

**Studies on Nucleophilic Cyclopropanation Reactions
with Bis(iodozincio)methane**

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Contents

Chapter 1	1
Introduction and General Summary	
Chapter 2	29
Diastereoselective Nucleophilic Cyclopropanation of 1,2-Diketones and α -Ketoimines with Bis(iodozincio)methane	
Chapter 3	59
Stereospecific and Stereoselective Preparation of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols from α,β -Epoxy Ketones and Bis(iodozincio)methane	
Chapter 4	85
A New Zincate-Mediated Rearrangement Reaction of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols	
Chapter 5	115
Stereospecific Construction of Chiral Tertiary and Quaternary Carbon by Nucleophilic Cyclopropanation with Bis(iodozincio)methane	
Chapter 6	151
Nucleophilic Cyclopropanation Reaction with Bis(iodozincio)methane by 1,4-Addition to α,β -Unsaturated Carbonyl Compounds	
Publication List	187
Acknowledgment	190

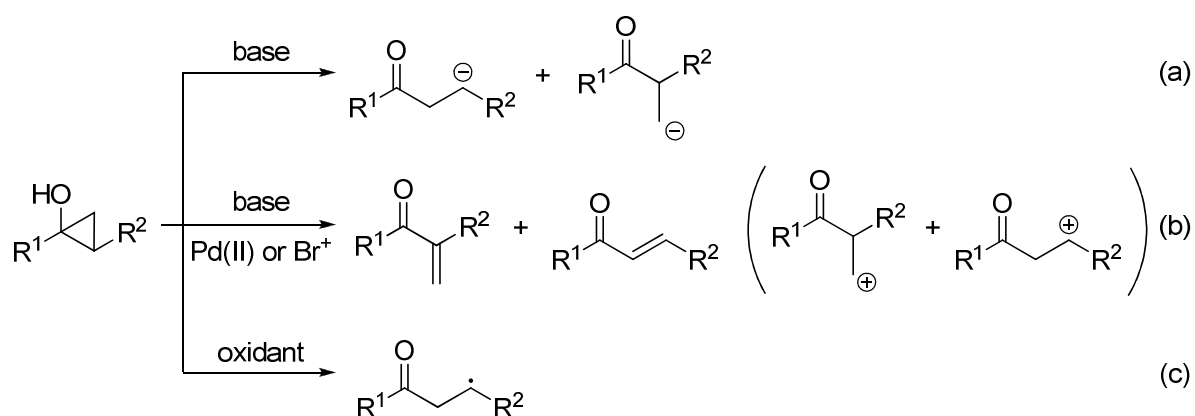
Chapter 1

Introduction and General Summary

Introduction

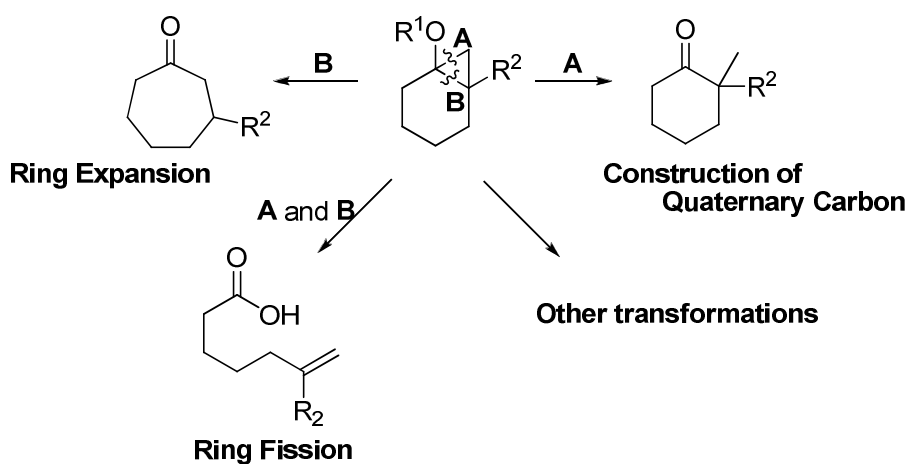
The cyclopropane-skeleton is often found in a wide range of natural products.¹ Some of these cyclopropane-containing natural compounds show high biological activities, and sometimes become potential drug candidates. In addition to these biological activities, cyclopropanes can also be recognized as variants of three-carbon chain units via ring-opening.² Actually, ring-opening reactions have been offering us many significant transformations in organic syntheses. For more efficient cyclopropane ring-opening reactions, we can postulate a use of cyclopropanols.³

The ring fission of cyclopropanols proceeds readily with the conversion of hydroxy-substituted carbon into carbonyl groups. This process affords various types of reactive intermediates. When cyclopropanols are treated with a base, carbanions at β -position of carbonyl groups, that is homoenolates, are formed (Scheme 1(a)).⁴ The reaction of the homoenolates with Pd(II) or bromine affords α,β -unsaturated ketones, which can be regarded as synthons of β -carbocation (Scheme 1(b)).⁵ Furthermore, it is known that treatment of cyclopropanols with one-electron oxidants, such as Fe(III) or Mn(III), generates β -radical species (Scheme 1(c)).⁶



Scheme 1. Building blocks from cyclopropanol.

In addition, one of the attractive aspects of cyclopropanols as synthetic intermediates is that the cyclopropane rings can be cleaved regioselectively depending on the reaction conditions. This advantage enables the constructions of various structures selectively. For example, in the case of 6-alkylbicyclo[4.1.0]heptan-1-ol derivative as a substrate, the cleavage of bond **A** affords a ketone having a stereogenic quaternary carbon at α -position, as shown in Scheme 2.⁷ In contrast, the fission of bond **B** allows ring expansion, and as a result, a seven-membered ring ketone is obtained.⁸ Furthermore, the reaction that cleaves both bond **A** and bond **B** to give acyclic carboxylic acid derivative has also been reported.⁹

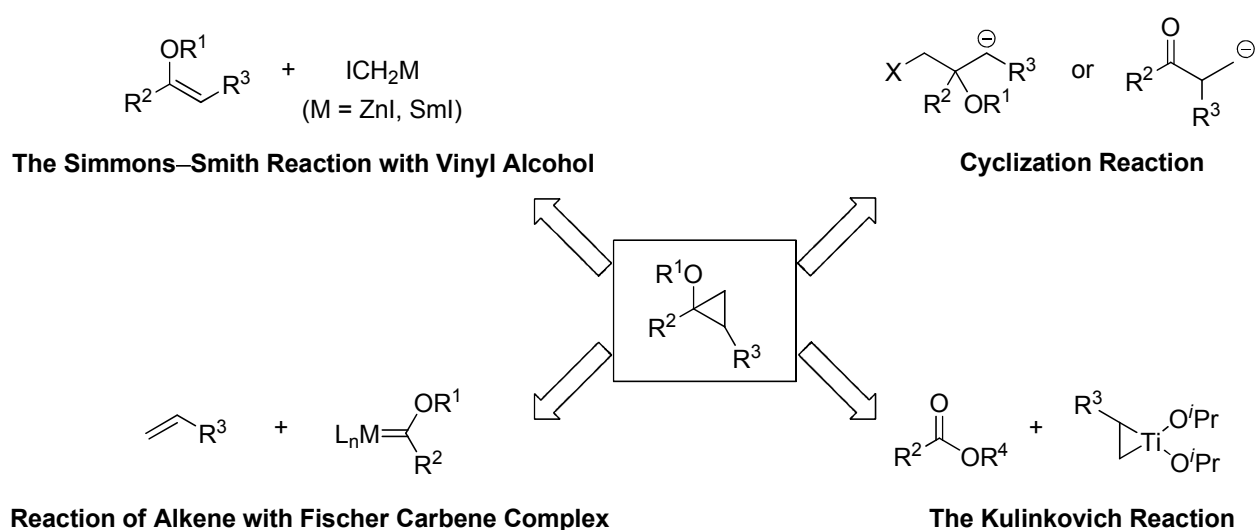


Scheme 2. Regioselective cleavage of cyclopropane ring in cyclopropanol.

Owing to the varieties of transformation reactions, cyclopropanols have been used as versatile synthetic tools. Hence the efficient methods for preparation of cyclopropanols have been required. Actually, many examples of cyclopropanol-preparation have been reported.³ However, the preparation of cyclopropanols having additional functional groups is insufficient by these methods. To achieve the preparation of more functionalized cyclopropanols, we must develop a new method for preparation of cyclopropanols.

Methods for Preparation of Cyclopropanols

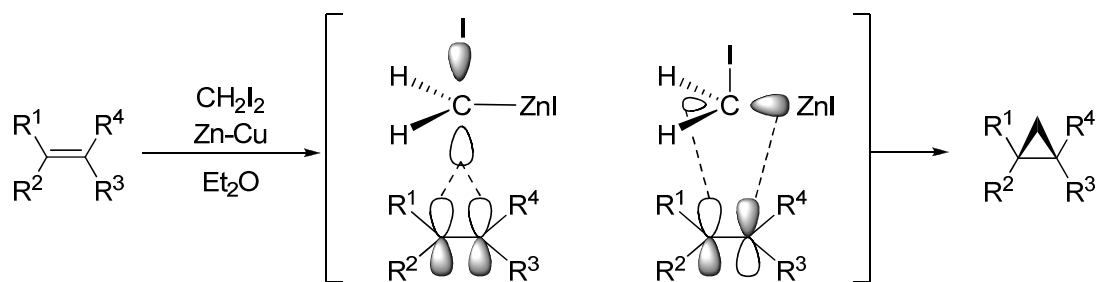
First of all, the author reviews the conventional methods of cyclopropanol syntheses. They can be represented by the following four methods, as shown in Scheme 3:¹⁰ 1) the Simmons–Smith reaction of vinyl alcohol equivalent; 2) the reaction of Fischer carbene complex with alkenes; 3) the cyclization reaction; and 4) the reaction of ester and titanacyclopropane, that is, the Kulinkovich reaction.



Scheme 3. Methods for preparation of cyclopropanol.

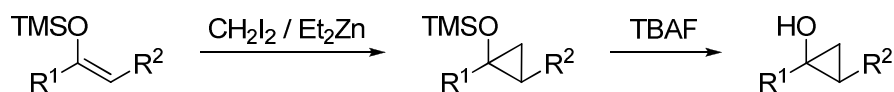
1) The Simmons–Smith Reaction

The most common electrophilic cyclopropanation method is the Simmons–Smith reaction:^{11,12} Treatment of alkenes with the Simmons–Smith reagent (IZnCH_2I), which is prepared from diiodomethane and zinc–copper couple in diethyl ether, affords cyclopropanes. The reaction proceeds stereospecifically, as shown in Scheme 4.



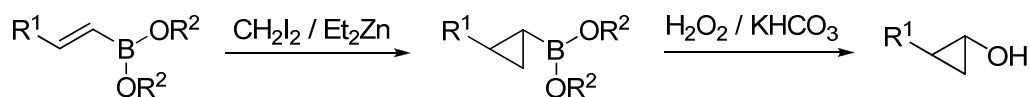
Scheme 4. The Simmons–Smith reaction.

The Simmons–Smith reaction with vinyl alcohol equivalents affords cyclopropanol derivatives. For example, the reaction of silyl enol ether with the reagent gave siloxycyclopropane efficiently.¹³ Desilylation with tetrabutylammonium fluoride afforded the corresponding cyclopropanol in a high yield (Scheme 5).



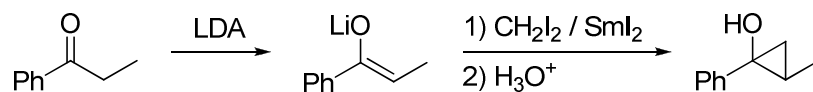
Scheme 5. The Simmons–Smith reaction (Furukawa method) with silyl enol ether.

Also, in the case of alkenylboronic acid ester as a substrate, the Simmons–Smith reaction proceeded to give a cyclopropylboronic acid ester. It can be converted into cyclopropanol by an oxidation with basic hydroperoxide (Scheme 6).¹⁴



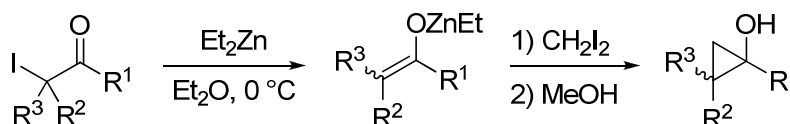
Scheme 6. The Simmons–Smith reaction (Furukawa method) with alkenylboronic acid ester.

The Simmons–Smith reaction of metal enolate also gave cyclopropanol. Imamoto showed the transformation of lithium enolate into cyclopropanol by using diiodomethane/samarium(II) iodide (Scheme 7).¹⁵



Scheme 7. Transformation of lithium enolate into cyclopropanol.

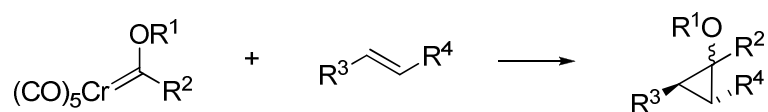
Oshima also reported that treatment of the prepared Reformatsky reagent with diiodomethane afforded the corresponding cyclopropanol (Scheme 8).¹⁶



Scheme 8. Transformation of zinc enolate into cyclopropanol.

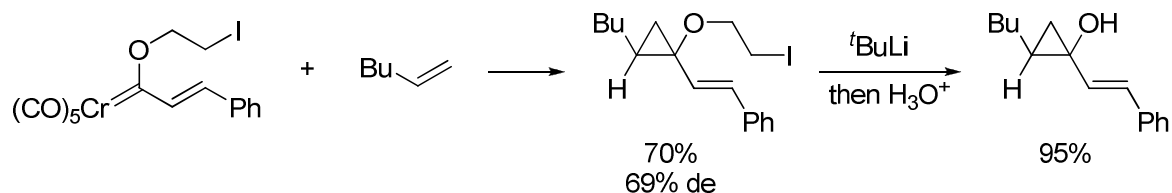
2) The Reaction of Fischer Carbene Complex

Instead of the Simmons–Smith reagent, metal carbene complexes are also applicable for the cyclopropanation of alkenes.^{12,17} For example, the Fischer carbene complex, which has an alkoxy group on the carbene atom, can be used for [2+1] cycloaddition to give cyclopropanol derivatives (Scheme 9).¹⁸



Scheme 9. Reaction of Fischer carbene complex with alkenes.

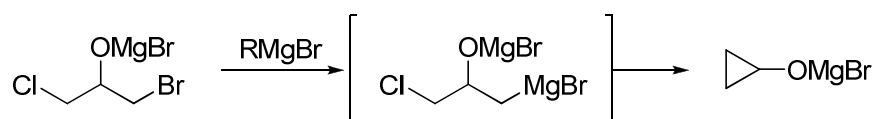
As shown in Scheme 10, treatment of 1-hexene with a Fischer carbene complex carrying an 2-iodoethoxy group afforded the corresponding cyclopropyl ether with moderate diastereoselectivity.¹⁹ The iodoethyl moiety could be removed easily by treatment with butyllithium to give the corresponding cyclopropanol.



Scheme 10. The reaction of Fischer carbene complex with alkene.

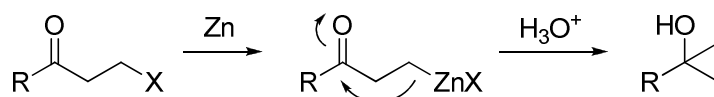
3) Cyclization Reaction

The cyclization reaction is also an efficient method to prepare cyclopropanols; actually, cyclopropanol was first synthesized via intramolecular nucleophilic substitution in 1942 by Cottle and co-workers.²⁰ When magnesium alkoxide of 3-bromo-1-chloro-2-propanol was treated with Grignard reagent, bromine-magnesium exchange proceeded, and the sequential intramolecular $\text{S}_{\text{N}}2$ reaction gave magnesium alkoxide of cyclopropanol (Scheme 11).



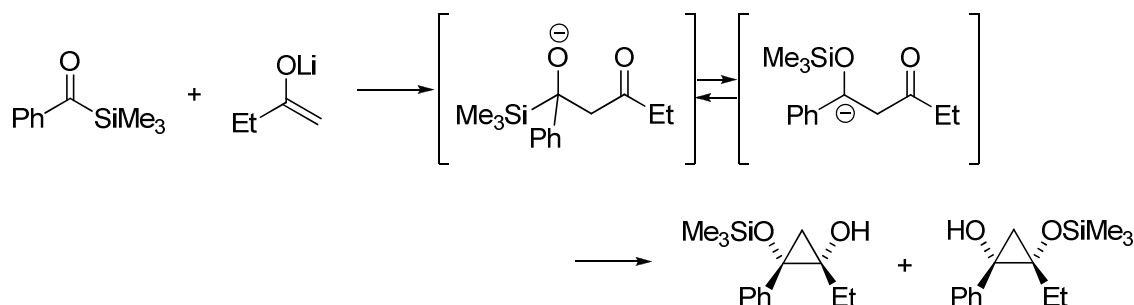
Scheme 11. Preparation of cyclopropanol by intramolecular $\text{S}_{\text{N}}2$ reaction.

A highly efficient intramolecular reaction proceeds when a carbanion equivalent is formed at the β -position of a ketone. For example, when β -haloketone was treated with zinc powder, the reduction proceeded to generate the corresponding zinc homoenolate; as a result, the corresponding cyclopropanol was obtained via intramolecular nucleophilic addition (Scheme 12).²¹



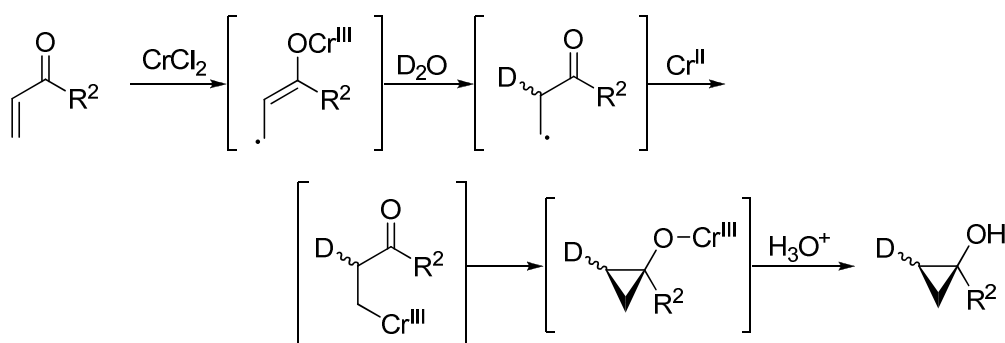
Scheme 12. Preparation of cyclopropanol by intramolecular nucleophilic addition.

Takeda showed the formation of a homoenolate after the nucleophilic reaction of enolate with acylsilane.²² This reaction involved 1,2-Brook rearrangement of the 1,2-adduct to form β -carbanion. The subsequent intramolecular nucleophilic addition afforded the corresponding cyclopropan-1,2-diol derivative (Scheme 13).



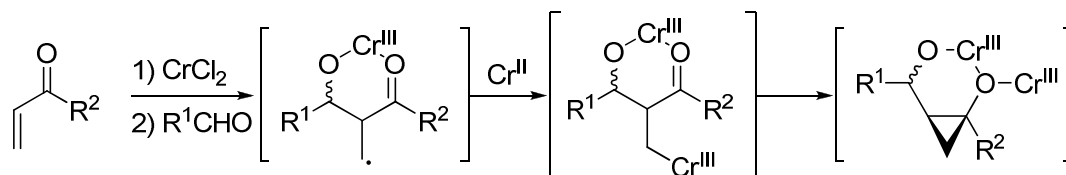
Scheme 13. Reaction of acylsilane and lithium enolate.

Takai showed the following method to generate carbanion at the β -position of the carbonyl group:²³ Treatment of α,β -unsaturated ketone with chromium(II) chloride afforded a ketone carrying C–Cr bond at the β -position via double single electron reduction (Scheme 14).



Scheme 14. Reaction of α,β -unsaturated ketone and D_2O in the presence of $CrCl_2$.

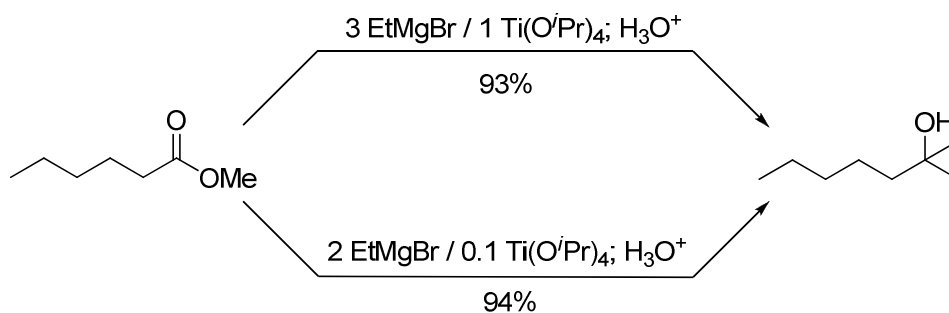
As shown in Scheme 15, 2-(1-hydroxyalkyl)-1-alkylcyclopropanol was also obtained via nucleophilic attack of the formed enolate to an aldehyde.²³



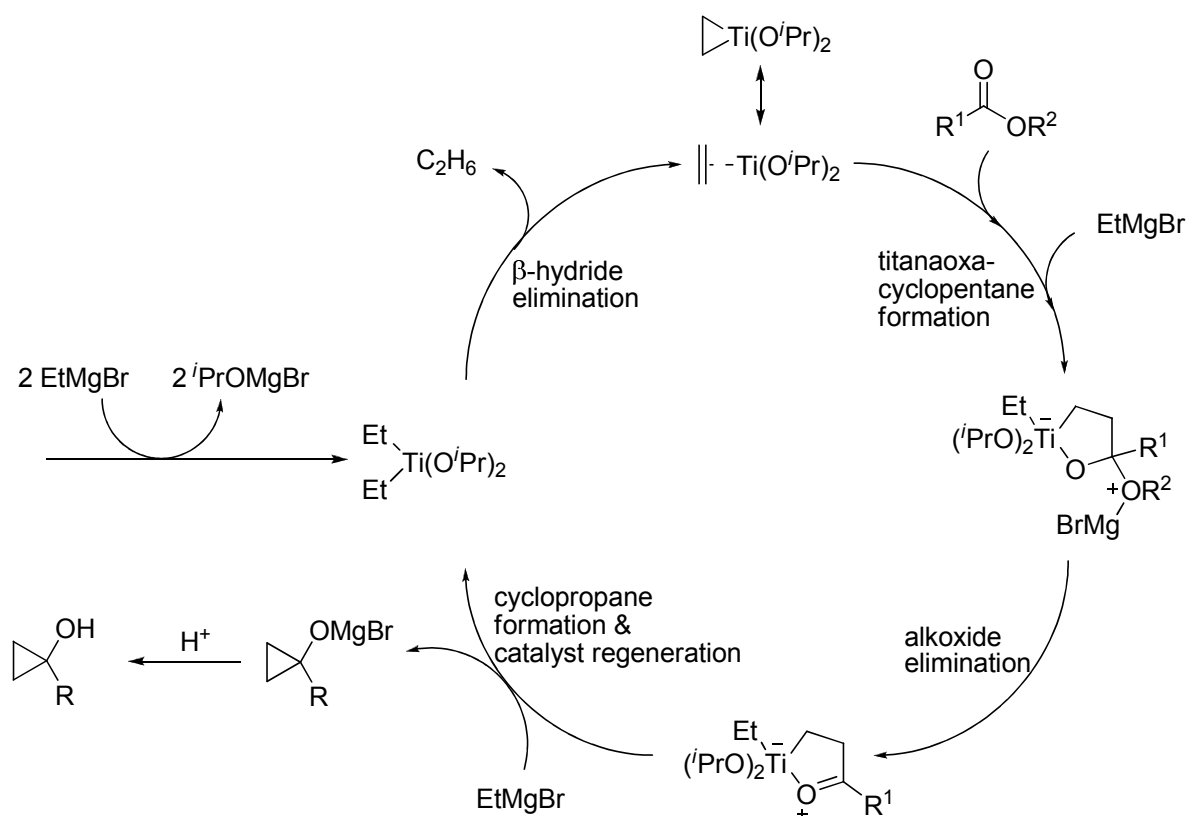
Scheme 15. Reaction of α,β -unsaturated ketone and aldehyde in the presence of CrCl_2 .

4) The Kulinkovich Reaction

In 1989, Kulinkovich reported an efficient method for preparation of cyclopropanols from ethylmagnesium bromide and esters.²⁴ Treatment of an ester with titanacyclopentane, which was prepared from ethylmagnesium bromide and titanium(IV) tetraisopropoxide, afforded 1-alkylcyclopropanol via successive nucleophilic addition of the dianion to the carbonyl group (Scheme 16). The mechanism is shown in Scheme 17.^{24,25}



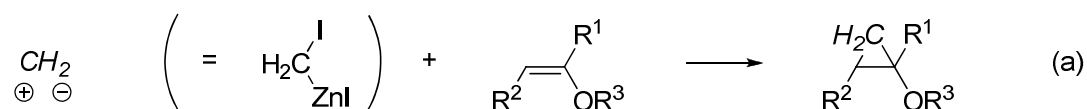
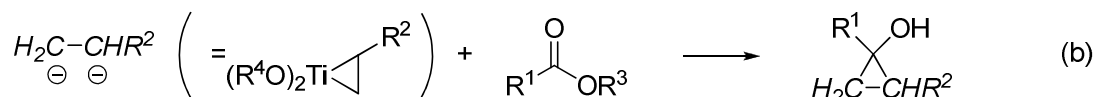
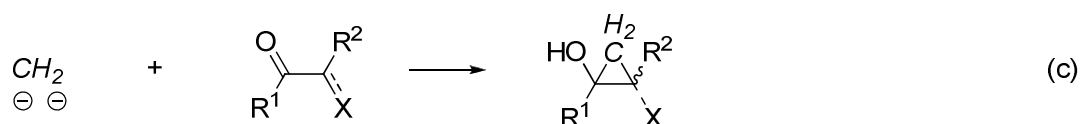
Scheme 16. The Kulinkovich reaction.



Scheme 17. Mechanism of the Kulinkovich reaction.

A New Approach for Preparation of Cyclopropanols

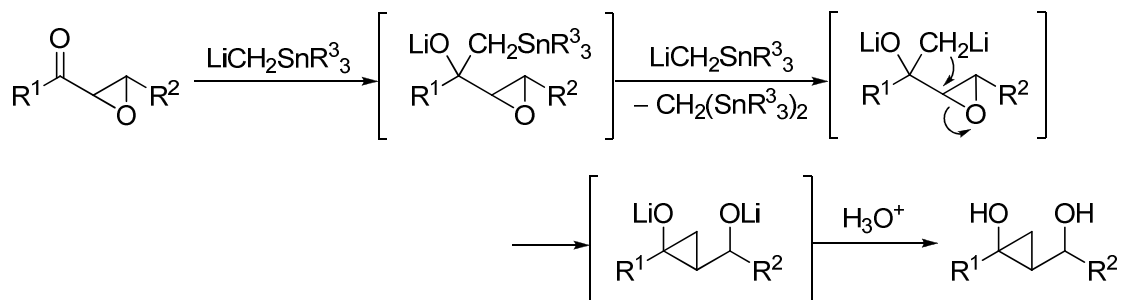
Among the conventional methods mentioned above, the more general methods for construction of cyclopropanols in practical syntheses are the Simmons–Smith reaction and the Kulinkovich reaction. In the Simmons–Smith reaction, one carbon unit of [2+1] cycloaddition is a carbenoid, which has both nucleophilic and electrophilic properties (Scheme 18(a)). Its electrophilic reaction with vinyl alcohol equivalents gives 1,2-dialkylcyclopropanols. Meanwhile, in the Kulinkovich reaction, successive nucleophilic addition of *vic*-dianion equivalent, that is titanacyclopentane, to esters affords 1,2-dialkylcyclopropanols (Scheme 18(b)). Different from these methods, the nucleophilic [2+1] cycloaddition with *gem*-dianion equivalent²⁶ would give a complete new strategy (Scheme 18(c)). In this context, the author focused on the nucleophilic [2+1] cycloaddition with *gem*-dianion equivalent.

the Simmons–Smith reaction**the Kulinkovich reaction****reaction with *gem*-dianion**

Scheme 18. Concept of (a) the Simmons–Smith reaction, (b) the Kulinkovich reaction, and (c) nucleophilic [2+1] cycloaddition with *gem*-dianion.

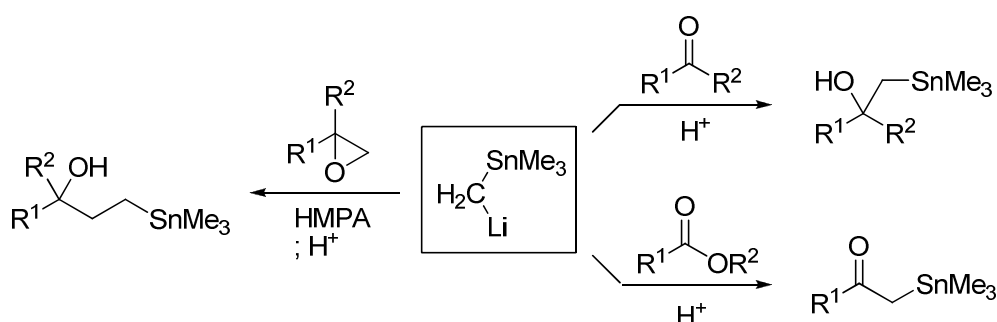
Nucleophilic [2+1] Cycloaddition with *gem*-Dianion Equivalent

In 1991, Sato and Murayama showed an example of nucleophilic [2+1] cycloaddition with *gem*-dianion equivalent to prepare cyclopropanols.²⁷ When α,β -epoxy ketone was treated with trialkylstannylmethyl lithium, sequential nucleophilic attack of the *gem*-dimetal species to the carbonyl group and the epoxy group proceeded to give 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (Scheme 19).



Scheme 19. Reaction of α,β -epoxy ketone and trialkylstannylmethyl lithium.

Further examples and applications in practical syntheses, however, have not been reported since then. One of the reasons may be the high reactivity of the C–Li bond of trialkylstannylmethyl lithium. Since the *gem*-dimetal readily attacks various electrophiles, such as ketones, esters, and epoxide (Scheme 20),²⁸ the chemoselective reaction seems to be difficult. So, its nucleophilic [2+1] cycloaddition would be restricted to simple substrates.

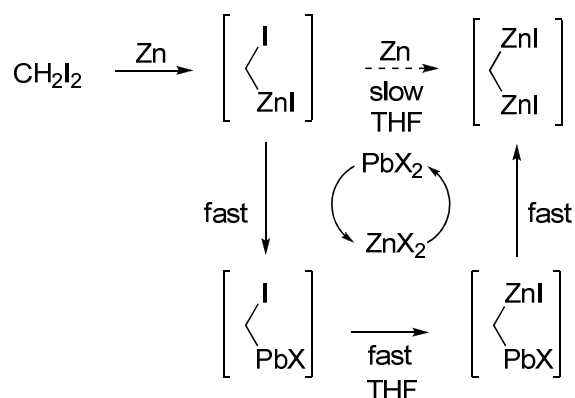


Scheme 20. Reaction of trimethylstannylmethyl lithium and various electrophiles.

If there are some *gem*-dianions which have moderate nucleophilicity to react with α,β -epoxy ketone moiety chemoselectively without affecting other functional groups, the nucleophilic [2+1] cycloaddition with *gem*-dianions would be an alternative method for preparing various types of cyclopropanols carrying additional functional groups. Thus, the author focused on bis(iodozincio)methane²⁹ as a *gem*-dianion equivalent, which consists of two C–Zn bonds.

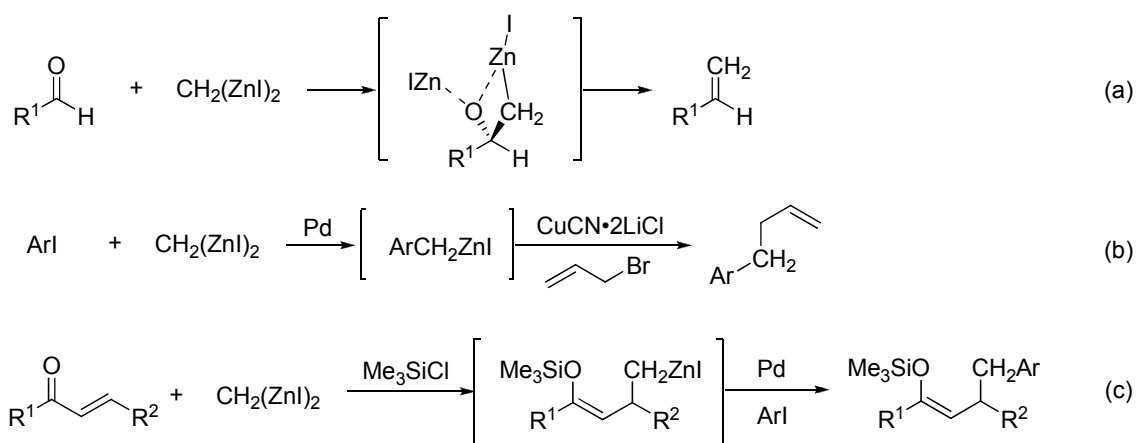
Preparation and Reactivity of Bis(iodozincio)methane

Treatment of diiodomethane with zinc powder in Et₂O affords the Simmons–Smith reagent (IZnCH₂I). When the same procedure is performed in THF in the presence of a catalytic amount of lead, the further reduction of the generated Simmons–Smith reagent proceeds to give bis(iodozincio)methane, as shown in Scheme 21.³⁰



Scheme 21. Preparation of bis(iodozincio)methane.

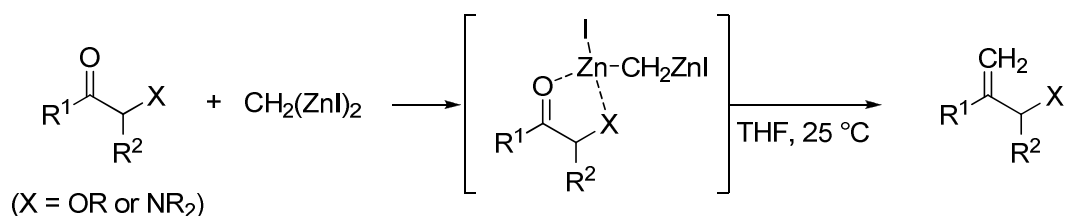
The dizinc reagent has an ability to form two C–C bonds on a carbon. Actually, several reactions with the dizinc, which include the construction of two C–C bonds, have been reported. The representative reaction is methylenation of an aldehyde, as shown in Scheme 22(a).^{29,31} Sequential coupling reactions of the dizinc with two different electrophiles, such as Scheme 22(b) and (c), are also good examples.^{32,33} Initially, these reactions undergo the introduction of iodozinciomethyl group to electrophiles.



Scheme 22. A couple of C–C bonds formation reactions with bis(iodozincio)methane.

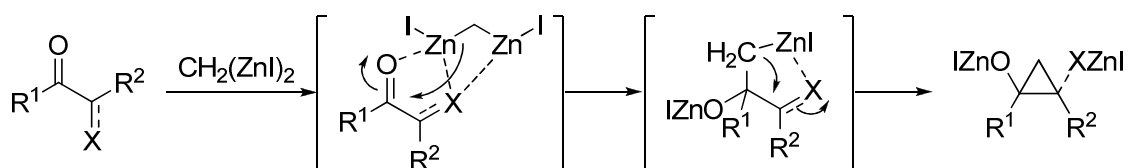
The dizinc reagent should be expected to have high nucleophilicity, because two electropositive zinc atoms substitute on a carbon. However, it does not have enough

nucleophilicity to attack carbonyl groups of ketones and esters. For example, the reaction of a simple ketone, such as acetophenone, with the dizinc results in a complete recovery of the starting material.^{34,35} Meanwhile, when an α -heteroatom-substituted ketone, such as α -alkoxy ketone or α -amino ketone, is treated with the dizinc, a coordination of the zinc atom with the carbonyl group and the heteroatom of the substrate enhances the nucleophilicity of the dizinc to the carbonyl group (Scheme 23).³⁴ In this case, a nucleophilic attack of *gem*-dizinc, which leads to methylenation, proceeds smoothly. Such activation of the organometallic reagent was also observed in the reaction of Grignard reagent and α -alkoxyketones via Cram's chelation.³⁶



Scheme 23. Methylenation of α -alkoxy and -amino ketone with bis(iodozincio)methane.

Considering these facts, the author proposed a nucleophilic cyclopropanation with bis(iodozincio)methane to prepare cyclopropanols, as shown in Scheme 24. The substrate is a ketone having an electrophilic carbon at α -position, which makes a chelation with the dizinc. The coordination would enhance the nucleophilicity of the reagent, and allow the nucleophilic addition of the dizinc to the carbonyl group. As a result of the nucleophilic addition, an iodozinciomethyl group is introduced to the adjacent carbon of the other electrophilic carbon. Sequential nucleophilic attack of the carbanion equivalent to the adjacent carbon would proceed readily to give a cyclopropanol. The author investigated details of the reactions with various types of substrates.

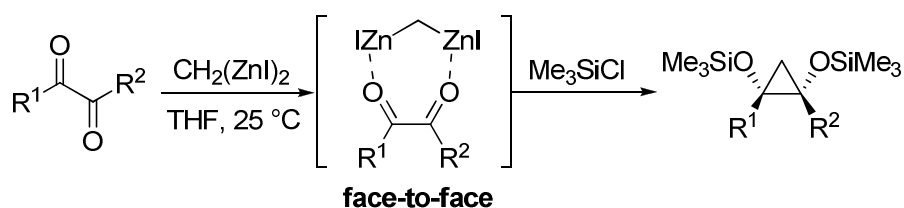


Scheme 24. Concept of nucleophilic cyclopropanation with bis(iodozincio)methane.

Overview of This Thesis

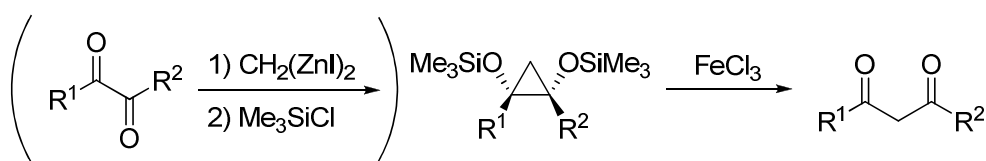
The author investigated a nucleophilic [2+1] cycloaddition of bis(iodozincio)methane and ketones having one other electrophilic site at the α -position, such as 1,2-diketones, α,β -epoxy ketones, α -sulfonyloxy ketones and γ -ethoxycarbonyl- α,β -unsaturated ketones, to establish a new general method of cyclopropanol syntheses. He showed the scopes, limitations, chemo- and stereoselectivities of the reaction. Additionally, he also developed further useful transformations of the obtained cyclopropanols, which allow the access to important building blocks, via cyclopropane ring opening.

In Chapter 2, the author describes diastereoselective nucleophilic cyclopropanation of 1,2-diketones and α -ketoimines with bis(iodozincio)methane.³⁷ When a 1,2-diketone was treated with bis(iodozincio)methane, a sequential nucleophilic attack of the dizinc reagent to vicinal two carbonyl group proceeded to give a *cis*-cyclopropan-1,2-diol, which can be converted into trimethylsilyl ether by quenching with chlorotrimethylsilane (Scheme 25). The reaction showed high diastereoselectivity to give *cis*-isomer via a specific coordination between the substrate and the dizinc.³⁸ The coordination was supposed to be face-to-face.



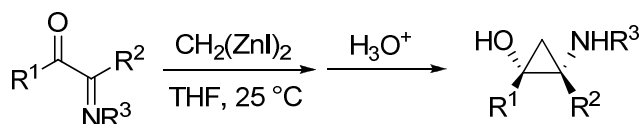
Scheme 25. Nucleophilic cyclopropanation of 1,2-diketone with bis(iodozincio)methane.

Treatment of the obtained *cis*-1,2-bis(trimethylsiloxy)cyclopropane with FeCl_3 afforded 1,3-diketone efficiently via cyclopropane ring opening (Scheme 26). Preparation of *cis*-1,2-bis(trimethylsiloxy)cyclopropane can be achieved from bis(iodozincio)methane, 1,2-diketone and chlorotrimethylsilane, as shown in Scheme 25, so the net transformation can be regarded as methylene insertion between two carbonyl groups in 1,2-diketone (Scheme 26).



Scheme 26. Synthesis of 1,3-diketone via oxidative cyclopropane ring opening reaction of *cis*-1,2-bis(trimethylsiloxy)cyclopropane.

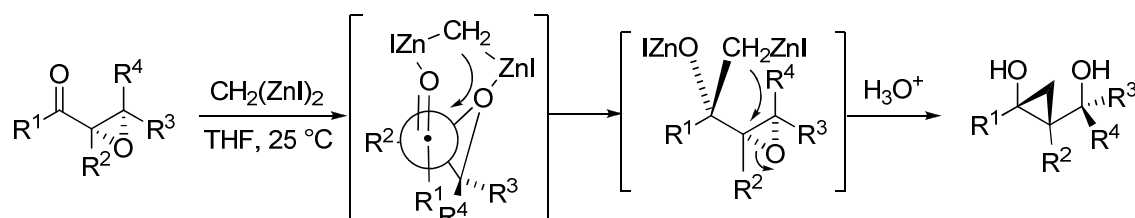
Furthermore, a reaction of a α -ketoimine with the dizinc also showed high diastereoselectivity to give a *cis*-2-aminocyclopropanol (Scheme 27).



Scheme 27. Nucleophilic cyclopropanation of α -ketoimine with bis(iodozincio)methane.

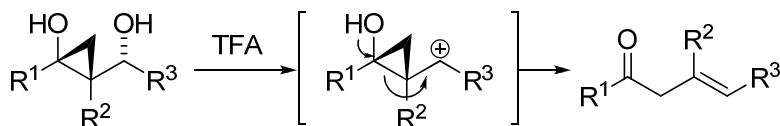
In Chapter 3, the author describes stereoselective and stereospecific nucleophilic cyclopropanation of α,β -epoxy ketone with bis(iodozincio)methane. The specific coordination with two oxygen atoms allows the dizinc to attack the carbonyl group diastereoselectively. When an α,β -epoxy ketone was treated with the dizinc, diastereoselective nucleophilic addition to the carbonyl group proceeded via a specific coordination, as shown in Scheme 28. Then the sequential stereospecific $\text{S}_{\text{N}}2$ reaction of the introduced zinciomethyl group to the epoxy group

also proceeded smoothly to give 2-(1-hydroxyalkyl)-1-alkylcyclopropanol diastereoselectively (Scheme 28).³⁹ In the case of an optically active α,β -epoxy ketone, the reaction afforded the corresponding cyclopropanol without loss of enantiomeric excess.



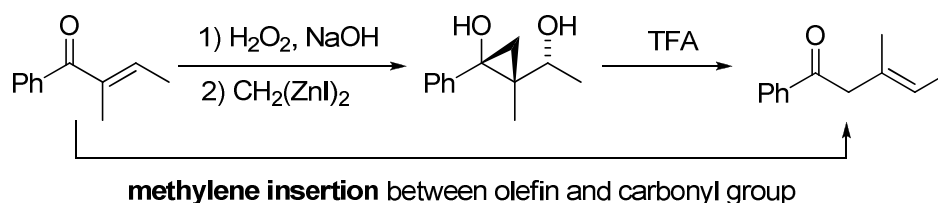
Scheme 28. Nucleophilic cyclopropanation of α,β -epoxy ketone with the dizinc.

When the obtained 2-(1-hydroxyalkyl)-1-alkylcyclopropanol was treated with trifluoroacetic acid, a ring-opening reaction proceeded via cyclopropyl cation intermediate to give the corresponding (*E*)- β,γ -unsaturated ketone diastereoselectively (Scheme 29).⁴⁰



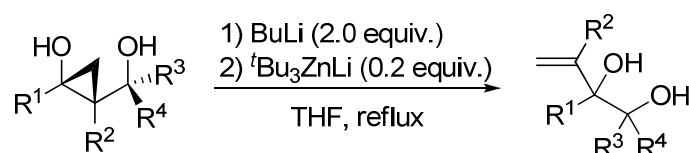
Scheme 29. Ring opening reaction of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol.

The substrate, α,β -epoxy ketone, can be prepared by the reaction of the corresponding α,β -unsaturated ketone with basic hydroperoxide, so the net transformation can be regarded as methylene insertion between a carbonyl group and an alkenyl group of α,β -unsaturated ketone (Scheme 30).



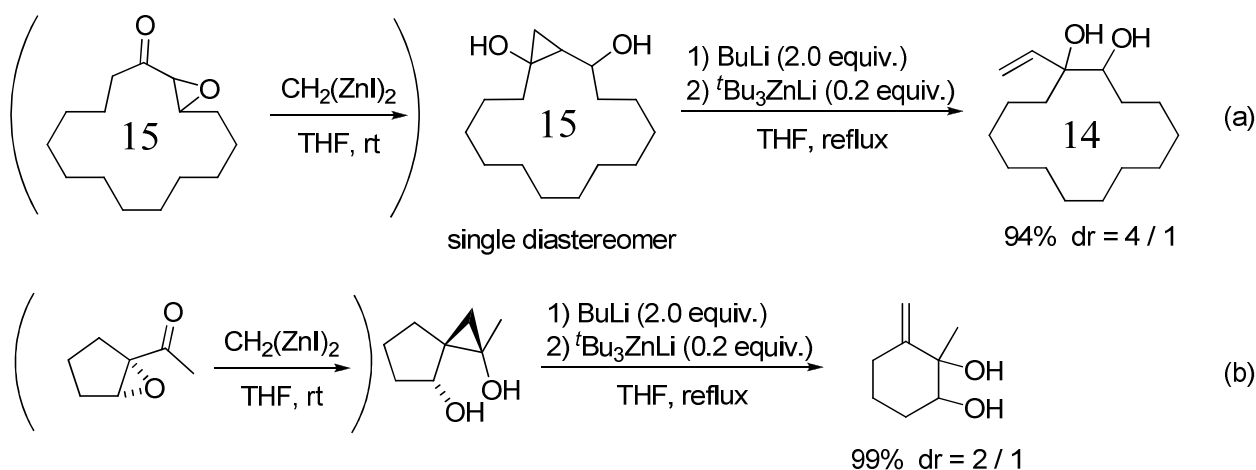
Scheme 30. The entire transformation to β,γ -unsaturated ketone via nucleophilic cyclopropanation.

In Chapter 4, the author describes a zincate-mediated novel rearrangement reaction of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol. When the reaction mixture of α,β -epoxy ketone and bis(iodozincio)methane was performed under reflux condition in THF, 1-alkenyl-1,2-diol was obtained in moderate yield. He investigated this reaction closely, and discovered that treatment of dilithium dialkoxide of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol with a catalytic amount of organozinc ate complex, $^t\text{Bu}_3\text{ZnLi}$, affords 1-alkenyl-1,2-diol in good yield (Scheme 31).⁴¹



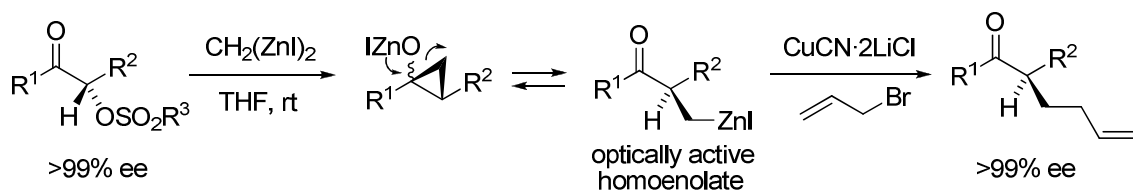
Scheme 31. Zincate-mediated rearrangement of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol.

The rearrangement can be applied for ring-size changing of the cyclic substrate. When bicyclo[13.1.0]pentadecane-1,15-diol was treated with organozinc ate complex, the corresponding 14-membered ring *vic*-diol was obtained (Scheme 32(a)). Meanwhile, treatment of lithium alkoxide of spirocyclic diol with $^t\text{Bu}_3\text{ZnLi}$ gave the corresponding ring-expanded product (Scheme 32(b)).



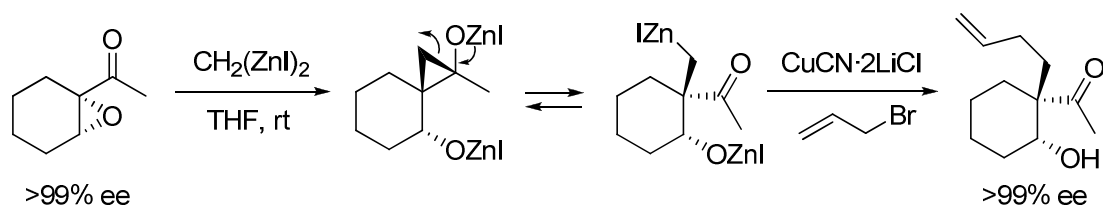
Scheme 32. (a) Ring contract and (b) ring expansion by means of the rearrangement.

In Chapter 5, the author describes a method to construct chiral tertiary and quaternary carbon via nucleophilic cyclopropanation with bis(iodozincio)methane. As mentioned above, it is well known that a cyclopropanol works as a homoenolate by a ring opening.⁴ The author speculated that treatment of optically active α -sulfonyloxy ketone with bis(iodozincio)methane affords the corresponding cyclopropanol via nucleophilic addition of the dizinc to carbonyl group, and sequential stereospecific $\text{S}_{\text{N}}2$ reaction to the original stereogenic carbon having sulfonyloxy group; the obtained cyclopropanol would work as a chiral homoenolate. Actually, treatment of optically active α -sulfonyloxy ketone with the dizinc gave the desired cyclopropanol in good yield with poor diastereoselectivity (Scheme 33).⁴² However, when the zinc alkoxides of cyclopropanols are utilized as zinc homoenolate equivalents, the stereogenic centers at oxygen atom-substituted carbon of zinc alkoxide of cyclopropanol will be converted into carbonyl groups, retaining the chirality of the tertiary carbon at the α -position. Treatment of the obtained zinc homoenolate equivalent with allyl bromide in the presence of copper cyanide gave an optically active α -tertiary ketone that retained a high enantiomeric ratio (Scheme 33).⁴²



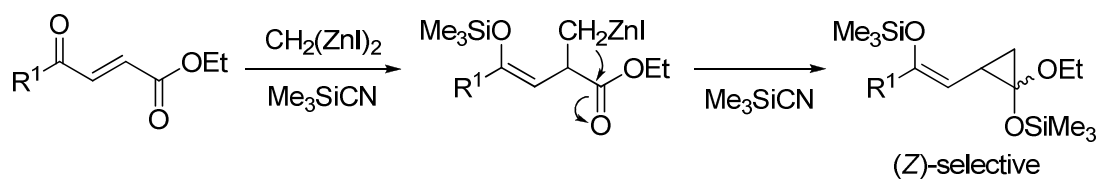
Scheme 33. Formation of optically active homoenolate, and its reaction with allyl bromide.

The cyclopropanols, which are obtained by the reaction of α,β -epoxy ketone and the dizinc,³⁹ can be also recognized as homoenolate. When an optically active α,β -epoxy ketone was applied as a substrate for the procedure shown in Scheme 33, an optically active α -quaternary ketone was obtained without loss of enantiomeric excess (Scheme 34).^{42b}



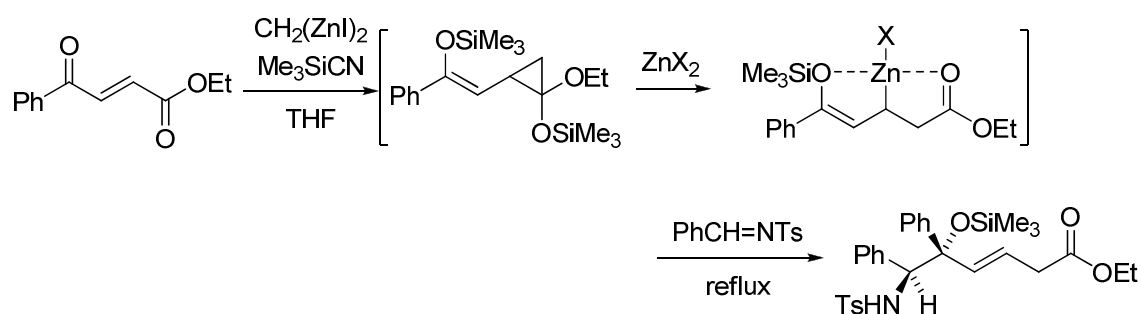
Scheme 34. Stereospecific construction of chiral quaternary carbon by nucleophilic cyclopropanation.

In Chapter 6, the author describes nucleophilic cyclopropanation with bis(iodozincio)methane via 1,4-addition to α,β -unsaturated carbonyl compounds. It is known that the dizinc undergoes 1,4-addition to α,β -unsaturated ketones in the presence of silylation reagent to give (*Z*)-silyl enol ethers.³³ So the author planned a sequential process of 1,4-addition and intramolecular cyclopropane formation using the dizinc and α,β -unsaturated ketone carrying an electrophilic site at γ -position. Treatment of γ -ethoxycarbonyl- α,β -unsaturated ketone with the dizinc in the presence of trimethylsilyl cyanide afforded 1-ethoxy-1-trimethylsiloxy-cyclopropane (Scheme 35).⁴³



Scheme 35. Nucleophilic cyclopropanation of γ -ethoxycarbonyl- α,β -unsaturated ketone with the dizinc by 1,4-addition.

A reaction of the obtained 1-ethoxy-1-siloxycyclopropane with imine gave β -siloxylamine derivative as a single diastereomer (Scheme 36). The author attributes the high diastereoselectivity to the stereoselective formation of a (Z)-3-siloxyallylzinc species via the cyclopropane ring opening with zinc(II) salt, and its diastereofacial selective addition to an imine.⁴³



Scheme 36. Preparation of zinc homoenolate by cyclopropane ring opening; its reaction with imine.

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Abbreviations

Ac	acetyl	mL	milliliter(s)
aq.	aqueous	mmol	millimole(s)
Ar	aryl	mp	melting point
bs	broad singlet (spectral)	Ms	methanesulfonyl
Bu	butyl	<i>n</i>	normal
°C	degrees Celsius	NMR	nuclear magnetic resonance
calcd	calculated	NOE	nuclear Overhauser effect
cat.	catalytic	Nu	nucleophile
Co.	company	<i>o</i>	ortho
δ	chemical shift in parts per million	<i>p</i>	para
d	doublet (spectral)	p. (pp.)	page(s)
<i>d</i>	deuterium	Pen	pentyl
dr	diastereomeric ratio	Ph	phenyl
Ed(s).	editor(s)	ppm	parts per million (spectral)
<i>E</i>	<i>entgegen</i> (means "opposite")	q	quartet (spectral)
ee	enantiomeric excess	quint	quintet (spectral)
<i>El</i>	electrophile	R	alkyl
equiv.	equivalent(s)	rac	racemic
Et	ethyl	ref	reference
<i>et al.</i>	<i>et alii</i> (and others)	rt	room temperature (<i>ca.</i> 25 °C)
g	gram(s)	s	singlet (spectral)
<i>gem</i>	geminal	sat.	saturated
GPC	gel permeation chromatography	<i>t (tert)</i>	tertiary
h	hour(s)	t	triplet (spectral)
HRMS	high-resolution mass spectrum	TFA	trifluoroacetic acid
Hz	hertz (s ⁻¹)	THF	tetrahydrofuran
IR	infrared (spectral)	TLC	thin-layer chromatography
<i>J</i>	coupling constant (spectral)	TMS	trimethylsilyl
m	multiplet (spectral)	Tf	trifluoromethanesulfonyl
M	molar (1 M = 1 mol dm ⁻³)	Ts	<i>p</i> -toluenesulfonyl
Me	methyl	<i>vic</i>	vicinal
mg	milligram(s)	Vol.	volume(s)
MHz	megahertz	wt	weight
min	minute(s)	Z	<i>zusammen</i> (means "together")

Instrumental and Materials

^1H NMR (500 MHz) and ^{13}C NMR (125 MHz) spectra were taken on a Varian UNITY INOVA 500 spectrometer and were obtained in CDCl_3 or C_6D_6 with tetramethylsilane as an internal standard. ^1H NMR (300 MHz), ^{13}C NMR (75 MHz) and ^{19}F NMR (282 MHz) spectra were recorded on a Varian GEMINI 300 spectrometer in CDCl_3 or C_6D_6 with tetramethylsilane as an internal standard. NOE analyses allowed the assignments of the signals of each compounds. IR spectra were determined on a SHIMADZU FTIR-8200PC spectrometer. Mass spectra were determined on a JEOL MStation 700 spectrometer. Melting points were determined on Yanaco micro melting point apparatus. Specific rotations were determined on a HORIBA SEPA-200 polarimeter. X-ray data were taken on a Bruker Smart APEX X-Ray diffractometer equipped with a large area CCD detector.¹ The structures were solved with the program system SHELXS-97 and refined with SHELXL-97 package from Bruker.² In-situ IR spectra were obtained with Mettler Toledo ReactIR 45M equipped with AgX Fiber (9.5 mm). TLC analyses were performed on commercial glass plates bearing a 0.25-mm layer of Merck Silica gel 60F₂₅₄. Silica gel (Wakogel 200 mesh) was used for column chromatography. GPC was performed by LC-908 (Japan Analytical Industry Ltd., two in-line JAIGEL-2H, toluene, 10 mL/min, RI detector). Elemental analyses were carried out at the Elemental Analysis Center of Kyoto University.

Unless otherwise noted, materials obtained from commercial suppliers were used without further purification. THF and Et_2O were purchased from Kanto Chemical Co., stored under argon, and used as they are. Benzene, toluene and hexane were dried over slices of sodium. Dichloromethane was dried with molecular sieves 4A.

¹ G. M. Sheldrick, SHELXS 97 program for the solution of crystal structures. University of Göttingen, Germany, 1997.

² G. M. Sheldrick, SHELXL 97 program for the refinement of crystal structures. University of Göttingen, Germany, 1997.

Chapter 2

Diastereoselective Nucleophilic Cyclopropanation of 1,2-Diketones and α -Ketoimines with Bis(iodozincio)methane

A reaction of 1,2-diketones and α -ketoimines with bis(iodozincio)methane gave cyclopropan-1,2-diol and 2-aminocyclopropanol respectively via nucleophilic [2+1] cycloaddition. The reaction proceeded via a sequential nucleophilic attack of the dizinc reagent to vicinal two carbonyl group. The reaction showed high diastereoselectivity to give *cis*-isomer via a face-to-face coordination between the substrate and bis(iodozincio)methane.

Introduction

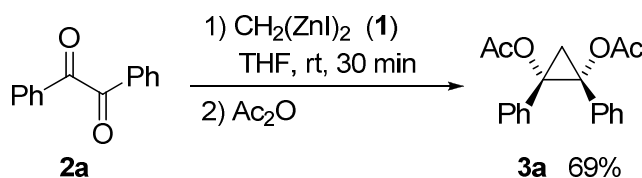
Cyclopropane-skeletons have been found in many natural products, and also used as versatile synthetic intermediates.¹ The most famous cyclopropanation is the Simmons–Smith reaction: Zinc carbenoid reacts with alkenes electrophilically to give a three-membered ring.² The zinc carbenoid can be prepared easily from diiodomethane and zinc–copper couple in diethyl ether. Meanwhile, when diiodomethane was treated with zinc in the presence of catalytic amount of lead in THF, the Simmons–Smith reagent is not obtained. In this condition, the further reduction of the reagent proceeds to give bis(iodozincio)methane (**1**).³ This dizinc reagent, which possesses a couple of zinc atoms on a carbon, works as a dianion equivalent.^{4,5} The reagent has an ability to form a couple of C–C bonds on the same carbon, so treatment of this reagent with the substrate carrying two electrophilic group vicinally, such as 1,2-diketones, may arise [2+1]cycloaddition. This nucleophilic cycloaddition would afford cyclopropan-1,2-diol.

In fact, treatment of benzil (**2a**) with bis(iodozincio)methane (**1**) gave *cis*-1,2-diphenylcyclopropan-1,2-diol in good yield.⁶ It is notable that treatment of a simple ketone with the reagent did not proceed satisfactorily. For example, treatment of acetophenone with the dizinc at room temperature resulted in the complete recovery of the starting material.⁷ The reason why the reaction with benzil proceed smoothly is that a double coordination with the substrate enhances the reactivity of the dizinc reagent. Such activation was also observed in the reaction of Grignard reagent and α -alkoxyketones via Cram's chelation.⁸ The reaction of benzil and the dizinc proceeded with high diastereoselectivity. The author investigated the scope and limitation of this nucleophilic [2+1] cycloaddition.

Results and Discussion

Benzil (**2a**) was treated with bis(iodozincio)methane (**1**) at 25 °C in THF for 0.5 h. Acetic anhydride was added to the reaction mixture to convert the formed diol to the stable diacetate,

and the whole was stirred for another 30 min at 25 °C. After aqueous work-up followed by purification with silica gel column chromatography, 1,2-diphenylcyclopropan-1,2-diol diacetate (**3a**) was obtained in 69% yield diastereoselectively (Scheme 1).



Scheme 1. Nucleophilic [2+1] cyclopropanation of bis(iodozincio)methane (**1**) with benzil (**2a**).

The stereochemistry of the product was confirmed by X-ray crystallographic analysis. The ORTEP figure of **3a** was shown in Figure 1.⁹ The figure shows that the product has *cis*-configuration. This, however, seems to be sterically unfavored.

By ab initio calculation, Matsubara *et al.* had shown the reason why the reaction affords a sterically unfavored *cis*-configuration.¹⁰ The study suggested that the reaction of bis(iodozincio)methane (**1**) with 1,2-diketone **2** proceeds via a double coordination, that is face-to-face coordination, to afford the *cis*-isomer **3** (Scheme 2).

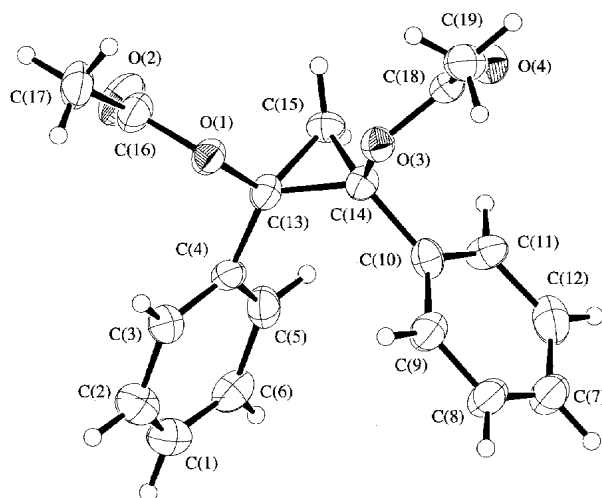
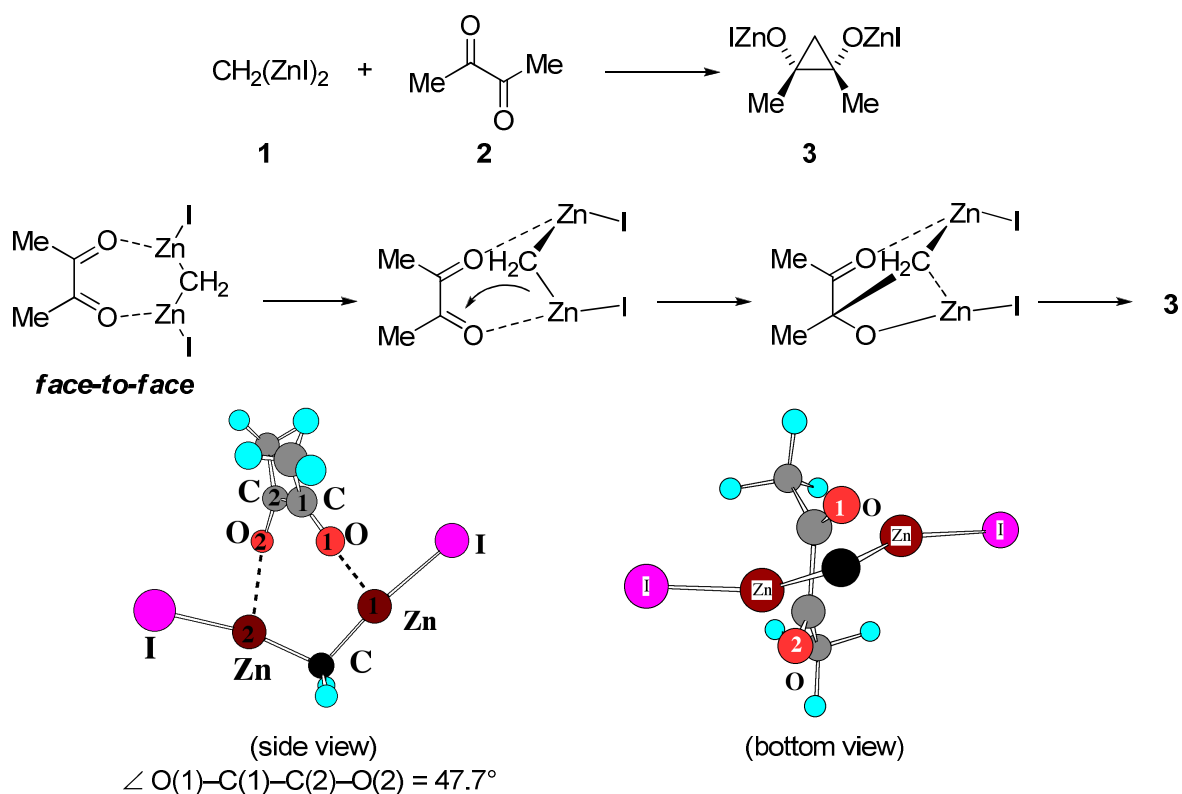
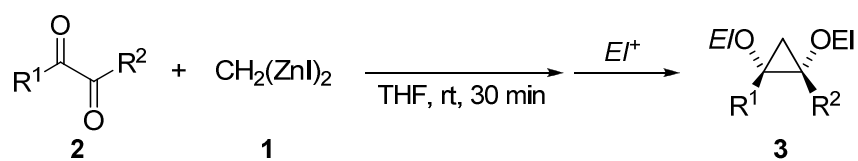


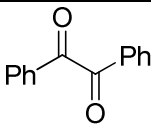
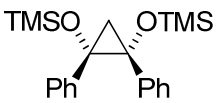
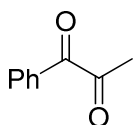
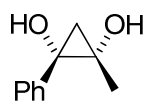
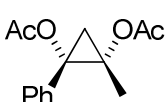
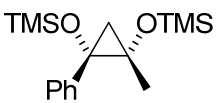
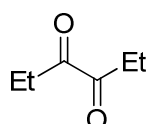
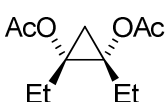
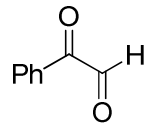
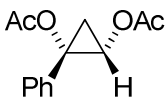
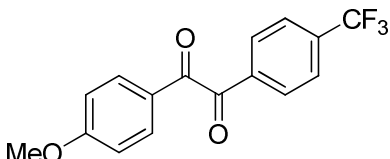
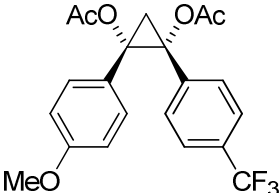
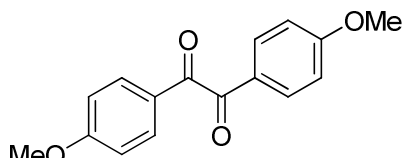
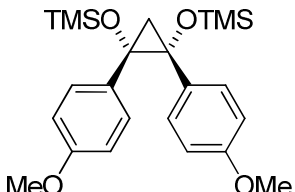
Figure 1. X-Ray analysis of *cis*-1,2-diacetoxy-1,2-diphenylcyclopropane (**3a**).

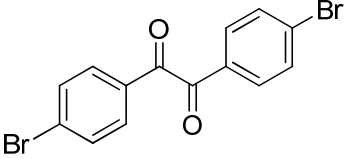
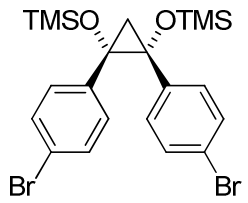
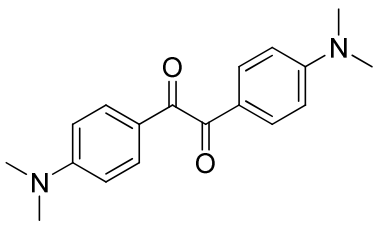
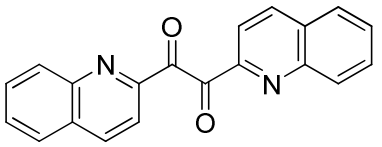
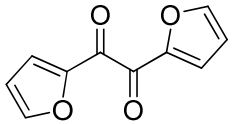
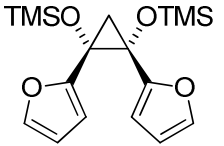
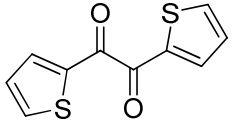
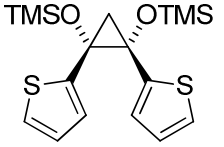
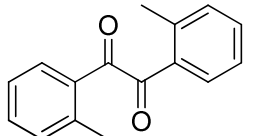
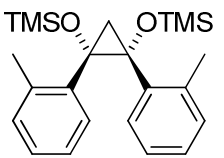
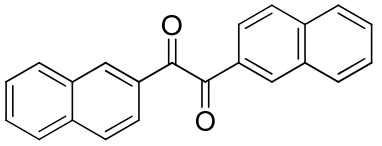
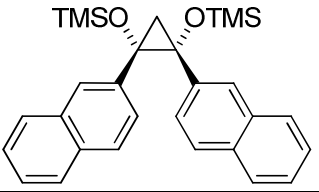


Scheme 2. Coordination pattern of bis(iodozincio)methane (**1**) with 2,3-butanedione (**2**).

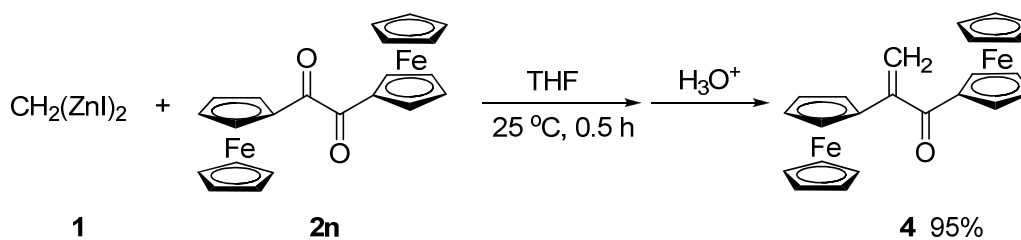
Other examples are summarized in Table 1. In all cases, the reaction proceeded to give *cis*-diol derivatives diastereoselectively. Instead of acetylation, an addition of chlorotrimethylsilane to the reaction mixture gave the silyl ether (entries 1 and 4). Depending on the substrate, the formed cyclopropan-1,2-diol possesses reasonable stability that enables isolation by silica gel column chromatography (entry 2). In the case of **2b** (entries 3, 4 and 5), this substrate tends to form a conjugated enolate. The dizinc reagent may work not only as nucleophile but also as base,¹¹ and the cyclopropanation proceeds prior to the enolization of 1,2-diketones. This fact was also explained by the *ab initio* calculation.¹⁰ The calculation suggested that the dihedral angle formed by two carbonyl groups of 1,2-diketone in face-to-face initial complex is 47.7° (Scheme 2). As the two carbonyl groups are not placed in the same plane, the carbonyl group at C-1 position cannot contribute to facilitate a deprotonation at C-3 position via conjugation in 1-phenylpropan-1,2-dione (**2b**). The reaction of α -ketoaldehyde accompanied methylenation to some extent (entry 6). The diketone which has either electron donating group or electron withdrawing group was also examined (entries 7-9). The reaction of basic nitrogen atom containing substrates, such as 4,4'-bis(*N,N*-dimethylamino)benzyl (**2h**) and 1,2-di(2-quinolinyl)ethanedione (**2i**), did not afford the cyclopropane adducts (entries 10 and 11). The coordination of basic nitrogen atom to dizinc **1** prevents the interaction of **1** with diketone. Meanwhile, the reaction of oxygen or sulfur atom containing substrates, 2,2'-furil (**2j**) and 1,2-di(2-thiophenyl)ethan-1,2-dione (**2k**), afforded the desired cycloadducts without any interruption of oxygen or sulfur atom (entries 12 and 13). 1,2-Di(*o*-tolyl)ethan-1,2-dione (**2l**) and 1,2-di(2-naphthyl)ethan-1,2-dione (**2m**) were also converted into sterically unfavored *cis*-cyclopropan-1,2-diol derivatives in good yields with high diastereoselectivity (entries 14 and 15). While the reaction with 1,2-diferrocenylethan-1,2-dione (**2n**) resulted in methylenation to give α,β -enone (**4**) (Scheme 3). It may be explained that **2n** is difficult to take the face-to-face coordination because of the steric hindrance of two ferrocenyl groups (Scheme 2).

Table 1. [2+1] Reaction of bis(iodozincio)methane (**1**) with 1,2-dicarbonyl compounds.^a

entry	substrate	EI^+	product	yield (%) ^b
1		2a TMSCl		3b 78
2		2b H ₃ O ⁺		3c 80
3		2b Ac ₂ O		3d 98
4		2b TMSCl		3e 97
5		2c Ac ₂ O		3f 59
6		2d Ac ₂ O		3g 58 ^c
7		2e Ac ₂ O		3h 94
8		2f TMSCl		3i 93

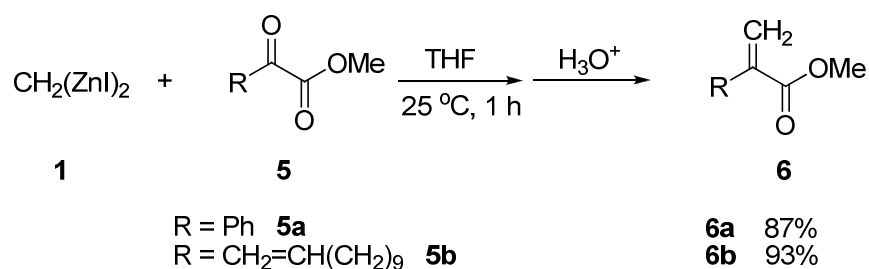
9		2g	TMSCl		3j	80
10		2h	TMSCl	—		0 ^d
11		2i	TMSCl	—		0 ^e
12		2j	TMSCl		3k	96
13		2k	TMSCl		3l	77
14		2l	TMSCl		3m	82
15		2m	TMSCl		3n	89

^a 1,2-Diketone **2** (1.0 mmol), *gem*-dizinc **1** (1.2 mmol) and Et^+ (2.4 mmol) were used. ^b Isolated yields. In each entry, only *cis*-isomer was obtained diastereoselectively. ^c The methylenated product (1-phenyl-2-propenone) was also isolated in 17% yield. ^d Starting material (**2h**) was recovered. ^e Complex mixture was obtained.

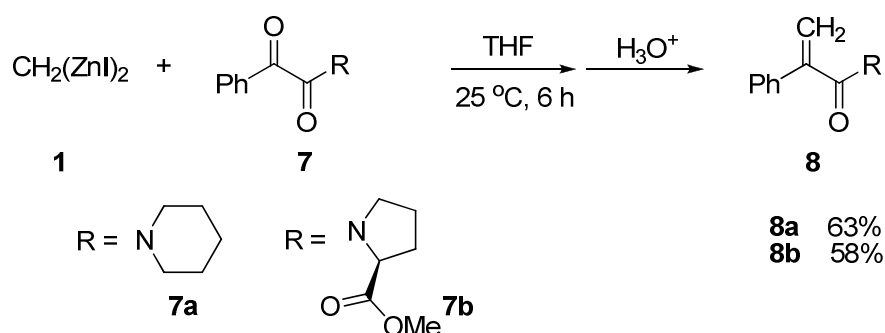


Scheme 3. Reaction of bis(iodozincio)methane (**1**) with 1,2-diferrocenyl-1,2-ethandione (**2n**).

Treatment of α -ketoester **5** and α -ketoamides **7** with the dizinc **1** gave the methylenation products **6** and **8** without forming the cyclopropan-1,2-diols (Scheme 4 and 5). The zinc reagent is not nucleophilic enough to attack ester or amide group.



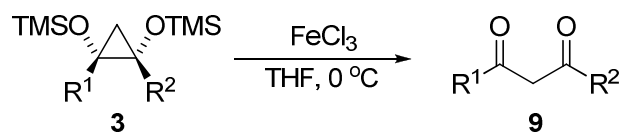
Scheme 4. Reaction of bis(iodozincio)methane (**1**) with α -ketoester (**5**).



Scheme 5. Reaction of bis(iodozincio)methane (**1**) with α -ketoamide (**7**).

The author also tried to perform a ring-opening reaction of the obtained silyl ethers of cyclopropan-1,2-diols with Lewis acid which has oxidizing ability.¹² As shown in Table 2,

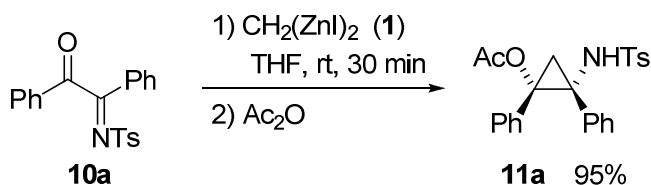
trimethylsilyl ethers of cyclopropanediols were converted into 1,3-diketone in good to excellent yields with iron(III) chloride¹³ in THF. Considering cyclopropanation of 1,2-diketones, the net transformation can be regarded as methylene insertion to 1,2-diketone compounds.¹⁴

Table 2. Ring opening isomerization into 1,3-diketones (**3**)^a

entry	substrate	product	Yield (%) ^b
1	 3b	 9a	96
2	 3e	 9b	83
3	 3i	 9c	85
4	 3j	 9d	89
5	 3k	 9e	97
6	 3l	 9f	99
7	 3n	 9g	72

^a 1,2-Bis(trimethylsiloxy)cyclopropane **3** (0.5 mmol) and FeCl₃ (0.75 mmol) were used. ^b Isolated yields.

Instead of 1,2-diketone, monotosylimide of benzil **10a**, which was prepared following the reported procedure,¹⁵ was treated with dizinc **1**. At the end of the reaction, addition of acetic anhydride to the reaction mixture gave *cis*-2-aminocyclopropanol acetate **11a** diastereoselectively in 95% yield (Scheme 6).



Scheme 6. Reaction of bis(iodozincio)methane (**1**) with α -ketoimine (**10a**).

The stereochemistry of **11a** was confirmed by X-ray analysis (Figure 2).¹⁶ The product was only *cis*-isomer. This result indicates that the reaction with α -ketoimine also proceeds via the face-to-face coordination.

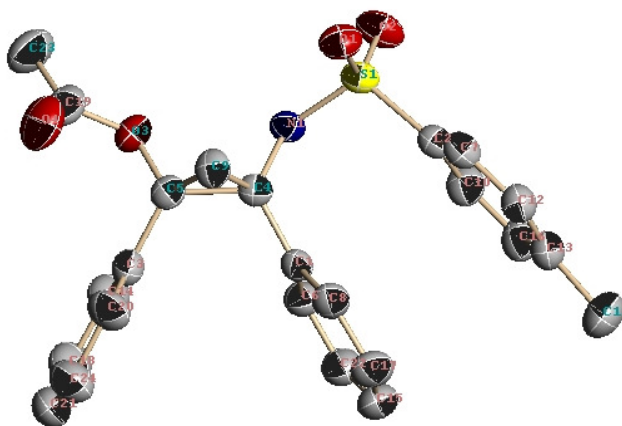
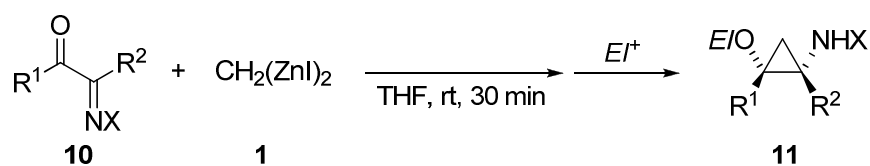
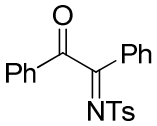
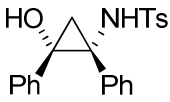
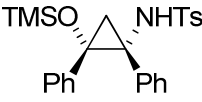
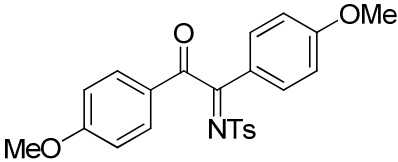
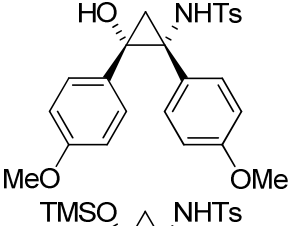
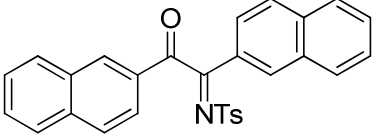
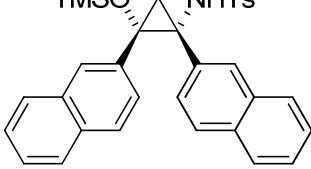
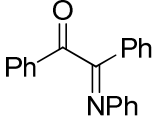
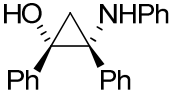
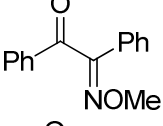
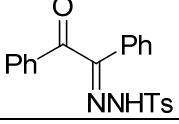


Figure 2 X-Ray analysis of *cis*-1,2-Diacetoxy-1,2-diphenylcyclopropane (**11a**).

Other examples are summarized in Table 3. An acidic aqueous work-up and quenching with chlorotrimethylsilane gave the corresponding products (entries 1 and 2). Electron-donating group, methoxy, on benzene ring did not disturb the cyclopropanation reaction (entry 3).

Tosylimine of 1,2-di(2-naphthyl)ethan-1,2-dione **10c** was also converted into *cis*-2-aminocyclopropanol derivative **11e** in 92% yield with high diastereoselectivity (entry 4). An attempt to isolate the corresponding 2-aminocyclopropanol without a protection with trimethylsilyl group was failed. The ring opening product, β -hydroxyimide, was isolated quantitatively. Instead of tosylimine, phenylimine was examined for the cyclopropanation reaction. Treatment of **10d** with dizinc **1** followed by aqueous work-up afforded *cis*-2-aminocyclopropanol **11f** quantitatively (entry 5). In the case of *O*-methyl oxime **10e** or tosylhydrazone **10f**, the reaction resulted in the complete recovery of the starting materials (entries 6 and 7).

Table 3. Nucleophilic [2+1]cycloaddition of the dizinc (**1**) with 1,2-ketoimines (**10**)^a

entry	substrate	Et^+	product	yield (%) ^b
1		10a H_3O^+		11b 97
2		10a TMSCl		11c >99
3		10b H_3O^+		11d >99
4		10c TMSCl		11e 92
5		10d H_3O^+		11f >99
6		10e H_3O^+	—	0 ^c
7		10f H_3O^+	—	0 ^c

^a α -Ketoimine **10** (1.0 mmol), *gem*-dizinc **1** (2.0 mmol) and Et^+ (2.4 mmol) were used. ^b Isolated yields. In each entry, only *cis*-isomer was found diastereoselectively. ^c Starting material was recovered.

Conclusion

The author showed the scope of the nucleophilic [2+1] cycloaddition of bis(iodozincio)methane and 1,2-diketones or α -ketoimines. Various substrates, which can coordinate with dizinc **1** as the face-to-face manner, were converted into *cis*-cyclopropan-1,2-diol derivatives diastereoselectively. These products have potential to apply for effective ligands of organometallic chemistry, pharmaceutical applications and functionalized materials.

Experimental Section

Unless otherwise noted, commercially available reagents were used without purification. Zinc powder was used after washing with 10% HCl according to the reported procedure.¹⁷ The compounds **2a**, **2b**, **2c**, **2d**, **2f**, **2g**, **2h**, **2j**, **2k** and **5a** are commercially available. 1,2-Diketones **2**¹⁸ and methyl 2-oxotridec-12-enoate (**5b**)¹⁹ were prepared according to the literature.

Preparation of bis(iodozincio)methane (1): A mixture of Zn (25 mmol), diiodomethane (1.0 mmol), and PbCl₂ (0.01 mmol) in THF (2.0 mL) was sonicated for 1 h in an ultrasonic cleaner bath under Ar. To the mixture, diiodomethane (10 mmol) in THF (20 mL) was added dropwise over 15 min at 0 °C with vigorous stirring. The mixture was stirred for 2 h at 0 °C. After the stirring was stopped, the reaction vessel was stood undisturbed for several hours. Excess zinc was separated by sedimentation. ¹H NMR spectra of the obtained supernatant showed a broad singlet at -1.2 ppm at 0 °C, which corresponded to the methylene proton of **1**. The supernatant was used for the further reaction as a solution of **1** in THF (0.5–0.6 M). Bis(Iodozincio)methane in THF can be kept unchanged at least for a month in the sealed reaction vessel.

General procedure for the preparation of cyclopropan-1,2-diol (3): To a solution of 1,2-diketone (**2**, 1.0 mmol) in THF (3 mL), bis(iodozincio)methane (**1**, 1.2 mmol) was added

dropwise at 25 °C. The mixture was stirred for 30 min. Quenching reagent (2.4 mmol, water, acetic anhydride, and chlorotrimethylsilane) was added dropwise and the resulting mixture was stirred for additional 30 min. The mixture was poured into sat. NH_4Cl and extracted with Et_2O . The combined organic phases were washed with brine and dried over Na_2SO_4 . Purification on a neutral silica gel column chromatography gave the corresponding cyclopropan-1,2-diol derivative **3**.

Preparation of α -ketoamide (7): The mixture of methyl benzoylformate (3.0 mmol) and amine (3.0 mmol) was stirred at 25 °C for 12 h. The product was purified by silica gel column chromatography to give the corresponding α -ketoamide **7**.

General Procedure for the preparation of 1,3-diketone (9): To a solution of *cis*-1,2-bis(trimethylsiloxy)-1,2-dialkylcyclopropane (**3**, 0.5 mmol) in THF (1 mL), FeCl_3 (0.75 mmol) was added at 0 °C. The mixture was stirred for 30 min. The mixture was poured into 1N HCl and extracted with EtOAc . The combined organic phases were washed with brine and dried over Na_2SO_4 . Purification on a neutral silica gel column chromatography gave the corresponding 1,3-diketone **9**.

General procedure for preparation of α -ketoimine (10): A solution of 1,2-diketone (10 mmol), amine (10 mmol), $\text{BF}_3 \cdot \text{OEt}_2$ (1.0 mmol) and benzene (30 mL) was heated to reflux for 12 h. Then the solvent was removed under the reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding α -ketoimine **10**.

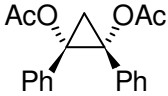
General procedure for the preparation of 2-aminocyclopropanol (11): To a solution of α -ketoimine (**10**, 1.0 mmol) in THF (4 mL), bis(iodozincio)methane (**1**, 2.0 mmol) was added dropwise at 25 °C. The mixture was stirred for 30 min. Quenching reagent (2.4 mmol, water, acetic anhydride, and chlorotrimethylsilane) was added dropwise and the resulting mixture was

stirred for additional 30 min. The mixture was poured into sat. NH_4Cl aq, then sat. NaHCO_3 aq was added to neutralize and extracted with Et_2O . The combined organic phases were washed with brine and dried over Na_2SO_4 . Purification on a neutral silica gel column chromatography gave the corresponding 2-aminocyclopropanol derivative **11**.

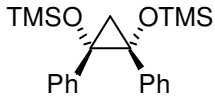
Characterization Data

The Spectral data of the substrates **2e**,²⁰ **2i**,²¹ **2l**,²² **2m**,²³ **2n**,¹⁸ **7a**,²⁴ **7b**²⁵ and **10d**²⁶ were found in the literature.

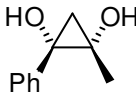
cis-1,2-Diacetoxy-1,2-diphenylcyclopropane (**3a**)

 ^1H NMR (300 MHz, CDCl_3) δ 7.28–7.20 (m, 4H), 7.18–7.10 (m, 6H), 2.51 (d, J = 9.0 Hz, 1H), 2.11 (s, 6H), 1.83 (d, J = 9.0 Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.1, 135.3, 128.8, 127.8, 64.9, 23.8, 21.1; IR (nujol) 2953, 1748, 1454, 1368, 1206, 1125, 1063, 1026, 934, 700 cm^{-1} ; mp 114.5–115.8 °C. Anal. Calcd for $\text{C}_{19}\text{H}_{18}\text{O}_4$: C, 73.53; H, 5.85%. Found: C, 73.25; H, 5.95%.

cis-1,2-Bis(trimethylsiloxy)-1,2-diphenylcyclopropane (**3b**)

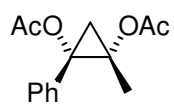
 ^1H NMR (300 MHz, CDCl_3) δ 7.17–6.90 (m, 10H), 2.18 (d, J = 7.5 Hz, 1H), 1.48 (d, J = 7.5 Hz, 1H), 0.08 (s, 18H); ^{13}C NMR (75 MHz, CDCl_3) δ 140.0, 127.9, 127.5, 126.5, 64.8, 23.1, 0.90; IR (neat) 2957, 1449, 1250, 1159, 1072, 1026, 966, 926, 843, 754, 700 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{30}\text{O}_2\text{Si}_2$: C, 68.05; H, 8.16%. Found: C, 67.80; H, 7.93%.

cis-1,2-Dihydroxy-1-methyl-2-phenylcyclopropane (**3c**)

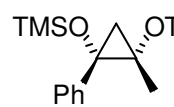
 ^1H NMR (500 MHz, CDCl_3) δ 7.60–7.20 (m, 5H), 3.85 (bs, 2H), 1.27 (d, J = 7.5 Hz, 1H), 1.13 (s, 3H), 0.98 (d, J = 7.5 Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 140.1, 128.4, 128.3, 127.3, 62.0, 58.8, 24.5, 20.5; IR (neat) 3352, 1604, 1447, 1221, 1132, 1076, 1057,

1024, 966, 910, 772, 700 cm^{-1} . HRMS (m/z) Found: 164.0834. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$: 164.0837.

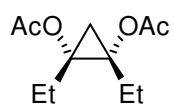
***cis*-1,2-Diacetoxy-1-methyl-2-phenylcyclopropane (3d)**

 ^1H NMR (300 MHz, CDCl_3) δ 7.65–7.56 (m, 2H), 7.38–7.20 (m, 3H), 2.09 (s, 3H), 1.92 (s, 3H), 1.68 (d, $J = 9.0$ Hz, 1H), 1.39 (d, $J = 9.0$ Hz, 1H), 1.21 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.6, 170.2, 135.6, 129.6, 128.3, 128.2, 125.9, 63.5, 60.5, 22.8, 21.0, 20.7, 18.3; IR (neat) 2936, 1748, 1449, 1370, 1229, 1126, 1018, 949, 889, 852, 762, 700 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_4$: C, 67.73; H, 6.50%. Found: C, 67.84; H, 6.59%.

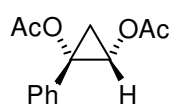
***cis*-1,2-Bis(trimethylsiloxy)-1-methyl-2-phenylcyclopropane (3e)**

 ^1H NMR (300 MHz, CDCl_3) δ 7.41–7.15 (m, 5H), 1.34 (d, $J = 6.9$ Hz, 1H), 1.06 (d, $J = 6.9$ Hz, 1H), 1.05 (s, 3H), 0.23 (s, 9H), 0.03 (s, 9H); ^{13}C NMR (75 MHz, CDCl_3) δ 141.1, 128.0, 127.9, 126.9, 63.7, 59.7, 24.1, 22.2, 1.24, 0.82; IR (neat) 2957, 1248, 1159, 1063, 1032, 950, 841, 752, 700 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}_2\text{Si}_2$: C, 62.28; H, 9.15%. Found: C, 61.98; H, 9.27%.

***cis*-1,2-Diacetoxy-1,2-diethylcyclopropane (3f)**

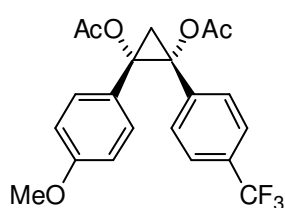
 ^1H NMR (300 MHz, CDCl_3) δ 1.98 (s, 6H), 1.84 (ddq, $J = 15.0, 7.5, 0.9$ Hz, 2H), 1.74 (dq, $J = 15.0, 7.5$ Hz, 2H), 1.07 (dt, $J = 8.4, 0.9$ Hz, 1H), 1.00 (t, $J = 7.5$ Hz, 6H), 0.87 (d, $J = 8.4$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 170.4, 64.1, 24.2, 23.1, 20.9, 9.4; IR (neat) 2976, 1748, 1454, 1371, 1240, 1215 cm^{-1} . HRMS (m/z) Found: 215.1289. Calcd for $\text{C}_{11}\text{H}_{19}\text{O}_4$ $[\text{MH}]^+$: 215.1283.

***cis*-1,2-Diacetoxy-1-phenylcyclopropane (3g)**

 ^1H NMR (300 MHz, CDCl_3) δ 7.51–7.40 (m, 2H), 7.41–7.28 (m, 3H), 4.26 (dd, $J = 8.4, 4.8$ Hz, 1H), 2.13 (s, 3H), 2.04 (s, 3H), 1.80 (dd, $J = 8.4, 8.4$ Hz, 1H), 1.49

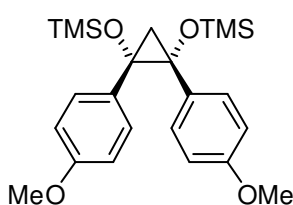
(dd, $J = 8.4, 4.8$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.2, 170.2, 137.5, 128.4, 128.1, 127.7, 59.9, 55.0, 20.8, 20.4, 18.8. HRMS (m/z) Found: 235.0963. Calcd for $\text{C}_{13}\text{H}_{15}\text{O}_4$ $[\text{MH}]^+$: 235.0970.

***cis*-1,2-Diacetoxy-1-(4-anisyl)-2-(4-trifluoromethylphenyl)cyclopropane (3h)**



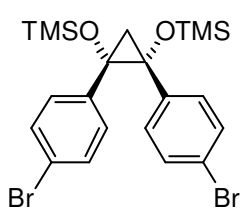
^1H NMR (500 MHz, CDCl_3) δ 7.40 (d, $J = 8.0$ Hz, 2H), 7.26 (d, $J = 8.0$ Hz, 2H), 7.25–7.22 (m, 2H), 6.70–6.67 (m, 2H), 3.72 (s, 3H), 2.43 (d, $J = 9.0$ Hz, 1H), 2.14 (s, 3H), 2.07 (s, 3H), 1.85 (d, $J = 9.0$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 170.2, 170.0, 159.4, 140.0, 131.3, 129.5 (q, $J = 32.5$ Hz), 128.0, 126.4, 124.8 (q, $J = 3.9$ Hz), 123.9 (q, $J = 270.6$ Hz), 113.4, 65.2, 64.0, 55.1, 24.3, 21.13, 21.07; IR (neat) 2938, 1747, 1733, 1616, 1583, 1520, 1368, 1121, 1073, 1016, 938, 914, 836, 735 cm^{-1} . HRMS (m/z) Found: 408.1193. Calcd for $\text{C}_{21}\text{H}_{19}\text{O}_5\text{F}_3$ $[\text{M}]^+$: 408.1185.

***cis*-1,2-Bis(trimethylsiloxy)-1,2-di(4-anisyl)cyclopropane (3i)**



^1H NMR (500 MHz, CDCl_3) δ 7.04–7.01 (m, 4H), 6.62–6.59 (m, 4H), 3.69 (s, 6H), 2.02 (d, $J = 7.5$ Hz, 1H), 1.37 (d, $J = 7.5$ Hz, 1H), 0.05 (s, 18H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.0, 132.4, 129.1, 112.8, 64.4, 55.0, 24.0, 1.08; IR (neat) 2925, 2360, 1611, 1514, 1458, 1297, 1250, 1177, 1155, 1071, 1037, 968, 921, 842 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}_2$: C, 64.14; H, 7.96%. Found: C, 64.27; H, 7.97%. HRMS (m/z) Found: 430.1993. Calcd for $\text{C}_{23}\text{H}_{34}\text{O}_4\text{Si}_2$ $[\text{M}]^+$: 430.1996.

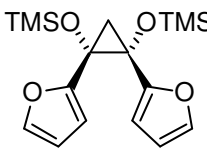
***cis*-1,2-Bis(trimethylsiloxy)-1,2-di(4-bromophenyl)cyclopropane (3j)**



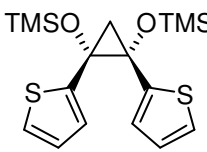
^1H NMR (500 MHz, CDCl_3) δ 7.22 (d, $J = 8.5$ Hz, 4H), 6.96 (d, $J = 8.5$ Hz, 4H), 2.08 (d, $J = 7.5$ Hz, 1H), 1.47 (d, $J = 7.5$ Hz, 1H), 0.06 (s, 18H); ^{13}C NMR (125 MHz, CDCl_3) δ 138.9, 130.9, 129.4, 120.8, 64.3, 23.8, 1.07; IR (neat) 2925, 2360, 1458, 1377, 1249, 1162, 1076, 1010, 924, 845 cm^{-1} . Anal.

Calcd for $C_{21}H_{28}O_2Br_2Si_2$: C, 47.73; H, 5.34%. Found: C, 47.64; H, 5.24%; HRMS (m/z) Found: 525.9988. Calcd for $C_{21}H_{28}O_2Br_2Si_2$ $[M]^+$: 525.9995.

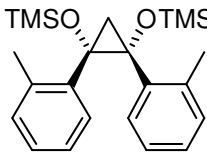
***cis*-1,2-di(2-furyl)-1,2-bis(trimethylsilyloxy)cyclopropane (3k)**

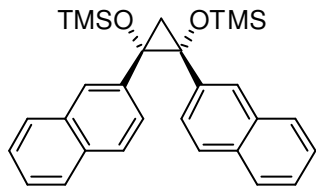
 1H NMR (500 MHz, $CDCl_3$) δ 7.22 (dd, J = 1.5, 1.0 Hz, 2H), 6.16 (dd, J = 3.5, 1.5 Hz, 2H), 5.92 (dd, J = 3.5, 1.0 Hz, 2H), 1.88 (d, J = 6.5 Hz, 1H), 1.41 (d, J = 6.5 Hz, 1H), 0.10 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 153.4, 141.4, 110.1, 107.6, 58.7, 25.1, 0.54; IR (neat) 2959, 1504, 1416, 1252, 1220, 1159, 1071, 1011, 966, 843 cm^{-1} . Anal. Calcd for $C_{17}H_{26}O_4Si_2$: C, 58.25; H, 7.48%. Found: C, 58.04; H, 7.41%; HRMS (m/z) Found: 350.1369. Calcd for $C_{17}H_{26}O_4Si_2$ $[M]^+$: 350.1370.

***cis*-1,2-di(thiophen-2-yl)-1,2-bis(trimethylsilyloxy)cyclopropane (3l)**

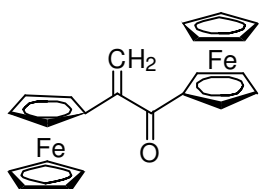
 1H NMR (500 MHz, $CDCl_3$) δ 7.07 (dd, J = 5.0, 1.0 Hz, 2H), 6.73 (dd, J = 5.0, 3.5 Hz, 2H), 6.59 (dd, J = 3.5, 1.0 Hz, 2H), 2.01 (d, J = 7.5 Hz, 1H), 1.66 (d, J = 7.5 Hz, 1H), 0.13 (s, 18H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 145.2, 125.8, 125.2, 125.0, 62.0, 28.9, 0.93; IR (neat) 2957, 1531, 1415, 1250, 1211, 1146, 1051, 1005, 961, 907, 843 cm^{-1} . HRMS (m/z) Found: 382.0915. Calcd for $C_{17}H_{26}O_2S_2Si_2$ $[M]^+$: 382.0913.

***cis*-1,2-Bis(trimethylsilyloxy)-1,2-di(2-tolyl)cyclopropane (3m)**

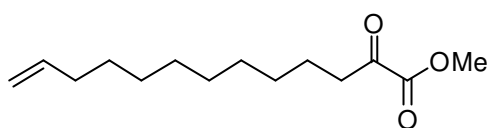
 1H NMR (300 MHz, $CDCl_3$) δ 7.05–6.95 (m, 4H), 6.82–6.77 (m, 4H), 2.57 (s, 6H), 2.01 (d, J = 7.2 Hz, 1H), 1.41 (d, J = 7.2 Hz, 1H), -0.01 (s, 18H); ^{13}C NMR (75 Hz, $CDCl_3$) δ 138.9, 138.2, 130.7, 127.7, 126.9, 124.5, 65.1, 25.8, 21.3, 1.38; IR (nujor) 2854, 1250, 1233, 843, 728, 668 cm^{-1} . Anal. Calcd for $C_{23}H_{34}O_2Si_2$: C, 69.29; H, 8.60%. Found: C, 69.02; H, 8.44%. HRMS (m/z) Found: 398.2094. Calcd for $C_{23}H_{34}O_2Si_2$ $[M]^+$: 398.2097.

cis-1,2-Bis(trimethylsiloxy)-1,2-di(2-naphthyl)cyclopropane (3n)

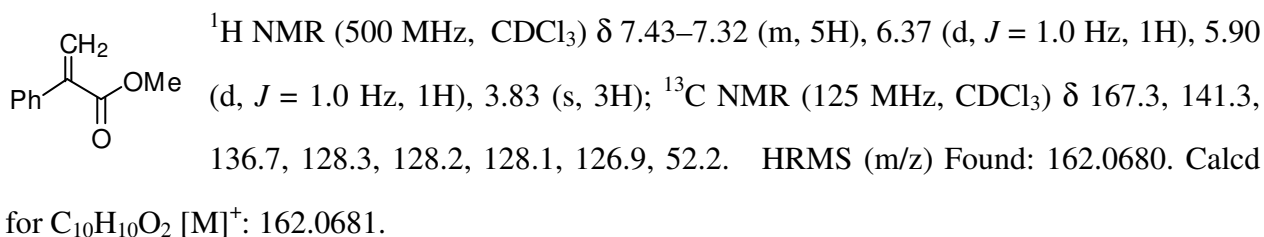
^1H NMR (500 MHz, CDCl_3) δ 7.63–7.59 (m, 6H), 7.47 (d, $J = 9.0\text{ Hz}$, 2H), 7.35–7.29 (m, 6H), 2.48 (d, $J = 7.5\text{ Hz}$, 1H), 1.62 (d, $J = 7.5\text{ Hz}$, 1H), 0.09 (s, 18H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.5, 132.6, 132.2, 127.8, 127.4, 127.3, 126.5, 126.2, 125.6, 125.5, 65.2, 24.0, 1.14; IR (neat) 2854, 2363, 1605, 1456, 1377, 1250, 1161, 1125, 1064, 952, 925, 842, 749 cm^{-1} . Anal. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_2\text{Si}_2$: C, 73.99; H, 7.28%. Found: C, 73.93; H, 7.32%; HRMS (m/z) Found: 470.2101. Calcd for $\text{C}_{29}\text{H}_{34}\text{O}_2\text{Si}_2$ $[\text{M}]^+$: 470.2097.

1,2-Diferrocenylpropenone (4)

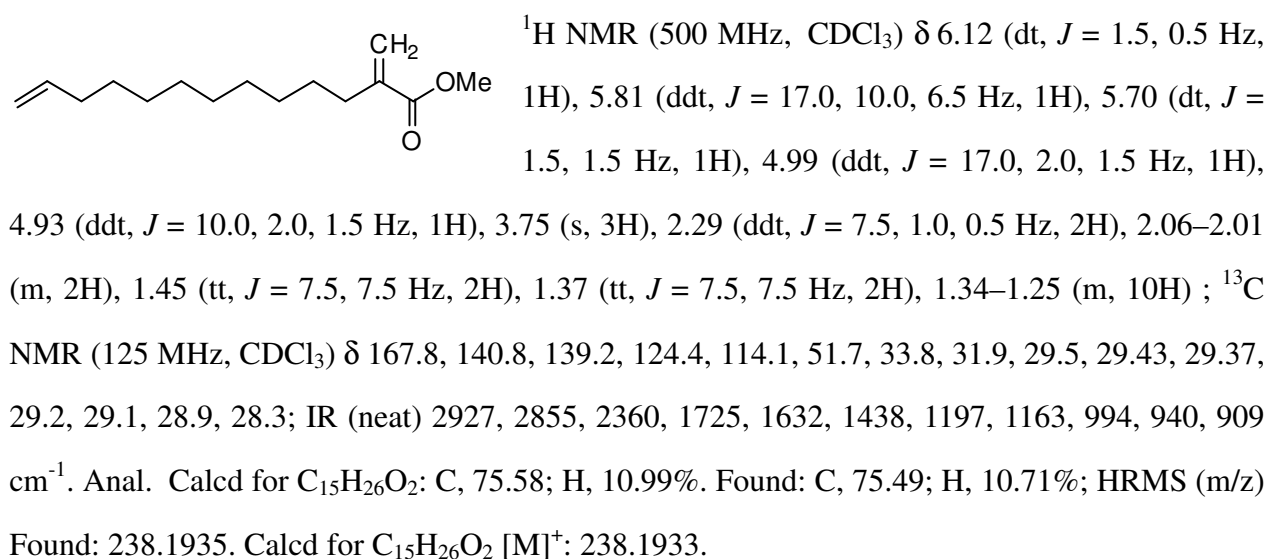
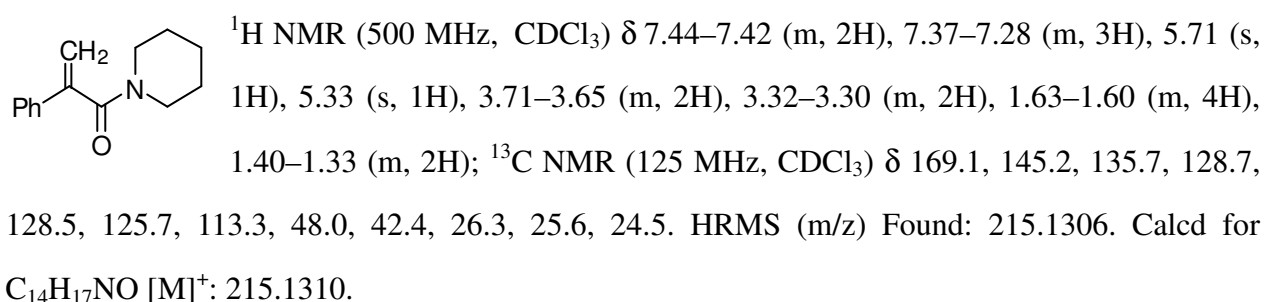
^1H NMR (500 MHz, CDCl_3) δ 5.77 (s, 1H), 5.68 (s, 1H), 4.84 (t, $J = 2.0\text{ Hz}$, 2H), 4.54 (t, $J = 2.0\text{ Hz}$, 2H), 4.52 (s, 2H), 4.29 (s, 2H), 4.23 (s, 5H), 4.14 (s, 5H); ^{13}C NMR (125 MHz, CDCl_3) δ 200.3, 147.4, 114.4, 80.8, 78.4, 72.3, 71.0, 70.0, 69.7, 69.0, 67.1; IR (nujol) 1635, 1246 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{20}\text{OFe}_2$: C, 65.14; H, 4.75%. Found: C, 64.86; H, 4.78%; HRMS (m/z) Found: 424.0209. Calcd for $\text{C}_{23}\text{H}_{20}\text{OFe}_2$ $[\text{M}]^+$: 424.0213.

Methyl 2-oxotridec-12-enoate (5b)

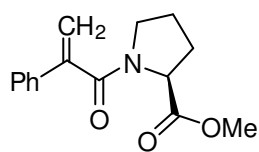
^1H NMR (300 MHz, CDCl_3) δ 5.80 (ddt, $J = 17.1, 10.2, 6.9\text{ Hz}$, 1H), 4.98 (ddt, $J = 17.1, 2.1, 1.5\text{ Hz}$, 1H), 4.92 (ddt, $J = 10.2, 2.1, 1.2\text{ Hz}$, 1H), 3.86 (s, 3H), 2.82 (t, $J = 7.2\text{ Hz}$, 2H), 2.06–1.99 (m, 2H), 1.68–1.57 (m, 2H), 1.40–1.27 (m, 12H); ^{13}C NMR (75 MHz, CDCl_3): δ 194.0, 161.4, 139.0, 114.0, 52.9, 39.4, 33.9, 29.5, 29.4, 29.3, 29.2, 29.0 (co-incident), 23.0; IR (neat) 2926, 1755, 1732, 1462, 1275, 1067, 910 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{24}\text{O}_3$: C, 69.96; H, 10.07%. Found: C, 69.69; H, 10.29%; HRMS (m/z) Found: 240.1724. Calcd for $\text{C}_{14}\text{H}_{24}\text{O}_3$ $[\text{M}]^+$: 240.1725.

Methyl 2-methylene-2-phenylacetate (6a)

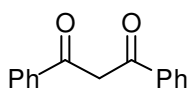
The spectral data of the product **6a** are in agreement with those published.²⁷

Methyl 2-methylene-12-tridecenoate (6b)**2-Phenyl-1-piperidin-1-ylpropenone (8a)**

The spectral data of the product **8a** are in agreement with those published.²⁸

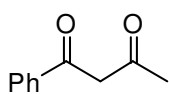
(S)-Methyl 1-(2-phenylacryloyl)pyrrolidine-2-carboxylate (8b)

^1H NMR (500 MHz, CDCl_3) δ 7.53–7.50 (m, 2H), 7.42–7.29 (m, 3H), 5.76 (s, 0.80H), 5.68 (s, 0.20H), 5.49 (s, 0.80H), 5.34 (s, 0.20H), 4.62 (dd, J = 8.0, 5.0 Hz, 0.80H), 4.24 (dd, J = 6.0, 2.5 Hz), 3.79 (s, 2.4H), 3.49 (s, 0.6H), 3.39–3.31 (m, 1.6H), 2.29–2.21 (m, 0.8H), 2.18–2.07 (m, 0.2H), 2.02–1.91 (m, 2H), 1.88–1.80 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 172.60, 172.58, 169.4, 169.3, 145.5, 145.4, 135.3, 135.1, 128.8, 128.7, 128.6, 128.5, 126.1, 125.9, 115.25, 115.17, 60.4, 58.4, 52.3, 52.1, 48.5, 46.0, 31.2, 29.4, 24.9, 22.6; IR (neat) 2922, 2360, 1744, 1642, 1436, 1175 cm^{-1} . HRMS (m/z) Found: 259.1205. Calcd for $\text{C}_{15}\text{H}_{17}\text{NO}_3$ $[\text{M}]^+$: 259.1208.

1,3-Diphenyl-1,3-propanedione (9a)

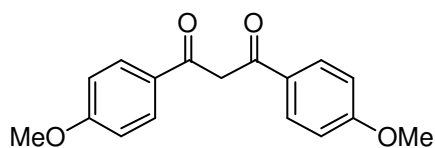
^1H NMR (300 MHz, CDCl_3) δ 8.00 (d, J = 7.0 Hz, 4H), 7.56 (t, J = 7.0 Hz, 2H), 7.50 (dd, J = 7.0, 7.0 Hz, 4H), 6.87 (s, 1H); ^{13}C NMR (75 MHz, CDCl_3) δ 185.7, 135.5, 132.4, 128.7, 127.1, 93.1. HRMS (m/z) Found: 224.0836. Calcd for $\text{C}_{15}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$: 224.0837.

The product **9a** is commercially available.

1-Methyl-3-phenyl-1,3-propanedione (9b)

^1H NMR (300 MHz, CDCl_3) δ 7.88 (d, J = 7.0 Hz, 2H), 7.52 (t, J = 7.5 Hz, 1H), 7.45 (dd, J = 7.5, 7.0 Hz, 2H), 6.18 (s, 1H), 2.20 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.8, 183.3, 134.8, 132.3, 128.6, 127.0, 96.7, 25.8. HRMS (m/z) Found: 162.0679. Calcd for $\text{C}_{10}\text{H}_{10}\text{O}_2$ $[\text{M}]^+$: 162.0681.

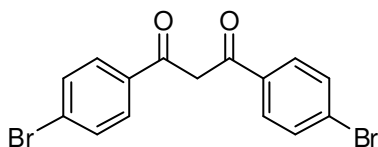
The product **9b** is commercially available.

1,3-di(4-Anisyl)-1,3-propanedione (9c)

^1H NMR (500 MHz, CDCl_3) δ 7.96 (d, J = 9.0 Hz, 4H), 6.98 (d, J = 9.0 Hz, 4H), 6.74 (s, 1H), 3.89 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3) δ 184.6, 163.0, 129.1, 128.2, 113.9, 91.5, 55.5.

HRMS (m/z) Found: 284.1048. Calcd for $\text{C}_{17}\text{H}_{16}\text{O}_4$ $[\text{M}]^+$: 284.1049.

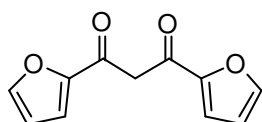
The product **9c** is commercially available.

1,3-di(4-Bromophenyl)-1,3-propanedione (9d)

^1H NMR (500 MHz, CDCl_3) δ 7.85 (d, J = 8.5 Hz, 4H), 7.63 (d, J = 8.5 Hz, 4H), 6.77 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 184.7, 134.2, 132.0, 128.7, 127.5, 92.9. HRMS (m/z) Found: 379.9044.

Calcd for $\text{C}_{15}\text{H}_{10}\text{O}_2^{79}\text{Br}_2$ $[\text{M}]^+$: 379.9048.

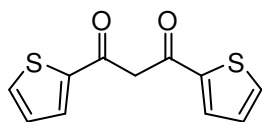
The spectral data of the product **9d** are in agreement with those published.²⁹

1,3-di(2-Furyl)-1,3-propanedione (9e)

^1H NMR (500 MHz, CDCl_3) δ 7.61 (dd, J = 1.5, 1.0 Hz, 2H), 7.20 (dd, J = 3.5, 1.0 Hz, 2H), 6.65 (s, 1H), 6.58 (dd, J = 3.5, 1.5 Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 174.7, 150.3, 146.1, 115.5, 112.6, 92.1. HRMS (m/z)

Found: 204.0421. Calcd for $\text{C}_{11}\text{H}_8\text{O}_4$ $[\text{M}]^+$: 204.0423.

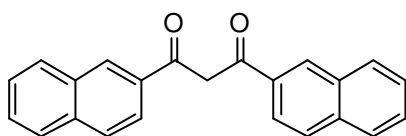
The spectral data of the product **9e** are in agreement with those published.³⁰

1,3-di(2-Thiophenyl)-1,3-propanedione (9f)

^1H NMR (500 MHz, CDCl_3) δ 7.78 (dd, J = 4.0, 1.0 Hz, 2H), 7.62 (dd, J = 5.0, 1.0 Hz, 2H), 7.17 (dd, J = 5.0, 4.0 Hz, 2H), 6.54 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 178.8, 140.6, 132.0, 130.0, 128.3, 92.6. HRMS (m/z)

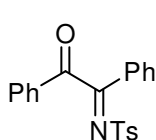
Found: 235.9971. Calcd for $\text{C}_{11}\text{H}_8\text{O}_2\text{S}_2$ $[\text{M}]^+$: 235.9966.

The spectral data of the product **9f** are in agreement with those published.³¹

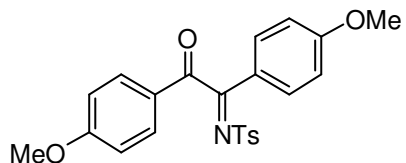
1,3-di(2-Naphtyl)-1,3-propanedione (9g)

^1H NMR (500 MHz, CDCl_3) δ 8.60 (d, $J = 1.5$ Hz, 2H), 8.08 (d, $J = 8.5$, 2.0 Hz, 2H), 8.02 (d, $J = 7.5$ Hz, 2H), 7.96 (d, $J = 8.5$ Hz, 2H), 7.91 (d, $J = 8.0$ Hz, 2H), 7.63–7.56 (m, 4H), 7.16 (s, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 185.6, 135.3, 132.8, 132.8, 129.4, 128.5, 128.4, 128.2, 127.8, 126.8, 123.3, 93.8. HRMS (m/z) Found: 324.1152. Calcd for $\text{C}_{23}\text{H}_{16}\text{O}_2$ [M] $^+$: 324.1150.

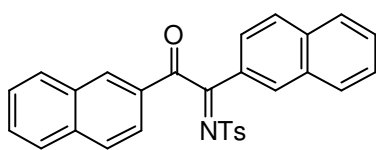
The spectral data of the product **9g** are in agreement with those published.³²

4-Methyl-*N*-(2-oxo-1,2-diphenylethylidene)benzenesulfonamide (10a)

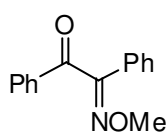
^1H NMR (500 MHz, CDCl_3) δ 7.94–7.92 (m, 2H), 7.87 (d, $J = 8.5$ Hz, 2H), 7.84–7.82 (m, 2H), 7.66–7.62 (m, 1H), 7.57–7.53 (m, 1H), 7.53–7.50 (m, 2H), 7.41–7.37 (m, 2H), 7.33 (d, $J = 8.5$ Hz, 2H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 196.1, 174.8, 144.8, 135.6, 134.7, 134.6, 134.5, 132.4, 130.1, 129.7, 129.13, 129.11, 129.0, 128.2, 21.6; IR (nujor) 3431, 1678, 1587, 1566, 1449, 1327, 1219, 1161, 1090, 904, 820, 773 cm^{-1} , mp 123.0–124.0 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{21}\text{H}_{17}\text{O}_3\text{NS}$: C, 69.40; H, 4.71%. Found: C, 69.66; H, 4.81%; HRMS (m/z) Found: 363.0914. Calcd for $\text{C}_{21}\text{H}_{17}\text{O}_3\text{NS}$ [M] $^+$: 363.0929.

***N*-(1,2-Bis(4-methoxyphenyl)-2-oxoethylidene)-4-methylbenzenesulfonamide (10b)**

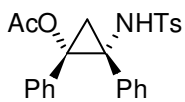
^1H NMR (500 MHz, CDCl_3) δ 7.89 (d, $J = 9.0$ Hz, 2H), 7.86 (d, $J = 8.5$ Hz, 2H), 7.80 (d, $J = 9.0$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 2H), 6.97 (d, $J = 9.0$ Hz, 2H), 6.85 (d, $J = 9.0$ Hz, 2H), 3.87 (s, 3H), 3.82 (s, 3H), 2.42 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 194.6, 174.1, 164.9, 164.6, 144.3, 136.3, 132.7, 131.6, 129.5, 128.2, 128.0, 125.1, 114.5, 114.4, 55.6 (co-incident), 21.6; IR (nujor) 3360, 1668, 1599, 1549, 1317, 1267, 1157, 1089, 1020, 908, 818, 787, 735 cm^{-1} . HRMS (m/z) Found: 424.1223. Calcd for $\text{C}_{23}\text{H}_{22}\text{O}_5\text{NS}$ [MH] $^+$: 424.1219.

***N*-(1,2-Di(2-naphthyl)-2-oxoethylidene)-4-methylbenzenesulfonamide (10c)**

^1H NMR (500 MHz, CDCl_3) δ 8.34 (s, 1H), 8.23–8.22 (m, 1H), 8.14 (dd, $J = 9.0, 2.0$ Hz, 1H), 8.10 (dd, $J = 9.0, 2.0$ Hz, 1H), 7.99 (d, $J = 9.0$ Hz, 1H), 7.91–7.85 (m, 5H), 7.83 (dd, $J = 8.0, 1.0$ Hz, 1H), 7.77 (dd, $J = 8.0, 1.0$ Hz, 1H), 7.65–7.46 (m, 4H), 7.32–7.30 (m, 2H), 2.43 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 196.1, 174.9, 144.7, 136.3, 136.2, 135.8, 133.8, 132.47, 132.43, 132.41, 132.3, 130.02, 129.97, 129.8, 129.7, 129.6, 129.4, 129.3, 129.1, 128.3, 128.0, 127.8, 127.15, 127.11, 124.2, 123.4, 21.6; IR (nujol) 3472, 1674, 1568, 1327, 1161, 1088, 910, 787, 731 cm^{-1} , mp 86.0–86.8 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{29}\text{H}_{21}\text{O}_3\text{NS}$: C, 75.14; H, 4.57%. Found: C, 75.11; H, 4.78%; HRMS (m/z) Found: 463.1246. Calcd for $\text{C}_{29}\text{H}_{21}\text{O}_3\text{NS}$ $[\text{M}]^+$: 463.1242.

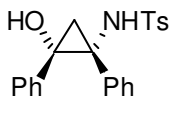
2-(methoxyimino)-1,2-diphenylethanone (10e)

^1H NMR (500 MHz, CDCl_3) δ 7.97–7.95 (m, 2H), 7.63–7.58 (m, 3H), 7.51–7.48 (m, 2H), 7.41–7.34 (m, 3H), 3.93 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 193.9, 155.7, 134.6, 134.2, 131.0, 130.1, 129.2, 128.9, 128.7, 126.2, 62.8; IR (neat) 2938, 1682, 1595, 1449, 1327, 1231, 1177, 1049, 928, 872, 772, 735, 691, 625 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{13}\text{NO}_2$: C, 75.30; H, 5.48%. Found: C, 75.17; H, 5.43%; HRMS (m/z) Found: 239.0954. Calcd for $\text{C}_{15}\text{H}_{13}\text{NO}_2$ $[\text{M}]^+$: 239.0946.

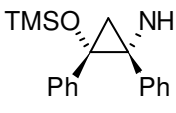
***cis*-*N*-(2-Acetoxy-1,2-diphenylcyclopropyl)-4-methylbenzenesulfonamide (11a)**

^1H NMR (300 MHz, CDCl_3) δ 7.41 (d, $J = 8.4$ Hz, 2H), 7.07–6.98 (m, 7H), 6.90–6.83 (m, 5H), 5.83 (s, 1H), 2.39 (d, $J = 8.4$ Hz, 1H), 2.30 (s, 3H), 2.18 (d, $J = 8.4$ Hz, 1H), 2.13 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 171.0, 143.1, 137.9, 135.9, 134.9, 129.3, 129.0, 128.5, 128.0, 127.93, 127.87, 127.4, 127.1, 66.2, 46.7, 22.4, 21.8, 21.7; IR (nujol) 3345, 2363, 1750, 1674, 1599, 1323, 1227 cm^{-1} . HRMS (m/z) Found: 421.1357. Calcd for $\text{C}_{24}\text{H}_{23}\text{NO}_4\text{S}$ $[\text{M}]^+$: 421.1348.

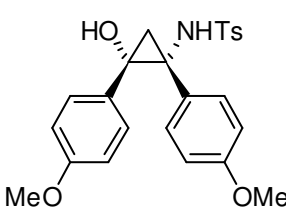
***cis*-N-(2-Hydroxy-1,2-diphenylcyclopropyl)-4-methylbenzenesulfonamide (11b)**

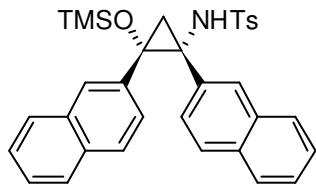

¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, *J* = 8.1 Hz, 2H), 7.06–7.02 (m, 7H), 6.89–6.83 (m, 5H), 6.04 (s, 1H), 3.39 (bs, 1H), 2.32 (s, 3H), 2.23 (d, *J* = 7.8 Hz, 1H), 1.77 (d, *J* = 7.8 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 143.2, 137.8, 137.7, 136.3, 129.3, 129.2, 128.0, 127.7, 127.5, 127.48, 127.3, 126.9, 63.4, 47.5, 23.8, 21.8; IR (neat) 3474, 3277, 1597, 1449, 1325, 1221, 1159, 1092 cm⁻¹. HRMS (*m/z*) Found: 379.1241. Calcd for C₂₂H₂₁NO₃S [M]⁺: 379.1242.

***cis*-N-(2-Trimethylsiloxy-1,2-diphenylcyclopropyl)-4-methylbenzenesulfonamide (11c)**

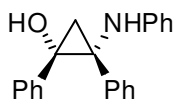

¹H NMR (500 MHz, CDCl₃) δ 7.49–7.47 (m, 2H), 7.10–7.07 (m, 2H), 7.04–6.98 (m, 5H), 6.95–6.92 (m, 2H), 6.90–6.86 (m, 3H), 5.91 (s, 1H), 2.34 (s, 3H), 2.31 (d, *J* = 8.0 Hz, 1H), 1.42 (d, *J* = 8.0 Hz, 1H), –0.01 (s, 9H); ¹³C NMR (125 MHz, CDCl₃) δ 142.8, 138.3, 137.5, 136.6, 129.1, 128.8, 127.8, 127.6, 127.31, 127.29, 127.28, 126.4, 64.0, 45.2, 21.8, 21.4, 0.72; IR (neat) 3327, 2955, 1599, 1497, 1449, 1323, 1252, 1159, 1092, 966, 928, 843 cm⁻¹. HRMS (*m/z*) Found: 451.1634. Calcd for C₂₅H₂₉NO₃SSi [M]⁺: 451.1637.

***cis*-N-(2-Hydroxy-1,2-di-4-anisylcyclopropyl)-4-methylbenzenesulfonamide (11d)**


¹H NMR (300 MHz, CDCl₃) δ 7.45 (d, *J* = 8.1 Hz, 2H), 7.06 (d, *J* = 8.1 Hz, 2H), 6.98 (d, *J* = 9.0 Hz, 2H), 6.78 (d, *J* = 8.7 Hz, 2H), 6.61 (d, *J* = 9.0 Hz, 2H), 6.40 (d, *J* = 8.7 Hz, 2H), 3.67 (s, 3H), 3.63 (s, 3H), 2.33 (s, 3H), 2.07 (d, *J* = 7.5 Hz, 1H), 1.61 (d, *J* = 7.5 Hz, 1H); ¹³C NMR (75 MHz, CDCl₃) δ 157.4, 157.1, 139.0, 130.7, 129.2, 128.9, 128.4, 127.8, 127.5, 127.2, 126.9, 126.2, 111.5, 111.4, 61.1, 53.3, 45.7, 22.4; IR (neat) 3271, 2936, 2359, 1599, 1549, 1514, 1317, 1267, 1159, 1090, 1024, 816, 669 cm⁻¹. HRMS (*m/z*) Found: 439.1453. Calcd for C₂₄H₂₅NO₅S [M]⁺: 439.1453.

***cis*-N-(2-Trimethylsiloxy-1,2-di-2-naphthylcyclopropyl)-4-methylbenzenesulfonamide (11e)**

^1H NMR (300 MHz, C_6D_6) δ 7.60–6.94 (m, 16H), 6.39–6.36 (m, 2H), 6.20 (s, 1H), 2.60 (d, $J = 8.1$ Hz, 1H), 2.15 (d, $J = 8.1$ Hz, 1H), 1.63 (s, 3H), 0.05 (s, 9H); ^{13}C NMR (75 MHz, C_6D_6) δ 142.0, 139.3, 135.8, 134.4, 132.8, 132.73, 132.66, 132.3, 128.6, 127.7, 127.6, 127.4, 127.3, 127.0, 126.5, 126.1, 126.0, 125.8, 125.6, 125.5, 64.8, 46.3, 23.6, 20.8, 0.9; IR (neat) 3312, 2955, 2344, 1250, 1159, 1092, 843, 752 cm^{-1} . HRMS (m/z) Found: 551.1950. Calcd for $\text{C}_{33}\text{H}_{33}\text{O}_3\text{NSSi}$ $[\text{M}]^+$: 551.1950.

1,2-Diphenyl-2-(phenylamino)cyclopropanol (11f)

^1H NMR (300 MHz, C_6D_6) δ 7.15–6.67 (m, 15H), 2.02 (d, $J = 7.2$ Hz, 1H), 1.08 (d, $J = 7.2$ Hz, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 147.2, 139.7, 138.6, 129.2, 128.8, 128.4, 128.0, 127.4, 126.1, 120.0, 118.5, 115.2, 66.5, 47.0, 25.0; IR (neat) 3509, 3423, 2363, 1605, 1314, 1208, 751, 693 cm^{-1} . Anal. Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}$: C, 83.69; H, 6.35%. Found: C, 83.39; H, 6.16%; HRMS (m/z) Found: 301.1459. Calcd for $\text{C}_{21}\text{H}_{19}\text{NO}$ $[\text{M}]^+$: 301.1463.

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9. Crystal structure data: Monoclinic, $a = 43.816(9)$, $b = 5.922(2)$, $c = 38.178(8)$ Å, $\beta = 100.53(3)^\circ$, $V = 9739(3)$ Å³, $Z = 24$, $\rho_{\text{calcd}} = 1.270$ Mgm⁻³, $\lambda(\text{Mo}_{\text{K}\alpha}) = 0.71069$ Å, $T = 296$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.130$ for 4583 reflections ($I > 2\sigma(I)$).
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 16. Crystal structure data: Monoclinic, $a = 12.7365(13)$, $b = 10.8102(11)$, $c = 16.3267(17)$ Å, $\beta = 105.936^\circ$, $V = 2161.5(4)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.295$ Mgm⁻³, $\lambda(\text{Mo}_{\text{K}\alpha}) = 0.71073$ Å, $T = 296$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.049$ for 4711 reflections ($I > 2\sigma(I)$).
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Chapter 3

Stereospecific and Stereoselective Preparation of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols from α,β -Epoxy Ketones and Bis(iodozincio)methane

A reaction of α,β -epoxy ketone with bis(iodozincio)methane gave 2-(1-hydroxyalkyl)-1-alkylcyclopropanol via nucleophilic [2+1] cycloaddition. The reaction proceeds via a coordination between the dizinc and α,β -epoxy ketone; this coordination allows the carbanion equivalent to nucleophilic attack onto carbonyl group stereoselectively. Subsequential nucleophilic attack to epoxy group proceeds in a stereospecific manner, and as a result, (*1R**,*2R**)-2-(1-hydroxyalkyl)-1-alkylcyclopropanol is obtained diastereoselectively.

Introduction

Bis(iodozincio)methane (**1**) possesses a couple of zinc atoms on a carbon, and it works as a dianion equivalent.¹ Because its reactivity is enhanced by doubly substituted electropositive zinc atoms, the dizinc **1** may have an enough nucleophilicity onto ketone. Treatment of a simple ketone, such as acetophenone with the dizinc **1**, however, resulted in the complete recovery of the starting material.² Meanwhile, Matsubara found that treatment of the dizinc **1** with an α -hydroxy ketone, which has Lewis basic atom at α -position of carbonyl, performed the nucleophilic addition smoothly to give a methylenated compounds.^{2a} The coordination between the dizinc and hydroxyl group at α -position might activate the reagent. The same activation is also observed in the reaction of Grignard reagent and α -hydroxy ketone under Cram's chelation control.³

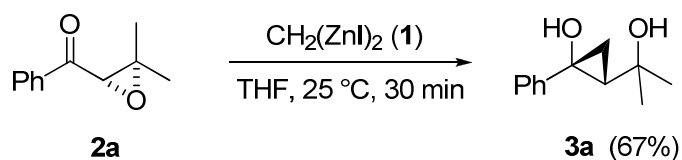
The author supposed that the similar activation may be observed, when the dizinc **1** is treated with other ketones having Lewis basic site at α -position, such as 1,2-diketone and α,β -epoxy ketone. Actually, in the case of 1,2-diketone as a substrate, the nucleophilic reaction of the dizinc **1** to a carbonyl group proceeded smoothly; sequential nucleophilic addition of the introduced iodozinciomethyl group to the other carbonyl group also proceeded readily to give *cis*-cyclopropan-1,2-diol diastereoselectively.⁴ The high stereoselectivity comes from the specific coordination between the dizinc and 1,2-diketone.⁵

Considering these results, when an α,β -epoxy ketone was treated with the dizinc **1**, diastereoselective nucleophilic addition to the carbonyl group would proceed via a specific coordination to give 2-(1-hydroxyalkyl)-1-alkylcyclopropanol diastereoselectively.

Results and Discussion

A solution of 2-benzoyl-1,1-dimethyloxirane (**2a**, 1.0 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 1.2 mmol, 0.5 M in THF) at 25 °C. After being stirred for 30

min, the mixture was quenched with a saturated aqueous solution of NH_4Cl . The reaction gave (*1R*,2R**)-2-(1-methyl-1-hydroxyethyl)-1-phenylcyclopropanol (**3a**) as the sole product (Scheme 1).



Scheme 1. Reaction of 2-benzoyl-1,1-dimethyloxirane (**2a**) with bis(iodozincio)methane (**1**).

The stereochemistry of the product was determined by a single-crystal X-ray analysis. The ORTEP figure of **3a** was shown in Figure 1.⁶ The figure shows that the product has *cis*-configuration.

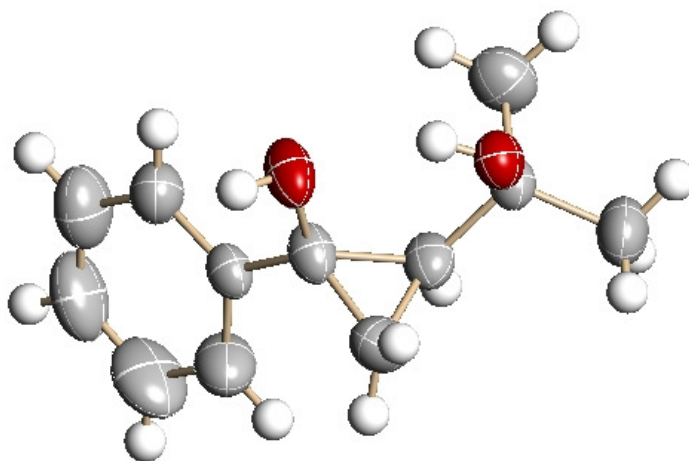


Figure 1. ORTEP of **3a**.

Other examples of reactions conducted that led to formation of a cyclopropane ring are shown in Table 1. In all cases, the reaction yielded a single diastereomer selectively. Various α,β -epoxy ketones **2b-e** could be applied for the reaction, and the reaction afforded the

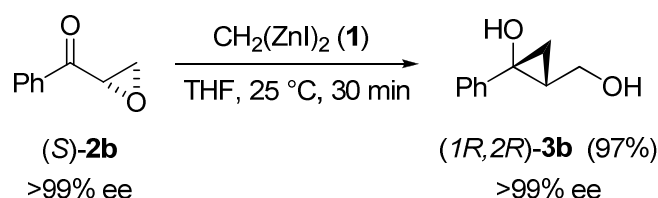
corresponding cyclopropanols in excellent yields (entries 1-4). The reaction of α,β -epoxy ketone **2g** having an acetyl group with **1** also proceeded chemoselectively to give the corresponding cyclopropanol **3g** in a good yield (entry 6). Bromo and cyclopropyl group tolerate the reaction condition (entries 7 and 8). The reaction of cyclic α,β -epoxy ketone **2j** with **1** afforded bicyclic product **3j** (entry 9).

Table 1. Reaction of α,β -epoxy ketone **2** with bis(iodozincio)methane (**1**).^a

entry	substrate	product	Yield (%) ^b
1	2b	3b	94
2	2c	3c	87
3	2d	3d	>99
4	2e	3e	95
5	2f	3f	90
6	2g	3g	95
7	2h	3h	95
8	2i	3i	83
9	2j	3j	37 ^c

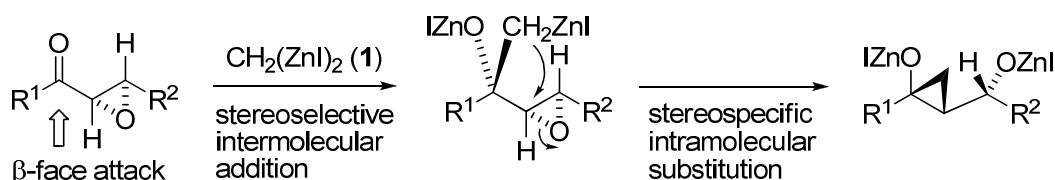
^a α,β -Epoxy ketone **2** (0.5 mmol), the dizinc **1** (0.6 mmol) and THF (2 mL) were used. ^b Isolated yields. ^c 2-methylene-16-oxabicyclo[13.1.0]hexadecane was also obtained in 13%.

Treatment of an optically active α,β -epoxy ketone (*S*)-**2b** with the dizinc **1** gave (*1R,2R*)-**3b** without a loss of enantiomeric excess as shown in Scheme 2.



Scheme 2. Reaction of (*S*)-**2b** with bis(iodozincio)methane (**1**).

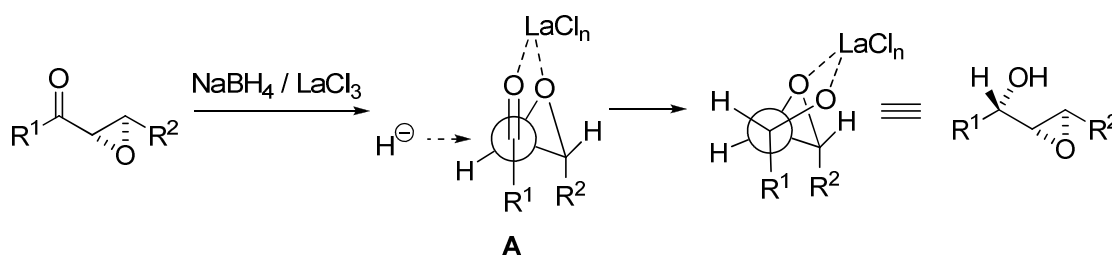
The diastereoselective formation of cyclopropanol **3** proceeded as follows. The reaction starts with the diastereoselective attack of **1** to the carbonyl group as a consequence of the stereogenic center at the α -carbon atom (Scheme 3).^{2a,4,5} This step is followed by stereospecific attack on the epoxide.



Scheme 3. Stereochemical requirements for the reaction.

The explanation shown in Scheme 3 requires diastereoselective attack to the β face of **2**, which needs to be rationalized, since previous reports concerning the diastereoselective metal-mediated nucleophilic attack to an α,β -epoxy ketone occurred from the α face of **2**.⁷

For example, treatment of **2c** with $\text{NaBH}_4/\text{LaCl}_3$ resulted in the exclusive formation of *erythro*-epoxy alcohol.⁸ The diastereoselective reaction was explained by chelation effects to form intermediate **A**, as shown in Scheme 4.



Scheme 4. Diastereoselective reduction of α,β -epoxy ketone with $\text{NaBH}_4/\text{LaCl}_3$.

Other metal salts, such as CaCl_2 , MnCl_2 , and ZnCl_2 as well as LaCl_3 showed the same effect. In the present cyclopropanation reaction, the addition of the dizinc **1** can not be explained by a simple chelation intermediate such as **A**,^{7,8} because the first nucleophilic attack also occurred by β -face attack on **2**. From ab initio calculation, Matsubara *et al.* proposed that coordination of the dizinc **1** to *vic*-diketone, 2,3-dioxobutane, occurs in a face-to-face arrangement, as shown in Figure 2.⁵ Such coordination has two characteristic features: First, the dihedral angle of the diketone part ($\angle\text{O}(1)\text{-C}(1)\text{-C}(2)\text{-O}(2) = 47.7^\circ$); second, the mechanism through which the zinc reagent coordinates to the diketone. A line drawn between the two oxygen atoms of the diketone, and another between the two zinc atoms in the initial complex, cross at almost right angles. In the same way, the nucleophilic attack of the dizinc **1** on α,β -epoxy ketone **2c** can be explained via intermediate **D** (Scheme 5). Attack from the other face via intermediate **E** will be constrained by steric hindrance between the dizinc **1** and the epoxide ring. Thus, face-to-face coordination will promote attack on the opposite face relative to traditional Cram-chelation intermediates such as **A**.

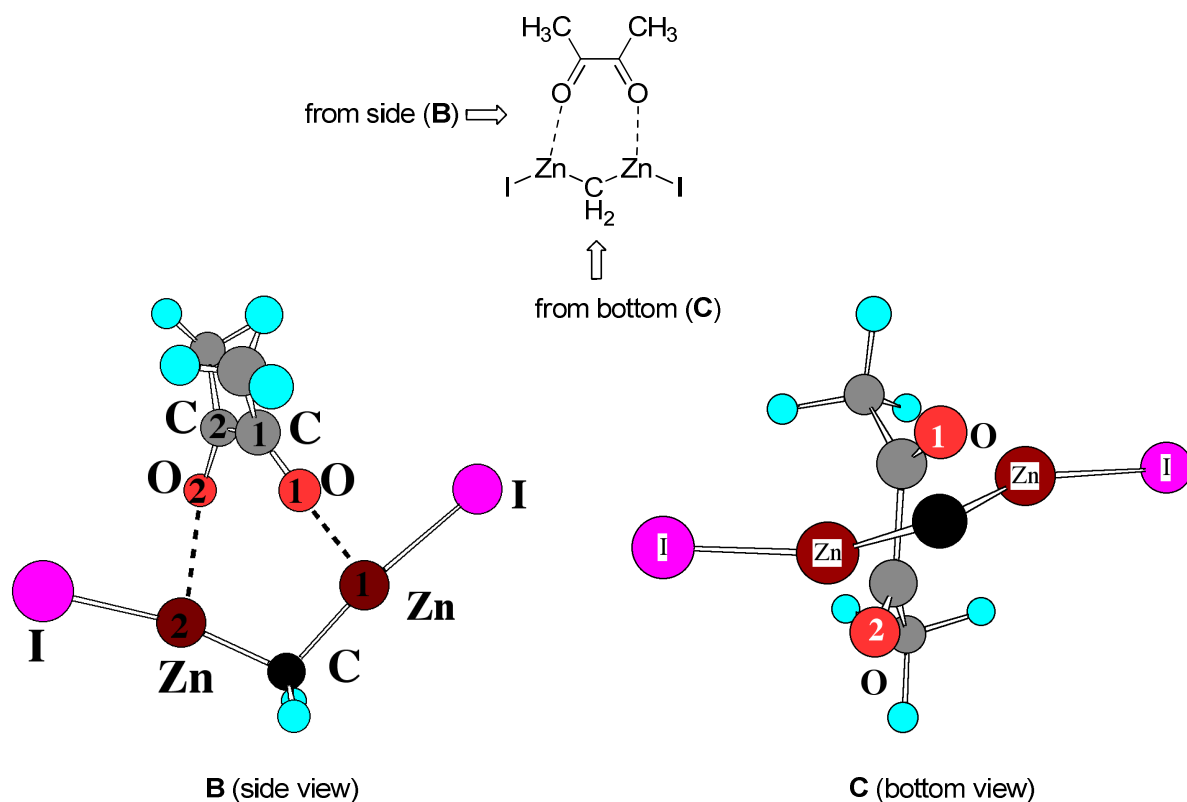
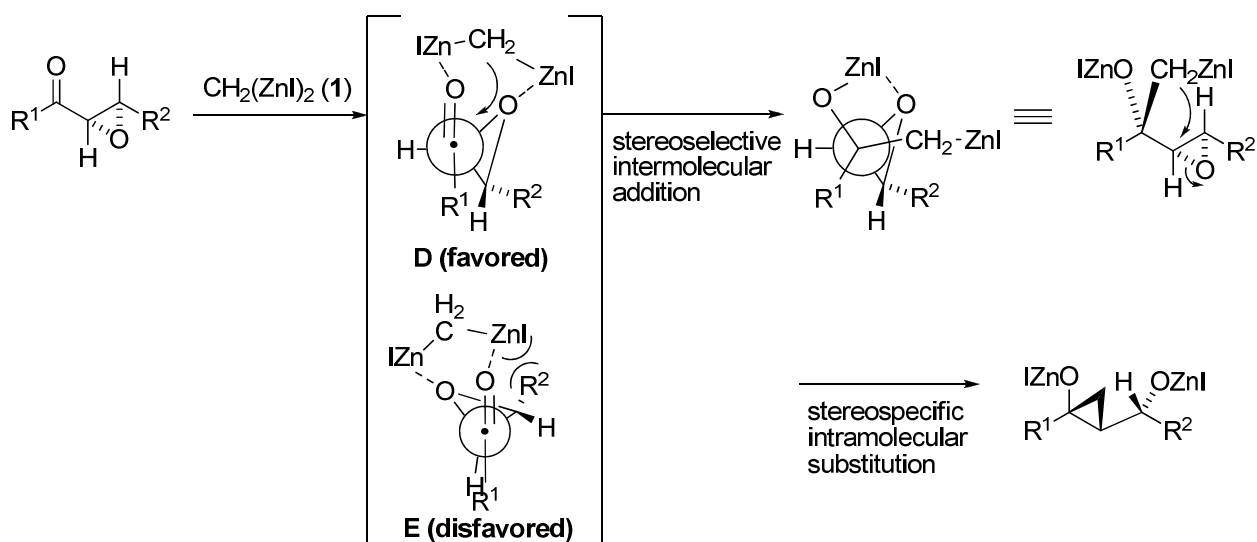
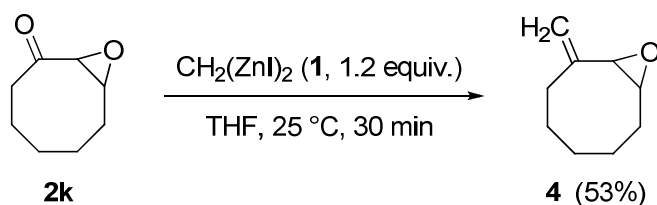


Figure 2. Initial complex formed in the reaction of 2,3-dioxobutane with **1** based on B3LYP/II/B3LYP/I calculations.



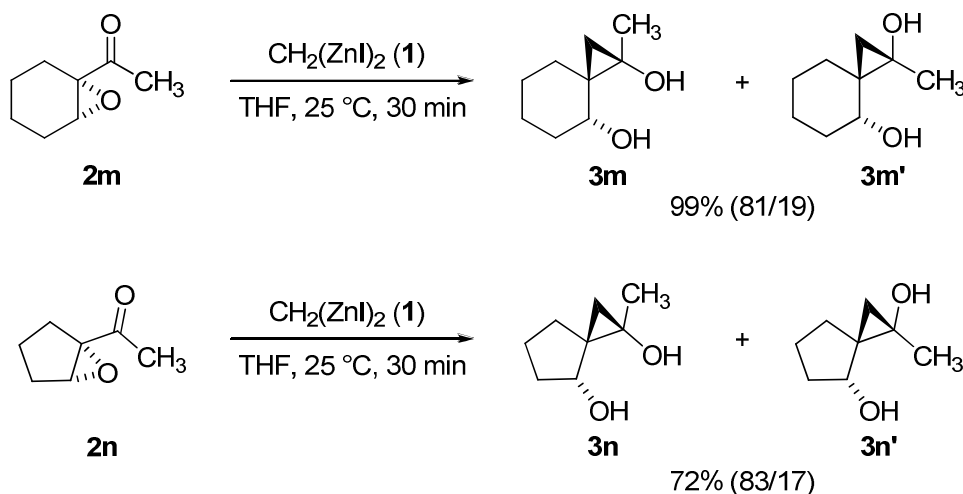
Scheme 5. Proposal for the stereoselective reaction of **2c** with **1**.

To coordinate with the dizinc properly as shown in Scheme 5, some structural flexibility of α,β -epoxy ketone is required. For example, the reaction of 1-oxo-2-cyclooctene oxide (**2k**) with the dizinc **1** afforded only methylation product **4** (Scheme 6).



Scheme 6. Reaction of **2k** with bis(iodozincio)methane (**1**).

In the case of cyclic substrate such as **2m** or **2n** (Scheme 7), they would experience some difficulty in differentiating between the intermediate corresponding to **D** and **E** because of steric hindrance of the carbocyclic moiety. Treatment of **2m** and **2n** with **1** gave the spiro compound with moderate diastereoselectivity. Figure 3 shows the results of the single-crystal X-ray analysis of the diester obtained from **3n** and 3,5-dinitrobenzoyl chloride.⁹



Scheme 7. Formation of spirocyclic derivatives.

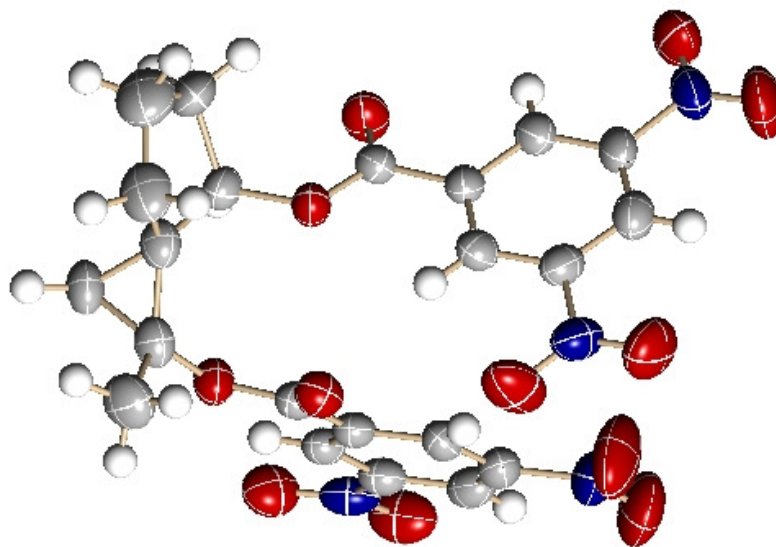
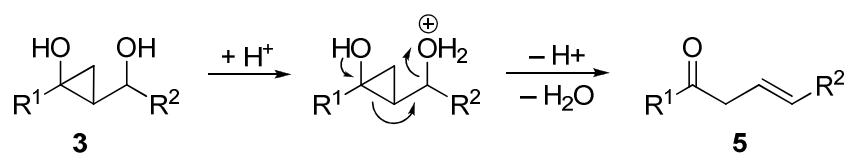


Figure 3. X-Ray analysis of bis(3,5-dinitrobenzoate) of **3n**.

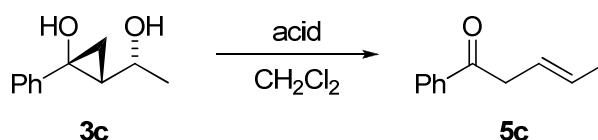
The product, 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, has a (1-hydroxyalkyl)cyclopropane moiety, and it is subject to cyclopropane ring opening reaction by acid. In 1960, Julia reported acid-catalyzed isomerization of (1-hydroxyalkyl)cyclopropanes to (*E*)-homoallylic alcohols.¹⁰ When it was applied to **3** as starting material, β,γ -unsaturated ketone **5** was obtained via carbocation intermediate (Scheme 8).¹¹ This transformation, however, has not been studied well, because the starting material was difficult to obtain. So the author also studied the acid-mediated ring-opening reaction of **3**.¹²



Scheme 8. Julia-type transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol into (*E*)- β,γ -unsaturated ketone.

As shown in Table 2, treatment of 2-(1-hydroxyethyl)-1-phenylcyclopropanol **3c** with a catalytic amount of various acids resulted in moderate *E/Z* selectivity (entries 1-3). Among them, TFA (trifluoroacetic acid) gave the best diastereoselectivity. Increasing the amount of TFA improved the yield and diastereoselectivity (entries 4 and 5). We found that treatment with 5 equiv. amounts of trifluoroacetic acid gave the desired β,γ -unsaturated ketone with high diastereoselectivity (entry 6).¹³

Table 2. Acid-mediated transformation of **3c** into **5c**.^a



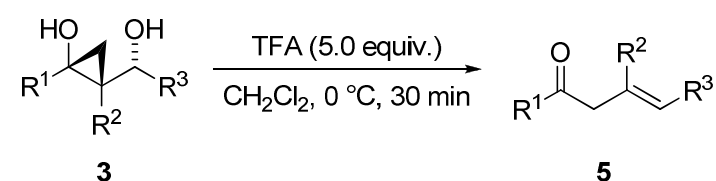
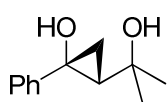
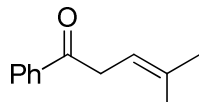
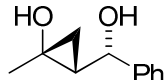
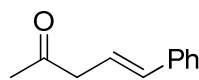
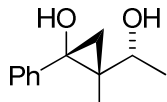
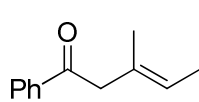
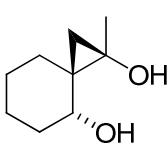
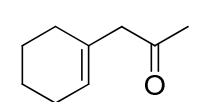
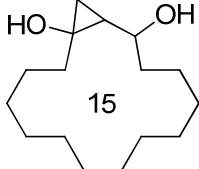
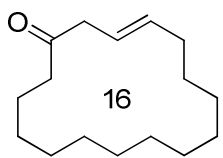
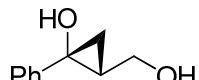
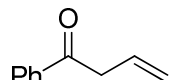
entry	acid (equiv.) ^b	time (h)	temp. (°C)	yield (%) ^c	<i>E</i> / <i>Z</i> ^d
1	TFA (0.2)	24	25	67	75/25
2	<i>p</i> -TsOH (0.2)	6	25	89	68/32
3	TfOH (0.2)	6	25	76	62/38
4	TFA (1.0)	24	25	90	88/12
5	TFA (2.0)	24	25	90	92/8
6	TFA (5.0)	0.5	0	90	95/5

^a The substrate **3c** (0.5 mmol) and dichloromethane (2 mL) were used. ^b TFA: trifluoroacetic acid, *p*-TsOH: *p*-toluenesulfonic acid, TfOH: trifluoromethanesulfonic acid. ^c Yields were determined by ¹H NMR using bromoform as internal standard. ^d The *E/Z* ratios were determined by ¹H NMR analysis.

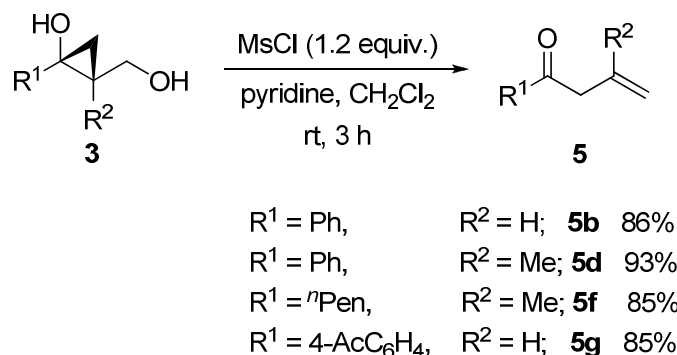
Other examples are shown in Table 3. Although a reaction of tertiary alcohol **3a** at 0 °C gave the desired product **5a** in 70%, it proceeded sluggishly (entry 1). The reaction at –78 °C, however, improved the yield (entry 2). Trisubstituted alkene **5e** was obtained with high diastereoselectivity from **3e** (entry 4). From bicyclic compound **3j**, ring-expanded (*E*)-cycloalkene **5j** was obtained in excellent yield (entry 6). In the case of a primary alcohol,

such as **3b**, this acid-mediated transformation did not proceed efficiently because of the lack of stability of the primary cation intermediate (entry 7). Treatment of **3b** with mesyl chloride and pyridine,¹⁴ however, gave the corresponding β,γ -unsaturated ketone **5b** in good yield (Scheme 9). This procedure worked well for the other primary alcohols **3d,f,g**.

Table 3. Examples of the transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanols **3** into (*E*)- β,γ -unsaturated ketones **5**.^a

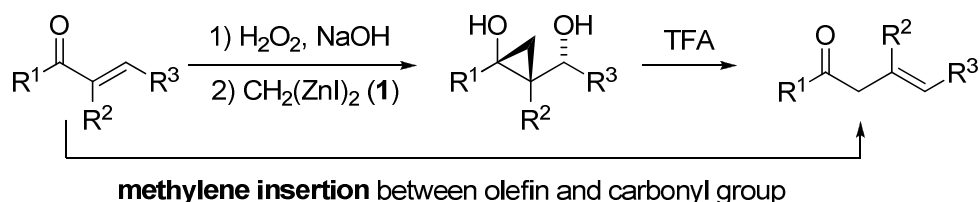
					
entry	substrate	product	yield (%) ^b	<i>E</i> / <i>Z</i> ^c	
1			70		
2 ^d			>99		
3			96	<i>E</i> only	
4			95	<i>E</i> only	
5			86		
6			>99	<i>E</i> only	
7 ^e			35 ^f		

^a The substrate **3** (0.5 mmol), TFA (2.5 mmol) and dichloromethane (2 mL) were used. ^b Isolated yields. ^c Stereochemistry was determined by NOE analysis. ^d Reaction was carried out at -78 °C. ^e Reaction was carried out at 25 °C for 24 h. ^f The corresponding α,β -unsaturated ketone was also obtained in 25% yield.



Scheme 9. Formation of β,γ -unsaturated ketones via mesylate elimination.

As mentioned above, the substrate **3** are available from the dizinc **1** and α,β -epoxy ketones **2** in one step, and α,β -epoxy ketones can be prepared from α,β -unsaturated ketones with basic hydroperoxide easily. So the net transformation can be regarded as methylene insertion between a carbonyl group and an alkenyl group of α,β -unsaturated ketone (Scheme 10).



Scheme 10. The schematic whole transformation.

Conclusion

The author showed the scope of the nucleophilic [2+1] cycloaddition of bis(iodozincio)methane (**1**) and α,β -epoxy ketones. Various substrates, which can coordinate with the dizinc **1**, were converted into (*1R**,*2R**)-2-(1-hydroxyalkyl)-1-alkylcyclopropanols **3** diastereoselectively. The author also demonstrated the stereoselective synthesis of β,γ -unsaturated ketones **7** by acid-mediated Julia-type transformation from

(1*R**,2*R**)-2-(1-hydroxyalkyl)-1-alkylcyclopropanols.

Experimental Section

Unless otherwise noted, commercially available reagents were used without purification. α,β -Epoxy ketones **2** were prepared according to the reported procedure.¹⁵

General procedure for preparation of (*S*)-2b**:** (*S*)-[(*R*)-Hydroxyphenylmethyl]oxirane was prepared from the corresponding allyl alcohol by Katsuki–Sharpless asymmetric epoxidation.¹⁶ The enantiomeric purity of (*S*)-[(*R*)-Hydroxyphenylmethyl]oxirane was determined by ¹H NMR after converting into the corresponding (*S*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetate. The obtained optically active epoxy alcohol was oxidized according to the reported procedure to give (*S*)-**2b**.¹⁷

General procedure for the preparation of 2-(hydroxyalkyl)-1-alkylcyclopropanol (3**):** To a solution of α,β -epoxy ketone (**2**, 1.0 mmol) in THF (4 mL), bis(iodozincio)methane (**1**, 1.2 mmol) was added at room temperature. The mixture was stirred at room temperature for 30 min. Then saturated aqueous solution of NH₄Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding 2-(hydroxyalkyl)-1-alkylcyclopropanol **3**.

General procedure for the transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (3a,c,e,j,m,o**) into β,γ -unsaturated ketone (**5**):** To a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3**, 0.5 mmol) in dichloromethane (2 mL), trifluoroacetic acid (2.5 mmol) was added at 0 °C. The mixture was stirred at 0 °C for 30 min, and then the solvent was removed under reduced pressure. The residue was purified by silica

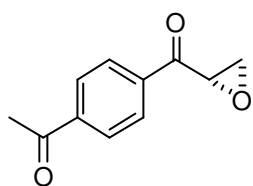
gel column chromatography (eluting with hexane–EtOAc) to give the corresponding β,γ -unsaturated ketone **5**.

General procedure for the transformation of 2-hydroxymethyl-1-alkylcyclopropanol (3b,d,f,g) into β,γ -unsaturated ketone (5): To a solution of 2-hydroxymethyl-1-alkylcyclopropanol **3** (0.5 mmol) in dichloromethane (2 mL), pyridine (2.0 mmol) and mesyl chloride (0.6 mmol) was added at room temperature. The mixture was stirred at room temperature for 3 h, then saturated aqueous solution of NaHCO_3 was added. The organic layer was extracted with EtOAc, and the combined organic layers were dried over Na_2SO_4 . The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography eluting with hexane and EtOAc to give the corresponding β,γ -unsaturated ketone **5**.

Characterization Data

The substrates **2a**,¹⁸ **2b**,¹⁸ **2c**,¹⁸ **2d**,¹⁹ **2e**,²⁰ **2f**,²¹ **2i**,²² **2k**,²³ **2m**²⁴ and **2n**²⁵ were be found in the literature.

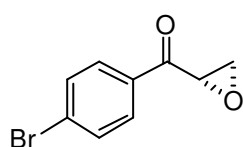
4-Acetylbenzoyloxirane (**2g**)



^1H NMR (300 MHz, CDCl_3) δ 8.12–8.02 (m, 4H), 4.21 (dd, J = 4.2, 2.4 Hz, 1H), 3.14 (dd, J = 6.6, 4.2 Hz, 1H), 2.97 (dd, J = 6.6, 2.4 Hz), 2.64 (s, 3H);

^{13}C NMR (75 MHz, CDCl_3): δ 197.0, 194.2, 140.5, 138.2, 128.44, 128.41, 51.4, 47.6, 27.0; IR (neat) 1694, 1682, 1505, 1408, 1360, 1310, 1267, 1233, 951 cm^{-1} . HRMS (m/z) Found: 190.0632. Calcd for $\text{C}_{11}\text{H}_{10}\text{O}_3$ $[\text{M}]^+$: 190.0630.

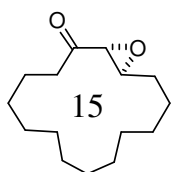
4-Bromobenzoyloxirane (**2h**)



^1H NMR (300 MHz, CDCl_3) δ 7.89 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 4.15 (dd, J = 4.5, 2.4 Hz, 1H), 3.11 (dd, J = 6.3, 4.5 Hz, 1H), 2.94 (dd,

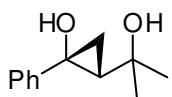
$J = 6.3, 2.4$ Hz, 1H); ^{13}C NMR (75 MHz, CDCl_3): δ 193.6, 133.8, 132.0, 129.7, 129.1, 51.2, 47.5; IR (neat) 1692, 1587, 1402, 1234, 1071, 1011, 955, 912, 741 cm^{-1} . HRMS (m/z) Found: 225.9630. Calcd for $\text{C}_9\text{H}_7\text{O}_2\text{Br}$ $[\text{M}]^+$: 225.9629.

16-Oxabicyclo[13.1.0]hexadecan-2-one (2j)



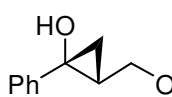
^1H NMR (300 MHz, CDCl_3) δ 3.27 (d, $J = 1.8$ Hz, 1H), 3.06 (ddd, $J = 8.7, 3.3, 1.8$ Hz, 1H), 2.52–2.31 (m, 2H), 2.08–1.99 (m, 1H), 1.72–1.68 (m, 2H), 1.55–1.43 (m, 2H), 1.36–1.25 (m, 17H); ^{13}C NMR (125 MHz, CDCl_3): δ 207.4, 60.3, 59.0, 37.2, 30.8, 27.5, 27.0, 26.8, 26.5, 26.4, 26.2, 26.1, 25.7, 24.7, 22.6; IR (nujol) 2928, 1712, 1444, 1368, 1240, 910, 856, 733 cm^{-1} , mp 56.2–56.7 $^\circ\text{C}$. Anal. Calcd for $\text{C}_{15}\text{H}_{26}\text{O}_2$: C, 75.58; H, 10.99%. Found: C, 75.73; H, 11.24%; HRMS (m/z) Found: 238.1936. Calcd for $\text{C}_{15}\text{H}_{26}\text{O}_2$ $[\text{M}]^+$: 238.1933.

(1*R**,2*R**)-2-(2-Hydroxypropyl)-1-phenylcyclopropanol (3a)



^1H NMR (300 MHz, C_6D_6) δ 7.22–7.19 (m, 2H), 7.16–7.12 (m, 2H), 7.05–7.00 (m, 1H), 4.19 (bs, 1H), 3.55 (bs, 1H), 1.37–1.33 (m, 1H), 1.31 (s, 3H), 1.20 (s, 3H), 1.03–0.95 (m, 1H), 0.89–0.79 (m, 1H); ^{13}C NMR (75 MHz, C_6D_6) δ 144.8, 128.4, 126.4, 124.7, 70.4, 60.6, 37.1, 31.0, 30.3, 17.1; IR (nujol) 3265, 2359, 1456, 1362, 1225 cm^{-1} ; mp 95.5–96.2 $^\circ\text{C}$. Anal. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$: C, 74.97; H, 8.39%. Found: C, 75.13; H, 8.19%; HRMS (m/z) Found: 193.1225. Calcd for $\text{C}_{12}\text{H}_{17}\text{O}_2$ $[\text{M}]^+$: 193.1229.

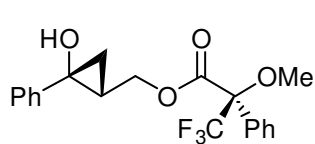
(1*R**,2*R**)-2-Hydroxymethyl-1-phenylcyclopropanol (3b)



^1H NMR (500 MHz, C_6D_6) δ 7.25–7.22 (m, 2H), 7.17–7.14 (m, 2H), 7.07–7.03 (m, 1H), 4.17 (bs, 1H), 3.86 (dd, $J = 11.5, 5.0$ Hz, 1H), 3.60 (dd, $J = 11.5, 9.0$ Hz, 1H), 3.22 (bs, 1H), 1.35–1.29 (m, 1H), 0.92–0.86 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 145.2, 128.4, 126.3, 124.6, 62.0, 59.2, 29.7, 20.9; IR (neat) 3362, 3354, 1497, 1449, 1402, 1375, 1238, 1111, 1078, 1024 cm^{-1} . HRMS (m/z) Found: 164.0837. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$:

164.0837.

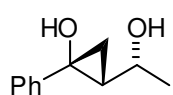
The enantiomeric excess of (*1R,2R*)-**3b** was determined by ^1H NMR after transformation into the corresponding (*S*)- α -methoxy- α -(trifluoromethyl)phenylacetate.



^1H NMR (500 MHz, CDCl_3) δ 7.37–7.23 (m, 8H), 7.15–7.12 (m, 2H), 4.67 (dd, 1H, $J = 11.5, 4.0$ Hz), 4.58 (dd, 1H, $J = 11.5, 10.0$ Hz), 3.89 (bs, 1H), 3.53 (s, 3H), 1.50–1.44 (dddd, 1H, $J = 10.0, 10.0, 7.0, 4.0$ Hz),

1.35 (dd, 1H, $J = 10.0, 6.0$ Hz), 1.14 (dd, 1H, $J = 7.0, 6.0$ Hz); ^{19}F NMR (282 MHz, CDCl_3) δ 89.7 (s).

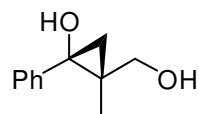
(*1R*,2R)-2-((*R**)-1-Hydroxyethyl)-1-phenylcyclopropanol (**3c**)**



^1H NMR (500 MHz, C_6D_6) δ 7.25–7.22 (m, 2H), 7.17–7.14 (m, 2H), 7.07–7.03 (m, 1H), 4.39 (bs, 1H), 3.81–3.75 (m, 1H), 3.44 (bs, 1H), 1.23 (d, $J = 6.5$ Hz, 3H),

1.20–1.14 (m, 1H), 0.89–0.85 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 145.3, 128.3, 126.3, 124.6, 69.0, 59.3, 35.5, 22.7, 21.5; IR (neat) 3363, 3273, 2362, 1602, 1498, 1451, 1235, 1077, 1022 cm^{-1} . Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$: C, 74.13; H, 7.92%. Found: C, 74.29, H, 8.03%; HRMS (m/z) Found: 178.0992. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$ $[\text{M}]^+$: 178.0994.

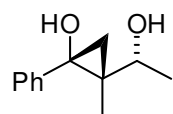
(*1S*,2R)-2-Hydroxymethyl-2-methyl-1-phenylcyclopropanol (**3d**)**



^1H NMR (300 MHz, CDCl_3) δ 7.39–7.23 (m, 5H), 3.91 (d, $J = 11.7$ Hz, 1H), 3.80 (d, $J = 11.7$ Hz, 1H), 3.06 (bs, 2H), 1.05 (s, 2H), 0.81 (s, 3H); ^{13}C NMR (75

MHz, C_6D_6) δ 140.6, 128.7, 128.6, 127.8, 67.7, 65.6, 29.5, 22.7, 19.0; IR (nujol) 3333, 3192, 1377, 1309, 1251, 1211, 1141, 1037, 1020 cm^{-1} ; mp 78.0–78.5 $^\circ\text{C}$. HRMS (m/z) Found: 178.0990. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$ $[\text{M}]^+$: 178.0994.

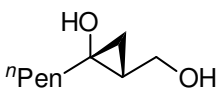
(*1S*,2R)-2-((*R**)-1-Hydroxyethyl)-2-methyl-1-phenylcyclopropanol (**3e**)**



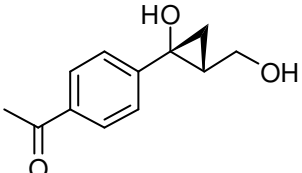
^1H NMR (500 MHz, C_6D_6) δ 7.29–7.26 (m, 2H), 7.18–7.14 (m, 2H), 7.10–7.07 (m, 1H), 4.03 (q, $J = 7.0$ Hz, 1H), 2.73 (bs, 1H), 2.62 (bs, 1H), 1.29 (d, $J = 7.0$ Hz,

2H), 0.83 (d, $J = 5.5$ Hz, 1H), 0.80 (d, $J = 5.5$ Hz, 1H), 0.70 (s, 3H); ^{13}C NMR (125 MHz, C_6D_6) δ 141.2, 128.7, 128.3, 127.4, 70.6, 65.6, 32.0, 22.3, 19.6, 14.9; IR (neat) 3358, 3350, 1446, 1290, 1227, 1130, 1099, 1074, 1047, 1026 cm^{-1} ; mp 68.5–69.3 °C. HRMS (m/z) Found: 192.1146. Calcd for $\text{C}_{12}\text{H}_{16}\text{O}_2$ $[\text{M}]^+$: 192.1150.

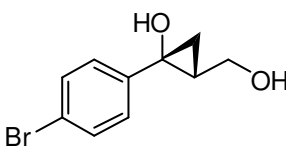
(1*R,2*R**)-2-Hydroxymethyl-1-pentylcyclopropanol (3f)**

 ^1H NMR (300 MHz, CDCl_3) δ 3.99 (dd, $J = 11.4, 5.1$ Hz, 1H), 3.59 (dd, $J = 11.4, 9.0$ Hz, 1H), 2.39 (bs, 2H), 1.56–1.46 (m, 4H), 1.35–1.26 (m, 4H), 1.07–0.97 (m, 1H), 0.89 (t, $J = 7.2$ Hz, 3H), 0.67–0.57 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 62.6, 59.0, 39.1, 31.8, 25.5, 25.4, 22.7, 17.4, 14.0; IR (neat) 3390, 3377, 2931, 2359, 1030, 1012 cm^{-1} . Anal. Calcd for $\text{C}_9\text{H}_{18}\text{O}_2$: C, 68.31; H, 11.47%. Found: C, 67.31; H, 11.08%; HRMS (m/z) Found: 158.1309. Calcd for $\text{C}_9\text{H}_{18}\text{O}_2$ $[\text{M}]^+$: 158.1307.

(1*R,2*R**)-1-(4-Acetylphenyl)-2-hydroxymethylcyclopropanol (3g)**

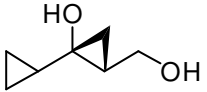
 ^1H NMR (500 MHz, CDCl_3) δ 7.85 (d, $J = 8.5$ Hz, 2H), 7.31 (d, $J = 8.5$ Hz, 2H), 4.15 (dd, $J = 11.5, 4.5$ Hz, 1H), 3.76 (dd, $J = 11.5, 9.0$ Hz, 1H), 3.71 (s, 1H), 2.56 (s, 3H), 2.55 (bs, 1H), 1.65–1.59 (m, 1H), 1.29 (dd, $J = 9.5, 6.5$ Hz, 1H), 1.22 (dd, $J = 7.0, 6.5$ Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 198.1, 150.5, 135.0, 128.5, 123.8, 62.3, 59.0, 31.0, 26.6, 22.4; IR (neat) 3381, 3362, 2359, 1667, 1605, 1566, 1406, 1360, 1277, 1238, 1111, 1030, 961, 829 cm^{-1} . Anal. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$: C, 49.41; H, 4.56%. Found: C, 49.11; H, 4.50%; HRMS (m/z) Found: 206.0942. Calcd for $\text{C}_{12}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$: 206.0943.

(1*R,2*R**)-1-(4-Bromophenyl)-2-hydroxymethylcyclopropanol (3h)**

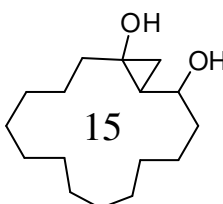
 ^1H NMR (500 MHz, CDCl_3) δ 7.43 (d, $J = 9.0$ Hz, 2H), 7.15 (d, $J = 9.0$ Hz, 2H), 4.13 (dd, $J = 11.5, 5.0$ Hz, 1H), 3.73 (dd, $J = 11.5, 9.0$ Hz, 1H), 3.19 (bs, 1H), 2.20 (bs, 1H), 1.54–1.48 (m, 1H), 1.22 (dd, $J = 9.5, 6.0$ Hz,

1H), 1.14 (dd, $J = 6.5, 6.0$ Hz); ^{13}C NMR (125 MHz, C_6D_6) δ 143.4, 131.4, 126.1, 120.3, 62.4, 59.1, 29.6, 21.2; IR (neat) 3283, 3271, 1487, 1433, 1395, 1283, 1240, 1115, 1018, 982, 918 cm^{-1} . Anal. Calcd for $\text{C}_{10}\text{H}_{11}\text{O}_2\text{Br}$: C, 49.41; H, 4.56%. Found: C, 49.11; H, 4.50%; HRMS (m/z) Found: 241.9938. Calcd for $\text{C}_{10}\text{H}_{11}\text{O}_2\text{Br}$ $[\text{M}]^+$: 241.9942.

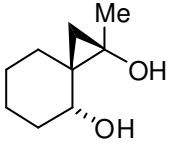
(1*R,2*R**)-1-Cyclopropyl-2-hydroxymethylcyclopropanol (3i)**

 ^1H NMR (500 MHz, CDCl_3) δ 3.98 (dd, $J = 11.5, 5.0$ Hz, 1H), 3.59 (dd, $J = 11.5, 9.0$ Hz, 1H), 2.61 (bs, 1H), 2.23 (bs, 1H), 1.33 (tt, $J = 8.0, 5.0$ Hz, 1H), 1.05–0.99 (m, 1H), 0.59 (dd, $J = 9.5, 5.5$ Hz, 1H), 0.54 (dd, $J = 6.0, 5.5$ Hz, 1H), 0.52–0.45 (m, 2H), 0.28–0.22 (m, 1H), 0.20–0.15 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 62.4, 60.2, 23.8, 17.1, 15.2, 2.69, 2.54; IR (neat) 3343, 2361, 1429, 1240, 1211, 1022, 934 cm^{-1} .

(1*R,14*R**,15*S**)-bicyclo[13.1.0]hexadecane-1,14-diol (3j)**

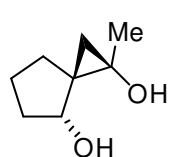
 ^1H NMR (500 MHz, CDCl_3) δ 4.05 (dt, $J = 6.0, 3.0$ Hz, 1H), 2.41 (bs, 2H), 2.12–2.05 (m, 1H), 1.75–1.71 (m, 2H), 1.58–1.25 (m, 20H), 1.02–0.88 (m, 3H), 0.62 (dd, $J = 10.0, 5.5$ Hz, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 71.2, 61.0, 39.2, 38.8, 28.1, 27.8, 27.2, 26.92, 26.85, 26.44, 26.42, 26.3, 25.9, 25.4, 24.2, 15.7; IR (nujol) 3275, 3263, 2359, 1375, 1015 cm^{-1} ; mp 70.5–71.5 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{16}\text{H}_{30}\text{O}_2$: C, 75.54; H, 11.89%. Found: C, 75.37, H, 12.03%; HRMS (m/z) Found: 255.2320. Calcd for $\text{C}_{16}\text{H}_{31}\text{O}_2$ $[\text{MH}]^+$: 255.2324.

1-methylspiro[2.5]octane-1,4-diol (3m)

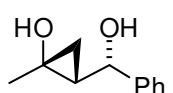
 (major isomer): ^1H NMR (500 MHz, C_6D_6) δ 4.21 (bs, 2H), 3.93–3.92 (m, 1H), 1.90–1.81 (m, 3H), 1.71–1.65 (m, 1H), 1.55–1.50 (m, 1H), 1.48–1.40 (m, 1H), 1.42 (s, 3H), 1.32–1.22 (m, 1H), 0.83 (dt, $J = 13.5, 4.5$ Hz, 1H), 0.79 (d, $J = 5.0$ Hz, 1H), 0.12 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 71.3, 59.2, 32.7, 32.0, 28.0, 24.9, 23.6, 21.5, 21.2. (minor isomer): ^1H NMR (500 MHz, C_6D_6) δ 3.40–3.30 (m, 1H), 1.90–1.84

(m, 1H), 1.79–1.73 (m, 2H), 1.70–1.61 (m, 2H), 1.59–1.51 (m, 3H), 1.55 (s, 3H), 1.42–1.34 (m, 3H), 0.56 (d, $J = 6.0$ Hz, 1H), 0.35 (d, $J = 6.0, 2.0$ Hz); ^{13}C NMR (125 MHz, C_6D_6) δ 72.1, 59.2, 32.7, 31.5, 24.7, 24.4, 24.3, 20.9, 20.0; IR (neat) 3379, 2931, 1444, 1290, 1246, 1200, 1163, 1140, 1071, 1036, 988 cm^{-1} ; HRMS (m/z) Found: 156.1148. Calcd for $\text{C}_9\text{H}_{16}\text{O}_2$ $[\text{M}]^+$: 156.1150.

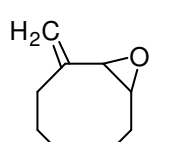
(1*R,3*R**,4*R**)-1-methylspiro[2.4]heptane-1,4-diol (3n)**

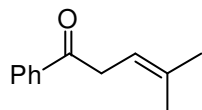
 (major isomer): ^1H NMR (500 MHz, C_6D_6) δ 4.13–4.12 (m, 1H), 3.71 (bs, 2H), 2.05–1.98 (m, 2H), 1.93–1.83 (m, 2H), 1.67–1.60 (m, 1H), 1.36 (s, 3H), 0.99–0.93 (m, 1H), 0.90–0.87 (m, 1H), 0.12 (d, $J = 5.0$ Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 81.1, 58.1, 37.9, 35.6, 30.6, 28.6, 24.0, 23.1, IR (neat) 3362, 2957, 1604, 1439, 1310, 1265, 1186, 1074, 1028, 978, 914 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{30}\text{O}_2$: C, 67.57; H, 9.92%. Found: C, 67.13; H, 9.92%.

(1*R,2*R**)-2-((*S**)-Hydroxyphenylmethyl)-1-methylcyclopropanol (3o)**

 ^1H NMR (500 MHz, CDCl_3) δ 7.47–7.45 (m, 2H), 7.24–7.20 (m, 2H), 7.14–7.10 (m, 1H), 4.63 (d, $J = 9.0$ Hz, 1H), 3.33 (bs, 2H), 1.27 (s, 3H), 0.95 (ddd, $J = 9.5, 9.0, 6.0$ Hz, 1H), 0.70 (dd, $J = 6.0, 6.0$ Hz, 1H), 0.36 (dd, $J = 9.5, 6.0$ Hz, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 143.9, 127.6, 126.5, 125.5, 74.2, 54.9, 31.7, 24.6, 18.0; IR (neat) 3345, 3335, 2359, 1454, 1265, 1074, 1015, 957, 916, 756, 698 cm^{-1} . Anal. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$: C, 74.13; H, 7.92%. Found: C, 74.07; H, 7.90%.

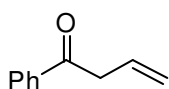
2-Methylene-9-oxabicyclo[6.1.0]nonane (4)

 ^1H NMR (300 MHz, CDCl_3) δ 5.02 (s, 1H), 4.99 (s, 1H), 3.38 (d, $J = 4.8$ Hz, 1H), 3.00 (ddd, $J = 9.9, 4.2, 4.2$ Hz, 1H), 2.25–2.21 (m, 2H), 2.06–1.98 (m, 1H), 1.70–1.14 (m, 7H); ^{13}C NMR (75 MHz, CDCl_3) δ 143.8, 112.5, 57.3, 56.4, 35.7, 27.4, 26.9, 26.4, 25.7; IR (neat) 2928, 1651, 1454, 1001, 899 cm^{-1} ; HRMS (m/z) Found: 138.1047. Calcd for $\text{C}_9\text{H}_{14}\text{O}$ $[\text{M}]^+$: 138.1045.

4-Methyl-1-phenyl-3-penten-1-one (5a)

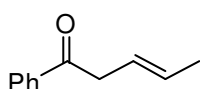
^1H NMR (300 MHz, CDCl_3) δ 7.99–7.94 (m, 2H), 7.58–7.53 (m, 1H), 7.49–7.44 (m, 2H), 5.48–5.41 (m, 1H), 3.69 (dd, $J = 7.2, 0.6$ Hz, 2H), 1.77 (s, 3H), 1.70 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 198.7, 137.1, 135.8, 133.2, 128.8, 128.6, 116.6, 38.9, 26.3, 18.7; HRMS (m/z) Found: 175.1124. Calcd for $\text{C}_{12}\text{H}_{15}\text{O}$ $[\text{MH}]^+$: 175.1123.

The spectral data of the product **5a** are in agreement with those published.²⁶

1-Phenyl-3-buten-1-one (5b)

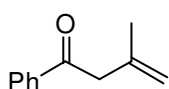
^1H NMR (500 MHz, CDCl_3) δ 7.99–7.96 (m, 2H), 7.59–7.55 (m, 1H), 7.49–7.45 (m, 2H), 6.09 (ddt, $J = 17.0, 10.5, 7.0$ Hz, 1H), 5.25–5.20 (m, 2H), 3.77 (dt, $J = 7.0, 1.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 198.0, 136.5, 133.2, 131.0, 128.6, 128.3, 118.7, 43.4. HRMS (m/z) Found: 145.0648. Calcd for $\text{C}_{10}\text{H}_9\text{O}$ $[\text{M}-\text{H}]^+$: 145.0653.

The spectral data of the product **5b** are in agreement with those published.²⁶

1-Phenyl-3-penten-1-one (5c)

^1H NMR (500 MHz, CDCl_3) δ 7.99–7.96 (m, 2H), 7.58–7.55 (m, 1H), 7.49–7.44 (m, 2H), 5.76–5.56 (m, 2H), 3.70–3.68 (m, 2H), 1.73–1.71 (m, 3H); ^{13}C NMR (75 MHz, CDCl_3) δ 198.8, 198.3, 137.0, 136.9, 133.3, 129.8, 128.9, 128.79, 128.77, 128.6, 128.5, 127.8, 123.7, 122.6, 42.9, 37.7, 18.7, 13.7. HRMS (m/z) Found: 160.0884. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}$ $[\text{M}]^+$: 160.0888.

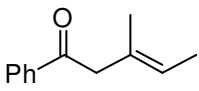
The spectral data of the product **5c** are in agreement with those published.²⁶

3-methyl-1-phenylbut-3-ene-1-one (5d)

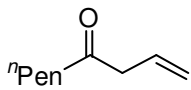
^1H NMR (500 MHz, CDCl_3) δ 8.00–7.97 (m, 2H), 7.58–7.55 (m, 1H), 7.48–7.44 (m, 2H), 5.00–4.98 (m, 1H), 4.86–4.85 (m, 1H), 3.69 (s, 2H), 1.82 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 198.1, 139.7, 136.8, 133.1, 128.5, 128.4, 115.0, 47.7, 22.8;

The spectral data of the product **5d** are in agreement with those published.²⁷

(E)-3-methyl-1-phenyl-3-penten-1-one (5e)

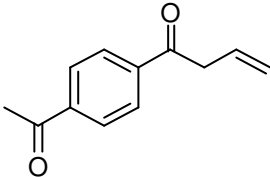
 ¹H NMR (500 MHz, CDCl₃) δ 7.99–7.97 (m, 2H), 7.57–7.53 (m, 1H), 7.47–7.43 (m, 2H), 5.39 (qqt, *J* = 7.0, 1.5, 1.5 Hz, 1H), 3.47 (t, *J* = 1.0 Hz, 2H), 1.69 (dt, *J* = 1.0, 1.0 Hz, 3H), 1.64 (dtq, *J* = 7.0, 1.5, 1.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 198.8, 136.9, 132.9, 130.0, 128.5, 128.3, 123.6, 49.2, 16.2, 13.6; IR (neat) 2918, 2363, 1683, 1597, 1448, 1333, 1278, 1202, 999 cm⁻¹. Anal. Calcd for C₁₂H₁₄O: C, 82.72; H, 8.10%. Found: C, 82.75; H, 8.13%; HRMS (*m/z*) Found: 174.1042. Calcd for C₁₂H₁₄O [*M*]⁺: 174.1045.

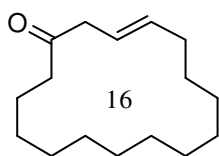
1-nonen-4-one (5f)

 ¹H NMR (500 MHz, CDCl₃) δ 5.92 (ddt, *J* = 17.0, 10.5, 7.0 Hz, 1H), 5.18 (ddt, *J* = 10.0, 1.5, 1.5 Hz, 1H), 5.13 (ddt, *J* = 17.0, 1.5, 1.5 Hz, 1H), 3.17 (ddd, *J* = 7.0, 1.5, 1.5 Hz, 2H), 2.43 (t, *J* = 7.5 Hz, 2H), 1.57 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.33–1.24 (m, 4H), 0.88 (t, *J* = 7.0 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 209.1, 130.7, 118.7, 47.7, 42.3, 31.3, 23.4, 22.4, 13.9;

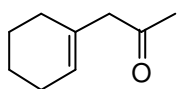
The spectral data of the product **5f** are in agreement with those published.²⁸

1-(4-Acetylphenyl)-3-buten-1-one (5g)

 ¹H NMR (500 MHz, CDCl₃) δ 8.04 (s, 4H), 6.08 (ddt, *J* = 17.0, 10.0, 7.0 Hz, 1H), 5.26 (ddt, *J* = 10.0, 1.5, 1.5 Hz, 1H), 5.23 (ddt, *J* = 17.0, 1.5, 1.5 Hz, 1H), 3.79 (ddd, *J* = 7.0, 1.5, 1.5 Hz, 2H), 2.66 (s, 3H); ¹³C NMR (125 MHz, C₆D₆) δ 197.45, 197.44, 140.2, 139.6, 130.4, 128.51, 128.46, 119.2, 43.7, 26.9; IR (neat) 2922, 2359, 1678, 1397, 1306, 1273, 1209, 1115, 928, 826 cm⁻¹. Anal. Calcd for C₁₂H₁₂O₂: C, 76.57; H, 6.43%. Found: C, 76.31, H, 6.56%; HRMS (*m/z*) Found: 188.0832. Calcd for C₁₂H₁₂O₂ [*M*]⁺: 188.0837.

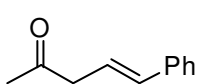
(E)-3-cyclohexadecen-1-one (5j)

^1H NMR (500 MHz, CDCl_3) δ 5.58–5.47 (m, 2H), 3.03 (d, J = 6.5 Hz, 2H), 2.49 (t, J = 7.0 Hz, 2H), 2.09 (dt, J = 6.5, 6.0 Hz, 2H), 1.59 (tt, J = 7.0, 7.0 Hz), 1.42–1.21 (m, 18H); ^{13}C NMR (125 MHz, CDCl_3) δ 210.4, 135.6, 123.2, 47.7, 40.9, 32.1, 28.2, 27.4, 27.2, 27.1, 26.9, 26.5, 26.2, 26.1, 25.6, 22.3; IR (neat) 2927, 2360, 1714, 1460, 970 cm^{-1} . Anal. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}$: C, 81.29; H, 11.94%. Found: C, 81.06; H, 11.99%; HRMS (m/z) Found: 236.2136. Calcd for $\text{C}_{16}\text{H}_{28}\text{O}$ $[\text{M}]^+$: 236.2140.

1-Cyclohexenylpropanone (5m)

^1H NMR (500 MHz, CDCl_3) δ 5.58–5.56 (m, 1H), 3.03 (s, 2H), 2.16 (s, 3H), 2.07–2.02 (m, 2H), 1.93–1.89 (m, 2H), 1.65–1.60 (m, 2H), 1.59–1.54 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.2, 131.5, 126.6, 53.4, 29.0, 28.5, 25.4, 22.7, 21.9. HRMS (m/z) Found: 138.1040. Calcd for $\text{C}_9\text{H}_{14}\text{O}$ $[\text{M}]^+$: 138.1045.

The spectral data of the product **5m** are in agreement with those published.²⁹

5-Phenyl-4-penten-2-one (5o)

^1H NMR (500 MHz, CDCl_3) δ 7.39–7.36 (m, 2H), 7.33–7.30 (m, 2H), 7.26–7.22 (m, 1H), 6.49 (d, J = 16.0 Hz, 1H), 6.30 (dt, J = 16.0, 7.0 Hz, 1H), 3.36 (dd, J = 7.0, 1.0 Hz, 2H), 2.24 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 208.0, 136.7, 134.0, 128.6, 127.6, 126.3, 121.5, 47.8, 29.6. HRMS (m/z) Found: 160.0888. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}$ $[\text{M}]^+$: 160.0888.

The spectral data of the product **5o** are in agreement with those published.³⁰

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6. Crystal structure data: Monoclinic, $a = 5.9500(9)$, $b = 22.439(3)$, $c = 17.496(3)$ Å, $\beta = 90.536(3)^\circ$, $V = 2335.9(6)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.508$ Mgm⁻³, $\lambda(\text{Mo}_{\text{K}\alpha}) = 0.71073$ Å, $T = 293(2)$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0838$ for 5098 reflections ($I > 2\sigma(I)$).
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9. Crystal structure data: Orthorhombic, $a = 6.1690(7)$, $b = 16.0965(17)$, $c = 22.395(2)$ Å, $\beta =$

- 90° , $V = 2223.8(4) \text{ \AA}^3$, $Z = 9$, $\rho_{\text{calcd}} = 1.148 \text{ Mgm}^{-3}$, $\lambda(\text{Mo}_{\text{K}\alpha}) = 0.71073 \text{ \AA}$, $T = 293(2) \text{ K}$, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0640$ for 4852 reflections ($I > 2\sigma(I)$).
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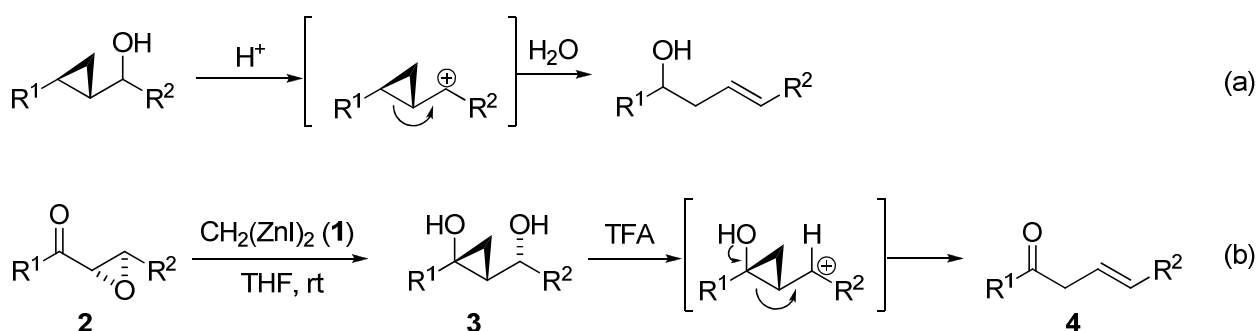
Chapter 4

A New Zincate-Mediated Rearrangement Reaction of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanol

A novel rearrangement of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol was found. It proceeds in the presence of a catalytic amount of organozinc ate complex to give *vic*-diols. The rearrangement can be applied to various types of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol, which can be prepared easily from the corresponding α,β -epoxy ketone and bis(iodozincio)methane. When bicyclo[13.1.0]pentadecane-1,15-diol was treated with organozinc ate complex, the corresponding 14-membered ring *vic*-diol was obtained. Thus, the rearrangement is also useful to change the ring size of the cyclic substrate.

Introduction

Cyclopropanes have been recognized as variants of three-carbon chain units in organic synthesis,¹ and a large number of cyclopropane ring opening reactions have been reported.² Triggered by the formation of a cation or a radical at the adjacent carbon of a cyclopropane ring, most of them proceed to release the three-membered ring strain.³ In 1960, Julia *et al.* reported acid-catalyzed ring opening isomerization of cyclopropyl alkyl carbinol (Scheme 1, (a)).⁴

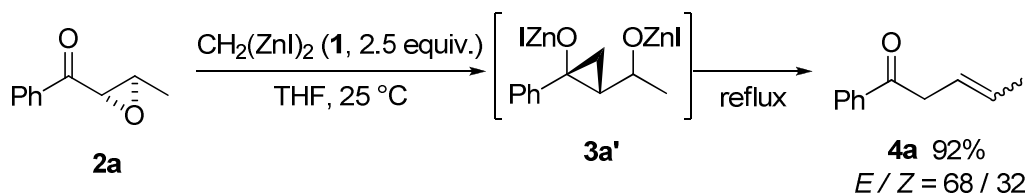


Scheme 1. Julia-type transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropane and 2-(1-hydroxyalkyl)-1-alkylcyclopropanol.

The reaction affords (*E*)-homoallylic alcohol via carbocation formation on the cyclopropyl-substituted carbon. The author had reported a preparation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3** from α,β -epoxy ketone **2** and bis(iodozincio)methane (**1**).⁵ When the Julia-type reaction was applied to 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, the carbocation-mediated ring opening reaction with trifluoroacetic acid (TFA) gives the corresponding β,γ -unsaturated ketone **4**, as shown in eq (b) in Scheme 1.^{6,7}

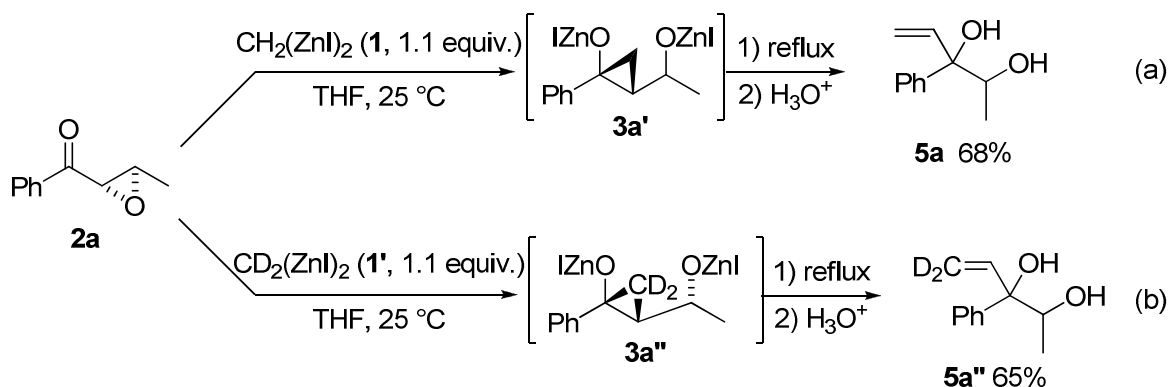
Meanwhile the author tried to convert the formed zinc alkoxide of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3a'** into the corresponding β,γ -unsaturated ketone directly, making use of the Lewis acidity of the zinc species in the reaction mixture.⁸ Actually, α,β -epoxy ketone **2a** (0.5 mmol) was treated with an excess amount of bis(iodozincio)methane (**1**,

1.25 mmol) at 25 °C; then, heating the reaction mixture to reflux for another 2 h afforded the desired β,γ -unsaturated ketone **4a** in good yield (Scheme 2).



Scheme 2. Tandem transformation of **2a** into **4a** via [2+1]cycloaddition of bis(iodozincio)methane (**1**).

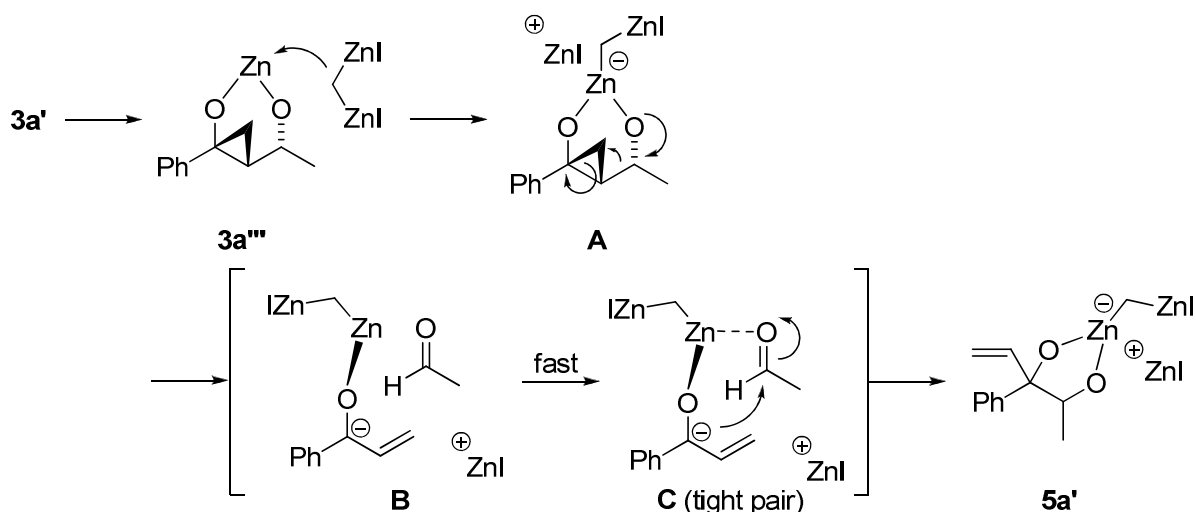
Treatment of **2a** with 1.1 equivalent amount of **1**, however, gave 2,3-dihydroxy-3-phenyl-4-pentene (**5a**) as a major product instead of the β,γ -unsaturated ketone **4a** (Scheme 3(a)).^{9,10} When the latter reaction was examined using the labeled reagent, $\text{CD}_2(\text{ZnI})_2$ (**1'**), 5,5-dideuterio-3-phenylpent-4-ene-2,3-diol **5a''** was obtained (Scheme 3(b)). The author investigated the details of this novel rearrangement.



Scheme 3. A novel rearrangement reaction of **3a'** or **3a''**.

Results and Discussion

The author speculated that the reaction proceeded via a zincate intermediate. The working hypothesis of this rearrangement is shown in Scheme 4. The zinc alkoxide **3a'''**, which was formed from **3a'** under heating, would be coordinated with the remaining **1**. The zincate **A** may fragment into aldehyde and carbanion as **B** through a strong electron-donating effect of the zincate. The two fragments, aldehyde and carbanion, will form a tight pair through zinc (**C**), and yield **5a'** via nucleophilic addition.¹¹



Scheme 4. The working hypothesis of the rearrangement.

Considering the role of zincate-complex, the author optimized the rearrangement starting from 2-hydroxymethyl-1-phenylcyclopropanol (**3b**) (Table 1). Treatment of **3b** with 2.0 equiv. of dimethylzinc (entry 2) or 3.0 equiv. of butyllithium (entry 3) resulted in the recovery of the starting material completely. One equiv. of zinc(II) chloride and 3.0 equiv. of butyllithium, however, gave the desired product in 88% yield (entry 4). The combination was expected to form a zincate-complex carrying alkoxy and butyl groups. The reaction became sluggish when the proportion of butyllithium to zinc(II) chloride was decreased (entries 5 and 6). The conditions in entries 5 and 6 would not allow formation of a zincate-complex such as

(RO)₂BuZnLi. The stoichiometric amount of zincate, ^tBu₃ZnLi^{12,13}, which can be prepared easily from ZnCl₂ and ^tBuLi, was also effective for this rearrangement (entry 7). Treatment of the prepared lithium alkoxide of **3b** with a catalytic amount of ^tBu₃ZnLi also gave **5b** (entries 8 and 9).

Table 1. The rearrangement of **3b** into **5b**.^a

Reaction scheme: **3b** (bicyclic alcohol with Ph and OH) $\xrightarrow[\text{reflux, THF, time}]{\text{reagent}}$ **5b** (acyclic alcohol with Ph and OH)

Entry	reagent	time (h)	yield (%) ^b
1	CH ₂ (ZnI) ₂ (1.0 equiv.)	3	18
2	Me ₂ Zn (2.0 equiv.)	3	0 ^c
3	BuLi (3.0 equiv.)	3	0 ^c
4	BuLi (3.0 equiv.) / ZnCl ₂ (1.0 equiv.)	3	88
5	BuLi (3.0 equiv.) / ZnCl ₂ (2.0 equiv.)	3	53
6	BuLi (2.0 equiv.) / ZnCl ₂ (1.0 equiv.)	3	0 ^d
7	^t Bu ₃ ZnLi (1.0 equiv.)	3	70
8	BuLi (2.0 equiv.) / ^t Bu ₃ ZnLi (0.2 equiv.)	6	88
9	BuLi (2.0 equiv.) / ^t Bu ₃ ZnLi (0.1 equiv.)	12	65

^a The substrate **3b** (0.5 mmol) was used. ^b Yield was determined by ¹H NMR using bromoform as internal standard. ^c The starting material was recovered completely. ^d Complex mixture was obtained.

The author traced the rearrangement of **3b** with reactIR (Figure 1).¹⁴ The reaction proceeded gradually, and almost completed after 4.5 h.

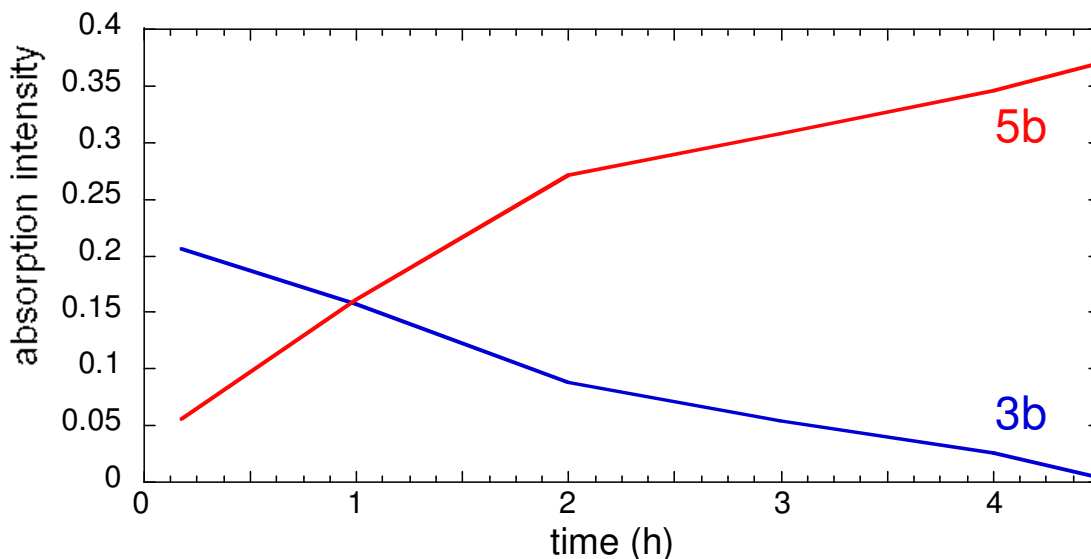


Figure 1. The result of IR during the reaction of **3b** into **5b**.

In order to determine the generality of the rearrangement, we treated various lithium alkoxides of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, with zincate complex as a catalyst (Table 2). The substrates **3c** and **3d** gave the corresponding 1,2-diols in good yields (entries 1 and 2). Cyclopropyl alkyl carbinols were also converted into the corresponding 1,2-diols in good yields with a low diastereoselectivity (entries 3-5). In the case of cyclopropyl dimethyl carbinol **3g**, the corresponding diol was obtained in 57% yield (entry 6). It is notable in this case that propiophenone was also obtained in 30% yield. Moreover, when the substrate **3h** was treated under the condition at 60 °C, 1-phenyl-1-propanone and cyclohexanone were obtained (entry 7). In this case, the rearranged product was not obtained. The ketones may come from the reaction intermediate, which corresponds to **B** in Scheme 4.¹¹

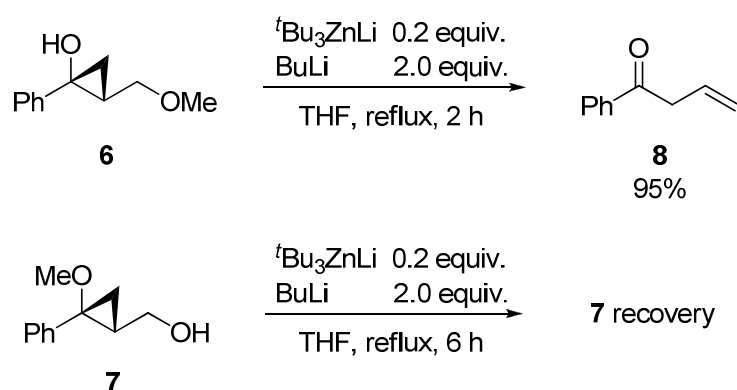
Table 2. Examples of the rearrangement of **3** into **5**.^a

Reaction scheme showing the conversion of substrate **3** to product **5** using $t\text{Bu}_3\text{ZnLi}$ (0.2 equiv.) and BuLi (2.0 equiv.) in THF, reflux.

entry	substrate	product	time (h)	yield (%) ^b
1	3c	5c	24	89
2	3d	5d	24	89
3	3a	5a	24	78 dr = 3/2 ^{c,d}
4	3e	5e	24	98 dr = 2/1 ^{c,e}
5	3f	5f	24	86 dr = 3/1 ^{c,f}
6 ^g	3g	5g	1	57 ^h
7 ⁱ	3h	5h	1	n.d. ^j

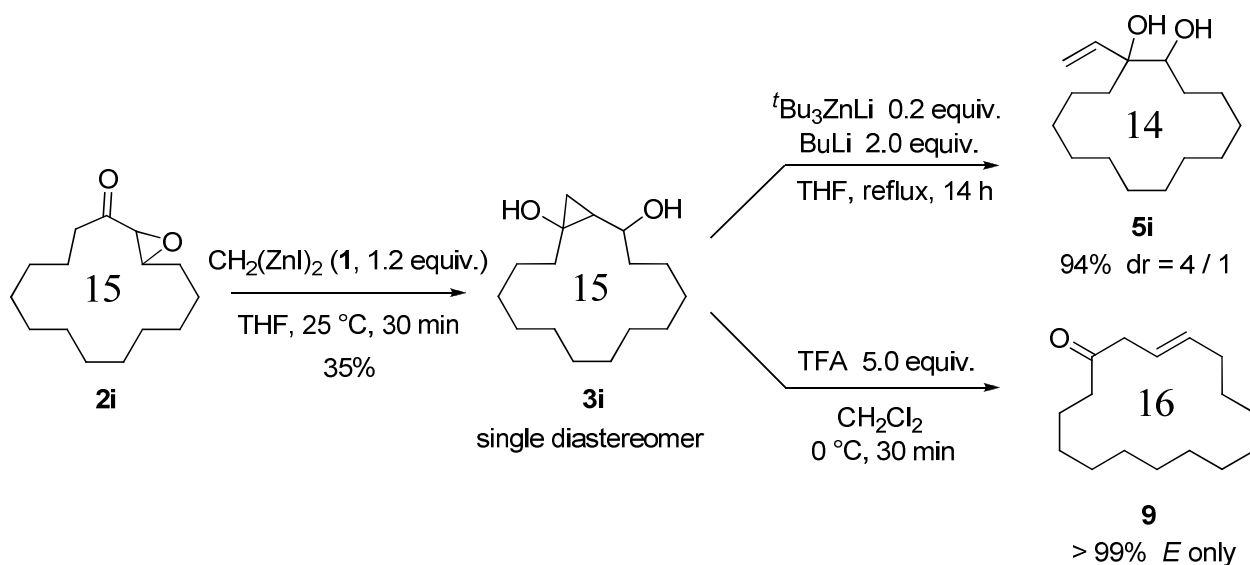
^a Substrate **3** (0.5 mmol), BuLi (1.0 mmol), $t\text{Bu}_3\text{ZnLi}$ (0.1 mmol) were used. ^b Isolated yields. ^c The diastereomeric ratios were determined by ^1H NMR. ^d The stereochemistry of major product was (2*S**,3*R**). ^e The stereochemistry of major product was (2*S**,3*S**). ^f The stereochemistry of major product was (2*S**,3*R**). ^g Reaction was carried out at 47 °C. ^h Propiophenone was also obtained in 30% yield. ⁱ Reaction was carried out at 60 °C. ^j Propiophenone and cyclohexanone was obtained in 68% and 52% yield, respectively.

As shown in Scheme 5, the author tried the rearrangement using mono-protected form of diols. The rearrangement did not proceed with the substrates carrying ether **6** or **7**. In the case of **6**, the corresponding β,γ -unsaturated ketone **8** was obtained quantitatively via cyclopropane ring-opening followed by elimination of methoxy group. Treatment of **7** resulted in complete recovery. These results imply the importance of zinc dialkoxide formation as **3a'''** in Scheme 4 for the rearrangement.



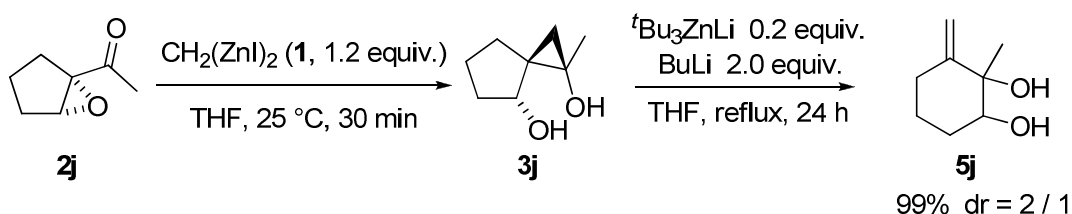
Scheme 5. The reaction of mono-protected substrate under the rearrangement condition.

When the rearrangement is applied to a lithium alkoxide of a bicyclic compound, the ring-contracting reaction occurs. In the case of bicyclo[13.1.0]hexadecane-1,14-diol (**3i**),¹⁵ the zincate-catalyzed reaction gave 14-membered diol (**5i**, 1-vinylcyclotetradecan-1,2-diol) (Scheme 6). The stereochemistry of the major product is (*1R**,*2S**). From the same substrate **3i**, the Julia-type reaction with trifluoroacetic acid gave the corresponding ring-expanded product **9**.



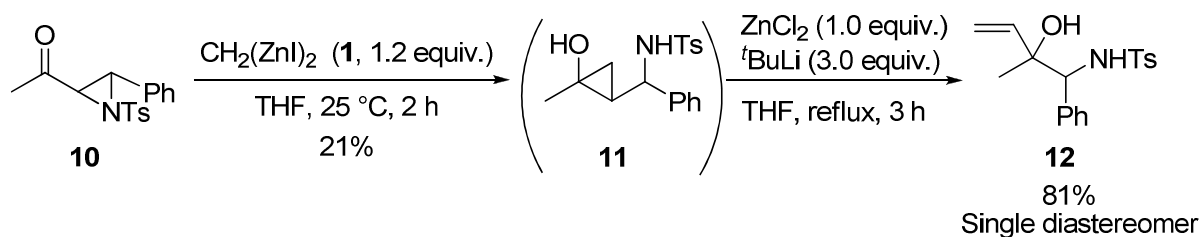
Scheme 6. The rearrangement of **3i** into **5i**.

Meanwhile, treatment of lithium alkoxide of spirocyclic diol **3j** with tBu_3ZnLi gave the corresponding ring-expanded product **5j** in good yield (Scheme 7).



Scheme 7. The rearrangement of **3j** into **5j**.

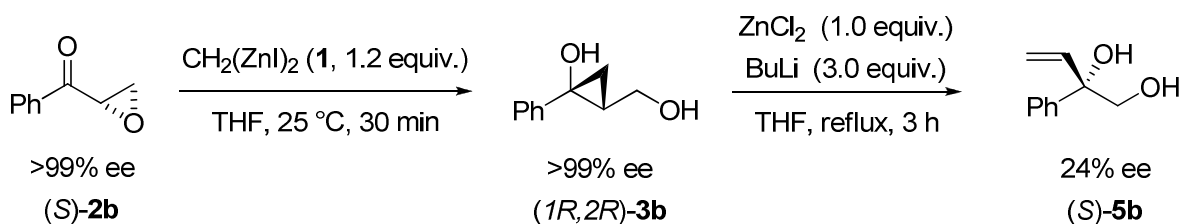
The substrate, 2-(1-hydroxyalkyl)-1-alkylcyclopropanol **3**, is prepared from the corresponding α,β -epoxy ketone **2** and dizinc **1**.⁵ The author applied this method to α,β -aziridinyl ketone **10**; the corresponding 2-(1-aminoalkyl)-1-alkylcyclopropanol **11** was obtained. This product **11** was also available as a substrate of the rearrangement, and in this case, the corresponding *vic*-amino alcohol **12** was obtained as a single isomer (Scheme 8).



Scheme 8. The transformation of **10** into **12** via [2+1]cyclization with bis(iodozincio)methane.

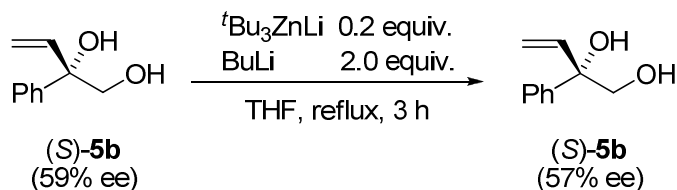
The enantioenriched **3** can be obtained easily from optically active **2**, which can be prepared via Katsuki-Sharpless asymmetric epoxidation followed by Swern oxidation. If the rearrangement proceeds in a stereospecific manner, this can be a useful method to construct enantioenriched *vic*-diols. So, the author studied the stereochemistry of the rearrangement in detail.

The reaction with the optically pure (*1R,2R*)-**3b** gave the corresponding product (*S*)-**5b**¹⁶ with a loss of enantiomeric purity (Scheme 9). The author proposes three possibilities to explain the loss of enantiomeric purity during the reaction: 1) A racemization of the product proceeds under the reaction condition; 2) the rearrangement is not stereospecific; and 3) a racemization of the substrate proceeds under the reaction condition. To clarify the cause of the loss of enantiomeric purity, the author conducted the following experiment.



Scheme 9. The rearrangement of optically active **3b**.

The obtained optically active product (*S*)-**5b** (59% ee) was treated under the same conditions as the rearrangement, and no significant loss of enantiomeric purity was detected (Scheme 10).



Scheme 10. Exposure of partially optically active (S)-**5b** under the rearrangement condition.

The author also tracked the enantiomeric purity of the substrate (*1R,2R*)-**3b** and the product (S)-**5b** during the reaction. The result is shown in Figure 2. Decreasing of the enantiomeric purity of **3b** was observed, and at the same time, that of **5b** was lost gradually. The result in Figure 2 implied that the enantiomeric purity of the product **5b** depends on that of the starting material **3b**. The rearrangement may proceed in a stereospecific manner, but the racemization of the substrate may determine the enantiomeric purity of the product.

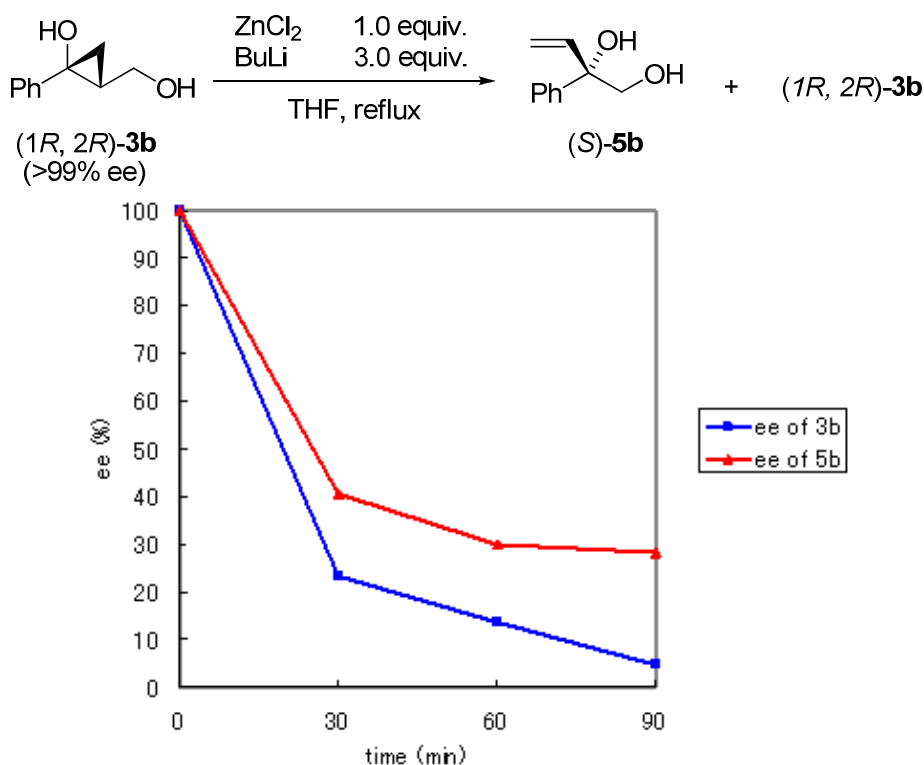
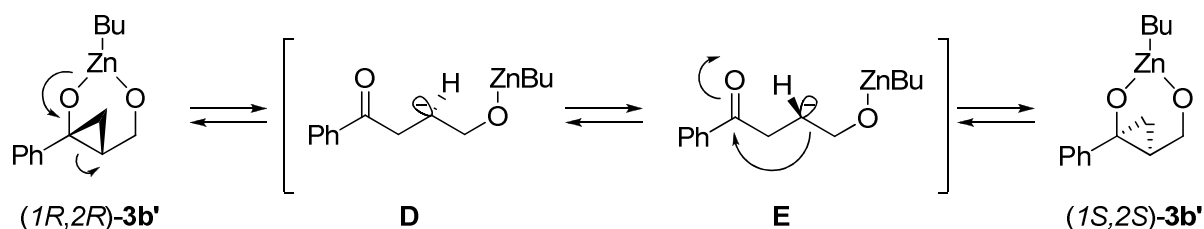


Figure 2. Tracking of ee of (*1R,2R*)-**3b** and (S)-**5b** during the reaction.

It should be noted that the diastereomer of **3b** was not observed during the reaction, although the enantiomeric purity was lost gradually. The recovered substrate at every period was *cis*-configuration. The author suppose that the racemization of **3b** proceeds as shown in Scheme 11.¹⁷ The zinc alkoxide, (*1R,2R*)-**3b'**, is converted into β -carbanion **D** via cyclopropane ring-opening with an electron-donating effect from the electron-rich zinc atom. Racemization of carbanion **D** may proceed in the THF reflux condition, and give **E**. Formation of cyclopropane ring from **E** gives the opposite enantiomer of the substrate, (*1S,2S*)-**3b'**.¹⁸



Scheme 11. Proposed mechanism of isomerization of **3b'** under the reaction condition.

Based on all these results, the author attributed the loss of enantiomeric purity of the product to the racemization of the substrate.

Conclusion

The author found some novel rearrangements of lithium alkoxides of 2-(hydroxyalkyl)-1-alkylcyclopropanols that were mediated by zincate-complex. Various types of substrates are available and the reaction can be applied for transformations of molecular skeleton. And at the same time, the author have proposed the ability of zincate complex to donate electrons.¹⁹ This electron-pushing effect may apply to other reactions.

Experimental Section

The substrates, 2-(1-hydroxyalkyl)-1-alkylcyclopropanols **3**, were prepared as mentioned in Chapter 3.⁵ In-situ IR spectra were obtained with Mettler Toledo ReactIR 45M equipped with AgX Fiber (9.5 mm).

General procedure of the rearrangement (method A): To a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3**, 1.0 mmol) and zinc chloride (1.0 mmol, 136.4 mg) in THF (8 mL), ^tBuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C. The mixture was heated to reflux. Then saturated aqueous solution of NH₄Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding *vic*-diol **5**.

General procedure of the rearrangement (method B): ^tBu₃ZnLi was prepared by liberated procedure.^{13a} To a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3**, 1.0 mmol) in THF (8 mL), ^tBuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C, and stirred for 10 min. To the solution, the prepared ^tBu₃ZnLi (THF solution, 0.2 mmol) was added at 0 °C. The mixture was heated to reflux. Then saturated aqueous solution of NH₄Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding *vic*-diol **5**.

The rearrangement using the labeled reagent, CD₂(ZnI)₂: To a solution of **2a** (1.0 mmol) in THF (4 mL), CD₂(ZnI)₂ (**1'**, 1.1 mmol) was added at room temperature, and the mixture was stirred at room temperature for 30 min. Then the mixture was heated to reflux for 2 h. To the resulting mixture, the saturated aqueous solution of NH₄Cl was added to quench the reaction and

extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give **5a''** in 65% yield (dr = 79/21) as a colorless oil.

Preparation of (*E*)-cyclohexadec-3-enone (9**):**⁶ To a solution of **3i** (1.0 mmol) in CH₂Cl₂ (4 mL), trifluoroacetic acid (5.0 mmol) was added at 0 °C, and stirred for 30 min. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give (*E*)-Cyclohexadec-3-enone (**9**, >99%).

Preparation of (*1R,*2R**)-2-(phenyl-*N*-tosylaminomethyl)-1-methylcyclopropanol (**11**):** To a solution of **10** (1.0 mmol) in THF (4 mL), bis(iodozincio)methane (**1**, 1.2 mmol) was added at room temperature. The mixture was stirred at room temperature for 30 min. The saturated aqueous solution of NH₄Cl was added to quench the reaction and the saturated aqueous solution of NaHCO₃ was added to neutralize. Then the organic layer was extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give **11** in 21% as a single diastereomer.

In-situ IR Spectra Analysis

Procedure for the rearrangement reaction of **3b:** The reaction was performed in a 50 mL round-bottomed flask equipped with a Teflon-coated magnetic stirrer bar and Dimroth reflux condenser. The top of condenser was connected with a balloon filled with argon gas (ca. 1 atm). To a solution of **3b** (1.0 mmol) in THF (8 mL), ^tBuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C, and stirred for 10 min. To the solution, the prepared ^tBu₃ZnLi (THF solution, 0.2 mmol) was added at 0 °C. The mixture was heated to reflux. The ReactIRTM probe was inserted directly into the reaction mixture. The measurement was started when the temperature of the reaction mixture was stabilized at 70 °C. The measurement was conducted every 30 sec.

(Figure 3). The consumed amount of **3b** and the generated amount of **5b** were determined by 1140–1020 cm^{-1} peak (Figure 4).

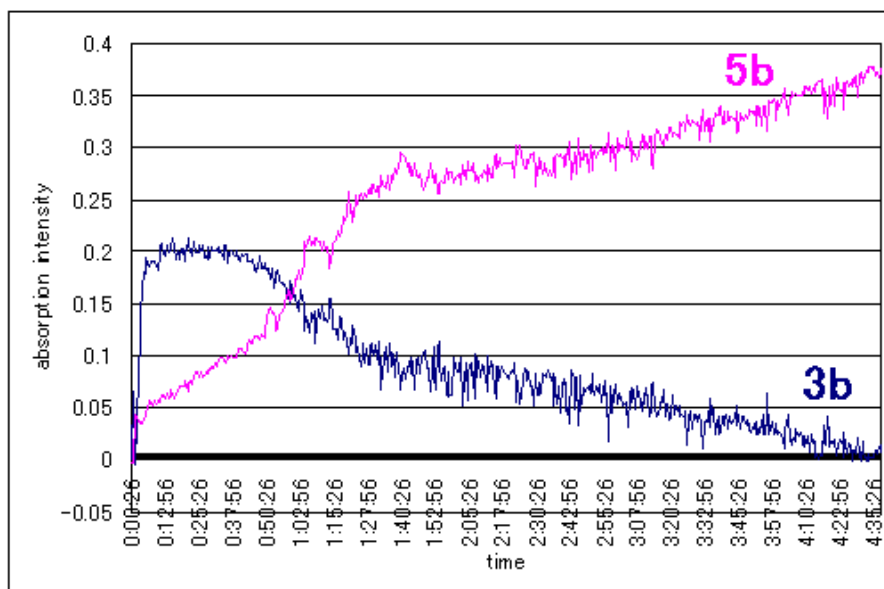


Figure 3. The absorption intensity of **3b** and **5b** plotted every 30 sec.

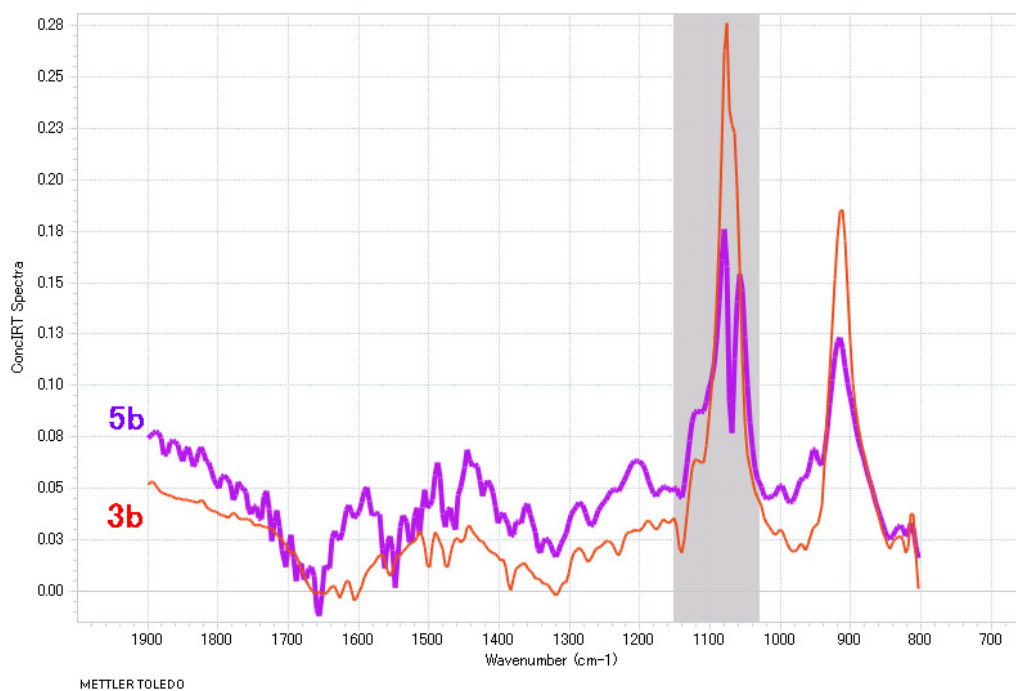


Figure 4. IR spectra of **3b** and **5b** in situ.

Tracking of ee of (*1R,2R*)-**3b** and (*S*)-**5b** during the reaction

Procedure for tracking of ee of (*1R,2R*)-3b** and (*S*)-**5b**:** To a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (**3**, 1.0 mmol) and zinc chloride (1.0 mmol) in THF (8 mL), ^tBuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C. The mixture was heated to reflux. The mixture (1 mL) was sampled every 30 min. The sampled mixture was poured into the saturated aqueous solution of NH₄Cl, and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the remained **3b** and the generated **5b**. The enantiomeric purity of (*1R,2R*)-**3b** was determined by ¹H NMR after converting into the corresponding (*S*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetate. To the solution of **3b** (0.1 mmol), dichloromethane (0.5 mL) and pyridine (0.24 mmol), (*R*)-(+)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (0.12 mmol) was added at 0 °C and stirred for 1 h. Then the solution was poured into sat. Na₂CO₃aq, and the organic layer was extracted with dichloromethane. The combined organic layers were dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding (*S*)- α -methoxy- α -(trifluoromethyl)phenylacetate. The enantiomeric excess of the product was determined by ¹H NMR focused on cyclopropyl carbinol group (the chemical shift at 4.67 ppm corresponds to (*1R,2R*)-isomer and that at 4.66 ppm, (*1S,2S*)-isomer).

¹H NMR (500 MHz, CDCl₃) δ 7.37–7.23 (m, 8H), 7.15–7.12 (m, 2H), 4.67 (dd, 1H, *J* = 11.5, 4.0 Hz), 4.58 (dd, 1H, *J* = 11.5, 10.0 Hz), 3.89 (bs, 1H), 3.53 (s, 3H), 1.50–1.44 (dddd, 1H, *J* = 10.0, 10.0, 7.0, 4.0 Hz), 1.35 (dd, 1H, *J* = 10.0, 6.0 Hz), 1.14 (dd, 1H, *J* = 7.0, 6.0 Hz); ¹⁹F NMR (282 MHz, CDCl₃) δ 89.7 (s)

Meanwhile, the enantiomeric purity of (*S*)-**5b** was determined by ¹H NMR after converting into

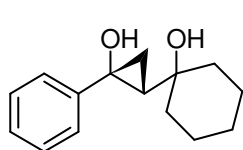
the corresponding (*S*)-(-)- α -methoxy- α -(trifluoromethyl)phenylacetate. To the solution of **5b** (0.1 mmol), dichloromethane (0.5 mL) and pyridine (0.24 mmol), (*R*)-(+)- α -methoxy- α -(trifluoromethyl)phenylacetyl chloride (0.12 mmol) was added at 0 °C and stirred for 1 h. Then the solution was poured into sat. Na₂CO₃aq, and extracted with dichloromethane. The combined organic layers were dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding (*S*)- α -methoxy- α -(trifluoromethyl)phenylacetate. The enantiomeric excess of the product was determined by ¹H NMR focused on methoxy group (the chemical shift at 3.40 ppm corresponds to (*S*)-isomer and that at 3.44 ppm, (*R*)-isomer).

¹H NMR (500 MHz, CDCl₃) δ 7.47–7.26 (m, 10H), 6.16 (dd, *J* = 17.0, 11.0 Hz, 0.33H), 6.13 (dd, *J* = 17.0, 11.0 Hz, 0.67H), 5.37 (dd, *J* = 17.0, 0.5 Hz, 0.33H), 5.35 (dd, *J* = 17.0, 0.5 Hz, 0.67H), 5.28 (dd, *J* = 11.0, 0.5 Hz, 0.33H), 5.26 (dd, *J* = 11.0, 0.5 Hz, 0.67H), 4.60 (dd, *J* = 38.5, 11.5 Hz, 1.34H), 4.59 (dd, *J* = 17.0, 11.5 Hz, 0.66H), 3.44 (d, *J* = 1.0 Hz, 0.99H), 3.40 (d, *J* = 1.0 Hz, 2.01H), 2.48 (s, 1H); ¹⁹F NMR (282 MHz, CDCl₃) δ 89.7 (s, 0.67F), 89.5 (s, 0.33F).

Characterization Data

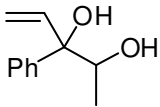
The spectral data of **7** can be found in the literature.²⁰

(1*R**,2*R**)-2-(1-Hydroxycyclohexyl)-1-phenylcyclopropanol (**3h**)

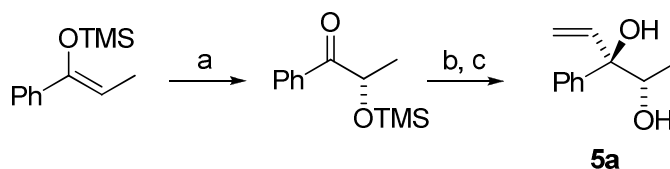


¹H NMR (500 MHz, CDCl₃) δ 7.33–7.30 (m, 2H), 7.27–7.23 (m, 2H), 7.16–7.12 (m, 1H), 3.00 (bs, 1H), 2.45 (bs, 1H), 1.87–1.84 (m, 1H), 1.79–1.70 (m, 3H), 1.58–1.36 (m, 6H), 1.23–1.15 (m, 1H), 1.07 (ddd, *J* = 10.5, 5.5, 2.0 Hz, 1H), 1.01 (dd, *J* = 10.5, 7.5 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 144.0, 127.4, 125.5, 123.9, 69.9, 59.5, 38.2, 37.6, 35.4, 25.1, 21.4, 21.1, 15.3; IR (neat) 3302, 3287, 2932, 1447, 1234, 1026, 951, 758, 696 cm⁻¹; mp 89.5–90.8 °C. Anal. Calcd for C₁₅H₂₀O₂: C, 77.55; H, 8.68%. Found: C, 77.29; H, 8.67%; HRMS (*m/z*) Found: 231.1377. Calcd for C₁₅H₁₉O₂ [M-H]⁺: 231.1385.

2,3-Dihydroxy-3-phenyl-4-pentene (5a)


¹H NMR (300 MHz, CDCl₃) δ 7.52–7.23 (m, 5H), 6.34 (dd, 0.28H, *J* = 17.1, 10.5 Hz), 6.27 (dd, 0.72H, *J* = 17.1, 10.5 Hz), 5.47 (dd, 0.28H, *J* = 17.1, 1.5 Hz), 5.46 (dd, 0.72H, *J* = 17.1, 1.5 Hz), 5.30 (dd, 0.28H, *J* = 10.5, 1.5 Hz), 5.29 (dd, 0.72H, *J* = 10.5, 1.5 Hz), 4.14 (q, 0.72H, *J* = 6.3 Hz), 4.10 (q, 0.28H, *J* = 6.3 Hz), 1.18 (d, 2.16H, *J* = 6.3 Hz), 0.97 (d, 0.84H, *J* = 6.3 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 143.8, 142.5, 139.3, 129.0, 128.8, 128.6, 127.7, 127.3, 126.3, 125.6, 115.7, 115.2, 79.7, 79.3, 73.9, 73.1, 17.4, 16.7; IR (neat) 3383, 1493, 1447, 1368, 1198, 1095 cm⁻¹. Anal. Calcd for C₁₁H₁₄O₂: C, 74.13; H, 7.92%. Found: C, 73.84; H, 8.03%; HRMS (*m/z*) Found: 178.0993. Calcd for C₁₁H₁₄O₂ [M]⁺: 178.0994.

To confirm the stereochemistry of the rearranged product **5a**, we synthesized an authentic sample of (2*S**,3*R**)-**5a** as shown in Scheme 12. Nucleophilic addition of vinylmagnesium bromide to the α-siloxyketone afforded a single isomer because of the chelation control.



Scheme 12. Synthesis of an authentic sample of **5a**: (a) mCPBA, CH₂Cl₂; (b) vinylmagnesium bromide, THF; (c) TBAF, THF.

The ORTEP figure of the authentic sample was shown in Figure 5. Compared with ¹H NMR spectrum of the authentic (2*S**,3*R**)-**5a**, it was found that the major isomer of the rearranged product **5a** was (2*S**,3*S**)-isomer.

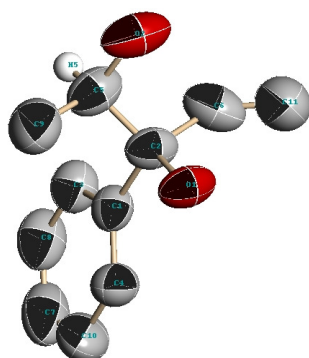


Figure 5. The ORTEP of the authentic **5a**.

For the X-ray diffraction study, a crystal was mounted on a glass fiber coated with epoxy resin. Measurements were made on a Rigaku Mercury charge-coupled device (CCD) system with graphite monochromated $\text{MoK}\alpha$ radiation. Crystal data: $M = 178.22$, Orthorhombic, Pbcn , $a = 25.693(7)$, $b = 7.699(2)$, $c = 10.478(3)$ Å, $\beta = 90^\circ$, $V = 2072.6(10)$ Å³, $Z = 9$, $\rho_{\text{calcd}} = 1.285$ Mg/m³, $\lambda(\text{MoK}\alpha) = 0.71073$ Å, $T = 293(2)$ K, $2\theta_{\text{max}} = 54.0^\circ$, $R = 0.1075$ for 2276 reflections ($I > 2\sigma(I)$).

5,5-Dideuterio-2,3-dihydroxy-3-phenyl-4-pentene (**5a''**)

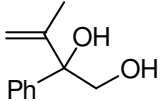
D2C=C(O)(O)C(c1ccccc1)C
¹H NMR (300 MHz, CDCl_3) δ 7.52–7.23 (m, 5H), 6.33 (bs, 0.21H), 6.26 (bs, 0.79H), 4.14 (q, 0.79H, $J = 6.3$ Hz), 4.10 (q, 0.21H, $J = 6.3$ Hz), 1.18 (d, 2.37H, $J = 6.3$ Hz), 0.97 (d, 0.63H, $J = 6.3$ Hz).

1,2-Dihydroxy-2-phenyl-3-butene (**5b**)

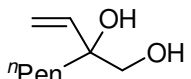
C=C(O)(O)C(c1ccccc1)C
¹H NMR (300 MHz, CDCl_3) δ 7.48–7.43 (m, 2H), 7.39–7.33 (m, 2H), 7.30–7.25 (m, 1H), 6.15 (dd, 1H, $J = 17.4, 10.5$ Hz), 5.39 (dd, 1H, $J = 17.4, 1.2$ Hz), 5.29 (dd, 1H, $J = 10.5, 1.2$ Hz), 3.78 (d, 2H, $J = 1.5$ Hz), 2.64 (bs, 2H); ¹³C NMR (75 MHz, CDCl_3) δ 142.7, 140.8, 128.7, 127.7, 125.9, 115.8, 77.8, 69.8. HRMS (m/z) Found: 164.0833. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$: 164.0837.

The spectral data are in agreement with those published.²¹

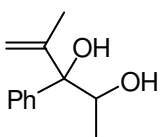
1,2-Dihydroxy-3-methyl-2-phenyl-3-butene (5c)


¹H NMR (300 MHz, CDCl₃) δ 7.47–7.25 (m, 5H), 5.16 (dq, 1H, *J* = 0.9, 0.9 Hz), 5.08 (dq, 1H, *J* = 1.2, 0.9 Hz), 4.05 (d, 1H, *J* = 11.1 Hz), 3.89 (d, 1H, *J* = 11.1 Hz), 1.64 (dd, 3H, *J* = 1.2, 0.9 Hz); ¹³C NMR (75 MHz, CDCl₃) δ 147.1, 142.2, 128.6, 127.8, 126.0, 112.2, 79.5, 68.4, 19.8; IR (neat) 3278, 1448, 1191, 1066, 1035 cm⁻¹; mp 30.0–30.5 °C. Anal. Calcd for C₁₁H₁₄O₂: C, 74.13; H, 7.92%. Found: C, 74.41; H, 7.94%; HRMS (*m/z*) Found: 178.0993. Calcd for C₁₁H₁₄O₂ [M]⁺: 178.0994.

1,2-Dihydroxy-2-vinylheptane (5d)

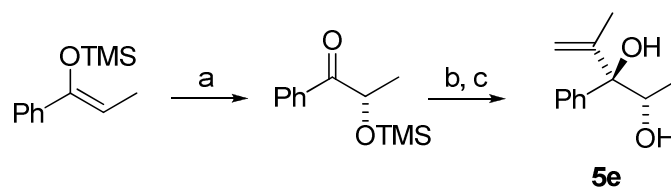

¹H NMR (300 MHz, CDCl₃) δ 5.80 (ddd, 1H, *J* = 17.4, 10.8, 0.6 Hz), 5.34 (ddd, 1H, *J* = 17.4, 1.5, 0.6 Hz), 5.25 (ddd, 1H, *J* = 10.8, 1.5, 0.6 Hz), 3.49 (s, 2H), 2.28 (bs, 1H), 1.97 (bs, 1H), 1.58–1.42 (m, 2H), 1.36–1.24 (m, 6H), 0.87 (t, 3H, *J* = 6.6 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 140.8, 115.0, 76.0, 68.7, 37.0, 32.2, 22.8, 22.5, 14.0; IR (neat) 3382, 2933, 2359, 1460, 1379, 1060 cm⁻¹. Anal. Calcd for C₉H₁₈O₂: C, 68.31; H, 11.47%. Found: C, 68.04; H, 11.54%; HRMS (*m/z*) Found: 157.1233. Calcd for C₉H₁₇O₂ [M-H]⁺: 157.1229.

2,3-Dihydroxy-4-methyl-3-phenyl-4-pentene (5e)


¹H NMR (500 MHz, CDCl₃) δ 7.57–7.20 (m, 5H), 5.28 (dq, 0.72H, *J* = 1.0, 1.0 Hz), 5.24 (dq, 0.28H, *J* = 1.0, 1.0 Hz), 5.07 (dq, 0.28H, *J* = 1.5, 1.0 Hz), 4.89 (dq, 0.72H, *J* = 1.5, 1.0 Hz), 4.61 (q, 0.72H, *J* = 6.0 Hz), 4.49 (q, 0.28H, *J* = 6.0 Hz), 1.65 (dd, 0.84H, *J* = 1.5, 1.0 Hz), 1.56 (dd, 2.16H, *J* = 1.5, 1.0 Hz), 1.24 (d, 2.16H, *J* = 6.0 Hz), 0.93 (d, 0.84H, *J* = 6.0 Hz); ¹³C NMR (125 MHz, CDCl₃) δ 149.1, 146.5, 143.7, 141.4, 128.3, 127.9, 127.2, 126.9, 126.1, 125.3, 110.8, 110.7, 80.9, 80.8, 70.0, 69.2, 19.4, 19.3, 16.5, 16.4; IR (neat) 3458 cm⁻¹. Anal. Calcd for C₉H₁₈O₂: C, 74.97; H, 8.39%. Found: C, 74.91; H, 8.56%.

To confirm the stereochemistry of the rearranged product **5e**, we synthesized an authentic sample

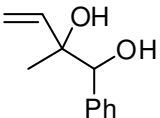
of (2*R**,3*S**)-**5e** as shown in Scheme 13. Nucleophilic addition of α -methylvinylmagnesium bromide to the α -siloxyketone afforded a single isomer because of the chelation control.



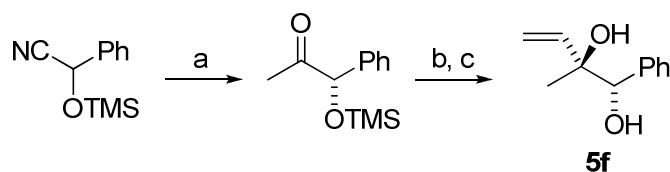
Scheme 13. Synthesis of an authentic sample of **5e**: (a) mCPBA, CH₂Cl₂; (b) α -methylvinylmagnesium bromide, THF; (c) TBAF, THF.

Compared with ¹H NMR spectrum of the authentic (2*R**,3*S**)-**5e**, it was found that the major isomer of the rearranged product **5e** was (2*S**,3*S**)-isomer.

1,2-Dihydroxy-2-methyl-1-phenyl-3-butene (**5f**)

 ¹H NMR (300 MHz, CDCl₃) δ 7.35–7.25 (m, 5H), 5.86 (dd, 1H, J = 17.4, 10.8 Hz), 5.25 (dd, 1H, J = 17.4, 1.5 Hz), 5.16 (dd, 1H, J = 10.8, 1.5 Hz), 2.17 (s, 1H), 1.27 (s, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 140.4, 128.22, 128.17, 128.0, 127.8, 114.9, 80.9, 76.1, 24.8; IR (neat) 3406, 2982, 1453, 1374, 1174, 1045 cm⁻¹. Anal. Calcd for C₁₁H₁₄O₂: C, 74.13; H, 7.92%. Found: C, 74.00; H, 8.11%.

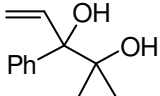
To confirm the stereochemistry of the rearranged product **5f**, we synthesized an authentic sample of (2*R**,3*R**)-**5f** as shown in Scheme 14. Nucleophilic addition of vinylmagnesium bromide to the α -siloxyketone afforded a single isomer because of the chelation control.



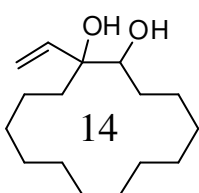
Scheme 14. Synthesis of an authentic sample of **5f**: (a) methylmagnesium iodide, Et₂O; (b) vinylmagnesium bromide, THF; (c) HCl(aq).

Compared with ¹H NMR spectrum of the authentic (2*R**,3*R**)-**5f**, it was found that the major isomer of the rearranged product **5f** was (2*R**,3*R**)-isomer.

2,3-Dihydroxy-2-methyl-3-phenyl-4-pentene (**5g**)

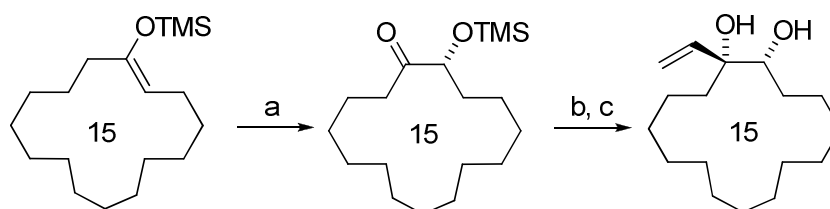
 ¹H NMR (300 MHz, CDCl₃) δ 7.57–7.53 (m, 2H), 7.37–7.23 (m, 3H), 6.74 (dd, *J* = 17.1, 10.8 Hz, 1H), 5.47 (dd, *J* = 17.1, 1.5 Hz, 1H), 5.34 (dd, *J* = 10.8, 1.5 Hz, 1H), 1.27 (d, *J* = 0.3 Hz, 3H), 1.10 (d, *J* = 0.3 Hz, 3H); ¹³C NMR (75 MHz, CDCl₃) δ 142.7, 140.5, 128.0, 127.4, 127.3, 115.8, 80.9, 75.9, 25.8, 25.0; IR (neat) 3462, 3326, 1446, 1360, 1161, 1008 cm⁻¹; mp 45.3–46.0 °C. Anal. Calcd for C₁₂H₁₆O₂: C, 74.97; H, 8.39%. Found: C, 74.70; H, 8.38%.

1,2-Dihydroxy-1-vinylcyclobutadecane (**5i**)

 ¹H NMR (500 MHz, CDCl₃) δ 5.92 (dd, 1H, *J* = 17.5, 10.5 Hz), 5.37 (dd, 1H, *J* = 17.5, 1.5 Hz), 5.23 (dd, 1H, *J* = 10.5, 1.5 Hz), 3.72 (d, 1H, *J* = 10.0 Hz), 1.71–1.04 (m, 24H); ¹³C NMR (125 MHz, CDCl₃) δ 140.5, 115.0, 77.5, 74.4, 36.9, 28.6, 26.43, 26.35, 25.8, 24.5, 23.7, 23.6, 23.5, 23.4, 19.2; IR (neat) 3325, 2922, 2359, 1456, 1377, 1043 cm⁻¹; mp 107.5–108.5 °C. Anal. Calcd for C₁₆H₃₀O₂: C, 75.54; H, 11.89%. Found: C, 75.26; H, 11.98%; HRMS (*m/z*) Found: 254.2247. Calcd for C₁₆H₃₀O₂ [M]⁺: 254.2246.

To confirm the stereochemistry of the rearranged product **5i**, we synthesized an authentic sample

of (*1R*,2R**)-1,2-dihydroxy-1-vinylcyclopentadecane as shown in Scheme 15. Nucleophilic addition of vinylmagnesium bromide to the α -siloxyketone afforded a single isomer because of the chelation control.



Scheme 15. Synthesis of an authentic sample of 1,2-dihydroxy-1-vinylcyclopentadecane: (a) mCPBA, CH_2Cl_2 ; (b) vinylmagnesium bromide, THF; (c) TBAF, THF.

Compared with ^1H NMR spectrum of the authentic (*1R*,2R**)-**5i**, it can be speculated that the major isomer of the rearranged product **5i** was (*1R*,2S**)-isomer.

1-Methyl-6-methylenecyclohexane-1,2-diol (**5j**)

major isomer (*syn*): ^1H NMR (500 MHz, C_6D_6) δ 5.16 (t, 1H, $J = 1.0$ Hz), 4.85 (s, 1H), 3.40 (s, 1H), 2.53 (bs, 1H), 2.33 (bs, 1H), 2.25–2.21 (m, 1H), 1.92–1.87 (m, 1H), 1.70–1.65 (m, 1H), 1.64–1.56 (m, 1H), 1.51–1.45 (m, 1H), 1.23 (s, 3H), 1.24–1.16 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 151.7, 108.9, 76.0, 74.5, 32.7, 30.3, 24.1, 22.5; IR (nujor) 3307, 2363, 1456, 1377, 1108, 1057 cm^{-1} ; mp 64.8–66.0 $^\circ\text{C}$. Anal. Calcd for $\text{C}_8\text{H}_{14}\text{O}_2$: C, 67.57; H, 9.92%. Found: C, 67.32; H, 9.64%; HRMS (m/z) Found: 142.0994. Calcd for $\text{C}_8\text{H}_{14}\text{O}_2$ [M] $^+$: 142.0994. minor isomer (*anti*): ^1H NMR (500 MHz, C_6D_6) δ 5.32 (s, 1H), 4.81 (t, 1H, $J = 1.5$ Hz), 3.82 (bs, 1H), 3.56 (dd, 1H, $J = 11.0, 5.0$ Hz), 3.38 (bs, 1H), 2.08–2.05 (m, 1H), 1.94–1.88 (m, 2H), 1.49–1.39 (m, 2H), 1.35 (s, 3H), 1.22–1.13 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 152.9, 107.4, 77.8, 77.4, 33.1, 31.5, 24.6, 20.0; HRMS (m/z) Found: 142.0994. Calcd for $\text{C}_8\text{H}_{14}\text{O}_2$ [M] $^+$: 142.0994.

The ORTEP of the ester obtained from 3,5-dinitrobenzoyl chloride and minor isomer of **5j** is shown in Figure 6.

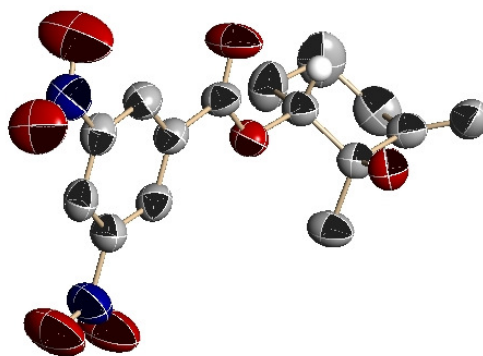
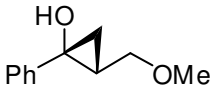


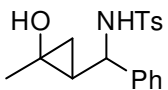
Figure 6. The ORTEP of derivative of **5j** (minor isomer).

Crystal data: $M = 336.30$, Monoclinic, $C2/c$, $a = 11.942(2)$, $b = 12.265(3)$, $c = 22.611(5)$ Å, $\beta = 102.343(4)^\circ$, $V = 3235.5(11)$ Å³, $Z = 8$, $\rho_{\text{calc}} = 1.381$ Mg/m³, λ (MoK α) = 0.71073 Å, $T = 296$ K, $2\theta_{\text{max}} = 54.0^\circ$, $R = 0.0569$ for 7050 reflections ($I > 2\sigma(I)$)

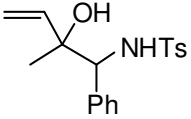
(1*R,2*R**)-2-Methoxymethyl-1-phenylcyclopropanol (6)**

 ¹H NMR (500 MHz, CDCl₃) δ 7.36–7.19 (m, 5H), 3.89 (dd, $J = 10.2, 5.4$ Hz, 1H), 3.59 (dd, $J = 10.2, 8.4$ Hz, 1H), 3.37 (s, 3H), 2.97 (bs, 1H), 1.64–1.54 (m, 1H), 1.26 (dd, $J = 9.6, 6.0$ Hz, 1H), 1.16 (dd, $J = 6.6, 6.0$ Hz, 1H).

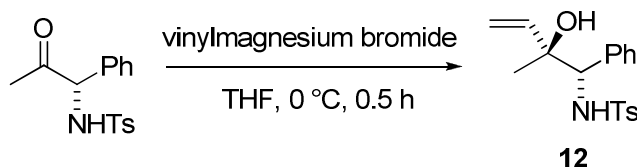
2-(Phenyl-*N*-tosylaminomethyl)-1-methylcyclopropanol (11)

 ¹H NMR (300 MHz, C₆D₆) δ 7.66 (d, 2H, $J = 8.4$ Hz), 6.97–6.89 (m, 5H), 6.68 (d, 2H, $J = 8.4$ Hz), 5.50 (d, 1H, $J = 6.3$ Hz), 4.39 (dd, 1H, $J = 9.3, 6.3$ Hz), 1.84 (s, 3H), 1.41 (s, 3H), 1.01 (ddd, 1H, $J = 9.3, 6.3, 6.0$ Hz), 0.57 (dd, 1H, $J = 6.0, 6.0$ Hz), 0.32 (dd, 1H, $J = 9.3, 6.0$ Hz).

2-Hydroxy-2-methyl-1-phenyl-1-*p*-toluenesulfonamino-3-butene (12)


¹H NMR (500 MHz, C₆D₆) δ 7.51–7.49 (m, 2H), 6.85–6.79 (m, 3H), 6.72–6.70 (m, 2H), 6.54–6.53 (m, 2H), 5.46 (dd, 1H, *J* = 17.5, 11.0 Hz), 5.39 (d, 1H, *J* = 8.5 Hz), 5.00 (dd, 1H, *J* = 17.5, 1.5 Hz), 4.78 (dd, 1H, *J* = 11.0, 1.5 Hz), 4.36 (d, 1H, *J* = 8.5 Hz), 1.78 (s, 3H), 1.17 (s, 3H), 0.45 (s, 1H); ¹³C NMR (125 MHz, C₆D₆) δ 141.3, 139.8, 137.7, 136.8, 128.1, 127.4, 127.3, 126.4, 126.2, 113.4, 74.1, 65.1, 25.0, 19.9; IR (nujol) 3480, 3245, 1377, 1318, 1158, 1089 cm⁻¹; mp 98.7–99.5 °C. Anal. Calcd for C₁₈H₂₁NO₃S: C, 65.23; H, 6.39%. Found: C, 65.27; H, 6.42%; HRMS (*m/z*) Found: 332.1320. Calcd for C₁₈H₂₂NO₃S [MH]⁺: 332.1320.

To confirm the stereochemistry of the rearranged product **12**, we synthesized an authentic sample as shown in Scheme 16. Nucleophilic addition of vinylmagnesium bromide to the α-aminoketone proceeded via the chelation control, and (2*R**,3*R**)-isomer was obtained.



Scheme 16. Synthesis of an authentic sample of **12**.

Compared with ¹H NMR spectrum of the authentic (2*R**,3*R**)-**12**, it was found that the obtained product **12** was (2*R**,3*R**)-isomer as a single diastereomer.

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14. The measurement of reactIR was conducted every 30 sec. Figure 1 shows the absorption intensity of **3b** and **5b** plotted every 30 min to simplify the figure.
 15. Although **3i** was used as a single diastereomer form, we could not determine the relative stereochemistry of **3i**.
 16. Compared with the result of specific rotation of the literature, it was found that the obtained **5b** has (*S*)-configuration. See: M. E. Vargas-Diaz, L. Chacon-Garcia, P. Valezquez, J. Tamariz, P. Joseph-Nathan, L. G. Zepeda, *Tetrahedron: Asymmetry* **2003**, 14, 3225.
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 19. Kondo and Uchiyama have reported the directed ortho metalation of aromatic compounds, such as ethyl benzoate, with di-*tert*-butyl-TMP zincate (LiZn(TMP)^tBu₂). The reaction affords *o*-zincated aromatic compound directly. This reactivity is contrast to the low basicity found for conventional zinc reagents. Because ligand on the zinc atom of the zincate has stronger basicity than that on conventional zinc reagents, we are expecting that a ligand of zincate complex, such as an alkoxy group, has an ability as electron-donor. See,

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Chapter 5

Stereospecific Construction of Chiral Tertiary and Quaternary Carbon by Nucleophilic Cyclopropanation with Bis(iodozincio)methane

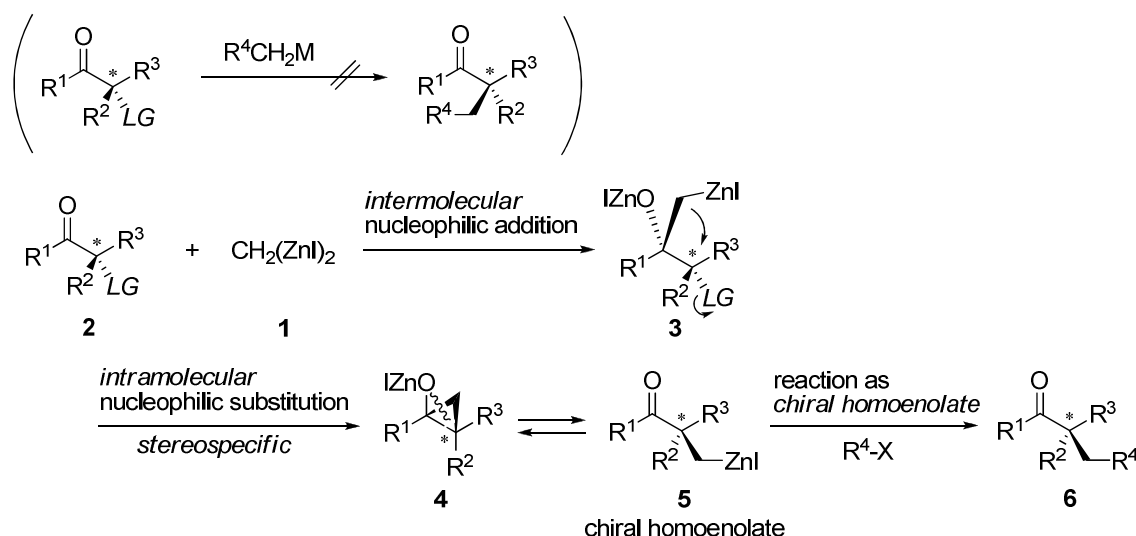
The reaction of a ketone having a leaving group at α -position, such as α,β -epoxy ketone or α -sulfonyloxy ketone, with bis(iodozincio)methane afforded a zinc alkoxide of cyclopropanol. The reaction proceeded by nucleophilic addition of the dizinc to the carbonyl group, and a sequential intramolecular nucleophilic substitution of the introduced iodozinciomethyl group to the adjacent electrophilic carbon that has a leaving group. When an optically active α,β -epoxy ketone or α -sulfonyloxy ketone was treated with the dizinc, a zinc alkoxide of cyclopropanol having a chiral tertiary or quaternary carbon in the cyclopropane ring was obtained. The obtained zinc alkoxide of cyclopropanol acts as a chiral homoenolate, and the treatment of it with an electrophile in the presence of copper cyanide gave an optically active α -tertiary or -quaternary ketone that retained high optical purity.

Introduction

The stereoselective construction of chiral tertiary and quaternary carbon is still a challenging subject in organic syntheses.¹ Among several important strategies, one of the most attractive routes would be a stereospecific substitution reaction of carbon nucleophile with an optically active secondary and tertiary carbon atom having a leaving group. This method, however, contains an unavoidable problem: An intermolecular S_N2 reaction by a carbon nucleophile would be difficult when there is a steric hindrance around the electrophilic carbon. Especially with the tertiary electrophilic carbon (R_3C-X), the S_N2 reaction does not proceed. However, in cases of intramolecular reactions, an S_N2 reaction, which affords a cyclopropane compound, proceeds efficiently and stereospecifically, even in the case of a substrate having a leaving group on a tertiary carbon.² Although the method seems to be attractive to construct a tertiary or quaternary carbon in a cyclopropane ring, it is not easy to prepare a substrate that has both a nucleophilic carbon and an optically active secondary or tertiary electrophilic carbon in the same molecule. As one idea for the preparation, the author proposed the nucleophilic addition of bis(iodozincio)methane (**1**)³, which possesses a couple of carbon–zinc bonds on a carbon atom, to a carbonyl group of a ketone carrying an enantiomeric enriched stereogenic center containing a leaving group at α -position, such as α,β -epoxy ketone⁴ or α -sulfonyloxy ketone⁵.

The author have already reported an efficient route for cyclopropane ring formation by a sequential nucleophilic reaction of bis(iodozincio)methane (**1**):⁴⁻⁶ As shown in Scheme 1, when α,β -epoxy ketone or α -sulfonyloxy ketone was treated with **1**, its nucleophilic addition to the carbonyl group proceeds and introduces a iodozinciomethyl group to adjacent carbon of the original stereogenic center (**3** in Scheme 1). The intermediate **3** would lead to a sequential intramolecular nucleophilic attack to afford a cyclopropane derivative. The intramolecular S_N2 reaction to a target tertiary carbon proceeds stereospecifically to afford the zinc alkoxide of cyclopropanol **4**, which has a quaternary center. So, treatment of an optically active substrate **2** with **1** afforded the zinc alkoxide of cyclopropanol **4**, which has the enantiomeric enriched

tertiary or quaternary carbon. Moreover, the obtained chiral zinc alkoxide of cyclopropanol can work as a homoenolate **5** by a ring opening.⁷ Treatment of an electrophile with the homoenolate **5** would afford an optically active α -tertiary or -quaternary ketone **6** that retains high enantiomeric purity.



Scheme 1. Strategy for construction of chiral tertiary or quaternary center at α -position of ketone via nucleophilic cyclopropanation with bis(iodozincio)methane (**1**).

Thus, the author attempted the preparation an optically active homoenolate equivalent by the reaction of a ketone that has stereogenic center containing a leaving group at α -position with **1**. The process leads to the sequential reaction of the obtained chiral homoenolate with an electrophile to prepare a ketone having optically active tertiary or quaternary carbon at α -position.

Results and Discussion

To prepare a homoenolate equivalent, the author treated ketones having leaving groups at α -position with bis(iodozincio)methane (**1**) as shown in Table 1. A solution of α -tosyloxy

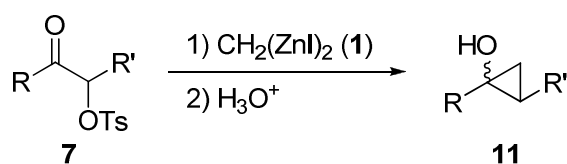
ketone (**7a**, 1.0 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 1.2 mmol, 0.5 M in THF) at 25 °C. After being stirred for 2 h, the mixture was quenched with a saturated aqueous solution of NH₄Cl. Purification by a silica gel column chromatography gave 1-phenyl-1-cyclopropanol (**11a**) and 1-phenyl-1-propanone (**12a**) (Table 1, entry 1). The ketone **12a** was generated by a cyclopropane ring opening by treatment with acid. When the α -tosyloxy ketone **7a** was treated with 3 equiv. amounts of the dizinc **1**, the substrate was consumed completely to convert the reactants into **11a** and **12a** (entry 3). Instead of α -tosyloxy ketone, the reaction of α -acetoxy ketone **8** with the dizinc **1** resulted in the complete recovery of the starting material (entry 4). Although a reaction of α -bromoketone **9** with the dizinc **1** afforded **11a** and **12a**, it proceeded sluggishly (entry 5). A reaction of α -iodoketone **10** with the dizinc **1** gave a complex mixture (entry 6).

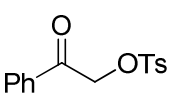
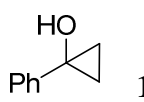
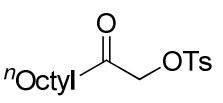
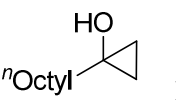
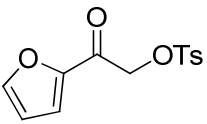
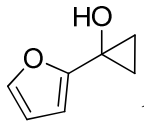
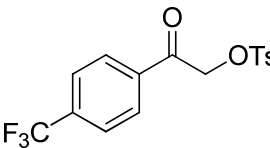
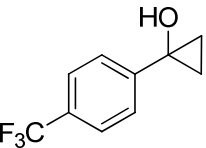
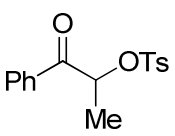
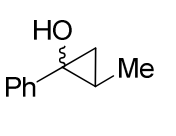
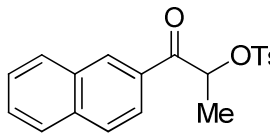
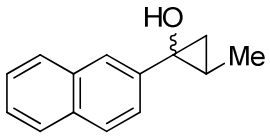
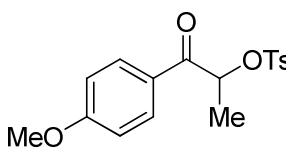
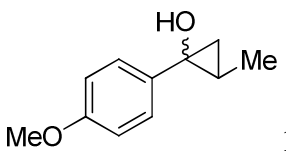
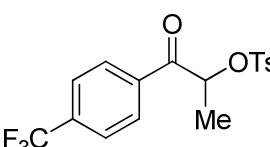
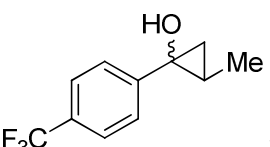
Table 1. Reactions of ketones having leaving group at α -position with bis(iodozincio)methane (**1**).^a

entry	X	y (equiv.)	t (h)	yield of 11a (%) ^b	yield of 12a (%) ^b
1 ^c	OTs (7a)	1.2	2	9	34
2	OTs (7a)	2.0	2	32	31
3	OTs (7a)	3.0	2	56	43
4 ^d	OAc (8)	3.0	2	0	0
5	Br (9)	3.0	15	17	21
6 ^e	I (10)	3.0	15	0	0

^a A ketone (**7-10**, 1.0 mmol), the dizinc **1** (0.5 M in THF), and THF (4 mL) were used. ^b Yields were determined by ¹H NMR using bromoform as internal standard. ^c The starting material was also obtained in 50% yield. ^d The starting material was recovered completely. ^e Complex mixture was obtained.

Other examples of the reaction of α -tosyloxy ketones with the dizinc **1** are shown in Table 2. In the cases of **7a-c**, ketones **12** were also obtained as by-products (entries 1-3). When the reaction of **1** and **7a** was quenched by chlorotrimethylsilane instead of by an aqueous solution of NH_4Cl , 1-phenyl-1-trimethylsiloxycyclopropane (**13**) was obtained in a high yield (Scheme 2). In the case of α -methyl- α -tosyloxy ketones **7e-h**, the reactions gave the 1-alkyl-2-methylcyclopropanols **11e-h** in high yields (entries 5-8). The obtained 2-alkylcyclopropanols **11e-h**, however, were diastereomeric mixtures (entries 5-8). After the nucleophilic addition of **1** to carbonyl group of **7**, the intramolecular $\text{S}_{\text{N}}2$ reaction of the existing iodozinciomethyl group to the adjacent stereogenic center that has a tosyloxy group will proceed in stereospecific $\text{S}_{\text{N}}2$ manner. So, the diastereofacial selectivity in nucleophilic addition of **1** to carbonyl group of **7e-h** would determine the diastereomeric ratio of **11e-h**. However, when the zinc alkoxides of cyclopropanols **11e-h** are utilized as zinc homoenolate equivalents, the stereogenic centers at oxygen atom-substituted carbon of zinc alkoxide of cyclopropanol will be converted into carbonyl groups retaining the chirality of tertiary carbon at α -position.^{7e} So the poor diastereofacial selectivity of the nucleophilic attack to carbonyl group will not be significant, when the reaction as zinc homoenolate is carried out as shown in Scheme 1.

Table 2. The reaction of α -tosyloxy ketone **7** with the dizinc **1**.^a

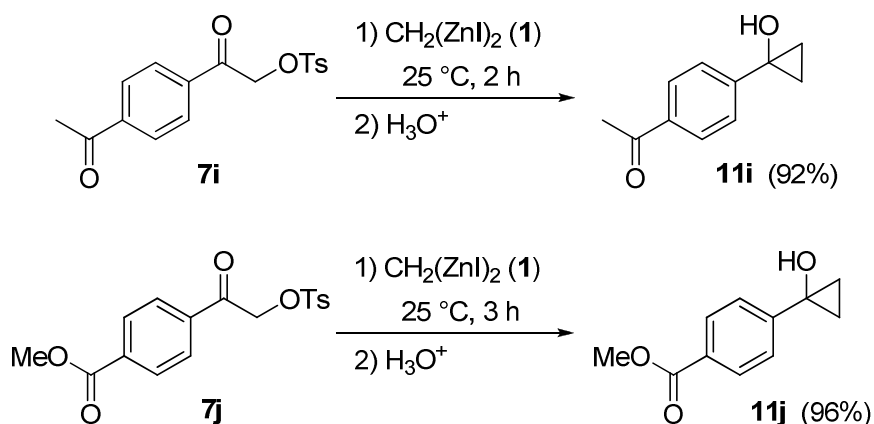
entry	substrate	product	t (h)	yield (%) ^b	d.r. ^c
1	 7a	 11a	2	56 ^d	
2	 7b	 11b	15	31 ^e	
3	 7c	 11c	12	38 ^f	
4	 7d	 11d	2	95	
5	 7e	 11e	10	86	76/24 ^g
6	 7f	 11f	15	99	67/33 ^g
7	 7g	 11g	20	81	67/33 ^g
8	 7h	 11h	4	88	72/28 ^g

^a A α -tosyloxy ketone **7** (1.0 mmol), the dizinc **1** (3.0 mmol, 0.5 M in THF), and THF (4 mL) were used. ^b Isolated yields. ^c The diastereomeric ratios were determined by ¹H NMR. ^d Propiophenone was also obtained in 43% yield. ^e 3-Undecanone was also obtained in 59% yield. ^f 1-(2-Furyl)-1-propanone was also obtained in 50% yield. ^g Stereochemistry of cyclopropane ring in major isomer was *trans*.



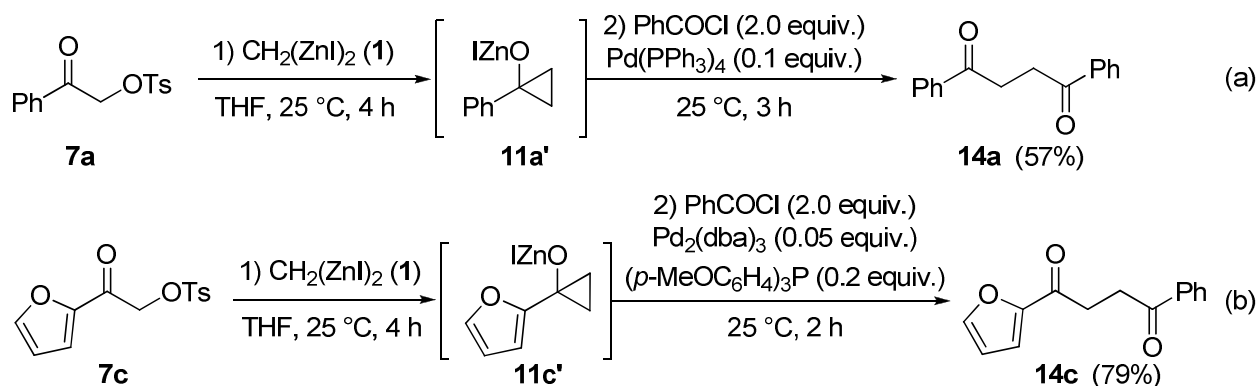
Scheme 2. Quench of the reaction mixture of **7a** and **1** with chlorotrimethylsilane.

Functional group tolerability of the transformation into cyclopropanols was demonstrated as shown in Scheme 3. It can be performed even in the presence of another carbonyl group in the substrate. The reaction of α -tosyloxy ketone having an additional carbonyl group, such as **7i** and **7j**, with **1** proceeded chemoselectively to give the corresponding cyclopropanols (**11i** and **11j**) in good yields without affecting the other carbonyl groups, as shown in Scheme 3.



Scheme 3. The reaction of **7i** or **7j** with **1**.

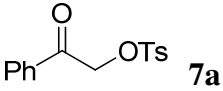
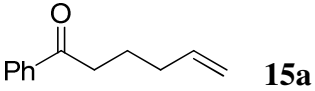
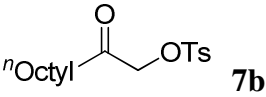
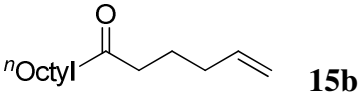
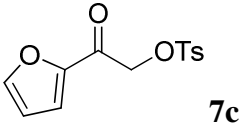
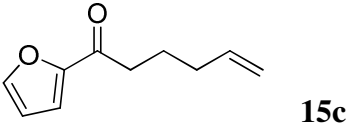
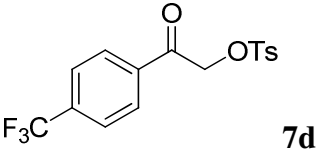
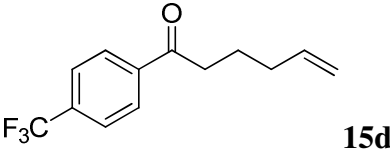
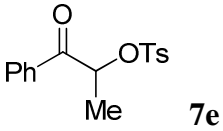
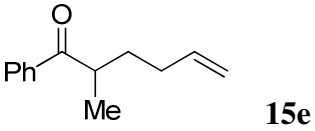
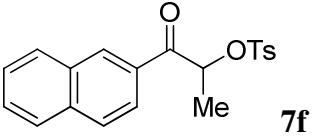
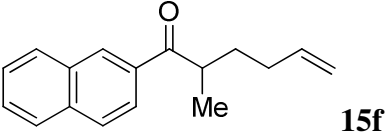
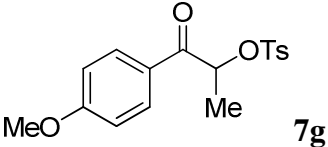
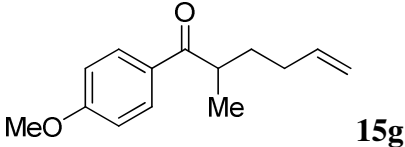
Instead of an isolation of cyclopropanol **11**, the acylation of the zinc homoenolate equivalent **11a',c'** was examined (Scheme 4).⁷¹ After the reaction of α -tosyloxy ketone **7** with the dizinc **1**, treatment of the resulting mixture with benzoyl chloride in the presence of palladium catalyst afforded the corresponding 1,4-diketone **14** in good yield.

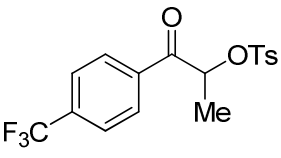
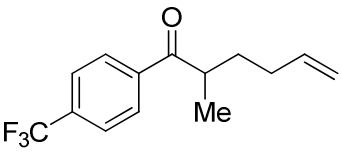
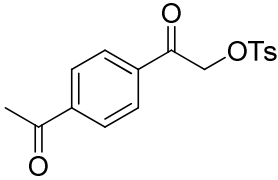
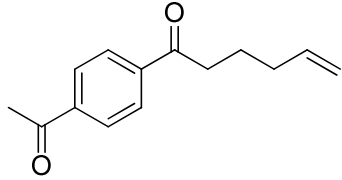
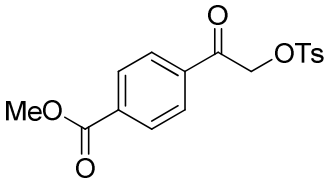
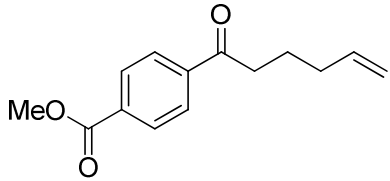


Scheme 4. The reaction of acid chloride and zinc homoenolate **11'** prepared from **1** and **7**.

The author also attempted a sequential reaction of the prepared zinc alkoxide of cyclopropanol **11'** with allyl bromide in the presence of copper cyanide.⁸ A solution of α -tosyloxy ketone **7** (1.0 mmol) in THF (4 mL) was treated with the dizinc (**1**, 2.0 mmol, 0.5 M in THF) at 25 °C. After being stirred for the period (t^1) shown in Table 3, the mixture was treated with CuCN•2LiCl (2.0 mmol) at -30 °C for 10 min. Allyl bromide was added to the resulting mixture, and the whole was stirred at 25 °C for the period (t^2) shown in Table 3. Purification by silica gel column chromatography gave α -homoallylated ketones **15** in good yields, as shown in Table 3. In the case of the reaction of α -methyl- α -tosyloxy ketones **7e-h**, the allylation proceeded regioselectively to give α -methyl ketones **15e-h** as sole products (entries 5-8). The reaction also tolerated the existence of other carbonyl groups (entries 9 and 10).

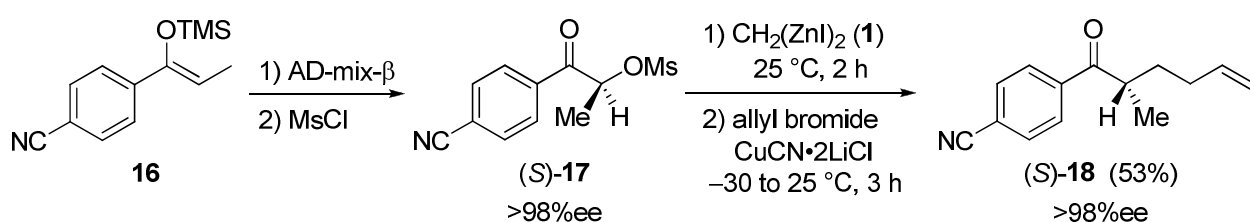
Table 3. The reaction of allyl bromide with the homoenolates prepared from **1** and **7**.^a

$ \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{CH}(\text{R}^2)-\text{OTs} \\ \mathbf{7} \end{array} \xrightarrow[\text{THF, 25 } ^\circ\text{C, } t^1 \text{ h}]{1) \text{ CH}_2(\text{ZnI})_2 \text{ (1)}} \left[\begin{array}{c} \text{IZnO} \\ \text{R}^1-\text{C}(\text{R}^2)-\text{C} \end{array} \right] \xrightarrow[\text{-30 to 25 } ^\circ\text{C, } t^2 \text{ h}]{2) \text{ allyl bromide, CuCN}\cdot\text{2LiCl}} \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{CH}(\text{R}^2)-\text{CH}_2\text{CH}_2\text{CH}=\text{CH}_2 \\ \mathbf{15} \end{array} $					
entry	substrate	Product	t^1 (h)	t^2 (h)	yield (%) ^b
1	 7a	 15a	4	4	85
2	 7b	 15b	24	3	84
3	 7c	 15c	15	6	79
4	 7d	 15d	3	5	88
5	 7e	 15e	4	4	76
6	 7f	 15f	18	20	78
7	 7g	 15g	24	12	55

8			3	5	87
9			2	2	86
10			3	4	81

^a A α -tosyloxy ketone **7** (1.0 mmol), the dizinc **1** (2.0 mmol, 0.5 M in THF), CuCN•2LiCl (2.0 mmol, 1 M in THF), allyl bromide (2.0 mmol), and THF (4 mL) were used. ^b Isolated yields.

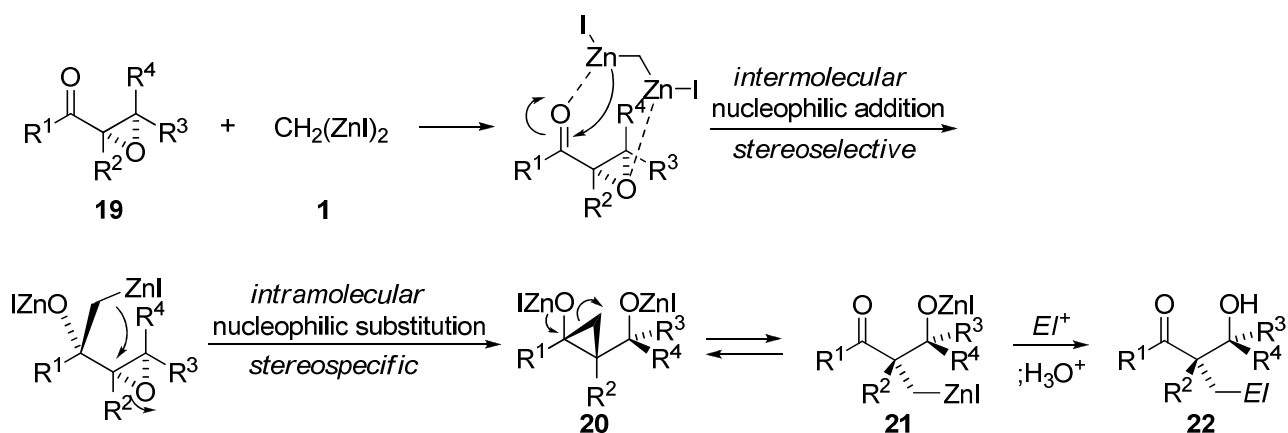
An optically active α -mesyloxy ketone (*S*)-**17** can be prepared easily by treatment of silyl enol ether **16** with AD-mix- β to form enantiomeric enriched α -hydroxy ketone,⁹ followed by mesylation of hydroxy group. As shown in Scheme 5, after the preparation of zinc alkoxide of cyclopropanol from the optically active α -mesyloxy ketone (*R*)-**17** with **1**, the resulting mixture was treated with allyl bromide in the presence of CuCN•2LiCl. The optically active α -tertiary ketone (*R*)-**18** was obtained without loss of enantiomeric purity.



Scheme 5. Preparation of chiral homoenolate from (*R*)-**17** and **1**, and its reaction with allyl bromide.

Though this method worked well to construct a chiral tertiary carbon at α -position of a ketone, it was difficult to apply for construction of a chiral quaternary carbon at α -position from

α -sulfonyloxy ketone: Treatment of 2-mesyloxy-2-methyl-1-phenyl-1-propanone with the dizinc **1** resulted in complete recovery of the starting material. That is, the preparation of zinc homoenolate equivalent containing quaternary carbon in cyclopropane ring is impossible from α,α -dialkyl- α -sulfonyloxy ketone with **1**. Meanwhile, as the author reported previously, the reaction of an α -alkyl- α,β -epoxy ketone **19** with **1** proceeds smoothly to afford a 2-(1-hydroxyalkyl)-1,2-dialkylcyclopropanol having quaternary center in the cyclopropane ring in a high yield.⁴ An epoxide is superior as a leaving group. The zinc alkoxide of 2-(1-hydroxyalkyl)-1,2-dialkylcyclopropanol **20** would act as a homoenolate equivalent. We speculated that the treatment of electrophiles with the obtained zinc alkoxide of cyclopropanol **20** in the presence of $\text{CuCN}\cdot 2\text{LiCl}$ would afford α -quaternary ketone **22** as shown in Scheme 6. So, the reactions of a zinc homoenolate, which was prepared from α,β -epoxy ketone **19** and the dizinc **1**, with electrophiles were examined.

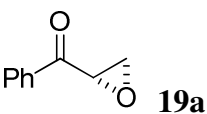
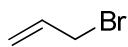
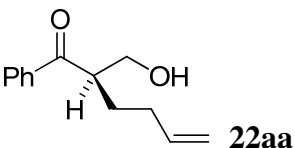
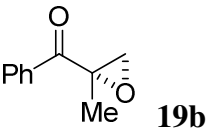
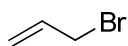
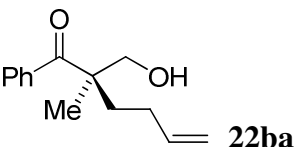
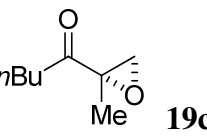
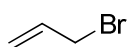
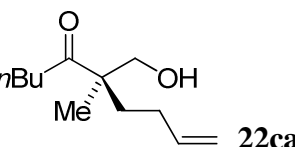


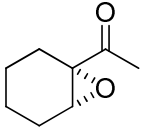
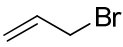
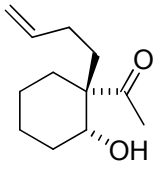
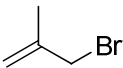
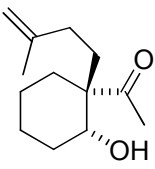
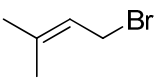
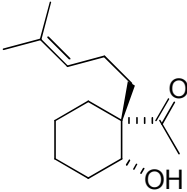
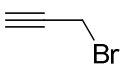
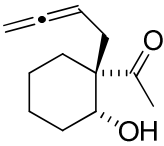
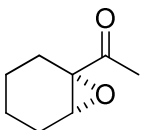
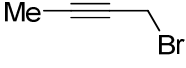
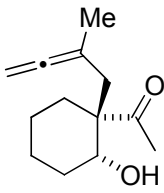
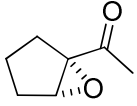
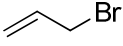
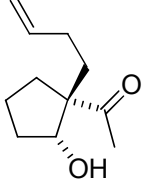
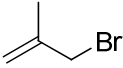
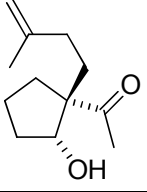
Scheme 6. Strategy for construction of chiral tertiary or quaternary carbon at α -position of a ketone via nucleophilic cyclopropanation of α,β -epoxy ketone **19** with **1**.

A solution of α,β -epoxy ketone **19a** (1.0 mmol) in THF (4 mL) was treated with the dizinc(**1**, 1.2 mmol, 0.5 M in THF) at 25 °C for 1 h. Then, the mixture was treated with $\text{CuCN}\cdot 2\text{LiCl}$ (2.4 mmol) at -30 °C for 10 min. Allyl bromide was added to the resulting mixture, and the whole was stirred at 25 °C for 12 h. After an aqueous work-up, a purification by a silica gel column

chromatography gave α -homoallylated ketone **22aa** in 69% yield (Table 4, entry 1). In the cases of α -methyl- α,β -epoxy ketone **19b** and **19c**, β -hydroxy ketones having quaternary carbon at α -position were obtained (entries 2 and 3). Treatment of 1-acetyl-1-cyclohexene oxide (**19d**) under the same conditions also gave the corresponding α -quaternary ketone **22da** in 67% yield (entry 4). Instead of allyl bromide, other electrophiles were also examined: Treatment of methallyl bromide with **20d** also afforded the corresponding product **22db** in good yield (entry 5). The reaction of prenyl bromide with **20d** proceeded regioselectively (entry 6). In the case of propargyl bromide and 1-bromo-2-butyne, the reaction with **20d** proceeded regioselectively in an S_N2' manner to give the corresponding allenes **22dd** and **22de** (entries 7 and 8). The reactions of electrophiles with a homoenolate prepared from 1-acetyl-1-cyclopentene oxide (**19e**) with **1** also afforded the corresponding α -quaternary ketones in good yields (entries 9 and 10).

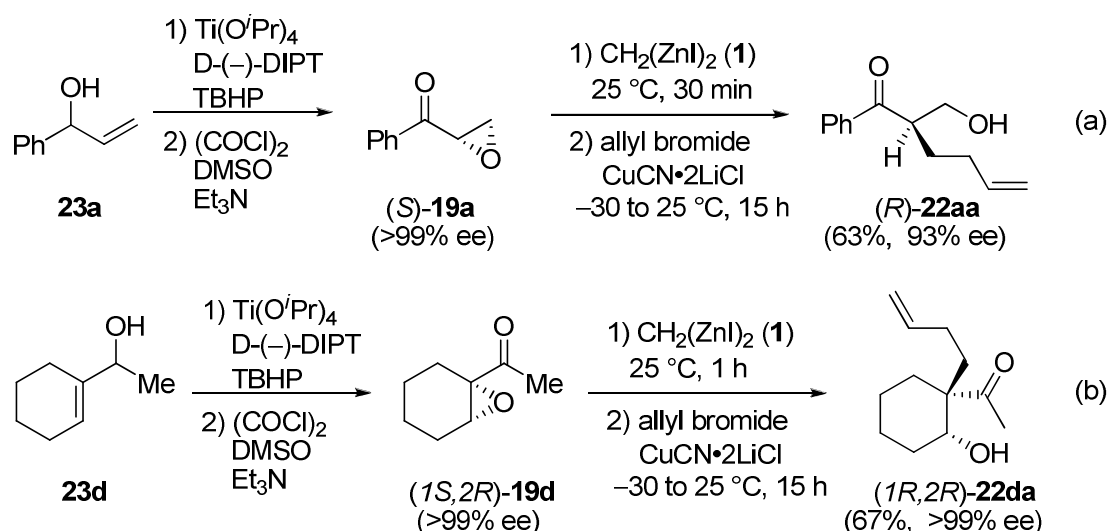
Table 4. Preparation of homoenolate from an α,β -epoxy ketone **19** and the dizinc **1**, and its reaction with electrophiles.^a

$ \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{C}(\text{R}^2)-\text{C}(\text{R}^3)-\text{O}-\text{C}(\text{R}^4) \\ \text{19} \end{array} \xrightarrow[\text{THF, 25 }^\circ\text{C, 1 h}]{1) \text{CH}_2(\text{ZnI})_2 \text{ (1)}} \left[\begin{array}{c} \text{IZnO} \quad \text{OZnI} \\ \text{R}^1 \quad \text{R}^2 \quad \text{R}^3 \quad \text{R}^4 \\ \text{20} \end{array} \right] \xrightarrow[\text{; H}_3\text{O}^+]{2) \text{El}^+ / \text{CuCN} \cdot 2\text{LiCl} \text{ } -30 \text{ to } 25^\circ\text{C, 12 h}} \begin{array}{c} \text{R}^1-\text{C}(=\text{O})-\text{C}(\text{R}^2)-\text{C}(\text{R}^3)-\text{OH} \\ \text{22} \end{array} $				
entry	substrate	El^+	product	Yield (%) ^b
1	 19a		 22aa	69
2 ^c	 19b		 22ba	52
3 ^c	 19c		 22ca	27

4				67
5	19d			70
6	19d			54
7	19d			27
8				73
9				57
10	19e			55

^a An α,β -epoxy ketone **19** (1.0 mmol), the dizinc **1** (1.2 mmol, 0.5 M in THF), $\text{CuCN} \cdot 2\text{LiCl}$ (2.4 mmol, 1 M in THF), electrophile (2.4 mmol), and THF (4 mL) were used. ^b Isolated yields. ^c The reaction of allyl bromide with the prepared homoenolate **20** were carried out at 40 °C.

An optically active α,β -epoxy ketone can be prepared easily by Katsuki-Sharpless asymmetric epoxidation of a corresponding allyl alcohol **23**, followed by Swern oxidation. As shown in Scheme 7(a), treatment of allyl bromide with a homoenolate prepared from (*S*)-**19a** and **1** under the same conditions afforded (*R*)-2-(hydroxymethyl)-1-phenyl-5-hexen-1-one ((*R*)-**22aa**), which possesses optically active tertiary carbon at α -position, in good yield. High enantiomeric excess was retained. In the case of (*1S,2R*)-1-acetyl-1-cyclohexene oxide ((*1S,2R*)-**19d**), the reaction gave optically active α -quaternary ketone (*1R,2R*)-**22da** without loss of enantiomeric excess (Scheme 7(b)). The ORTEP figure of a compound derived from (*1R,2R*)-**22da** and 3,5-dinitrobenzoyl chloride is shown in Figure 1.¹⁰



Scheme 7. Preparation of optically active homoenolates, and their reactions with allyl bromide.

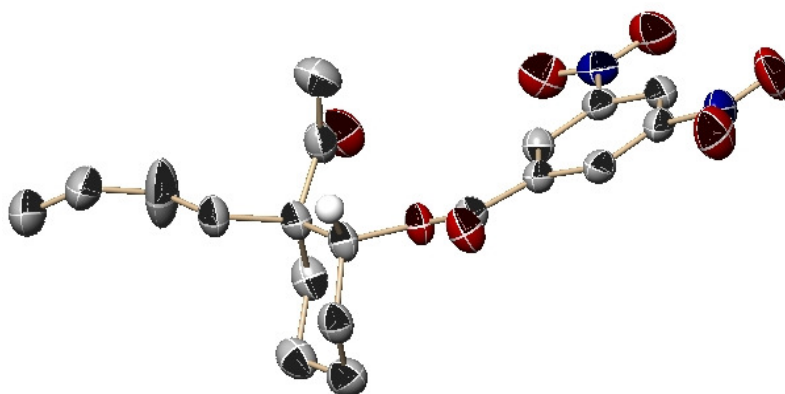


Figure 1. The ORTEP of the compound derived from (*1R,2R*)-**22da** and 3,5-dinitrobenzoyl chloride.

Conclusion

The author demonstrated the preparation of zinc homoenolate equivalent from α -sulfonyloxy ketone and bis(iodozincio)methane. The prepared zinc homoenolate reacted with allyl bromide mediated by $\text{CuCN} \cdot 2\text{LiCl}$ to give α -tertiary ketone. The reaction proceeded regioselectively and chemoselectively. The zinc homoenolate prepared by the reaction of a α,β -epoxy ketone with the dizinc also reacted with various electrophiles under the same condition to give a α -tertiary or -quaternary ketone. The transformation proceeded in a stereospecific manner, so treatment of electrophile with the homoenolate prepared by the reaction of optically active α -sulfonyloxy ketone or α,β -epoxy ketone with the dizinc gave the corresponding optically active α -tertiary or -quaternary ketone; high enantiomeric purity was retained. The high optical purity of the substrate can be introduced easily by the reliable asymmetric reactions, so this stereospecific method can be applied for pharmaceuticals or natural product syntheses containing tertiary or quaternary carbons.

Experimental Section

Unless otherwise noted, commercially available reagents were used without purification. Phenacyl acetate **8** and phenacyl bromide **9** are commercially available. α -Tosyloxy ketones **7**¹¹ and 2-iodoacetophenone **10**¹² were prepared according to the literature. α,β -Epoxy ketones **19** were prepared according to the procedure mentioned in Chapter 3.

General procedure for the nucleophilic cyclopropanation of α -sulfonyloxy ketone with bis(iodozincio)methane: A solution of α -sulfonyloxy ketone (**7**, 1.0 mmol) in THF (4.0 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 3.0 mmol) at 25 °C. Then saturated aqueous solution of NH₄Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding cyclopropanol **11**.

Preparation of 1-Phenyl-1-trimethylsiloxycyclopropane (13): A solution of **7a** (1.0 mmol) in THF (4.0 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 3.0 mmol) at 25 °C for 2 h. Then chlorotrimethylsilane (2.0 mmol) was added and the whole was stirred for additional 30 min. Water was added and the organic layer was extracted with hexane. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding cyclopropanol **13**.

General procedure for the preparation of 1,4-diketone: A solution of α -sulfonyloxy ketone (**7**, 1.0 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M in THF, 2.0 mmol) at 25 °C. The resulting mixture was added to a solution of benzoyl chloride (2.0 mmol), palladium catalyst (5~10 mol%), ligand (~20 mol%), and THF. The whole mixture was stirred

at 25 °C. Then saturated aqueous solution of NH₄Cl was added and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding 1,4-diketone **14**.

General procedure for the homoallylation of α -sulfonyloxy ketone: A solution of α -sulfonyloxy ketone (**7**, 1.0 mmol) in THF (4.0 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 2.0 mmol) at 25 °C. The mixture was cooled at –30 °C. To the mixture, CuCN•2LiCl (1.0 M solution in THF, 2.2 mmol) was added and stirred for 10 min at –30 °C. Then allyl bromide (2.0 mmol) was added and the cool bath was removed. After stirring at 25 °C, saturated aqueous solution of NH₄Cl was added and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding homoallylated ketone **15**.

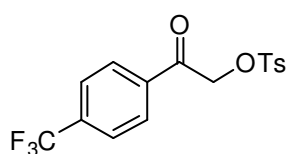
General procedure for the homoallylation of α,β -epoxy ketone: A solution of α,β -epoxy ketone (**19**, 1.0 mmol) in THF (4.0 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C. The mixture was cooled at –30 °C. To the mixture, CuCN•2LiCl (1.0 M solution in THF, 2.4 mmol) was added and stirred for 10 min at –30 °C. Then electrophile (2.4 mmol) was added and the cool bath was removed. After stirring at 25 °C, saturated aqueous solution of NH₄Cl was added and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding product **22**.

Characterization Data

The substrates **7a**,¹³ **7b**,¹⁴ **7c**,¹⁵ **7e**,¹³ **10**,¹² **19a**,¹⁶ **19b**,¹⁷ **19c**,¹⁸ **19d**¹⁹ and **19e**²⁰ were found in

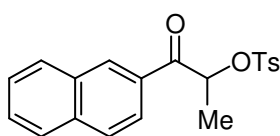
the literature.

2-Tosyloxy-1-(4-trifluoromethylphenyl)-1-ethanone (7d)



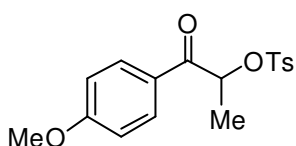
^1H NMR (500 MHz, CDCl_3) δ 7.95 (d, J = 8.1 Hz, 2H), 7.83 (d, J = 8.1 Hz, 2H), 7.73 (d, J = 8.4 Hz, 2H), 7.35 (d, J = 8.4 Hz, 2H), 5.24 (s, 2H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 190.0, 145.5, 136.5, 135.3 (q, J = 33.0 Hz), 132.5, 129.9, 128.5, 128.1, 125.9 (q, J = 3.9 Hz), 123.3 (q, J = 271.5 Hz), 69.9, 21.6; ^{19}F NMR (282 MHz, CDCl_3) δ 97.84; IR (nujor) 1709, 1364, 1327, 1175, 1130, 1057, 966, 910, 739 cm^{-1} , mp 117.5–118.0 $^\circ\text{C}$. Anal. Calcd for $\text{C}_{16}\text{H}_{13}\text{O}_4\text{F}_3\text{S}$: C, 53.63; H, 3.66%. Found: C, 53.56; H, 3.80%; HRMS (m/z) Found: 358.0490. Calcd for $\text{C}_{16}\text{H}_{13}\text{O}_4\text{F}_3\text{S}$ $[\text{M}]^+$: 358.0487.

1-(2-Naphthyl)-2-tosyloxy-1-propanone (7f)



^1H NMR (300 MHz, CDCl_3) δ 8.40 (s, 1H), 7.96–7.86 (m, 4H), 7.75 (d, J = 8.4 Hz, 2H), 7.66–7.55 (m, 2H), 7.20 (d, J = 7.8 Hz, 2H), 5.94 (q, J = 6.9 Hz, 1H), 2.35 (s, 3H), 1.67 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 194.7, 145.0, 135.8, 133.5 (co-incident), 132.3, 131.0, 130.7, 129.7, 129.0, 128.7, 127.9, 127.8, 127.0, 124.0, 77.4, 21.5, 18.9; IR (nujor) 1694, 1626, 1597, 1470, 1362, 1190, 1177, 1071, 1017, 920, 816 cm^{-1} , mp 98.2–98.6 $^\circ\text{C}$. Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_4\text{S}$: C, 67.78; H, 5.12%. Found: C, 67.81; H, 5.30%; HRMS (m/z) Found: 354.0920. Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_4\text{S}$ $[\text{M}]^+$: 354.0926.

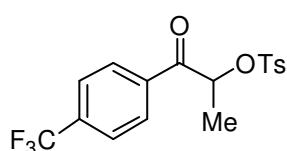
1-(4-Methoxyphenyl)-2-tosyloxy-1-propanone (7g)



^1H NMR (300 MHz, CDCl_3) δ 7.88 (d, J = 9.0 Hz, 2H), 7.75 (d, J = 8.4 Hz, 2H), 7.26 (d, J = 8.4 Hz, 2H), 6.92 (d, J = 9.0 Hz, 2H), 5.73 (q, J = 6.9 Hz, 1H), 3.87 (s, 3H), 2.40 (s, 3H), 1.57 (d, J = 6.9 Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 193.0, 164.1, 144.9, 133.6, 131.2, 129.7, 127.9, 126.5, 114.0, 77.3, 55.5, 21.6, 18.8; IR (nujor) 1694, 1601, 1514, 1354, 1267, 1234, 1177, 1030, 1009, 928, 843, 820,

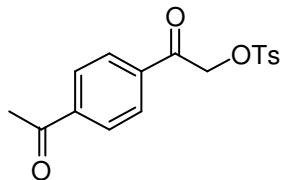
735 cm^{-1} , mp 87.0–87.5 °C. Anal. Calcd for $\text{C}_{17}\text{H}_{18}\text{O}_5\text{S}$: C, 61.06; H, 5.43%. Found: C, 61.00; H, 5.44%; HRMS (m/z) Found: 334.0875. Calcd for $\text{C}_{17}\text{H}_{18}\text{O}_5\text{S} [\text{M}]^+$: 334.0875.

2-Tosyloxy-1-(4-trifluoromethylphenyl)-1-propanone (7h)



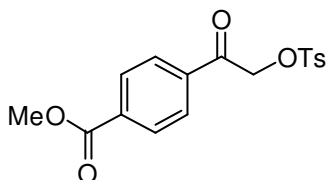
^1H NMR (500 MHz, CDCl_3) δ 8.00 (d, $J = 8.4$ Hz, 2H), 7.73 (d, $J = 8.1$ Hz, 2H), 7.71 (d, $J = 8.1$ Hz, 2H), 7.27 (d, $J = 8.4$ Hz, 2H), 5.71 (q, $J = 6.9$ Hz, 1H), 2.42 (s, 3H), 1.61 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 194.4, 145.3, 136.6, 134.9 (q, $J = 32.4$ Hz), 133.3, 129.8, 129.2, 127.9, 125.7 (q, $J = 3.75$ Hz), 123.4 (q, $J = 271.5$ Hz), 77.6, 21.6, 18.4; ^{19}F NMR (282 MHz, CDCl_3) δ 97.84; IR (nujor) 1703, 1597, 1360, 1323, 1176, 1142, 1067, 1011, 924, 665 cm^{-1} , mp 92.5–93.0 °C. Anal. Calcd for $\text{C}_{17}\text{H}_{15}\text{O}_4\text{F}_3\text{S}$: C, 54.83; H, 4.06%. Found: C, 54.86; H, 4.16%; HRMS (m/z) Found: 372.0641. Calcd for $\text{C}_{17}\text{H}_{15}\text{O}_4\text{F}_3\text{S} [\text{M}]^+$: 372.0643.

1-(4-Acetylphenyl)-2-tosyloxy-1-ethanone (7i)



^1H NMR (300 MHz, CDCl_3) δ 8.03 (d, $J = 8.4$ Hz, 2H), 7.93 (d, $J = 8.4$ Hz, 2H), 7.85 (d, $J = 8.4$ Hz, 2H), 7.36 (d, $J = 8.4$ Hz, 2H), 5.25 (s, 2H), 2.65 (s, 3H), 2.46 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 197.1, 190.2, 145.5, 140.9, 136.9, 132.6, 130.0, 128.7, 128.4, 128.2, 70.0, 26.8, 21.7; IR (nujor) 1717, 1690, 1362, 1263, 1179, 968, 910, 735 cm^{-1} , mp 116.0–117.0 °C. HRMS (m/z) Found: 332.0722. Calcd for $\text{C}_{17}\text{H}_{16}\text{O}_5\text{S} [\text{M}]^+$: 332.0718.

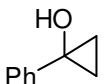
1-(4-Methoxycarbonylphenyl)-2-tosyloxy-1-ethanone (7j)



^1H NMR (300 MHz, CDCl_3) δ 8.12 (d, $J = 8.1$ Hz, 2H), 7.89 (d, $J = 8.1$ Hz, 2H), 7.84 (d, $J = 8.1$ Hz, 2H), 7.35 (d, $J = 8.1$ Hz, 2H), 5.26 (s, 2H), 3.96 (s, 3H), 2.45 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 190.2, 165.8, 145.4, 137.0, 134.8, 132.6, 130.0, 129.9, 128.2, 128.0, 69.9, 52.6, 21.7; IR (nujor) 1720, 1715, 1373, 1283, 1179, 1111, 1065, 968, 910, 733 cm^{-1} , mp 109.5–110.2 °C. Anal. Calcd for

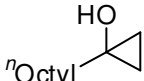
$C_{17}H_{16}O_6S$: C, 58.61; H, 4.63%. Found: C, 58.48; H, 4.68%; HRMS (m/z) Found: 348.0673. Calcd for $C_{17}H_{16}O_6S$ $[M]^+$: 348.0668.

1-phenylcyclopropanol (**11a**)

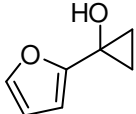
 1H NMR (500 MHz, $CDCl_3$) δ 7.36–7.30 (m, 4H), 7.25–7.21 (m, 1H), 2.17 (bs, 1H), 1.27 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H), 1.05 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 144.2, 128.3, 126.4, 124.4, 56.6, 17.9.

The spectral data of the product **11a** are in agreement with those published.²¹

1-octylcyclopropanol (**11b**)

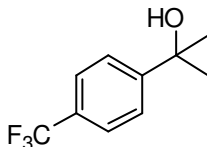
 1H NMR (500 MHz, $CDCl_3$) δ 1.77 (bs, 1H), 1.56–1.27 (m, 14H), 0.88 (t, $J = 6.5$ Hz, 3H), 0.72 (dd, $J = 7.0, 5.5$ Hz, 2H), 0.43 (dd, $J = 7.0, 5.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 55.9, 38.3, 31.9, 29.7, 29.6, 29.3, 25.9, 22.7, 14.1, 13.5; IR (neat) 3321, 2926, 1466, 1377, 1258, 1101, 1007 cm^{-1} . Anal. Calcd for $C_{11}H_{22}O$: C, 77.58; H, 13.02%. Found: C, 77.69; H, 13.01%; HRMS (m/z) Found: 170.1665. Calcd for $C_{11}H_{22}O$ $[M]^+$: 170.1671.

1-(2-furyl)cyclopropanol (**11c**)

 1H NMR (500 MHz, $CDCl_3$) δ 7.32 (dd, $J = 2.0, 1.0$ Hz, 1H), 6.32 (dd, $J = 3.5, 2.0$ Hz, 1H), 6.22 (dd, $J = 3.5, 1.0$ Hz, 1H), 1.18–1.15 (m, 2H), 1.09–1.06 (m, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 156.5, 141.4, 110.3, 104.7, 52.3, 15.2.

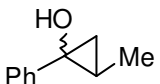
The spectral data of the product **11c** are in agreement with those published.²²

1-(4-trifluoromethylphenyl)cyclopropanol (**11d**)

 1H NMR (500 MHz, $CDCl_3$) δ 7.56 (d, $J = 8.0$ Hz, 2H), 7.36 (d, $J = 8.0$ Hz, 2H), 2.35 (bs, 1H), 1.35 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H), 1.10 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 148.7, 128.4 (q, $J = 31.9$ Hz), 125.2 (q, $J = 3.3$ Hz), 124.2 (q, $J = 270.1$ Hz), 124.1, 56.1, 19.1; ^{19}F NMR (282 MHz, $CDCl_3$) δ

98.75; IR (neat) 3350, 2922, 1456, 1377, 1328, 1240, 1130, 1099, 1016 cm^{-1} ; mp 53.8–54.5 $^{\circ}\text{C}$.
 Anal. Calcd for $\text{C}_{10}\text{H}_9\text{F}_3\text{O}$: C, 59.41; H, 4.49%. Found: C, 59.17; H, 4.29%.

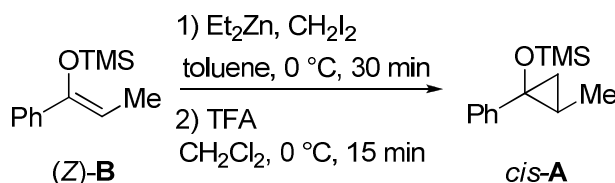
2-methyl-1-phenylcyclopropanol (**11e**)

 (major isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.43–7.41 (m, 2H), 7.38–7.34 (m, 2H), 7.30–7.27 (m, 1H), 2.27 (bs, 1H), 1.49–1.45 (m, 1H), 1.15 (dd, $J = 10.0$, 5.5 Hz, 1H), 0.87 (dd, $J = 6.5$, 5.5 Hz, 1H), 0.77 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 140.2, 128.2 (co-incident), 127.4, 61.8, 21.2, 19.5, 14.6. Anal. Calcd for $\text{C}_{10}\text{H}_{12}\text{O}$: C, 84.81; H, 7.12%. Found: C, 84.75; H, 7.08%. (minor isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.35–7.31 (m, 2H), 7.29–7.27 (m, 2H), 7.23–7.19 (m, 1H), 2.15 (bs, 1H), 1.33–1.32 (m, 3H), 1.28–1.23 (m, 2H), 0.84–0.82 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 145.4, 128.3, 126.0, 123.8, 59.0, 24.2, 23.2, 12.5.

The spectral data of the product **11e** are in agreement with those published.²³

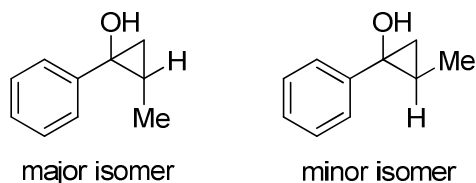
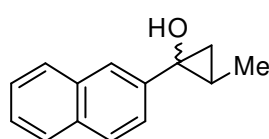
To determine the stereochemistry of **11e**, the following experiment was performed.

The authentic sample of cyclopropanol **A** was synthesized from the corresponding (Z)-silyl enol ether **B**. (Z)-Silyl enol ether **B** was treated with diethylzinc and diiodomethane at 0 $^{\circ}\text{C}$ for 30 min. The obtained siloxycyclopropane was treated with trifluoroacetic acid to give *cis*-2-methyl-1-phenylcyclopropanol **A** (Scheme 8).

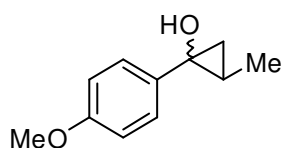


Scheme 8. Synthesis of an authentic sample of **11e**.

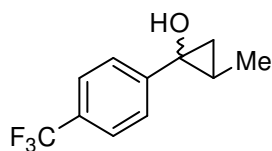
Compared with ^1H NMR spectrum of the authentic sample **A**, it was found that the stereochemistry of cyclopropane ring in major isomer was *trans*.

**2-methyl-1-(2-naphthyl)cyclopropanol (11f)**

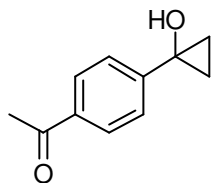
(major isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.86–7.81 (m, 4H), 7.61 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.51–7.46 (m, 2H), 2.19 (bs, 1H), 1.58–1.51 (m, 1H), 1.23 (dd, $J = 10.0, 6.0$ Hz, 1H), 1.02 (dd, $J = 7.0, 6.0$ Hz, 1H), 0.79 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 137.7, 133.2, 132.8, 128.0, 127.9, 127.6, 126.8, 126.6, 126.1, 125.9, 62.1, 21.3, 19.5, 14.6; IR (nujol) 3228, 2924, 1456, 1377, 1195, 1135, 1094 cm^{-1} ; mp 71.9–72.5 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}$: C, 84.81; H, 7.12%. Found: C, 84.63; H, 7.17%; HRMS (m/z) Found: 198.1040. Calcd for $\text{C}_{14}\text{H}_{14}\text{O}$ $[\text{M}]^+$: 198.1045. (minor isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.83–7.79 (m, 4H), 7.49–7.43 (m, 2H), 7.28 (dd, $J = 8.5, 2.0$ Hz, 1H), 2.37 (bs, 1H), 1.38 (d, $J = 2.5$ Hz, 3H), 1.39–1.32 (m, 2H), 0.91 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 142.7, 133.2, 132.0, 128.0, 127.7, 127.5, 126.1, 125.4, 122.6, 122.4, 59.3, 24.0, 23.0, 12.5; IR (nujol) 3210, 2925, 1458, 1377, 1366 cm^{-1} ; mp 77.5–78.5 $^{\circ}\text{C}$.

1-(4-methoxyphenyl)-2-methylcyclopropanol (11g)

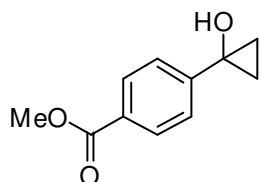
(major isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.36–7.26 (m, 2H), 6.90–6.87 (m, 2H), 3.81 (s, 3H), 2.23 (bs, 1H), 1.46–1.39 (m, 1H), 1.11 (dd, $J = 10.0, 5.5$ Hz, 1H), 0.78–0.76 (m, 1H), 0.76 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.9, 132.3, 129.7, 113.6, 61.5, 55.2, 20.7, 19.4, 14.9. HRMS (m/z) Found: 178.1001. Calcd for $\text{C}_{11}\text{H}_{14}\text{O}_2$ $[\text{M}]^+$: 178.0994. (minor isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.24–7.21 (m, 2H), 6.88–6.85 (m, 2H), 3.80 (s, 3H), 2.06 (bs, 1H), 1.30 (d, $J = 6.0$ Hz, 3H), 1.20–1.12 (m, 2H), 0.75 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 158.2, 137.4, 125.8, 113.7, 59.1, 55.3, 23.1, 22.0, 12.5; IR (neat) 3401, 2957, 2344, 1670, 1601, 1514, 1458, 1375, 1302, 1250, 1177, 1031 cm^{-1} .

2-methyl-1-(4-trifluoromethylphenyl)cyclopropanol (11h)

(major isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.61 (d, $J = 8.0$ Hz, 2H), 7.52 (d, $J = 8.0$ Hz, 2H), 2.33 (bs, 1H), 1.56–1.49 (m, 1H), 1.23 (dd, $J = 10.0, 6.0$ Hz, 1H), 0.95 (dd, $J = 6.5, 6.0$ Hz, 1H), 0.77 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 144.4, 129.4 (q, $J = 32.0$ Hz), 128.2, 125.2 (q, $J = 3.8$ Hz), 124.2 (q, $J = 270.5$ Hz), 61.3, 22.0, 20.1, 14.2; ^{19}F NMR (282 MHz, CDCl_3) δ 97.89. HRMS (m/z) Found: 216.0760. Calcd for $\text{C}_{11}\text{H}_{11}\text{OF}_3$: 216.0762. (minor isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.57–7.55 (m, 2H), 7.36–7.34 (m, 2H), 2.04 (bs, 1H), 1.34–1.33 (m, 3H), 1.31–1.26 (m, 2H), 0.95–0.90 (m, 1H); ^{13}C NMR (125 MHz, CDCl_3) δ 149.9, 128.1 (q, $J = 32.0$ Hz), 125.2 (q, $J = 3.8$ Hz), 124.3 (q, $J = 270.1$ Hz), 123.7, 58.7, 25.3, 24.5, 12.5; ^{19}F NMR (282 MHz, CDCl_3) δ 98.12; IR (nujol) 3338, 2923, 1456, 1377, 1328, 1167, 1111, 1072 cm^{-1} ; mp 66.8–67.4 $^{\circ}\text{C}$.

1-(4-acetylphenyl)cyclopropanol (11i)

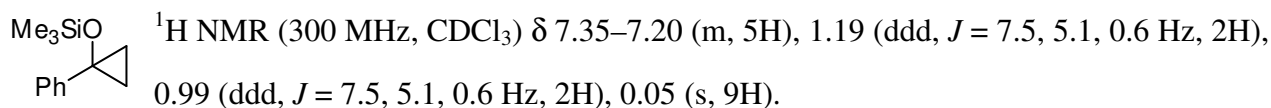
^1H NMR (500 MHz, CDCl_3) δ 7.91 (d, $J = 8.5$ Hz, 2H), 7.34 (d, $J = 8.5$ Hz, 2H), 2.59 (s, 3H), 1.38 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H), 1.14 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 197.7, 150.5, 135.1, 128.5, 123.8, 56.3, 26.6, 19.5; IR (neat) 3381, 1681, 1607, 1566, 1408, 1360, 1308, 1273, 1236, 1190, 1121, 1101, 1015 cm^{-1} . Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_2$: C, 74.98; H, 6.86%. Found: C, 75.12; H, 6.93%; HRMS (m/z) Found: 176.0836. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_2$ $[\text{M}]^+$: 176.0837.

1-(4-ethoxycarbonylphenyl)cyclopropanol (11j)

^1H NMR (500 MHz, CDCl_3) δ 8.00–7.98 (m, 2H), 7.33–7.31 (m, 2H), 3.91 (s, 3H), 2.04 (bs, 1H), 1.37 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H), 1.13 (ddd, $J = 7.5, 5.5, 0.5$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 167.1, 150.3, 129.6, 127.7, 123.6, 56.1, 52.0, 19.4; IR (nujol) 3450, 2925, 1456, 1377, 1288, 1240, 1183, 1119 cm^{-1} ; mp 78.0–78.8 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{11}\text{H}_{12}\text{O}_3$: C, 68.74; H, 6.29%. Found: C, 68.79; H, 6.32%;

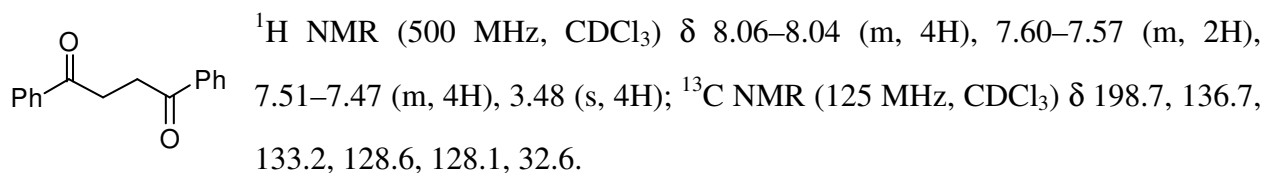
HRMS (m/z) Found: 193.0857. Calcd for $C_{11}H_{13}O_3$ $[MH]^+$: 193.0865.

1-Phenyl-1-trimethylsiloxycyclopropane (**13**)



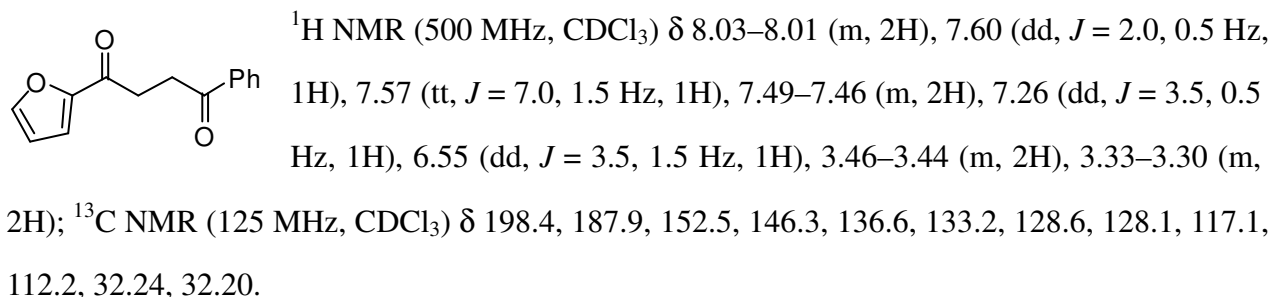
The spectral data of the product **13** are in agreement with those published.²⁴

1,4-diphenylbutan-1,4-dione (**14a**)



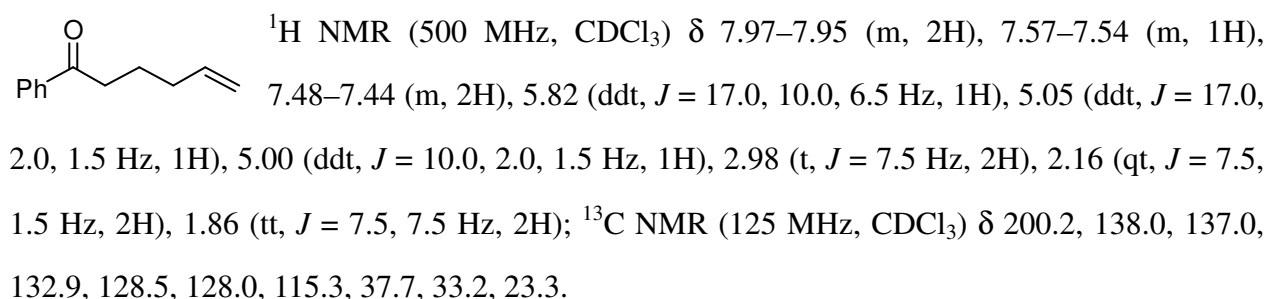
The spectral data of the product **14a** are in agreement with those published.²⁵

1-furyl-4-phenylbutan-1,4-dione (**14c**)



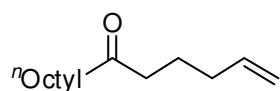
The spectral data of the product **14c** are in agreement with those published.²⁶

1-phenyl-5-hexen-1-one (**15a**)



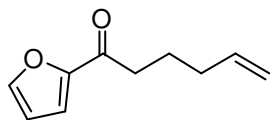
The spectral data of the product **15a** are in agreement with those published.²⁷

1-tetradecen-6-one (**15b**)



¹H NMR (500 MHz, CDCl₃) δ 5.76 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.01 (ddt, *J* = 17.0, 2.0, 1.5 Hz, 1H), 4.96 (ddt, *J* = 10.0, 2.0, 1.5 Hz, 1H), 2.42–2.36 (m, 4H), 2.05 (qt, *J* = 7.5, 1.5 Hz, 2H), 1.67 (tt, *J* = 7.5, 7.5 Hz, 2H), 1.56–1.53 (m, 2H), 1.30–1.25 (m, 10H), 0.87 (t, *J* = 6.5 Hz, 3H); ¹³C NMR (125 MHz, CDCl₃) δ 211.3, 138.0, 115.1, 42.9, 41.8, 33.1, 31.8, 29.3, 29.2, 29.1, 23.9, 22.8, 22.6, 14.1; IR (neat) 2928, 1713, 1674, 1641, 1605, 1454, 1410, 1371, 1273, 1130, 1074 cm⁻¹. Anal. Calcd for C₁₄H₂₆O: C, 79.94; H, 12.46%. Found: C, 80.21; H, 12.53%; HRMS (*m/z*) Found: 210.1990. Calcd for C₁₄H₂₆O [M]⁺: 210.1984.

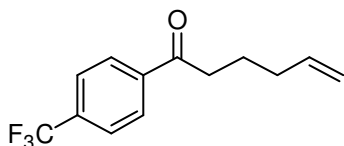
1-furyl-5-hexen-1-one (**15c**)



¹H NMR (500 MHz, CDCl₃) δ 7.57 (dd, *J* = 2.0, 1.0 Hz, 1H), 7.17 (dd, *J* = 4.0, 1.0 Hz, 1H), 6.52 (dd, *J* = 4.0, 2.0 Hz, 1H), 5.80 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.04 (ddt, *J* = 17.0, 2.0, 1.5 Hz, 1H), 4.99 (ddt, *J* = 10.0, 2.0, 1.5 Hz, 1H), 2.82 (t, *J* = 7.5 Hz, 2H), 2.14 (qt, *J* = 7.5, 1.5 Hz, 2H), 1.83 (tt, *J* = 7.5, 7.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 189.5, 152.8, 146.2, 137.9, 116.8, 115.3, 112.1, 37.6, 33.1, 23.2.

The spectral data of the product **15c** are in agreement with those published.²⁸

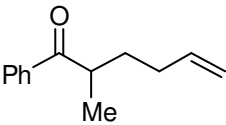
1-(4-trifluoromethylphenyl)-5-hexen-1-one (**15d**)



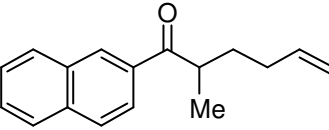
¹H NMR (500 MHz, CDCl₃) δ 8.04 (d, *J* = 8.0 Hz, 2H), 7.71 (d, *J* = 8.0 Hz, 2H), 5.81 (ddt, *J* = 17.0, 10.0, 6.5 Hz, 1H), 5.04 (ddt, *J* = 17.0, 2.0, 1.5 Hz, 1H), 5.00 (ddt, *J* = 10.0, 2.0, 1.5 Hz, 1H), 2.99 (t, *J* = 7.5 Hz, 2H), 2.16 (qt, *J* = 7.0, 1.5 Hz, 2H), 1.86 (tt, *J* = 7.5, 7.5 Hz, 2H); ¹³C NMR (125 MHz, CDCl₃) δ 199.1, 139.6, 137.8, 134.2 (q, *J* = 32.9 Hz), 128.3, 125.6 (q, *J* = 3.8 Hz), 123.6 (q, *J* = 271.1 Hz), 115.5, 37.9, 33.0, 23.0; ¹⁹F NMR (282MHz, CDCl₃) δ 98.06; IR (neat) 2938, 2359,

1694, 1410, 1327, 1170, 1132, 1067, 1016 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{13}\text{OF}_3$: C, 64.46; H, 5.41%. Found: C, 64.21; H, 5.43%; HRMS (m/z) Found: 242.0918. Calcd for $\text{C}_{13}\text{H}_{13}\text{OF}_3$ $[\text{M}]^+$: 242.0918.

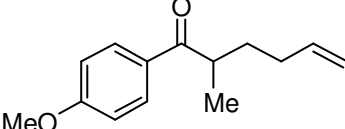
2-methyl-1-phenyl-5-hexen-1-one (15e)

 ^1H NMR (500 MHz, CDCl_3) δ 7.96–7.94 (m, 2H), 7.57–7.54 (m, 1H), 7.48–7.45 (m, 2H), 5.79 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 4.99 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 4.96 (ddt, $J = 10.0, 2.0, 1.5$ Hz, 1H), 3.50 (qt, $J = 14.0, 6.5$ Hz, 1H), 2.11–2.06 (m, 2H), 1.98–1.91 (m, 1H), 1.56–1.47 (m, 1H), 1.20 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.3, 138.1, 136.7, 132.8, 128.6, 128.3, 115.1, 39.7, 32.6, 31.5, 17.3. The spectral data of the product **15e** are in agreement with those published.²⁹

2-methyl-1-(2-naphthyl)-5-hexen-1-one (15f)

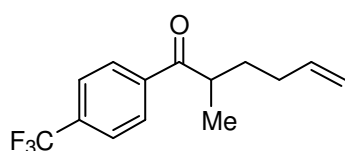
 ^1H NMR (500 MHz, CDCl_3) δ 8.47 (s, 1H), 8.04 (dd, $J = 8.5, 1.5$ Hz, 1H), 7.97 (d, $J = 8.0$ Hz, 1H), 7.90 (d, $J = 8.5$ Hz, 1H), 7.88 (d, $J = 8.0$ Hz, 1H), 7.62–7.54 (m, 2H), 5.82 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.03–4.97 (m, 2H), 3.68 (qt, $J = 14.0, 6.5$ Hz, 1H), 2.16–2.11 (m, 2H), 2.04–2.02 (m, 1H), 1.62–1.56 (m, 1H), 1.27 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 204.2, 138.1, 135.5, 133.9, 132.6, 129.7, 129.5, 128.5, 128.3, 127.7, 126.7, 124.2, 115.2, 39.7, 32.7, 31.5, 17.5; IR (neat) 2932, 1678, 1467, 1276, 1185, 1123 cm^{-1} . Anal. Calcd for $\text{C}_{17}\text{H}_{18}\text{O}$: C, 85.67; H, 7.61%. Found: C, 85.52; H, 7.64%; HRMS (m/z) Found: 238.1362. Calcd for $\text{C}_{17}\text{H}_{18}\text{O}$ $[\text{M}]^+$: 238.1358.

1-(4-methoxyphenyl)-2-methyl-5-hexen-1-one (15g)

 ^1H NMR (500 MHz, CDCl_3) δ 7.94 (d, $J = 9.0$ Hz, 2H), 6.94 (d, $J = 9.0$ Hz, 2H), 5.79 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.00–4.94 (m, 2H), 3.87 (s, 3H), 3.46 (qt, $J = 14.0, 6.5$ Hz, 1H), 2.11–2.03 (m, 2H), 1.96–1.89 (m, 1H), 1.55–1.48 (m, 1H), 1.18 (d, $J = 6.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 202.9, 163.3, 138.2, 130.5, 129.6, 115.0, 113.7, 55.4, 39.3, 32.8, 31.5, 17.5; IR (neat) 2970, 1672,

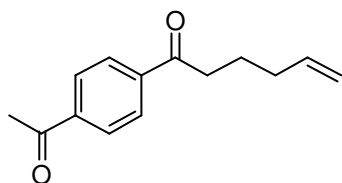
1601, 1510, 1460, 1420, 1371, 1308, 1260, 1173, 1031 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$: C, 77.03; H, 8.31%. Found: C, 76.95; H, 8.27%; HRMS (m/z) Found: 218.1306. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2 [\text{M}]^+$: 218.1307.

2-methyl-1-(4-trifluoromethylphenyl)-5-hexen-1-one (15h)



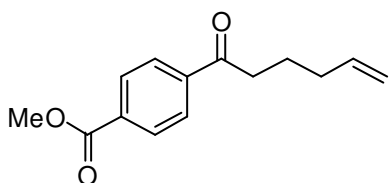
^1H NMR (500 MHz, CDCl_3) δ 8.04 (d, $J = 8.0$ Hz, 2H), 7.73 (d, $J = 8.0$ Hz, 2H), 5.77 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.00–4.96 (m, 2H), 3.49 (dq, $J = 14.0, 6.5$ Hz, 1H), 2.12–2.07 (m, 2H), 1.97–1.90 (m, 1H), 1.57–1.51 (m, 1H), 1.21 (d, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 203.3, 139.3 (d, $J = 0.9$ Hz), 137.8, 134.2 (q, $J = 32.9$ Hz), 128.6, 125.7 (q, $J = 3.8$ Hz), 123.6 (q, $J = 271.5$ Hz), 115.4, 40.1, 32.3, 31.4, 17.0; ^{19}F NMR (282 MHz, CDCl_3) δ 97.96; IR (neat) 2935, 1690, 1410, 1326, 1172, 1132, 1068, 1017 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{OF}_3$: C, 65.62; H, 5.90%. Found: C, 65.54; H, 5.88%; HRMS (m/z) Found: 256.1074. Calcd for $\text{C}_{14}\text{H}_{15}\text{OF}_3 [\text{M}]^+$: 256.1075.

1-(4-acetylphenyl)-5-hexen-1-one (15i)



^1H NMR (500 MHz, CDCl_3) δ 8.03 (s, 4H), 5.82 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.05 (ddt, $J = 17.0, 2.0, 1.5$ Hz, 1H), 5.01 (ddt, $J = 10.0, 2.0, 1.5$ Hz, 1H), 3.01 (t, $J = 7.5$ Hz, 2H), 2.65 (s, 3H), 2.17 (qt, $J = 7.0, 1.5$ Hz, 2H), 1.86 (tt, $J = 7.0, 7.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 199.7, 197.5, 140.1, 140.0, 137.9, 128.5, 128.2, 115.5, 38.1, 33.1, 26.9, 23.0; IR (neat) 2923, 2360, 1679, 1456, 1404, 1312, 1268 cm^{-1} ; mp 49.5–51.0 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2$: C, 77.75; H, 7.46%. Found: C, 77.74; H, 7.46%; HRMS (m/z) Found: 216.1153. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_2 [\text{M}]^+$: 216.1150.

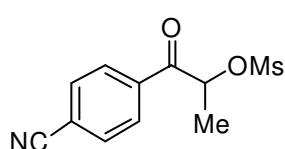
1-(4-ethoxycarbonylphenyl)-5-hexen-1-one (15j)



^1H NMR (500 MHz, CDCl_3) δ 8.12 (d, $J = 9.0$ Hz, 2H), 8.00 (d, $J = 9.0$ Hz, 2H), 5.82 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.05 (ddt, $J = 17.0, 2.0, 2.0$ Hz, 1H), 5.00 (ddt, $J = 10.0, 2.0, 1.5$ Hz, 1H),

3.00 (t, $J = 7.5$ Hz, 2H), 2.16 (qt, $J = 7.0, 1.5$ Hz, 2H), 1.86 (tt, $J = 7.0, 7.0$ Hz, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 199.7, 166.3, 140.2, 137.9, 133.7, 129.8, 127.9, 115.5, 52.5, 38.0, 33.1, 23.0; IR (nujol) 2924, 1722, 1677, 1457, 1407, 1378, 1284, 1112 cm^{-1} ; mp 55.5–57.0 $^{\circ}\text{C}$. HRMS (m/z) Found: 232.1097. Calcd for $\text{C}_{14}\text{H}_{16}\text{O}_3$ $[\text{M}]^+$: 232.1099.

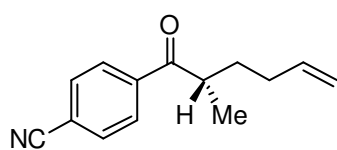
1-(4-Cyanophenyl)-2-mesyloxy-1-propanone (17)



^1H NMR (500 MHz, CDCl_3) δ 8.03 (d, $J = 8.4$ Hz, 2H), 7.81 (d, $J = 8.4$ Hz, 2H), 5.96 (q, $J = 7.2$ Hz, 1H), 3.12 (s, 3H), 1.65 (d, $J = 7.2$ Hz, 3H);

^{13}C NMR (125 MHz, CDCl_3): δ 194.3, 136.8, 132.7, 129.0, 117.5, 117.3, 76.6, 39.3, 18.2; IR (nujol) 1709, 1352, 1221, 1179, 976, 910, 735 cm^{-1} , mp 112.0–113.2 $^{\circ}\text{C}$. HRMS (m/z) Found: 253.0413. Calcd for $\text{C}_{11}\text{H}_{11}\text{O}_4\text{NS}$ $[\text{M}]^+$: 253.0409.

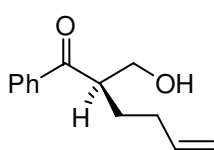
(*R*)-1-(4-cyanophenyl)-2-methyl-5-hexen-1-one ((*R*)-18)



^1H NMR (500 MHz, CDCl_3) δ 8.02 (d, $J = 8.5$ Hz, 2H), 7.77 (d, $J = 8.5$ Hz, 2H), 5.76 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.00–4.96 (m, 2H), 3.45 (tq, $J = 7.0, 7.0$ Hz, 1H), 2.11–2.07 (m, 2H), 1.96–1.89 (m, 1H), 1.57–1.50 (m, 1H);

^{13}C NMR (125 MHz, CDCl_3) δ 202.9, 139.6, 137.7, 132.5, 128.6, 118.0, 116.1, 115.6, 40.1, 32.2, 31.3, 17.0; IR (neat) 2931, 2360, 2232, 1689, 1458, 1406, 1280, 1226 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{15}\text{ON}$: C, 78.84; H, 7.09%. Found: C, 79.06; H, 7.20%; HRMS (m/z) Found: 213.1156. Calcd for $\text{C}_{14}\text{H}_{15}\text{ON}$ $[\text{M}]^+$: 213.1154. $[\alpha]_{\text{D}}^{25} = -24$ ($c = 0.0105$ g/mL, benzene); HPLC conditions: Daisel CHIRALCEL AD-H, hexane/2-propanol = 99.9/0.1, 1.5 mL/min, retention time: 23.85 min (*S*); 25.00 min (*R*).

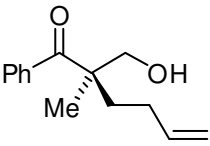
(*R*)-2-(hydroxymethyl)-1-phenyl-5-hexen-1-one (22aa)



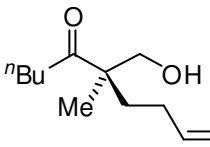
^1H NMR (500 MHz, CDCl_3) δ 7.97–7.94 (m, 2H), 7.60–7.57 (m, 1H), 7.50–7.46 (m, 2H), 5.77 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.02–4.98 (m, 2H), 3.94 (dd, $J = 11.0, 7.0$ Hz, 1H), 3.85 (dd, $J = 11.0, 4.0$ Hz, 1H), 3.67–3.62 (m,

1H), 2.43 (bs, 1H), 2.16–2.08 (m, 2H), 1.86–1.79 (m, 1H), 1.77–1.69 (m, 1H); ^{13}C NMR (125 MHz, C_6D_6) δ 204.5, 137.5, 136.6, 133.4, 128.7, 128.4, 115.7, 62.7, 47.1, 31.3, 28.0; IR (neat) 3447, 2934, 2361, 1678, 1597, 1449, 1375, 1234, 1053, 1001 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$: C, 76.44; H, 7.90%. Found: C, 76.69; H, 8.02%; HRMS (m/z) Found: 204.1154. Calcd for $\text{C}_{13}\text{H}_{16}\text{O}_2$ $[\text{M}]^+$: 204.1150. HPLC conditions: Daisel CHIRALCEL OJ-H, hexane/2-propanol = 95/5, 1.0 mL/min, retention time: 9.36 min (*R*); 10.42 min (*S*).

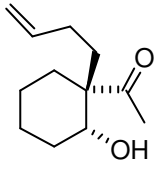
2-(hydroxymethyl)-2-methyl-1-phenyl-5-hexen-1-one (22ba)

 ^1H NMR (500 MHz, CDCl_3) δ 7.74–7.72 (m, 2H), 7.51–7.48 (m, 1H), 7.44–7.40 (m, 2H), 5.74 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 4.97 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 4.93 (ddt, $J = 10.0, 2.0, 1.5$ Hz, 1H), 3.91 (dd, $J = 11.5, 7.0$ Hz, 1H), 3.61 (dd, $J = 11.5, 7.0$ Hz, 1H), 2.41 (t, $J = 7.0$ Hz, 1H), 2.15–2.07 (m, 1H), 2.04–1.96 (m, 1H), 1.93 (ddd, $J = 14.0, 12.0, 4.5$ Hz, 1H), 1.86 (ddd, $J = 14.0, 12.0, 5.5$ Hz, 1H), 1.38 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 209.2, 138.3, 137.9, 131.5, 128.3, 127.8, 114.9, 68.8, 52.6, 35.5, 28.6, 21.0; IR (neat) 3403, 2934, 2360, 1668, 1445, 1214, 1046 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$: C, 77.03; H, 8.31%. Found: C, 77.11; H, 8.24%; HRMS (m/z) Found: 218.1305. Calcd for $\text{C}_{14}\text{H}_{18}\text{O}_2$ $[\text{M}]^+$: 218.1307.

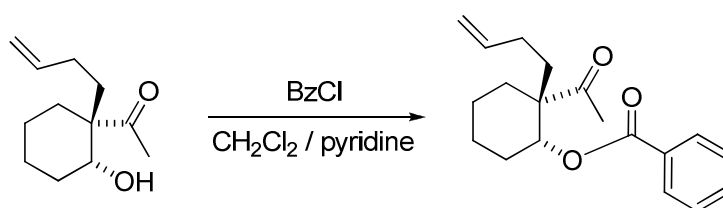
6-(hydroxymethyl)-6-methyl-9-decen-5-one (22ca)

 ^1H NMR (500 MHz, CDCl_3) δ 5.77 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 5.02 (ddt, $J = 17.0, 10.0, 6.5$ Hz, 1H), 4.96 (ddt, $J = 10.0, 2.0, 1.5$ Hz, 1H), 3.74 (dd, $J = 11.0, 6.5$ Hz, 1H), 3.50 (dd, $J = 11.0, 6.5$ Hz, 1H), 2.47 (dt, $J = 6.5, 4.5$ Hz, 2H), 2.25 (dd, $J = 6.5, 6.5$ Hz, 1H), 2.04–1.90 (m, 2H), 1.64 (dd, $J = 9.0, 7.5$ Hz, 2H), 1.57–1.51 (m, 2H), 1.34–1.27 (m, 2H), 1.17 (s, 3H), 0.91 (t, $J = 7.5$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3) δ 216.9, 138.0, 114.9, 67.7, 52.2, 37.5, 34.6, 28.4, 25.6, 22.4, 19.3, 13.9; IR (neat) 3415, 2927, 1698, 1464, 1377, 1261, 1116, 1023 cm^{-1} . HRMS (m/z) Found: 199.1696. Calcd for $\text{C}_{12}\text{H}_{23}\text{O}_2$ $[\text{MH}]^+$: 199.1698.

(1*R*,2*R*)-2-acetyl-2-(3-butenyl)cyclohexanol (22da)

 ^1H NMR (500 MHz, CDCl_3) δ 5.77 (ddt, J = 17.0, 10.0, 6.0 Hz, 1H), 5.02 (ddt, J = 17.0, 2.0, 1.5 Hz, 1H), 4.96 (ddt, J = 10.0, 2.0, 1.5 Hz, 1H), 3.66 (bs, 1H), 3.07 (bs, 1H), 2.15 (d, J = 0.5 Hz, 3H), 2.10–1.95 (m, 3H), 1.85–1.45 (m, 8H), 1.39–1.25 (m, 2H); ^{13}C NMR (125 MHz, C_6D_6) δ 216.5, 138.1, 114.9, 73.5, 55.5, 34.7, 31.0, 30.4, 28.5, 26.4, 22.7, 22.2; IR (neat) 3420, 2936, 1699, 1448, 1355, 1232, 1170, 1138, 1064 cm^{-1} . HRMS (m/z) Found: 197.1540. Calcd for $\text{C}_{12}\text{H}_{21}\text{O}_2$ $[\text{MH}]^+$: 197.1542. $[\alpha]_{\text{D}}^{25}$ = +16 (c = 0.0188 g/mL, benzene).

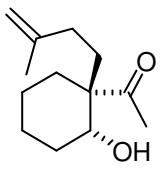
HPLC analysis was conducted after transformation of (1*R*,2*R*)-**22da** into the corresponding benzoate by treatment with benzoyl chloride.



Scheme 9. Preparation of benzoate of (1*R*,2*R*)-**22da**.

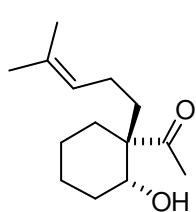
HPLC conditions: Daisel CHIRALCEL AD-H, hexane/2-propanol = 98/2, 1.0 mL/min, retention time: 8.07 min (1*R*,2*R*); 9.23 min (1*S*,2*S*).

(1*R,2*R**)-2-acetyl-2-(3-methyl-3-butenyl)cyclohexanol (22db)**

 ^1H NMR (500 MHz, CDCl_3) δ 4.71–4.70 (m, 1H), 4.68–4.67 (m, 1H), 3.69 (ddd, J = 8.0, 8.0, 3.5 Hz, 1H), 3.02 (d, J = 8.0 Hz, 1H), 2.15 (s, 3H), 2.02–1.88 (m, 3H), 1.85–1.73 (m, 3H), 1.72 (s, 3H), 1.69–1.46 (m, 4H), 1.40–1.27 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 216.3, 145.5, 110.0, 73.4, 55.5, 33.6, 32.2, 30.9, 30.1, 26.3, 22.5, 22.2; IR (neat) 3420, 2936, 1695, 1450, 1355, 1263, 1232, 1170, 1046 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{22}\text{O}_2$: C, 74.24; H, 10.54%. Found: C, 74.34; H, 10.31%; HRMS (m/z) Found: 210.1621. Calcd for

$\text{C}_{13}\text{H}_{22}\text{O}_2$ $[\text{M}]^+$: 210.1620.

(1*R,2*R**)-2-acetyl-2-(4-methyl-3-pentenyl)cyclohexanol (22dc)**

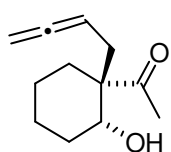


^1H NMR (500 MHz, CDCl_3) δ 5.07–5.03 (m, 1H), 3.70 (ddd, $J = 8.0, 8.0, 4.0$ Hz, 1H), 3.05 (d, $J = 8.0$ Hz, 1H), 2.15 (s, 3H), 1.99–1.78 (m, 4H), 1.70–1.46 (m, 6H), 1.67 (d, $3J = 1.0$ Hz, 3H), 1.58 (d, $J = 1.0$ Hz, 3H), 1.39–1.26 (m, 2H);

^{13}C NMR (125 MHz, CDCl_3) δ 216.4, 132.3, 123.7, 73.3, 55.7, 35.4, 30.9, 30.1,

26.3, 25.6, 22.8, 22.5, 22.2, 17.6; IR (neat) 3458, 2934, 2344, 1697, 1449, 1375, 1354, 1265, 1236, 1217, 1167, 1138, 1064 cm^{-1} . HRMS (m/z) Found: 224.1774. Calcd for $\text{C}_{14}\text{H}_{24}\text{O}_2$ $[\text{M}]^+$: 224.1776.

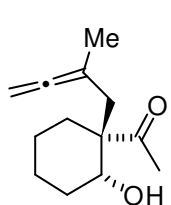
(1*R,2*R**)-2-acetyl-2-(2,3-butadienyl)cyclohexanol (22dd)**



^1H NMR (500 MHz, CDCl_3) δ 5.10 (m, 1H), 4.67 (dt, $J = 6.5, 2.5$ Hz, 2H), 3.62 (ddd, $J = 9.0, 9.0, 4.0$ Hz, 1H), 3.21 (d, $J = 9.0$ Hz, 1H), 2.44–2.31 (m, 2H), 2.16 (s, 3H), 2.02 (dddd, $J = 14.0, 6.5, 3.5, 1.5$ Hz, 1H), 1.86–1.80 (m, 1H), 1.72–1.54

(m, 3H), 1.47 (ddd, $J = 14.0, 10.0, 3.5$ Hz, 1H), 1.38–1.22 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 216.2, 209.7, 84.8, 74.5, 74.0, 56.1, 35.1, 31.2, 30.8, 26.8, 23.1, 22.4; IR (neat) 3389, 2936, 2359, 1954, 1693, 1604, 1447, 1408, 1360, 1273, 1244, 1177, 1123 cm^{-1} . HRMS (m/z) Found: 195.1382. Calcd for $\text{C}_{12}\text{H}_{19}\text{O}_2$ $[\text{MH}]^+$: 195.1385.

(1*R,2*R**)-2-acetyl-2-(2-methyl-2,3-butadienyl)cyclohexanol (22de)**

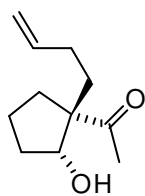


^1H NMR (500 MHz, CDCl_3) δ 4.60–4.57 (m, 2H), 3.74 (ddd, $J = 7.5, 7.5, 3.5$ Hz, 1H), 3.19 (d, $J = 7.5$ Hz, 1H), 2.34 (dd, $J = 2.5, 2.5$ Hz, 2H), 2.18 (s, 3H), 2.06–2.01 (m, 1H), 1.84–1.79 (m, 1H), 1.70 (t, $J = 3.0$ Hz, 3H), 1.69–1.52 (m, 4H), 1.40–1.30 (m, 2H); ^{13}C NMR (125 MHz, CDCl_3) δ 216.4, 208.0, 93.8, 74.3, 72.9,

56.0, 38.1, 30.7, 29.9, 27.2, 22.2, 22.1, 20.8; IR (neat) 3460, 2938, 2360, 1958, 1697, 1449, 1424, 1354, 1136, 1078, 1060 cm^{-1} . Anal. Calcd for $\text{C}_{13}\text{H}_{20}\text{O}_2$: C, 74.96; H, 9.68%. Found: C, 74.71; H,

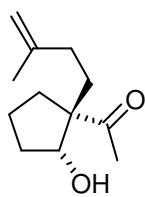
9.78%; HRMS (m/z) Found: 208.1471. Calcd for $C_{13}H_{20}O_2$ $[M]^+$: 208.1463.

(1*R,2*R**)-2-acetyl-2-(3-butenyl)cyclopentanol (22ea)**



1H NMR (500 MHz, $CDCl_3$) δ 5.75 (ddt, J = 17.0, 10.0, 6.5 Hz, 1H), 5.00 (ddt, J = 17.0, 2.0, 1.5 Hz, 1H), 4.95 (ddt, J = 10.0, 2.0, 1.5 Hz, 1H), 4.15 (ddd, J = 5.0, 5.0, 3.0 Hz, 1H), 2.74 (dd, J = 5.0, 0.5 Hz, 1H), 2.20–2.14 (m, 1H), 2.18 (s, 3H), 2.05–1.82 (m, 4H), 1.72–1.52 (m, 5H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.1, 137.7, 115.0, 78.7, 63.8, 35.1, 32.6, 30.8, 29.1, 27.8, 20.5; IR (neat) 3420, 2936, 1695, 1448, 1355, 1232, 1170, 1046 cm^{-1} . Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95%. Found: C, 72.31; H, 9.87%; HRMS (m/z) Found: 183.1380. Calcd for $C_{11}H_{19}O_2$ $[MH]^+$: 183.1385.

(1*R,2*R**)-2-acetyl-2-(3-methyl-3-butenyl)cyclopentanol (22eb)**



1H NMR (500 MHz, $CDCl_3$) δ 4.71–4.70 (m, 1H), 4.66–4.65 (m, 1H), 4.16 (ddd, J = 5.0, 5.0, 2.5 Hz, 1H), 2.74 (d, J = 5.0 Hz, 1H), 2.21–2.15 (m, 1H), 2.18 (s, 3H), 2.06–1.56 (m, 9H), 1.70 (s, 3H); ^{13}C NMR (125 MHz, $CDCl_3$) δ 214.1, 145.1, 110.0, 78.8, 63.9, 34.1, 32.8, 32.6, 30.8, 27.7, 22.6, 20.5; IR (neat) 3461, 2936, 1694, 1447, 1357, 1167, 1052 cm^{-1} . HRMS (m/z) Found: 197.1542. Calcd for $C_{12}H_{21}O_2$ $[MH]^+$: 197.1542.

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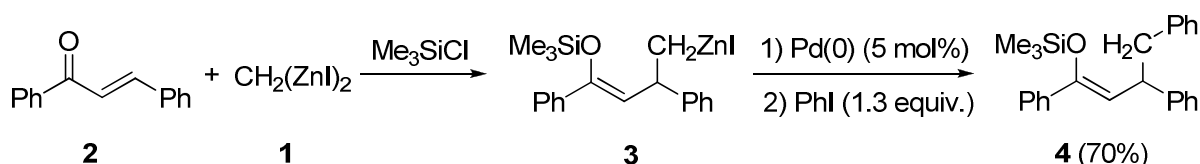
Chapter 6

Nucleophilic Cyclopropanation Reaction with Bis(iodozincio)methane by 1,4-Addition to α,β -Unsaturated Carbonyl Compounds

Treatment of α,β -unsaturated ketones carrying electrophilic site at γ -position in the presence of trimethylsilyl cyanide with bis(iodozincio)methane afforded (*Z*)-silyl enol ether of β -cyclopropyl substituted ketone in good yields. The reaction proceeds via 1,4-addition to form enolate, and its sequential intramolecular nucleophilic attack to an adjacent electrophilic site. The reaction of γ -ethoxycarbonyl- α,β -unsaturated ketone and bis(iodozincio)methane in the presence of trimethylsilyl cyanide afforded 1-ethoxy-1-trimethylsiloxycyclopropane derivatives, which can be regarded as the homoenolate equivalent. The author also demonstrated the reactions of the obtained homoenolate equivalents with imines to give 1-(*E*)-alkenyl-2-(1-aminoalkyl)alkanols diastereoselectively.

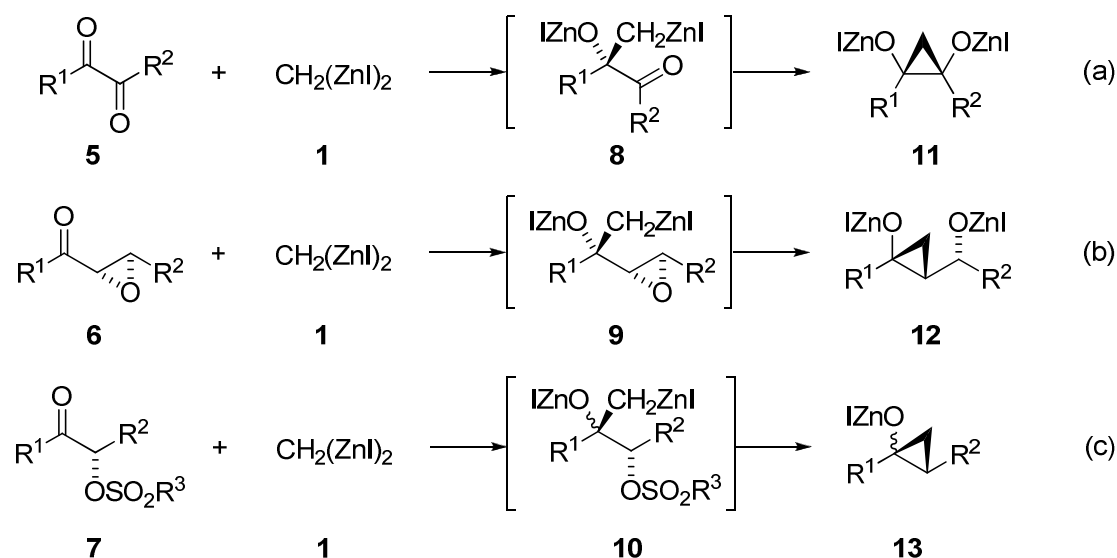
Introduction

Many examples of 1,4-addition of organozinc reagent to α,β -unsaturated ketones have been reported.¹ Matsubara *et al.* had also reported that the *gem*-dizinc reagent undergoes 1,4-addition to α,β -unsaturated ketones.² For example, treatment of chalcone (**2**) with bis(iodozincio)methane (**1**) in the presence of chlorotrimethylsilane afforded (*Z*)-trimethylsilyl enol ethers of β -iodozinciomethylketone **3** via 1,4-addition (Scheme 1).³ The sequential coupling reaction at the introduced zinciomethyl group with other electrophiles, such as phenyl iodide, was also possible in the presence of Pd(0).



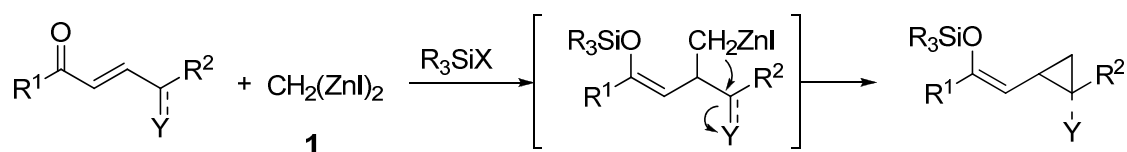
Scheme 1. 1,4-Addition of bis(iodozincio)methane (**1**) to chalcone (**2**) and sequential coupling with phenyl iodide in the presence of Pd(0).

Instead of performing the intermolecular coupling shown in Scheme 1, an intramolecular process would afford cyclic compounds. The author had already shown that a sequential nucleophilic reaction is an efficient route for cyclopropane ring formation in Chapter 2, 3, and 5.⁴ When 1,2-diketone **5**, α,β -epoxy ketone **6**, or α -sulfonyloxy ketone **7** was treated with **1**, 1,2-addition to carbonyl group proceeds to generate organozinc species, **8**, **9**, or **10** respectively. In this case, a sequential intramolecular nucleophilic attack of the carbon–zinc bond to another carbonyl group or the leaving group, epoxy group or sulfonyloxy group, had proceeded readily, and the corresponding zinc alkoxide of cyclopropanol **11**, **12**, or **13** was obtained (Scheme 2).



Scheme 2. Nucleophilic cyclopropanation of bis(iodozincio)methane (**1**) with 1,2-diketone (**5**), α,β -epoxy ketone (**6**) or α -sulfonyloxy ketone (**7**) via iodozinciomethylation.

In this context, the author planned a sequential process of 1,4-addition and cyclopropane formation using *gem*-dizinc **1** to produce β -cyclopropyl substituted silyl enol ether. As shown in Scheme 3, the author examined the treatment of α,β -unsaturated ketone carrying an electrophilic site at γ -position with bis(iodozincio)methane (**1**) in the presence of silylation reagent (R_3SiX).

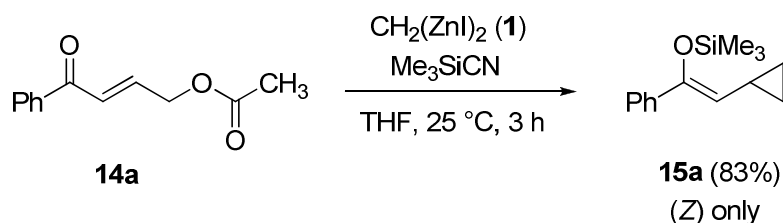


Scheme 3. Nucleophilic cyclopropanation of bis(iodozincio)methane (**1**) via 1,4-addition.

Results and Discussion

A mixture of γ -acetoxy- α,β -unsaturated ketone **14a** (1.0 mmol), triethylamine (2.5 mmol), and trimethylsilyl cyanide (2.2 mmol) in THF was treated with **1** (1.2 mmol) at 25 °C for 5 min.

After aqueous work up, (Z)-silyl enol ether of β -cyclopropyl ketone **15a** was obtained in 83 % yield stereoselectively (Scheme 4).^{2,5}



Scheme 4. Reaction of γ -acetoxy- α,β -unsaturated ketone **14a** with the dizinc **1**.

Other examples are shown in Table 1. In all cases, the products were obtained as (Z)-form enolates selectively. When γ -acetoxy- γ -methyl- α,β -enone **14e** was treated with **1** in the presence of trimethylsilyl cyanide, (Z)-enolate **15e** was obtained in 80% yield with low diastereoselectivity concerning the stereochemistry of cyclopropane ring (entry 4). Starting the reaction at -40 $^\circ\text{C}$ did not improve the diastereomeric ratio (entry 5). In these cases, the diastereofacial selectivity of 1,4-addition to α,β -enone will determine the diastereomeric ratio of the product, because the subsequent intramolecular nucleophilic substitution of the remaining carbanion site to the adjacent acyloxy substituted carbon should be stereospecific. Yamamoto had reported the diastereofacial selectivity of 1,4-addition of carbon nucleophiles to α,β -unsaturated carbonyl derivatives.⁶ In general, the diastereoselectivity can be explained by the modified Felkin–Anh model when 1,4-additions proceed through the Bürgi–Dunitz trajectory⁷ (Figure 1). The model could be applied to our reaction, so the size of the substituents on γ -position was examined to determine the diastereoselectivity. The reaction of γ -(2,4,6-trimethylbenzoyloxy)- α,β -enone **14f** improved the diastereomeric ratio only slightly (entry 6). In the case of γ -isopropyl-substituted enone **14h**, the diastereomeric ratio was improved to 85 / 15, but the reaction became sluggish (entry 8).

Table 1. Cyclopropanation of γ -acyloxy- α,β -unsaturated ketone **14** with bis(iodozincio)methane (**1**) via 1,4-addition.^a

entry	substrate	conditions	product	yield (%) ^b	dr ^c
1	14b	25 °C, 3 h	15b	86	
2	14c	25 °C, 3 h	15c	83	
3	14d	25 °C, 3 h	15d	51 ^d	
4	14e	0 to 25 °C 12 h	15e	80	59/41 ^e
5	14e	-40 to 25 °C 12 h	15e	80	60/40
6	14f	0 to 25 °C 12 h	15e	75	66/34
7	14g	0 to 25 °C 12 h	15g	82	79/21 ^f
8	14h	0 to 25 °C 12 h	15h	27 ^g	85/15

^a Ketone **14** (1.0 mmol), the dizinc **1** (1.2 mmol, 0.5 M in THF), triethylamine (2.5 mmol), R₃SiX (2.2 mmol), and THF (4 mL) were used. ^b Isolated yields. ^c The diastereomeric ratios were determined by ¹H NMR. ^d **15d** was obtained as equimolar mixture of (*E*)- and (*Z*)-isomers after purification. ^e The stereochemistry of substituents on cyclopropane ring in major isomer was trans. ^f The diastereomeric ratio was determined after converting to the corresponding ketone with 1N aqueous HCl. ^g The starting material was recovered in 65% yield.

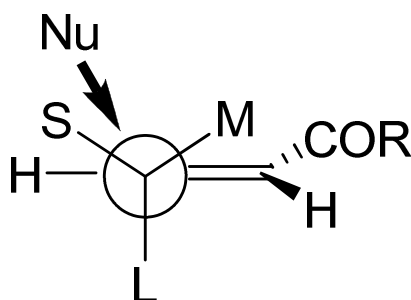
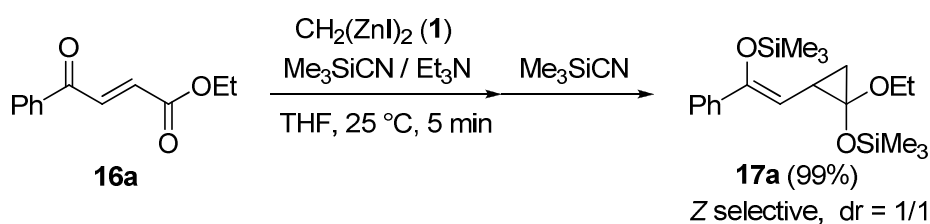


Figure 1. Modified Felkin-Anh Model by Yamamoto.

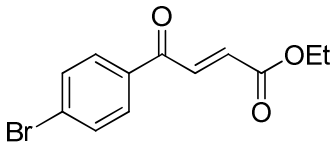
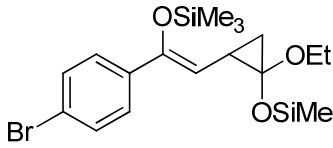
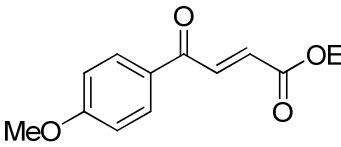
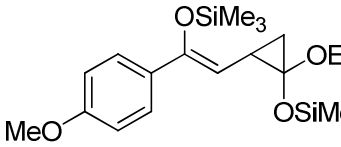
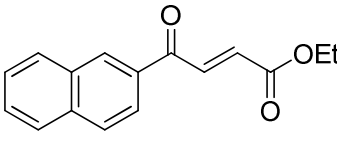
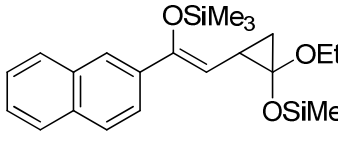
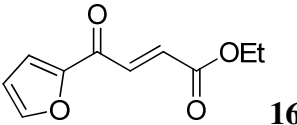
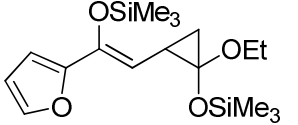
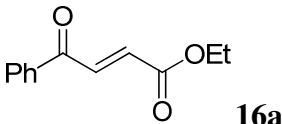
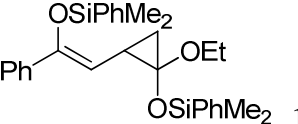
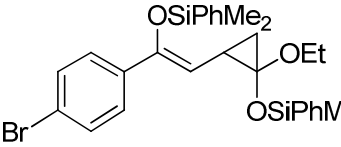
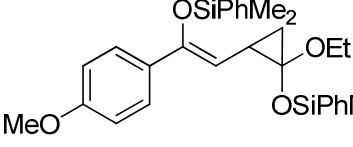
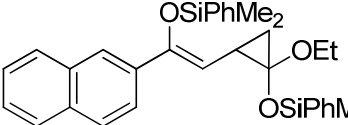
Instead of **14**, γ -ethoxycarbonyl- α,β -enone **16** was also examined as a substrate. A mixture of ethyl (*E*)-3-benzoylacrylate (**16a**, 1.0 mmol), triethylamine (2.5 mmol), and trimethylsilyl cyanide (1.1 mmol) in THF was treated with **1** (1.2 mmol) at 25 °C for 5 min. Additional trimethylsilyl cyanide (1.1 mmol) was added and the mixture was stirred for 10 min at room temperature. After aqueous work-up, 1-ethoxy-1-trimethylsiloxycyclopropane **17a** was obtained in 99% yield (Scheme 5). The configuration of enolate was (*Z*)-form without any diastereoselectivity of cyclopropane formation reaction.



Scheme 5. Cyclopropanation of ketoester **16a** with bis(iodozincio)methane (**1**).

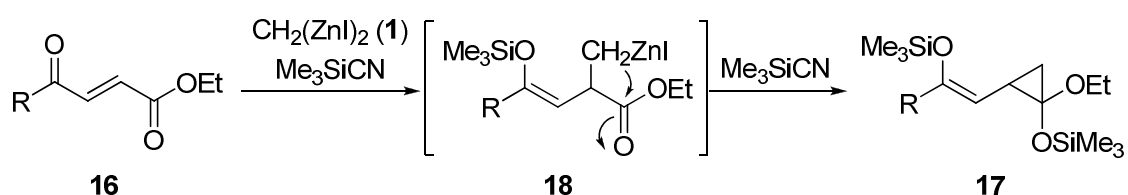
Other examples are shown in Table 2. In all cases, the products **17** were obtained as an equimolar mixture of diastereomers, as the intramolecular cyclopropanation proceeded without diastereoselectivity (from **18** to **17** in Scheme 6). When chlorodimethylphenylsilane was used as silylation reagent instead of trimethylsilyl cyanide, the corresponding phenyldimethylsilyl ether derivatives **17a'-d'** were obtained (entries 5-8).

Table 2. Cyclopropanation of ketoesters **16** with bis(iodozincio)methane (**1**).^a

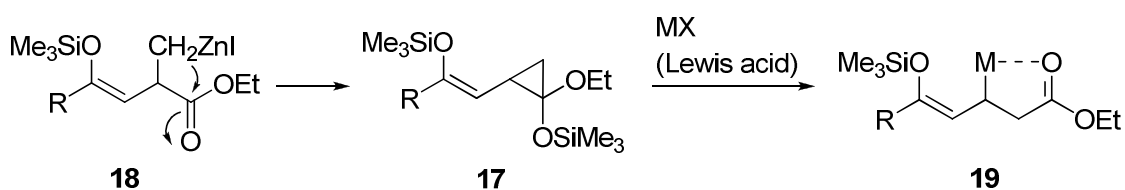
$ \begin{array}{c} \text{R}-\text{C}(=\text{O})-\text{CH}=\text{CH}-\text{C}(=\text{O})\text{OEt} \\ \mathbf{16} \end{array} \xrightarrow[\text{THF, 25 }^{\circ}\text{C, 5 min}]{\begin{array}{c} \text{CH}_2(\text{ZnI})_2 \text{ (1)} \\ \text{R}'_3\text{SiX} \end{array}} \begin{array}{c} \text{R}'_1-\text{C}(\text{OSiR}'_3)=\text{CH}-\text{C}(\text{OSiR}'_3)_2\text{OEt} \\ \mathbf{17} \end{array} $				
entry	substrate	R' ₃ SiX	product	yield (%) ^b
1	 16b	Me ₃ SiCN	 17b	99
2	 16c	Me ₃ SiCN	 17c	73
3	 16d	Me ₃ SiCN	 17d	99
4	 16e	Me ₃ SiCN	 17e	83
5	 16a	PhMe ₂ SiCl	 17a'	93
6	16b	PhMe ₂ SiCl	 17b'	90
7	16c	PhMe ₂ SiCl	 17c'	65
8	16d	PhMe ₂ SiCl	 17d'	97

^a (*E*)-Ethyl 4-oxoalk-2-enoate **16** (1.0 mmol), the dizinc **1** (1.2 mmol, 0.5 M in THF), triethylamine (2.5 mmol), R'₃SiX (2.2 mmol), and THF (4 mL) were used. ^b Isolated yields.

The product **17** has 1-ethoxy-1-siloxycyclopropane moiety, which is known as an ester homoenolate via cyclopropane ring opening. Nakamura and Kuwajima had reported that treatment of 1-siloxy-1-alkoxycyclopropanes with Lewis acid generates homoenolates,⁸ which can be applied for the C–C bond forming reactions.⁹ When **17** was activated by Lewis acid, the homoenolate **19** would be generated via cyclopropane ring opening (Scheme 7); the homoenolate **19** is considered to be as 3-siloxyallylmetal species.¹⁰ This reagent might have an allylmetal form **19**, because of the coordination between metal and carbonyl group. The silyl enol ether was formed as (Z)-form selectively. So, the nucleophilic reaction of **19** as 3-siloxyallylmetal reagent was expected to proceed regio- and diastereoselectively.¹¹

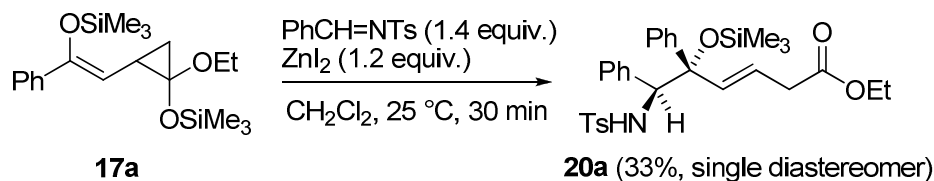


Scheme 6. Formation of cyclopropane **17** via 1,4-addition.



Scheme 7. Strategy of migration of iodozincio group from homoallyl metal into allyl metal.

Treatment of tosylimine of benzaldehyde with **17a** in the presence of zinc(II) iodide gave the β -siloxylamine derivative **20a** as a single diastereomer (Scheme 8). The stereochemistry of **20a** was determined by X-ray analysis (Figure 2).¹² Meanwhile, the same reaction from **17a** without zinc(II) iodide resulted in a complete recovery.



Scheme 8. The reaction of **17a** as homoenolate with imine.

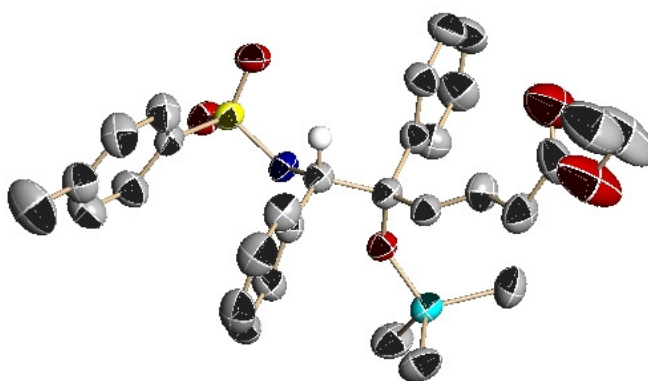
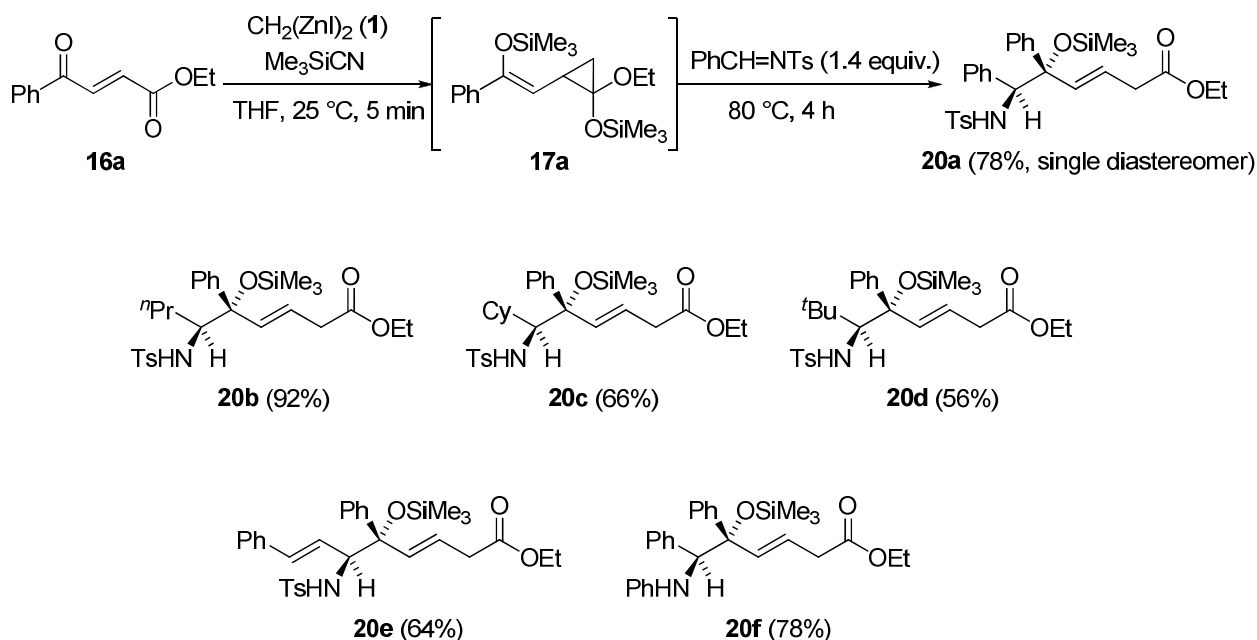


Figure 2. The ORTEP of **20a**.

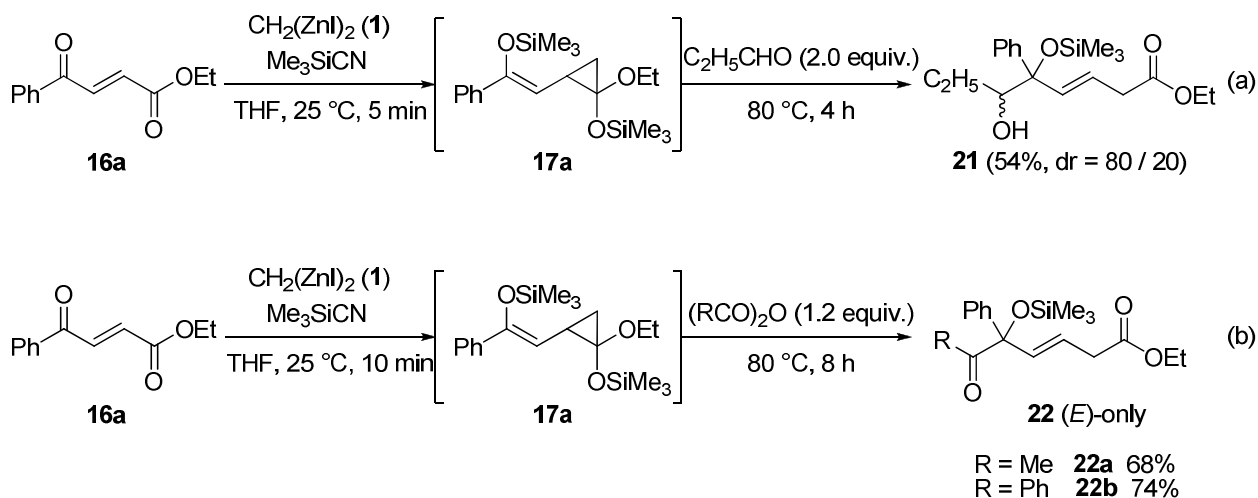
When the ketoester **16a** was treated with bis(iodozincio)methane (**1**) in the presence of trimethylsilyl cyanide as in Scheme 5, zinc(II) salts such as zinc(II) iodide and cyanide were also generated in situ. These zinc salts might mediate the conversion of the 1-trimethylsiloxy-1-ethoxycyclopropane moiety in **17a** into the zinc homoenolate. So we tried the cyclopropanation reaction and the addition reaction in one pot without the isolation of silyl ether **17a**. For this purpose, after the procedure for preparation of **17a** from **16a** without addition of triethylamine, we added the tosylimines and then raised the reaction temperature to 80 °C for 4 h. As shown in Scheme 9, β -siloxylamine derivatives **20** were obtained with high

diastereoselectivity. Instead of tosylimine, treatment of phenylimine of benzaldehyde with **17a** also gave the corresponding β -siloxylamine derivative **20f** diastereoselectively.



Scheme 9. Reaction of various imines with the homoenolate prepared from **16a**.

Instead of imines, other electrophiles were also examined. Treatment of in situ formed **17a** with propanal under the reflux condition afforded the *vic*-diol **21** in moderate yield. The product **21**, however, was given as a diastereo mixture (Scheme 10 (a)). The reaction of acid anhydrides with **17a** afforded α -(*E*)-alkenyl- α -siloxylketones **22** in good yields with high (*E*)-selectivity (Scheme 10 (b)).



Scheme 10. Reaction of propanal or acid anhydride with the homoenolate from **16a**.

The author proposes the explanation for the high diastereoselectivities in the reaction of imines with the homoenolate, as shown in Figure 3. The conformation of 3-siloxyallylzinc intermediate might be fixed by the chelation between zinc atom and two oxygen atoms as (Z)-**23a**. The nucleophilic reaction proceeds regioselectively, retaining the conformation, and as a result, the product is afforded as (*E*)-form dominantly. Furthermore, considering the trajectory of nucleophile to imine, we propose the reaction pathway shown as **24**. In comparison with another possible intermediate **24'**, **24** is much more favourable, since the intermediate **24'** contains a steric interaction between alkyl group on imine and phenyl group in the reagent. In addition, an intermolecular chelation between siloxy group and nitrogen atom of imine would benefit the intermediate **24**. So, the nucleophilic attack of (Z)-**23a** to imine proceeds via **24** to generate a couple of stereogenic centers diastereoselectively, and as a result, the *threo* isomer **20a** will be a major product.

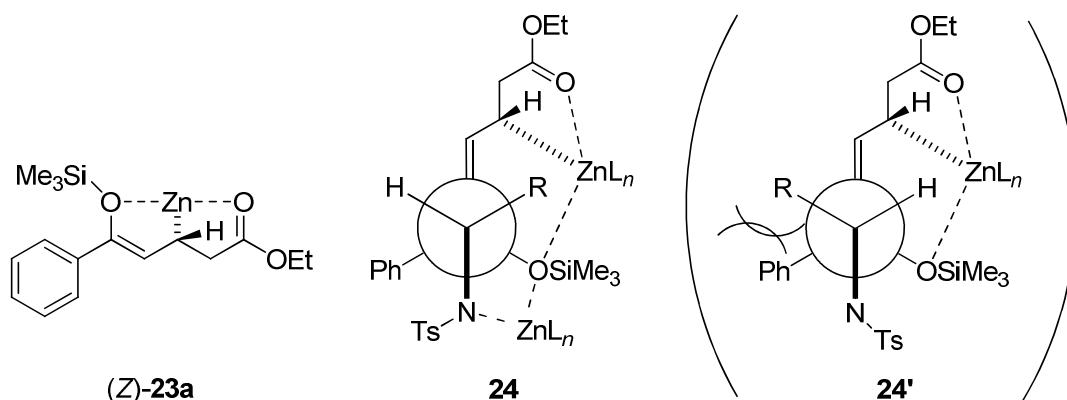


Figure 3. Proposed conformation of (Z)-23 and the transition state 24.

Conclusion

The author have demonstrated the nucleophilic cyclopropanation reaction of γ -acyloxy- α,β -unsaturated ketone or γ -ethoxycarbonyl- α,β -unsaturated ketone with bis(iodozincio)methane in the presence of silylating reagent. The reaction proceeded via 1,4-addition and sequential intramolecular nucleophilic attack to adjacent electrophilic sites to afford cyclopropane derivatives or 1-ethoxy-1-siloxycyclopropane derivatives in good yield. Furthermore, he also demonstrated the reaction with imines of (Z)-3-siloxyallylzinc species, which can be prepared easily from the obtained 1-ethoxy-1-siloxycyclopropane derivative with the aid of zinc salts existing in the reaction mixture. The reaction proceeded with high diastereoselectivity to give 1-(*E*)-alkenyl-2-(1-aminoalkyl)alkanol.

Experimental Section

Unless otherwise noted, commercially available reagents were used without purification. The compounds **16a** is commercially available.

General procedure for preparation of γ -acyloxy- α,β -unsaturated ketone (**14**):

γ -Hydroxy- α,β -unsaturated ketone was prepared according to the literature.¹³ To a solution of γ -hydroxy- α,β -unsaturated ketone (1.0 mmol), pyridine (1 mL) and dichloromethane (1 mL), acid chloride (1.2 mmol) or acid anhydride (1.2 mmol) was added at 0 °C. The mixture was stirred for 3 h, and saturated aqueous solution of Na₂CO₃ was added. The organic layer was extracted with dichloromethane. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding γ -acyloxy- α,β -unsaturated ketone **14**.

General procedure for the nucleophilic cyclopropanation of γ -acyloxy- α,β -unsaturated ketone (**14**):

A mixture of γ -acyloxy- α,β -unsaturated ketone (**14**, 1.0 mmol), triethylamine (2.5 mmol) and trimethylsilyl cyanide (2.2 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C for 3 h. Then water was added to quench the reaction and extracted with hexane. The combined organic layers were washed with brine, and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding cyclopropane **15**.

General procedure for preparation of (*E*)-ethyl 4-oxoalk-2-enoate (16**):** A phosphonium bromide was prepared from 1-alkyl-2-bromoethanone and triphenylphosphine by the conventional method. To a mixture of sodium hydride (5.5 mmol) and THF (5 mL), the prepared phosphonium bromide was added and stirred for 1.5 h. To the resulted mixture, ethyl

glyoxylate (6.0 mmol, 47% in toluene) was added. The whole was stirred for 12 h, and saturated aqueous solution of NH_4Cl was added. The organic layer was extracted with ethyl acetate, and the solvent was removed under reduced pressure. The residue was purified by silica gel column chromatography to give the corresponding (*E*)-ethyl 4-oxoalk-2-enoate **16**.

General procedure for the nucleophilic cyclopropanation of (*E*)-ethyl 4-oxoalk-2-enoate

(16): A mixture of (*E*)-ethyl 4-oxoalk-2-enoate (**16**, 1.0 mmol), triethylamine (2.5 mmol) and trimethylsilyl cyanide (1.1 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C for 5 min. Additional trimethylsilyl cyanide (1.1 mmol) was added and the mixture was stirred for 10 min at room temperature. Triethylamine was added and the whole mixture was poured into water, and the organic layer was extracted with hexane–EtOAc. The combined organic layers were washed with brine, and dried over Na_2SO_4 . The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding cyclopropane **17**.

General procedure for the tandem reaction of bis(iodozincio)methane (1**), **16a**, and imines:**

A mixture of (*E*)-ethyl 4-oxoalk-2-enoate (**16**, 1.0 mmol) and trimethylsilyl cyanide (1.1 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C for 5 min. Additional trimethylsilyl cyanide (1.1 mmol) was added and the mixture was stirred for 10 min at room temperature. A solution of imine (1.2 mmol) in THF (1.5 mL) was added, and the resulting mixture was heated to reflux for 4h. The mixture was cooled to 0 °C and poured into water to quench the reaction. The organic layer was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na_2SO_4 . The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding (*E*)-1-alkenyl-2-(1-aminoalkyl)alkanol **20**.

Preparation of ethyl (*E*)-6-hydroxy-5-phenyl-5-trimethylsiloxy-3-octenoate (21**):** A mixture

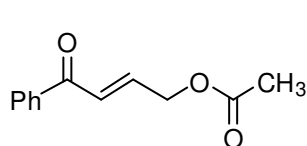
of (*E*)-ethyl 4-oxoalk-2-enoate (**16**, 1.0 mmol) and trimethylsilyl cyanide (1.1 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C for 5 min. Additional trimethylsilyl cyanide (1.1 mmol) was added and the mixture was stirred for 10 min at room temperature. A solution of propanal (1.2 mmol) in THF (1.5 mL) was added, and the resulting mixture was heated to reflux for 4 h. The mixture was cooled to 0 °C and poured into water to quench the reaction. The organic layer was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding *vic*-diol **21**.

General procedure for the tandem reaction of bis(iodozincio)methane (1**), **16a**, and acid anhydride:** A mixture of (*E*)-ethyl 4-oxoalk-2-enoate (**16**, 1.0 mmol) and trimethylsilyl cyanide (1.1 mmol) in THF (4 mL) was treated with bis(iodozincio)methane (**1**, 0.5 M solution in THF, 1.2 mmol) at 25 °C for 5 min. Additional trimethylsilyl cyanide (1.1 mmol) was added and the mixture was stirred for 10 min at room temperature. A solution of acid anhydride (1.2 mmol) in THF (1.5 mL) was added, and the resulting mixture was heated to reflux for 8 h. The mixture was cooled to 0 °C and poured into water to quench the reaction. The organic layer was extracted with EtOAc. The combined organic layers were washed with brine and dried over Na₂SO₄. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding α -siloxyketone **22**.

Characterization Data

The spectral data of the substrates **16b** and **16c** can be found in the literature.¹⁴

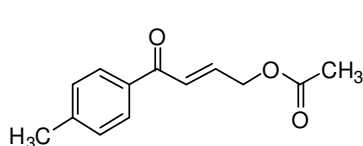
(*E*)-4-Acetoxy-1-phenyl-2-buten-1-one (**14a**)



¹H NMR (500 MHz, CDCl₃) δ 7.96–7.92 (m, 2H), 7.60–7.54 (m, 1H), 7.50–7.44 (m, 2H), 7.08 (dt, *J* = 15.6, 1.2 Hz, 1H), 6.99 (dt, *J* = 15.6,

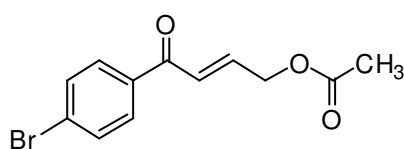
4.2 Hz, 1H), 4.84 (dd, $J = 4.2, 1.2$ Hz, 2H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 190.0, 170.3, 141.0, 137.3, 133.0, 128.61, 128.56, 126.0, 63.1, 20.7; IR (neat) 1746, 1674, 1632, 1449, 1364, 1284, 1231, 1082, 1036, 756, 692 cm^{-1} . HRMS (m/z) Found: 204.0796. Calcd for $\text{C}_{12}\text{H}_{12}\text{O}_3$ $[\text{M}]^+$: 204.0786.

(*E*)-4-Acetoxy-1-(4-methylphenyl)-2-buten-1-one (14b)



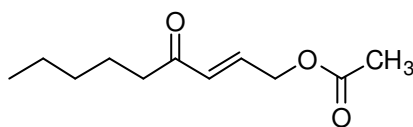
^1H NMR (300 MHz, CDCl_3) δ 7.84 (d, $J = 7.8$ Hz, 2H), 7.26 (d, $J = 7.8$ Hz, 2H), 7.08 (dt, $J = 15.6, 0.9$ Hz, 1H), 6.97 (dt, $J = 15.6, 4.5$ Hz, 1H), 4.83 (dd, $J = 4.5, 0.9$ Hz, 2H), 2.40 (s, 3H), 2.14 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 189.1, 170.1, 143.8, 140.3, 134.6, 129.2, 128.6, 125.9, 63.2, 21.7, 20.8; IR (neat) 1746, 1672, 1630, 1605, 1445, 1364, 1285, 1231, 1084, 1036, 797 cm^{-1} . HRMS (m/z) Found: 218.0940. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$: 218.0943.

(*E*)-4-Acetoxy-1-(4-bromophenyl)-2-buten-1-one (14c)



^1H NMR (500 MHz, CDCl_3) δ 7.80 (d, $J = 9.0$ Hz, 2H), 7.62 (d, $J = 9.0$ Hz, 2H), 7.02–7.01 (m, 2H), 4.84 (d, $J = 3.0$ Hz, 2H), 2.15 (s, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 188.8, 170.3, 141.7, 136.1, 131.9, 130.1, 128.2, 125.4, 63.1, 20.7; IR (nujol) 1742, 1674, 1630, 1586, 1285, 1233, 1072, 1034, 1011, 910, 733 cm^{-1} , mp 52.5–53.5 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{12}\text{H}_{11}\text{O}_3\text{Br}$: C, 50.91; H, 3.92%. Found: C, 51.03; H, 3.88%; HRMS (m/z) Found: 281.9891. Calcd for $\text{C}_{12}\text{H}_{11}\text{O}_3\text{Br}$ $[\text{M}]^+$: 281.9892.

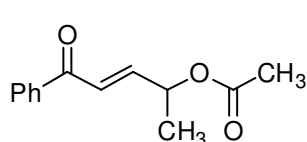
(*E*)-1-Acetoxy-2-nonen-4-one (14d)



^1H NMR (300 MHz, CDCl_3) δ 6.76 (dt, $J = 16.2, 4.8$ Hz, 1H), 6.26 (dt, $J = 16.2, 1.8$ Hz, 1H), 4.74 (dd, $J = 4.8, 1.8$ Hz, 2H), 2.54 (t, $J = 7.5$ Hz, 2H), 2.11 (s, 3H), 1.65–1.55 (m, 2H), 1.34–1.25 (m, 4H), 0.88 (t, $J = 6.9$ Hz, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 199.6, 170.1, 138.4,

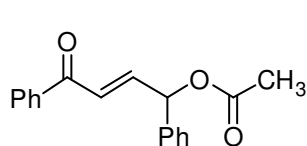
130.0, 62.8, 40.6, 31.5, 23.7, 22.5, 20.8, 14.0; IR (neat) 2932, 1746, 1701, 1678, 1640, 1381, 1364, 1227, 1088, 1034, 976, 731 cm^{-1} . Anal. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_3$: C, 66.64; H, 9.15%. Found: C, 66.84; H, 9.36%; HRMS (m/z) Found: 198.1249. Calcd for $\text{C}_{11}\text{H}_{18}\text{O}_3$ $[\text{M}]^+$: 198.1256.

(*E*)-4-Acetoxy-1-phenyl-2-penten-1-one (14e)



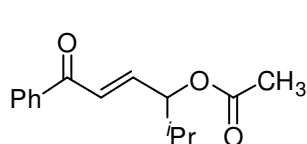
^1H NMR (300 MHz, CDCl_3) δ 7.95–7.91 (m, 2H), 7.60–7.54 (m, 1H), 7.50–7.45 (m, 2H), 7.02 (dd, $J = 15.6, 1.2$ Hz, 1H), 6.91 (dd, $J = 15.6, 4.8$ Hz, 1H), 5.59 (ddq, $J = 6.6, 4.8, 1.2$ Hz, 1H), 2.12 (s, 3H), 1.42 (d, $J = 6.6$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 190.1, 169.8, 145.9, 137.3, 132.9, 128.5, 128.4, 124.7, 69.4, 21.3, 19.9; IR (neat) 2984, 1738, 1674, 1626, 1449, 1371, 1238, 1049, 1015, 974, 773, 698 cm^{-1} . HRMS (m/z) Found: 218.0947. Calcd for $\text{C}_{13}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$: 218.0943.

(*E*)-4-Acetoxy-1,4-diphenyl-2-buten-1-one (14g)



^1H NMR (300 MHz, CDCl_3) δ 7.95–7.91 (m, 2H), 7.60–7.55 (m, 1H), 7.51–7.45 (m, 2H), 7.41–7.34 (m, 5H), 7.08 (d, $J = 2.1$ Hz, 1H), 7.08 (d, $J = 1.5$ Hz, 1H), 6.51 (dd, $J = 2.1, 1.5$ Hz, 1H), 2.17 (s, 3H); ^{13}C NMR (75 MHz, CDCl_3): δ 189.9, 169.5, 144.2, 137.3, 137.2, 132.9, 128.72, 128.65, 128.50, 128.47, 127.3, 125.4, 74.8, 21.2; IR (neat) 3063, 1738, 1672, 1626, 1495, 1449, 1371, 1287, 1229, 1069, 1020, 978, 760, 698 cm^{-1} . Anal. Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_3$: C, 77.12; H, 5.75%. Found: C, 77.09; H, 5.93%; HRMS (m/z) Found: 280.1103. Calcd for $\text{C}_{18}\text{H}_{16}\text{O}_3$ $[\text{M}]^+$: 280.1099.

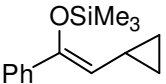
(*E*)-4-Acetoxy-5-methyl-1-phenyl-2-hexen-1-one (14h)



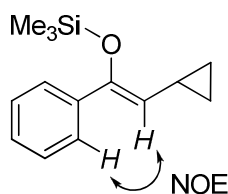
^1H NMR (300 MHz, CDCl_3) δ 7.95–7.91 (m, 2H), 7.60–7.54 (m, 1H), 7.50–7.44 (m, 2H), 7.00 (dd, $J = 15.9, 0.9$ Hz, 1H), 6.90 (dd, $J = 15.9, 5.4$ Hz, 1H), 5.33 (ddd, $J = 5.4, 5.4, 0.9$ Hz, 1H), 2.14 (s, 3H), 2.01 (dsept, $J = 6.9, 5.4$ Hz, 1H), 0.98 (d, $J = 6.9$ Hz, 3H), 0.96 (d, $J = 6.9$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 190.1, 170.2, 143.9, 137.5, 132.9, 128.58, 128.56, 126.5, 77.5, 32.1, 21.0, 18.1,

17.9; IR (neat) 2966, 1743, 1674, 1626, 1449, 1371, 1292, 1236, 1022, 986 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_3$: C, 73.15; H, 7.37%. Found: C, 73.20; H, 7.46%; HRMS (m/z) Found: 246.1264. Calcd for $\text{C}_{15}\text{H}_{18}\text{O}_3$ $[\text{M}]^+$: 246.1256.

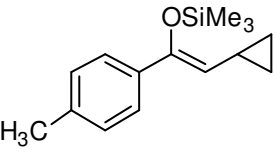
[(Z)-2-trimethysiloxy-2-phenylethenyl]cyclopropane (15a)

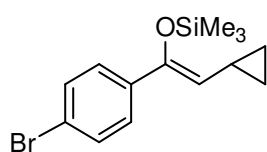
 ^1H NMR (500 MHz, CDCl_3) δ 7.44–7.42 (m, 2H), 7.30–7.26 (m, 2H), 7.22–7.19 (m, 1H), 4.76 (d, $J = 9.5$ Hz, 1H), 1.76 (dt, $J = 9.5, 8.0, 4.5$ Hz, 1H), 0.81 (ddd, $J = 8.0, 6.0, 4.5$ Hz, 2H), 0.42 (ddd, $J = 6.0, 4.5, 4.5$ Hz, 2H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 148.6, 138.8, 128.0, 127.1, 124.7, 115.9, 9.3, 7.2, 0.52; IR (neat) 2959, 1647, 1599, 1493, 1447, 1368, 1306, 1283, 1252, 1065, 1028 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{20}\text{OSi}$: C, 72.36; H, 8.67%. Found: C, 72.22; H, 8.94%; HRMS (m/z) Found: 232.1284. Calcd for $\text{C}_{14}\text{H}_{20}\text{OSi}$ $[\text{M}]^+$: 232.1283.

The structure of **15a** was assigned based on NOE experiments of ^1H NMR.



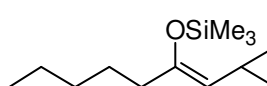
[(Z)-2-trimethysiloxy-2-(4-tolyl)ethenyl]cyclopropane (15b)

 ^1H NMR (500 MHz, CDCl_3) δ 7.32 (d, $J = 8.0$ Hz, 2H), 7.08 (d, $J = 8.0$ Hz, 2H), 4.71 (d, $J = 9.5$ Hz, 1H), 2.32 (s, 3H), 1.74 (dt, $J = 9.5, 8.0, 4.5$ Hz, 1H), 0.79 (ddd, $J = 8.0, 6.0, 4.5$ Hz, 2H), 0.40 (ddd, $J = 6.0, 4.5, 4.5$ Hz, 2H), 0.17 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 148.7, 136.8, 136.0, 128.7, 124.7, 115.0, 21.1, 9.3, 7.2, 0.55; IR (neat) 2960, 1648, 1511, 1366, 1311, 1252, 1065 cm^{-1} . Anal. Calcd for $\text{C}_{15}\text{H}_{22}\text{OSi}$: C, 73.11; H, 9.00%. Found: C, 72.87; H, 8.89%; HRMS (m/z) Found: 246.1445. Calcd for $\text{C}_{15}\text{H}_{22}\text{OSi}$ $[\text{M}]^+$: 246.1440.

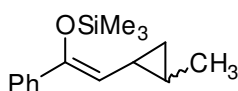
[(Z)-2-trimethylsiloxy-2-(4-bromophenyl)ethenyl]cyclopropane (15c)

^1H NMR (500 MHz, CDCl_3) δ 7.39 (d, $J = 8.5$ Hz, 2H), 7.30 (d, $J = 8.5$ Hz, 2H), 4.76 (d, $J = 9.5$ Hz, 1H), 1.74 (dtt, $J = 9.5, 8.0, 4.5$ Hz, 1H), 0.82 (ddd, $J = 8.0, 6.0, 4.5$ Hz, 2H), 0.42 (ddd, $J = 6.0, 4.5, 4.5$ Hz, 2H), 0.17 (s, 9H);

^{13}C NMR (125 MHz, CDCl_3): δ 147.7, 137.8, 131.1, 126.3, 120.8, 116.6, 9.4, 7.3, 0.52; IR (neat) 2959, 1645, 1486, 1398, 1366, 1310, 1252, 1065, 1008 cm^{-1} . Anal. Calcd for $\text{C}_{14}\text{H}_{19}\text{BrOSi}$: C, 54.02; H, 6.15%. Found: C, 54.08; H, 6.11%; HRMS (m/z) Found: 310.0385. Calcd for $\text{C}_{14}\text{H}_{19}\text{BrOSi}$ $[\text{M}]^+$: 310.0389.

(2-Trimethylsiloxyhept-1-enyl)cyclopropane (15d)

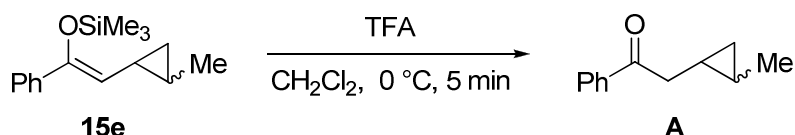
^1H NMR (500 MHz, CDCl_3) δ 4.16 (d, $J = 8.5$ Hz, 0.5H), 3.95 (d, $J = 9.5$ Hz, 0.5H), 2.16 (t, $J = 7.5$ Hz, 1H), 1.97 (t, $J = 7.5$ Hz, 1H), 1.56–1.41 (m, 3H), 1.35–1.23 (m, 4H), 0.90 (t, $J = 7.0$ Hz, 1.5H), 0.88 (t, $J = 7.0$ Hz, 1.5H), 0.66–0.62 (m, 2H), 0.24–0.18 (m, 2H), 0.21 (s, 4.5H), 0.15 (s, 4.5H); ^{13}C NMR (125 MHz, CDCl_3): δ 151.8, 150.5, 112.4, 111.6, 36.4, 31.7, 31.49, 31.46, 26.71, 26.65, 22.6, 22.5, 14.1, 14.0, 8.5, 8.1, 6.6, 6.5, 0.62, 0.35; IR (neat) 2957, 1670, 1458, 1379, 1296, 1252, 1215, 1152, 1101 cm^{-1} . HRMS (m/z) Found: 226.1759. Calcd for $\text{C}_{13}\text{H}_{26}\text{OSi}$ $[\text{M}]^+$: 226.1753.

1-[(Z)-2-trimethylsiloxy-2-phenylethenyl]-2-methylcyclopropane (15e)

^1H NMR (500 MHz, CDCl_3) δ 7.47–7.42 (m, 2H), 7.30–7.25 (m, 2H), 7.22–7.18 (m, 1H), 5.02 (d, $J = 9.5$ Hz, 0.35H), 4.79 (d, $J = 10.0$ Hz, 0.65H), 1.83–1.77 (m, 0.35H), 1.50–1.45 (m, 0.65H), 1.14 (s, 1.05H), 1.13 (s, 1.95H), 1.14–1.07 (m, 0.65H), 1.03–0.98 (m, 0.35H), 0.86–0.79 (m, 0.65H), 0.60–0.55 (m, 1.35H), 0.18 (s, 5.85H), 0.17 (s, 3.15H); ^{13}C NMR (125 MHz, CDCl_3): δ 149.8, 148.0, 139.0, 138.8, 128.00, 127.99, 127.1, 127.0, 124.8, 124.7, 115.7, 111.3, 18.7, 18.3, 15.7, 15.5, 15.3, 14.4, 12.8, 0.51; IR (neat) 2955, 1645, 1599, 1493, 1447, 1375, 1335, 1296, 1252, 1065, 1026 cm^{-1} . HRMS (m/z) Found: 246.1434. Calcd for $\text{C}_{15}\text{H}_{22}\text{OSi}$ $[\text{M}]^+$: 246.1440.

To determine the stereochemistry of **15e**, the following experiment was performed.

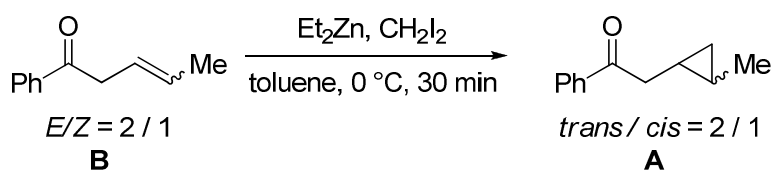
The product **15e** was treated with trifluoroacetic acid to give the corresponding α -cyclopropyl ketone **A** (Scheme 11).



Scheme 11. Preparation of α -cyclopropyl ketone **A**.

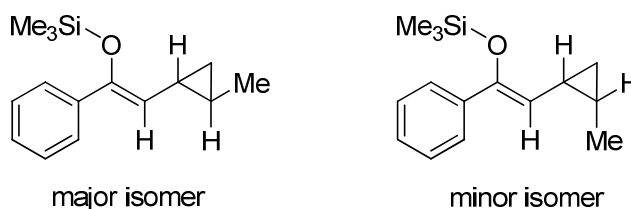
2-(2-methylcyclopropyl)-1-phenylethanone (A): ^1H NMR (500 MHz, CDCl_3) δ 7.99–7.96 (m, 0.7H), 7.96–7.93 (m, 0.13H), 7.58–7.53 (m, 1H), 7.48–7.44 (m, 2H), 3.01 (dd, $J = 17.0, 7.0$ Hz, 0.35H), 2.93 (dd, $J = 17.0, 7.0$ Hz, 0.35H), 2.91 (dd, $J = 17.0, 7.0$ Hz, 0.65H), 2.86 (dd, $J = 17.0, 7.0$ Hz, 0.65H), 1.22–1.14 (m, 0.35H), 1.06 (d, $J = 5.5$ Hz, 1.95H), 1.05 (d, $J = 6.5$ Hz, 1.05H), 0.99–0.90 (m, 0.35H), 0.89–0.82 (m, 0.65H), 0.78 (ddd, $J = 8.5, 8.5, 4.5$ Hz, 0.35H), 0.62–0.55 (m, 0.65H), 0.37–0.31 (m, 1.3H), -0.14 (dd, $J = 10.0, 5.0$ Hz, 0.35H); ^{13}C NMR (125 MHz, CDCl_3): δ 200.4, 200.1, 137.0, 136.9, 132.9, 128.5, 128.11, 128.06, 43.4, 38.0, 18.7, 15.1, 13.6, 13.0, 12.9, 12.2, 11.2, 9.3.

The authentic sample of β -cyclopropylketone **A** was synthesized from the corresponding β,γ -unsaturated ketone **B** ($E/Z = 2/1$). Treatment of **B** with diethylzinc and diiodomethane gave **A** ($trans/cis = 2/1$) (Scheme 12).

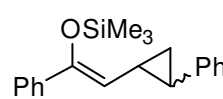


Scheme 12. Synthesis of an authentic sample of **A**.

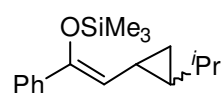
Compared with ^1H NMR spectrum of the authentic sample **A**, it was found that the stereochemistry of cyclopropane ring in major isomer was *trans*.

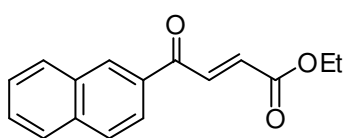


1-[2-trimethylsiloxy-2-phenylethenyl]-2-phenylcyclopropane (**15g**)

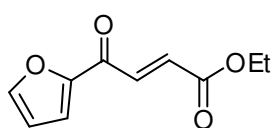
 ^1H NMR (500 MHz, CDCl_3) δ 7.50–7.08 (m, 10H), 5.50 (s, 0.29H), 4.95 (d, J = 9.5 Hz, 0.59H), 4.65 (d, J = 10.0 Hz, 0.12H), 2.46–2.41 (m, 0.12H), 2.26–2.20 (m, 0.12H), 2.19–2.15 (m, 0.29H), 2.09–2.03 (m, 0.59H), 2.00–1.96 (m, 0.59H), 1.81–1.77 (m, 0.29H), 1.42–1.38 (m, 0.29H), 1.38–1.34 (m, 0.12H), 1.32–1.28 (m, 0.59H), 1.21–1.17 (m, 0.29H), 1.14–1.10 (m, 0.59H), 1.06–1.02 (m, 0.12H); ^{13}C NMR (125 MHz, CDCl_3): δ 152.6, 149.2, 142.5, 142.0, 138.6, 136.6, 129.0, 128.8, 128.5, 128.4, 128.3, 128.12, 128.06, 128.0, 127.9, 127.3, 127.1, 126.6, 125.9, 125.8, 125.6, 125.5, 125.45, 125.43, 124.8, 124.8, 29.0, 25.5, 25.0, 23.6, 22.6, 17.7, 17.6, 16.0, 12.8, 0.84, 0.58, 0.42; IR (neat) 2959, 1593, 1491, 1445, 1344, 1253, 1057 cm^{-1} . HRMS (m/z) Found: 308.1595. Calcd for $\text{C}_{20}\text{H}_{24}\text{OSi}$ [M] $^+$: 308.1596.

1-[2-trimethylsiloxy-2-phenylethenyl]-2-isopropylcyclopropane (**15h**)

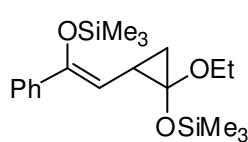
 (major isomer): ^1H NMR (500 MHz, CDCl_3) δ 7.45–7.41 (m, 2H), 7.29–7.25 (m, 2H), 7.21–7.18 (m, 1H), 4.78 (d, J = 9.5 Hz, 1H), 1.58–1.53 (m, 1H), 1.11–1.05 (m, 1H), 1.01 (d, J = 6.0 Hz, 3H), 0.96 (d, J = 7.0 Hz, 3H), 0.69–0.61 (m, 2H), 0.52–0.49 (m, 1H), 0.18 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 147.8, 138.9, 128.0, 126.9, 124.7, 116.0, 32.7, 29.6, 22.2, 21.7, 16.2, 13.3, 0.59; IR (neat) 2957, 1448, 1252, 1070 cm^{-1} . HRMS (m/z) Found: 274.1753. Calcd for $\text{C}_{17}\text{H}_{26}\text{OSi}$ [M] $^+$: 274.1753.

(E)-Ethyl 4-(2-naphthyl)-4-oxobut-2-enoate (16d)

^1H NMR (300 MHz, CDCl_3) δ 8.52 (s, 1H), 8.08 (d, $J = 15.6$ Hz, 1H), 8.08–7.88 (m, 4H), 7.67–7.56 (m, 2H), 6.96 (d, $J = 15.6$ Hz, 1H), 4.33 (q, $J = 7.2$ Hz, 2H), 1.38 (t, $J = 7.2$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 189.2, 165.7, 136.3, 135.8, 134.0, 132.44, 132.40, 131.0, 129.7, 129.0, 128.9, 127.8, 127.0, 124.0, 61.4, 14.2; IR (nujor) 2982, 1717, 1667, 1622, 1470, 1368, 1300, 1171, 1125, 1034, 974, 862, 775 cm^{-1} , mp 62.0–62.7 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{16}\text{H}_{14}\text{O}_3$: C, 75.57; H, 5.55%. Found: C, 75.54; H, 5.66%; HRMS (m/z) Found: 254.0948. Calcd for $\text{C}_{16}\text{H}_{14}\text{O}_3$ $[\text{M}]^+$: 254.0943.

(E)-Ethyl 4-(2-furyl)-4-oxobut-2-enoate (16e)

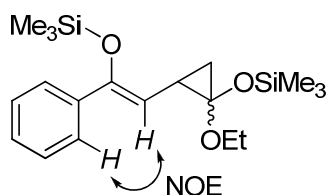
^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, $J = 15.5$ Hz, 1H), 7.70 (d, $J = 1.5$ Hz, 1H), 7.38 (d, $J = 3.5$ Hz, 1H), 6.98 (d, $J = 15.5$ Hz, 1H), 6.63 (dd, $J = 3.5, 1.5$ Hz, 1H), 4.30 (q, $J = 7.0$ Hz, 2H), 1.35 (t, $J = 7.0$ Hz, 3H); ^{13}C NMR (125 MHz, CDCl_3): δ 176.2, 165.2, 152.6, 147.6, 135.3, 132.0, 119.4, 112.8, 61.4, 14.2; IR (nujor) 2984, 2255, 1721, 1667, 1630, 1568, 1464, 1397, 1302, 1182, 1028, 910, 733 cm^{-1} , mp 49.8–50.5 $^{\circ}\text{C}$. HRMS (m/z) Found: 194.0575. Calcd for $\text{C}_{10}\text{H}_{10}\text{O}_4$ $[\text{M}]^+$: 194.0579.

2-[(Z)-2-trimethylsiloxy-2-phenylethenyl]-1-ethoxy-1-trimethylsiloxy-2-cyclopropane (17a)

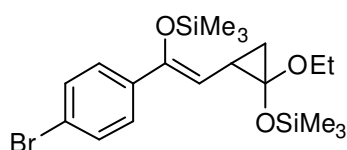
^1H NMR (500 MHz, CDCl_3) δ 7.48–7.42 (m, 2H), 7.31–7.26 (m, 2H), 7.24–7.19 (m, 1H), 5.08 (d, $J = 9.5$ Hz, 0.55H), 5.07 (d, $J = 9.5$ Hz, 0.45H), 3.76–3.60 (m, 2H), 2.18 (ddd, $J = 10.0, 10.0, 6.5$ Hz, 0.55H), 2.16 (ddd, $J = 10.5, 9.5, 6.0$ Hz, 0.45H), 1.39 (dd, $J = 10.5, 5.5$ Hz, 0.55H), 1.28 (dd, $J = 10.5, 5.5$ Hz, 0.45H), 1.21 (t, $J = 9.0$ Hz, 1.35H), 1.20 (t, $J = 9.0$ Hz, 1.65H), 0.88 (dd, $J = 6.0, 5.5$ Hz, 0.45H), 0.76 (dd, $J = 6.0, 5.5$ Hz, 0.55H), 0.22 (s, 5H), 0.20 (s, 4H), 0.16 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 149.6, 149.5, 139.10, 139.08, 128.24, 128.23, 127.44, 127.42, 125.21, 125.17, 110.0, 109.7,

89.9, 89.5, 62.1, 61.9, 25.4, 23.7, 22.6, 22.2, 15.5, 0.94, 0.83; IR (neat) 2960, 1645, 1440, 1273, 1251, 1193, 1065 cm^{-1} . Anal. Calcd for $\text{C}_{19}\text{H}_{32}\text{O}_3\text{Si}_2$: C, 62.59; H, 8.85%. Found: C, 62.52; H, 8.63%; HRMS (m/z) Found: 364.1883. Calcd for $\text{C}_{19}\text{H}_{32}\text{O}_3\text{Si}_2 [\text{M}]^+$: 364.1890.

The structure of **17a** was assigned based on NOE experiments of ^1H NMR.

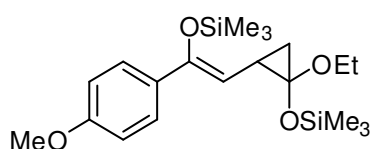


2-[(Z)-2-trimethylsiloxy-2-(4-bromophenyl)ethenyl]-1-ethoxy-1-trimethylsiloxycyclopropane (17b)



^1H NMR (500 MHz, CDCl_3) δ 7.41 (d, J = 8.5 Hz, 1.1H), 7.40 (d, J = 8.5 Hz, 0.9H), 7.31 (d, J = 8.5 Hz, 2H), 5.06 (d, J = 9.5 Hz, 0.55H), 5.05 (d, J = 9.5 Hz, 0.45H), 3.75–3.64 (m, 2H), 2.14 (ddd, J = 11.0, 9.5, 6.0 Hz, 0.55H), 2.12 (ddd, J = 11.0, 9.5, 6.5 Hz, 0.45H), 1.39 (dd, J = 10.5, 5.5 Hz, 0.55H), 1.27 (dd, J = 10.5, 6.0 Hz, 0.45H), 1.20 (t, J = 7.0 Hz, 1.35H), 1.19 (t, J = 7.0 Hz, 1.65H), 0.87 (dd, J = 6.5, 5.5 Hz, 0.45H), 0.76 (dd, J = 6.0, 5.5 Hz, 0.55H), 0.20 (s, 5H), 0.19 (s, 4H), 0.15 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 148.4, 148.3, 137.9, 137.8, 131.15, 131.12, 126.52, 126.48, 121.0, 110.5, 110.2, 89.6, 89.2, 61.9, 61.7, 25.2, 23.5, 22.5, 22.0, 15.2, 0.68, 0.58; IR (neat) 2960, 2360, 2683, 1587, 1253, 1194, 1071 cm^{-1} . HRMS (m/z) Found: 442.0993. Calcd for $\text{C}_{19}\text{H}_{31}\text{BrO}_3\text{Si}_2 [\text{M}]^+$: 442.0995.

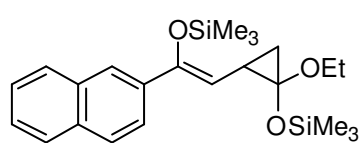
2-[(Z)-2-trimethylsiloxy-2-(4-methoxyphenyl)ethenyl]-1-ethoxy-1-trimethylsiloxycyclopropane (17c)



^1H NMR (500 MHz, C_6D_6) δ 7.51 (d, J = 9.5 Hz, 1.1H), 7.47 (d, J = 9.0 Hz, 0.9H), 6.71 (d, J = 9.0 Hz, 1.1H), 6.70 (d, J = 9.0 Hz,

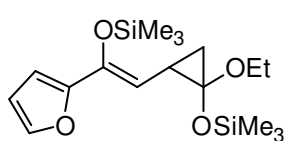
0.9H), 5.27 (d, $J = 10.0$ Hz, 0.55H), 5.24 (d, $J = 9.5$ Hz, 0.45H), 3.89 (q, $J = 7.0$ Hz, 0.9H), 3.69 (q, $J = 7.0$ Hz, 1.1H), 3.29 (s, 1.65H), 3.28 (s, 1.35H), 2.51 (ddd, $J = 9.5, 9.5, 6.0$ Hz, 0.45H), 2.48 (ddd, $J = 10.0, 9.5, 6.0$ Hz, 0.55H), 1.45–1.35 (m, 1H), 1.13 (t, $J = 7.0$ Hz, 1.35H), 1.11 (t, $J = 7.0$ Hz, 1.65H), 0.85 (dd, $J = 6.0, 5.5$ Hz, 1H), 0.27 (s, 5H), 0.25 (s, 4H), 0.20 (s, 4H), 0.18 (s, 5H); ^{13}C NMR (125 MHz, CDCl_3): δ 158.9, 149.1, 149.0, 131.7, 126.3, 126.2, 113.4, 108.0, 107.7, 89.7, 89.2, 61.8, 61.6, 55.2, 25.1, 23.4, 22.3, 21.9, 15.3, 0.72, 0.62; IR (neat) 2959, 1651, 1609, 1511, 1440, 1371, 1252, 1192, 1067 cm^{-1} . HRMS (m/z) Found: 394.1997. Calcd for $\text{C}_{20}\text{H}_{34}\text{O}_4\text{Si}_2$ $[\text{M}]^+$: 394.1996.

2-[(Z)-2-trimethylsiloxy-2-(2-naphthyl)ethenyl]-1-ethoxy-1-trimethylsiloxycyclopropane (17d)



^1H NMR (500 MHz, CDCl_3) δ 7.89 (s, 1H), 7.81–7.73 (m, 3H), 7.58 (d, $J = 8.5$ Hz, 1H), 7.45–7.39 (m, 2H), 5.24 (d, $J = 10.0$ Hz, 0.59H), 5.23 (d, $J = 10.0$ Hz, 0.41H), 3.76–3.64 (m, 2H), 2.24 (ddd, $J = 10.0, 10.0, 6.5$ Hz, 0.59H), 2.22 (ddd, $J = 10.5, 10.0, 6.5$ Hz, 0.41H), 1.42 (dd, $J = 10.5, 5.5$ Hz, 0.59H), 1.31 (dd, $J = 10.0, 5.5$ Hz, 0.41H), 1.22 (t, $J = 7.5$ Hz, 1.23H), 1.21 (t, $J = 7.0$ Hz, 1.77H), 0.93 (dd, $J = 6.0, 5.5$ Hz, 0.41H), 0.81 (dd, $J = 6.0, 5.5$ Hz, 0.59H), 0.23 (s, 5.3H), 0.21 (s, 3.7H), 0.20 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 149.34, 149.26, 136.14, 136.12, 133.3, 132.78, 132.76, 128.20, 128.18, 127.59, 127.57, 127.52, 126.08, 126.07, 125.7, 123.51, 123.49, 123.44, 110.6, 110.3, 89.8, 89.4, 61.9, 61.7, 25.4, 23.7, 22.5, 22.2, 15.3, 0.74, 0.65; IR (neat) 2959, 1645, 1440, 1363, 1252, 1191, 1062 cm^{-1} . HRMS (m/z) Found: 414.2044. Calcd for $\text{C}_{23}\text{H}_{34}\text{O}_3\text{Si}_2$ $[\text{M}]^+$: 414.2046.

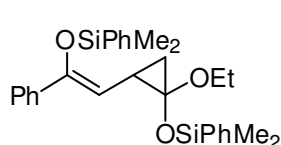
2-[(Z)-2-trimethylsiloxy-2-(2-furyl)ethenyl]-1-ethoxy-1-trimethylsiloxycyclopropane (17e)



^1H NMR (500 MHz, CDCl_3) δ 7.32 (d, $J = 2.0$ Hz, 1H), 6.34 (dd, $J = 3.5, 2.0$ Hz, 1H), 6.23 (d, $J = 3.5$ Hz, 1H), 5.16 (d, $J = 10.0$ Hz, 0.55H), 5.15 (d, $J = 10.0$ Hz, 0.45H), 3.75–3.66 (m, 2H), 2.10 (ddd, $J = 10.0, 10.0, 6.5$

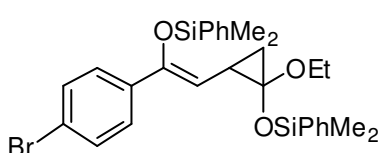
Hz, 0.55H), 2.08 (ddd, $J = 10.0, 10.0, 6.5$ Hz, 0.45H), 1.38 (dd, $J = 10.5, 5.5$ Hz, 0.55H), 1.30 (dd, $J = 10.0, 5.5$ Hz, 0.45H), 1.21 (t, $J = 7.5$ Hz, 1.35H), 1.18 (t, $J = 7.5$ Hz, 1.65H), 0.89 (dd, $J = 6.5, 5.5$ Hz, 0.45H), 0.77 (dd, $J = 6.0, 5.5$ Hz, 0.55H), 0.23 (s, 5H), 0.22 (s, 4H), 0.19 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 152.6, 141.41, 141.36, 141.2, 141.1, 110.94, 110.93, 108.5, 108.2, 105.19, 105.17, 89.7, 89.3, 62.0, 61.6, 24.7, 22.9, 22.5, 22.1, 15.22, 15.19, 0.69, 0.50; IR (neat) 2960, 1657, 1435, 1326, 1252, 1193, 1070 cm^{-1} . Anal. Calcd for $\text{C}_{17}\text{H}_{30}\text{O}_4\text{Si}_2$: C, 57.58; H, 8.53%. Found: C, 57.46; H, 8.31%; HRMS (m/z) Found: 354.1685. Calcd for $\text{C}_{17}\text{H}_{30}\text{O}_4\text{Si}_2$ $[\text{M}]^+$: 354.1683.

2-[(Z)-2-dimethylphenylsiloxy-2-phenylethenyl]-1-ethoxy-1-dimethylphenylsilocyclopropane (17a')



^1H NMR (300 MHz, CDCl_3) δ 7.61–7.50 (m, 4H), 7.42–7.32 (m, 9H), 7.26–7.19 (m, 2H), 5.06 (d, $J = 9.3$ Hz, 0.55H), 5.02 (d, $J = 9.9$ Hz, 0.45H), 3.69–3.51 (m, 2H), 2.10 (ddd, $J = 9.9, 9.9, 6.0$ Hz, 0.55H), 2.05 (ddd, $J = 9.9, 9.6, 6.0$ Hz, 0.45H), 1.20 (dd, $J = 10.5$ Hz, 0.55H), 1.09 (t, $J = 7.5$ Hz, 1.35H), 1.08 (dd, $J = 9.9, 6.0$ Hz, 0.45H), 1.03 (t, $J = 7.2$ Hz, 1.65H), 0.77 (dd, $J = 6.3, 6.0$ Hz, 0.45H), 0.66 (dd, $J = 6.3, 6.0$ Hz, 0.55H), 0.48 (s, 1.65H), 0.47 (s, 1.65H), 0.44 (s, 1.35H), 0.42 (s, 1.35H), 0.38 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 149.29, 149.27, 138.70, 138.65, 138.3, 137.5, 137.4, 133.5, 133.4, 133.3, 129.7, 129.5, 127.98, 127.94, 127.7, 127.21, 127.19, 125.11, 125.08, 110.0, 109.7, 89.9, 89.5, 62.0, 61.8, 25.3, 23.5, 22.5, 22.1, 15.1, 15.0, -0.71, -0.80, -0.85, -0.89, -0.90, -0.96, -1.1; IR (neat) 2959, 1645, 1428, 1321, 1252, 1193, 1119, 1064 cm^{-1} . HRMS (m/z) Found: 488.2200. Calcd for $\text{C}_{29}\text{H}_{36}\text{O}_3\text{Si}_2$ $[\text{M}]^+$: 488.2203.

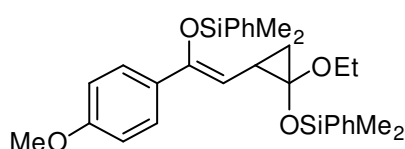
2-[(Z)-2-dimethylphenylsiloxy-2-(4-bromophenyl)ethenyl]-1-ethoxy-1-dimethylphenylsilocyclopropane (17b')



^1H NMR (300 MHz, CDCl_3) δ 7.62–7.50 (m, 4H), 7.43–7.27 (m, 8H), 7.25 (d, $J = 6.9$ Hz, 1H), 7.17 (d, $J = 6.9$ Hz, 1H), 5.03 (d, J

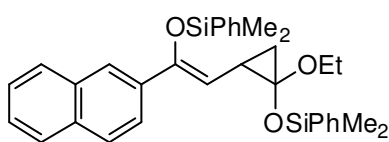
= 9.3 Hz, 0.55H), 5.01 (d, J = 9.5 Hz, 0.45H), 3.65–3.40 (m, 2H), 2.15–2.05 (m, 1H), 1.24 (dd, J = 9.9, 5.1 Hz, 0.55H), 1.09 (dd, J = 9.9, 5.7 Hz, 0.45H), 1.08 (t, J = 7.2 Hz, 1.35H), 1.04 (t, J = 6.9 Hz, 1.65H), 0.77 (dd, J = 6.0, 5.7 Hz, 0.45H), 0.67 (dd, J = 6.0, 5.7 Hz, 0.55H), 0.47 (s, 1.65H), 0.46 (s, 1.65H), 0.44 (s, 1.35H), 0.42 (s, 1.35H), 0.38 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 148.33, 148.28, 138.2, 137.7, 137.6, 137.2, 137.0, 133.43, 133.37, 133.31, 131.08, 131.03, 129.84, 129.82, 129.6, 129.5, 127.80, 127.78, 127.76, 127.75, 126.63, 126.60, 121.01, 120.97, 110.7, 110.4, 89.9, 89.5, 62.0, 61.9, 25.3, 23.5, 22.6, 22.1, 15.1, 15.0, -0.75, -0.84, -0.85, -0.90, -0.95, -0.98, -1.0, -1.1; IR (neat) 2961, 2363, 1645, 1486, 1428, 1319, 1253, 1194, 1120, 1061, 1008 cm^{-1} . HRMS (m/z) Found: 566.1305. Calcd for $\text{C}_{29}\text{H}_{36}\text{BrO}_3\text{Si}_2$ $[\text{M}]^+$: 566.1308.

2-[(Z)-2-dimethylphenylsiloxy-2-(4-methoxyphenyl)ethenyl]-1-ethoxy-1-dimethylphenylsiloxycyclopropane (17c')



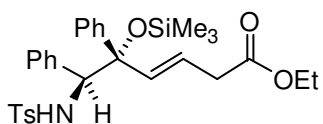
^1H NMR (300 MHz, CDCl_3) δ 7.69–7.61 (m, 4H), 7.44–7.39 (m, 6H), 7.40 (d, J = 9.0 Hz, 1H), 7.34 (d, J = 8.7 Hz, 1H), 6.84 (d, J = 8.7 Hz, 1H), 6.82 (d, J = 9.0 Hz, 1H), 5.02 (d, J = 9.6 Hz, 0.55H), 4.97 (d, J = 9.9 Hz, 0.45H), 3.84 (s, 1.65H), 3.83 (s, 1.35H), 3.72–3.42 (m, 2H), 2.17 (ddd, J = 9.9, 9.9, 6.3 Hz, 0.55H), 2.12 (ddd, J = 10.2, 9.3, 6.3 Hz, 0.45H), 1.27 (dd, J = 10.5, 5.4 Hz, 0.55H), 1.16 (t, J = 7.2 Hz, 1.35H), 1.15 (dd, J = 9.9, 5.4 Hz, 0.45H), 1.09 (t, J = 7.2 Hz, 1.65H), 0.83 (dd, J = 6.3, 5.7 Hz, 0.45H), 0.71 (dd, J = 6.3, 5.4 Hz, 0.55H), 0.55 (s, 1.65H), 0.54 (s, 1.65H), 0.51 (s, 1.35H), 0.49 (s, 1.35H), 0.45 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 158.93, 158.91, 149.1, 149.0, 138.3, 137.6, 137.4, 133.5, 133.4, 133.3, 131.5, 131.4, 129.7, 129.5, 127.7, 126.40, 126.38, 113.32, 113.28, 108.2, 107.9, 89.9, 89.5, 61.9, 61.8, 55.2, 25.2, 23.4, 22.5, 22.0, 15.1, 15.0, -0.70, -0.79, -0.84, -0.88, -0.93, -1.1; IR (neat) 2960, 2363, 1608, 1511, 1428, 1253, 1193, 1119, 1065 cm^{-1} . HRMS (m/z) Found: 518.2312. Calcd for $\text{C}_{30}\text{H}_{38}\text{O}_4\text{Si}_2$ $[\text{M}]^+$: 518.2309.

2-[(Z)-2-dimethylphenylsiloxy-2-(2-naphthyl)ethenyl]-1-ethoxy-1-dimethylphenylsiloxypropene (17d')



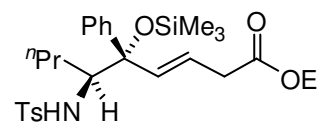
^1H NMR (300 MHz, CDCl_3) δ 7.81–7.73 (m, 2H), 7.73–7.56 (m, 6H), 7.53–7.31 (m, 9H), 5.25 (d, $J = 9.6$ Hz, 0.55H), 5.20 (d, $J = 9.9$ Hz, 0.45H), 3.69–3.53 (m, 2H), 2.18 (ddd, $J = 10.2, 9.6, 6.6$ Hz, 0.55H), 2.13 (ddd, $J = 10.2, 9.6, 6.3$ Hz, 0.45H), 1.26 (dd, $J = 10.5, 5.4$ Hz, 0.55H), 1.15 (dd, $J = 10.5, 5.4$ Hz, 0.45H), 1.12 (t, $J = 7.2$ Hz, 1.35H), 1.06 (t, $J = 7.2$ Hz, 1.65H), 0.84 (dd, $J = 6.3, 5.4$ Hz, 0.45H), 0.73 (dd, $J = 6.0, 6.0$ Hz, 0.55H), 0.51 (s, 1.65H), 0.49 (s, 1.65H), 0.47 (s, 1.35H), 0.44 (s, 1.35H), 0.42 (s, 6H); ^{13}C NMR (125 MHz, CDCl_3): δ 149.23, 149.19, 138.2, 137.5, 137.4, 135.75, 135.72, 133.51, 133.45, 133.41, 133.3, 133.2, 132.7, 129.8, 129.5, 128.21, 128.19, 127.78, 127.77, 127.75, 127.53, 127.48, 127.46, 126.04, 125.99, 125.67, 125.65, 123.7, 123.4, 110.8, 110.4, 90.0, 89.6, 62.0, 61.9, 25.5, 23.7, 22.7, 22.2, 15.12, 15.05, $-0.72, -0.78, -0.85, -0.88, -1.0, -1.1$; IR (neat) 2959, 2333, 1428, 1252, 1188, 1119, 1060 cm^{-1} . HRMS (m/z) Found: 538.2357. Calcd for $\text{C}_{33}\text{H}_{38}\text{O}_3\text{Si}_2$ $[\text{M}]^+$: 538.2359.

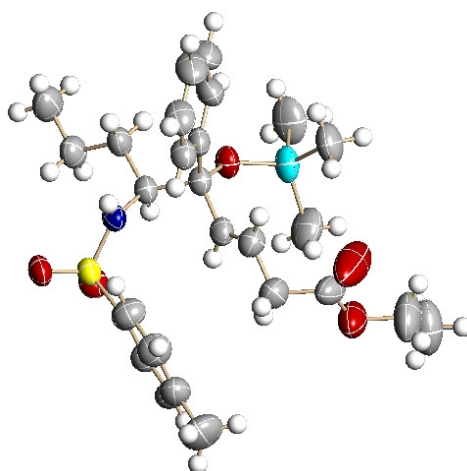
Ethyl (5*S,6*S**)-(*E*)-5,6-diphenyl-6-tosylamino-5-trimethylsiloxy-3-hexenoate (20a)**



^1H NMR (500 MHz, CDCl_3) δ 7.28–7.14 (m, 10H), 7.06 (d, $J = 8.0$ Hz, 2H), 7.01 (d, $J = 8.0$ Hz, 2H), 5.59–5.58 (m, 2H), 5.20 (d, $J = 7.0$ Hz, 1H), 4.48 (d, $J = 7.0$ Hz, 1H), 4.09 (q, $J = 7.0$ Hz, 2H), 3.05–3.01 (m, 1H), 3.00–2.96 (m, 1H), 2.35 (s, 3H), 1.22 (t, $J = 7.0$ Hz, 3H), -0.08 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.0, 142.7, 141.3, 137.8, 137.5, 135.1, 129.5, 129.4, 128.1, 128.0, 127.8, 127.7, 127.6, 127.1, 127.0, 82.1, 67.1, 61.0, 38.3, 21.6, 14.4, 2.4; IR (nujol) 3279, 2855, 1733, 1599, 1447, 1377, 1328, 1250, 1162, 1073, 1022 cm^{-1} ; mp 143.5–144.5 $^{\circ}\text{C}$. Anal. Calcd for $\text{C}_{30}\text{H}_{37}\text{NO}_3\text{SSi}$: C, 65.30; H, 6.76%. Found: C, 65.21; H, 6.50%; HRMS (m/z) Found: 552.2245. Calcd for $\text{C}_{30}\text{H}_{38}\text{NO}_3\text{SSi}$ $[\text{MH}]^+$: 552.2240.

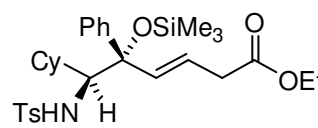
Ethyl (5*S,6*S**)-(*E*)-5-phenyl-6-tosylamino-5-trimethylsiloxy-3-nonenoate (20b)**


¹H NMR (500 MHz, CDCl₃) δ 7.69 (d, *J* = 6.5 Hz, 2H), 7.33 (d, *J* = 6.5 Hz, 2H), 7.30–7.20 (m, 5H), 5.99 (d, *J* = 15.5 Hz, 1H), 5.76 (dt, *J* = 15.5, 7.0 Hz, 1H), 4.55 (d, *J* = 9.0 Hz, 1H), 4.14 (q, *J* = 7.5 Hz, 2H), 3.76 (ddd, *J* = 9.0, 9.0, 2.5 Hz, 1H), 3.08 (d, *J* = 7.0 Hz, 2H), 2.39 (s, 3H), 1.42–1.20 (m, 2H), 1.27 (t, *J* = 7.5 Hz, 3H), 1.19–1.06 (m, 1H), 0.95–0.85 (m, 1H), 0.71 (t, *J* = 7.0 Hz, 3H), 0.16 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 171.5, 142.7, 142.3, 139.8, 135.8, 129.6, 128.2, 127.9, 127.8, 127.1, 126.8, 81.5, 63.7, 61.1, 38.1, 34.6, 21.7, 19.9, 14.4, 14.1, 2.2; IR (nujol) 3298, 2928, 1733, 1599, 1448, 1325, 1251, 1160 cm⁻¹. Anal. Calcd for C₂₇H₃₉NO₃SSi: C, 62.63; H, 7.59%. Found: C, 62.48; H, 7.72%.

**Figure 4.** The ORTEP of **20b**.

Crystal structure data: Triclinic, *a* = 10.842(10), *b* = 12.134(11), *c* = 13.608(13) Å, β = 110.316(15)°, *V* = 1489(2) Å³, *Z* = 2, ρ_{calcd} = 1.154 Mg m⁻³, λ(Mo Kα) = 0.71073 Å, *T* = 293(2) K, θ_{max} = 54.0°, *R* = 0.0514 for 6267 reflections (*I* > 2σ(*I*)).

Ethyl (5*S,6*S**)-(*E*)-6-cyclohexyl-5-phenyl-6-tosylamino-5-trimethylsiloxy-3-hexenoate (20c)**


¹H NMR (500 MHz, CDCl₃) δ 7.65 (d, *J* = 8.5 Hz, 2H), 7.31–7.21 (m, 7H), 5.95 (d, *J* = 16.0 Hz, 1H), 5.71 (dt, *J* = 16.0, 7.0 Hz, 1H), 4.59 (d, *J* = 9.5 Hz, 1H), 4.14 (q, *J* = 7.0 Hz, 2H), 3.49 (d, *J* = 9.5 Hz, 1H), 3.07 (d, *J* = 7.0 Hz, 2H), 2.39

(s, 3H), 1.25 (t, $J = 7.0$ Hz, 3H), 1.66–0.91 (m, 11H), –0.15 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.4, 142.9, 142.2, 139.3, 136.1, 129.6, 128.1, 127.9, 127.7, 127.4, 126.6, 82.0, 67.7, 61.1, 38.2, 33.8, 29.0, 27.1, 26.5, 26.2, 21.7, 14.4, 14.3, 2.3; IR (nujol) 3334, 2921, 2360, 1733, 1447, 1325, 1253, 1154, 1061, 1024 cm^{-1} . Anal. Calcd for $\text{C}_{30}\text{H}_{43}\text{NO}_3\text{SSi}$: C, 64.59; H, 7.77%. Found: C, 64.32; H, 7.78%.

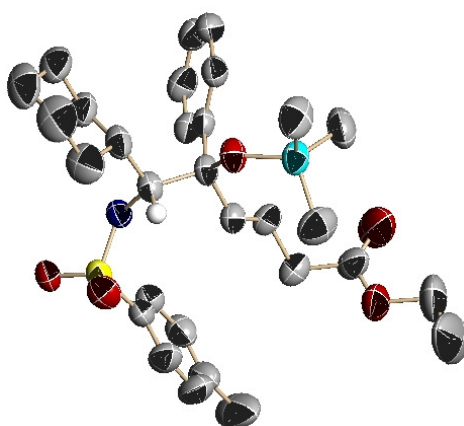
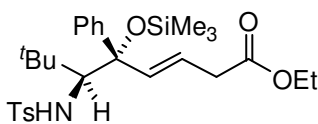


Figure 5. The ORTEP of **20c**.

Crystal structure data: $a = 10.7006(7)$, $b = 12.0632(8)$, $c = 14.3473(10)$ Å, $\beta = 69.7620(10)^\circ$, $V = 1578.31(18)$ Å³, $Z = 2$, $\rho_{\text{calcd}} = 1.174$ Mg m^{–3}, $\lambda(\text{Mo K}\alpha) = 0.71073$ Å, $T = 293(2)$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0573$ for 6726 reflections ($I > 2\sigma(I)$).

Ethyl (5*S,6*S**)-(*E*)-7,7-dimethyl-5-phenyl-6-tosylamino-5-trimethylsiloxy-3-octanoate (20d)**



^1H NMR (500 MHz, CDCl_3) δ 7.76 (d, $J = 8.5$ Hz, 2H), 7.48 (d, $J = 7.0$ Hz, 2H), 7.33–7.25 (m, 5H), 6.15 (d, $J = 15.5$ Hz, 1H), 5.74 (dt, $J = 15.5, 7.0$ Hz, 1H), 4.66 (d, $J = 10.0$ Hz, 1H), 4.15 (q, $J = 7.0$ Hz, 2H), 3.96 (d, $J = 10.0$ Hz, 1H), 3.09 (dd, $J = 17.5, 8.5$ Hz, 1H), 3.01 (dd, $J = 17.5, 8.0$ Hz, 1H), 2.40 (s, 3H), 1.26 (t, $J = 7.0$ Hz, 3H), 0.57 (s, 9H), –0.09 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.5, 143.3, 142.5, 141.0, 137.2, 129.6, 128.4, 128.1, 128.0, 126.7, 125.4, 81.7, 71.9, 61.1, 37.9, 36.1, 29.4, 21.7, 14.5, 2.4; IR (nujol) 3317, 2924, 2360, 1734, 1314, 1250, 1153, 1067, 1026 cm^{-1} ; mp 147.0–148.5 °C. Anal.

Calcd for $C_{28}H_{41}NO_3SSi$: C, 63.24; H, 7.77%. Found: C, 63.10; H, 7.73%; HRMS (m/z) Found: 530.2397. Calcd for $C_{28}H_{40}NO_3Ssi$ $[M-H]^+$: 530.2396.

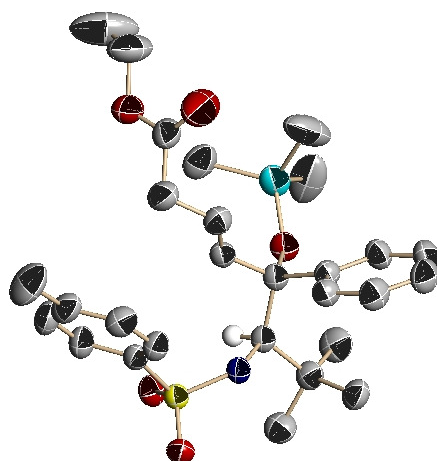
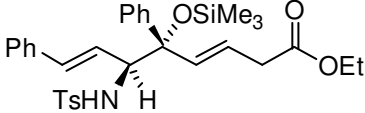
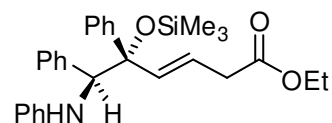


Figure 6. The ORTEP of **20d**.

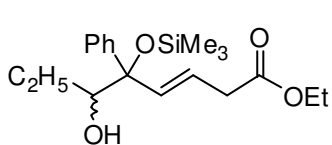
Crystal structure data: $a = 10.7467(6)$, $b = 11.8295(7)$, $c = 13.8357(8)$ Å, $\beta = 97.4430(10)^\circ$, $V = 1498.38(15)$ Å³, $Z = 2$, $\rho_{\text{calcd}} = 1.176$ Mg m⁻³, $\lambda(\text{MoK}\alpha) = 0.71073$ Å, $T = 293(2)$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0506$ for 5493 reflections ($I > 2\sigma(I)$).

Ethyl (5*S,6*S**)-(3*E*,7*E*)-5,8-diphenyl-6-tosylamino-5-trimethylsiloxy-3,7-octadienoate (**20e**)**

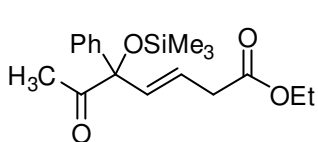
 ¹H NMR (500 MHz, CDCl₃) δ 7.54 (d, $J = 8.5$ Hz, 2H), 7.35–7.09 (m, 12H), 6.29 (d, $J = 16.0$ Hz, 1H), 6.00 (d, $J = 16.0$ Hz, 1H), 5.83 (dd, $J = 16.0, 7.5$ Hz, 1H), 5.75 (dt, $J = 15.5, 7.0$ Hz, 1H), 4.90 (d, $J = 7.5$ Hz, 1H), 4.26 (dd, $J = 7.5, 7.5$ Hz, 1H), 4.12 (q, $J = 7.0$ Hz, 2H), 3.11 (d, $J = 7.0$ Hz, 2H), 2.30 (s, 3H), 1.26 (t, $J = 7.0$ Hz, 3H), 0.02 (s, 9H); ¹³C NMR (125 MHz, CDCl₃): δ 170.9, 142.8, 141.3, 136.4, 135.0, 133.9, 129.3, 129.0, 128.4, 128.2, 127.9, 127.7, 127.6, 127.4, 127.2, 126.4, 125.6, 81.6, 64.9, 60.8, 38.0, 21.3, 14.1, 2.2; IR (nujol) 3286, 2957, 1733, 1605, 1496, 1448, 1330, 1252, 1163, 1071 cm⁻¹; mp 103.0–104.0 °C. Anal. Calcd for $C_{32}H_{39}NO_3SSi$: C, 66.52; H, 6.80%. Found: C, 66.53; H, 6.81%; HRMS (m/z) Found: 577.2313. Calcd for $C_{32}H_{39}NO_3Ssi$ $[M]^+$: 577.2318.

Ethyl (5*S,6*S**)-(*E*)-5,6-diphenyl-6-phenylamino-5-trimethylsiloxy-3-hexenoate (20f)**

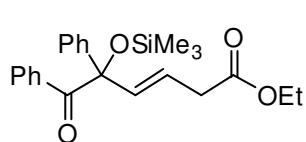
^1H NMR (500 MHz, CDCl_3) δ 7.43 (d, $J = 7.0$ Hz, 2H), 7.34 (dd, $J = 7.5$, 7.0 Hz, 2H), 7.30–7.24 (m, 6H), 7.00 (dd, $J = 9.0$, 7.0 Hz, 2H), 6.56 (dd, $J = 7.5$, 7.0 Hz, 1H), 6.37 (d, $J = 7.5$ Hz, 2H), 5.85 (d, $J = 15.5$ Hz, 1H), 5.72 (dt, $J = 15.5$, 7.0 Hz, 1H), 4.62 (s, 1H), 4.15 (q, $J = 7.0$ Hz, 2H), 3.12 (dd, $J = 16.0$, 7.0 Hz, 1H), 3.10 (dd, $J = 16.0$, 7.0 Hz, 1H), 1.27 (t, $J = 7.0$ Hz, 3H), 0.03 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.3, 147.6, 142.8, 139.8, 136.2, 129.8, 129.1, 128.0, 127.9, 127.7, 127.5, 127.4, 126.9, 117.0, 113.6, 82.5, 67.7, 61.0, 38.4, 14.5, 2.5; IR (nujol) 3372, 2957, 1733, 1602, 1499, 1447, 1373, 1253, 1176, 1028 cm^{-1} . HRMS (m/z) Found: 472.2318. Calcd for $\text{C}_{29}\text{H}_{34}\text{NO}_3\text{Si}$ $[\text{M}-\text{H}]^+$: 472.2308.

Ethyl (*E*)-6-hydroxy-5-phenyl-5-trimethylsiloxy-3-octenoate (21)

^1H NMR (300 MHz, CDCl_3) δ 7.45–7.42 (m, 2H), 7.35–7.26 (m, 3H), 6.02 (d, $J = 15.9$ Hz, 1H), 5.93 (dt, $J = 15.6$, 6.6 Hz, 1H), 4.15 (q, $J = 7.2$ Hz, 2H), 3.72 (dd, $J = 10.2$, 2.1 Hz, 1H), 3.19 (d, $J = 6.3$ Hz, 2H), 1.48–1.36 (m, 1H), 1.26 (t, $J = 7.2$ Hz, 3H), 1.13–1.01 (m, 1H), 0.91 (t, $J = 7.5$ Hz, 3H), –0.01 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 171.5, 142.4, 134.8, 128.1, 128.0, 127.8, 126.0, 82.4, 80.7, 61.1, 38.8, 24.5, 14.7, 11.7, 2.7. HRMS (m/z) Found: 349.1835. Calcd for $\text{C}_{19}\text{H}_{29}\text{O}_4\text{Si}$ $[\text{M}-\text{H}]^+$: 349.1835.

Ethyl (*E*)-6-oxo-5-phenyl-5-trimethylsiloxy-3-heptenoate (22a)

^1H NMR (500 MHz, CDCl_3) δ 7.37–7.27 (m, 5H), 6.16 (d, $J = 15.5$ Hz, 1H), 5.76 (dt, $J = 15.5$, 7.0 Hz, 1H), 4.12 (q, $J = 7.0$ Hz, 2H), 3.15 (d, $J = 7.0$ Hz, 2H), 2.11 (s, 3H), 1.24 (t, $J = 7.0$ Hz, 3H), 0.09 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 209.2, 171.2, 141.1, 135.0, 128.4, 128.2, 127.4, 127.3, 86.0, 61.0, 38.3, 25.4, 14.4, 2.29; IR (nujol) 2958, 1733, 1717, 1447, 1252, 1159, 1070, 1030 cm^{-1} . HRMS (m/z) Found: 334.1594. Calcd for $\text{C}_{18}\text{H}_{26}\text{O}_4\text{Si}$ $[\text{M}]^+$: 334.1600.

Ethyl (*E*)-5,6-diphenyl-6-oxo-5-trimethylsiloxy-3-hexenoate (22b)

^1H NMR (500 MHz, CDCl_3) δ 7.86 (d, $J = 7.0$ Hz, 2H), 7.46 (d, $J = 7.5$ Hz, 2H), 7.40 (dd, $J = 7.5, 7.0$ Hz, 1H), 7.34 (dd, $J = 7.5, 7.5$ Hz, 2H), 7.28–7.25 (m, 3H), 6.43 (d, $J = 15.5$ Hz, 1H), 5.51 (dt, $J = 15.5, 7.0$ Hz, 1H), 4.10 (q, $J = 7.0$ Hz, 2H), 3.11 (d, $J = 7.5$ Hz, 2H), 1.22 (t, $J = 7.0$ Hz, 3H), 0.00 (s, 9H); ^{13}C NMR (125 MHz, CDCl_3): δ 200.4, 171.3, 141.9, 137.2, 132.6, 131.0, 130.8, 128.6, 128.0, 127.9, 126.5, 126.2, 85.5, 60.9, 38.3, 14.4, 2.1; IR (nujol) 2959, 1733, 1683, 1599, 1448, 1253, 1159, 1071, 1028 cm^{-1} . Anal. Calcd for $\text{C}_{23}\text{H}_{28}\text{O}_4\text{Si}$: C, 69.66; H, 7.12%. Found: C, 69.54; H, 7.11%; HRMS (m/z) Found: 396.1758. Calcd for $\text{C}_{23}\text{H}_{28}\text{O}_4\text{Si}$ $[\text{M}]^+$: 396.1757.

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12. Crystal structure data: Monoclinic, $a = 15.6500(9)$, $b = 20.3324(12)$, $c = 9.7522(6)$ Å, $\beta = 104.3280(10)^\circ$, $V = 3006.6(3)$ Å³, $Z = 4$, $\rho_{\text{calcd}} = 1.219$ Mgm⁻³, $\lambda(\text{Mo}_{\text{K}\alpha}) = 0.71073$ Å, $T = 293(2)$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0613$ for 6494 reflections ($I > 2\sigma(I)$).
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Publication List

1. Parts of the present thesis have been published in the following journals.

Chapter 2 Preparation of *cis*-2-Aminocyclopropanol: [2+1] Cycloaddition Reaction of Bis(iodozincio)methane

Kenichi Nomura, Koichiro Oshima, and Seiji Matsubara

Tetrahedron Lett. **2004**, 45, 5957–5959.

Diastereoselective Nucleophilic Cyclopropanation of 1,2-Diketones and α -Ketoimines with Bis(iodozincio)methane

Kenichi Nomura, Keisuke Asano, Takuya Kurahashi, and Seiji Matsubara

Heterocycles **2008**, 76, 1381–1399.

Chapter 3 Stereospecific and Stereoselective Preparation of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols from α,β -Epoxy Ketones and Bis(iodozincio)methane

Kenichi Nomura, Koichiro Oshima, and Seiji Matsubara

Angew. Chem. Int. Ed. **2005**, 44, 5860–5863.

Stereoselective Synthesis of β,γ -Unsaturated Ketones by Acid-Mediated Julia-Type Transformation from 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols

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Synlett **2008**, 1412–1414.

Chapter 4 Zincate-Mediated Rearrangement Reaction of
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Chapter 5 Preparation of Zinc–Homoenolate from α -Sulfonyloxy Ketone and
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Chapter 6 Nucleophilic cyclopropanation Reaction with Bis(iodozincio)methane by
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Kenichi Nomura, Takaharu Hirayama, and Seijiro Matsubara
Chem. Asian J. **2009**, *4*, 1298–1303.

2. Following publications are not included in this thesis.

- (1) A Mild Ring Opening Fluorination of Epoxide with Ionic Liquid 1-Ethyl-3-methylimidazolium Oligo Hydrogenfluoride (EMIMF(HF)_{2.3})
Hideaki Yoshino, Kenichi Nomura, Seijiro Matsubara, Koichiro Oshima, Kazuhiko Matsumoto, Rika Hagiwara, and Yasuhiko Ito
J. Fluorine Chem. **2004**, 125, 1127–1129.
- (2) Pentamethylcyclopentadienide in Organic Synthesis: Nucleophilic Addition of Lithium Pentamethylcyclopentadienide to Carbonyl Compounds and Carbon–Carbon Bond Cleavage of The Adducts Yielding The Parent Carbonyl Compounds
Minoru Uemura, Kazunari Yagi, Masayuki Iwasaki, Kenichi Nomura, Hideki Yorimitsu, and Koichiro Oshima
Tetrahedron **2006**, 62, 3523–3535.
- (3) Stereoselective Preparation of 3-Alkanoylprop-2-en-1-ol Derivatives
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