Xiao-Yu Sun

Total Synthesis of Plakortide E and Biomimetic Synthesis of Plakortone B

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Xiao-Yu Sun

Total Synthesis of Plakortide E and Biomimetic Synthesis of Plakortone B

Doctoral Thesis accepted by
The Chinese University of Hong Kong

Springer

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X.-Y. Sun, X.-Y. Tian, Z.-W. Li, X.-S. Peng, H. N. C. Wong, *Chem. Eur. J.* **2011**, *17*, 5874–5880. *Reproduced with permission.*

Supervisor's Foreword

This thesis describes the first total synthesis of all possible stereoisomers of the peroxide natural product plakortide E. This includes the first confirmation of the absolute configuration of natural plakortide E, based on the conversion of plakortide E to plakortone B. This transformation also suggests a biomimetic conversion of plakortide E to plakortone B.

A new synthetic approach involving palladium-catalyzed reaction of vinyl cyclopropanes with hydrogen peroxide to form highly substituted 1,2-dioxolanes was developed. A lipase-catalyzed kinetic resolution was employed to provide optically pure 1,2-dioxolane central cores. The efficient conversion of these optically pure 1,2-dioxolane central cores into four possible 3,5-*cis*-stereoisomers of the plakortide E structure is very interesting and challenging. The successful application of the Corey-Fuchs homologation on the framework of 1,2-dioxolane, involving a metal-halogen exchange, is particularly impressive. This pathway may be the first reported example of metal-halogen exchange on cyclic peroxides. Two palladium-mediated reactions in the presence of 1,2-dioxolanes were used during the homologation sequence: a palladium-catalyzed hydrostannylation of an alkyne and Negishi olefination. Our results may widen the synthetic scope of hindered peroxide chemistry. Furthermore, these results will be of interest to scientists interested in organic peroxides as well as in the marine natural products containing five-membered cyclic peroxides.

For the following reasons I am convinced that the research presented in this thesis is outstanding and significant.

I. Plakortide E and plakortone B have attractive bioactivities and the synthetic studies toward them and their analogs will be pivotal both for the evaluation of the biological activity of these molecules and their analogs, and for drug discovery.

II. The methodology study for the syntheses of highly substituted cyclic peroxides is novel and useful, which not only extends the field of Pd-catalyzed reactions, but also provides a convenient synthetic approach to prepare 1,2-dioxolanes series.

III. It goes without saying that construction and functionalization of 1,2-diox-
olanes are particularly difficult because of the low O–O bond dissociation
energy, so the syntheses in the thesis are full of challenges.

IV. The convergent synthetic strategy was employed in the total synthesis of
plakortide E, so the synthesis is step-economical, starting from (+)-*cis*-**137a**,
the plakortide candidate structure (10*S*)-(+)-*cis*-**86a** was efficiently synthe-
sized in ten simple chemical operations.

V. The thesis is well prepared and the chemistry inside clearly described.

Hong Kong, September 2011   Henry N. C. Wong

Acknowledgments

April 2011

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Contents

Abbreviations

[α]	Specific rotation
Å	Ångstrom (s)
Ac	Acetyl
AIBN	Azobisisobutyronitrile
Anal.	Analytical
aq.	Aqueous
9-BBN	9-Borabicyclo[3.3.1]nonane
Bn	Benzyl
BDE	Bond dissociation energy
BHT	2,6-di-*tert*-butyl-4-methyl phenol
cat.	Catalytic
conc.	Concentrated
δ	Chemical shift in parts per million downfield from tetramethylsilane
d	Day (s), doublet (spectral)
DBU	1,8-diazabicyclo[5.4.0]undec-7-ene
DIPEA	Diisopropylethylamine
DMAP	4-(dimethylamino)pyridine
DMF	Dimethyl formamide
DMP	Dess-Martin periodinane
DMSO	Dimethyl sulfoxide
EA	Ethyl acetate
Et	Ethyl
EI	Electron impact (in mass spectrometry)
ESI	Electrospray ionization
equiv	Equivalent
FAB	Fast atom bombardment
FT	Fourier transform

HPLC	High-performance liquid chromatography
HRMS	High-resolution mass spectrum
HWE	Horner-Wadsworth-Emmons
IR	Infrared
J	Coupling constant (in NMR)
KHMDS	Potassium hexamethyldisilazide
LDA	Lithium diisopropylamide
lit.	Literature
DCC	*N*,*N*′-Dicyclohexylcarbodiimide
m	Multiplet (spectral),milli-
Me	Methyl
m.p	Melting point
MS	Mass spectrometry; molecular sieves
m/z	Mass to charge ratio (in mass spectrometry)
NMR	Nuclear magnetic resonance
NOE	Nuclear overhauser effect
NOESY	Nuclear overhauser effect spectroscopy
PDC	Pyridinium dichromate
Ph	Phenyl
ppm	Parts per million (in NMR)
^{i}Pr	Isopropyl
q	Quartet
R_f	Retention factor
rt	Room temperature
t	Triplet
TBAF	Tetrabutylammonium fluoride
TBS	*t*-butyldimethylsilyl
TEA	Triethylamine
tert-	Tertiary
THF	Tetrahydrofuran
TLC	Thin-layer chromatography
p-TsOH	*p*-toluenesulfonic acid

Chapter 1
Introduction

1.1 Introduction to Organic Peroxides

Organic peroxides are compounds containing an O–O bond. The O–O group is called the peroxide group. The peroxide bond is one of the weakest bonds in organic molecules, with BDE of approximately 34 kcal/mol (C–C: 81 kcal/mol, C–H: 98 kcal/mol, C–O: 79 kcal/mol, C–N: 66 kcal/mol) [1, 2]. The O–O bond is unstable and easily splits into reactive radicals via homolytic cleavage. For this reason, peroxides are found in nature only in small quantities, in water, atmosphere, plants, animals and man. According to the substitution patterns, organic peroxides can be classified into hydroperoxides, acyclic dialkyl peroxide and cyclic peroxides (Fig. 1.1).

1.2 Cyclic Peroxide Natural Products and Their Potential Biological Activities

Ascaridole, used as a remedy for worms, which was isolated from chenopodium oil and named by Hüthig in 1908 [3], was the first studied naturally occurring organic peroxide (Fig. 1.2). Hüthig described its explosive character and determined its chemical formula as $C_{10}H_{16}O_2$. In 1911, these results were confirmed by Nelson in his detailed study of ascaridole [3].

One of the most important medical applications of organic peroxides has been in the treatment of malarial. In the worldwide scale, there are 300–500 million clinical cases of people that are infected by malaria every year, and between one to three million deaths, mostly of children, are attributable to this disease. Every 40 s a child dies of malaria, resulting in a daily loss of more than 2,000 young lives worldwide. These estimates made malaria one of the top three killers among communicable diseases [4].

R−O−O−H   R₁−O−O−R₂

Hydroperoxides   Acyclic dialkyl peroxide   Cyclic peroxides
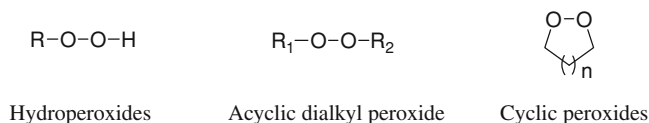
Fig. 1.1 Categories of peroxides

Fig. 1.2 The first studied
naturally occurring organic
peroxide
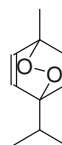
Ascaridole

In the search for antimalarial drugs, yingzhaosu A was isolated by Liang et al. in 1979 from *Artabotrys uncinatus* (Annonaceae) [5], which was used in China as a traditional remedy for the treatment of malaria (Fig. 1.3). Further work from this lab resulted in the isolation of yingzhaosu C (Fig. 1.3) [6]. Yingzhaosus A and C both contain a 1,2-dioxane core structure. These compounds have been extensively studied for their potential antimalarial activity.

At about the same time, artemisinin, a naturally occurring organic peroxide with a 1,2,4-trioxane core, also known as qinghaosu, was isolated from the plant *Artemisia annua*, a herb described in Chinese traditional medicine by Wu and coworkers (Figs. 1.3 and 1.4) [7]. Artemisinin and its derivatives are a group of drugs that possess the most rapid action of all current drugs against falciparum malaria. The discovery of strong antimalarial activity from artemisinin and yinghaosu motivated the worldwide exploration of antimalarial cyclic peroxide drugs. Since scientists recognized the pivotal role of cyclic peroxides in various vital biological processes [8], the chemistry of cyclic peroxides has been rejuvenated in the 1970s. More and more naturally occurring cyclic peroxides have been isolated and identified.

Chondrillin, isolated from a Great Barrier Reef sponge of the genus *Chondrilla* by Wells in 1976, was the first cyclic peroxide to be isolated from marine sources [9]. Later, it was also isolated from another marine sponge *Plakortis lita* by DeGuzman and Christophersen [10, 11], and its diastereomer plakorin and a number of other alkoxydioxines were isolated from this marine sponge (Fig. 1.5) [12].

These peroxides have shown interesting biological properties. For example, chondrillin was found to have an *in vitro* IC$_{50}$ of 5 µg/mL against P388 leukemia cells [10, 11]. Plakorin is a potent activator of sarcoplasmic reticulum calcium-ATPase, and it also has an *in vitro* IC$_{50}$ = 0.85 µg/mL against murine lymphoma L1210 cells and IC$_{50}$ = 1.8 µg/mL against human epidermoid carcinoma KB cells [13].
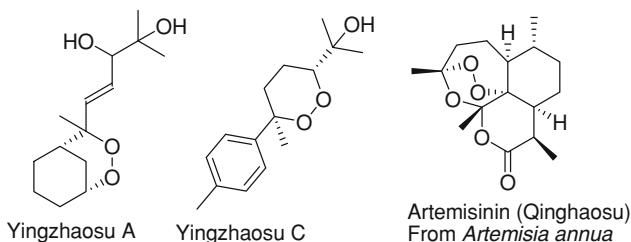
Fig. 1.3 Antimalarial natural cyclic peroxides

Fig. 1.4 *Artemisia annua*

Fig. 1.5 Six-membered cyclic peroxides

Chondrillin
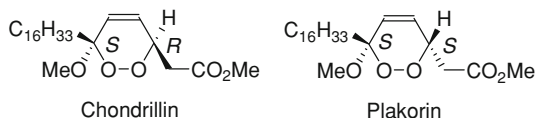
Plakorin

Many natural peroxides with 1,2-dioxine or 1,2-dioxane subunits have been isolated from the marine sponge, *Plakortis sp.*, especially from *Plakortis halichondrioides*. For example, plakortin (**1**), 3-epi-plakortin (**2**), plakortic acid (**3**) all share a common six-membered cyclic peroxide core (Fig. 1.6). The marine cyclic peroxide plakortic acid (**3**) is a potent antifungal and antibacterial agent; however, the corresponding methyl ester, plakortin (**1**), is inactive [14, 15].

Plakinic acid A, a 3,3,5,5-tetrasubstituted 1,2-dioxolane isolated from a Caribbean sponge, was the first isolated five-membered ring peroxide among marine natural products (Fig. 1.7) [16, 17]. In the last decades, many additional plakinates have been isolated and characterized, which usually exhibited remarkable cytotoxicity against fungal and cancer cell lines [17–25]. As shown in Table 1.1, all the plakinic acids contained a 3,3,5,5-tetrasubstituted 1,2-dioxolane core.

The highly unstable prostaglandin H_2 (PGH_2) and prostaglandin G_2 (PGG_2), containing a five-membered ring peroxide, were isolated and identified as key intermediates in prostaglandin's biosynthesis from arachidonic acid (Fig. 1.8) [26–28]. PGH_2 and PGG_2 were also biosynthetic precursors for many other physiological important compounds, such as prostacyclins and thromboxanes [29, 30]. Afterwards, the total syntheses of PGH_2 and PGG_2 were reported by Porter and coworkers [102] and Johnson and coworkers [110]. The early studies on prostaglandin endoperoxides and their analogs were reviewed by Nicolaou and Salomon [31, 32].

1 R = Me
3 R = H

2
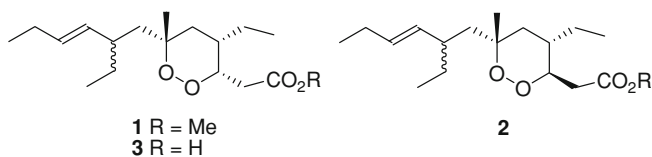
Fig. 1.6 Natural products with 1,2-dioxane cores

Plakinic acid A

Fig. 1.7 The first isolated five-membered ring peroxide
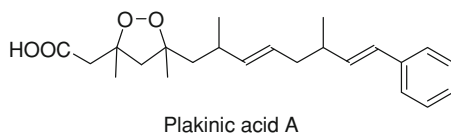
Table 1.1 Plakinates from marine sponge

R		Plakinate	Reference
$C_{16}H_{33}$	$C_{15}H_{31}$	unnamed	[18]
	n = 4	C (3,5-*cis*); epi-C (3,5-*trans*)	[17]
	n = 2	D (3,5-c*is*); epi-D (3,5-t*rans*)	[17]
		epi-E (3,5-t*rans*)	[20]
		F (3,5-c*is*); epi-F (3,5-t*rans*)	[21]
		G (3,5-c*is*); epi-G (3,5-t*rans*)	[22]
		unnamed (3,5-cis); unnamed (3,5-trans)	[108]
$Ph(CH_2)_{10}-\xi-$		andavadoic acid (3,5-t*rans*)	[24]

Fig. 1.8 Prostaglandin G_2 and H_2

R =OOH, Prostaglandin G_2
R = OH, Prostaglandin H_2
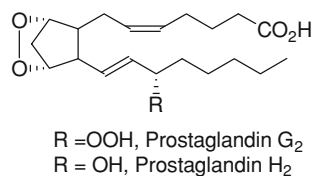
Fig. 1.9 A polycyclic natural product with 1,2-dioxane core
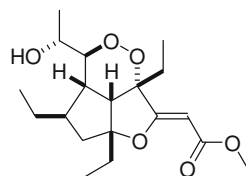
Gracilioether A

Fig. 1.10 A novel linear polyene peroxide
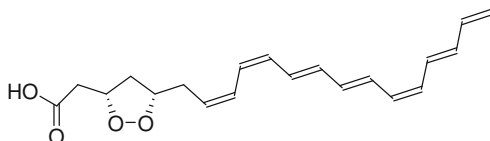
Mycangimycin

Fig. 1.11 Natural products containing medium ring cyclic peroxides
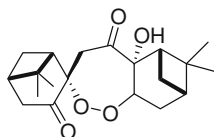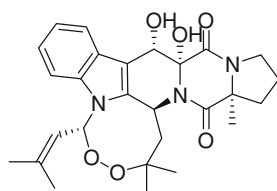
4   Verruculogen (**5**)

In the course of their continuing search for drug leads from Japanese marine invertebrates, Nakao and Fusetani isolated graciliorther A from the deep-sea sponge *Agelas gracilis* in 2009, which show considerable antimalarial activity (Fig. 1.9) [33]. The absolute stereochemistry of graciliorther A was confirmed by application of the modified Mosher's method.

Clardy and coworkers in their study of the southern pine beetle system, have discovered another symbiont (Streptomyces sp. SPB74) that produces a polyene peroxide, which was named mycangimycin (Fig. 1.10). It was found that mycangimycin selectively inhibits the beetle's fungal antagonist. The complete structure was fully elucidated including the absolute configuration [34, 35].

Although majority of cyclic peroxide natural products contain dioxanes or dioxolanes, some medium ring cyclic peroxides discovered in nature (Fig. 1.11). The terpenic peroxide **4** was isolated from the spice cardamom, the fruit of *Amomum krervanh* Pierre, which contained a seven-membered cyclic peroxide core. Compound **4** also exhibited moderate antimalarial activity *in vitro* against *Plasmodium falciparum* ($IC_{50} = 170$ nM) [36]. Verruculogen (**5**), containing a novel eight-membered cyclic peroxide core, was obtained from a strain of *Penicillium verruculosum* Peyronel isolated from peanuts, which was fully characterized by Clardy and coworkers in 1974 [37, 38].

Plakortin   Plakorin   Plakortolides

Plakinidone   Peroxyplakoric acids   Plakinic acids
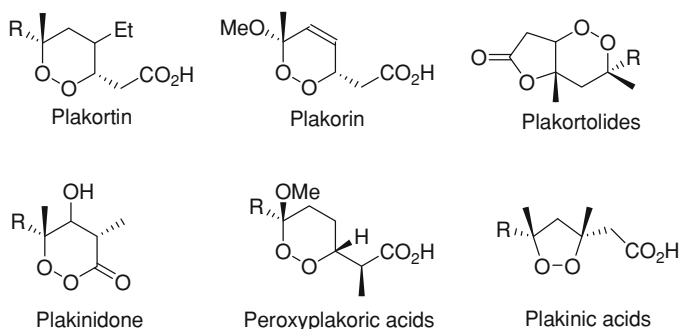
Fig. 1.12 Natural products from the genus *Plakortis*

1.3 Natural Products from Marine Sponges of the Genus Plakortis

Marine sponges have been among the most studied of marine organisms. The genus *Plakortis* has attracted particularly interests as a source of novel metabolites. Many unusual metabolites isolated from the genus *Plakortis* exhibited anti-fungal, anti-tumor, anti-bacterial and other important pharmacological activities. Based on their work, the structures, stereochemistry, pharmacological activities and selected syntheses of the *Plakortis* derived metabolites have been reviewed by Kitching and coworkers in 2004 [39–41].

Examples of cyclic peroxides isolated from the genus *Plakortis* are illustrated in Fig. 1.12. These cyclic peroxide natural products are very fascinating because of their novel structure and activities.

In their continuing search for biologically active natural products to cure cardiac disease, Patil and coworkers employed a high throughput screening to evaluate the ability of natural products to stimulate cardiac SR-Ca^{2+} ATPase [42]. A screening of over 2400 plant and marine extracts found an extract of sponge *Plakortis halichondrioides* with the ability to stimulate cardiac SR-Ca^{2+} ATPase activity. This led to the discovery of four novel polyketides, plakortones A–D, four novel acids, plakortides E–H and one known compound 3-epi-plakortin (**2**) were isolated from the sponge *Plakortis halichondrioides* (Fig. 1.13).

In 2002, Kitching and coworkers reported the first total synthesis of plakortone D, which not only confirmed the absolute stereochemistry of plakortone D, but also enabled the acquisition of other plakortones and analogs [39]. In 2010, they reported the total syntheses and configuration assignments of plakortone C and F [41]. Our group were also interested in the synthetic chemistry of the *Plakortis* derived metabolites. Our preliminary synthetic efforts towards plakortide E were recorded in 2007 [43]. In 2010, we have reported the total syntheses and configuration assignments of all four isomers of plakortone B [44], whose total synthesis was reported by Semmelhack and coworkers in 2006 [45]. In consideration that plakortone B was isolated from the same animal source together with plakortide E [42], we reasoned

Plakortones A (R = Et), B (R = Me)

Plakortones C (R = Me), D (R = H)

Plakortide E

Plakortide F

Plakortide G
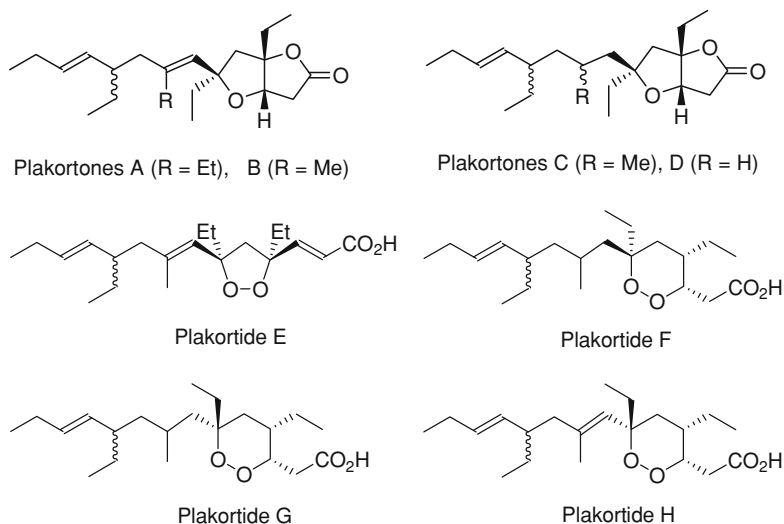
Plakortide H

Fig. 1.13 Natural products from the sponge *Plakortis halichondrioides*

Plakortide E (**85**)

Plakortone B (**87**)

6
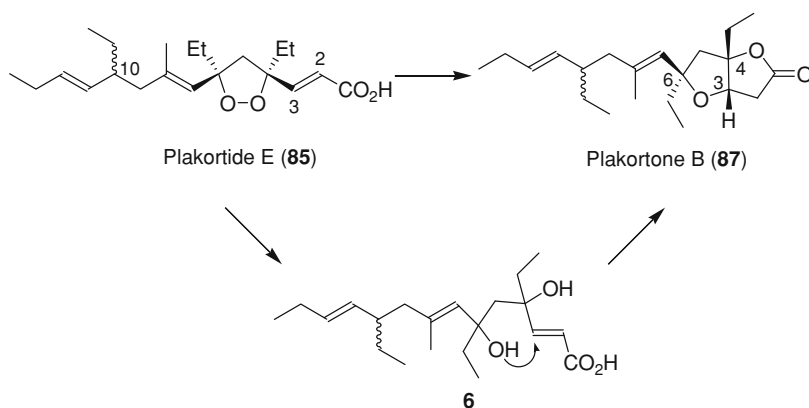
Scheme 1.1 Biosynthesis of plakortone B

that diol **6** could be converted to plakortone B (Scheme 1.1) [109]. Kitching has also suggested that the 1,3-diol notionally derived from reductive cleavage of 1,2-dioxolane are perhaps the actual precursors of the plakortone series [40, 41].

1.4 Methodologies for Synthesis of Cyclic Peroxides

Construction of cyclic peroxides is a particularly challenging issue because of the low O–O bond dissociation energy (37 ± 1 kcal mol^{-1}) [1]. Numerous approaches have been developed in the past for the synthesis of five- and six-membered
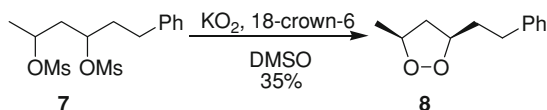
Scheme 1.2 Corey's synthesis of 1,2-dioxolanes
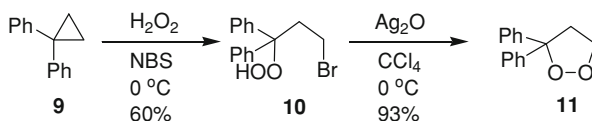
Scheme 1.3 Adam's route to 1,2-dioxolanes
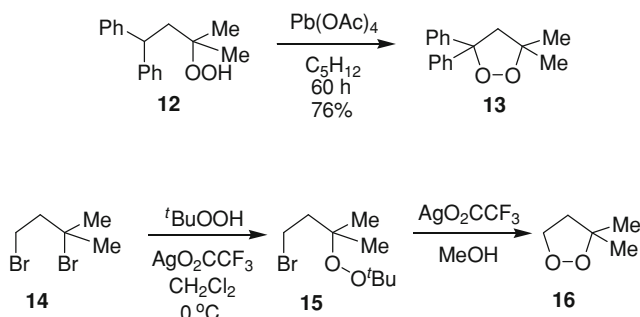
Scheme 1.4 Formations of 1,2-dioxolanes via nucleophilic reactions

ring peroxides [48–90]. Syntheses of cyclic peroxides were well-reviewed by Nojima and coworkers [46], and Bachi and coworker [47]. Many of these methodologies demand low temperature operations and mild conditions. These approaches can be categorized into three types: (1) cyclization of hydroperoxides through intramolecular nucleophilic reactions; (2) cycloaddition of triplet oxygen with radicals; (3) cycloaddition of singlet oxygen with 1,3-dienes.

Cyclization via intramolecular nucleophilic reaction. In 1975, Corey and coworkers reported a method to obtain the 1,2-dioxolane through a intramolecular substitution. Bis (mesylate) **7** was treated with potassium superoxide to give the *cis*-disubstituted 1,2-dioxolane **8** in a moderate yield (Scheme 1.2) [87].

In 1978, Adam treated cyclopropane **9** with H_2O_2/NBS to afford β-bromohydro peroxide **10**, which was cyclized to 1,2-dioxolane **11** in the presence of silver(I) oxide in good yield (Scheme 1.3) [88].

Kropf [56] prepared 1,2-dioxolanes by treating hydroperoxides with $Pb(OAc)_4$, which involves 1,5-hydrogen abstraction by an intermediate peroxyl radical. Alternatively, the treatment of 1,3-dibromopropane **14** with *tert*-butylhydroperoxide in the presence of AgO_2CCF_3 also led to 1,2-dioxolane **16** (Scheme 1.4) [89].
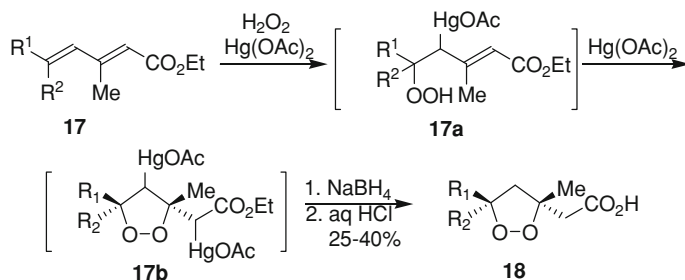
Scheme 1.5 Intramolecular hydroperoxide addition to double bond
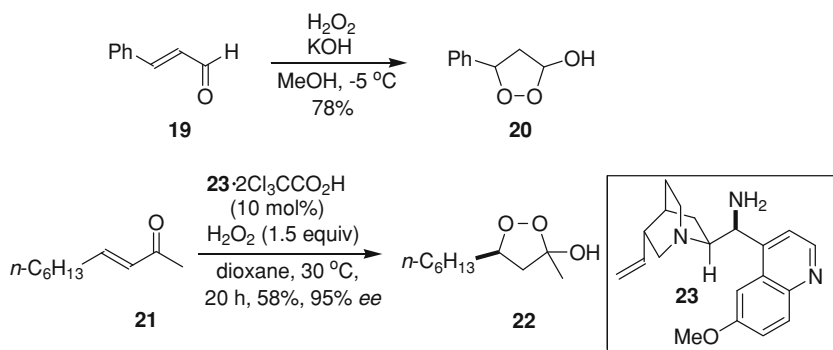
Scheme 1.6 Intramolecular hydroperoxide addition to carbonyl group

Bloodworth [66–69] prepared four non-natural plakinic acids via a peroxymercuration reaction as shown below (Scheme 1.5). A similar strategy was used by Gunstone [70] for his preparation of 1,2-dioxolanes from methyl oleate. A cycloperoxyiodination route also gave rise to 1,2-dioxolane frameworks. The difference between Bloodwoworth's and Gunstone's approach is five-*exo* vs. 5-*endo* peroxymercuration.

Intramolecular nucleophilic addition of hydroperoxide to a carbonyl group was one of the earliest methods to prepare cyclic peroxides. For example, the α,β-unsaturated aldehyde **19** reacted with hydrogen peroxide at room temperature in the presence of KOH to form the 1,2-dioxolane **20** in 78% yield [91–93]. An asymmetric version of this reaction was reported by List and coworkers in 2008 (Scheme 1.6) [93].

Acid-catalyzed intramolecular attack of hydroperoxide on an epoxide to form the 1,2-dioxolane was reported in 1976 (Scheme 1.7) [94]. This type of reaction was applicable to more complex substrates, and has been applied to the total syntheses of natural products [101].

Methods to synthesize the cyclic peroxides by the intramolecular opening of oxetanes with hydroperoxides have been developed by Dussault and coworkers
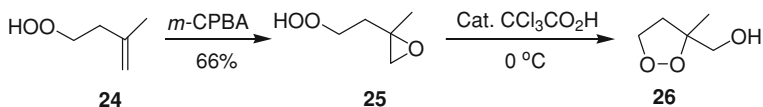
Scheme 1.7 Formation of 1,2-dioxolane via intramolecular opening of epoxide with hydroperoxide
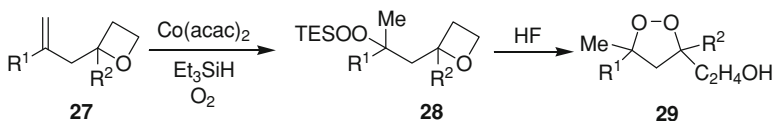
$R^1 = R^2 = Me$, 1) 78%, 2) 80%
$R^1 = Hex$; $R^2 = Me$, 1) 71%, 2) 82%
$R^1 = Hex$; $R^2 = H$, 1) 80%, 2) 85%

R = Me, 73%; R = H, 77%
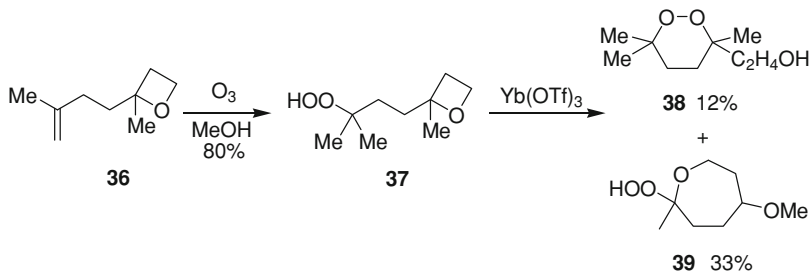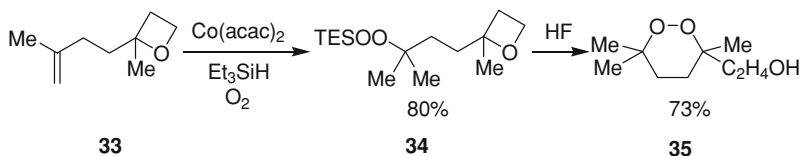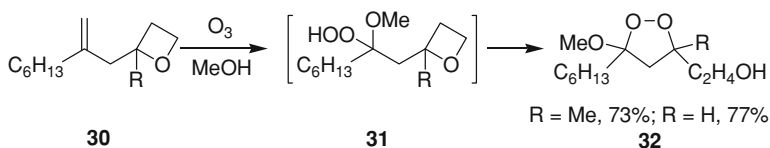
Scheme 1.8 Formations of 1,2-dioxolane via intramolecular opening of oxetanes with hydroperoxides

[78]. The method was used to synthesize the 1,2-dioxolanes, 1,2-dioxanes and 3-alkoxy-1,2-dioxolanes with good stereoselectivity and good yields (Scheme 1.8).

Cycloaddition of triplet oxygen with radicals. As can be seen in Scheme 1.9, pentasubstituted 3-hydroxy-1,2-dioxolanes were realized via oxygen trapping during thermolysis of cyclic α-azohydroperoxides [90].
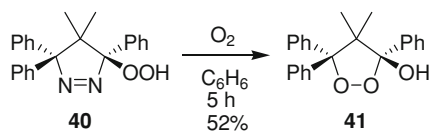
Scheme 1.9 Cycloaddition of triplet oxygen with diradicals
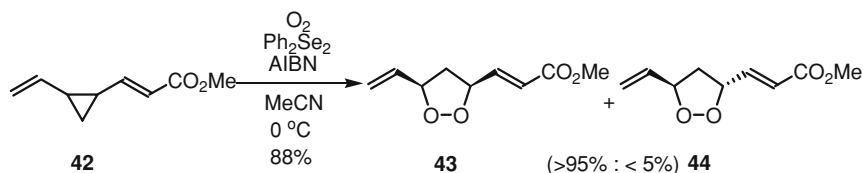
Scheme 1.10 Formations of 1,2-dioxolanes reported by Feldman and coworkers

Ergosteryl Acetate (**45**)   **46**
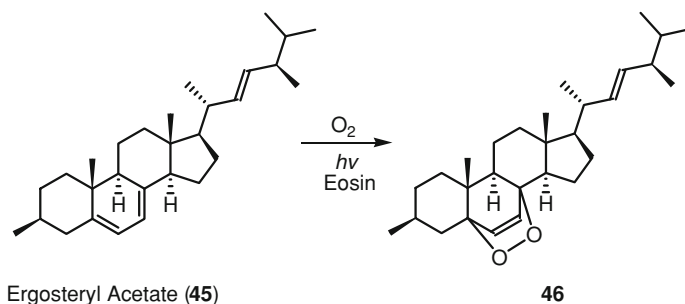
Scheme 1.11 Ergosteryl acetate oxidation with oxygen

Feldman developed a convenient approach for the formation of 1,2-dioxolanes from vinylcyclopropanes by a free radical-mediated ring expansion with oxygen as demonstrated in Scheme 1.10. In their experiments, the *cis*-1,2-dioxolanes **43** were obtained in good yield [83–86].

Cycloaddition of singlet oxygen with 1,3-dienes. Singlet oxygen ($^1O_2$) can be generated by a chemical process on a synthetically useful scale or in a photo-sensitized process by energy transfer from dye molecules such as rose bengal, methylene blue or porphyrins [95]. The electron occupancy of the shells of the singlet oxygen is different from those of ground state oxygen. The energy difference between ground state and singlet oxygen is 94.3 kJ/mol [96]. The damages caused by the sunlight to many organic materials are always attributed to the effects of singlet oxygen. Singlet oxygen reacting with a variety of 1,3-dienes gives the corresponding six-membered cyclic peroxides. This is one of the oldest and the most general methods to generate cyclic peroxides. Windaus and Brunken isolated the cyclic peroxide of ergosteryl acetate in 1928 [97], which was prepared through singlet oxygen cycloaddition to ergosteryl acetate (**45**) (Scheme 1.11).

Scheme 1.12 Anthracene derivatives peroxydation with singlet oxygen

Scheme 1.13 Application of singlet oxygen [4+2]-cycloaddition to 1,3-dienes in total synthesis of brevetoxin A
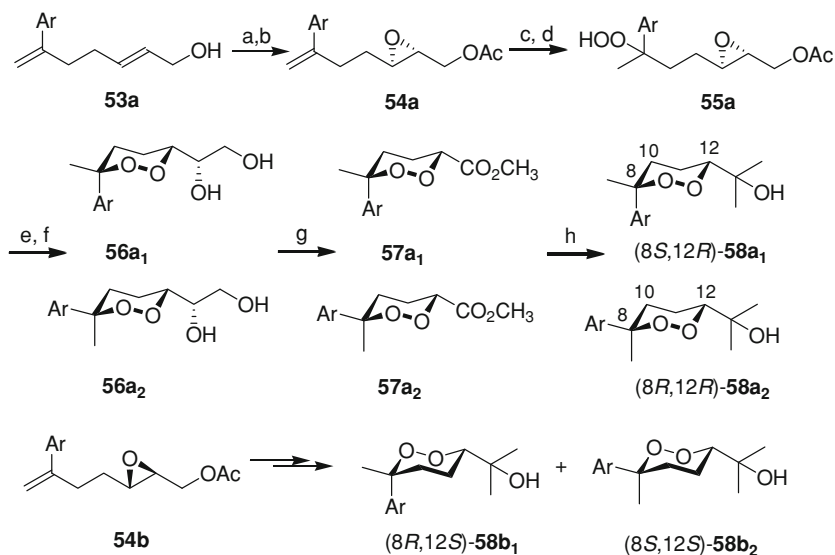
Scheme 1.14 Total syntheses of yingzhaosu C and its isomers. **Reagents and conditions:** (a) L-(+)-DIPT, Ti(Oi-Pr)$_4$, t-BuOOH, CH$_2$Cl$_2$; (b) Ac$_2$O/Pyr; (c) Et$_3$SiH, O$_2$, Co(modh)$_2$; (d) KF/18-crown-6, THF; (e) Amberlyst-15, CH$_2$Cl$_2$; (f) K$_2$CO$_3$/MeOH, then H$_2$C$_2$O$_4$ 2H$_2$O; (g) NaIO$_4$/RuC$_{13}$, MeCN:CC$_{14}$:H$_2$O (2:2:3, v/v), rt, then CH$_2$N$_2$/Et$_2$O; (h) 2 equiv of MeLi/Et$_2$O, −78 °C, then aqueous NH$_4$C1
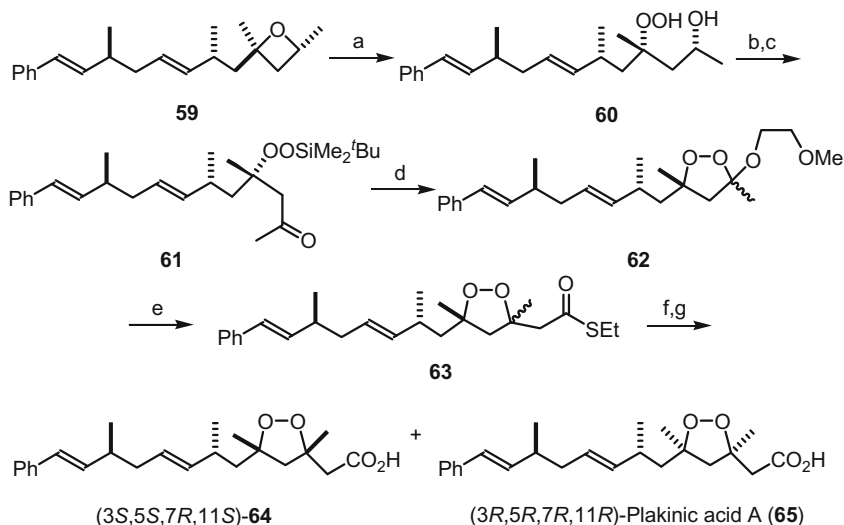
Scheme 1.15 Total synthesis of plakinic acid A. **Reagents and conditions:** (a) Me$_3$SiOTf, H$_2$O$_2$, Et$_2$O, −78 °C, 57%; (b) LiN(SiMe$_3$)$_2$, t-BuMe$_2$SiCl; (c) Dess-Martin periodinane, 80%; (d) HF, MeOCH$_2$CH$_2$OH, 2 days, 88%; (e) TiCl$_4$, CH$_2$=CH$_2$(OSiMe$_3$)SEt, −50 to 0 °C, 88%; (f) NaOMe, MeOH; g. LiOH, H$_2$O$_2$, THF, 71%
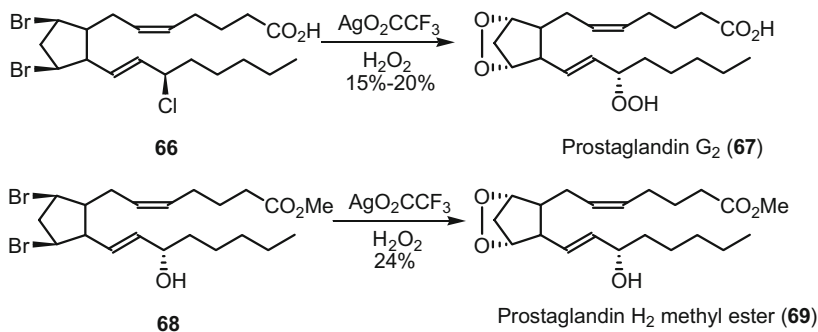
Scheme 1.16 Semi-syntheses of prostaglandin H_2 and prostaglandin G_2
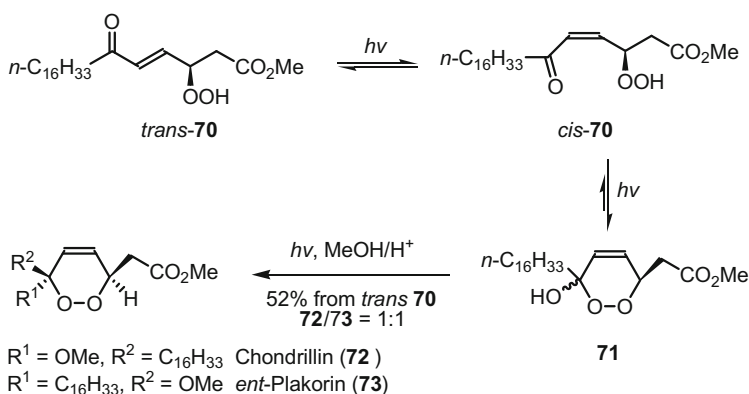
Scheme 1.17 Total syntheses of chondrillin and *ent*-plakorin

Anthracene derivatives reacted with singlet oxygen to furnish the corresponding 1,4-endoperoxides or 9,10-endoperoxides. For example, singlet oxygen cycloaddition to 1,2,3,4,5,6,7,8-octamethylanthracene (**47**) mainly led to 1,4-endoperoxide **48** (Scheme 1.12) [98].

Singlet oxygen [4+2]-cycloadditions to 1,3-dienes were widely used in the total syntheses of non-peroxide containing natural products. For example, in the total synthesis of brevetoxin A (**52**), 1,3-diene **49** reacted with singlet oxygen to furnish the cyclic peroxide containing intermediate **50** (Scheme 1.13) [99, 100].

1.5 Total Syntheses of Cyclic Peroxide Natural Products

The discovery of antimalarial and anticancer activity in cyclic peroxide natural products has resulted in increased interest in the total syntheses of cyclic peroxide natural products in the last decades. In this section, the total syntheses of cyclic peroxide natural products will be reviewed.
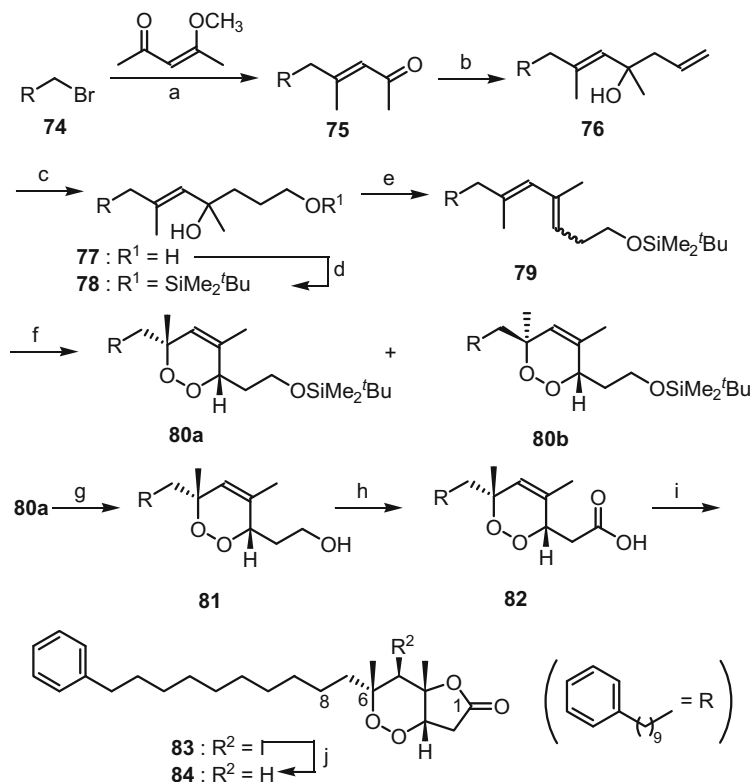
Scheme 1.18 Total synthesis of 6-epiplakortolide E. **Reagents and conditions:** (a) Mg/ether, rt, 2 h, 69%; (b) allylmagnesium bromide, ether, 0 °C, 1.5 h, 60%; (c) 9-BBN, rt, 3 N NaOH/H$_2$O$_2$, 2 h, 90%; (d) *t*-BuMe2SiCl, imidazole, DMF, rt, 4 h, 98%; (e) TsOH/CaCl$_2$, benzene, rt, 2 h, 80%; (f) O$_2$, 500-W lamp, rose bengal, 0 °C, 6 h, CH$_2$Cl$_2$/MeOH (19:1), 45%; (g) 10% HCl, THF/MeOH, rt, 1 h, 87%; (h) Jones' reagent, acetone, rt, 1.5 h, 78%; (i) NaHCO$_3$/I$_2$, CHCl$_3$/ H$_2$O, rt, 2 days, 55%; (j) AIBN/Bu$_3$SnH, benzene, 80 °C, 1 h, 68%

Xu and coworkers reported the total synthesis of all four stereoisomers of yingzhaosu C in 1995 [101]. The core structure of the 1,2-dioxane was constructed by intramolecular epoxide opening under acidic conditions (Amberlyst-15), with the stereochemistry of the ring-closure controlled by the stereochemistry of the epoxide (Scheme 1.14). Compounds **58a$_1$** and **58a$_2$** were prepared from **53a**. Dioxanes **58b$_1$** and **58b$_2$** were synthesized in a similar manner. These four samples are two pairs of enantiomers (**58a$_1$** and **58b$_1$**, **58a$_2$** and **58b$_2$**). The NMR spectra of **58a$_1$** and **58b$_1$** were identical with that of the natural yingzhaosu C. On the basis of the observed optical rotation, Xu and coworkers concluded that natural yingzhaosu C may be considered to be a mixture of enantiomeric (8*S*,12*R*)-**58a$_1$** and (8*R*,12*S*)-**58b$_1$** with the former being in excess, because the optical rotation of the natural yingzhaosu C was only +2.89 (MeOH). However, the strategy employed in this study is not suitable for the substrates with unsaturated side chains.

Based on elegant synthetic routes [72–82], Dussault and coworkers achieved for the first time the asymmetric synthesis and configurational assignment of plakinic acid A (**65**) in 2006 [79]. The synthetic pathway for the (3*S*,5*S*,7*R*,11*S*)-stereoisomer of plakinic acid is shown in Scheme 1.15. As can be seen, a regio- and stereoselective opening of an enantiomerically enriched oxetane by hydrogen peroxide led to an intermediate, which was further elaborated into the 1,2-dioxolane product. After preparing four possible structural candidates of plakinic acid A (**65**), Dussault concluded that the most likely configuration for plakinic acid A should be (3*R*,5*R*,7*R*,11*R*).

Porter and coworkers reported the semi-syntheses of prostaglandin H_2 and prostaglandin G_2 (Scheme 1.16). 1,3-Dibromide **68** was treated with hydrogen peroxide and silver trifluoroacetate to give prostaglandin H_2 (**69**) in 24% yield. In a similar manner, prostaglandin G_2 was obtained in 15–20% yield [102–104].

Total syntheses of chondrillin and *ent*-plakorin were accomplished by Dussault and coworkers. The final key step was based on the cyclization of *trans*-**70** as shown in Scheme 1.17. Compound *trans*-**70** was subjected to photocyclization and transetherification to give a mixture of chondrillin (**72**) and *ent*-plakorin (**73**) in good yield [105, 106].

In 2002, Jung and coworkers reported the first total synthesis of racemic 6-epiplakortolide E (Scheme 1.18) [107]. Thus, the intermediate diene **79** underwent singlet oxygen [4+2]-cycloaddition to provide the six-membered cyclic peroxide containing compound **80**, which was a mixture of *cis*-**80a** and *trans*-**80b**. The ability to perform a [4+2]-cycloaddition on intermediate **79** was related to a substitution pattern. Compound *cis*-**80a** was subjected to desilylation giving alcohol **81** in 87% yield. Oxidation of **81** with Jones' reagent furnished acid **82**, which was subjected to iodolactonization to give **83**. A chemoselective free-radical reductive deiodination of **83** led to the natural product 6-epiplakortolide E (**84**).

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Chapter 2
Results and Discussion

2.1 Introduction

Plakortide E (**85**) and plakortone B (**87**) were first isolated from the Jamaican marine sponge *Plakortis halichondrioides* along with plakortones A, C, D in 1996 by Patil and coworkers (Figs. 2.1, 2.2) [1]. In 1999, plakortone B (**87**) was also isolated from the Caribbean sponge *Plakortis simplex* along with plakortones C–F by Fattorusso and coworkers [2]. In their continuing program to identify compounds with antifungal properties, Wright and coworkers also isolated a molecule identified as plakortide E (**85**) from the sponge *Plakortis halichondrioides* in 2002 [3].

Plakortide E (**85**), $[\alpha]_D^{20} = 63.9(c = 2.0, \text{CHCl}_3)$, isolated as a low melting solid, was first characterized in 1996 by Patil and coworkers [1]. The molecular formula of plakortide E (**85**) was determined as $C_{22}H_{36}O_4$ from the LRESIMS $351(M + H)^+$. The basic skeleton was determined by interpretation of the IR, ^{1}H NMR (Table 2.1), ^{13}C NMR (Table 2.1), COSY, and HMBC spectra. In the IR spectrum, a sharp and intense absorption at 1,690 cm^{-1} indicated that the carbonyl was an α, β-unsaturated acid. Treatment of **85** with diazomethane furnished methyl ester **86**, confirming the presence of an acid group in **85**. The data of methyl ester **86** is summarized in Table 2.2. The NMR spectra indicated that plakortide E (**85**) contained five methyl groups and two double bonds. The methyl group was at C-8 in the side chain. The coupling constants of the double bond (15.8 Hz) suggested *trans* stereochemistry. Additionally, the NMR data indicated that the remaining oxygen in **85** must be attached via a peroxide functionality in the form of a 1,2-dioxolane. A combination of COSY, and HMBC spectra confirmed that plakortide E (**85**) contained a *tetra*-substituted *cis*-1,2-dioxolane, whose oxygen atoms were linked to two tertiary C4 and C6 centers. However, only the relative configuration was established. The absolute configuration at C4, C6 and C10 were not revealed in the initial structure elucidation.

Fig. 2.1 The Jamaican
marine sponge *Plakortis
halichondrioides*

In 2002, Wright and coworkers [3] also characterized plakortide E (**85**), however, the absolute configurations of C4, C6 and C10 were still unknown. The NMR and specific rotation data, depicted in Table 2.3, were nearly identical to those reported by Patil and coworkers. However, a chemical shift difference at C3 was observed in both the ^{1}H NMR and ^{13}C NMR spectra, although both samples were measured in CDCl$_3$ (Tables 2.1, 2.3). The proton and carbon signals were observed at δ 6.69 (d, J = 15.8 Hz) and 146.9 respectively by Patil and coworkers. While the proton and carbon were observed at δ 6.93 (d, J = 15 Hz) and 152.07 respectively by Wright and coworkers. The isolation procedures used in both isolations were similar. Wright and coworkers have not given any explanations on the differences of the chemical shift at C3 in the NMR spectra. They thought that some form of tautomerism was occurring, and it was possible that their isolation was of the sodium or other salt [3].

So far, the absolute configuration of plakortide E has not been determined. Based on the stereochemical data of the isolation papers, we can conclude that plakortide E had four possible configurations (Fig. 2.3).

Plakortone B (**87**), $[\alpha]_D^{20}$ = −9.2 (c = 0.72, CHCl$_3$), isolated as a colorless oil, was first characterized in 1996 by Patil and coworkers. The molecular formula of plakortone B (**87**) was determined as C$_{21}$H$_{34}$O$_3$ by 335.2586 (M + H)$^+$. The basic skeleton was established by NMR methods (Table 2.4). NOE difference data provided the relative configuration. Many similarities were observed between the ^{1}H NMR spectra of plakortone B (**87**) and plakortide E (**85**). However, the absolute configurations of their stereocenters were not revealed in the initial structure elucidation [1].

According to the stereochemical data, there are four possible structures for plakortone B (Fig. 2.4). In 2006, the absolute configuration of plakortone B was established as **87a** by total synthesis [4]. Recently, our group has reported the total syntheses and stereochemical assignments of all four isomers of plakortone B [5].

The novel structural features of plakortide E (**85**) as well as its potential bioactivities have stimulated our considerable interest in the quest for its total synthesis. Our first plan was to synthesize all four possible isomers of plakortide E (Fig. 2.3) and to realize the determination of the absolute configuration of plakortide E. We were also intrigued by the biosynthesis of plakortone B (**87**). So our second plan was to convert plakortide E to plakortone B, which would support the hypothesis that plakortide E was the precursor of plakortone B in nature.

cis-1,2-dioxolane

R = H plakortide E (**85**)
R = Me plakortide E methyl ester (**86**)

(3*S*,4*S*,6*R*,10*R*)-Plakortone B (**87**)
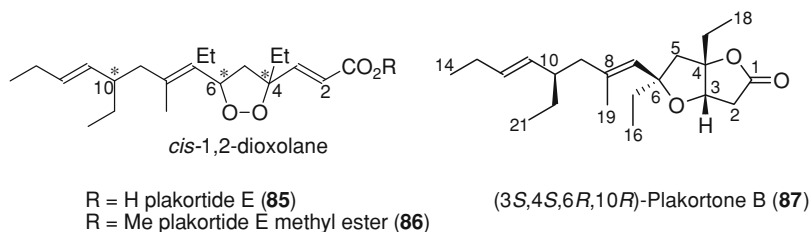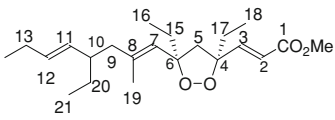
Fig. 2.2 Plakortide E (**85**) and plakortone B (**87**)

Table 2.1 The data of plakortide E (**85**) reported by Patil and coworkers

Source	Natural product [1]		
Reference	[1]		
Assigned structure			
EIHRMS	m/z [M + H]$^+$: 351		
$[\alpha]_D^T$	$[\alpha]_D^{20} = 63.9 (c = 2.0,\ CHCl_3)$		
NMR (CDCl$_3$)	^{1}H (ppm)		^{13}C (ppm)
Equipment	Bruker AMX-400 spectrometer		
H-1		C-1	173.0
H-2	5.98 (1 H, d, 15.8)	C-2	123.9
H-3	6.69 (1 H, d, 15.8)	C-3	146.9
H-4		C-4	87.2
H-5	2.53 β (1 H, d, 12.0)	C-5	55.8
	2.42 α (1 H, d, 12.0)		
H-6		C-6	89.1
H-7	5.12 (1 H, m)	C-7	126.9
H-8		C-8	136.5
H-9	2.00 (1 H, m)	C-9	46.6
	1.85 (1 H, m)		
H-10	2.00 (1 H, m)	C-10	42.6
H-11	5.05 (1 H, ddt, 15.2, 8.3, 1.4)	C-11	132.8
H-12	5.34 (1 H, dt, 6.3, 15.2)	C-12	131.9
H-13	1.98 (2 H, m)	C-13	25.6
H-14	0.93 (3 H, t, 7.4)	C-14	14.0
H-15	1.85 (1 H, m)	C-15	32.1
	1.63 (1 H, m)		
H-16	0.87 (3 H, t, 7.4)	C-16	8.8
H-17	1.77 (2 H, m)	C-17	31.0
H-18	0.87 (3 H, t, 7.4)	C-18	8.9
H-19	1.61 (3 H, d, 1.0)	C-19	17.7
H-20	1.35 (1 H, m)	C-20	27.6
	1.11 (1 H, m)		
H-21	0.80 (3 H, t, 7.4)	C-21	11.6

Table 2.2 The data of plakortide E methyl ester (**86**) reported by Patil and coworkers

Source	Natural product [1]		
Reference	[1]		
Assigned structure			

EIHRMS	*m/z* [M + H]$^+$: calcd for $C_{22}H_{37}O_4$: 365.2692, found: 365.2681		
$[\alpha]_D^T$	$[\alpha]_D^{20} = 75.1(c = 2.23, \text{ CHCl}_3)$		
NMR (CDCl$_3$)	^{1}H (ppm)	^{13}C (ppm)	
Equipment	Bruker AMX-400 spectrometer		
H-1		C-1	166.9
H-2	6.07 (1 H, d, 15.8)	C-2	119.9
H-3	6.85 (1 H, d, 15.8)	C-3	149.6
H-4		C-4	87.1
H-5	2.54 β (1 H, d, 12.0)	C-5	55.9
	2.44 α (1 H, d, 12.0)		
H-6		C-6	89.1
H-7	5.11 (1 H, q, 1.3)	C-7	126.7
H-8		C-8	136.4
H-9	2.00 (1 H, m); 1.85 (1 H, m)	C-9	46.5
H-10	2.00 (1 H, m)	C-10	42.5
H-11	5.05 (1 H, ddt, 1.5, 8.4, 15.3)	C-11	132.7
H-12	5.34 (1 H, dt, 6.43, 15.3)	C-12	131.9
H-13	1.97 (2 H, m)	C-13	25.5
H-14	0.93 (3 H, t, 7.4)	C-14	14.0
H-15	1.86 (1 H, m); 1.64 (1 H, m)	C-15	32.1
H-16	0.88 (3 H, t, 7.4)	C-16	8.8
H-17	1.78 (2 H, m)	C-17	30.8
H-18	0.90 (3 H, t, 7.4)	C-18	8.8
H-19	1.61 (3 H, d, 1.3)	C-19	17.7
H-20	1.35 (1 H, m); 1.10 (1 H, m)	C-20	27.6
H-21	0.80 (3 H, t, 7.4)	C-21	11.5
	3.73 (3 H, s, OCH$_3$)		51.1

2.2 Retrosynthesis

Our studies of the total synthesis of plakortide E (**85**) began as early as 2002. Initially, in consideration of the instability of the cyclic peroxide, we planned to construct the cyclic peroxide ring in the final step. We designed the model substrate **88** to investigate the Feldman reaction (Scheme 2.1). However, to our disappointment, the starting material decomposed, but no desired product **89** was obtained [6]. Assuming that the failure resulted from the steric hindrance in **88**, we designed an alternative convergent strategy.

Table 2.3 The data of plakortide E (**85**) reported by Wright and coworkers

Source	Natural product [3]		
Reference	[3]		
Assigned structure			
EIHRMS			
$[\alpha]_D^T$	$[\alpha]_D^{20} = 63(c = 0.001, \ CHCl_3)$		
NMR ($CDCl_3$)	^{1}H (ppm)		^{13}C (ppm)
Equipment	Bruker AMX-500 spectrometer		
H-1		C-1	172.0
H-2	6.09 (1 H, d, 15)	C-2	120.5
H-3	6.93 (1 H, d, 15)	C-3	152.1
H-4		C-4	87.2
H-5	2.53 β (1 H, d, 12.0)	C-5	56.0
	2.42 α (1 H, d, 12.0)		
H-6		C-6	89.3
H-7	5.10 (1 H, s)	C-7	126.6
H-8		C-8	136.7
H-9	2.00 (1 H, m)	C-9	46.6
	1.85 (1 H, m)		
H-10	2.00 (1 H, m)	C-10	42.6
H-11	5.04 (1 H, dd, 15, 8)	C-11	132.8
H-12	5.33 (1 H, dt, 6.5, 15)	C-12	132.0
H-13	1.95 (2 H, m)	C-13	25.6
H-14	0.92 (3 H, t, 7.5)	C-14	14.1
H-15	1.86 (1 H, m)	C-15	32.2
	1.64 (1 H, m)		
H-16	0.86 (3 H, t, 7.5)	C-16	8.9
H-17	1.78 (2 H, m)	C-17	30.8
H-18	0.88 (3 H, t, 7.5)	C-18	8.9
H-19	1.60 (3 H, s)	C-19	17.8
H-20	1.37 (1 H, m)	C-20	27.7
	1.24 (1 H, m)		
H-21	0.80 (3 H, t, 7.5)	C-21	11.6

Retrosynthetic analysis. According to the convergent synthetic strategy as shown in Scheme 2.2, we envisioned that the assembly of the target molecule **86** can be achieved by coupling the corresponding central core **90** with the side chain **91**. Formation of the C8–C9 single bond is realized by a metal-catalyzed sp^2–sp^3 coupling reaction [7–10]. Realization of the *trans* double bond, in turn, can be accomplished by a Horner–Wadsworth–Emmons olefination reaction [11–13]. Variations in the structure of central core **90** and the side chain **91** would provide the four possible absolute configurations of plakortide E. In our synthetic strategy,
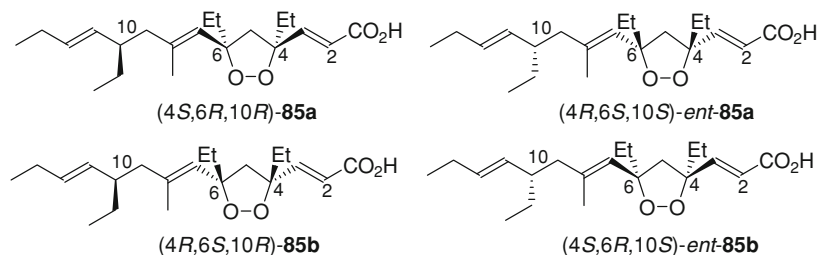
Fig. 2.3 Four possible isomers of plakortide E

Table 2.4 The data of plakortone B (**87**) reported by Patil and coworkers

Source	Natural product [1]		
Reference	[1]		
Assigned structure			
EIHRMS	m/z [M + H]$^+$: calcd for $C_{21}H_{35}O_3$: 335.2586, found: 335.2541		
$[\alpha]_D^T$	$[\alpha]_D^{20} = -9.2(c = 0.72, \text{ CHCl}_3)$		
NMR (CDCl$_3$)	^{1}H (ppm)		^{13}C (ppm)
Equipment	Bruker AMX-400 spectrometer		
H-1		C-1	175.6
H-2	2.71 β (dd, 5.1, 18.4, 1 H)	C-2	36.7
	2.64 α (dd, 1.3, 18.4, 1 H)		
H-3	4.21 (dd, 1.3, 5.1, 1 H)	C-3	79.5
H-4		C-4	97.2
H-5	2.24 α (d, 13.7, 1 H)	C-5	49.0
	2.13 β (d, 13.7, 1 H)		
H-6		C-6	86.9
H-7	5.03 (q, 1.3, 1 H)	C-7	129.5
H-8		C-8	137.1
H-9	2.00 (m, 1 H); 1.85 (m, 1 H)	C-9	46.9
H-10	1.98 (m, 1 H)	C-10	42.6
H-11	5.06 (ddt, 1.5, 8.4, 15.3, 1 H)	C-11	132.7
H-12	5.36 (dt, 6.3, 15.3, 1 H)	C-12	131.9
H-13	1.96 (m, 2 H)	C-13	25.5
H-14	0.95 (t, 7.4, 3 H)	C-14	14.0
H-15	1.73 (m, 2 H)	C-15	33.7
H-16	0.86 (t, 7.4, 3 H)	C-16	8.7
H-17	1.73 (m, 2 H)	C-17	30.3
H-18	0.96 (t, 7.4, 3 H)	C-18	8.3
H-19	1.69 (d, 1.3, 3 H)	C-19	16.7
H-20	1.35 (m, 1 H); 1.15 (m, 1 H)	C-20	27.8
H-21	0.83 (t, 7.4, 3 H)	C-21	11.5
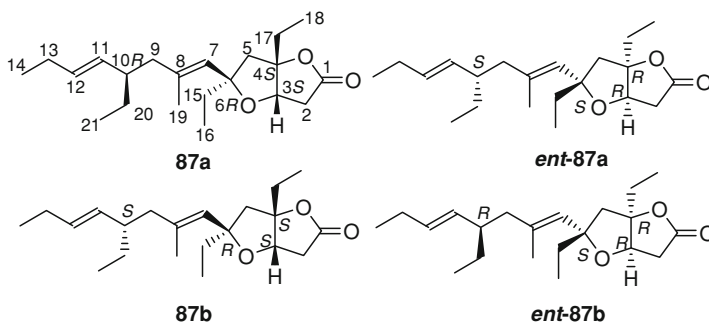
Fig. 2.4 Four possible isomers of plakortone B
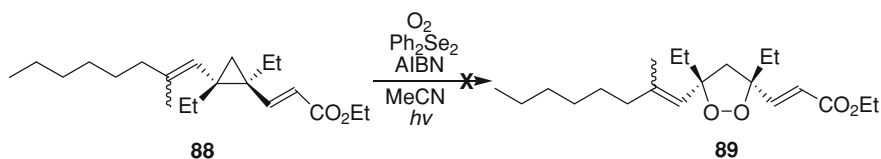
Scheme 2.1 Feldman reaction of the model substrate

lipase-catalyzed kinetic resolution of racemic 1,2-dioxolane **90** would be employed to generate the two enantiomerically pure central cores [14, 15]. The racemic 1,2-dioxolane **90** would be prepared from vinylcyclopropane **92**. When the four possible isomers of plakortide E are obtained, we plan to convert them into the four possible isomers of plakortone B (**87**), whose total synthesis has been reported by us recently [5]. This conversion will not only provide a biomimetic synthesis towards plakortone B, but will also help to confirm the absolute configuration of plakortide E (Scheme 2.2).

2.3 Synthesis of *cis*-1,2-Dioxolane

2.3.1 Syntheses of 1,2-Dioxolanes by the Feldman Reaction

In 1986, Feldman developed a convenient method for the synthesis of 1,2-dioxolanes. In this reaction, vinylcyclopropanes react with molecular oxygen via a radical-mediated [3 + 2] addition to form 1,2-dioxolanes (Scheme 2.3). The experimental results support the notion that *cis*-1,2-dioxolanes should predominate [16–19].

The mechanism of the Feldman reaction is depicted in Scheme 2.4. The free radical PhSe· is produced by using AIBN as an initiator, which reacts with the

87 (plakortone B)

Biomimetic synthesis of   (Determination of the absolute
Plakortone B   configuration of plakortide E)

I: Negishi coupling   *cis*-1, 2-dioxolane **86**   II: Horner-Wadsworth
                                                    -Emmons olefination

91   *cis*-1, 2-dioxolane **90**

92
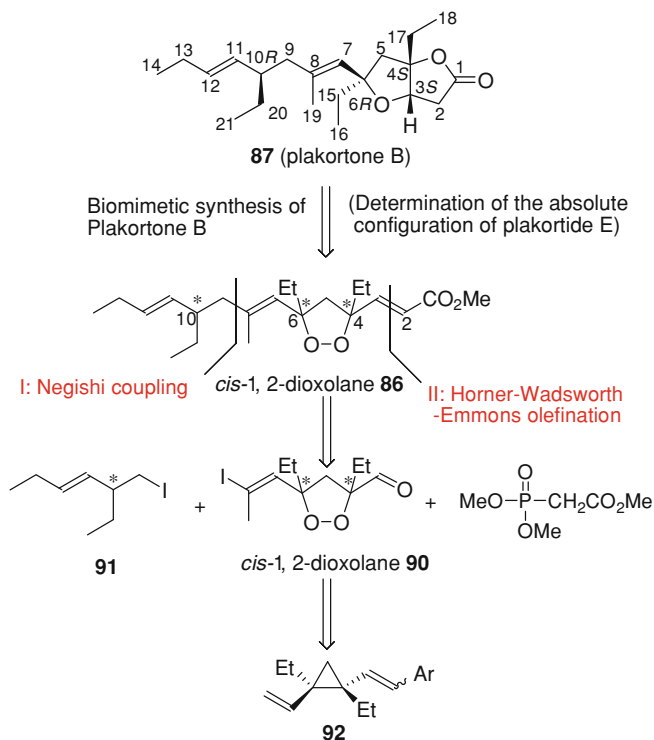
Scheme 2.2 Retrosynthetic analysis of plakortide E and plakortone B

42   **43**   (>95%: <5%)   **44**

93   **94**
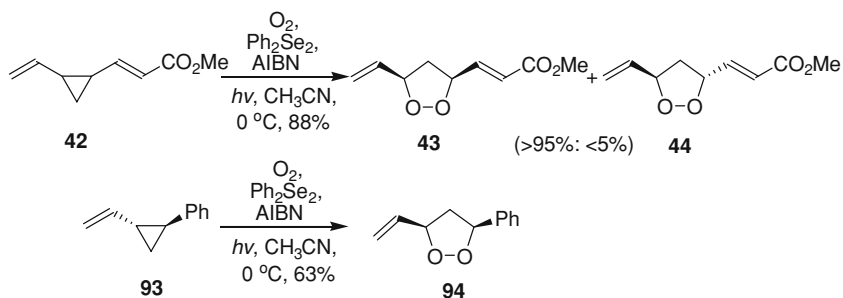
Scheme 2.3 Formations of 1,2-dioxolanes via Feldman reactions

double bond of vinylcyclopropane **95**, leading to cyclopropylcarbinyl radical **96**. Then cyclopropylcarbinyl radical **96** opens to the homoallylic radical **97**, which is trapped by oxygen to generate 5-hexenylperoxy **98**. Cyclization of the intermediate **98** leads to **99**. Finally, expulsion of PhSe· radical from peroxyl radical **99**
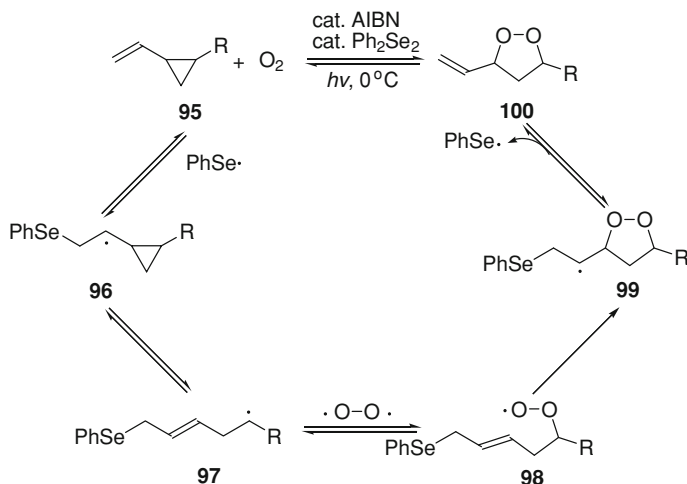
Scheme 2.4 The mechanism of the Feldman reaction

results in the formation of 1,2-dioxolane **100**. The rate-determining step is the irreversible cyclization of 5-hexenylperoxy **98** to peroxyl radical **99** [16–19].

Our previous research. Our preliminary synthetic efforts towards plakortide E were recorded in 2007 [20], in which Zhao studied the application of the Feldman reaction to synthesize highly substituted 1,2-dioxolanes. Initially, substrate **101d** was prepared and used to investigate the Feldman reaction. Irradiation with a 300 W sunlamp at 0 °C under an atmosphere of oxygen and in the presence of catalytic amounts of Ph$_2$Se$_2$ and AIBN furnished 1,2-dioxolane in 88% yield and as a 1/7 mixture of diastereomers, as determined by ^{1}H NMR and HPLC. The major product was determined to have *trans* configuration based upon nOe studies. A subsequent study applied the same peroxidation to a series of vinyl cyclopropanes. The results are depicted in Table 2.5.

In studies on less substituted vinylcyclopropane substrates, Feldman found that *cis*-1,2-dioxolanes predominated [16–19]. Weinreb and Feldman [19] utilized ab initio computation methods at the MP2/6-31G*//UHF/6-31G* level to probe the predicted energies between these species (5-hexenylperoxy **98** and peroxyl radical **99** in Scheme 2.4) in order to explain the *cis/trans* ratio in the product. Their results indicate that a chair-like transition state is always favorable, and an electron-withdrawing group would prefer an axial disposition that leads to a *trans*-product. On the other hand, an electron-donating group will occupy an equatorial position to give a *cis*-product (Scheme 2.5).

In the less substituted substrates, both experimental and computational results support the notion that *cis*-1,2-dioxolanes should predominate [16–19]. However, to our disappointment, during our construction of 3,5-tetrasubstituted-1,2-dioxolanes, we observed that the Feldman reaction predominantly furnished the

Table 2.5 Investigations of Feldman reaction

Entry	Substrate	Yield (%)	cis/trans[a]
1	**101a**	Quant	*trans*
2	**101b**	75	1/22
3	**101c**	Quant	1/13
4	**101d**	88	1/7
5	**92a**	82	1/2.8

[a] Determined by ^{1}H NMR analysis
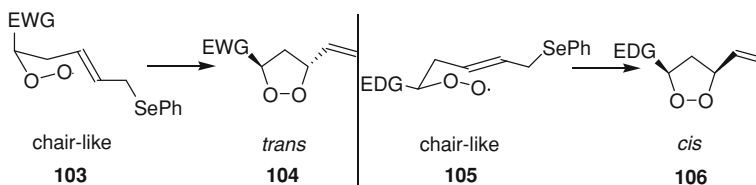
Scheme 2.5 Chair-like transition states in Feldman reaction

trans-stereoisomer when both oxygen atoms were on tertiary carbons (Table 2.5) [20]. Even substrate **92a**, which had an electron-rich styrenyl substituent, under Feldman reaction conditions as described above furnished the *trans*-product (*cis/trans* = 1:2.8) as the major product. These results were different from the traditional results as reported by Feldman and coworkers.

To explain our experimental results, we reinvestigate the transition states for cyclization of the hexenyl peroxyl radical which were developed by Feldman and coworkers to interpret the stereochemistry of 1,2-dioxolane formation [17]. After the equilibration studies with 1,2-dioxolanes and a trapping experiment with 1,2-dioxolane, Feldman and coworkers had predicted that the cyclization was irreversible and that the stereoselectivity reflected kinetic control. In the cyclization of 5-hexenylperoxy radical **108**, there were four transition states, the chair-like
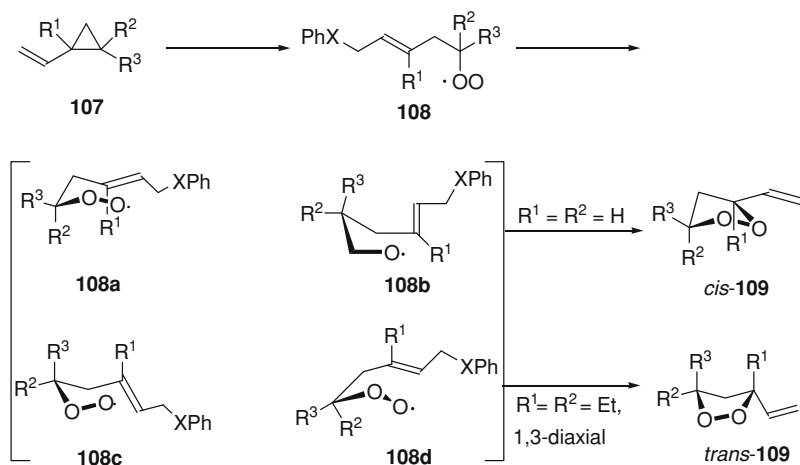
Scheme 2.6 Stereochemistry of 1,2-dioxolane formation

transition state **108a** featuring a pseudoequatorial substituent R^3, a boat-like transition state **108b** with pseudoaxial R^3, the chair-like transition state **108c** featuring a pseudoaxial substituent R^3 and a boat-like transition state **108d** with pseudoequatorial R^3 (Scheme 2.6). Reaction is believed to proceed through the more stable chair-like transition states **108a** or **108c** to generate the *cis*-product or *trans*-product respectively. When $R^1 = R^2 = H$, the reaction mainly proceeded through conformer **108a** to furnish the *cis*-1,2-dioxolane as the major product. However, when $R^1 = R^2 = Et$, the two Et groups would suffer from a 1,3-diaxial interaction in **108a**. As a result, cyclizations of substrates with $R^1 = R^2 = R^3 = $ alkyl proceed mainly via conformer **108c**, leading to the *trans*-1,2-dioxolane as the major product.

We also have studied this issue by employing DFT computional methods (courtesy of Dr. Yu-Xue Li, Shanghai Institute of Organic Chemistry, The Chinese Academy of Science). As expected, UB3LYP/6-31G* level computations indicated that the chair-like transition state going towards tertiary *trans*-peroxide was about 0.2 kcal/mol more stable in energy than those leading to *cis*-products.

Comparing the *cis/trans* ratio of the peroxides in Table 2.5, we found that the substrate **92a** gave the best value (*cis/trans* = 1:2.8). We envisioned that *cis/trans* ratio can be improved with a benzyl group. This result might suggest that the aryl group plays an important role in the stereocontrol process. We presumed that a π–π stacking interaction might be a crucial factor to control *cis*-selectivity (Fig. 2.5). To address this issue, we planned to reinvestigate the Feldman reaction with a series of divinylcyclopropanes containing a range of arene substituents on the alkenes. It was anticipated that the realization of *cis*-1,2-dioxolane could be accomplished by this strategy.

Syntheses of *trans*-divinyl cyclopropanes. The key intermediate **113** was prepared according to McCoy's procedure [21–23]. As depicted in Scheme 2.7,
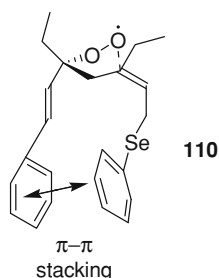
Fig. 2.5 π–π stacking interaction in the formation of 1,2-dioxolane
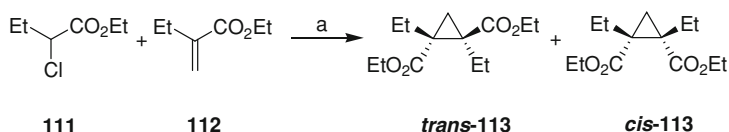
Scheme 2.7 Preparation of diethyl 1,2-diethyl-1,2-cyclopropanedicarboxylate. **Reagents and conditions**: (a) NaH, DMF, 88%

Scheme 2.8 Preparation of ethyl α-chlorobutyrate. **Reagents and conditions**: (a) DMF, SO_2Cl_2, 90–95 °C, 29%; (b) EtOH, H_2SO_4, benzene, 70%
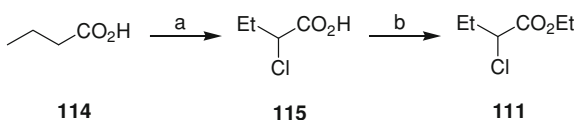
Scheme 2.9 Preparation of ethyl α-ethylacrylate. **Reagents and conditions**: (a) KOH, EtOH; (b) Piperidine, $(HCHO)_2$, Pyridine, 70% (2 steps)
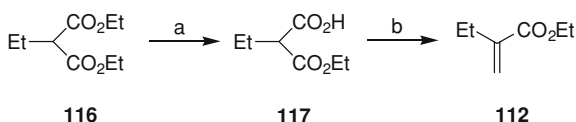
ethyl α-chlorobutyrate (**111**) and ethyl α-ethylacrylate (**112**) underwent tandem Michael/alkylation for the generation of diethyl 1,2-diethyl-1,2-cyclopropanedi-carboxylate (**113**). Ethyl α-chlorobutyrate (**111**) [24–26] was prepared from butyric acid (**114**) (Scheme 2.8) and ethyl α-ethylacrylate (**112**) [27] was formed from diethy l,2-ethylmalonate (**116**) (Scheme 2.9).

Our previous studies towards plakortide E showed that the *cis*-divinyl cyclo-propane might undergo Cope rearrangement to furnish cycloheptadiene [20]. Therefore, we resorted to the use of the *trans*-divinyl cyclopropane as a precursor for our investigation of the Feldman reaction (Scheme 2.10). Reduction of diester **113** gave diol **118** in 93% yield by employing $LiAlH_4$ [6, 20].

After reduction with $LiAlH_4$, mono-protection of alcohol group was necessary. Diol **118** was treated with Et_3N and t-$BuMe_2SiCl$ to afford the desired mono-protected product **119** as a colorless oil in 80% yield (Scheme 2.10) [6, 20].
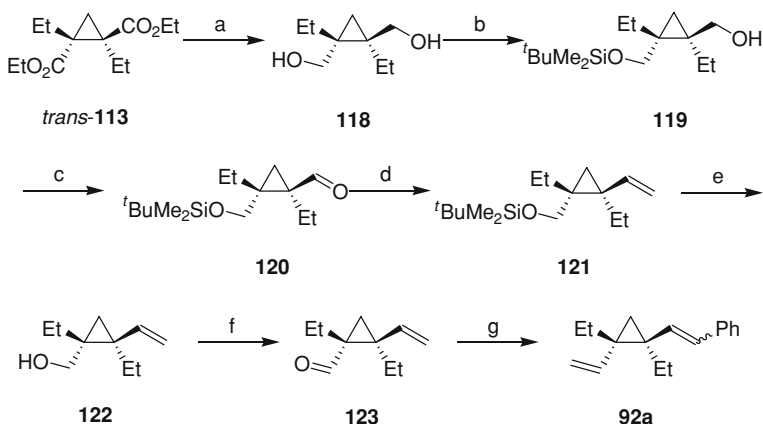
Scheme 2.10 Synthesis of *trans*-divinyl cyclopropane. **Reagents and conditions**: (a) LiAlH$_4$, Et$_2$O, rt, 84%; (b) *t*-BuMe$_2$SiCl, Et$_3$N, CH$_2$Cl$_2$, 0 °C, 2 h, 78%; (c) (COCl)$_2$, DMSO, Et$_3$N, CH$_2$Cl$_2$, −78 °C, 81%; (d) *n*-BuLi, PPh$_3$CH$_3$I, THF, −78 °C to rt, 74%; (e) *p*-TsOH, CH$_2$Cl$_2$/CH$_3$OH, 90%; (f) (COCl)$_2$, DMSO, Et$_3$N, CH$_2$Cl$_2$, −78 °C; (g) *n*-BuLi, PPh$_3$BnBr, THF, −78 °C to rt, 70% (2 steps)

Scheme 2.11 Syntheses of *trans*-divinyl cyclopropanes
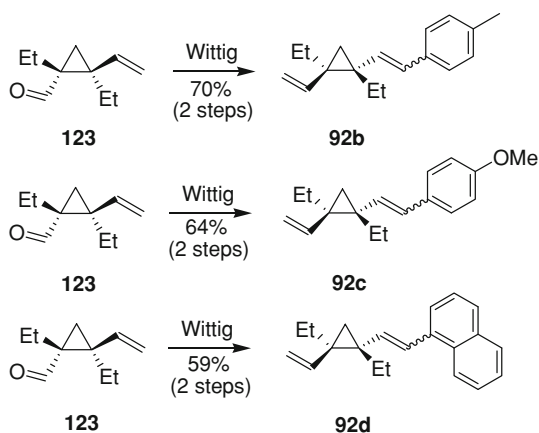
The mono-protected alcohol **119** was then subjected to Swern oxidation to generate aldehyde **120** as a colorless oil. Subsequently, aldehyde **120** was used directly for the Wittig reaction affording vinylcyclopropane **121** as a colorless oil in 65% yield (Scheme 2.10) [6, 20].

Then *p*-TsOH mediated desilylation of **121** furnished the free hydroxyl intermediate **122** as a colorless oil in 98% yield. Then the alcohol was subjected to Swern oxidation as above to furnish aldehyde **123** a colorless oil. Subsequently, Wittig reaction was performed, and the desired product divinylcyclopropane **92a** was prepared in 70% yield (two steps) (Scheme 2.10) [6, 20].

Table 2.6 Syntheses of 1,2-dioxolanes by Feldman reaction

Entry	Substrate	Yield (%)	cis/trans[a]
1	**92a**	72	1:3.1
2	**92b**	75	1:4
3	**92c**	84	1:2.6
4	**92d**	62	1:2.5

[a] Determined by ^{1}H NMR analysis

   Starting from the 1,2-diethyl-2-vinyl- cyclopropanecarbaldehyde (**123**), three other aryl-substituted divinylcyclopropanes were prepared by Wittig reactions in a similar manner (Scheme 2.11) [6, 20].

   Syntheses of 1,2-dioxolanes by the Feldman reaction. With the desired substrates in hand, we began our studies on the effect of aryl π–π stacking interaction in the Feldman reaction. The reactions were performed under standard Feldman reaction conditions. All the experimental results are summarized in Table 2.6. However, to our disappointment, we found that there was no significant improvement to the *cis/trans* ratio when various substrates were used. The best value in the table was *cis/trans* = 1:2.6, when the substrate **92c** was used. However, the major product was still the *trans*-1,2-dioxolane. The natural product plakortide E [1] was a *cis*-tetrasubstituted peroxide, so we sought to develop a complementary approach to synthesize the *cis*-tetrasubstituted 1,2-dioxolanes.

2.3.2 Palladium-Catalyzed Approach Towards 1,2-Dioxolanes

Ru-catalyzed oxidation of amides with *tert*-butyl hydroperoxide to give the corresponding *tert*-butyldioxy amides has been reported [28]. A Co-mediated peroxidation of alkenes in the presence of oxygen and triethylsilane was also known [29–34]. To the best of our knowledge, only two examples of Pd-catalyzed reaction resulting in peroxide-containing products have been reported [35, 36].

Pd(OAc)$_2$, K$_2$CO$_3$,
t-BuOOH
CH$_2$Cl$_2$, 0 °C

125   **126**

6 examples (yield: 40%-72%)
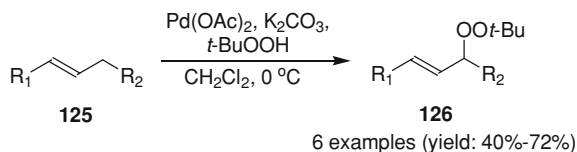
Scheme 2.12 Formation of allylic *tert*-butylperoxy ethers catalyzed by Pd(OAc)$_2$

5 mol% Pd(OAc)$_2$
20 mol% pyr
Ag$_2$CO$_3$ or BQ
80 °C, 3h

127   **128**

7 examples (30%-35%)

5 mol% Pd(OAc)$_2$
20 mol% pyr
Ag$_2$CO$_3$ or BQ
80 °C, 3h

129   **130**
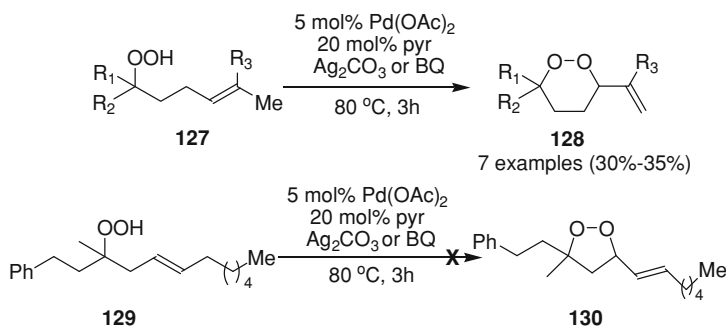
Scheme 2.13 Formations of 1,2-dioxanes reported by Woerpel and coworkers

Table 2.7 Catalyst screening

cat.
O$_2$ (balloon)
MeCN, rt

92a   **cis-124a**   **trans-124a**

Catalyst (mol%)	Temperature (°C)	Time (h)	Yield (%)	cis/trans[a]
No catalyst	25	48	NR[b]	–
Pd(PCy$_3$)$_2$Cl$_2$ (10)	25	24	NR[b]	–
Pd(PPh$_3$)$_4$ (10)	25	24	25	1:1
Pd$_2$(dba)$_3$ (10)	25	48	20	1:1
PdCl$_2$ (10)	25	24	NR[b]	–
Pd(OAc)$_2$ (10)	25	24	NR[b]	–
CuSO$_4$ (100)	25	24	NR[b]	–

[a] Determined by ^{1}H NMR analysis, [b] *NR* No reaction

Corey's method only furnished allylic *tert*-butylperoxy ethers as the major products (Scheme 2.12) [35].

Woerpel reported a palladium-catalyzed intramolecular cyclization of unsaturated hydroperoxides for the formation six-membered cyclic peroxides [36]. However, yields of this method were reportedly low (30–35%). Furthermore, this method has not been known to afford 1,2-dioxolanes (Scheme 2.13).

Our initial studies involved the use of **92a** [20] as a substrate. Thus, under O$_2$ (oxygen balloon), we examined a number of catalysts to identify the optimal catalytic system. Our results are summarized in Table 2.7. As can be seen, Pd(PPh$_3$)$_4$ was found to give the best result. In the absence of the catalyst, the reaction did not take place. In the presence of the CuSO$_4$, or Pd^{2+} [Pd(OAc)$_2$,

Table 2.8 Solvent screening

Entry	Solvent	Time (h)	Yield (%)	cis/trans[a]
1	THF	48	19	1:1
2	DMF	48	13	1:1
3	Toluene	48	15	1:1
4	DMSO	48	NR[b]	–
5	MeNO2	48	NR[b]	–
6	MeCN	24	25	1:1

[a] Determined by ^{1}H NMR analysis, [b] *NR* No reaction

Table 2.9 Catalyst screening

Entry	Catalyst (mol%)	Time (h)	Yield (%)	cis/trans[a]
1	Pd(PPh$_3$)$_4$ (10)	24	15	1:1.5
2	Pd(PPh$_3$)$_4$ (20)	24	26	1:1.5
3	CuCl$_2$ (20)	24	NDP[b]	–
4	Pd(PPh$_3$)$_4$ (10) CuCl$_2$ (20)	24	Trace	–
5	PdCl$_2$ (10)	24	NDP[b]	–
6	Pd$_2$(dba)$_3$ (10)	24	9	1:1.5

[a] Determined by ^{1}H NMR analysis, [b] *NDP* No desired product

Pd(PCy$_3$)$_2$Cl$_2$ and PdCl$_2$], no 1,2-dioxolane was resulted. In the presence of the Pd(0) catalyst, the desired product was obtained, and the ratio of the *cis/trans* is 1:1. When Pd(PPh$_3$)$_4$ was used as the catalyst, the yield of the reaction was found to be higher than that of Pd$_2$(dba)$_3$.

For further optimization, we examined the reaction in a variety of solvents. All results are summarized in Table 2.8. In DMSO or MeNO$_2$, there was no reaction. When MeCN was used as the solvent, the reaction gave a higher yield than in other solvents.

In the syntheses of peroxides, H$_2$O$_2$ is a widely used reagent. For further screening of reaction conditions for the oxidation of **92a**, aqueous H$_2$O$_2$ (30%) was used instead of oxygen balloon. The reaction was performed at room temperature in the presence of various catalysts with aqueous H$_2$O$_2$ solution in MeCN. The results are shown in Table 2.9. To our delight, in the presence of Pd (0) catalyst, substrate **92a** reacted with aqueous H$_2$O$_2$ solution, leading to the desired 1,2-dioxolane. However, the yields were not good. In the presence of 20 mol%

Table 2.10 Optimizations for the Pd-catalyzed approach towards 1,2-dioxolane

Entry	Catalyst (mol%)	H_2O_2 (equiv)	Solvent	Time (h)	Yield (%)	cis/trans[a]
1	Pd(PPh₃)₄ (10)	2.0	MeCN	12	33	1:1.5
2	Pd(PPh₃)₄ (20)	2.0	MeCN	12	53	1:1.5
3	Pd(PPh₃)₄ (20)	2.0	Benzene	36	46	1:1.9
4	Pd(PPh₃)₄ (20)	2.0	THF	12	17	1:1.2
5	Pd(PPh₃)₄ (20)	3.0	MeCN	12	57	1:1.5

[a] Determined by ¹H NMR analysis

Table 2.11 Palladium-catalyzed approach towards 1,2-dioxolanes

Entry	Substrate	Yield (%)	cis/trans[a]
1	a	57	1:1.5
2	b	70	1:1.4
3	c	40	1:1.6
4	d	67	1:1.8
5	e	NR[b]	–

[a] Determined by ¹H NMR analysis, [b] NR No product formed

Pd(PPh₃)₄, the mixture of 1,2-dioxolanes (*cis/trans* = 1:1.5) was obtained in 26% yield (Table 2.9).

Consideration of the effect of water in the reaction, urea hydrogen peroxide (UHP), a white crystalline solid, was used instead of aqueous H_2O_2. The reaction was performed at room temperature in the presence of Pd(PPh₃)₄ with urea hydrogen peroxide in dry organic solvents. The experimental results are summarized in Table 2.10. In these studies, we observed that the reaction with urea peroxide led to a better result (yield = 33%, *cis/trans* = 1:1.5) than that with aqueous H_2O_2 solution (yield = 15%, *cis/trans* = 1:1.5). By increasing the Pd(PPh₃)₄ catalyst loading from 10 mol% to 20 mol%, an isolated yield of 57% was realized. We also screened other solvents (THF and benzene), but it was found that MeCN was the best solvent for this reaction.
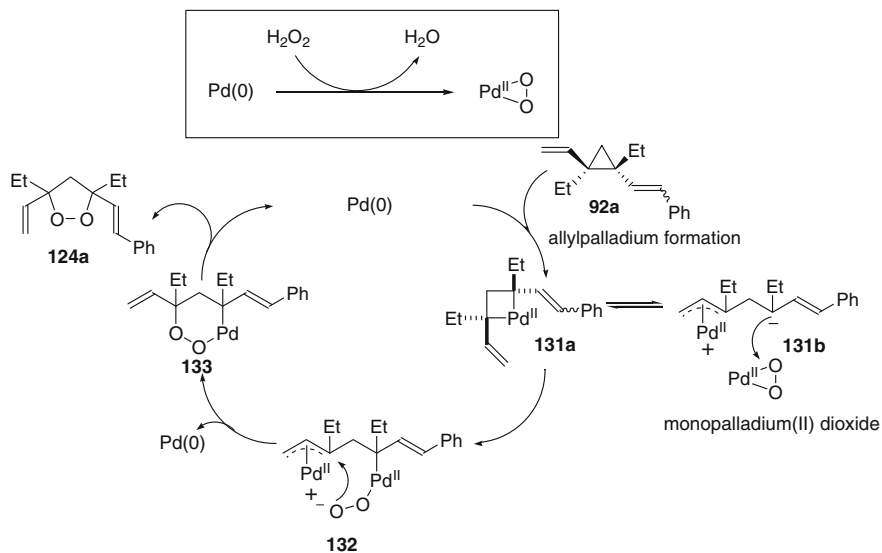
Scheme 2.14a Proposed mechanism for a palladium-catalyzed approach towards 1,2-dioxolane

The application of this palladium-catalyzed approach towards various 1,2-dioxolanes under the optimized condition is shown in Table 2.11. We have still not been able to obtain exclusively *cis*-1,2-dioxolanes by this method although the *cis/trans* ratio of this palladium approach (*cis/trans* = 1:1.4) is much better than that of the Feldman reaction (*cis/trans* = 1:2.8) [20]. Further optimization and search for asymmetric versions of this palladium-catalyzed process towards 1,2-dioxolanes are in progress.

An attempt to gain insight into the mechanism of this reaction was carried out. A radical scavenger, 2,6-di-*tert*-butyl-4-methylphenol (BHT), was used in the reaction between **92a** and urea peroxide. Despite the presence of a radical scavenger, the desired product was still obtained in 42% yield. This result implies that the reaction is not expected to proceed through a free radical process. As illustrated in Scheme 2.14a, a mechanism is proposed in light of other palladium-catalyzed reactions involving vinylcyclopropanes [37]. Divinylcyclopropane **92a** may react with Pd(0) to generate a π-allylpalladium complex **131b**, which can attack the monopalladium(II) dioxide [O_2Pd^{II}] [38] to form **132**. Ring closure by an intramolecular attack therefore yields **133**, which undergoes reductive elimination to yield the 1,2-dioxolane **124a** and regenerate the Pd(0) catalyst.

2.3.3 Synthesis of cis-*1,2-Dioxolane*

The mixture of *cis/trans* 1,2-dioxolanes **124a** was subjected to ozonolysis, which on reductive workup with NaBH$_4$ gave two chromatographically separable diols *trans*-**134** and *cis*-**135**. (Scheme 2.14b) [20]. Peroxide *cis*-**135** was isolated as a
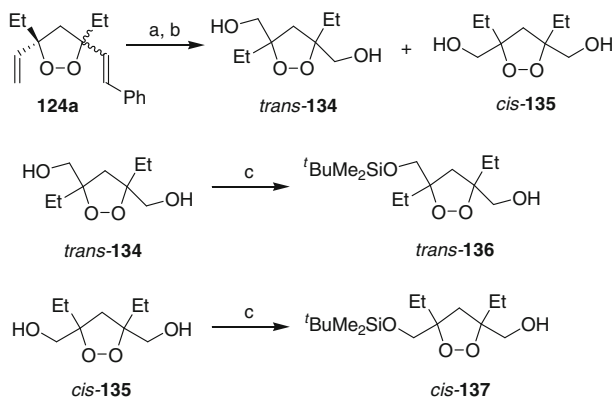
Scheme 2.14b Synthesis of *cis*-1,2-dioxolane **137**. **Reagents and conditions**: (a) O_3, CH_2Cl_2/MeOH (7:1), 78 °C; (b) $NaBH_4$ (1.5 equiv), −78 to 0 °C, 5 h, 90% (2 steps); (c) t-$BuMe_2SiCl$ (1.0 equiv), imidazole (1.0 equiv), DMAP (5 mol%), DMF, 0 °C to rt, 74% (reacted yield)

Fig. 2.6 X-ray crystallographic analysis of *cis*-135
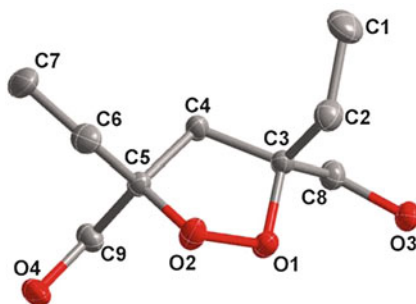
colorless solid, whose stereochemistry was confirmed by an X-ray crystallographic analysis (Fig. 2.6). Peroxides *trans*-**134** and *cis*-**135** were monoprotected with *t*-$BuMe_2SiCl$ to give *trans*-**136** and *cis*-**137**, respectively.

2.4 Studies on the Model Reactions

cis-1,2-Dioxolane **137** is the key synthetic precursor towards the total synthesis of plakortide E, while the *trans*-product **136** is useful for model studies. Due to the weak O–O bond dissociation energy (37 ± 1 kcal mol^{-1}) [39], the functionalization of the 1,2-dioxolanes are expectedly difficult. Generally, it is widely believed that peroxides are unstable compounds. Metals and metal ions such as Co and Pd, Sn(II), Fe(II) and Zn(II) are able to function as single- or two electron donors or Lewis acids to decompose peroxides. Strong bases, strong acids and high
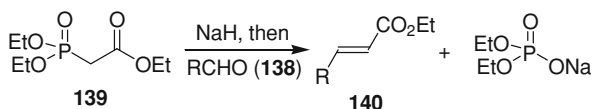
Scheme 2.15 Horner–Wadsworth–Emmons reaction
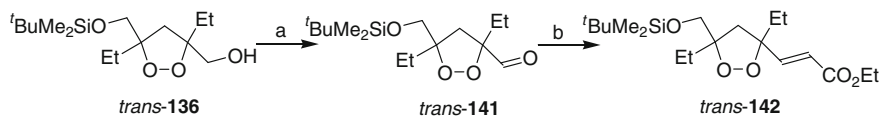
Scheme 2.16 Construction of *trans*-double bond. **Reagents and conditions**: (a) Dess–Martin periodinane (1.5 equiv), CH_2Cl_2; (b) $(EtO)_2P(O)CH_2CO_2Et$ (3.0 equiv), NaH (2.8 equiv), THF, 0 °C, 79% (2 steps)

temperature are all detrimental to peroxides [39, 40]. According to these facts, it goes without saying that the studies on the model reactions for the total synthesis are by no means trivial.

2.4.1 Construction of **trans-***Double Bond*

In 1958, Horner developed a modified Wittig reaction between aldehydes or ketones **138** and stabilized phosphonate **139** (Scheme 2.15) [11–13, 41]. Compared to phosphonium ylides, phosphonate-stabilized carbanions are more nucleophilic and more basic. Wadsworth and Emmons did further studies on this reaction [12]. The stereoselectivity of Horner–Wadsworth–Emmons reaction is usually pretty high, which favors the formation of *E*-alkenes. Another advantage is that the phosphate by-product can be washed away by aqueous solution of $pH > 2$.

Starting from the mono-protected *trans*-1,2-dioxolane containing alcohol **136**, we began to construct the *trans* double bond, which is a substituent of the tertiary peroxide center. In light of the good stereoselectivity and mild reaction conditions of Horner–Wadsworth–Emmons olefination reaction, we envisioned that this reaction would meet our requirements. The synthetic route is depicted in Scheme 2.16. Oxidation of **136** with Dess–Martin periodinane (DMP) generated the 1,2-dioxolane-containing aldehyde **141**. Aldehyde **141** as an unstable species that had to be freshly prepared for each olefination. To our delight, the Horner–Wadsworth–Emmons olefination of aldehyde **141** with triethyl phosphonoacetate resulted exclusively in the desired product **142** in 79% yield (two steps) [11–13, 41]. The stereochemistry was determined by the ^1H NMR, with the 15.8 Hz $^3J_{H–H}$ coupling confirming the *trans* stereochemistry.

Encouraged by the success of the Horner–Wadsworth–Emmons olefination, we next investigated the application of a Wittig olefination for introduction of *tri*-substituted alkene adjacent to the 1,2-dioxolane. The model reaction is shown in Scheme 2.17. Although two kinds of Wittig reactions have been tried, we failed to obtain the desired product (Table 2.12). In both cases, no obvious product spot
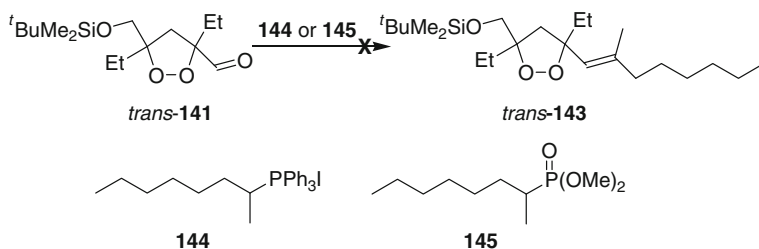
Scheme 2.17 Construction of trisubstituted double bond

Table 2.12 Reaction conditions for Wittig reaction

Entry	Reaction conditions	Results
1	*n*-BuLi (1.2 equiv), **144** [6] (1.3 equiv), THF, −78 °C to rt	Decomposed
2	*n*-BuLi (1.2 equiv), **145** [6] (1.3 equiv), THF, −78 °C to rt	Decomposed
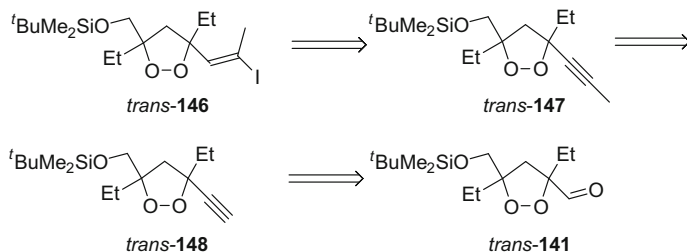
Scheme 2.18 Retrosynthesis of alkenyl iodide **146**

was observed on TLC, although all starting material was consumed. We presumed that the steric hindrance between the 1,2-dioxolane-containing aldehyde **141** and the side chain **144** [6] or **145** [6] led to the failure of these coupling reactions. When the desired Wittig reaction did not take place, the unstable 1,2-dioxolane-containing aldehyde decomposed under these conditions. For this reason, we abandoned this Wittig reaction approach. Next, we place our focus on the Pd-catalyzed cross-coupling reaction, which has been widely used in carbon–carbon bond-forming reactions.

2.4.2 Synthesis of Alkenyl Iodide

In our retrosynthesis of plakortide E, 1,2-dioxolane-containing-alkenyl iodide **90** was an important key precursor. To prepare for the synthesis of the *cis*-1,2-dioxolane-containing alkenyl iodide **90**, we intended to initially model the

Scheme 2.19 Seyferth–
Gilbert homologation

aldehyde or ketone
149   **151**
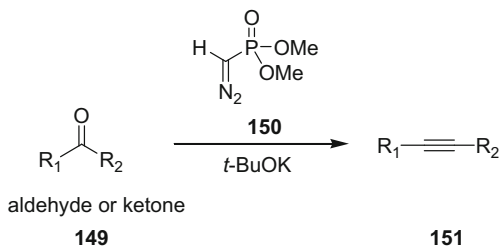
Scheme 2.20 Modification
of Seyferth–Gilbert
homologation (Ohira–
Bestmann reagent)

152   **154**
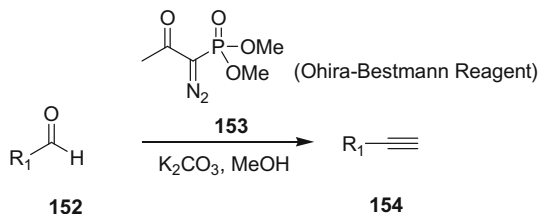
synthetic steps on the *trans* isomer, **146**. As shown in Scheme 2.18, starting from
the *trans*-1,2-dioxolane-containing-aldehyde **141** to prepare the *trans*-1,2-dioxolane-
containing-alkenyl iodide **146**, we need as the first step to prepare the intermediate
terminal alkyne **148**. With terminal alkyne **148** in hand, subsequent methylation
afforded the alkyne **147**. The conversion of an alkyne to an alkenyl iodide has been
reported in the literature [4, 5, 42].

Preparation of terminal alkyne 148. The one-pot conversion of ketones or
aldehydes to the corresponding internal or terminal alkynes by using dia-
zophosphonates under basic conditions is called Seyferth–Gilbert homologation
(Scheme 2.19). In 1973, Colvin and coworkers reported that aryl ketone **149**
(or aldehyde) reacted with dimethyl (diazomethyl)phosphonate **150** in the presence
of a base to give substituted alkynes **151** [43, 44]. Dimethyl (diazomethyl)phos-
phonate **150** was often called the Seyferth–Gilbert reagent [45], which was first
synthesized by Seyferth. In 1979 Gilbert and coworkers improved the procedure of
the reaction, and extended its scope [46, 47]. Ohira and Bestmann made a further
modification of this reaction based upon generation of the dimethyl(diazometh-
yl)phosphonate in situ from dimethyl(1-diazo-2-oxopropyl)phosphonate (**153**),
which was called Ohira–Bestmann reagent (Scheme 2.20) [48, 49]. The Ohira–
Bestmann procedure is now widely used in organic syntheses. The mild reaction
conditions are tolerant most functional groups and various aldehydes can be
homologated in excellent yields.

In the light of the advantages of the Ohira–Bestmann procedure and its wide
synthetic applications, we planned to use this reaction to introduce the terminal
alkyne to our 1,2-dioxolane-containing substrate. As shown in Scheme 2.21,
freshly prepared aldehyde **141** was subjected to the standard Ohira–Bestmann
procedure [48, 49]. To our disappointment, none of the desired terminal alkyne
148 was obtained, although the TLC showed that all starting material was
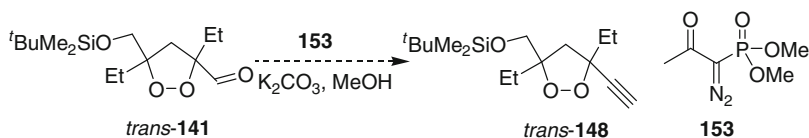
Scheme 2.21 Synthesis of terminal alkyne via Ohira–Bestmann procedure
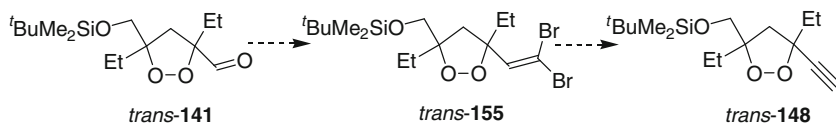
Scheme 2.22 Synthesis of terminal alkyne

Scheme 2.23 Corey–Fuchs reaction
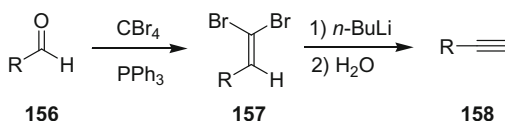
Table 2.13 Reaction conditions for the preparation of 1,1-dibromoalkene **155**
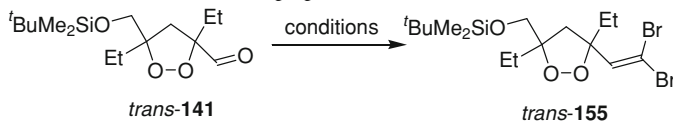
Entry	Reaction conditions	Results
1	CBr$_4$, Ph$_3$P, CH$_2$Cl$_2$ (Corey–Fuchs reaction)	Decomposed
2	CBr$_2$HPPh$_3$Br, t-BuOK	79% (2 steps)

consumed. We presumed that the 1,2-dioxolane-containing aldehyde **141** decomposed under the basic conditions due to its instability.

Due to the fact that a one-pot conversion of the 1,2-dioxolane-containing aldehyde **141** to terminal alkyne **148** failed, we planned to convert the 1,2-dioxolane-containing aldehyde **141** to the 1,1-dibromoalkene **155**, which can be treated with n-BuLi to generate the desired terminal alkyne **148** (Scheme 2.22).

The Corey–Fuchs reaction [50] included two sequential reactions, the formation of the 1,1-dibromoolefin and the formation of the terminal alkyne. Starting from aldehyde **156**, and through these two sequential transformations, a terminal alkyne **158** was obtained (Scheme 2.23). The formation of 1,1-dibromoolefins via phosphine-dibromomethane was originally developed by Desai and McKelvie [51].

In consideration of the good functional group tolerance of the Corey–Fuchs reaction, we intended to employ it in our preparation of the terminal alkyne **148**. Freshly prepared aldehyde **141** was used to investigate the Corey–Fuchs reaction. The reaction was performed under standard Corey–Fuchs reaction conditions [50].
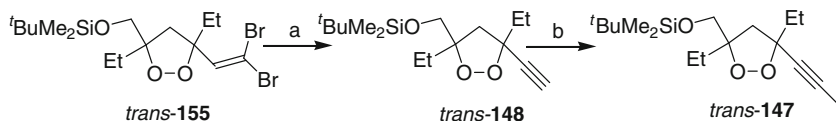
Scheme 2.24 Preparation of *trans*-1,2-dioxolane-containing alkyne. **Reagents and conditions**: (a) *n*-BuLi (2.2 equiv), THF, −78 °C, 0.5 h, 95%; (b) *n*-BuLi (1.2 equiv), MeOTf (1.5 equiv), THF, −78 °C, 1 h, 70%

Fig. 2.7 Schwartz reagent
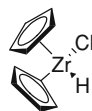
However, to our disappointment, we failed to obtain the desired 1,1-dibromoalkene **155** (Table 2.13). Under these reaction conditions, no obvious spot was observed on TLC although all starting material was consumed. We thought that the 1,2-dioxolane-containing aldehyde **141** decomposed during the reaction.

Then we adopted the Rassat's procedure which has also been widely used in total synthesis [52]. Thus to a slurry of freshly prepared Ph₃P-CHBr₃ [53] (2.5 equiv) in THF at 0 °C was added *t*-BuOK (2.4 equiv). The bright yellow slurry was stirred for 15 min and the temperature was allowed to warm to room temperature. Then the solution of the aldehyde **141** (1.0 equiv) in THF was added to the mixture and stirred for 30 min, the reaction was complete as monitored by TLC. To our delight, the desired 1,1-dibromoalkene **155** was prepared in 79% yield starting from the 1,2-dioxolane-containing alcohol **136** (two steps). It was necessary to warm the reaction system after the addition of *t*-BuOK. If the reaction were kept at 0 °C, an inseparable side product was formed along with the 1,1-dibromoalkene **155**. The reaction time for the Wittig salt Ph₃P-CHBr₃ and *t*-BuOK and the amount of *t*-BuOK were also important. It is essential to allow a complete consumption of the base *t*-BuOK; otherwise, the base would decompose 1,2-dioxolane-containing aldehyde **141**.

Preparation of the alkyne 147. With dibromoalkene **155** in hand, we treated it with *n*-BuLi (2.2 equiv) at −78 °C to provide the terminal alkyne **148** in 95% yield. Then the terminal alkyne **148** was deprotonated with *n*-BuLi (1.2 equiv) at −78 °C, followed by methylation to afford *trans*-1,2-dioxolane-containing alkyne **147** in 70% yield (Scheme 2.24) [4, 5].

Preparation of the alkenyl iodide 146. In 1970, Wailes and Weigold first prepared zirconocene hydrochloride (Cp₂ZrHCl) by the reduction of Cp₂ZrCl₂ [54], and then Schwartz examined the reactions of Cp₂ZrHCl with a wide range of substrates and developed it to become a useful reagent for organic synthesis (Fig. 2.7) [42, 55]. Zirconocene hydrochloride reacts with alkenes or alkynes to form alkenylzirconium or alkylzirconium compounds and this reaction is called
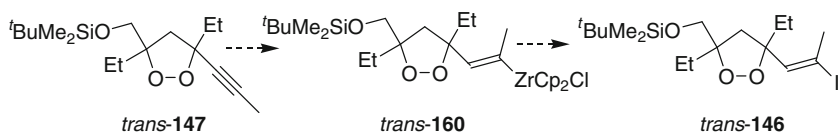
Scheme 2.25 Preparation of *trans*-1,2-dioxolane-containing alkenyl iodide 23 by Schwartz hydrozirconation

Table 2.14 Reaction conditions for Schwartz hydrozirconation

Entry	Reaction conditions	Results
1	Cp$_2$Zr(H)Cl, benzene, THF, 0 °C to rt	No reaction
2	Cp$_2$Zr(H)Cl, benzene, THF, 50 °C	Complicated

Schwartz hydrozirconation. Zirconocene hydrochloride (Cp$_2$ZrHCl) is called the Schwartz reagent. Generally, the addition of the Zr–H proceeds with *syn*-addition [56].

To prepare the alkenyl iodide **146**, we attempted to employ the Schwartz reagent in our transformation. Hydrozirconation of the alkyne **147** should lead to the formation of the alkenylzirconium **160**, iodination of which affords the desired alkenyl iodide **146** (Scheme 2.25).

The Schwartz hydrozirconation reaction of the alkyne **147** was performed under standard reaction conditions reported in the literature [42, 55, 57]. To a suspension of Cp$_2$Zr(H)Cl in THF at 0 °C was added a solution of the alkyne **147** in benzene under nitrogen. The temperature was allowed to warm to room temperature. The reaction was examined by ^{1}H NMR. Although the reaction mixture was stirred for 24 h, no reaction took place (Table 2.14). Then the reaction was performed at 50 °C, and was monitored by ^{1}H NMR. To our disappointment, no desired product **160** resulted. However, the starting material was consumed. Decomposition of the starting material made the reaction very messy.

After the failure of the Schwartz hydrozirconation reaction, we sought to employ a milder reaction to prepare the 1,2-dioxolane-containing alkenyl iodide **146**. This time, we resorted to the palladium-catalyzed hydrostannylation of alkynes. Compared to other methods, the palladium-catalyzed hydrostannylation offers these advantages: (1) mild reaction conditions; (2) good functional group tolerance; (3) good stereoselectivity (*cis*-addition) [58, 59]; (4) wide application in total synthesis. It was recently reported that hexane minimized the competitive stannane dimerization in palladium-catalyzed hydrostannylations [60]. In light of these findings, our synthetic route was designed in Scheme 2.26. The palladium-catalyzed hydrostannylation of the alkyne **147** regiospecifically furnished **161**. Then subsequent iodination of **161** cleanly led to the 1,2-dioxolane-containing alkenyl iodide **146**.
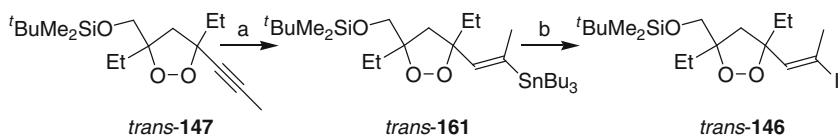
Scheme 2.26 Preparation of *trans*-1,2-dioxolane-containing alkenyl iodide **146** by palladium-catalyzed hydrostannylation of the alkyne **147**. **Reagents and conditions**: (a) Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%), *n*-Bu$_3$SnH (3.0 equiv), Hexane, 1 h, 84%; (f) I$_2$ (1.0 equiv), CH$_2$Cl$_2$, 0 °C, 86%

Table 2.15 Optimization of the palladium-catalyzed hydrostannylation

Catalyst	Solvent	(n-Bu)$_3$SnH (equiv)	**161**	**162**	SM
Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%)	THF	4.0	33%	33%	–
Pd(PCy$_3$)$_2$Cl$_2$ (10 mol%)	THF	2.0	Trace	Trace	56%
Pd(OAc)$_2$ (10 mol%) PCy$_3$ (20 mol%)	THF	4.0	24%	Trace	–
Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%) PCy$_3$ (30 mol%)	THF	4.0	30%	33%	–
Pd(PPh$_3$)$_4$ (10 mol%)	THF	4.0	31%	35%	–
Pd(OAc)$_2$ (10 mol%) PCy$_3$ (30 mol%)	Hexane	2.0	17%	7%	46%
Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%)	Hexane	4.0	84%	Trace	–
Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%)	Hexane	2.0	71%	Trace	SM residual
Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%)	Hexane	2.5	80%	Trace	–

Employing alkyne **147** as the substrate, we studied the palladium-catalyzed hydrostannylation of 1,2-dioxolane-containing alkyne. To a solution of Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%) and alkyne **147** in THF, tributyltin hydride was added dropwise at room temperature. The dark brown reaction mixture was stirred for 1 h, and the reaction was monitored by TLC. The starting material alkyne **147** was completely consumed. After flash column chromatography, both **161** and **162** were obtained in 66% yield, and the **161**/**162** ratio is 1:1. Although we obtained our desired product **161**, the regioselectivity was not acceptable. We optimized the reactions by screening several palladium catalysts, ligands and solvents. All the results are summarized in Table 2.15. Gratifyingly, we found the best reaction conditions. In the presence of Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%), alkyne **147** reacted with tributyltin hydride in hexane, and regioselectively resulted in the desired product in 84% yield. With the intermediate **161** in hand, its iodination led to 1,2-dioxolane-containing alkenyl iodide **146** in 86% yield.
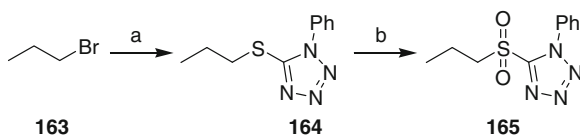
Scheme 2.27 Preparation of the Julia reagent. **Reagents and conditions**: (a) NaH, Hspt, THF, 0 °C to rt, overnight, 96%; (b) $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$, H_2O_2(30%), EtOH, overnight, 92%
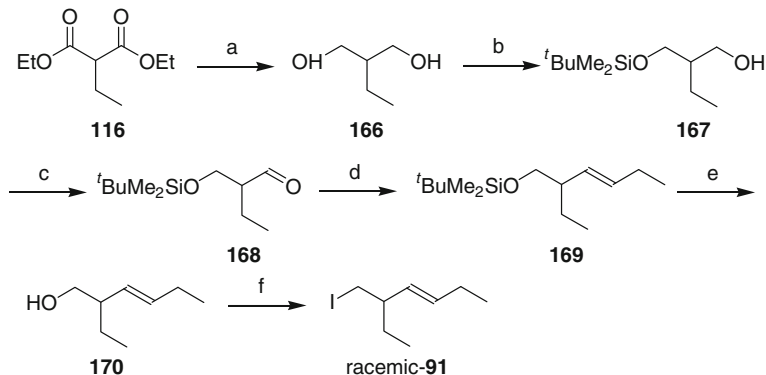
Scheme 2.28 Synthesis of the racemic side chain. **Reagents and conditions**: (a) LiAlH$_4$, THF, reflux, 24 h, 60%; (b) n-BuLi, t-BuMe$_2$SiCl, THF, −78 °C to rt, 99%; (c) (COCl)$_2$, DMSO, Et$_3$N, CH$_2$Cl$_2$, −78 °C; (d) KHMDS (solid), Julia reagent, THF, −78 °C to rt, 89% (2 steps); (e) p-TsOH, CH$_2$Cl$_2$/CH$_3$OH, 86%; f. PPh$_3$, imidazole, I$_2$, CH$_2$Cl$_2$, 0 °C to rt, 86%

2.4.3 Synthesis of the Racemic Side Chain

To continue our basic model study, the racemic side chain needed to be prepared. The route is shown in Scheme 2.28. The synthetic paradigm was step-economical and starting material was commercially available and cheap.

As shown in Scheme 2.28, Julia olefination was used to construct the *trans*-double bond of the side chain. We first prepared the Julia reagent **165** by literature reported methods (Scheme 2.27) [6]. Commercially available *n*-propyl bromide **163** was allowed to react with 1-phenyl-1H-tetrazole-5-thiol (Hspt) in THF in the presence of NaH furnishing the intermediate thioether **164** in 96% yield, which was in turn oxidized to the sulfone **165** with H_2O_2 in the presence of a catalytic amounts of $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ in 92% yield.

We next prepared the aldehyde substrate for the Julia olefination. Commercially available ethyl diethyl malonate (**116**) was reduced to diol **166** in 60% yield by using LiAlH$_4$. Diol **166** was then treated with *n*-BuLi and *t*-BuMe$_2$SiCl at −78 °C to afford the desired mono-protected product **167** as a colorless oil in excellent

Table 2.16   Optimization of the Julia olefination
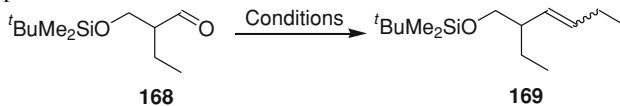
Entry	Reaction conditions	trans/cis[a]	Yield (2 steps) (%)
1	LDA, THF, −78 °C to rt	10:1.2	56
2	KHMDS (Toluene), THF, −78 °C to rt	11:1	30
3	KHMDS (solid), THF, −78 °C to rt	25:1	89

[a] Determined by ^{1}H NMR analysis

yield [61]. The mono-protected alcohol **167** was then subjected to Swern oxidation. After oxidation, a colorless oil of aldehyde **168** was obtained and was directly used for the Julia olefination (Scheme 2.28).

When we used Julia olefination to construct the *trans*-double bond, we found that the stereoselectivity of the reaction was problematic. We found that the *trans/cis* ratio was affected by the base. Initially, LDA was used, the *trans/cis* ratio is 10:1.2 as determined by ^{1}H NMR spectrometry. Then we optimized the reaction by screening bases and solvents. The results are summarized in Table 2.16. When KHMDS was used as a base, the desired 1,2-disubstituted olefin **169** was obtained in 89% yield (two steps). The *trans/cis* ratio of the 1,2-disubstituted olefin **169** obtained under these reaction conditions was also acceptable (*trans/cis* = 25:1).

The 1,2-disubstituted alkene **169** underwent *p*-TsOH mediated desilylation to furnish the free hydroxy intermediate **170** as a colorless oil in 86% yield. Alcohol **170** was converted to (±)-**91** in 86% yield with PPh$_3$/I$_2$/imidazole (Scheme 2.28) [4, 5].

2.4.4 Pd-Catalyzed sp^2–sp^3 Coupling

In studying the evolution of organic chemistry and grasping its essence, one comes quickly to the conclusion that no other type of reaction plays as large a role in shaping this domain of science than carbon–carbon bond-forming reactions.—K. C. Nicolaou [62]

In the last quarter of the 20th century, transition metal-catalyzed cross coupling reactions have been greatly developed. Nowadays, these types of cross coupling reactions have become the most powerful and useful C–C formation reactions in synthetic organic chemistry. Amongst them, the palladium-catalyzed cross coupling reactions are the most visible. It is only natural that Pd-catalyzed coupling has been used as a pivotal reaction in many total syntheses [63, 64].

Palladium-catalyzed cross-coupling reactions in total synthesis have been comprehensively reviewed by Nicolaou and coworkers [65]. Below, I have provided some examples relevant to our total synthesis of plakortide E.
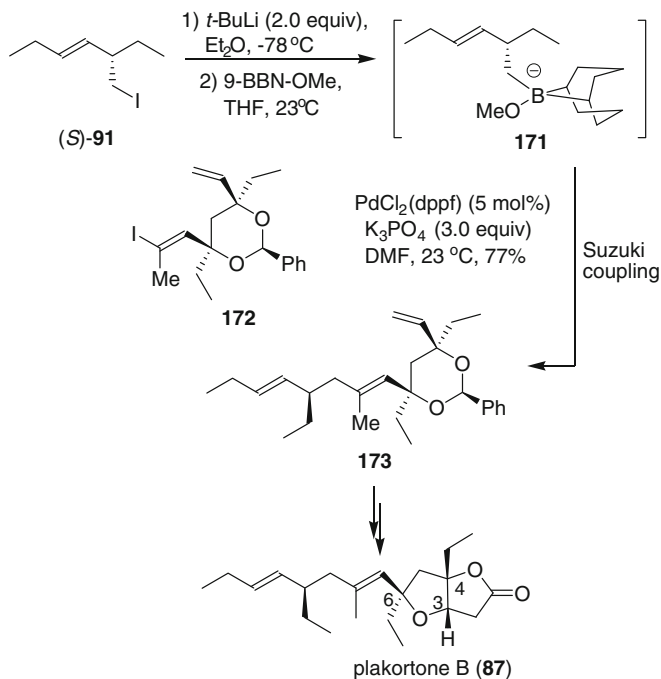
Scheme 2.29 Application of Suzuki reaction in total synthesis of plakortone B

These beautiful applications of palladium-catalyzed cross-coupling reactions in total synthesis have shed light on our own program in the quest for plakortide E.

In 2006, Semmelhack and coworkers reported the synthesis of plakortone B (**87**) and analogs [4]. The connection of the side chain (S)-**91** to the core structure **172** was achieved by a palladium-catalyzed Suzuki reaction (Scheme 2.29).

Recently, starting from D-mannitol (**174**), our group accomplished the total syntheses of all four possible isomers of plakortone B [5]. And one of these molecules, **87**, was found to be identical with the natural plakortone B on the basis of ^{1}H, ^{13}C NMR spectra and specific rotation, demonstrating that absolute configuration of the natural plakortone B is (3S,4S,6R,10R). In our synthesis, a Suzuki reaction was also used to connect the central core **175** and side chain (S)-**91** (Scheme 2.30).

In 1977, Negishi and coworkers developed a new carbon–carbon bond formation reaction, which was used to couple organozinc reagents and organic halides [65]. The synthesis of β-carotene demonstrates the utility of this reaction both as a sp–sp^2 and sp^2–sp^2 coupling method [66]. Generally, diorganozinc species (R_2Zn) and organozinc halides ($RZnX$) can be employed in the Negishi reaction. Organozinc halides ($RZnX$), typically prepared either by the direct insertion of zinc (zinc dust) into organic halides or by transmetalation from other
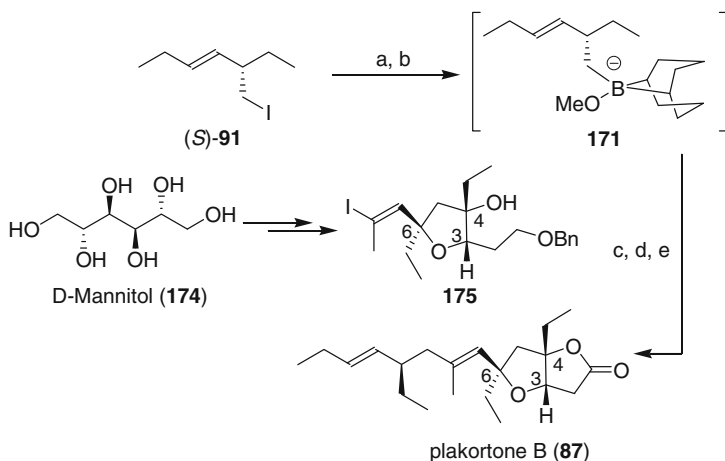
Scheme 2.30 Application of Suzuki reaction in total synthesis of plakortone B. **Reagents and conditions**: (a) *t*-BuLi, Et$_2$O, −78 °C, 5 min; (b) 9-BBN-OMe, THF, −78 °C, 10 min, then warm to 23 °C, 1 h; (c) 3 N K$_3$PO$_4$ (aq.), 3 min; then **175**, [PdCl$_2$ (dppf)$_2$]·CH$_2$Cl$_2$, DMF, 23 °C, 20 h; (d) Na/NH$_3$ (liq.), THF, −78 °C, 0.5 h; (e) PDC, DMF, 23 °C, 20 h, 60% over 3 steps

organometallic species, are widely used in organic synthesis [67, 68]. Alkylzinc reagents were used in the cross coupling process, which have greatly expanded the scope of the Negishi reaction beyond standard C(sp^2)–C(sp^2) couplings. Smith and coworkers reported a gram-scale synthesis of discodermolide (**180**), which was a clinically relevant microtubule-stabilizing agent. In their total synthesis, the Negishi coupling reaction was beautifully utilized to achieve the coupling of two fragments (Scheme 2.31). This application was a good example of the use of alkylzinc reagents in the process of sp^2–sp^3 carbon–carbon bond-formation [8, 9].

In this approach, the two fragments **176** and **178** were coupled to form the C$_{14}$–C$_{15}$ bond of the target product. Significantly, it was found that 3 equivalents of *t*-BuLi were needed in the initial lithium–halogen exchange process after the optimization. If the customary 2 equivalents were used, the product was a 1:1 mixture of the iodide starting material **176** and the expected product **179**. To explain such modified Negishi protocol, they speculated that the mixed *tert*-butyl-alkyl zinc intermediate (**177**) was in fact the reactive alkyl donor in the coupling process (Scheme 2.31) [8, 9].

Recently, Aggarwal and coworkers reported the total synthesis of (+)-faranal. Remarkably, this synthesis was completed in only six steps from propyne, which was quite step-economical. The key reaction in the total synthesis was the coupling of the two fragments **182** and **181** from Negishi coupling. Zinc bromide was used to generate the alkyl-zinc intermediate from the corresponding organolithium (Scheme 2.32). This application was also an example of sp^2–sp^3 carbon–carbon bond-formation achieved by Negishi cross-coupling [10].
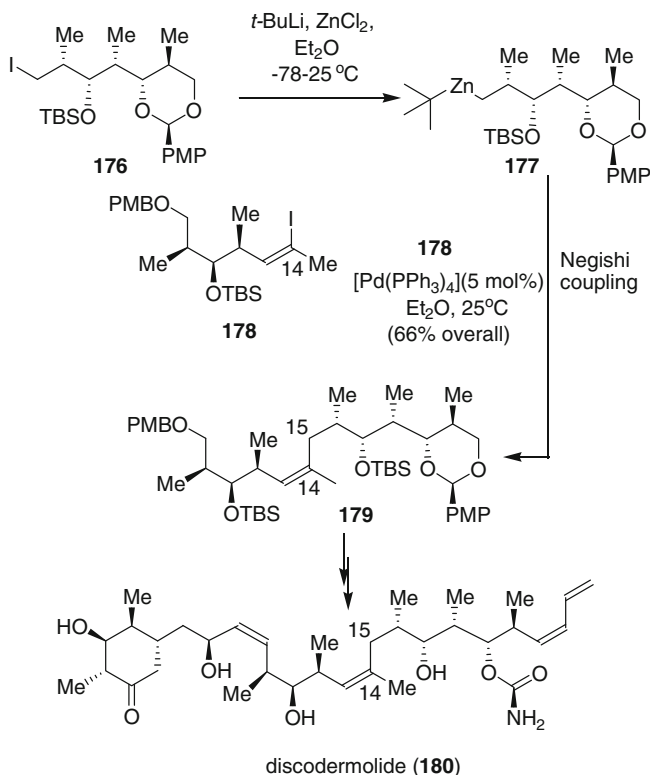
Scheme 2.31 Application of the Negishi reaction in the total synthesis of discodermolide
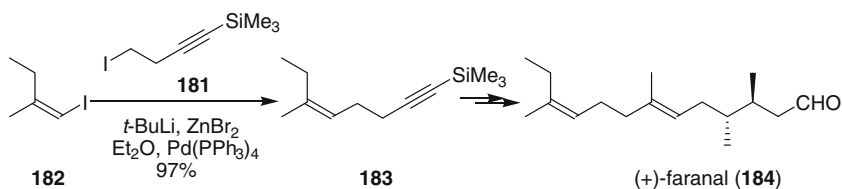
Scheme 2.32 Application of Negishi reaction in the total synthesis of (+)-faranal

In 1998, Dussault and coworker reported their studies on the application of palladium-mediated carbon–carbon bond forming reactions to functionalized peroxides [69]. They found that the peroxides are compatible with a series of Pd-catalyzed cross coupling reactions. In that paper, they used acyclic peroxides in Stille (Scheme 2.33), Heck (Scheme 2.34), and Pd-catalyzed carbonylation reactions of vinyl iodides (Scheme 2.35). These examples demonstrated that peroxides
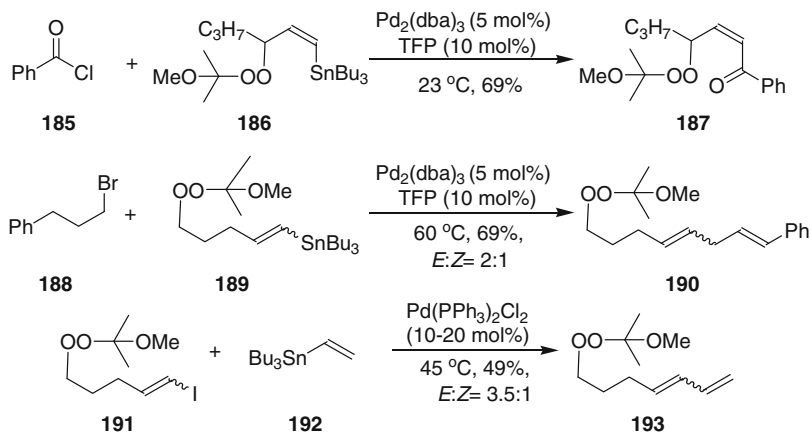
Scheme 2.33 Stille reaction
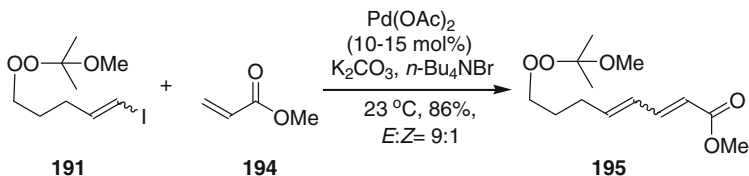
Scheme 2.34 Heck reaction
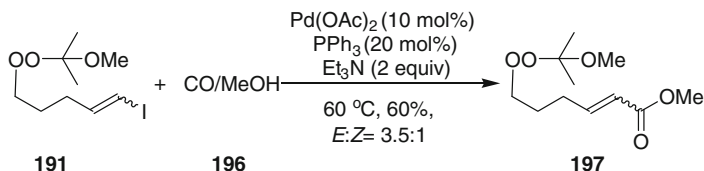
Scheme 2.35 Pd-catalyzed carbonylations of vinyl iodide reactions

are stable to the conditions for a series of palladium-catalyzed carbon–carbon bond formation reactions.

Dussault and coworkers observed that acyclic peroxides were reduced under the conditions of the Sonogashira reaction. However, in the syntheses of polyunsaturated peroxides peroxyacarnoate A (**203**) and peroxyacarnoate D (**204**) [70], the Sonogashira reaction was successfully employed for the key coupling reactions (Scheme 2.36). Taken together, these results encouraged us in our planned use of Pd-catalyzed cross coupling reactions in our total synthesis of plakortide E.
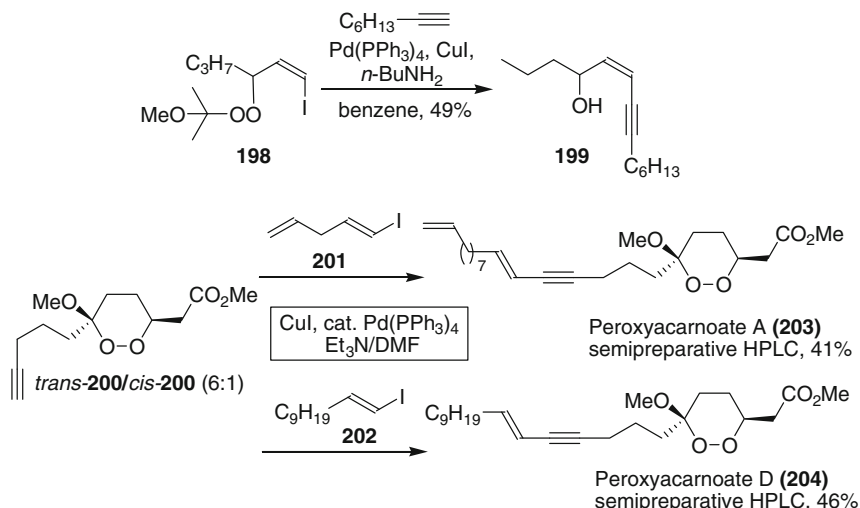
Scheme 2.36 Syntheses of polyunsaturated peroxides
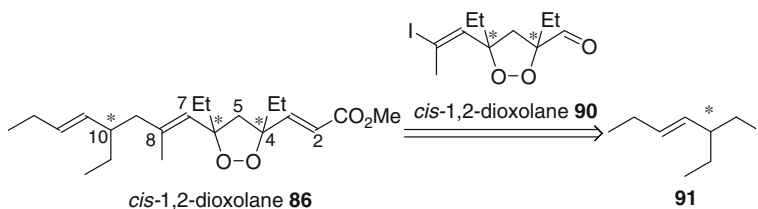
Scheme 2.37 The coupling of the side chain **91** and the central core **90**

In our retrosynthetic analysis of the total synthesis of plakortide E, the coupling of the side chain **91** with the cyclic peroxide containing central core **90** is one of the challenging issues (Scheme 2.37). Side chain **91** is an alkyl iodide, and the centre core is an 1,2-dioxolane-containing alkenyl iodide. So the C7–C8 bond formation is in fact an issue concerning $C(sp^2)$–$C(sp^3)$ coupling.

The organozinc reagents mentioned before show only moderate reactivity towards many organic electrophiles, However, they are among the most reactive of nucleophilic species in palladium-catalyzed cross-coupling reactions. This is due to the fact that in contrast to other organometallic reagents, organozinc reagents undergo rapid transmetalation with transition-metal salts, most notably those of palladium [62]. Based on these facts, we thought the Negishi cross-coupling reaction was suitable for application to the peroxide-containing substrate, because the moderate nucleophilicity of organozinc reagents would decrease their reactivity towards organic peroxides.
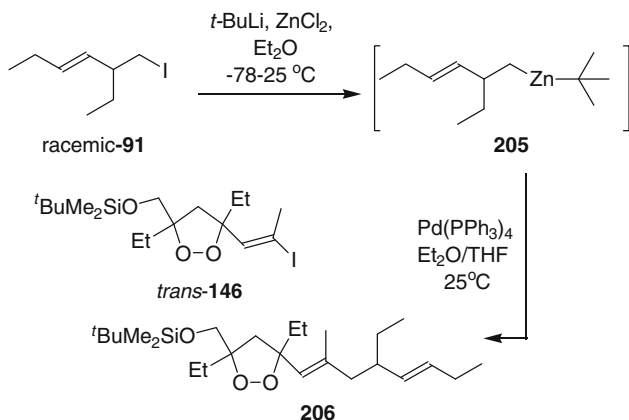
Scheme 2.38 Negishi coupling (condition I)

We proceeded to test this reaction with a model study. With the side chain (±)-**91** and *trans*-1,2-dioxolane-containing alkenyl iodide **146** in hand, we attempted to couple the two components together. The modified Negishi coupling protocol developed by Smith's group was demonstrated as an efficient method for $C(sp^2)$–$C(sp^3)$ bond formation in their gram-scale synthesis of discodermolide [8, 9]. Inspired by their success, we directly employed the modified Negishi coupling protocol to our model reaction (Scheme 2.38). To a solution of iodide (±)-**91** (1.2 equiv) and $ZnCl_2$ (1.2 equiv) in Et_2O at −78 °C, *t*-BuLi (3.6 equiv) was added, and was followed by warming the reaction mixture to room temperature. Then alkenyl iodide **146** (1.0 equiv) and $Pd(PPh_3)_4$ (10 mol%) in THF were added to the reaction mixture. The reaction mixture was stirred at room temperature for 16 h. After work-up and flash column chromatography, a colorless oil was obtained. The ^1H NMR spectrum indicated that a 4:1 mixture of our expected coupling product **206** and an unknown side product was furnished. Unfortunately the side product cannot be removed by column chromatography.

To obtain the pure coupling product **206**, we optimized the Negishi cross-coupling reaction. The side chain was easily prepared by reported methods [5, 61]. However, the 1,2-dioxolane-containing alkenyl iodide was not readily available. Due to the above facts, we considered to use an excess of the side chain in order to improve the yield and the purity of the expected coupling product. In accordance with the literature, $ZnBr_2$ was used instead of $ZnCl_2$ [10]. The reaction was then performed under the improved conditions (Scheme 1.3). To a solution of iodide (±)-**91** (1.0 equiv) and $ZnBr_2$ (1.3 equiv) in Et_2O, *t*-BuLi (2.0 equiv) was added at −78 °C. The mixture was stirred at −78 °C for 30 min. Then the temperature was allowed to warm to room temperature and the reaction mixture was stirred for 1 h. Subsequently, alkenyl iodide **146** (0.4 equiv) and $Pd(PPh_3)_4$ (4 mol%) in THF were added to the above reaction mixture. The reaction mixture was stirred at
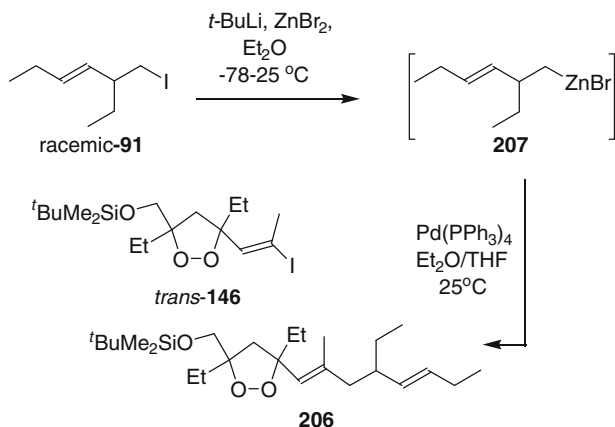
Scheme 2.39 Negishi coupling (condition II)
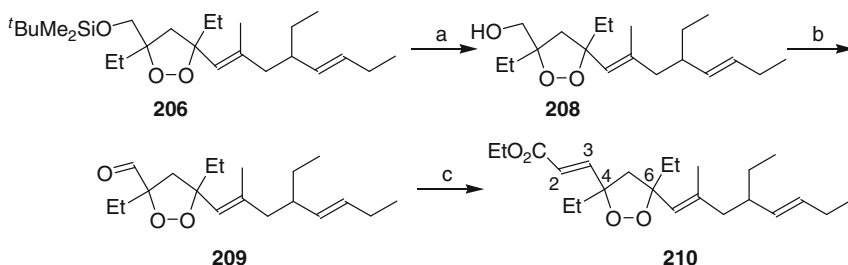
Scheme 2.40 Synthesis of model product **210**. **Reagents and conditions**: (a) *p*-TsOH (10 mol%), CH$_2$Cl$_2$/MeOH (1:2), 89%; (b) Dess–Martin periodinane (1.5 equiv), CH$_2$Cl$_2$; (c) (EtO)$_2$P(O)CH$_2$CO$_2$Et (2.0 equiv), NaH (1.9 equiv), THF, 0 °C, 80% (2 steps)

room temperature for 16 h (Scheme 2.39). After flash column chromatography, the desired coupling product was obtained in good yield (>80%) as the only product. No side product was found by ^{1}H NMR spectroscopy.

After we successfully obtained the crossing coupling product **206**, we continued to study the total synthesis of plakortide E. To our delight, the successive conversions were achieved smoothly (Scheme 2.40). The crossing coupling product **206** was subjected to a *p*-TsOH mediated desilylation to give the free hydroxy intermediate **208** in 89% yield [20]. Dess–Martin oxidation of **208** afforded an aldehyde **209**, whose Horner–Wadsworth–Emmons olefination with triethyl phosphonoacetate gave **210** in a good yield [11–13]. The coupling constant between H-2 and H-3 of **210** was found to be 15.8 Hz, indicating *trans* stereochemistry of the C2–C3 disubstituted double bond (Scheme 1.6). Until now, all fundamental reactions related to the total synthesis of plakortide E were well

studied. The successful completion of this model sequence was very helpful to our total synthesis of plakortide E.

2.5 Synthesis of Chiral Side Chains

In our project, the four possible structures of plakortide E will be synthesized. For this reason, both chiral side chains (R)-**91** and (S)-**91** were needed (Fig. 2.8). The syntheses of these two compounds have been reported in the literature (Scheme 2.41) [4, 5, 71–75].

Commercially available L-phenylalanine (**211**) was reduced by LiAlH$_4$ to give amino alcohol **212** in good yield, which was converted to (S)-4-benzyl-2-oxazo-lidinone (**213**) with potassium dicarbonate/diethyl carbonate [75]. Then the Evans reagent **213** was treated with n-BuLi/butyryl chloride to furnish imide **214** [74]. The subsequent reaction of **214** with (benzyloxy)methyl chloride (BOMCl) in the presence of TiCl$_4$ and Et$_3$N at 0 °C produced imide **215** as a single stereoisomer in 77% yield. Hydrogenolysis of **215**, followed by protection of the resulting alcohol **216** with t-BuMe$_2$Si group, quantitatively provided **217** (Scheme 2.41) [73]. Reduction of **217** with LiBH$_4$ furnished (S)-**167** in 85% yield [73].

As shown in Scheme 2.41, 7 steps were needed in the synthesis of the chiral intermediate (S)-**167**, starting from the commercial available L-phenylalanine (**211**). The synthesis of its enantiomer of (R)-**167** also should involve similar steps. In consideration of a step-economic synthetic strategy, we sought to develop an alternative synthetic route to realize the chiral side chain (R)-**91** and (S)-**91** (Scheme 2.42). In our model studies for the synthesis of the racemic side chain, the racemic-**167** as the intermediate was easily prepared in only two steps from commercially available ethyl diethyl malonate (**116**). The lipase catalyzed kinetic resolution of racemic-**167** was employed in the total synthesis of rutamycin B and oligomycin C, and showed excellent enantiomeric excess [61]. We envisioned to use this method to prepare the optically pure (S)-**167** and (R)-**167** in only one step. If we employed the synthetic route described in Scheme 2.41, there were totally 14 steps required to prepare (S)-**167** and (R)-**167**. According to the literature, the kinetic resolution of racemic **167** was performed. To a solution of racemic **167** in pentane, the lipase extract and vinyl acetate were added. The reaction mixture was stirred vigorously for 24 h. Then the reaction mixture was filtered to remove the lipase catalyst. Purification by column chromatography furnished acetate (R)-**218** in 47% yield and alcohol (S)-**167** in 46% yield. On the other hand, hydrolysis of acetate (R)-**218** gave the enantiomeric alcohol (R)-**167** (Scheme 2.42). A comparison of the specific rotation with literature values is shown in Table 2.17 [76, 77].

We also assessed the enantiomeric purity of (S)- and (R)-**167** by analyses of the ^{1}H NMR and ^{13}C NMR spectra of the diastereomeric derivative **220**. Our synthetic chiral compound (R)-**167** reacted with optically pure N-Boc protected L-phenylalanine (**219**) to afford the diastereomeric derivative **220** [78], which was

Fig. 2.8 Enantiomerically pure side chains
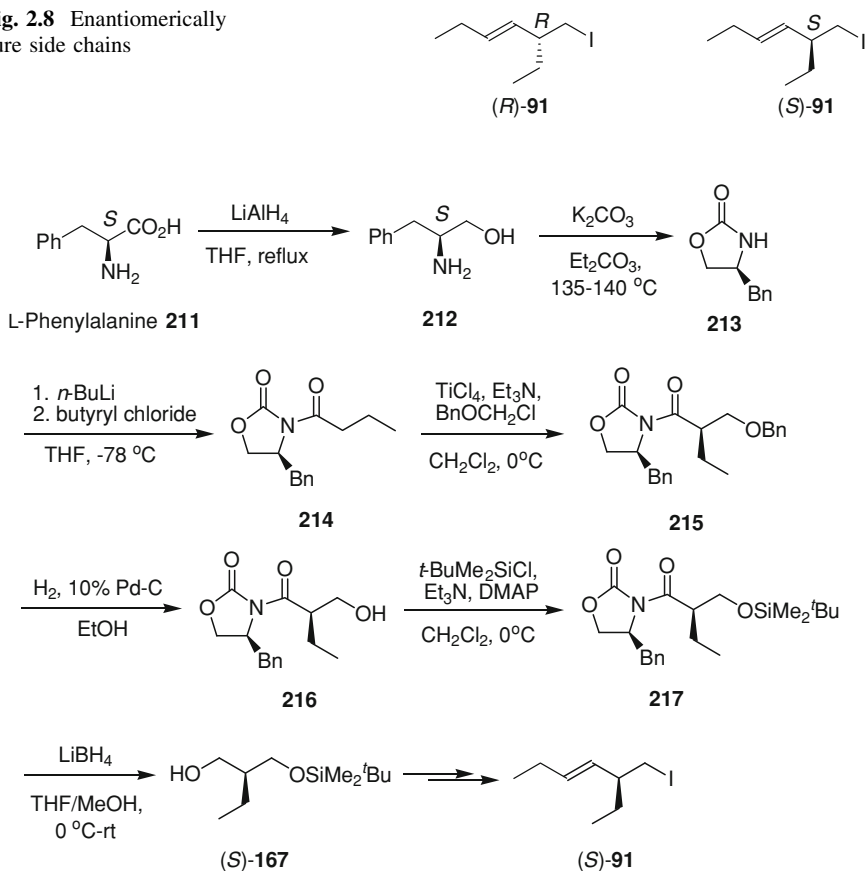
Scheme 2.41 Synthesis of side enantiomerically pure side chain

analyzed by the ^{1}H NMR and ^{13}C NMR spectroscopy (Scheme 2.43). The NMR spectra indicated that compound **220** was very pure, with virtually no trace of the diastereoisomer (dr > 95%).

After the enantiomerically pure (R)-**167** and (S)-**167** were obtained, we proceeded to continue the syntheses of enantiomerically pure side chains of plakortide E. Since all related reactions have been well studied in model studies, we found it straightforward to convert the desired enantiomerically pure side chains (R)-**91** and (S)-**91**. The synthetic route is shown in Scheme 2.44. The enantiomerically pure alcohol (R)-**167** was first subjected to Swern oxidation. After oxidation, a colorless oil of aldehyde **221a** was generated and was used immediately in the Julia olefination. When KHMDS was used as the base, the desired 1,2-disubstituted olefin **222a** was obtained in 89% yield (two steps) [4, 5]. From 1,2-disubstituted olefin **222a**, p-TsOH mediated desilylation helped to remove the t-BuMe$_2$Si group to
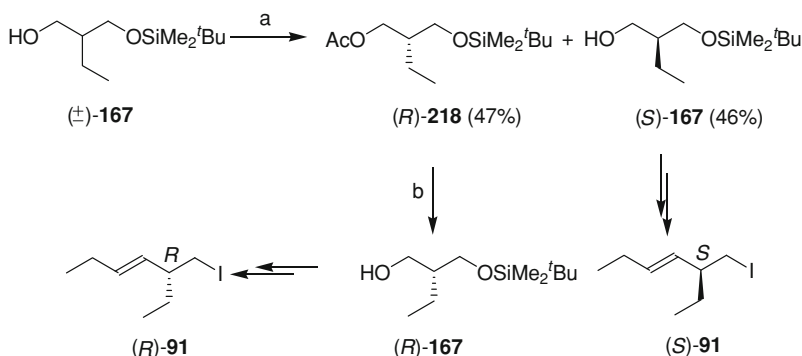
Scheme 2.42 An alternative synthetic route for enantiomerically pure side chains. **Reagents and conditions** : (a) Lipase PS30, vinyl acetate, pentane, rt, 24 h; (b) K$_2$CO$_3$, MeOH, 99%

Table 2.17 Comparison of specific rotations

Entry	Compound	$[\alpha]_D^{20}$	Literature
1	HO OSiMe$_2{}^t$Bu	$[\alpha]_D^{20} = -10.6$ (c, 0.99, CHCl$_3$) (nearly 100% ee)	[76]
2	HO OSiMe$_2{}^t$Bu	$[\alpha]_D^{20} = -11.41$ (c, 1.42, CHCl$_3$) (>99% ee)	[77]
3	HO OSiMe$_2{}^t$Bu (S)-**167**	$[\alpha]_D^{20} = -10.7$ (c, 1.37, CHCl$_3$)	Our synthetic compound
4	HO OSiMe$_2{}^t$Bu (R)-**167**	$[\alpha]_D^{20} = 10.6$ (c, 1.67, CHCl$_3$)	Our synthetic compound

give the free hydroxy intermediate **223a** as a colorless oil in 86% yield. Alcohol **223a** was converted with PPh$_3$/I$_2$/imidazole to iodide (R)-**91** in 86% yield. In a similar manner, enantiomerically pure side chain (S)-**91** was also synthesized [4, 5].

2.6 Syntheses of Enantiomerically Pure Dioxolane Cores

Syntheses of enantiomerically pure central cores via chemical resolution. Chemical resolution is an established method for producing optically pure compound as single enantiomers. A racemic compound is reacted with an optically
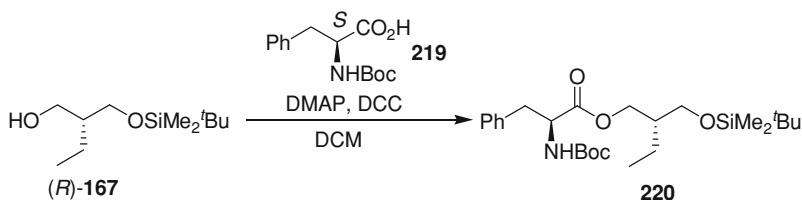
Scheme 2.43 Formation of the diastereomeric derivative **220**
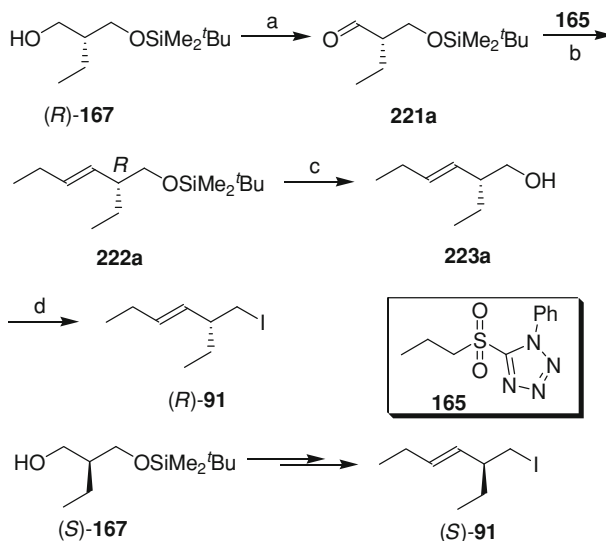
Scheme 2.44 Syntheses of enantiomerically pure side chains. **Reagents and conditions**: (a) $(COCl)_2$, DMSO, Et_3N, CH_2Cl_2, -78 °C; (b) KHMDS (*solid*), Julia reagent , THF, -78 °C to rt, 89% (2 steps); (c) *p*-TsOH, CH_2Cl_2/CH_3OH, 86%; (d) PPh_3, imidazole, I_2, CH_2Cl_2, 0 °C to rt, 86%

pure reagent to form a pair of diastereomers, which can be separated by conventional techniques, such as column chromatography. This method was first introduced by Louis Pasteur in 1853, who successfully resolved racemic tartaric acid with optically active (+)-cinchotoxine.

Scheme 2.45 illustrates the planned resolution. To prepare the optically pure cyclic peroxide, we planned to start from *cis*-**137**. Thus, oxidation of the aldehyde **224** leads to the acid **225**, which is allowed to react with the chiral amine **226** to furnish a pair of diastereomers **227** and **228**. Then the diastereomers are separated by column chromatography.

To our disappointment, oxidation of aldehyde **224** with $NaClO_2$ did not successfully furnish the corresponding acid **225**; instead, the aldehyde decomposed. TLC indicated that the reaction was very complicated. On the other hand, attempts
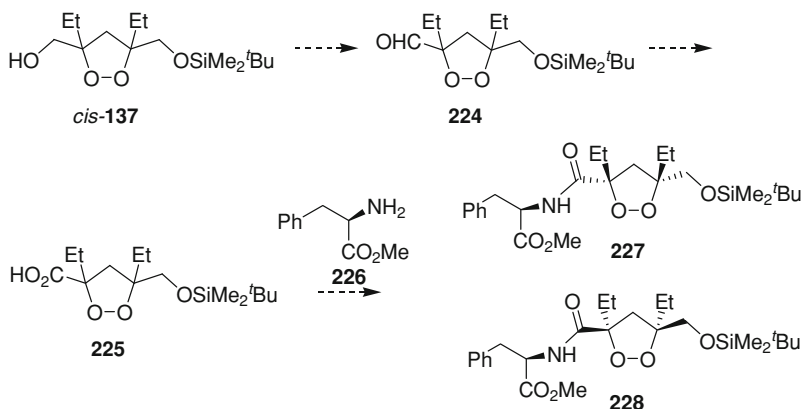
Scheme 2.45 Chemical resolution of racemic *cis*-1,2-dioxolane alcohol

Table 2.18 Oxidations of racemic *cis*-1,2-dioxolane alcohol

Entry	Reaction conditions	Results
1	NaClO$_2$, H$_2$O$_2$, NaH$_2$PO$_4$, THF, rt	Complicated
2	PDC, DMF, rt, 10 h	Complicated

to oxidize aldehyde **224** with PDC in DMF also did not lead to the desired acid **225** [79]. The results are summarized in Table 2.18.

One reason for these failures was presumably due to the sensitivity of the *t*-BuMe$_2$Si group. We therefore designed an alternate route replacing the *t*-BuMe$_2$Si protecting group with a Bn group. Another route of chemical resolution was therefore designed (Scheme 2.46). Thus, racemic *cis*-1,2-dioxolane alcohol **137** is protected with Bn group to give **229**, whose *t*-BuMe$_2$Si group is removed to afford the free alcohol **230**. Oxidation of the racemic *cis*-1,2-dioxolane alcohol **230** leads to the acid **231**, which reacts with enantiomerically pure amine **226** to furnish the diastereomers **231** and **232**. Then the diastereomers are separated by column chromatography.

However, the protection of the racemic *cis*-1,2-dioxolane alcohol **137** with benzyl bromide is problematic. The reaction conditions are depicted in Table 2.19 [80–82]. In all cases, TLC indicated that no expected product was produced. However, the starting material was consumed. The racemic *cis*-1,2-dioxolane alcohol **137** was found to decompose easily under these reaction conditions. For this reason, we had to abandon this chemical resolution route.

Due to the aforementioned failure, we had to seek other milder reactions to accomplish the resolution of racemic *cis*-1,2-dioxolane alcohol **137**. Finally,
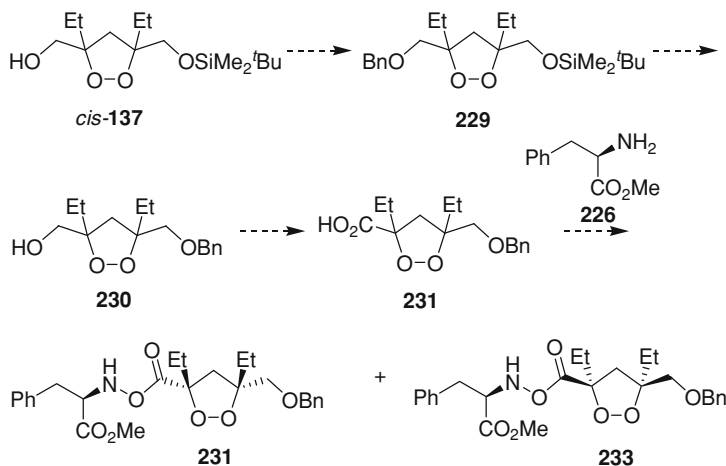
Scheme 2.46 An alternative chemical resolution route of racemic *cis*-1,2-dioxolane alcohol **137**

Table 2.19 Reaction conditions for protection of the racemic *cis*-1,2-dioxolane alcohol 137 with benzyl bromide
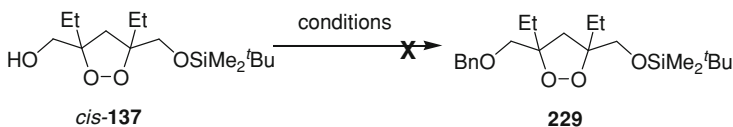
Entry	Reaction conditions	Results
1	BnBr, NaH, DMF	Complicated
2	BnBr, Ag₂O, DMF	Complicated
3	BnBr, NaH, TBAI, THF	Complicated

we found the racemic *cis*-1,2-dioxolane alcohol **137** reacted with *N*-Boc protected L-phenylalanine (**219**) smoothly in the presence of DMAP/DCC to furnish the diastereomers **234** and **235** (Scheme 2.47) [78]. However, their diastereomers could not be separated by column chromatography. In principle, diastereomers **234** and **235** could be converted to other derivatives that might be separable. However, this approach is not step-economical for our total synthesis of plakortide E. We therefore moved onto enzymatic resolution of the 1,2-dioxolane core.

Syntheses of enantiomerically pure central cores by lipase-catalyzed kinetic resolution. Enzymes are proteins that catalyze a vast number of chemical reactions [14, 15, 83, 84]. The history of enzyme is very long, which can go back to thousands of years to ancient Egypt [14, 15]. Over the last few years, more and more organic chemists have recognized the potential of biocatalysis as a viable and popular technique in organic synthesis. Compared to other catalysts, the
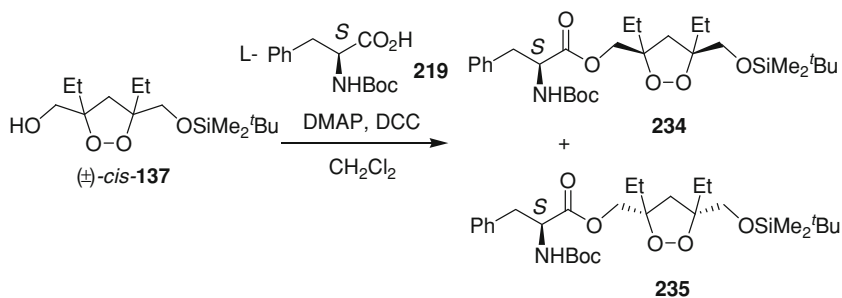
Scheme 2.47 Formation of diastereomeric derivatives of racemic *cis*-1,2-dioxolane alcohol

Fig. 2.9 A computer-generated image of a type of pancreatic lipase (PLRP2) from the guinea pig
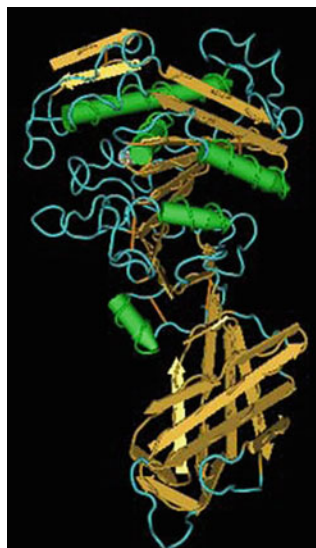
advantages of enzymes are quite obvious. It is known that reactions catalyzed by enzymes are more selective and efficiently performed.

There has been a dramatic increase in the number of publications in the field of lipase-catalyzed reactions. Lipases are ubiquitous water-soluble enzymes that catalyze the hydrolysis of ester chemical bonds and can be found in animals, plants, fungi and bacteria [14, 15, 85–88]. A computer-generated image of a type of pancreatic lipase from the guinea pig is showed in Fig. 2.9. Traditionally, biocatalysis are performed in aqueous medium. However, water is a poor solvent for organic chemistry, since most organic compounds are very sparingly soluble and are sometimes unstable in aqueous solutions. Side reactions such as hydrolysis, racemization, polymerization and decomposition often take place easily in water medium. As a result, chemists have developed procedures for the use of enzymes in organic solvents. Now, enzymatic catalysis in non-aqueous media has significantly benefited the chemistry of lipase catalysis [89, 90].

1. Hydrolysis
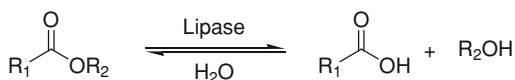
2. Esterification
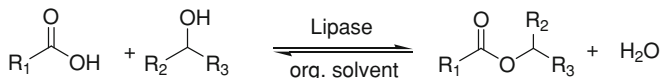
3. Transesterification
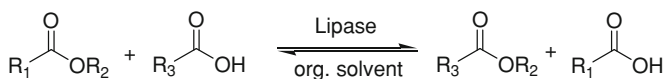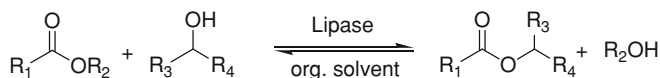
4. Interesterification
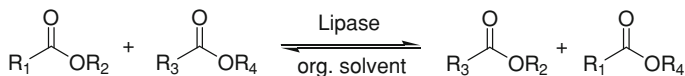
Scheme 2.48 Reactions catalyzed by lipase

Lipases as organocatalysts are widely used in three main types of asymmetric transformations [91]. They are (a) kinetic resolution of racemic carboxylic acids or alcohols, (b) transformations of meso dicarboxylic acids or meso diols and (c) transformations of prochiral dicarboxylic acid and diol derivatives. In kinetic resolutions, theoretical yields are limited to 50%. Through enantiotopic group differentiation of meso dicarboxylic acids or meso diols, yields of up to 100% are possible [92]. Some typical reactions catalyzed by lipases are depicted in Scheme 2.48.

According to IUPAC recommendation, kinetic resolution (KR) is defined as the achievement of partial or complete resolution by virtue of unequal rates of reaction of the enantiomers in a racemate with a chiral agent (reagent, catalyst, solvent, etc.) [92].

The enzyme catalyzed reactions and the lipase-catalyzed kinetic resolutions have been reviewed [14, 15]. The following section describes some selected examples of lipase-catalyzed resolutions.

In 1997, an efficient method [93, 94] to prepare enantiomerically pure (S)-(+)-**236** and (R)-(+)-**237** by a lipase-catalyzed kinetic resolution was reported by Sakai. Their reactions were carried out preferentially at −40 °C (Scheme 2.49). Recently, in their continuing program, porous ceramic (Toyonite)-immobilized lipase (PSCII) was used in the resolution of (±)-**238** at low temperature, giving the
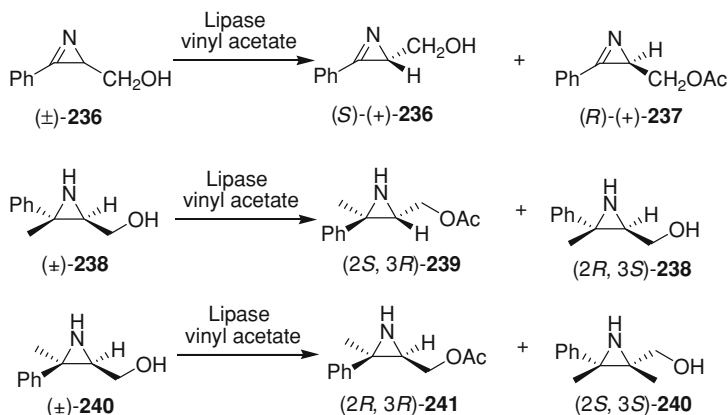
Scheme 2.49 An efficient method to prepare enantiomerically pure alcohols by lipase-catalyzed kinetic resolution
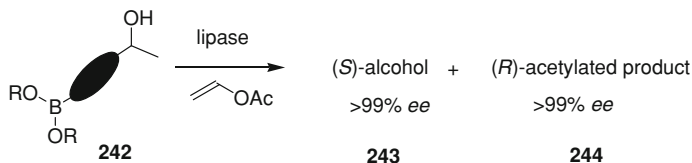
Scheme 2.50 The lipase-catalyzed kinetic resolution of boron-containing alcohols

synthetically useful (2R, 3S)-**238** and its acetate (2S, 3R)-**239** with (2S)-selectivity ($E = 55$ at -40 °C), while a similar reaction of ($\pm$)-**240** gave (2S, 3S)-**240** and its acetate (2R, 3R)-**241** with (2R)-selectivity ($E = 73$ at -20 °C) (Scheme 2.49). Two special points in this example are intriguing and are worthy of mentioning. First, substrates ($\pm$)-**238** and ($\pm$)-**240** belong to an interesting class of primary aziridine alcohols, which feature two stereogenic centers at the β- and γ-carbons. Before this report, there were few examples of the lipase-catalyzed reaction for such 2-aziridinemethanols. Second, the substrates without N-protection were directly used in the reactions. These outcomes inspired us to use the lipase-catalyzed resolution to realize the enantiomerically pure *cis*-1,2-dioxolane containing alcohols, which also feature two stereogenic centers [93, 94].

Boron compounds are useful as potential enzyme inhibitors. Recently, a highly enantioselective lipase-catalyzed kinetic resolution of boron-containing alcohols was reported. It was found that aromatic, allylic, and aliphatic secondary alcohols containing a boronate ester or boronic acid group (*viz.* **242**) were resolved by lipase from *Candida antartica* (CALB). Excellent E values ($E > 200$) and high enantiomeric excesses (>99%) of **243** and **244** were obtained (Scheme 2.50) [95]. This example extends the scope of the lipase-catalyzed kinetic resolutions.

Table 2.20 Optimization for the kinetic resolution of (±)-*cis*-**137**

HO~~O−O~~OSiMe₂ᵗBu (±)-*cis*-**137** → Lipase / vinyl acetate / Hexane →

HO~~O−O~~OSiMe₂ᵗBu *cis*-**137**
+
AcO~~O−O~~OSiMe₂ᵗBu *cis*-**245**

Lipase source	Time	Alcohol			Ester		
		Yield (%)	ee (%)	Specific rotation	Yield (%)	ee (%)	Specific rotation
Lipase CR	40	68	34	−6.6	31	49	10.0
Lipase BC	3	53	78	23.5	45	94	−21.5
	5	49	89	26.3	46		−21.5
	29	43	>99	28.5	55		
	3	56			41	>99ᵃ	−21.5

Lipase CR Candida rugosa lipase, *Lipase BC* Lipase PS from *Burkholderia cepaci*
[a] Resolution two times, the *ee* was determined by chiral HPLC

With the desired mono-protected alcohol (±)-*cis*-**137** in hand, the lipase-catalyzed kinetic resolution of *cis*-1,2-dioxolane-containing alcohol was investigated [14, 15, 61]. Results of these studies are summarized in Table 2.20. Lipase PS from *Burkholderia cepaci* was found to give the best kinetic resolution outcome. We observed that prolongation of the reaction time to 29 h provided the optically pure alcohol, which showed excellent enantiomeric excess (>99% *ee*). When the reaction was quenched after 3 h, the optically pure ester was obtained (94% *ee*). We were able to secure the optically pure ester in excellent enantiomeric excess (>99% *ee*) by repeating the resolution on partially resolved material.

2.7 Total Synthesis of Four Possible Structures of Plakortide E Methyl Ester

With the enantiomerically pure 1,2-dioxolane-containing alcohol *cis*-**137** and ester *cis*-**245**, enantiomerically pure side chain (*R*)-**91** and (*S*)-**91** in hand, we assembled the four possible plakortide E methyl esters structures using the chemistry worked out in our model sequences. The routes are illustrated in Scheme 2.51.

Preparation of enantiomerically pure *cis*-1,2-dioxolane-containing alkenyl iodide 246a and 246b. As shown in Scheme 2.52, oxidation of **137a** with Dess–Martin periodinane (DMP) produced a 1,2-dioxolane-containing aldehyde. Thus, the 1,2-dioxolane-containing aldehyde was treated with freshly prepared CHBr₂PPh₃Brand *t*-BuOK, giving dibromoalkene **247a** in good yield with
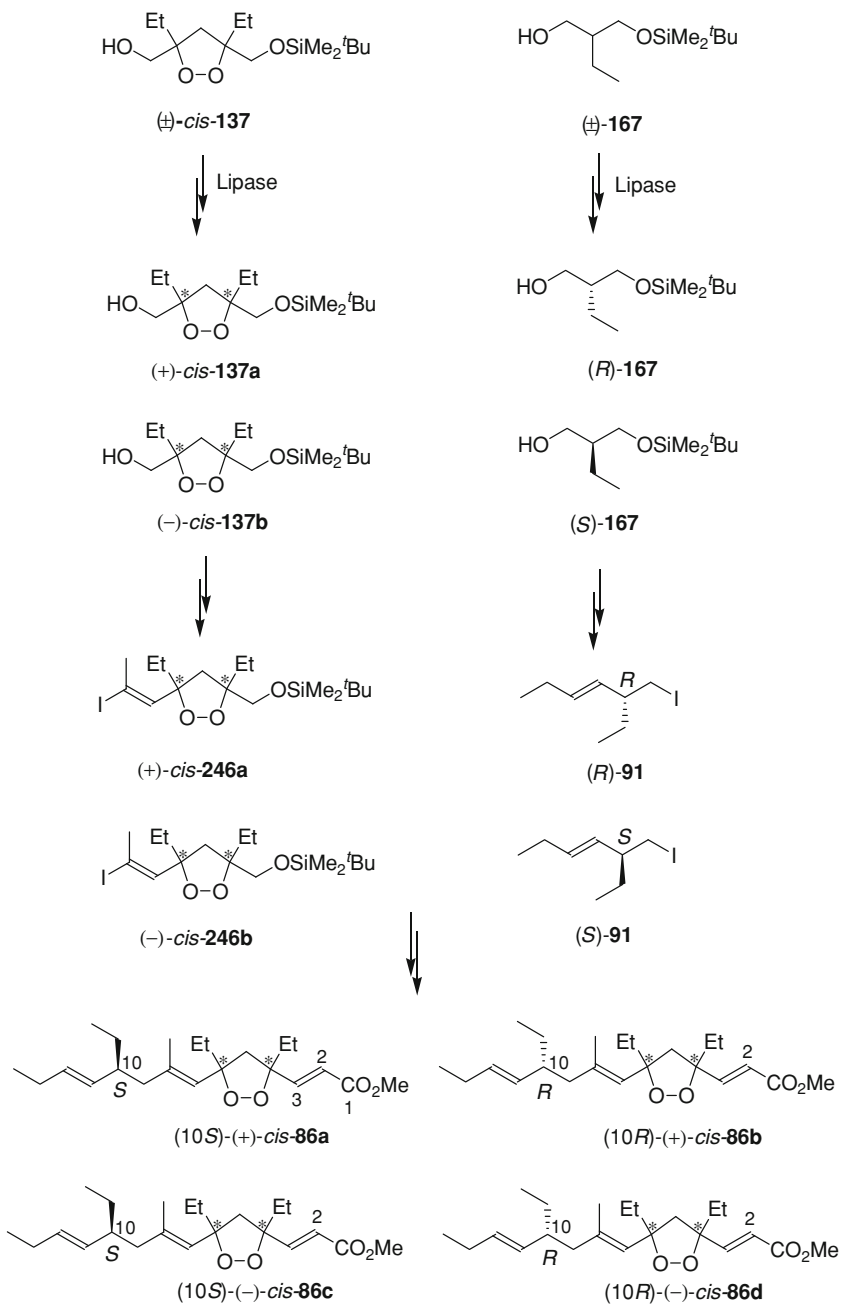
Scheme 2.51 Total synthesis of four possible structures of Plakortide E methyl ester
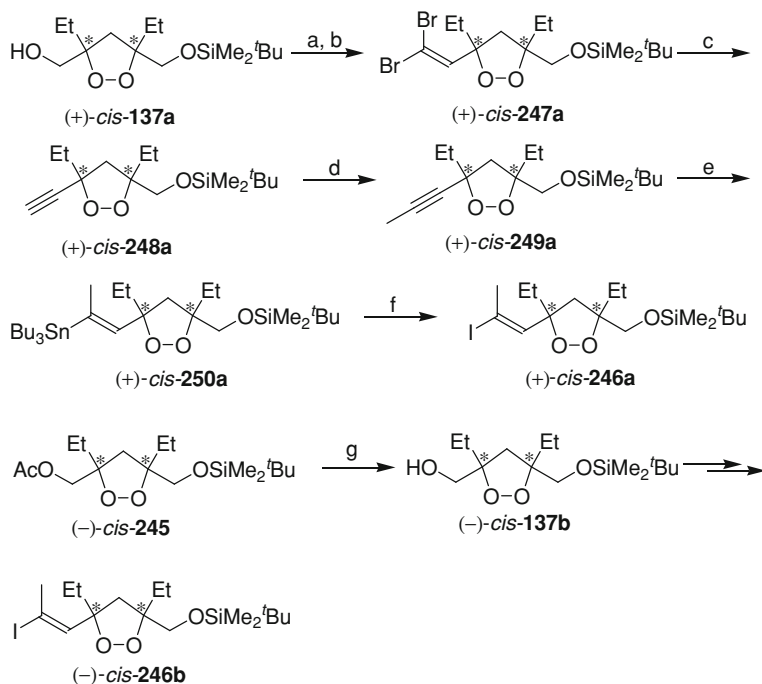
Scheme 2.52 Syntheses of enantiomerically pure **246a** and **246b**. **Reagents and conditions**: (a) Dess–Martin periodinane (1.5 equiv), CH_2Cl_2; (b) $CHBr_2P^+Ph_3Br^-$ (2.5 equiv), t-BuOK (2.4 equiv), THF, rt, 79% (2 steps); (c) n-BuLi (2.2 equiv), THF, −78 °C, 0.5 h, 95%; (d) n-BuLi (1.2 equiv), MeOTf (1.5 equiv), THF, −78 °C, 1 h, 70%; (e) $Pd(PPh_3)_2Cl_2$ (10 mol%), n-Bu_3SnH (3.0 equiv), Hexane, 1 h, 84%; (f) I_2 (1.0 equiv), CH_2Cl_2, 0 °C, 86%; (g) K_2CO_3 (1.0 equiv), MeOH, 94%

excellent reproducibility [52]. Preparation of terminal alkyne **248a** was subsequently achieved by treatment of **247a** with n-BuLi, followed by methylation to provide **249a** [5]. In the presence of a catalytic amount of $PdCl_2(PPh_3)_2$, **249a** underwent regiospecific hydrostannylation to furnish **250a** in 84% yield. Subsequent iodination of **250a** led to the formation of the key alkenyl iodide **246a**. On the other hand, hydrolysis of **245** gave the enantiomeric **137b** in a good yield. In a similar manner, optically pure **246b** was also synthesized (Scheme 2.52). Because all the related reactions had been well executed in the model studies, the syntheses of **246a** and **246b** were achieved smoothly.

   Total synthesis of four possible isomers of plakortide E methyl ester. With the central core (+)-**246a** and side chain (R)-**91** in hand, the Negishi cross coupling reaction was carried out to join the two partners together [10], from which the desired molecule **251a** was generated as the only product. Subsequent p-TsOH mediated desilylation of the t-BuMe$_2$Si group furnished the free hydroxy intermediate **252a** in 89% yield [20]. Dess–Martin oxidation of **252a** afforded an
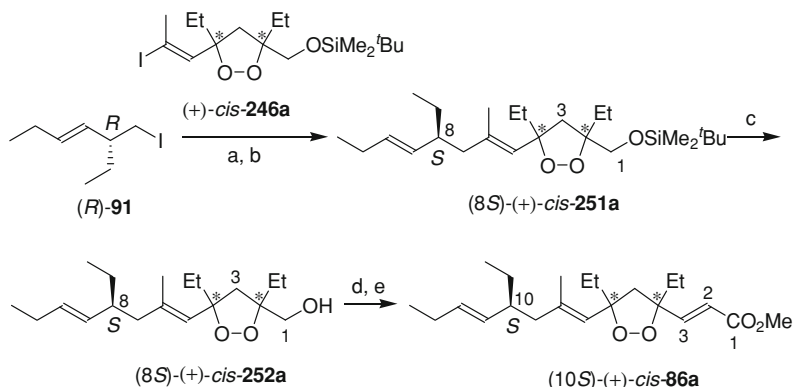
Scheme 2.53 Synthesis of **86a**. **Reagents and conditions**: (a) ZnBr$_2$ (1.3 equiv), *t*-BuLi (2.0 equiv), Et$_2$O/THF, −78 °C to rt; (b) Pd(PPh$_3$)$_4$ (10 mol%), THF, 16 h, 93%; (c) *p*-TsOH (10 mol%), CH$_2$Cl$_2$/MeOH (1:2), 89%; (d) Dess–Martin Periodinane (1.5 equiv), CH$_2$Cl$_2$; (e) (MeO)$_2$P(O)CH$_2$CO$_2$Me (10.0 equiv), NaH (10.0 equiv), THF, 0 °C, 80% (2 steps)
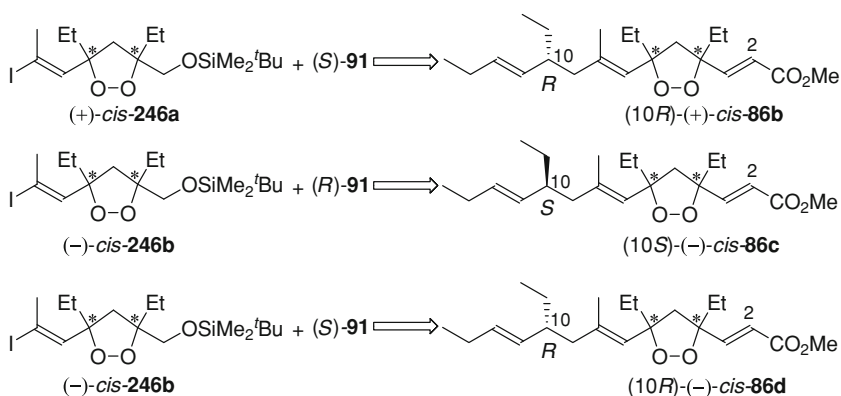
Scheme 2.54 Syntheses of three other possible isomers of plakortide E methyl ester

aldehyde, whose Horner–Wadsworth–Emmons olefination with trimethyl phosphonoacetate gave **86a** in a good yield [11–13]. The coupling constant between H-2 and H-3 of **86a** was found to be 15.8 Hz, indicating the *trans* stereochemistry of the C2–C3 disubstituted double bond (Scheme 2.53).

With the two enantiomerically pure central cores (**246a** and **246b**) and two side chains (*R*)-**91** and (*S*)-**91** available, the other three possible isomers of plakortide E methyl ester were synthesized through similar sequences. All reactions proceeded smoothly to give the other three isomers in good yields (Scheme 2.54).

All four possible isomers of plakortide E methyl ester were synthesized so that a comparison of their NMR spectral data with those of the natural plakortide E

Table 2.21 Comparison of selected ^{1}H NMR chemical shifts (*J* values) and specific rotations

	H5	H7	H19	$[\alpha]_D^{20}$
86a	2.54 (11.9)	5.11	1.61	−86.0
	2.44 (11.9)			
86b	2.58 (11.8)	5.15	1.59	−74.8
	2.44 (11.8)			
86c	2.58 (11.9)	5.15	1.59	+75.0
	2.44 (11.9)			
86d	2.54 (11.9)	5.11 (1.3)[a]	1.61 (1.3)[a]	+87.0
	2.44 (11.9)			
Plakortide E methyl ester [1]	2.54 (12.0)	5.11 (1.3)	1.61 (1.3)	+75.1
	2.44 (12.0)			

[a] Coupling constants were measured by 2D *J*-resolved NMR experiment on an advance Bruker 600M spectrometer

Table 2.22 Comparison of selected ^{13}C chemical shifts

	C-1	C-2	C-3	C-5	C-7	C-8	C-11	C-12
86d	167.1	119.9	149.8	56.0	126.7	136.6	132.8	132.0
Plakortide E methyl ester	166.9	119.9	149.6	55.9	126.7	136.4	132.7	131.9

methyl ester could be made [1]. All ^{1}H and ^{13}C NMR spectra and specific rotation data are included in the experimental section, with the most crucial data being summarized in Tables 2.21 and 2.22. As can be seen, the four synthetic samples can be divided into two pairs of enantiomers (**86a** and **86d**, **86b** and **86c**). Although the differences in their ^{1}H NMR spectra are generally very small, there are considerable differences in the chemical shifts of H-5, H-7 and H-19. While the ^{1}H NMR spectra of the synthetic molecules **86a** and **86d** show good agreement with those of the natural compound, the ^{1}H NMR spectra of compounds **86b** and **86c** exhibit significant differences. It is therefore clear that **86b** and **86c** are not related to the natural product. Because the specific rotation $[\alpha]_D^{20}$ of the natural plakortide E methyl ester ($[\alpha]_D^{20} = +75.1, c = 2.23$ in CHCl$_3$) [1] was found to be in positive value, the value of **86a** is negative ($[\alpha]_D^{20} = -86, c = 0.28$ in CHCl$_3$), indicating that this enantiomer can also be ruled out. It was found therefore that only the ^{1}H NMR spectrum and specific rotation ($[\alpha]_D^{20} = +87.1, c = 0.39$ in CHCl$_3$) of **86d** fit closely with those of the natural plakortide E methyl ester. These results confirm that **86d** possesses an identical structure to the natural plakortide E methyl ester.
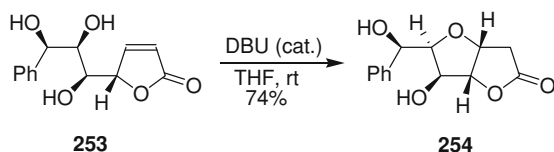
Scheme 2.55 Application of intramolecular Michael addition reaction in the total synthesis of (+)-goniofufurone
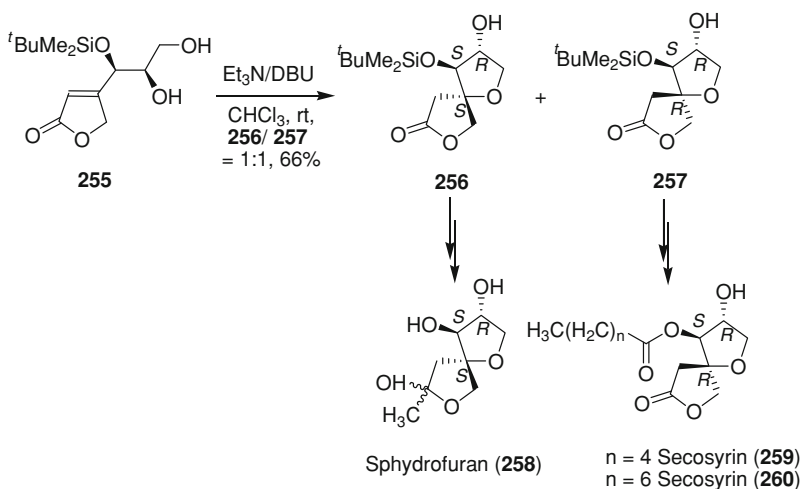
Scheme 2.56 Application of intramolecular Michael addition in the total syntheses of sphydrofuran and secosyrins

2.8 Biomimetic Synthesis of Plakortone B and Determination of the Absolute Configuration of Plakortide E

Over the past few years, the intramolecular Michael addition has become one of the most efficient and simple approaches to the synthesis of furanofuran bicyclic lactone skeleton, which has been widely applied to the total synthesis of natural products containing furanofuran bicyclic lactone skeleton. For example, Shing and coworkers [96] reported the total synthesis of (+)-goniofufurone through an intramolecular Michael addition reaction (Scheme 2.55). Thus, treatment of the butenolide **253** with a catalytic amount of DBU in THF provided the desired lactone **254** in 74% yield.

Our group has used intramolecular Michael addition to prepare the dioxaspiro framework in the syntheses of natural products, including the total synthesis of sphydrofuran and secosyrin (Scheme 2.56) [97].
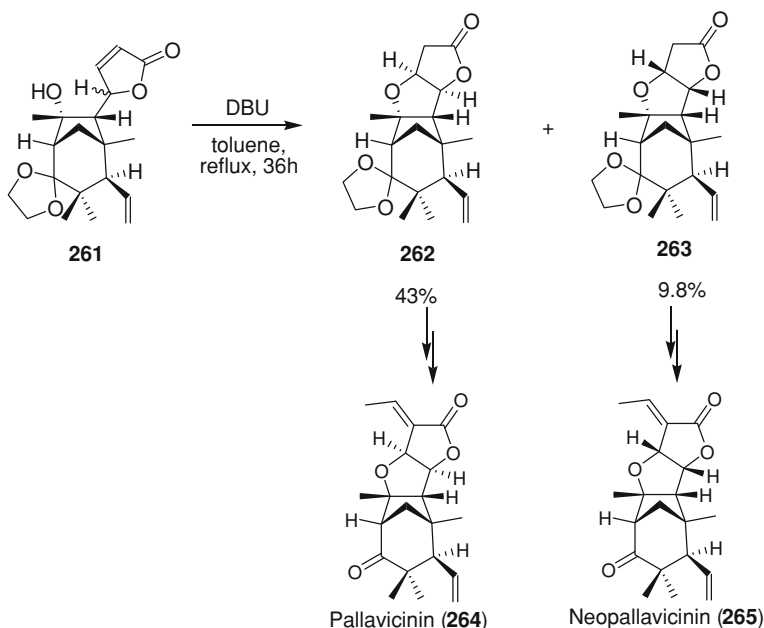
Scheme 2.57 Application of intramolecular Michael addition in the total syntheses of pallavicinin and neopallavicinin

Scheme 2.58 Application of intramolecular Michael addition in the total synthesis of plakortone B
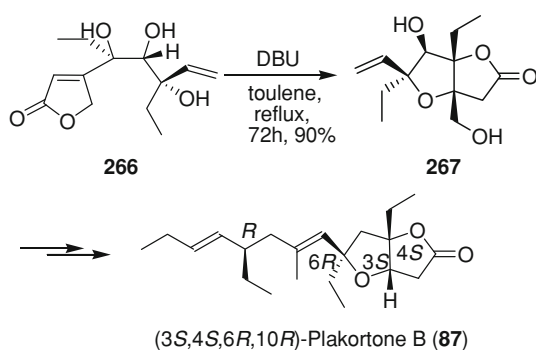
Peng also applied the same protocol to realize the total syntheses of natural products pallavicinin (**264**) and neopallavicinin (**265**) (Scheme 2.57). Treatment of the butenolide mixture **261** with DBU in toluene provided a 4:1 mixture of **262** and **263** [98, 99].

Recently, our group has reported the total syntheses and configuration assignments of all four isomers of plakortone B. The synthesis of the furanofuran bicyclic lactone skeleton was achieved through a stereoselective intramolecular
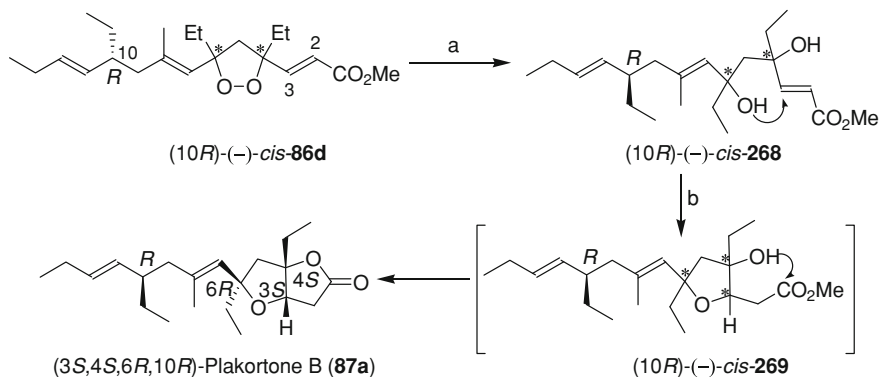
Scheme 2.59 Biomimetic synthesis of plakortone B. **Reagents and conditions**: (a) Zn (50 equiv), AcOH/CH$_2$Cl$_2$ (1:2), 0 °C to rt, 2 h, 99%; (b) DBU (0.2 equiv), toluene, reflux, overnight, 90%
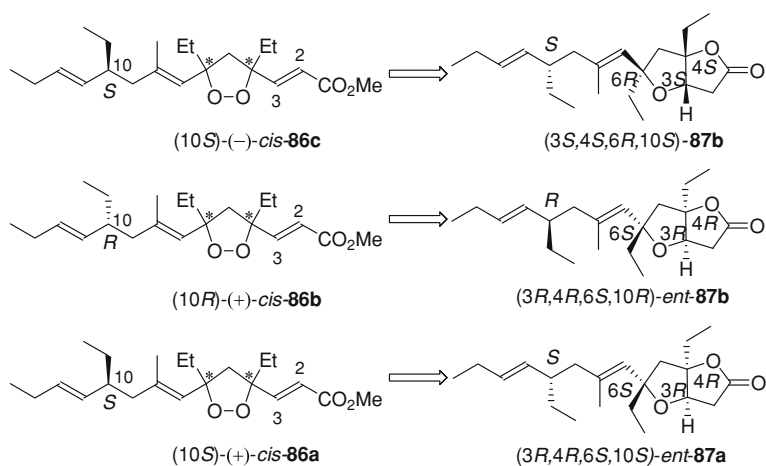
Scheme 2.60 Syntheses of the other three isomers of plakortone B

conjugate addition of an alcohol to an unsaturated lactone; the transformation is chemoselective for one alcohol in the triol substrate (Scheme 2.58) [5].

In consideration that plakortone B (**87a**) was isolated from the same marine sponge together with plakortide E (**85**) [1], we reasoned that plakortide E methyl ester **86d** could be converted to plakortone B (**87a**). In this way, the determination of the absolute configuration of plakortide E methyl ester (**86d**) would be achieved, and this conversion would also provide a concise biomimetic synthesis pathway to plakortone B (**87a**). To begin with, cleavage of the O–O bond of plakortide E methyl ester (**86d**) with zinc in acetic acid provided 1,3-diol **268** in an excellent yield [100]. With the 1,3-diol **268** in hand, our next objective was to

(4R,6S,10S)-**86a**

(4R,6S,10R)-**86b**

(4S,6R,10S)-**86c**

(4S,6R,10R)-**86d**

Plakortide E Methyl Ester
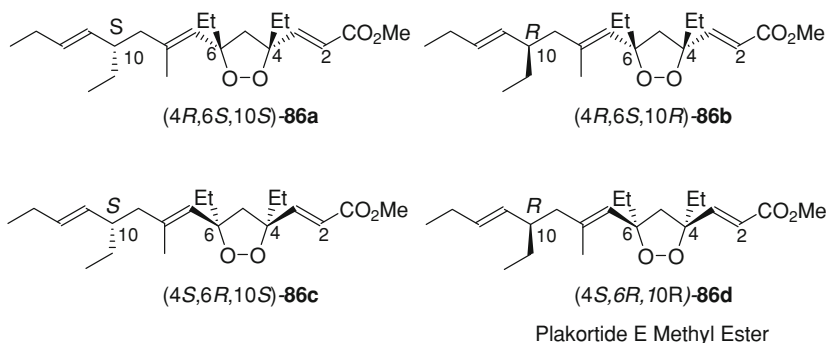
Fig. 2.10 Absolute configurations of four isomers of plakortide E methyl ester

(4S,6R,10R)-**86d**   (4S,6R,10R)-**85a**
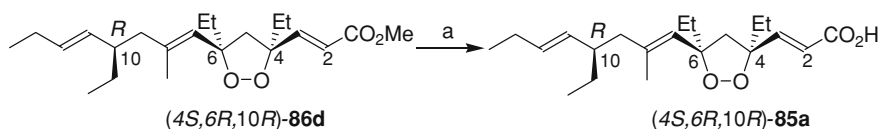
Scheme 2.61 Synthesis of plakortide E. **Reagents and conditions**: (a) LiOH (5.0 equiv), THF/
H_2O (4:1), 0 °C to rt, 24 h, 90%

Table 2.23 Comparison of selected NMR shifts (J values) and specific rotations

	H-2	H-3	H-5	C-1	C-2	C-3	C-5	$[\alpha]_D^{20}$
85a	6.09 (15.7)	6.93 (15.7)	2.43 (12.0)	171.1	119.6	152.1	56.0	66.6
			2.53 (12.0)					
Wright [3]	6.09 (15)	6.93 (15)	2.43 (12)	172.0	120.5	152.1	56.0	63
			2.53 (12)					
Patil et al. [1]	5.98 (15.8)	6.69 (15.8)	2.43 (12)	173.0	123.9	146.9	55.8	63.9
			2.53 (12)					

convert it to the corresponding isomer of plakortone B. Encouraged by our recent success in the preparation of various tetrahydrofurofuranone frameworks towards the syntheses of naturally occurring molecules, an intramolecular Michael addition was employed to achieve this conversion. Thus, the 1,3-diol **268** was subjected to an intramolecular oxa-Michael addition/lactonization cascade reaction. To our delight, our target **87a** was afforded exclusively in 90% yield (Scheme 2.59) [98, 99, 101].

The other three possible isomers of plakortone B were prepared in a similar manner from the three corresponding isomers of plakortide E methyl ester, as can be seen in Scheme 2.60. A comparison of the NMR spectra and the specific rotations of the four synthetic isomers and the reported data of plakortone B (**87a**) and its isomers [5] confirms the absolute configurations of **86a**, **86b**, **86c** and **86d**

to be (4*R*,6*S*,10*S*), (4*R*,6*S*,10*R*), (4*S*,6*R*,10*S*) and (4*S*,6*R*,10*R*). All absolute configurations of plakortide E methyl ester and its isomers are depicted in Fig. 2.10.

2.9 Synthesis of Plakortide E

As depicted in Scheme 2.61, compound **86d** was then saponified to provide the plakortide E (**85a**). Comparisons of the chemical shifts and coupling constants for the synthetic compound and the literature values for plakortide E are summarized in Table 2.23. Our values are identical to those reported by Wright [3]. However, our results and those of Patil [1] show some differences for the ^{13}C NMR chemical shifts of C-1, C-2 and C-3.

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Chapter 3
Conclusion

The key steps included the synthesis of enantiomerically pure dioxolane cores through lipase resolution of a racemic precursor, the introduction of an alkynyl sidechain on a 1,2-dioxolane via a Corey-Fuchs homologation, and the introduction of the sidechain of the natural product through Pd-catalyzed sp^2/sp^3 cross-coupling.

Synthesis of plakortide E methyl ester **86a** (one of the plakortide E candidate structures) was completed in ten steps from (+)-*cis*-**137a** (Scheme 1). The other three possible isomers of plakortide E methyl ester (**86b**, **86c** and **86d**) were synthesized in a similar manner. One of these molecules **86d** was identical to the natural plakortide E methyl ester on the basis of ^{1}H, ^{13}C NMR spectra and specific rotation comparisons.

With the plakortide E methyl ester **86d** and its other three isomers in hand, we successfully converted them into plakortone B (3*S*,4*S*,6*R*,10*R*)-(**87a**), and its isomers *ent*-**87a**, **87b** and *ent*-**87b** via an intramolecular oxa-Michael addition/lactonization cascade reaction. A comparison of the NMR spectra and the specific rotations of the four synthetic isomers (**87a**, *ent*-**87a**, **87b** and *ent*-**87b**) and the reported data of plakortone B and its isomers [1] confirmed the absolute configurations of **86a**, **86b**, **86c and 86d** to be (4*R*,6*S*,10*S*), (4*R*,6*S*,10*R*), (4*S*,6*R*,10*S*) and (4*S*,6*R*,10*R*). The conversion not only provided a concise biomimetic synthesis pathway to plakortone B (**87a**), but also proved the hypothesis that plakortide E was the precursor of the plakortone B in nature.

Saponification converted 1,2-dioxolane **86d** into plakortide E (**85a**) whose absolute configuration (4*S*,6*R*,10*R*) was confirmed by comparison of spectral and physical data with those of reported.
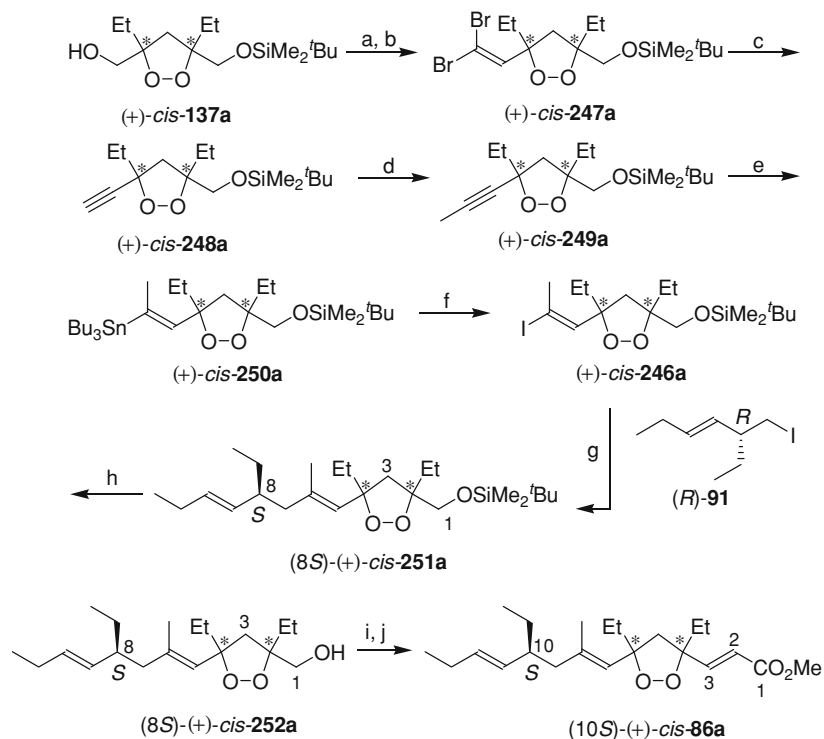
Scheme 1 Synthesis of **86a**. **Reagents and conditions**: (a) Dess–Martin periodinane (1.5 equiv), CH$_2$Cl$_2$; (b) CHBr$_2$P$^+$Ph$_3$Br$^-$ (2.5 equiv), t-BuOK (2.4 equiv), THF, rt, 79% (2 steps); (c) n-BuLi (2.2 equiv), THF, −78 °C, 0.5 h, 95%; (d) n-BuLi (1.2 equiv), MeOTf (1.5 equiv), THF, −78 °C, 1 h, 70%; (e) Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%), n-Bu$_3$SnH (3.0 equiv), Hexane, 1 h, 84%; (f) I$_2$ (1.0 equiv), CH$_2$Cl$_2$, 0 °C, 86%; (g) ZnBr$_2$ (1.3 equiv), t-BuLi(2.0 equiv), Et$_2$O/THF, −78 °C to rt, then Pd(PPh$_3$)$_4$ (10 mol%), THF, 16 h, 93%; (h) p-TsOH (10 mol%), CH$_2$Cl$_2$/MeOH (1:2), 89%; (i) Dess–Martin periodinane (1.5 equiv), CH$_2$Cl$_2$; (j) (MeO)$_2$P(O)CH$_2$CO$_2$Me (10.0 equiv), NaH (10.0 equiv), THF, 0 °C, 80% (2 steps)

Reference

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Chapter 4
Experimental Section

4.1 General Information

All non-aqueous reactions were carried out using oven-dried glassware under a positive pressure of dry nitrogen unless otherwise noted. All reagents and solvents were reagent grade. Further purifications and drying by standard methods were used when necessary. Except as indicated otherwise, reactions were magnetically stirred and monitored by thin layer chromatography (TLC) using Merck silica gel 60 F254 plates and visualized by fluorescence quenching under UV light. In addition, compounds on TLC plate were visualized with a spray of 5% w/v dodecamolybdophosphoric acid in ethanol and with subsequent heating. Chromatographic purification of products (flash chromatography) was performed on E. Merck silica gel 60 (230–400 mesh). All evaporation of organic solvents was carried out with a rotary evaporator. Yields refer to chromatographically and spectroscopically pure compounds, unless otherwise stated.

NMR spectra were recorded on Bruker DRX300 spectrometer, Brucker Advanced III 400 spectrometer and Advanced Brucker 600 M spectrometer. Chemical shifts (δ) are reported in ppm with the solvent resonance as the internal standard relative to chloroform (δ 7.26) or tetramethylsilane (δ 0.00) for ^{1}H and chloroform (δ 77.1) for ^{13}C. Data are reported as follows: brs = broad singlet, s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet; coupling constants in Hz. ^{1}H NMR measurements were carried out at room temperature in deuterated chloroform solution unless otherwise stated. Mass spectra (EIMS and HRMS (ESI)) were obtained with a HP 5989B spectrometer and determined at an ionizing voltage of 70 eV unless otherwise stated; relevant data were tabulated as *m/z*. HPLC analysis was performed on a Hewlett Packard Series 1050 HPLC, or Hewlett Packard Series 1100 HPLC, or Agilent 1100 HPLC with a diode array UV detector (λ = 214–258 nm), using Chiralpak AD-H (0.46 cm × 25 cm). Optical rotations were measured on a Perkin-Elmer model 241 polarimeter operating at the

sodium D line with a 100 mm path length cell and at 20 °C, and were reported as follows: $[\alpha]_D^T$, concentration (g/100 mL), and solvent.

2-Chlorobutyric acid (115) [1, 2]

$$\underset{\underset{\text{Cl}}{|}}{\text{Et}}\diagdown\diagup\text{CO}_2\text{H}$$

115
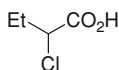
Sulfuryl chloride (366 mL, 4.5 mol) was added dropwise to a solution of butyric acid **114** (265 g, 3 mol) in dimethylformamide (5 mL) in a three-necked round flask fitted with a condenser, drying tube and HCl gas convertor. The reaction mixture was heated to 80–85 °C and then the yellow solution was heated to 90–95 °C for 2 h. Colour change from yellow to colorless was observed. The resulting mixture was distilled carefully to yield 2-chlorobutyric acid (**115**) (106 g) in 29% yield. b.p.: 112 °C/25 torr (Lit: [2] 123 °C/34 torr); ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.08 (t, J = 7.2 Hz, 3H), 1.93–2.17 (m, 2H), 4.28 (t, J = 6 Hz, 1H), 10.77 (s, 1H) ppm; MS (ESI): m/z (M)$^+$ 122.

Ethyl 2-chlorobutyrate (111) [1, 3]

$$\underset{\underset{\text{Cl}}{|}}{\text{Et}}\diagdown\diagup\text{CO}_2\text{Et}$$
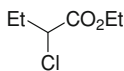
111

Concentrated sulfuric acid (9 mL) was added to a solution of 2-chlorobutyric acid (**115**) (76.1 g, 0.62 mol) in ethanol (95%, 110 mL) and benzene (40 mL) in a three-necked round flask fitted with condenser, thermometer. The reaction mixture was heated to reflux for 14 h (monitored by TLC) and the solvent was removed *in vacuo*. The residue was washed with water (70 mL × 2) and the *p*H of solution was adjusted to *p*H 5–6 using saturated sodium hydrogen carbonate. The solution was extracted with Et$_2$O (70 mL × 2) and the combined layers were dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo* to yield **111** (65.0 g) as a colorless oil in 70% yield. b.p.: 85 °C/35 torr (Lit: [3] 64 °C/20 torr); ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.00 (t, J = 7.5 Hz, 3H), 1.27 (t, J = 7.5 Hz, 3H), 1.92–2.10 (m, 2H), 4.16–4.26 (m, 3H) ppm; MS (ESI): m/z (M + H)$^+$ 151.

Ethyl 2-ethylacrylate (112) [1, 4]

$$\underset{\|}{\text{Et}}\diagdown\diagup\text{CO}_2\text{Et}$$
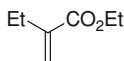
112

Diethyl 2-ethylmalonate (35 g, 186 mmol, 1 equiv) in anhydrous ethanol (50 mL) was added to potassium hydroxide (10.5 g, 186 mmol, 1 equiv) in anhydrous ethanol (100 mL) at 0 °C. The reaction mixture was stirred for 10 h. White precipitate was formed and solvent was removed. Water (10 mL) was added to dissolve the white solid and the solution was acidified to pH 3–4 using hydrochloric acid (10%). The solution was extracted with Et_2O (70 mL × 3). The combined organic layers were dried over Na_2SO_4, filtered and the solvent was concentrated *in vacuo* to yield a colorless oil.

Pyridine (40 mL) was added to the crude, $(HCHO)_n$ (5.58 g, 186 mmol, 1 equiv) and piperidine (1.8 mL) were added to the solution. The reaction mixture was heated to reflux for 1 h and then cooled to room temperature. The mixture was poured into water (100 mL), and washed with *n*-pentane (70 mL × 3). The combined layers were washed with hydrochloric acid (10%, 100 mL), water (100 mL), sodium hydrogen carbonate (5%, 100 mL), then dried over Na_2SO_4, filtered and concentrated *in vacuo*. It was purified by using distillation at 68 °C *in vacuo* to yield a colorless oil (16.7 g, 70%). ^{1}H NMR (400 MHz, CDCl$_3$) δ = 1.04 (t, *J* = 7.5 Hz, 3H), 1.26 (t, *J* = 7.3 Hz, 3H), 2.30 (q, *J* = 7.5 Hz, 2H), 4.17 (q, *J* = 7.5 Hz, 2H), 5.47 (s, 1H), 6.09 (s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 12.7, 14.2, 24.8, 60.5, 123.2, 142.5, 167.3 ppm; MS (ESI): *m/z* (M + Na)$^+$ 151.

Diethyl *cis*-1,2-diethylcyclopropane-1,2-dicarboxylate (*cis*-113) and Diethyl *trans*-1,2-diethylcyclopropane-1,2-dicarboxylate (*trans*-113) [1, 5]
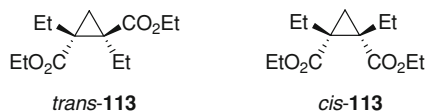
NaH (60%, 5.6 g, 140.4 mmol, 1.5 equiv) in DMF (25 mL) was cooled in an ice-bath. A solution of α-ethylacrylate **112** (12.0 g, 93.6 mmol) and α-chlorobutyrate **111** (11.1 g, 93.6 mmol) in DMF (50 mL) were added dropwise to the solution with temperature below 30 °C (gas released). The reaction mixture was stirred at room temperature for 17 h (monitored by TLC). MeOH (15 mL) was added to quench the excess NaH, then washed with water (100 mL). The mixture was extracted with Et_2O (70 mL × 3) and the combined layers were dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was subjected to purification using column chromatography on silica gel (800 g) eluting with hexanes/EtOAc (20:1) to yield *trans*-**113** (14.3 g, 63%), and *cis*-**113** (5.7 g, 25%). *trans*-**113** R_f = 0.6 (hexanes/EtOAc, 20:1); *cis*-**113** R_f = 0.4 (hexanes/EtOAc, 20:1); *cis*-**113**: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.65 (d, 1H, *J* = 4.5 Hz), 1.01 (t, *J* = 7.5 Hz, 6H), 1.24 (t, *J* = 7.5 Hz, 6H), 1.43–1.50 (m, 2H), 1.86 (d, *J* = 4.5 Hz, 1H), 1.94–2.02 (m, 2H), 4.10 (q, *J* = 7.5 Hz, 4H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 11.8, 14.2, 23.0, 23.9, 38.1, 60.8, 172.1 ppm; MS (ESI): *m/z* (M + Na)$^+$ 265.

trans-**113**: ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.89 (t, *J* = 7.5 Hz, 6H), 1.10–1.15 (m, 2H), 1.24 (t, *J* = 7.5 Hz, 6H), 1.28 (s, 2H), 1.98–2.06 (m, 2H),

4.08–4.20 (m, 4H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 11.6, 14.3, 20.1, 23.6, 38.0, 60.9, 171.6 ppm; IR (Film): 2974, 2939, 2880, 1729, 1458, 1382, 1309, 1234, 1182, 1139, 1031 cm^{-1}; MS (ESI): *m/z* (M + Na)$^+$ 265.

trans-1,2-Diethyl-1,2-bis (hydroxymethyl) cyclopropane (118) [1, 6]

118

Compound *trans*-**113** (10 g, 41.3 mmol) in Et$_2$O (50 mL) was added dropwise to a solution of LiAlH$_4$ (3.4 g, 90.8 mmol, 2.2 equiv) in Et$_2$O (50 mL) at 0 °C and the reaction mixture was heated to reflux for 17 h (monitored by TLC). NaOH (5%, 20 mL) was added to the reaction mixture to quench the excess LiAlH$_4$, then filtered and extracted with Et$_2$O (50 mL × 3). The combined organic layers were dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The crude material was subjected to purification using column chromatography on silica gel (250 g) eluting with hexanes/EtOAc (1:2) to yield a colorless oil (6.1 g, 93%). R_f = 0.3 (hexanes/EtOAc, 1:2); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.19 (s, 2H), 0.93 (t, *J* = 7.4 Hz, 6H), 1.25–1.34 (m, 2H), 1.82–1.91 (m, 2H), 3.28 (d, *J* = 11.3 Hz, 2H), 3.69 (s, 2H), 3.79 (d, *J* = 11.4 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 11.2, 19.2, 21.9, 32.9, 63.4 ppm; MS (ESI): *m/z* (M + Na)$^+$ 181.

trans-1,2-Diethyl-2-(hydroxymethyl)-[(*tert*-butyl-dimethylsiloxy)methyl]-cyclopropane (119) [1, 6]
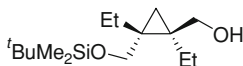
119

Et$_3$N (11.0 g, 15.1 mL, 108.4 mmol, 2.2 equiv) was added to a solution of **118** (7.8 g, 49.3 mmol) in CH$_2$Cl$_2$ (60 mL) at 0 °C and stirred for 10 min. *t*-BuMe$_2$SiCl (8.2 g, 54.2 mmol, 1.1 equiv) in CH$_2$Cl$_2$ (20 mL) was then added dropwise to the solution at 0 °C and stirred for 4 h (monitored by TLC). White precipitate was formed. The reaction mixture was washed with water (100 mL), dried over Na$_2$SO$_4$, filtered and concentrated *in vacuo*. The crude material was subjected to purification using column chromatography on silica gel (400 g) eluting with hexanes:ethyl acetate (5:1) to yield a colorless oil **119** (10.73 g) in 80% yield. R_f = 0.3 (hexanes/EtOAc, 5:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.02 (s, 3H), 0.03 (s, 3H), 0.28 (q, *J* = 4.8 Hz, 2H), 0.88 (s, 9H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.98 (t, *J* = 7.5 Hz, 3H), 1.24 (s, 1H), 1.41–1.70 (m, 4H), 3.40 (d, *J* = 10.7 Hz, 1H), 3.54 (d, *J* = 11.5 Hz, 1H), 3.65 (d, *J* = 11.6 Hz, 1H), 3.70 (d, *J* = 10.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, −5.4, 11.3, 11.4, 18.3, 20.3, 22.9, 23.1, 26.0, 32.7, 32.9, 64.1, 64.9 ppm; MS (ESI): *m/z* (M + Na)$^+$ 295.

***trans*-1,2-Diethyl-1-(*tert*-butyldimethylsiloxymethyl)-2-vinylcyclopropane (121)** [1]

121
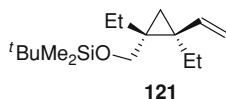
DMSO (7.2 g, 6.6 mL, 91.7 mmol, 2.5 equiv) in CH_2Cl_2 (20 mL) was added carefully to a solution of $(COCl)_2$ (5.6 g, 3.8 mL, 44.0 mmol, 1.2 equiv) in CH_2Cl_2 (60 mL) at −78 °C and stirred for 15 min. **119** (10 g, 36.7 mmol) in CH_2Cl_2 (20 mL) was added to the mixture and followed by Et_3N (19.3 g, 26.6 mL, 190.8 mmol, 5.2 equiv). The reaction mixture was allowed to stir at room temperature for 20 min. Water (50 mL) was added to the mixture and stirred for a further 30 min. The mixture was extracted with CH_2Cl_2 (70 mL × 3) and the combined layers were washed with hydrochloric acid (10%, 70 mL) sodium hydrogen carbonate solution (10%, 70 mL) and saturated brine solution (70 mL), then dried over Na_2SO_4, filtered and concentrated *in vacuo*. The crude material was used directly for the next step.

n-BuLi (1.6 M, 35 mL, 30.3 mmol, 1.3 equiv) was added to a solution of PPh_3CH_3I (19.3 g, 47.7 mmol, 1.3 equiv) in THF (100 mL) at −78 °C. The solution was stirred at room temperature until no solid left and then re-cooled to −78 °C. The crude material in THF (10 mL) was added dropwise to the solution and left stirring at room temperature for overnight. saturated aq. NH_4Cl (70 mL) was added to the reaction mixture and extracted with Et_2O (70 mL × 3). The combined layers were washed with water (100 mL), saturated brine solution (100 mL), dried over Na_2SO_4, filtered and concentrated *in vacuo* to yield a yellow solid. The crude material was subjected to purification using column chromatography on silica gel (250 g) eluting with hexane to yield a colorless oil **121** (5.9 g) in 60% yield (two steps); $R_f = 0.3$ (hexanes/EtOAc, 20:1); ^1H NMR (400 MHz, $CDCl_3$) δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.34 (d, J = 4.2 Hz, 1H), 0.57 (d, J = 4.7 Hz, 1H), 0.87 (t, J = 7.5 Hz, 3H), 0.90 (s, 9H), 0.92 (t, J = 7.5 Hz, 3H), 1.39–1.49 (m, 3H), 1.57–1.62 (m, 1H), 3.56 (d, J = 10.7 Hz, 1H), 3.70 (d, J = 10.7 Hz, 1H), 4.95 (d, J = 17.2 Hz, 1H), 5.07 (d, J = 10.5 Hz, 1H), 5.86 (dd, J = 10.5, 17.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.3, −5.4, 11.2, 11.7, 18.4, 20.6, 23.8, 25.7, 26.0, 33.3, 34.4, 64.2, 114.6, 140.8 ppm; MS (EI): *m/z* (M)$^+$ 268.

***trans*-1,2-Diethyl-2-vinylcyclopropyl)methanol (122)** [1]

122
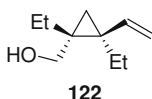
p-TsOH (242.5 mg, 1.42 mmol, 10 mol%) was added to a solution of **121** (3.8 g, 14.2 mmol) in CH_2Cl_2/MeOH (1:2, 80 mL) at 0 °C with stirring. The reaction mixture was stirred at room temperature for 4 h (monitored by TLC). The mixture

was then extracted with CH_2Cl_2 (40 mL $\times$ 3). The combined layers were washed with $NaHCO_3$ solution (5%, 40 mL), saturated brine solution (40 mL) and dried over Na_2SO_4, filtered and concentrated *in vacuo* to the crude. The crude material was subjected to purification using column chromatography on silica gel (100 g) eluting with hexane/EtOAc (5:1) to yield a colorless oil (2.0 g, 90%); R_f = 0.3 (hexanes/EtOAc, 5:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.34 (d, *J* = 4.8 Hz, 1H), 0.63 (d, *J* = 4.8 Hz, 1H), 0.90 (t, *J* = 7.4 Hz, 3H), 0.91 (t, *J* = 7.4 Hz, 3H), 1.37–1.52 (m, 4H), 1.60–1.68 (m, 1H), 3.64 (d, *J* = 12.5 Hz, 1H), 3.72 (d, *J* = 12.5 Hz, 1H), 4.97 (d, *J* = 17.2 Hz, 1H), 5.10 (d, *J* = 10.5 Hz, 1H), 5.83 (dd, *J* = 10.5, 17.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 11.2, 11.7, 20.7, 23.4, 25.7, 33.7, 34.7, 64.4, 115.3, 139.9 ppm; MS (ESI): *m/z* (M + Na)$^+$ 177.

1-(2-(*trans*-1,2-Diethyl-2-vinylcyclopropyl)vinyl)benzene (92a) [1, 7]

92a
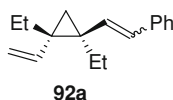
A solution of DMSO (0.13 mL, 1.85 mmol) in CH_2Cl_2 (2 mL) was added to a solution of (COCl)$_2$ (0.07 mL, 0.74 mmol) in CH_2Cl_2 (2 mL) at −78 °C over 30 min, followed by a solution of *trans*-**122** (114 mg, 0.74 mmol) in CH_2Cl_2 (2 mL). The resulting mixture was stirred at the same temperature for 30 min, and then Et$_3$N (0.5 mL, 3.7 mmol) was added. After another 20 min, water (10 mL) and CH_2Cl_2 (10 mL) were added, and the whole was partitioned. The aqueous layer was extracted with CH_2Cl_2 (20 mL $\times$ 3). The combined organic layers were successively washed with 1% HCl (30 mL), H$_2$O (30 mL), saturated aq. NaHCO$_3$ (30 mL), and brine (30 mL), and dried over Na$_2$SO$_4$. After removal of the solvents, the crude product was used without purification in the next step. BnPPh$_3$Br (415.6 mg, 1.0 mmol, 1.3 equiv) was suspended in anhydrous THF (5 mL) under nitrogen. *n*-BuLi (1.6 M in hexane, 0.63 mL, 1.00 mmol) was added into the reaction flask dropwise at −78 °C. After warming to room temperature, the resulting ylide mixture was allowed to stir for 30 min and then cooled to 0 °C again. A solution of the crude aldehyde in THF (2 mL) was added dropwise into the cooled reaction mixture, and was then allowed to warm slowly to room temperature. After 20 h, saturated aq. NH$_4$Cl (10 mL) was added to the mixture followed by Et$_2$O (30 mL). The organic layer was separated, and the aqueous layer was extracted with Et$_2$O (30 mL $\times$ 2). The combined organic layers were dried over Na$_2$SO$_4$, filtered, and concentrated. The crude product was purified by flash chromatography on silica gel (8 g) eluting with hexane to afford **92a** as a colorless oil (117.1 mg, 70% in 2 steps): R_f = 0.85 (Hexane); ^{1}H NMR (300 MHz, CDCl$_3$): δ = 0.41 (d, *J* = 4.5 Hz, 1H), 0.87 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.5 Hz, 3H), 1.34–2.04 (m, 4H), 1.87 (d, *J* = 4.5 Hz, 1H), 4.93–5.22 (d, *J* = 17.1 Hz, 2H), 5.23–5.37 (m, 1H), 5.75–6.05 (m, 1H), 6.22–6.75 (m, 1H), 7.09–7.50 (m, 5H) ppm; IR (Film): 3082, 3026, 2961, 2854, 1640, 1601, 1495, 1463, 1378, 1164, 959, 694 cm^{-1}; MS (EI): *m/z* 226 [M$^+$];

1-(2-(*trans*-1,2-Diethyl-2-vinylcyclopropyl)vinyl)-4-methylbenzene (92b) [1]

92b
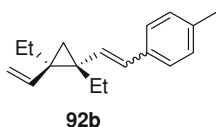
Compound **92b** was prepared by a similar procedure as **92a** : yield $= 70\%$ (2 steps); ($E/Z = 7/3$); $R_f = 0.85$ (Hexane); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.44$ (d, $J = 4.7$ HZ, 0.3 H), 0.79–0.96 (m, 7.7H), 1.25–1.65 (m, 4H), 2.34 (s, 2.1 H), 2.35 (s, 0.9 H), 4.99 (dd, 1H, $J = 1.1$, 11.9 Hz), 5.16 (m, 1H), 5.74 (d, $J = 11.9$ Hz, 0.3H), 5.86–5.96 (m, 1H), 6.26–6.45 (m, 1.7H), 7.12 (d, $J = 7.6$ Hz, 2H), 7.27 (d, $J = 8.2$ Hz, 1.4H), 7.33 (d, $J = 7.8$ Hz, 0.6 H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.6$, 11.7, 11.8, 12.4, 21.2, 21.2, 24.8, 26.4, 26.5, 26.7, 27.2, 32.9, 35.6, 36.6, 36.6, 115.3, 115.4, 125.9, 128.7, 129.1, 129.3, 130.5, 131.3, 131.5, 132.5, 134.3, 135.1, 136.5, 136.7, 139.7, 139.9 ppm; MS (EI): m/z 240 [M$^+$]; HRMS (EI) m/z [M]$^+$ calcd for C$_{18}$H$_{24}$: 240.1873, found: 240.1884.

1-(2-(*trans*-1,2-Diethyl-2-vinylcyclopropyl)vinyl)-4-methoxybenzene (92c)

92c
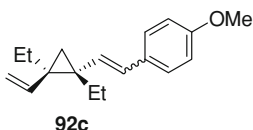
Compound **92c** was prepared by a similar procedure as **92a** : yield $= 64\%$ (2 steps); $R_f = 0.60$ (Hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.43$ (d, $J = 4.8$ HZ, 1H), 0.84 (t, $J = 7.3$ Hz, 3H), 0.87 (d, $J = 4.7$ HZ, 1H), 0.94 (t, $J = 7.4$ Hz, 3H), 1.48–1.68 (m, 4H), 3.81 (s, 3H), 4.99 (dd, 1H, $J = 1.8$, 17.2 Hz), 5.16 (dd, 1H, $J = 1.7$, 10.5 Hz), 5.67 (d, $J = 11.9$ Hz, 1H), 5.86 (dd, $J = 10.5$, 17.2 Hz, 1H), 6.38 (d, $J = 12.0$ Hz, 1H), 6.84 (d, $J = 6.8$ Hz, 2H), 7.37 (d, $J = 8.7$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.6$, 12.3, 24.8, 26.5, 27.2, 32.8, 36.6, 55.3, 113.4, 115.3, 130.0, 130.4, 131.0, 131.3, 139.7, 158.5 ppm; MS (FAB): m/z 256 [M$^+$]; HRMS (FAB) m/z [M]$^+$ calcd for C$_{18}$H$_{24}$O: 256.1822, found: 256.1811.

1-(2-(*trans*-1,2-Diethyl-2-vinylcyclopropyl)vinyl)naphthalene (92d)

92d
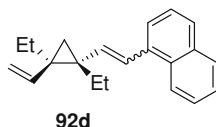
Compound **92d** was prepared by a similar procedure as **92a** (the E/Z ratio is about 5/2): yield $= 59\%$ (2 steps); $R_f = 0.85$ (Hexane); ^{1}H NMR (400 MHz,

CDCl$_3$) δ = 0.11 (d, J = 5.1 HZ, 0.4 H), 0.60 (d, J = 5.0 HZ, 0.4 H),0.79–0.96 (m, 7.7H), 0.80 (t, J = 7.3 Hz, 1.2H), 0.86–0.96 (m, 8H), 1.4–1.67 (m, 5.6H), 4.90 (dd, J = 1.8, 17 Hz, 0.4H), 5.04–5.10 (m, 1.4H), 5.17 (dd, J = 1.6, 10.5 Hz, 1H), 5.84 (dd, J = 10.4, 17.2 Hz, 0.4H), 5.96 (dd, J = 10.5, 17.2 Hz, 1H), 6.05 (d, J = 11.8 Hz, 0.4H), 6.33 (d, J = 15.6 Hz, 1H), 7.03 (d, J = 11.8 Hz, 0.4H), 7.10 (d, J = 15.7 Hz, 1H), 7.40–7.56 (m, 5.6H), 7.75 (d, J = 8.1 Hz, 1.4H), 7.84 (d, J = 7.4 Hz, 1.4H), 8.0 (d, J = 8.0 Hz, 0.4H), 8.11 (d, J = 8.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 11.6, 11.7, 11.8, 12.2, 21.6, 23.9, 26.5, 26.6, 26.8, 28.0, 31.9, 33.1, 35.9, 36.1, 36.6, 115.2, 115.4, 123.4, 124.0, 124.7, 125.1, 125.6, 125.6, 125.7, 125.8, 126.5, 127.1, 127.3, 127.9, 128.4, 128.5, 129.3, 131.1, 131.5, 133.4, 133.6, 134.7, 134.8, 135.8, 139.5, 139.7 ppm; MS (ESI): m/z 277 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{21}$H$_{25}$: 277.1951, found: 277.1957.

(E)-cis-3,5-Diethyl-3-styryl-5-vinyl-1,2-dioxolane (cis-124a) and (E)-trans-3,5-Diethyl-3-styryl-5-vinyl-1,2-dioxolane (trans-124a) [1]

cis-**124a**   trans-**124a**
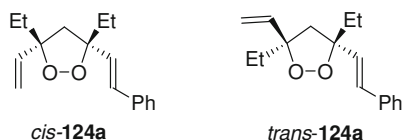
Feldman procedure. To a stirring solution of the vinylcyclopropane **92a** (226 mg, 1 mmol) in CH$_3$CN (10 mL) at room temperature was added diphenyl diselenide (32 mg, 0.1 mmol) and AIBN (13 mg, 0.08 mmol). The reaction was placed under a balloon of oxygen and irradiated with a 300 W sunlamp. When starting material was consumed as shown by TLC, the reaction mixture was concentrated *in vacuo*, and the residue was purified by flash chromatography on silica gel (8 g, hexane/EtOAc, 10/1) to afford **124** (*cis/trans* = 1:3.1) as a colorless oil (185.8 mg, 72%); R_f = 0.50 (hexanes/EtOAc, 20:1);

Pd-catalyzed procedure. To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stirring bar was added **92a** (57 mg, 0.25 mmol), urea peroxide (35%, 73 mg, 0.75 mmol, 3.0 equiv) and Pd (PPh$_3$)$_4$ (57 mg, 20 mol%). The flask was placed under an argon atmosphere, and MeCN (2 mL) was added via syringe. The resulting mixture was stirred at room temperature for 24 h. The reaction mixture concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (8 g, hexanes/EtOAc, 20:1) to give the pure product in which the *cis/trans* ratio is about 1/1.5 as a colorless oil (37 mg, 57%); R_f = 0.50 (hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.86–0.98 (m, 15 H), 1.67–1.83 (m, 10H), 2.38 (d, J = 12.1 Hz, 1H), 2.52 (s, 3H), 2.64 (d, J = 12.0 Hz, 1H), 5.16 (dd, J = 1.0, 11.0 Hz, 1H), 5.20 (dd, J = 1.0, 10.9 Hz, 1.5H), 5.25 (dd, J = 1.0, 17.6 Hz, 1H), 5.31 (dd, J = 1.0, 17.5 Hz, 1.5H), 5.82–5.94 (m, 2.5H), 6.21 (t, J = 16.5 Hz, 2.5H), 6.62 (t, J = 16.3 Hz, 2.5H), 7.23–7.25 (m, 2.5H), 7.28–7.41 (m, 10H) ppm; ^{13}C NMR

(100 MHz, CDCl$_3$) δ = 8.7, 8.9, 30.5, 30.9, 31.0, 31.5, 53.3, 53.9, 88.4, 88.5, 88.5, 88.6, 114.1, 114.8, 126.4, 127.5, 128.5, 128.9, 129.6, 130.8, 131.8, 136.7, 139.4, 140.2 ppm; MS (EI): m/z 258 [M]$^+$; HRMS (EI) m/z [M]$^+$ calcd for C$_{17}$H$_{22}$O$_2$: 258.1614, found: 258.1613.

(E)-3-(4-Methystyryl)-*cis*-3,5-diethyl-5-vinyl-1,2-dioxolane (*cis*-124b) and (E)-3-(4-Methystyryl)-*trans*-3,5-diethyl-5-vinyl-1,2-dioxolane (*trans*-124b) [1]

cis-**124b**   *trans*-**124b**
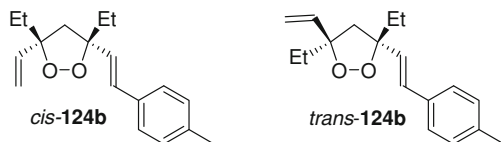
Compound **124b** was prepared by a similar procedure as **124a**; Feldman procedure: yield = 75%, (*cis/trans* = 1:4); Pd-catalyzed procedure: yield = 70% (*cis/trans* = 1:1.4); R_f = 0.50 (hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.86–0.97 (m, 14.4H), 1.69–1.84 (m, 9.6H), 2.33 (s, 3H), 2.34 (s, 4.2H), 2.37 (d, J = 12.0 Hz, 1H), 2.52 (s, 2.8H), 2.65 (d, J = 12.0 Hz, 1H), 5.16 (dd, J = 1.1, 11.0 Hz, 1H), 5.19 (dd, J = 1.1, 10.9 Hz, 1.4H), 5.26 (dd, J = 1.1, 17.6 Hz, 1H), 5.30 (dd, J = 1.1, 17.5 Hz, 1.4H), 5.86–5.93 (m, 2.4H), 6.16 (t, J = 16.4 Hz, 2.4H), 6.57 (t, J = 17.0 Hz, 2.4H), 7.11–7.14 (m, 4.8H), 7.28–7.31 (m, 4.8H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 8.9, 9.0, 9.0, 21.2, 30.7, 31.1, 31.2, 31.6, 53.4, 54.0, 88.6, 88.7, 88.7, 88.7, 114.2, 114.9, 126.4, 126.4, 128.9, 129.3, 129.3, 129.7, 129.9, 130.9, 134.1, 137.5, 139.7, 140.4 ppm; MS(ESI): m/z 290 [M + NH$_4$]$^+$; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for C$_{18}$H$_{28}$NO$_2$: 290.2115, found: 290.2113.

(E)-3-(4-Methoxystyryl)-*cis*-3,5-diethyl-5-vinyl-1,2-dioxolane (*cis*-124c) and (E)-3-(4-Methoxystyryl)-*trans*-3,5-diethyl-5-vinyl-1,2-dioxolane (*trans*-124c)
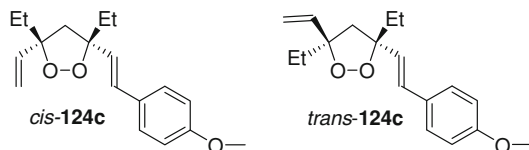
cis-**124c**   *trans*-**124c**

Compound **124c** was prepared by a similar procedure as **124a**; Feldman procedure: yield = 84%,   (*cis/trans* = 1:2.6);   Pd-catalyzed   procedure: yield = 40% (*cis/trans* = 1:1.6); R_f = 0.50 (hexanes/EtOAc, 10:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.86–0.97 (m, 16.2H), 1.67–1.84 (m, 10.8H), 2.37 (d, J = 12.0 Hz, 1H), 2.51 (s, 3.4H), 2.64 (d, J = 12.0 Hz, 1H), 3.80 (s, 3H), 3.81 (s, 5.1H), 5.16 (dd, J = 1.0, 11.0 Hz, 1H), 5.19 (dd, J = 1.0, 11.0 Hz, 1.7H), 5.28 (dt, J = 1.0, 17.6 Hz, 2.7H), 5.82–5.93 (m, 2.7H), 6.07 (t, J = 16.8 Hz, 2.7H), 6.54 (t, J = 16.6 Hz, 2.7H), 6.84–6.88 (m, 5.4H), 7.30–7.35 (m, 5.4H) ppm; ^{13}

C NMR (100 MHz, CDCl$_3$) δ = 8.9, 9.0, 30.7, 31.0, 31.2, 31.6, 53.4, 53.9, 55.4, 88.6, 88.6, 88.7, 88.7, 114.0, 114.0, 114.2, 114.9, 127.7,128.5, 128.6, 129.3, 129.6, 139.7, 140.3, 159.3 ppm; IR (Neat): 2964, 2934, 1607, 1511, 1251, 1175, 1036, 839 cm^{-1}; MS (FAB): *m/z* 288 [M]$^+$; HRMS (EI) *m/z* [M]$^+$ calcd for C$_{18}$H$_{24}$O$_3$: 288.1720, found: 288.1716.

(*E*)-*cis*-3,5-Diethyl-3-(2-(naphthalen-1-yl)vinyl)-5-vinyl-1,2-dioxolane (*cis*-124d) and **(*E*)-*trans*-3,5-Diethyl-3-(2-(naphthalen-1-yl)vinyl)-5-vinyl-1, 2-dioxolane (*trans*-124d)**
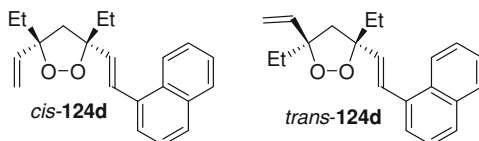
cis-**124d**   *trans*-**124d**

Compound **124d** was prepared by a similar procedure as **124a**; Feldman procedure: yield = 62%,   (*cis/trans* = 1:2.5);   Pd-catalyzed   procedure: yield = 67% (*cis/trans* = 1:1.8); R_f = 0.50 (hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.91–1.06 (m, 16.8H), 1.73–1.91 (m, 11.2H), 2.44 (d, *J* = 12.1 Hz, 1H), 2.61 (s, 3.6H), 2.75 (d, *J* = 12.0 Hz, 1H), 5.20 (dd, *J* = 1.1, 10.8 Hz, 1H), 5.23 (dd, *J* = 1.1, 10.9 Hz, 1.8H), 5.31 (dd, *J* = 1.0, 18 Hz, 1H), 5.36 (dd, *J* = 1.0, 17.4 Hz, 1.8H), 5.89–5.98 (m, 2.8 Hz), 5.18 (d, *J* = 16 Hz, 1H), 6.22 (d, *J* = 16 Hz, 1.8H), 7.36–7.60 (m, 14H), 7.79 (dd, *J* = 3.8, 8.2 Hz, 2.8H), 7.85 (dd, *J* = 2.6, 7.4 Hz, 2.8H), 8.09 (d, *J* = 7.4 Hz, 1H), 8.13 (d, *J* = 7.9 Hz, 1.8H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 8.9, 9.1, 30.7, 31.2, 31.7, 53.5, 54.2, 88.6, 88.7, 88.8, 88.8, 114.2, 115.0, 123.7, 124.0, 124.0, 125.6, 125.8, 126.1, 126.1, 126.5, 127.3, 127.9, 128.5, 131.4, 133.6. 134.3, 135.0, 135.1, 139.6, 140.5 ppm; MS (ESI): *m/z* 326 [M + NH$_4$]$^+$; HRMS (ESI) *m/z* [M + NH$_4$]$^+$ calcd for C$_{21}$H$_{28}$NO$_2$: 326.2115, found: 326.2120.

(*trans*-3,5-Diethyl-1,2-dioxolane-3,5-diyl)dimethanol (*trans*-134) and (*cis*-3, 5-Diethyl-1,2-dioxolane-3,5-diyl)dimethanol (*cis*-135) [1]

trans-**134**   *cis*-**135**
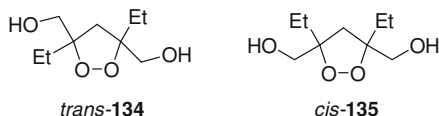
To a -78 °C solution of **92a** (440 mg, 1.6 mmol) in CH$_2$Cl$_2$ (14 mL)/MeOH (2 mL) was bubbled O$_3$. After the mixture turned light blue and TLC analysis displayed little or no starting material, ozonolysis was stopped and the ozone was removed by passage of O$_2$ or N$_2$ through the solution. NaBH$_4$ (91 mg, 2.4 mmol) was added to the reaction mixture at the same temperature and the reaction was slowly (5 h) warm to room temperature. The reaction was diluted with water

(2 mL) and the mixture extracted with EtOAc (15 mL × 2). The organic extracts were dried over Na$_2$SO$_4$, filtered, and concentrated *in vacuo*. The residue was purified by flash chromatography on silica gel (10 g, hexanes/EtOAc, 2:1–1:1) to afford firstly *trans*-**134** (178 mg, 55%), followed by *cis*-**135** (113 mg, 35%); *trans*-**134**: R_f = 0.25 (hexanes/EtOAc, 1:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.93 (t, J = 7.6 Hz, 6H), 1.51–1.60 (m, 2H), 1.74–1.83 (m, 2H), 2.05 (s, 2H), 2.25 (brs, 2H), 3.43 (d, J = 11.8 Hz, 2H), 3.72 (d, J = 11.8 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 9.2, 25.0, 44.7, 64.5, 89.5 ppm; MS (ESI): m/z 208 [M + NH$_4$]$^+$; HRMS (ESI) m/z [M + NH$_4$]$^+$ calcd for C$_9$H$_{22}$NO$_4$: 208.1543, found: 208.1540.

cis-**135**: R_f = 0.22 (hexanes/EtOAc, 1:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.94 (t, J = 7.6 Hz, 6H), 1.58–1.67 (m, 2H), 1.74–1.83 (m, 2H), 2.14 (d, J = 12.4 Hz, 1H), 2.46 (d, J = 12.4 Hz, 1H), 2.60 (s, 2H), 3.63 (q, J = 12.2 Hz, 4H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 8.7, 27.4, 44.2, 63.9, 89.5 ppm; MS (ESI): m/z 213 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_9$H$_{18}$O$_4$Na: 213.1097, found: 213.1093.

(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl) methanol (*cis*-137) and 3,5-bis((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3, 5-diethyl-1,2-dioxolane (*cis*-270)

cis-**137**   *cis*-**270**

To a stirring solution of *cis*-**135** (741 mg, 3.89 mmol) in DMF (10 mL) cooled at 0 °C were added imidazole (265 mg, 3.89 mmol), DMAP (24 mg, 0.19 mmol), and *tert*-butyldimethylsilyl chloride (587 mg, 3.89 mmol). The reaction was stirred overnight, and it was allowed to warm to room temperature slowly. Then quenched by addition of saturated aq. NH$_4$Cl (10 mL), and the resulting solution was stirred at room temperature for 30 min. The mixture was extracted with Et$_2$O (3 × 10 mL). The combined extracts were washed with brine (15 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated on the rotary evaporator. The residue was purified by flash chromatography on silica gel (8 g, hexane/EtOAc, 20:1 − 10:1) to afford *cis*-**270** (83 mg, 5%), *cis*-**137** (532 mg, 45%) and *cis*-**135** (259 mg, 35%) as colorless oil. *cis*-1**37**: R_f = 0.50 (hexanes/EtOAc, 8:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.06 (s, 6H), 0.89 (s, 9H), 0.90 (t, J = 7.5 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H), 1.57–1.66 (m, 2H), 1.75–1.83 (m, 2H), 2.07–2.12 (m, 1H), 2.06 (d, J = 12.3 Hz, 1H), 2.32 (d, J = 12.3 Hz, 1H), 3.46 (dd, J = 7.6 Hz, 11.9 Hz, 1H), 3.58 (d, J = 3.0 Hz, 2H), 3.72 (dd, J = 4.6 Hz, 11.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, 8.5, 8.9, 18.4, 25.9, 26.4, 28.0, 44.8, 63.9, 64.1, 89.1, 89.2 ppm; IR (Neat): 2956, 2931, 2883, 2858, 1463, 1254, 1113, 1060, 838, 778 cm^{-1}; MS (ESI): m/z 305 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{15}$H$_{33}$O$_4$Si: 305.2143, found: 305.2141.

cis-**270**: $R_f = 0.9$ (hexane); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.06$ (s, 12H), 0.89 (s, 18 H), 0.90 (t, $J = 7.5$ Hz, 6H), 1.55–1.64 (m, 2H), 1.75–1.84 (m, 2H), 1.98 (d, $J = 12.4$ Hz, 1H), 2.28 (d, $J = 12.3$ Hz, 1H), 3.49 (d, $J = 10.6$ Hz, 2H), 3.65 (d, $J = 10.7$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3$, 8.6, 18.3, 25.9, 27.2, 45.3, 64.0, 88.8, ppm; MS (ESI): *m/z* 419 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{21}$H$_{47}$O$_4$Si$_2$: 419.3007, found: 419.3018.

(5-((*tert*-Butyldimethylsilyloxy)methyl)-*trans*-3,5-diethyl-1,2-dioxolan-3-yl)methanol (*trans*-136) and 3,5-bis((*tert*-Butyldimethylsilyloxy)methyl)-*trans*-3,5-diethyl-1,2-dioxolane (*trans*-271)
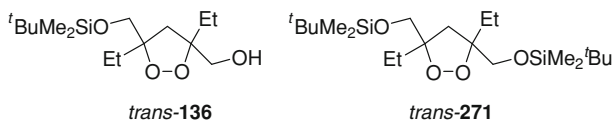
trans-**136**   *trans*-**271**

trans-**136** and *trans*-**271** were prepared by a similar procedure as *cis*-**137** and *cis*-**270**; *trans*-**137**: $R_f = 0.50$ (hexanes/EtOAc, 9:1); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.06$ (s, 6H), 0.89 (s, 9H), 0.91 (t, $J = 7.4$ Hz, 3H), 0.94 (t, $J = 7.4$ Hz, 3H), 1.49–1.59 (m, 2H), 1.70–1.80 (m, 2H), 1.96 (d, $J = 12.6$ Hz, 1H), 2.04–2.10 (m, 1H), 2.17 (d, $J = 12.6$ Hz, 1H), 3.44 (dd, $J = 8.3$ Hz, 11.6 Hz, 1H), 3.49 (d, $J = 10.9$ Hz, 1H), 3.68 (d, $J = 10.9$ Hz, 1H), 3.71 (dd, $J = 8.3$ Hz, 11.6 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3$, 8.8, 9.0, 18.3, 25.4, 25.9, 25.9, 44.6, 64.4, 65.0, 88.9, 89.1 ppm; IR (Neat): 2955, 2933, 2884, 2862, 1464, 1254, 1112, 1059, 842, 779 cm^{-1}; MS (ESI): *m/z* 305 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{15}$H$_{33}$O$_4$Si: 305.2143, found: 305.2141.

trans-**271**: $R_f = 0.9$ (hexane); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.06$ (s, 12H), 0.89 (s, 18H), 0.91 (t, $J = 7.5$ Hz, 6H), 1.55–1.62 (m, 2H), 1.72–1.80 (m, 2H), 2.10 (s, 2H), 3.50 (d, $J = 10.2$ Hz, 2H), 3.65 (d, $J = 10.2$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, -5.3$, 8.6, 18.3, 25.9, 26.3, 44.4, 64.9, 88.5 ppm; MS (ESI): *m/z* 441 [M +Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{21}$H$_{46}$O$_4$Si$_2$Na: 441.2827, found: 441.2831.

(*E*)-Ethyl 3-(5-((butyldimethylsilyloxy)methyl)-*trans*-3,5-diethyl-1,2-dioxolan-3-yl)acrylate *trans*-142
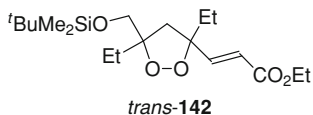
trans-**142**

To a solution of *trans*-**136** (38 mg, 0.125 mmol) in CH$_2$Cl$_2$ (2.0 mL) was added DMP (80 mg, 0.188 mmol). The reaction mixture was stirred until the starting material had disappeared, NaHCO$_3$ (84 mg, 1.0 mmol) was added. Then added saturated aq. NaHCO$_3$ (5.0 mL), and the mixture was extracted with Et$_2$O

(3 × 10 mL). The combined extracts were washed with brine (25 mL), dried over anhydrous Na_2SO_4, and concentrated on the rotary evaporator. The residue was purified by flash chromatography on silica gel (8 g, hexanes/EtOAc, 10:1) to afford the desired aldehyde *trans*-**141**, which was used in the next step. To a 0 °C spension of NaH (14 mg, 60% in mineral oil, 2.8 equiv) in THF (1 mL) was added a solution of triethyl phosphonoacetate (84 mg, 0.375 mmol, 3.0 equiv) in THF (0.5 mL). After stirring for 0.5 h, the aldehyde **141** in THF (1 mL) was added slowly. The reaction mixture was warmed to room temperature, stirred until no starting material remained (TLC). Quenched the reaction with saturated aq. NH_4Cl extracted with Et_2O three times and combined the organic layers and washed with brine and water, and dried over $MgSO_4$ and filtered. Removed the solvent with rotary evaporation. Flash chromatography on silica gel (8 g) of the residue gave the product (37 mg, 79% in 2 steps) as a colorless oil. $R_f = 0.50$ (hexanes/EtOAc, 10:1); ^1H NMR (400 MHz, $CDCl_3$) $\delta = 0.07$ (s, 6H), 0.86 (t, $J = 7.5$ Hz, 3H), 0.89 (s, 9H), 0.91 (t, $J = 7.5$ Hz, 3H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.52–1.58 (m, 1H), 1.68–1.78 (m, 3H), 2.31 (q, $J = 12.5$ Hz, 2H), 3.50 (d, $J = 10.3$ Hz, 1H), 3.65 (d, $J = 10.3$ Hz, 1H), 4.20 (q, $J = 7.1$ Hz, 2H), 6.11 (d, $J = 15.8$ Hz, 1H), 6.87 (d, $J = 15.8$ Hz, 1H)ppm; ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -5.5, -5.3$, 8.7, 8.8, 14.3, 18.3, 25.9, 26.2, 30.4, 49.0, 60.6, 65.0, 87.7, 89.0, 120.5, 149.8, 166.7 ppm; IR (Neat): 2956, 2930, 2857, 1722, 1658, 1463, 1304, 1259, 1178, 1113, 1039, 838, 778 cm^{-1}; MS (ESI): m/z $[M + H]^+$ 373; HRMS (ESI) m/z $[M + H]^+$ calcd for $C_{19}H_{37}O_5Si$: 373.2405, found: 373.2402.

tert-Butyl((5-(2,2-dibromovinyl)-*trans*-3,5-diethyl-1,2-dioxolan-3-yl)methoxy)dimethylsilane (*trans*-155)

trans-**155**
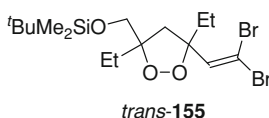
To a slurry of Ph_3P-$CHBr_3$ [8] (322 mg, 0.625 mmol) in THF (2.0 mL) at 0 °C was added *t*-BuOK (67 mg, 0.6 mmol). The bright yellow slurry was stirred for 15 min and the temperature was allowed to warm to room temperature. Then added the aldehyde **141** in THF (1.0 mL) to the mixture and stirred for 30 min, TLC, the reaction completed. Quenched the reaction with saturated aq. NH_4Cl extracted with Et_2O three times and combined the organic layers and washed with brine and water, and dried over $MgSO_4$ and filtered. Removed the solvent with rotary evaporation. Flash chromatography on silica gel (8 g) of the residue gave the product (90 mg, 79%, 2 steps) as a colorless oil : $R_f = 0.75$ (hexanes/EtOAc, 20:1); ^1H NMR (400 MHz, $CDCl_3$) $\delta = 0.07$ (s, 6H), 0.89 (s, 9H), 0.91 (t, $J = 7.5$ Hz, 3H), 0.93 (t, $J = 7.4$ Hz, 3H), 1.56–1.63 (m, 1H), 1.70–1.81 (m, 2H), 2.15–2.20 (m, 1H), 2.25 (d, $J = 12.7$ Hz, 1H), 2.69 (d, $J = 12.7$ Hz, 1H), 3.48 (d, $J = 10.2$ Hz, 1H), 3.63 (d, $J = 10.2$ Hz, 1H), 6.91 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -5.4, -5.3$, 8.5, 8.9, 18.3, 25.9, 26.2, 28.0, 49.1, 65.5,

87.1, 88.8, 90.3, 144.9 ppm; IR (Neat): 2954, 2930, 2858, 1461, 1256, 1115, 838 cm^{-1}; MS (ESI): *m/z* 481 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{16}$H$_{30}$Br$_2$O$_3$SiNa: 481.0203, found: 481.0190.

tert-Butyl((*trans*-3,5-diethyl-5-ethynyl-1,2-dioxolan-3-yl)methoxy)dimethylsilane (*trans*-148)
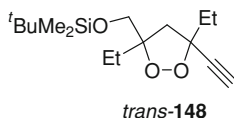
trans-**148**

To a two necked round-bottomed flask equipped with a magnetic stirring bar was added *trans*-**155** (114 mg, 0.25 mmol) under an argon atmosphere, and THF (2 mL) was added via syringe. The mixture was cooled to −78 °C and *n*-butyllithium (0.55 mmol, 1.6 M solution in hexanes, 0.344 mL) was added dropwise via syringe. The mixture was stirred at −78 °C for 30 min, then saturated aq. NH$_4$Cl water solution was added. The mixture was warmed to 25 °C, diluted with Et$_2$O, transferred to a separatory flask, and the layers separated. The aqueous layer was extracted with Et$_2$O and the combined organic extracts washed with saturated brine and water, dried by MgSO$_4$, filtered and the solvent removed by rotary evaporation. The residue was purified by column chromatography on silica gel (8 g) to yield **148** (71 mg, 95%) as a colorless oil, R_f = 0.55 (hexanes/Et$_2$O 20:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.06 (s, 3H), 0.06 (s, 3H), 0.88 (s, 9H), 0.95 (t, J = 7.5 Hz, 3H), 1.08 (t, J = 7.4 Hz, 3H), 1.70–1.81 (m, 2H), 1.80–1.87 (m, 2H), 2.33 (d, J = 12.4 Hz, 1H), 2.51 (s, 1H), 2.56 (d, J = 12.4 Hz, 1H), 3.47 (d, J = 10.3 Hz, 1H), 3.63 (d, J = 10.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.5, −5.3, 8.5, 9.6, 18.3, 25.9, 26.2, 31.2, 51.6, 65.3, 73.0, 82.7, 84.8, 89.0, ppm; IR (Neat): 3311, 2955, 2930, 2858, 1471, 1463, 1258, 1111, 1007, 839 cm^{-1}; MS (ESI): *m/z* 321 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{16}$H$_{30}$O$_3$SiNa: 321.1856, found: 321.1854.

tert-Butyl((*trans*-3,5-diethyl-5-(prop-1-ynyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane (*trans*-147)

trans-**147**
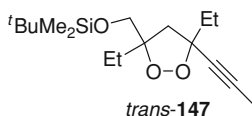
To a 25-mL, two-necked, round-bottomed flask equipped with a magnetic stirring bar was added **148** (89 mg, 0.3 mmol). The flask was placed under an argon atmosphere, and THF (2.5 mL) was added via syringe. The mixture was cooled to −78 °C and *n*-butyllithium (0.36 mmol, 1.6 M solution in hexanes, 0.225 mL) was added dropwise via syringe. The mixture was stirred at −78 °C for

5 min and methyl trifluoromethanesulfonate (0.45 mmol, 74 mg, 0.052 mL) was added dropwise via syringe. The mixture was stirred at $-78\,°C$ for 30 min, then saturated aq. NaHCO$_3$ was added. The mixture was warmed to $25\,°C$, diluted with Et$_2$O, transferred to a separatory flask, and the layers separated. The aqueous layer was extracted with Et$_2$O and the combined organic extracts washed with saturated brine and water, dried by MgSO$_4$, filtered and the solvent removed by rotary evaporation. The residue was purified by column chromatography on silica gel (8 g) to yield **147** (66 mg, 70%) as a colorless oil, $R_f = 0.55$ (hexanes/Et$_2$O 20:1); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.05$ (s, 3H), 0.05 (s, 3H), 0.87 (s, 9H), 0.96 (t, $J = 7.5$ Hz, 3H), 1.04 (t, $J = 7.4$ Hz, 3H), 1.66–1.73 (m, 2H), 1.73–1.83 (m, 2H), 1.85 (s, 3H), 2.27 (d, $J = 12.3$ Hz, 1H), 2.48 (d, $J = 12.3$ Hz, 1H), 3.45 (d, $J = 10.4$ Hz, 1H), 3.60 (d, $J = 10.3$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, -5.3, 3.7, 8.5, 9.8, 18.3, 25.9, 26.4, 31.7, 51.9, 65.3, 80.2, 81.1, 83.1, 88.9$ ppm; MS (ESI): m/z 335 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{17}$H$_{32}$O$_3$SiNa: 335.2013, found: 335.2017.

(*E*)-*tert*-Butyl((*trans*-3,5-diethyl-5-(2-iodoprop-1-enyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane (*trans*-146)
(*E*)-*tert*-Butyl((*trans*-3,5-diethyl-5-(1-iodoprop-1-enyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane (*trans*-162b)

trans-**146**   *trans*-**162b**
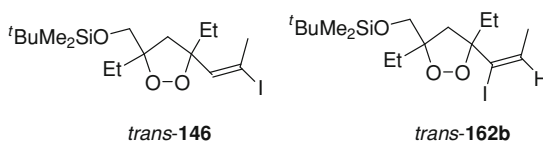
Procedure I: To a 10-mL, argon-filled, two-necked round-bottomed flask equipped with a magnetic stirring bar was added *trans*-**147** (64 mg, 0.206 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%). The flask was evacuated and filled with argon three times, and then freshly distilled THF (2 mL) was added via a syringe. Tributyltin hydride (4.0 equiv) was added slowly (about over 10 min) via a syringe. The reaction was stirred at $23\,°C$ for 1 h, then immediately transferred to a silica gel column (8 g) and rapidly eluted with hexanes until the excess Bu$_3$SnH/(Bu$_3$Sn)$_2$ is removed, followed by elution with a mixture of hexanes and EtOAc (10:1) to afford *trans*-**161** (41 mg, 33%), *trans*-**162** (41 mg, 33%) as colorless oil; *trans*-**162**: $R_f = 0.70$ (hexanes/EtOAc, 20:1); *trans*-**161**: $R_f = 0.60$ (hexanes/EtOAc, 20:1); The obtained stannane compound *trans*-**162** was dissolved in CH$_2$Cl$_2$ (2 mL) and cooled to $0\,°C$. I$_2$ (17 mg, 0.07 mmol) in CH$_2$Cl$_2$ (1 mL) was added and the resulting mixture was stirred at $0\,°C$ for 5–8 min then worked up by a saturated aq. Na$_2$S$_2$O$_3$ solution (3 mL) and extracted by Et$_2$O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (8 g, hexanes/EtOAc, 20:1) to give **162b** (26 mg, 86%) as an oil: $R_f = 0.60$ (hexanes/EtOAc, 20:1);

In a similar manner of iodination, *trans*-**146** was prepared as a colorless oil: $R_f = 0.50$ (hexanes/EtOAc, 20:1);

trans-**146**: ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.06$ (s, 6H), 0.90 (s, 9H), 0.92 (t, $J = 7.5$ Hz, 3H), 0.93 (t, $J = 7.5$ Hz, 3H), 1.55–1.64 (m, 1H), 1.70–1.76 (m, 3H), 2.28 (d, $J = 1.6$ Hz, 2H), 2.58 (d, $J = 1.3$ Hz, 3H), 3.48 (d, $J = 10.2$ Hz, 1H), 3.61 (d, $J = 10.2$ Hz, 1H), 6.17 (d, $J = 1.4$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3, 8.5, 9.1, 18.3, 25.9, 26.4, 29.8, 30.9, 50.8, 65.4, 88.4, 90.8, 96.4, 144.1$ ppm; MS (ESI): *m/z* [M + Na]$^+$ 463; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{17}$H$_{33}$IO$_3$SiNa: 463.1136, found: 463.1137.

trans-**162b**: ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.06$ (s, 6H), 0.90 (s, 9H), 0.92 (t, $J = 7.5$ Hz, 6H), 1.60–1.68 (m, 1H), 1.70–1.77 (m, 2H), 1.87 (d, $J = 7.5$ Hz, 3H), 2.11–2.19 (m, 1H), 2.26 (d, $J = 12.9$ Hz, 1H), 2.87 (q, $J = 12.8$ Hz, 1H), 3.50 (d, $J = 10.1$ Hz, 3H), 3.62 (d, $J = 10.1$ Hz, 1H), 6.45 (d, $J = 7.5$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3, 8.2, 8.6, 18.0, 18.4, 26.0, 26.0, 30.9, 51.7, 65.8, 88.6, 93.2, 107.1, 138.8$ ppm; MS (ESI): *m/z* [M + Na]$^+$ 463; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{17}$H$_{33}$IO$_3$SiNa: 463.1136, found: 463.1138.

Procedure II (*trans*-**146**): To a 10-mL, argon-filled, two-necked round-bottomed flask equipped with a magnetic stirring bar was added *trans*-**147** (64 mg, 0.206 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%). The flask was evacuated and filled with argon three times, and then freshly distilled *n*-hexane (2 mL) was added via a syringe. Tributyltin hydride (4.0 equiv) was added slowly (about over 10 min) via a syringe. The reaction was stirred at 23 °C for 1 h, then immediately transferred to a silica gel column (8 g) and rapidly eluted with hexanes until the excess Bu$_3$SnH/(Bu$_3$Sn)$_2$ is removed, followed by elution with a mixture of hexanes and ethyl acetate (10:1) to give the stannane compound *trans*-**161** (105 mg, 84%) as a colorless oil: $R_f = 0.60$ (hexanes/EtOAc, 20:1). The obtained stannane compound was dissolved in CH$_2$Cl$_2$ (3 mL) and cooled to 0 °C. I$_2$ (43 mg, 0.17 mmol) in CH$_2$Cl$_2$ (1 mL) was added and the resulting mixture was stirred at 0 °C for 5–8 min then worked up by a saturated aq. Na$_2$S$_2$O$_3$ solution (3 mL) and extracted by Et$_2$O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na$_2$SO$_4$, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (8 g, /EtOAc, 20:1) to give *trans*-**146** (64 mg, 86%) as an oil: $R_f = 0.50$ (hexanes/EtOAc, 20:1);

1-Phenyl-5-(propylthiol)-1*H*-tetrazole (164) [1, 9]
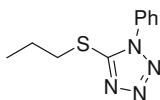
164

To a solution of *n*-propyl bromide **163** (1.3 g, 10.6 mmol) in THF (40 mL) was added NaH (424 mg, 60% in mineral oil, 12 mmol) and 1-phenyl-1h-tetrazole-5-thiol

(HSPT) (2.16 g, 12 mmol) at 0 °C. The reaction mixture was allowed to warm to room temperature and stirred overnight. The reaction mixture was quenched with saturated aq. NH_4Cl and extracted with EtOAc. The organic layer were dried over MgSO4, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (100 g, hexanes/EtOAc, 20:1) to give the desired **164** (2.25 g) in 96% yield. R_f = 0.70 (hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.03 (t, J = 7.4 Hz, 3H), 1.79–1.89 (m, 2H), 3.35 (t, 2H, J = 7.2 Hz), 7.52–7.56 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 13.2, 22.6, 35.2, 123.9, 129.8, 130.1, 133.7, 154.5 ppm; MS (ESI): m/z [M + H]$^+$ 221;

1-Phenyl-5-(propylsulfonyl)-1H-tetrazole (165) [1, 9]
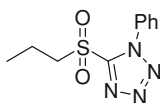
165

To a solution of **164** (0.22 g, 1.0 mmol) in EtOH (5 mL) was added $(NH_4)_6Mo_7O_{24}\cdot 4H_2O$ (0.13 g, 0.1 mmol) and H_2O_2 (30% in H_2O, 1 mL, 10 mmol) at room temperature. The reaction mixture was stirred for 14 h. The reaction mixture was extracted with Et_2O (25 mL × 3). The organic layer were dried over $MgSO_4$, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (8 g, hexanes/EtOAc, 6:1) to give the desired **165** (0.23 g) in 92% yield; R_f = 0.50 (hexanes/EtOAc, 5:1); ^{1}H NMR (400 MHz, $CDCl_3$) δ = 1.12 (t, J = 7.4 Hz, 3H), 1.94–2.01 (m, 2H), 3.68–3.72 (m, 2H), 7.56–7.68 (m, 5H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = 12.8, 16.0, 57.6, 125.1, 129.7, 131.5, 133.0, 153.5 ppm; MS (ESI): m/z [M + H]$^+$ 253;

2-Ethylpropane-1,3-diol (166) [10]
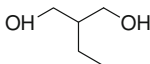
166

To a solution of ethyl diethyl malonate (10 g, 0.053 mol) in THF (90 mL) was slowly added $LiAlH_4$ (3.9 g, 0.103 mol) at 0 °C. The reaction mixture was stirred at rt for 1 h and refluxed for 15 h. The reaction mixture was cooled to 0 °C and quenched with 20% NaOH solution. The mixture was further diluted with Et_2O (300 mL), filtered and the precipitated aluminum salts were washed with additional 200 mL of Et_2O. The combined filtrates were concentrated under reduced pressure to give a yellow oil which was distilled under reduced pressure at 110 °C, to provide diol as a colorless oil in a 60% yield (3.3 g). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 0.89 (t, J = 7.4 Hz, 3H), 1.20–1.27 (m, 2H), 1.55–1.61 (m, 1H),

3.52–3.58 (m, 2H), 3.67–3.71 (m, 2H), 3.81 (s, 1H), 3.87 (s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.6$, 20.6, 43.7, 64.8, 64.9 ppm; MS (ESI): *m/z* [M + H]$^+$ 105;

2-((*tert*-Butyldimethylsilyloxy)methyl)butan-1-ol (167) [10]

167
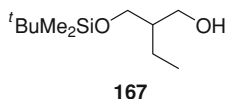
To a solution of diol **166** (3.3 g, 0.032 mol) in THF (90 mL) was slowly added *n*-BuLi (1.6 M, 19.8 mL, 1.0 equiv) at −78 °C. The reaction mixture was stirred at −78 °C for 1 h, the reaction mixture was warmed to −30 °C, and *t*-BuMe$_2$SiCl was added (1.0 equiv). After stirring for 1 at −30 °C, the reaction mixture was allowed to warm to room temperature, quenched with saturated aq. NH$_4$Cl and extracted with EtOAc. The organic layer were dried over MgSO4, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexanes/EtOAc, 20:1) to give the desired mono protected alcohol **167** (7.0 g) as an oil in quantitative yield.

$R_f = 0.50$ (hexanes/EtOAc, 10:1); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.06$ (s, 6H), 0.88 (s, 9H); 0.91 (t, $J = 7.4$ Hz, 3H), 1.22–1.30 (m, 2H), 1.60–1.65 (m, 1H), 2.95 (s, 1H), 3.60 (q, $J = 7.4$ Hz, 2H), 3.72 (d, $J = 10.4$ Hz, 1H), 3.79 (dd, $J = 3.8$, 9.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.6$, −5.5, 11.8, 18.2, 20.6, 25.9, 43.7, 66.4, 67.2 ppm; MS (ESI): *m/z* [M + H]$^+$ 219;

(*E*)-*tert*-Butyl(2-ethylhex-3-enyloxy)dimethylsilane (169) [11]

169
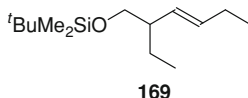
To a stirring solution of (COCl)$_2$ (0.75 mL, 8.6 mmol) in CH$_2$Cl$_2$ (50 mL) was added DMSO (1 mL, 14.0 mmol) dropwise via a syringe at −78 °C. The mixture was stirred at −78 °C for 15 min and then a solution of **167** (1.08 g, 4.95 mmol) in CH$_2$Cl$_2$ (10 mL) was added dropwise to the reaction mixture via a syringe. After stirring for 1 h at −78 °C, Et$_3$N (2.5 mL, 18.0 mmol) was added and the reaction was allowed to warm to 23 °C and stirred at this temperature for 0.5 h. Then it was successively washed with an aq. HCl solution (10 mL, 1 N), a saturated aq. NaHCO$_3$ solution (10 mL) and brine (10 mL). The organic phase was dried over anhydrous Na$_2$SO$_4$, filtered, and concentrated under reduced pressure to provide the crude aldehyde **168** as a pale yellow oil which was used directly in the next step without further purification.

To a solution of compound **165** (1.26 g, 5 mmol) of THF (20 mL) was added dropwise KHMDS (4.5 mL, 1.0 M in THF, 4.5 mmol) at −78 °C. After stirring at

−78 °C for 2 h, a solution of the above freshly prepared aldehyde **168** in THF (5 mL) was added dropwise. The resulting mixture was stirred from −78 to 23 °C overnight, and quenched with a saturated aq. NH_4Cl solution (10 mL). The organic layer was separated and the aqueous layer was extracted with Et_2O (3 × 50 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered, and concentrated under reduced pressure to provide a residue which was purified by flash column chromatography on silica gel (40 g, hexanes/Et_2O 20:1) to give **169** (1.07 g, 89% in 2 steps) as a 25:1 *E/Z* mixture: $R_f = 0.35$ (hexanes/Et_2O 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.03$ (s, 6H), 0.85 (t, $J = 7.4$ Hz, 3H), 0.90 (s, 9H), 0.98 (t, $J = 7.6$ Hz, 3H), 1.16–1.26 (m, 1H), 1.49–1.59 (m, 1H), 1.97–2.05 (m, 3H), 3.43–3.51 (m, 2H), 5.15 (ddt, $J = 1.4$, 7.2, 15.4 Hz, 1H), 5.48 (dt, $J = 6.5$, 15.2 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -5.2, -5.2, 11.7, 14.0, 18.5, 24.1, 25.9, 26.0, 47.2, 67.0, 130.4, 133.4$ ppm; MS (ESI): *m/z* [M + Na]$^+$ 265; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for $C_{14}H_{30}NaOSi$: 265.1958, found: 265.1955.

(*E*)-2-Ethylhex-3-en-1-ol (170) [11, 12]

170
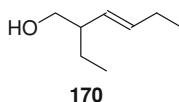
To a solution of **169** (35 mg, 0.14 mmol) in CH_2Cl_2/MeOH (0.7/1.4 mL) was added *p*-TsOH (10 mol%). The reaction was stirred at room temperature until no starting material remained (TLC). After removal of the solvents, the crude product was purified by column chromatography on silica gel (8 g, hexanes/EtOAc, 5:1) to yield **170** (18 mg, 86%); $R_f = 0.35$ (hexanes/Et_2O 9:1); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.85$ (t, $J = 7.4$ Hz, 3H), 0.98 (t, $J = 7.6$ Hz, 3H), 1.16–1.27 (m, 1H), 1.38–1.43 (m, 2H), 2.01–2.09 (m, 3H), 3.35 (t, $J = 10.6$ Hz, 1H), 3.51–3.57 (m, 1H), 5.13 (ddt, $J = 1.4$, 7.4, 15.4 Hz, 1H), 5.60 (dt, $J = 6.3$, 15.3 Hz, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 11.7, 14.1, 24.1, 25.8, 47.7, 65.8, 130.0, 135.9$ ppm; MS (EI): *m/z* [M + Na]$^+$ 151;

(*E*)-5-(Iodomethyl)hept-3-ene (recemic-91) [11, 12]

racemic-**91**
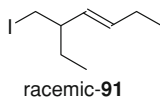
170 (179 mg, 1.40 mmol) was dissolved in CH_2Cl_2 (5 mL) and stirred at 0 °C. PPh$_3$ (628 mg, 2.4 mmol) and imidazole (204 mg, 3 mmol) was added to the solution followed by I_2 (558 mg, 2.2 mmol) at 0 °C. The resulting mixture was stirred from 0 °C to 23 °C for 4 h and then worked up by adding a saturated aq. $Na_2S_2O_3$ solution (5 mL). The organic layer was separated and the aqueous layer

was extracted with pentane (3 × 15 mL). The combined organic phase was dried over anhydrous Na_2SO_4 and concentrated at 25 °C under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (10 g, pentane) to give recemic-**91** (286 mg, 86%): $R_f = 0.80$ (hexanes); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.86$ (t, $J = 7.4$ Hz, 3H), 0.99 (t, $J = 7.5$ Hz, 3H), 1.26–1.33 (m, 1H), 1.52–1.58 (m, 1H), 1.96–2.07 (m, 3H), 3.16 (d, $J = 6.1$ Hz, 2H), 5.13 (dd, $J = 8.4$, 15.2 Hz, 1H), 5.52 (dt, $J = 6.4$, 15.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = 11.6$, 13.9, 14.8, 25.7, 27.9, 45.9, 130.9, 134.5 ppm; MS (ESI): m/z [M]$^+$ 238.

tert-Butyl((*trans*-3,5-diethyl-5-((1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane (206)

206
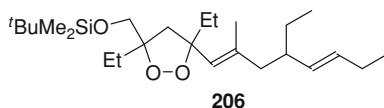
Negishi Coupling: To a 25-mL, two-necked, round-bottomed flash equipped with a magnetic stirring bar was added $ZnBr_2$ (70 mg, 0.312 mmol). The flask was placed under an argon atmosphere, and the side chain racemic-**91** (57 mg, 0.24 mmol) in Et_2O (3 mL) was added via syringe. The solution was cooled to −78 °C and *t*-butyllithium (0.48 mmol, 1.6 M solution in hexanes, 0.32 mL) was added dropwise via syringe. The mixture was stirred at −78 °C for 30 min and THF (0.75 mL) was stirred for1 h and the temperature was allowed to warm to room temperature. The core **146** (40 mg, 0.09 mmol) in THF (1.5 mL) with $Pd(PPh_3)_4$ was added via syringe. The mixture was stirred overnight in the absence of light. Quenched with saturated aq. NH_4Cl. The mixture was diluted with Et_2O, and the layers was separated. The water layer was separated with Et_2O, and the combined organic layers were washed with brine and water, dried over $MgSO_4$, filtered and solvent was removed by rotary evaporation. Chromatography on silica gel (8 g) gave the product **206** (36 mg, 93%) as a colorless oil: $R_f = 0.50$ (hexanes/EtOAc, 20:1); ^{1}H NMR (400 MHz, $CDCl_3$) $\delta = 0.06$ (s, 3H), 0.07 (s, 3H), 0.83 (t, $J = 7.4$ Hz, 3H), 0.86 (t, $J = 7.4$ Hz, 3H), 0.87 (t, $J = 7.4$ Hz, 3H), 0.89 (s, 9H), 0.95 (t, $J = 7.4$ Hz, 3H), 1.09–1.20 (m, 1H), 1.32–1.44 (m, 1H), 1.52–1.62 (m, 1H), 1.63 (s, 1.5 H), 1.64 (s, 1.5 H), 1.66–1.81 (m, 3H), 1.90–2.04 (m, 5H), 2.21–2.45 (m, 2H), 3.49 (d, $J = 12.4$ Hz, 1H), 3.61 (d, $J = 12.8$ Hz, 1H), 5.08 (dd, $J = 8.3$, 15.3 Hz, 1H), 5.27 (s, 0.5H), 5.30 (s, 0.5H), 5.33–5.40 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) $\delta = -5.4$, −5.3, 8.6, 9.1, 9.2, 11.7, 11.7, 14.1, 14.1, 17.5, 17.6, 18.4, 25.7, 26.0, 27.0, 27.8, 27.9, 31.3, 42.6, 42.8, 46.6, 46.7, 51.5, 51.7, 64.9, 65.0, 88.3, 88.4, 88.8, 130.0, 130.5, 131.9, 133.0, 135.1, 135.5 ppm; IR (Neat): 2962, 2930, 2880, 2857, 1462, 1438, 1263, 1118, 838 cm^{-1}; MS (ESI): m/z 447 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{25}H_{48}O_3SiNa$: 447.3265, found: 447.3269.

(*trans*-3,5-Diethyl-5-((1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methanol (208)

208
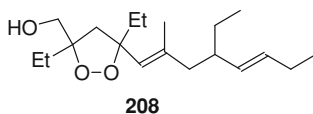
To a solution of **206** (35 mg, 0.08 mmol) in CH_2Cl_2/MeOH (0.7/1.4 mL) was added *p*-TsOH (10 mol%). The reaction was stirred at room temperature until no starting material remained (TLC). After removal of the solvents, the crude product was purified by column chromatography on silica gel (8 g, hexanes/EtOAc, 5:1) to yield **208** (22 mg, 89%): R_f = 0.30 (hexanes/EtOAc, 10:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.84 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 0.90 (t, J = 7.4 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 1.11–1.20 (m, 1H), 1.33–1.44 (m, 1H), 1.56–1.60 (m, 1H), 1.65 (d, J = 1.0 Hz, 1.5 H), 1.67 (d, J = 1.0 Hz, 1.5 H), 1.72–1.79 (m, 3H), 1.19–2.07 (m, 6H), 2.24 (dd, J = 3.2, 11.8 Hz, 1H), 2.40 (t, J = 11.8 Hz, 1H), 3.49 (dd, J = 7.5, 11.7 Hz, 1H), 3.64 (dd, J = 5.8, 11.7 Hz, 1H), 5.09 (dd, J = 8.1, 15.3 Hz, 1H), 5.26 (s, 0.5H), 5.30 (s, 0.5H), 5.33–5.40 (m, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 9.0, 9.2, 9.3, 11.7, 11.7, 14.0, 14.1, 17.3, 17.5, 25.7, 26.1, 27.9, 27.9, 31.1, 42.6, 42.8, 46.7, 46.8, 51.1, 51.2, 65.3, 88.6, 88.7, 89.3, 130.0, 130.4, 132.0, 132.0, 132.9, 133.0, 135.6, 136.0 ppm; MS (ESI): *m/z* 333 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{19}$H$_{34}$O$_3$Na: 333.2400, found: 333.2403.

(*E*)-Ethyl 3-(*trans*-3,5-diethyl-5-((1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)acrylate (*E*)-ethyl acrylate (210)

210
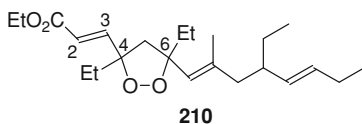
To a solution of **208** (22 mg, 0.07 mmol) in CH_2Cl_2 (1 mL) was added DMP (45 mg, 0.105 mmol). The reaction mixture was stirred until the starting material had disappeared, NaHCO$_3$ (25 mg, 0.30 mmol) was added. Then added saturated aq. NaHCO$_3$ solution (5 mL), and the mixture was extracted with Et$_2$O (3 × 10 mL). The combined extracts were washed with brine (25 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated on the rotary evaporator. The residue was purified by flash chromatography (hexanes/ethyl acetate) to afford the desired aldehyde, which was used in the next step. To a 0 °C suspension of NaH (5.3 mg, 60% in mineral oil, 0.13 mmol) in THF (0.8 mL) was added a solution of triethyl phosphonoacetate (31.4 mg, 0.14 mmol) in THF (0.5 mL). After stirring for 0.5 h, the aldehyde in THF (0.7 mL) was added slowly. The reaction mixture was warmed to room temperature, stirred until no starting material remained (TLC).

Quenched the reaction with saturated aq. NH_4Cl extracted with Et_2O three times and combined the organic layers and washed with brine and water, and dried over $MgSO_4$ and filtered. Removed the solvent with rotary evaporation. Flash chromatography on silica gel (8 g) of the residue gave the product **210** (21 mg, 80% in 2 steps) as a colorless oil : $R_f = 0.50$ (hexanes/EtOAc, 10:1); ^1H NMR (400 MHz, CDCl$_3$) $\delta = 0.81$ (t, $J = 7.4$ Hz, 3H), 0.85 (t, $J = 7.4$ Hz, 3H), 0.89 (t, $J = 7.5$ Hz, 3H), 0.94 (t, $J = 7.3$ Hz, 3H), 1.10–1.20 (m, 1H), 1.30 (t, $J = 7.1$ Hz, 3H), 1.33–1.40 (m, 1H), 1.63 (d, $J = 1.1$ Hz, 1.5H), 1.64 (d, $J = 1.0$ Hz, 1.5H), 1.65–1.70 (m, 2H), 1.72–1.86 (m, 2H), 1.87–1.93 (m, 1H), 1.94–2.10 (m, 4H), 2.49 (s, 1H), 2.51 (d, $J = 2.3$ Hz, 1H), 4.20 (q, $J = 7.2$ Hz, 1H), 5.07 (dd, $J = 8.3, 15.2$ Hz, 1H), 5.27 (d, $J = 10.6$ Hz, 1H), 5.33–5.40 (m, 1H), 6.06 (d, $J = 15.8$ Hz, 1H), 6.88 (d, $J = 15.8$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 8.8, 9.0, 9.1, 11.7, 11.7, 14.1, 14.1, 14.3, 17.6, 17.7, 25.7, 27.9, 28.0, 30.9, 31.0, 31.5, 31.5, 42.7, 42.8, 46.6, 46.6, 55.9, 56.0, 60.6, 87.3, 87.4, 89.3, 120.1, 129.0, 129.3, 132.0, 132.1, 132.8, 132.9, 135.9, 136.2, 149.2, 149.2, 166.7$ ppm; MS (ESI): m/z 382 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{23}H_{38}O_4Na$: 401.2662, found: 401.2661.

(R)-2-((tert-Butyldimethylsilyloxy)methyl)butyl acetate ((R)-218) and (S)-2-((tert-butyldimethylsilyloxy)methyl)butan-1-ol ((S)-167) [10, 13, 14]

(R)-**218**   (S)-**167**
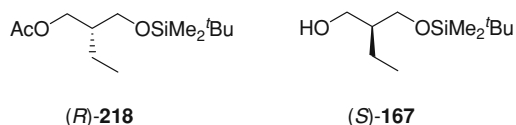
To a solution of racemic primary alcohol **167** (5.16 g,) in pentane was added the lipase extract PS3O (250 mg) and freshly distilled vinyl acetate. The heterogeneous mixture is stirred vigorously at room temperature for 24 h. Then filtered through a sintered glass funnel to recover the enzymatic extract. The extracted was washed with Et_2O, and combined the solutions and removed the solvents under vacuum. Purification by column chromatography on silica gel (200 g, hexanes/EtOAc, 10:1) to afford (R)-**218** (2.91 g, 47%) and (S)-**167** (2.40 g, 46%);

(R)-**218** : $R_f = 0.60$ (hexanes/EtOAc, 10:1); $[\alpha]_D^{20} = 1.2$ (c, 1.40, CHCl$_3$); ^1H NMR (400 MHz, CDCl$_3$) $\delta = 0.02$ (s, 6H), 0.87 (s, 9H); 0.91 (t, $J = 7.4$ Hz, 3H), 1.30–1.40 (m, 2H), 1.68–1.70 (m, 1H), 2.03 (s, 3H), 3.52–3.60 (m, 2H), 4.05 (d, $J = 5.8$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, 11.5, 18.3, 20.8, 21.0, 25.9, 41.9, 62.4, 64.5, 171.3$ ppm; MS (ESI): m/z [M + Na]$^+$ 283; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{13}H_{28}O_3SiNa$: 283.1700, found: 283.1704.

(S)-**167** : $R_f = 0.50$ (hexanes/EtOAc, 10:1); $[\alpha]_D^{20} = -10.7$ (c, 1.37, CHCl3); ^1H NMR (400 MHz, CDCl$_3$) $\delta = 0.06$ (s, 6H), 0.88 (s, 9H); 0.91 (t, $J = 7.4$ Hz, 3H), 1.22–1.30 (m, 2H), 1.60–1.65 (m, 1H), 2.95 (s, 1H), 3.60 (q, $J = 7.4$ Hz, 2H), 3.72 (d, $J = 10.4$ Hz, 1H), 3.79 (dd, $J = 3.8, 9.8$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.6, -5.5, 11.8, 18.2, 20.6, 25.9, 43.7, 66.4, 67.2$ ppm; MS (ESI): m/z [M + H]$^+$ 219;

(*R*)-2-((*tert*-Butyldimethylsilyloxy)methyl)butan-1-ol ((*R*)-167) [10, 11]

(*R*)-**167**
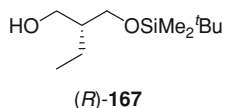
To a solution of (*R*)-**218** (426.4 mg, 1.64 mmol) in MeOH (30 mL) was added K$_2$CO$_3$ (226 mg, 1.64 mmol). The reaction mixture was stirred until the starting material had disappeared. Removed the solvent under reduced pressure. Water (20 mL) was added. The mixture was extracted with Et$_2$O (3 × 20 mL). The combined extracts were washed with brine (25 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated on the rotary evaporator. The residue was purified by flash chromatography on silica gel (20 g, hexanes/EtOAc, 8:1) to afford (*R*)-**167** (354 mg, 99%) as colorless oil; R_f = 0.50 (hexanes/EtOAc, 10:1); (*R*)-**167** : $[\alpha]_D^{20}$ = 10.6 (*c*, 1.67, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.06 (s, 6H), 0.88 (s, 9H); 0.91 (t, *J* = 7.4 Hz, 3H), 1.22–1.30 (m, 2H), 1.60–1.65 (m, 1H), 2.95 (s, 1H), 3.60 (q, *J* = 7.4 Hz, 2H), 3.72 (d, *J* = 10.4 Hz, 1H), 3.79 (dd, *J* = 3.8, 9.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.6, −5.5, 11.8, 18.2, 20.6, 25.9, 43.7, 66.4, 67.2 ppm; MS (ESI): *m/z* [M + H]$^+$ 219;

(*S*)-((*R*)-2-((*tert*-Butyldimethylsilyloxy)methyl)butyl) 2-(*tert*-butoxycarbonyl)-3-phenylpropanoate (220)

220
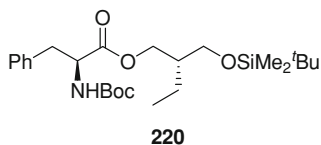
To a solution of (*R*)-**167** (34.9 mg, 0.16 mmol) and optically pure *N*-Boc protected L-phenylalanine **219** (46 mg, 1.05 equiv) in CH$_2$Cl$_2$ (2 mL) was added DMAP (10 mol%) and DCC (41 mg, 1.2 equiv) at 0 °C. The temperature was allowed to warm to room temperature. The reaction mixture was stirred overnight. Quenched the reaction with saturated aq. NH$_4$Cl extracted with Et$_2$O three times and combined the organic layers and washed with 10% aqueous HCl, brine and water, and dried over MgSO$_4$ and filtered. Removed the solvent with rotary evaporation. Flash chromatography on silica gel (8 g) of the residue gave the product (74.0 mg, 99%) as a colorless oil; R_f = 0.40 (hexanes/EtOAc, 5:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.03 (s, 6H), 0.88 (s, 9H); 0.91 (t, *J* = 7.5 Hz, 3H), 1.23–1.38 (m, 2H), 1.41 (s, 9H), 1.61–1.67 (m, 1H), 3.02–3.12 (m, 2H), 3.50 (d, *J* = 5.0 Hz, 2H), 4.07 (dd, *J* = 5.4, 10.8 Hz, 1H), 4.14 (dd, *J* = 6.2, 10.8 Hz, 1H), 4.56–4.60 (m, 1H), 4.97 (d, *J* = 8.1 Hz, 1H), 7.13 (d, *J* = 6.8 Hz, 2H), 7.2–7.3 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, −5.4, 11.4, 18.3, 20.6, 25.9, 28.4, 38.6, 42.0, 54.5, 62.2, 65.4, 79.9, 127.0, 128.6, 129.4, 136.2,

155.1, 172.0 ppm; MS (ESI): m/z [M + Na]$^+$ 488; HRMS (ESI) m/z [M + Na]$^+$
calcd for C$_{25}$H$_{43}$NNaO$_5$Si: 488.2803, found: 488.2811.

(R,E)-*tert*-Butyl(2-ethylhex-3-enyloxy)dimethylsilane (222a) [11]
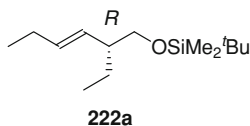
222a

The procedure was similar to that for the preparation of **169** (vide supra):
yield = 89% (two steps); R_f = 0.35 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = −16.6 (c, 1.49,
CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.03 (s, 6H), 0.85 (t, J = 7.4 Hz, 3H), 0.90
(s, 9H), 0.98 (t, J = 7.6 Hz, 3H), 1.16–1.26 (m, 1H), 1.49– 1.59 (m, 1H), 1.97–2.05
(m, 3H), 3.43–3.51 (m, 2H), 5.15 (ddt, J = 1.4, 7.2, 15.4 Hz, 1H), 5.48 (dt, J = 6.5,
15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.2, −5.2, 11.7, 14.0, 18.5,
24.1, 25.9, 26.0, 47.2, 67.0, 130.4, 133.4 ppm; MS (ESI): m/z [M + Na]$^+$ 265; HRMS
(ESI) m/z [M + Na]$^+$ calcd for C$_{14}$H$_{30}$NaOSi: 265.1958, found: 265.1952.

(R,E)-2-Ethylhex-3-en-1-ol (223a) [11]
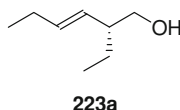
223a

The procedure was similar to that for the preparation of **170** (vide supra):
yield = 86%; R_f = 0.35 (hexanes/EtOAc, 9:1); $[\alpha]_D^{20}$ = −3.0 (c, 0.32, CHCl$_3$); ^{1}H
NMR (400 MHz, CDCl$_3$) δ = 0.85 (t, J = 7.4 Hz, 3H), 0.98 (t, J = 7.6 Hz, 3H),
1.16–1.27 (m, 1H), 1.38–1.43 (m, 2H), 2.01–2.09 (m, 3H), 3.35 (t, J = 10.6 Hz,
1H), 3.51–3.57 (m, 1H), 5.13 (ddt, J = 1.4, 7.4, 15.4 Hz, 1H), 5.60 (dt, J = 6.3,
15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 11.7, 14.1, 24.1, 25.8, 47.7,
65.8, 130.0, 135.9 ppm; MS (EI): m/z [M]$^+$ 128; HRMS (EI) m/z [M]$^+$ calcd for
C$_8$H$_{16}$O: 128.1196, found: 128.1197.

(R,E)-5-(Iodomethyl)hept-3-ene ((R)-91) [11, 15]
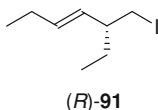
(R)-**91**

The procedure was similar to that for the preparation of recemic-**91** (vide supra);
yield = 86%; R_f = 0.80 (hexanes); R_f = 0.80 (hexanes); ^{1}H NMR (400 MHz,
CDCl$_3$) δ = 0.86 (t, J = 7.4 Hz, 3H), 0.99 (t, J = 7.5 Hz, 3H), 1.26–1.33 (m, 1H),
1.52–1.58 (m, 1H), 1.96–2.07 (m, 3H), 3.16 (d, J = 6.1 Hz, 2H), 5.13 (dd, J = 8.4,

15.2 Hz, 1H), 5.52 (dt, $J = 6.4$, 15.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.6$, 13.9, 14.8, 25.7, 27.9, 45.9, 130.9, 134.5 ppm; MS (ESI): m/z [M]$^+$ 238.

(S,E)-*tert*-Butyl(2-ethylhex-3-enyloxy)dimethylsilane (222b) [11]
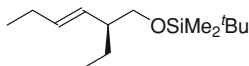
222b

The procedure was similar to that for the preparation of **169** (vide supra): yield = 89% (two steps); $R_f = 0.35$ (hexanes/EtOAc, 20:1); $[\alpha]_D^{20} = 16.2$ (c, 0.95, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.03$ (s, 6H), 0.85 (t, $J = 7.4$ Hz, 3H), 0.90 (s, 9H), 0.98 (t, $J = 7.6$ Hz, 3H), 1.16–1.26 (m, 1H), 1.49–1.59 (m, 1H), 1.97–2.05 (m, 3H), 3.43–3.51 (m, 2H), 5.15 (ddt, $J = 1.4$, 7.2, 15.4 Hz, 1H), 5.48 (dt, $J = 6.5$, 15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.2$, -5.2, 11.7, 14.0, 18.5, 24.1, 25.9, 26.0, 47.2, 67.0, 130.4, 133.4 ppm; MS (ESI): m/z [M + Na]$^+$ 265; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{14}$H$_{30}$NaOSi: 265.1958, found: 265.1948.

(S,E)-2-Ethylhex-3-en-1-ol (223b) [11, 12]
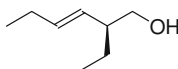
223b

The procedure was similar to that for the preparation of **170** (vide supra): yield = 86%; $R_f = 0.35$ (hexanes/EtOAc, 9:1); $[\alpha]_D^{20} = 2.9$ (c, 0.40, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.85$ (t, $J = 7.4$ Hz, 3H), 0.98 (t, $J = 7.6$ Hz, 3H), 1.16–1.27 (m, 1H), 1.38–1.43 (m, 2H), 2.01–2.09 (m, 3H), 3.35 (t, $J = 10.6$ Hz, 1H), 3.51–3.57 (m, 1H), 5.13 (ddt, $J = 1.4$, 7.4, 15.4 Hz, 1H), 5.60 (dt, $J = 6.3$, 15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.7$, 14.1, 24.1, 25.8, 47.7, 65.8, 130.0, 135.9 ppm; MS (EI): m/z [M]$^+$ 128; HRMS (EI) m/z [M]$^+$ calcd for C$_8$H$_{16}$O: 128.1196, found: 128.1196.

(S,E)-5-(Iodomethyl)hept-3-ene ((S)-91) [11, 12]
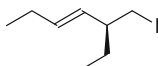
(S)-**91**

The procedure was similar to that for the preparation of recemic-**91** (vide supra); yield = 86%; $R_f = 0.80$ (hexanes); ^{1}H NMR (400 MHz, CDCl$_3$) $= 0.86$ (t, $J = 7.4$ Hz, 3H), 0.99 (t, $J = 7.5$ Hz, 3H), 1.26–1.33 (m, 1H), 1.52–1.58 (m, 1H), 1.96–2.07 (m, 3H), 3.16 (d, $J = 6.1$ Hz, 2H), 5.13 (dd, $J = 8.4$, 15.2 Hz,

1H), 5.52 (dt, $J = 6.4$, 15.0 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = 11.6$, 13.9, 14.8, 25.7, 27.9, 45.9, 130.9, 134.5 ppm; MS (ESI): m/z [M]$^+$ 238.

(*S*)-((3*R*,5*S*)-5-((*tert*-Butyldimethylsilyloxy)methyl)-3,5-diethyl-1,2-dioxolan-3-yl)methyl 2-(*tert*-butoxycarbonyl)-3-phenylpropanoate (234) and (*S*)-((3*S*,5*R*)-5-((*tert*-Butyldimethylsilyloxy)methyl)-3,5-diethyl-1,2-dioxolan-3-yl)methyl 2-(*tert*-butoxycarbonyl)-3-phenylpropanoate (235)
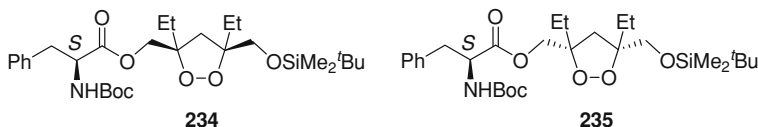
To a solution of *cis*-**137** (53.7 mg, 0.18 mmol) and optically pure *N*-Boc protected L-phenylalanine **219** (70.2 mg, 1.5 equiv) in CH$_2$Cl$_2$ (2 mL) was added DMAP (10 mol%) and DCC (54.7 mg, 1.5 equiv) at 0 °C. The temperature was allowed to warm to room temperature. The reaction mixture was stirred overnight. Quenched the reaction with saturated aq. NH$_4$Cl extracted with Et$_2$O three times and combined the organic layers and washed with 10% aqueous HCl, brine and water, and dried over MgSO$_4$ and filtered. Removed the solvent with rotary evaporation. Flash chromatography on silica gel (10 g) of the residue gave the product (90.9 mg, 93%) as a colorless oil; $R_f = 0.30$ (hexanes/EtOAc, 5:1); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.08$ (s, 6H), 0.87–0.93 (m, 6H), 0.90 (s, 9H), 1.41 (s, 9H), 1.54–1.64 (m, 2H), 1.70–1.82 (m, 2H), 2.05 (dd, $J = 4.5$ Hz, 12.4 Hz, 1H), 2.25–2.30 (m, 1H), 3.03–3.15 (m, 2H), 3.52–3.62 (m, 2H), 3.97–4.03 (m, 1H), 4.33 (d, $J = 11.6$ Hz, 1H), 4.58–4.63 (m, 1H), 4.98 (s, 1H), 7.13–7.16 (m, 2H), 7.21–7.30 (m, 3H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, -5.4$, -5.4, 8.5, 8.7, 8.7, 18.4, 18.4, 25.9, 26.4, 26.7, 27.8, 28.2, 28.4, 38.4, 45.6, 45.6, 54.4, 54.5, 63.4, 63.6, 65.2, 65.2, 79.9, 86.8, 86.9, 89.1, 127.0, 127.1, 128.6, 129.3, 129.5, 136.0, 136.0, 155.1, 171.7, 171.7 ppm; IR (Neat): 3381, 2957, 2931, 2883, 2858, 1745, 1718, 1497, 1472, 1462, 1366, 1253, 1169, 1115, 1007, 838, 779, 738, 701 cm^{-1}; MS (ESI): m/z [M + Na]$^+$ 574; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{29}$H$_{49}$NNaO$_7$Si: 574.3171, found: 574.3190.

(−)-(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methyl acetate ((−)-*cis*-245) and (+)-(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methanol ((+)-*cis*-137a)
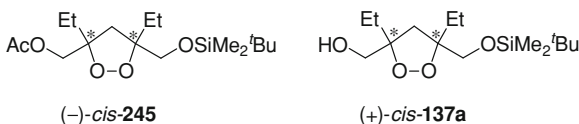
To a solution of racemic alcohol (±)-*cis*-**137** (1.11 g, 3.65 mmol) in hexane (40 mL) was added the Lipase PS from *Burkholderia cepaci* (555 mg) and vinyl

acetate (1.68 mL, 18.3 mmol). The heterogeneous mixture was stirred vigorously at rt for 29 h before being filtered through a sintered glass funnel to recover the lipase catalyst. The catalyst was washed with Et$_2$O (20 mL), and the combined filtrates were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (25 g, hexanes/EtOAc, 10:1) to afford (−)-*cis*-**245** (695 mg, 55%) and (+)-*cis*-**137a** (477 mg, 43%) as colorless oil;

(−)-*cis*-**245**: R_f = 0.50 (hexanes/EtOAc, 10:1); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.05 (s, 6H), 0.88 (s, 9H), 0.90 (t, J = 7.5 Hz, 3H), 0.92 (t, J = 7.6 Hz, 3H), 1.56–1.66 (m, 2H), 1.73–1.82 (m, 2H), 2.05 (d, J = 12.4 Hz, 1H), 2.06 (s, 3H), 2.33 (d, J = 12.4 Hz, 1H), 3.53 (d, J = 10.8 Hz, 1H), 3.60 (d, J = 10.8 Hz, 1H), 4.02 (d, J = 11.8 Hz, 1H), 4.21 (d, J = 11.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.5, −5.4, 8.4, 8.6, 18.3, 20.9, 25.9, 27.0, 27.7, 45.5, 63.6, 64.4, 86.9, 89.0, 170.8 ppm; MS (ESI): *m/z* 347 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{17}$H$_{35}$O$_5$Si: 347.2248, found: 347.2248.

(+)-*cis*-**137a**: R_f = 0.35 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 28.5 (*c* 1.13, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.06 (s, 6H), 0.89 (s, 9H), 0.90 (t, J = 7.5 Hz, 3H), 0.94 (t, J = 7.5 Hz, 3H), 1.57–1.66 (m, 2H), 1.75–1.83 (m, 2H), 2.02 (s, 1H), 2.06 (d, J = 12.3 Hz, 1H), 2.32 (d, J = 12.3 Hz, 1H), 3.46 (dd, J = 7.6 Hz, 11.9 Hz, 1H), 3.58 (d, J = 3.0 Hz, 2H), 3.72 (dd, J = 4.6 Hz, 11.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, 8.5, 8.9, 18.4, 25.9, 26.3, 28.0, 44.8, 63.8, 64.00, 89.1, 89.2 ppm; MS (ESI): *m/z* 305 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{15}$H$_{33}$O$_4$Si: 305.2143, found: 305.2141.

(+)-(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methyl 4-methylbenzenesulfonate ((+)-*cis*-272a)

(+)-*cis*-**272a**
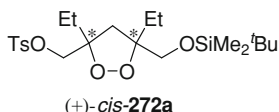
To a solution of acetate (+)-*cis*-**137a** (46 mg, 0.15 mmol) in CH$_2$Cl$_2$ (1 mL) was added *p*-TsCl (34 mg, 1.8 mmol), Et$_3$N (2.0 eq) and DMAP (10 mol %). The reaction mixture was stirred until the starting material had disappeared. Removed the solvent, the residue was purified by flash chromatography on silica gel (10 g, hexanes/EtOAc, 10:1) to afford **272a** (61 mg, 89%): R_f = 0.40 (hexanes/EtOAc, 10: 1); *ee* > 99%; The *ee* values were determined by chiral HPLC; CHIRALPAK AD-H column; hexane/2-propanol 95/5; flow rate 1.0 mL/min; temp 25 °C; wavelength = 254 nm; retention time: 4.9 min; ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.00 (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 0.87 (t, J = 7.0 Hz, 6H), 1.52–1.66 (m, 2H), 1.71–1.82 (m, 2H), 2.03 (d, J = 12.6 Hz, 1H), 2.33 (d, J = 12.6 Hz, 1H), 2.44 (s, 3H), 3.48 (s, 2H), 3.91 (d, J = 10.1 Hz, 1H), 4.15 (d, J = 10.1 Hz, 1H), 7.33 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.3 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.5, −5.4, 8.4, 18.3, 21.7, 25.9, 26.4, 28.1, 45.3, 63.2, 69.4, 86.7,

89.2, 128.0, 129.9, 132.9, 144.9 ppm; MS (ESI): *m/z* 459 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{22}H_{39}O_6SSi$: 459.2231, found: 459.2225.

(−)-(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methanol ((−)-*cis*-137b)
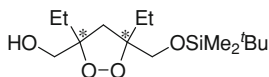
(–)-*cis*-**137b**

To a solution of racemic alcohol (±)-*cis*-**137** (1.11 g, 3.65 mmol) in hexane (40 mL) was added the Lipase PS from Burkholderia cepaci (555 mg) and vinyl acetate (1.68 mL, 18.3 mmol). The heterogeneous mixture is stirred vigorously at rt for 3 h before being filtered through a sintered glass funnel to recover the lipase catalyst. The catalyst was washed with Et$_2$O (20 mL), and the combined filtrates were concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (30 g, hexanes/EtOAc, 10:1) to afford (−)-*cis*-**245** (568 mg, 45%) and (+)-*cis*-**137a** (588 mg, 53%). (−)-*cis*-**245**: R_f = 0.50 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −21.5 (*c*, 0.89, CHCl$_3$);

To a solution of acetate (−)-*cis*-**245** (568 mg, 1.64 mmol) in MeOH (30 mL) was added K$_2$CO$_3$ (226 mg, 1.64 mmol). The reaction mixture was stirred until the starting material had disappeared, the reaction mixture was acidified to *p*H 6 with 10% aqueous HCl. Removed the solvent under reduced pressure. The residue was extracted with Et$_2$O (3 × 20 mL). The combined extracts were washed with brine (25 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated on the rotary evaporator. The residue was purified by flash chromatography on silica gel (30 g, hexanes/EtOAc, 10:1) to afford (−)-*cis*-**137b** (469 mg, 94%) as colorless oil : R_f = 0.35 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −27.5 (*c* 0.47, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.06 (s, 6H), 0.89 (s, 9H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H), 1.57–1.66 (m, 2H), 1.75–1.83 (m, 2H), 2.02 (bs, 1H), 2.06 (d, *J* = 12.3 Hz, 1H), 2.32 (d, *J* = 12.3 Hz, 1H), 3.46 (dd, *J* = 7.6 Hz, 11.9 Hz, 1H), 3.58 (d, *J* = 3.0 Hz, 2H), 3.72 (dd, *J* = 4.6 Hz, 11.9 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = –5.4, 8.5, 8.9, 18.4, 25.9, 26.3, 28.0, 44.8, 63.9, 64.00, 89.1, 89.2 ppm; MS (ESI): *m/z* 327 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for $C_{15}H_{32}O_4SiNa$: 327.1962, found: 327.1968.

(−)-(5-((*tert*-Butyldimethylsilyloxy)methyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methyl 4-methylbenzenesulfonate ((−)-*cis*-272b)
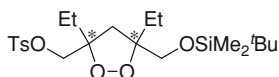
(–)-*cis*-**272b**

To increase the *ee*, (−)-*cis*-**137b** was resolved again. Then it was converted into (−)-*cis*-**272b** to determine the *ee* value. The procedure was similar to that for the preparation of (+)-*cis*-**272a** (vide supra): $R_f = 0.40$ (hexanes/EtOAc, 10:1); *ee* > 99%; The *ee* values were determined by chiral HPLC; CHIRALPAK AD-H column; hexane/2-propanol 95/5; flow rate 1.0 mL/min; temp 25 °C; wavelength = 254 nm; retention time: 5.4 min; ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.00$ (s, 3H), 0.01 (s, 3H), 0.85 (s, 9H), 0.87 (t, $J = 7.0$ Hz, 6H), 1.52–1.66 (m, 2H), 1.71–1.82 (m, 2H), 2.03 (d, $J = 12.6$ Hz, 1H), 2.33 (d, $J = 12.6$ Hz, 1H), 2.44 (s, 3H), 3.48 (s, 2H), 3.91 (d, $J = 10.1$ Hz, 1H), 4.15 (d, $J = 10.1$ Hz, 1H), 7.33 (d, $J = 8.1$ Hz, 2H), 7.79 (d, $J = 8.3$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, -5.4, 8.4, 18.3, 21.7, 25.9, 26.4, 28.1, 45.3, 63.2, 69.4, 86.7, 89.2,$ 128.0, 129.9, 132.9, 144.9 ppm; MS (ESI): *m/z* 459 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{22}$H$_{39}$O$_6$SSi: 459.2231, found: 459.2225.

(+)-*tert*-Butyl((5-(2,2-dibromovinyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((+)-*cis*-247a)
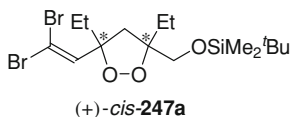
(+)-*cis*-**247a**

The procedure was similar to that for the preparation of *trans*-**155** (vide supra); yield = 79% (two steps); $R_f = 0.75$ (hexanes/EtOAc, 20:1); $[\alpha]_D^{20} = -11.0$ (*c*, 0.75, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.07$ (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 0.92 (t, $J = 7.5$ Hz, 3H), 0.94 (t, $J = 7.4$ Hz, 3H), 1.60–1.66 (m, 1H), 1.75–1.87 (m, 2H), 2.07–2.12 (m, 1H), 2.23 (d, $J = 12.5$ Hz, 1H), 2.80 (d, $J = 12.5$ Hz, 1H), 3.49 (d, $J = 10.5$ Hz, 1H), 3.58 (d, $J = 10.5$ Hz, 1H), 6.79 (s, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3, 8.5, 8.9, 18.4, 25.9,$ 27.4, 29.1, 50.0, 64.1, 87.4, 88.9, 90.1, 142.5 ppm; IR (Neat): 2955, 2929, 2883, 2858, 1462, 1256, 1115, 838, 777 cm^{-1}; MS (ESI): *m/z* 459 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for C$_{16}$H$_{31}$Br$_2$O$_3$Si: 459.0383, found: 459.0391.

(+)-*tert*-Butyl((*cis*-3,5-diethyl-5-ethynyl-1,2-dioxolan-3-yl)methoxy)dimethyl-silane ((+)-*cis*-248a)
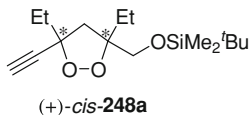
(+)-*cis*-**248a**

The procedure was similar to that for the preparation of *trans*-**148** (vide supra); yield = 95%; $R_f = 0.55$ (hexanes/Et$_2$O 20:1); $[\alpha]_D^{20} = 17.0$ (*c*, 1.60, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) $\delta = 0.07$ (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 0.92

(t, $J = 7.5$ Hz, 3H), 1.07 (t, $J = 7.4$ Hz, 3H), 1.60–1.67 (m, 1H), 1.67–1.80 (m, 2H), 1.85–1.92 (m, 1H), 2.25 (d, $J = 12.4$ Hz, 1H), 2.51 (s, 1H), 2.70 (d, $J = 12.4$ Hz, 1H), 3.70 (q, $J = 10.3$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.4, -5.3, 8.4, 9.4, 18.3, 25.9, 27.1, 32.1, 52.5, 64.2, 73.7, 82.3, 83.4, 89.2$, ppm; IR (Neat): 3311, 2956, 2931, 2883, 2858, 1472, 1463, 1259, 1111, 1007, 838, 670 cm^{-1}; MS (ESI): m/z 299 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{16}$H$_{31}$O$_3$Si: 299.2037, found: 299.2037.

(+)-*tert*-Butyl((*cis*-3,5-diethyl-5-(prop-1-ynyl)-1,2-dioxolan-3-yl)methoxy) dimethylsilane ((+)-*cis*-249a)

(+)-*cis*-**249a**
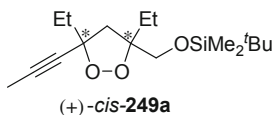
The procedure was similar to that for the preparation of *trans*-**147** (vide supra); yield = 70%; $R_f = 0.55$ (hexanes/Et$_2$O 20:1); $[\alpha]_D^{20} = 9.5$ (*c*, 1.70, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.07$ (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.90 (t, $J = 7.5$ Hz, 3H), 1.03 (t, $J = 7.4$ Hz, 3H), 1.61–1.67 (m, 2H), 1.69–1.77 (m, 1H), 1.81–1.88 (m, 1H), 1.85 (s, 3H), 2.20 (d, $J = 12.3$ Hz, 1H), 2.60 (d, $J = 12.3$ Hz, 1H), 3.68 (q, $J = 10.2$ Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) $\delta = -5.5, -5.3, 3.7, 8.4, 9.5, 18.3, 25.9, 26.9, 32.5, 52.3, 64.4, 78.6, 82.0, 82.7, 89.1$, ppm; MS (ESI): m/z 335 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{17}$H$_{32}$O$_3$SiNa: 335.2013, found: 335.2008.

(+)-(*E*)-*tert*-Butyl((*cis*-3,5-diethyl-5-(2-iodoprop-1-enyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((+)-*cis*-246a)
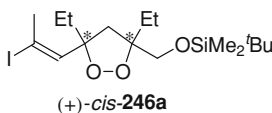
(+)-*cis*-**246a**

To a 10-mL, argon-filled, two-necked round-bottomed flask equipped with a magnetic stirring bar was added (+)-*cis*-**249a** (64 mg, 0.206 mmol) and Pd(PPh$_3$)$_2$Cl$_2$ (10 mol%). The flask was evacuated and filled with argon three times, and then freshly distilled *n*-hexane (2 mL) was added via a syringe. Tributyltin hydride (4.0 equiv) was added slowly (about over 10 min) via a syringe. The reaction was stirred at 23 °C for 1 h, then immediately transferred to a silica gel column and rapidly eluted with hexanes until the excess Bu$_3$SnH/ (Bu$_3$Sn)$_2$ is removed, followed by elution with a mixture of hexanes and ethyl acetate (10:1) to obtain the stannane compound **250a** (104 mg, 84%) as a colorless oil: $R_f = 0.60$ (hexanes/EtOAc, 20:1). The obtained stannane compound was

dissolved in CH_2Cl_2 (3 mL) and cooled to 0 °C. I_2 (43 mg, 0.17 mmol) in CH_2Cl_2 (1 mL) was added and the resulting mixture was stirred at 0 °C for 5–8 min then worked up by a saturated aq. $Na_2S_2O_3$ solution (3 mL) and extracted by Et_2O (3 × 10 mL). The combined organic layers were washed with brine (10 mL), dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexanes/EtOAc, 20:1) to give **246a** (65 mg, 86%) as an oil: R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = 1.2 (*c*, 2.24, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$): δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.93 (t, *J* = 7.5 Hz, 3H), 1.58–1.74 (m, 2H), 1.76–1.88 (m, 2H), 2.18 (d, *J* = 12.2 Hz, 1H), 2.42 (d, *J* = 12.2 Hz, 1H), 2.53 (d, *J* = 0.7 Hz, 3H), 3.50 (d, *J* = 10.4 Hz, 1H), 3.62 (d, *J* = 10.4 Hz, 1H), 6.14 (d, *J* = 0.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.4, −5.3, 8.5, 9.0, 18.3, 25.9, 27.0, 30.3, 31.8, 51.3, 64.4, 88.4, 90.6, 96.6, 142.2 ppm; MS (ESI): *m/z* 441 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{17}H_{34}IO_3Si$: 441.1316, found: 441.1320.

(−)-*tert*-Butyl((5-(2,2-dibromovinyl)-*cis*-3,5-diethyl-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((−)-*cis*-247b)
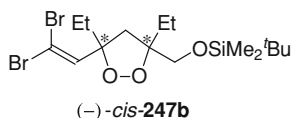
(−)-*cis*-**247b**

The procedure was similar to that for the preparation of *trans*-**155** (vide supra); yield = 79% (two steps); R_f = 0.75 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = 10.0 (*c*, 2.55, $CHCl_3$); ^1H NMR (400 MHz, $CDCl_3$) δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.90 (s, 9H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 3H), 1.60–1.66 (m, 1H), 1.75–1.87 (m, 2H), 2.07–2.12 (m, 1H), 2.23 (d, *J* = 12.5 Hz, 1H), 2.80 (d, *J* = 12.5 Hz, 1H), 3.49 (d, *J* = 10.5 Hz, 1H), 3.58 (d, *J* = 10.5 Hz, 1H), 6.79 (s, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ = −5.4, −5.3, 8.5, 8.9, 18.4, 25.9, 27.4, 29.1, 50.0, 64.1, 87.4, 88.9, 90.1, 142.5 ppm; MS (ESI): *m/z* 459 [M + H]$^+$; HRMS (ESI) *m/z* [M + H]$^+$ calcd for $C_{16}H_{31}Br_2O_3Si$: 459.0383, found: 459.0385.

(−)-*tert*-Butyl((*cis*-3,5-diethyl-5-ethynyl-1,2-dioxolan-3-yl)methoxy)dimethyl-silane ((−)-*cis*-248b)
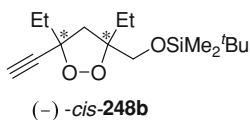
(−)-*cis*-**248b**

The procedure was similar to that for the preparation of *trans*-**148** (vide supra); yield = 95%; R_f = 0.55 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = −17.5 (*c* 0.64, $CHCl_3$);

^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.89 (s, 9H), 0.92 (t, J = 7.5 Hz, 3H), 1.07 (t, J = 7.4 Hz, 3H), 1.56–1.65 (m, 1H), 1.67–1.80 (m, 2H), 1.85–1.94 (m, 1H), 2.25 (d, J = 12.4 Hz, 1H), 2.52 (s, 1H), 2.70 (d, J = 12.4 Hz, 1H), 3.70 (q, J = 10.3 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, −5.3, 8.4, 9.4, 18.3, 25.9, 27.1, 32.1, 52.5, 64.2, 73.7, 82.3, 83.4, 89.2 ppm; MS (ESI): m/z 299 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{16}$H$_{31}$O$_3$Si: 299.2037, found: 299.2032.

(−)-*tert*-Butyl((*cis*-3,5-diethyl-5-(prop-1-ynyl)-1,2-dioxolan-3-yl)methoxy) dimethylsilane ((−)-*cis*-249b)

(−)-*cis*-249b
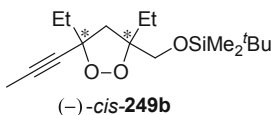
The procedure was similar to that for the preparation of *trans*-147 (vide supra); yield = 70%; R_f = 0.75 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = −9.0 (*c*, 2.05, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.90 (t, J = 7.5 Hz, 3H), 1.03 (t, J = 7.4 Hz, 3H), 1.61–1.67 (m, 2H), 1.69–1.77 (m, 1H), 1.81–1.88 (m, 1H), 1.85 (s, 3H), 2.20 (d, J = 12.3 Hz, 1H), 2.60 (d, J = 12.3 Hz, 1H), 3.69 (q, J = 10.2 Hz, 2H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.5, −5.3, 3.7, 8.4, 9.5, 18.3, 25.9, 26.9, 32.5, 52.3, 64.4, 78.6, 82.0, 82.7, 89.1 ppm; MS (ESI): m/z 335 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{17}$H$_{32}$O$_3$SiNa: 335.2013, found: 335.2016.

(−)-(*E*)-*tert*-Butyl((*cis*-3,5-diethyl-5-(2-iodoprop-1-enyl)-1,2-dioxolan-3-yl) methoxy)dimethylsilane ((−)-*cis*-246b)
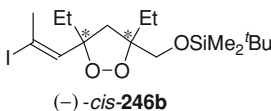
(−)-*cis*-246b

The procedure was similar to that for the preparation of (+)-*cis*-246a (vide supra): yield = 72% (two steps); R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = −1.5 (*c*, 1.60, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.07 (s, 3H), 0.08 (s, 3H), 0.88 (s, 9H), 0.91 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.5 Hz, 3H), 1.58–1.74 (m, 2H), 1.76–1.88 (m, 2H), 2.18 (d, J = 12.2 Hz, 1H), 2.42 (d, J = 12.2 Hz, 1H), 2.53 (d, J = 0.7 Hz, 3H), 3.50 (d, J = 10.4 Hz, 1H), 3.62 (d, J = 10.4 Hz, 1H), 6.14 (d, J = 0.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.4, −5.3, 8.5, 9.0, 18.3, 25.9, 27.0, 30.3, 31.8, 51.3, 64.4, 88.4, 90.6, 96.6, 142.2 ppm; MS (ESI): m/z 441 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{17}$H$_{34}$IO$_3$Si: 441.1316, found: 441.1322.

tert-Butyl(((+)-cis-3,5-diethyl-5-((S,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((8S)-(+)-cis-251a)
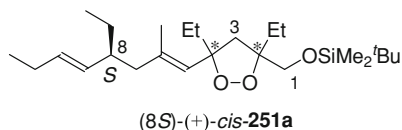
(8S)-(+)-cis-**251a**

The synthesis of (8S)-(+)-cis-**251a** was similar to that for the preparation of **206** (vide supra): yield = 93%; R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = 60.5 (c, 0.47, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ = −0.04 (s, 3H), 0.05 (s, 3H), 0.83 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H), 0.88 (s, 9H), 0.92 (t, J = 7.4 Hz, 3H), 0.96 (t, J = 7.4 Hz, 3H), 1.09–1.17 (m, 1H), 1.34–1.41 (m, 1H), 1.58–1.65 (m, 2H), 1.63 (d, J = 1.1 Hz, 3H), 1.73–1.83 (m, 1H), 1.85–1.92 (m, 2H), 1.94–2.04 (m, 4H), 2.03 (d, J = 12.6 Hz, 1H), 2.24 (s, 2H), 3.42 (d, J = 10.3 Hz, 1H), 3.64 (d, J = 10.3 Hz, 1H), 5.07 (dd, J = 8.3, 15.3 Hz, 1H), 5.18 (s, 1H), 5.36 (dt, J = 6.3, 15.3 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ = −5.5, −5.2, 8.8, 9.0, 11.7, 14.1, 17.9, 18.3, 25.7, 25.9, 26.3, 27.6, 32.2, 42.6, 46.6, 51.9, 64.5, 88.3, 88.7, 127.3, 131.9, 132.9, 135.9 ppm; MS (ESI): m/z 447 [M + Na]⁺; HRMS (ESI) m/z [M + Na]⁺ calcd for $C_{25}H_{48}O_3SiNa$: 447.3265, found: 447.3279.

((+)-cis-3,5-Diethyl-5-((S,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methanol ((8S)-(+)-cis-252a)

(8S)-(+)-cis-**252a**
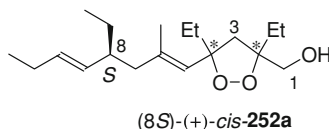
The procedure was similar to that for the preparation of **208** (vide supra): yield = 89%; R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = -81.2 (c, 0.29, CHCl₃); ¹H NMR (400 MHz, CDCl₃) δ = 0.83 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 0.94 (t, J = 7.6 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 1.09–1.20 (m, 1H), 1.31–1.40 (m, 1H), 1.54–1.68 (m, 2H), 1.64 (d, J = 0.8 Hz, 3H), 1.73–1.83 (m, 1H), 1.85–1.92 (m, 2H), 1.94–2.06 (m, 5H), 2.28 (q, J = 11.9 Hz, 2H), 3.40 (dd, J = 7.0, 11.7 Hz, 1H), 3.62 (dd, J = 4.0, 11.8 Hz, 1H), 5.05 (dd, J = 8.4, 15.2 Hz, 1H), 5.17 (s, 1H), 5.36 (dt, J = 6.3, 15.2 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ = 9.0, 9.0, 11.7, 14.1, 17.9, 25.7, 26.0, 27.9, 32.2, 42.7, 46.6, 51.2, 64.5, 88.8, 89.5, 126.7, 132.1, 132.7, 136.7 ppm; MS (ESI): m/z 333 [M + Na]⁺; HRMS (ESI) m/z [M + Na]⁺ calcd for $C_{19}H_{34}O_3Na$: 333.2400, found: 333.2400.

(*E*)-Methyl 3-((+)-*cis*-3,5-diethyl-5-((*S*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-die-nyl)-1,2-dioxolan-3-yl)acrylate (*S*-(+)-*cis*-86a)
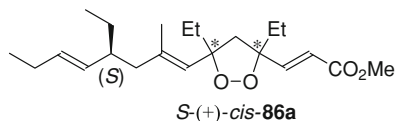
S-(+)-*cis*-**86a**

The procedure was similar to that for the preparation of **210** (vide supra): yield = 80% (two steps); R_f = 0.50 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −86.0 (*c*, 0.26, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.80 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H), 1.07–1.14 (m, 1H), 1.31–1.38 (m, 1H), 1.61 (d, *J* = 0.7 Hz, 3H), 1.62–1.69 (m, 1H), 1.70–1.82 (m, 2H), 1.83–1.93 (m, 2H), 1.94–2.02 (m, 4H), 2.44 (d, *J* = 11.9 Hz, 1H), 2.54 (d, *J* = 11.9 Hz, 1H), 3.73 (s, 3H), 5.05 (dd, *J* = 8.3, 15.2 Hz, 1H), 5.11 (s, 1H), 5.34 (dt, *J* = 15.2, 6.3 Hz, 1H), 6.07 (d, *J* = 15.8 Hz, 1H), 6.85 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.9, 8.9, 11.6, 14.1, 17.8, 25.6, 27.6, 30.9, 32.2, 42.6, 46.6, 51.6, 56.0, 87.2, 89.3, 119.9 126.7, 132.0, 132.8, 136.6, 149.80, 167.1 ppm; IR (Neat): 2963, 2919, 2849, 1720, 1656, 1461, 1262, 798 cm^{-1}; MS (ESI): *m/z* 382 [M + NH$_4$]$^+$; HRMS (ESI) *m/z* [M + NH$_4$]$^+$ calcd for C$_{22}$H$_{40}$O$_4$N: 382.2952, found: 382.2943.

tert-Butyl(((−)-*cis*-3,5-diethyl-5-((*R*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((8*R*)-(−)-*cis*-251d)

(8*R*)-(−)-*cis*-**251d**
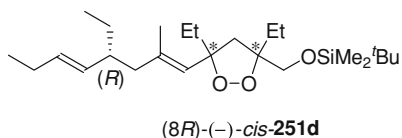
The synthesis of **251d** was similar to that for the preparation of **206** (vide supra): yield = 93%; R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = 62.0 (*c*, 1.12, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.83 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.88 (s, 9H), 0.92 (t, *J* = 7.4 Hz, 3H), 0.96 (t, *J* = 7.4 Hz, 3H), 1.09–1.17 (m, 1H), 1.34–1.41 (m, 1H), 1.58–1.65 (m, 2H), 1.63 (d, *J* = 1.1 Hz, 3H), 1.73–1.83 (m, 1H), 1.85–1.92 (m, 2H), 1.94–2.04 (m, 4H), 2.03 (d, *J* = 12.6 Hz, 1H), 2.24 (s, 2H), 3.42 (d, *J* = 10.3 Hz, 1H), 3.64 (d, *J* = 10.3 Hz, 1H), 5.07 (dd, *J* = 8.3, 15.3 Hz, 1H), 5.18 (s, 1H), 5.36 (dt, *J* = 6.3, 15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = −5.5, −5.2, 8.8, 9.0, 11.7, 14.1, 17.9, 18.3, 25.7, 25.9, 26.3, 27.6, 32.2, 42.6, 46.6, 51.9, 64.5, 88.3, 88.7, 127.3, 131.9, 132.9, 135.9 ppm; IR (Neat): 2961, 2930, 2857, 1463, 1263, 1119, 741 cm^{-1}; MS (ESI): *m/z* 447 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{25}$H$_{48}$O$_3$SiNa: 447.3265, found: 447.3259.

((−)-*cis*-3,5-Diethyl-5-((*R*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methanol ((8*R*)-(−)-*cis*-252d)
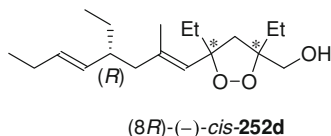
(8*R*)-(−)-*cis*-**252d**

The procedure was similar to that for the preparation of **208** (vide supra): yield = 86%; R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 80.0 (*c*, 0.80, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$) δ = 0.82 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.6 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 1.09–1.20 (m, 1H), 1.31–1.40 (m, 1H), 1.54–1.68 (m, 2H), 1.63 (d, *J* = 0.5 Hz, 3H), 1.73–1.83 (m, 1H), 1.85–1.92 (m, 2H), 1.94–2.06 (m, 5H), 2.28 (q, *J* = 11.9 Hz, 2H), 3.40 (dd, *J* = 7.8, 11.8 Hz, 1H), 3.62 (dd, *J* = 5.3, 11.8 Hz, 1H), 5.05 (dd, *J* = 8.4, 15.2 Hz, 1H), 5.17 (s, 1H), 5.35 (dt, *J* = 6.3, 15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 9.0, 9.0, 11.7, 14.1, 17.9, 25.7, 26.0, 27.9, 32.2, 42.7, 46.6, 51.2, 64.5, 88.8, 89.5, 126.7, 132.1, 132.7, 136.7 ppm; MS (ESI): *m/z* 333 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{19}$H$_{34}$O$_3$Na: 333.2400, found: 333.2404.

(*E*)-Methyl 3-((−)-*cis*-3,5-diethyl-5-((*R*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)acrylate (*R*-(−)-*cis*-86d) [16]
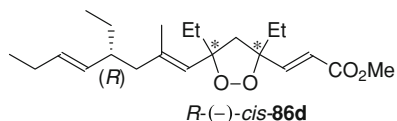
R-(−)-*cis*-**86d**

The procedure was similar to that for the preparation of **210** (vide supra): yield = 80% (two steps); R_f = 0.50 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 87.0 (*c*, 0.85, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.80 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.90 (t, *J* = 7.5 Hz, 3H), 0.93 (t, *J* = 7.3 Hz, 3H), 1.07–1.14 (m, 1H), 1.31–1.38 (m, 1H), 1.61 (d, *J* = 0.7 Hz, 3H), 1.62–1.69 (m, 1H), 1.70–1.82 (m, 2H), 1.83–1.93 (m, 2H), 1.94–2.02 (m, 4H), 2.44 (d, *J* = 11.9 Hz, 1H), 2.54 (d, *J* = 11.9 Hz, 1H), 3.73 (s, 3H), 5.05 (dd, *J* = 8.3, 15.2 Hz, 1H), 5.11 (s, 1H), 5.34 (dt, *J* = 15.2, 6.3 Hz, 1H), 6.07 (d, *J* = 15.8 Hz, 1H), 6.85 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.9, 8.9, 11.6, 14.1, 17.8, 25.6, 27.6, 30.9, 32.2, 42.6, 46.6, 51.6, 56.0, 87.2, 89.3, 119.9 126.7, 132.0, 132.8, 136.6, 149.80, 167.1 ppm; IR (Neat): 2963, 2920, 2875, 2850, 1720, 1657, 1462, 1303, 1262, 1038, 798 cm^{-1}; MS (ESI): *m/z* 387 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{22}$H$_{36}$O$_4$Na: 387.2506, found: 387.2505.

tert-Butyl(((+)-cis-3,5-diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((8R)-(+)-cis-251b)
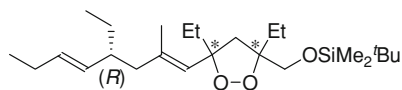
(8R)-(+)-cis-**251b**

The synthesis of **251b** was similar to that for the preparation of **206** (vide supra): yield = 93%; R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_D^{20}$ = −47.1 (c, 0.93, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.81 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H), 0.88 (s, 9H), 0.92 (t, J = 7.5 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 1.59–1.64 (m, 2H), 1.61 (d, J = 0.6 Hz, 3H), 1.74–1.81 (m, 2H), 1.83–1.92 (m, 2H), 1.94–2.04 (m, 4H), 2.23 (d, J = 12.0 Hz, 1H), 2.31 (d, J = 12.0 Hz, 1H), 3.43 (d, J = 10.2 Hz, 1H), 3.64 (d, J = 10.2 Hz, 1H), 5.06 (dd, J = 8.3, 15.2 Hz, 1H), 5.20 (s, 1H), 5.36 (dt, J = 6.3, 15.2 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = −5.5, −5.2, 8.7, 8.9, 11.7, 14.1, 17.8, 18.3, 25.7, 25.9, 26.4, 27.9, 32.2, 42.7, 46.6, 51.8, 64.7, 88.3, 88.7, 127.6, 132.0, 132.9, 135.5 ppm; MS (ESI): m/z 447 [M + Na]⁺; HRMS (ESI) m/z [M + Na]⁺ calcd for $C_{25}H_{48}O_3SiNa$: 447.3265, found: 447.3265.

**((+)-cis-3,5-Diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methanol ((8R)-(+)-cis-252b)**
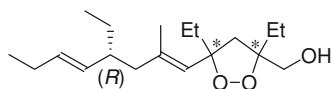
(8R)-(+)-cis-**252b**

The procedure was similar to that for the preparation of **208** (vide supra): yield = 86%; R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −43.5 (c, 0.85, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.83 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 0.94 (t, J = 7.4 Hz, 6H), 1.13–1.18 (m, 1H), 1.31–1.41 (m, 1H), 1.56–1.68 (m, 2H), 1.62 (d, J = 1.2 Hz, 3H), 1.72–1.80 (m, 1H), 1.82–1.91 (m, 2H), 1.94–2.07 (m, 5H), 2.31 (s, 2H), 3.41 (dd, J = 6.3, 11.8 Hz, 1H), 3.61 (dd, J = 4.0, 11.8 Hz, 1H), 5.05 (ddt, J = 1.4, 8.5, 15.2 Hz, 1H), 5.18 (s, 1H), 5.36 (dt, J = 6.3, 15.2 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃) δ = 8.9, 9.0, 11.7, 14.1, 17.8, 25.7, 26.2, 28.0, 32.1, 42.7, 46.6, 51.2, 64.5, 88.8, 89.5, 126.9, 132.3, 132.7, 136.5 ppm; MS (ESI): m/z 333 [M + Na]⁺; HRMS (ESI) m/z [M + Na]⁺ calcd for $C_{19}H_{34}O_3Na$: 333.2400, found: 333.2391.

(E)-Methyl   3-((+)-*cis*-3,5-diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-die-nyl)-1,2-dioxolan-3-yl)acrylate (R-(+)-*cis*-86b)
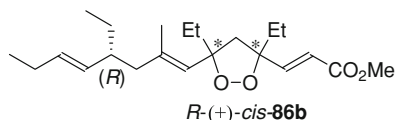
R-(+)-*cis*-**86b**

The procedure was similar to that for the preparation of **210** (vide supra): yield = 80% (two steps); R_f = 0.50 (hexanes/EtOAc, 10:1); $[\alpha]_\text{D}^{20}$ = −74.8 (*c*, 0.39, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.81 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H), 1.10–1.13 (m, 1H), 1.30–1.35 (m, 1H), 1.59 (s, 3H), 1.61–1.67 (m, 1H), 1.70–1.81 (m, 2H), 1.82–1.89 (m, 2H), 1.89–2.02 (m, 4H), 2.44 (d, *J* = 11.9 Hz, 1H), 2.58 (d, *J* = 11.8 Hz, 1H), 3.74 (s, 3H), 5.04 (dd, *J* = 8.0, 15.2 Hz, 1H), 5.15 (s, 1H), 5.34 (dt, *J* = 15.2, 6.4 Hz, 1H), 6.08 (d, *J* = 15.8 Hz, 1H), 6.86 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.9, 8.9, 11.7, 14.1, 17.8, 25.7, 27.8, 30.9, 32.2, 42.7, 46.5, 51.7, 55.8, 87.4, 89.2, 120.0, 127.1, 132.0, 132.8, 136.1, 149.8, 167.1 ppm; MS (ESI): *m/z* 387 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{22}$H$_{36}$O$_4$Na: 387.2506, found: 387.2507.

***tert*-Butyl(((−)-*cis*-3,5-diethyl-5-((S,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methoxy)dimethylsilane ((8S)-(−)-*cis*-251c)**

(8S)-(−)-*cis*-**251c**
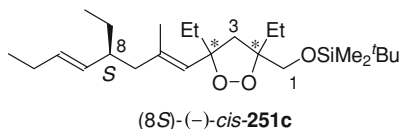
The synthesis of **251c** was similar to that for the preparation of **206** (vide supra): yield = 93%; R_f = 0.50 (hexanes/EtOAc, 20:1); $[\alpha]_\text{D}^{20}$ = 46.5 (*c*, 0.55, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.04 (s, 3H), 0.05 (s, 3H), 0.81 (t, *J* = 7.4 Hz, 3H), 0.87 (t, *J* = 7.4 Hz, 3H), 0.88 (s, 9H), 0.92 (t, *J* = 7.5 Hz, 3H), 0.95 (t, *J* = 7.4 Hz, 3H), 1.59–1.64 (m, 2H), 1.61 (s, 3H), 1.74–1.81 (m, 2H), 1.83–1.92 (m, 2H), 1.94–2.04 (m, 4H), 2.23 (d, *J* = 12.0 Hz, 1H), 2.31 (d, *J* = 12.0 Hz, 1H), 3.43 (d, *J* = 10.2 Hz, 1H), 3.64 (d, *J* = 10.2 Hz, 1H), 5.06 (dd, *J* = 8.2, 15.2 Hz, 1H), 5.20 (s, 1H), 5.36 (dt, *J* = 6.2, 15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = -5.5, −5.2, 8.7, 8.9, 11.7, 14.1, 17.8, 18.3, 25.7, 25.9, 26.4, 27.9, 32.2, 42.7, 46.6, 51.8, 64.7, 88.3, 88.7, 127.6, 132.0, 132.9, 135.5 ppm; MS (ESI): *m/z* 447 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{25}$H$_{48}$O$_3$SiNa: 447.3265, found: 447.3254.

((−)-*cis*-3,5-Diethyl-5-((*S*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)methanol ((8*S*)-(−)-*cis*-252c)
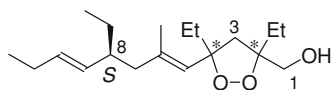
(8*S*)-(−)-*cis*-**252c**

The procedure was similar to that for the preparation of **208** (vide supra): yield = 86%; R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 44.0 (*c*, 0.27, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.83 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.4 Hz, 3H), 0.94 (t, *J* = 7.4 Hz, 6H), 1.13–1.18 (m, 1H), 1.31–1.41 (m, 1H), 1.56–1.68 (m, 2H), 1.62 (d, *J* = 1.2 Hz, 3H), 1.72–1.80 (m, 1H), 1.82–1.91 (m, 2H), 1.94–2.07 (m, 5H), 2.31 (s, 2H), 3.41 (dd, *J* = 6.3, 11.8 Hz, 1H), 3.61 (dd, *J* = 4.0, 11.8 Hz, 1H), 5.05 (ddt, *J* = 1.4, 8.5, 15.2 Hz, 1H), 5.18 (s, 1H), 5.36 (dt, *J* = 6.3, 15.2 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$) δ = 8.9, 9.0, 11.7, 14.1, 17.8, 25.7, 26.2, 28.0, 32.1, 42.7, 46.6, 51.2, 64.5, 88.8, 89.5, 126.9, 132.3, 132.7, 136.5 ppm; MS (ESI): *m/z* 333 [M + Na]$^+$; HRMS (ESI) *m/z* [M + Na]$^+$ calcd for C$_{19}$H$_{34}$O$_3$Na: 333.2400, found: 333.2395.

(*E*)-Methyl   3-((−)-*cis*-3,5-diethyl-5-((*S*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-die-nyl)-1,2-dioxolan-3-yl)acrylate (*S*-(−)-*cis*-86c)
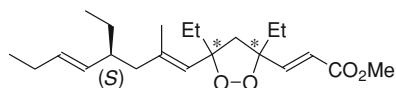
S-(−)-*cis*-**86c**

The procedure was similar to that for the preparation of **210** (vide supra): yield = 80% (two steps); R_f = 0.50 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 75.0 (*c*, 0.15, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.81 (t, *J* = 7.4 Hz, 3H), 0.88 (t, *J* = 7.3 Hz, 3H), 0.91 (t, *J* = 7.5 Hz, 3H), 0.94 (t, *J* = 7.5 Hz, 3H), 1.10–1.13 (m, 1H), 1.30–1.35 (m, 1H), 1.59 (s, 3H), 1.61–1.67 (m, 1H), 1.70–1.81 (m, 2H), 1.82–1.89 (m, 2H), 1.89–2.02 (m, 4H), 2.44 (d, *J* = 11.9 Hz, 1H), 2.58 (d, *J* = 11.8 Hz, 1H), 3.74 (s, 3H), 5.04 (dd, *J* = 8.0, 15.2 Hz, 1H), 5.15 (s, 1H), 5.34 (dt, *J* = 15.2, 6.4 Hz, 1H), 6.08 (d, *J* = 15.8 Hz, 1H), 6.86 (d, *J* = 15.8 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.9, 8.9, 11.7, 14.1, 17.8, 25.7, 27.8, 30.9, 32.2, 42.7, 46.5, 51.7, 55.8, 87.4, 89.2, 120.0, 127.1, 132.0, 132.8, 136.1, 149.8, 167.1 ppm; MS (ESI): *m/z* 382 [M + NH$_4$]$^+$; HRMS (ESI) *m/z* [M + NH$_4$]$^+$ calcd for C$_{22}$H$_{40}$O$_4$N: 382.2952, found: 382.2961.

**(−)-(2E,7E,10R,11E)-Methyl   4,6,10-triethyl-4,6-dihydroxy-8-methyltetra-
deca-2,7,11-trienoate (R-(−)-cis-268d)**
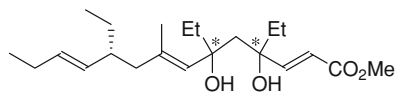
R-(−)-cis-**268d**

To a 25-mL round-bottomed flask equipped with a magnetic stirring bar was added **86d** (18 mg, 0.05 mmol) and Zn power (160 mg, 2.5 mmol), CH_2Cl_2 (1 mL) was added via syringe, and then 0.5 mL AcOH was added dropwiseat 0 °C. The mixture was stirred at room temperature, TLC monitor the reaction until the starting material disappeared. Two hours later, the reaction completed. Chromatography gave the product (18 mg, 99%): R_f = 0.30 (hexanes/EtOAc, 4:1); $[\alpha]_D^{20}$ = −34.4 (c, 0.33, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.81 (t, J = 7.4 Hz, 3H), 0.83 (t, J = 7.4 Hz, 3H), 0.83 (t, J = 7.5 Hz, 3H), 0.93 (t, J = 7.4 Hz, 3H), 1.09–1.19 (m, 1H), 1.28–1.35 (m, 2H), 1.45–1.60 (m, 5H), 1.63 (d, J = 0.7 Hz, 3H), 1.75–1.81 (m, 1H), 1.87–2.06 (m, 6H), 3.71 (s, 3H), 4.87 (s, 1H), 5.02 (dd, J = 8.6, 15.2 Hz, 1H), 5.32 (dt, J = 15.2, 6.3 Hz, 1H), 6.03 (d, J = 15.5 Hz, 1H), 6.93 (d, J = 15.5 Hz, 1H) ppm; ¹³C NMR (100 MHz, CDCl₃): δ = 7.4, 7.5, 11.8, 14.1, 17.1, 25.9, 28.3, 35.6, 37.1, 42.7, 47.7, 50.4, 51.4, 76.0, 78.6, 117.6, 130.5, 132.0, 133.0, 135.7, 155.0, 167.4 ppm; MS (ESI): m/z 389 [M + Na]⁺; HRMS (ESI) m/z [M + Na]⁺ calcd for $C_{22}H_{38}O_4Na$: 389.2662, found: 389.2668 (Table 4.1).
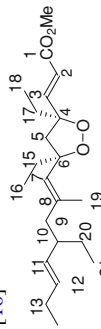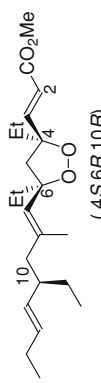
**(3aS,5R,6aS)-5,6a-Diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)
-tetrahydrofuro[3,2-b]furan-2(5H)-one ((3S,4S,6R,10R)-Plakortone B (87a))**
[11, 12, 16]
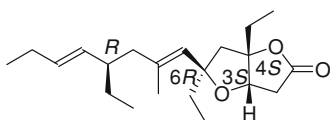
(3S,4S,6R,10R)-Plakortone B (**87a**)

To a solution of **268d** (16 mg, 0.044 mmol) in toluene (5 mL) was added DBU (20 mol%) at 25 °C. The reaction mixture was allowed to reflux for 24 h and then concentrated under reduced pressure to give a residue which was purified by flash column chromatography on silica gel (hexanes/EtOAc, 10:1) to afford **87a** (13 mg, 90%). R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −15.4 (c, 0.17, CHCl₃); ¹H NMR (400 MHz, CDCl₃): δ = 0.83 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 0.97 (t, J = 7.4 Hz, 3H), 1.09–1.17 (m, 1H), 1.32–1.39 (m, 1H), 1.63–1.67 (m, 2H), 1.69 (d, J = 1.1 Hz, 3H), 1.70–1.81 (m, 2H), 1.82–1.90 (m, 1H), 1.94–2.04 (m, 4H), 2.14 (d, J = 13.8 Hz, 1H), 2.24

Table 4.1 The data reported for natural plakortide E methyl ester and the data for our synthetic compound **86d** (for comparison)

Source	Natural Product [16]	Our synthetic compound **86d**
Reference	[16]	
Assigned Structure		(4S,6R,10R)
EIHRMS	m/z [M + H]+: calcd for $C_{22}H_{37}O_4$: 365.2692, found: 365.2681	m/z [M + Na]+: calcd for $C_{22}H_{36}O_4Na$: 387.2506, found: 387.2509
$[\alpha]_D^{20}$	$[\alpha]_D^{20} = 75.1(c = 2.23,\ CHCl_3)$	$[\alpha]_D^{20} = 87.0(c = 0.85,\ CHCl_3)$
NMR ($CDCl_3$)		
Equipment	Bruker AMX-400 spectrometer	Bruker advance III 400 spectrometer

Natural Product [16]

^1H (ppm)		^{13}C (ppm)	
H-1		C-1	166.9
H-2	6.07 (1H, d, 15.8)	C-2	119.9
H-3	6.85 (1H, d, 15.8)	C-3	149.6
H-4		C-4	87.1
H-5	2.54 β (1H, d, 12.0) 2.44 α (1H, d, 12.0)	C-5	55.9
H-6		C-6	89.1
H-7	5.11 (1H, q, 1.3)	C-7	126.7
H-8		C-8	136.4
H-9	2.00 (1H, m) 1.85 (1H, m)	C-9	46.5
H-10	2.00 (1H, m)	C-10	42.5
H-11	5.05 (1H, ddt, 1.5, 8.4, 15.3)	C-11	132.7
H-12	5.34 (1H, dt, 6.43, 15.3)	C-12	131.9
H-13	1.97 (2H, m)	C-13	25.5
H-14	0.93 (3H, t, 7.4)	C-14	14.0
H-15	1.86 (1H, m) 1.64 (1H, m)	C-15	32.1
H-16	0.88 (3H, t, 7.4)	C-16	8.8
H-17	1.78 (2H, m)	C-17	30.8
H-18	0.90 (3H, t, 7.4)	C-18	8.8
H-19	1.61 (3H, d, 1.3)	C-19	17.7
H-20	1.35 (1H, m) 1.10 (1H, m)	C-20	27.6
H-21	0.80 (3H, t, 7.4) 3.73 (3H, S, OCH₃)	C-21	11.5 51.1

Our synthetic compound **86d**

^1H (ppm)		^{13}C (ppm)	
H-1		C-1	167.1
H-2	6.07 (1H, d, 15.8)	C-2	119.9
H-3	6.85 (1H, d, 15.8)	C-3	149.8
H-4		C-4	87.2
H-5	2.54 β (1H, d, 11.9) 2.44 α (1H, d, 11.9)	C-5	56.0
H-6		C-6	89.3
H-7	5.11 (1H, q, 1.3)	C-7	126.7
H-8		C-8	136.6
H-9	2.00 (1H, m) 1.85 (1H, m)	C-9	46.5
H-10	2.00 (1H, m)	C-10	42.6
H-11	5.05 (1H, dd, 15.1, 8.3)[a]	C-11	132.8
H-12	5.34 (1 H, dt, 6.3, 15.2)	C-12	132.0
H-13	1.97 (2H, m)	C-13	25.6
H-14	0.93 (3H, t, 7.4)	C-14	14.1
H-15	1.86 (1H, m) 1.64 (1H, m)	C-15	32.2
H-16	0.88 (3H, t, 7.4)	C-16	8.9
H-17	1.78 (2H, m)	C-17	30.9
H-18	0.90 (3H, t, 7.4)	C-18	8.9
H-19	1.61 (3H, d, 1.3)	C-19	17.8
H-20	1.35 (1H, m) 1.10 (1H, m)	C-20	27.6
H-21	0.81 (t, 7.4, 3H) 3.74 (3H, s, OCH₃)	C-21	11.6 51.6

[a] Coupling constants were measured by 2D J-Resolved NMR experiment on an Advance Bruker 600 M spectrometer

(d, J = 13.8 Hz, 1H), 2.64 (dd, J = 1.2, 18.4 Hz, 1H), 2.71 (dd, J = 5.1, 18.4 Hz, 1H), 4.21 (dd, J = 1.1, 5.0 Hz, 1H), 5.03 (s, 1H), 5.06 (ddt, J = 1.0, 8.4, 15.3 Hz, 1H), 5.36 (dt, J = 6.3, 15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.4, 8.8, 11.7, 14.1, 16.8, 25.7, 27.9, 30.4, 33.9, 36.8, 42.8, 47.0, 49.1, 79.6, 87.1, 97.4, 129.6, 132.1, 132.8, 137.3, 175.8 ppm; MS (ESI): m/z 335 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{21}$H$_{35}$O$_3$: 335.2581, found: 335.2574.

(−)-(2E,7E,10S,11E)-Methyl 4,6,10-triethyl-4,6-dihydroxy-8-methyltetradeca-2,7,11-trienoate (S-(−)-cis-268c)
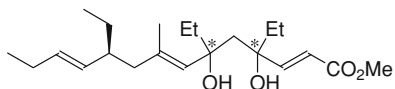
S-(−)-*cis*-**268c**

The procedure was similar to that for the preparation of *R*-(−)-*cis*-**268d** (vide supra): R_f = 0.30 (hexanes/EtOAc, 4:1); $[\alpha]_D^{20}$ = −48.5 (*c*, 0.20, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.81 (t, J = 7.5 Hz, 3H), 0.83 (t, J = 7.4 Hz, 6H), 0.94 (t, J = 7.4 Hz, 3H), 1.07–1.14 (m, 1H), 1.28–1.38 (m, 2H), 1.45–1.65 (m, 5H), 1.63 (d, J = 0.8 Hz, 3H), 1.75–1.77 (m, 1H), 1.92–2.01 (m, 6H), 3.71 (s, 3H), 4.93 (s, 1H), 5.04 (dd, J = 8.3, 15.2 Hz, 1H), 5.34 (dt, J = 15.3, 6.3 Hz, 1H), 6.03 (d, J = 15.5 Hz, 1H), 6.93 (d, J = 15.5 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 7.4, 7.5, 11.6, 14.1, 17.3, 25.7, 27.8, 35.6, 36.8, 42.6, 47.5, 50.3, 51.4, 76.0, 78.3, 117.7, 131.1 132.0, 133.1, 135.5, 155.2, 167.4 ppm; MS (ESI): m/z 389 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{22}$H$_{38}$O$_4$Na: 389.2662, found: 389.2663.

(3aS,5R,6aS)-5,6a-Diethyl-5-((S,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-tetrahydrofuro[3,2-b]furan-2(5H)-one ((3S,4S,6R,10S)-87b) [11]
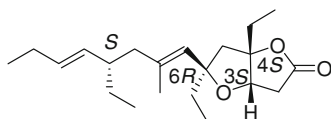
(3*S*,4*S*,6*R*,10*S*)-**87b**

The procedure was similar to that for the preparation of **87a** (vide supra): R_f = 0.3 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = −31.0 (*c*, 0.20, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.83 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H), 1.09–1.17 (m, 1H), 1.32–1.38 (m, 1H), 1.63–1.76 (m, 4H), 1.68 (d, J = 1.1 Hz, 3H), 1.82–1.90 (m, 1H), 1.94–2.04 (m, 4H), 2.14 (d, J = 13.7 Hz, 1H), 2.24 (d, J = 13.7 Hz, 1H), 2.64 (dd, J = 1.2, 18.6 Hz, 1H), 2.71 (dd, J = 5.1, 18.6 Hz, 1H), 4.19 (dd, J = 1.1, 5.0 Hz, 1H), 5.04 (s, 1H), 5.05 (dd, J = 8.8, 15.3 Hz, 1H), 5.36 (dt, J = 6.3,

15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.5, 8.9, 11.7, 14.2, 16.8, 25.8, 28.1, 30.4, 33.8, 36.8, 42.7, 47.0, 48.9, 79.7, 87.0, 97.4, 129.7, 132.1, 132.9, 137.3, 175.7 ppm; MS (ESI): m/z 357 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{22}$H$_{34}$O$_3$Na: 357.2400, found: 357.2403.

(+)-(2E,7E,10R,11E)-Methyl 4,6,10-triethyl-4,6-dihydroxy-8-methyltetradeca-2,7,11-trienoate (R-(+)-cis-268b)
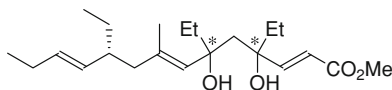
R-(−)-cis-**268b**

The procedure was similar to that for the preparation of **268d** (vide supra): R_f = 0.30 (hexanes/EtOAc, 4:1); $[\alpha]_D^{20}$ = 45.5 (c, 0.24, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.81 (t, J = 7.5 Hz, 3H), 0.83 (t, J = 7.4 Hz, 6H), 0.94 (t, J = 7.4 Hz, 3H), 1.07–1.14 (m, 1H), 1.28–1.38 (m, 2H), 1.45–1.65 (m, 5H), 1.63 (d, J = 0.8 Hz, 3H), 1.75–1.77 (m, 1H), 1.92–2.01 (m, 6H), 3.71 (s, 3H), 4.93 (s, 1H), 5.04 (dd, J = 8.3, 15.2 Hz, 1H), 5.34 (dt, J = 15.3, 6.3 Hz, 1H), 6.03 (d, J = 15.5 Hz, 1H), 6.93 (d, J = 15.5 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 7.3, 7.4, 11.6, 14.0, 17.1, 25.6, 27.7, 35.5, 36.7, 42.5, 47.4, 50.1, 51.3, 76.0, 78.3, 117.6, 131.0, 132.0, 133.0, 135.4, 155.2, 167.4 ppm; MS (ESI): m/z 389 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for C$_{22}$H$_{38}$O$_4$Na: 389.2662, found: 389.2677.

(3aR,5S,6aR)-5,6a-Diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-tetrahydrofuro[3,2-b]furan-2(5H)-one ((3R,4R,6S,10R)-ent-87b) [11]
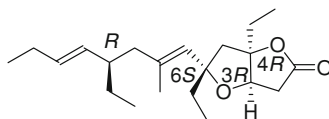
(3R,4R,6S,10R)-ent-**87b**

The procedure was similar to that for the preparation of **87a** (vide supra): R_f = 0.30 (hexanes/EtOAc, 10:1); $[\alpha]_D^{20}$ = 33.0 (c, 0.25, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.83 (t, J = 7.4 Hz, 3H), 0.87 (t, J = 7.4 Hz, 3H), 0.95 (t, J = 7.4 Hz, 3H), 0.98 (t, J = 7.4 Hz, 3H), 1.09–1.17 (m, 1H), 1.32–1.38 (m, 1H), 1.63–1.76 (m, 4H), 1.68 (d, J = 1.1 Hz, 3H), 1.82–1.90 (m, 1H), 1.94–2.04 (m, 4H), 2.14 (d, J = 13.7 Hz, 1H), 2.24 (d, J = 13.7 Hz, 1H), 2.64 (dd, J = 1.2, 18.6 Hz, 1H), 2.71 (dd, J = 5.1, 18.6 Hz, 1H), 4.19 (dd, J = 1.1, 5.0 Hz, 1H), 5.04 (s, 1H), 5.05 (dd, J = 8.8, 15.3 Hz, 1H), 5.36 (dt, J = 6.3, 15.3 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.5, 8.9, 11.7, 14.2, 16.8, 25.8, 28.1, 30.4, 33.8, 36.8, 42.7, 47.0, 48.9, 79.7, 87.0, 97.4, 129.7, 132.1, 132.9,

137.3, 175.8 ppm; MS (ESI): m/z 335 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{21}H_{35}O_3$: 335.2581, found: 335.2580.

(+)-(2*E*,7*E*,10*S*,11*E*)-Methyl 4,6,10-triethyl-4,6-dihydroxy-8-methyltetradeca-2,7,11-trienoate (*S*-(+)-*cis*-268a)
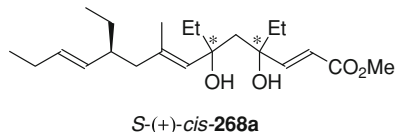
S-(+)-*cis*-**268a**

The procedure was similar to that for the preparation of **268d** (vide supra): $R_f = 0.30$ (hexanes/EtOAc, 4:1); $[\alpha]_D^{20} = 33.9$ (c, 0.14, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.81$ (t, $J = 7.4$ Hz, 3H), 0.83 (t, $J = 7.4$ Hz, 3H), 0.83 (t, $J = 7.5$ Hz, 3H), 0.93 (t, $J = 7.4$ Hz, 3H), 1.09–1.19 (m, 1H), 1.28–1.35 (m, 2H), 1.45–1.60 (m, 5H), 1.63 (d, $J = 0.7$ Hz, 3H), 1.75–1.81 (m, 1H), 1.87–2.06 (m, 6H), 3.71 (s, 3H), 4.87 (s, 1H), 5.02 (dd, $J = 8.6, 15.2$ Hz, 1H), 5.32 (dt, $J = 15.2, 6.3$ Hz, 1H), 6.04 (d, $J = 15.5$ Hz, 1H), 6.94 (d, $J = 15.5$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 7.4, 7.5, 11.8, 14.1, 17.1, 25.9, 28.3, 35.6, 37.1, 42.7, 47.7, 50.4, 51.4, 76.0, 78.6, 117.6, 130.5, 132.0, 133.0, 135.7, 155.0, 167.4$ ppm; MS (ESI): m/z 389 [M + Na]$^+$; HRMS (ESI) m/z [M + Na]$^+$ calcd for $C_{22}H_{38}O_4Na$: 389.2662, found: 389.2657.

(3a*R*,5*S*,6a*R*)-5,6a-Diethyl-5-((*S*,1*E*,5*E*)-4-ethyl-2-methylocta-1,5-dienyl)-tetrahydrofuro[3,2-b]furan-2(5*H*)-one ((3*R*,4*R*,6*S*,10*S*)-*ent*-87a) [11]
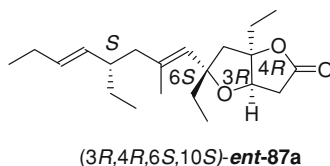
(3*R*,4*R*,6*S*,10*S*)-**ent-87a**

The procedure was similar to that for the preparation of **87a** (vide supra): $R_f = 0.30$ (hexanes/EtOAc, 10:1); $[\alpha]_D^{20} = 15.0$ (c, 0.12, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): $\delta = 0.83$ (t, $J = 7.4$ Hz, 3H), 0.86 (t, $J = 7.4$ Hz, 3H), 0.95 (t, $J = 7.4$ Hz, 3H), 0.97 (t, $J = 7.4$ Hz, 3H), 1.09–1.17 (m, 1H), 1.32–1.39 (m, 1H), 1.63–1.67 (m, 2H), 1.69 (d, $J = 1.1$ Hz, 3H), 1.70–1.81 (m, 2H), 1.82–1.90 (m, 1H), 1.94–2.04 (m, 4H), 2.14 (d, $J = 13.8$ Hz, 1H), 2.24 (d, $J = 13.8$ Hz, 1H), 2.64 (dd, $J = 1.2, 18.4$ Hz, 1H), 2.71 (dd, $J = 5.1, 18.4$ Hz, 1H), 4.21 (dd, $J = 1.1, 5.0$ Hz, 1H), 5.03 (s, 1H), 5.06 (ddt, $J = 1.0, 8.4, 15.3$ Hz, 1H), 5.36 (dt, $J = 6.3, 15.3$ Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): $\delta = 8.4, 8.8, 11.7, 14.1, 16.8, 25.7, 27.9, 30.4, 33.9, 36.8, 42.8, 47.0, 49.1, 79.6, 87.1, 97.4, 129.6, 132.1, 132.8, 137.3, 175.8$ ppm; MS (ESI): m/z 335 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for $C_{21}H_{35}O_3$: 335.2581, found: 335.2590

Table 4.2 The data reported for natural plakortide E and the data for our synthetic compound **85a** (for comparison)

Source	Natural Product [16]	Our synthetic compound **85a**
Reference	[16]	
Structure		
		(4S,6R,10R)
EIHRMS	m/z [M + H]+: 351	m/z [M + H]+: calcd for $C_{21}H_{35}O_4$: 351.2530, found: 365.2522
$[\alpha]_D^T$	$[\alpha]_D^{20} = 63.9\,(c = 2.0,\ CHCl_3)$	$[\alpha]_D^{20} = 66.6\,(c = 0.24,\ CHCl_3)$
NMR ($CDCl_3$) 1H (ppm) equipment	Bruker AMX-400 spectrometer	Bruker advance III 400 spectrometer

	Natural Product [16] 1H (ppm)		Our synthetic compound **85a** 1H (ppm)
H-1			
H-2	5.98 (1H, d, 15.8)	H-2	6.09 (1H, d, 15.7)
H-3	6.69 (1H, d, 15.8)	H-3	6.93 (1H, d, 15.7)
H-4		H-4	
H-5	2.53 β (1H, d, 12.0) 2.42 α (1H, d, 12.0)	H-5	2.53 β (1H, d, 12.0) 2.43 α (1H, d, 12.0)
H-6		H-6	
H-7	5.12 (1H, m)	H-7	5.11 (1H, s)
H-8		H-8	
H-9	2.00 (1H, m) 1.85 (1H, m)	H-9	2.00 (1H, m) 1.85 (1H, m)
H-10	2.00 (1 H, m)	H-10	2.00 (1H, m)
H-11	5.05 (1H, ddt, 15.2, 8.3, 1.4)	H-11	5.05 (1H, dd, 15.2, 8.3)[a]
H-12	5.34 (1H, dt, 6.3, 15.2)	H-12	5.34 (1H, dt, 6.4, 15.2)
H-13	1.98 (2H, m)	H-13	1.97 (2H, m)
H-14	0.93 (3H, t, 7.4)	H-14	0.92 (3H, t, 7.4)
H-15	1.85 (1H, m) 1.63 (1H, m)	H-15	1.86 (1H, m) 1.64 (1H, m)
H-16	0.87 (3 H, t, 7.4)	H-16	0.86 (3 H, t, 7.4)
H-17	1.77 (2H, m)	H-17	1.78 (2H, m)
H-18	0.87 (3H, t, 7.4)	H-18	0.88 (3H, t, 7.4)
H-19	1.61 (3H, d, 1.0)	H-19	1.61 (3H, d, 0.9)
H-20	1.35 (1H, m) 1.11 (1H, m)	H-20	1.36 (1H, m) 1.11 (1H, m)
H-21	0.80 (3H, t, 7.4)	H-21	0.80 (t, 7.4, 3H)

	Natural Product [16] 13C (ppm)		Our synthetic compound **85a** 13C (ppm)
C-1	173.0	C-1	171.1
C-2	123.9	C-2	119.6
C-3	146.9	C-3	152.1
C-4	87.2	C-4	87.2
C-5	55.8	C-5	56.0
C-6	89.1	C-6	89.3
C-7	126.9	C-7	126.6
C-8	136.5	C-8	136.7
C-9	46.6	C-9	46.6
C-10	42.6	C-10	42.6
C-11	132.8	C-11	132.8
C-12	131.9	C-12	132.0
C-13	25.6	C-13	25.6
C-14	14.0	C-14	14.1
C-15	32.1	C-15	32.3
C-16	8.8	C-16	8.9
C-17	31.0	C-17	30.8
C-18	8.9	C-18	8.9
C-19	17.7	C-19	17.8
C-20	27.6	C-20	27.7
C-21	11.6	C-21	11.6

Table 4.3 The data reported for natural plakortide E and the data for our synthetic compound **85a** (for comparison)

Source	Natural product [16]		Our synthetic compound **85a**	
Reference	[17]			
Assigned structure				
EIHRMS			$(4S,6R,10R)$ m/z [M + H]$^+$: calcd for $C_{21}H_{35}O_4$: 351.2530, found: 365.2522	
$[\alpha]_D^T$	$[\alpha]_D^{20} = 63(c = 0.001, CHCl_3)$		$[\alpha]_D^{20} = 66.6(c = 0.24, CHCl_3)$	
NMR (CDCl$_3$)	^{1}H (ppm)	^{13}C (ppm)	^{1}H (ppm)	^{13}C (ppm)
Equipment	Bruker AMX-500 spectrometer		Bruker advance III 400 spectrometer	
H-1		C-1 172.0		C-1 171.1
H-2	6.09 (1H, d, 15)	C-2 120.5	6.09 (1H, d, 15.7)	C-2 119.6
H-3	6.93 (1H, d, 15)	C-3 152.1	6.93 (1H, d, 15.7)	C-3 152.1
H-4		C-4 87.2		C-4 87.2
H-5	2.53 β (1H, d, 12.0) 2.42 α (1H, d, 12.0)	C-5 56.0	2.53 β (1H, d, 12.0) 2.43 α (1H, d, 12.0)	C-5 56.0
H-6		C-6 89.3		C-6 89.3
H-7	5.10 (1H, s)	C-7 126.6	5.11 (1H, s)	C-7 126.6
H-8		C-8 136.7		C-8 136.7
H-9	2.00 (1H, m) 1.85 (1H, m)	C-9 46.6	2.00 (1H, m) 1.85 (1H, m)	C-9 46.6
H-10	2.00 (1H, m)	C-10 42.6	2.00 (1H, m)	C-10 42.6
H-11	5.04 (1H, dd, 15, 8)	C-11 132.8	5.05 (1H, dd, 15.2, 8.3)^a	C-11 132.8
H-12	5.33 (1H, dt, 6.5, 15)	C-12 132.0	5.34 (1H, dt, 6.4, 15.2)	C-12 132.0
H-13	1.95 (2H, m)	C-13 25.6	1.97 (2H, m)	C-13 25.6
H-14	0.92 (3H, t, 7.5)	C-14 14.1	0.92 (3H, t, 7.4)	C-14 14.1
H-15	1.86 (1H, m) 1.64 (1H, m)	C-15 32.2	1.86 (1H, m) 1.64 (1H, m)	C-15 32.3
H-16	0.86 (3H, t, 7.5)	C-16 8.9	0.86 (3H, t, 7.4)	C-16 8.9
H-17	1.78 (2H, m)	C-17 30.8	1.78 (2H, m)	C-17 30.8
H-18	0.88 (3H, t, 7.5)	C-18 8.9	0.88 (3H, t, 7.4)	C-18 8.9
H-19	1.60 (3H, s)	C-19 17.8	1.61 (3H, d, 0.9)	C-19 17.8
H-20	1.37 (1H, m) 1.24 (1H, m)	C-20 27.7	1.36 (1H, m) 1.11 (1H, m)	C-20 27.7
H-21	0.80 (3H, t, 7.5)	C-21 11.6	0.80 (3H, t, 7.4)	C-21 11.6

Table 4.4 The data reported for natural plakortone B and the data for our synthetic compound **87a** (for comparison)

Source	Natural Product [16]	Our synthetic compound **87a**
Reference	[16]	
Assigned structure	plakortone B (relative configuration) The biclyclic furanolactone core is *cis* confused	(3*S*,4*S*,6*R*,10*R*) (3*S*,4*S*,6*R*,10*R*)
EI HRMS	m/z [M + H]$^+$: calcd for $C_{21}H_{35}O_3$: 335.2586, found: 335.2541	[M + H]$^+$ calcd for $C_{21}H_{35}O_3$: 335.2581, found: 335.2574
$[\alpha]_D^T$	$_D^{20}$ = −9.2(c = 0.72, CHCl$_3$)	$[\alpha]_D^{20}$ = −15.5(c = 0.17, CHCl$_3$)
NMR (CDCl$_3$)	^{1}H (ppm) ^{13}C (ppm)	^{1}H (ppm) ^{13}C (ppm)
Equipment	Bruker AMX-400 spectrometer	Bruker advance III 400 spectrometer

Label	Natural ^{1}H (ppm)	Natural ^{13}C (ppm)	Synthetic ^{1}H (ppm)	Synthetic ^{13}C (ppm)
1	H-1	C-1 175.6	H-1	C-1 175.8
2	H-2 2.71 β (dd, 5.1, 18.4, 1H) 2.64 α (dd, 1.3, 18.4, 1H)	C-2 36.7	H-2 2.71 β (dd, 5.1, 18.6, 1H) 2.64 α (dd, 1.1, 18.6, 1H)	C-2 36.8
3	H-3 4.21 (dd, 1.3, 5.1, 1H)	C-3 79.5	H-3 4.21 (dd, 1.1, 5.0, 1H)	C-3 79.6
4	H-4	C-4 97.2	H-4	C-4 97.4
5	H-5 2.24 α (d, 13.7, 1H) 2.13 β (d, 13.7, 1H)	C-5 49.0	H-5 2.24 α (d, 13.7, 1H) 2.14 β (d, 13.7, 1H)	C-5 49.1
6	H-6	C-6 86.9	H-6	C-6 87.1
7	H-7 5.03 (q, 1.3, 1H)	C-7 129.5	H-7 5.03 (s, 1H)	C-7 129.6
8	H-8	C-8 137.1	H-8	C-8 137.3
9	H-9 2.00 (m, 1H) 1.85 (m, 1H)	C-9 46.9	H-9 1.99–2.04 (m, 1H) 1.82–1.87 (m, 1H)	C-9 47.0
10	H-10 1.98 (m, 1H)	C-10 42.6	H-10 1.99–2.04 (m, 1H)	C-10 42.8
11	H-11 5.06 (ddt, 1.5, 8.4, 15.3, 1H)	C-11 132.7	H-11 5.06 (dd, 8.4, 15.3, 1H)	C-11 132.8
12	H-12 5.36 (dt, 6.3, 15.3, 1H)	C-12 131.9	H-12 5.36 (dt, 6.3, 15.3, 1H)	C-12 132.1
13	H-13 1.96 (m, 2H)	C-13 25.5	H-13 1.99–2.04 (m, 2H)	C-13 25.7
14	H-14 0.95 (t, 7.4, 3H)	C-14 14.0	H-14 0.95 (t, 7.4, 3H)	C-14 14.1
15	H-15 1.73 (m, 2H)	C-15 33.7	H-15 1.66–1.77 (m, 2H)	C-15 33.9
16	H-16 0.86 (t, 7.4, 3H)	C-16 8.7	H-16 0.86 (t, 7.4, 3H)	C-16 8.8
17	H-17 1.73 (m, 2H)	C-17 30.3	H-17 1.66–1.77 (m, 2H)	C-17 30.4
18	H-18 0.96 (t, 7.4, 3H)	C-18 8.3	H-18 0.96 (t, 7.2, 3H)	C-18 8.4
19	H-19 1.69 (d, 1.3, 3H)	C-19 16.7	H-19 1.69 (d, 1.4, 3H)^a	C-19 16.8
20	H-20 1.35 (m, 1H) 1.15 (m, 1H)	C-20 27.8	H-20 1.32–1.38 (m, 1H) 1.10–1.17 (m, 1H)	C-20 27.9
21	H-21 0.83 (t, 7.4, 3H)	C-21 11.5	H-21 0.83 (t, 7.4, 3H)	C-21 11.7

(E)-3-((3S,5R)-3,5-Diethyl-5-((R,1E,5E)-4-ethyl-2-methylocta-1,5-dienyl)-1,2-dioxolan-3-yl)acrylic acid ((4S,6R,10R)-Plakortide E (85a)) [16, 17] (Tables 4.2, 4.3)
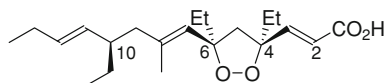
(4S,6R,10R)-Plakortide E (**85a**)

To a 0 °C solution of **86d** (13 mg, 0.037 mmol) in THF/H$_2$O (4:1, 2 mL) was added LiOH (4.5 mg, 0.19 mmol). The reaction mixture was allowed to warm to room temperature and stirred overnight. TLC monitor the reaction until the starting material disappeared. The reaction mixture was acidified to pH 2 with 10% aqueous HCl. The resulting solution was extracted with Et$_2$O (3 × 10 mL). The combined extracts were washed with brine (15 mL), dried over anhydrous Na$_2$SO$_4$, and concentrated on the rotary evaporator. The residue was purified by flash chromatography (hexanes//EtOAc/AcOH 100/10/1) to afford **85a** (11.6 mg, 90%) as a colorless oil: R_f = 0.25 (hexanes/EtOAc/AcOH, 100:10:1); $[\alpha]_D^{20}$ = 66.6 (c, 0.24, CHCl$_3$); ^{1}H NMR (400 MHz, CDCl$_3$): δ = 0.80 (t, J = 7.4 Hz, 3H), 0.86 (t, J = 7.4 Hz, 3H), 0.88 (t, J = 7.4 Hz, 3H), 0.92 (t, J = 7.4 Hz, 3H), 1.07–1.14 (m, 1H), 1.31–1.38 (m, 1H), 1.61 (d, J = 0.6 Hz, 3H), 1.62–1.69 (m, 1H), 1.70–1.82 (m, 2H), 1.83–1.93 (m, 2H), 1.94–2.02 (m, 4H), 2.43 (d, J = 12.0 Hz, 1H), 2.53 (d, J = 12.0 Hz, 1H), 5.05 (dd, J = 8.3, 15.2 Hz, 1H), 5.11 (s, 1H), 5.34 (dt, J = 6.4, 15.2 Hz, 1H), 6.09 (d, J = 15.7 Hz, 1H), 6.93 (d, J = 15.7 Hz, 1H) ppm; ^{13}C NMR (100 MHz, CDCl$_3$): δ = 8.9, 8.9, 11.6, 14.1, 17.8, 25.6, 27.7, 30.8, 32.3, 42.6, 46.6, 56.0, 87.2, 89.3, 119.6, 126.6, 132.0, 132.8, 136.7, 152.1, 171.1 ppm; MS (ESI): m/z 351 [M + H]$^+$; HRMS (ESI) m/z [M + H]$^+$ calcd for C$_{21}$H$_{35}$O$_4$: 351.2530, found: 351.2533 (Table 4.4).

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Appendix

Table A.1 Crystal data and structure refinement for xysun-1

Identification code	xysun-1
Empirical formula	C9 H18 O4
Formula weight	190.23
Temperature	296(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 5.6535(3) Å, α = 77.5980(10)°
	b = 8.1968(5) Å, β = 86.4690(10)°
	c = 11.5406(7) Å, γ = 77.1180(10)°
Volume	509.12(5) A^3
Z, Calculated density	2, 1.241 Mg/m^3
Absorption coefficient	0.096 mm^{-1}
F(000)	208
Crystal size	0.4 × 0.3 × 0.3 mm
Theta range for data collection	1.81–25.25°
Limiting indices	−6<=h<=6, −9<=k<=9, −13<=l<=13
Reflections collected/unique	9128/1842 [R(int) = 0.0585]
Completeness to θ = 25.25	100.0%
Absorption correction	None
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	1842/0/118
Goodness-of-fit on F^2	1.036
Final R indices [I>2σ(I)]	R1 = 0.0517, wR2 = 0.1433
R indices (all data)	R1 = 0.0569, wR2 = 0.1504
Largest diff. peak and hole	0.539 and −0.501 e A^{-3}

Table A.2 Atomic coordinates ($\times 10^4$) and equivalent isotropic displacement parameters ($A^2 \times 10^3$) for A. U(eq) is defined as one third of the trace of the orthogonalized Uij tensor

	x	y	z	U(eq)
O(1)	−4154(2)	8764(2)	6738(1)	43(1)
O(2)	−5883(2)	10086(2)	7204(1)	46(1)
O(3)	−77(3)	6246(2)	6413(1)	46(1)
O(4)	−7398(3)	13420(2)	5588(1)	58(1)
C(1)	247(5)	7491(3)	9301(2)	65(1)
C(2)	−1905(4)	7587(3)	8560(2)	46(1)
C(3)	−1906(3)	8680(2)	7313(2)	31(1)
C(4)	−1943(3)	10564(2)	7284(2)	34(1)
C(5)	−4623(3)	11467(2)	7088(2)	32(1)
C(6)	−5750(4)	12407(3)	8058(2)	47(1)
C(7)	−4723(5)	13945(3)	8099(2)	66(1)
C(8)	62(3)	7922(2)	6510(2)	39(1)
C(9)	−4946(4)	12574(3)	5847(2)	43(1)

Table A.3 Bond lengths (Å) and angles (°) for A

O(1)–C(3)	1.451(2)
O(1)–O(2)	1.4596(18)
O(2)–C(5)	1.446(2)
O(3)–C(8)	1.422(2)
O(3)–H(3)	0.8200
O(4)–C(9)	1.424(2)
O(4)–H(4)	0.8200
C(1)–C(2)	1.508(3)
C(1)–H(1A)	0.9600
C(1)–H(1B)	0.9600
C(1)–H(1C)	0.9600
C(2)–C(3)	1.523(3)
C(2)–H(2A)	0.9700
C(2)–H(2B)	0.9700
C(3)–C(8)	1.515(2)
C(3)–C(4)	1.533(2)
C(4)–C(5)	1.538(2)
C(4)–H(4B)	0.9700
C(4)–H(4C)	0.9700
C(5)–C(9)	1.519(3)

Table A.3 (continued)

C(5)–C(6)	1.522(2)
C(6)–C(7)	1.512(3)
C(6)–H(6A)	0.9700
C(6)–H(6B)	0.9700
C(7)–H(7A)	0.9600
C(7)–H(7B)	0.9600
C(7)–H(7C)	0.9600
C(8)–H(8A)	0.9700
C(8)–H(8B)	0.9700
C(9)–H(9C)	0.9700
C(9)–H(9A)	0.9700
C(3)–O(1)–O(2)	103.37(11)
C(5)–O(2)–O(1)	104.13(11)
C(8)–O(3)–H(3)	109.5
C(9)–O(4)–H(4)	109.5
C(2)–C(1)–H(1A)	109.5
C(2)–C(1)–H(1B)	109.5
H(1A)–C(1)–H(1B)	109.5
C(2)–C(1)–H(1C)	109.5
H(1A)–C(1)–H(1C)	109.5
H(1B)–C(1)–H(1C)	109.5
C(1)–C(2)–C(3)	115.21(18)
C(1)–C(2)–H(2A)	108.5
C(3)–C(2)–H(2A)	108.5
C(1)–C(2)–H(2B)	108.5
C(3)–C(2)–H(2B)	108.5
H(2A)–C(2)–H(2B)	107.5
O(1)–C(3)–C(8)	104.45(13)
O(1)–C(3)–C(2)	109.22(14)
C(8)–C(3)–C(2)	113.30(15)
O(1)–C(3)–C(4)	102.98(13)
C(8)–C(3)–C(4)	111.98(14)
C(2)–C(3)–C(4)	113.90(14)
C(3)–C(4)–C(5)	104.29(13)
C(3)–C(4)–H(4B)	110.9
C(5)–C(4)–H(4B)	110.9
C(3)–C(4)–H(4C)	110.9
C(5)–C(4)–H(4C)	110.9
H(4B)–C(4)–H(4C)	108.9

(continued)

Table A.3 (continued)

O(2)–C(5)–C(9)	109.98(15)
O(2)–C(5)–C(6)	104.07(14)
C(9)–C(5)–C(6)	113.55(15)
O(2)–C(5)–C(4)	104.27(13)
C(9)–C(5)–C(4)	110.01(15)
C(6)–C(5)–C(4)	114.32(15)
C(7)–C(6)–C(5)	113.66(18)
C(7)–C(6)–H(6A)	108.8
C(5)–C(6)–H(6A)	108.8
C(7)–C(6)–H(6B)	108.8
C(5)–C(6)–H(6B)	108.8
H(6A)–C(6)–H(6B)	107.7
C(6)–C(7)–H(7A)	109.5
C(6)–C(7)–H(7B)	109.5
H(7A)–C(7)–H(7B)	109.5
C(6)–C(7)–H(7C)	109.5
H(7A)–C(7)–H(7C)	109.5
H(7B)–C(7)–H(7C)	109.5
O(3)–C(8)–C(3)	112.50(15)
O(3)–C(8)–H(8A)	109.1
C(3)–C(8)–H(8A)	109.1
O(3)–C(8)–H(8B)	109.1
C(3)–C(8)–H(8B)	109.1
H(8A)–C(8)–H(8B)	107.8
O(4)–C(9)–C(5)	113.31(16)
O(4)–C(9)–H(9C)	108.9
C(5)–C(9)–H(9C)	108.9
O(4)–C(9)–H(9A)	108.9
C(5)–C(9)–H(9A)	108.9
H(9C)–C(9)–H(9A)	107.7

Symmetry transformations used to generate equivalent atoms

Table A.4 Anisotropic displacement parameters ($A^2 \times 10^3$) for A. The anisotropic displacement factor exponent takes the form: $-2 \, pi^2 \, [h^2 \, a^{*2} \, U11 + \ldots + 2 \, h \, k \, a^* \, b^* \, U12]$

	U11	U22	U33	U23	U13	U12
O(1)	33(1)	36(1)	63(1)	−23(1)	−10(1)	−2(1)
O(2)	27(1)	39(1)	75(1)	−22(1)	0(1)	−6(1)
O(3)	46(1)	37(1)	56(1)	−23(1)	−8(1)	7(1)
O(4)	55(1)	54(1)	60(1)	−27(1)	−28(1)	21(1)
C(1)	75(2)	66(2)	45(1)	−4(1)	−16(1)	1(1)
C(2)	56(1)	40(1)	41(1)	−7(1)	2(1)	−10(1)
C(3)	29(1)	28(1)	36(1)	−10(1)	−4(1)	−4(1)
C(4)	28(1)	29(1)	46(1)	−10(1)	−5(1)	−3(1)
C(5)	27(1)	30(1)	40(1)	−12(1)	−2(1)	−3(1)
C(6)	43(1)	52(1)	44(1)	−20(1)	1(1)	1(1)
C(7)	69(2)	55(1)	80(2)	−42(1)	−21(1)	6(1)
C(8)	39(1)	36(1)	42(1)	−12(1)	1(1)	−2(1)
C(9)	41(1)	43(1)	40(1)	−12(1)	−7(1)	6(1)

Et﹨ ╱CO₂Et

112

Bruker Advance III 400

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4.0857
4.0832
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4.0655

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1.9787
1.9610
1.9431
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1.8670
1.8548
1.6315
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1.4889
1.4675
1.4502
1.4319
1.4135
1.2465
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EtO2C — CO2Et

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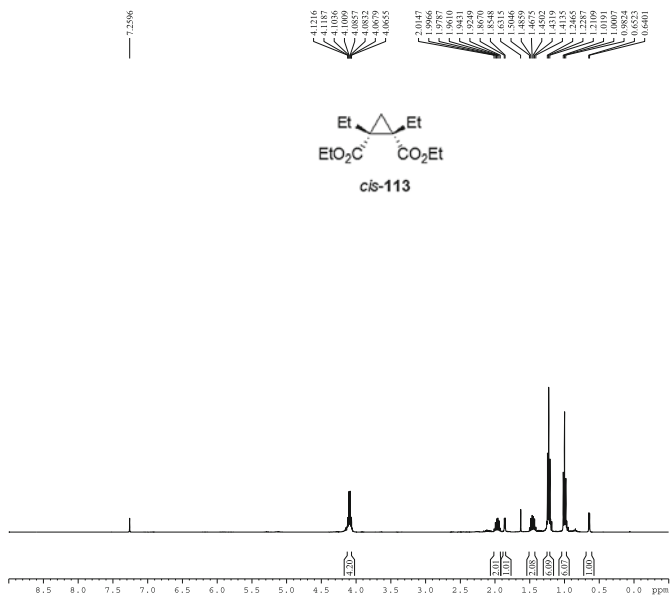
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PULPROG           zg30
TD               65536
SOLVENT          CDCl3
NS                  14
DS                   2
SWH         8223.685 Hz
FIDRES     0.125483 Hz
AQ        3.9846387 sec
RG                  64
DW           60.800 usec
DE            6.50 usec
TE            297.7 K
D1       1.00000000 sec
TD0                  1

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NUC1                1H
P1           14.00 usec
PL1          -1.00 dB
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SFO1    400.1924713 MHz
SI               32768
SF      400.1900138 MHz
WDW                 EM
SSB                  0
LB            0.30 Hz
GB                   0
PC                1.00
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8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

Bruker Advance III 400

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76.778

60.777

38.134

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22.964

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11.797
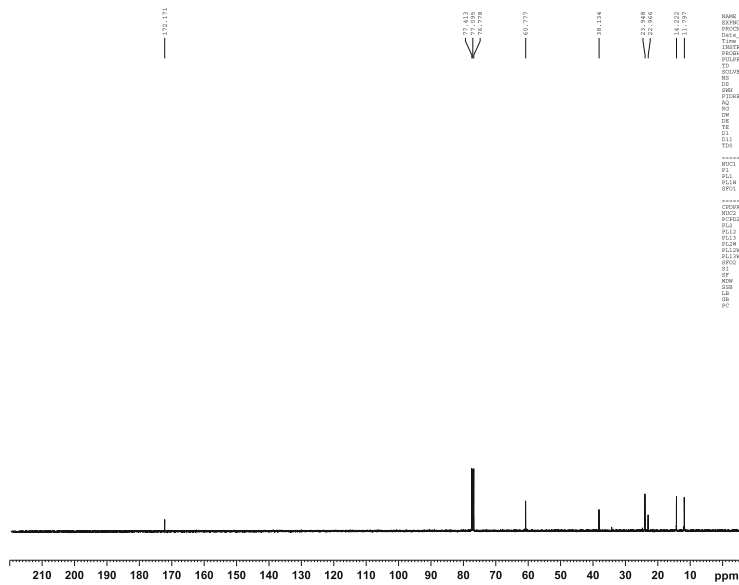
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PULPROG         zgpg30
TD               65536
SOLVENT          CDCl3
NS                 111
DS                   4
SWH        24038.461 Hz
FIDRES    0.366798 Hz
AQ        1.3631988 sec
RG                 161
DW           20.800 usec
DE            6.50 usec
TE            298.3 K
D1       2.00000000 sec
D11      0.03000000 sec
TD0                  1

-------- CHANNEL f1 ========
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P1            9.90 usec
PL1          -2.00 dB
PL1W     55.33689699 W
SFO1    100.6379163 MHz

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NUC2                1H
PCPD2        90.00 usec
PL2          -1.00 dB
PL12         15.16 dB
PL13         18.62 dB
PL2W     13.56617069 W
PL12W    0.32944094 W
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Bruker Advance III 400

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PROCNO   1
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TD   65536
SOLVENT   CDCl3
NS   16
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   45.2
DW   60.800 usec
DE   6.50 usec
TE   295.3 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300096 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

Et   OH
HO   Et

118

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0.1916

1.970
2.007
2.040
2.017
2.010
6.000
2.011

8.5   8.0   7.5   7.0   6.5   6.0   5.5   5.0   4.5   4.0   3.5   3.0   2.5   2.0   1.5   1.0   0.5   0.0   ppm

Bruker Advance III 400

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DS   4
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AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   295.4 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.68 usec
PL1   -0.60 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22589411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127658 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

77.419
77.101
76.783
63.436
32.994
21.963
19.229
11.161

210   200   190   180   170   160   150   140   130   120   110   100   90   80   70   60   50   40   30   20   10   ppm

Bruker Advance III 400

NAME   sunxy-cycloprane-TBS-OH
EXPNO   1
PROCNO   1
Date_   20110111
Time   13.09
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   45.2
DW   60.800 usec
DE   6.50 usec
TE   295.2 K
D1   1.00000000 sec
TD0   1

-------- CHANNEL f1 --------
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300096 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

119

Bruker Advance III 400

NAME   sunxy-cycloprane-TBS-OH-C13
EXPNO   1
PROCNO
Date_   20110111
Time   13.12
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   202
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   295.2 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

-------- CHANNEL f1 --------
NUC1   13C
P1   9.68 usec
PL1   -0.40 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22585411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127614 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

206

7.2599

5.9006 5.8744 5.8576 5.8314 5.0887 5.0841 5.0625 5.0579 4.9729 4.9683 4.9298 4.9253

3.7235 3.6967 3.5728 3.5460

1.6247 1.6066 1.5890 1.5763 1.5709 1.5524 1.5150 1.4965 1.4783 1.4606 1.4534 1.4425 1.4338 1.4241 1.4153 1.3969

0.9380 0.9196 0.9008 0.8888 0.8702 0.8517 0.5806 0.5689

0.97 1.02 0.98 1.10 0.90 1.10 3.12 15.19 1.00 1.02 6.00

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

140.758

114.980

77.415 77.098 76.780

64.211

34.353 33.396 26.011 23.795 23.468 18.362 11.735 11.225

-5.337 -5.372

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Bruker Advance III 400

NAME	sunxy-4-38-72
EXPNO	3
PROCNO	1
Date_	20100817
Time	13.28
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	11160.714 Hz
FIDRES	0.340598 Hz
AQ	1.4680564 sec
RG	40.3
DW	44.800 usec
DE	6.50 usec
TE	298.4 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

NUC1	1H
P1	14.00 usec
PL1	-1.00 dB
PL1W	13.56617069 W
SFO1	400.1933363 MHz
SI	16384
SF	400.1900137 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

Bruker Advance III 400

NAME	sunxy-4-38-72-C13
EXPNO	1
PROCNO	1
Date_	20100817
Time	13.48
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	969
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

-------- CHANNEL f1 --------

NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127614 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

92b

92c

Bruker Advance III 400

NAME   sunxy-4-43-89-2
EXPNO   1
PROCNO   1
Date_   20100827
Time   20.59
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zg
TD   65536
SOLVENT   CDCl3
NS   16
DS   0
SWH   10000.000 Hz
FIDRES   0.152588 Hz
AQ   3.2768500 sec
RG   57
DW   50.000 usec
DE   6.50 usec
TE   298.2 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   7.10 usec
PL1   -2.00 dB
PL1W   13.17734718 W
SFO1   400.1316005 MHz
SI   65536
SF   400.1300050 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

92d

Bruker Advance III 400

NAME   sunxy-4-43-89-C13
EXPNO   3
PROCNO   1
Date_   20100828
Time   22.12
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   11763
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.5 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   14.50 usec
PL1   -4.00 dB
PL1W   90.22689819 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   80.00 usec
PL2   -2.00 dB
PL12   18.00 dB
PL13   18.00 dB
PL2W   13.17734718 W
PL12W   0.10960442 W
PL13W   0.10960442 W
SFO2   400.1316005 MHz
SF   100.6127690 MHz
SI   32768
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

211

cis-**124b**   trans-**124b**

cis-124c   trans-124c

cis-124d   trans-124d

trans-**134**

cis-**135**

(+)-*cis*-**137a**

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

(−)-*cis*-245

Bruker Advance III 400

```
NAME           sunxy-4-40-79
EXPNO                     1
PROCNO                    1
Date_              20100727
Time                  15.02
INSTRUM               spect
PROBHD    5 mm PABBI 1H/
PULPROG               zg30
TD                    65536
SOLVENT               CDCl3
NS                       14
DS                        0
SWH          10000.000 Hz
FIDRES        0.152588 Hz
AQ            3.2768500 sec
RG                      101
DW              50.000 usec
DE               6.50 usec
TE                 294.2 K
D1            1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1               7.10 usec
PL1              -2.00 dB
PL1W        13.17734718 W
SFO1        400.1316005 MHz
SI                    65536
SF          400.1300053 MHz
WDW                      EM
SSB                       0
LB               0.30 Hz
GB                        0
PC                     1.00
```

Bruker Advance III 400

```
NAME        sunxy-4-40-79-C13
EXPNO                     1
PROCNO                    1
Date_              20100727
Time                  15.04
INSTRUM               spect
PROBHD    5 mm PABBI 1H/
PULPROG             zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      116
DS                        4
SWH          24038.461 Hz
FIDRES        0.366798 Hz
AQ            1.3631988 sec
RG                      203
DW              20.800 usec
DE               6.50 usec
TE                 294.4 K
D1            2.00000000 sec
D11           0.03000000 sec
TD0                       1

-------- CHANNEL f1 --------
NUC1                    13C
P1              14.50 usec
PL1              -4.00 dB
PL1W        90.22689819 W
SFO1        100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2              waltz16
PCPD2           80.00 usec
NUC2                     1H
PL2              -2.00 dB
PL12            18.80 dB
PL13            18.80 dB
PL2W        13.17734718 W
PL12W        0.10960442 W
PL13W        0.10960442 W
SFO2        400.1316005 MHz
SI                    32768
SF          100.6127614 MHz
WDW                      EM
SSB                       0
LB               1.00 Hz
GB                        0
PC                     1.40
```

cis-**270**

7.2599

3.6695
3.6328
3.4999
3.4733

2.3080
2.2772
1.9913
1.9624
1.8436
1.8247
1.8060
1.7900
1.7713
1.7526
1.6372
1.6184
1.5996
1.5918
1.5838
1.5651
1.5464
1.0279
0.9902
0.8901
0.0597

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

88.818

77.420
77.102
76.785

61.975

48.146

26.139
25.951
18.336

8.652

-5.315
-5.388

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

224

Bruker Advance III 400

Bruker Advance III 400

225

trans-**136**

Bruker Advance III 400

NAME   sunxy-5-3-8
EXPNO   1
PROCNO   1
Date_   20101108
Time   15.19
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   15
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   57
DW   60.800 usec
DE   6.50 usec
TE   297.2 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900141 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

trans-**155**

Bruker Advance III 400

NAME   sunxy-5-3-8-C13
EXPNO   1
PROCNO   1
Date_   20101108
Time   16.43
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.8 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

-------- CHANNEL f1 --------
NUC1   13C
P1   9.68 usec
PL1   -0.60 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22585411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127606 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

Bruker Advance III 400

```
NAME         sunxy-5-3-9
EXPNO              1
PROCNO             1
Date_         20101115
Time            14.59
INSTRUM         spect
PROBHD    5 mm PADUL 13C
PULPROG         zg30
TD             65536
SOLVENT        CDCl3
NS                16
DS                 2
SWH        8223.685 Hz
FIDRES     0.125483 Hz
AQ         3.9846387 sec
RG               144
DW            60.800 usec
DE             6.50 usec
TE            296.0 K
D1       1.00000000 sec
TD0                1

======== CHANNEL f1 ========
NUC1               1H
P1            14.83 usec
PL1            0.00 dB
PL1W       8.31434441 W
SFO1     400.1324710 MHz
SI             32768
SF       400.1300099 MHz
WDW               EM
SSB                0
LB             0.30 Hz
GB                 0
PC              1.00
```


^{t}BuMe$_2$SiO, Et, Et

trans-**148**

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

Bruker Advance III 400

```
NAME       sunxy-5-3-9-C13
EXPNO              1
PROCNO             1
Date_         20101201
Time            10.32
INSTRUM         spect
PROBHD    5 mm PABBI 1H/
PULPROG        zgpg30
TD             65536
SOLVENT        CDCl3
NS               123
DS                 4
SWH       24038.461 Hz
FIDRES     0.366798 Hz
AQ        1.3631988 sec
RG               203
DW            20.800 usec
DE             6.50 usec
TE            294.5 K
D1       2.00000000 sec
D11      0.03000000 sec
TD0                1

======== CHANNEL f1 ========
NUC1              13C
P1            14.50 usec
PL1           -4.00 dB
PL1W      90.22689819 W
SFO1     100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2        waltz16
NUC2               1H
PCPD2         90.00 usec
PL2           -2.00 dB
PL12          20.06 dB
PL13          22.00 dB
PL2W      13.17734718 W
PL12W      0.08200268 W
PL13W      0.05245997 W
SFO2     400.1316005 MHz
SI             32768
SF       100.6127628 MHz
WDW               EM
SSB                0
LB             1.00 Hz
GB                 0
PC              1.40
```


190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

trans-**162b**

Bruker Advance III 400

```
NAME          sunxy-5-12-33
EXPNO                      1
PROCNO                     1
Date_               20101230
Time                   19.29
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         2
SWH              8223.685 Hz
FIDRES         0.125483 Hz
AQ             3.98463387 sec
RG                       128
DW                60.800 usec
DE                  6.50 usec
TE                   297.9 K
D1          1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                 14.00 usec
PL1                -1.00 dB
PL1W         13.56617069 W
SFO1        400.1924713 MHz
SI                     32768
SF          400.1900138 MHz
WDW                       EM
SSB                        0
LB                   0.30 Hz
GB                         0
PC                      1.00
```

Bruker Advance III 400

```
NAME         sunxy-5-12-33-C13
EXPNO                      1
PROCNO                     1
Date_               20101230
Time                   19.33
INSTRUM                spect
PROBHD    5 mm PABBO BB-
PULPROG                zgpg30
TD                     65536
SOLVENT                CDCl3
NS                      2809
DS                         4
SWH             24038.461 Hz
FIDRES         0.366798 Hz
AQ             1.3631988 sec
RG                      71.8
DW                20.800 usec
DE                  6.50 usec
TE                   298.2 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                     13C
P1                  9.90 usec
PL1                -2.00 dB
PL1W         55.33689499 W
SFO1        100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2               waltz16
NUC2                      1H
PCPD2              90.00 usec
PL2                -1.00 dB
PL12               15.16 dB
PL13               18.62 dB
PL2W         13.56617069 W
PL12W         0.32844096 W
PL13W         0.14806664 W
SFO2        400.1916008 MHz
SI                     32768
SF          100.6278480 MHz
WDW                       EM
SSB                        0
LB                   1.00 Hz
GB                         0
PC                      1.40
```

166

7.5594
7.5575
7.5527
7.5450
7.5303
7.5234
7.2597

3.3719
3.3538
3.3357

1.8854
1.8670
1.8487
1.8304
1.8123
1.7941

1.0521
1.0338
1.0153

Ph

164

4.81   1.99   2.05   3.00

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

154.597

131.785
130.491
129.779

123.862

77.414
77.097
76.779

35.216

22.575

13.206

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10   ppm

235

7.6816
7.6661
7.6414
7.6124
7.5961
7.5820
7.5773
7.5631
7.2596

3.7203
3.7063
3.7007
3.6944
3.6877
3.6811

2.0164
1.9973
1.9779
1.9590
1.9408

1.1361
1.1175
1.0991

165

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

1.92 2.94   2.03   2.00   3.00

153.515

133.054
130.462
129.711
128.120

77.419
77.101
76.782

57.560

15.947
13.835

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 ppm

Bruker Advance III 400

NAME   sunxy-rac-sidechain-TBS-julia
EXPNO   1
PROCNO   1
Date_   20110124
Time   16.33
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   9
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   32
DW   60.800 usec
DE   6.50 usec
TE   297.5 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900141 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

^{t}BuMe$_2$SiO

169

Bruker Advance III 400

NAME sunxy-rac-sidechain-TBS-julia-C13
EXPNO   1
PROCNO   1
Date_   20110124
Time   18.29
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   158
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   73.8
DW   20.800 usec
DE   6.50 usec
TE   298.3 K
D1   1.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -2.00 dB
PL1W   53.33689499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   16.62 dB
PL2W   13.56617069 W
PL12W   0.32844096 W
PL13W   0.34800664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6276465 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

237

170

Bruker Advance III 400

NAME   sunxy-3-54-164
EXPNO   1
PROCNO   1
Date_   20090928
Time   20.15
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   71.8
DW   60.800 usec
DE   6.50 usec
TE   294.7 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300051 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

AcO⌇⌇OTBS

(R)

AcO⌇⌇OSiMe₂ᵗBu

(R)-218

2.014 2.056   3.000 1.443 2.090 3.094 9.047   0.024

8   7   6   5   4   3   2   1   ppm

Bruker Advance III 400

NAME   sunxy-3-54-164-C13
EXPNO   2
PROCNO   1
Date_   20090928
Time   20.39
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   209
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.9 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.68 usec
PL1   -0.60 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22585411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127606 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

AcO⌇⌇OTBS

(R)

180   160   140   120   100   80   60   40   20   0   ppm

239

Bruker Advance III 400

NAME   sunxy-racemic-sidechain
EXPNO   1
PROCNO   1
Date_   20110410
Time   16.08
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   9
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   114
DW   60.800 usec
DE   6.50 usec
TE   293.7 K
D1   1.00000000 sec
TD0   1

======= CHANNEL f1 =======
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300099 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

racemic-91

Bruker Advance III 400

NAME   sunxy-racemic-sidechain-C13
EXPNO   1
PROCNO   1
Date_   20110410
Time   16.24
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   200
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.0 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======= CHANNEL f1 =======
NUC1   13C
P1   9.68 usec
PL1   -0.60 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

======= CHANNEL f2 =======
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22585411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127621 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

220

222a

Bruker Advance III 400

```
NAME       sunxy-R-sidechain-OH-julia-H
EXPNO                     1
PROCNO                    1
Date_              20110125
Time                  12.44
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG                zg30
TD                    65536
SOLVENT               CDCl3
NS                       16
DS                        2
SWH              8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9846387 sec
RG                     80.6
DW                60.800 usec
DE                  6.50 usec
TE                  298.2 K
D1         1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                     1H
P1                14.00 usec
PL1                -1.00 dB
PL1W         13.56617069 W
SFO1       400.1924713 MHz
SI                    32768
SF         400.1900141 MHz
WDW                      EM
SSB                       0
LB                  0.30 Hz
GB                        0
PC                     1.00
```

223a

Bruker Advance III 400

```
NAME       sunxy-R-sidechain-OH-julia-C13
EXPNO                     1
PROCNO                    1
Date_              20110125
Time                  12.15
INSTRUM               spect
PROBHD    5 mm PABBO BB-
PULPROG              zgpg30
TD                    65536
SOLVENT               CDCl3
NS                      443
DS                        4
SWH             24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                      203
DW                20.800 usec
DE                  6.50 usec
TE                  298.2 K
D1         2.00000000 sec
D11        0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                    13C
P1                 9.90 usec
PL1                 2.00 dB
PL1W        55.31689409 W
SFO1       100.6379163 MHz

======== CHANNEL f2 ========
CPDPRG2             waltz16
NUC2                     1H
PCPD2             90.00 usec
PL2                -1.00 dB
PL12               15.16 dB
PL13               18.62 dB
PL2W        13.56617069 W
PL12W        0.32464096 W
PL13W        0.14800604 W
SFO2       400.1916008 MHz
SI                    32768
SF         100.6279480 MHz
WDW                      EM
SSB                       0
LB                  1.00 Hz
GB                        0
PC                     1.40
```

(R)-91

Bruker Advance III 400

NAME   sunxy-8-sidechain-TBS-julia
EXPNO   1
PROCNO   1
Date_   20110124
Time   16.37
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   12
DS   2
SWH   8223.685 Hz
FIDRES   0.125493 Hz
AQ   3.9846387 sec
RG   32
DW   60.800 usec
DE   6.50 usec
TE   297.5 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900141 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

Bruker Advance III 400

NAME   sunxy-8-sidechain-TBS-julia-C13
EXPNO   1
PROCNO   1
Date_   20110124
Time   16.42
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   102
DS   4
SWH   24038.461 Hz
FIDRES   0.366796 Hz
AQ   1.3631988 sec
RG   161
DW   20.800 usec
DE   6.50 usec
TE   298.0 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -3.00 dB
PL1W   55.15989499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   18.62 dB
PL2W   13.56617069 W
PL12W   0.32864098 W
PL13W   0.14806664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6278465 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

Bruker Advance III 400

NAME   sunxy-S-sidechain-OH-julia
EXPNO   1
PROCNO   1
Date_   20110125
Time   10.30
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   11
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   80.6
DW   60.800 usec
DE   6.50 usec
TE   297.7 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900138 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

223b

Bruker Advance III 400

NAME   sunxy-S-sidechain-OH-julia-C13
EXPNO   1
PROCNO   1
Date_   20110125
Time   11.32
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   675
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   181
DW   20.800 usec
DE   4.50 usec
TE   297.8 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -2.00 dB
PL1W   55.33689499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   18.62 dB
PL2W   13.56617069 W
PL12W   0.32844096 W
PL13W   0.14606664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6278480 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

Bruker Advance III 400

NAME   sunxy-S-sidechain
EXPNO   1
PROCNO   1
Date_   20110410
Time   16.16
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   114
DW   60.800 usec
DE   6.50 usec
TE   293.7 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300099 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

(S)-91

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

Bruker Advance III 400

NAME   sunxy-S-sidechain-C13
EXPNO   1
PROCNO   1
Date_   20110410
Time   16.20
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   82
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.1 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.68 usec
PL1   -0.68 dB
PL1W   41.24164963 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   0.00 dB
PL12   15.66 dB
PL13   15.92 dB
PL2W   8.31434441 W
PL12W   0.22585411 W
PL13W   0.21272963 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127628 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10   0 ppm

208

250

Bruker Advance III 400

NAME   sunny-trans-finalproduct
EXPNO   2
PROCNO   1
Date_   20110411
Time   16.10
INSTRUM   spect
PROBHD   5 mm PADUL 13C
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   203
DW   60.800 usec
DE   6.50 usec
TE   294.1 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.83 usec
PL1   0.00 dB
PL1W   8.31434441 W
SFO1   400.1324710 MHz
SI   32768
SF   400.1300098 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

210

7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

Bruker Advance III 400

NAME   sunny-trans-finalproduct-C13
EXPNO   1
PROCNO   1
Date_   20110411
Time   0.41
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   8254
DS   4
SWH   24038.461 Hz
FIDRES   0.366790 Hz
AQ   1.3631988 sec
RG   64
DW   20.800 usec
DE   6.50 usec
TE   297.2 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -2.00 dB
PL1W   55.33689499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   18.62 dB
PL2W   13.56617069 W
PL12W   0.52864096 W
PL13W   0.14806664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6278487 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Bruker Advance III 400

8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0 ppm

3.139
2.075
1.032
1.028
1.025
0.999
2.009
2.079
1.000
1.042
1.974
2.219
9.571
15.432
6.106

Bruker Advance III 400

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

(+)-cis-248a

Et Et

\>—\<*\>*\<—OSiMe₂ᵗBu

O–O

(+)-*cis*-**249a**

Bruker Advance III 400

Bruker Advance III 400

(+)-*cis*-246a

Bruker Advance III 400

NAME	sunxy-4-19-34
EXPNO	1
PROCNO	1
Date_	20100517
Time	22.49
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2768500 sec
RG	57
DW	50.000 usec
DE	6.50 usec
TE	294.4 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1316005 MHz
SI	65536
SF	400.1300052 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Bruker Advance III 400

NAME	sunxy-4-19-34-C13
EXPNO	1
PROCNO	1
Date_	20100517
Time	23.00
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	318
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.7 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127606 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Et   Et

OSiMe₂ᵗBu

O—O

(−)-*cis*-248b

Bruker Advance III 400

NAME	sunxy-4-22-40-2
EXPNO	2
PROCNO	1
Date_	20100618
Time	17.21
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2768500 sec
RG	144
DW	50.000 usec
DE	6.50 usec
TE	294.4 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1316005 MHz
SI	65536
SF	400.1300053 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

(8S)-(+)-cis-251a

Bruker Advance III 400

NAME	sunxy-4-22-40-C13
EXPNO	1
PROCNO	1
Date_	20100618
Time	21.22
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	565
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.6 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

======== CHANNEL f1 ========
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127599 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Bruker Advance III 400

NAME   sunxy-4-23-42
EXPNO   2
PROCNO   1
Date_   20100602
Time   8.43
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   0
SWH   10000.000 Hz
FIDRES   0.152588 Hz
AQ   3.2768500 sec
RG   144
DW   50.000 usec
DE   6.50 usec
TE   294.4 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   7.10 usec
PL1   -2.00 dB
PL1W   13.17734718 W
SFO1   400.1316005 MHz
SI   65536
SF   400.1300053 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

(8S)-(+)-cis-252a

Bruker Advance III 400

NAME   sunxy-4-23-42-C13
EXPNO   1
PROCNO   1
Date_   20100602
Time   8.46
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   787
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.6 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   14.50 usec
PL1   -4.00 dB
PL1W   90.22689819 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   80.00 usec
PL2   -2.00 dB
PL12   18.80 dB
PL13   18.80 dB
PL2W   13.17734718 W
PL12W   0.10960442 W
PL13W   0.10960442 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127606 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

Bruker Advance III 400

```
NAME         sunxy-4-25-45
EXPNO               2
PROCNO              1
Date_        20100603
Time            17.11
INSTRUM         spect
PROBHD   5 mm PABBI 1H/
PULPROG          zg30
TD              65536
SOLVENT         CDCl3
NS                 16
DS                  0
SWH        10000.000 Hz
FIDRES      0.152588 Hz
AQ          3.2768500 sec
RG                203
DW            50.000 usec
DE             6.50 usec
TE             294.5 K
D1          1.00000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1               1H
P1            7.10 usec
PL1           -2.00 dB
PL1W      13.17734718 W
SFO1      400.1316005 MHz
SI              65536
SF        400.1300052 MHz
WDW                EM
SSB                 0
LB             0.30 Hz
GB                  0
PC               1.00
```


Bruker Advance III 400

```
NAME       sunxy-4-25-45-C13
EXPNO               1
PROCNO              1
Date_        20100607
Time            22.22
INSTRUM         spect
PROBHD   5 mm PABBI 1H/
PULPROG         zgpg30
TD              65536
SOLVENT         CDCl3
NS              10644
DS                  4
SWH        24038.461 Hz
FIDRES      0.366798 Hz
AQ          1.3631988 sec
RG                203
DW            20.800 usec
DE             6.50 usec
TE             294.6 K
D1          2.00000000 sec
D11         0.03000000 sec
TD0                 1

======== CHANNEL f1 ========
NUC1              13C
P1           14.50 usec
PL1           -4.00 dB
PL1W      90.22689819 W
SFO1      100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2        waltz16
NUC2               1H
PCPD2         80.00 usec
PL2           -2.00 dB
PL12          18.80 dB
PL13          18.80 dB
PL2W      13.17734718 W
PL12W     0.10960442 W
PL13W     0.10960442 W
SFO2      400.1316005 MHz
SI              32768
SF        100.6127606 MHz
WDW                EM
SSB                 0
LB             1.00 Hz
GB                  0
PC               1.40
```

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(8R)-(+)-*cis*-251b

Bruker Advance III 400

NAME	sunxy-4-36-69
EXPNO	1
PROCNO	1
Date_	20100709
Time	15.44
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	zg30
TD	65536
SOLVENT	CDCl3
NS	12
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2768500 sec
RG	101
DW	50.000 usec
DE	6.50 usec
TE	294.7 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========

NUC1	1H
P1	14.83 usec
PL1	0.00 dB
PL1W	8.31434441 W
SFO1	400.1316005 MHz
SI	65536
SF	400.1300049 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

(8R)-(+)-cis-252b

Bruker Advance III 400

NAME	sunxy-4-36-69-C13
EXPNO	1
PROCNO	1
Date_	20100709
Time	15.53
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	303
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.8 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

-------- CHANNEL f1 --------

NUC1	13C
P1	9.68 usec
PL1	-0.60 dB
PL1W	41.24164963 W
SFO1	100.6228298 MHz

======== CHANNEL f2 ========

CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	0.00 dB
PL12	15.66 dB
PL13	15.92 dB
PL2W	8.31434441 W
PL12W	0.22585411 W
PL13W	0.21272963 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127606 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

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R-(+)-*cis*-**86b**

Bruker Advance III 400

NAME	sunxy-4-14-29
EXPNO	1
PROCNO	1
Date_	20100715
Time	15.54
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	12
DS	2
SWH	11160.714 Hz
FIDRES	0.340598 Hz
AQ	1.4680564 sec
RG	57
DW	44.800 usec
DE	6.50 usec
TE	297.8 K
D1	1.00000000 sec
TD0	1
======== CHANNEL f1 ========	
NUC1	1H
P1	14.00 usec
PL1	-1.00 dB
PL1W	13.56617069 W
SFO1	400.1933363 MHz
SI	16384
SF	400.1900137 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

(8S)-(−)-*cis*-251c

Bruker Advance III 400

NAME	sunxy-4-14-29-C13
EXPNO	1
PROCNO	1
Date_	20100715
Time	15.57
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	402
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	298.1 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1
-------- CHANNEL f1 --------	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz
======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916009 MHz
SI	32768
SF	100.6278480 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

(8*S*)-(−)-*cis*-**252c**

S-(−)-cis-86c

Bruker Advance III 400

NAME   sunxy-4-31-55
EXPNO   2
PROCNO   1
Date_   20100618
Time   17.04
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   16
DS   0
SWH   10000.000 Hz
FIDRES   0.152588 Hz
AQ   3.2768500 sec
RG   45.2
DW   50.000 usec
DE   6.50 usec
TE   294.5 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   7.10 usec
PL1   -2.00 dB
PL1W   13.17734718 W
SFO1   400.1316005 MHz
SI   65536
SF   400.1300053 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

(8R)-(−)-cis-251d

Bruker Advance III 400

NAME   sunxy-4-31-55-C13
EXPNO   1
PROCNO   1
Date_   20100618
Time   17.09
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   238
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.7 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

-------- CHANNEL f1 --------
NUC1   13C
P1   14.50 usec
PL1   -4.00 dB
PL1W   90.22689819 W
SFO1   100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2   waltz16
NUC2   1H
PCPD2   80.00 usec
PL2   -2.00 dB
PL12   18.80 dB
PL13   18.80 dB
PL2W   13.17734718 W
PL12W   0.10960442 W
PL13W   0.10960442 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127599 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

(8R)-(−)-cis-**252d**

Bruker Advance III 400

```
NAME           sunxy-4-32-56
EXPNO                      1
PROCNO                     1
Date_               20100619
Time                   15.33
INSTRUM                spect
PROBHD     5 mm PABBI 1H/
PULPROG                 zg30
TD                     65536
SOLVENT                CDCl3
NS                        16
DS                         0
SWH            10000.000 Hz
FIDRES           0.152588 Hz
AQ             3.2768500 sec
RG                        57
DW                50.000 usec
DE                 6.50 usec
TE                  294.1 K
D1             1.00000000 sec
TD0                        1

======== CHANNEL f1 ========
NUC1                      1H
P1                7.10 usec
PL1               -2.00 dB
PL1W        13.17734718 W
SFO1        400.1316005 MHz
SI                     65536
SF          400.1300052 MHz
WDW                      EM
SSB                       0
LB                 0.30 Hz
GB                        0
PC                     1.00
```
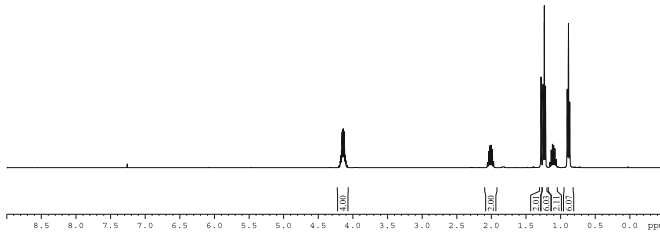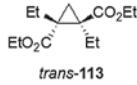
Bruker Advance III 400

```
NAME         sunxy-4-32-56-C13
EXPNO                      1
PROCNO                     1
Date_               20100619
Time                   15.37
INSTRUM                spect
PROBHD     5 mm PABBI 1H/
PULPROG              zgpg30
TD                     65536
SOLVENT                CDCl3
NS                       382
DS                         4
SWH            24038.461 Hz
FIDRES           0.366798 Hz
AQ             1.3631988 sec
RG                       203
DW                20.800 usec
DE                 6.50 usec
TE                  294.3 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                        1

-------- CHANNEL f1 --------
NUC1                     13C
P1                14.50 usec
PL1               -4.00 dB
PL1W        90.22689819 W
SFO1        100.6228298 MHz

-------- CHANNEL f2 --------
CPDPRG2             waltz16
NUC2                      1H
PCPD2             80.00 usec
PL2               -2.00 dB
PL12              18.80 dB
PL13              18.80 dB
PL2W        13.17734718 W
PL12W        0.10960442 W
PL13W        0.10960442 W
SFO2        400.1316005 MHz
SI                     32768
SF          100.6127606 MHz
WDW                      EM
SSB                       0
LB                 1.00 Hz
GB                        0
PC                     1.40
```


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R-(−)-cis-**86d**

J–Resolved CDCl3 4–32–57

J–Resolved CDCl3 4–32–57

Bruker Advance III 400

NAME	sunxy-4-41-83
EXPNO	1
PROCNO	1
Date_	20100813
Time	16.03
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg
TD	65536
SOLVENT	CDCl3
NS	16
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2768500 sec
RG	90.5
DW	50.000 usec
DE	6.50 usec
TE	294.3 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========	
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1316005 MHz
SI	65536
SF	400.1300052 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

S-(+)-cis-268a

Bruker Advance III 400

NAME	sunxy-4-41-83-C13
EXPNO	2
PROCNO	1
Date_	20100813
Time	22.42
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	11020
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	203
DW	20.800 usec
DE	6.50 usec
TE	294.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

-------- CHANNEL f1 --------	
NUC1	13C
P1	14.50 usec
PL1	-4.00 dB
PL1W	90.22689819 W
SFO1	100.6228298 MHz

-------- CHANNEL f2 --------	
CPDPRG2	waltz16
NUC2	1H
PCPD2	80.00 usec
PL2	-2.00 dB
PL12	18.80 dB
PL13	18.80 dB
PL2W	13.17734718 W
PL12W	0.10960442 W
PL13W	0.10960442 W
SFO2	400.1316005 MHz
SI	32768
SF	100.6127606 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

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(3R,4R,6S,10S)-ent-87a

Bruker Advance III 400

NAME	sunxy-4-42-85
EXPNO	2
PROCNO	1
Date_	20100817
Time	19.47
INSTRUM	spect
PROBHD	5 mm PABBI 1H/
PULPROG	zg
TD	65536
SOLVENT	CDCl3
NS	8
DS	0
SWH	10000.000 Hz
FIDRES	0.152588 Hz
AQ	3.2768500 sec
RG	57
DW	50.000 usec
DE	6.50 usec
TE	294.5 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========	
NUC1	1H
P1	7.10 usec
PL1	-2.00 dB
PL1W	13.17734718 W
SFO1	400.1316005 MHz
SI	65536
SF	400.1300056 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

Bruker Advance III 400

NAME	sunxy-4-42-85-C13
EXPNO	2
PROCNO	1
Date_	20100817
Time	15.45
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1353
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	181
DW	20.800 usec
DE	6.50 usec
TE	298.0 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

-------- CHANNEL f1 --------	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz

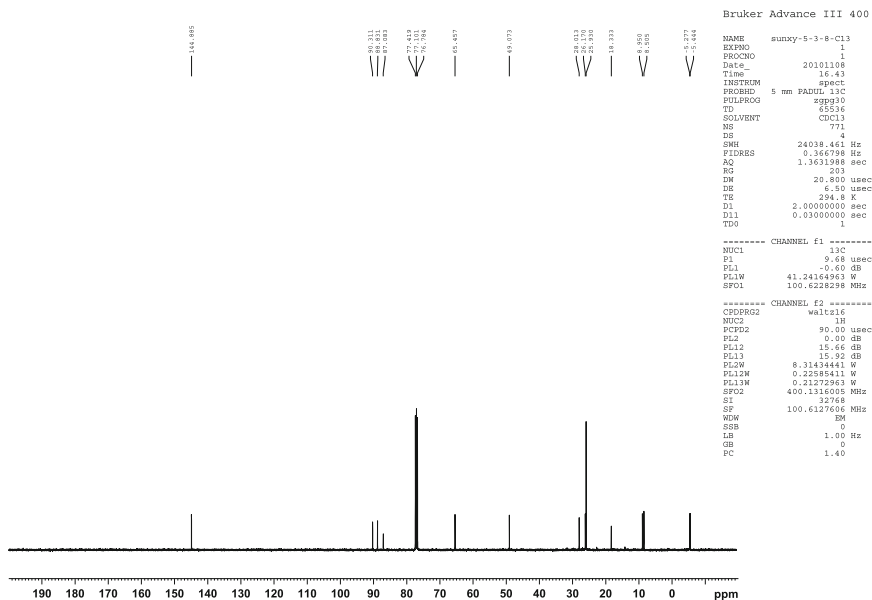| -------- CHANNEL f2 -------- | |
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278480 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Bruker Advance III 400
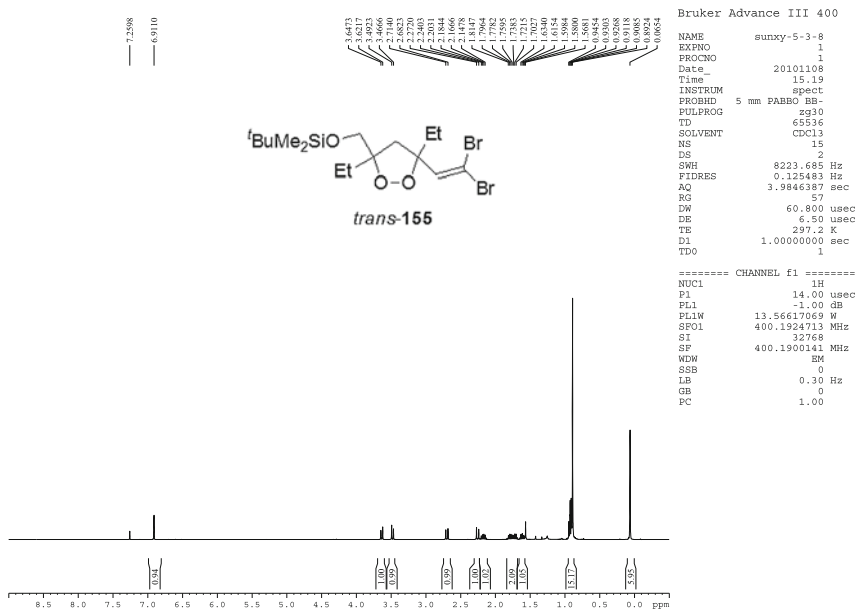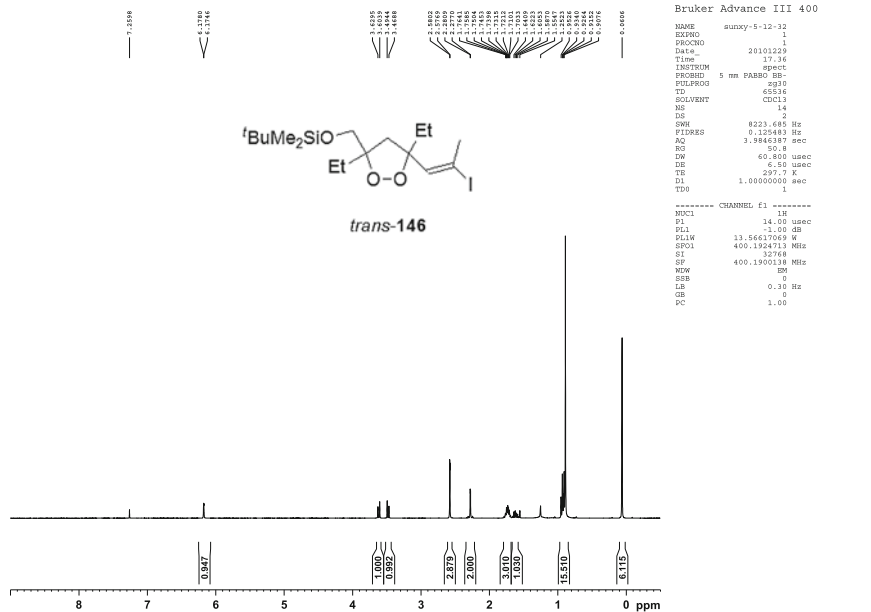
NAME   sunxy-4-24-43
EXPNO   1
PROCNO   1
Date_   20100601
Time   20.32
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   18
DS   0
SWH   10000.000 Hz
FIDRES   0.152588 Hz
AQ   3.2768500 sec
RG   161
DW   50.000 usec
DE   6.50 usec
TE   294.5 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   7.10 usec
PL1   -2.00 dB
PL1W   13.17734718 W
SFO1   400.1316005 MHz
SI   65536
SF   400.1300052 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

R-(+)-cis-268b

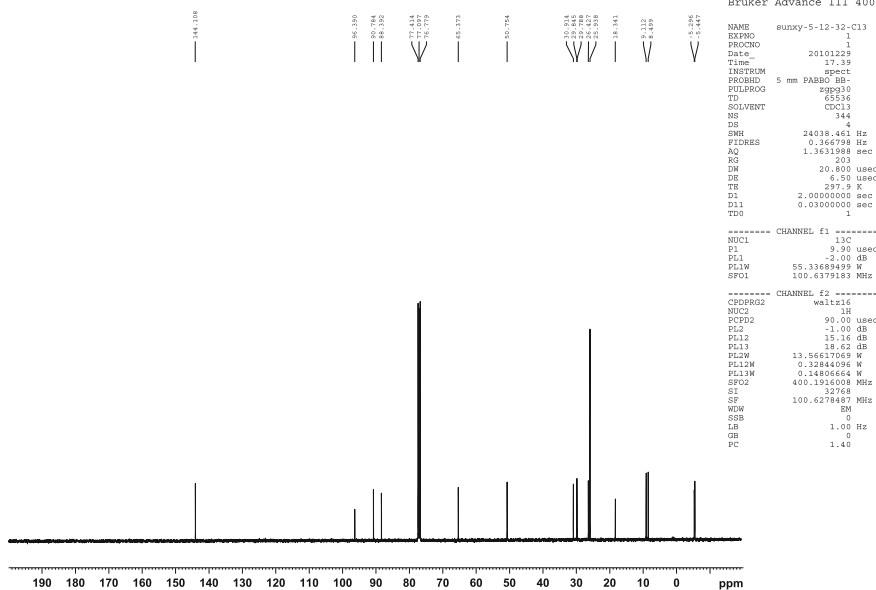Bruker Advance III 400

NAME   sunxy-4-24-43-C13
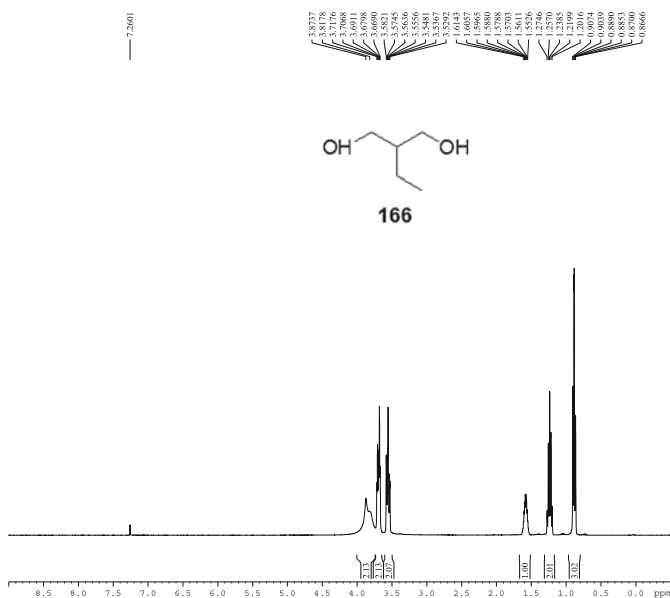EXPNO   1
PROCNO   1
Date_   20100601
Time   20.35
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   423
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   294.6 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   14.50 usec
PL1   -4.00 dB
PL1W   90.22689819 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   80.00 usec
PL2   -2.00 dB
PL12   18.80 dB
PL13   18.80 dB
PL2W   13.17734718 W
PL12W   0.10960442 W
PL13W   0.10960442 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127606 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

Bruker Advance III 400

NAME   sunxy-4-24-44
EXPNO   2
PROCNO   1
Date_   20100818
Time   22.10
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   8
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   90.5
DW   60.800 usec
DE   6.50 usec
TE   298.7 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900138 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

(3R,4R,6S,10R)-ent-87b

Bruker Advance III 400

NAME   sunxy-4-24-44-C13
EXPNO   1
PROCNO   1
Date_   20100818
Time   21.21
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   783
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   181
DW   20.800 usec
DE   6.50 usec
TE   298.8 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -2.00 dB
PL1W   55.33689499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   18.62 dB
PL2W   13.56617069 W
PL12W   0.32844096 W
PL13W   0.14806664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6278480 MHz
WDW   EM
SSB   0
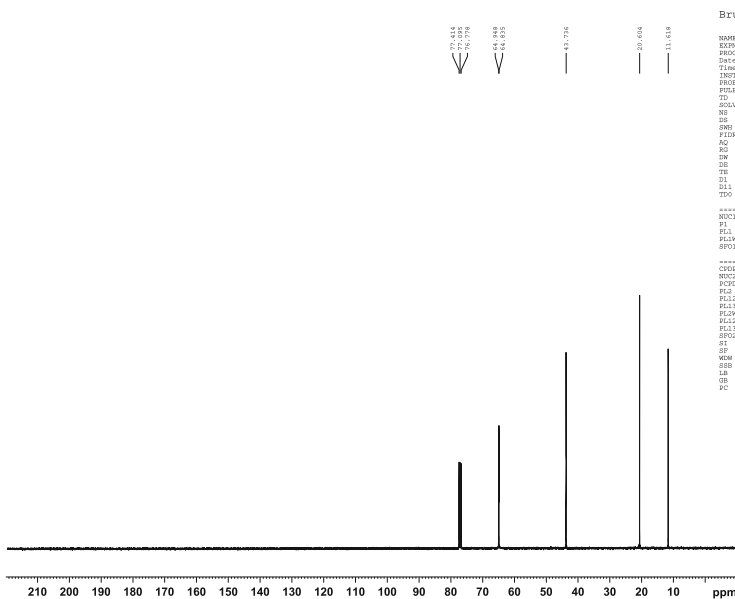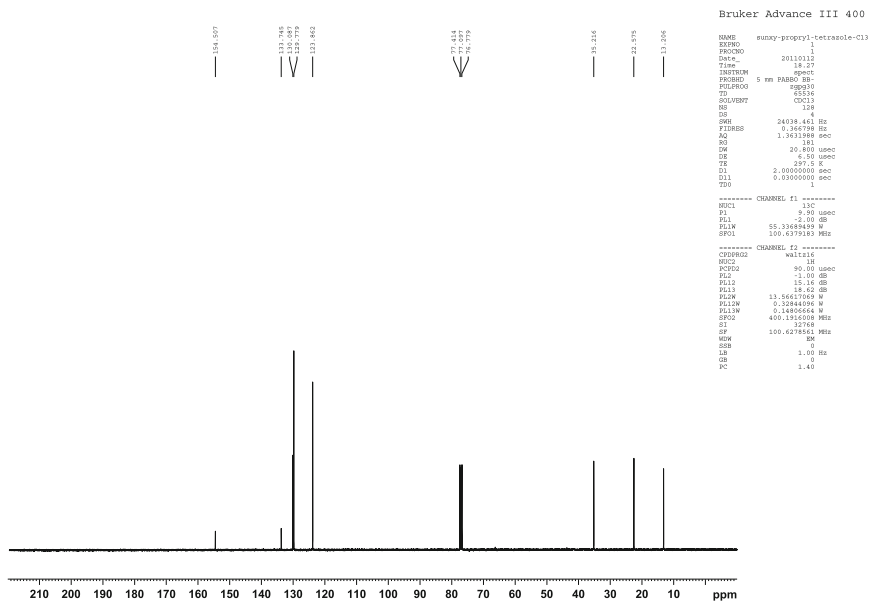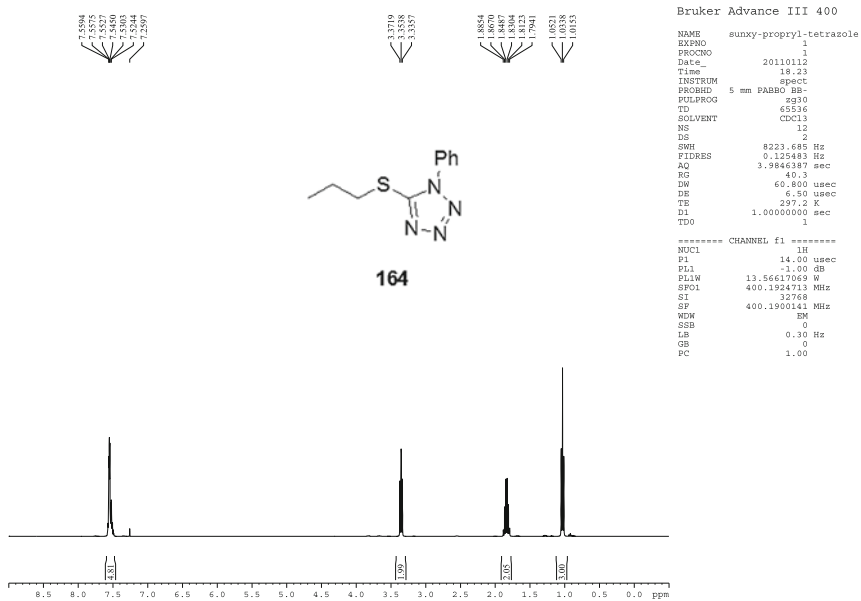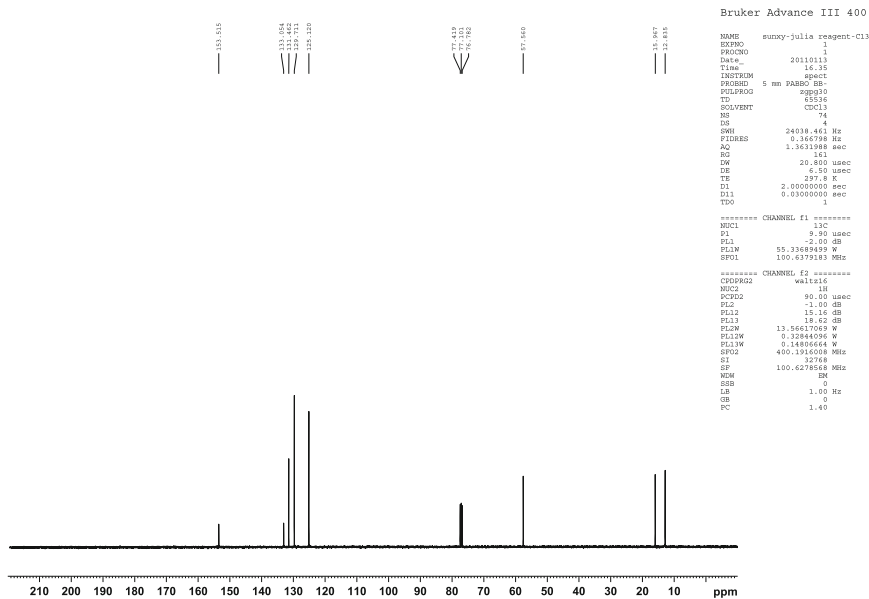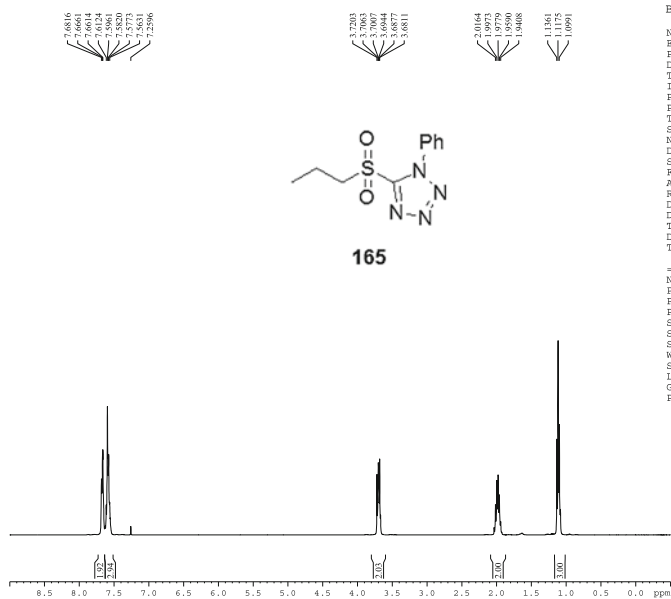LB   1.00 Hz
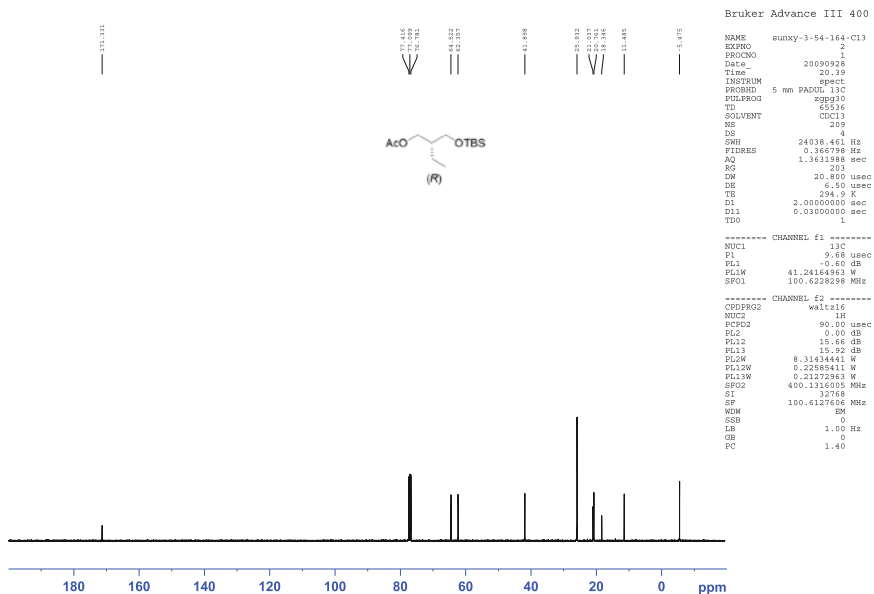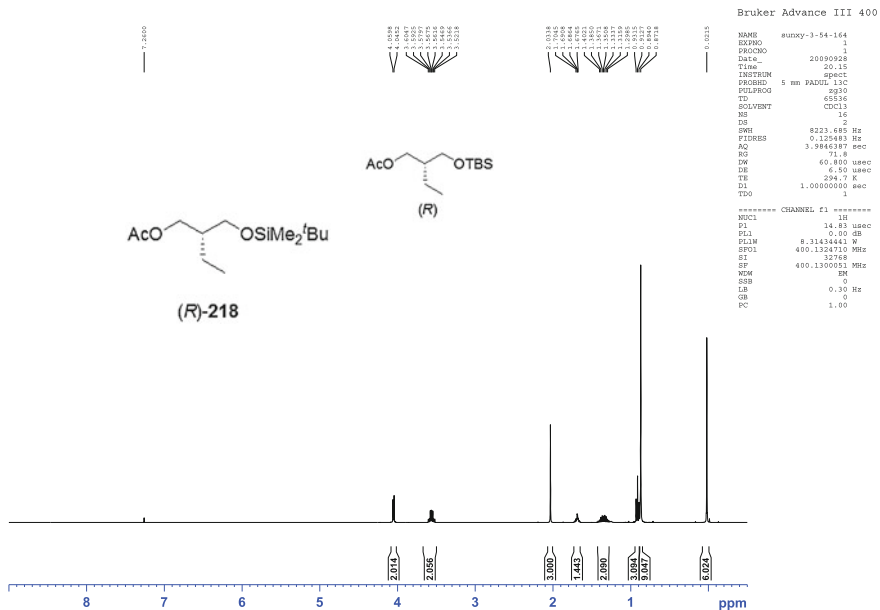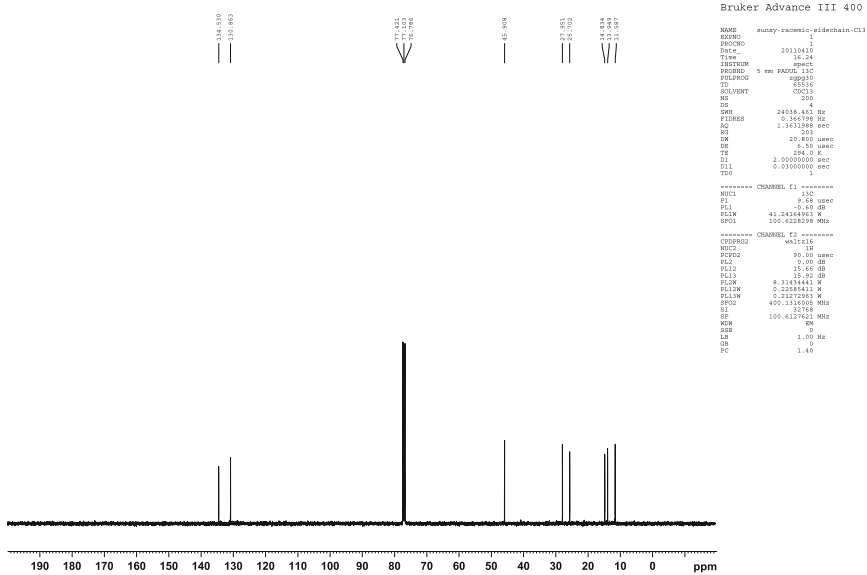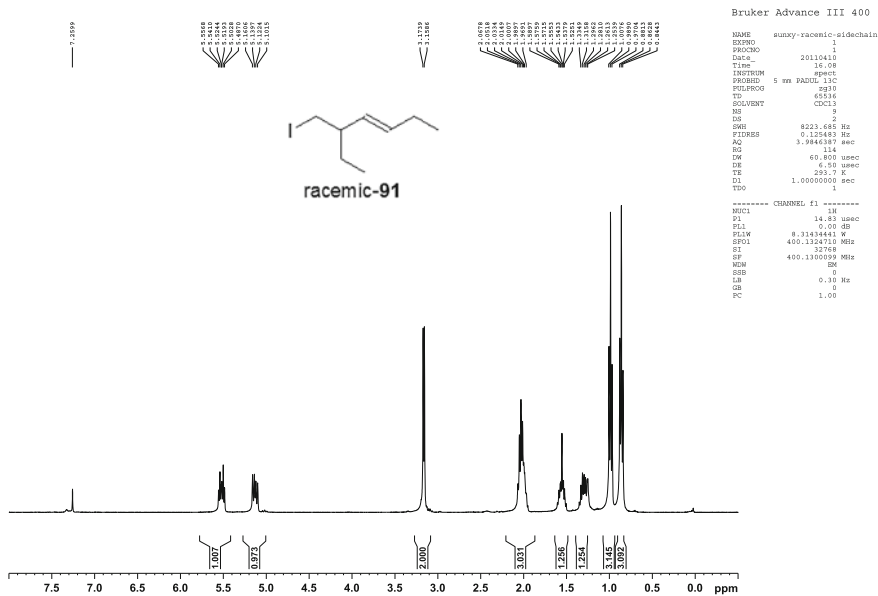GB   0
PC   1.40

190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 ppm

Bruker Advance III 400

NAME	sunxy-4-6-10
EXPNO	1
PROCNO	1
Date_	20100806
Time	14.07
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	11160.714 Hz
FIDRES	0.340598 Hz
AQ	1.4680564 sec
RG	114
DW	44.800 usec
DE	6.50 usec
TE	298.2 K
D1	1.00000000 sec
TD0	1

======== CHANNEL f1 ========	
NUC1	1H
P1	14.00 usec
PL1	-1.00 dB
PL1W	13.56617069 W
SFO1	400.1933363 MHz
SI	16384
SF	400.1900144 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.00

S-(−)-cis-268c

Bruker Advance III 400

NAME	sunxy-4-6-10-C13
EXPNO	1
PROCNO	1
Date_	20100806
Time	18.55
INSTRUM	spect
PROBHD	5 mm PABBO BB-
PULPROG	zgpg30
TD	65536
SOLVENT	CDCl3
NS	1128
DS	4
SWH	24038.461 Hz
FIDRES	0.366798 Hz
AQ	1.3631988 sec
RG	90.5
DW	20.800 usec
DE	6.50 usec
TE	298.5 K
D1	2.00000000 sec
D11	0.03000000 sec
TD0	1

-------- CHANNEL f1 --------	
NUC1	13C
P1	9.90 usec
PL1	-2.00 dB
PL1W	55.33689499 W
SFO1	100.6379183 MHz

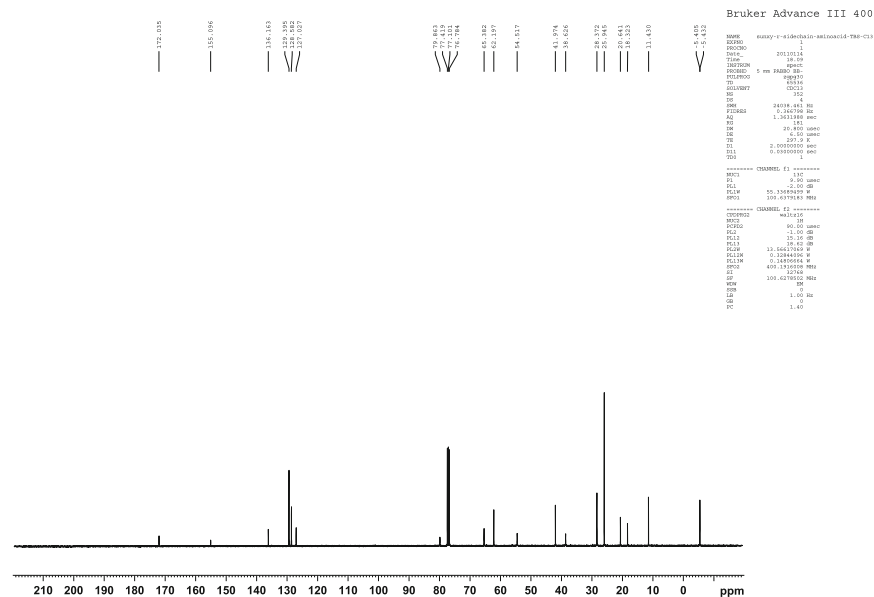| ======== CHANNEL f2 ========	
CPDPRG2	waltz16
NUC2	1H
PCPD2	90.00 usec
PL2	-1.00 dB
PL12	15.16 dB
PL13	18.62 dB
PL2W	13.56617069 W
PL12W	0.32844096 W
PL13W	0.14806664 W
SFO2	400.1916008 MHz
SI	32768
SF	100.6278480 MHz
WDW	EM
SSB	0
LB	1.00 Hz
GB	0
PC	1.40

Bruker Advance III 400

NAME   sunxy-4-6-11
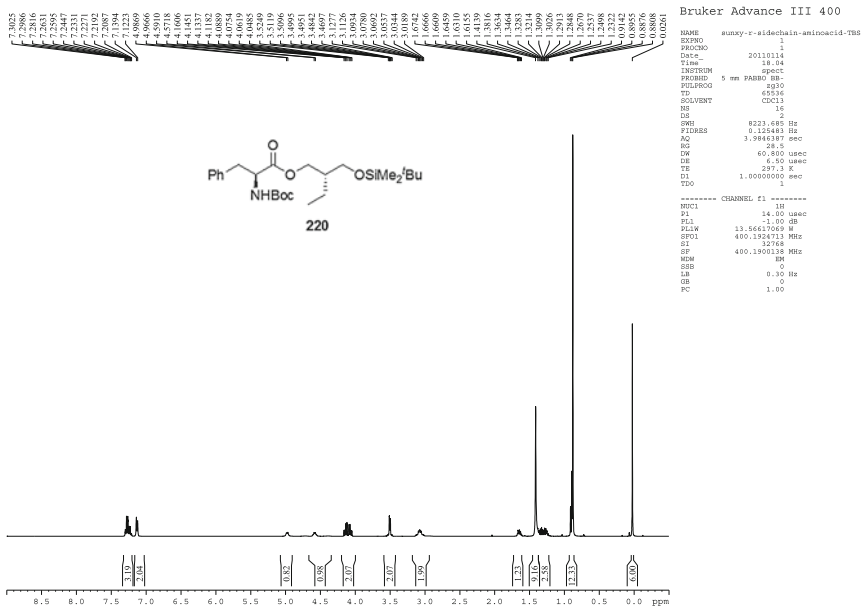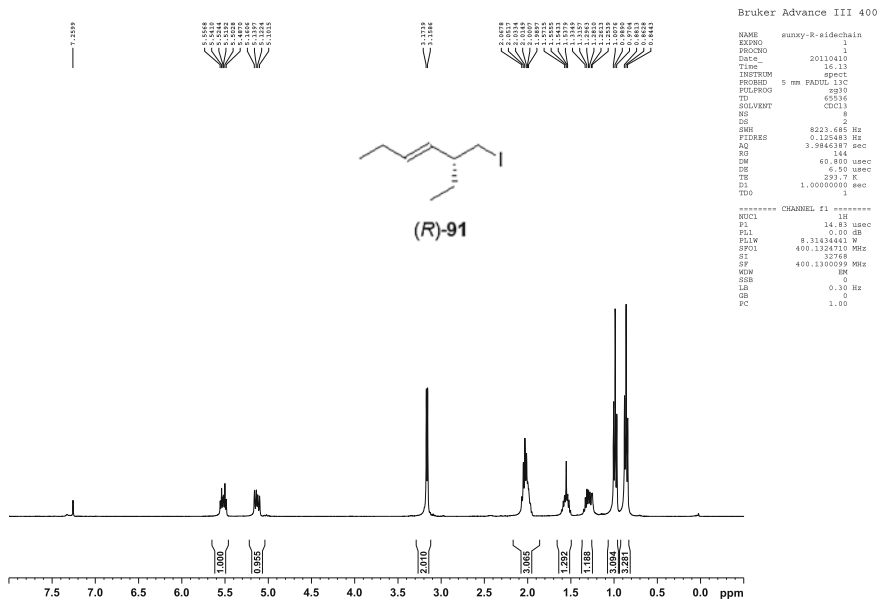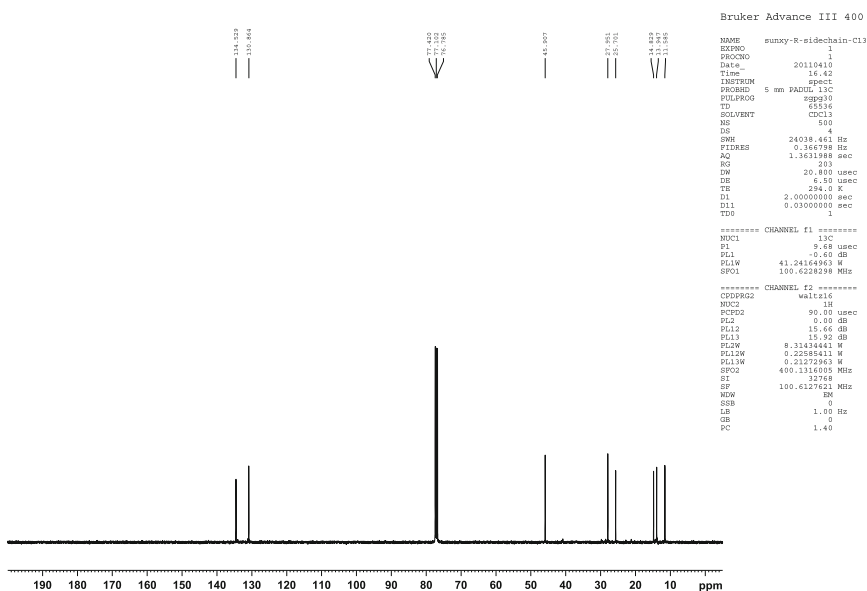EXPNO   1
PROCNO   1
Date_   20100818
Time   19.26
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   8
DS   2
SWH   8223.685 Hz
FIDRES   0.125483 Hz
AQ   3.9846387 sec
RG   90.5
DW   60.800 usec
DE   6.50 usec
TE   298.3 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   14.00 usec
PL1   -1.00 dB
PL1W   13.56617069 W
SFO1   400.1924713 MHz
SI   32768
SF   400.1900138 MHz
WDW   EM
SSB   0
LB   0.30 Hz
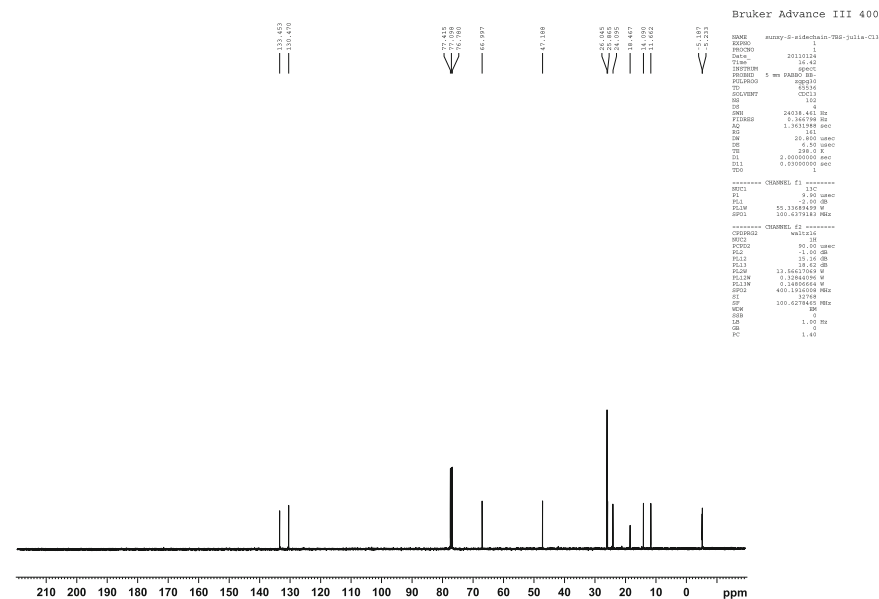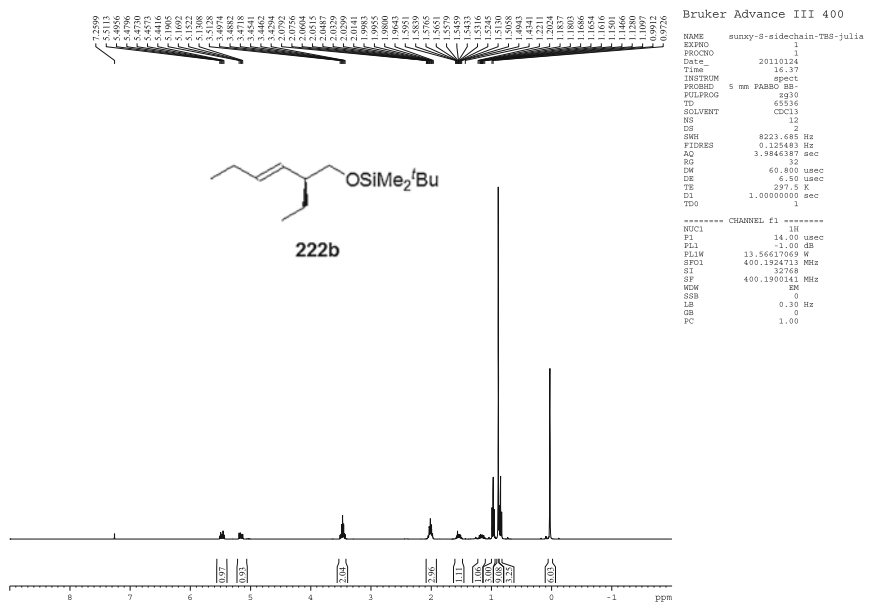GB   0
PC   1.00

(3S,4S,6R,10S)-87b

Bruker Advance III 400

NAME   sunxy-4-6-11-C13
EXPNO   1
PROCNO   1
Date_   20100818
Time   19.38
INSTRUM   spect
PROBHD   5 mm PABBO BB-
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   492
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
DE   6.50 usec
TE   299.0 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   9.90 usec
PL1   -2.00 dB
PL1W   55.33668499 W
SFO1   100.6379183 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   90.00 usec
PL2   -1.00 dB
PL12   15.16 dB
PL13   18.62 dB
PL2W   13.56617069 W
PL12W   0.32844096 W
PL13W   0.14806664 W
SFO2   400.1916008 MHz
SI   32768
SF   100.6278560 MHz
WDW   EM
SSB   0
LB   1.00 Hz
GB   0
PC   1.40

R-(−)-cis-268d

Bruker Advance III 400

NAME   sunxy-4-33-58
EXPNO   1
PROCNO   1
Date_   20100621
Time   23.46
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zg30
TD   65536
SOLVENT   CDCl3
NS   12
DS   0
SWH   10000.000 Hz
FIDRES   0.152588 Hz
AQ   3.2768500 sec
RG   128
DW   50.000 usec
DE   6.50 usec
TE   294.3 K
D1   1.00000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   1H
P1   7.10 usec
PL1   -2.00 dB
PL1W   13.17734718 W
SFO1   400.1316005 MHz
SI   65536
SF   400.1300045 MHz
WDW   EM
SSB   0
LB   0.30 Hz
GB   0
PC   1.00

Bruker Advance III 400

NAME   sunxy-4-33-58-C13
EXPNO   1
PROCNO   1
Date_   20100621
Time   23.50
INSTRUM   spect
PROBHD   5 mm PABBI 1H/
PULPROG   zgpg30
TD   65536
SOLVENT   CDCl3
NS   9139
DS   4
SWH   24038.461 Hz
FIDRES   0.366798 Hz
AQ   1.3631988 sec
RG   203
DW   20.800 usec
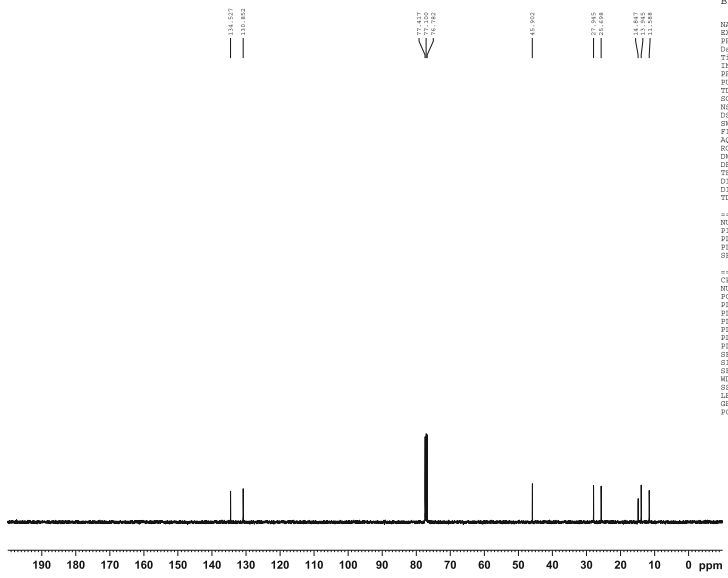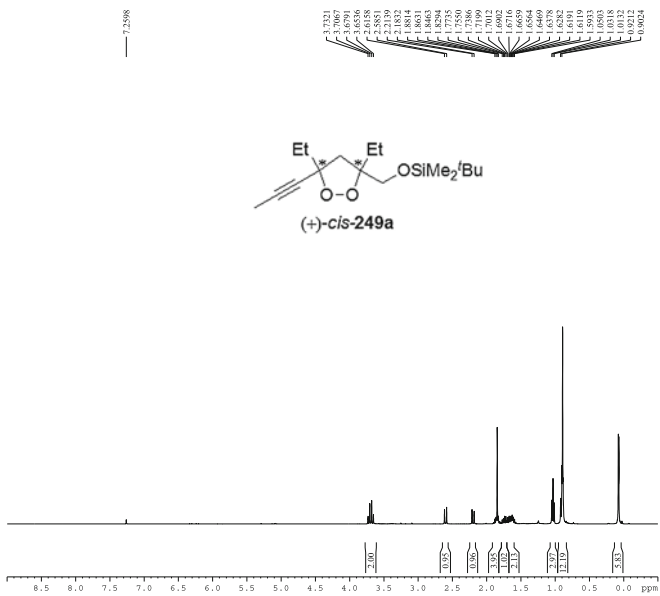DE   6.50 usec
TE   294.6 K
D1   2.00000000 sec
D11   0.03000000 sec
TD0   1

======== CHANNEL f1 ========
NUC1   13C
P1   14.50 usec
PL1   -4.00 dB
PL1W   90.22689819 W
SFO1   100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2   waltz16
NUC2   1H
PCPD2   80.00 usec
PL2   -2.00 dB
PL12   18.80 dB
PL13   18.80 dB
PL2W   13.17734718 W
PL12W   0.10960442 W
PL13W   0.10960442 W
SFO2   400.1316005 MHz
SI   32768
SF   100.6127606 MHz
WDW   EM
SSB   0
LB   1.00 Hz
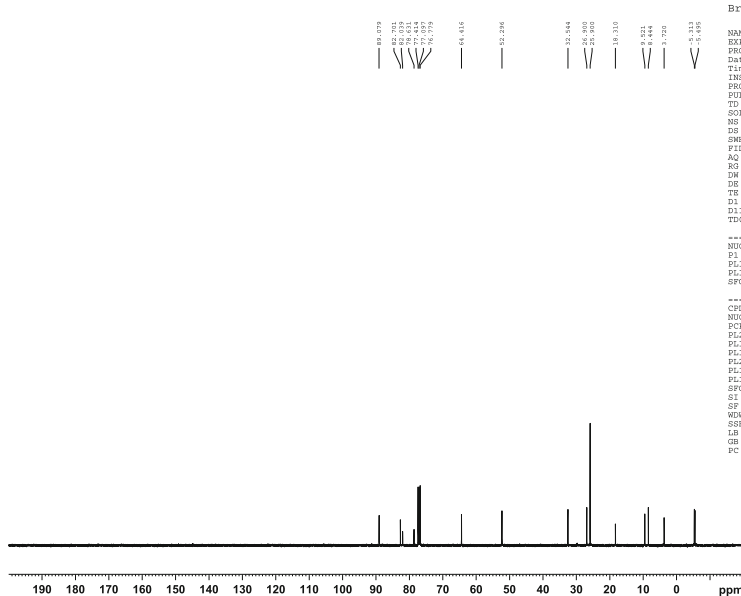GB   0
PC   1.40

(3S,4S,6R,10R)-Plakortone B (87a)

(4S,6R,10R)-Plakortide E (85a)

Data File I:\HPLC\DATA\HEHAO\051-0101.D   Sample Name: XYS_PO-OTs_rac

MP: 95% Hexane : 5% IPA   Flow: 1.0ml/min
Column: ~~CHIRALCEL~~ AD-H
         CHIRALPAK ·
==
Injection Date : 7/31/2009 1:26:31 PM   Seq. Line :   1
Sample Name   : XYS_PO-OTs_rac   Location : Vial 51
Acq. Operator   : lqh   Inj :   1
Acq. Instrument : Instrument 1   Inj Volume : 20 µl
Acq. Method   : I:\HPLC\METHODS\SAM-POT2.M
Last changed   : 7/31/2009 1:36:35 PM by lqh
                  (modified after loading)
Analysis Method : I:\HPLC\METHODS\SAM-POTS.M
Last changed   : 7/31/2009 2:17:30 PM by SAM
                  (modified after loading)
For AD-mix DIOL Reaction Product
Channel A: IPA
Channel B: Hexane
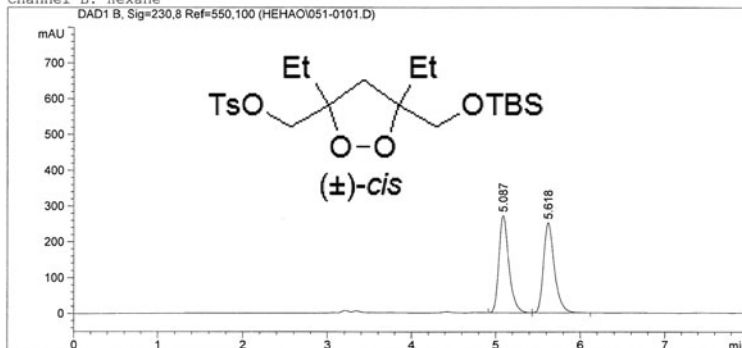
==
                        Area Percent Report
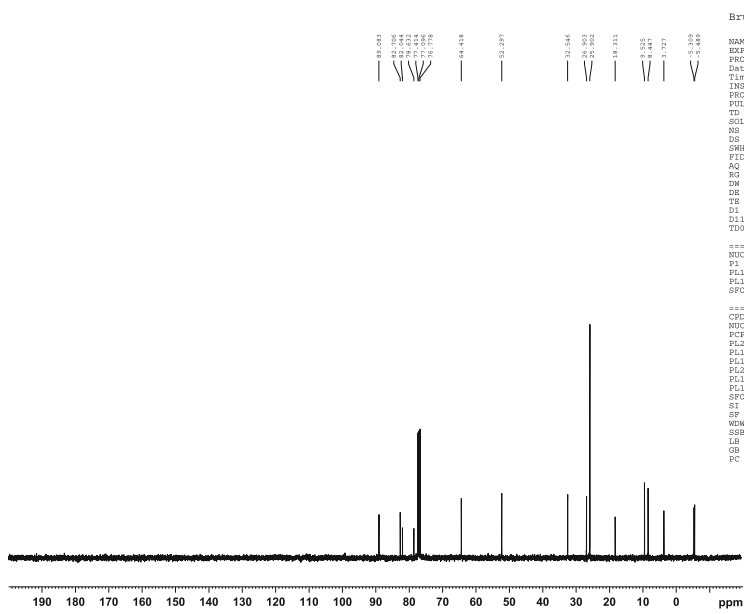==

Sorted By   :   Signal
Multiplier   :   1.0000
Dilution   :   1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=230,8 Ref=550,100

Peak RetTime Type Width   Area   Height   Area
 #   [min]   [min]   [mAU*s]   [mAU]   %
----|-------|----|-------|----------|----------|--------|
  1   5.087 VV   0.1248 2249.16724   271.19827   49.9087
  2   5.618 VB   0.1368 2257.39478   251.29340   50.0913

Totals :   4506.56201   522.49167

 Results obtained with enhanced integrator!
==
                       *** End of Report ***

Data File I:\HPLC\DATA\HEHAO\021-0101.D   Sample Name: XYSun_132

    MP: 95% Hexane : 5% IPA   Flow: 1.0ml/min   Sun xy -3 - 132
    Column: CHIRALPAK AD-H
            CHIRALPAK.
===
    Injection Date : 8/25/2009 1:48:47 PM   Seq. Line :   1
    Sample Name   : XYSun_132   Location : Vial 21
    Acq. Operator   : SAM   Inj :   1
    Acq. Instrument : Instrument 1   Inj Volume : 20 µl
    Acq. Method   : I:\HPLC\METHODS\SAM-POT2.M
    Last changed   : 8/10/2009 12:50:39 PM by SAM
    Analysis Method : I:\HPLC\METHODS\SAM-POT2.M
    Last changed   : 8/25/2009 2:06:25 PM by SAM
                      (modified after loading)
    For XYSun Peroxide-OTs Product
    Channel A: IPA
    Channel B: Hexane
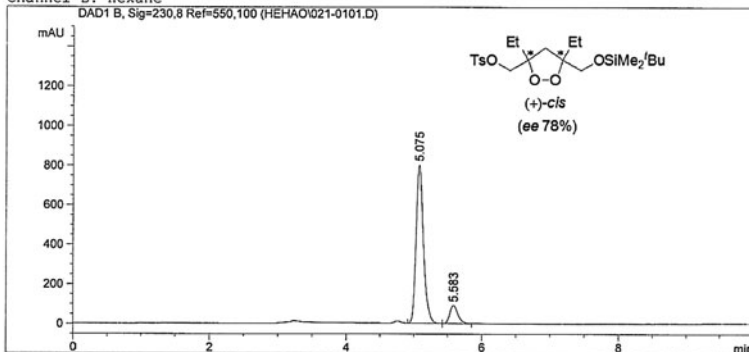
                          Area Percent Report
===

    Sorted By   :   Signal
    Multiplier   :   1.0000
    Dilution   :   1.0000
    Do not use Multiplier & Dilution Factor with ISTDs

    Signal 1: DAD1 B, Sig=230,8 Ref=550,100

    Peak RetTime Type Width   Area   Height   Area
     #   [min]   [min]   [mAU*s]   [mAU]   %
    ---|-------|----|-------|----------|----------|--------|
      1   5.075 VV   0.1166 6080.63818 800.48834 89.1612
      2   5.583 VV   0.1228 739.18622   90.93532 10.8388

    Totals :   6819.82440 891.42366

     Results obtained with enhanced integrator!
===
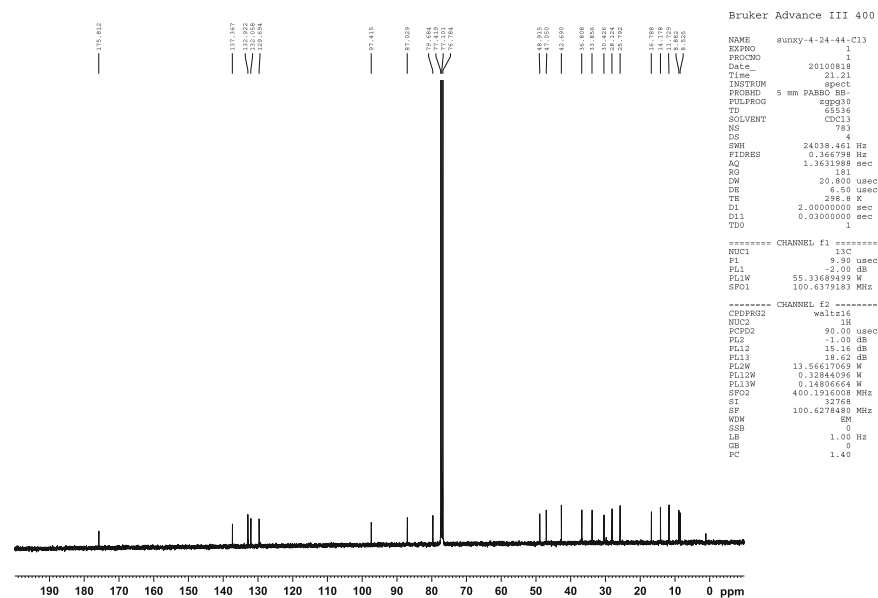   *** End of Report ***

ata File I:\HPLC\DATA\HEHAO\022-0201.D   Sample Name: XYSun_135

MP: 95% Hexane : 5% IPA   Flow: 1.0ml/min $Sunny-3-135$
Column: CHIRALPAK AD-H

===

Injection Date   : 8/25/2009 2:05:46 PM   Seq. Line :   2
Sample Name   : XYSun_135   Location : Vial 22
Acq. Operator   : SAM   Inj :   1
Acq. Instrument : Instrument 1   Inj Volume : 20 µl
Acq. Method   : I:\HPLC\METHODS\SAM-POT2.M
Last changed   : 8/10/2009 12:50:39 PM by SAM
Analysis Method : I:\HPLC\METHODS\SAM-POT2.M
Last changed   : 8/25/2009 2:24:42 PM by SAM
                   (modified after loading)
For XYSun Peroxide-OTs Product
Channel A: IPA
Channel B: Hexane

===
                              Area Percent Report
===
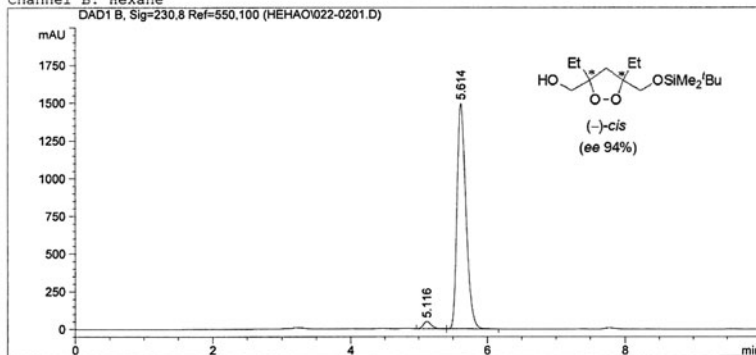
Sorted By   :   Signal
Multiplier   :   1.0000
Dilution   :   1.0000
Do not use Multiplier & Dilution Factor with ISTDs

Signal 1: DAD1 B, Sig=230,8 Ref=550,100

Peak RetTime Type Width   Area   Height   Area
 #   [min]   [min]   [mAU*s]   [mAU]   %
----|-------|----|-------|----------|----------|--------|
  1   5.116 VP   0.1233 404.39487   49.52249   2.9286
  2   5.614 VB   0.1366 1.34042e4 1495.09082 97.0714

Totals :   1.38086e4 1544.61331

 Results obtained with enhanced integrator!
===
                            *** End of Report ***
===

ta File I:\HPLC\DATA\HEHAO\023-0301.D   Sample Name: XYSun_136

MP: 95% Hexane : 5% IPA   Flow: 1.0ml/min   *SunXY-3-136*
Column: CHIRALPAK AD-H

```
============================================================================
Injection Date   : 8/25/2009 2:22:44 PM          Seq. Line :    3
Sample Name      : XYSun_136                      Location : Vial 23
Acq. Operator    : SAM                                 Inj :    1
Acq. Instrument  : Instrument 1             Inj Volume : 20 µl
Acq. Method      : I:\HPLC\METHODS\SAM-POT2.M
Last changed     : 8/10/2009 12:50:39 PM by SAM
Analysis Method  : I:\HPLC\METHODS\SAM-POT2.M
Last changed     : 8/25/2009 2:38:31 PM by SAM
                   (modified after loading)
For XYSun Peroxide-OTs Product
Channel A: IPA
Channel B: Hexane
```


DAD1 B, Sig=230,8 Ref=550,100 (HEHAO\023-0301.D)

(+)-*cis*
(*ee* 89%)
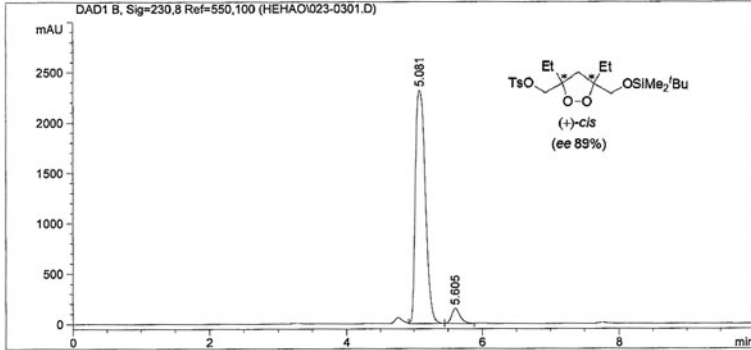
```
============================================================================
                        Area Percent Report
============================================================================

Sorted By            :       Signal
Multiplier           :       1.0000
Dilution             :       1.0000
Do not use Multiplier & Dilution Factor with ISTDs


Signal 1: DAD1 B, Sig=230,8 Ref=550,100

Peak RetTime Type  Width     Area       Height     Area
 #   [min]        [min]    [mAU*s]      [mAU]        %
---|-------|----|-------|----------|----------|--------|
  1   5.081 VV   0.1580 2.30140e4  2315.59375  94.6720
  2   5.605 VV   0.1305 1295.19531  150.39812   5.3280

Totals :                 2.43092e4  2465.99187

 Results obtained with enhanced integrator!
============================================================================
                       *** End of Report ***
```

Data File C:\HPCHEM\1\DATA\20100825\XYSRAC2.D   Sample Name: XYS-rac-2

    XYS-rac-1
    IPA: 5%, Hexanes: 95%
    Column: CHIRALPAK AD-H

    ===
    Injection Date : 8/25/2010 1:21:30 PM
    Sample Name   : XYS-rac-2   Location : Vial 1
    Acq. Operator   : SAM
                                                       Inj Volume : 5 µl
    Acq. Method   : C:\HPCHEM\1\METHODS\TERMS04.M
    Last changed   : 8/25/2010 12:34:47 PM by SAM
                      (modified after loading)
    Analysis Method : C:\HPCHEM\1\METHODS\TERMS04.M
    Last changed   : 8/25/2010 1:37:29 PM by SAM
                      (modified after loading)

    ===
                          Area Percent Report
    ===
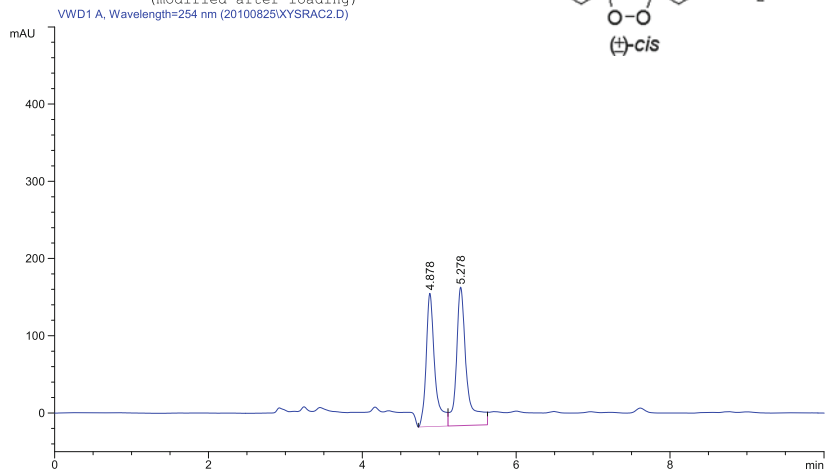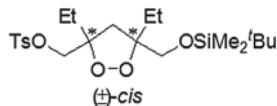
    Sorted By   :   Signal
    Multiplier   :   1.0000
    Dilution   :   1.0000

    Signal 1: VWD1 A, Wavelength=254 nm

    Peak RetTime Type Width   Area   Height   Area
     #   [min]   [min] mAU   *s   [mAU   ]   %
    ----|-------|----|-------|----------|----------|--------|
      1   4.878 VV   0.1183 1362.06201 172.57300 45.0561
      2   5.278 VV   0.1376 1660.97363 178.62419 54.9439

    Totals :   3023.03564 351.19719

     Results obtained with enhanced integrator!
    ===
                          *** End of Report ***

XYS-4-40-79
IPA: 5%, Hexanes: 95%
Column: CHIRALPAK AD-H

```
====================================================================
Injection Date  : 8/25/2010 12:01:49 PM
Sample Name     : XYS-4-79                          Location : Vial 1
Acq. Operator   : SAM
                                                    Inj Volume : 5 µl
Acq. Method     : C:\HPCHEM\1\METHODS\TERMS04.M
Last changed    : 8/25/2010 11:55:15 AM by CYW
                  (modified after loading)
Analysis Method : C:\HPCHEM\1\METHODS\TERMS04.M
Last changed    : 8/25/2010 12:34:47 PM by SAM
                  (modified after loading)
```

VWD1 A, Wavelength=230 nm (20100825\XYS7901.D)

$(-)$-*cis*-**272b**

$ee > 99\%$

```
====================================================================
                    Area Percent Report
====================================================================

Sorted By             :      Signal
Multiplier            :      1.0000
Dilution              :      1.0000


Signal 1: VWD1 A, Wavelength=230 nm

Peak RetTime Type  Width     Area       Height     Area
  #   [min]        [min]  mAU  *s   [mAU   ]       %
---|-------|----|-------|----------|----------|--------|
  1   5.438 VV    0.1676 1.11494e4  1025.61499 100.0000

Totals :                  1.11494e4  1025.61499
```

 Results obtained with enhanced integrator!
```
====================================================================
                    *** End of Report ***
```

    XYS-4-40-80
    IPA: 5%, Hexanes: 95%
    Column: CHIRALPAK AD-H

    ==
    Injection Date : 8/25/2010 12:51:32 PM
    Sample Name   : XYS-4-80   Location : Vial 1
    Acq. Operator   : SAM
                                                      Inj Volume : 5 µl
    Acq. Method   : C:\HPCHEM\1\METHODS\TERMS04.M
    Last changed   : 8/25/2010 12:34:47 PM by SAM
                      (modified after loading)
    Analysis Method : C:\HPCHEM\1\METHODS\TERMS04.M
    Last changed   : 8/25/2010 1:37:29 PM by SAM
                      (modified after loading)

    ==
                         Area Percent Report
    ==

    Sorted By   :   Signal
    Multiplier   :   1.0000
    Dilution   :   1.0000

    Signal 1: VWD1 A, Wavelength=254 nm

    Peak RetTime Type Width   Area   Height   Area
     #   [min]   [min] mAU   *s   [mAU   ]   %
    ----|-------|----|-------|----------|----------|--------|
       1   4.870 PB   0.1113 2507.12842 343.81906 100.0000

    Totals :   2507.12842 343.81906

     Results obtained with enhanced integrator!
    ==
                         *** End of Report ***