The zirconium center is bonded with two Cp rings, one imine nitrogen atom, and one nitrogen atom of the pyrrolo ring. The silicon atom is bonded with one quaternary carbon atom, one imine nitrogen atom, and two methyl groups. Two imine carbon atoms neighboring the silicon and zirconium atoms in **2-4a** showed a singlet at δ = 183.9 and 188.2 ppm in the ^{13}C NMR spectrum in [D_6]benzene, respectively.



Scheme 2.3 Formation of zirconocene-containing intermediate **2-4a** from three molecules of nitrile and the hydrolysis reaction

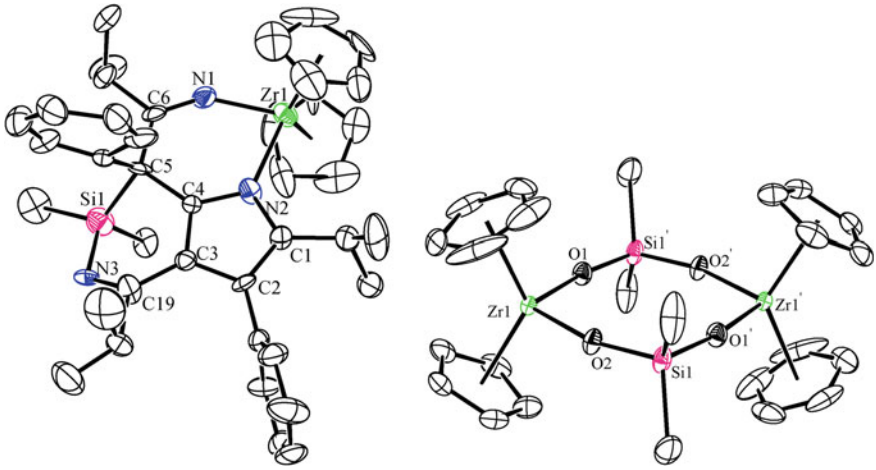
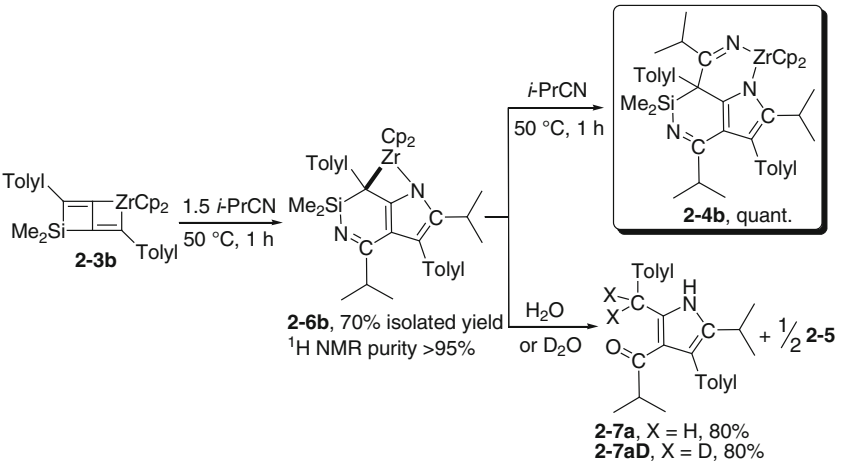


Fig. 2.2 ORTEP drawing of **2-4a** and **2-5** with 30 % thermal ellipsoids. Reproduced from Ref. [11] with the permission from Wiley

Hydrolysis of this isolated **2-4a** with a certain amount of H_2O afforded its corresponding 5-azaindole **2-2a** in a quantitative yield. In addition to **2-2a**, formation of NH_3 in the reaction solution was detected using in situ ^1H NMR spectra. Furthermore, the whereabouts of the Cp_2Zr moiety and the $SiMe_2$ moiety was determined by successful isolation of the cyclic zirconasiloxane **2-5**. This cyclic zirconasiloxane **2-5**, which was obtained in 45 % isolated yield, formed nice crystals suitable for X-ray structural analysis (Fig. 2.2).

With these results in hands, the author expected to understand more about the reaction mechanism. How is **2-4a** formed from the reaction of **2-3a** with *i*-PrCN? And what are the structures of reactive intermediates involving only one or two molecules

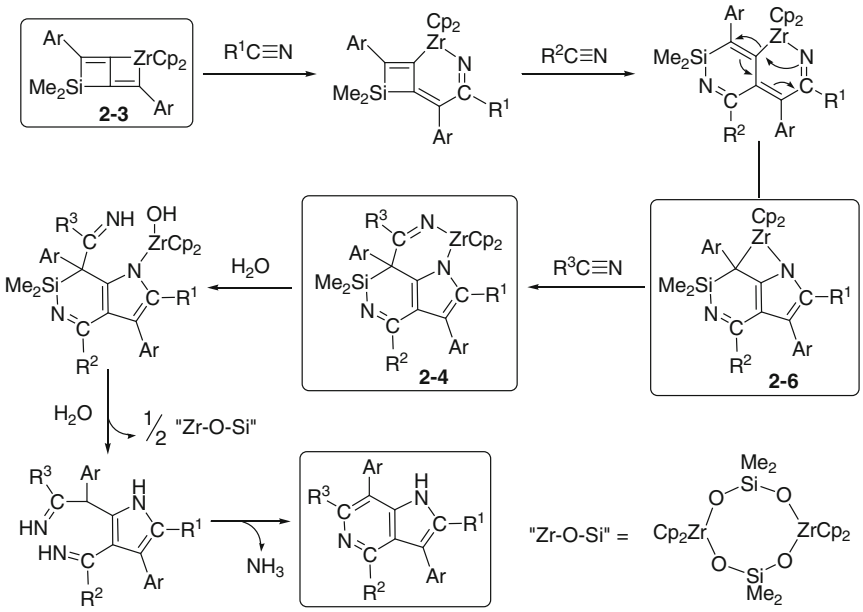


Scheme 2.4 Formation of zirconocene-containing intermediate **2-6b** from two molecules of nitrile and the hydrolysis reaction

of nitriles? The reaction of tolyl-substituted **2-3b** with 1.5 equivalents of *i*-PrCN in benzene at 50 °C for 1 h afforded a green solid **2-6b** in 70 % yield. Although single crystals of **2-6b** suitable for X-ray crystallographic analysis were not obtained, its ^{1}H and ^{13}C NMR data were rather informative for the elucidation of the structure. The imine carbon atoms in **2-6b** showed a singlet at $\delta = 181.5$, and the quaternary carbon atom linked by zirconium and silicon atoms gave a singlet at $\delta = 80.9$ ppm in the ^{13}C NMR spectrum in [D_6]benzene. Hydrolysis of **2-6b** with 1–3 equiv. of H_2O gave the compound **2-7** in 80 % yield after a short column chromatography. The cyclic zirconasiloxane **2-5** was also obtained in 45 % isolated yield (Scheme 2.4).

Based on all the above experimental results, we proposed a reaction mechanism for the formation of 5-azaindole (Scheme 2.5). Insertion of the C≡N triple bond of the first organonitrile (R^1CN) into one of the Zr–C bonds of **2-3** would afford the first intermediate, which might immediately undergo insertion of the C≡N triple bond of the second organonitrile (R^2CN) into one of the Si–C bonds. This intermediate is thermodynamically unstable and would undergo skeletal rearrangement through 1,2-shift of the Cp_2Zr moiety in the azazirconacyclic ring to afford the key intermediate **2-6**, which is stable enough at room temperature and could be characterized by ^{1}H NMR and ^{13}C NMR. The insertion chemistry of the C≡N triple bond of organonitriles into Zr–C bonds affording azazirconacycles and into Si–C bonds has been documented [12–14]. Insertion of the C≡N triple bond of the third organonitrile (R^3CN) to the Zr–C bond in **2-6** would lead to the formation of **2-4**.

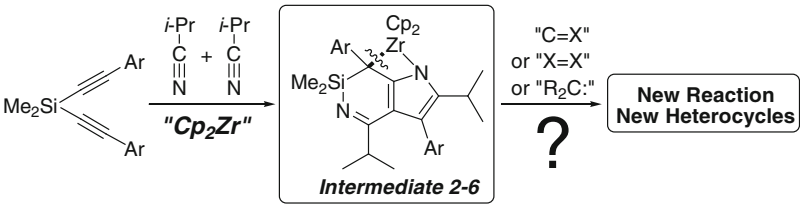
A proposed hydrolysis process of **2-4** leading to the formation of NH_3, 5-azaindole, and **2-5** is also shown in Scheme 2.5. Cleavage of the Zr–N (imine) bond in **2-4** by the first molecule of water and further hydrolysis with 2 molecules of water afforded the diimine. **2-5** was formed and eliminated through the coupling between the Me_2SiOH and Cp_2ZrOH moieties. The final product **2-2** was generated via the cyclization of the diimine, along with the loss of NH_3 [15].



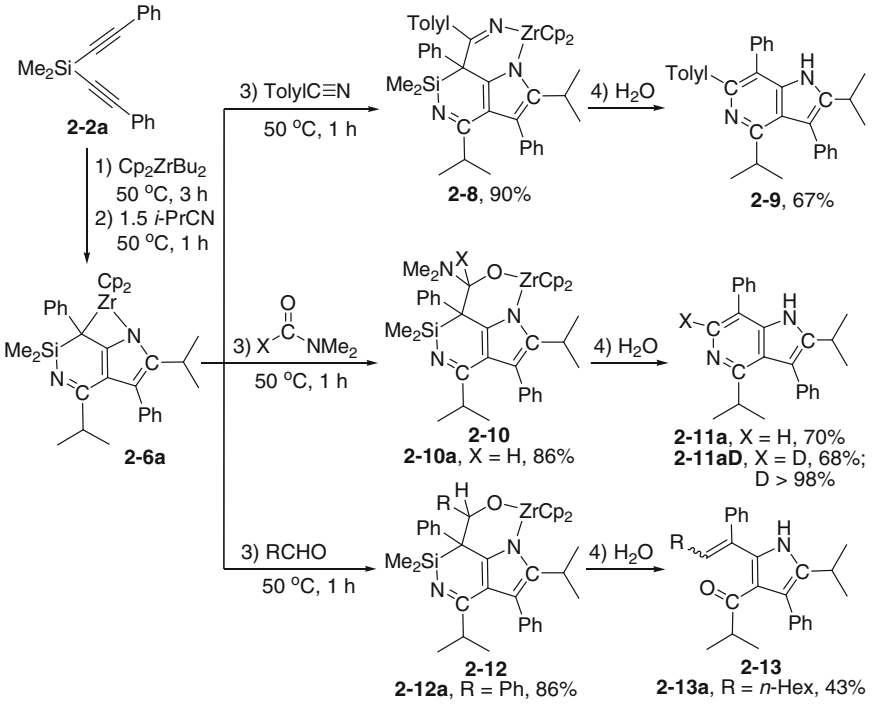
Scheme 2.5 Proposed reaction mechanism involving one bis(alkynyl)silane and three organonitriles

2.2.3 *Synthetic Application of Zr/Si-Containing Organometallic Reactive Intermediates*

The structural investigation of organometallic intermediates benefits the understanding of reaction mechanism and further reaction chemistry (Scheme 2.6). The reactive intermediate **2-6** features Zr–C(sp^3) bond, which was proved to be useful for further synthetic application. **2-6** could react with several unsaturated compounds or electrophiles such as isocyanide, formamide, acid chloride, and aldehyde, affording a series of *N*-heterocycles upon hydrolysis (Scheme 2.7).



Scheme 2.6 Reaction modes of intermediate **2-6**



Scheme 2.7 Reaction chemistry and synthetic application of **2-6**

Firstly, insertion of the third nitrile into reactive intermediate **2-6a** took place and afforded 5-azaindole with the same substituents on 2,4-positions and different substituent on 6-position. The azazirconacyclobutane-containing intermediate **2-6a** was isolated directly from reaction of **2-2a** with 1.5 equivalents of *i*-PrCN mediated by Cp_2ZrBu_2 in toluene solution (Scheme 2.7). Treatment of a benzene solution of **2-6a** with *p*-TolylCN at 50 °C for 1 h gave a deep brown solution, which was dried up under vacuum and then crystallized in THF/hexane mixed solvent to afford the complex **2-8** as brown crystals in 90 % isolated yield (Fig. 2.3). Single-crystal X-ray structural analysis of **2-8** clearly showed the three-ring-fused skeleton containing the Me_2Si and Cp_2Zr moieties. Hydrolysis of **2-8** gave 5-azaindole **2-9** quantitatively. 5-Azaindole **2-9** could also be obtained from one bis(alkynyl)silane, two molecules of *i*-PrCN, and one molecule of *p*-TolylCN in good isolated yields.

When a formamide Me_2NCHO was used instead of the third nitrile, 5-azaindole **2-11a** was obtained in 70 % isolated yield upon hydrolysis with saturated aq. $NaHCO_3$. When hydrolyzed with D_2O instead of saturated aq. $NaHCO_3$, again **2-11a** was obtained in a similar yield. The deuterium-labeled product **2-11aD** was not formed. When Me_2NCDO was used instead of Me_2NCHO, hydrolysis of the reaction mixture with aq. $NaHCO_3$ afforded the deuterated product **2-11aD** in 68 % isolated yield with D > 98 % (Scheme 2.7). These results indicate that the CH or CD moiety of the carbonyl groups (–CHO or –CDO) in formamides is incorporated

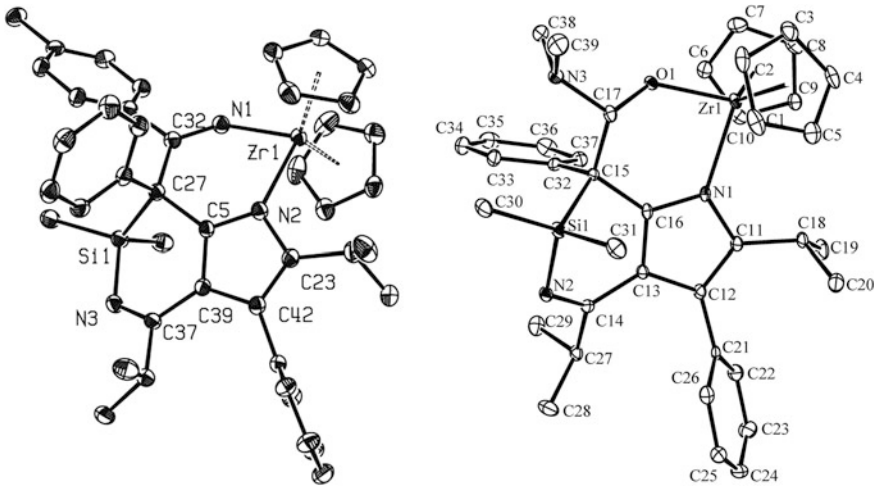


Fig. 2.3 X-ray structures of **2-8** and **2-10a.** Reproduced from Ref. [14] with the permission from Wiley

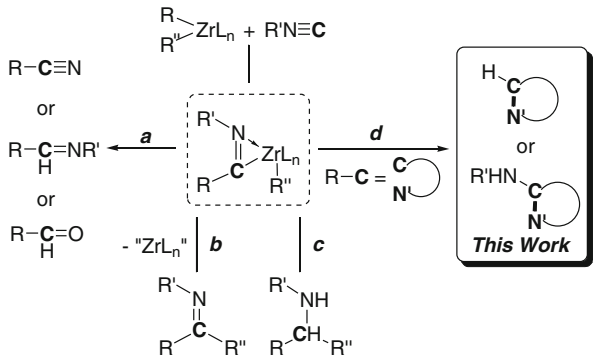
into the product. Other moieties in formamides were removed. Insertion of DMF into the Zr–C bond in **2-6a** has been demonstrated by isolation and characterization of the key intermediate **2-10a**, which is formed in 86 % isolated yield and characterized by X-ray single-crystal structural analysis (Fig. 2.3). Hydrolysis of **2-10a** with aq. $NaHCO_3$ gave azaindole **2-11a** in a quantitative yield.

When **2-6a** was treated with heptanal, formation of a new type of pyrrole derivative **2-13** was observed as a mixture of two isomers. When benzaldehyde was subjected to the reaction under the same condition, the reactive intermediate **2-12a** was isolated. Thus, the insertion of C=O bond of aldehyde into Zr–C bond in **2-6** is similar to the insertion reaction of DMF.

Besides, the reaction of **2-6a** with CO and alkynes (including diphenylacetylene, DMAD, and 4-octyne) did not show promising reactivity or no reaction occurred.

2.2.4 One-Pot Multi-component Coupling of Bis(alkynyl) silanes, Nitriles and Isocyanides and Synthesis of N*-Containing Heterocycles via Intramolecular Cyclization of Iminoacyl–Zr Intermediates*

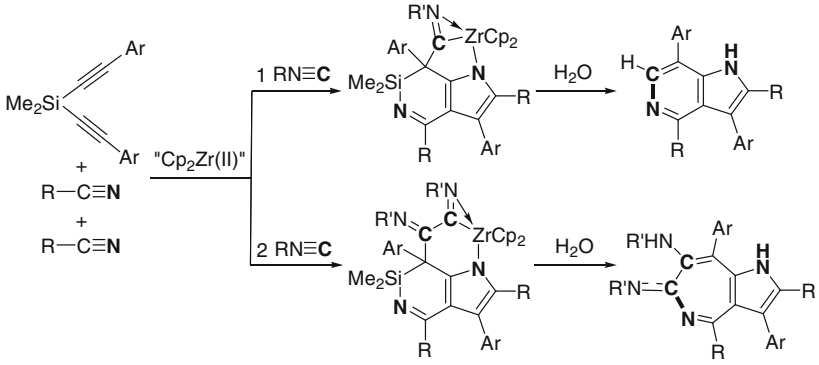
Isocyanide has been widely utilized as a key reagent in organic synthesis. Besides, the insertion of isocyanides into M–C bonds is one of the powerful means for carbon chain construction [16–34]. Insertion of isocyanide into M–C bonds afforded η^2-iminoacyl–metal intermediates, such as η^2-iminoacyl–Zr complexes [19–27], which can be conveniently converted to one-carbon elongated products such as imines, aldehydes, or nitriles via various chemical bond cleavage including Zr–C, C=N, and N–R′ bonds (Scheme 2.8) [29–32]. η^2-Iminoacyl–Zr complexes



Scheme 2.8 Reactivities of iminoacyl–Zr intermediates

also displayed other useful reactivities including reductive elimination [1, 2], -alkyl shift of non-acyl Zr–C bonds, and other types of rearrangements [28]. However, intramolecular cyclization of the iminoacyl–Zr intermediates yielding *N*-containing heterocycles has not been reported.

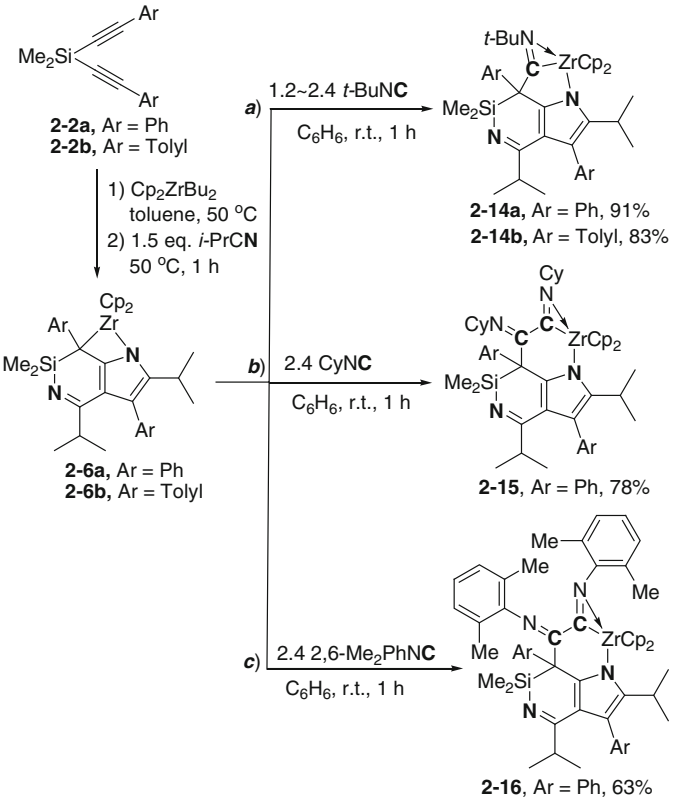
The author explored the reaction chemistry of intermediates **2-6** with isocyanides. Isocyanides bearing less-bulky and bulky substituents led to mono- and bis (iminoacyl)–Zr intermediates, respectively. Upon hydrolysis, the isolated mono (iminoacyl)–Zr intermediates underwent intramolecular cyclization to afford tetra-substituted 5-azaindoles, while intramolecular cyclization of bis(iminoacyl)–Zr intermediates led to the formation of dihydropyrrolo[3,2-*c*]azepines. Based on the above results, the author developed zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides. The structure of a bis(iminoacyl)–Zr intermediate, formed via insertion of two molecules of CyNC into the Zr–C bond, and structures of two dihydropyrrolo[3,2-*c*]azepines were characterized by single-crystal X-ray structural analysis (Scheme 2.9).



Scheme 2.9 One-pot synthesis of *N*-containing heterocycles by multi-component coupling of bis (alkynyl)silanes, nitriles, and isocyanides via intramolecular cyclization of iminoacyl–Zr intermediates

2.2.4.1 Isolation and Structural Characterization of Iminoacyl-Zr and Bis(iminoacyl)–Zr Intermediates via Mono- and Double Insertion of Isocyanides into Azazirconacycles

At room temperature, treatment of **2-6a** with 1.2 equivalents of aliphatic isocyanide *t*-BuNC led to the mono-insertion of isocyanide into the Zr–C(sp^3) σ bond giving **2-14a** in 91 % isolated yield (Scheme 2.10a). Even in the presence of excess amount of *t*-BuNC, only **2-14a** was obtained and the double-insertion product was not observed, probably due to the steric hindrance of *t*-Bu group. Similarly, the insertion of *t*-BuNC into tolyl-substituted **2-6b** gave **2-14b** under the same condition (Scheme 2.10b). However, when 2.4 equivalents of less steric-hindered isocyanide CyNC were used, the double-insertion product **2-15** was formed exclusively in 78 % isolated yield (Scheme 2.10b), showing that the steric hinderance of isocyanides strongly affects the insertion reaction. The double-insertion product **2-16** could also be obtained in good isolated yield when 2.4 equivalents of 2,6-dimethylphenyl isocyanide were used to react with **2-6a** (Scheme 2.10c). It should be noted that



Scheme 2.10 Formation of iminoacyl–Zr complexes by insertion of isocyanides into Zr–C(sp^3) bond

double insertion of isocyanides into Zr–C bonds is rare, and this work represents an efficient preparation of bis(iminoacyl)–Zr complexes [24–27].

These η^2-iminoacyl–Zr complexes **2-14**–**2-16** were all characterized by ^{1}H NMR and ^{13}C NMR spectra. The imine carbon atom neighboring the silicon in **2-14a** showed a singlet at δ = 186.88 ppm in the ^{13}C NMR spectrum in C_6D_6. In comparison, the characteristic carbon of η^2-iminoacyl–Zr moiety displayed a singlet at down-shielded δ = 234.17 ppm. The chemical shift of iminoacyl–Zr carbon in **2-14a** was comparable with that found in $Cp_2ZrCl(C(=N\mathit{t}Bu)C(Ph)=C(PPh_2)C{\equiv}CPh)$ (223.4 ppm) [19] and $Cp_2ZrCl(C(=N\mathit{t}Bu)CH_2SiMePhC(Ph)=CHPh)$ (228.77 ppm) [23]. The two imine carbons of bis(iminoacyl)–Zr moiety in **2-15** showed the respective singlet at δ = 164.95, 222.57 ppm in the ^{13}C NMR spectrum, which are consistent with those data in a reported bis(iminoacyl)–Zr complex [27]. Compared with mono(iminoacyl)–Zr carbon in **2-14a**, the iminoacyl carbon in **2-15** (222.57 ppm) appeared up-shielded in the ^{13}C NMR spectrum, probably due to the electron-withdrawing effect of the adjacent imino group. Similar to **2-15**, the two imine carbon atoms of bis(iminoacyl)–Zr moiety in **2-16** showed two singlets at δ = 180.93 and 237.10 ppm in the ^{13}C NMR spectra, respectively.

The structure of **2-15** was confirmed by single-crystal X-ray structural analysis, which featured four-ring-fused structure (Fig. 2.4). Zirconium center is bonded to a η^2-iminoacyl moiety in an "edge-on" fashion, forming a three-membered azazirconacycle [27]. The Zr1–N4 bond of 2.245(2) Å and the Zr–C18 bond of 2.175 (3) Å in Zr–C–N three-membered ring are close to the value of the reported bis(iminoacyl)–Zr complex [27]. The Zr1–N4 bond length of 2.245(2) Å is even shorter than the Zr1–N1 σ-bond of 2.347(2) Å, indicating a strong coordinative driving

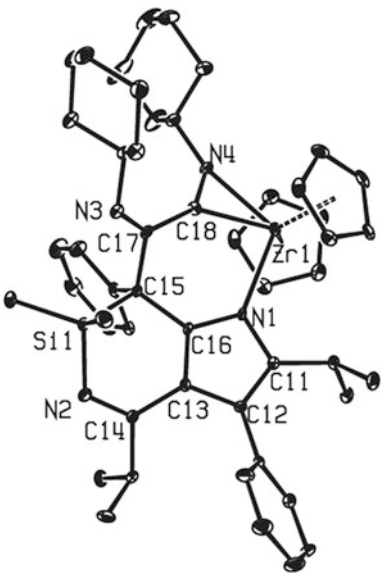


Fig. 2.4 ORTEP drawing of **2-15** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond length (Å): Zr1–N1 2.347(2), Zr1–N4 2.245(2), Zr1–C18 2.175(3), Si1–C15 1.924(3), Si1–N2 1.744(3), C13–C16 1.389(4), C15–C16 1.539(4), C15–C17 1.521(4), C17–C18 1.470(4), C17–N3 1.276(4), C18–N4 1.254(3). Reproduced from Ref. [35] with the permission from Wiley

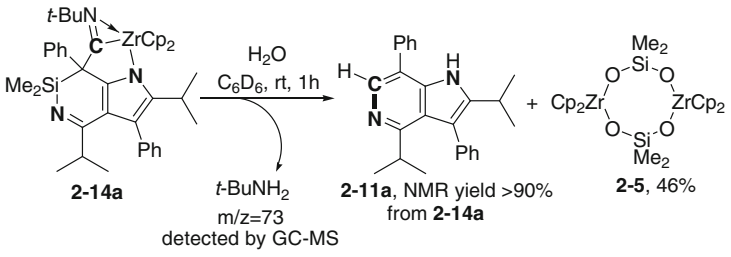
effect between Zr1 and N4 atoms. The bond length of two imine bonds C17–N3 and C18–N4 is 1.276(4) and 1.254(3) Å, respectively, demonstrating a strong C=N double-bond behavior.

2.2.4.2 Intramolecular Cyclization of η^2-Iminoacyl–Zr Complexes to Form Tetra-substituted 5-Azaindoles or Dihydropyrrolo[3,2-*c*]azepine Derivatives

Hydrolysis of the mono-insertion product **2-14a** with H_2O afforded a tetra-substituted 5-azaindole derivative **2-11a** in >90 % NMR yield, showing that the η^2-iminoacyl–Zr moiety cyclized with the *N*-silyl imine moiety by an unexpected C–N bond-forming fashion (Scheme 2.11). Along with **2-11a**, formation of *t*-$BuNH_2$ after quenching with water was detected using GC–MS. In addition, the Cp_2Zr moiety and the $SiMe_2$ moiety were coupled to form the cyclic zirconasiloxane **2-5**.

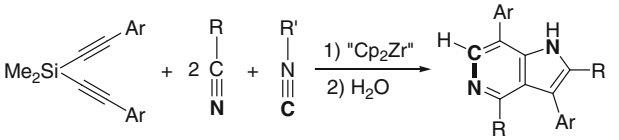
5-Azaindoles could be prepared conveniently in one pot via zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides as shown in Table 2.2. When bis(alkynyl)silane **2-2a**, *i*-PrCN, and *t*-BuNC were used, tetra-substituted 5-azaindole **2-11a** was formed in 63 % isolated yield, with only the isocyanide carbon atom being integrated into the product. The newly formed carbon–hydrogen bond was found to be originated from the hydrolysis process. Changing the isocyanide from *t*-BuNC to both aliphatic CyNC and aromatic 2,6-dimethylphenyl isocyanide led to the same 5-azaindole **2-11a** as main product in 65 and 54 % yields, respectively. In addition to *i*-PrCN, the scope of nitriles could be expanded to 2-methylbutyronitrile, CyCN and 1-phenyl cyclopropanecarbonitrile, affording their corresponding tetra-substituted 5-azaindoles **2-11b, 2-11c**, **2-11e**–**2-11f** in moderate to good isolated yields.

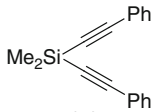
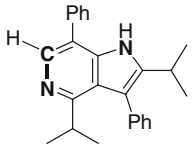
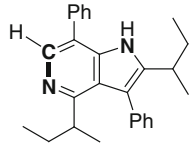
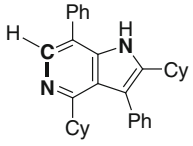
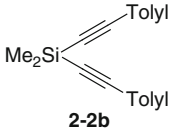
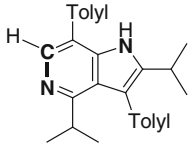
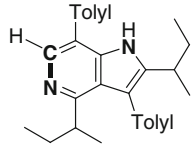
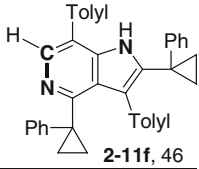
When the double-insertion intermediate **2-16** was hydrolyzed with water, two dihydropyrrolo[3,2-*c*]azepine derivatives **2-18a** and **2-19a** were obtained in 46 and 24 % yields, respectively (Scheme 2.12). Single-crystal X-ray structural analysis of **2-18a** and **2-19a** demonstrated their pyrrole-fused seven-membered azacycle (Fig. 2.5) [36]. The bond length of C6–N4 in **2-18a** is 1.277(7) Å, while the bond length of C47–N7 in **2-19a** is 1.481(3) Å. In their ^{13}C NMR spectra, the imine C6



Scheme 2.11 Hydrolysis of the iminoacyl–Zr intermediates **2-14a**

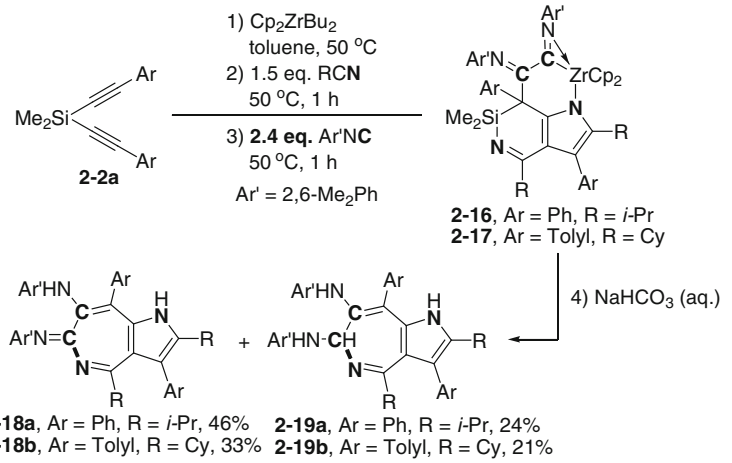
Table 2.2 Formation of 5-azaindoles **2-11** via zirconocene-mediated multi-component coupling of bis(alkynyl)silanes, nitriles, and isocyanides



entry	bis(alkynyl)silane **2-2**	RC**N**	R'N**C**	product **2-11** (yield/%) [a]
1	 **2-2a**	*i*-Pr—C**N**	*t*-BuN**C**	 **2-11a**, 63
2	**2-2a**	*i*-Pr—C**N**	CyN**C**	**2-11a**, 65 [b]
3	**2-2a**	*i*-Pr—C**N**	2,6-Me_2PhN**C**	**2-11a**, 54
4	**2-2a**		CyN**C**	 **2-11b,** 55
5	**2-2a**	Cy—C**N**	*t*-BuN**C**	 **2-11c**, 66
6	 **2-2b**	*i*-Pr—C**N**	*t*-BuN**C**	 **2-11d**, 41
7	**2-2b**		*t*-BuN**C**	 **2-11e**, 53
8	**2-2b**		*t*-BuN**C**	 **2-11f**, 46

[a] Isolated yields

[b] Main product yield, with trace amount of other products



Scheme 2.12 Intramolecular cyclization of bis(iminoacyl)–Zr complexes to form dihydropyrrolo [3,2-*c*]azepines

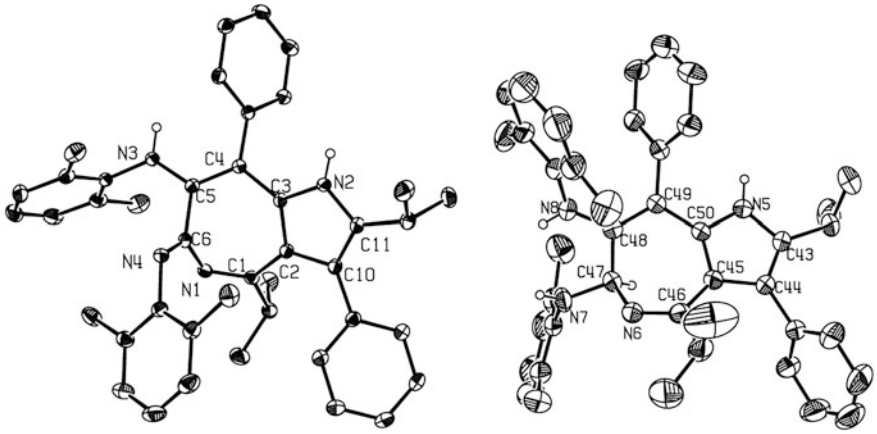


Fig. 2.5 ORTEP drawing of **2-18a** and **2-19a** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reproduced from Ref. [35] with the permission from Wiley

atom in **2-18a** shows a singlet at δ = 167.18 ppm, while the C47 atom in **2-19a** appears at 79.79 ppm. Dihydropyrrolo[3,2-*c*]azepine derivatives **2-18b** and **2-19b** could also be obtained. The hydrolysis mechanism from the bis(iminoacyl)–Zr intermediates to dihydropyrrolo[3,2-*c*]azepine derivatives **2-18** and **2-19** is not clear yet [37–39].

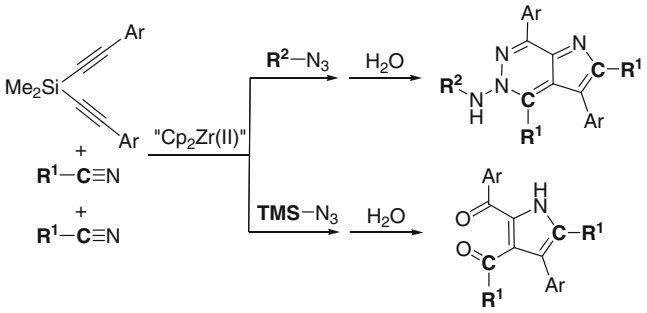
2.2.5 One-Pot Synthesis of Pyrrolo[3,2-d]pyridazines and Pyrrole-2,3-Diones via Zirconocene-Mediated Four-Component Coupling of Bis(alkynyl)silane, Nitriles, and Azide

Pyrrolo[3,2-*d*]pyridazines are a class of interesting and useful *N*-heterocycles [40–42]. However, synthetic methods for such heterocyclic compounds have been very much limited such as condensation of pyrrole-2,3-diones with hydrazine. There are no reports on one-pot multi-component synthesis of pyrrolo[3,2-*d*]pyridazines [43]. Moreover, synthetic methods for pyrrole-2,3-diones are also very limited [43]. On the other hand, transition-metal-mediated reactions of azides are of great importance and versatility in organic synthesis, because azides could be readily transformed into a wide variety of valuable *N*-containing natural products and medicinal agents [44–50].

Based on the mechanistic investigation and chemistry of reactive intermediates in zirconocene-mediated reactions, the author subjected organic azide to the reaction and developed a one-pot synthesis of pyrrolo[3,2-*d*]pyridazine derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide. When $TMSN_3$ was used as a special azide, pyrrole-2,3-diones were isolated in high yields. These functionalized pyrrole-2,3-diones could be efficiently further transformed into pyrrole-fused heterocycles (Scheme 2.13).

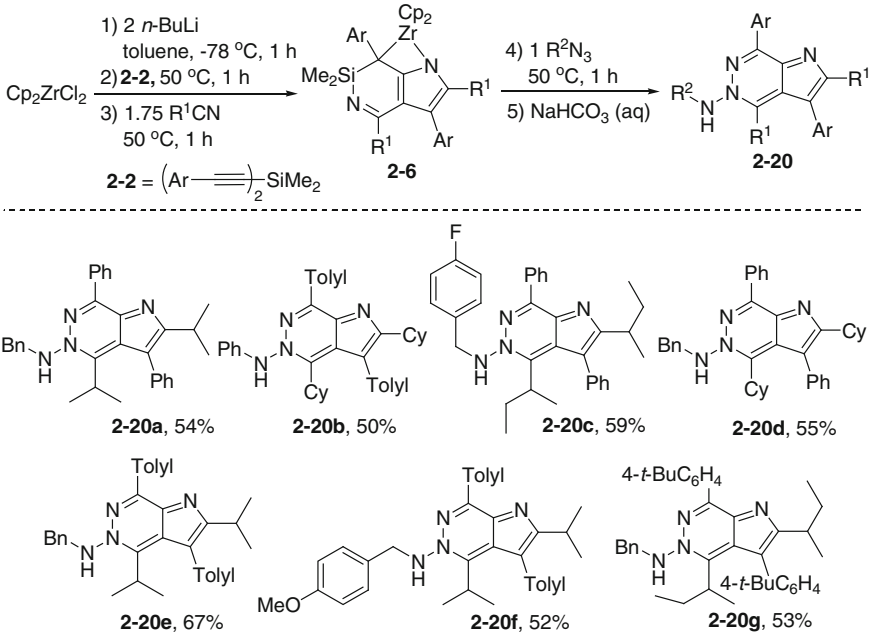
2.2.5.1 One-Pot Synthesis of Pyrrolo[3,2-*d*]pyridazine Derivatives via Zirconocene-Mediated Cyclization of One Bis(alkynyl) silane, Two Nitriles, and One Azide

As introduced in the previous section, reactive organometallic intermediates **2-6** were synthesized in situ in high yields via multi-component coupling of Cp_2ZrBu_2, bis(alkynyl)silane, and nitriles. Reaction of benzyl azide BnN_3 with **2-6a** (Ar = Ph,



Scheme 2.13 One-pot synthesis of pyrrolo[3,2-*d*]pyridazine or pyrrole-2,3-dione derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide

Table 2.3 One-pot synthesis of pyrrolo[3,2-*d*]pyridazine derivatives via zirconocene-mediated cyclization of one bis(alkynyl)silane, two nitriles, and one azide



R^1 = *i*-Pr) at 50 °C for 1 h followed by quenching with saturated aqueous $NaHCO_3$ afforded a yellow solid **2-20a** in 54 % isolated yield (Table 2.3). The structure of product **2-20a** was confirmed by X-ray single-crystal structure analysis as a pyrrolo [3,2-*d*]pyridazine derivative (Fig. 2.6). Various aryl or benzyl azides with both electron-withdrawing groups (F) and electron-donating groups (MeO) could be applied to afford pyrrolo[3,2-*d*]pyridazine derivatives **2-20** in good isolated yields.

A proposed mechanism is shown in Scheme 2.14 for reaction of azides with reactive organometallic intermediate **2-6** and hydrolysis process affording the pyrrolo[3,2-*d*]pyridazine derivative. 1,1-Insertion of an azide into the C–Zr bond of **2-6** and delocalization leads to the formation of triazenido-ligated zirconium intermediate **2-21**. According to the literature, a 1,3-insertion of an azide into the C–Zr bond of **2-6** may be also possible to generate the intermediate **2-21** [52–54]. Although it is not clear that which one is formed in this reaction, only one insertion organometallic intermediate was obtained in 87 % isolated yield and was characterized by NMR spectroscopy. Hydrolysis of the insertion product, either **2-21a** or **2-21a′**, affords pyrrole derivatives **2-22** or **2-22′**. These intermediates **2-22** or **2-22′** would undergo cyclization of the triazene moiety with the imine C=N bond to afford **2-23** [55, 56]. Dehydration and aromatization of **2-23** led to the final product **2-20**.

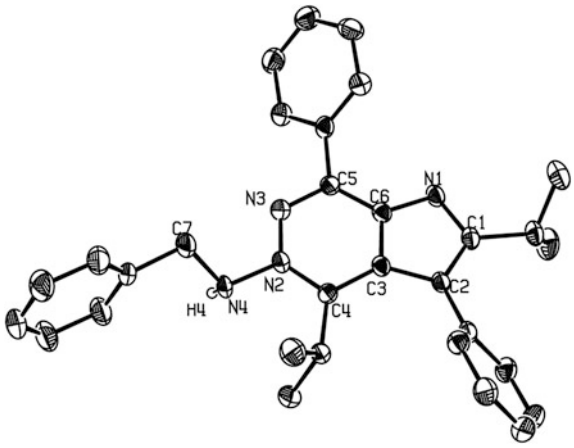
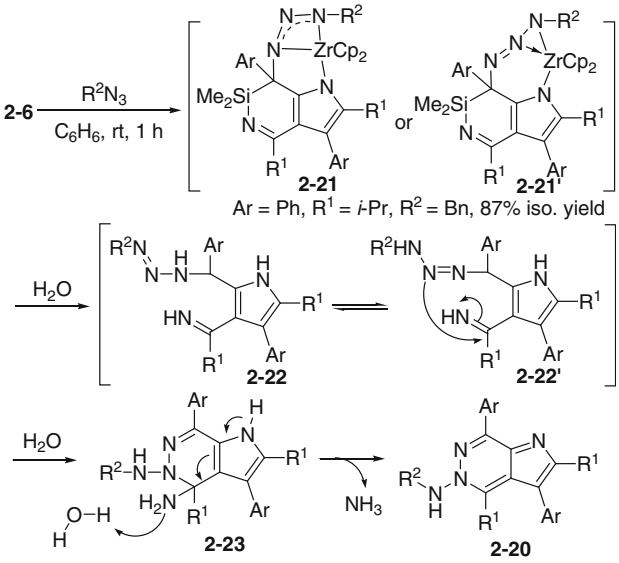


Fig. 2.6 Single-crystal X-ray structure of **2-20a**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Selected bond length (Å): N1–C1 1.390(2), N1–C6 1.363(2), N2–N3 1.350(2), N2–C4 1.372(2), N3–C5 1.327(2), N4–N2 1.438(2). Reprinted with the permission from Ref. [51]. Copyright 2011 American Chemical Society

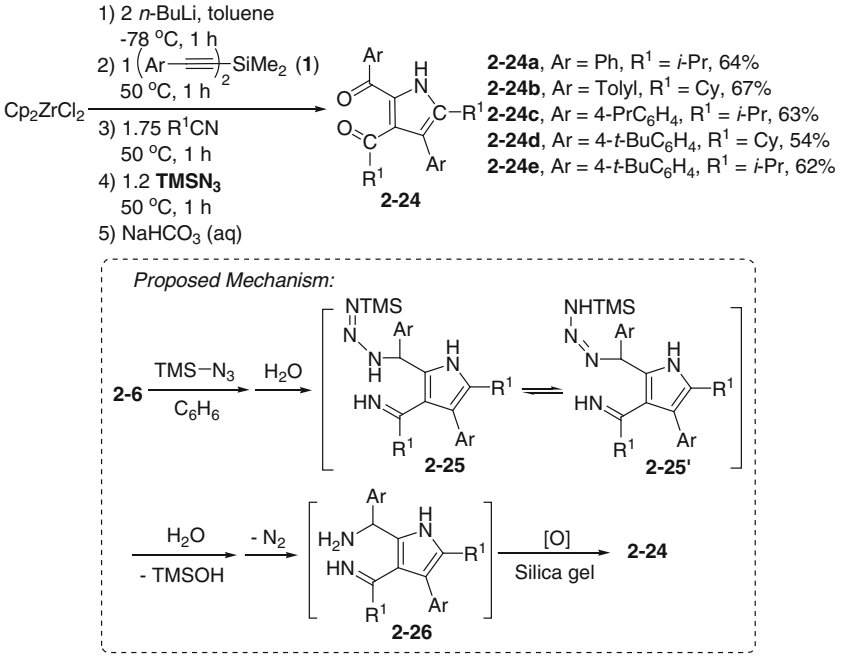


Scheme 2.14 Proposed mechanisms

2.2.5.2 One-Pot Synthesis of Pyrrole-2,3-Dione Derivatives via Zirconocene-Mediated Cyclization of One Bis(alkynyl) silane, Two Nitriles, and One $TMSN_3$

When $TMSN_3$ was used as an azide in this zirconocene-mediated reaction, pyrrolo [3,2-*d*]pyridazine derivative **2-20** was not isolated as product. Instead, pyrrole-2,3-diones **2-24** were formed in good isolated yields (Scheme 2.15). The structure of product **2-24a** was confirmed by single-crystal X-ray structural analysis (Fig. 2.7). Bis(alkynyl)silanes with functional groups as well as bulky nitriles such as *t*-BuCN could not lead to products **2-24** because their corresponding intermediates **2-6** could not be formed efficiently.

On mechanistic aspects, it is proposed that after insertion of $TMSN_3$ into the C–Zr bond, hydrolytic cleavage of N–Si and N–Zr bonds would give triazene **2-25** or **2-25′**. Hydrolysis of N-$SiMe_3$ bond followed by the elimination of dinitrogen would afford the imine **2-26**, which might be oxidized and hydrolyzed on the silica gel during column chromatography to give the final product pyrrole-2,3-dione **2-24** [57]. Although plenty of synthetic methods for pyrrole derivatives have been developed [58], synthetic methods for pyrrole-2,3-diones, which are highly functionalized pyrroles, are very rare.



Scheme 2.15 One-pot synthesis of pyrrole-2,3-diones **2-24** via zirconocene-mediated cyclization of bis(alkynyl)silane, nitriles, and $TMSN_3$

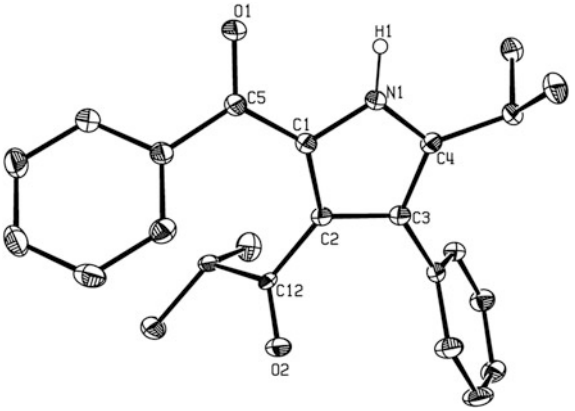
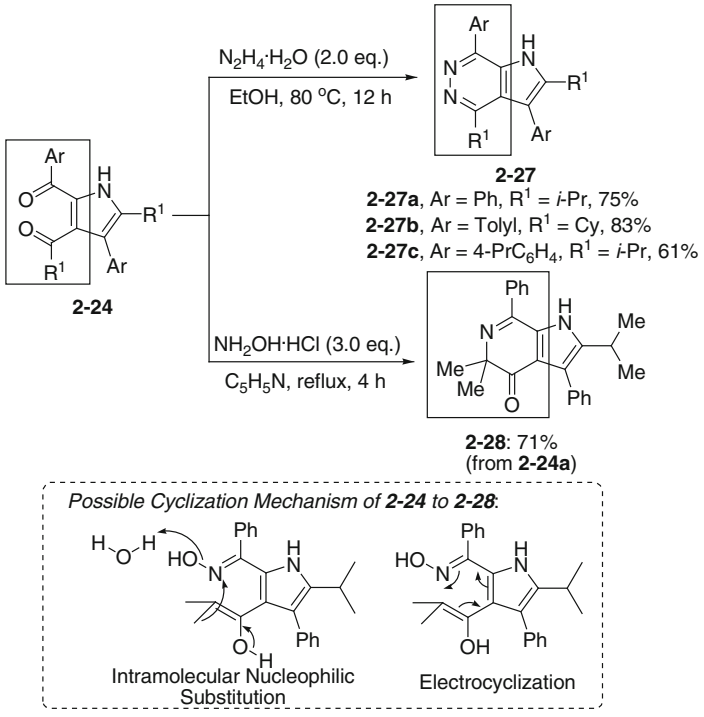


Fig. 2.7 Single-crystal X-ray structure of **2-24a**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reprinted with the permission from Ref. [51] Copyright 2011 American Chemical Society

Condensation of **2-24** with hydrazine hydrate and hydroxylamine hydrochloride was carried out. The pyrrole-fused heterocycles pyrrolo[3,2-*d*]pyridazine **2-27** and pyrrolo[2,3-*c*]pyridinone **2-28** were generated in high isolated yields, respectively (Scheme 2.16). These further applications of **2-24** demonstrate that the two carbonyl groups on the pyrrole ring of **2-24** are useful for the preparation of other valuable pyrrole-fused *N*-heterocyclic compounds [59, 60].



Scheme 2.16 Preparation of pyrrole-fused *N*-heterocyclic compounds via annulation of pyrrole-2,3-diones **2-24**

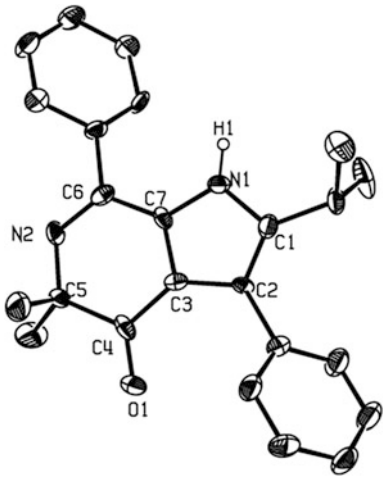


Fig. 2.8 Single-crystal X-ray structure of **2-28**. Hydrogen atoms are omitted for clarity except polar N–H bonds. Reprinted with the permission from Ref. [51]. Copyright 2011 American Chemical Society

Condensation of **2-24** with hydrazine hydrate in ethanol at 80 °C gave pyrrolo[3,2-*d*]pyridazines **2-27** as products. However, condensation of **2-24a** with hydroxylamine hydrochloride in refluxing pyridine led to the pyrrolo[2,3-*c*]pyridinone **2-28** as the single product, which was confirmed by single-crystal X-ray structural analysis (Fig. 2.8). The C_{sp3}–H bond of *i*-Pr was coupled with the in situ generated oxime moiety to form the pyridinone ring via intramolecular nucleophilic substitution or 6π-electrocyclization.

2.3 Summary

The author developed zirconocene-mediated one-pot multi-component synthesis of 5-azaindole derivatives from bis(alkynyl)silane and three molecules of nitriles. Isolation and characterization of Zr/Si-containing three-ring-fused organometallic complexes **2-4a** and **2-6** were achieved as three or two nitriles involved reactive intermediates, respectively. The 8-membered cyclic zirconasiloxane was characterized as fate of Cp_2Zr and Me_2Si in hydrolysis process. Ammonia was observed by NMR spectrum, showing that the nitrile C≡N bond was cleaved in hydrolysis process. Based on the reaction chemistry of reactive intermediates **2-6** with unsaturated compounds such as formamides, aldehydes, isocyanides, and azides, various *N*-heterocycles were synthesized, including 5-azaindoles, 3-acylpyrrole, dihydropyrrolo[3,2-*c*]azepines, pyrrolo[3,2-*d*]pyridazine, and pyrrolo[2,3-*c*]pyridinone derivatives.

2.4 Experimental Section

All reactions were conducted under a slightly positive pressure of dry nitrogen using standard Schlenk line techniques or under a nitrogen atmosphere in a Mikrouna Super (1220/750) glove box. The nitrogen in the glove box was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glove box atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure that both were always below 1 ppm. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Solvents were purified by an Mbraun SPS-800 Solvent Purification System and dried over fresh Na chips in the glove box.

Organometallic samples for NMR spectroscopic measurements were prepared in the glove box by use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer (FT, 400 MHz for ^{1}H; 100 MHz for ^{13}C) or a JEOL-AL300 spectrometer (FT, 300 MHz for ^{1}H; 75 MHz for ^{13}C) at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Microelemental analyses were performed on an Elemental Analyzer Vario EL apparatus.

Formation of 5-azaindoles Derivatives 2-1 from One Molecule of the Bis(alkynyl)silane with Three Molecules of Identical Organonitriles: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(alkynyl)silane (**2-2**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 3 h. After benzonitrile (3.5 mmol, 361 mg) was added, the reaction mixture was stirred at this temperature for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and the resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using hexane and diethyl ether (10:1) as the eluent.

2-1a: White solid, isolated yield 58 % (404 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.86–7.72 (m, 22H), 8.42 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.78, 118.34, 121.33, 121.56, 121.94, 122.62, 126.94, 127.33, 128.04, 128.10, 128.26, 128.63, 129.04, 129.51, 130.03, 130.07, 130.10, 130.44, 130.53, 130.96, 131.13, 132.74, 133.34, 133.56, 133.66, 134.83, 135.14, 140.96, 141.05, 142.34, 146.73, 151.42. HRMS calcd for $C_{37}H_{23}Br_3N_2$ 733.9391; found: 733.9388. Elemental Analysis Calcd (%) for $C_{37}H_{23}Br_3N_2$: C, 60.44; H, 3.15; N, 3.81. Found: C, 60.40; H, 3.35; N, 3.51.

2-1b: White solid, isolated yield 61 % (448 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.86–7.48 (m, 22H), 8.38 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.35, 117.88, 121.53, 121.80, 122.47, 126.62, 128.01, 128.16, 129.04,

129.54, 129.89, 130.02, 130.09, 130.57, 130.78, 130.85, 131.02, 131.87, 132.05, 133.98, 135.14, 135.46, 138.11, 139.27, 141.07, 146.99, 151.73. HRMS calcd for $C_{37}H_{23}Br_3N_2$ 733.9391; found: 733.9385. Elemental Analysis Calcd (%) for $C_{37}H_{23}Br_3N_2$: C, 60.44; H, 3.15; N, 3.81. Found: 60.24; H, 3.33; N, 3.67.

2-1c: White solid, isolated yield 60 % (393 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.74 (*d*, *J* = 7.8 Hz, 2H), 7.04–7.55 (m, 21H), 8.36 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 114.73, 116.37, 120.29, 121.27, 121.95, 127.13, 127.45, 127.80, 128.33, 128.49, 128.77, 129.53, 130.46, 130.71, 131.45, 131.80, 132.33, 132.49, 133.43, 134.96, 136.22, 139.23, 140.16, 148.69, 153.04. HRMS calcd for $C_{37}H_{24}N_2Br_2$ 656.0286; found: 656.0281.

2-1d: White solid, isolated yield 48 % (358 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.56 (*d*, *J* = 7.8 Hz, 2H), 6.73–6.82 (m, 6H), 7.11–7.25 (m, 6H), 7.28 (*d*, *J* = 8.4 Hz, 2H), 7.37 (*d*, *J* = 8.1 Hz, 2H), 7.55 (*d*, *J* = 7.5 Hz, 2H), 8.29 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 115.38, 117.11, 121.50, 122.24, 122.92, 124.85, 124.90, 124.95, 125.00, 126.46, 126.51, 126.56, 126.60, 127.61, 127.84, 128.97, 129.28, 130.37, 130.55, 130.61, 130.77, 130.91, 131.13, 131.79, 132.85, 132.92, 133.37, 135.68, 137.39, 139.09, 140.64, 140.68, 141.69, 147.35, 151.84. HRMS calcd for $C_{40}H_{30}Br_2N_2O_3$ 746.0603; found: 746.0597. Elemental Analysis Calcd (%) for $C_{40}H_{30}Br_2N_2O_3$: C, 64.36; H, 4.05; N, 3.75. Found: C, 64.53; H, 3.99; N, 3.60.

2-1e: White solid, isolated yield 42 % (365 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.91–7.77 (m, 20H), 8.46 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 115.38, 117.11, 121.50, 122.24, 122.92, 124.95, 125.00, 126.46, 126.51, 126.56, 126.60, 127.61, 127.85, 128.97, 129.28, 130.37, 130.55, 130.61, 130.77, 130.90, 131.13, 131.79, 132.85, 132.92, 133.37, 135.68, 137.39, 139.09, 140.64, 140.68, 141.69, 147.35, 151.84. HRMS calcd for $C_{39}H_{21}N_2F_6Br_2$ 869.9139; found: 869.9146. Elemental Analysis Calcd (%) for $C_{39}H_{21}N_2F_6Br_2$: C, 53.76; H, 2.43; N, 3.22. Found: C, 53.60; H, 2.68; N, 3.00.

2-1f: White solid, isolated yield 32 % (230 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 3.69 (s, 3H), 3.77 (s, 3H), 3.78 (s, 3H), 6.52 (*d*, *J* = 8.4 Hz, 2H), 6.75 (*d*, *J* = 8.7 Hz, 2H), 6.82 (*d*, *J* = 8.7 Hz, 2H), 7.00 (*d*, *J* = 8.1 Hz, 2H), 7.15 (*d*, *J* = 7.2 Hz, 4H), 7.26 (*d*, *J* = 8.4 Hz, 2H), 7.36 (*d*, *J* = 8.7 Hz, 2H), 7.55 (*d*, *J* = 8.4 Hz, 2H), 7.70 (*d*, *J* = 8.4 Hz, 2H), 8.30 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 55.10, 55.22, 55.32, 112.61, 113.34, 113.83, 114.34, 115.41, 120.98, 123.61, 124.37, 124.39, 124.44, 124.49, 126.20, 126.22, 126.30, 126.34, 129.91, 130.63, 130.71, 131.15, 131.72, 131.87, 132.61, 136.42, 138.86, 140.48, 148.02, 152.60, 158.99, 159.48, 159.80. HRMS calcd for $C_{42}H_{30}F_6N_2O_3$ 724.2161; found: 724.2166. Elemental Analysis Calcd (%) for $C_{42}H_{30}F_6N_2O_3$: C, 69.61; H, 4.17; N, 3.87. Found: C, 69.31; H, 4.36; N, 3.67.

2-1g: White solid, isolated yield 45 % (270 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 2.05 (s, 3H), 2.26 (s, 3H), 2.28 (s, 3H), 6.53–7.44 (m, 20H), 8.35 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 21.05, 21.43, 21.51, 55.26, 55.30,

113.11, 114.62, 115.59, 117.14, 121.42, 125.79, 126.71, 127.09, 127.26, 127.56, 127.66, 127.86, 128.24, 128.41, 128.64, 128.79, 130.97, 131.28, 131.74, 132.10, 133.42, 135.76, 136.33, 137.16, 138.24, 139.29, 140.55, 141.07, 148.00, 152.69, 158.00, 159.01. HRMS calcd for $C_{42}H_{36}N_2O_2$ 600.2777; found: 600.2768.

Formation of 5-Azaindoles 2-1h and 2-1i via Suzuki Coupling of 1n and 1o and Benzeneboronic Acid: To a mixture of **2-1b** (368 mg, 0.5 mmol) and benzeneboronic acid (244 mg, 2.0 mmol) in THF (5 mL) was added a solution of potassium carbonate (690 mg, 5.0 mmol) in water (2.5 mL). After the mixture was degassed and backfilled with nitrogen, $Pd(PPh_3)_4$ (29 mg, 0.025 mmol) was added, and then, the reaction mixture was refluxed for 16 h. The mixture was extracted with dichloromethane and washed with brine (100 mL × 3). The organic extracts were dried with anhydrous $MgSO_4$. After the removal of the solvent, the residue was purified by column chromatography (silica gel, hexane, and ethyl acetate (10:1) as eluent) to afford **2-1i** as a white solid.

2-1h: White solid, isolated yield 53 % (385 mg), m.p. > 300 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.70–7.91 (m, 37H), 8.51 (s, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.23, 117.61, 121.70, 125.77, 125.81, 126.11, 126.37, 126.92, 127.00, 127.04, 127.09, 127.12, 127.22, 127.61, 127.77, 127.84, 128.64, 128.67, 128.74, 128.85, 129.38, 129.91, 130.22, 130.79, 130.92, 131.00, 134.66, 135.63, 136.13, 138.50, 139.50, 139.61, 139.92, 140.14, 140.65, 140.97, 141.11, 141.46, 147.61, 152.55. HRMS calcd for $C_{55}H_{38}N_2$: 726.3035; found: 726.3096.

2-1i: White solid, isolated yield 82 % (300 mg). m.p. > 300 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 6.95–7.66 (m, 37H), 8.51 (s, 1H). ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 116.31, 117.79, 121.43, 125.74, 126.05, 126.30, 126.68, 126.80, 126.91, 126.94, 126.98, 127.12, 127.21, 127.47, 127.67, 127.80, 128.23, 128.27, 128.46, 128.51,128.69, 129.02, 129.43, 129.52, 129.62, 130.27, 130.83, 132.28, 134.48, 136.15, 136.25, 139.87, 140.02, 140.16, 140.29, 140.77, 141.06, 141.13, 141.34, 141.35, 147.88, 152.81. HRMS calcd for $C_{55}H_{38}N_2$: 726.3035; found: 726.3022. Elemental Analysis Calcd (%) for $C_{55}H_{38}N_2$: C, 90.88; H, 5.27; N, 3.85. Found: C, 90.72; H, 5.30; N, 4.08.

Isolation of 2-4a: In a 20-mL Schlenk tube, the *i*-PrCN (159 μL, 1.743 mmol) was added to the benzene solution of compound **2-3a** (240 mg, 0.498 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the clear filtrate was reduced under vacuum to precipitate **2-4a** as red powder (309 mg, 0.448 mmol, 90 % yield).

2-4a: Red solid, isolated yield 90 % (309 mg, 0.448 mmol). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.28 (s, 3H, $SiMe_2$), 0.52 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 0.65 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 0.93 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.03 (s, 3H, $SiMe_2$), 1.11 (*t*, *J* = 6.4 Hz, 6H, $CHMe_2$), 1.47 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 2.03–2.10 (m, 1H, $CHMe_2$), 2.34–2.40 (m, 1H, $CHMe_2$), 2.72–2.78 (m, 1H, $CHMe_2$), 5.86 (s, 5H,

C_5H_4), 6.07 (s, 5H, C_5H_4), 6.95 (*t*, *J* = 7.2 Hz, 1H, C_6H_5), 7.06–7.19 (m, 6H, C_6H_5), 7.39 (*d*, *J* = 8.0 Hz, 2H, C_6H_5), 7.49 (*d*, *J* = 8.0 Hz, 1H, C_6H_5); ^{13}C NMR (100 MHz, C_6D_6): $\delta = -2.9$, 3.0, 19.3, 21.4, 21.9, 22.4, 22.5, 26.7, 35.6, 35.9, 36.3, 60.6, 111.3, 111.4, 120.6, 125.8, 126.2, 127.4, 127.6, 127.7, 129.3, 129.9, 131.4, 132.5, 140.9, 141.3, 142.6, 143.4, 183.9, 188.2. Anal. Calcd for $C_{40}H_{47}N_3SiZr$: C, 69.72; H, 6.87; N, 6.10. Found: C, 69.95; H, 6.60; N, 6.30. Single crystals of **2-4a** suitable for X-ray analysis were grown in benzene at room temperature for one week.

Isolation of 2-5: A J. Young valve NMR tube was charged with **2-4a** (69 mg, 0.1 mmol) and $CDCl_3$ (0.5 mL). 1–3 equivalents of H_2O were added to the $CDCl_3$ solution of **2-4a** with a syringe at room temperature, and then, the NMR tube was shaken immediately and stayed at room temperature. Single crystals of **2-5** suitable for X-ray analysis were grown after staying for one day. **2-5** was obtained in 45 % yield, which was insoluble in common organic solvents. Anal. Calcd for $C_{24}H_{32}O_4Si_2Zr_2$: C, 46.26; H, 5.18. Found: C, 46.20; H, 5.50.

Isolation of 2-6b: In a 20-mL Schlenk tube, the *i*-PrCN (70 μL, 0.765 mmol) was added to the benzene solution of compound **2-3b** (260 mg, 0.51 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the clear filtrate was reduced under vacuum to precipitate **2-6b** as green powder, which was recrystallized at −40 °C to give **2-6b** in 70 % isolated yield. The purity of **2-6b** is >95 % determined by ^{1}H NMR spectroscopy.

2-6b: Green powder, isolated yield 70 % (210 mg) ^{1}H NMR (400 MHz, C_6D_6): $\delta = 0.22$ (s, 3H, $SiMe_2$), 0.76 (s, 3H, $SiMe_2$), 0.77 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.15 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.24 (dd, *J* = 7.2, 6.4 Hz, 6H, $CHMe_2$), 2.16 (s, 3H, 4-MeC_6H_4), 2.21 (s, 3H, 4-MeC_6H_4), 2.69–2.79 (m, 1H, $CHMe_2$), 3.05–3.16 (m, 1H, $CHMe_2$), 5.67 (s, 5H, C_5H_4), 5.74 (s, 5H, C_5H_4), 6.94–7.14 (m, 6H, 4-MeC_6H_4), 7.34 (*d*, *J* = 7.6 Hz, 2H, 4-MeC_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = 4.3, 6.3, 21.5, 21.8, 21.9, 22.1, 24.6, 27.7, 32.4, 35.4, 80.9 (Zr–C), 111.1, 115.0, 124.1, 124.9, 125.7, 128.0, 128.8, 129.1, 129.2, 129.5, 130.6, 130.8, 131.7, 133.2, 136.2, 136.3, 153.7, 157.0, 181.5. Anal. Calcd for $C_{38}H_{44}N_2SiZr$: C, 70.42; H, 6.84; N, 4.32. Found: C, 70.02; H, 6.37; N, 4.00.

Isolation of 2-7: 2-6b was quenched with 1–3 equivalents of water, and the resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a white solid **2-7**, which was subjected to a short SiO_2 column using petroleum ether and diethyl ether (1:1) as the eluent.

2-7: White solid, isolated yield 80 %, m.p.: 168 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): $\delta = 0.86$ (*d*, *J* = 6.9 Hz, 6H), 1.04 (*d*, *J* = 6.9 Hz, 6H), 2.28 (s, 3H), 2.40 (s, 3H), 2.45–2.62 (m, 1H), 2.72–2.30 (m, 1H), 4.22 (s, 2H), 6.68–7.32 (m, 8H), 7.81 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 18.94, 21.07, 21.24, 22.88, 24.88, 33.37, 37.71, 119.87, 120.49, 128.94, 129.46, 129.80, 130.19, 133.54, 133.71, 135.04, 136.05, 136.13, 205.03. HRMS calcd for $C_{26}H_{31}NO$: 373.2406. Found: 373.2413.

Isolation of Reactive Intermediate 2-8 from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and *p*-TolylCN: In a 20-mL Schlenk tube, *p*-tolunitrile (60 μL, 0.50 mmol) was added to the benzene solution of compound **2-3a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **2-8** as brown powder (331 mg, 0.45 mmol, 90 % yield).

2-8: Brown powder, isolated yield 90 % (331 mg, 0.45 mmol) ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.11 (s, 3H, $SiMe_2$), 0.17 (s, 3H, $SiMe_2$), 0.52 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.72 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.85 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.39 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.12–2.29 (m, 2H, $CHMe_2$), 2.34 (s, 3H, CH_3), 6.23 (s, 5H, C_5H_5), 6.45 (s, 5H, C_5H_5), 7.03 (s, 4H, C_6H_5), 7.13–7.37 (m, 9H, C_6H_5), 7.55 (*d*, *J* = 8.1 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −5.0, 0.3, 18.5, 20.3, 21.0, 25.5, 26.2, 34.7, 35.6, 57.2, 111.3, 111.7, 119.6, 125.6, 125.8, 126.9, 127.0, 127.7, 127.9, 128.6, 128.7, 131.0, 132.1, 137.9, 138.6, 141.3, 142.7, 144.2, 145.0, 175.7, 185.7. Elemental Analysis Calcd (%) for $C_{48}H_{55}N_3OSiZr$: C, 71.24; H, 6.85; N, 5.19. Found: C, 70.84; H, 6.90; N, 5.00. Single crystals of **2-8** suitable for X-ray analysis were grown in tetrahydrofuran/hexane at room temperature for one week.

Isolation of 2-10a: In a 20-mL Schlenk tube, DMF (39 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-10a** as yellow powder (298 mg, 0.43 mmol, 86 % yield).

2-10a: Yellow powder, isolated yield 86 % (298 mg, 0.43 mmol). ^{1}H NMR (300 MHz, C_4D_8O): δ = 0.30 (s, 3H, $SiMe_2$), 0.33 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 0.60 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.76 (s, 3H, $SiMe_2$), 1.01 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.58 (*t*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.92–2.10 (m, 2H, $CHMe_2$), 2.22 (s, 6H, NMe_2), 5.39 (s, 1H, CH), 6.45 (s, 5H, C_5H_5), 6.48 (s, 5H, C_5H_5), 7.06–7.39 (m, 9H, C_6H_5), 7.60 (*d*, *J* = 7.8 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O): δ = −4.1, 0.3, 18.0, 21.5, 22.1, 25.4, 35.1, 35.5, 42.1, 49.8, 100.3, 113.5, 114.1, 120.0, 124.7, 125.6, 125.8, 126.8, 127.1, 127.4, 128.1, 131.3, 131.4, 132.1, 140.7, 141.1, 141.4, 143.1, 195.0. Anal. Calcd for $C_{43}H_{55}N_3OSiZr$: C, 67.49; H, 7.24; N, 5.49. Found: C, 67.14; H, 7.51; N, 5.31. Single crystals of **2-10a**·THF suitable for X-ray analysis were grown in tetrahydrofuran at room temperature for three days.

Formation of 2-11: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-1a**) was added and warmed up to 50 °C for 3 h to yield **2-3a**. After *i*-PrCN (1.5 mmol, 0.135 ml) was added to the toluene solution of **2-3a**, the reaction mixture was stirred at 50 °C for 1 h. Then, *t*-BuNC (1.2 mmol, 100 mg) or CyNC (1.2 mmol, 131 mg) was added to the above reaction mixture. After

stirring at 50 °C for 1 h, it was quenched with saturated aqueous $NaHCO_3$ and extracted with diethyl ether for three times. The extract was washed with water and brine and dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to Al_2O_3 column using petroleum ether and diethyl ether (5:1) as the eluent to give **2-11a**. When *t*-BuNC was used and quenched by D_2O, **2-11aD** could be obtained through the similar procedure as shown above.

2-11a: White solid, isolated yield 70 % (247 mg), m.p.: 106–107 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.22 (*d*, *J* = 6.9 Hz, 6H), 2.86–3.18 (m, 2H), 7.30–7.80 (m, 10H), 8.29 (s, 1H), 8.31 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 22.03, 22.70, 25.59, 30.75, 113.71, 118.52, 121.84, 127.19, 127.73, 128.03, 128.22, 129.47, 131.06, 136.22, 136.58, 136.97, 139.31, 142.31, 159.95. HRMS calcd for $C_{25}H_{26}N_2$: 354.2096. Found: 354.2093.

2-11aD: White solid, isolated yield 56 % (197 mg), D > 98 %, m.p: 106 °C. ^{1}H NMR ($CDCl_3$, Me_4Si): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.22 (*d*, *J* = 6.9 Hz, 6H), 2.79–3.20 (m, 2H), 7.14–7.88 (m, 10H), 8.29 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 22.03, 22.71, 25.58, 30.75, 113.70, 118.40, 121.83, 127.19, 128.03, 128.32, 129.48, 131.05, 136.20, 136.55, 136.94, 139.31, 142.28, 159.95. HRMS calcd for $C_{25}H_{25}N_2D$: 355.2156. Found: 355.2151.

Isolation of 2-12a: In a 20-mL Schlenk tube, PhCHO (50 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 50 °C for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-12a** as yellow powder.

2-12a: Yellow powder, isolated yield 93 % (336 mg, 0.465 mmol). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.66 (s, 3H, $SiMe_2$), 0.71 (s, 3H, $SiMe_2$), 0.89 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.08 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.12 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.53 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.68–1.75 (m, 1H, $CHMe_2$), 2.51–2.58 (m, 1H, $CHMe_2$), 5.63 (s, 1H, CH), 5.99 (s, 5H, C_5H_5), 6.18 (s, 5H, C_5H_5), 6.91 (*d*, *J* = 6.8 Hz, 2H, C_6H_5), 7.16–7.44 (m, 12H, C_6H_5), 7.78 (*d*, *J* = 7.2 Hz, 1H, C_6H_5); ^{13}C NMR (100 MHz, C_6D_6): δ = −3.3, 1.0, 18.8, 22.3, 23.3, 25.0, 25.5, 35.9, 36.0, 50.4, 88.4, 112.8, 113.9, 120.1, 125.5, 126.2, 127.1, 127.2, 127.6, 128.3, 128.6, 129.1, 131.7, 131.8, 132.4, 140.4, 141.2, 141.5, 142.1, 142.9, 186.1. Single crystals of **2-12a** suitable for X-ray analysis were grown in tetrahydrofuran at room temperature for a week.

Formation of 2-13: To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added and warmed up to 50 °C for 3 h. After *i*-PrCN (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, *n*-heptanal (1.2 mmol, 137 mg) was added, and the

reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was performed for crude ^1H NMR to give the ratio of *trans* to *cis* of the product before purified by Al_2O_3 column, using petroleum ether and diethyl ether (2:1) as the eluent. Yellow liquid, total isolated yield (*trans* + *cis*) 43 % (190 mg) (*trans*/*cis* = 1: 0.5).

2-13: Yellow liquid, isolated yield 43 % (190 mg, *trans*/*cis* = 1:0.5). ^1H NMR ($CDCl_3$, Me_4Si): δ = 0.78 (*d*, *J* = 7.2 Hz, 12H), 0.81–0.93 (m, 6H), 1.00–1.54 (m, 28H), 2.03–2.30 (m, 4H), 2.54–3.12 (m, 4H), 5.99 (*t*, *J* = 7.5 Hz, 1H), 6.33 (*t*, *J* = 7.5 Hz, 1H),6.99–7.50 (m, 20H), 7.67 (s, 1H), 7.85 (s, 1H); ^{13}C NMR ($CDCl_3$, Me_4Si): δ = 13.99, 14.09, 18.65, 18.81, 22.59, 22.88, 23.04, 24.77, 24.88, 29.09, 29.56, 29.65, 29.92, 30.40, 31.68, 31.73, 38.19, 39.64, 120.84, 120.93, 122.53, 122.66, 126.20, 126.29, 126.36, 127.22, 127.34, 127.86, 127.93, 128.03, 128.12, 128.39, 128.61, 129.00, 129.76, 130.07, 130.36, 131.21, 131.23, 132.72, 133.14, 133.48, 133.50, 133.95, 134.27, 134.35, 135.17, 135.20, 135.86, 136.14, 136.17, 138.38, 140.63, 203.09, 205.74. HRMS calcd for $C_{31}H_{39}NO$: 441.3032; found: 441.3030.

Isolation of Iminoacyl–Zr Intermediate 2-14a from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and *t*-BuNC: In a 20-mL Schlenk tube, *t*-BuNC (56 μL, 0.50 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-14a** as yellow powder (319 mg, 0.455 mmol, 91 % yield).

2-14a: Yellow powder, isolated yield 91 % (319 mg). ^1H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.38 (s, 3H, $SiMe_2$), 0.91 (s, 3H, $SiMe_2$), 1.11 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.18–1.28 (m, 15H, $CHMe_2$ + ^{t}Bu), 0.93 (*d*, *J* = 6.8 Hz, 3H, $CHMe_2$), 1.66 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.69–2.78 (m, 1H, $CHMe_2$), 3.03–3.12 (m, 1H, $CHMe_2$), 5.67 (s, 5H, C_5H_5), 5.71 (s, 5H, C_5H_5), 7.03–7.51 (m, 9H, C_6H_5), 7.88 (*d*, *J* = 7.2 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6, 25 °C): δ = −2.97, 1.15, 14.32, 19.35, 22.66, 26.08, 30.08, 33.17, 35.36, 54.49, 60.89, 107.22, 108.08, 120.26, 124.20, 126.14, 126.34, 127.33, 127.54, 127.92, 129.68, 132.17, 132.88, 140.15, 141.35, 144.34, 156.76, 186.88, 234.17. Elemental analysis calcd (%) for $C_{41}H_{49}N_3SiZr$: C, 70.03; H, 7.02; N, 5.98. Found: C, 69.95; H, 7.20; N, 5.60.

2-14b: Yellow powder, isolated yield 83 % (302 mg). ^1H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.20 (s, 3H, $SiMe_2$), 0.68 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$ + $SiMe_2$), 0.73 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.05 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.61 (s, 9H, ^{t}Bu), 1.49 (*t*, *J* = 6.9 Hz, 3H, $CHMe_2$), 2.31 (s, 3H, CH_3), 2.36–2.43 (m, 1H, $CHMe_2$), 2.46 (s, 3H, CH_3), 3.04–3.14 (m, 1H, $CHMe_2$), 5.77 (s, 5H, C_5H_5), 6.85 (s, 5H, C_5H_5), 7.06–7.25 (m, 7H, C_6H_5), 7.54 (*d*, *J* = 7.5 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −4.12, −0.13, 18.24, 20.07, 20.47, 21.76, 21.98,

25.29, 29.68, 32.75, 34.32, 61.09, 106.92, 107.80, 119.31, 123.33, 127.40, 127.60, 128.07, 129.32, 131.66, 132.28, 134.65, 135.10, 136.85, 138.10, 143.96, 156.42, 185.50. Elemental analysis calcd (%) for $C_{43}H_{53}N_3SiZr$: C, 70.63; H, 7.31; N, 5.75. Found: C, 70.42; H, 7.51; N, 5.40.

Isolation of Iminoacyl–Zr Intermediate 2-15 or 2-16 from Bis(alkynyl)silane, Two Molecules of *i*-PrCN, and Two Molecules of CyNC: In a 20-mL Schlenk tube, CyNC (124 μL, 1.0 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, *the solid was* dried up under vacuum to precipitate **2-15** or **2-16** as yellow powder (326 mg, 0.39 mmol, 78 % yield).

2-15: Yellow powder, isolated yield 78 % (326 mg). ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.29 (s, 3H, $SiMe_2$), 0.39 (s, 3H, $SiMe_2$), 0.58 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.90 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.10 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 1.31 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.30–1.52 (m, 14H, $CHMe_2$ + C_6H_{11}), 1.70–2.00 (m, 11H, C_6H_{11}), 2.21–2.30 (m, 1H, $CHMe_2$), 2.78–2.87 (m, 1H, $CHMe_2$), 5.83 (s, 5H, C_5H_5), 6.06 (s, 5H, C_5H_5), 7.08–7.40 (m, 9H, C_6H_5), 7.73 (*d*, *J* = 7.5 Hz, 1H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −2.94, −1.48, 18.60, 22.20, 23.35, 24.25, 24.42, 24.76, 24.95, 25.25, 25.74, 32.16, 34.70, 35.07, 35.54, 50.90, 64.13, 68.07, 109.45, 110.31, 119.90, 124.79, 125.47, 126.30, 126.85, 127.08, 127.41, 128.07, 128.12, 132.78, 140.76, 141.16, 141.47, 143.99, 164.95, 183.63, 222.57. Elemental analysis calcd (%) for $C_{54}H_{70}N_4OSiZr$ (**2-15**·THF): C, 71.63; H, 7.45; N, 6.68. Found: C, 71.95; H, 7.81; N, 6.50. Single crystals of **2-15**·THF suitable for X-ray analysis were grown in tetrahydrofuran/hexane at room temperature for three days.

2-16: Yellow powder, isolated yield 63 % (277 mg). ^{1}H NMR (300 MHz, C_4D_8O, 25 °C): δ = 0.49 (s, 3H, $SiMe_2$), 0.54 (s, 3H, $SiMe_2$), 1.04 (*d*, *J* = 7.2 Hz, 3H, $CHMe_2$), 1.25 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.74 (s, 3H, 2,6-Me_2Ph), 1.90 (s, 3H, 2,6-Me_2Ph), 2.21 (s, 3H, 2,6-Me_2Ph), 2.44 (s, 3H, 2,6-Me_2Ph), 2.83–2.92 (m, 1H, $CHMe_2$), 3.07–3.16 (m, 1H, $CHMe_2$), 5.89 (s, 5H, C_5H_5), 5.92 (s, 5H, C_5H_5), 6.15–6.65 (m, 6H, 2,6-Me_2Ph), 7.32–7.40 (m, 8H, C_6H_5), 8.03 (*d*, *J* = 8.1 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_4D_8O, 25 °C): δ = −0.97, 0.10, 0.43, 18.80, 19.47, 19.68, 20.81, 20.87, 21.59, 21.85, 25.66, 32.36, 33.51, 108.48, 109.17, 116.64, 118.15, 125.34, 126.03, 126.64, 126.98, 127.07, 127.15, 126.46, 127.64, 128.24, 129.04, 129.98, 130.19, 136.58, 138.41, 138.82, 139.14, 145.54, 151.96, 154.92, 161.63, 180.93, 184.93. Elemental analysis calcd (%) for $C_{54}H_{58}N_4SiZr$: C, 73.50; H, 6.63; N, 6.35. Found: C, 73.66; H, 6.48; N, 6.50.

Hydrolysis of Iminoacyl–Zr Intermediate 2-14a to Give 1*H*-Pyrrolo[3,2-*c*] pyridine 2-11a, *t*-BuNH$_2$, and Zirconasiloxane 2-5: Under a nitrogen atmosphere, a J. Young valve NMR tube was charged with **2-14a** (70 mg, 0.10 mmol) and C_6D_6 (0.5 mL). Three equivalents of H_2O (5.4 μL, 0.30 mmol) were added to the C_6D_6 solution of **2-14a** with a syringe at room temperature, and then, the NMR tube was shaken immediately. The mixture in NMR tube was monitored by ^{1}H and

^{13}C NMR spectroscopy, and **2-11a** was found to be the main product over 90 % yield by ^{1}H NMR. Then, the mixture was filtered in the glove box, and the filtrate was subjected to GC–MS. The obvious peak of *m/z* = 73 as the relative molecular weight of *t*-BuNH$_2$ was found. The residue was washed with diethyl ether for several times until it turned out to be a pale solid and further characterized by elemental analysis to be **2-5**.

Formation of 1*H*-Pyrrolo[3,2-*c*]pyridine 2-11 from One Molecule of the Bis (alkynyl)silane with Two Molecules of Nitrile and One Isocyanide. A General Procedure for the Formation of 2,4-Diisopropyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*] pyridine (2-11d): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(*p*-tolylethynyl) dimethylsilane (**2-2b**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, *t*-BuNC (1.2 mmol, 100 mg, 136 μl) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine (100:10:1) as the eluent to give product **2-11d**.

2-11b: White solid, isolated yield: 55 % (231 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.54–0.63 (m, 3H), 0.74–0.87 (m, 3H), 1.10–1.24 (m, 6H), 1.36–1.42 (m, 1H), 1.53–1.59 (m, 2H), 1.73–1.79 (m, 1H), 2.67–2.80 (m, 2H), 7.22–7.48 (m, 6H), 7.55 (*t*, *J* = 7.6 Hz, 2H), 7.64 (*d*, *J* = 7.6 Hz, 2H), 8.28 (s, 1H), 8.33 (Br, 1H); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 12.12, 12.19, 12.21, 12.24, 19.36, 19.42, 20.91, 29.43, 29.47, 29.62, 29.71, 30.28, 32.50, 32.55, 37.51, 114.85, 114.94, 118.27, 122.56, 122.58, 127.07, 127.19, 127.45, 127.64, 127.87, 127.93, 127.95, 128.13, 128.16, 128.19, 128.32, 128.52, 128.93, 129.36, 131.07, 131.12, 131.39, 131.47, 131.85, 136.15, 136.18, 136.50, 137.03, 138.59, 139.13, 141.09, 141.16, 159.18, 159.24. HRMS: *m/z*: calcd for $C_{27}H_{31}N_2$ $[M + H]^+$: 383.2487; found: 383.2473.

2-11c: White solid, isolated yield: 66 % (287 mg), m.p.: 218–220 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.74–1.88 (m, 20H), 2.58–2.68 (m, 2H), 7.24–7.66 (m, 10H), 8.25 (s, 1H), 8.31 (Br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 25.79, 26.00, 26.30, 26.60, 32.21, 33.27, 35.67, 41.30, 114.13, 118.64, 122.28, 127.33, 127.88, 128.16, 128.43, 129.64, 131.38, 136.43, 136.83, 137.03, 139.36, 141.76, 159.55. HRMS: *m/z*: calcd for $C_{31}H_{35}N_2$ $[M + H]^+$: 435.2800; found: 435.2780.

2-11d: White solid, isolated yield: 41 % (156 mg), m.p.: 181–184 °C. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.14 (*d*, *J* = 6.9 Hz, 6H), 1.20 (*d*, *J* = 6.9 Hz, 6H),

2.44 (s, 3H), 2.45 (s, 3H), 2.95–3.13 (m, 2H), 7.24 (s, 4H), 7.36 (*d*, *J* = 7.8 Hz, 2H), 7.53 (*d*, *J* = 7.5 Hz, 2H), 8.25 (s, 1H), 8.32 (br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 21.26, 21.35, 22.05, 22.70, 25.55, 30.61, 113.58, 118.47, 121.84, 128.08, 128.75, 130.14, 130.84, 133.03, 133.55, 136.70, 137.04, 137.56, 139.05, 142.34, 159.70. HRMS: *m/z*: calcd for $C_{27}H_{31}N_2$ $[M + H]^+$: 383.2487; found: 383.2469.

2-11e: White solid, isolated yield: 53 % (217 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.55–0.65 (m, 3H), 0.74–0.83 (m, 3H), 1.10–1.23 (m, 6H), 1.35–1.45 (m, 1H), 1.48–1.61 (m, 2H), 1.71–1.84 (m, 1H), 2.45 (s, 3H), 2.46 (s, 3H), 2.66–2.77 (m, 1H), 2.78–2.85 (m, 1H), 7.23 (s, 4H), 7.37 (*d*, *J* = 8.1 Hz, 2H), 7.54 (*d*, *J* = 7.8 Hz, 2H), 8.22 (br, 1H), 8.26 (s, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 12.20, 12.29, 12.35, 19.57, 19.61, 21.05, 21.07, 21.29, 21.36, 29.58, 29.74, 29.77, 29.84, 32.54, 32.58, 37.52, 114.96, 115.05, 118.38, 122.84, 128.27, 128.83, 128.87, 128.92, 130.33, 131.16, 131.24, 131.46, 131.58, 133.32, 133.86, 136.82, 137.30, 137.71, 139.37, 141.20, 141.28, 159.40. HRMS: *m/z*: calcd for $C_{29}H_{35}N_2$ $[M + H]^+$: 411.2800; found: 411.2795.

2-11f: White solid, isolated yield: 46 % (487 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.83–1.38 (m, 8H), 2.30 (s, 3H), 2.45 (s, 3H), 6.56 (*d*, *J* = 7.8 Hz, 2H), 6.64–78 (m, 4H), 6.93 (*d*, *J* = 8.1 Hz, 2H), 7.01–7.25 (m, 6H), 7.36 (*d*, *J* = 7.8 Hz, 2H), 7.56 (*d*, *J* = 7.8 Hz, 2H), 8.36 (s, 1H), 8.50 (Br, 1H); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 17.79, 19.23, 21.27, 21.30, 22.19, 29.46, 117.98, 119.67, 124.11, 124.59, 125.06, 125.87, 125.95, 127.70, 127.86, 128.33, 128.56, 130.35, 131.33, 132.11, 133.23, 135.82, 138.01, 138.08, 139.40, 144.97, 145.97, 155.12. HRMS: *m/z*: calcd for $C_{39}H_{35}N_2$ $[M + H]^+$: 531.2800; found: 531.2783.

Formation of Dihydropyrrolo[3,2-*c*]azepine 2-18 and 2-19 from One Molecule of the Bis(alkynyl)silane with Two Molecules of *i*-PrCN and Two Molecules of 2,6-Dimethylphenyl Isocyanides. A General Procedure for the Formation of *N*-(2,6-dimethylphenyl)-6-(2,6-dimethylphenylimino)-2,4-diisopropyl-3,8-diphenyl-1,6-dihydropyrrolo[3,2-*c*]azepin-7-amine (2-18a) and N^6,N^7-bis(2,6-dimethylphenyl)-2,4-diisopropyl-3,8-diphenyl-1,6-dihydropyrrolo[3,2-*c*]azepine-6,7-diamine (2-19a): To a toluene (20 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 50-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *i*-PrCN (1.5 mmol, 0.135 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, 2,6-dimethylphenyl isocyanide (2.4 mmol, 314 mg) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine

(100:7.5:1) as the eluent to give product **2-19a** and using petroleum ether, diethyl ether, and triethylamine (100:15:1) as the eluent to give product **2-18a**.

2-18a: Colorless crystal, isolated yield: 46 % (278 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.59 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 1.01 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.81 (s, 6H, Me), 2.23 (s, 6H, Me), 2.94–3.03 (m, 2H, $CHMe_2$), 6.08 (s, 1H, NH), 6.81 (*t*, *J* = 8.1 Hz, 4H, CH), 6.92 (*d*, *J* = 7.2 Hz, 2H, CH), 7.10–7.33 (m, 10H, CH), 7.44 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 17.76, 19.17, 20.73, 22.70, 24.77, 33.24, 106.65, 118.38, 118.61, 122.10, 125.27, 126.16, 127.05, 127.38, 127.80, 128.04, 128.09, 128.64, 129.72, 130.21, 134.36, 134.97, 135.18, 135.91, 136.27, 137.82, 147.28, 158.59, 167.17. HRMS: *m/z*: calcd for $C_{42}H_{45}N_4$ $[M + H]^+$: 605.3644; found: 605.3678. Single crystals of **2-18a**·1.5**DME** suitable for X-ray analysis were grown in 1,2-dimethoxyethane/diethyl ether at room temperature for three days.

2-18b: White solid, isolated yield: 33 % (235 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.57–0.63 (m, 2H, CH_2), 0.83–0.90 (m, 3H, CH_2), 1.05–1.14 (m, 4H, CH_2), 1.17–1.25 (m, 2H, CH_2), 1.37–1.45 (m, 3H, CH_2), 1.57–1.71 (m, 6H, CH_2), 1.75 (s, 6H, Me), 1.79–1.85 (m, 1H, CH), 2.22 (s, 6H, Me), 2.31 (s, 3H, Me), 2.35 (s, 3H, Me), 2.53–5.59 (m, 1H, CH), 5.97 (s, 1H, NH), 6.81 (*t*, *J* = 7.6 Hz, 4H, CH), 6.89 (*d*, *J* = 7.6 Hz, 2H, CH), 6.96 (*d*, *J* = 8.0 Hz, 2H, CH), 7.08 (*q*, *J* = 7.6 Hz, 4H, CH), 7.19 (*d*, *J* = 8.0 Hz, 2H, CH), 7.43 (Br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 17.72, 19.15, 21.12, 21.15, 25.71, 25.96, 26.11, 26.33, 30.97, 33.27, 34.81, 43.24, 106.47, 118.49, 118.76, 121.92, 125.14, 126.94, 127.79, 128.20, 128.67, 129.00, 129.37, 129.67, 130.05, 132.88, 133.36, 133.47, 135.18, 135.24, 135.54, 135.92, 136.99, 138.06, 147.41, 158.59, 168.16. HRMS: *m/z*: calcd for $C_{50}H_{57}N_4$ $[M + H]^+$: 713.4578; found: 713.4560.

2-19a: Yellow solid, isolated yield: 24 % (145 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.80 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.88 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 0.99 (*d*, *J* = 6.0 Hz, 3H, $CHMe_2$), 1.22 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.68 (s, 3H, Me), 2.35 (s, 3H, Me), 2.38–2.45 (m, 1H, $CHMe_2$), 2.57 (s, 6H, Me), 3.02–3.09 (m, 1H, $CHMe_2$), 4.33 (*d*, *J* = 5.1 Hz, 1H, CHNH), 4.68 (*d*, *J* = 5.1 Hz, 1H, CHNH), 6.39 (*d*, *J* = 7.5 Hz, 1H, CH), 6.57 (*t*, *J* = 7.2 Hz, 1H, CH), 6.75 (*d*, *J* = 7.2 Hz, 1H, CH), 6.85–7.34 (m, 13H, CH), 7.53 (Br, 1H, NH), 7.89 (br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, 25 °C): δ = 19.30, 19.99, 20.42, 22.28, 22.71, 23.03, 24.70, 33.04, 79.79, 101.03, 118.20, 118.97, 121.82, 123.35, 125.59, 125.83, 127.06, 127.43, 128.00, 128.55, 128.68, 128.77, 129.66, 129.72, 130.52, 130.60, 131.92, 133.62, 133.70, 136.38, 136.98, 137.04, 137.78, 147.01, 167.69. HRMS: *m/z*: calcd for $C_{42}H_{47}N_4$ $[M + H]^+$: 607.3801; found: 607.3794. Single crystals of **2-19a** suitable for X-ray analysis were grown in diethyl ether/hexane at room temperature for one week.

2-19b: Yellow solid, isolated yield: 21 % (150 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.55–0.67 (m, 1H, CH_2), 0.80–0.88 (m, 1H, CH_2), 0.94–1.05 (m, 5H, CH_2), 1.08–1.25 (m, 2H, CH_2), 1.43–1.61 (m, 9H, CH_2), 1.64 (s, 3H, Me), 1.72–1.77 (m, 1H, CH_2), 1.98–2.00 (m, 2H, CH), 2.14 (s, 3H, Me), 2.32 (s, 3H,

Me), 2.37 (s, 3H, Me), 2.56 (s, 3H, Me), 2.59–5.62 (m, 1H, CH), 4.27 (*d*, *J* = 5.2 Hz, 1H, CHNH), 4.63 (*d*, *J* = 5.2 Hz, 1H, CHNH), 6.35 (*d*, *J* = 7.6 Hz, 1H, CH), 6.53 (*t*, *J* = 7.6 Hz, 1H, CH), 6.62 (*d*, *J* = 7.6 Hz, 1H, CH), 6.73 (*t*, *J* = 8.0 Hz, 2H, CH), 6.77 (s, 2H, CH), 6.84 (t, *J* = 8.0 Hz, 1H, CH), 7.04 (*d*, *J* = 7.6 Hz, 2H, CH), 7.11 (*q*, *J* = 7.6 Hz, 4H, CH), 7.51 (Br, 1H, NH), 7.69 (br, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 19.07, 19.33, 19.98, 20.94, 21.18, 25.76, 26.23, 26.31, 26.39, 26.47, 26.86, 30.89, 32.75, 33.03, 33.69, 34.70, 43.20, 79.85, 100.99, 118.31, 119.18, 121.73, 123.06, 126.98, 127.61, 128.11, 128.27, 12860, 128.70, 129.71, 130.26, 130.44, 131.94, 132.78, 133.07, 133.90, 134.11, 135.08, 135.19, 136.26, 137.93, 148.13, 167.01. HRMS: *m/z*: calcd for $C_{50}H_{59}N_4$ $[M + H]^+$: 715.4740; found: 715.4728.

Formation of pyrrolo[3,2-*d*]pyridazine 2-20 from One Molecule of the Bis (alkynyl)silane with Two nitriles and One Azide. A General Procedure for the Formation of N-benzyl-2, 4-diisopropyl-3, 7-diphenyl-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.75 mmol, 0.157 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, BnN_3 (1.2 mmol, 154 mg) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine (100:15:1) as the eluent to give product **2-20a**.

***N*-Benzyl-2,4-diisopropyl-3,7-diphenyl-5*H*-pyrrolo[3,2-*d*]pyridazin-5-amine (2-20a):** Yellow crystal, isolated yield 54 % (248 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.34 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.36 (*d*, *J* = 6.9 Hz, 6H, CH_3), 3.05–3.14 (m, 1H, C*H*Me_2), 3.48–3.57 (m, 1H, C*H*Me_2), 4.55 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.34 (*t*, *J* = 7.2 Hz, 1H, NH), 7.24–7.59 (m, 13H, CH), 8.81 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.88, 23.19, 28.55, 29.32, 56.63, 118.02, 126.70, 127.74, 127.91, 128.18, 128.22, 128.86, 128.93, 129.49, 129.78, 130.91, 135.21, 135.51, 137.50, 140.08, 145.31, 153.62, 168.22. HRMS calcd for $C_{31}H_{33}N_4$ $[M + H]^+$: 461.2705; found: 461.2761. Elemental Analysis Calcd (%) for $C_{31}H_{32}N_4$: C, 80.83; H, 7.00; N, 12.16. Found: C, 80.63; H, 7.20; N, 11.99. Single crystals of **2-20a** suitable for X-ray analysis were grown in hexane at room temperature for one day.

2,4-Dicyclohexyl-*N*-phenyl-3,7-di*p*-tolyl-5*H*-pyrrolo[3,2-*d*]pyridazin-5-amine (2-20b): Pale yellow crystal, isolated yield 50 % (277 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.21–2.17 (m, 20H, CH_2), 2.37 (s, 3H, CH_3), 2.45 (s, 3H, CH_3),

2.71–2.78 (m, 1H, CH), 3.00–3.16 (m, 1H, CH), 6.43 (*d*, *J* = 8.4 Hz, 2H, CH), 6.97 (*t*, *J* = 7.2 Hz, 1H, CH), 7.16–7.27 (m, 8H, CH), 7.75 (Br, 1H, NH), 8.47 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 21.34, 21.47, 25.40, 26.10, 26.36, 26.63, 29.23, 30.96, 33.13, 38.77, 39.91, 114.89, 118.77, 122.23, 127.90, 128.63, 128.92, 129.08, 129.81, 130.78, 132.00, 134.24, 136.24, 139.51, 139.89, 146.99, 147.12, 154.87, 167.50. HRMS calcd for $C_{38}H_{43}N_4$ $[M + H]^+$: 555.3488; found: 555.3486. Elemental Analysis Calcd (%) for $C_{38}H_{42}N_4$: C, 82.27; H, 7.63; N, 10.10. Found: C, 82.11; H, 7.89; N, 9.91.

2,4-Di-*sec*-butyl-*N*-(4-fluorobenzyl)-3,7-diphenyl-5*H*-pyrrolo[2,3-*d*]pyridazin-5-amine (2-20c): White solid, isolated yield 59 % (298 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.57–0.64 (m, 3H), 0.74–0.84 (m, 5H), 1.26–1.36 (m, 6H), 1.60–1.77 (m, 2H), 1.90–1.95 (m, 2H), 2.76–2.80 (m, 1H), 3.27–3.35 (m, 1H), 4.51 (*d*, *J* = 7.6 Hz, 2H, CH_2), 5.26 (*t*, *J* = 7.2 Hz, 1H, NH), 7.08 (*t*, *J* = 8.4 Hz, 2H), 7.23–7.55 (m, 10H), 8.85 (*d*, *J* = 7.2 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 12.36, 12.61, 12.72, 17.60, 17.73, 21.18, 21.22, 27.43, 27.46, 29.97, 30.15, 35.59, 35.65, 36.27, 36.30, 55.66, 115.68, 115.90, 119.12, 119.26, 126.67, 127.77, 127.86, 127.94, 128.21, 129.48, 129.76, 130.70, 130.79, 131.09, 131.17, 131.29, 131.33, 131.37, 131.40, 135.67, 137.63, 137.66, 139.98, 145.01, 145.05, 152.73, 152.81, 161.35, 163.81, 167.51, 167.58. HRMS calcd for $C_{33}H_{36}FN_4$ $[M + H]^+$: 507.2924; found: 507.2920. Elemental Analysis Calcd (%) for $C_{33}H_{35}FN_4$: C, 78.23; H, 6.96; N, 11.06. Found: C, 78.12; H, 7.09; N, 10.90.

***N*-Benzyl-2,4-dicyclohexyl-3,7-diphenyl-5*H*-pyrrolo[2, 3-*d*]pyridazin-5-amine (2-20d):** Yellow solid, isolated yield 55 % (297 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.66–2.24 (m, 20H, CH_2), 2.72–2.80 (m, 1H, C*H*), 3.03–3.11 (m, 1H, C*H*), 4.50 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.30 (*t*, *J* = 7.2 Hz, 1H, NH), 7.33–7.57 (m, 13H, CH), 8.83 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 25.89, 26.09, 26.42, 26.67, 29.41, 33.16, 38.89, 40.13, 56.80, 118.33, 126.68, 127.94, 128.15, 128.23, 128.84, 129.44, 129.76, 131.02, 135.25, 135.61, 137.73, 139.90, 145.33, 152.73, 167.23. HRMS calcd for $C_{37}H_{41}N_4$ $[M + H]^+$: 541.3331; found: 541.3320. Elemental Analysis Calcd (%) for $C_{37}H_{40}N_4$: C, 82.18; H, 7.46; N, 10.36. Found: C, 82.00; H, 7.93; N, 10.08.

***N*-Benzyl-2, 4-diisopropyl-3, 7-di*p*-tolyl-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20e):** Yellow crystal, isolated yield 67 % (327 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.33 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.36 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.44 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.03–3.12 (m, 1H, $CHMe_2$), 3.53–3.62 (m, 1H, $CHMe_2$), 4.54 (*d*, *J* = 7.5 Hz, 2H, CH_2), 5.35 (*t*, *J* = 7.2 Hz, 1H, NH), 7.22–7.50 (m, 11H, CH), 8.72 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.91, 21.34, 21.54, 23.22, 28.49, 29.20, 56.68, 117.88, 127.54, 128.19, 128.66, 128.88, 128.97, 129.66, 130.75, 132.45, 134.34, 135.63, 136.14, 139.46, 139.98, 145.47, 153.55, 168.14. HRMS calcd for $C_{33}H_{37}N_4$ $[M + H]^+$: 489.3018; found: 489.3024. Elemental Analysis Calcd (%) for $C_{33}H_{36}N_4$: C, 80.94; H, 7.62; N, 11.44. Found: C, 80.63; H, 7.90; N, 11.21.

2,4-Diisopropyl-*N*-(4-methoxybenzyl)-3,7-di*p*-tolyl-5*H*-pyrrolo[2,3-*d*]pyridazin-5-amine (2-20f): Yellow oily solid, isolated yield 52 % (275 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 1.33 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.34 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.44 (s, 3H, CH_3), 2.45 (s, 3H, CH_3), 3.03–3.13 (m, 1H, $CHMe_2$), 3.52–3.61 (m, 1H, $CHMe_2$), 3.82 (s, 3H, OCH_3), 4.49 (*d*, *J* = 7.2 Hz, 2H, CH_2), 5.25 (*t*, *J* = 7.2 Hz, 1H, NH), 6.93 (*d*, *J* = 8.7 Hz, 2H, CH), 7.22–7.42 (m, 8H, CH), 8.72 (*d*, *J* = 6.9 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 19.91, 21.34, 21.54, 23.22, 28.46, 29.18, 55.29, 56.10, 114.17, 117.85, 127.49, 128.65, 128.97, 129.65, 130.36, 130.73, 132.45, 134.32, 136.12, 139.45, 139.94, 145.47, 153.55, 159.44, 168.06. HRMS calcd for $C_{34}H_{40}N_4O$ $[M + H]^+$: 519.3108; found: 519.3124.

***N*-Benzyl-2, 4-di-*sec*-butyl-3, 7-bis(4-*tert*-butylphenyl)-5*H*-pyrrolo[3, 2-*d*]pyridazin-5-amine (2-20g):** Yellow solid, isolated yield 53 % (312 mg). ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.76–0.85 (m, 4H, CH_2CH_3), 1.13–1.17 (m, 6H, $CHCH_3$), 1.39 (s, 9H, CMe_3), 1.40 (s, 9H, CMe_3), 1.61–1.70 (m, 3H, CH_2CH_3), 1.77–1.86 (m, 3H, CH_2CH_3), 2.77–2.87 (m, 1H, $CHCH_3$), 3.17–3.21 (m, 1H, $CHCH_3$), 4.53 (*d*, *J* = 7.2 Hz, 2H, CH_2), 5.27 (*t*, *J* = 7.2 Hz, 1H, NH), 7.23–8.72 (m, 11H, CH), 8.73 (*d*, *J* = 8.1 Hz, 2H, CH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = −0.82, 11.43, 11.87, 11.95, 16.42, 16.53, 20.48, 20.56, 26.43, 26.48, 29.16, 29.31, 30.52, 30.65, 33.73, 33.97, 34.74, 35.24, 55.71, 118.20, 118.30, 123.68, 123.73, 123.92, 124.46, 127.33, 127.51, 127.70, 128.04, 128.15, 128.60, 129.77, 129.93, 129.99, 130.17, 131.71, 133.57, 134.87, 139.15, 148.58, 151.54, 152.08, 152.16, 166.33, 166.39. HRMS calcd for $C_{41}H_{53}N_4$ $[M + H]^+$: 601.4270; found: 601.4274.

Isolation of Reactive Intermediate 2-21a or 2-21a′ with the Proposed Structure: In a 20-mL Schlenk tube, benzyl azide (59 mg, 0.5 mmol) was added to the benzene solution of compound **2-6a** (310 mg, 0.50 mmol). After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **2-21a** or **2-21a′** as brown powder (328 mg, 0.43 mmol, 87 % yield). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.47 (s, 3H, $SiMe_2$), 0.59 (s, 3H, $SiMe_2$), 1.03 (*d*, *J* = 6.9 Hz, 3H, $CHMe_2$), 1.36 (*d*, *J* = 6.6 Hz, 3H, $CHMe_2$), 2.37–2.46 (m, 1H, $CHMe_2$), 2.73–2.82 (m, 1H, $CHMe_2$), 4.58 (s, 2H, CH_2Ph), 5.55 (s, 5H, C_5H_5), 5.76 (s, 5H, C_5H_5), 7.08–7.42 (m, 12H, C_6H_5), 7.57 (*d*, *J* = 7.5 Hz, 2H, C_6H_5), 7.75 (*d*, *J* = 6.9 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.61, −1.38, 19.64, 22.28, 22.60, 26.11, 32.67, 35.63, 61.88, 65.59, 111.11, 111.58, 120.21, 123.07, 126.22, 126.43, 126.76, 127.34, 128.53, 128.73, 129.08, 132.25, 132.96, 139.36, 141.25, 143.48, 143.94, 144.48, 185.29. Elemental Analysis Calcd (%) for $C_{43}H_{47}N_5SiZr$: C, 68.57; H, 6.29; N, 9.30. Found: C, 68.46; H, 6.40; N, 9.18.

Formation of Pyrrole-2,3-diones 2-24 from One Molecule of the Bis(alkynyl)silane, Two Nitriles, and One $TMSN_3$. A General Procedure for the Formation of 1-(2-benzoyl-5-isopropyl-4-phenyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.2 mmol, 350 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.4 mmol, 1.6 M, 1.5 ml) with a syringe. After the addition was complete, the reaction mixture

was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane (**2-2a**) was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After *iso*-butyronitrile (1.75 mmol, 0.157 ml) was added, the reaction mixture was stirred at this temperature for 1 h. Then, $TMSN_3$ (1.2 mmol) was added, and the reaction mixture was stirred at 50 °C for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:15:1) as the eluent to give product **2-24a**.

1-(2-Benzoyl-5-isopropyl-4-phenyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24a): Yellow crystal, isolated yield 64 % (228 mg), m.p.: 135–136 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) δ = 0.55 (*d*, *J* = 6.9 Hz, 6H, CH_3), 1.24 (*d*, *J* = 6.9 Hz, 6H, CH_3), 2.09–2.18 (m, 1H, $CHMe_2$), 2.99–3.08 (m, 1H, $CHMe_2$), 7.26–7.77 (m, 10H, CH), 10.08 (Br, 1H, NH); ^{13}C NMR ($CDCl_3$, Me_4Si) δ = 17.65, 22.40, 25.52, 43.44, 123.60, 127.07, 127.19, 128.00, 128.55, 129.17, 130.54, 131.99, 132.30, 133.71, 138.96, 142.65, 186.32, 206.07. IR (film): 1,689, 1,602 cm^{-1}. HRMS calcd for $C_{24}H_{26}NO_2$ $[M + H]^+$: 360.1964; found: 360.1952. Elemental Analysis Calcd (%) for $C_{24}H_{25}NO_2$: C, 80.19; H, 7.01; N, 3.90. Found: C, 80.36; H, 6.97; N, 3.68. Single crystals of **2-24a** suitable for X-ray analysis were grown in hexane/diethyl ether/ethyl acetate (2:1:1) at room temperature for one day.

(3-(Cyclohexanecarbonyl)-5-cyclohexyl-4-*p*-tolyl-1*H*-pyrrol-2-yl)(*p*-tolyl)methanone (2-24b): Yellow solid, isolated yield 67 % (315 mg), m.p.: 200–202 °C. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.79–1.88 (m, 20H, CH_2), 2.37 (s, 3H, Me), 2.39 (s, 3H, Me), 2.51–2.67 (m, 2H, CH), 7.14 (s, 4H, C_6H_4), 7.23 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 7.63 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 9.30 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 21.20, 21.53, 25.58, 26.21, 28.07, 32.81, 35.22, 53.32, 123.69, 127.18, 128.61, 129.10, 129.19, 130.29, 130.73, 131.76, 136.51, 136.58, 141.71, 142.79, 186.15, 205.37. IR (film): 1,685, 1,597 cm^{-1}. HRMS calcd for $C_{32}H_{38}NO_2$ $[M + H]^+$: 468.2903; found: 468.2907. Elemental Analysis Calcd (%) for $C_{32}H_{37}NO_2$: C, 82.19; H, 7.97; N, 3.00. Found: C, 82.10; H, 8.09; N, 2.97.

1-(5-Isopropyl-2-(4-propylbenzoyl)-4-(4-propylphenyl)-1H-pyrrol-3-yl)-2-methylpropan-1-one (2-24c): Yellow oil, isolated yield 63 % (264 mg). ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.55 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 0.90–0.97 (m, 6H, $CH_2CH_2CH_3$), 1.24 (*d*, *J* = 6.9 Hz, 6H, $CHMe_2$), 1.60–1.70 (m, 4H, $CH_2CH_2CH_3$), 2.10–2.19 (m, 1H, $CHMe_2$), 2.57–2.65 (m, 4H, $CH_2CH_2CH_3$), 2.99–3.09 (m, 1H, $CHMe_2$), 7.13–7.26 (m, 6H, C_6H_4), 7.68 (*d*, *J* = 8.1 Hz, 2H, C_6H_4), 9.88 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 13.68, 13.88, 17.64, 22.45, 24.27, 24.33, 25.40, 37.73, 37.98, 43.50, 123.52, 127.08, 127.99, 128.65, 129.28, 130.27, 130.82, 131.75, 136.55, 141.39, 142.29, 147.66, 186.02, 206.30. IR (film): 1,691, 1,597 cm^{-1}. HRMS calcd for $C_{30}H_{38}NO_2$ $[M + H]^+$: 444.2903; found: 444.2901.

(2-(4-*tert*-Butylbenzoyl)-4-(4-*tert*-butylphenyl)-5-cyclohexyl-1*H*-pyrrol-3-yl) (cyclohexyl)methanone (2-24d): Yellow oil, isolated yield 54 % (298 mg). ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) δ = 0.79–0.90 (m, 5H, C_6H_{11}), 1.05–1.20 (m, 6H, C_6H_{11}), 1.30 (s, 9H, CMe_3), 1.34 (s, 9H, CMe_3), 1.42–1.45 (m, 3H, C_6H_{11}), 1.62–1.75 (m, 6H, C_6H_{11}), 1.86–1.92 (m, 1H, C_6H_{11}), 2.53–2.59 (m, 1H, C_6H_{11}), 7.12 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.33 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.38 (*d*, *J* = 8.4 Hz, 2H, C_6H_4), 7.45 (*d*, *J* = 8.1 Hz, 2H, C_6H_4), 9.27 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 25.70, 25.91, 26.27, 29.83, 31.04, 31.34, 32.87, 34.47, 34.99, 35.34, 49.89, 123.82, 124.97, 125.28, 125.84, 128.85, 130.05, 130.73, 132.27, 136.73, 142.48, 149.45, 155.31, 180.90, 186.20. IR (film): 1,607, 1,558 cm^{-1}. HRMS calcd for $C_{38}H_{49}NO_2$ $[M + H]^+$: 551.3763; found: 551.3995.

1-(2-(4-*tert*-Butylbenzoyl)-4-(4-*tert*-butylphenyl)-5-isopropyl-1*H*-pyrrol-3-yl)-2-methylpropan-1-one (2-24e): Yellow solid, isolated yield 62 % (294 mg), ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 0.49 (*d*, *J* = 6.3 Hz, 6H, $CHMe_2$), 1.13 (*d*, *J* = 6.6 Hz, 6H, $CHMe_2$), 1.29 (s, 9H, CMe_3), 1.30 (s, 9H, CMe_3), 2.18–2.26 (m, 1H, $CHMe_2$), 2.92–3.01 (m, 1H, $CHMe_2$), 7.13 (*d*, *J* = 8.2 Hz, 2H, C_6H_4), 7.30 (*d*, *J* = 7.8 Hz, 2H, C_6H_4), 7.38 (*d*, *J* = 7.2 Hz, 2H, C_6H_4), 7.46 (*d*, *J* = 7.5 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 17.84, 22.62, 25.14, 31.06, 31.32, 34.37, 34.76, 42.29, 122.05, 124.63, 125.54, 127.48, 127.89, 128.00, 129.87, 131.80, 137.03, 139.18, 149.02, 153.87, 170.02, 205.71. IR (film): 1,670, 1,609 cm^{-1}. HRMS calcd for $C_{32}H_{41}NO_2$ $[M + H]^+$: 471.3137; found: 471.3367.

Formation of Pyrrolo[3,2-*d*]pyridazines 2-27 from Pyrrole-2,3-diones 2-24 and Hydrazine Hydrate. A General Procedure for Preparation of 2,4-diisopropyl-3,7-diphenyl- 1*H*-pyrrolo[3,2-*d*]pyridazine (2-27a): In a 20-mL Schlenk tube, hydrazine hydrate (1.0 mmol, 0.057 mL) was added to the ethanol solution (5 mL) of compound **2-24** (180 mg, 0.5 mmol). After the reaction mixture was refluxed for 12 h, the solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:30:1) as the eluent to give product **2-27a**.

2,4-Diisopropyl-3,7-diphenyl-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27a): Yellow solid, isolated yield 75 % (133 mg), m.p.: 249–251 °C. ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 1.21 (*d*, *J* = 7.2 Hz, 6H, $CHMe_2$), 1.24 (*d*, *J* = 7.2 Hz, 6H, $CHMe_2$), 3.05–3.14 (m, 2H, $CHMe_2$), 7.26–7.45 (m, 8H, C_6H_4), 7.81–7.84 (m, 2H, C_6H_4), 10.00 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 21.86, 22.32, 25.98, 30.25, 113.43, 122.37, 127.45, 128.02, 128.31, 128.63, 128.77, 129.60, 130.96, 135.04, 135.99, 145.32, 146.61, 160.36. HRMS calcd for $C_{24}H_{26}N_3$ $[M + H]^+$: 356.2127; found: 356.2123. Elemental Analysis Calcd (%) for $C_{24}H_{25}N_3$: C, 81.09; H, 7.09; N, 11.82. Found: C, 81.07; H, 7.15; N, 11.80.

2,4-Dicyclohexyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27b): Yellow solid, isolated yield 83 % (192 mg), m.p.: >300 °C. ^{1}H NMR (THF-d8, Me_4Si) δ = 1.45–1.92 (m, 20H, CH_2), 2.58 (s, 3H, CH_3), 2.60 (s, 3H, CH_3), 2.89–2.93 (m, 2H, CH), 7.39–7.47 (m, 4H, CH), 7.39–7.47 (m, 4H, CH), 7.68–7.71 (m, 2H, CH), 7.83–7.86 (m, 2H, CH), 10.72 (Br, 1H, CH); ^{13}C NMR (THF-d8, Me_4Si) δ = 13.18,

19.19, 20.47, 25.88, 26.18, 26.46, 26.66, 29.75, 30.69, 32.22, 128.535, 128.69, 128.86, 130.67, 131.12, 132.75, 166.77. HRMS calcd for $C_{32}H_{38}N_3$ $[M + H]^+$: 464.3066; found: 464.3060. Elemental Analysis Calcd (%) for $C_{32}H_{37}N_3$: C, 82.89; H, 8.04; N, 9.06. Found: C, 82.78; H, 8.20; N, 8.99.

2,4-Diisopropyl-3,7-bis(4-propylphenyl)-1*H*-pyrrolo[3,2-*d*]pyridazine (2-27c): Yellow solid, isolated yield 61 % (134 mg), m.p.: 271–272 °C. ^{1}H NMR (400 MHz, $CDCl_3$, Me_4Si) $\delta = 0.95$–1.21 (m, 6H, $CHMe_2$), 1.25 (*t*, $J = 9.5$ Hz, 6H, $CH_2CH_2CH_3$), 1.67–1.77 (m, 4H, $CH_2CH_2CH_3$), 2.63–2.71 (m, 4H, $CH_2CH_2CH_3$), 3.08–3.15 (m, 2H, $CHMe_2$), 7.26 (s, 4H, C_6H_4), 7.32 (*d*, $J = 8.1$ Hz, 2H, C_6H_4), 7.84 (*d*, $J = 8.0$ Hz, 2H, C_6H_4), 9.00 (Br, 1H, NH); ^{13}C NMR (100.0 MHz, $CDCl_3$, Me_4Si) δ = 13.31, 13.41, 21.45, 22.11, 23.92, 25.35, 29.84, 37.31, 37.41, 113.31, 122.00, 127.55, 127.74, 128.71, 129.00, 130.29, 131.45, 133.10, 141.47, 143.36, 144.79, 145.23, 159.99. HRMS calcd for $C_{30}H_{38}N_3$ $[M + H]^+$: 440.3066; found: 440.3060. Elemental Analysis Calcd (%) for $C_{30}H_{37}N_3$: C, 81.96; H, 8.48; N, 9.56. Found: C, 81.90; H, 8.53; N, 9.47.

Formation of Pyrrolo[2,3-*c*]pyridinone 2-28 from Pyrrole-2,3-diones 2-24 and Hydroxylamine Hydrochloride. In a 20-mL Schlenk tube, hydroxylamine hydrochloride (1.5 mmol, 104 mg) was added to the pyridine solution (10 mL) of compound **2-24a** (180 mg, 0.5 mmol). After the reaction mixture was refluxed for 4 h, the solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, ethyl acetate, and triethylamine (100:20:1) as the eluent to give product **2-28**.

2-Isopropyl-5,5-dimethyl-3,7-diphenyl-1*H*-pyrrolo[2,3-*c*]pyridin-4(5*H*)-one (2-28): Yellow crystal, isolated yield 71 % (126 mg), m.p.: 274–276 °C. ^{1}H NMR ($CDCl_3$, Me_4Si) ^{1}H NMR (300 MHz, $CDCl_3$, Me_4Si) δ = 1.28 (*d*, J = 4.0 Hz, 6H, $CHMe_2$), 1.57 (s, 6H, CMe_2), 3.23–3.30 (m, 1H, $CHMe_2$), 7.30–7.46 (m, 5H, C_6H_5), 7.61–7.63 (m, 3H, C_6H_5), 7.74–7.76 (m, 2H, C_6H_5), 8.27 (Br, 1H, NH); ^{13}C NMR (75.4 MHz, $CDCl_3$, Me_4Si) δ = 22.76, 24.92, 26.96, 69.54, 118.13, 119.89, 127.04, 127.39, 127.85, 129.43, 130.00, 130.15, 130.52, 132.98, 136.97, 140.13, 152.88, 201.55. IR (film): 1,648 cm^{-1}. HRMS calcd for $C_{24}H_{25}N_2O$ $[M + H]^+$: 357.1967; found: 357.1962. Elemental Analysis Calcd (%) for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.79; N, 7.86. Found: C, 80.81; H, 6.86; N, 7.86. Single crystals of **2-28** suitable for X-ray analysis were grown in dichloromethane/ethyl acetate (1:1) at room temperature for one day.

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Chapter 3
Bulky Nitrile Coordination-Induced Skeleton Rearrangement of Zr-/Si-Containing Metallacycles and Selective Synthesis of 5-Azaindoles

3.1 Introduction

Among the most fundamental reactions of organometallic compounds, the reaction initiated by the incoming coordinating ligand (**L**) is central to virtually all organometallic reactions of great significance for organic synthesis [1]. In particular, besides commonly observed ligand substitution, the coordination of the ligand (**L**) may greatly alter the steric and electronic environment around the metal center and thus activates the whole compound, resulting in novel skeletal rearrangement or cleavage of chemical bonds (Fig. 3.1) [2–4]. Depending on its steric or electronic property, the **L** may behave as a brake handle to stabilize the **L**-coordinated complexes. When the coordinating **L** is substituted by a different substrate (**S**), the whole complex will become reactive again (Fig. 3.1). Consequently, in this way, the reactivity-control, synthetic application and otherwise unavailable reaction patterns can be expected. The steric and electronic match (or cooperation) between the **[M]** and the **L** is essential to realize such a process [5–11].

The zirconacyclobutene–silacyclobutene-fused compound **3-1** could be readily generated in high yields from the zirconocene-mediated reaction of its corresponding Si-tethered diyne **3-3** [12, 13]. Because of its concomitance of two Zr–C bonds and two Si–C bonds in the skeleton, this compound **3-1** is structurally unique and should display novel reaction chemistry and synthetic applications.

In Chap. 2, the author disclosed zirconocene-mediated cyclization of bis(alkynyl)silanes, nitriles, and unsaturated compounds. The reactive intermediates involving two or three molecules of nitriles were isolated and characterized. Thus, the author expects to further isolate the one molecule of nitrile involved intermediate and demonstrates the reaction mechanism toward the formation of Zr-/Si-containing three-ring fused intermediates (Scheme 3.1). The author tried to use only one equivalents of nitrile, lower the reaction temperature, and quench the reaction mixture generated in situ or trap with electrophiles. However, all these attempts failed, and the isolation and characterization of one-nitrile-involved intermediates

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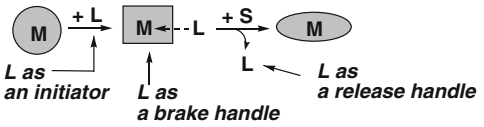
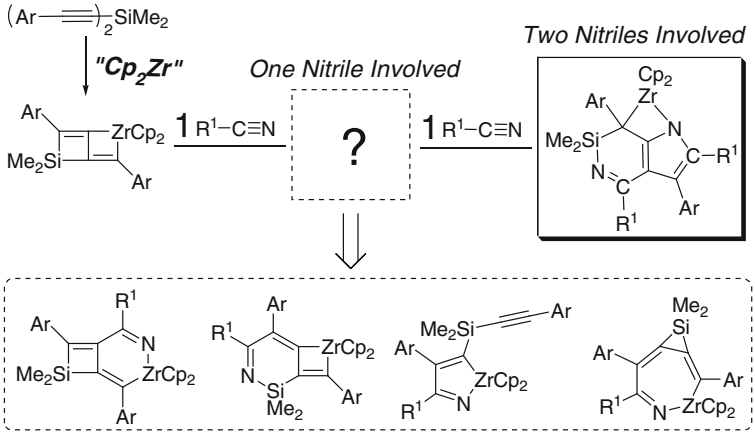


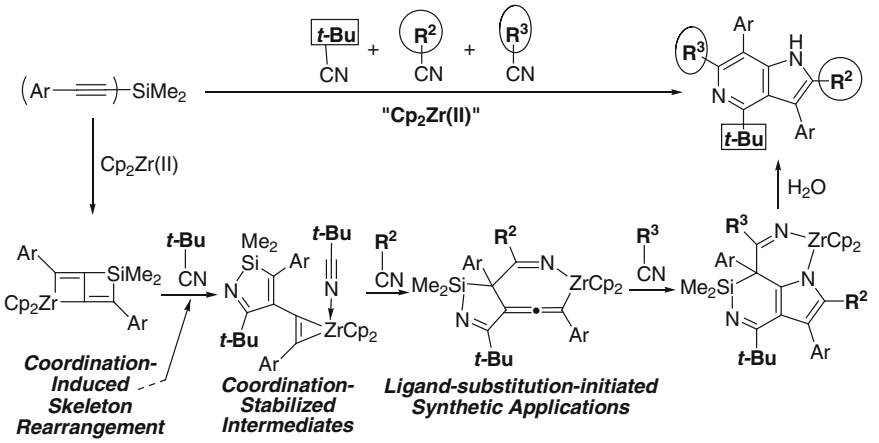
Fig. 3.1 An coordination-induced initiating–braking–releasing process model of organometallic complexes: An incoming ligand (**L**) behaves as both an initiator and a brake/release handle. The different shapes around the metal center indicate different structure and bonding



Scheme 3.1 Proposed structure of one-nitrile-involved reactive intermediate in zirconocene-mediated cyclization of bis(alkynyl)silanes and nitriles

were not successful, probably because the presumed one nitrile involved intermediate was unstable and the activation barrier for the further reaction with the second nitrile was quite low at the reaction temperature.

Trimethylacetonitrile (*t*-BuCN) as a steric bulky nitrile might prevent the further reaction of one nitrile involved intermediate with the second nitrile. The coupling reaction of intermediates **3-1** and *t*-BuCN in situ generated the *t*-BuCN-stabilized zirconacyclopropene–azasilacyclopentadiene complexes **3-2** in high yields, via a coordination-induced Zr–C/Si–C bond cleavage and reorganization. Complexes **3-2** have shown various synthetically useful reaction patterns. A variety of novel Zr/Si organo-*bi*-metallic compounds and Si/N heterocyclic compounds, such as azasilacyclopentadienes, azasilacyclohexadienes, and allenyl-aza-zirconacycles, were obtained in high yields. The reaction pathway of coupling of complex **3-1** with bulky nitriles was different from the reaction with less-bulky nitriles, which behaved as "chemical transformer" reactivity. In this chemistry, bulky *t*-BuCN behaved as both an initiator and a brake/release handle to initiate and control the reaction process. Based on the reaction chemistry of complexes **3-2** and two different molecules of nitrile, the author investigated zirconocene-mediated



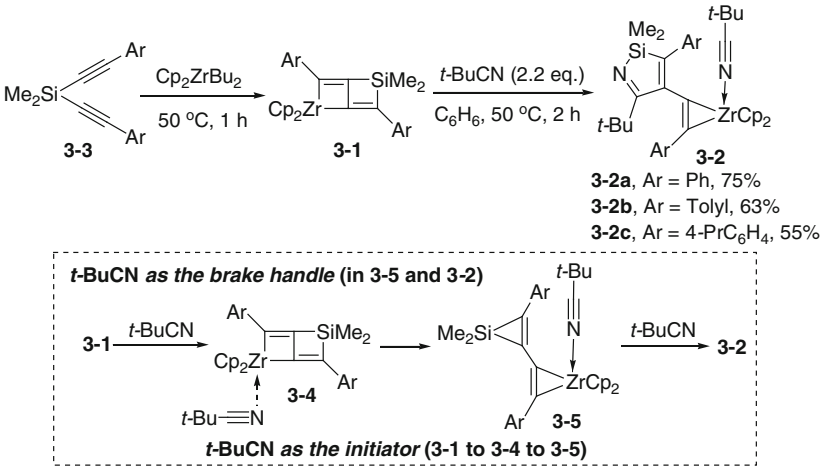
Scheme 3.2 Bulky nitrile coordination-induced skeleton rearrangement of Zr-/Si-containing metallacycles and selective synthesis of 5-azaindoles

multi-component coupling of bis(alkynyl)silanes and three different nitriles toward synthesis of 5-azaindoles with different substituents at 2,4,6-positions. The reactive intermediates involving one, two, and three molecules of nitriles were all isolated and well characterized, which clearly showed the positions of three different nitriles and the regioselectivity (Scheme 3.2).

3.2 Results and Discussion

3.2.1 Bulky Nitriles Coordination-Induced Skeleton Rearrangement of Zirconacyclopropene–Azasilacyclopentadiene Complexes

Based on the proposed reaction mechanism, bulky trimethylacetonitrile (*t*-BuCN) was subjected to the reaction with reactive intermediate **3-1**. When we treated **3-1** with 2 equivalents of *t*-BuCN, the reaction mixture turned out to be a suspension. An unprecedented skeletal rearrangement took place to afford the compounds **3-2** in 55–75 % isolated yields (Scheme 3.3). An X-ray analysis of **3-2b** unambiguously revealed the structure of the C_{sp2}–C_{sp2} linked zirconacyclopropene–azasilacyclopentadiene (Fig. 3.2). The dihedral angle of 88.10° between the two cyclic planes demonstrates a near perpendicular conformation. The azasilacyclopentadiene species, though structurally and chemically interesting, are very rare in terms of synthetic methods and reaction chemistry study. This transformation of silacyclobutenes to azasilacyclopentadienes represents an unprecedented and useful reaction pattern of silacycles [14, 15].



Scheme 3.3 *t*-BuCN-induced formation of zirconacyclopropene–azasilacyclopentadienes **3-2**

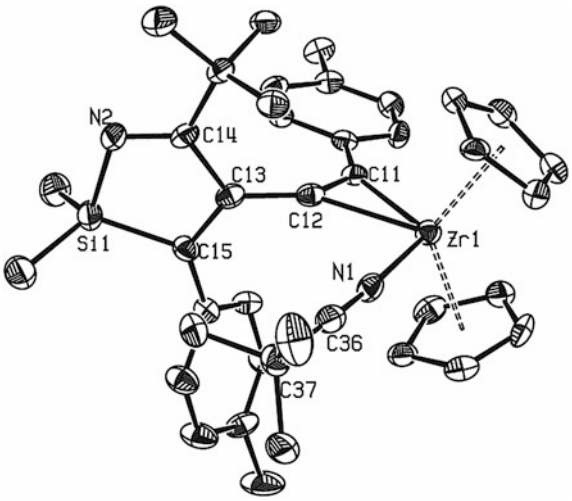


Fig. 3.2 ORTEP drawing of **3-2b** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond length (Å): Zr1–C11 2.197(6), Zr1–C12 2.289(7), C11–C12 1.322(8), C12–C13 1.480(9), C13–C15 1.358(9), C13–C14 1.547(8), C14–N2 1.281(8), Si1–C15 1.875(7), Si1–N2 1.760(6), C36–N1 1.150(9). Reprinted with the permission from Ref. [16]. Copyright 2010 American Chemical Society

A proposed mechanism involving coordination-induced formation of silacyclopropene–zirconacyclopropene species **3-5** is given in (Scheme 3.3). Zirconacyclopropene species is known to be very reactive. However, in this case, one *t*-BuCN is coordinated to the zirconium center and thus deactivates the

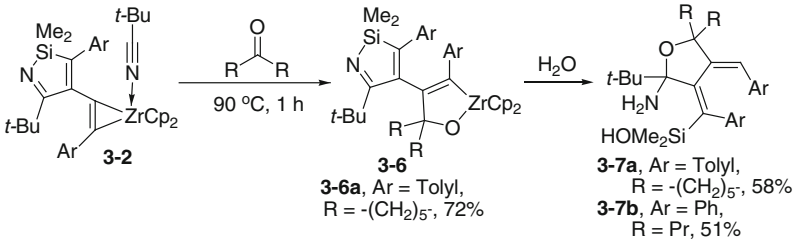
zirconacyclopropene moiety. A second *t*-BuCN inserted into the C–Si bond of the reactive silacyclopropene moiety in **3-5** to form the azasilacyclopentadiene moiety in **3-2** [14].

This successful transformation could be attributed to the strong coordinating ability and the steric effect of *t*-BuCN (as the **L** in Scheme 3.1). *t*-BuCN behaved as both an initiator and a brake handle [17, 18]. The reactivity of the resulted zirconacyclopropene moiety in **3-2** was controlled (or shut down) by the coordinating *t*-BuCN.

3.2.2 Reaction and Synthetic Application of Zirconacyclopropene–Azasilacyclopentadiene Complexes: Reactions of the Zirconacyclopropene Moiety

The compound **3-2** has been demonstrated to be indeed very reactive and synthetically useful. Whenever the coordinating *t*-BuCN, functioning as the brake handle in **3-2**, is substituted by a different substrate (as the **S** in Scheme 3.1), the stabilized zirconacyclopropene moiety will become reactive and thus generates diversified zirconacycles (Scheme 3.3) or even initiates the whole molecule including the azasilacyclopentadiene moiety to undergo further reactions generating heterocycles of novel structures (Scheme 3.4).

In the reactions of **3-2** with different substrates such as ketone, carbodiimide, alkyne, element sulfur, CO, and iodine, the zirconacyclopropene moiety is independently involved and the azasilacyclopentadiene moiety in **3-2** does not participate in these cases. Firstly, ketones were used to substitute the coordinating *t*-BuCN. Selective insertion of the C=O double bond into the zirconacyclopropene ring afforded the corresponding oxazirconacyclopentene derivative **3-6** (Scheme 3.4) [19]. The compound **3-6a** was isolated in 72 % yield, and its structure was determined by single-crystal X-ray structural analysis. Although the azasilacyclopentadiene moiety did not participate in this transformation, however, the cooperation



Scheme 3.4 Reaction of **3-2** with ketones and hydrolysis of the resulting intermediates

between the azasilacycle and the zirconacycle resulted in an unprecedented cyclization chemistry upon hydrolysis. Hydrolysis of **3-6** afforded the butadiene-fused aminotetrahydrofuran derivatives **3-7**, which are useful but not accessible by other means [20] (Fig. 3.3).

Similarly, selective insertion of a C=N double bond of *N*,*N*′-diisopropylcarbodiimide was also observed to afford the complex **3-8** in 86 % isolated yield [21]. In addition to the above C=O and C=N double bond insertion reactions, the C≡C triple bond of alkynes was also found to react smoothly and selectively with the

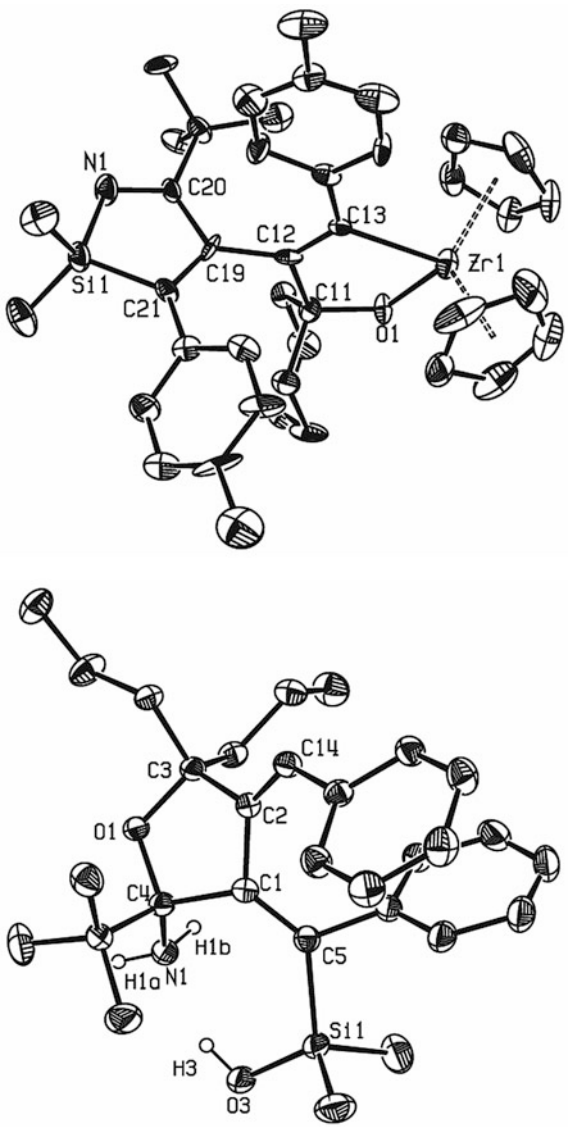
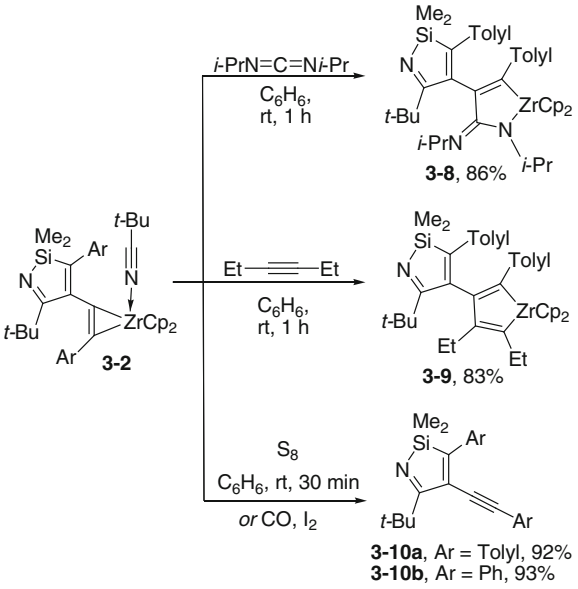


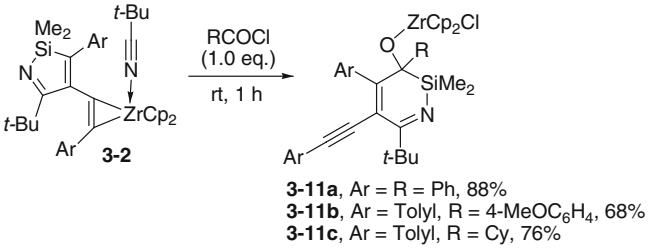
Fig. 3.3 X-ray structures of **3-6a** and **3-7b**. Reprinted with the permission from Ref. [16]. Copyright 2010 American Chemical Society



Scheme 3.5 Reactions of **3-2** with carbodiimide, alkyne, element sulfur, CO, and I_2

zirconacyclopropene moiety to afford its corresponding zirconacyclopentadiene derivative **3-9** (Scheme 3.5) [22].

The reaction of **3-2** with elemental sulfur (S_8) resulted in demetallation of **3-2** to afford the alkynyl azasilacyclopentadienes **3-10** in excellent yields (Scheme 3.6). The structure of **3-10a**, as the first case of azasilacyclopentadiene derivatives [23], was determined by single-crystal X-ray structural analysis. As far as we know, no other method could efficiently afford alkynyl azasilacyclopentadienes. Compound **3-10** was also obtained when **3-2** was treated with CO or I_2.



Scheme 3.6 Reaction of **3-2** with acid chlorides

3.2.3 *Reaction and Synthetic Application of Zirconacyclopropene–Azasilacyclopentadiene Complexes: Reactions Involving Both the Zirconacycle and Silacycle Moiety*

3.2.3.1 Reaction of 3-2 with Acid Chloride

In the reactions of **3-2** with acid chlorides, the whole molecule **3-2** including the azasilacyclopentadiene moiety was involved the reaction initiated by the substitution of the coordinating *t*-BuCN with other substrates. The reaction of **3-2** with acid chloride gave the formally silacycle-ring expansion products azasilacyclohexadienes **3-11** in good to excellent isolated yields. The single-crystal structure of **3-11a** confirmed its 6-membered silacycle bonding with the oxychlorozirconocene moiety (Fig. 3.4). Both aromatic and aliphatic acid chlorides showed high efficiency. To the best of our knowledge, this is the first example of such aza-silacyclic skeletons. The isolated azasilacyclopentadienes **3-10** did not show any reaction with RCOCl. Thus, we assume the RCOCl replace the coordinating *t*-BuCN and react with the zirconacyclopropene moiety as the first step. The azasilacyclopentadiene moiety then takes part (or cooperates) in a further skeletal rearrangement to generate **3-11** (Scheme 3.6).

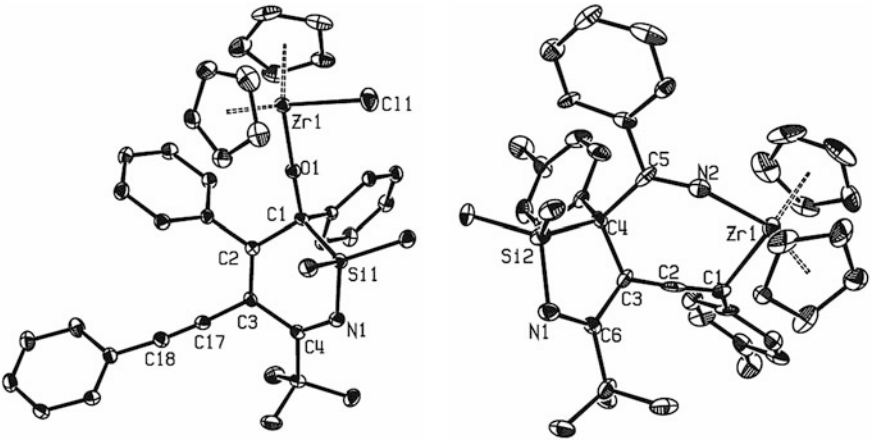


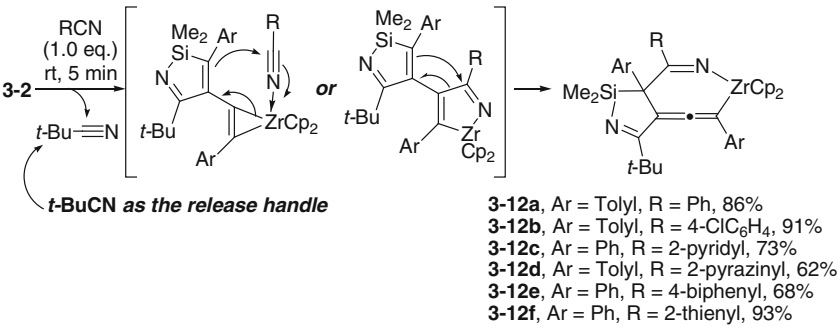
Fig. 3.4 ORTEP drawing of **3-11a** (on the *left*) and **3-12a** (on the *right*) with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond length (Å) and angles (°): **3-11a**: Zr1–O1 1.938(2), Si1–C1 1.919(4), Si1–N1 1.744(3); C2–C3 1.367(5), C17–C18 1.203(5), C4–N1 1.275(5); **3-12a**: Zr1–C1 2.379(13), Zr1–N2 2.032(10), C1–C2 1.331(17), C2–C3 1.365 (18), C3–C4 1.521(15), C5–N2 1.292(13), C6–N1 1.295(14), C1–C2–C3 175.7(13). Reprinted with the permission from Ref. [16]. Copyright 2010 American Chemical Society

3.2.3.2 Reaction of 3-2 with Second Molecule of Nitrile

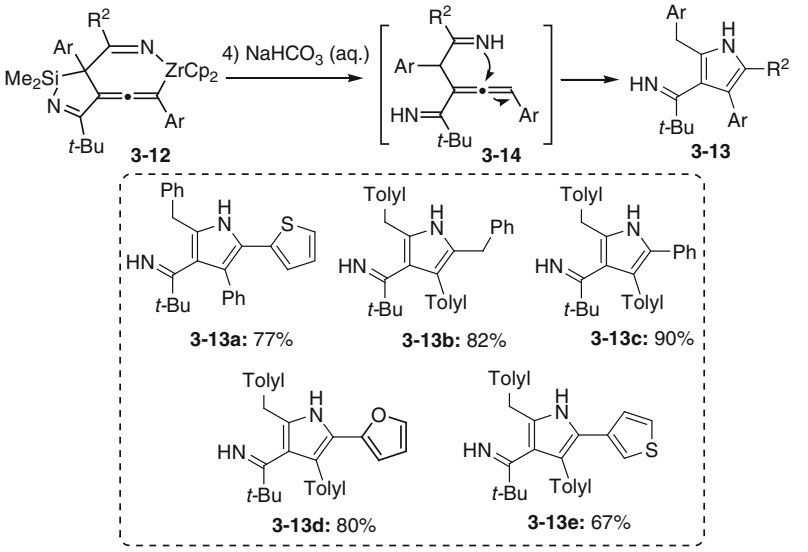
The cooperative effect between the azasilacyclopentadiene moiety and the zirconacycle showed unexpected and very interesting impact on the reaction of **3-2** with nitriles. Based on the above discussion, the complex **3-2** could be considered as reactive intermediate of **3-1** with one molecule of nitrile. When **3-2** was further treated with the second molecule of nitrile, the incoming nitrile substituted the *t*-BuCN and initiated an unprecedented reaction process. As shown in Scheme 3.7, the reaction of PhCN with **3-2b** resulted in the formation of **3-12a** in 86 % isolated yield [24–28]. The structure of **3-12a**, unambiguously confirmed by single-crystal X-ray structural analysis (Fig. 3.4), featured a 5-membered azasilacyclopentene-fused 7-membered azazirconacycle incorporating an allenyl moiety. This is the first synthesis and well-defined cyclic allenyl azazirconocene complex [24–28]. The angle of C1–C2–C3 was measured as 175.7°, while the bond length of C1–C2 and C2–C3 is 1.331(17) and 1.365(18) Å, respectively, showing its slightly bent allene nature. The singlet at 193.4 ppm of **3-12a** in its ^{13}C NMR spectrum in [D_6]benzene confirmed its *sp*-hybrided allenic carbon character, which is well comparable with reported allenyl zirconocene complexes [24–28]. A variety of aromatic and heteroaromatic nitriles could be used to form complexes **3-12** in high yields. A proposed reaction mechanism is given in **3-7**.

The reaction of **3-2** with the second molecule of nitrile does not give three-ring fused reactive intermediate **2-6** in Chap. 2, which was isolated and identified as intermediates of complex **3-1** with two molecules of less-bulky nitrile. Despite zirconacycle **3-12** could also be considered as product of **3-1** with two molecules of nitrile, however, the generation pathway toward **3-12** is totally different from the one of **2-6**. The different reaction pathways of **3-1** and nitriles could be attributed to different steric bulkiness and electronic effect of nitriles.

When the allenyl-aza-zirconacycle **3-12**, generated in situ from two different organonitriles and a Si-tethered diyne, was hydrolyzed with water, a wide variety of iminopyrrole derivatives **3-13a**–**3-13e** were obtained in 67–90 % yields



Scheme 3.7 A proposed mechanism for the formation of cyclic allenyl zirconocene complexes **3-12**

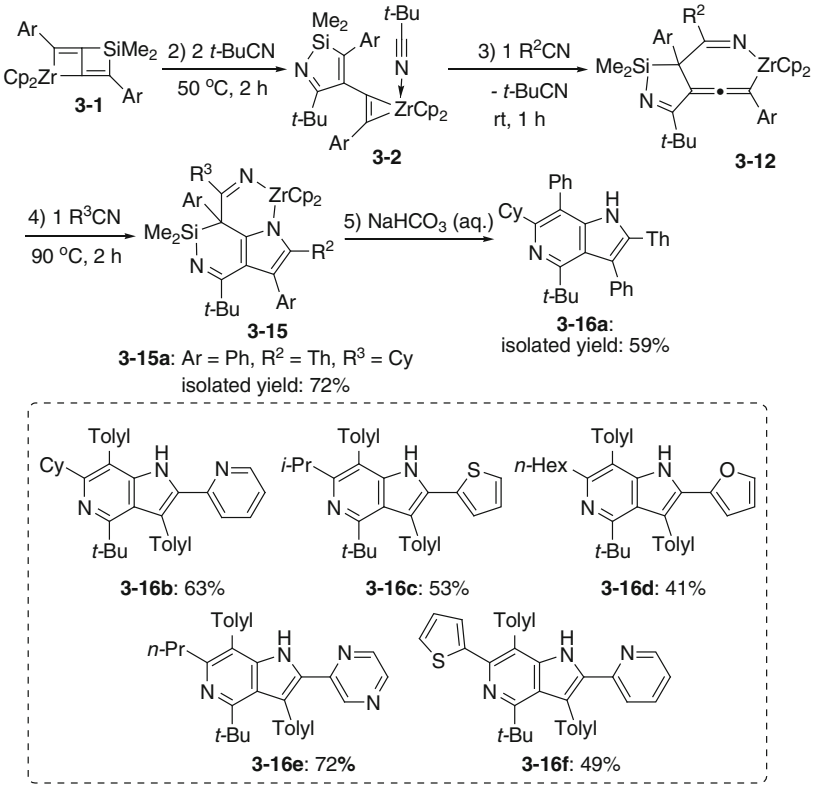


Scheme 3.8 Formation of iminopyrroles with all different substituents via hydrolysis of allenyl-aza-zirconacycles **3-12**

(Scheme 3.8). These types of pyrroles **3-13** are functionalized with an imino group and are substituted with all different substituents. The formation of **3-13** was proposed via the nucleophilic attack-induced hydroamination cyclization of the iminoallene species **3-14** [29–31].

3.2.3.3 Reactions of Intermediate 3-2 with the Second and Third Molecules of Nitrile: Formation of 5-Azaindoles from One Si-Tethered Diyne, One *t*-BuCN, and Two Identical or Different Organonitriles

The reactive intermediates **3-12**, as the fate in the reaction of **3-2** with the second nitrile, was found to further react with the third nitrile. When the in situ generated allenyl-aza-zirconacycle **3-12f** (Ar = Ph, R^2 = Th) was treated with a third organonitrile CyCN at 90 °C in benzene for 1 h, the reaction afforded the three-ring fused Zr-/Si-containing compound **3-15a** (Ar = Ph, R^2 = Th, R^3 = Cy) in 72 % isolated yield (Scheme 3.9). The structure of **3-15a** was characterized by X-ray single-crystal structural analysis (Fig. 3.5), which clearly showed the positions of the three different nitriles. Hydrolysis of **3-15a** afforded the 5-azaindole derivative **3-16a** in 59 % isolated yield. The structure of **3-16a** was confirmed by X-ray single-crystal structural analysis (Fig. 3.5). The *t*-Bu group from the first nitrile was fixed at position 4, while the thienyl group from the second nitrile was found at position 2 on the pyrrole ring, and the cyclohexyl group from the third nitrile was bonded at



Scheme 3.9 Formation of 5-azaindoles with three different substituents at positions 2,4,6

position 6 on the pyridine ring. In addition to CyCN, other organonitriles either aromatic or aliphatic could be also applied as the third different organonitrile to afford 5-azaindoles **3-16b**–**3-16f** in good to high yields upon hydrolysis of the reaction mixture. In all these cases, only one regioisomer was obtained. These results clearly demonstrate that 5-azaindoles are substituted with three different substituents at positions 2,4,6.

When the second nitrile and the third nitrile are the same, the 5-azaindole could be generated directly from the intermediate **3-2** with two identical nitriles. Treatment of **3-2a** (Ar = Ph) with 2 equivalents of CyCN at 90 °C in benzene for 1 h afforded the three-ring fused compound **3-17a** (Ar = Ph, R^2 = Cy) in 81 % isolated yield (Scheme 3.10). The X-ray structure of **3-17a** revealed clearly the *t*Bu group was located on the 6-membered azasilacycle, adjacent to the *N*-silyl imine moiety (Fig. 3.6). Hydrolysis of **3-17a** afforded the 5-azaindole derivative **3-18a** in 69 % isolated yield. In addition to CyCN, other organonitriles such as the aromatic organonitrile 2-ThCN and the aliphatic organonitriles *i*-PrCN and *n*-PrCN could be also applied to afford 5-azaindoles **3-18b**–**3-18e** in good to high yields, respectively, with the same substituents (R^2) at positions 2,6 and a different substituent

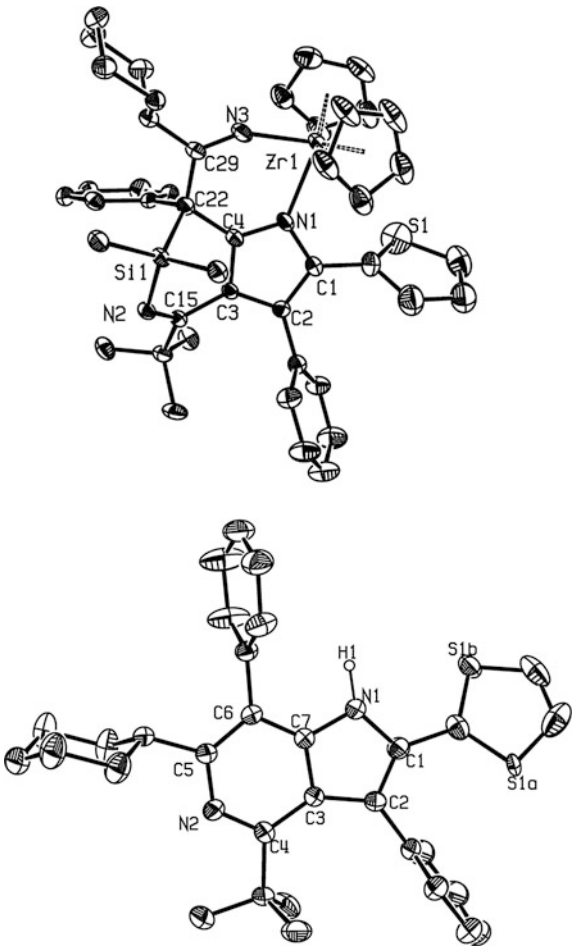
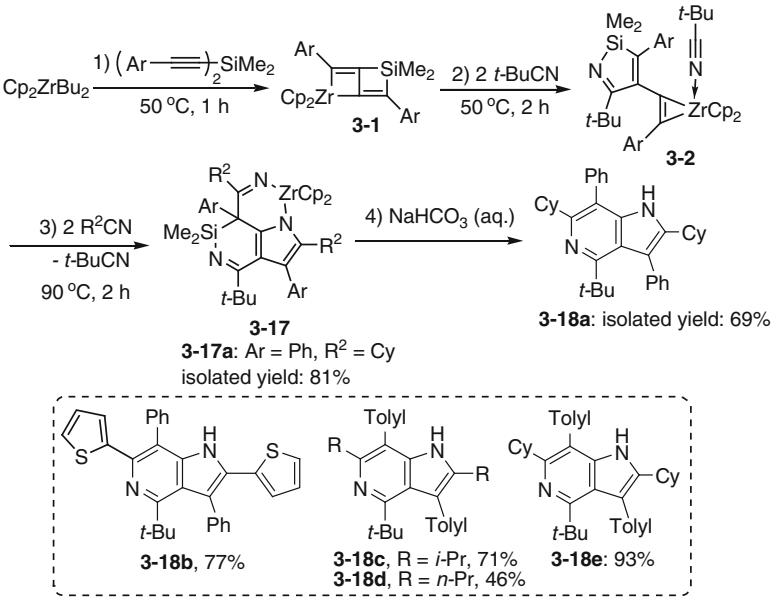


Fig. 3.5 ORTEP drawings of **3-15a** and **3-16a** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity except polar N–H bond. Reproduced from Ref. [32] by permission of John Wiley and Sons Ltd.

(*t*-Bu) at position 4. The X-ray single-crystal structure of **3-18c** (Fig. 3.6) again confirmed the *t*-Bu group being bonded at position 4 of the azaindoles, and the two cyclohexyl groups at positions 2,6 of the azaindoles.

Based on the above experimental evidences, a possible mechanism for the formation of **3-15** or **3-17** from **3-2** is proposed and shown in Scheme 3.11. For the first step, one R^2CN is proposed to replace the bulky *t*-BuCN and revive the reactivity of the zirconacyclopropene moiety. The coordinating R^2CN, which is generally smaller than *t*-BuCN, may insert into the zirconacyclopropene moiety in **3-2** and generate the allenyl-aza-zirconacycle **3-12**. The third R^3CN may then insert into the Zr–C bond of the allenyl-aza-zirconacycle **3-12** to generate a nine-membered allenyl-aza-zirconacycle **3-19**. This cyclic intermediate **3-19** is unstable and would undergo intramolecular nucleophilic attack or via 1,3-silyl shift to give the final three-ring fused compound **3-15**. When $R^2 = R^3$, it gives the corresponding compound **3-17**.



Scheme 3.10 Formation of 5-azaindoles with the same substituents at positions 2,6 and a different substituent at position 4

3.3 Summary

Bulky nitrile coordination-induced Zr–C/Si–C bond cleavage and reorganization of zirconacyclobutene–silacyclobutene complex **3-1**, affording zirconacyclopropene–azasilacyclopentadiene complexes **3-2** as only one nitrile involved intermediate. The experimental results showed that the reaction pathways of **3-1** with bulky nitrile and less-bulky nitriles were different, which behaved as "chemical transformer" reactivity. Complexes **3-2** have shown various synthetically useful reaction patterns. A variety of novel Zr/Si organo-*bi*-metallic compounds and Si/N heterocyclic compounds, such as azasilacyclopentadienes, azasilacyclohexadienes, and allenyl-aza-zirconacycles, were obtained in high yields. Based on the reaction chemistry of complexes **3-2** and two different molecules of nitrile, the author investigated zirconocene-mediated multi-component coupling of bis(alkynyl) silanes and three different nitriles toward synthesis of 5-azaindoles with different substituents at 2,4,6-positions. The reactive intermediates involving one, two, and three molecules of nitriles were all isolated and well characterized, which clearly showed the positions of three different nitriles and the regioselectivity (Scheme 3.12).

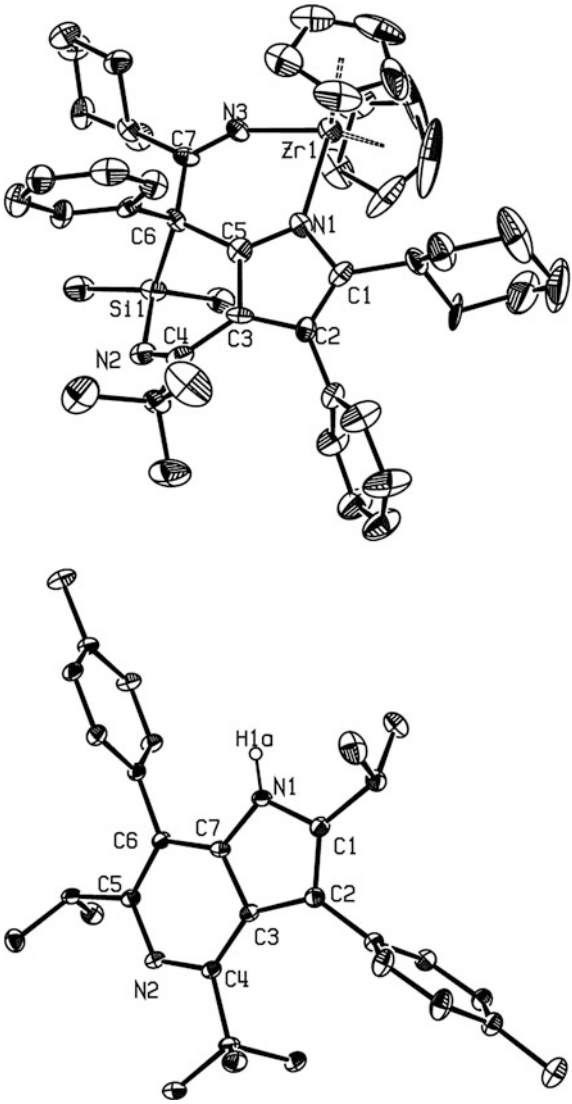
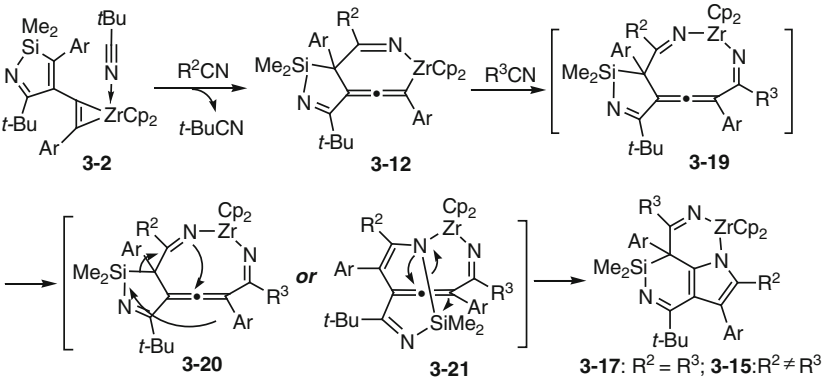


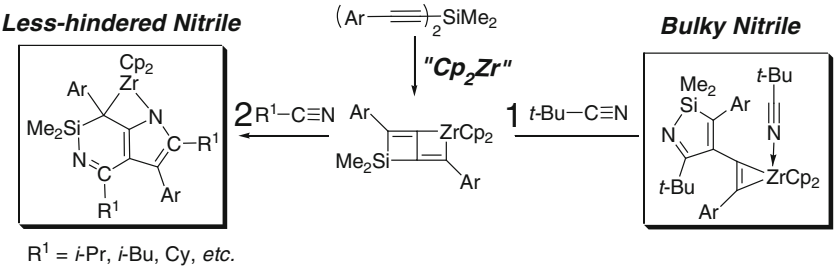
Fig. 3.6 ORTEP drawings of **3-17a** and **3-18c** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reproduced from Ref. [32] by permission of John Wiley and Sons Ltd.

3.4 Experimental Section

All reactions were conducted under a slightly positive pressure of dry nitrogen using standard Schlenk line techniques or under a nitrogen atmosphere in a Mikrouna Super (1220/750) glove box. The nitrogen in the glove box was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glove box atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure both were always below 1 ppm. Unless otherwise noted,



Scheme 3.11 Proposed mechanism



Scheme 3.12 Reaction mode of Zr-/Si-containing intermediates with bulky nitrile or less-bulky nitrile

all starting materials were commercially available and were used without further purification. Solvents were purified by an Mbraun SPS-800 Solvent Purification System and dried over fresh Na chips in the glove box.

Organometallic samples for NMR spectroscopic measurements were prepared in the glove box by use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer (FT, 400 MHz for ^{1}H; 100 MHz for ^{13}C) or a JEOL-AL300 spectrometer (FT, 300 MHz for ^{1}H; 75 MHz for ^{13}C) at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Microelemental analyses were performed on an Elemental Analyzer vario EL apparatus.

Isolation of Zirconacyclobutene–Silacyclobutene Fused Complex 3-1c: To a toluene (10 mL) solution of Cp_2ZrCl_2 (307 mg, 1.05 mmol) at –78 °C (dry ice/acetone bath) in a 20-mL Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 mL) with a syringe. After the addition was complete, the reaction mixture was stirred at –78 °C for 1 h. Then, bis(4-propylphenylethynyl) dimethylsilane (346 mg, 1 mmol) was added, and the reaction mixture was warmed up to

50 °C and stirred at this temperature for 3 h. The reaction mixture was dried up under vacuum, and the residue was extracted with hexane. The precipitated LiCl was separated using a frit under a nitrogen atmosphere. The clear filtrate was reduced under vacuum to precipitate **3-1c** as orange powder, which was recrystallized at –40 °C to give orange solid in 88 % isolated yield. ^{1}H NMR (400 MHz, C_6D_6): δ = 0.53 (s, 6H, $SiMe_2$), 0.95 (t, J = 7.2 Hz, 6H, $CH_2CH_2CH_3$), 1.66 (m, 4H, $CH_2CH_2CH_3$), 2.60 (t, J = 7.2 Hz, 4H, $CH_2CH_2CH_3$), 5.58 (s, 10H, C_5H_5), 7.29 (d, J = 8.0 Hz, 2H, C_6H_4), 7.33 (d, J = 8.0 Hz, 2H, C_6H_4), 7.68 (d, J = 8.0 Hz, 2H, C_6H_4), 7.92 (d, J = 8.0 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = 0.72, 14.44, 14.51, 25.57, 25.58, 38.75, 38.83, 106.82, 127.75, 129.46, 129.69, 130.84, 139.48, 140.72, 142.42, 142.52, 162.24, 203.14.

Isolation of Zirconacyclopropene–Azasilacyclopentadiene Complex 3-2a: In a 20-mL Schlenk tube, trimethylacetonitrile (221 μl, 2.0 mmol) was added to the benzene solution (1 mL) of compound **3-1a** (480 mg, 1.0 mmol). After the reaction mixture was stirred at 50 °C for 2 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **3-2a** as bright yellow powder (477 mg, 75 %). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.42 (s, 3H, $SiMe_2$), 0.61 (s, 3H, $SiMe_2$), 0.93 (s, 9H, CMe_3), 1.65 (s, 9H, CMe_3), 5.31 (s, 5H, C_5H_5), 5.91 (s, 5H, C_5H_5), 6.99 (d, J = 6.9 Hz, 2H, C_6H_5), 7.13 (m, 3H, C_6H_5), 7.57 (t, J = 7.5 Hz, 3H, C_6H_5), 7.81 (d, J = 6.9 Hz, 2H, C_6H_5).

Isolation of Zirconacyclopropene–Azasilacyclopentadiene Complex 3-2b: In a 20-mL Schlenk tube, trimethylacetonitrile (221 μl, 2.0 mmol) was added to the benzene solution (1 mL) of compound **3-1b** (510 mg, 1.0 mmol). After the reaction mixture was stirred at 50 °C for 2 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **3-2b** as bright yellow powder (424 mg, 63 %). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.47 (s, 3H, $SiMe_2$), 0.66 (s, 3H, $SiMe_2$), 0.92 (s, 9H, CMe_3), 1.68 (s, 9H, CMe_3), 2.09 (s, 3H, Me), 2.29 (s, 3H, Me), 5.33 (s, 5H, C_5H_5), 5.93 (s, 5H, C_5H_5), 6.92 (d, J = 7.8 Hz, 2H, C_6H_4), 7.08 (d, J = 7.8 Hz, 2H, C_6H_4), 7.38 (d, J = 7.5 Hz, 2H, C_6H_4), 7.75 (d, J = 7.8 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −3.32, −2.38, 21.01, 21.40, 27.60, 28.90, 42.23, 105.94, 106.15, 128.02, 128.17, 129.01, 129.50, 131.44, 133.31, 134.78, 135.65, 136.63, 138.62, 139.60, 140.01, 162.45, 167.97, 183.93, 191.68. Single crystals of **3-2b** suitable for X-ray analysis were grown in benzene/hexane (1:2) at room temperature.

Isolation of Zirconacyclopropene–Azasilacyclopentadiene Complex 3-2c: In a 20-mL Schlenk tube, trimethylacetonitrile (221 μl, 2.0 mmol) was added to the benzene solution (1 mL) of compound **3-1c** (566 mg, 1.0 mmol). After the reaction mixture was stirred at 50 °C for 2 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to precipitate **3-2c** as bright yellow powder (396 mg, 55 %). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.35 (s, 3H, $SiMe_2$), 0.55 (s, 3H, $SiMe_2$), 0.71 (t, J = 7.2 Hz, 3H, $CH_2CH_2CH_3$), 0.83 (s, 9H, CMe_3), 0.92 (t, J = 7.2 Hz, 3H, $CH_2CH_2CH_3$), 1.37 (m, 2H, $CH_2CH_2CH_3$), 1.56 (s, 9H, CMe_3), 1.66 (m, 2H, $CH_2CH_2CH_3$), 2.28 (t, J = 7.2 Hz,

2H, $CH_2CH_2CH_3$), 2.60 (t, J = 7.2 Hz, 2H, $CH_2CH_2CH_3$), 5.22 (s, 5H, C_5H_5), 5.83 (s, 5H, C_5H_5), 6.84 (d, J = 8.0 Hz, 2H, C_6H_4), 7.00 (d, J = 8.0 Hz, 2H, C_6H_4), 7.34 (d, J = 8.0 Hz, 2H, C_6H_4), 7.70 (d, J = 8.0 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = −2.83, −1.88, 14.40, 14.70, 25.40, 25.43, 28.11, 29.42, 31.21, 38.48, 38.87, 42.70, 106.44, 106.62, 128.64, 128.92, 129.33, 131.92, 133.84, 137.15, 139.48, 140.27, 140.37, 141.05, 141.49, 162.94, 168.70, 184.46, 192.20.

Isolation of Oxazirconacyclopentene–Azasilacyclopentadiene Complex 3-6a: In a 20-mL Schlenk tube, cyclohexanone (51 μl, 0.5 mmol) was added to the benzene solution (3 mL) of compound **3-2b** (337 mg, 0.5 mmol). After the reaction mixture was stirred at 90 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the filtrate was dried up under vacuum to precipitate **3-6a** as bright yellow powder (248 mg, 72 %). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.49 (s, 3H, $SiMe_2$), 0.77 (s, 3H, $SiMe_2$), 1.29–1.82 (m, 10H, C_6H_{10}), 1.87 (s, 9H, CMe_3), 2.19 (s, 3H, Me), 2.31 (s, 3H, Me), 6.33 (s, 5H, C_5H_5), 6.39 (s, 5H, C_5H_5), 7.16–7.31 (m, 6H, C_6H_4), 7.75 (d, J = 8.1 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.50, −2.07, 21.12, 21.29, 22.35, 22.42, 25.95, 26.33, 32.36, 36.40, 36.54, 92.31, 113.27, 113.30, 128.72, 128.78, 129.20, 129.35, 130.45, 135.36, 136.74, 138.79, 144.71, 154.75, 155.87, 164.19, 183.38, 194.01. Single crystals of **3-6a** suitable for X-ray analysis were grown in benzene/hexane (1:1) at room temperature.

Formation of Aminotetrahydrofuran Derivatives 3-7 from Complexes 3-2 and Ketones. A General Procedure for Preparation of ((*Z*)-((*E*)-2-Amino-2-*tert*-butyl-4- (4-methylbenzylidene)-1-oxaspiro[4.5]decan-3-ylidene)(p-tolyl)methyl) dimethylsilanol (3-7a): In a 20-mL Schlenk tube, a ketone (0.5 mmol, 1.0 eq.) was added to the benzene solution (3 mL) of compound **3-2** (318 mg for **3-2a**, 337 mg for **3-2b**, 0.5 mmol). After the reaction mixture was stirred at 90 °C for 1 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using petroleum ether, diethyl ether, and triethylamine (100:15:1) as the eluent to give product **3-7a**.

((*Z*)-((*E*)-2-Amino-2-*tert*-butyl-4-(4-methylbenzylidene)-1-oxaspiro[4.5]decan-3-ylidene)(*p*-tolyl)methyl)dimethylsilanol (3-7a): Yellow solid, isolated yield 58 % (141 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.35 (s, 3H, $SiMe_2$), 0.30 (s, 3H, $SiMe_2$), 1.22 (s, 9H, CMe_3), 1.50–1.83 (m, 8H, C_6H_{10}), 1.99 (m, 2H, C_6H_{10}), 2.10 (s, 3H, Me), 2.31 (s, 3H, Me), 5.69 (s, 1H, CH), 6.16 (d, J = 8.1 Hz, 1H, C_6H_4), 6.24 (d, J = 8.1 Hz, 1H, C_6H_4), 6.65 (d, J = 7.2 Hz, 1H, C_6H_4), 6.76–6.87 (m, 5H, C_6H_4); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 1.07, 2.08, 20.88, 21.16, 22.02, 22.52, 25.75, 26.59, 35.25, 39.36, 40.11, 79.50, 95.35, 121.80, 126.65, 127.16, 127.83, 128.25, 128.89, 134.00, 134.49, 136.41, 140.68, 145.03, 149.09, 149.27. HRMS: *m/z*: calcd for $C_{31}H_{41}O_2Si$

$[M\text{-}NH_2]^+$: 473.2876, found: 473.2871. Elemental Analysis Calcd (%) for $C_{31}H_{43}NO_2Si$: C, 76.02; H, 8.85; N, 2.86; found: C, 75.83; H, 8.96; N, 2.72.

((*Z*)-((*E*)-2-Amino-4-benzylidene-2-*tert*-butyl-5,5-dipropyldihydrofuran-3(2*H*)-ylidene)(phenyl)methyl)dimethylsilanol (3-7b): Yellow solid, isolated yield 51 % (121 mg). ^{1}H NMR (300 MHz, $CDCl_3$): δ = −0.39 (s, 3H, $SiMe_2$), 0.31 (s, 3H, $SiMe_2$), 0.92–1.97 (m, 14H, C_3H_7), 1.23 (s, 9H, CMe_3), 5.64 (s, 1H, CH), 6.20 (d, J = 7.5 Hz, 1H, C_6H_5), 6.44 (t, J = 7.8 Hz, 1H, C_6H_5), 6.60 (d, J = 7.5 Hz, 1H, C_6H_5), 6.77 (t, J = 7.5 Hz, 1H, C_6H_5), 6.95–7.26 (m, 6H, C_6H_5); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 0.92, 1.92, 14.37, 14.89, 16.83, 17.82, 26.72, 38.13, 40.15, 41.34, 82.77, 95.41, 124.06, 124.75, 126.21, 126.81, 127.07, 127.14, 127.68, 128.36, 128.46, 137.37, 144.00, 144.71, 149.12, 149.88. HRMS: *m/z*: calcd for $C_{30}H_{41}O_2Si$ $[M\text{-}NH_2]^+$: 461.2876, found: 461.2879. Elemental Analysis Calcd (%) for $C_{30}H_{43}NO_2Si$: C, 75.42; H, 9.07; N, 2.93; found: C, 75.31; H, 9.09; N, 2.84. Single crystals of **3-7b** suitable for X-ray analysis were grown in hexane at room temperature.

Isolation of Azazirconacyclopentene–Azasilacyclopentadiene Complex 3-8: In a 20-mL Schlenk tube, *N*,*N*′-diisopropylcarbodiimide (78 μl, 0.5 mmol) was added to the benzene solution (3 mL) of compound **3-2b** (337 mg, 0.5 mmol). After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the filtrate was dried up under vacuum to precipitate **3-8** as orange solid (308 mg, 86 %). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.48 (s, 3H, $SiMe_2$), 0.51 (s, 3H, $SiMe_2$), 1.24 (d, J = 6.0 Hz, 6H, $CHMe_2$), 1.55 (d, J = 5.7 Hz, 6H, $CHMe_2$), 1.78 (s, 9H, CMe_3), 2.19 (s, 3H, Me), 2.28 (s, 3H, Me), 4.32 (m, 1H, $CHMe_2$), 5.85 (s, 5H, C_5H_5), 6.23 (s, 5H, C_5H_5), 6.88 (d, J = 8.1 Hz, 2H, C_6H_4), 7.00 (d, J = 8.1 Hz, 2H, C_6H_4), 7.36 (d, J = 8.1 Hz, 2H, C_6H_4), 7.85 (d, J = 8.4 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.35, −2.58, 20.29, 20.46, 20.76, 23.90, 24.34, 26.91, 27.53, 31.30, 42.06, 49.91, 111.90, 112.97, 125.67, 127.78, 129.00, 130.20, 132.81, 136.27, 136.97, 143.64, 144.85, 150.56, 153.89, 158.39, 191.72, 194.13. Single crystals of **3-8** suitable for X-ray analysis were grown in THF/hexane (1:2) at room temperature.

Isolation of Zirconacyclopentadiene–Azasilacyclopentadiene Complex 3-9: In a 20-mL Schlenk tube, 3-hexyne (55 μl, 0.5 mmol) was added to the benzene solution (3 mL) of compound **3-2b** (337 mg, 0.5 mmol). After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the filtrate was dried up under vacuum to precipitate **3-9** as red solid (279 mg, 83 %). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.57 (s, 3H, $SiMe_2$), 0.60 (s, 3H, $SiMe_2$), 0.89–1.06 (m, 6H, CH_2CH_3), 1.66 (s, 9H, CMe_3), 2.19 (s, 3H, Me), 2.24 (s, 3H, Me), 2.27–2.60 (m, 4H, CH_2CH_3), 6.12 (s, 5H, C_5H_5), 6.29 (s, 5H, C_5H_5), 6.66 (d, J = 7.5 Hz, 2H, C_6H_4), 6.95 (d, J = 7.8 Hz, 2H, C_6H_4), 7.33 (d, J = 7.8 Hz, 2H, C_6H_4), 7.92 (d, J = 8.1 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −3.34, −2.89, 15.45, 15.95, 20.59, 20.83, 25.51, 29.96, 30.13, 42.05, 110.34, 110.68, 126.85, 128.07, 128.18, 128.82, 130.29, 132.49,

136.56, 136.78, 140.46, 142.93, 144.08, 152.24, 153.66, 184.02, 191.69, 198.44. Single crystals of **3-9** suitable for X-ray analysis were grown in benzene/hexane (1:1) at room temperature.

Formation of Alkynyl Azasilacyclopentadienes 3-10 from Complexes 3-2 and Element Sulfur. A General Procedure for the Preparation of 5-*tert*-Butyl-2,2-dimethyl-3-*p*-tolyl-4-(*p*-tolylethynyl)-2*H*-1,2-azasilole (3-10a): In a 20-mL Schlenk tube, element sulfur (0.5 mmol, 16 mg, 1.0 eq.) was added to the benzene solution (3 mL) of compound **3-2** (318 mg for **3-2a**, 337 mg for **3-2b**, 0.5 mmol). After the reaction mixture was stirred at room temperature for 1 h, the reaction mixture was filtered and the filtrate was dried up under vacuum to give product **3-10a**.

5-*tert*-Butyl-2,2-dimethyl-3-*p*-tolyl-4-(p-tolylethynyl)-2*H*-1,2-azasilole(3-10a): Yellow solid, isolated yield 92 % (170 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.47 (s, 6H, $SiMe_2$), 1.88 (s, 9H, CMe_3), 2.11 (s, 3H, Me), 2.23 (s, 3H, Me), 6.97 (d, J = 8.1 Hz, 2H, C_6H_4), 7.17 (d, J = 8.1 Hz, 2H, C_6H_4), 7.54 (d, J = 7.8 Hz, 2H, C_6H_4), 7.99 (d, J = 8.1 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −3.31, 21.31, 28.62, 41.44, 90.00, 99.36, 121.09, 128.54, 128.88, 129.00, 129.44, 129.57, 131.40, 135.66, 138.43, 138.77, 165.30, 187.77. Elemental Analysis Calcd (%) for $C_{25}H_{29}NSi$: C, 80.81; H, 7.87; N, 3.77; Found: C, 80.60; H, 8.00; N, 3.64. Single crystals of **3-10a** suitable for X-ray analysis were grown in benzene/hexane (2:1) at room temperature.

5-*tert*-Butyl-2,2-dimethyl-3-phenyl-4-(phenylethynyl)-2*H*-1,2-azasilole(3-10b): Yellow solid, isolated yield 93 % (159 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.49 (s, 6H, $SiMe_2$), 1.92 (s, 9H, CMe_3), 7.14–7.42 (m, 6H, C_6H_5), 7.58 (t, J = 7.8 Hz, 2H, C_6H_5), 8.00 (d, J = 7.5 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −3.51, 28.53, 41.41, 90.06, 98.92, 123.81, 128.49, 128.66, 128.75, 128.78, 129.63, 131.45, 138.42, 166.23, 187.42. Elemental Analysis Calcd (%) for $C_{23}H_{25}NSi$: C, 80.41; H, 7.34; N, 4.08; found: C, 80.29; H, 7.40; N, 4.00.

A General Procedure for Isolation of Azasilacyclohexadiene Complexes 3-11: In a 20-mL Schlenk tube, acid chloride (0.5 mmol, 1.0 eq.) was added to the benzene solution (3 mL) of compound **3-2** (318 mg for **3-2a**, 337 mg for **3-2b**, 0.5 mmol). After the reaction mixture was stirred at room temperature for 1 h, it was dried up under vacuum and the residue was washed with hexane. After filtering, the solid was dried up under vacuum to give **3-11**.

3-11a: Yellow crystal, isolated yield: 88 % (305 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.69 (s, 3H, $SiMe_2$), 0.84 (s, 3H, $SiMe_2$), 1.69 (s, 9H, CMe_3), 5.79 (s, 5H, C_5H_5), 5.84 (s, 5H, C_5H_5), 7.09–7.49 (m, 13H, C_6H_5), 7.94 (d, J = 7.5 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.86, −1.90, 29.19, 43.49, 87.34, 91.34, 95.68, 114.06, 114.18, 115.70, 119.12, 124.10, 127.46, 127.49, 128.53, 128.56, 128.95, 131.03, 131.24, 139.33, 140.99, 159.12, 182.79. Single crystals of **3-11a** suitable for X-ray analysis were grown in benzene/hexane (1:1) at room temperature.

3-11b: Orange solid, isolated yield: 68 % (255 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.60 (s, 3H, $SiMe_2$), 0.77 (s, 3H, $SiMe_2$), 1.60 (s, 9H, CMe_3), 1.98 (s, 3H,

CMe), 2.23 (s, 3H, CMe), 3.27 (s, 3H, OMe), 5.74 (s, 5H, C_5H_5), 5.75 (s, 5H, C_5H_5), 6.83 (d, J = 6.6 Hz, 4H, C_6H_4), 7.03 (d, J = 8.1 Hz, 2H, C_6H_4), 7.19 (d, J = 8.1 Hz, 4H, C_6H_4), 7.74 (d, J = 8.7 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −4.86, −1.64, 21.26, 21.31, 29.28, 43.47, 54.77, 87.00, 91.02, 95.63, 113.98, 114.12, 118.89, 121.28, 129.41, 130.02, 130.99, 132.88, 136.35, 137.10, 138.30, 158.96, 159.42, 183.06.

3-11c:: Yellow solid, isolated yield: 76 % (280 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.67 (s, 3H, $SiMe_2$), 0.91 (s, 3H, $SiMe_2$), 1.23–2.32 (m, 11H, C_6H_{11}), 1.78 (s, 9H, CMe_3), 2.07 (s, 3H, Me), 2.37 (s, 3H, Me), 5.87 (s, 5H, C_5H_5), 6.00 (s, 5H, C_5H_5), 6.91 (d, J = 7.5 Hz, 2H, C_6H_4), 7.11 (d, J = 8.1 Hz, 2H, C_6H_4), 7.25–7.28 (m, 2H, C_6H_4), 7.142 (d, J = 6.9 Hz, 2H, C_6H_4); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −3.16, 0.76, 21.16, 21.28, 24.91, 25.38, 26.97, 27.54, 27.77, 29.07, 29.21, 30.35, 31.42, 43.29, 49.42, 54.81, 87.67, 90.95, 96.48, 113.78, 114.23, 119.34, 121.34, 128.54, 128.72, 129.23, 130.99, 136.61, 137.71, 138.00, 163.05, 182.39.

A General Procedure for Isolation of Cyclic Allenyl Azazirconocenes 3-12: In a 20-mL Schlenk tube, nitrile (0.5 mmol, 1.0 eq.) was added to the benzene solution (3 mL) of compound **3-2** (318 mg for **3-2a**, 337 mg for **3-2b**, 0.5 mmol). After the reaction mixture was stirred at room temperature for 5 min, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the filtrate was dried up under vacuum to give **3-12**.

3-12a: Red crystal, isolated yield: 86 % (298 mg). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.00 (s, 3H, $SiMe_2$), 0.93 (s, 3H, $SiMe_2$), 1.71 (s, 9H, CMe_3), 2.23 (s, 3H, Me), 2.37 (s, 3H, Me), 5.82 (s, 5H, C_5H_5), 6.22 (s, 5H, C_5H_5), 6.67 (d, J = 7.6 Hz, 2H, C_6H_4), 7.08 (d, J = 7.6 Hz, 2H, C_6H_4), 7.15 (d, J = 7.6 Hz, 2H, C_6H_4), 7.30–7.38 (m, 5H, C_6H_4), 8.05 (d, J = 7.6 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = −1.84, 1.02, 21.46, 21.61, 30.24, 41.69, 69.67, 108.57, 110.56, 123.17, 128.83, 129.32, 129.70, 129.77, 129.80, 130.20, 134.81, 135.33, 139.00, 140.21, 147.41, 171.66, 177.70, 193.75. Single crystals of **3-12a** suitable for X-ray analysis were grown in benzene/hexane (1:1) at room temperature.

3-12b: Orange solid, isolated yield: 91 % (331 mg). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.20 (s, 3H, $SiMe_2$), 0.70 (s, 3H, $SiMe_2$), 1.53 (s, 9H, CMe_3), 2.08 (s, 3H, Me), 2.18 (s, 3H, Me), 5.60 (s, 5H, C_5H_5), 5.97 (s, 5H, C_5H_5), 6.48 (d, J = 7.6 Hz, 2H, C_6H_4), 6.90 (d, J = 7.6 Hz, 2H, C_6H_4), 6.97 (d, J = 7.6 Hz, 2H, C_6H_4), 7.04 (d, J = 7.6 Hz, 2H, C_6H_4), 7.13 (d, J = 7.6 Hz, 2H, C_6H_4), 7.66 (d, J = 7.6 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, C_6D_6): δ = −1.90, 1.05, 21.42, 21.57, 30.20, 41.74, 69.32, 108.45, 110.66, 124.16, 128.38, 128.58, 129.08, 129.42, 129.67, 129.85, 131.11, 135.05, 135.52, 136.29, 137.28, 140.09, 147.01, 170.48, 177.55, 193.88.

3-12c: Red solid, isolated yield: 73 % (239 mg). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.00 (s, 3H, $SiMe_2$), 0.98 (s, 3H, $SiMe_2$), 1.60 (s, 9H, CMe_3), 5.64 (s, 5H, C_5H_5), 6.00 (s, 5H, C_5H_5), 6.60–8.00 (m, 14H, C_6H_5 and C_5H_4N); ^{13}C NMR (100 MHz, C_6D_6): δ = −1.36, 2.87, 30.29, 41.50, 66.35, 68.71, 108.82, 110.65,

123.30, 124.81, 126.09, 127.53, 128.38, 128.60, 129.03, 129.09, 129.26, 129.52, 130.22, 143.99, 147.33, 150.11, 153.58, 173.05, 178.80, 188.11.

3-12d: Brown solid, isolated yield: 62 % (215 mg). ^{1}H NMR (400 MHz, C_6D_6): δ = −0.06 (s, 3H, $SiMe_2$), 0.93 (s, 3H, $SiMe_2$), 1.58 (s, 9H, CMe_3), 2.07 (s, 3H, Me), 2.09 (s, 3H, Me), 5.59 (s, 5H, C_5H_5), 5.95 (s, 5H, C_5H_5), 6.53–7.16 (m, 8H, C_6H_4), 7.53 (s, 1H, $C_4H_3N_2$), 8.03 (s, 1H, $C_4H_3N_2$), 9.47 (s, 1H, $C_4H_3N_2$); ^{13}C NMR (100 MHz, C_6D_6): δ = −1.40, 2.24, 21.35, 21.56, 30.28, 41.64, 68.01, 108.93, 110.91, 128.39, 129.03, 129.13, 129.54, 129.84, 134.19, 135.49, 140.61, 142.01, 145.44, 146.30, 146.50, 147.99, 171.73, 177.66, 190.08.

3-12e: Red solid, isolated yield: 68 % (249 mg). ^{1}H NMR (400 MHz, C_6D_6): δ = 0.10 (s, 3H, $SiMe_2$), 0.80 (s, 3H, $SiMe_2$), 1.54 (s, 9H, CMe_3), 5.60 (s, 5H, C_5H_5), 6.03 (s, 5H, C_5H_5), 6.58–7.90 (m, 19H, C_6H_4 and C_6H_5); ^{13}C NMR (100 MHz, C_6D_6): δ = −1.78, 1.16, 30.20, 41.72, 70.04, 108.63, 110.57, 123.03, 125.61, 126.19, 127.56, 127.80, 129.12, 129.62, 129.64, 130.34, 137.47, 141.11, 143.09, 143.14, 150.32, 171.25, 177.84, 193.80.

3-12f: Orange solid, isolated yield: 93 % (307 mg). ^{1}H NMR (300 MHz, C_6D_6): δ = 0.22 (s, 3H, $SiMe_2$), 0.87 (s, 3H, $SiMe_2$), 1.66 (s, 9H, CMe_3), 5.86 (s, 5H, C_5H_5), 6.18 (s, 5H, C_5H_5), 6.68–6.77 (m, 3H, C_4H_3S), 7.07–7.43 (m, 10H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6): δ = −2.36, −0.00, 29.83, 41.49, 69.92, 108.63, 110.61, 124.92, 125.31, 125.97, 127.14, 128.43, 128.73, 128.84, 129.25, 129.86, 142.75, 146.87, 148.75, 165.90, 177.32, 193.75.

Formation of Iminopyrroles 3-13 with All Different Substituents via Hydrolysis of the Allenyl-aza-zirconacycles 3-3. A General Procedure for the Preparation of 1-(2-benzyl-4-phenyl-5-(thiophen-2-yl)-1*H*-pyrrol-3-yl)-2,2-dimethylpropan-1-imine (3-13a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl) dimethylsilane was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After trimethylacetonitrile (2.0 mmol, 166 mg, 220 μl) was added, the reaction mixture was stirred at this temperature for 2 h. Then, thiophene-2-carbonitrile (0.9 mmol, 98 mg, 84 μl) was added and the reaction mixture was stirred at room temperature for 1 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using hexane, ethyl acetate, and triethylamine (100:40:1) as the eluent.

1-(2-Benzyl-4-phenyl-5-(thiophen-2-yl)-1*H*-pyrrol-3-yl)-2,2-dimethylpropan-1-imine (3-13a): Yellow solid, isolated yield: 77 % (306 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.89 (s, 9H, CMe_3), 3.92 (s, 2H, CH_2), 6.76–6.86 (m, 2H, C_4H_3S), 7.02–7.05 (m, 1H, C_4H_3S), 7.26–7.34 (m, 10H, C_6H_5), 8.22 ppm (brs, 1H,

NH); ^{13}C NMR (75.5 MHz, $CDCl_3$, 25 °C, TMS): δ = 28.51, 32.60, 40.68, 120.75, 121.66, 123.77, 126.56, 126.78, 127.05, 128.08, 128.63, 128.88, 130.55, 134.68, 135.84, 138.57, 187.77 ppm. HRMS: *m/z*: calcd for $C_{26}H_{27}N_2S$ $[M + H]^+$: 399.1895, found: 399.1892. Elemental Analysis Calcd (%) for $C_{26}H_{26}N_2S$: C, 78.35; H, 6.58; N, 7.03. Found: C, 78.25; H, 6.66; N, 7.08.

1-(5-Benzyl-2-(4-methylbenzyl)-4-*p*-tolyl-1*H*-pyrrol-3-yl)-2,2-dimethylpropan-1-imine (3-13b): Yellow solid, isolated yield: 82 % (355 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.93 (s, 9H, CMe_3), 2.31 (s, 3H, CMe), 2.33 (s, 3H, CMe), 3.80 (s, 2H, CH_2), 3.92 (s, 2H, CH_2), 7.01–7.29 (m, 13H, C_6H_4 and C_6H_5), 7.46 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.00, 21.16, 28.70, 29.70, 31.85, 31.94, 40.74, 120.29, 122.83, 125.13, 125.86, 126.30, 128.27, 128.36, 128.59, 128.90, 129.25, 129.35, 133.80, 135.34, 136.04, 139.84, 188.67 ppm. HRMS: *m/z*: calcd for $C_{31}H_{35}N_2$ $[M + H]^+$: 435.2795, found: 435.2793. Elemental Analysis Calcd (%) for $C_{31}H_{34}N_2$: C, 85.67; H, 7.89; N, 6.45. Found: C, 85.54; H, 7.66; N, 6.58.

2,2-Dimethyl-1-(2-(4-methylbenzyl)-5-phenyl-4-*p*-tolyl-1*H*-pyrrol-3-yl)propan-1-imine (3-13c): White solid, isolated yield: 90 % (378 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.93 (s, 9H, CMe_3), 2.32 (s, 3H, CMe), 2.34 (s, 3H, CMe), 3.90 (s, 2H, CH_2), 7.01–7.25 (m, 13H, C_6H_4 and C_6H_5), 7.73 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.04, 21.20, 28.59, 32.37, 40.85, 126.28, 126.95, 127.00, 128.41, 128.67, 128.91, 129.60, 130.04, 132.92, 133.47, 135.46, 135.61, 136.39, 188.33 ppm. HRMS: *m/z*: calcd for $C_{30}H_{33}N_2$ $[M + H]^+$: 421.2638, found: 421.2635.

1-(5-(Furan-2-yl)-2-(4-methylbenzyl)-4-*p*-tolyl-1*H*-pyrrol-3-yl)-2,2-dimethylpropan-1-imine (3-13d): Yellow solid, isolated yield: 80 % (328 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.91 (s, 9H, CMe_3), 2.34 (s, 3H, CMe), 2.35 (s, 3H, CMe), 3.88 (s, 2H, CH_2), 5.98 (d, J = 3.3 Hz, 1H, C_4H_3O), 6.22–6.23 (m, 1H, C_4H_3O), 7.12–7.22 (m, 9H, C_6H_4 and C_4H_3O), 8.23 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.00, 21.21, 28.59, 32.26, 40.59, 103.44, 111.34, 119.05, 119.66, 124.67, 127.24, 128.54, 128.87, 129.53, 130.06, 132.88, 135.42, 136.27, 136.31, 139.89, 147.21, 187.68 ppm. HRMS: *m/z*: calcd for $C_{28}H_{31}N_2O$ $[M + H]^+$: 411.2431, found: 411.2408.

2,2-Dimethyl-1-(2-(4-methylbenzyl)-5-(thiophen-3-yl)-4-*p*-tolyl-1*H*-pyrrol-3-yl) propan-1-imine (3-13e): Yellow solid, isolated yield: 67 % (285 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.93 (s, 9H, CMe_3), 2.29 (s, 3H, CMe), 2.30 (s, 3H, CMe), 3.89 (s, 2H, CH_2), 6.78–6.79 (m, 1H, C_4H_3S), 6.93–6.94 (m, 1H, C_4H_3S), 7.06–7.15 (m, 9H, C_6H_4 and C_4H_3S), 7.82 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.01, 21.19, 28.60, 32.31, 40.73, 119.21, 123.18, 125.30, 126.56, 128.53, 128.61, 128.74, 128.83, 129.41, 129.45, 129.56, 130.11, 133.39, 133.58, 135.51, 135.82, 136.35, 188.12 ppm. HRMS: *m/z*: calcd for $C_{28}H_{31}N_2S$ $[M + H]^+$: 427.2202, found: 427.2205.

Isolation of Reactive Intermediate 3-15a from One Bis(alkynyl)silane, One *t*-BuCN, One Thiophene-2-carbonitrile, and One CyCN: In a 20-mL Schlenk tube, thiophene-2-carbonitrile (47 μl, 0.50 mmol) was added to the benzene solution of compound **3-2** (Ar = Ph, 318 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at room temperature for 1 h, cyclohexanecarbonitrile (118 μl, 1.0 mmol) was added, and the reaction mixture was stirred at 90 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the solid was dried up under vacuum to precipitate **3-15a** as orange powder (277 mg, 0.36 mmol, 72 % yield). Single crystals of **3-15a** suitable for X-ray analysis were grown in hexane at room temperature for 1 week. ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.20 (s, 3H, $SiMe_2$), 0.88 (s, 3H, $SiMe_2$), 1.04 (s, 9H, CMe_3), 1.21–1.91 (m, 10H, C_6H_{11}), 2.73–2.81 (m, 1H, C_6H_{11}), 5.62 (s, 5H, C_5H_5), 6.20 (s, 5H, C_5H_5), 6.77–7.44 (m, 11H, C_6H_5 and C_4H_3S), 7.74 ppm (d, J = 8.1 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6, 25 °C): δ = −3.8, 3.0, 26.32, 30.28, 31.21, 32.16, 42.00, 46.33, 59.91, 108.41, 110.41, 111.62, 111.98, 125.62, 126.01, 126.15, 126.69, 127.80, 129.18, 130.36, 130.82, 132.81, 132.84, 140.12, 141.65, 143.20, 145.50, 179.71, 195.99 ppm. Elemental Analysis Calcd (%) for $C_{45}H_{49}N_3SSiZr$: C, 69.00; H, 6.31; N, 5.36. Found: C, 68.92; H, 6.41; N, 5.18.

Formation of 5-Azaindoles 3-16 (Type IV) from One Si-tethered Diyne, One *t*-BuCN, and Two Different Organonitriles. A Typical Procedure for the Preparation of 4-*tert*-Butyl-6-cyclohexyl-3,7-diphenyl-2-(thiophen-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine(3-16a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl)dimethylsilane was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After trimethylacetonitrile (2.0 mmol, 166 mg, 220 μl) was added, the reaction mixture was stirred at this temperature for 2 h. Then, thiophene-2-carbonitrile (0.9 mmol, 98 mg, 84 μl) was added and the reaction mixture was stirred at room temperature for 1 h. Then, cyclohexanecarbonitrile (2.0 mmol, 218 mg, 238 μl) was added, and the reaction mixture was stirred at 90 °C for 2 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$. The resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using hexane, diethyl ether, and triethylamine (100:5:1) as the eluent.

4-*tert*-Butyl-6-cyclohexyl-3,7-diphenyl-2-(thiophen-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine(3-16a): White solid, isolated yield: 59 % (289 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.16–1.30 (m, 2H, CH_2), 1.25 (s, 9H, CMe_3), 1.62–1.96 (m, 8H, CH_2), 2.63–2.71 (m, 1H, CH), 6.67 (d, J = 2.1 Hz, 1H, C_4H_3S), 6.80 (t, J = 5.4 Hz, 1H, C_4H_3S), 7.03 (d, J = 5.4 Hz, 1H, C_4H_3S), 7.42–7.57 (m, 10H, C_6H_5), 8.02 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 26.20, 26.61, 30.81, 32.98, 39.49, 41.65, 115.59, 115.81, 119.97, 124.32,

125.76, 126.63, 127.72, 127.97, 128.21, 129.11, 129.78, 129.93, 133.61, 134.63, 135.95, 137.91, 140.82, 152.09, 161.17 ppm. HRMS: *m/z*: calcd for $C_{33}H_{35}N_2S$ $[M + H]^+$: 491.2521, found: 491.2516. Elemental Analysis Calcd (%) for $C_{33}H_{34}N_2S$: C, 80.77; H, 6.98; N, 5.71. Found: C, 80.54; H, 7.03; N, 5.55.

4-*tert*-Butyl-6-cyclohexyl-3,7-di*p*-tolyl-2-(pyridin-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine(3-16b): White solid, isolated yield: 63 % (323 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.19–1.31 (m, 2H, CH_2), 1.26 (s, 9H, CMe_3), 1.63–1.95 (m, 8H, CH_2), 2.49 (s, 3H, CMe), 2.50 (s, 3H, CMe), 2.69–2.75 (m, 1H, CH), 6.32 (d, J = 8.2 Hz, 1H, C_5H_4N), 6.94–6.97 (m, 9H, C_6H_4 and C_5H_4N), 8.40–8.41 (m, 1H, C_5H_4N), 9.54 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.38, 21.46, 26.27, 26.64, 30.96, 33.00, 39.54, 41.56, 116.11, 116.88, 120.76, 121.36, 129.24, 129.69, 129.85, 132.67, 133.05, 133.07, 135.63, 135.88, 137.02, 137.48, 140.35, 148.69, 150.13, 152.25, 161.76 ppm. HRMS: *m/z*: calcd for $C_{36}H_{40}N_3$ $[M + H]^+$: 514.3217, found: 514.3216. Elemental Analysis Calcd (%) for $C_{36}H_{39}N_3$: C, 84.17; H, 7.65; N, 8.18. Found: C, 84.12; H, 7.77; N, 8.10.

4-*tert*-Butyl-6-isopropyl-3,7-di*p*-tolyl-2-(thiophen-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine(3-16c): White solid, isolated yield: 53 % (253 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.24 (d, J = 7.2 Hz, 6H, $CHMe_2$), 1.26 (s, 9H, CMe_3), 2.45 (s, 3H, CMe), 2.47 (s, 3H, CMe), 3.03–3.12 (m, 1H, $CHMe_2$), 6.67 (d, J = 3.6 Hz, 1H, C_4H_3S), 6.79–6.82 (m, 1H, C_4H_3S), 7.03 (d, J = 5.1 Hz, 1H, C_4H_3S), 7.21–7.35 (m, 8H, C_6H_4), 8.02 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.33, 21.49, 23.05, 30.81, 31.22, 39.49, 115.55, 120.12, 124.09, 125.64, 126.57, 128.97, 129.78, 129.81, 132.86, 133.36, 134.64, 134.79, 137.39, 137.65, 140.89, 152.58, 161.28 ppm. HRMS: *m/z*: calcd for $C_{32}H_{35}N_2S$ $[M + H]^+$: 479.2521, found: 479.2518. Elemental Analysis Calcd (%) for $C_{32}H_{34}N_2S$: C, 80.29; H, 7.16; N, 5.85. Found: C, 80.31; H, 7.08; N, 5.95.

4-*tert*-Butyl-2-(furan-2-yl)-6-hexyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*]pyridine(3-16d): Yellow solid, isolated yield: 41 % (206 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.84 (t, J = 6.5 Hz, 3H, CH_3), 1.20–1.27 (m, 4H, CH_2), 1.29 (s, 9H, CMe_3), 1.73–1.76 (m, 2H, CH_2), 2.34–2.42 (m, 2H, CH_2), 2.47 (s, 3H, CMe), 2.48 (s, 3H, CMe), 2.69 (t, J = 7.6 Hz, 2H, CH_2), 5.02 (d, J = 3.4 Hz, 1H, C_4H_3O), 6.16–6.17 (m, 1H, C_4H_3O), 7.27 (d, J = 4.1 Hz, 1H, C_4H_3O), 7.28 (s, 4H, C_6H_4), 7.31 (s, 4H, C_6H_4), 8.43 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.10, 21.33, 21.43, 22.60, 29.13, 29.55, 30.79, 31.78, 34.28, 39.06, 106.86, 111.89, 114.27, 117.06, 119.83, 127.10, 128.94, 129.22, 129.75, 129.84, 132.52, 133.04, 135.29, 137.27, 137.38, 140.72, 140.85, 146.87, 148.07, 161.14 ppm. HRMS: *m/z*: calcd for $C_{35}H_{41}N_2O$: 505.3213, found: 505.3210.

4-*tert*-Butyl-3,7-di*p*-tolyl-6-propyl-2-(pyrazin-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine (3-16e): White solid, isolated yield: 72 % (341 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.86 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.27 (s, 9H, CMe_3), 1.77–1.83 (m, 2H, $CH_3CH_2CH_2$), 2.48 (s, 3H, CMe), 2.49 (s, 3H, CMe), 2.69 (t, J = 7.6 Hz, 2H, $CH_3CH_2CH_2$), 7.29–7.35 (m, 4H, C_6H_4), 7.37 (s, 4H, C_6H_4), 7.51 (d, J = 1.6 Hz, 1H, $C_4H_3N_2$), 8.21 (d, J = 2.5 Hz, 1H, $C_4H_3N_2$), 8.35–8.36 (m, 1H,

$C_4H_3N_2$), 9.35 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.14, 21.36, 21.46, 22.74, 30.88, 36.46, 39.25, 117.34, 118.75, 120.72, 129.62, 129.78, 129.81, 130.92, 132.33, 132.88, 134.80, 137.30, 138.22, 141.24, 141.55, 142.48, 143.15, 146.28, 148.84, 162.51 ppm. HRMS: *m/z*: calcd for $C_{32}H_{35}N_4$ $[M + H]^+$: 475.2862, found: 475.2858. Elemental Analysis Calcd (%) for $C_{32}H_{34}N_4$: C, 80.98; H, 7.22; N, 11.80. Found: C, 80.90; H, 7.36; N, 11.54.

4-*tert*-Butyl-3,7-di*p*-tolyl-2-(pyridin-2-yl)-6-(thiophen-2-yl)-1*H*-pyrrolo[3,2-*c*] pyridine(3-16f): White solid, isolated yield: 49 % (251 mg). ^1H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.31 (s, 9H, CMe_3), 2.50 (s, 3H, CMe), 2.53 (s, 3H, CMe), 6.34 (d, *J* = 8.3 Hz, 1H, C_5H_4N), 6.45 (d, *J* = 3.2 Hz, 1H, C_4H_3S), 6.79–6.81 (m, 1H, C_4H_3S), 7.18–7.42 (m, 9H, C_5H_4N and C_6H_4), 8.43 (d, *J* = 4.8 Hz, 1H, C_5H_4N), 9.57 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.47, 21.52, 30.74, 39.62, 115.05, 117.36, 120.91, 121.59, 121.66, 125.25, 126.19, 127.37, 129.33, 129.91, 130.47, 132.60, 132.65, 134.18, 135.07, 136.01, 137.75, 138.08, 139.04, 141.25, 148.77, 149.74, 162.35 ppm. HRMS: *m/z*: calcd for $C_{34}H_{32}N_3S$: 514.2311, found: 514.2305.

Isolation of Reactive Intermediate 3-17a from One Bis(alkynyl)silane, One *t*-BuCN, and Two CyCN: Compound **3-2** was isolated according to the method we reported previously. In a 20-mL Schlenk tube, cyclohexanecarbonitrile (178 μl, 1.50 mmol) was added to the benzene solution of compound **2** (Ar = Ph, 318 mg, 0.50 mmol) with a syringe. After the reaction mixture was stirred at 90 °C for 1 h, it was dried up under vacuum and the residue was extracted with hexane. After filtering, the solid was dried up under vacuum to precipitate **3-17a** as orange powder (312 mg, 0.405 mmol, 81 % yield). Single crystals of **3-17a** suitable for X-ray analysis were grown in benzene/hexane at room temperature for 1 week. ^1H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.29 (s, 3H, $SiMe_2$), 1.01 (s, 9H, CMe_3), 1.02 (s, 3H, $SiMe_2$), 1.23–2.18 (m, 20H, C_6H_{11}), 2.28–2.36 (m, 1H, C_6H_{11}), 2.71–2.77 (m, 1H, C_6H_{11}), 6.11 (s, 5H, C_5H_5), 6.26 (s, 5H, C_5H_5), 7.12–7.46 (m, 6H, C_6H_5), 7.66 (d, *J* = 7.8 Hz, 2H, C_6H_5),7.90 ppm (d, *J* = 7.5 Hz, 2H, C_6H_5); ^{13}C NMR (75.4 MHz, C_6D_6, 25 °C): δ = −3.35, 2.95, 15.54, 25.76, 26.31, 27.82, 28.16, 29.74, 31.33, 32.09, 32.22, 37.45, 41.42, 46.44, 46.86, 60.53, 111.29, 111.41, 119.54, 125.82, 126.47, 126.94, 127.50, 127.68, 130.70, 132.45, 134.66, 140.07, 141.24, 142.02, 144.23, 181.56, 194.26 ppm. Elemental Analysis Calcd (%) for $C_{47}H_{57}N_3SiZr$: C, 72.07; H, 7.33; N, 5.36. Found: C, 72.00; H, 7.56; N, 5.00.

Formation of 5-Azaindoles 3-18 (Type III) from One Si-tethered Diyne, One *t*-BuCN, and Two Identical Organonitriles. A Typical Procedure for the Preparation of 4-*tert*-Butyl-2,6-dicyclohexyl-3,7-diphenyl-1*H*-pyrrolo[3,2-*c*] pyridine(3-18a): To a toluene (10 ml) solution of Cp_2ZrCl_2 (1.05 mmol, 307 mg) at −78 °C (dry ice/acetone) in a 20-ml Schlenk tube was added dropwise *n*-BuLi (2.1 mmol, 1.6 M, 1.32 ml) with a syringe. After the addition was complete, the reaction mixture was stirred at −78 °C for 1 h. Then, 1 mmol of bis(phenylethynyl) dimethylsilane was added, and the reaction mixture was warmed up to 50 °C and stirred at this temperature for 1 h. After trimethylacetonitrile (2.0 mmol, 166 mg,

220 μl) was added, the reaction mixture was stirred at this temperature for 2 h. Then, cyclohexanecarbonitrile (3.0 mmol, 327 mg, 356 μl) was added, and the reaction mixture was stirred at 90 °C for 2 h. The reaction mixture was quenched with saturated aqueous $NaHCO_3$, and the resulting mixture was extracted with diethyl ether for three times and then washed with water and brine. The extract was dried over anhydrous $MgSO_4$. The solvent was evaporated in vacuo to give a yellow solid, which was subjected to SiO_2 column using hexane, diethyl ether, and triethylamine (100:5:1) as the eluent.

4-*tert*-Butyl-2,6-dicyclohexyl-3,7-diphenyl-1*H*-pyrrolo[3,2-*c*]pyridine(3-18a): Pale yellow solid, isolated yield 69 % (338 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.19–1.90 (m, 29H, CH_2 + CMe_3), 2.19–2.26 (m, 1H, CH), 2.59–2.66 (m, 1H, CH), 7.34–7.54 (m, 10H, C_6H_5), 7.74 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 23.59, 24.77, 25.21, 25.79, 26.22, 27.50, 29.01, 30.30, 32.48, 32.65, 35.23, 38.87, 41.08, 112.93, 115.30, 118.64, 122.17, 126.52, 126.99, 127.09, 128.54, 129.51, 132.54, 136.01, 138.47, 139.33, 141.10, 150.39, 159.73 ppm. HRMS: *m/z*: calcd for $C_{35}H_{43}N_2$ $[M + H]^+$: 491.3426, found: 491.3428. Elemental Analysis Calcd (%) for $C_{35}H_{42}N_2$: C, 85.66; H, 8.63; N, 5.71. Found: C, 85.60; H, 8.82; N, 5.59.

4-*tert*-Butyl-3,7-diphenyl-2,6-di(thiophen-2-yl)-1*H*-pyrrolo[3,2-*c*]pyridine(3-18b): White solid, isolated yield 77 % (377 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.31 (s, 9H, CMe_3), 6.40 (d, J = 3.5 Hz, 1H, C_4H_3S), 6.70–6.82 (m, 3H, C_4H_3S), 7.06 (d, J = 5.2 Hz, 1H, C_4H_3S), 7.16 (d, J = 5.2 Hz, 1H, C_4H_3S), 7.44 (s, 5H, C_6H_5), 7.50–7.60 (m, 5H, C_6H_5), 8.05 ppm (brs, 1H, NH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 30.60, 39.55, 114.56, 116.05, 120.86, 124.64, 125.16, 126.17, 126.34, 126.72, 127.37, 128.20, 128.31, 128.61, 129.87, 130.04, 130.98, 133.58, 134.16, 135.52, 137.36, 138.84, 141.71, 147.21, 161.69 ppm. HRMS: *m/z*: calcd for $C_{31}H_{27}N_2S_2$ $[M + H]^+$: 491.1616, found: 491.1608.

4-*tert*-Butyl-2,6-diisopropyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*]pyridine(3-18c): White solid, isolated yield 71 % (310 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.05 (d, J = 6.9 Hz, 6H, $CHMe_2$), 1.23 (d, J = 6.9 Hz, 6H, $CHMe_2$), 1.24 (s, 9H, CMe_3), 2.43 (s, 3H, CMe), 2.47 (s, 3H, CMe), 2.59–2.69 (m, 1H, $CHMe_2$), 3.00–3.08 (m, 1H, $CHMe_2$), 7.18–7.34 (m, 8H, C_6H_4), 7.72 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.33, 22.50, 23.16, 25.65, 30.75, 31.10, 39.33, 113.08, 115.54, 119.21, 128.31, 129.72, 129.80, 132.84, 133.34, 135.80, 136.48, 137.12, 139.98, 142.05, 151.40, 160.31 ppm. HRMS: *m/z*: calcd for $C_{31}H_{39}N_2$ $[M + H]^+$: 439.3108, found: 439.3100. Elemental Analysis Calcd (%) for $C_{31}H_{38}N_2$: C, 84.88; H, 8.73; N, 6.39. Found: C, 84.72; H, 8.79; N, 6.21. Single crystals of **5c** suitable for X-ray analysis were grown in hexane/diethyl ether at room temperature for 1 day.

4-*tert*-Butyl-2,6-dipropyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*]pyridine(3-18d): White solid, isolated yield 46 % (201 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.77 (t, J = 6.6 Hz, 3H, CH_2CH_3), δ = 0.86 (t, J = 7.2 Hz, 3H, CH_2CH_3), 1.24 (s, 9H, CMe_3), 1.38–1.46 (m, 2H, $CH_2CH_2CH_3$), 1.74–1.81 (m, 2H, $CH_2CH_2CH_3$),

2.25 (t, J = 7.1 Hz, 2H, $CH_2CH_2CH_3$), 2.42 (s, 3H, CMe), 2.46 (s, 3H, CMe), 2.64 (t, J = 6.8 Hz, 2H, $CH_2CH_2CH_3$), 7.16–7.33 (m, 8H, C_6H_4), 7.76 ppm (brs, 1H, NH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 13.85, 14.19, 21.35, 22.92, 22.99, 28.44, 30.71, 36.35, 38.96, 114.58, 116.72, 119.39, 128.24, 129.67, 129.83, 132.85, 133.43, 135.72, 136.39, 137.07, 137.09, 140.31, 146.62, 160.09 ppm. HRMS: *m/z*: calcd for $C_{31}H_{39}N_2$ $[M + H]^+$: 439.3108, found: 439.3102.

4-*tert*-Butyl-2,6-dicyclohexyl-3,7-di*p*-tolyl-1*H*-pyrrolo[3,2-*c*]pyridine(3-18e): White solid, isolated yield 93 % (483 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.09–1.93 (m, 29H, CH_2 + CMe_3), 2.19–2.27 (m, 1H, CH), 2.42 (s, 3H), 2.47 (s, 3H), 2.61–2.68 (m, 1H, CH), 7.15–7.37 (m, 8H), 7.72 ppm (brs, 1H); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.37, 25.71, 26.24, 26.67, 30.78, 32.97, 33.12, 35.60, 39.32, 41.43, 113.24, 115.66, 119.15, 128.27, 129.72, 129.79, 132.78, 133.33, 135.71, 136.37, 136.98, 139.84, 141.55, 150.85, 160.03 ppm. HRMS: *m/z*: calcd for $C_{31}H_{39}N_2$ $[M + H]^+$: 519.3739, found: 519.3736.

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Chapter 4
Introduction to Semibullvalenes and Azasemibullvalenes

Semibullvalene (SBV) as well as azasemibullvalene (NSBV) is a class of organic molecules featuring unique polycyclic skeleton. Since Zimmerman et al. reported the first example of SBV in 1966, both SBV and NSBV have attracted much attention to their structures and reactions (Fig. 4.1) [1–20]. SBV and NSBV both feature 5/3/5 tricyclic-strained ring skeleton and the bis(allyl) system shows rapid degenerate Cope rearrangement in both solution-phase and gas-phase [21–23], with very low activation barrier. The unsymmetrical, localized structure features three-membered cyclopropane or aziridine ring, while the delocalized structure is symmetrical and does not have classical three-membered ring structure. The transition-state of Cope arrangement in SBV or NSBV is aromatic transition-state and features 6π electrons, high delocalization, symmetrical structure, and relatively low energy close to the value of localized structure [24]. Gas-phase structure of unsubstituted SBV has revealed that it is not a static, neutral homoaromatic molecule. The activation barrier of Cope rearrangement in unsubstituted SBV was determined as 5.5 kcal/mol [4]. Structural derivation by both theoretical/computational propose and experimental synthesis was expected to lower the activation barrier and stabilize the delocalized structure to become a homoaromatic minimum in energy. The following strategies have been applied in this chemistry: (1) electronic stabilization by substituents (Dewar–Hoffmann SBV); (2) small ring annulation; (3) introduction of heteroatom into skeleton; (4) coordination with metal ion; (5) solvation or other methods [1]. Based on these strategies, the SBV or NSBV derivatives synthesized have lower activation barrier of Cope rearrangement than unsubstituted SBV. However, until now, there is no real neutral homoaromatic SBV or NSBV derivative.

4.1 Homoaromaticity

Aromaticity refers to a chemical property that a conjugated ring of unsaturated bonds, lone pairs, or empty orbitals exhibits stronger stabilization than without conjugation [2, 24]. For monocyclic aromatic compound, it should be planar, cyclic delocalized system of $(4n + 2)\pi\, e^-$ (Huckel's rule). The feature of aromatic compounds includes:

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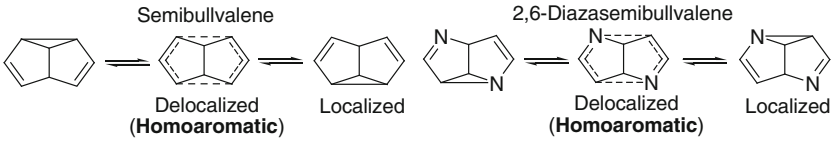


Fig. 4.1 Semibullvalene and azasemibullvalene

(1) thermodynamically stable; (2) bond length equalization; (3) diamagnetic exaltation (ring current); (4) easier for substitution to occur rather than addition or oxidation. The commonly referred aromatic compounds include benzene, cycloheptatriene cation, and cyclpentadiene anion.

The concept of homoaromaticity, introduced by Winstein et al. in 1959, describes a type of aromaticity in which conjugation is interrupted by an sp^3-hybridized carbon atom [2, 24]. Homotropylium cation is one of the most common homoaromatic species, in which conjugation and ring current skip the saturated CH_2 to form diamagnetic exaltation. Thus, two H atoms in CH_2 show different chemical shifts in ^1H NMR spectrum (Fig. 4.2).

Since the publication of Winstein's paper, much research has focused on understanding the bonding mode in these molecules, broadening definition of aromaticity as well as reaction chemistry of homoaromatic molecules. Homoaromatic compounds include cationic, anionic, and neutral homoaromatic molecules. Cationic homoaromatic compounds are relatively more common. The "homotropylium" cation ($C_8H_9^+$) is among the most studied example of a cationic homoaromatic compound.

Anionic homoaromatic compounds are quite few, such as the bis-diazene dianion in Fig. 4.3. However, whether or not neutral species can be homoaromatic is still a matter of debate. Some of neutral molecules used to be considered as homoaromatic, such as the fulleroid, 1,2-diboroetane and triquinacene in Fig. 4.3 but their homoaromaticity characters are either in question or denied. Thus, the establishment of experimental models for potential neutral homoaromatic molecules has long been an exciting pursuit in synthetic and theoretical chemistry. The central challenges remain the development of efficient synthesis, and the collection of detailed experimental data, in order to gain a deep insight into the structure–reactivity relationship.

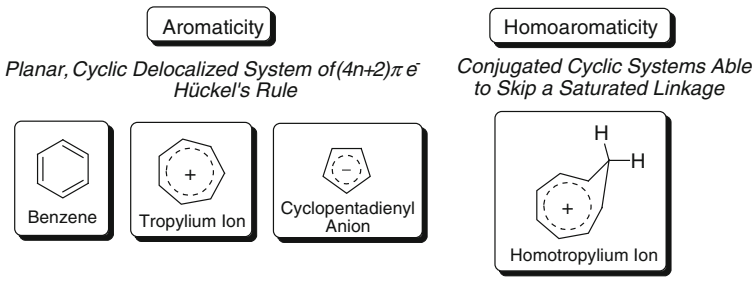


Fig. 4.2 Aromaticity and homoaromaticity

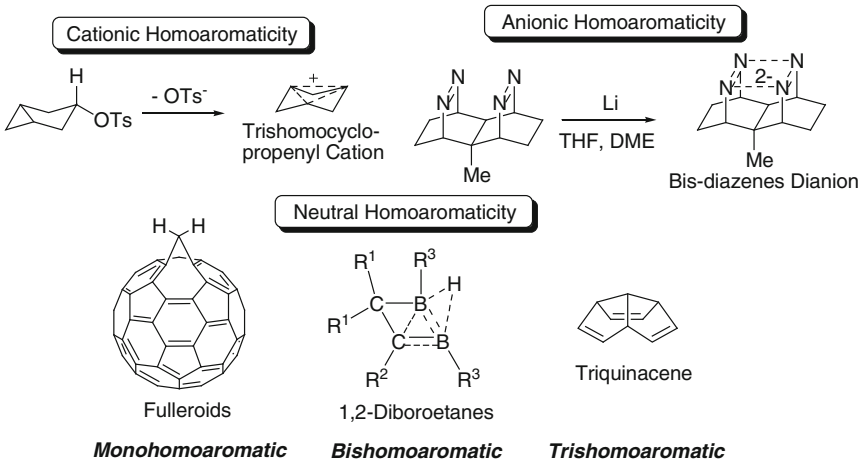
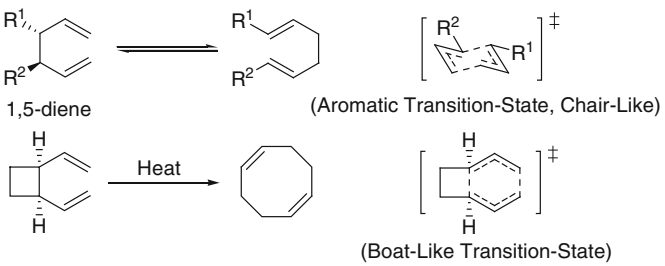


Fig. 4.3 Cationic, anionic, and neutral homoaromatic molecules

4.2 Cope Rearrangement

In 1959, Cope rearrangement was reported for the first time by A. C. Cope, which refers to [3,3]-sigmatropic rearrangement reaction of "bis(allyl) system" in 1,5-diene under thermal condition. In many cases, Cope rearrangement features high yield and good selectivity and is thus widely applied in organic synthesis (Scheme 4.1) [21–23].

The mechanism of Cope rearrangement is considered as concerted and pericyclic, via a six-membered cyclic transition-state. The transition-state of Cope rearrangement is considered as 6π electrons aromatic transition-state. The transition-state of the Cope rearrangement can be either chair conformation or boat conformation. Alternatively, the Cope rearrangement can also be considered to occur via a diradical transition-state.



Scheme 4.1 Cope rearrangement and chair and boat transition-state

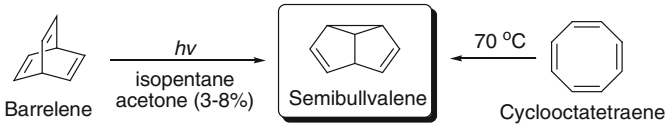
4.3 Semibullvalene

SBV (tricycle-[4.2.0.0^{2,5}]-3,7-octadiene) was first synthesized in 1966 by Zimmermann and Grunewald [3]. They found photo-irradiation of barrelene gave SBV as a new product rather than cyclooctatetraene. In 1980, Zimmermann et al. found that photo-irradiation of cyclooctatetraene in acetone at 70 °C could give SBV in quantitative yield [25] (Scheme 4.2).

The classical structure of SBV features two cyclopentene rings and one cyclopropane ring. Thus, the ring system in SBV is expected to be highly strained. More interestingly, the "bis(allyl) system" of SBV was found to undergo rapid degenerate Cope rearrangement. Thus, due to the low activation barrier and high rearrangement rate, in solution, the "fluxional" SBV molecule shows averaging signals and symmetrical structure in NMR spectrum.

Not only SBV is important structural model in theoretical chemistry, but the unique polycyclic skeleton is challenging in synthetic chemistry. SBV features two structures, C_s-symmetrical localized structure **4-1** and C_{2v}-symmetrical delocalized structure **4-1**^{deloc}. **4-1**^{deloc} is considered as 6π electrons aromatic transition-state with low energy in Cope rearrangement, and thus SBV has long been recognized as the system most closely approaching neutral homoaromaticity [1] (Fig. 4.4).

In 1972, Bauer demonstrated the localized structure is the stable structure of SBV in gas-phase by gas-phase electron diffraction. The C2–C8 distance of 1.600 Å suggested a C–C single bond while the C3–C4 distance of 1.350 Å suggested a C=C double bond. The whole molecule showed unsymmetrical structure [26]. In 1974, Meinwald and Anet determined the activation barrier of SBV at 5.5 kcal/mol (130 K) for the first time. Thus, SBV shows rapid Cope rearrangement but is not a homoaromatic molecule [4]. In 1989, Quast et al. revised the value of activation barrier of SBV as 6.2 kcal/mol (298 K) according to the line-shape analysis of low-temperature ^{13}C NMR spectrum [27].



Scheme 4.2 Synthesis of unsubstituted semibullvalene

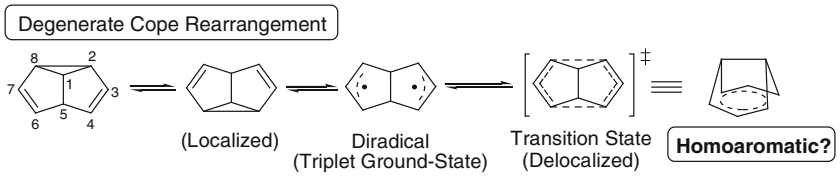


Fig. 4.4 Localized, delocalized, and diradical structures of semibullvalene

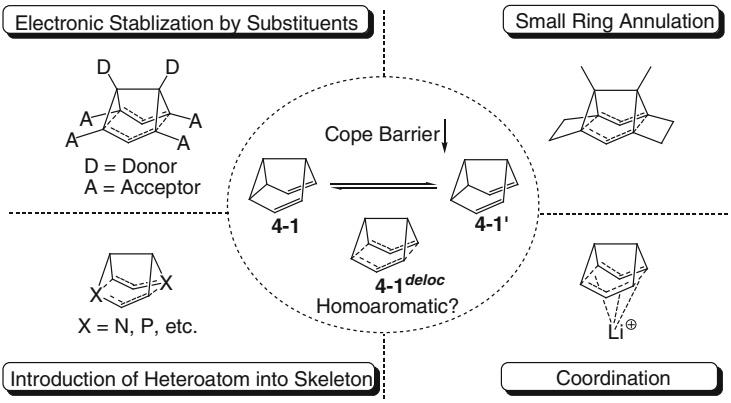


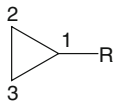
Fig. 4.5 Derivation of semibullvalenes

Tuning the substituent effect or further derivation of SBV structures was expected to further lower or even eliminate the activation barrier of Cope rearrangement and thus stabilize the energy of delocalized structure to become a minimum. In that case, the delocalized structure **4-1**^{deloc} might become a stable, static homoaromatic molecule rather than a transition-state. These strategies include: (1) electronic stabilization by substituents (Dewar-Hoffmann SBV); (2) small ring annulation; (3) introduction of heteroatom into skeleton; (4) coordination with metal ion; (5) solvation or other methods (Fig. 4.5). Several different types of SBV derivatives have been synthesized and studied.

Most of SBV derivatives have lower activation barrier of Cope rearrangement than the value of unsubstituted SBV. However, they are all still in rapid Cope rearrangement and the activation barrier is not eliminated. Thus, these SBV derivatives are all not homoaromatic. There were only few reports on homoaromatic SBV derivatives and they are not widely accepted.

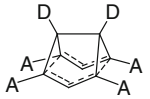
4.3.1 Electronic Stabilization by Substituents (Dewar–Hoffmann SBV)

In 1971, Dewar and Hoffmann demonstrated tuning electronic effect of substituents on SBVs could stabilize the delocalized structure and approach homoaromatic SBV [28, 29]. Electron-withdrawing groups on C1 would weaken C1–C2 and C2–C3 bonds and activate C2–C3 bonds, and electron-donating groups on C1 would have opposite effect. For SBVs, electron-donating groups at 1,5-positions and electron-withdrawing groups at 2,4,6,8-positions would weaken C2–C8 and C4–C6 bonds, and thus stabilize the delocalized structures. The SBV with electron-donating groups at 1,5-positions and electron-withdrawing groups at 2,4,6,8-positions is also referred as Dewar–Hoffmann SBVs **4-2** (Fig. 4.6).



R	C1-C2	C1-C3	C2-C3
Acceptor	*W*	*W*	*S*
Donor	*S*	*S*	*W*

W = Weaken *S = Strengthen*



4-2
Dewar-Hoffmann SBVs

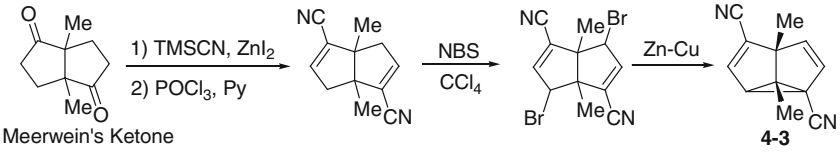
Fig. 4.6 Electronic effect on structure of cyclopropane and Dewar–Hoffmann semibullvalenes

A lot of Dewar–Hoffmann SBVs have lower activation barrier than unsubstituted SBV. Even some of them were considered to be homoaromatic in polar solvent or in the gas-phase.

In 1985, Quast et al. synthesized 2,6-dicyanosemibullvalene **4-3** starting from Meerwein's ketone via zinc iodide-catalyzed cyanation, bromination, and reduction. At −158 °C, the peaks of C2/C6 and C4/C8 in solution-phase ^{13}C NMR showed line broadening. At this temperature, the activation barrier for the degenerate Cope rearrangement of **4-3** is estimated from the broadening of the ^{13}C NMR signals to be 3.2 kcal/mol, which is lower than the value 5.4 kcal/mol of unsubstituted SBV at the same temperature (Scheme 4.3) [30]. In the IR spectrum, two wave numbers (2,218, 2,230 cm^{-1}) were observed for cyano groups, thus **4-3** is not a static homoaromatic compound.

4-3 forms two polymorphs (α and β-forms) in hexane and ethyl acetate solution. X-ray crystallographic structure of α-form showed unsymmetrical localized structure, however, the structure of β-form showed highly symmetrical delocalized structure, which is the first report of C_2 symmetrical structure of SBV derivatives (Fig. 4.7). Further, in 2000, Quast et al. studied the variable-temperature X-ray crystallographic structure of β-form and found that at other temperatures, the structure of β-form shows unsymmetrical nature, which is "accidentally" degenerate and symmetrical at room temperature [31].

In 1980, Sauer et al. synthesized 3,7-dicyanosemibullvalene **4-4** (Scheme 4.4). Cycloaddition of 1,2,4,5-tetrazines with 3,3′-bicyclopropenyl in a cycloaddition-cycloelimination sequence followed by hydrolysis, amination, and dehydration gave 3,7-dicyanosemibullvalene **4-4**. The author also determined the activation barrier of Cope arrangement of **4-4** at −158 °C as 5.7 kcal/mol, slightly higher than the value 5.4 kcal/mol of unsubstituted SBV at the same temperature. This result indicates that electro-deficient cyano group at 3,7-position has little effect on the stabilization of delocalized structure [32].



Scheme 4.3 Synthesis of 2,6-dicyanosemibullvalene

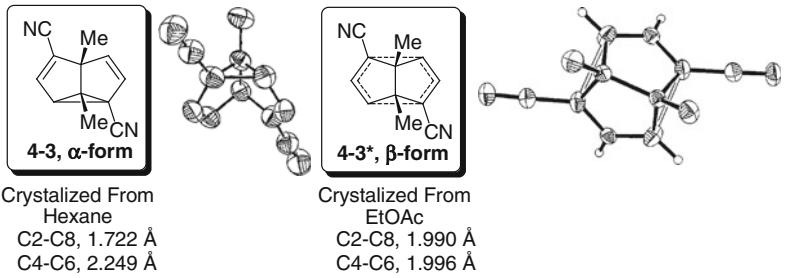
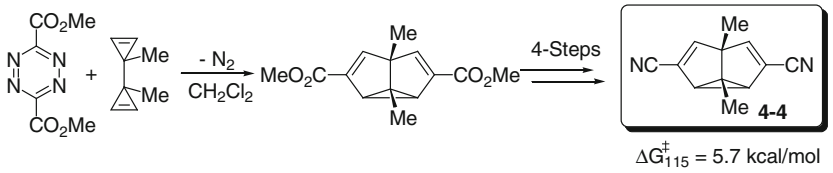


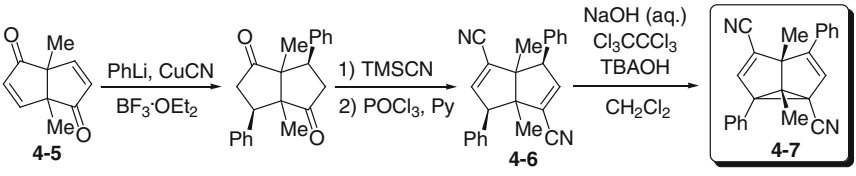
Fig. 4.7 Two polymorphs (α and β-forms) of 2,6-dicyanosemibullvalene



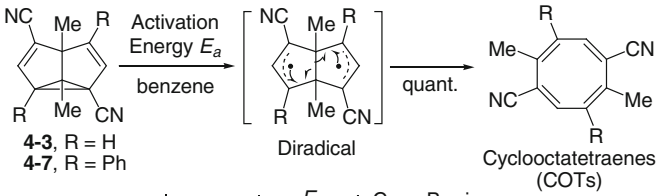
Scheme 4.4 Synthesis of 3,7-dicyanosemibullvalene

In 1994, Quast et al. designed and synthesized 2,6-dicyano-4,8-diphenylsemibullvalene **4-7**, aiming at elongation of conjugation by introducing phenyl groups and thus stabilizing the delocalized structure to be homoaromatic (Scheme 4.5). Copper-mediated conjugate addition of phenyl lithium to dione **4-5** introduced two phenyl groups. Cyanation and elimination gave bicyclic diene **4-6**. The red SBV **4-7** was formed in a single step by treatment with hexachloroethane and concentrated aqueous sodium hydroxide in the presence of tetrabutylammonium hydroxide as phase-transfer catalyst. In the solid state, **4-7** exhibits apparent C_2 symmetry and equal atomic distances C2–C8 and C4–C6. The red color of **4-7** in the crystal and in solution is due to a maximum at 444 nm which disappears on cooling. Thus, **4-7** was considered as one thermochromic SBV and showed the most intensive maximum at the longest wavelength observed by far. The activation barrier of Cope rearrangement of **4-7** was determined as 2.6 kcal/mol [33].

Thermolysis of several SBVs gives cyclooctatetraenes. The mechanism was considered as following: homolysis of C–C bond in cyclopropane ring gives bis



Scheme 4.5 Synthesis of 2,6-dicyano-4,8-diphenylsemibullvalene



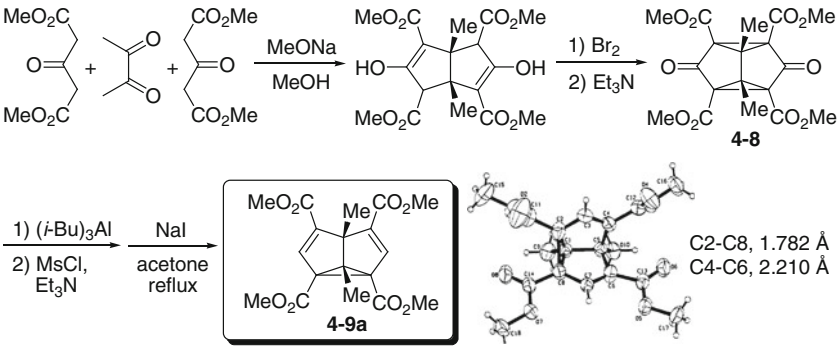
	Temp.	E_a (kcal/mol)	Cope Barrier (kcal/mol)
R = H	130 °C	32.0	3.1
R = Ph	70 °C	25.4	2.6

Scheme 4.6 Thermolysis of 2,6-dicyano-4,8-diphenylsemibullvalene

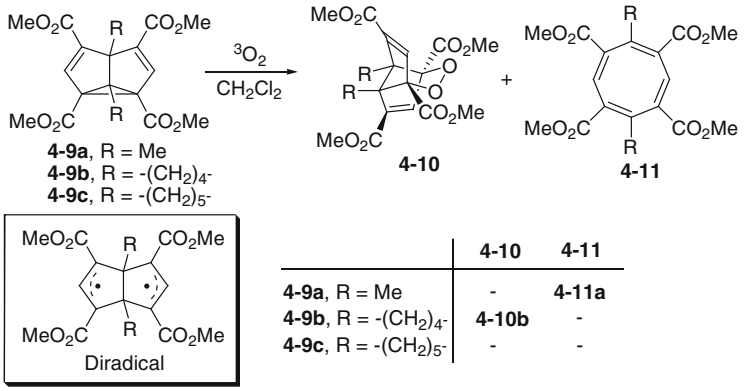
(allyl) diradical, which triggers further ring opening to form cyclooctatetraenes. The temperature for unsubstituted SBV is around 270 °C. In comparison, 2,6-dicyanosemibullvalene **4-3** undergoes thermolysis at 130 °C, while 2,6-dicyano-4,8-diphenylsemibullvalene undergoes thermolysis at 70 °C as a even lower temperature (Scheme 4.6). Generally, it is considered that the SBV with lower barrier of Cope rearrangement has lower barrier of thermolysis and is more prone to thermo-rearrange at lower temperature [33].

In 1981, Grohmann et al. reported synthesis, structure, and reaction of SBV 2,4,6,8-tetracarboxylic acid ester (Scheme 4.7). Condensation of 3-oxoglutaric acid dimethyl ester with butadione in the presence of base followed by bromination and elimination afforded tetracyclic diketone **4-8** [34]. Diketone **4-8** was stereospecifically reduced to exo-diol by using Al(*i*-Bu)$_3$. The corresponding dimesyl derivative was treated with sodium iodide to give the product **4-9a**. The solution-phase ^{13}C NMR did not show obvious line broadening at −120 °C, which indicated the low activation barrier of Cope rearrangement of **4-9a**. The room temperature crystal structure of **4-9a** showed localized structure, and thus **4-9a** is not homoaromatic.

Cycloaddition of 1,5-cyclohexano-2,4,6,8-tetracarbomethoxysemibullvalene **4-9a** with dioxygen yielded a doubly bridged *trans*-dioxadecalin structure **4-10b**



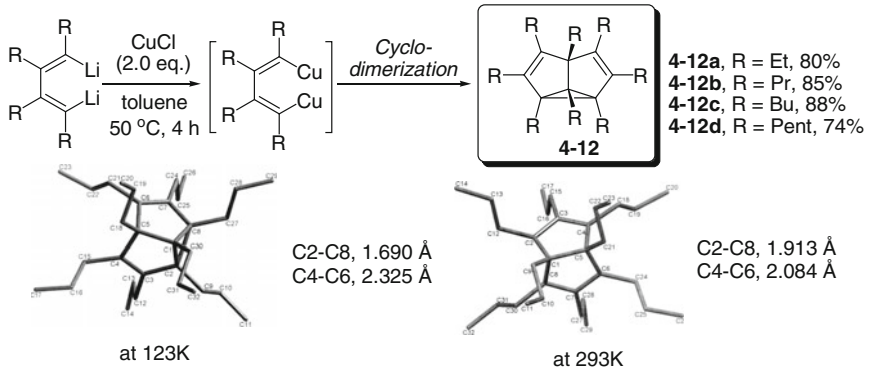
Scheme 4.7 Synthesis of semibullvalene 2,4,6,8-tetracarboxylic acid ester



Scheme 4.8 Reaction of semibullvalene 2,4,6,8-tetracarboxylic acid ester with dioxygen

selectively. The reaction mechanism might be homolysis of cyclopropane C–C bond to form bis(allyl) diradical followed by dioxygen addition (Scheme 4.8). 1,5-Cycloheptano-2,4,6,8-tetracarbomethoxysemibullvalene **4-9c** does not react with dioxygen and is stable. In contrast, 1,5-dimethyl-2,4,6,8-tetracarbomethoxysemibullvalene does not react with dioxygen but undergoes thermo-rearrangement to produce cyclooctatetraene **4-11**. These results showed that the 1,5-bridge in SBV has striking effect on the reactivity [35].

Other types of SBV derivatives were also studied and showed different structural features. Our group found that 1,4-dilithio-1,3-butadienes **1** could react with stoichiometric amount of CuCl to give octa-substituted SBVs **4-12** in high yields (Scheme 4.9). This is the first example of metal-mediated synthesis of SBVs via C–C bond forming process. Crystal structure of octapropylsemibullvalene **4-12b** showed highly symmetrical structures at room temperature, which might be due to a dynamic or static disorder of two non-degenerate SBV molecules in the solid state. At −150 °C, **4-12b** showed unsymmetrical localized structure [12].



Scheme 4.9 Synthesis and structure of octaalkylsemibullvalenes

4.3.2 Destabilization of Localized Structure by Small Ring Annulation

In 1978, Paquette et al. suggested that the small-ring fused SBV might destabilize the cyclopropane ring in SBV and thus drive the equilibrium to the delocalized structure. Semiempirical and ab initio quantum mechanical calculations on other bisannelated SBVs supported this hypothesis. The delocalized structure of bisannelated SBV **4-13** was optimized at MNDO Cl2 level and showed lower energy than SBV for 2.5 kcal/mol (Fig. 4.8) [36–38]. The NICS (nucleus-independent chemical shifts) of **4-13** was calculated as −22.6, which is more negative than the NICS value of benzene (−11.5). This suggests **4-13** might be more aromatic. However, the synthetic approach toward small-ring fused SBV is much limited [39, 40].

In 1989, Müllen et al. reported the first example of 2,8:4,6-biannulated SBV (Scheme 4.10) [38]. Starting from tetraester **4-14**, after four steps the tetrabromo compound **4-15** was synthesized. Further, four steps in synthesis constructed the biannulated tetracyclic skeleton. Finally, reduction with magnesium gave biannulated SBV **4-16**. Line broadening of solution-phase ^{13}C NMR of **4-16** at −160 °C was not observed. At this temperature, the upper limit of activation barrier of Cope rearrangement was determined as 3.6 kcal/mol, which is lower than the value 5.5 kcal/mol of unsubstituted SBV.

1,5-Dimethyl-2,4,6,8-semibullvalene tetracarboxylic dianhydride **4-17** is a close approach to a neutral homoaromatic SBV [7]. Theoretical studies predicted that the bisanhydride **4-17** has a single minimum potential energy surface with a homoaromatic ground-state. In 1996, Williams et al. developed two-step synthesis of **4-17** from tetraester **4-9a** (Scheme 4.11). **4-17** is thermostable at 200 °C and also stable toward oxygen and moisture. The solid-phase ^{13}C CP-MAS NMR spectra of **4-17** are temperature independent over the range −50 to 20 °C. The solution-phase ^{13}C NMR spectra of the bisanhydride **4-17** show no line broadening of C(2,4,6,8) signal caused by exchanging at −83 °C. The crystal structure of **4-17** showed symmetrical structure at room temperature but turned out to be unsymmetrical structure at −150 °C. The author suggested in the solution and solid states SBV **4-17** is not homoaromatic. The activation barrier of Cope rearrangement in **4-17** was determined as low as 3.3 kcal/mol which could be attributed to stabilization of delocalized structure due to four electron-withdrawing groups on 2,4,6,8-positions as well as destabilization of localized structure due to bis-annulation.

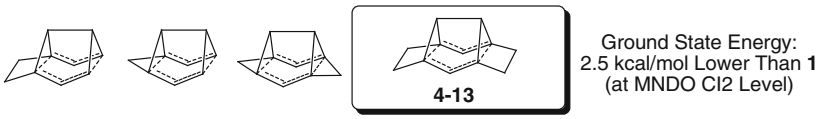
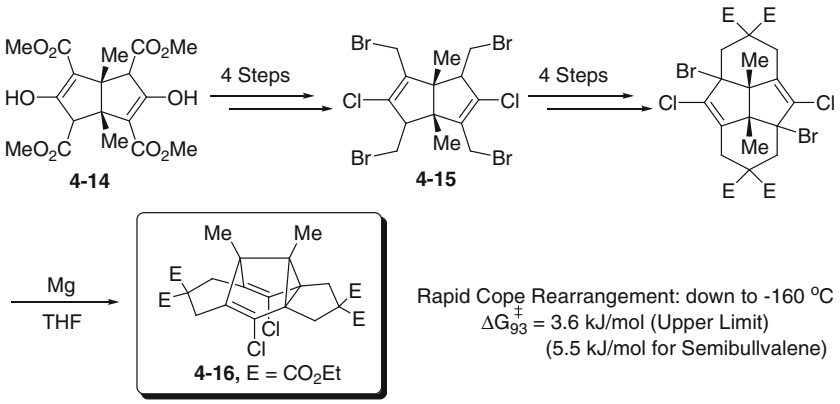
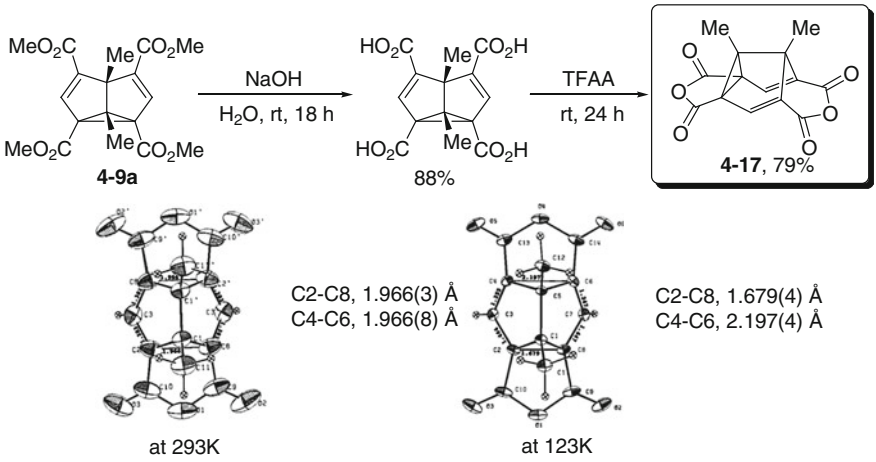


Fig. 4.8 Small-ring annulated semibullvalenes



Scheme 4.10 Synthesis of 2,8:4,6-biannulated semibullvalene



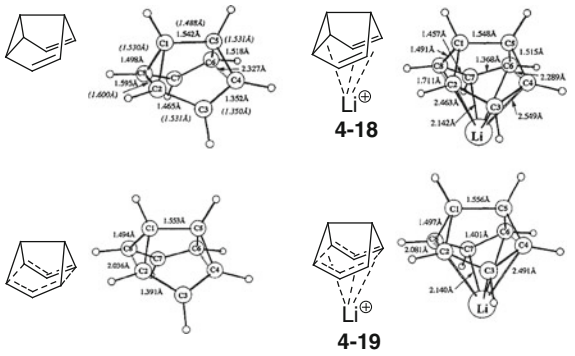
Scheme 4.11 Synthesis of 2,4,6,8-semibullvalene tetracarboxylic acid anhydride

4.3.3 Coordination with Metal Ion

In 1993, Schleyer et al. reported computational results on complexion of SBV with metal ion and suggested more delocalized structure might have homoaromaticity. According to ab initio calculations, complexation of a Li^+ ion stabilizes delocalized structure of SBV **4-1**^{deloc} more effectively than localized structure **4-1**. And the delocalized structure does have bishomoaromatic character [13]. Geometries of localized structure **4-1**, delocalized structure **4-1**^{deloc}, and their corresponding coordination complexes with Li^+ ion were fully optimized at the RHF2(full)/6-31G*. Li^+ complexation polarizes **4-1a** and results in a partially delocalized structure. The C2–C8 bond length in **4-18** and **4-19** increases to 1.711 and 2.081 Å

Complex	σ	δ
Li^+	95.4	0.0
4-18	101.1	-5.7
Li^+-Cp	102.3	-6.9
Li^+-C_6H_6	102.8	-7.4
4-19	106.2	-10.8
Li^+-Cp_2	106.2	-10.8

Calculated by the IGLO Method
(IGLO/DZ//RMP2(full)/6-3lG*)



The RMP2(full), 6-31G* optimized structures

Fig. 4.9 Optimized structures of semibullvalene and Li^+ complexes, absolute lithium shielding constants (σ) and chemical shifts (δ)

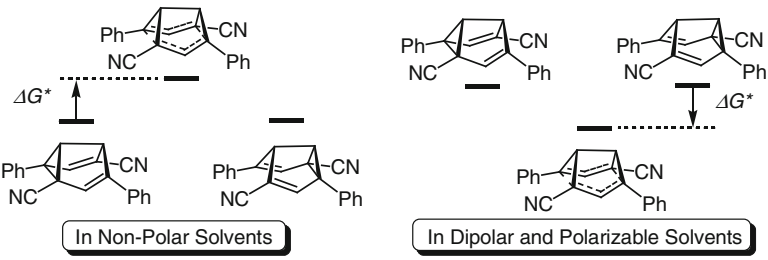
(from 1.595 Å in **4-1** and 2.036 Å in **4-1**^{deloc}), indicating more delocalized character of the electron system of **4-18** and **4-19**. The C_{2v}-symmetrical structure **4-19** is only 0.1 kcal/mol less stable than the C_s-symmetrical structure **4-18** at level of (MP2 (fu11)/6-31G*). Absolute lithium shielding constants (σ) and chemical shifts (δ) of **4-18** and **4-19** were calculated at IGLO/DZ//RMP2(full)/6-3lG* level and compared with lithium cyclopentadienide and lithium benzene complex. The homoaromaticity of **4-19** and the partial homoaromaticity in **4-18** are indicated by the upfield chemical shifts (Fig. 4.9) [13].

4.3.4 Stabilization of Delocalized Structure by Solvation

In 1999, Quast found dipolar and polarizable solvents such as *N,N′*-dimethylpropylene urea (DMPU) strongly affect and even may reverse the relative stabilities of the localized and delocalized structures of 4,8-diphenylsemibullvalene-2,6-dicarbonitrile. The author calculated electrical dipole and quadrupole moments and molecular polarizabilities using the B3LYP/6-31G* method and computed solvation energies with the conductor-like polarized continuum model (CPCM). The results indicate that the solvent effects are due to the greater polarity and polarizability of the delocalized structures relative to the localized structures (Fig. 4.10) [10].

4.3.5 Introduction of Heteroatom into Skeleton

Boron carbonyl (BCO) fragment is isolobal to a CH group. This relationship predicts BCO might mimic the aromaticity of their hydrocarbon counterparts. In 2003, Schleyer et al. applied this strategy to convert delocalized structure of SBV into bishomoaromatic minima by BCO replacement at appropriate positions (Fig. 4.11).



Solvent	λ_{max} (nm)	ΔG^* (kJ/mol)	f^* X 100%
C_6H_{12}	436	7.9	2
MeCN	439	3.4	12
DMF	447	1.8	20
DMSO	453	0.4	30
DMPU	452	-3	60

f^*: Percentages of Delocalized Structures

Fig. 4.10 Stabilization of delocalized structure by solvation

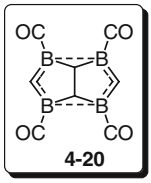


Fig. 4.11 2,4,6,8-tetra BCO-substituted semibullvalene

The structure of 2,4,6,8-tetra BCO-substituted SBV **4-20** was optimized at B3P86/6-311+G** as a C_{2v} symmetrical delocalized structure. The bond length of B2–C3 was optimized as 1.494 Å, which was close to the B–C bond length (1.503 Å) in 1,3,5-tri BCO-substituted benzene. The nucleus-independent chemical shift (NICS) of **4-20** was calculated as −16.6 and confirmed the delocalization and its neutral bishomoaromaticity. The author ascribed the stabilization of the allylic moieties in delocalized structure to the greater radial extension of the orbitals of the more electropositive boron, which favors bridged structures. However, no synthesis effort toward **4-20** has been successful [17].

4.3.6 Azasemibullvalene

In 1971, Dewar et al. theoretically predicted by MINDO/2 calculations that the introduction of heteroatoms such as nitrogen into the SBV skeleton (e.g., 2,6-diazasemibullvalene, NSBV) could further reduce or even eliminate the barrier

of the Cope rearrangement and thus result in a delocalized, homoaromatic ground-state [15]. Based on the results of calculation, the delocalized structures of 2,6-diazasemibullvalene and 3,7-diazasemibullvalene in Fig. 4.12 were both stable homoaromatic structures. In 2011, Greve suggested the localized structure of 2,6-diazasemibullvalene is more stable by MP4/cc-pVDZ//MP2/cc-pVDZ and CCSD (T)/cc-pVDZ//MP2/cc-pVDZ calculations. However, the activation barrier was only calculated as 0.56 kcal/mol. Thus, it might be possible that the experimental model gives more stable delocalized homoaromatic structure [16]. Moreover, the delocalized structures of 2,6-diazasemibullvalene and 3,7-diazasemibullvalene were both calculated as large negative NICS value (Fig. 4.12).

However, the difficulties in the synthesis, isolation, and structural characterization of NSBV hampered chemists to find an experimental probe as real model to prove the theoretical assumption. The only experimental model of NSBV was reported by Müllen et al. in 1982 (Scheme 4.12) [18]. Bipyrroline **4-22** was

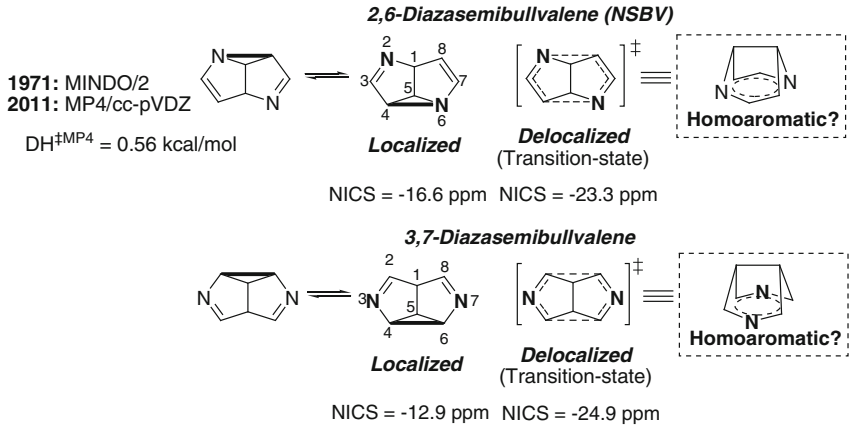
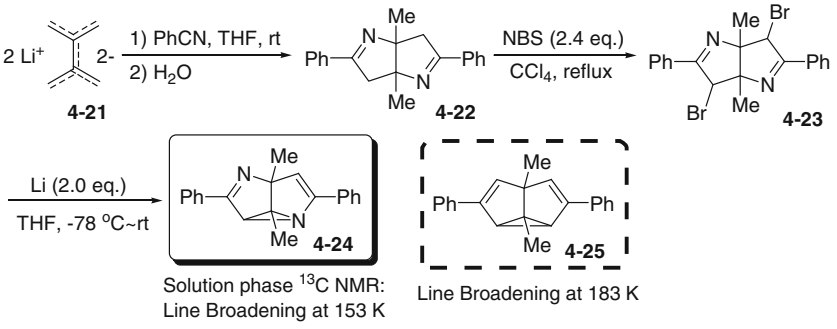


Fig. 4.12 Azasemibullvalene



Scheme 4.12 Synthesis of 1,5-dimethyl-3,7-diphenyl-2,6-semibullvalene

synthesized from dilithio compound **4-21** and benzonitrile. Bromination with NBS gave dibromo compound **4-23**, which was reduced by metal lithium in [D_8]tetrahydrofuran (THF-d_8) to in situ generate 1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene **4-24**. **4-24** was shown to have a lower barrier of the Cope rearrangement as compared to its carbon-analogue, although the authors did not consider **4-24** to be homoaromatic. In 1985, Müllen et al. reported a thermo-rearrangement of **4-24** to give 1,5-diazocine, which has been recorded as the only example on the reaction chemistry of NSBV [19]. During the past 30 years, no further report followed in the literature, leaving the structure and reaction chemistry of NSBV almost unknown [20].

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Chapter 5
2,6-Diazasemibullvalenes: Synthesis, Structural Characterization, and Theoretical Analysis

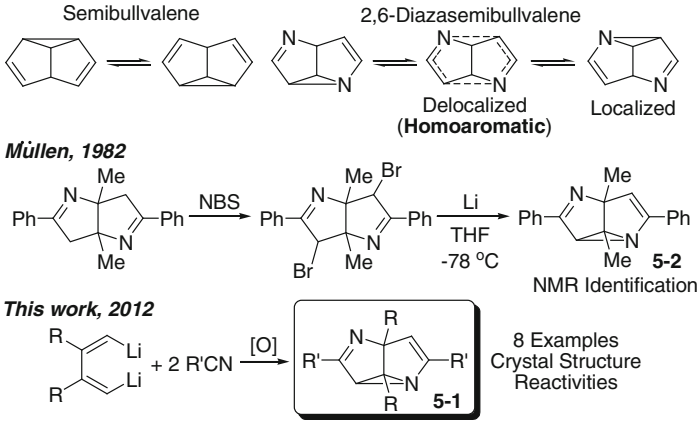
5.1 Introduction

The term homoaromaticity, introduced by Winstein et al. in 1959, describes a type of aromaticity in which conjugation is interrupted by an sp^3-hybridized carbon atom [1]. Since then, the concept of homoaromaticity has attracted much attention both theoretically and experimentally, focusing on the "non-classical" bonding mode and new chemical reactions. Although many cationic species and a few anionic species have been confirmed to be homoaromatic, whether or not neutral species can be homoaromatic is still a matter of debate. Thus, the establishment of experimental models for potential neutral homoaromatic molecules has long been an exciting pursuit in synthetic and theoretical chemistry.

Semibullvalenes (SBVs) and azasemibullvalenes have long been considered as potentially neutral homoaromatic [2–21]. However, this topic has been long in a controversy since SBVs and azasemibullvalenes undergo rapid, degenerate Cope rearrangement, and their true structure could be in equilibrium of two localized C_s symmetric structure or the delocalized bishomoaromatic C_{2v} symmetric structure. In order to further lower the barrier of the Cope rearrangement as well as the relative energy of the delocalized transition state, and finally realize neutral homoaromatic molecules, several novel classes of SBVs have been designed and synthesized during the past four decades.

In 1971, based on the theoretical study, Dewar predicted that the introduction of heteroatoms like nitrogen into the semibullvalene skeleton (e.g., 2,6-diazasemibullvalene, NSBV) could further reduce or even eliminate the barrier of the Cope rearrangement and thus result in a delocalized, homoaromatic ground state [16]. However, the difficulties in the synthesis, isolation, and structural characterization of NSBV hampered chemists to find an experimental probe as real model to prove the theoretical assumption. In 1982, Müllen reported the only experimental

S. Zhang, *The Chemistry of Zirconacycles and 2,6-Diazasemibullvalenes*,
Springer Theses, DOI 10.1007/978-3-662-45021-5_5



Scheme 5.1 2,6-diazasemibullvalene

probe of NSBV, 1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene (**5-2**), for the first time [19]. In 1985, Müllen et al. reported a thermo-rearrangement of **5-2** to give 1,5-diazocine, which has been recorded as the only example on the reaction chemistry of NSBV.

During the past 30 years, due to the difficulty in synthesis of NSBV, no further report followed in the literature, leaving the structure and reaction chemistry of NSBV almost totally unknown. In this chapter, we report the synthesis and isolation of a series of NSBVs, the first single-crystal structure of NSBV (**5-1a**), and theoretical/computational calculation and analysis (Scheme 5.1).

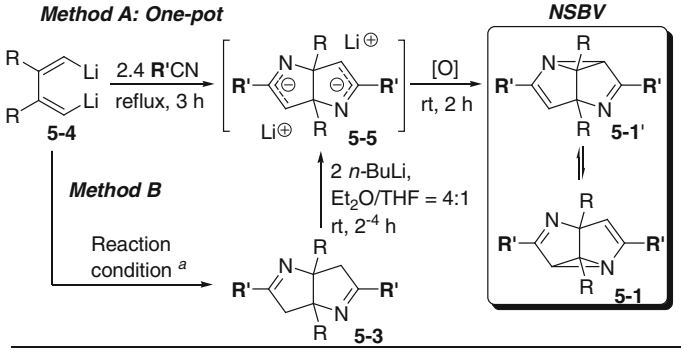
5.2 Result and Discussion

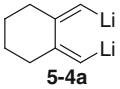
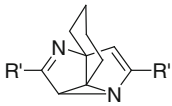
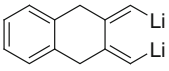
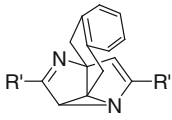
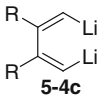
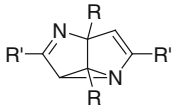
5.2.1 2,6-Diazasemibullvalenes: Synthesis

The author developed two preparative methods for the efficient synthesis of NSBV derivatives from the reaction of dilithio reagents **5-4** and nitriles (Table 5.1) [22]. Both methods involved lithiation and oxidant-induced intramolecular C–N bond formation [23].

Method A represents a one-pot synthesis of NSBVs **5-1**. The dilithio reagent **5-4a** was generated in situ from its corresponding 1,4-diiodo compound and *t*-BuLi (Table 5.1). Reaction of **5-4a** with 2.4 equiv of trimethylacetonitrile (*t*-BuCN) readily afforded the dianion **5-5a** [22]. Addition of di-*tert*-butyl peroxide ($(t\text{-BuO})_2$, 4.0 equiv) as oxidant led to NSBV derivative **5-1a** via intramolecular C–N bond formation. Decomposition of **5-1a** was observed when normal work-up procedure and column chromatography using silica gel or alumina were used to purify the product. Finally, the bulb-to-bulb distillation (220 °C, 0.01 kPa) was found to be an

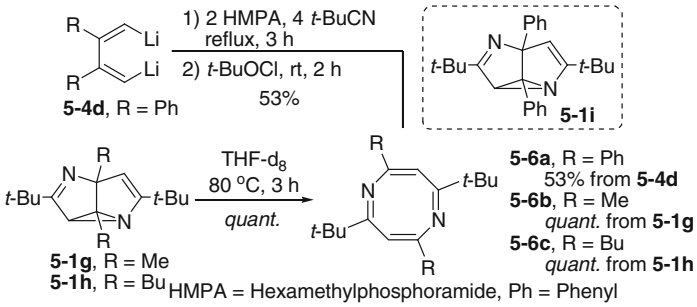
Table 5.1 Synthetic strategies toward 2,6-diazasemibullvalenes



	1,4-Dilithio-1,3-diene	NSBV	Isolated Yield (%) Method A	Method B
Type I	 **5-4a**			
		5-1a, R' = *t*-Bu[b]	66 [c]	83 [d]
		5-1b, R' = Ad	53 [c]	68 [d]
		5-1c, R' = Et_2MeC	43 [c]	72 [d]
		5-1d, R' = $BuMe_2C$	30 [c]	83 [d]
		5-1e, R' = $EtMe_2C$	51 [c]	72 [d]
Type II	 **5-4b**			
		5-1f, R' = *t*-Bu	51 [e]	
Type III	 **5-4c**			
		5-1g, R = Me, R' = *t*-Bu		72 [e]
		5-1h, R = Bu, R' = *t*-Bu		73 [e]

a. HMPA (2.0 eq.), rt, 0.5 h; **R'**CN (2.4 eq.), reflux, 3 h; then $NaHCO_3$ (aq.);
b. Me = methyl; Et = Ethyl; Bu = Butyl; Ad = Adamantyl;
c. [O] = $(t\text{-BuO})_2$ (4.0 eq.); *d*. [O] = $PhI(OAc)_2$ (1.0 eq.); *e*. [O] = *t*-BuOCl (1.0 eq.)

efficient way and the pure product **5-1a** as light-yellow crystallines was obtained in 66 % isolated yield. Reaction of **5-4a** with different nitriles followed by treatment with $(t\text{-BuO})_2$ afforded 1,5-bridged-2,6-diazasemibullvalenes **5-1b–5-1e** with different substituents at 3,7-position (**Type I**) in moderate yields. Furthermore, the



Scheme 5.2 Thermolysis of NSBVs **5-1** to 1,5-diazocines **5-6**

dilithio reagent **5-4b** was successfully applied to one-pot synthesis of the NSBV derivative **5-1f** (**Type II**) in 51 % isolated yield.

Method B represents a stepwise synthesis of NSBV **5-1**. The dianions **5-5** could be readily in situ generated via dilithiation of Δ^1-bipyrrolines **5-3**. Sequential addition of phenyliodine diacetate ($PhI(OAc)_2$) as oxidant afforded their corresponding NSBVs **5-1** in good isolated yields. The use of $(t\text{-BuO})_2$ led to a slightly lower yield. By using ***Method B***, **5-1a–5-1e** could all be obtained in higher isolated yields. 1,5-Dialkyl-substituted Δ^1-bipyrrolines **5-3** could also be converted to their corresponding non-bridged NSBVs **5-1g** and **5-1h** (**Type III**) in 72 % and 73 % isolated yield, respectively. For the synthesis of **Type I** NSBV derivatives, ***Method B*** was found to be more efficient than ***Method A***. All NSBV derivatives are stable in inert atmosphere at room temperature.

However, as given in Scheme 5.2, when 2,3-diphenyl-1,4-dilithio-1,3-butadiene **5-4d** was applied following ***Method A***, 1,5-diazocine **5-6a** was obtained in 53 % isolated yield and was structurally characterized. The author assumed that the expected NSBV derivative **5-1i** might be unstable at room temperature and readily transformed to the thermodynamically more stable **5-6a**, which was also obtained via ***Method B***. Those non-bridged NSBV derivatives **5-1g** and **5-1h** could be quantitatively converted to their corresponding 1,5-diazocines **5-6b** and **5-6c,** but at a higher temperature [10, 20]. On the contrary, 1,5-bridged NSBVs **5-1a–5-1f** showed good thermostability under 200 °C and did not undergo the transformation. These results demonstrated that the substituents at the 1,5-positions of NSBVs **5-1** played an important role in their thermostability [6].

5.2.2 2,6-Diazasemibullvalenes: Structural Characterization

A single crystal of **5-1a** suitable for X-ray structural determination, obtained at −20 °C in hexane/diethyl ether solution, provided the first example of single-crystal structure of NSBV. Thus, in the solid state, the single-crystal structure of **5-1a** (space group P2(1)2(1)2(1)) shows a localized structure with a strained aziridine

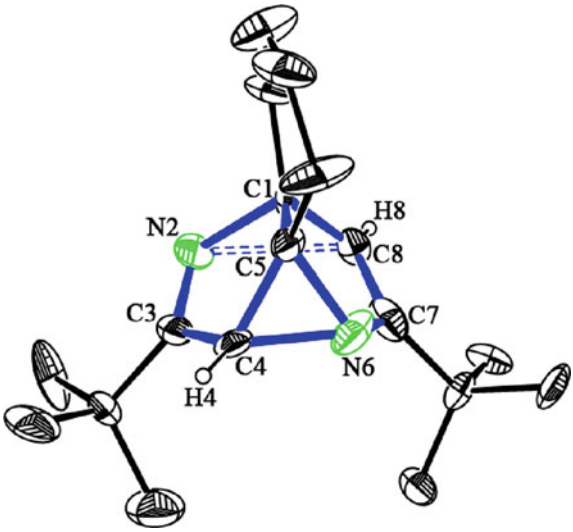


Fig. 5.1 Single-crystal X-ray structure of **5-1a** with 30 % thermal ellipsoids. Hydrogen atoms except H4 and H8 are omitted for clarity. Reprinted with the permission from ref. [25]. Copyright 2012 American Chemical Society

ring (Fig. 5.1). This is in good agreement with the observation using the solid-state ^{13}C NMR. The 1,5-bridge exists as a distorted boat-like cyclohexane ring. The C4-N6 bond (1.628 Å) is much longer than that in simple aziridine compounds (1.520 Å), indicating enhanced strain and through-bond coupling in the NSBV molecule [24]. The other bond lengths of the NSBV core are all in the normal range, comparable to the calculated localized structure of unsubstituted NSBV [17]. Thus, this NSBV molecule **5-1a** does not have C_2 symmetry in the crystal phase.

The solid-state ^{13}C NMR of **5-1a** at room temperature showed a "frozen" unsymmerical structure, consistent with its X-ray structure. C4 and C8 showed two broad singlets at $\delta = 74.7$ and 125.3 ppm, respectively. Other peaks of **5-1a** such as C1/C5 and C3/C7 all showed different chemical shifts from one another, indicating that the degenerate aza-Cope rearrangement was "frozen" in the solid state.

On the other hand, the solution-phase NMR spectra of all isolated NSBVs **5-1a–5-1h** showed interesting and characteristic patterns, indicating a rapid equilibrium between two localized structure **5-1a** and **5-1a′** in solution. For example, the aziridinyl H4 and vinyl H8 in **5-1a** displayed only one singlet at $\delta = 4.79$ ppm in the ^1H NMR spectrum in THF-d_8, whereas C1/C5, C3/C7, and C4/C8 of **5-1a** displayed three singlets at $\delta = 79.2$, 162.9, and 99.1 ppm, respectively, in the ^{13}C NMR spectrum in THF-d_8, due to the rapid degenerate Cope rearrangement. The chemical shift of C4/C8 in **5-1a** was comparable with those found in 1,5-dimethyl-3,7-diphenyl-2,6-diazasemibullvalene **5-2** (99.4 ppm for C4/C8) [19].

Low-temperature ^1H and ^{13}C NMR data of **5-1a** in THF-d_8 or THF-d_8/CS_2(1:3) solution were recorded on a 600-MHz spectrometer to study the solution-phase structure of **5-1a**. The low-temperature NMR spectra unambiguously showed that, even down to −100 °C **5-1a** was still undergoing rapid aza-Cope rearrangement. At −100 °C, the line widths at half-height $W_{1/2}$ of the singlet peak for C4/C8 and CH_3

carbon of the *t*-Bu group were 4.2 Hz and 4.5 Hz, respectively. However, at −110°C with addition of CS_2 in the solvent, line broadening (width at half-height $W_{1/2}$ = 41.9 Hz) of the singlet peak for C4/C8 was observed, while no obvious line broadening of the peak ($W_{1/2}$ = 8.8 Hz) for the CH_3 carbon on the *t*-Bu group took place, suggesting that the aza-Cope rearrangement was slowed down. This experimental observation indicated that **5-1a** was not a static homoaromatic form but a dynamically balanced form in the rapid degenerated aza-Cope rearrangement. This trend is in good agreement with Müllen's report. By using the line shape analysis of the low-temperatue ^{13}C NMR spectra reported by Quast et al., the upper limit of the activation barrier $\Delta G^{\ddagger}_{163K}$ of the aza-Cope rearrangement was determined [7].

$$k = \frac{\pi(\Delta v)^2}{2W_{1/2}} \tag{5.1}$$

$$\Delta G^{\ddagger} = RT\left[\ln\frac{k_B T}{h} - \ln\frac{\pi(\Delta v)^2}{2W_{1/2}}\right] \tag{5.2}$$

R: Gas constant, 8.31 J K^{-1} mol^{-1}

T: Temperature, 163 K

k_B: Boltzmann constant, 1.38 × 10^{-23} J K^{-1}

h: Planck constant, 6.63 × 10^{-34} J s

Δν: Difference in chemical shifts for the exchange-related carbon nuclei (C4/C8) under slow-exchange conditions. Here, the chemical shifts of C4 and C8 in solid-state ^{13}C NMR spectrum are used to give the difference value (125.28 ppm, 74.65 ppm, respectively), 7.6 × 10^3 Hz.

$W_{1/2}$: Line widths at half-height of C4/C8, 41.9 Hz

According to the equations above, the rate constant *k* and the upper limit of the activation barrier $\Delta G^{\ddagger}_{163K}$ were calculated:

$$k = 2.16 \times 10^6\ s^{-1}$$

$$\Delta G^{\ddagger}_{163K} = 4.4\ \text{kcal/mol}$$

Thus, at 163 K, **5-1a** is still undergoing rapid aza-Cope rearrangement. Because of limitation of instrument, it is not feasible to collect data at or near the coalescence temperature for variable-temperature ^{13}C NMR spectra. Therefore, the author could only determine an upper limit for the activation barrier of the aza-Cope rearrangement at the lowest available temperature (163 K), which is indeed lower than that of its corresponding all-carbon analogs [7, 11].

5.2.3 2,6-Diazasemibullvalenes: Theoretical Analysis and Computational Results

In collaboration with Mr. Junnian Wei from the same research group, the structures of both localized NSBV **5-1a** and delocalized **5-1a**^{deloc} were optimized using DFT calculations [26–28]. At the B3LYP/6-31G* level, both localized ground-state **5-1a** and delocalized ground-state **5-1a**^{deloc} were found to be energy minima, as confirmed by frequency calculations (Fig. 5.2). The calculated C4-N6 and C2-N8 distances in **5-1a** are 1.58 and 2.33 Å, respectively. The other bond lengths are comparable to the values measured in the single-crystal structure. The calculated ^{13}C NMR spectrum of the localized structure utilizing (GIAO)B3LYP/6-311 + g** was similar to the solid-state ^{13}C NMR spectrum (the calculated chemical shifts of C3, C4, C7, and C8 are 178.1, 73.1, 172.9, and 129.3 ppm, respectively). The geometric parameters of **5-1a**^{deloc} were close to the values of the optimized delocalized structure of the unsubstituted NSBV reported by Greve [17]. However, its Gibbs free energy at 163 K was 1.8 kcal/mol higher than the value of the calculated localized **5-1a**. This trend is consistent with the calculations on unsubstituted NSBV at the MP2/cc-pVDZ level by Greve [17].

In addition, transition-state **5-1a*** of the aza-Cope rearrangement was optimized and shown in Fig. 5.2. The C4-N6 and C2-N8 distances are 1.97 and 2.21 Å, respectively. Calculations indicate that **5-1a*** and **5-1a**^{deloc} are very close in energy ($\Delta E^{\ddagger}_{\mathbf{1a}-deloc/\mathbf{1a}*} = 0.1$ kcal/mol, $\Delta G^{\ddagger}_{\mathbf{1a}-deloc/\mathbf{1a}*} = 0.3$ kcal/mol) and the potential energy surface has a broad, flat transition-state region. The activation barrier of the aza-Cope rearrangement at 163 K was calculated to be only 2.1 kcal/mol, which is comparable with the experimental results. Because of the small activation barrier from **5-1a**^{deloc} to **5-1a**, the rearrangement of **5-1a**^{deloc} to **5-1a** should be extremely

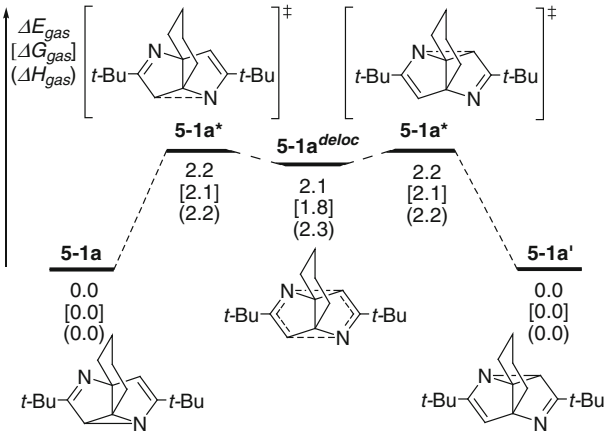
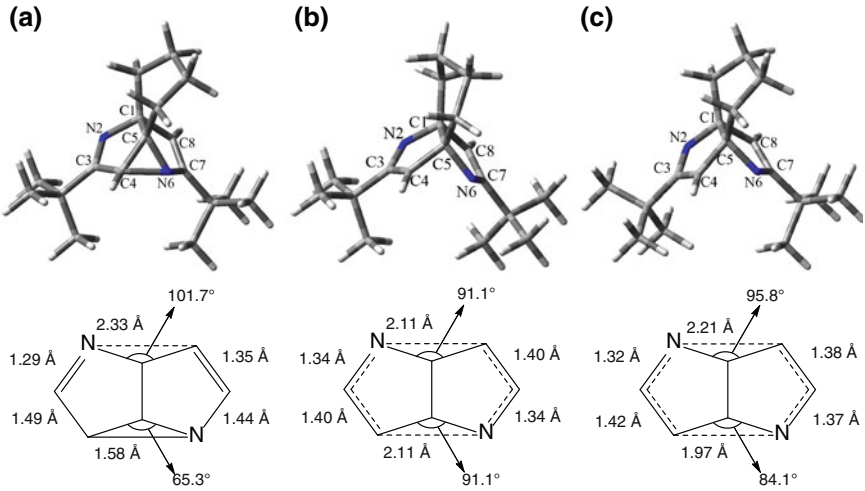


Fig. 5.2 Calculated relative energy, Gibbs free energy, and enthalpy (kcal/mol) at 163 K, 1 atm



Scheme 5.3 Optimized localized structure of **5-1a**, optimized delocalized structure of **5-1a**^{deloc}, and optimized structure of transition-state **5-1a*** at the B3LYP/6-31G* level. Selected bond length (Å) and angles (°) of all structures are also shown. Reprinted with the permission from ref. [25]. Copyright 2012 American Chemical Society

fast. Since the homoaromatic **5-1a**^{deloc} was calculated to be an intermediate but not a transition state, its existence in the solution and gas phase is for sure, although its percentage could be about 0.2 %, based on the Boltzmann distribution analysis. This result again supports the suggestion that the 2,6-diazasemibullvalene rearrangement has an even lower barrier than that for its corresponding all-carbon analog.

As introduced in Chap. 4, nucleus-independent chemical shift (NICS) is defined as the negativity of the absolute magnetic shielding and is often used as a simple, efficient measure of aromaticity [29, 30]. A more negative NICS value indicates a more aromatic structure. NICS(0) represents the negativity value at the center of aromatic ring, while NICS(−1) represents the negativity value at 1 Å above the center of aromatic ring. The calculated B3LYP/6-311 + g** NICS(0) and NICS(−1) values of **5-1a**^{deloc} were −19.0 and −14.2, respectively, all large and negative, and in good accordance with the values reported by Greve using GIAO-HF/cc-pVDZ [17]. In addition, the NICS(0) and NICS(−1) values of the transition-state **5-1a*** were −17.6 and −13.3, respectively. Thus, both **5-1a**^{deloc} and transition-state **5-1a*** could be homoaromatic based on their NICS values (Scheme 5.3 and Table 5.2).

5.3 Summary

The author successfully established experimental models for structurally and theoretically interesting 2,6-diazasemibullvalenes (NSBVs). Efficient one-pot synthesis and isolation of a series of NSBVs were developed by oxidant-induced C–N bond

Table 5.2 Selected bond lengths (Å) and angles (°) from the single-crystal structure of **5-1a**, optimized structure of **5-1a**, **5-1a*deloc***, **5-1a***, and optimized structure of 2,6-diazasemibullvalene at the MP2/cc-pVDZ level [17]

	5-1a[a]	**5-1a**[b]	**5-1a*deloc*** [b]	**5-1a***[b]	**NSBV**[c]	**NSBV*deloc*** [c]
N2-C3	1.340(14)	1.29	1.34	1.32	1.31	1.35
C3-C4	1.408(14)	1.49	1.47	1.42	1.46	1.40
N6-C7	1.465(15)	1.44	1.34	1.37	1.42	1.35
C7-C8	1.265(16)	1.35	1.47	1.38	1.36	1.40
C4-N6	1.628(7)	1.58	2.11	1.97		2.08
N2-C8	2.266(3)	2.33	2.11	2.21	2.27	2.08
C4-C5-N6	64.9(4)	65.3	91.1	84.1		
N2-C1-C8	96.5(5)	101.7	91.1	95.8		

[a] Single-crystal structure
[b] Optimized structure at B3LYP/6-31G* level
[c] From Ref. [18]

formation. For the first time, the single-crystal structure of an NSBV (**5-1a**) was determined and the molecule showed a localized structure. The C_2-symmetrical structure of **5-1a** in solution along with line broadening of the NMR signal at −110 °C indicates an extremely low barrier of the rapid degenerate aza-Cope rearrangement. DFT calculations at B3LYP/6-31G* level show that both localized **5-1a** and delocalized **5-1a*deloc*** are energy minima, with the Gibbs free energy of **5-1a** being 1.8 kcal/mol lower than that of **5-1a*deloc***. Thus, **5-1a** should be the predominant form in the gas or condensed phase; however, the existence of the homoaromatic **5-1a*deloc*** is highly possible. This is in good agreement with the observed localized single-crystal structure, solid-state NMR spectra, and previous computational results. The activation barrier $\Delta G^{\ddagger}$ was determined to be 4.4 kcal/mol by line shape analysis of low-temperature ^{13}C NMR spectra, comparable with 2.1 kcal/mol calculated value. Both experimental and computational results show that NSBV has a lower activation barrier than its corresponding all-carbon analog (SBV).

5.4 Experimental Section

All reactions were conducted under a slightly positive pressure of dry nitrogen using standard Schlenk line techniques or under a nitrogen atmosphere in a Mikrouna Super (1,220/750) glovebox. The nitrogen in the glove box was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glovebox atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure that both were always below 1 ppm. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Solvents were purified by an Mbraun SPS-800 Solvent Purification System and dried over fresh Na chips in the glovebox.

Organometallic samples for NMR spectroscopic measurements were prepared in the glovebox by use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-400 spectrometer (FT, 400 MHz for ^{1}H; 100 MHz for ^{13}C) or a JEOL-AL300 spectrometer (FT, 300 MHz for ^{1}H; 75 MHz for ^{13}C) at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Microelemental analyses were performed on an Elemental Analyzer vario EL apparatus. Low-temperature ^{1}H and ^{13}C NMR data of **5-1a** in THF-d_8 or THF-d_8/CS_2 (1:3) were recorded on a BRUKER AVANCE 600-M spectrometer (FT, 600 MHz for ^{1}H; 150 MHz for ^{13}C). Solid-state NMR spectrum of **5-1a** was recorded on BRUKER AVANCE III 400-M spectrometer (FT, 100 MHz for ^{13}C).

n-BuLi and *t*-BuLi were obtained from Acros. 2,2-Dimethylbutyronitrile, 2,2-dimethylhexanenitrile, diiodo compounds **5-7a**, **5-7c–5-7e,** and bipyrrolines **5-3a–5-3c, 5-3g** were prepared according to the reported literature.

Synthesis of (2*Z*,3*Z*)-2,3-bis(iodomethylene)-1,2,3,4-tetrahydronaphthalene (15b): To a solution of Cp_2ZrCl_2 (7.7 g, 26.4 mmol) in 70 mL of THF in a 200-ml Schlenk tube was added *n*-BuLi (1.6 M hexane solution, 33.0 mL, 52.8 mmol) at −78 °C (dry ice/acetone), and the mixture was stirred for 1 h. 1,2-Bis(3-(trimethylsilyl)prop-2-ynyl)benzene (6.5 g, 22.0 mmol) was added to the solution, and it was warmed to room temperature. After stirring for 3 h, CuCl (2.8 g, 28.6 mmol) and I_2 (16.7 g, 66.0 mmol) were added to the mixture, and it was stirred for 3 h at room temperature. The mixture was quenched with 3 N HCl and extracted with petroleum ether. The combined organic phase was washed with saturated aqueous $NaHCO_3$ solution, saturated aqueous $Na_2S_2O_3$ solution, water, and brine. The solution was dried over anhydrous Na_2SO_4. The solvent was evaporated, and the resulting brown solid was directly dissolved into CH_2Cl_2 (1.0 mmol in 4.0 mL of CH_2Cl_2) and then mixed with freshly prepared CH_3ONa in CH_3OH (15.0 mL, 2.0 M). The reaction mixture was stirred at 50 °C for 3 h. The reaction mixture was added to 50 mL of 3 N HCl and extracted with petroleum ether (3 × 60.0 mL). The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give crude products. Chromatography using petroleum ether as the eluent provided the corresponding pure product **5-7b**.

5-7b: Yellow solid, isolated yield 56 % (5.0 g). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 4H, CH_2), 6.36 (s, 2H, CH), 7.04–7.17 (m, 4H, C_6H_4); ^{13}C NMR (75.4 MHz, $CDCl_3$): δ = 40.80 (2 CH_2), 74.99 (2 CH), 126.46 (2 CH), 128.24 (2 CH), 134.71 (2 quat. C), 147.71 (2 quat. C). HRMS: *m/z*: calcd for $C_{12}H_{11}I_2$ $[M + H]^+$: 408.8950, found: 408.8955. Elemental analysis calcd (%) for $C_{12}H_{10}I_2$: C, 35.32; H, 2.47; found: C, 35.41; H, 2.36.

General procedure for preparation of 2,6-diazasemibullvalene 5-1a (*Type I*, *Method A*) from cyclic 2,3-disubstituted 1,4-diiodo-1,3-dienes 5-7a: *t*-BuLi (4.0 mmol, 1.6 M in pentane) was added to a solution of cyclic 2,3-disubstituted 1,4-diiodo-1,3-diene **5-7a** (1.0 mmol) in diethyl ether (5 mL) in a 20-ml Schlenk

tube at −78 °C (dry ice/acetone). The reaction mixture was then stirred at −78 °C for 30 min to generate 1,4-dilithio-1,3-diene, and then, the reaction mixture was stirred at room temperature for 30 min. After addition of *t*-BuCN (2.4 mmol, 264 μl) at −78 °C, the mixture was heated to reflux and maintained for 3 h. Then, $(t\text{-BuO})_2$ (4.0 mmol, 361 μl) was added and the reaction mixture was kept at room temperature for 2 h. After dried up, the reaction mixture was extracted with hexane (10 mL) for three times. The solvent was evaporated in vacuum to give yellow solid, which was purified by bulb-to-bulb distillation (220 °C, 0.01 kPa) to afford the 2,6-diazasemibullvalene **5-1a**.

Similarly, 2,6-diazasemibullvalenes **5-1b–5-1e** were obtained.

1,5-Tetramethylene-3,7-di-*tert*-butyl-2,6-diazasemibullvalene (5-1a): Yellow solid, isolated yield 66 % (180 mg). ^{1}H NMR (300 MHz, THF-d_8, 25 °C): δ = 1.05 (s, 18H, CH_3), 1.16–1.27 (m, 4H, CH_2), 1.48–1.56 (m, 2H, CH_2), 1.91–1.96 (m, 2H, CH_2), 4.77 (s, 2H, CH); ^{13}C NMR (75 MHz, THF-d_8, 25 °C): δ = 22.26 (2 CH_2), 28.90 (2 CH_2), 28.96 (6 CH_3), 34.75 (2 quat. C), 79.56 (2 quat. C), 99.56 (2 CH), 163.25 (2 quat. C). HRMS: *m/z*: calcd for $C_{18}H_{29}N_2$ $[M + H]^+$: 273.2331, found: 273.2326. Elemental analysis calcd (%) for $C_{18}H_{28}N_2$: C, 79.07; H, 10.69; N, 10.24; found: C, 79.00; H, 10.78; N, 10.12. Single crystals of **5-1a** suitable for X-ray analysis were grown in hexane/diethyl ether (2:1) at −20 °C.

1,5-Tetramethylene-3,7-di-adamantyl-2,6-diazasemibullvalene (5-1b): Yellow solid, isolated yield 53 % (226 mg). ^{1}H NMR (300 MHz, THF-d_8, 25 °C): δ = 1.12–2.01 (m, 6H, CH; 32H, CH_2), 4.73 (s, 2H, CH); ^{13}C NMR (75 MHz, THF-d_8, 25 °C): δ = 22.29 (2 CH_2), 28.94 (2 CH_2), 29.41 (6 CH), 36.94 (2 quat. C), 37.71 (6 CH_2), 41.46 (6 CH_2), 79.00 (2 quat. C), 99.26 (2 CH), 163.22 (2 quat. C). Elemental analysis calcd (%) for $C_{30}H_{40}N_2$: C, 84.06; H, 9.41; N, 6.54; found: C, 83.85; H, 9.72; N, 6.22.

1,5-Tetramethylene-3,7-di-(1-methyl-1-ethylpropyl)-2,6-diazasemibullvalene (5-1c): Yellow oil, isolated yield 43 % (153 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.83–0.89 (m, 12H, CH_3), 1.02 (s, 6H, CH_3), 1.34–1.71 (m, 14H, CH_2), 1.94–2.00 (m, 2H, CH_2), 4.71 (s, 2H, CH); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 8.83 (4 CH_3), 8.97 (2 CH_3), 21.76 (2 CH_2), 22.26 (2 CH_2), 28.73 (2 CH_2), 30.65 (2 CH_2), 40.84 (2 quat. C), 79.26 (2 quat. C), 100.53 (2 CH), 161.18 (2 quat. C). Elemental analysis calcd (%) for $C_{22}H_{36}N_2$: C, 80.43; H, 11.04; N, 8.53; found: C, 80.19; H, 11.28; N, 8.33.

1,5-Tetramethylene-3,7-di-(1,1-dimethylpentyl)-2,6-diazasemibullvalene (5-1d): Yellow oil, isolated yield 30 % (115 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.91–0.93 (m, 12H, CH_3), 1.07–1.08 (m, 6H, CH_3), 1.13–1.14 (m, 4H, CH_2), 1.31–1.33 (m, 8H, CH_2), 1.40–1.42 (m, 2H, CH_2), 1.64-1.67 (m, 4H, CH_2), 1.93–1.98 (m, 2H, CH_2), 4.74 (s, 2H, CH); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 14.42 (2 CH_3), 21.74 (2 CH_3), 23.77 (2 CH_3), 26.29 (2 CH_2), 26.44 (2 CH_2), 27.21 (2 CH_2), 28.58 (2 CH_2), 37.47 (2 CH_2), 41.60 (2 quat. C), 79.25 (2 quat. C), 99.84 (2 CH), 162.12 (2 quat. C). Elemental analysis calcd (%) for $C_{24}H_{40}N_2$: C, 80.84; H, 11.31; N, 7.86; found: C, 80.60; H, 11.59; N, 7.56.

1,5-Tetramethylene-3,7-di-(1,1-dimethylpropyl)-2,6-diazasemibullvalene (5-1e): Yellow oil, isolated yield 51 % (154 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C): $\delta = 0.87$ (t, $J = 7.2$ Hz, 6H, CH_3), 1.08 (s, 12H, CH_3), 1.37–1.43 (m, 6H, CH_2), 1.59–1.66 (m, 4H, CH_2), 1.90–1.95 (m, 2H, CH_2), 4.70 (s, 2H, CH); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): $\delta = 8.97$ (2 CH_3), 21.76 (4 CH_3), 22.26 (2 CH_2), 28.73 (2 CH_2), 30.21 (2 CH_2), 40.85 (2 quat. C), 79.26 (2 quat. C), 100.53 (2 CH), 161.18 (2 quat. C). Elemental analysis calcd (%) for $C_{20}H_{32}N_2$: C, 79.94; H, 10.73; N, 9.32; found: C, 79.81; H, 10.70; N, 9.28.

Procedure for preparation of 2,6-diazasemibullvalene 5-1f (*Type II*, *Method A*) from cyclic 2,3-disubstituted 1,4-diiodo-1,3-dienes 5-7b: *t*-BuLi (4.0 mmol, 1.6 M in pentane) was added to a solution of cyclic 2,3-disubstituted 1,4-diiodo-1,3-diene **5-7b** (1.0 mmol) in diethyl ether (10 mL) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). The reaction mixture was then stirred at −78 °C for 30 min to generate 1,4-dilithio-1,3-diene, and then, the reaction mixture was stirred at room temperature for 30 min. After addition of *t*-BuCN (2.4 mmol, 264 μl) at −78 °C, the mixture was heated to reflux and maintained for 3 h. Then, *t*-BuOCl (1.0 mmol, 119 μl) was added and the reaction mixture was kept at room temperature for 2 h. After dried up, the reaction mixture was extracted with hexane (20 mL) and filtered. The solvent was evaporated in vacuum. Repeat this extraction–filtration–drying procedure for three times to afford 2,6-diazasemibullvalene **5-1f**.

1,5-Xylylene-3,7-di-*tert*-butyl-2,6-diazasemibullvalene (5-1f): Yellow solid, isolated yield 51 % (164 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 1.21 (s, 18H, CH_3), 3.04–3.17 (m, 4H, CH_2), 4.93 (s, 2H, CH), 7.10 (s, 4H, C_6H_4); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 28.68 (6 CH_3), 34.57 (2 CH_2), 46.89 (2 quat. C), 82.33 (2 quat. C), 96.39 (2 CH), 126.87 (2 quat. C), 128.45 (2 quat. C), 136.22 (2 quat. C), 165.05 (2 quat. C). Elemental analysis calcd (%) for $C_{22}H_{28}N_2$: C, 82.45; H, 8.81; N, 8.74; found: C, 82.34; H, 8.96; N, 8.70.

General procedure for preparation of Δ^1-bipyrroline 5-3: *t*-BuLi (4.0 mmol, 1.6 M in pentane) was added to a solution of cyclic 2,3-disubstituted 1,4-diiodo-1,3-diene **5-7** (1.0 mmol) in diethyl ether (5 mL) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). The reaction mixture was then stirred at −78 °C for 30 min to generate 1,4-dilithio-1,3-diene, and then, the reaction mixture was stirred at room temperature for 30 min. HMPA (2.0 mmol, 347 μl) was then added, and the reaction mixture was stirred at room temperature for 30 min. After addition of nitrile (4.0 mmol), the mixture was heated to reflux and maintained for 3 h. The reaction mixture was quenched by saturated aqueous $NaHCO_3$, extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:2:1) to afford the corresponding Δ^1-bipyrroline **5-3**.

5-3d: Colorless oil, isolated yield 75 % (268 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.87 (t, J = 7.2 Hz, 6H, CH_3), 1.07 (s, 12H, CH_3), 1.12–1.16 (m, 4H,

CH_2), 1.19–1.26 (m, 8H, CH_2), 1.36–1.46 (m, 6H, CH_2), 2.28–2.32 (m, 2H, CH_2), 2.59–2.97 (m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 14.08 (2 CH_3), 21.13 (2 CH_3), 23.35 (2 CH_3), 25.74 (2 CH_2), 26.38 (2 CH_2), 26.79 (2 CH_2), 33.05 (2 CH_2), 38.62 (2 quat. C), 41.03 (2 CH_2), 43.23 (2 CH_2), 78.88 (2 quat. C), 180.49 (2 quat. C). HRMS: *m/z*: calcd for $C_{24}H_{43}N_2$ $[M + H]^+$: 359.3426, found: 359.3435. Elemental analysis calcd (%) for $C_{24}H_{42}N_2$: C, 80.38; H, 11.81; N, 7.81; found: C, 80.31; H, 11.87; N, 7.71.

5-3e: Colorless oil, isolated yield 61 % (187 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.73 (t, J = 7.2 Hz, 6H, CH_3), 1.01 (s, 12H, CH_3), 0.93–1.20 (m, 4H, CH_2), 1.45–1.50 (m, 4H, CH_2), 1.50–1.60 (m, 2H, CH_2), 2.29–2.33 (m, 2H, CH_2), 2.60–2.98 (m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 8.96 (2 CH_3), 21.08 (2 CH_2), 25.33 (2 CH_3), 25.78 (2 CH_3), 33.02 (2 CH_2), 33.53 (2 CH_2), 38.83 (2 quat. C), 43.27 (2 CH_2), 78.89 (2 quat. C), 180.31 (2 quat. C). HRMS: *m/z*: calcd for $C_{20}H_{35}N_2$ $[M + H]^+$: 303.2800, found: 303.2806. Elemental analysis calcd (%) for $C_{20}H_{34}N_2$: C, 79.41; H, 11.33; N, 9.26; found: C, 79.32; H, 11.36; N, 9.20.

5-3f: Colorless crystal, isolated yield 62 % (151 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.08 (s, 18H, CH_3), 1.22 (s, 6H, CH_3), 2.51–3.07 (m, 4H, CH_2); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.80 (2 CH_3), 27.91 (6 CH_3), 35.41 (2 quat. C), 46.04 (2 CH_2), 80.46 (2 quat. C), 181.21 (2 quat. C). HRMS: *m/z*: calcd for $C_{16}H_{29}N_2$ $[M + H]^+$: 249.2331, found: 249.2336. Elemental analysis calcd (%) for $C_{16}H_{28}N_2$: C, 77.36; H, 11.36; N, 11.28; found: C, 77.32; H, 11.39; N, 11.22.

5-3h: Yellow solid, isolated yield 57 % (212 mg). ^1H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.29 (s, 18H, CH_3), 3.19–3.38 (m, 4H, CH_2), 6.74–7.03 (m, 10H, C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 28.13 (6 CH_3), 36.10 (2 quat. C), 47.06 (2 CH_2), 89.13 (2 quat. C), 126.17 (2 CH), 126.23 (4 CH), 127.40 (4 CH), 139.89 (2 quat. C), 183.70 (2 quat. C). HRMS: *m/z*: calcd for $C_{26}H_{33}N_2$ $[M + H]^+$: 373.2644, found: 373.2648. Elemental analysis calcd (%) for $C_{26}H_{32}N_2$: C, 83.82; H, 8.66; N, 7.52; found: C, 83.71; H, 8.72; N, 7.40.

General procedure for preparation of 2,6-diazasemibullvalenes 5-1a–5-1e (*Type I, Method B*) from Δ^1-bipyrroline 5-3: *n*-BuLi (0.64 mmol, 1.6 M in hexane, 0.4 mL) was added to a solution of Δ^1-bipyrroline **5-3** (0.32 mmol) in 5 mL of diethyl ether/THF (4:1) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). After 10 min, the reaction mixture was stirred at room temperature for 2 h. Then, $PhI(OAc)_2$ (0.32 mmol, 103 mg) was added and the reaction mixture was kept at room temperature for 2 h. After dried up, the reaction mixture was extracted with hexane (10 mL) and filtered. The solvent was evaporated in vacuum. Repeat this extraction–filtration–drying procedure for three times to afford 2,6-diazasemibullvalenes **5-1a–5-1e** in 68–83 % isolated yields.

5-1a: Yellow solid, isolated yield 83 % (72 mg).
5-1b: White solid, isolated yield 68 % (93 mg).
5-1c: Yellow oil, isolated yield 72 % (76 mg).
5-1d: Yellow oil, isolated yield 83 % (102 mg).
5-1e: Yellow oil, isolated yield 72 % (69 mg).

General procedure for preparation of 2,6-diazasemibullvalenes 5-1g–5-1h (*Type III, Method B*) from Δ^1-bipyrroline 5-3: *n*-BuLi (0.64 mmol, 1.6 M in hexane, 0.4 mL) was added to a solution of Δ^1-bipyrroline **5-3** (0.32 mmol) in 5 mL of diethyl ether/THF (4:1) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). After 10 min, the reaction mixture was stirred at room temperature for 4 h. Then, *t*-BuOCl (0.32 mmol, 39 μl) was added and the reaction mixture was kept at room temperature for 2 h. After dried up, the reaction mixture was extracted with hexane (10 mL) and filtered. The solvent was evaporated in vacuum. Repeat this extraction–filtration–drying procedure for three times to afford 2,6-diazasemibullvalenes **5-1g–5-1h** in 72–73 % isolated yields.

1,5-Dimethyl-3,7-di-*tert*-butyl-2,6-diazasemibullvalene (5-1g): Colorless solid, isolated yield 72 % (57 mg). ^{1}H NMR (300 MHz, THF-d_8, 25 °C): δ = 0.98 (s, 18H, CH_3), 1.09 (s, 6H, CH_3), 4.65 (s, 2H, CH); ^{13}C NMR (75 MHz, THF-d_8, 25 °C): δ = 14.70 (2 CH_3), 27.98 (6 CH_3), 33.80 (2 quat. C), 79.33 (2 quat. C), 97.40 (2 CH), 161.81 (2 quat. C). Elemental analysis calcd (%) for $C_{16}H_{26}N_2$: C, 77.99; H, 10.64; N, 11.37; found: C, 78.00; H, 10.60; N, 11.43.

1,5-Dibutyl-3,7-di-*tert*-butyl-2,6-diazasemibullvalene (5-1h): Colorless oil, isolated yield 73 % (77 mg). ^{1}H NMR (300 MHz, THF-d_8, 25 °C): δ = 0.83 (t, J = 6.9 Hz, 6H, CH_3), 0.99 (s, 18H, CH_3), 1.21–1.29 (m, 8H, CH_2), 1.49 (t, J = 11.7 Hz, 4H, CH_2), 4.72 (s, 2H, CH); ^{13}C NMR (75 MHz, THF-d_8, 25 °C): δ = 13.45 (2 CH_3), 23.12 (2 CH_2), 27.41 (2 CH_2), 27.98 (6 CH_3), 29.07 (2 CH_2), 33.97 (quat. C), 82.54 (2 quat. C), 95.60 (2 CH), 161.95 (2 quat. C). Elemental analysis calcd (%) for $C_{22}H_{38}N_2$: C, 79.94; H, 11.59; N, 8.47; found: C, 79.86; H, 11.73; N, 8.22.

Procedure for preparation of 1,5-diazocine 5-6a from 2,3-diphenyl-1,4-diiodo-1,3-diene 5-7e *(Method A)*: *t*-BuLi (4.0 mmol, 1.6 M in pentane) was added to a solution of 2,3-diphenyl-1,4-diiodo-1,3-diene **5-7e** (1.0 mmol, 458 mg) in diethyl ether (4 mL) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). The reaction mixture was then stirred at −78 °C for 30 min to generate 1,4-dilithio-1,3-diene. HMPA (2.0 mmol, 347 μl) was then added, and the reaction mixture was stirred at room temperature for 30 min. After addition of *t*-BuCN (4.0 mmol, 440 μl) at −78 °C, the mixture was heated to reflux and maintained for 3 h. Then, *t*-BuOCl (1.0 mmol, 119 μl) was added and the reaction mixture was kept at room temperature for 2 h. The reaction mixture was quenched by saturated aqueous $NaHCO_3$, extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:2:1) to afford the corresponding 1,5-diazocine **5-6a** in 57 % isolated yield.

Procedure for preparation of 1,5-diazocine 5-6a from Δ^1-bipyrroline 5-3h *(Method B)*: *n*-BuLi (0.64 mmol, 1.6 M in hexane, 0.4 mL) was added to a solution of Δ^1-bipyrroline **5-3h** (0.32 mmol, 119 mg) in 5 mL of diethyl ether/THF (4:1) in a 20-ml Schlenk tube at −78 °C (dry ice/acetone). After 10 min, the reaction mixture

was stirred at room temperature for 2 h. Then, *t*-BuOCl (0.32 mmol, 39 μl) was added and the reaction mixture was kept at room temperature for 2 h. After dried up, the reaction mixture was suspended in C_6D_6 and monitored by ^{1}H NMR and ^{13}C NMR. Instead of **5-2i**, **5-6a** was confirmed as the only product. The reaction mixture was quenched by saturated aqueous $NaHCO_3$, extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give a yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:2:1) to afford the corresponding 1,5-diazocine **5-6a** in 73 % isolated yield.

In $CDCl_3$, **5-6a** turned out to be 1:1 mixture of **5-6a** and its valence isomer **5-6a′** (according to the integration of ^{1}H NMR spectra).

2,6-di-*tert*-butyl-4,8-diphenyl-1,5-diazocine (5-6a): Colorless crystal. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.26 (s, 18H + 18H, CH_3, **5-6a** + **5-6a′**), 5.52 (s, 2H, CH, **5-6a′**), 5.96 (s, 2H, CH, **5-6a**), 7.21–7.84 (m, 10H + 10H, C_6H_5, **5-6a** + **5-6a′**); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 28.16 (6 CH_3), 28.33 (6 CH_3), 37.48 (2 quat. C), 40.13 (2 quat. C), 102.18 (2 CH), 104.10 (2 CH), 125.68 (4 CH), 128.11 (4 CH), 128.21 (4 CH), 128.26 (4 CH), 128.50 (2 CH), 130.36 (2 CH), 136.79 (2 quat. C), 138.14 (2 quat. C), 154.88 (2 quat. C), 166.53 (2 quat. C), 169.13 (2 quat. C), 178.98 (2 quat. C). HRMS: *m/z*: calcd for $C_{26}H_{31}N_2$ $[M + H]^+$: 371.2487, found: 371.2487. Elemental analysis calcd (%) for $C_{26}H_{30}N_2$: C, 84.28; H, 8.16; N, 7.56; found: C, 84.12; H, 8.40; N, 7.34. Single crystals of **5-6a** suitable for X-ray analysis were grown in hexane/ethyl acetate (2:1) at room temperature.

General procedure for preparation of 1,5-diazocine 5-6b-5-6c from thermolysis of 2,6-diazasemibullvalene 5-1g–5-1h. 2,6-diazasemibullvalene **5-1g** or **5-1h** (0.23 mmol) in 0.5 mL of THF-d_8 was heated to 80 °C and maintained for 3 h. ^{1}H and ^{13}C NMR showed quantitative transformation to 1,5-diazocine **5-6b–5-6c.** Further purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:1:1) gave **5-6b–5-6c** as colorless oil.

In $CDCl_3$, **5-6b** turned out to be 1:1.6 mixture of **5-6b** and its valence isomer **5-6b′**, while **5-6c** turned out to be 2.5:1 mixture of **5-6c** and its valence isomer **5-6c′** (according to the integration of ^{1}H NMR spectra). [7]

2,6-di-*tert*-butyl-4,8-dimethyl-1,5-diazocine (5-6b): Colorless oil. ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 0.95 (s, 18H + 18H, CH_3, **5-6b** + **5-6b′**), 1.60 (s, 6H, CH_3, **5-6b′**), 1.94 (m, 6H, CH_3, **5-6b**), 4.54 (s, 2H, CH, **5-6b′**), 4.98 (s, 2H, CH, **5-6b**); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 19.51 (2 CH_3), 21.83 (2 CH_3), 28.36 (6 CH_3), 29.39 (6 CH_3), 104.03 (2 CH), 104.21 (2 CH), 155.56 (2 quat. C), 155.58 (2 quat. C). HRMS: *m/z*: calcd for $C_{16}H_{27}N_2$ $[M + H]^+$: 247.2174, found: 247.2176. Elemental analysis calcd (%) for $C_{16}H_{26}N_2$: C, 77.99; H, 10.64; N, 11.37; found: C, 77.64; H, 10.88; N, 11.15.

2,6-di-*tert*-butyl-4,8-dibutyl-1,5-diazocine (5-6c): Colorless oil. ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.89 (t, *J* = 8.7 Hz, 6H + 6H, CH_3, **5-6c** + **5-6c′**), 1.10 (s, 18H + 18H, CH_3, **5-6c** + **5-6c′**), 1.25-1.36 (m, 12H + 12 H, CH_2, **5-6c** + **5-**

6c′), 5.08 (s, 2H, CH, **5-6c′**), 5.19 (s, 2H, CH, **5-6c**); ^{13}C NMR (75 MHz, THF-d_8, 25 °C): δ = 13.29 (2 CH_3), 13.36 (2 CH_3), 22.06 (2 CH_2), 22.28 (2 CH_2), 27.61 (6 CH_3 + 6 CH_3), 28.41 (2 CH_2), 28.49 (2 CH_2), 35.23 (2 CH_2), 35.95 (2 CH_2), 38.69 (2 quat. C), 39.00 (2 quat. C), 158.79 (2 quat. C), 165.92 (2 quat. C), 171.22 (2 quat. C), 178.98 (2 quat. C). HRMS: *m/z*: calcd for $C_{22}H_{39}N_2$ $[M + H]^+$: 331.3113, found: 331.3119. Elemental analysis calcd (%) for $C_{22}H_{38}N_2$: C, 79.94; H, 11.59; N, 8.47; found: C, 79.82; H, 11.83; N, 8.26.

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Chapter 6
2,6-Diazasemibullvalenes: Reaction Chemistry and Synthetic Application

6.1 Introduction

The reaction chemistry and further synthetic application of organic compounds are of great importance and have direct relationship to the structures. 2,6-Diazasemibullvalene (NSBV, **6-1**) features rapid intramolecular *aza*-Cope rearrangement and highly strained ring system. Thus, novel reaction types and different selectivity with reactions of standard aziridines are expected, which could be also applied to the synthetic application of functionalized heterocycles [1–6].

NSBV **6-1** is highly reactive and useful in organic and organometallic synthesis because of their unique strained ring system, multiple reaction sites, and intramolecular *aza*-Cope rearrangement. These reaction sites in NSBV **6-1** enable its unprecedented and diversified reaction patterns toward several different substrates: (1) aziridine ring (C–N bond cleavage, nucleophilic ring opening, cycloaddition, and reaction with metal complexes); (2) C–H bonds (C–H functionalization, oxidation); (3) imine C=N bond (coordination with Lewis acid or metal complexes); (4) olefin (or enamine) C=C bond (cycloaddition, coordination, or metal complexes); (5) the polycyclic skeleton as a whole could be involved in the reaction and thus generates different reaction pattern and selectivity from those of standard aziridines. The reaction modes of NSBV are summarized in Fig. 6.1.

However, due to the limitation of synthetic methods toward 2,6-diazasemibullvalene (NSBV, **6-1**), the reaction chemistry of NSBV was unknown except for its thermolysis to give 1,5-diazocine by Müllen et al. [4]. Thus, our well-established efficient synthesis and isolation of NSBV **6-1** were greatly beneficial for investigation into its reaction chemistry.

Although all the isolated NSBVs **6-1** are stable in an inert atmosphere, they are sensitive to acid, base, and silica gel and decompose slowly when exposed to moisture. These observations indicated their highly reactive nature and suggested that the reaction chemistry of such fluxional molecules **6-1** should be very interesting.

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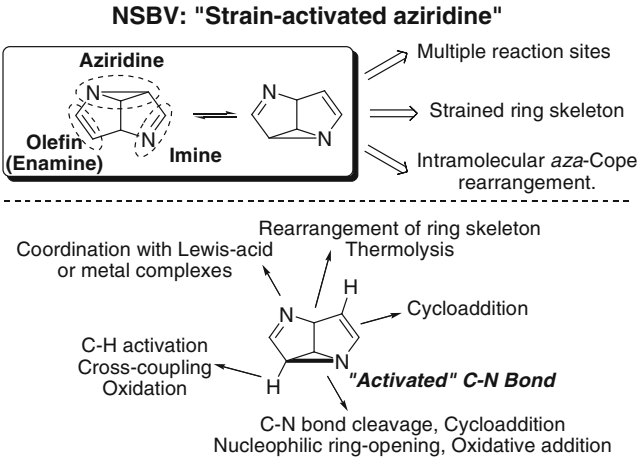


Fig. 6.1 Reaction modes of 2,6-diazasemibullvalenes

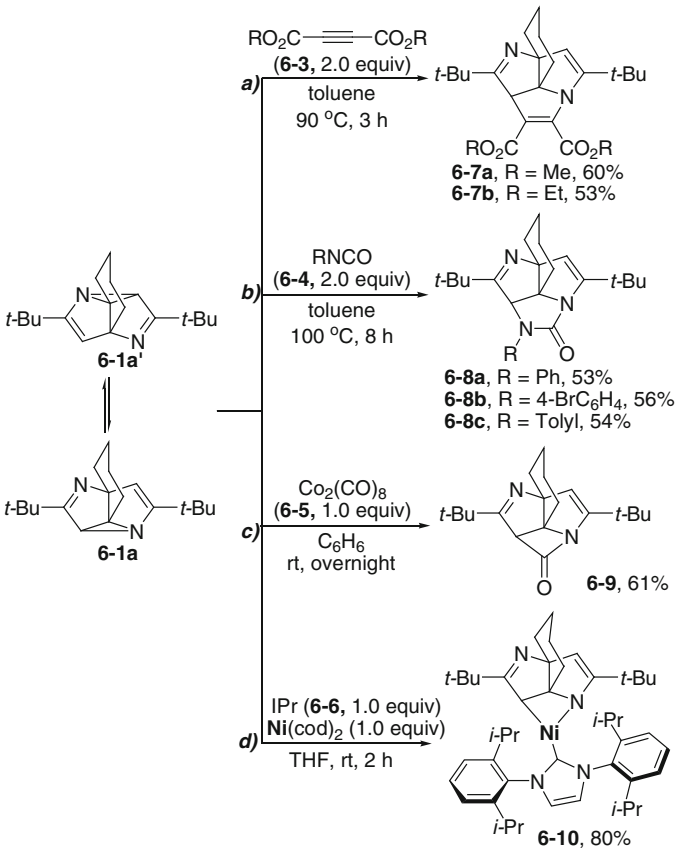
6.2 Result and Discussion

6.2.1 Insertion Reaction of Unsaturated Compounds or Low-Valent Metals into the Weakened C–N Bonds of 2,6-Diazasemibullvalenes

Insertion of unsaturated compounds as well as low-valent metal complexes into the weakened C–N bonds interrupts the rapid Cope rearrangement and leads to the diversified ring expansion products (Scheme 6.1) [7–9]. Regiospecific cycloaddition of **6-1a** with activated alkynes such as dimethyl acetylenedicarboxylate (DMAD) or its diethyl analogue (DEAD) in toluene at 90 °C readily afforded the 1,5-diazatriquinacenes **6-7a** and **6-7b** in 60 and 53 % isolated yields, respectively [10, 11]. To the best of our knowledge, the synthesis of triquinacene and azatriquinacene generally require multi-step procedures; thus, this straightforward synthesis of 1,5-diazatriquinacene should be useful for construction of structurally interesting yet otherwise unavailable "bowl-shaped" polycyclic frameworks [10, 11].

The cycloaddition of **6-1a** with isocyanates without any catalyst led to tetracyclic imidazolidinone derivatives **6-8a–6-8c** in moderate yields. Note that all reported reactions of simple aziridines with isocyanates require a catalyst such as transition metal salt [12], indicating that the C–N bonds in NSBV molecule might be more reactive than simple aziridine due to the enhanced ring strain caused by rigid ring system as well as rapid *aza*-Cope rearrangement. Single-crystal structures of **6-7a** and **6-8a** were determined by X-ray diffraction (Fig. 6.2).

Carbonylation of **6-1a** using $CO_2(CO)_8$ at room temperature gave the tetracyclic β-lactam **6-9** in 61 % yield. In contrast, carbonylation reactions of simple aziridines



Scheme 6.1 Insertion reaction of unsaturated compounds or low-valent metals into the weakened C–N bonds

all occurred at elevated temperatures, high pressures of CO gas, or in the presence of promoters [14].

Metal complexation was reported to accelerate the Cope rearrangement; however, the interaction of metal centers with azasemibullvalene in *aza*-Cope rearrangements is unknown. Insertion of a low-valent transition metal into the weakened C–N bonds was demonstrated by the reaction of an *N*-heterocyclic carbene-ligated Ni(0) complex with **6-1a**. Addition of **6-1a** into a 1:1 mixture of bis (1,5-cyclooctadiene)nickel(0) ($Ni(cod)_2$) and 1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene (IPr) in THF solution resulted in a rapid color change from dark brown to red. A three-coordinated, 4-membered azanickelacycle **6-10** was isolated in 80 % yield, the structure of which is shown in Fig. 6.3. Only one IPr ligand coordinates to the Ni(II) center, probably due to steric hinderance. The N2-Ni1-C19 (159.7°) and C5-Ni1-C19 (109.9°) angles reveal a distorted T-shape Ni coordination environment. Besides, the author suggests the mechanism for oxidative

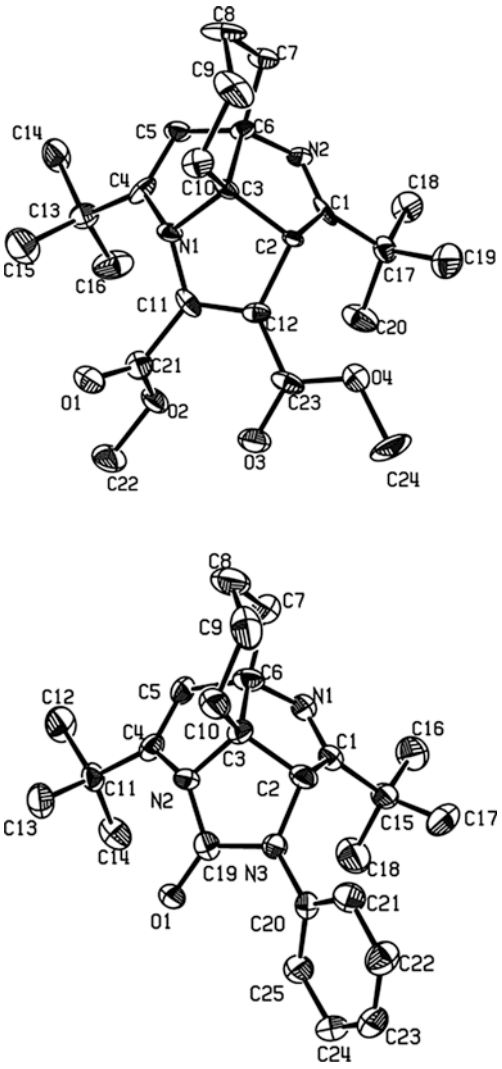


Fig. 6.2 Single-crystal X-ray structures of **6-7a** (*left*) and **6-8a** (*right*) with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reprinted with the permission from Ref. [13]. Copyright 2012 American Chemical Society

addition of **6-1a** with IPr-Ni(0) complex is totally different from S_N2 mechanism proposed by Hillhouse for their reaction [15]. Since **6-1a** features multi-substitution and rigid ring system, it is impossible to rotate around the C–C bond after an S_N2 attack. Thus, the mechanism for oxidative addition might be concerted or via diradical pathway.

Clearly, the rapid *aza*-Cope rearrangement in NSBV molecules in solution weakens the C–N bonds greatly, leading to reactivities different from simple aziridine analogues.

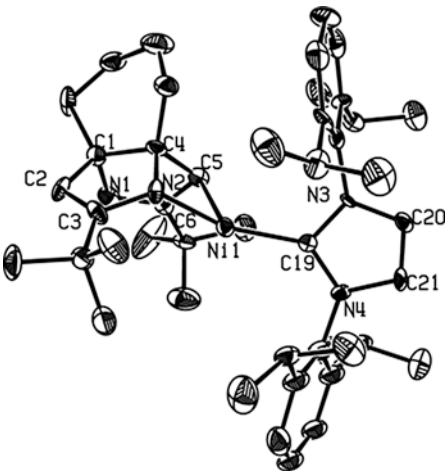


Fig. 6.3 Single-crystal X-ray structures of **6-10** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond length (Å) and angels (°): Ni1-N2 1.858(5), Ni1-C5 2.018(7), N2–C4 1.507(9), C4–C5 1.521(9), Ni1-C19 1.947(7), N2-Ni1-C5 73.5(3), N2-Ni1-C19 159.7(3), C5-Ni1-C19 109.9(3). Reprinted with the permission from Ref. [13]. Copyright 2012 American Chemical Society

6.2.2 *Lewis Acid-Catalyzed Cycloadditions of 2,6-Diazasemibullvalenes with Isocyanides, Azides, and Diazo Compounds: Novel Reaction Patterns Leading to* N-*Heterocyclic Cage-Shaped Compounds*

Organic cage-shaped compounds such as adamantane and cubane are attractive and important in both structural organic chemistry and synthetic chemistry, yet in most cases, the development of new organic cage-shaped compounds suffers from the difficulty in multi-step synthesis and low yields [16–18]. Brexanes (tricyclo [4.3.0.$0^{3,7}$] nonanes), brexadienes, as well as their aza-analogues are structurally interesting cage-shaped architectures and important intermediates for organic synthesis (Fig. 6.4) [19–22]. However, efficient synthetic methods toward brexane derivatives and their aza-analogues are very rare.

Herein, the author reports Lewis acid-catalyzed diverse cycloaddition reactions of NSBVs **6-1** with a wide variety of isocyanides, azides, and diazo compounds. These reactions afforded 5,8-diaza- and 2,5,9-triaza-brexadiene derivatives as highly fused *N*-containing polycyclic frameworks, which are structurally and chemically interesting cage-shaped compounds, but not readily accessible by other means. Unique and unprecedented "rearrangement–cycloaddition" patterns are revealed. These reaction patterns are not only different from our previously reported reaction with DMAD or RNCO, but most notably, very different from the reactions

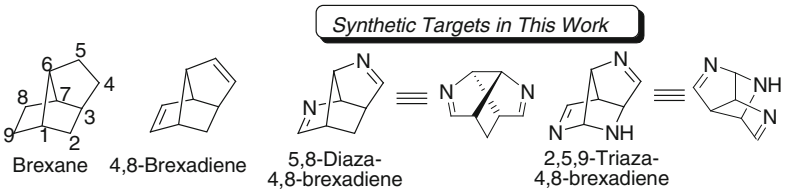


Fig. 6.4 Brexane, brexadiene, and their aza-analogue

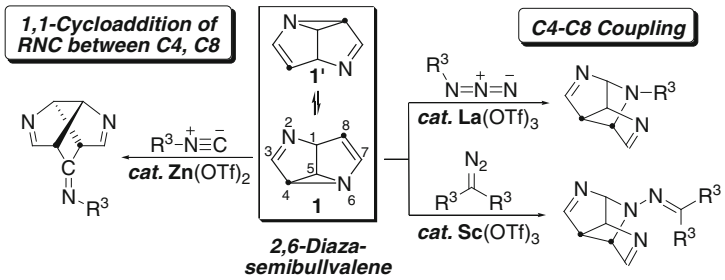


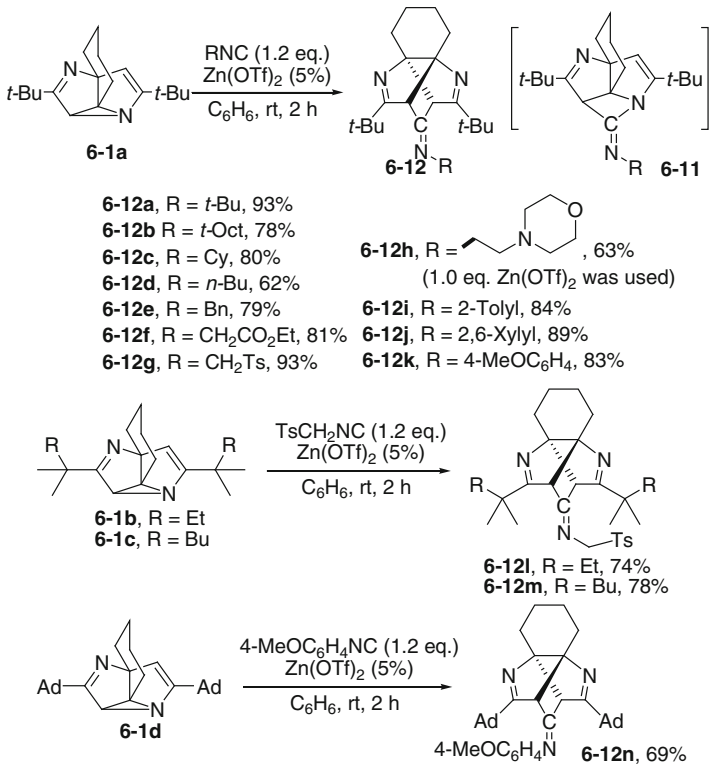
Fig. 6.5 Cycloaddition patterns of 2,6-diazasemibullvalenes with isocyanides, azides, and diazo compounds catalyzed by different lewis acids

of standard aziridines [21–29], because of the active involvement of the whole ring skeleton of the NSBV compound (Fig. 6.5).

6.2.2.1 Zinc Triflate-Catalyzed [5 + 1] Cycloadditions of 2,6-Diazasemibullvalenes with Isocyanides: Synthesis of Diazabrexadienes

The reaction of NSBV **6-1a** with *tert*-butyl isocyanide (*t*-BuNC) in toluene was first monitored by ^{1}H NMR spectra. No reaction took place even when the reaction mixture was heated to 120 °C for 12 h in a sealed tube. However, in the presence of a catalytic amount of zinc triflate (5 mol%), reaction of the above mixture proceeded smoothly at room temperature. The reaction was very clean and finished within 2 h, affording the 5,8-diaza-4,8-brexadiene derivative **6-12a** as a tetracyclic triimine in 93 % isolated yield (Scheme 6.2). No formation of the C–N bond "insertion" product **6-11** was detected. Single-crystal X-ray structural analysis of **6-12a** revealed a cage-shaped skeleton containing a cyclopentanimine core fused with one cyclohexane ring and two pyrroline rings (Fig. 6.6).

The reaction scope was found to be very broad. Both aliphatic and aromatic isocyanides bearing either less-hindered or bulky substituent could undergo clean reactions with NSBVs to afford their corresponding products **6-12a–6-12n** in good to excellent isolated yields under the $Zn(OTf)_2$-catalyzed reaction condition



Scheme 6.2 Zinc triflate-catalyzed [5 + 1] cycloaddition of 2,6-diazasemibullvalenes and isocyanides. *t*-Oct = 1,1,3,3-tetra-methylbutyl; 2,6-Xylyl = 2,6-Me_2Ph; Ad = Adamantyl

(Scheme 6.3). Tertiary, secondary, and primary alkyl isocyanides could all be applied. Functional groups such as ester and sulfonyl groups could be tolerated. NSBVs with different substituents were also tested and various diazabrexadiene derivatives were isolated in good yields (**6-12l–6-12n**).

The above Lewis acid-catalyzed reaction between NSBVs **6-1** and isocyanides represents a formal [5 + 1] cycloaddition pattern. This cycloaddition reaction has several features. (1) Site-selective. The cyclization occurred exclusively at the 4,8-positions, other than the 4,6-positions. (2) Highly reactive. The strained ring tension remarkably weakens the C–N bond in **6-1**. In comparison, insertion of isocyanides with simple aziridines is very rare [30, 31]. (3) The active involvement of the whole ring skeleton of the NSBV compound makes it unusual. (4) Synthetically useful. Poly-*N*-heterocyclic skeletons are constructed efficiently in one-pot.

Given in Scheme 6.3 are three proposed reaction pathways. ***Pathway A*** shows a "ring-opening/ring-closure" process, demonstrating an "*N*-alkenyl aziridine" reaction pattern of NSBV [27–29]. Coordination of Lewis acid with aziridine-N in NSBV **6-1** would promote nucleophilic ring opening to give nitrilium intermediate

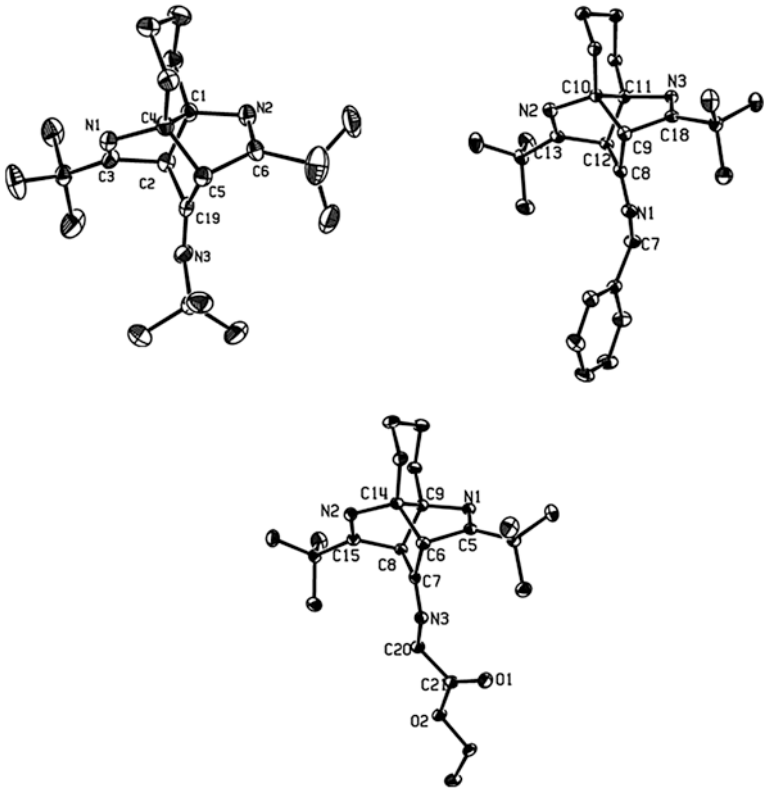
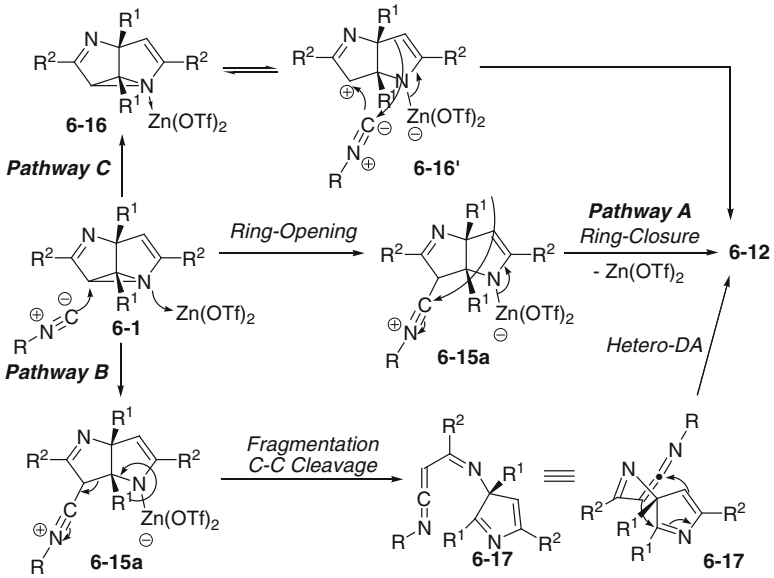


Fig. 6.6 ORTEP drawing of **6-12a**, **6-12e**, **6-12f** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reproduced from Ref. [32] by permission of John Wiley & Sons Ltd

6-15a. Nucleophilic cyclization of zinc enamide with nitrilium moiety leads to **6-12** accompanied by elimination of Lewis acid. ***Pathway B*** proposes a tandem "ring opening–rearrangement–cyclization" process. Fragmentation of C–C bond and ring opening of one pyrroline ring in **6-15a** would form an iminoacyl ketenimine **6-17** as a key intermediate. Then, an intramolecular [4 + 2] cycloaddition of 2*H*-pyrrole ring and iminoacyl ketenimine moiety would construct the cyclopentanimine ring and polycyclic skeleton in regiospecific and diastereospecific fashion. ***Pathway C*** represents a concerted [5 + 1] cheletropic cycloaddition mechanism. Coordination of Lewis acid activated C–N bond in **6-1**, followed by two C–C bonds formation process. Although ***Pathway A*** and ***Pathway C*** cannot be ruled out, ***Pathway B*** is assumed to be more probable because it could explain the regio- and- diastereo-specificity of the cycloaddition reaction.

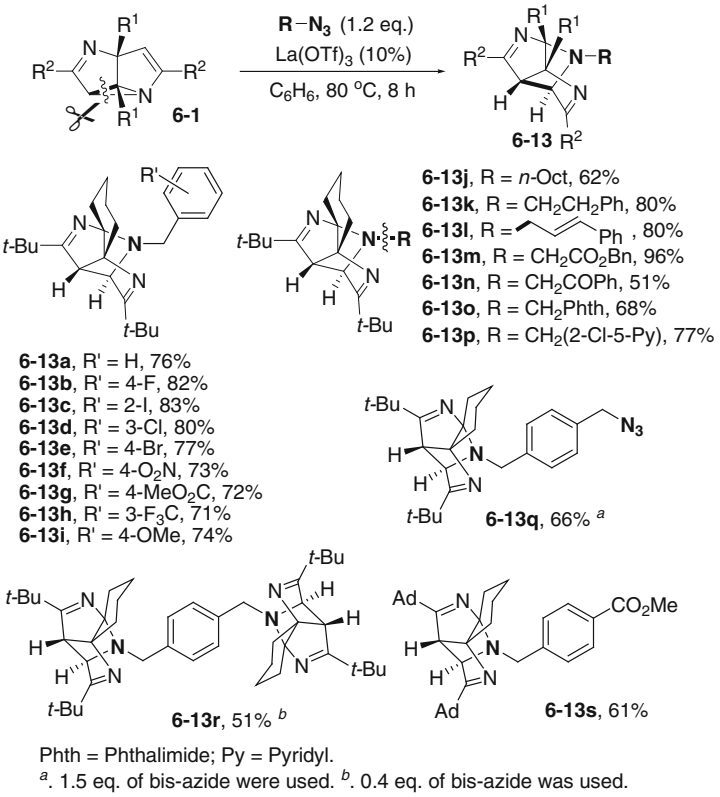


Scheme 6.3 Proposed mechanism for Zinc Triflate-catalyzed [5 + 1] cycloaddition of 2,6-diazasemibullvalenes and isocyanides

6.2.2.2 Lanthanum Triflate-Catalyzed Rearrangement–Cycloaddition of 2,6-Diazasemibullvalenes and Azides: Synthesis of Triazabrexadienes

In addition to isocyanides, azides were found to react with NSBVs **1** cleanly and efficiently in the presence of a catalytic amount of $La(OTf)_3$, affording multi-substituted 2,5,9-triaza-4,8-brexadiene **6-3** as a single diastereomer in good to excellent isolated yields (Scheme 6.4) [33–36]. $La(OTf)_3$ was found to be the most efficient catalyst, while $Zn(OTf)_2$ gave slightly lower yields. When $Sc(OTf)_3$ was used, substrate decomposition was observed. Single-crystal X-ray structural analysis of **6-13e** revealed its new, different cage-shaped skeleton (Fig. 6.7).

A wide variety of azides could be applied. Good functional group tolerance was demonstrated. Benzyl azides bearing halogen atoms (F, Cl, Br, I), electron-withdrawing groups (CO_2Me, NO_2, CF_3), and electron-donating groups (OMe) all gave satisfied yields (**6-13a–6-13i**). Alkyl azides bearing ester or carbonyl groups and cinnamyl azide showed good reactivity as well (**6-13j–6-13n**). Azides bearing heterocycles such as phthalimide and pyridine ring also afforded the corresponding products in good yields (**6-13o–6-13p**). 1,4-Bis(azidomethyl)benzene reacted chemoselectively with 1 or 2 equiv of NSBV **6-1a** to afford the corresponding highly fused mono(diazabrexadiene) **6-13q** and bis(diazabrexadiene) derivatives **6-13r** in 66 and 51 % isolated yields, respectively. NSBV with different substituents could also be readily applied (**6-13s**). Bulky azides such as 1,1-diphenylethyl azide did not give satisfied result. Besides, when aromatic azides such as 4-methoxyphenyl



Scheme 6.4 Lanthanum triflate-catalyzed ring opening-rearrangement-cycloaddition of 2,6-diazasemibullvalenes and azides

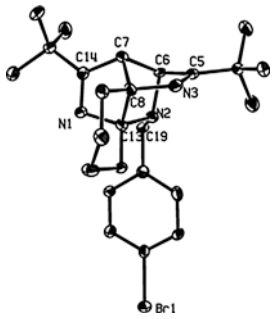


Fig. 6.7 ORTEP drawing of **6-13e** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reproduced from Ref. [32] by permission of John Wiley & Sons Ltd

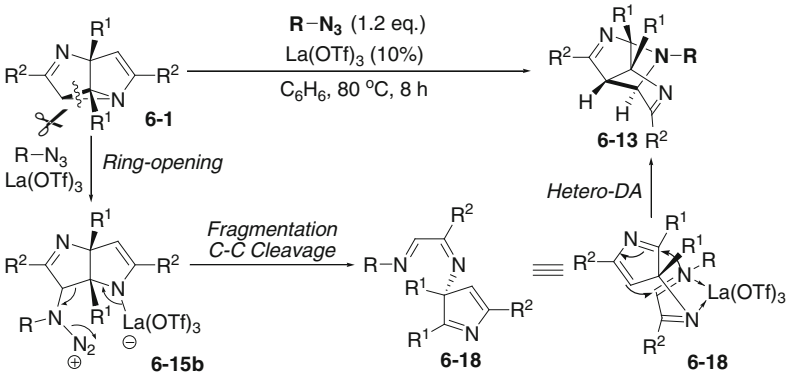
azide and 4-chlorophenyl azide were applied, the reactions with NSBV **6-1** gave no cycloaddition products, probably due to their low nucleophilicity.

As far as we know, there is no report on the reaction of organic azides with simple aziridines in the literature [37–39]. Obviously, during this present reaction process, skeletal rearrangement of NSBV **6-1** and loss of N_2 in azide took place. Normal reactions such as [3 + 2] cycloaddition of azide 1,3-dipole or [2 + 1] cycloaddition of nitrene did not occur [37–39]. Besides, this reaction features cleavage of the unstrained C4–C5 bond of NSBV **6-1** as well as C4–C8 coupling. All these features are different from the reaction of **6-1** with isocyanides.

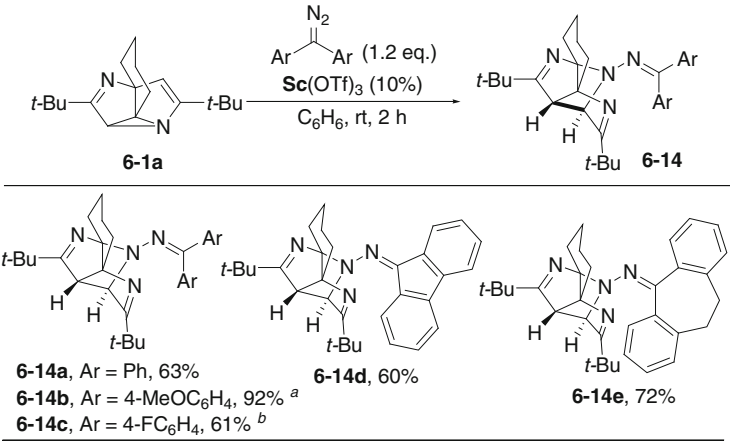
The reaction mechanism is proposed as following. Firstly, Lewis acid would promote nucleophilic attack of azide α-N to NSBV **6-1**, leading to the ring-opening intermediate **6-15b**. Fragmentation of C–C bond and ring opening of one pyrroline ring in **6-15b** gives *N*-2-pyrrolyl diimine **6-18** as a key intermediate with elimination of both Lewis acid and dinitrogen. Finally, intramolecular hetero-Diels-Alder reaction of 2*H*-pyrrole ring and less-bulky, remote imine moiety affords the pyrrolidine ring in regiospecific and diastereospecific fashion.

6.2.2.3 Scandium Triflate-Catalyzed Rearrangement–Cycloaddition of 2,6-Diazasemibullvalenes and Diazo Compounds: Synthesis of Triazabrexadienes

The unusual reactivity of NSBVs **6-1** was further demonstrated by their reaction with diazo compounds (Scheme 6.5). The reaction chemistry of diazo compounds as carbene precursors has been well developed and reviewed [40, 41]. However, transition metal or Lewis acid-catalyzed cyclization of diazo compounds with normal aziridines is very rare [42–44]. There are few examples including copper-catalyzed coupling of 2-acylaziridines or 2-vinylaziridines with diazo compounds, giving bicyclic aziridines, indolizidines, or seven-membered lactams as products.



Scheme 6.5 Proposed mechanism for lanthanum triflate-catalyzed cycloaddition of 2,6-diazasemibullvalenes and azides



a. Reaction time: 0.5 h. b. Reaction time: 12 h.

Scheme 6.6 Scandium triflate-catalyzed ring opening-rearrangement-cycloaddition of 2,6-diazasemibullvalenes and diazo compounds

Interestingly, in the presence of a catalytic amount of $Sc(OTf)_3$, the reaction between NSBV **6-1a** and a variety of diaryl diazomethane all completed in 2 h at room temperature without loss of dinitrogen. The structure of product was further confirmed as *N*-ylideneamino-2,5,9-triaza-brexadiene **6-14**, which is similar to the cycloaddition product of NSBV **1** with azides (Fig. 6.8). The electronic effect of substituents on diaryl diazomethane is remarkable for this reaction. When a methoxy group substituted diaryl diazomethane was applied, the reaction completed within 0.5 h, affording its corresponding product **6-14b** in 92 % isolated yield. However, when a diazo compound bearing an electron-withdrawing group such as a fluoro atom was used, the reaction rate was slowed down and the yield of the product **6-14c** was 61 % after 12 h. Thus, a nucleophilic ring opening of NSBV **6-1** with diazo compounds is assumed as the key step (Scheme 6.6).

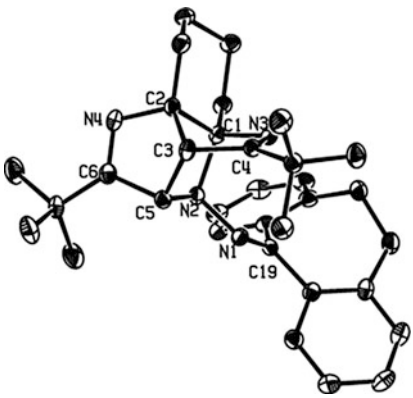
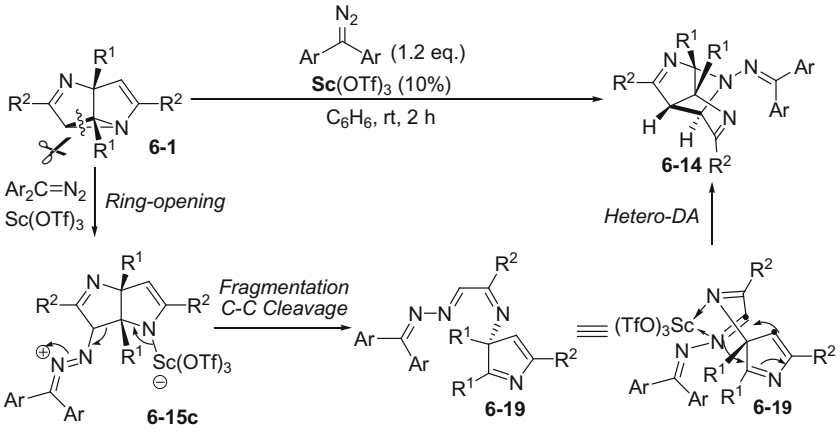


Fig. 6.8 ORTEP drawing of **6-14e** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reproduced from Ref. [32] by permission of John Wiley & Sons Ltd



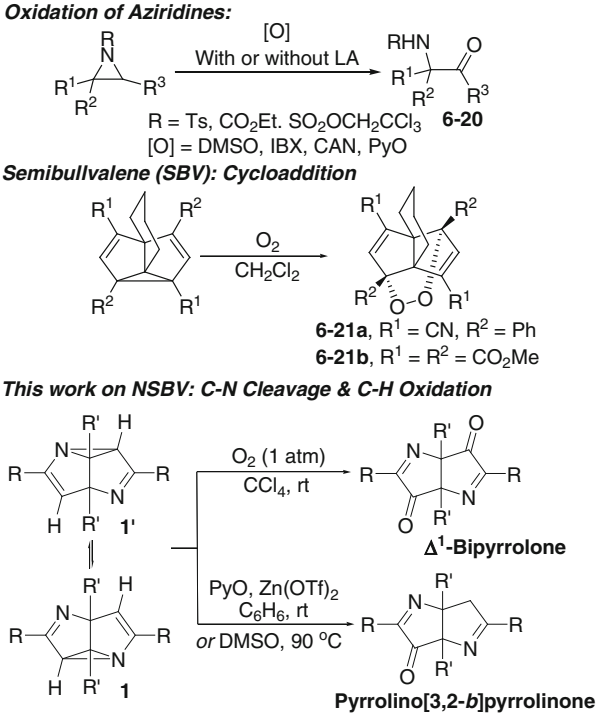
Scheme 6.7 Proposed mechanism for scandium triflate-catalyzed cycloaddition of 2,6-diazasemibullvalenes and diazo compounds

Notably, the diaryl diazomethane here showed the reactivity of a nitrene, rather than a carbene, forming two C–N bonds in one cycloaddition reaction [45]. This is probably because the α-C in diaryl diazomethane is less nucleophilic and steric-hindered, while the γ-N behaves as nucleophile and initiates the ring opening of NSBV **6-1a** [46–48]. Although [3 + 2] cycloaddition of diazo compounds with other unsaturated compounds have been reported with the preservation of the dinitrogen moiety, few reports show nitrene reactivity with formation of two C–N bonds [49–51] (Scheme 6.7).

The proposed reaction mechanism of cycloaddition of NSBV **6-1** with diazo compounds is similar to the reaction with azides. Lewis acid would promote nucleophilic attack of terminal N-atom of diazo compounds to NSBV **6-1**, leading to the ring-opening intermediate **6-15c**. Fragmentation of C–C bond and ring opening of one pyrroline ring in **6-15c** give hydrazine **6-19** as a key intermediate. Finally, intramolecular hetero-Diels-Alder reaction of 2*H*-pyrrole ring and the least bulky C=N bond affords the pyrrolidine ring in regiospecific and diastereospecific fashion [52–55].

6.2.3 *Oxidation of 2,6-Diazasemibullvalenes by O_2 or* N*-Oxides: Synthesis of Δ^1-Bipyrrolinones and Pyrrolino[3,2-b]Pyrrolinones*

Oxidation of C–H bonds to C=O bonds by oxygen (O_2) is a very important and useful process [56]. In general, additives or promoters such as bases, transition metal complexes, and photosensitizers are required to realize such a process [57–60]. On the contrary, to the best of our knowledge, there are very few reports



Scheme 6.8 Oxidation of aziridines, semibullvalenes (SBVs), and 2,6-diazasemibullvalenes (NSBVs)

on oxidation of a C–H bond to a C=O bond by oxygen ***only***, without any additives or promoters.

2,6-Diazasemibullvalenes is featured with a strained aziridine core as well as rapid *aza*-Cope rearrangement. Both features have significant impacts on its reaction chemistry, as our preliminary research has demonstrated. Normal aziridines were reported to be readily oxidized to afford β-amino ketones [61–63]; however, in most cases, an activation group on the nitrogen atom such as a tosyl group is required for realizing the oxidation reaction. Meanwhile, SBV derivatives such as semibullvalene tetracarboxylates were reported to react with O_2 to afford cycloaddition products regioselectively [24, 26]. However, the oxidation reaction of NSBV is unknown (Scheme 6.8).

As our continued interest in reaction chemistry of NSBVs, we envisioned NSBVs would show a different oxidation reaction pattern from that of normal aziridines and SBVs. The author found selective and efficient oxidation reaction of NSBVs by oxygen or *N*-oxide to afford Δ^1-bipyrrolone and mono-pyrrolone derivatives [64, 65]. The C–N bond cleavage and C–H bond oxidation proceeded in the reaction process. Both Δ^1-bipyrrolones and mono-pyrrolones were further

transformed into other heterocyclic compounds, which are not available by other means.

6.2.3.1 Oxidation of 2,6-Diazasemibullvalenes by O_2: Synthesis of Δ^1-Bipyrrolinones

The CCl_4 solution of **6-1a** was treated with oxygen (balloon, 1 atm) at room temperature for 12 h (Scheme 6.2). The resulted yellow solution was dried up and subjected to flash column chromatography to yield Δ^1-bipyrrolinone **6-22a** in 93 % isolated yield. Heating of neat **6-1a** to 270 °C in open air for about 10 min also afforded **6-22a** in 89 % isolated yield. Both the ^1H and ^{13}C NMR spectra of **6-22a** clearly showed its symmetrical structure. The imine and the carbonyl carbons of **6-22a** showed the respective singlets at $\delta = 177.72$ and 197.98 ppm in the ^{13}C NMR spectrum in $CDCl_3$. 1,5-Bridged NSBVs **6-1** bearing different alkyl or aryl substituents could be also applied in this oxidation reaction, affording their corresponding Δ^1-bipyrrolinones **6-22a–6-2h** in good to excellent isolated yields. Non-bridged NSBVs **6-1i–6-1j** could also undergo this selective oxidation reaction with O_2 to form their corresponding Δ^1-bipyrrolinones **6-22i–6-22j**. The X-ray single-crystal structure of Δ^1-bipyrrolinone **6-22b** was unambiguously determined (Fig. 6.9; Scheme 6.9).

Oxidation of NSBVs **1** by oxygen resulted in oxidation of two C–H bonds and C–N bond cleavage. Formation of cycloaddition products **6-23** or **6-24** were not observed, demonstrating different oxidation reaction pattern of NSBVs from SBVs. The possible mechanism for this oxidation process is given in Scheme 6.3. The triplet-state, diradical form **6-1*** of NSBV **1** would react with oxygen to form a cycloaddition product **6-25**. Homolysis of O–O bond leads to bis(oxy) diradical **6-26**. Double abstraction of two α-H in bis(oxy) diradical **6-26** by oxygen and the

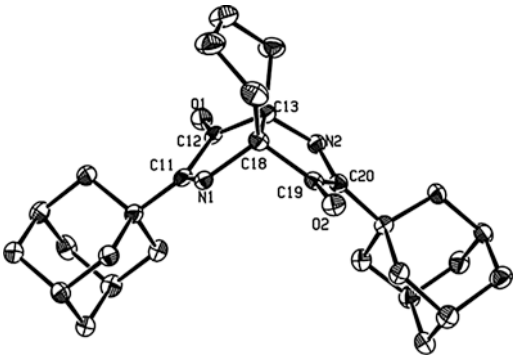
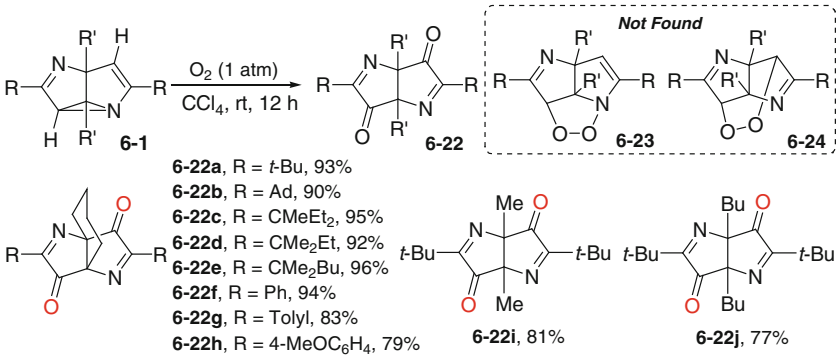
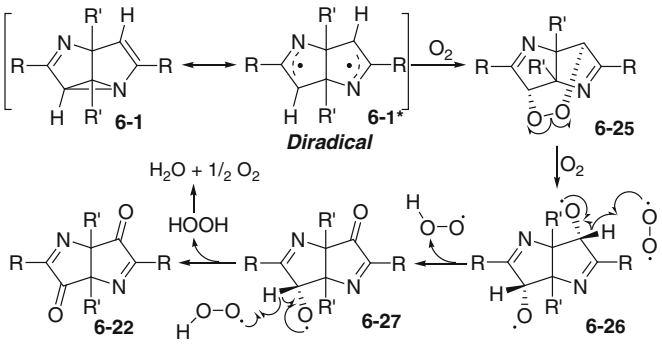


Fig. 6.9 ORTEP drawings of **6-22b** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å]: C12–O1 1.157(7), C19–O2 1.204(7), C11–N1 1.309(6), C20–N2 1.297(6), C11–C12 1.490(7), C19–C20 1.513(7). Reproduced from Ref. [66] with permission from The Royal Society of Chemistry



Scheme 6.9 Oxidation of NSBVs **6-1** by oxygen: Synthesis of Δ^1-bipyrrolinones **6-22**

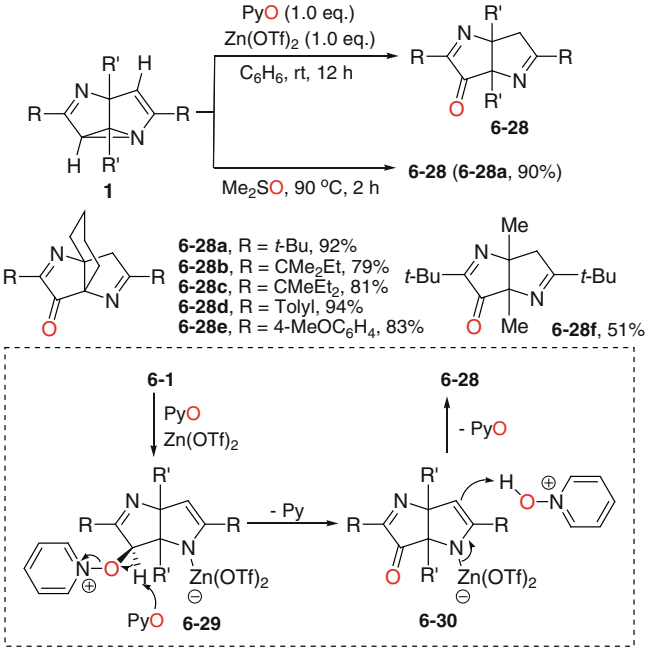


Scheme 6.10 Proposed mechanism for the reaction of NSBV **1** with O_2

in situ generated hydrogen peroxide radical would construct two C=O bonds in Δ^1-bipyrrolinones **6-22**. We ascribed the different oxidation process of NSBV **6-1** from SBVs to the unique structure of **6-1** (Scheme 6.10).

6.2.3.2 Oxidation of 2,6-Diazasemibullvalenes by *N*-Oxides: Synthesis of Pyrrolino[3,2-*b*]Pyrrolinones

The above results via oxidation of NSBVs **6-1** by oxygen prompted us to further study the oxidation reaction chemistry of NSBVs **6-1** using other oxidants, such as *N*-oxide or *S*-oxide. Initially, it was found that NSBV **6-1a** was inert toward oxidation by pyridine oxide (PyO), even when heated to 120 °C in C_6D_6, as monitored by in situ ^{1}H NMR spectra. Then, we tested the effect of Lewis acids and found that zinc triflate could effectively promote the oxidation of NSBV **6-1a** with pyridine oxide (PyO) at room temperature (Scheme 6.11). However, interestingly, instead of the double oxidized products **6-22** obtained using O_2 as the oxidant, selective mono-oxidation took place in this case, affording the corresponding pyrrolino



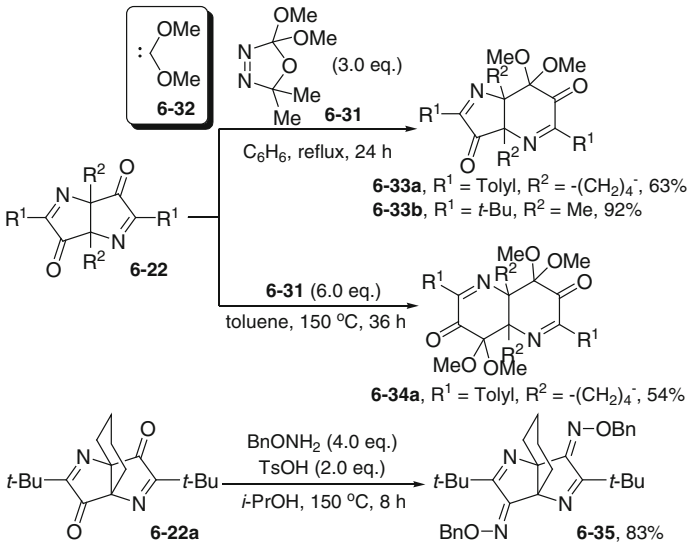
Scheme 6.11 Lewis acid-promoted oxidation of NSBV **6-1** by *N*-oxide or *S*-oxide: Synthesis of pyrrolino[3,2-*b*]pyrrolinones **6-28**

[3,2-*b*]pyrrolinone derivative **6-28a** in 92 % isolated yield. Similarly, pyrrolino[3,2-*b*]pyrrolinone derivatives **6-28b–6-28f** could be all obtained in good to excellent isolated yields. Moreover, without the aid of Lewis acid, the NSBV **6-1a** could also be highly efficiently oxidized by DMSO at 90 °C. Both the methylene and the carbonyl carbon of **6-28a** showed their respective singlets at δ = 44.88 and 200.43 ppm in the ^{13}C NMR spectrum in $CDCl_3$, while the methylene CH_2 also clearly showed two doublets at δ = 2.89 and 3.00 ppm in the ^{1}H NMR spectrum.

A proposed mechanism for this Lewis acid-promoted oxidation of NSBVs **6-1** with *N*-oxides is given in Scheme 6.4. Firstly, Lewis acid would promote the nucleophilic attack of PyO to NSBV **6-1**, leading to the ring-opening intermediate **6-29**. Deprotonation of α-H by another PyO molecule and subsequent elimination of pyridine molecule would give the intermediate **6-30**. Finally, protonation of the zinc enamide **6-30** affords the pyrrolino[3,2-*b*]pyrrolinone derivative **6-28**.

6.2.3.3 Synthetic Applications of Δ^1-Bipyrrolinones and Pyrrolino[3,2-b] Pyrrolinones

Δ^1-Bipyrrolinones **6-22** are valuable cyclic α-acyl imines and could be subjected for further synthetic transformations toward the synthesis of other *N*-heterocycles.



Scheme 6.12 Further synthetic applications of Δ^1-bipyrrolinones **2**

Oxadiazoline **6-31** is well known as precursor of singlet, dimethoxycarbene **6-32** [67, 68]. When the benzene solution of Δ^1-bipyrrolinone **6-22** and 3 equivalents of **6-31** was refluxed for 24 h, dihydropyrrolo[3,2-*b*]pyridine-3,6-dione **6-33** could be isolated in high yields as regioselective ring expansion products (Scheme 6.5). The structure of **6-33a** was unambiguously determined by X-ray single-crystal structural analysis (Fig. 6.2). Reaction of **6-22** with 6 equivalents of **6-31** at higher temperature and longer reaction time would give tetrahydro-1,5-naphthyridine-3,7-dione **6-34a** as double ring expansion product. In all the above reactions, carbene **6-32** formally inserts into the C–C bond adjacent to the C=O bond in the pyrrolinone ring and thus generated the dihydropyridone ring. Although insertion of carbene **6-32** into a C–C bond of three- or four-membered cyclic ketones has been reported, insertion of **6-32** into the C–C bond of less-strained five-membered carbocycles is rarely known and suffered from low yields [67, 68]. Thus, our results showed the fused-ring skeleton of Δ^1-bipyrrolinones has higher reactivity (Scheme 6.12; Fig. 6.10).

We proposed two possible reaction pathways. Under the heat, **6-31** decomposes and releases dinitrogen, acetone, and carbene **6-32**. In **Pathway A**, nucleophilic addition of in situ generates **6-32** to C=O bond generated zwitterionic intermediate **6-36**. Migration of more substituted and electron-rich α-carbon leads to ring expansion product **6-33**. In **Pathway B**, [2 + 1] cycloaddition of **6-32** with C=O bond affords spiro compounds **6-37**. Homolysis of C–O bond gives diradical

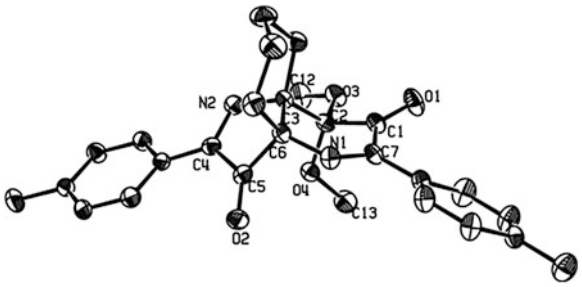
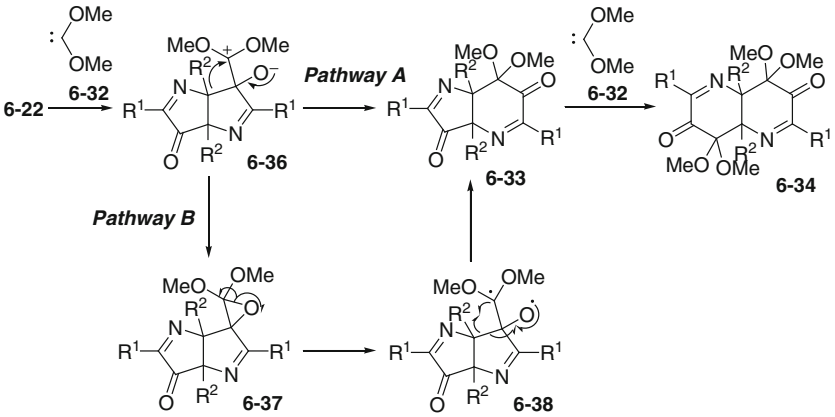


Fig. 6.10 ORTEP drawings of **6-33a** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Selected bond lengths (Å): C1–O1 1.195(4), C2–O3 1.392(4), C2–O4 1.399(4), C5–O2 1.207(4), C4–N2 1.298(4), C7–N1 1.282(4), C1–C2 1.557(5), C1–C7 1.515(5), C4–C5 1.529(5). Reproduced from Ref. [66] with permission from The Royal Society of Chemistry

intermediate **6-38** and promoted C–C bond cleavage of pyrrolinone ring and radical C–C coupling to construct dihydropyridone ring in **6-33**. Further reaction of pyrroline ring in **6-33** with carbene **6-32** gives double ring expansion product **6-34** (Scheme 6.13).

Furthermore, direct transformation of the C=O bonds in Δ^1-bipyrrolinone **6-22a** was demonstrated by condensation reaction with *O*-benzylhydroxylamine under acidic condition, affording the tricyclic dioxime **6-35** in 83 % isolated yield (Scheme 6.5) [69].



Scheme 6.13 Proposed mechanism for the reactions of Δ^1-bipyrrolinones **6-22** with oxadiazoline **6-31**

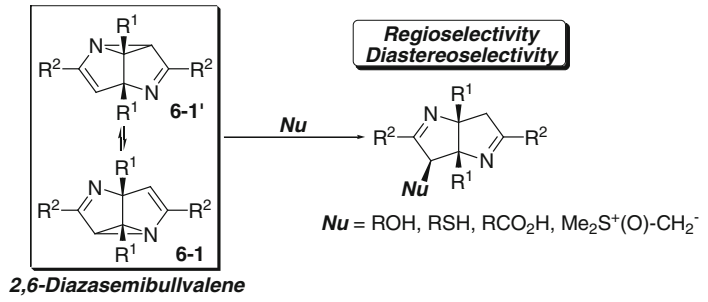
6.2.4 Nucleophilic Ring-Opening Reactions of 2,6-Diazasemibullvalenes for the Synthesis of Diverse Functionalized Δ^1-Bipyrroline Derivatives

As a strained nitrogen-containing three-membered heterocyclic compound, aziridines are among the most important compounds in organic and pharmaceutical chemistry [23–26]. Among all the reaction patterns of aziridine, the nucleophilic ring-opening reaction is very important and has been well investigated and reviewed [23–26]. Based on the ring opening of aziridine toward different nucleophilic reagents, a wide variety of synthetically valuable compounds, such as β-amino alcohols, 1,2-diamines, chiral ligands, as well as natural products and biologically active compounds, have been prepared.

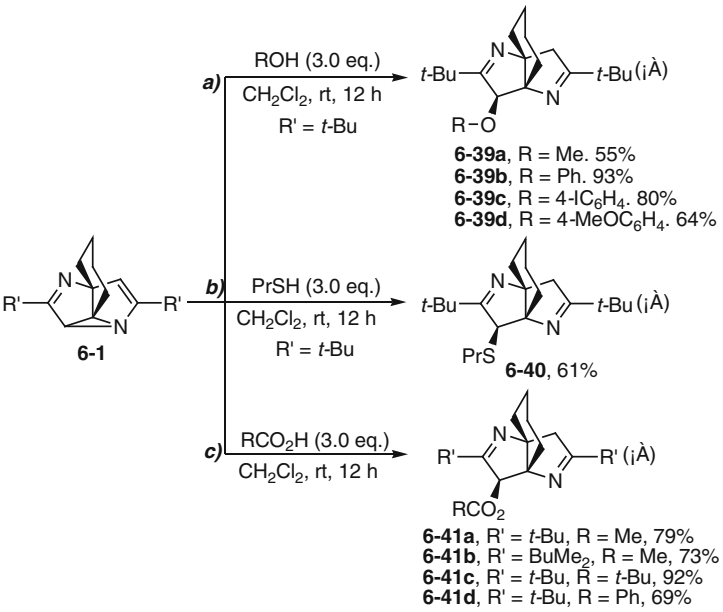
In the oxidation and cycloaddition chemistry of NSBVs, nucleophilic ring opening of the aziridine core with oxidants or cycloaddition reagents was proposed as the key step. As far as we are aware, nucleophilic ring-opening reaction of NSBV with nucleophiles is unknown, although nucleophilic ring-opening reaction of SBV has been reported [70, 71]. The author investigated the ring-opening reactions of NSBV toward a series of nucleophiles with different structures and reactivities. Diverse functionalized Δ^1-bipyrroline derivatives were obtained in good yields with high regio- and diastereoselectivity. NSBV did show higher reactivity than common aziridine and derivatives. In the reaction of NSBV with sulfoxonium ylides, different reaction pattern and chemoselectivity from aziridines were observed (Scheme 6.14).

6.2.4.1 Nucleophilic Ring Opening of 2,6-Diazasemibullvalenes with Proton-Bearing Nucleophiles

Ring-opening reactions of **6-1** with alcohols, phenols, thiol, and carboxylic acids as *O*- or *S*-nucleophiles all proceeded smoothly at room temperature, giving unsymmetrical Δ^1-bipyrroline derivatives **6-39–6-41** (Scheme 6.15). According to the ^{1}H



Scheme 6.14 Nucleophilic ring-opening reaction of NSBV



Scheme 6.15 Nucleophilic ring opening of 2,6-diazasemibullvalenes with proton-bearing nucleophiles

NMR spectra, all compounds **6-39–6-41** were formed as single diastereoisomers. The X-ray structure of **6-39c** and **6-41d** (Fig. 6.11) unambiguously revealed that nucleophiles attacked at the *exo*-face of the aziridine core in NSBV **6-1**, probably because the *exo*-face is less hindered while the nucleophilic attack at the *endo*-face would be suffered from repulsion of bulky substituents at 3,7-positions on NSBV **6-1**. This *exo*-face selectivity was also observed for the nucleophilic ring opening of SBV derivatives.

6.2.4.2 Nucleophilic Ring Opening of 2,6-Diazasemibullvalenes with Sulfoxonium Ylides

Ring expansion of aziridines with sulfoxonium ylides has been reported to generate structurally interesting and synthetically useful azetidines [73–75]. The mechanism is a double S_N2 process, featuring nucleophilic ring opening of aziridines with sulfoxonium ylides followed by nucleophilic ring closure along with elimination of sulfoxide. Since we have interest in construction of novel bowl- or cage-shaped compounds via reaction of NSBV **6-1**, we are curious whether ring expansion of aziridines core in NSBV **6-1** with sulfoxonium ylides could generate new "bowl-shaped" polycyclic frameworks containing strained 4-membered azetidine ring. However, to our surprise, when **6-1a** was treated with 4.0 equivalents of

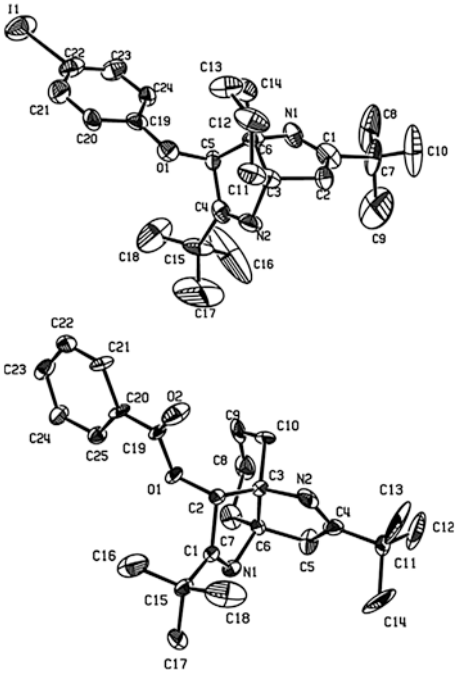
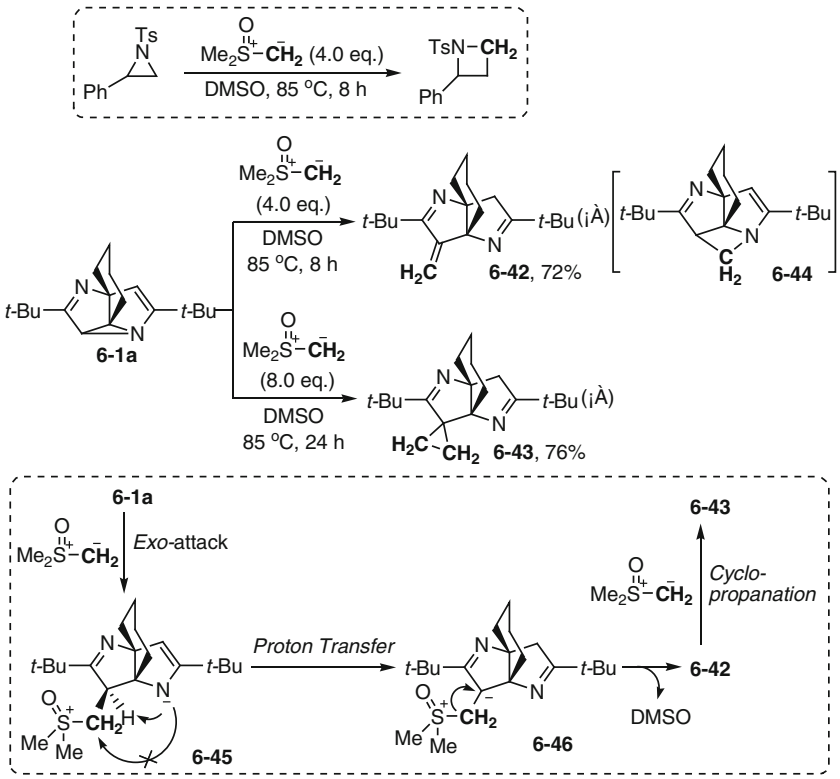


Fig. 6.11 ORTEP drawings of **6-39c** and **6-41d** with 30 % thermal ellipsoids. Hydrogen atoms are omitted for clarity. Reproduced from Ref. [72] by permission of John Wiley & Sons Ltd

dimethylsulfoxonium ylide in DMSO at 90 °C for 4 h, methylidene Δ^1-bipyrroline **6-42** was isolated in 72 % isolated yield as sole product instead of ring expansion product **6-44**. The methylene CH_2 unambiguously showed two singlets at $\delta = 5.54$ and 5.76 ppm in the ^{1}H NMR spectrum in $CDCl_3$, which is in good accordance with structure **6-42**. Treatment of **6-1a** with much more excess of sulfoxonium ylides for a longer time afforded Δ^1-bipyrroline-based spiro compound **6-43** in 76 % isolated yield (Scheme 6.16).

For the mechanistic aspect, we proposed that the sulfoxonium ylide would attack the *exo*-face of the aziridine ring of NSBV **6-1** to give intermediate **6-45**, according to the results of diastereoselectivity in ring opening of NSBV **1** with other nucleophiles. Because of the rigid ring system, the C–C bond in pyrroline ring could not rotate. Thus, the methylene group is distant from enamide moiety and nucleophilic ring closure is not preferred. Instead, intramolecular proton transfer followed by elimination of DMSO via the intermediate **6-46** would afford the ring-opening product **6-42**. Michael addition of excess sulfoxonium ylide to **6-42** followed by ring closure would give cyclopropanation product **6-43**. The different reaction patterns of NSBV **6-1** and aziridines toward sulfoxonium ylides demonstrated again that the strained rigid ring system and substitution patterns have obvious impact on the unique reactivity of NSBVs, making it remarkably different from common aziridines.



Scheme 6.16 Nucleophilic ring opening of 2,6-diazasemibullvalenes with sulfoxonium ylides

We suggest the rigid ring skeleton of NSBV enhances the reactivity of its aziridine core toward nucleophiles, thus leading to new types of reactions as well as selectivity.

6.3 Summary

The reaction chemistry of 2,6-diazasemibullvalenes (NSBV **6-1**) has been explored and disclosed, such as C–N bond insertion, rearrangement–cycloaddition, oxidation, and nucleophilic ring-opening reaction. Insertion of unsaturated compounds or low-valent metal complex into C–N bond of NSBV leads to several different kinds of ring expansion products or metallacycles. Lewis acid-catalyzed rearrangement–cycloaddition of NSBV with isocyanides, azides, or diazo compounds affords novel *N*-containing organic cage-shaped skeletons. Oxidation of NSBV by O_2 or *N*-oxides gives Δ^1-bilyrrolinones or pyrrolino[3,2-*b*]pyrrolinone derivatives, respectively. C–H bond oxidation and C–N bond cleavage occur in these processes. Nucleophilic

ring-opening reaction of NSBV with a series of nucleophiles results in highly functionalized Δ^1-bipyrroline derivatives with exclusive regioselectivity and diastereoselectivity. Some reactions even show different reactivities and selectivities with standard aziridines. These synthesized ring expansion products and "bowl-shaped" or "cage-shaped" *N*-containing polycyclic frameworks could be hardly accessed by other means.

The author attributes the highly reactive nature and usefulness in *N*-heterocycle synthesis to their unique strained ring system, multiple reaction sites, and intramolecular *aza*-Cope rearrangement. Moreover, the ring skeleton as a whole could be involved in the reaction.

6.4 Experimental Section

All reactions were conducted under a slightly positive pressure of dry nitrogen using standard Schlenk line techniques or under a nitrogen atmosphere in a Mikrouna Super (1220/750) glove box. The nitrogen in the glove box was constantly circulated through a copper/molecular sieves catalyst unit. The oxygen and moisture concentrations in the glove box atmosphere were monitored by an O_2/H_2O Combi-Analyzer to ensure both were always below 1 ppm. Unless otherwise noted, all starting materials were commercially available and were used without further purification. Solvents were purified by an Mbraun SPS-800 Solvent Purification System and dried over fresh Na chips in the glove box.

Organometallic samples for NMR spectroscopic measurements were prepared in the glove box by use of J. Young valve NMR tubes (Wilmad 528-JY). ^{1}H and ^{13}C NMR spectra were recorded on a Bruker-500 spectrometer (FT, 500 MHz for ^{1}H; 126 MHz for ^{13}C), Bruker-400 spectrometer (FT, 400 MHz for ^{1}H; 100 MHz for ^{13}C), or a JEOL-AL300 spectrometer (FT, 300 MHz for ^{1}H; 75 MHz for ^{13}C) at room temperature, unless otherwise noted. High-resolution mass spectra (HRMS) were recorded on a Bruker Apex IV FTMS mass spectrometer using ESI (electrospray ionization). Microelemental analyses were performed on an Elemental Analyzer vario EL apparatus.

IPr (1,3-bis(2,6-diisopropylphenyl)imidazol-2-ylidene), azides, and diaryl diazomethanes used in this work were prepared according to the reported procedures. 2,6-Diazasemibullvalenes **6-1d** were prepared according to the previous chapter.

General procedure for insertion reaction of alkynes into 2,6-diazasemibullvalene 6-1a. 2,6-Diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of toluene was treated with dimethyl acetylenedicarboxylate (1.0 mmol, 123 μl) or diethyl analogue (1.0 mmol, 160 μl), and the reaction mixture was stirred at 90 °C for 3 h. After the removal of solvent in vacuum, purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:3:1) gave **6-7a** or **6-7b** as pure products.

6-7a: Colorless crystal, isolated yield 60 % (124 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C): δ = 1.05 (s, 9H, CH_3), 1.13–1.23 (m, 6H, CH_2), 1.39 (s, 9H, CH_3), 1.89–1.94 (m, 1H, CH_2), 2.13–2.20 (m, 1H, CH_2), 3.41 (s, 3H, CH_3), 3.48 (s, 3H, CH_3), 3.93 (s, 1H, CH), 5.29 (s, 1H, CH); ^{13}C NMR (75 MHz, C_6D_6, 25 °C): δ = 19.84 (1 CH_2), 21.14 (1 CH_2), 28.04 (1 CH_2), 28.37 (3 CH_3), 29.06 (3 CH_3), 32.19 (1 quat. C), 33.57 (1 CH_2), 37.19 (1 quat. C), 50.95 (1 CH_3), 52.32 (1 CH_3), 57.34 (1 CH), **6-7** 9.89 (1 quat. C), 87.01 (1 quat. C), 112.61 (1 CH), 120.90 (1 quat. C), 148.25 (1 quat. C), 155.91 (1 quat. C), 164.75 (1 quat. C), 165.44 (1 quat. C), 180.52 (1 quat. C). HRMS: *m/z*: calcd for $C_{24}H_{35}N_2O_4$ $[M + H]^+$: 415.2597, found: 415.2592. Elemental Analysis Calcd (%) for $C_{24}H_{34}N_2O_4$: C, 69.54; H, 8.27; N, 6.76; found: C, 69.40; H, 8.46; N, 6.52. Single crystals of **6-7a** suitable for X-ray analysis were grown in hexane/ethyl acetate (4:1) at room temperature.

6-7b: Colorless solid, isolated yield 53 % (117 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.10 (s, 9H, CH_3), 1.20 (s, 9H, CH_3), 1.26–1.33 (m, 10H, CH_3 + CH_2), 1.56–1.61 (m, 2H, CH_2), 2.18–2.22 (m, 1H, CH_2), 2.32–2.36 (m, 1H, CH_2), 3.83 (s, 1H, CH), 4.18–4.30 (m, 4H, CH_2), 5.40 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 13.56 (1 CH_3), 14.31 (1 CH_3), 19.98 (1 CH_2), 21.21 (1 CH_2), 27.78 (1 CH_2), 27.99 (3 CH_3), 28.90 (3 CH_3), 32.03(1 quat. C), 33.41 (1 CH_2), 36.68 (1 quat. C), 56.48 (1 CH), 62.03 (1 CH_2), 60.05 (1 CH_2), 79.14 (1 quat. C), 86.16 (1 quat. C), 111.04 (1 CH), 120.13 (1 quat. C), 147.41 (1 quat. C), 155.88 (1 quat. C), 164.28 (1 quat. C), 165.33 (1 quat. C), 181.35 (1 quat. C). HRMS: *m/z*: calcd for $C_{26}H_{39}N_2O_4$ $[M + H]^+$: 443.2910, found: 443.2916. Elemental Analysis Calcd (%) for $C_{26}H_{38}N_2O_4$: C, 70.56; H, 8.65; N, 6.33; found: C, 70.42; H, 8.80; N, 6.19.

General procedure for insertion reaction of isocyanates into 2,6-diazasemibullvalene 6-1a. 2,6-Diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of toluene was treated with isocyanate (1.0 mmol), and the reaction mixture was stirred at 100 °C for 8 h. After the removal of solvent in vacuum, purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) gave **6-8a**, **6-8b,** or **6-8c** as pure products.

6-8a: Colorless crystal, isolated yield 53 % (103 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.03 (s, 9H, CH_3), 1.03–1.20 (m, 2H, CH_2), 1.28 (s, 9H, CH_3), 1.39–1.42 (m, 2H, CH_2), 1.56-1.64 (m, 2H, CH_2), 2.27–2.36 (m, 2H, CH_2), 5.06 (s, 1H, CH), 5.17 (s, 1H, CH), 7.14 (t, J = 7.5 Hz, 1H, CH), 7.38 (t, J = 7.5 Hz, 2H, CH), 7.53 (t, J = 7.8 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.31 (1 CH_2), 21.02 (1 CH_2), 27.87 (1 CH_2), 28.43 (3 CH_3), 28.70 (3 CH_3), 32.43 (1 quat. C), 32.49 (1 quat. C), 35.19 (1 CH_2), 70.85 (1 CH), 72.48 (1 quat. C), 78.20 (1 quat. C), 114.34 (1 CH), 121.95 (2 quat. C), 124.36 (1 CH), 128.87 (2 quat. C), 139.70 (1 quat. C), 153.57 (1 quat. C), 155.68 (1 quat. C), 178.09 (1 quat. C). HRMS: *m/z*: calcd for $C_{25}H_{34}N_3O$ $[M + H]^+$: 392.2702, found: 392.2708. Elemental Analysis Calcd (%) for $C_{25}H_{33}N_3O$: C, 76.69; H, 8.49; N, 10.73; found: C, 76.61; H, 8.37; N, 10.51. Single crystals of **6-8a** suitable for X-ray analysis were grown in hexane/diethyl ether/ethyl acetate (4:1:1) at room temperature.

6-8b: Colorless solid, isolated yield 56 % (131 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 0.78–0.82 (m, 2H, CH_2), 0.95 (s, 9H, CH_3), 1.05–1.12 (m, 2H, CH_2), 1.19 (s, 9H, CH_3), 1.43–1.64 (m, 2H, CH_2), 2.17–2.31 (m, 2H, CH_2), 4.93 (s, 1H, CH), 5.11 (s, 1H, CH), 7.36–7.44 (m, 4H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.42 (1 CH_2), 21.09 (1 CH_2), 28.42 (3 CH_3), 28.62 (3 CH_3), 29.66 (1 CH_2), 32.42 (2 quat. C), 35.22 (1 CH_2), 70.65 (1 CH), 72.51 (1 quat. C), 78.08 (1 quat. C), 114.64 (1 CH), 117.18 (1 quat. C), 123.23 (2 CH), 131.89 (2 CH), 138.85 (1 quat. C), 153.14 (1 quat. C), 155.48 (1 quat. C), 177.67 (1 quat. C). HRMS: *m/z*: calcd for $C_{25}H_{33}BrN_3O$ $[M + H]^+$: 470.1807, found: 470.1806. Elemental Analysis Calcd (%) for $C_{25}H_{32}BrN_3O$: C, 63.83; H, 6.86; N, 8.93; found: C, 63.89; H, 6.74; N, 9.00.

6-8c: Colorless solid, isolated yield 54 % (109 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.01 (s, 9H, CH_3), 1.05–1.24 (m, 6H, CH_2), 1.25 (s, 9H, CH_3), 2.32 (s, 3H, CH_3), 2.24–2.31 (m, 2H, CH_2), 4.99 (s, 1H, CH), 5.14 (s, 1H, CH), 7.16 (d, *J* = 8.1 Hz, 2H, CH), 7.37 (d, *J* = 7.5 Hz, 2H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 20.32 (1 CH_2), 20.86 (1 CH_2), 21.06 (1 CH_3), 28.53 (3 CH_3), 28.78 (3 CH_3), 29.69 (1 CH_2), 32.50 (1 quat. C), 32.55 (1 quat. C), 35.26 (1 CH_2), 71.16 (1 CH), 72.57 (1 quat. C), 78.34 (1 quat. C), 114.21 (1 CH), 122.12 (2 CH), 129.43 (2 CH), 134.15 (1 quat. C), 137.20 (1 quat. C), 153.84 (1 quat. C), 155.81 (1 quat. C), 178.30 (1 quat. C). HRMS: *m/z*: calcd for $C_{26}H_{36}N_3O$ $[M + H]^+$: 406.2858, found: 406.2862. Elemental Analysis Calcd (%) for $C_{26}H_{35}N_3O$: C, 77.00; H, 8.70; N, 10.36; found: C, 77.20; H, 8.59; N, 10.48.

Procedure for reaction of 2,6-diazasemibullvalene 6-1a with $Co_2(CO)_8$. 2,6-Diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of benzene was treated with dicobalt octacarbonyl (0.5 mmol, 171 mg). The reaction mixture was stirred at room temperature overnight. The reaction mixture was quenched by water, extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:2:1) to afford the corresponding **6-9**.

6-9: Colorless oil, isolated yield 61 % (91 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C): δ = 1.12 (s, 9H, CH_3), 1.17 (s, 9H, CH_3), 1.24–1.29 (m, 4H, CH_2), 1.31–1.61 (m, 2H, CH_2), 2.08–2.20 (m, 2H, CH_2), 4.05 (s, 1H, CH), 5.33 (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 18.84 (1 CH_2), 19.02 (1 CH_2), 26.51 (1 CH_2), 28.33 (3 CH_3), 28.76 (3 CH_3), 30.44 (1 CH_2), 32.21 (1 quat. C), 32.65 (1 quat. C), 67.60 (1 CH), 71.55 (1 quat. C), 84.66 (1 quat. C), 116.50 (1 CH), 158.42 (1 quat. C), 166.54 (1 quat. C), 174.60 (1 quat. C). HRMS: *m/z*: calcd for $C_{19}H_{29}N_2O$ $[M + H]^+$: 301.2280, found: 301.2269. Elemental Analysis Calcd (%) for $C_{19}H_{28}N_2O$: C, 75.96; H, 9.39; N, 9.32; found: C, 75.80; H, 9.42; N, 9.30.

Procedure for insertion reaction of 2,6-diazasemibullvalene 6-1a with IPr-Ni complex. In glove box $Ni(cod)_2$ (0.2 mmol, 55 mg) in 2 mL of THF was treated with IPr (0.2 mmol, 77 mg) at room temperature. After 2 h, 2,6-diazasemibullvalene **6-1a** (0.2 mmol, 55 mg) was added and the reaction mixture was stirred at room

temperature for additional 2 h. The reaction mixture was dried up in vacuum to give dark red solid, which was washed with hexane (5 mL) twice and dried up to yield the complex **6-10**.

6-10: Black red solid, isolated yield 80 % (115 mg). Elemental Analysis Calcd (%) for $C_{45}H_{65}N_4Ni$: C, 74.99; H, 9.09; N, 7.77; found: C, 74.69; H, 9.21; N, 7.49. Single crystals of **6-10** suitable for X-ray analysis were grown in hexane/THF (2:1) at room temperature.

General procedure for the preparation of 5,8-diaza-4,8-brexadienes 6-12 from NSBV 6-1 and isocyanides: To a solution of NSBV **6-1** (0.5 mmol) in 5 mL of benzene in a 50-ml round-bottom flask was added *t*-BuNC (0.6 mmol, 67 μl) and $Zn(OTf)_2$ (0.025 mmol, 9 mg) at room temperature, and the mixture was stirred for 2 h. The solvent was evaporated in vacuum to give crude product, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) to afford the desired product.

6-12a: Colorless crystal, isolated yield 93 % (165 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.21 (s, 9H, CH_3), 1.25 (s, 9H, CH_3), 1.28 (s, 9H, CH_3), 1.56–1.58 (m, 2H, CH_2), 1.35–1.42 (m, 4H, CH_2), 2.08–2.08 (m, 2H, CH_2), 3.28 (s, 1H, CH), 3.70 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.34, 20.66, 24.30, 24.47, 28.19, 28.99, 30.89, 36.32, 36.54, 56.31, 58.69, 61.99, 87.48, 92.03, 166.15, 185.15, 187.33. HRMS: *m/z*: calcd for $C_{23}H_{38}N_3$ $[M + H]^+$: 356.3066, found: 356.3069. Elemental Analysis Calcd (%) for $C_{23}H_{37}N_3$: C, 77.69; H, 10.49; N, 11.82; found: C, 77.53; H, 10.61; N, 11.74. Single crystals of **6-12a** suitable for X-ray analysis were grown in hexane at room temperature.

6-12b: Colorless oil, isolated yield 78 % (160 mg). ^{1}H NMR (400 MHz, THF-d_8, 25 °C): δ = 0.98 (s, 9H, CH_3), 1.10 (s, 6H, CH_3), 1.22 (s, 9H, CH_3), 1.27 (s, 9H, CH_3), 1.39–1.36 (m, 4H, CH_2), 1.53 (s, 2H, CH_2), 1.60–1.54 (m, 2H, CH_2), 2.07 (t, *J* = 8.9 Hz, 2H, CH_2), 3.23 (s, 1H, CH), 3.64 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.35, 20.69, 24.4, 24.56, 27.95, 28.21, 29.14, 29.77, 31.75, 32.04, 36.29, 36.45, 55.75, 56.59, 61.48, 87.35, 92.37, 164.45, 185.39, 187.58. HRMS: *m/z*: calcd for $C_{27}H_{46}N_3$ $[M + H]^+$: 412.3692, found: 412.3660. Elemental Analysis Calcd (%) for $C_{27}H_{45}N_3$: C, 78.77; H, 11.02; N, 10.21; found: C, 78.71; H, 11.08; N, 10.15.

6-12c: White solid, isolated yield 80 % (153 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.21 (s, 18H, CH_3), 1.24–1.25 (m, 4H, CH_2), 1.37–1.39 (m, 4H, CH_2), 1.54–1.59 (m, 3H, CH_2), 1.63–1.65 (m, 2H, CH_2), 1.73–1.79 (m, 3H, CH_2), 2.08–2.10 (m, 2H, CH_2), 3.27–3.29 (m, 1H, CH_2), 3.33 (s, 1H, CH), 3.60 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.43, 20.52, 24.24, 24.31, 24.51, 24.84, 25.51, 28.01, 28.27, 29.70, 33.45, 36.32, 36.51, 53.46, 59.78, 63.65, 88.13, 90.91, 171.59, 184.36, 186.24. HRMS: *m/z*: calcd for $C_{25}H_{40}N_3$ $[M + H]^+$: 382.3222, found: 382.3225. Elemental Analysis Calcd (%) for $C_{25}H_{39}N_3$: C, 78.69; H, 10.30; N, 11.01; found: C, 78.69; H, 10.30; N, 11.01.

6-12d: Yellow oil, isolated yield 62 % (110 mg). ^{1}H NMR (500 MHz, $CDCl_3$, 25 °C): δ = 0.90 (t, J = 7.2 Hz, 3H, CH_3), 1.20–1.21 (m, 2H, CH_2), 1.31 (s, 9H, CH_3), 1.32 (s, 9H, CH_3), 1.33–1.37 (m, 6H, CH_2), 1.58–1.59 (m, 2H, CH_2), 2.09–2.12 (m, 2H, CH_2), 3.24–3.31 (m, 1H, CH_2), 3.31 (s, 1H, CH), 3.48–3.54 (m, 1H, CH_2), 3.63 (s, 1H, CH); ^{13}C NMR (126 MHz, $CDCl_3$, 25 °C): δ = 13.91, 20.39, 20.53, 20.55, 24.21, 24.26, 27.87, 28.17, 32.96, 35.96, 36.53, 53.32, 55.84, 59.85, 88.55, 90.69, 173.25, 184.20, 186.08. HRMS: *m/z*: calcd for $C_{23}H_{38}N_3$ $[M + H]^+$: 356.3066, found: 356.3068. Elemental Analysis Calcd (%) for $C_{23}H_{37}N_3$: C, 77.69; H, 10.49; N, 11.82; found: C, 77.81; H, 10.57; N, 11.90.

6-12e: Colorless crystal, isolated yield 79 % (154 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.09 (s, 9H, CH_3), 1.24 (s, 9H, CH_3), 1.39–1.47 (m, 4H, CH_2), 1.57–1.59 (m, 2H, CH_2), 2.14–2.17 (m, 2H, CH_2), 3.39 (s, 1H, CH), 3.83 (s, 1H, CH), 4.51 (d, J = 13.6 Hz, 1H, CH_2), 4.66 (d, J = 13.6 Hz, 1H, CH_2), 7.20–7.24 (m, 3H, C_6H_5), 7.27–7.31 (m, 2H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.37, 20.46, 24.17, 24.23, 27.65, 28.20, 36.03, 36.40, 53.71, 59.75, 60.07, 88.59, 90.97, 127.08, 127.97, 128.41, 138.64, 174.32, 183.94, 186.14. HRMS: *m/z*: calcd for $C_{26}H_{36}N_3$ $[M + H]^+$: 390.2909, found: 390.2905. Elemental Analysis Calcd (%) for $C_{26}H_{35}N_3$: C, 80.16; H, 9.06; N, 10.79; found: C, 80.08; H, 9.18; N, 10.59. Single crystals of **6-12e** suitable for X-ray analysis were grown in hexane/diethyl ether (2:1) at room temperature.

6-12f: White solid, isolated yield 81 % (155 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.16–1.18 (m, 1H, CH_2), 1.23 (s, 9H, CMe_3), 1.25 (s, 9H, CMe_3), 1.27 (t, J = 7.5 Hz, 3H, $CH_2C\mathit{H}_3$), 1.39–1.40 (m, 3H, CH_2), 1.59–1.60 (m, 2H, CH_2), 2.10–2.13 (m, 2H, CH_2), 3.46 (s, 1H, CH), 3.62 (s, 1H, CH), 4.08 (d, J = 14.0 Hz, 1H, CH_2), 4.19 (q, J = 6.8 Hz, 2H, CH_2), 4.29 (d, J = 13.6 Hz, 1H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.21, 20.30, 20.42, 24.11, 24.17, 27.72, 28.05, 35.94, 36.61, 53.86, 57.32, 60.33, 61.13, 88.76, 91.10, 169.44, 177.82, 183.41, 185.90. HRMS: *m/z*: calcd for $C_{23}H_{36}N_3O_2$ $[M + H]^+$: 386.2808, found: 386.2811. Elemental Analysis Calcd (%) for $C_{23}H_{35}N_3O_2$: C, 71.65; H, 9.15; N, 10.90; found: C, 71.49; H, 9.18; N, 10.36. Single crystals of **6-12f** suitable for X-ray analysis were grown in hexane/ethyl acetate (2:1) at room temperature.

6-12g: White solid, isolated yield 93 % (217 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.15 (s, 9H, CH_3), 1.16 (s, 9H, CH_3), 1.31–1.42 (m, 4H, CH_2), 1.58–1.59 (m, 2H, CH_2), 2.08–2.12 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 3.38 (s, 1H, CH), 3.56 (s, 1H, CH), 4.59 (d, J = 14.0 Hz, 1H, CH_2), 4.81 (d, J = 14.0 Hz, 1H, CH_2), 7.34 (d, J = 8.0 Hz, 2H, C_6H_4), 7.80 (d, J = 7.6 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.16, 20.27, 21.65, 24.01, 27.55, 28.09, 35.89, 36.55, 55.05, 60.49, 75.61, 89.18, 91.63, 128.99, 129.72, 134.88, 144.98, 181.79, 182.90, 185.36. HRMS: *m/z*: calcd for $C_{27}H_{38}N_3O_2S$ $[M + H]^+$: 468.2685, found: 468.2681. Elemental Analysis Calcd (%) for $C_{27}H_{37}N_3O_2S$: C, 69.34; H, 7.97; N, 8.99; found: C, 69.27; H, 7.99; N, 8.77.

6-12h: White solid, isolated yield 63 % (129 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 1.18–1.11 (m, 4H, CH_2), 1.20 (s, 9H, CH_3), 1.21 (s, 9H, CH_3), 1.40–1.37 (m, 2H, CH_2), 1.64–1.56 (m, 2H, CH_2), 2.15–2.06 (m, 2H, CH_2), 2.52–2.41 (m, 4H, CH_2), 2.66–2.55 (m, 1H, CH_2), 3.34 (s, 1H, CH), 3.51–3.38 (m, 1H, CH_2), 3.63 (s, 1H, CH), 3.77–3.67 (m, 4H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.34, 20.48, 24.17, 24.21, 27.90, 28.14, 35.96, 36.60, 53.20, 53.62, 53.98, 59.19, 60.04, 66.88, 88.66, 90.80, 174.71, 183.96, 185.97. HRMS: *m/z*: calcd for $C_{25}H_{41}N_4O$ $[M + H]^+$: 413.3280, found: 413.3278. Elemental Analysis Calcd (%) for $C_{25}H_{40}N_4O$: C, 72.77; H, 9.77; N, 13.58; found: C, 72.70; H, 9.91; N, 13.44.

6-12i: Yellow solid, isolated yield 84 % (163 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.85 (s, 9H, CH_3), 1.25 (s, 9H, CH_3), 1.38–1.42 (m, 4H, CH_2), 1.60–1.61 (m, 2H, CH_2), 2.12 (s, 3H, CH_3), 2.14–2.21 (m, 2H, CH_2), 3.58 (s, 1H, CH), 3.81 (s, 1H, CH), 6.49 (d, J = 7.6 Hz, 1H, C_6H_4), 7.01 (t, J = 7.2 Hz, 1H, C_6H_4), 7.08–7.15 (m, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 18.04, 20.37, 24.12, 24.22, 27.41, 27.88, 35.69, 36.67, 53.74, 60.88, 88.55, 91.37, 118.22, 124.59, 126.15, 130.06, 130.71, 148.13, 174.18, 184.63, 185.73. HRMS: *m/z*: calcd for $C_{26}H_{36}N_3$ $[M + H]^+$: 390.2909, found: 390.2907. Elemental Analysis Calcd (%) for $C_{26}H_{35}N_3$: C, 80.16; H, 9.06; N, 10.79; found: C, 80.04; H, 9.26; N, 10.61.

6-12j: Yellow solid, isolated yield 89 % (179 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.86 (s, 9H, CH_3), 1.25–1.27 (m, 2H, CH_2), 1.28 (s, 9H, CH_3), 1.40–1.44 (m, 4H, CH_2), 1.60–1.62 (m, 2H, CH_2), 1.89 (s, 3H, CH_3), 2.09 (s, 3H, CH_3), 2.08–2.14 (m, 2H, CH_2), 3.25 (s, 1H, CH), 3.54 (s, 1H, CH), 6.87–6.98 (m, 3H, C_6H_3); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C): δ = 18.21, 19.05, 20.30, 24.13, 24.35, 27.47, 27.72, 29.71, 35.75, 36.80, 55.67, 59.59, 89.16, 91.88, 123.80, 124.89, 127.98, 128.89, 129.89, 147.20, 173.21, 185.07. HRMS: *m/z*: calcd for $C_{27}H_{38}N_3$ $[M + H]^+$: 404.3066, found: 404.3064. Elemental Analysis Calcd (%) for $C_{27}H_{37}N_3$: C, 80.35; H, 9.24; N, 10.41; found: C, 80.24; H, 9.33; N, 10.35.

6-12k: Yellow oil, isolated yield 83 % (168 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (s, 9H, CH_3), 1.25 (s, 9H, CH_3), 1.40–1.41 (m, 4H, CH_2), 1.60–1.62 (m, 2H, CH_2), 2.12–2.20 (m, 2H, CH_2), 3.57 (s, 1H, CH), 3.79 (s, 3H, OCH_3), 3.91 (s, 1H, CH), 6.70 (d, J = 7.6 Hz, 2H, C_6H_4), 6.84 (d, J = 7.2 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 20.34, 20.38, 24.05, 24.12, 27.80, 27.92, 35.71, 36.64, 53.97, 55.43, 61.27, 88.44, 91.08, 114.18, 121.44, 143.06, 156.73, 175.40, 184.34, 185.72. HRMS: *m/z*: calcd for $C_{26}H_{36}N_3O$ $[M + H]^+$: 406.2858, found: 406.2851. Elemental Analysis Calcd (%) for $C_{26}H_{35}N_3O$: C, 77.00; H, 8.70; N, 10.36; found: C, 76.93; H, 8.81; N, 10.25.

6-12l: White solid, isolated yield 74 % (183 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.81 (t, J = 7.5 Hz, 6H, CH_2CH_3), 0.89–0.84 (m, 2H, CH_2), 1.08 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.10 (s, 6H, CH_3), 1.43–1.36 (m, 2H, CH_2), 1.52–1.47 (m, 4H, CH_2 CH_3), 1.63–1.56 (m, 2H, CH_2), 2.15–2.07 (m, 2H, CH_2), 2.44 (s, 3H, CH_3), 3.37 (s, 1H, CH), 3.52 (s, 1H, CH), 4.57 (d, J = 14.2 Hz, 1H, CH_2SO_2), 4.81 (d, J = 14.2 Hz, 1H, CH_2SO_2), 7.34 (d, J = 8.1 Hz, 2H, C_6H_4), 7.82 (d, J = 8.2 Hz,

2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 8.51, 8.58, 20.24, 20.32, 21.66, 24.09, 24.13, 24.20, 24.74, 25.26, 25.70, 32.23, 32.89, 39.35, 39.64, 55.29, 60.60, 75.41, 89.26, 91.87, 129.03, 129.70, 134.92, 144.96, 181.83, 182.31, 184.97. HRMS: *m/z*: calcd for $C_{29}H_{42}N_3O_2S$ $[M + H]^+$: 496.2998, found: 496.2998. Elemental Analysis Calcd (%) for $C_{29}H_{41}N_3O_2S$: C, 70.26; H, 8.34; N, 8.48; found: C, 70.21; H, 8.50; N, 8.31.

6-12m: Colorless oil, isolated yield 78 % (214 mg). ^1H NMR (400 MHz, $CDCl_3$, 25 °C): δ = 0.87 (dt, J = 9.8, 6.8 Hz, 6H, CH_3), 1.08 (s, 3H, CH_3), 1.09 (s, 3H, CH_3), 1.10 (s, 3H, CH_3), 1.11 (s, 3H, CH_3), 1.15–1.31 (m, 4H, CH_2), 1.63–1.33 (m, 14H, CH_2), 2.11 (d, J = 11.6 Hz, 2H, CH_2), 2.44 (s, 3H, CH_3), 3.38 (s, 1H, CH), 3.52 (s, 1H, CH), 4.56 (d, J = 14.2 Hz, 1H, CH_2), 4.81 (d, J = 14.2 Hz, 1H, CH_2), 7.34 (d, J = 8.0 Hz, 2H, C_6H_4), 7.82 (d, J = 8.2 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C): δ = 14.10, 14.26, 20.25, 20.35, 21.67, 23.28, 23.30, 24.09, 24.15, 24.70, 25.46, 25.96, 26.02, 26.34, 26.39, 29.71, 39.04, 39.42, 39.51, 40.24, 55.30, 60.57, 101.47, 76.72, 77.04, 77.36, 89.25, 91.84, 129.02, 129.70, 134.96, 144.95, 182.03, 182.59, 185.16. HRMS: *m/z*: calcd for $C_{33}H_{50}N_3O_2S$ $[M + H]^+$: 552.3624, found: 552.3620. Elemental Analysis Calcd (%) for $C_{33}H_{49}N_3O_2S$: C, 71.83; H, 8.95; N, 7.61; found: C, 71.77; H, 9.02; N, 7.47.

6-12n: White solid, isolated yield 69 % (193 mg). ^1H NMR (400 MHz, $CDCl_3$): δ = 0.91–0.81 (m, 2H, CH_2), 1.26–1.38 (m, 14H, CH_2 + CH), 2.04–1.61 (m, 16H, CH_2 + CH), 2.19–2.09 (m, 2H, CH), 3.56 (s, 1H, CH), 3.79 (s, 3H, OCH_3), 3.87 (s, 1H, CH), 6.73 (d, J = 8.8 Hz, 2H, C$_6H_4$), 6.87 (d, J = 8.8 Hz, 2H, C$_6H_4$); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 20.40, 20.45, 24.05, 24.16, 27.89, 27.97, 36.35, 36.56, 37.60, 38.75, 39.85, 39.88, 53.66, 55.64, 60.33, 88.53, 90.82, 114.23, 121.56, 143.40, 156.84, 176.08, 184.19, 185.18. HRMS: *m/z*: calcd for $C_{38}H_{48}N_3O$ $[M + H]^+$: 561.3719, found: 561.3717.

General procedure for the preparation of 2,5,9-triaza-4,8-brexadienes 6-13 from NSBV 6-1 and azides: To a solution of NSBV **6-1** (0.5 mmol) in 5 mL of benzene in a 25-ml Schlenk tube was added benzyl azide (0.6 mmol, 76 μl) and La $(OTf)_3$ (0.05 mmol, 29 mg) at room temperature, and the mixture was stirred at 80 °C for 8 h. The solvent was evaporated in vacuum to give crude products, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:3:1) to afford the desired product.

6-13a: Colorless oil, isolated yield 76 % (143 mg). ^1H NMR (500 MHz, $CDCl_3$): δ = 0.92 (s, 9H, CH_3), 1.17–1.11 (m, 2H, CH_2), 1.25 (s, 9H, CH_3), 1.49–1.41 (m, 2H, CH_2), 1.53 (d, J = 13.5 Hz, 1H, CH_2), 1.67 (d, J = 12.7 Hz, 1H, CH_2), 1.94 (d, J = 12.7 Hz, 1H, CH_2), 2.17 (d, J = 13.2 Hz, 1H, CH_2), 3.00 (d, J = 13.1 Hz, 1H, CH_2), 3.22 (s, 1H, CH), 3.26 (s, 1H, CH), 3.96 (d, J = 13.1 Hz, 1H, CH), 7.27–7.20 (m, 5H, C_6H_5); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.90, 22.06, 27.02, 27.57, 27.79, 28.66, 35.01, 36.06, 51.97, 67.18, 69.83, 83.60, 90.79, 127.02, 128.09, 129.86, 139.63, 183.57, 189.39. HRMS: *m/z*: calcd for $C_{25}H_{36}N_3$ $[M + H]^+$:

378.2909, found: 378.2902. Elemental Analysis Calcd (%) for $C_{25}H_{35}N_3$: C, 79.53; H, 9.34; N, 11.13; found: C, 79.42; H, 9.40; N, 11.08.

6-13b: Colorless oil, isolated yield 82 % (162 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (s, 9H, CH_3), 1.27 (s, 9H, CH_3), 1.42–1.59 (m, 5H, CH_2), 1.65 (d, J = 12.7 Hz, 1H, CH_2), 1.93 (d, J = 12.7 Hz, 1H, CH_2), 2.10 (d, J = 13.2 Hz, 1H, CH_2), 3.00 (d, J = 13.1 Hz, 1H, CH_2), 3.22 (s, 2H, CH), 3.90 (d, J = 13.1 Hz, 1H, CH_2), 6.95 (d, J = 6.9 Hz, 2H, C_6H_4), 7.12–7.27 (m, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.83, 22.05, 27.01, 27.56, 27.82, 28.77, 35.04, 36.08, 51.26, 67.33, 69.83, 83.59, 90.86, 114.79, 115.00, 131.18, 131.26, 135.42, 135.45, 160.86, 163.29, 183.67, 189.29. HRMS: *m/z*: calcd for $C_{25}H_{35}FN_3$ $[M + H]^+$: 396.2815, found: 396.2815. Elemental Analysis Calcd (%) for $C_{25}H_{34}FN_3$: C, 75.91; H, 8.66; N, 10.62; found: C, 75.80; H, 8.91; N, 10.35.

6-13c: Colorless oil, isolated yield 83 % (208 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.82 (s, 9H, CH_3), 0.86 (m, 1H, CH_2), 1.27 (s, 9H, CH_3), 1.38 (m, 1H, CH_2), 1.47 (dd, J = 12.3, 6.0 Hz, 1H, CH_2), 1.59 (m, 2H, CH_2), 1.76 (m, 1H, CH_2), 1.95 (d, J = 12.9 Hz, 1H, CH_2), 2.52 (d, J = 13.1 Hz, 1H, CH_2), 3.10 (d, J = 13.7 Hz, 1H, CH_2), 3.24 (s, 1H, CH), 3.41 (d, J = 1.4 Hz, 1H, CH), 4.10 (d, J = 13.6 Hz, 1H), 6.91 (td, J = 7.6, 1.9 Hz, 1H, C_6H_4), 7.30–7.19 (m, 2H, C_6H_4), 7.78 (dd, J = 7.9, 0.9 Hz, 1H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.87, 22.00, 26.93, 27.57, 27.65, 28.66, 35.05, 36.01, 55.56, 66.23, 69.94, 84.04, 90.53, 101.31, 127.96, 128.88, 131.78, 139.60, 141.60, 183.88, 189.44. HRMS: *m/z*: calcd for $C_{25}H_{35}IN_3$ $[M + H]^+$: 504.1876, found: 504.1871. Elemental Analysis Calcd (%) for $C_{25}H_{34}IN_3$: C, 59.64; H, 6.81; N, 8.35; found: C, 59.59; H, 6.86; N, 8.27.

6-13d: Colorless oil, isolated yield 80 % (164 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.96 (s, 9H, CH_3), 1.19–1.13 (m, 1H, CH_2), 1.24 (s, 9H, CH_3), 1.49–1.40 (m, 2H, CH_2), 1.56–1.50 (m, 1H, CH_2), 1.60–1.56 (m, 1H, CH_2), 1.95 (d, J = 12.9 Hz, 1H, CH_2), 2.17 (d, J = 13.3 Hz, 1H, CH_2), 2.95 (d, J = 13.5 Hz, 1H, CH_2), 3.22 (d, J = 1.3 Hz, 1H, CH), 3.23 (s, 1H, CH), 3.96 (d, J = 13.5 Hz, 1H, CH_2), 7.11 (t, J = 3.7 Hz, 1H, C_6H_4), 7.19 (d, J = 5.2 Hz, 2H, C_6H_4), 7.25–7.23 (m, 1H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.81, 22.00, 26.98, 27.53, 27.78, 28.65, 35.08, 36.06, 51.49, 67.48, 69.93, 83.61, 90.75, 127.18, 127.71, 129.33, 129.82, 133.91, 141.86, 183.79, 189.34. HRMS: *m/z*: calcd for $C_{25}H_{35}ClN_3$ $[M + H]^+$: 412.2520, found: 412.2518. Elemental Analysis Calcd (%) for $C_{25}H_{34}ClN_3$: C, 72.88; H, 8.32; N, 10.20; found: C, 72.72; H, 8.46; N, 10.15.

6-13e: Colorless crystal, isolated yield 77 % (175 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 9H, CH_3), 1.23 (s, 9H, CH_3), 1.47–1.37 (m, 2H, CH_2), 1.51 (d, J = 12.8 Hz, 1H, CH_2), 1.61–1.54 (m, 2H, CH_2), 1.66 (d, J = 12.6 Hz, 1H, CH_2), 1.94 (d, J = 12.9 Hz, 1H, CH_2), 2.08 (d, J = 13.1 Hz, 1H, CH_2), 2.97 (d, J = 13.3 Hz, 1H, CH_2), 3.21 (d, J = 1.3 Hz, 1H, CH), 3.23 (s, 1H, CH), 3.89 (d, J = 13.3 Hz, 1H, CH_2), 7.12 (d, J = 8.3 Hz, 2H, C_6H_4), 7.39 (d, J = 8.3 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.79, 22.02, 27.00, 27.54, 27.82, 28.83, 35.06, 36.08, 51.42, 67.57, 69.83, 83.62, 90.84, 120.86, 131.18, 131.37, 138.73,

183.76, 189.25. HRMS: *m/z*: calcd for $C_{25}H_{35}BrN_3$ $[M + H]^+$: 456.2014, found: 456.2010. Elemental Analysis Calcd (%) for $C_{25}H_{34}BrN_3$: C, 65.78; H, 7.51; N, 9.21; found: C, 65.56; H, 7.80; N, 9.07. Single crystals of **6-13e** suitable for X-ray analysis were grown in hexane/ethyl acetate (3:1) at room temperature.

6-13f: White solid, isolated yield 73 % (154 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01 (s, 9H, CH_3), 1.11 (dd, J = 13.1, 4.3 Hz, 1H, CH_2), 1.25 (s, 9H, CH_3), 1.70–1.38 (m, 5H, CH_2), 1.98 (t, J = 13.3 Hz, 2H, CH_2), 3.13 (d, J = 13.8 Hz, 1H, CH_2), 3.23 (d, J = 1.4 Hz, 1H, CH), 3.28 (s, 1H, CH), 4.06 (d, J = 13.8 Hz, 1H, CH_2), 7.44 (d, J = 8.6 Hz, 2H, C_6H_4), 8.14 (d, J = 8.7 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.66, 21.96, 26.99, 27.49, 27.79, 29.00, 35.11, 36.14, 51.52, 68.19, 69.91, 83.7, 90.88, 123.36, 130.21, 147.16, 147.47, 184.25, 189.13. HRMS: *m/z*: calcd for $C_{25}H_{35}N_4O_2$ $[M + H]^+$: 423.2760, found: 423.2764. Elemental Analysis Calcd (%) for $C_{25}H_{34}N_4O_2$: C, 71.06; H, 8.11; N, 13.26; found: C, 71.01; H, 8.13; N, 13.20.

6-13g: White crystal, isolated yield 72 % (156 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.94 (s, 9H, CH_3), 1.17–1.04 (m, 2H, CH_2), 1.25 (s, 9H, CH_3), 1.54 1.41 (m, 2H, CH_2), 1.67 (d, J = 12.3 Hz, 1H, CH_2), 1.95 (d, J = 12.8 Hz, 1H, CH_2), 2.12 (d, J = 13.1 Hz, 1H, CH_2), 3.05 (d, J = 13.5 Hz, 1H, CH_2), 3.23 (s, 1H, CH), 3.24 (s, 1H, CH), 3.90 (s, 3H, CH_3), 4.01 (d, J = 13.4 Hz, 1H, CH_2), 7.32 (d, J = 8.1 Hz, 2H, C_6H_4), 7.95 (d, J = 8.2 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.77, 21.99, 26.98, 27.54, 27.80, 28.74, 35.07, 36.10, 51.78, 52.02, 67.67, 69.89, 83.68, 90.78, 128.93, 129.46, 129.66, 145.08, 167.05, 183.89, 189.31. HRMS: *m/z*: calcd for $C_{27}H_{38}N_3O_2$ $[M + H]^+$: 436.2964, found: 436.2964. Elemental Analysis Calcd (%) for $C_{27}H_{37}N_3O_2$: C, 74.45; H, 8.56; N, 9.65; found: C, 74.48; H, 8.42; N, 9.60.

6-13h: White solid, isolated yield 71 % (158 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.92 (s, 9H, CH_3), 1.14–1.21 (m, 1H, CH_2) 1.25 (s, 9H, CH_3), 1.41–1.53 (m, 2H, CH_2), 1.54–1.63 (m, 2H, CH_2), 1.70 (d, J = 13.0 Hz, 1H, CH_2),1.96 (d, J = 13.1 Hz, 1H, CH_2), 2.19 (d, J = 13.3 Hz, 1H, CH_2), 3.02 (d, J = 13.6 Hz, 1H, CH_2), 3.22 (d, J = 1.4 Hz, 1H, CH), 3.26 (s, 1H, CH), 4.06 (d, J = 13.6 Hz, 1H, CH_2), 7.35–7.44 (m, 2H, C_6H_4), 7.46–7.54 (m, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.77, 21.97, 26.94, 27.54, 27.73, 28.60, 35.08, 36.12, 51.55, 67.59, 69.99, 83.69, 90.74, 123.84–123.96 (q, J = 3.8 Hz), 126.39–126.50 (q, J = 3.8 Hz), 120.12–128.24 (q, J = 272.3 Hz), 128.55, 130.04–131.00 (q, J = 32.1 Hz), 132.88, 140.80, 184.02, 189.44. HRMS: *m/z*: calcd for $C_{26}H_{35}F_3N_3$ $[M + H]^+$: 446.2783, found: 446.2780. Elemental Analysis Calcd (%) for $C_{26}H_{34}F_3N_3$: C, 70.09; H, 7.69; N, 9.43; found: C, 70.08; H, 7.81; N, 9.23.

6-13i: Yellow oil, isolated yield 74 % (151 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.95 (s, 9H, CH_3), 1.13–1.07 (m, 2H, CH_2), 1.24 (s, 9H, CH_3), 1.54–1.37 (m, 3H, CH_2), 1.65 (d, J = 12.5 Hz, 1H, CH_2), 1.93 (d, J = 12.9 Hz, 1H, CH_2), 2.12 (d, J = 13.1 Hz, 1H, CH_2), 2.98 (d, J = 13.0 Hz, 1H, CH_2), 3.20 (s, 1H, CH), 3.24 (d, J = 1.3 Hz, 1H, CH), 3.78 (s, 1H, OCH_3), 3.87 (d, J = 13.0 Hz, 1H, CH_2), 6.80 (d,

J = 8.6 Hz, 2H, C_6H_4), 7.14 (d, J = 8.5 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.91, 22.09, 27.04, 27.58, 27.85, 28.74, 35, 36.04, 51.28, 55.29, 67.11, 69.75, 83.53, 90.85, 113.49, 130.86, 131.82, 158.74, 183.43, 189.32. HRMS: *m/z*: calcd for $C_{26}H_{38}N_3O$ $[M + H]^+$: 408.3015, found: 408.3013. Elemental Analysis Calcd (%) for $C_{26}H_{37}N_3O$: C, 76.62; H, 9.15; N, 10.31; found: C, 76.39; H, 9.18; N, 10.18.

6-13j: Colorless oil, isolated yield 62 % (123 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3H, CH_3), 1.08 (d, J = 1.9 Hz, 1H, CH_2), 1.12 (d, J = 1.3 Hz, 1H, CH_2), 1.17 (s, 9H, CH_3), 1.22 (s, 9H, CH_3), 1.30–1.23 (m, 9H, CH_2), 1.44–1.35 (m, 3H, CH_2), 1.61–1.49 (m, 3H, CH_2), 1.70 (d, J = 14.1 Hz, 1H, CH_2), 1.92 (dd, J = 12.7, 6.1 Hz, 2H, CH_2), 2.37 (d, J = 13.3 Hz, 1H, CH_2), 2.76 (dt, J = 12.7, 7.8 Hz, 1H, CH_2), 3.17 (s, 1H, CH), 3.22 (s, 1H, CH); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 14.08, 21.93, 22.00, 22.64, 26.90, 27.32, 27.52, 28.15, 28.75, 29.34, 29.40, 30.27, 31.86, 35.36, 35.92, 48.08, 68.20, 69.77, 83.64, 90.53, 183.27, 189.12. HRMS: *m/z*: calcd for $C_{26}H_{46}N_3$ $[M + H]^+$: 400.3692, found: 400.3688. Elemental Analysis Calcd (%) for $C_{26}H_{45}N_3$: C, 78.14; H, 11.35; N, 10.51; found: C, 78.08; H, 11.50; N, 10.29.

6-13k: Colorless oil, isolated yield 80 % (156 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.91–0.82 (m, 1H, CH_2), 1.16 (s, 9H, CH_3), 1.23 (s, 9H, CH_3), 1.51–1.38 (m, 2H, CH_2), 1.63–1.54 (m, 2H, CH_2), 1.71 (d, J = 14.0 Hz, 1H, CH_2), 1.94 (d, J = 12.9 Hz, 1H, CH_2), 2.22 (ddd, J = 12.7, 10.8, 5.1 Hz, 1H, CH_2), 2.41 (d, J = 13.3 Hz, 1H, CH_2), 2.86–2.66 (m, 2H, CH_2), 3.08 (ddd, J = 12.6, 11.1, 6.0 Hz, 1H, CH_2), 3.20 (s, 1H, CH), 3.28 (d, J = 1.3 Hz, 1H, CH), 7.15 (t, J = 6.1 Hz, 3H, C_6H_5), 7.24 (d, J = 7.5 Hz, 2H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.87, 22.08, 26.98, 27.47, 28.13, 29.16, 35.32, 35.97, 37.23, 50.13, 68.4, 69.62, 83.68, 90.75, 125.95, 128.26, 128.59, 140.28, 183.53, 188.91. HRMS: *m/z*: calcd for $C_{26}H_{38}N_3$ $[M + H]^+$: 392.3066, found: 392.3064.

6-13i: Colorless oil, isolated yield 80 % (161 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 1.18 (s, 9H, CH_3) 1.21 (s, 9H, CH_3),1.45 (dd, J = 12.2, 5.1 Hz, 1H, CH_2), 1.57–1.48 (m, 2H, CH_2), 1.59 (s, 2H, CH_2), 1.72 (d, J = 12.8 Hz, 1H, CH_2), 1.95 (d, J = 13.0 Hz, 1H, CH_2), 2.41 (d, J = 13.3 Hz, 1H, CH_2), 2.71 (dd, J = 13.8, 8.7 Hz, 1H, CH_2), 3.21 (s, 1H, CH), 3.32 (s, 1H, CH), 3.69 (dd, J = 13.7, 4.9 Hz, 1H, CH_2), 6.25–6.15 (m, 1H, CH), 6.34 (d, J = 15.9 Hz, 1H, CH), 7.22 (t, J = 6.9 Hz, 1H, C_6H_5), 7.35–7.27 (m, 4H, C_6H_5); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.88, 21.98, 26.87, 27.48, 28.10, 28.36, 35.38, 36.04, 50.07, 66.33, 69.62, 83.49, 90.65, 126.21, 127.37, 128.56, 129.32, 131.29, 136.90, 183.70, 189.30. HRMS: *m/z*: calcd for $C_{27}H_{38}N_3$ $[M + H]^+$: 404.3066, found: 404.3061. Elemental Analysis Calcd (%) for $C_{27}H_{37}N_3$: C, 80.35; H, 9.24; N, 10.41; found: C, 80.30; H, 9.29; N, 10.35.

6-13m: Colorless oil, isolated yield 96 % (208 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.16 (s, 9H, CH_3), 1.18 (s, 9H, CH_3), 1.24–1.20 (m, 1H, CH_2), 1.46–1.38 (m, 1H, CH_2), 1.53–1.46 (m, 1H, CH_2), 1.63–1.53 (m, 2H, CH_2), 1.72 (d, J = 12.8 Hz, 1H, CH_2), 1.95 (d, J = 13.1 Hz, 1H, CH_2), 2.31 (d, J = 13.3 Hz, 1H, CH_2), 2.67 (d,

J = 15.2 Hz, 1H, CH_2), 3.23 (s, 1H, CH), 3.52 (d, J = 1.3 Hz, 1H, CH), 3.71 (d, J = 15.2 Hz, 1H, CH_2), 5.16–5.02 (m, 2H, CH_2), 7.36–7.31 (m, 5H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.66, 21.81, 26.85, 27.35, 27.85, 27.90, 35.19, 36.05, 49.24, 66.37, 68.39, 69.90, 83.83, 90.23, 126.87, 128.22, 128.52, 135.60, 171.11, 184.83, 189.49. HRMS: *m/z*: calcd for $C_{27}H_{38}N_3O_2$ $[M + H]^+$: 436.2964, found: 436.2961.

6-13n: Orange solid, isolated yield 51 % (103 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.97 (s, 9H, CH_3), 1.18–1.16 (m, 1H, CH_2), 1.23 (s, 9H, CH_3), 1.46–1.41 (m, 1H, CH_2), 1.65–1.55 (m, 3H, CH_2), 1.87–1.76 (m, 1H, CH_2), 1.98 (d, J = 12.5 Hz, 1H, CH_2), 2.59 (d, J = 12.4 Hz, 1H, CH_2), 2.73 (d, J = 13.7 Hz, 1H, CH_2), 3.28 (s, 1H, CH), 3.53 (d, J = 1.3 Hz, 1H, CH), 4.48 (d, J = 13.6 Hz, 1H, CH_2), 7.42 (t, J = 7.6 Hz, 2H, C_6H_5), 7.53 (t, J = 7.2 Hz, 1H, C_6H_5), 7.99 (d, J = 7.2 Hz, 2H, C_6H_5); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.72, 21.95, 26.90, 27.48, 27.70, 28.12, 35.29, 36.16, 53.44, 67.01, 70.15, 84.31, 90.52, 128.42, 128.98, 133.14, 136.12, 190.06, 197.68. HRMS: *m/z*: calcd for $C_{26}H_{36}N_3O$ $[M + H]^+$: 406.2858, found: 406.2855.

6-13o: White solid, isolated yield 68 % (151 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.98 (s, 9H, CH_3), 1.20 (s, 9H, CH_3), 1.47–1.41 (m, 1H, CH_2), 1.63–1.49 (m, 3H, CH_2), 1.83–1.74 (m, 1H, CH_2), 1.94 (d, J = 12.5 Hz, 2H, CH_2), 2.69 (d, J = 13.1 Hz, 1H, CH_2), 3.29 (s, 1H, CH), 3.83 (d, J = 1.4 Hz, 1H, CH), 3.98 (d, J = 13.5 Hz, 1H, CH_2), 4.87 (d, J = 13.5 Hz, 1H, CH_2), 7.72 (m, 2H, C_6H_4), 7.84 (m, 2H, C_6H_4). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.71, 21.79, 26.42, 27.36, 27.41, 27.56, 35.30, 36.05, 50.49, 67.67, 70.05, 84.53, 89.86, 123.36, 131.94, 134.15, 168.11, 184.58, 188.81. HRMS: *m/z*: calcd for $C_{27}H_{35}N_4O_2$ $[M + H]^+$: 447.2760, found: 447.2761. Elemental Analysis Calcd (%) for $C_{27}H_{34}N_4O_2$: C, 72.62; H, 7.67; N, 12.55; found: C, C, 72.56; H, 7.72; N, 12.48.

6-13p: White solid, isolated yield 77 % (159 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (s, 9H, CH_3), 1.24 (s, 9H, CH_3), 1.47–1.38 (m, 2H, CH_2), 1.61–1.52 (m, 2H, CH_2), 1.67 (d, J = 12.7 Hz, 1H, CH_2), 1.95 (d, J = 12.6 Hz, 1H, CH_2), 2.06 (d, J = 12.8 Hz, 2H, CH_2), 3.02 (d, J = 13.8 Hz, 1H, CH_2), 3.21 (d, J = 1.4 Hz, 1H, CH), 3.26 (s, 1H, CH), 3.95 (d, J = 13.8 Hz, 1H, CH_2), 7.27 (d, J = 4.3 Hz, 1H, C_6H_3N), 7.58 (dd, J = 8.1, 2.4 Hz, 1H, C_6H_3N), 8.23 (d, J = 2.2 Hz, 1H, C_6H_3N); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.65, 21.93, 26.92, 27.48, 27.81, 28.90, 35.17, 36.15, 48.58, 67.79, 69.85, 83.68, 90.84, 123.85, 134.15, 140.29, 150.11, 150.24, 184.25, 189.15. HRMS: *m/z*: calcd for $C_{24}H_{34}ClN_4$ $[M + H]^+$: 413.2472, found: 413.2469. Elemental Analysis Calcd (%) for $C_{24}H_{33}ClN_4$: C, 69.80; H, 8.05; N, 13.57; found: C, 69.73; H, 8.19; N, 13.46.

6-13q: Colorless oil, isolated yield 66 % (143 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.93 (s, 9H, CH_3), 1.13–1.06 (m, 2H), 1.25 (s, 9H, CH_3), 1.55–1.42 (m, 3H, CH_2), 1.67 (d, J = 12.0 Hz, 1H, CH_2), 1.94 (d, J = 12.8 Hz, 1H, CH_2), 2.14 (d, J = 13.2 Hz, 1H, CH_2), 3.02 (d, J = 13.2 Hz, 1H, CH_2), 3.23 (s, 1H, CH), 3.24 (s, 1H, CH), 3.96 (d, J = 13.2 Hz, 1H, CH_2), 4.28 (s, 2H, CH_2N_3), 7.33–7.17 (m, 4H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.84, 22.03, 26.99, 27.55, 27.78, 28.68, 29.70, 35.02, 36.07, 51.63, 54.52, 67.31, 69.82, 83.60, 90.78, 128.19, 130.30,

133.96, 139.97, 183.69, 189.37. HRMS: *m/z*: calcd for $C_{26}H_{37}N_6$ $[M + H]^+$: 433.3080, found: 433.3078.

6-13r: White solid, isolated yield 51 % (86 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.99 (s, 9H, CH_3), 1.00 (s, 9H, CH_3), 1.15–1.13 (m, 4H, CH_2), 1.24 (s, 9H, CH_3), 1.24 (s, 9H, CH_3), 1.47–1.40 (m, 4H, CH_2), 1.69–1.58 (m, 4H, CH_2), 1.93 (d, J = 12.6 Hz, 2H, CH_2), 2.05 (dd, J = 13.1, 2.9 Hz, 2H, CH_2), 3.00 (d, J = 13.2, 1H, CH_2), 3.01 (d, J = 13.2, 1H, CH_2), 3.21 (s, 1H, CH), 3.22 (s, 1H, CH), 3.24 (s, 1H, CH), 3.25 (s, 1H, CH), 3.89 (d, J = 13.2, 1H, CH_2), 3.92 (d, J = 13.2, 1H, CH_2), 7.17–7.13 (m, 4H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.86, 22.08, 27.05, 27.55, 27.82, 27.92, 27.96, 28.01, 28.94, 28.98, 29.71, 35.00, 35.03, 36.05, 51.72, 51.77, 67.74, 67.79, 69.76, 69.80, 83.56, 83.61, 90.85, 129.33, 129.36, 138.41, 138.46, 183.46, 183.55, 189.21, 189.24. HRMS: *m/z*: calcd for $C_{44}H_{65}N_6$ $[M + H]^+$: 677.5271, found: 677.5270.

6-13s: White solid, isolated yield 61 % (180 mg). ^{1}H NMR (500 MHz, $CDCl_3$): δ = 0.87–0.88 (m, 2H, CH_2), 0.88–0.89 (m, 2H, CH_2), 1.43–1.84 (m, 31H, CH + CH_2), 2.13–2.16 (m, 2H, CH), 2.20–2.21 (m, 1H, CH_2), 3.02 (d, J = 13.4 Hz, 1H, CH_2), 3.21 (d, J = 3.1 Hz, 2H, CH), 3.91 (s, 3H, CO_2CH_3), 4.01 (d, J = 13.4 Hz, 1H, CH_2), 7.33 (d, J = 8.2 Hz, 2H, C_6H_4), 7.95 (d, J = 8.2 Hz, 2H, C_6H_4); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 14.13, 21.82, 21.97, 22.70, 26.97, 27.93, 27.97, 28.58, 36.52, 36.67, 37.16, 38.17, 39.74, 39.81, 51.72, 52.07, 66.53, 68.96, 83.27, 90.75, 128.90, 129.41, 129.92, 145.15, 167.07, 183.90, 189.08. HRMS: *m/z*: calcd for $C_{39}H_{50}N_3O_2$ $[M + H]^+$: 592.3903, found: 592.3906.

General procedure for the preparation of 2,5,9-triaza-4,8-brexadienes 6-14 from NSBV 6-1 and diazo compounds: To a solution of NSBV **6-1** (0.5 mmol) in 5 mL of benzene in a 25-ml Schlenk tube was added diphenyl diazomethane (0.6 mmol, 116 mg) and $Sc(OTf)_3$ (0.05 mmol, 24 mg) at room temperature, and the mixture was stirred for 2 h. The solvent was evaporated in vacuum to give crude products, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:3:1) to afford the desired product.

6-14a: Yellow solid, isolated yield 63 % (146 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.78 (dd, J = 13.1, 3.7 Hz, 1H, CH_2), 1.08 (d, J = 3.4 Hz, 1H, CH_2), 1.12 (d, J = 3.2 Hz, 1H, CH_2), 1.20 (s, 9H, CH_3), 1.23 (s, 9H, CH_3), 1.45 (dd, J = 14.2, 6.8 Hz, 3H, CH_2), 1.90 (t, J = 9.3 Hz, 2H, CH_2), 3.33 (s, 1H, CH_3), 3.90 (d, J = 1.4 Hz, 1H, CH_3), 7.35–7.28 (m, 6H, C_6H_5), 7.43–7.39 (m, 2H, C_6H_5), 7.46 (dd, J = 6.6, 3.0 Hz, 2H, C_6H_5); ^{13}C NMR (126 MHz, $CDCl_3$): δ = 21.30, 22.14, 27.12, 27.41, 27.74, 27.96, 35.37, 36.02, 68.82, 70.26, 89.37, 91.05, 127.67, 127.82, 128.54, 128.59, 129.26, 130.25, 136.83, 139.80, 162.62, 183.59, 189.04. HRMS: *m/z*: calcd for $C_{31}H_{39}N_4$ $[M + H]^+$: 467.3175, found: 467.3176.

6-14b: Yellow solid, isolated yield 92 % (241 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 0.89–0.82 (m, 2H, CH_2), 1.23 (s, 9H, CMe_3), 1.24 (s, 9H, CMe_3), 1.51–1.41 (m, 4H, CH_2), 1.85 (d, J = 13.4 Hz, 1H, CH_2), 1.92 (d, J = 5.6 Hz, 1H, CH_2), 3.33

(s, 1H, CH), 3.78 (s, 3H, OCH_3), 3.84 (s, 3H, OCH_3), 3.87 (d, J = 1.4 Hz, 1H, CH), 6.78 (d, J = 8.9 Hz, 2H, C_6H_4), 6.84 (d, J = 8.8 Hz, 2H, C_6H_4), 7.36 (d, J = 8.9 Hz, 2H, C_6H_4), 7.45 (d, J = 8.8 Hz, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.30, 22.19, 27.13, 27.43, 28.00, 28.73, 35.40, 36.00, 55.23, 55.28, 68.79, 70.18, 89.29, 91.20, 112.80, 113.19, 129.26, 130.21, 131.87, 132.80, 159.59, 160.72, 163.16, 183.37, 189.24. HRMS: *m/z*: calcd for $C_{33}H_{43}N_4O_2$ $[M + H]^+$: 527.3386, found: 527.3390. Elemental Analysis Calcd (%) for $C_{33}H_{42}N_4O_2$: C, 75.25; H, 8.04; N, 10.64; found: C, 75.15; H, 8.12; N, 10.56.

6-14c: Yellow solid, isolated yield 61 % (154 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.01–0.96 (m, 1H, CH_2), 1.22 (s, 9H, CH_3), 1.23 (s, 9H, CH_3), 1.50–1.39 (m, 4H, CH_2), 1.66–1.59 (m, 1H, CH_2),1.80 (d, J = 13.4 Hz, 1H, CH_2), 1.92 (d, J = 6.5 Hz, 1H, CH_2), 3.36 (s, 1H, CH), 3.87 (d, J = 1.4 Hz, 1H, CH), 6.96 (t, J = 8.7 Hz, 2H, C_6H_4), 7.05 (t, J = 8.7 Hz, 2H, C_6H_4), 7.41–7.35 (m, 2H, C_6H_4), 7.51–7.45 (m, 2H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.11, 22.09, 27.07, 27.30, 27.92, 28.77, 35.41, 36.07, 69.01, 70.06, 89.68, 91.26, 114.71, 114.79, 114.92, 115.00, 115.15, 115.36, 128.14, 128.22, 130.42, 130.50, 132.20, 132.28, 161.42, 161.82, 163.90, 164.14, 164.99, 183.97, 189.09. HRMS: *m/z*: calcd for $C_{31}H_{37}F_2N_4$ $[M + H]^+$: 503.2986, found: 503.2982.

6-14d: Yellow solid, isolated yield 60 % (139 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.23 (s, 9H, CMe_3), 1.26 (s, 9H, CMe_3), 1.41–1.35 (m, 1H, CH_2), 1.65–1.58 (m, 4H, CH_2), 2.16–2.06 (m, 2H, CH_2), 2.29 (d, J = 12.1 Hz, 1H, CH_2), 3.43 (s, 1H, CH), 4.01 (d, J = 1.4 Hz, 1H, CH), 7.27–7.20 (m, 2H, C_6H_4), 7.40–7.33 (m, 2H, C_6H_4), 7.58 (dd, J = 11.0, 7.5 Hz, 2H, C_6H_4), 7.67 (d, J = 7.5 Hz, 1H, C_6H_4), 8.62 (d, J = 7.7 Hz, 1H, C_6H_4); ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.87, 22.14, 26.93, 27.66, 28.03, 32.70, 35.94, 36.10, 66.03, 70.23, 91.12, 92.63, 119.47, 119.61, 122.43, 127.83, 127.92, 129.17, 130.42, 130.88, 130.92, 137.28, 140.96, 142.37, 162.66, 183.28, 191.22. HRMS: *m/z*: calcd for $C_{31}H_{37}N_4$ $[M + H]^+$: 465.3018, found: 465.3015.

6-14e: Yellow crystal, isolated yield 72 % (177 mg). ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.50 (d, J = 6.8 Hz, 1H, C_6H_4), 7.39 (d, J = 7.5 Hz, 1H, C_6H_4), 7.21–7.14 (m, 3H, C_6H_4), 7.11 (t, J = 7.4 Hz, 2H, C_6H_4), 7.04 (d, J = 7.4 Hz, 1H, C_6H_4), 3.89 (s, 1H, CH), 3.34 (s, 2H, CH_2), 3.34 (s, 1H, CH), 3.30 (d, J = 7.1 Hz, 1H, CH), 3.07–2.84 (m, 2H, CH_2), 2.21 (s, 1H, CH_2), 1.89 (d, J = 5.3 Hz, 1H, CH_2), 1.49–1.39 (m, 5H, CH_2), 1.19 (s, 9H, CH_3), 1.08 (s, 9H, CH_3). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 21.19, 22.44, 27.01, 27.49, 27.81, 27.95, 32.35, 33.44, 35.22, 35.94, 69.53, 70.65, 89.11, 91.51, 125.42, 125.50, 127.93, 128.12, 128.19, 128.69, 128.81, 129.81, 138.08, 138.27, 138.70, 139.12, 184.05, 188.26. HRMS: *m/z*: calcd for $C_{33}H_{41}N_4$ $[M + H]^+$: 493.3331, found: 493.3329. Elemental Analysis Calcd (%) for $C_{33}H_{40}N_4$: C, 80.45; H, 8.18; N, 11.37; found: C, 80.40; H, 8.21; N, 11.26. Single crystals of **6-14e** suitable for X-ray analysis were grown in hexane/diethyl ether (2:1) at room temperature.

General procedure for the preparation of Δ^1-bipyrrolinones 6-22 from NSBV 6-1 and oxygen: O_2 gas was bubbled into a solution of NSBV **6-1** (0.5 mmol) in 5 mL of CCl_4 at room temperature for ca.10 min. The reaction mixture was allowed to stir for 12 h under O_2 atmosphere. Solvents were removed, and the crude product was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:1:1) to afford the desired product.

6-22a: Yellow solid, isolated yield 93 % (140 mg); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.50–2.42 (m, 2H, CH_2), 1.65–1.53 (m, 6H, CH_2), 1.23 (s, 18H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.98, 177.72, 74.97, 35.02, 28.70, 26.91, 18.93. IR (neat): ν = 1742 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{18}H_{27}N_2O_2$ $[M + H]^+$: 303.2073, found 303.2070. Elemental Analysis Calcd (%) for $C_{18}H_{26}N_2O_2$: C, 71.49; H, 8.67; N, 9.26; found: C, 71.31; H, 8.70; N, 9.13.

6-22b: Yellow solid, isolated yield 90 % (206 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.47–2.35 (m, 2H, CH_2), 2.03 (s, 4H, CH_2), 1.90 (s, 8H, CH_2), 1.76–1.71 (m, 8H, CH and CH_2), 1.65–1.47 (m, 4H, CH), 1.25 (s, 12H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 198.11, 176.98, 75.13, 38.45, 37.54, 36.51, 29.71, 28.65, 27.77, 18.70. IR (neat): ν = 1744 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{30}H_{39}N_2O_2$ $[M + H]^+$: 459.3012, found 459.3006. Elemental Analysis Calcd (%) for $C_{30}H_{38}N_2O_2$: C, 78.56; H, 8.35; N, 6.11; found: C, 78.42; H, 8.58; N, 5.99. Single crystals of **6-22b** suitable for X-ray analysis were grown in hexane/CH_2Cl_2 (1:1) at room temperature.

6-22c: Yellow oil, isolated yield 95 % (170 mg); ^{1}H NMR (300 MHz, $CDCl_3$): δ = 2.47–2.42 (m, 2H, CH_2), 1.85–1.71 (m, 4H, CH_2), 1.56–1.44 (m, 8H, CH_2), 1.21–1.03 (m, 2H, CH_2), 1.07 (s, 6H, CH_3), 0.62 (t, J = 7.5 Hz, 6H, CH_3), 0.55 (t, J = 7.5 Hz, 6H, CH_3). ^{13}C NMR (75 MHz, $CDCl_3$): δ = 197.81, 176.45, 75.26, 42.05, 30.01, 29.97, 29.34, 20.51, 19.20, 8.57, 8.47. IR (neat): ν = 1745 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{22}H_{35}N_2O_2$ $[M + H]^+$: 359.2699, found 359.2697.

6-22d: Yellow oil, isolated yield 92 % (151 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.54–2.44 (m, 2H, CH_2), 1.72 (q, J = 7.4 Hz, 4H, CH_2), 1.64–1.50 (m, 4H, CH_2), 1.28–1.23 (m, 2H, CH_2), 1.21 (s, 6H, CH_3), 1.17 (s, 6H, CH_3), 0.64 (t, J = 7.5 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.01, 177.12, 75.23, 38.66, 31.79, 29.06, 24.88, 24.67, 19.22, 9.08. IR (neat): ν = 1743 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{20}H_{31}N_2O_2$ $[M + H]^+$: 331.2386, found 331.2381.

6-22e: Yellow oil, isolated yield 96 % (183 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.57–2.45 (m, 2H, CH_2), 1.78–1.69 (m, 2H, CH_2), 1.67–1.60 (m, 2H, CH_2), 1.29–1.23 (m, 4H, CH_2), 1.22 (s, 6H, CH_3), 1.18 (s, 6H, CH_3), 1.59–1.51 (m, 4H, CH_2), 1.05–0.85 (m, 6H, CH_2), 0.82 (t, J = 7.3 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.03. 177.22, 75.19, 38.84, 38.36, 29.12, 27.16, 25.57, 25.12, 23.12, 19.40, 13.97. IR (neat): ν = 1747 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{24}H_{39}N_2O_2$ $[M + H]^+$: 387.3012, found 387.3008.

6-22f: Yellow solid, isolated yield 94 % (160 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.30 (d, J = 7.2 Hz, 4H, C_6H_5), 7.54 (t, J = 7.4 Hz, 2H, C_6H_5), 7.46 (t, J = 7.5 Hz, 4H, C_6H_5), 2.66 (dt, J = 14.3, 5.3 Hz, 2H, CH_2), 2.00–1.89 (m, 2H, CH_2), 1.72–1.61 (m, 2H, CH_2), 1.49–1.37 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.99, 165.45, 132.34, 129.59, 128.76, 128.67, 75.99, 29.17, 18.74. IR (neat): ν = 1741 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{22}H_{19}N_2O_2$ [M + H]$^+$: 343.1447, found 343.1449. Elemental Analysis Calcd (%) for $C_{22}H_{18}N_2O_2$: C, 77.17; H, 5.30; N, 8.18; found: C, 77.10; H, 5.28; N, 8.17.

6-22g: Yellow solid, isolated yield 83 % (155 mg);^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, J = 8.2 Hz, 4H, C_6H_4), 7.23 (d, J = 8.1 Hz, 4H, C_6H_4), 2.60 (dt, J = 14.2, 5.2 Hz, 2H, CH_2), 2.38 (s, 6H, CH_3), 1.95–1.84 (m, 2H, CH_2), 1.68–1.57 (m, 2H, CH_2), 1.46–1.33 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.36, 165.21,142.93, 129.38, 128.71, 126.93, 75.80, 29.12, 21.67, 18.69. IR (neat): ν = 1743 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{24}H_{23}N_2O_2$ [M + H]$^+$: 371.1760, found 371.1762. Elemental Analysis Calcd (%) for $C_{24}H_{22}N_2O_2$: C, 77.81; H, 5.99; N, 7.56; found: C, 77.67; H, 6.13; N, 7.42.

6-22h: Yellow solid, isolated yield 79 % (158 mg);^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.27 (dd, J = 8.8, 1.5 Hz, 4H, C_6H_4), 6.92 (dd, J = 8.8, 1.5 Hz, 4H, C_6H_4), 3.82 (s, 6H, CH_3), 2.62–2.53 (m, 2H, CH_2), 1.94–1.83 (m, 2H, CH_2), 1.63–1.56 (m, 2H, CH_2), 1.43–1.34 (m, 2H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 198.81, 164.43, 162.92, 130.61, 130.56, 122.32, 114.07, 113.93, 75.60, 55.40, 29.09, 18.63. IR (neat): ν = 1740 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{24}H_{23}N_2O_4$ [M + H]$^+$: 403.1658, found 403.1654.

6-22i: Yellow solid, isolated yield 81 % (111 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 1.43 (s, 6H, CH_3), 1.22 (s, 18H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.39, 176.88, 75.31, 34.99, 26.91, 16.95. IR (neat): ν = 1746 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{16}H_{25}N_2O_2$ [M + H]$^+$: 277.1916, found 277.1916. Elemental Analysis Calcd (%) for $C_{16}H_{24}N_2O_2$: C, 69.53; H, 8.75; N, 10.14; found: C, 69.43; H, 8.72; N, 10.18.

6-22j: Yellow oil, isolated yield 77 % (138 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.32 (ddd, J = 14.1, 12.4, 5.1 Hz, 2H, CH_2), 1.60–1.52 (m, 2H, CH_2), 1.37–1.29 (m, 8H, CH_2), 1.21 (s, 18H, CH_3), 0.89 (t, J = 7.3 Hz, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.68, 176.95, 78.38, 35.16, 29.52, 26.96, 26.08, 23.11, 13.74. IR (neat): ν = 1744 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{22}H_{37}N_2O_2$ [M + H]$^+$: 361.2855, found 361.2859.

General procedure for the preparation of pyrrolino[3,2-*b*]pyrrolinones 6-28 from NSBV 6-1 and pyridine oxide or DMSO: To a solution of NSBV **6-1** (0.5 mmol) in 5 mL of benzene in a 25-ml Schlenk tube was added pyridine oxide (0.5 mmol, 47 mg) and $Zn(OTf)_2$ (0.5 mmol, 181 mg) at room temperature, and the mixture was stirred for 12 h. The solvent was evaporated in vacuum to give crude products, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:1:1) to afford the desired product.

The solution of NSBV **6-21** (0.5 mmol) in 5 mL of DMSO in a 25-ml round-bottom flask was stirred at 90 °C for 2 h. The reaction mixture was poured into 20 mL of water and extracted with diethyl ether. The organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give crude products, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethyl amine = 100:1:1) to afford **6-28**.

6-28a: Yellow solid, isolated yield 92 % (133 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.95 (dd, J = 43.6, 18.1 Hz, 2H, CH_2), 2.54 (dt, J = 13.9, 3.7 Hz, 1H, CH_2), 2.32 (dt, J = 8.1, 3.7 Hz, 1H, CH_2), 1.65–1.45 (m, 2H, CH_2), 1.41–1.30 (m, 2H, CH_2), 1.24 (s, 9H, CH_3), 1.22–1.18 (m, 1H, CH_2), 1.08 (s, 9H, CH_3), 1.03–0.91 (m, 1H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.43, 186.23, 175.47, 80.72, 73.71, 44.88, 36.08, 34.36, 32.93, 28.45, 27.86, 27.06, 20.41, 20.37. IR (neat): v = 1740 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{18}H_{29}N_2O$ $[M + H]^+$: 289.2280, found 289.2284. Elemental Analysis Calcd (%) for $C_{18}H_{28}N_2O$: C, 74.96; H, 9.78; N, 9.71; found: C, 74.84; H, 9.82; N, 9.69.

6-28b: Yellow oil, isolated yield 79 % (136 mg); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 2.99 (d, J = 18.1 Hz, 1H, CH_2), 2.83 (d, J = 18.1 Hz, 1H, CH_2), 2.58 (d, J = 13.9 Hz, 1H, CH_2), 2.38–2.33 (m, 1H, CH_2), 1.92–1.84 (m, 2H, CH_2), 1.61–1.51 (m, 8H, CH_2), 1.46–1.38 (m, 4H, CH_2), 1.15 (s, 3H, CH_3), 0.99 (s, 3H, CH_3), 0.77–0.72 (m, 6H, CH_3), 0.70–0.65 (m, 6H, CH_3).^{13}C NMR (126 MHz, $CDCl_3$): δ = 200.73, 184.90, 174.38, 80.92, 74.23, 45.36, 42.96, 41.47, 33.84, 32.07, 31.78, 30.33, 30.10, 20.93, 20.92, 20.73, 20.69, 8.80, 8.67, 8.64, 8.54. IR (neat): v = 1739 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{22}H_{37}N_2O$ $[M + H]^+$: 345.2906, found 345.2904.

6-28c: Yellow oil, isolated yield 81 % (128 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 2.99 (d, J = 18.1 Hz, 1H, CH_2), 2.86 (d, J = 18.1 Hz, 1H, CH_2), 2.56 (dt, J = 14.0, 3.4 Hz, 1H, CH_2), 2.35 (dt, J = 13.5, 3.5 Hz, 1H, CH_2), 1.77–1.72 (m, 2H, CH_2), 1.63–1.50 (m, 3H, CH_2), 1.49–1.43 (m, 2H, CH_2), 1.22 (s, 3H, CH_3), 1.19 (s, 3H, CH_3), 1.06 (s, 3H, CH_3), 1.03 (s, 3H, CH_3), 0.90–0.82 (m, 3H, CH_3), 0.74–0.65 (m, 6H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 200.56, 185.45, 174.85, 80.82, 74.00, 45.03, 39.53, 37.94, 33.63, 33.37, 31.84, 29.71, 28.91, 25.72, 25.29, 25.04, 24.81, 20.58, 20.53, 9.13, 8.96. IR (neat): v = 1741 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{20}H_{33}N_2O$ $[M + H]^+$: 317.2593, found 317.2591.

6-28d: Yellow solid, isolated yield 94 % (168 mg); ^{1}H NMR (400 MHz, C_6D_6): δ = 8.51 (d, J = 8.1 Hz, 2H, C_6H_4), 7.71 (d, J = 8.1 Hz, 2H, C_6H_4), 6.92 (d, J = 8.1 Hz, 2H, C_6H_4), 6.85 (d, J = 8.0 Hz, 2H, C_6H_4), 3.36 (d, J = 17.9 Hz, 1H, CH_2), 2.92 (d, J = 17.9 Hz, 1H, CH_2), 2.87 (t, J = 3.9 Hz, 1H, CH_2), 2.17 (dt, J = 13.6, 4.1 Hz, 1H, CH_2), 1.99 (s, 3H, CH_3), 1.95 (s, 3H, CH_3), 1.46–1.37 (m, 1H, CH_2), 1.32–1.26 (m, 2H, CH_2), 1.23–1.16 (m, 1H, CH_2), 1.08–0.97 (m, 1H, CH_2), 0.93–0.85 (m, 1H, CH_2). ^{13}C NMR (101 MHz, C_6D_6): δ = 200.58, 173.14, 163.57, 141.63, 141.13, 131.83, 129.36, 129.12, 128.83, 128.66, 128.30, 82.31, 74.92, 46.39, 33.17, 29.18, 21.22, 21.18, 20.19. IR (neat): v = 1737 (C=O), cm^{-1}; HRMS: *m/z*: calcd for

$C_{24}H_{25}N_2O$ $[M + H]^+$: 356.1889, found 356.1891. Elemental Analysis Calcd (%) for $C_{24}H_{24}N_2O$: C, 80.87; H, 6.79; N, 7.86; found: C, 80.88; H, 6.81; N, 7.66.

6-28e: Yellow solid, isolated yield 83 % (161 mg); ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.22 (d, J = 8.9 Hz, 2H, C_6H_4), 7.75 (d, J = 8.8 Hz, 2H, C_6H_4), 6.93 (d, J = 8.9 Hz, 2H, C_6H_4), 6.86 (d, J = 8.8 Hz, 2H, C_6H_4), 3.82 (s, 3H, OCH_3), 3.80 (s, 3H OCH_3), 3.48 (d, J = 17.9 Hz, 1H, CH_2), 3.36 (d, J = 17.9 Hz, 1H, CH_2), 2.64 (dt, J = 13.9, 4.3 Hz, 1H, CH_2), 2.48–2.39 (m, 1H, CH_2), 1.69–1.61 (m, 1H, CH_2), 1.60–1.45 (m, 4H, CH_2), 1.17–1.08 (m, 1H, CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 200.90, 173.06, 162.82, 162.31, 162.05, 130.18, 129.64, 126.54, 123.20, 113.95, 113.78, 81.79, 77.35, 77.09, 76.84, 74.59, 55.35, 55.34, 46.46, 33.08, 28.92, 19.98, 19.89. IR (neat): ν = 1742 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{24}H_{23}N_2O_3$ $[M + H]^+$: 389.1865, found 389.1861.

6-28f: Yellow solid, isolated yield 51 % (66 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.01 (d, J = 18.3 Hz, 1H, CH_2), 2.81 (d, J = 18.3 Hz, 1H, CH_2), 1.35 (s, 3H, CH_3), 1.24 (s, 9H, CH_3), 1.23 (s, 3H, CH_3), 1.07 (s, 9H, CH_3). ^{13}C NMR (75 MHz, $CDCL_3$): δ = 200.68, 186.07, 175.58, 81.78, 74.45, 46.99, 27.86, 27.09, 22.18, 15.59. IR (neat): ν = 1741 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{16}H_{27}N_2O$ $[M + H]^+$: 263.2123, found 263.2119. Elemental Analysis Calcd (%) for $C_{16}H_{26}N_2O$: C, 73.24; H, 9.99; N, 10.68; found: C, 73.18; H, 10.02; N, 10.64.

Reactions of Δ^1-bipyrrolinones 6-22 with oxadiazoline 6-31: The solution of Δ^1-bipyrrolinones **6-22** (0.25 mmol, 65 mg) and oxadiazoline **6-31** (0.75 mmol, 120 mg) in 5 mL of benzene in a 25-ml Schlenk tube was refluxed for 24 h. The solvent was evaporated and the crude product was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) to afford **6-33**.

The solution of Δ^1-bipyrrolinones **6-22** (0.25 mmol, 65 mg) and oxadiazoline **6-31** (1.5 mmol, 240 mg) in 5 mL of toluene in a 25-ml Schlenk tube was refluxed for 36 h. The solvent was evaporated, and the crude product was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) to afford **6-34**.

6-33a: Yellow solid, isolated yield 63 % (69 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.20 (d, J = 8.1 Hz, 2H, C_6H_4), 7.86 (d, J = 8.2 Hz, 2H, C_6H_4), 7.31 (d, J = 8.0 Hz, 2H, C_6H_4), 7.23 (d, J = 8.1 Hz, 2H, C_6H_4), 3.51 (s, 3H, OCH_3), 3.12 (s, 3H, OCH_3), 2.52 (d, J = 14.8 Hz, 1H, CH_2), 2.44 (s, 3H, CH_3), 2.39 (s, 3H, CH_3), 2.35 (d, J = 15.6 Hz, 1H, CH_2), 1.76–1.66 (m, 2H, CH_2), 1.62–1.49 (m, 2H, CH_2), 1.34–1.27 (m, 1H, CH_2), 1.18–1.07 (m, 1H, CH_2). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 196.99, 192.78, 166.59, 160.94, 142.59, 141.59, 130.54, 129.45, 129.09, 128.75, 128.49, 128.07, 99.38, 77.92, 73.10, 53.31, 51.87, 33.74, 28.99, 21.71, 21.49, 21.14, 20.79. IR (neat): ν = 1749 (C=O), 1727 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{27}H_{29}N_2O_4$ $[M + H]^+$: 445.2127, found 445.2125. Elemental Analysis Calcd (%) for $C_{27}H_{28}N_2O_4$: C, 72.95; H, 6.35; N, 6.30; found: C, 72.81; H, 6.50; N, 6.16. Single crystals of **6-33a** suitable for X-ray analysis were grown in hexane/EtOAc/CH_2Cl_2 (1:1:1) at room temperature.

6-33b: Yellow oil, isolated yield 92 % (80 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 3.41 (s, 3H, OCH_3), 3.08 (s, 3H, OCH_3), 1.31 (s, 9H, CH_3), 1.30 (s, 3H, CH_3), 1.27 (s, 9H, CH_3), 1.20 (s, 3H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 197.16, 191.61, 177.95, 169.09, 98.32, 77.42, 72.34, 53.02, 51.41, 38.94, 35.18, 28.36, 26.89, 23.11, 16.10. IR (neat): ν = 1751 (C=O), 1729 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{19}H_{31}N_2O_4$ $[M + H]^+$: 351.2284, found 351.2280.

6-34a: Yellow solid, isolated yield 54 % (70 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.74 (d, J = 8.1 Hz, 4H, C_6H_4), 7.25 (d, J = 7.5 Hz, 4H, C_6H_4), 3.39 (s, 6H, OCH_3), 3.30 (s, 6H, CH_3), 2.41 (s, 6H, CH_3), 2.18 (d, J = 13.3 Hz, 2H, CH_2), 1.84–1.75 (m, 2H, CH_2), 1.63–1.57 (m, 4H, CH_2). ^{13}C NMR (126 MHz, $CDCl_3$): δ = 184.66, 164.22, 140.86, 132.28, 128.96, 128.89, 95.71, 68.54, 52.79, 52.37, 30.72, 21.47, 21.44. IR (neat): ν = 1734 (C=O), cm^{-1}; HRMS: *m/z*: calcd for $C_{30}H_{35}N_2O_6$ $[M + H]^+$: 519.2495, found 519.2492. Elemental Analysis Calcd (%) for $C_{30}H_{34}N_2O_6$: C, 69.48; H, 6.61; N, 5.40; found: C, 69.35; H, 6.89; N, 5.28.

Reactions of Δ^1-bipyrrolinones 6-22 and *O*-benzylhydroxylamine: The solution of Δ^1-bipyrrolinones **6-22** (0.25 mmol, 65 mg), *p*-toluenesulfonic acid hydrate (0.5 mmol, 95 mg), and *O*-benzylhydroxylamine (1.0 mmol, 121 mg) in 3 mL of isopropanol in a 25-ml Schlenk tube was stirred at 150 °C for 8 h. The solvent was evaporated, and the crude product was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) to afford **6-35**.

6-35: Yellow oil, isolated yield 63 % (80 mg); ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.38 (d, J = 7.4 Hz, 4H, C_6H_5), 7.31 (t, J = 7.2 Hz, 4H, C_6H_5), 7.26 (d, J = 5.0 Hz, 2H, C_6H_5), 5.25 (s, 4H, OCH_2), 2.32 (d, J = 14.0 Hz, 2H, CH_2), 2.04 (d, J = 14.0 Hz, 2H, CH_2), 1.32–1.28 (m, 4H, CH_2), 1.21 (s, 18H, CH_3). ^{13}C NMR (101 MHz, $CDCl_3$): δ = 177.16, 157.96, 138.40, 128.15, 127.69, 127.48, 79.82, 76.89, 36.21, 28.11, 26.36, 15.76. HRMS: *m/z*: calcd for $C_{32}H_{41}N_4O_2$ $[M + H]^+$: 513.3230, found 513.3226.

General procedure for nucleophilic ring opening of 2,6-diazasemibullvalene 6-1a with alcohol or phenol derivatives: 2,6-diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of CH_2Cl_2 was treated with alcohol or phenol derivatives (1.5 mmol), and the reaction mixture was stirred at room temperature overnight. After the removal of solvent in vacuum, purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:3:1) gave **6-39** as pure products.

6-39a: Yellow oil, isolated yield 55 % (84 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.09 (s, 9H, CH_3), 1.13–1.14 (m, 4H, CH_2), 1.28 (s, 9H, CH_3), 1.55–1.56 (m, 4H, CH_2), 2.25–2.30 (m, 1H, CH_2), 2.80–2.86 (m, 1H, CH_2), 3.27 (s, 3H, CH_3), 4.43 ppm (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.44, 21.68, 28.00, 28.95, 30.13, 32.80, 35.32, 35.66, 43.24, 59.42, 79.82, 81.76, 92.54, 178.95, 181.16 ppm. HRMS: *m/z*: calcd for $C_{19}H_{33}N_2O$ $[M + H]^+$: 305.2593, found 305.2589.

6-39b: Colorless solid, isolated yield 93 % (170 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.55 (s, 9H, CH_3), 0.56 (s, 9H, CH_3), 0.66–0.78 (m, 6H, CH_2), 1.85–1.92 (m, 2H, CH_2), 2.16–2.41 (m, 2H, CH_2), 4.92 (s, 1H, CH), 6.40 (t, J = 7.5 Hz, 1H, C_6H_5), 6.55 (d, J = 8.4 Hz, 2H, C_6H_5), 6.74 ppm (t, J = 8.7 Hz, 2H, C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 20.87, 21.04, 27.89, 28.62, 29.69, 32.28, 35.04, 35.53, 43.35, 79.89, 81.05, 86.44, 114.88, 120.83, 129.46, 157.99, 178.54, 182.47 ppm. HRMS: *m/z*: calcd for $C_{24}H_{35}N_2O$ $[M + H]^+$: 367.2749, found: 367.2751. Elemental Analysis Calcd (%) for $C_{24}H_{34}N_2O$: C, 78.64; H, 9.35; N, 7.64; found: C, 78.39; H, 9.63; N, 7.56.

6-39c: Colorless solid, isolated yield 80 % (195 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.10 (s, 18H, CH_3), 1.23–1.25 (m, 5H, CH_2), 1.78–1.80 (m, 1H, CH_2), 2.24–2.32 (m, 2H, CH_2), 2.72–2.96 (m, 2H, CH_2), 5.40 (s, 1H, CH), 6.90 (d, J = 8.7 Hz, 2H, C_6H_4), 7.57 ppm (d, J = 9.0 Hz, 2H, C_6H_4); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.53, 22.40, 27.81, 28.20, 30.48, 32.81, 35.28, 35.61, 43.16, 79.68, 80.07, 81.92, 128.55, 129.55, 129.84, 133.24, 164.77, 178.07, 182.47 ppm. HRMS: *m/z*: calcd for $C_{24}H_{34}IN_2O$ $[M + H]^+$: 493.1716, found: 493.1710. Elemental Analysis Calcd (%) for $C_{24}H_{33}IN_2O$: C, 58.54; H, 6.75; N, 5.69; found: C, 58.50; H, 6.86; N, 5.43. Single crystals of **6-39c** suitable for X-ray analysis were grown in hexane/diethyl ether (2:1) at room temperature.

6-39d: Colorless solid, isolated yield 64 % (150 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.10 (s, 9H, CH_3), 1.11 (s, 9H, CH_3), 1.30–1.41 (m, 5H, CH_2), 2.27–2.37 (m, 3H, CH_2), 2.63–2.98 (m, 2H, CH_2), 3.78 (s, 3H, OCH_3), 5.38 (s, 1H, CH), 6.84 (d, J = 8.7 Hz, 2H, C_6H_4), 7.03 ppm (d, J = 9.0 Hz, 2H, C_6H_4); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 20.99, 21.21, 27.95, 28.70, 29.84, 32.35, 35.10, 35.64, 43.38, 55.65, 79.85, 81.03, 87.06, 114.58, 115.61, 152.17, 153.74, 178.82, 182.67 ppm. HRMS: *m/z*: calcd for $C_{25}H_{37}N_2O_2$ $[M + H]^+$: 397.2855, found: 397.2852.

General procedure for nucleophilic ring opening of 2,6-diazasemibullvalene 6-1a with thiol derivatives: 2,6-diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of CH_2Cl_2 was treated with 1-propanethiol (1.5 mmol, 58 μL), and the reaction mixture was stirred at room temperature overnight. After the removal of solvent in vacuum, purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:2:1) gave **6-40** as pure products.

6-40: Colorless oil, isolated yield 61 % (106 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.00 (t, J = 7.2 Hz, 3H, CH_3), 1.03 (s, 9H, CH_3), 1.07–1.19 (m, 8H, CH_2), 1.24 (s, 9H, CH_3), 1.64–1.72 (m, 2H, CH_2), 2.23–2.28 (m, 1H, CH_2), 2.53–2.60 (m, 1H, CH_2), 2.77 (t, J = 7.2 Hz, 2H, CH_2), 4.01 ppm (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 13.65, 21.31, 22.51, 23.22, 28.02, 29.78, 31.74, 31.82, 35.46, 35.67, 37.73, 43.35, 61.18, 79.57, 81.10, 180.96, 181.08 ppm. HRMS: *m/z*: calcd for $C_{21}H_{37}N_2S$ $[M + H]^+$: 349.2677, found 349.2675.

General procedure for nucleophilic ring opening of 2,6-diazasemibullvalene 6-1a with carboxylic acid derivatives: 2,6-diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) in 2 mL of CH_2Cl_2 was treated with carboxylic acid (1.5 mmol), and the reaction mixture was stirred at room temperature overnight. After the removal of solvent in vacuum, purification by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:5:1) gave **6-41** as pure products.

6-41a: Colorless oil, isolated yield 79 % (131 mg). ^{1}H NMR (300 MHz, C_6D_6, 25 °C, TMS): δ = 1.07 (s, 9H, CH_3), 1.16 (s, 9H, CH_3), 1.31–1.39 (m, 4H, CH_2), 1.48–1.53 (m, 4H, CH_2), 1.70 (s, 3H, CH_3), 2.28–2.90 (m, 2H, CH_2), 6.55 ppm (s, 1H, CH); ^{13}C NMR (75 MHz, C_6D_6, 25 °C, TMS): δ = 20.55, 21.93, 22.93, 27.94, 28.38, 31.24, 33.31, 35.47, 35.67, 43.41, 80.02, 80.45, 82.08, 169.02, 177.15, 181.45 ppm. HRMS: *m/z*: calcd for $C_{20}H_{33}N_2O_2$ $[M + H]^+$: 333.2542, found 333.2540.

6-41b: Colorless oil, isolated yield 73 % (152 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.87 (td, *J* = 7.3, 2.4 Hz, 6H, CH_3), 1.04 (s, 3H, CH_3), 1.06 (s, 6H, CH_3), 1.10 (s, 3H, CH_3), 1.17– 1.31 (m, 11H, CH_2), 1.33–1.49 (m, 5H, CH_2), 1.52–1.60 (m, 1H, CH_2), 1.69– 1.77 (m, 1H, CH_2), 2.11 (s, 3H, CH_3), 2.26 (d, *J* = 14.3 Hz, 1H, CH_2), 2.34 (d, *J* = 11.3 Hz, 1H, CH_2), 2.69 (d, *J* = 17.5 Hz, 1H, CH_2), 2.93 (d, *J* = 17.4 Hz, 1H, CH_2), 6.14 ppm (s, 1H, CH). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 14.04, 14.08, 21.08, 21.63, 22.47, 23.34, 23.37, 25.79, 26.13, 26.33, 26.60, 26.75, 26.82, 31.01, 32.90, 38.46, 38.82, 40.94, 41.18, 43.31, 79.57, 79.88, 82.01, 169.36, 177.19, 181.90 ppm. HRMS: *m/z*: calcd for $C_{26}H_{45}N_2O_2$ $[M + H]^+$: 417.3481, found 417.3480.

6-41c: Colorless oil, isolated yield 92 % (172 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.07 (m, 13H, CH_3 and CH_2), 1.09 (s, 9H, CH_3), 1.24 (s, 9H, CH_3), 1.52–1.73 (m, 2H, CH_2), 2.19–2.37 (m, 2H, CH_2), 2.70–2.96 (m, 2H, CH_2), 6.16 ppm (s, 1H, CH); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.27, 22.26, 27.33, 27.78, 28.85, 32.52, 35.17, 35.41, 38.84, 43.21, 79.48, 79.94, 81.27, 176.63, 177.95, 182.00. HRMS: *m/z*: calcd for $C_{23}H_{39}N_2O_2$ $[M + H]^+$: 375.3012, found 375.3010.

6-41d: Colorless solid, isolated yield 69 % (136 mg). ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.10 (s, 9H, CH_3), 1.12 (s, 9H, CH_3), 1.22–1.25 (m, 4H, CH_2), 1.61–1.76 (m, 2H, CH_2), 2.29–2.45 (m, 2H, CH_2), 2.64–2.81 (m, 1H, CH_2), 2.93–3.02 (m, 1H, CH_2), 6.44 (s, 1H, CH), 7.28–7.47 (m, 2H, C_6H_5), 7.57–7.62 (m, 1H, C_6H_5), 8.04–8.07 ppm (m, 2H, C_6H_5); ^{13}C NMR (75 MHz, $CDCl_3$, 25 °C, TMS): δ = 21.53, 22.40, 27.81, 28.20, 30.48, 32.82, 35.28, 35.62, 43.16, 79.68, 80.01, 81.93, 128.55, 129.55, 129.85, 133.24, 164.77, 178.08, 182.47 ppm. HRMS: *m/z*: calcd for $C_{25}H_{35}N_2O_2$ $[M + H]^+$: 395.2699, found 395.2701. Single crystals of **6-41d** suitable for X-ray analysis were grown in hexane/ethyl acetate (2:1) at room temperature.

Procedure for nucleophilic ring opening of 2,6-diazasemibullvalene 6-1a with sulfoxonium ylide: Trimethyl sulfoxonium iodide (2.0 mmol, 440 mg) in 2 mL of DMSO was treated with NaH (2.0 mmol, 48 mg), and the reaction mixture was stirred at 85 °C for 1 h and then cooled down. 2,6-Diazasemibullvalene **6-1a**

(0.5 mmol, 136 mg) was added, and the reaction mixture was stirred at 85 °C for 8 h. The reaction mixture was quenched with water and extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:1:1) to afford the corresponding product **6-42**.

Trimethyl sulfoxonium iodide (4.0 mmol, 880 mg) in 2 mL of DMSO was treated with NaH (2.0 mmol, 96 mg), and the reaction mixture was stirred at 85 °C for 1 h and then cooled down. 2,6-Diazasemibullvalene **6-1a** (0.5 mmol, 136 mg) was added, and the reaction mixture was stirred at 85 °C for 24 h. The reaction mixture was quenched with water and extracted with diethyl ether (10 mL) for three times. The combined organic layer was washed with water and brine and dried over $MgSO_4$. The solvent was evaporated in vacuum to give yellow oil, which was purified by column chromatography (silica gel, petroleum ether/diethyl ether/triethylamine = 100:1:1) to afford the corresponding product **6-43**.

6-42: Colorless solid, isolated yield 72 % (103 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 1.07 (s, 9H, CH_3), 1.22–1.24 (m, 4H, CH_2), 1.25 (s, 9H, CH_3), 1.47–1.54 (m, 2H, CH_2), 2.17–2.30 (m, 2H, CH_2), 2.72–2.98 (m, 2H, CH_2), 5.54 (s, 1H, CH_2), 5.76 ppm (s, 1H, CH_2); ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 20.29, 20.31, 21.11, 27.95, 28.93, 31.05, 32.50, 32.72, 35.45, 35.52, 35.70, 43.23, 43.49, 78.96, 82.00, 148.69, 113.54, 177.10, 181.24 ppm. HRMS: *m/z*: calcd for $C_{19}H_{31}N_2$ $[M + H]^+$: 287.2487, found 287.2485.

6-43: Colorless solid, isolated yield 76 % (114 mg). ^{1}H NMR (400 MHz, $CDCl_3$, 25 °C, TMS): δ = 0.82–0.90 (m, 2H, CH_2), 1.07 (s, 9H, CH_3), 1.08–1.10 (m, 9H, CH_3), 1.12–1.26 (m, 5H, CH_2), 1.35–1.42 (m, 1H, CH_2), 1.47–1.57 (m, 2H, CH_2), 1.59–1.68 (m, 1H, CH_2), 2.26 (d, J = 13.5 Hz, 1H, CH_2), 2.76 (d, J = 16.9 Hz, 1H, CH_2), 2.95 ppm (d, J = 16.9 Hz, 1H, CH_2). ^{13}C NMR (100 MHz, $CDCl_3$, 25 °C, TMS): δ = 8.09, 11.35, 21.56, 22.42, 28.00, 28.73, 29.84, 32.47, 35.45, 35.64, 36.68, 44.52, 76.28, 79.97, 179.99, 180.90 ppm. HRMS: *m/z*: calcd for $C_{20}H_{33}N_2$ $[M + H]^+$: 301.2644, found 301.2640.

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