Title
Studies on a Nucleophilic Cyclopropanation Reactions with Bis(iodozincio)methane

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Citation
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Issue Date
2010-03-23

URL
https://doi.org/10.14989/doctor.k15384

Type
Thesis or Dissertation

Textversion
author

Kyoto University
Studies on Nucleophilic Cyclopropanation Reactions

with Bis(iodozincio)methane

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2010
# Contents

Chapter 1  
Introduction and General Summary  
1

Chapter 2  
Diastereoselective Nucleophilic Cyclopropanation of 1,2-Diketones and  
α-Ketoimines with Bis(iodozincio)methane  
29

Chapter 3  
Stereospecific and Stereoselective Preparation of  
2-(1-Hydroxyalkyl)-1-alkylcyclopropanols from α,β-Epoxy Ketones and  
Bis(iodozincio)methane  
59

Chapter 4  
A New Zincate-Mediated Rearrangement Reaction of  
2-(1-Hydroxyalkyl)-1-alkylcyclopropanols  
85

Chapter 5  
Stereospecific Construction of Chiral Tertiary and Quaternary Carbon  
by Nucleophilic Cyclopropanation with Bis(iodozincio)methane  
115

Chapter 6  
Nucleophilic Cyclopropanation Reaction with Bis(iodozincio)methane  
by 1,4-Addition to α,β-Unsaturated Carbonyl Compounds  
151

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 $\beta$-position of carbonyl groups, that is homoenolates, are formed (Scheme 1(a)).\(^4\) The reaction of the homoenolates with Pd(II) or bromine affords $\alpha,\beta$-unsaturated ketones, which can be regarded as synthons of $\beta$-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 $\beta$-radical species (Scheme 1(c)).\(^6\)

![Scheme 1. Building blocks from cyclopropanol.](image-url)
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. In contrast, the fission of bond B allows ring expansion, and as a result, a seven-membered ring ketone is obtained. Furthermore, the reaction that cleaves both bond A and bond B to give acyclic carboxylic acid derivative has also been reported.

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. 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: 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.


1) The Simmons–Smith Reaction

The most common electrophilic cyclopropanation method is the Simmons–Smith reaction: Treatment of alkenes with the Simmons–Smith reagent (IZnCH₂I), which is prepared from diiodomethane and zinc–copper couple in diethyl ether, affords cyclopropanes. The reaction proceeds stereospecifically, as shown in Scheme 4.
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. Desilylation with tetrabutylammonium fluoride afforded the corresponding cyclopropanol in a high yield (Scheme 5).

![Scheme 4. The Simmons–Smith reaction.](image)

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).

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

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

\[
\begin{align*}
\text{O} & \quad \text{Et}_2\text{Zn} \\
\text{R}^1\text{R}^2 & \quad \text{Et}_2\text{O}, 0^\circ \text{C} \\
\text{I} & \quad \text{R}^3\text{OZnEt} \\
\text{Et}_2\text{Zn} & \quad \text{Et}_2\text{O}, 0^\circ \text{C} \\
\text{R}^3\text{OZnEt} & \quad \text{CH}_2\text{I}_2 \\
\text{R}^3\text{OZnEt} & \quad \text{MeOH} \\
\end{align*}
\]

**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).\(^{18}\)

\[
\begin{align*}
\text{OR}^1 & \quad \text{R}^3\text{R}^4 \\
\text{R}^3\text{R}^4 & \quad \text{R}^4 \\
\end{align*}
\]

**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.
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. When magnesium alkoxide of 3-bromo-1-chloro-2-propanol was treated with Grignard reagent, bromine-magnesium exchange proceeded, and the sequential intramolecular S_N2 reaction gave magnesium alkoxide of cyclopropanol (Scheme 11).

![Scheme 11. Preparation of cyclopropanol by intramolecular S_N2 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).

![Scheme 12. Preparation of cyclopropanol by intramolecular nucleophilic addition.]

Takeda showed the formation of a homoenolate after the nucleophilic reaction of enolate with acylsilane. 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. 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 D2O in the presence of CrCl2.

As shown in Scheme 15, 2-(1-hydroxyalkyl)-1-alkycyclopropanol was also obtained via nucleophilic attack of the formed enolate to an aldehyde.
Scheme 15. Reaction of α,β-unsaturated ketone and aldehyde in the presence of CrCl₂.

4) The Kulinkovich Reaction

In 1989, Kulinkovich reported an efficient method for preparation of cyclopropanols from ethylmagnesium bromide and esters. Treatment of an ester with titanacyclopropane, 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.  

Scheme 16. 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 titanacyclop propane, to esters affords 1,2-dialkylcyclopropanols (Scheme 18(b)). Different from these methods, the nucleophilic [2+1] cycloaddition with gem-dianion equivalent 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

\[
\text{CH}_2 \quad \left( \begin{array}{c}
\text{ZnI} \\
\text{H}_2\text{C} \\
\text{I}
\end{array} \right) + \quad \text{CH}_2 \quad \begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} \quad \text{OR}^3
\quad \rightarrow \quad \text{H}_2\text{C} \quad \begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} \quad \text{OR}^3
\]

(a)

the Kulinkovich reaction

\[
\text{H}_2\text{C-CH}_2\text{R}^2 \quad \left( \begin{array}{c}
\text{(R}_4\text{O})_2\text{Ti} \\
\text{R}^2
\end{array} \right) + \quad \text{CH}_2 \quad \begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} \quad \text{OR}^3
\quad \rightarrow \quad \text{R}^1\text{OH} \quad \text{H}_2\text{C-CH}_2\text{R}^2
\]

(b)

reaction with gem-dianion

\[
\text{CH}_2 \quad \begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} \quad \begin{array}{c}
\text{X} \\
\text{X}
\end{array} \quad \rightarrow \quad \text{HO} \quad \text{CH}_2 \quad \begin{array}{c}
\text{R}^1 \\
\text{R}^2
\end{array} \quad \begin{array}{c}
\text{X} \\
\text{X}
\end{array}
\]

(c)

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.\textsuperscript{27} When \( \alpha,\beta \)-epoxy ketone was treated with trialkylstannylmethyllithium, sequential nucleophilic attack of the gem-dimetal species to the carbonyl group and the epoxy group proceeded to give 2-(1-hydroxyalkyl)-1-alkycyclopropanol (Scheme 19).

Scheme 19. Reaction of \( \alpha,\beta \)-epoxy ketone and trialkylstannylmethyllithium.
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 trialkylstannylmethyllithium. Since the \textit{gem}-dimetal readily attacks various electrophiles, such as ketones, esters, and epoxide (Scheme 20),\textsuperscript{28} the chemoselective reaction seems to be difficult. So, its nucleophilic [2+1] cycloaddition would be restricted to simple substrates.

\begin{center}
\textbf{Scheme 20.} Reaction of trimethylstannylmethyllithium and various electrophiles.
\end{center}

If there are some \textit{gem}-dianions which have moderate nucleophilicity to react with \(\alpha,\beta\)-epoxy ketone moiety chemoselectively without affecting other functional groups, the nucleophilic [2+1] cycloaddition with \textit{gem}-dianions would be an alternative method for preparing various types of cyclopropanols carrying additional functional groups. Thus, the author focused on bis(iodozincio)methane\textsuperscript{29} as a \textit{gem}-dianion equivalent, which consists of two C–Zn bonds.

\textbf{Preparation and Reactivity of Bis(iodozincio)methane}

Treatment of diiodomethane with zinc powder in Et\textsubscript{2}O affords the Simmons–Smith reagent (IZnCH\textsubscript{3}I). 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.\textsuperscript{30}
The representative reaction is methylenation of an aldehyde, as shown in Scheme 22(a). Sequential coupling reactions of the dizinc with two different electrophiles, such as Scheme 22(b) and (c), are also good examples. Initially, these reactions undergo the introduction of iodozinciomethyl group to electrophiles.
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.\textsuperscript{34,35} Meanwhile, when an \(\alpha\)-heteroatom-substituted ketone, such as \(\alpha\)-alkoxy ketone or \(\alpha\)-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).\textsuperscript{34} In this case, a nucleophilic attack of \(\text{gem}\)-dizinc, which leads to methylenation, proceeds smoothly. Such activation of the organometallic reagent was also observed in the reaction of Grignard reagent and \(\alpha\)-alkoxyketones via Cram’s chelation.\textsuperscript{36}

![Scheme 23](image)

**Scheme 23.** Methylenation of \(\alpha\)-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 \(\alpha\)-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.
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.
Treatment of the obtained *cis*-1,2-bis(trimethylsiloxy)cyclopropane with FeCl₃ 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](image)

**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](image)

**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 *S_N*2 reaction of the introduced zinciomethyl group to the epoxy group
also proceeded smoothly to give 2-(1-hydroxyalkyl)-1-alkycyclopropanol diastereoselectively (Scheme 28). 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-alkycyclopropanol 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).

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

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).
Chapter 1

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, 3Bu3ZnLi, affords 1-alkenyl-1,2-diol in good yield (Scheme 31).41


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 3Bu3ZnLi gave the corresponding ring-expanded product (Scheme 32(b)).
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. 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 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). 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).
Chapter 1

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

The cyclopropanols, which are obtained by the reaction of α,β-epoxy ketone and the dizinc,\textsuperscript{39} can be also recognized as homoenoate. 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).\textsuperscript{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.\textsuperscript{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-trimethylsiloxycyclopropane (Scheme 35).\textsuperscript{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.
References and Notes


Chapter 1


Chapter 1

2001, 513.


Instrumental and Materials

$^1$H 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$_6$D$_6$ with tetramethylsilane as an internal standard. $^1$H 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$_6$D$_6$ 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 60F$_{254}$. 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$_2$O 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.
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.
Chapter 2

Introduction

Cyclopropane-skeletons have been found in many natural products, and also used as versatile synthetic intermediates.\textsuperscript{1} The most famous cyclopropanation is the Simmons–Smith reaction: Zinc carbenoid reacts with alkenes electrophilically to give a three-membered ring.\textsuperscript{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).\textsuperscript{3} This dizinc reagent, which possesses a couple of zinc atoms on a carbon, works as a dianion equivalent.\textsuperscript{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 \textit{cis}-1,2-diphenylcyclopropan-1,2-diol in good yield.\textsuperscript{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.\textsuperscript{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 $\alpha$-alkoxyketones via Cram’s chelation.\textsuperscript{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).](image1)

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, and the cyclopropanation proceeds prior to the enolization of 1,2-diketones. This fact was also explained by the ab initio calculation. 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.\textsuperscript{a}

$$
\begin{align*}
\text{R}^1\text{C}O\text{R}^2 & + \text{CH}_2(\text{ZnI})_2 & \xrightarrow{\text{THF, rt, 30 min}} & \text{EI}^+ & \xrightarrow{\text{EI}^+} & \text{EI}_\text{O} \text{O}_{\text{EI}} \\
\text{R}^1 & & & \text{R}^2 & & \text{R}^1 & \text{R}^2
\end{align*}
$$

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>$\text{EI}^+$</th>
<th>product</th>
<th>yield (%)\textsuperscript{b}</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>$\text{Ph}\text{C}O\text{Ph}$</td>
<td>$2\text{a}$ TMSCl</td>
<td>TMSO\text{Ph}O\text{TMS} \text{EI}_\text{O}</td>
<td>$3\text{b}$ 78</td>
</tr>
<tr>
<td>2</td>
<td>$\text{Ph}\text{C}O$</td>
<td>$2\text{b}$ H$_3$O$^+$</td>
<td>HO\text{Ph}OH</td>
<td>$3\text{c}$ 80</td>
</tr>
<tr>
<td>3</td>
<td>$2\text{b}$ Ac$_2$O</td>
<td></td>
<td>TMSO\text{Ph}OAc</td>
<td>$3\text{d}$ 98</td>
</tr>
<tr>
<td>4</td>
<td>$2\text{b}$ TMSCl</td>
<td></td>
<td>TMSO\text{Ph}O\text{TMS}</td>
<td>$3\text{e}$ 97</td>
</tr>
<tr>
<td>5</td>
<td>$\text{Et}\text{C}O\text{Et}$</td>
<td>$2\text{c}$ Ac$_2$O</td>
<td>AcO\text{Et}OAc</td>
<td>$3\text{f}$ 59</td>
</tr>
<tr>
<td>6</td>
<td>$\text{Ph}\text{C}O\text{H}$</td>
<td>$2\text{d}$ Ac$_2$O</td>
<td>AcO\text{Ph}OAc</td>
<td>$3\text{g}$ 58\textsuperscript{c}</td>
</tr>
<tr>
<td>7</td>
<td>$\text{MeO}\text{C}O\text{Ph}$</td>
<td>$2\text{e}$ Ac$_2$O</td>
<td>AcO\text{MeO}OAc</td>
<td>$3\text{h}$ 94</td>
</tr>
<tr>
<td>8</td>
<td>$\text{MeO}\text{C}O\text{Me}$</td>
<td>$2\text{f}$ TMSCl</td>
<td>TMSO\text{MeO}O\text{TMS}</td>
<td>$3\text{i}$ 93</td>
</tr>
<tr>
<td>Entry</td>
<td>Structure</td>
<td>Reagent</td>
<td>Yield (%)</td>
<td></td>
</tr>
<tr>
<td>-------</td>
<td>-----------</td>
<td>---------</td>
<td>-----------</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td><img src="image1" alt="Structure" /></td>
<td>2g TMSCl</td>
<td>3j 80</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td><img src="image2" alt="Structure" /></td>
<td>2h TMSCl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>11</td>
<td><img src="image3" alt="Structure" /></td>
<td>2i TMSCl</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td><img src="image4" alt="Structure" /></td>
<td>2j TMSCl</td>
<td>3k 96</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td><img src="image5" alt="Structure" /></td>
<td>2k TMSCl</td>
<td>3l 77</td>
<td></td>
</tr>
<tr>
<td>14</td>
<td><img src="image6" alt="Structure" /></td>
<td>2l TMSCl</td>
<td>3m 82</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td><img src="image7" alt="Structure" /></td>
<td>2m TMSCl</td>
<td>3n 89</td>
<td></td>
</tr>
</tbody>
</table>

*Note: 1,2-Diketone 2 (1.0 mmol), gem-dizinc 1 (1.2 mmol) and Et2 (2.4 mmol) were used. Isolated yields. In each entry, only cis-isomer was obtained diastereoselectively. The methylenated product (1-phenyl-2-propenone) was also isolated in 17% yield. Starting material (2h) was recovered. 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. As shown in Table 2,
trimethylsilyl ethers of cyclopropanediols were converted into 1,3-diketone in good to excellent yields with iron(III) chloride in THF. Considering cyclopropanation of 1,2-diketones, the net transformation can be regarded as methylene insertion to 1,2-diketone compounds.
Table 2. Ring opening isomerization into 1,3-diketones (3)\textsuperscript{a}

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>Yield (%)\textsuperscript{b}</th>
</tr>
</thead>
</table>
| 1     | \[
\begin{align*}
\text{Ph} & \quad \text{TMSO} \\
\text{Ph} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | 96 |
| 2     | \[
\begin{align*}
\text{Ph} & \quad \text{TMSO} \\
\text{Me} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | 83 |
| 3     | \[
\begin{align*}
\text{MeO} & \quad \text{TMSO} \\
\text{OMe} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{MeO} & \quad \text{O} \\
\text{OMe} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{MeO} & \quad \text{O} \\
\text{OMe} & \quad \text{O}
\end{align*}
\] | 85 |
| 4     | \[
\begin{align*}
\text{Br} & \quad \text{TMSO} \\
\text{Br} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{Br} & \quad \text{O} \\
\text{Br} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{Br} & \quad \text{O} \\
\text{Br} & \quad \text{O}
\end{align*}
\] | 89 |
| 5     | \[
\begin{align*}
\text{O} & \quad \text{TMSO} \\
\text{O} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{O} & \quad \text{O} \\
\text{O} & \quad \text{O}
\end{align*}
\] | 97 |
| 6     | \[
\begin{align*}
\text{S} & \quad \text{TMSO} \\
\text{S} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{S} & \quad \text{O} \\
\text{S} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{S} & \quad \text{O} \\
\text{S} & \quad \text{O}
\end{align*}
\] | 99 |
| 7     | \[
\begin{align*}
\text{Ph} & \quad \text{TMSO} \\
\text{Ph} & \quad \text{OTMS}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | \[
\begin{align*}
\text{Ph} & \quad \text{O} \\
\text{Ph} & \quad \text{O}
\end{align*}
\] | 72 |

\textsuperscript{a} 1,2-Bis(trimethylsiloxy)cyclopropane 3 (0.5 mmol) and FeCl\textsubscript{3} (0.75 mmol) were used. \textsuperscript{b} Isolated yields.
Instead of 1,2-diketone, monotosylimide of benzil 10a, which was prepared following the reported procedure,\textsuperscript{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).](image)

The stereochemistry of 11a was confirmed by X-ray analysis (Figure 2).\textsuperscript{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).](image)

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)\textsuperscript{a}

\[
\begin{array}{cccc}
\text{entry} & \text{substrate} & EI^+ & \text{product} \\
1 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{Ph}
\end{array} & 10a & \text{\textbf{H}_3O}^+ & \begin{array}{c}
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
\text{11b} & 97 \\
2 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{Ph}
\end{array} & 10a & \text{TMSO}^- & \begin{array}{c}
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
\text{11c} & >99 \\
3 & \begin{array}{c}
\text{MeO} \\
\text{NC} \\
\text{MeO}
\end{array} & 10b & \text{\textbf{H}_3O}^+ & \begin{array}{c}
\text{MeO} \\
\text{Ph} \\
\text{NHTs} \\
\text{MeO}
\end{array} \\
\text{11d} & >99 \\
4 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{Ph}
\end{array} & 10c & \text{TMSO}^- & \begin{array}{c}
\text{Ph} \\
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
\text{11e} & 92 \\
5 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{Ph}
\end{array} & 10d & \text{\textbf{H}_3O}^+ & \begin{array}{c}
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
\text{11f} & >99 \\
6 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{MeO}
\end{array} & 10e & \text{\textbf{H}_3O}^+ & \begin{array}{c}
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
& 0^c \\
7 & \begin{array}{c}
\text{Ph} \\
\text{NC} \\
\text{NHTs}
\end{array} & 10f & \text{\textbf{H}_3O}^+ & \begin{array}{c}
\text{Ph} \\
\text{NHTs} \\
\text{Ph}
\end{array} \\
& 0^c
\end{array}
\]

\textsuperscript{a} \alpha-Ketoimine 10 (1.0 mmol), gem-dizinc 1 (2.0 mmol) and $EI^+$ (2.4 mmol) were used. \textsuperscript{b} Isolated yields. In each entry, only cis-isomer was found diastereoselectively. \textsuperscript{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. The compounds 2a, 2b, 2c, 2d, 2f, 2g, 2h, 2j, 2k and 5a are commercially available. 1,2-Diketones 218 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 ºC with vigorous stirring. The mixture was stirred for 2 h at 0 ºC. 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 ºC, 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. NH₄Claq and extracted with Et₂O. The combined organic phases were washed with brine and dried over Na₂SO₄. 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), FeCl₃ (0.75 mmol) was added at 0 °C. The mixture was stirred for 30 min. The mixture was poured into 1N HClaq and extracted with EtOAc. The combined organic phases were washed with brine and dried over Na₂SO₄. 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), BF₃•OEt₂ (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. NH₄Claq, then sat. NaHCO₃aq was added to neutralize and extracted with Et₂O. The combined organic phases were washed with brine and dried over Na₂SO₄. Purification on a neutral silica gel column chromatography gave the corresponding 2-aminocyclopropanol derivative 11.

**Characterization Data**

The Spectral data of the substrates 2e, 2f, 2l, 2m, 2n, 7a, 7b and 10d were found in the literature.

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

\[
\begin{align*}
\text{Ac} & \quad \text{Ph} \\
\quad & \quad \text{Ph}
\end{align*}
\]

\( ^1\text{H NMR (300 MHz, CDCl}_3\) \( \delta 7.28–7.20 \text{ (m, 4H), 7.18–7.10 \text{ (m, 6H), 2.51 (d, } J = 9.0 \text{ Hz, 1H), 2.11 (s, 6H), 1.83 (d, } J = 9.0 \text{ Hz, 1H); } ^{13}\text{C NMR (75 MHz, CDCl}_3\) \( \delta 170.1, 135.3, 128.8, 127.8, 64.9, 23.8, 21.1; \text{ IR (nujol) 2953, 1748, 1454, 1368, 1206, 1125, 1063, 1026, 934, 700 cm}^{-1}; \text{ mp 114.5–115.8 °C. Anal. Calcd for 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)**

\[
\begin{align*}
\text{TMSO} & \quad \text{Ph} \\
\quad & \quad \text{Ph}
\end{align*}
\]

\( ^1\text{H NMR (300 MHz, CDCl}_3\) \( \delta 7.17–6.90 \text{ (m, 10H), 2.18 (d, } J = 7.5 \text{ Hz, 1H}, 1.48 (d, } J = 7.5 \text{ Hz, 1H), 0.08 (s, 18H); } ^{13}\text{C NMR (75 MHz, CDCl}_3\) \( \delta 140.0, 127.9, 127.5, 126.5, 64.8, 23.1, 0.90; \text{ IR (neat) 2953, 1449, 1250, 1159, 1072, 1026, 966, 926, 843, 754, 700 cm}^{-1}. \text{ Anal. Calcd for 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)**

\[
\begin{align*}
\text{HO} & \quad \text{Ph} \\
\quad & \quad \text{OH}
\end{align*}
\]

\( ^1\text{H NMR (500 MHz, CDCl}_3\) \( \delta 7.60–7.20 \text{ (m, 5H), 3.85 (bs, 2H), 1.27 (d, } J = 7.5 \text{ Hz, 1H), 1.13 (s, 3H), 0.98 (d, } J = 7.5 \text{ Hz, 1H); } ^{13}\text{C NMR (125 MHz, C}_6\text{D}_6\) \( \delta 140.1, 128.4, 128.3, 127.3, 62.0, 58.8, 24.5, 20.5; \text{ IR (neat) 3352, 1604, 1447, 1221, 1132, 1076, 1057,}
\]
cis-1,2-Diacetoxy-1-methyl-2-phenylcyclopropane (3d)

\[
\text{cis} \quad 1,2\text{-Diacetoxy-1-methyl-2-phenylcyclopropane (3d)} \quad \text{AcO} \quad \text{Ph} \\
\quad \text{OAc} \\
\]

\[\text{H NMR (300 MHz, CDCl}_3) \delta 7.65–7.56 \text{ (m, 2H)}, 7.38–7.20 \text{ (m, 3H)}, 2.09 \text{ (s, 3H)}, 1.92 \text{ (s, 3H)}, 1.68 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 1.39 \text{ (d, } J = 9.0 \text{ Hz, 1H)}, 1.21 \text{ (s, 3H)}; ^{13}\text{C NMR (75 MHz, CDCl}_3) \delta 170.6, 170.2, 135.6, 129.6, 128.3, 128.2, 125.9, 63.5, 60.5, 22.8, 21.0, 20.7, 18.3; \text{IR (neat) 2936}, 1748, 1449, 1370, 1229, 1126, 1018, 949, 889, 852, 762, 700 \text{ cm}^{-1}. \]

Anal. Calcd for C_{10}H_{12}O_2: C, 67.73; H, 6.50%. Found: C, 67.84; H, 6.59%.

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

\[
\text{cis} \quad 1,2\text{-Bis(trimethylsiloxy)-1-methyl-2-phenylcyclopropane (3e)} \quad \text{TMSO} \quad \text{Ph} \\
\quad \text{OTMS} \\
\]

\[\text{H NMR (300 MHz, CDCl}_3) \delta 7.41–7.15 \text{ (m, 5H)}, 1.34 \text{ (d, } J = 6.9 \text{ Hz, 1H)}, 1.06 \text{ (d, } J = 6.9 \text{ Hz, 1H)}, 1.05 \text{ (s, 3H)}, 0.23 \text{ (s, 9H)}, 0.03 \text{ (s, 9H)}; ^{13}\text{C NMR (75 MHz, CDCl}_3) \delta 141.1, 128.0, 127.9, 126.9, 63.7, 59.7, 24.1, 22.2, 1.24, 0.82; \text{IR (neat) 2957}, 1248, 1159, 1063, 1032, 950, 841, 752, 700 \text{ cm}^{-1}. \]

Anal. Calcd for C_{16}H_{28}O_2Si_2: C, 62.28; H, 9.15%. Found: C, 61.98; H, 9.27%.

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

\[
\text{cis} \quad 1,2\text{-Diacetoxy-1,2-diethylcyclopropane (3f)} \quad \text{AcO} \quad \text{Et} \\
\quad \text{OAc} \quad \text{Et} \\
\]

\[\text{H NMR (300 MHz, CDCl}_3) \delta 1.98 \text{ (s, 6H)}, 1.84 \text{ (ddq, } J = 15.0, 7.5, 0.9 \text{ Hz, 2H)}, 1.74 \text{ (dq, } J = 15.0, 7.5 \text{ Hz, 2H)}, 1.07 \text{ (dt, } J = 8.4, 0.9 \text{ Hz, 1H)}, 1.00 \text{ (t, } J = 7.5 \text{ Hz, 6H)}, 0.87 \text{ (d, } J = 8.4 \text{ Hz, 1H})\); ^{13}\text{C NMR (75 MHz, CDCl}_3) \delta 170.4, 64.1, 24.2, 23.1, 20.9, 9.4; \text{IR (neat) 2976}, 1748, 1454, 1371, 1240, 1215 \text{ cm}^{-1}. \text{HRMS (m/z) Found: 215.1289. Calcd for } C_{11}H_{19}O_4\text{ [MH]}^+: 215.1283. \]

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

\[
\text{cis} \quad 1,2\text{-Diacetoxy-1-phenylcyclopropane (3g)} \quad \text{AcO} \quad \text{Ph} \\
\quad \text{OAc} \quad \text{H} \\
\]

\[\text{H NMR (300 MHz, CDCl}_3) \delta 7.51–7.40 \text{ (m, 2H)}, 7.41-7.28 \text{ (m, 3H)}, 4.26 \text{ (dd, } J = 8.4, 4.8 \text{ Hz, 1H)}, 2.13 \text{ (s, 3H)}, 2.04 \text{ (s, 3H)}, 1.80 \text{ (dd, } J = 8.4, 8.4 \text{ Hz, 1H)}, 1.49 \text{ cm}^{-1}. \]
(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 C$_{13}$H$_{15}$O$_4$ [MH]$^+$: 235.0970.

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

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

cis-1,2-Bis(trimethylsiloxy)-1,2-di(4-bromophenyl)cyclopropane (3j)
Calcd for C_{21}H_{28}O_{2}Br_{2}Si_{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_{2}Br_{2}Si_{2} [M]^+: 525.9995.

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

\[
\text{TMSO} \quad \text{OTMS}  \\
\text{OTMS} \quad \text{TMSO}
\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_{4}$Si$_{2}$: 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$_{4}$Si$_{2}$ [M]$^+$: 350.1370.

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

\[
\text{TMSO} \quad \text{OTMS}  \\
\text{OTMS} \quad \text{TMSO}
\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_{2}$S$_{2}$Si$_{2}$ [M]$^+$: 382.0913.

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

\[
\text{TMSO} \quad \text{OTMS}  \\
\text{OTMS} \quad \text{TMSO}
\]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 138.9, 138.2, 130.7, 127.7, 126.9, 124.5, 65.1, 25.8, 21.3, 1.38; IR (nujor) 2854, 2650, 1233, 843, 728, 668 cm$^{-1}$. Anal. Calcd for C$_{23}$H$_{34}$O$_{2}$Si$_{2}$: 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$_{2}$Si$_{2}$ [M]$^+$: 398.2097.
cis-1,2-Bis(trimethylsiloxy)-1,2-di(2-naphthyl)cyclopropane (3n)

\[
\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.63–7.59 (m, 6H), 7.47 (d, J = 9.0Hz, 2H), 7.35–7.29 (m, 6H), 2.48 (d, J = 7.5 Hz, 1H), 1.62 (d, J = 7.5 Hz, 1H), 0.09 (s, 18H); ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)} \delta 137.5, 132.6, 132.2, 127.8, 127.4, 127.3, 126.5, 126.2, 125.6, 125.5, 65.2, 24.0, 1.14; \text{IR (neat) 2854, 2363, 1605, 1456, 1377, 1250, 1161, 1125, 952, 925, 842, 749 cm}^{-1}. \text{Anal. Calcd for C}_{29}\text{H}_{34}\text{O}_{2}\text{Si}_{2}: C, 73.99; H, 7.28%. \text{Found: C, 73.93; H, 7.32%; HRMS (m/z) Found: 470.2101. Calcd for C}_{29}\text{H}_{34}\text{O}_{2}\text{Si}_{2}[^{13}\text{M}]^{+}: 470.2097.\]

1,2-Diferrocenylpropenone (4)

\[
\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 5.77 (s, 1H), 5.68 (s, 1H), 4.84 (t, J = 2.0 Hz, 2H), 4.54 (t, J = 2.0 Hz, 2H), 4.52 (s, 2H), 4.29 (s, 2H), 4.23 (s, 5H), 4.14 (s, 5H); ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)} \delta 200.3, 147.4, 114.4, 80.8, 78.4, 72.3, 71.0, 70.0, 69.7, 69.0, 67.1; \text{IR (nujor) 1635, 1246 cm}^{-1}. \text{Anal. Calcd for C}_{23}\text{H}_{20}\text{OFe}_{2}: C, 65.14; H, 4.75%. \text{Found: C, 64.86; H, 4.78%; HRMS (m/z) Found: 424.0209. Calcd for C}_{23}\text{H}_{20}\text{OFe}_{2}[^{13}\text{M}]^{+}: 424.0213.\]

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

\[
\text{H NMR (300 MHz, CDCl}_3\text{)} \delta 5.80 (ddt, J = 17.1, 10.2, 6.9 Hz, 1H), 4.98 (ddt, J = 17.1, 2.1, 1.5 Hz, 1H), 4.92 (ddt, J = 10.2, 2.1, 1.2 Hz, 1H), 3.86 (s, 3H), 2.82 (t, J = 7.2 Hz, 2H), 2.06–1.99 (m, 2H), 1.68–1.57 (m, 2H), 1.40–1.27 (m, 12H); ^{13}\text{C NMR (75 MHz, CDCl}_3\text{)}: \delta 194.0, 161.4, 139.0, 114.0, 52.9, 39.4, 33.9, 29.5, 29.4, 29.3, 29.2, 29.0 (co-incident), 23.0; \text{IR (neat) 2926, 1755, 1732, 1462, 1275, 1067, 910 cm}^{-1}. \text{Anal. Calcd for C}_{14}\text{H}_{24}\text{O}_{3}: C, 69.96; H, 10.07%. \text{Found: C, 69.69; H, 10.29%; HRMS (m/z) Found: 240.1724. Calcd for C}_{14}\text{H}_{24}\text{O}_{3}[^{13}\text{M}]^{+}: 240.1725.\]
Methyl 2-methylene-2-phenylacetate (6a)

\[\text{Ph} \begin{array}{c}
\text{H} \\
\text{CH}_2 \\
\text{O} \\
\text{Me}
\end{array} \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.43–7.32 (m, 5H), 6.37 (d, $J = 1.0$ Hz, 1H), 5.90 (d, $J = 1.0$ Hz, 1H), 3.83 (s, 3H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 167.3, 141.3, 136.7, 128.3, 128.2, 128.1, 126.9, 52.2. HRMS (m/z) Found: 162.0680. Calcd for C$_{10}$H$_{10}$O$_2$ [M]$^+$: 162.0681.

The spectral data of the product 6a are in agreement with those published.$^{27}$

Methyl 2-methylene-12-tridecenoate (6b)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 6.12 (dt, $J = 1.5$, 0.5 Hz, 1H), 5.81 (ddt, $J = 17.0$, 10.0, 6.5 Hz, 1H), 5.70 (dt, $J = 1.5$, 1.5 Hz, 1H), 4.99 (ddt, $J = 17.0$, 2.0, 1.5 Hz, 1H), 4.93 (ddt, $J = 10.0$, 2.0, 1.5 Hz, 1H), 3.75 (s, 3H), 2.29 (ddt, $J = 7.5$, 1.0, 0.5 Hz, 2H), 2.06–2.01 (m, 2H), 1.45 (tt, $J = 7.5$, 7.5 Hz, 2H), 1.37 (tt, $J = 7.5$, 7.5 Hz, 2H), 1.34–1.25 (m, 10H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 167.8, 140.8, 139.2, 124.4, 114.1, 51.7, 33.8, 31.9, 29.5, 29.43, 29.37, 29.2, 29.1, 28.9, 28.3; IR (neat) 2927, 2855, 2360, 1725, 1632, 1438, 1197, 1163, 994, 940, 909 cm$^{-1}$. Anal. Calcd for C$_{15}$H$_{26}$O$_2$: C, 75.58; H, 10.99%. Found: C, 75.49; H, 10.71%; HRMS (m/z) Found: 238.1935. Calcd for C$_{15}$H$_{26}$O$_2$ [M]$^+$: 238.1933.

2-Phenyl-1-piperidin-1-ylpropenone (8a)

\[\text{Ph} \begin{array}{c}
\text{H} \\
\text{CH}_2 \\
\text{N} \\
\text{O} \\
\text{Me}
\end{array} \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 7.44–7.42 (m, 2H), 7.37–7.28 (m, 3H), 5.71 (s, 1H), 5.33 (s, 1H), 3.71–3.65 (m, 2H), 3.32–3.30 (m, 2H), 1.63–1.60 (m, 4H), 1.40–1.33 (m, 2H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 169.1, 145.2, 135.7, 128.7, 128.5, 125.7, 113.3, 48.0, 42.4, 26.3, 25.6, 24.5. HRMS (m/z) Found: 215.1306. Calcd for C$_{14}$H$_{19}$NO [M]$^+$: 215.1310.

The spectral data of the product 8a are in agreement with those published.$^{28}$
(S)-Methyl 1-(2-phenylacryloyl)pyrrolidine-2-carboxylate (8b)

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

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

\[ \text{HNMR (300 MHz, CDCl}_3\text{) } \delta \text{ 8.00 (d, } J = 7.0 \text{ Hz, 4H), 7.56 (t, } J = 7.0 \text{ Hz, 2H), 7.50 (dd, } J = 7.0, 7.0 \text{ Hz, 4H), 6.87 (s, 1H); } ^{13}\text{C NMR (75 MHz, CDCl}_3\text{) } \delta \text{ 185.7, 135.5, 132.4, 128.7, 127.1, 93.1. HRMS (m/z) Found: 224.0836. Calcd for C}_{15}\text{H}_{12}\text{O}_2 \text{[M]^+: 224.0837.} \]

The product 9a is commercially available.

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

\[ \text{HNMR (300 MHz, CDCl}_3\text{) } \delta \text{ 7.88 (d, } J = 7.0 \text{ Hz, 2H), 7.52 (t, } J = 7.5 \text{ Hz, 1H), 7.45 (dd, } J = 7.5, 7.0 \text{ Hz, 2H), 6.18 (s, 1H), 2.20 (s, 3H); } ^{13}\text{C NMR (75 MHz, CDCl}_3\text{) } \delta \text{ 193.8, 183.3, 134.8, 132.3, 128.6, 127.0, 96.7, 25.8. HRMS (m/z) Found: 162.0679. Calcd for C}_{10}\text{H}_{10}\text{O}_2 \text{[M]^+: 162.0681.} \]

The product 9b is commercially available.
1,3-di(4-Anisyl)-1,3-propanedione (9c)

\[ \text{MeO} \quad \text{O} \quad \text{O} \quad \text{Me} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta \quad 7.96 (d, J = 9.0 \text{ Hz, 4H}), \quad 6.98 \quad (d, J = 9.0 \text{ Hz, 4H}), \quad 6.74 \quad (s, \text{ 1H}), \quad 3.89 \quad (s, \text{ 6H}); \quad \text{C NMR (125 MHz, CDCl}_3\text{)} \delta \quad 184.6, \quad 163.0, \quad 129.1, \quad 128.2, \quad 113.9, \quad 91.5, \quad 55.5. \]

HRMS (m/z) Found: 284.1048. Calcd for C_{17}H_{16}O_4 [M]^+: 284.1049.

The product 9c is commercially available.

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

\[ \text{Br} \quad \text{O} \quad \text{O} \quad \text{Br} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta \quad 7.85 (d, J = 8.5 \text{ Hz, 4H}), \quad 7.63 \quad (d, J = 8.5 \text{ Hz, 4H}), \quad 6.77 \quad (s, \text{ 1H}); \quad \text{C NMR (125 MHz, CDCl}_3\text{)} \delta \quad 184.7, \quad 134.2, \quad 132.0, \quad 128.7, \quad 127.5, \quad 92.9. \quad \text{HRMS (m/z) Found: 379.9044.} \]

Calcd for C_{15}H_{10}O_2^7Br_2 [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)

\[ \text{\text{O}} \quad \text{O} \quad \text{\text{O}} \quad \text{\text{O}} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta \quad 7.61 (dd, J = 1.5, 1.0 \text{ Hz, 2H}), \quad 7.20 \quad (dd, J = 3.5, 1.0 \text{ Hz, 2H}), \quad 6.65 \quad (s, \text{ 1H}), \quad 6.58 \quad (dd, J = 3.5, 1.0 \text{ Hz, 2H}); \quad \text{C NMR (125 MHz, CDCl}_3\text{)} \delta \quad 174.7, \quad 150.3, \quad 146.1, \quad 115.5, \quad 112.6, \quad 92.1. \quad \text{HRMS (m/z) Found: 204.0421.} \]

Calcd for C_{11}H_{8}O_4 [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)

\[ \text{\text{S}} \quad \text{S} \quad \text{\text{O}} \quad \text{O} \quad \text{\text{O}} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{)} \delta \quad 7.78 (dd, J = 4.0, 1.0 \text{ Hz, 2H}), \quad 7.17 \quad (dd, J = 5.0, 4.0 \text{ Hz, 2H}), \quad 6.54 \quad (s, \text{ 1H}); \quad \text{C NMR (125 MHz, CDCl}_3\text{)} \delta \quad 178.8, \quad 140.6, \quad 132.0, \quad 130.0, \quad 128.3, \quad 92.6. \quad \text{HRMS (m/z) Found: 235.9971.} \]

Calcd for C_{11}H_{8}O_2S_2 [M]^+: 235.9966.

The spectral data of the product 9f are in agreement with those published.\(^{31}\)
Chapter 2

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

\[
\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 8.60 \text{ (d, } J = 1.5 \text{ Hz, 2H), 8.08 \text{ (d, } J = 8.5 \text{ Hz, 2H), 8.02 \text{ (d, } J = 7.5 \text{ Hz, 2H), 7.96 \text{ (d, } J = 8.5 \text{ Hz, 2H), 7.91 \text{ (d, } J = 8.0 \text{ Hz, 2H), 7.63–7.56 \text{ (m, 4H), 7.16 (s, 1H); \[13C NMR (125 MHz, CDCl}_3\text{) } \delta 185.6, 135.3, 132.8, 132.8, 129.4, 128.5, 128.4, 128.2, 127.8, 126.8, 123.3, 93.8. \]}\]


The spectral data of the product 9g are in agreement with those published.\textsuperscript{32}

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

\[
\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 7.94–7.92 \text{ (m, 2H), 7.87 \text{ (d, } J = 8.5 \text{ Hz, 2H), 7.84–7.82 \text{ (m, 2H), 7.66–7.62 \text{ (m, 1H), 7.57–7.53 \text{ (m, 1H), 7.53–7.50 \text{ (m, 2H), 7.41–7.37 \text{ (m, 2H), 7.33 (d, } J = 8.5 \text{ Hz, 2H), 2.43 (s, 3H); \[13C NMR (125 MHz, CDCl}_3\text{): } \delta 196.1, 174.8, 144.8, 135.6, 134.7, 134.6, 134.5, 132.4, 130.1, 129.7, 129.13, 129.11, 129.0, 128.2, 21.6; IR (nujor) 3431, 1678, 1587, 1566, 1449, 1327, 1219, 1161, 1090, 904, 820, 773 cm\textsuperscript{-1}, mp 123.0–124.0 °C. Anal. Calcd for C\text{21H}_{17}O_3NS: C, 69.40; H, 4.71%. Found: C, 69.66; H, 4.81%; HRMS (m/z) Found: 363.0914. Calcd for C\text{21H}_{17}O_3NS [M]+: 363.0929. \]

\[
\text{N-(1,2-Bis(4-methoxyphenyl)-2-oxoethyldiene)-4-methylbenzenesulfonamide (10b) } \]

\[
\text{H NMR (500 MHz, CDCl}_3\text{) } \delta 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); \[13C NMR (125 MHz, CDCl}_3\text{): } \delta 194.6, 174.1, 164.9, 164.6, 144.3, 136.3, 132.7, 131.6, 129.5, 128.2, 128.0, 125.1, 114.5, 114.4, 55.6 (co-incident), 21.6; IR (nujor) 3360, 1668, 1599, 1549, 1317, 1267, 1157, 1089, 1020, 908, 818, 787, 735 cm\textsuperscript{-1}. HRMS (m/z) Found: 424.1223. Calcd for C\text{23H}_{22}OsNS [MH]+: 424.1219. \]}\]
Chapter 2

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

\[ \text{NHTs} \]

\[ \text{Ph} \]

\[ \text{Ph} \]

\[ \text{O} \]

\[ \text{AcO} \]

\[ \text{Ph} \]

\[ \text{Ph} \]

\[ \text{Ts} \]

\[ \text{N} \]

\[ \text{O} \]

\[ \text{Me} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{) } \delta \]

\[ 8.34 \text{ (s, 1H), 8.23–8.22 (m, 1H), 8.14 (dd, } J = 9.0, 2.0 \text{ Hz, 1H), 8.10 (dd, } J = 9.0, 2.0 \text{ Hz, 1H), 7.99 (d, } J = 9.0 \text{ Hz, 1H), 7.91–7.85 (m, 5H), 7.83 (dd, } J = 8.0, 1.0 \text{ Hz, 1H), 7.77 (dd, } J = 8.0, 1.0 \text{ Hz, 1H), 7.65–7.46 (m, 4H), 7.32–7.30 (m, 2H), 2.43 (s, 3H); } \]

\[ \text{13C NMR (125 MHz, CDCl}_3\text{): } \delta \]

\[ 196.1, 174.9, 144.7, 136.3, 136.2, 135.8, 133.8, 132.47, 132.43, 132.41, 132.3, 130.02, 129.97, 129.8, 129.7, 129.6, 129.4, 129.3, 129.1, 128.3, 128.0, 127.8, 127.15, 127.11, 124.2, 123.4, 21.6; IR (nujor) 3472, 1674, 1568, 1327, 1161, 1088, 910, 787, 731 \text{ cm}^{-1}, \text{ mp 86.0–86.8 °C.} \]

Anal. Calcd for C\textsubscript{29}H\textsubscript{21}O\textsubscript{3}NS: C, 75.14; H, 4.57%. Found: C, 75.11; H, 4.78%; HRMS (m/z) Found: 463.1246. Calcd for C\textsubscript{29}H\textsubscript{21}O\textsubscript{3}NS [M]+: 463.1242.

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

\[ \text{Ph} \]

\[ \text{Ph} \]

\[ \text{NOMe} \]

\[ \text{H NMR (500 MHz, CDCl}_3\text{) } \delta \]

\[ 7.97–7.95 (m, 2H), 7.63–7.58 (m, 3H), 7.51–7.48 (m, 2H), 7.41–7.34 (m, 3H), 3.93 (s, 3H); } \]

\[ \text{13C NMR (75 MHz, CDCl}_3\text{) } \delta \]

\[ 193.9, 155.7, 134.6, 134.2, 131.0, 130.1, 129.2, 128.9, 128.7, 126.2, 62.8; IR (neat) 2938, 1682, 1595, 1449, 1327, 1231, 1177, 1049, 928, 872, 772, 735, 691, 625 \text{ cm}^{-1}. \]

Anal. Calcd for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{2}: C, 75.30; H, 5.48%. Found: C, 75.17; H, 5.43%; HRMS (m/z) Found: 239.0954. Calcd for C\textsubscript{15}H\textsubscript{13}NO\textsubscript{2} [M]+: 239.0946.

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

\[ \text{AcO} \]

\[ \text{Ph} \]

\[ \text{Ph} \]

\[ \text{H NMR (300 MHz, CDCl}_3\text{) } \delta \]

\[ 7.41 (d, } J = 8.4 \text{ Hz, 2H), 7.07–6.98 (m, 7H), 6.90–6.83 (m, 5H), 5.83 (s, 1H), 2.39 (d, } J = 8.4 \text{ Hz, 1H), 2.30 (s, 3H), 2.18 (d, } J = 8.4 \text{ Hz, 1H), 2.13 (s, 3H); } \]

\[ \text{13C NMR (75 MHz, CDCl}_3\text{) } \delta \]

\[ 171.0, 143.1, 137.9, 135.9, 134.9, 129.3, 129.0, 128.5, 128.0, 127.93, 127.87, 127.4, 127.1, 66.2, 46.7, 22.4, 21.8, 21.7; IR (nujor) 3345, 2363, 1750, 1674, 1599, 1323, 1227 \text{ cm}^{-1}. \]

HRMS (m/z) Found: 421.1357. Calcd for C\textsubscript{24}H\textsubscript{23}NO\textsubscript{4}S [M]+: 421.1348.
cis-N-(2-Hydroxy-1,2-diphenylcyclopropyl)-4-methylbenzenesulfonamide (11b)

\[
\begin{align*}
\text{HO} & \quad \text{NH} \quad \text{Ts} \\
\text{Ph} & \quad \text{Ph} \\
\end{align*}
\]

$^1$H NMR (300 MHz, CDCl$_3$) 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); $^{13}$C NMR (75 MHz, CDCl$_3$) 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 C$_{22}$H$_{21}$NO$_3$S [M]$^+$: 379.1242.

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

\[
\begin{align*}
\text{TMSO} & \quad \text{NH} \quad \text{Ts} \\
\text{Ph} & \quad \text{Ph} \\
\end{align*}
\]

$^1$H NMR (500 MHz, CDCl$_3$) 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); $^{13}$C NMR (125 MHz, CDCl$_3$) δ 142.8, 138.3, 137.5, 136.5, 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 C$_{25}$H$_{29}$NO$_3$SSi [M]$^+$: 451.1637.

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

\[
\begin{align*}
\text{HO} & \quad \text{NH} \quad \text{Ts} \\
\text{MeO} & \quad \text{O} \quad \text{Me} \\
\end{align*}
\]

$^1$H NMR (300 MHz, CDCl$_3$) 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); $^{13}$C NMR (75 MHz, CDCl$_3$) 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 C$_{24}$H$_{23}$NO$_5$S [M]$^+$: 439.1453.
cis-N-(2-Trimethylsiloxy-1,2-di-2-naphthylcyclopropyl)-4-methylbenzenesulfonamide (11e)

\[ \text{cis-N} \]

\[
\begin{array}{c}
\text{TMSO} \setminus \text{NHTs} \\
\text{NHPh} \setminus \text{NHPh}
\end{array}
\]

\[ ^{1}H \text{ NMR} (300 \text{ MHz}, \text{ C}_6\text{D}_6) \delta 7.60–6.94 (m, 16H), 6.39–6.36 (m, 2H), 6.20 (s, 1H), 2.60 (d, \text{ J} = 8.1 \text{ Hz}, 1H), 2.15 (d, \text{ J} = 8.1 \text{ Hz}, 1H), 1.63 (s, 3H), 0.05 (s, 9H); ^{13}C \text{ NMR} (75 \text{ MHz}, \text{ C}_6\text{D}_6) \delta 142.0, 139.3, 135.8, 134.4, 132.8, 132.73, 132.66, 132.3, 128.6, 127.7, 127.6, 127.4, 127.3, 127.0, 126.5, 126.1, 126.0, 125.8, 125.6, 125.5, 64.8, 46.3, 23.6, 20.8, 0.9; \text{ IR (neat)} 3312, 2955, 2344, 1250, 1159, 1092, 843, 752 \text{ cm}^{-1}. \text{ HRMS (m/z) Found: 551.1950. Calcd for C}_{33}\text{H}_{33}\text{O}_3\text{NSSi} [\text{M}^+] : 551.1950. \]

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

\[ \text{HO} \]

\[
\begin{array}{c}
\text{NHPH} \\
\text{Ph} \setminus \text{Ph}
\end{array}
\]

\[ ^{1}H \text{ NMR} (300 \text{ MHz}, \text{ C}_6\text{D}_6) \delta 7.15–6.67 (m, 15H), 2.02 (d, \text{ J} = 7.2 \text{ Hz}, 1H), 1.08 (d, \text{ J} = 7.2 \text{ Hz}, 1H); ^{13}C \text{ NMR} (75 \text{ MHz}, \text{ C}_6\text{D}_6) \delta 147.2, 139.7, 138.6, 129.2, 128.8, 128.4, 128.0, 127.4, 126.1, 120.0, 118.5, 115.2, 66.5, 47.0, 25.0; \text{ IR (neat)} 3509, 3423, 2363, 1605, 1314, 1208, 751, 693 \text{ cm}^{-1}. \text{ Anal. Calcd for C}_{21}\text{H}_{19}\text{NO}: \text{ C}, 83.69; \text{ H}, 6.35\%. \text{ Found: C}, 83.39; \text{ H}, 6.16\%; \text{ HRMS (m/z) Found: 301.1459. Calcd for C}_{21}\text{H}_{19}\text{NO} [\text{M}^+] : 301.1463. \]
References and Notes


Chapter 2


9. Crystal structure data: Monoclinic, a = 43.816(9), b = 5.922(2), c = 38.178(8) Å, β = 100.53(3)°, V = 9739(3) Å³, Z = 24, ρ_{calc} = 1.270 Mgm⁻³, λ(MoKα) = 0.71069 Å, T = 296 K, θ_{max} = 54.0°, R = 0.130 for 4583 reflections (I > 2σ(I)).


11. Treatment of 1-dodecyne with 1 in THF at 25 °C for 12 h gave zinc acetylide quantitatively.


16. Crystal structure data: Monoclinic, a = 12.7365(13), b = 10.8102(11), c = 16.3267(17) Å, β = 105.936°, V = 2161.5(4) Å³, Z = 4, ρ_{calc} = 1.295 Mgm⁻³, λ(MoKα) = 0.71073 Å, T = 296 K, θ_{max} = 54.0°, R = 0.049 for 4711 reflections (I > 2σ(I)).


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. Subsequent 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. Because its reactivity is enhanced by doubly substituted electronegative zinc atoms, the dizinc 1 may have 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. Meanwhile, Matsubara found that treatment of the dizinc 1 with an \( \alpha \)-hydroxy ketone, which has a Lewis basic atom at \( \alpha \)-position of carbonyl, performed the nucleophilic addition smoothly to give a methylenated compounds. The coordination between the dizinc and hydroxyl group at \( \alpha \)-position might activate the reagent. The same activation is also observed in the reaction of Grignard reagent and \( \alpha \)-hydroxy ketone under Cram’s chelation control.

The author supposed that the similar activation may be observed, when the dizinc 1 is treated with other ketones having a Lewis basic site at \( \alpha \)-position, such as 1,2-diketone and \( \alpha,\beta \)-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 iodozincioethyl group to the other carbonyl group also proceeded readily to give cis-cyclopropan-1,2-diol diastereoselectively. The high stereoselectivity comes from the specific coordination between the dizinc and 1,2-diketone.

Considering these results, when an \( \alpha,\beta \)-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 NH₄Cl. 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. 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 \(\alpha,\beta\)-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).\(^a\)

![Chemical structure](image)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>Yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>2b</td>
<td>3b</td>
<td>94</td>
</tr>
<tr>
<td>2</td>
<td>2c</td>
<td>3c</td>
<td>87</td>
</tr>
<tr>
<td>3</td>
<td>2d</td>
<td>3d</td>
<td>&gt;99</td>
</tr>
<tr>
<td>4</td>
<td>2e</td>
<td>3e</td>
<td>95</td>
</tr>
<tr>
<td>5</td>
<td>2f</td>
<td>3f</td>
<td>90</td>
</tr>
<tr>
<td>6</td>
<td>2g</td>
<td>3g</td>
<td>95</td>
</tr>
<tr>
<td>7</td>
<td>2h</td>
<td>3h</td>
<td>95</td>
</tr>
<tr>
<td>8</td>
<td>2i</td>
<td>3i</td>
<td>83</td>
</tr>
<tr>
<td>9</td>
<td>2j</td>
<td>3j</td>
<td>37(^c)</td>
</tr>
</tbody>
</table>

\(^a\) 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 $\alpha,\beta$-epoxy ketone (S)-2b with the dizinc 1 gave ($IR,2R$)-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 $\alpha$-carbon atom (Scheme 3). 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 $\beta$ face of 2, which needs to be rationalized, since previous reports concerning the diastereoselective metal-mediated nucleophilic attack to an $\alpha,\beta$-epoxy ketone occurred from the $\alpha$ face of 2.

For example, treatment of 2c with NaBH$_4$/LaCl$_3$ resulted in the exclusive formation of erythro-epoxy alcohol. The diastereoselective reaction was explained by chelation effects to form intermediate A, as shown in Scheme 4.
Scheme 4. Diastereoselective reduction of $\alpha,\beta$-epoxy ketone with NaBH$_4$/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 $\beta$-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 ($\angle$O(1)-C(1)-C(2)-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 $\alpha,\beta$-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 methylanation 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.
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.\textsuperscript{10} When it was applied to 3 as starting material, \(\beta,\gamma\)-unsaturated ketone 5 was obtained via carbocation intermediate (Scheme 8).\textsuperscript{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.\textsuperscript{12}

**Scheme 8.** Julia-type transformation of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol into (E)-\(\beta,\gamma\)-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 $\beta,\gamma$-unsaturated ketone with high diastereoselectivity (entry 6).\textsuperscript{13}

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

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

$^a$ 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 $^1$H NMR using bromoform as internal standard. $^d$ The $E/Z$ ratios were determined by $^1$H 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 alcolol,
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, however, gave the corresponding $\beta,\gamma$-unsaturated ketone 5b in good yield (Scheme 9). This procedure worked well for the other primary alcohols 3d-f.

Table 3. Examples of the transformation of 2-(1-hydroxyalkyl)-1-alkycyclopropanols 3 into $(E)$-$\beta,\gamma$-unsaturated ketones 5.

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
<th>E / Z&lt;sup&gt;c&lt;/sup&gt;</th>
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<tr>
<td>1</td>
<td>[image]</td>
<td>3a</td>
<td>5a</td>
<td>70</td>
</tr>
<tr>
<td>2&lt;sup&gt;d&lt;/sup&gt;</td>
<td>3a</td>
<td>5a</td>
<td></td>
<td>$&gt;99$</td>
</tr>
<tr>
<td>3</td>
<td>[image]</td>
<td>3o</td>
<td>5o</td>
<td>96  E only</td>
</tr>
<tr>
<td>4</td>
<td>[image]</td>
<td>3e</td>
<td>5e</td>
<td>95  E only</td>
</tr>
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</tr>
<tr>
<td>6</td>
<td>[image]</td>
<td>3j</td>
<td>5j</td>
<td>$&gt;99$  E only</td>
</tr>
<tr>
<td>7&lt;sup&gt;e&lt;/sup&gt;</td>
<td>[image]</td>
<td>3b</td>
<td>5b</td>
<td>35&lt;sup&gt;f&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

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

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 (IR*,2R*)-2-(1-hydroxyalkyl)-1-alkycyclopropanols 3 diastereoselectively. The author also demonstrated the stereoselective synthesis of β,γ-unsaturated ketones 7 by acid-mediated Julia-type transformation from
(\(R^*,2R^*\))-2-(1-hydroxyalkyl)-1-alkylcyclopropanols.

**Experimental Section**

Unless otherwise noted, commercially available reagents were used without purification. \(\alpha,\beta\)-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 \(^1\)H NMR after converting into the corresponding (S)-(–)-\(\alpha\)-methoxy-\(\alpha\)-(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 \(\alpha,\beta\)-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 \(\text{NH}_4\text{Cl}\) was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over \(\text{Na}_2\text{SO}_4\). 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 \(\beta,\gamma\)-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 NaHCO₃ was added. The organic layer was extracted with EtOAc, and the combined organic layers were dried over Na₂SO₄. 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,²ᵃ 2b,²ᵇ 2c,²ᶜ 2d,²ᵈ 2e,²ᵉ 2f,²ᶠ 2i,²ⁱ 2k,²ᴷ 2m²ᵐ and 2n²ⁿ were be found in the literature.

**4-Acetylbenzoyloxirane (2g)**

\[
\begin{align*}
\text{1H NMR (300 MHz, CDCl}_3\text{)} & : \delta 8.12–8.02 (m, 4H), 4.21 (dd, J = 4.2, 2.4 Hz, 1H), 3.14 (dd, J = 6.6, 4.2 Hz, 1H), 2.97 (dd, J = 6.6, 2.4 Hz), 2.64 (s, 3H); \\
\text{13C NMR (75 MHz, CDCl}_3\text{)}: \delta 197.0, 194.2, 140.5, 138.2, 128.44, 128.41, 51.4, 47.6, 27.0; \text{ IR (neat) 1694, 1682, 1505, 1408, 1360, 1310, 1267, 1233, 951 cm}^{-1}. \text{ HRMS (m/z) Found: 190.0632. Calcd for C}_{11}H_{10}O_3 \text{[M]}^+: 190.0630.}
\end{align*}
\]

**4-Bromobenzoyloxirane (2h)**

\[
\begin{align*}
\text{1H NMR (300 MHz, CDCl}_3\text{)} & : \delta 7.89 (d, J = 8.7 Hz, 2H), 7.62 (d, J = 8.7 Hz, 2H), 4.15 (dd, J = 4.5, 2.4 Hz, 1H), 3.11 (dd, J = 6.3, 4.5 Hz, 1H), 2.94 (dd,}
\end{align*}
\]
$J = 6.3, 2.4 \text{ Hz}, 1\text{H}); ^{13}\text{C NMR (75 MHz, CDCl}_3): \delta 193.6, 133.8, 132.0, 129.7, 129.1, 51.2, 47.5; \text{ IR (neat)} 1692, 1587, 1402, 1234, 1071, 1011, 955, 912, 741 \text{ cm}^{-1}. \text{ HRMS (m/z) Found: 225.9630. Calcd for C}_9\text{H}_7\text{O}_2\text{Br [M]$: 225.9629.}

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

$^1\text{H NMR (300 MHz, CDCl}_3)$ $\delta 3.27 (d, J = 1.8 \text{ Hz}, 1\text{H}), 3.06 (ddd, J = 8.7, 3.3, 1.8 \text{ Hz, 1H}), 2.52–2.31 (m, 2\text{H}), 2.08-1.99 (m, 1\text{H}), 1.72–1.68 (m, 2\text{H}), 1.55–1.43 (m, 2\text{H}), 1.36–1.25 (m, 17\text{H}); ^{13}\text{C NMR (125 MHz, CDCl}_3): \delta 207.4, 60.3, 59.0, 37.2, 30.8, 27.5, 27.0, 26.8, 26.5, 26.4, 26.2, 26.1, 25.7, 24.7, 22.6; \text{ IR (nujor) 2928, 1712, 1444, 1368, 1240, 910, 856, 733 cm}^{-1}$. mp 56.2–56.7 \text{ °C. Anal. Calcd for 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 C_{15}H_{26}O_2 [M]$: 238.1933.

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

$^1\text{H NMR (300 MHz, C}_6\text{D}_6)$ $\delta 7.22–7.19 (m, 2\text{H}), 7.16–7.12 (m, 2\text{H}), 7.05–7.00 (m, 1\text{H}), 4.19 (bs, 1\text{H}), 3.55 (bs, 1\text{H}), 1.37–1.33 (m, 1\text{H}), 1.31 (s, 3\text{H}), 1.20 (s, 3\text{H}), 1.03–0.95 (m, 1\text{H}), 0.89–0.79 (m, 1\text{H}); ^{13}\text{C NMR (75 MHz, C}_6\text{D}_6)$ $\delta 144.8, 128.4, 126.4, 124.7, 70.4, 60.6, 37.1, 31.0, 30.3, 17.1; \text{ IR (nujor) 3265, 2359, 1456, 1362, 1225 cm}^{-1}$. mp 95.5–96.2 \text{ °C. Anal. Calcd for 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 C_{12}H_{17}O_2 [M]$: 193.1229.

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

$^1\text{H NMR (500 MHz, C}_6\text{D}_6)$ $\delta 7.25–7.22 (m, 2\text{H}), 7.17–7.14 (m, 2\text{H}), 7.07–7.03 (m, 1\text{H}), 4.17 (bs, 1\text{H}), 3.86 (dd, J = 11.5, 5.0 \text{ Hz, 1H}), 3.60 (dd, J = 11.5, 9.0 \text{ Hz, 1H}), 3.22 (bs, 1\text{H}), 1.35–1.29 (m, 1\text{H}), 0.92–0.86 (m, 2\text{H}); ^{13}\text{C NMR (125 MHz, C}_6\text{D}_6)$ $\delta 145.2, 128.4, 126.3, 124.6, 62.0, 59.2, 29.7, 20.9; \text{ IR (neat) 3362, 3354, 1497, 1449, 1402, 1375, 1238, 1111, 1078, 1024 cm}^{-1}$. HRMS (m/z) Found: 164.0837. Calcd for C_{10}H_{12}O_2 [M]$: 

74
164.0837.

The enantiomeric excess of \((IR,2R)\)-3b was determined by \(^1\text{H}\) NMR after transformation into the corresponding \((S)\)-\(\alpha\)-methoxy-\(\alpha\)-(trifluoromethyl)phenylacetate.

\[
\begin{align*}
\text{\(^1\text{H}\) NMR (500 MHz, CDCl}_3\delta & 7.37−7.23 (m, 8H), 7.15−7.12 (m, 2H), \\
& 4.67 (dd, 1H, \text{ }J = 11.5, 4.0 Hz), 4.58 (dd, 1H, \text{ }J = 11.5, 10.0 Hz), 3.89 \\
& (bs, 1H), 3.53 (s, 3H), 1.50−1.44 (dddd, 1H, \text{ }J = 10.0, 10.0, 7.0, 4.0 Hz), \\
& 1.35 (dd, 1H, \text{ }J = 10.0, 6.0 Hz), 1.14 (dd, 1H, \text{ }J = 7.0, 6.0 Hz); \\
\text{\(^{19}\text{F}\) NMR (282 MHz, CDCl}_3\delta & 89.7 \\
\end{align*}
\]

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

\[
\begin{align*}
\text{\(^1\text{H}\) NMR (500 MHz, C}_6\text{D}_6\delta & 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, \text{ }J = 6.5 Hz, 3H), \\
& 1.20−1.14 (m, 1H), 0.89−0.85 (m, 2H); \\
\text{\(^{13}\text{C}\) NMR (125 MHz, C}_6\text{D}_6\delta & 145.3, 128.3, 126.3, 124.6, \\
& 69.0, 59.3, 35.5, 22.7, 21.5; \text{IR (neat) 3363, 3273, 2362, 1602, 1498, 1451, 1235, 1077, 1022 cm}^{-1}. \\
\text{Anal. Calcd for } & \text{C}_{11}\text{H}_{14}\text{O}_2: } \text{C, 74.13; H, 7.92\%; Found: C, 74.29, H, 8.03\%; } \\
\text{HRMS (m/z) Found: } & 178.0992. \text{Calcd for } \text{C}_{11}\text{H}_{14}\text{O}_2 \text{ [M]^+ : 178.0994.}
\end{align*}
\]

\((IS^*,2R^*)\)-2-Hydroxymethyl-2-methyl-1-phenylcyclopropanol (3d)

\[
\begin{align*}
\text{\(^1\text{H}\) NMR (300 MHz, } & \text{CDCl}_3\delta 7.39−7.23 (m, 5H), 3.91 (d, \text{ }J = 11.7 Hz, 1H), \\
& 3.80 (d, \text{ }J = 11.7 Hz, 1H), 3.06 (bs, 2H), 1.05 (s, 2H), 0.81 (s, 3H); \\
\text{\(^{13}\text{C}\) NMR (75 MHz, C}_6\text{D}_6\delta & 140.6, 128.7, 128.6, 127.8, 67.7, 65.6, 29.5, 22.7, 19.0; \text{IR (nujol) 3333, 3192, \\
& 1377, 1309, 1251, 1211, 1141, 1037, 1020 cm}^{-1}; \text{mp 78.0−78.5 °C. HRMS (m/z) Found: 178.0990.} \\
\text{Calcd for } & \text{C}_{11}\text{H}_{14}\text{O}_2 \text{ [M]^+ : 178.0994.}
\end{align*}
\]

\((IS^*,2R^*)\)-2-\((R^*)\)-1-Hydroxyethyl)-2-methyl-1-phenylcyclopropanol (3e)

\[
\begin{align*}
\text{\(^1\text{H}\) NMR (500 MHz, C}_6\text{D}_6\delta & 7.29−7.26 (m, 2H), 7.18−7.14 (m, 2H), 7.10−7.07 (m, \\
& 1H), 4.03 (q, \text{ }J = 7.0 Hz, 1H), 2.73 (bs, 1H), 2.62 (bs, 1H), 1.29 (d, \text{ }J = 7.0 Hz, \\
& 3.89 (bs, 1H), 3.53 (s, 3H), 1.50−1.44 (dddd, 1H, \text{ }J = 10.0, 10.0, 7.0, 4.0 Hz), \\
& 1.35 (dd, 1H, \text{ }J = 10.0, 6.0 Hz), 1.14 (dd, 1H, \text{ }J = 7.0, 6.0 Hz); \\
\text{\(^{19}\text{F}\) NMR (282 MHz, CDCl}_3\delta & 89.7 \\
\end{align*}
\]
Chapter 3

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$_6$D$_6$) 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 C$_{12}$H$_{16}$O$_2$ [M]$^+$: 192.1150.

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

\[
\text{HO}
\]
\[
\text{\_n\text{Pen}}\text{OH}
\]

$^1$H 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$_6$D$_6$) 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 C$_9$H$_{18}$O$_2$: C, 68.31; H, 11.47%. Found: C, 67.31; H, 11.08%; HRMS (m/z) Found: 158.1309. Calcd for C$_9$H$_{18}$O$_2$ [M]$^+$: 158.1307.

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

\[
\text{HO}
\]
\[
\text{\_\text{Acy}}\text{OH}
\]

$^1$H 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$_6$D$_6$) 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 C$_{12}$H$_{14}$O$_3$: C, 49.41; H, 4.56%. Found: C, 49.11; H, 4.50%; HRMS (m/z) Found: 206.0942. Calcd for C$_{12}$H$_{14}$O$_3$ [M]$^+$: 206.0943.

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

\[
\text{HO}
\]
\[
\text{\_\text{Br}}\text{OH}
\]

$^1$H 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,
Chapter 3

1H, 1.14 (dd, J = 6.5, 6.0 Hz); $^{13}$C NMR (125 MHz, C$_6$D$_6$) 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 C$_{10}$H$_{11}$O$_2$Br: C, 49.41; H, 4.56%. Found: C, 49.11; H, 4.50%; HRMS (m/z) Found: 241.9938. Calcd for C$_{10}$H$_{11}$O$_2$Br [M]+: 241.9942.

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

$^1$H 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$_6$D$_6$) 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$^{-1}$.

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

$^1$H 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 (nujor) 3275, 3263, 2359, 1375, 1015 cm$^{-1}$; mp 70.5–71.5 °C. Anal. Calcd for C$_{16}$H$_{30}$O$_2$: C, 75.54; H, 11.89%. Found: C, 75.37, H, 12.03%; HRMS (m/z) Found: 255.2320. Calcd for C$_{16}$H$_{31}$O$_2$ [MH]+: 255.2324.

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

(major isomer): $^1$H NMR (500 MHz, C$_6$D$_6$) 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$_6$D$_6$) δ 71.3, 59.2, 32.7, 32.0, 28.0, 24.9, 23.6, 21.5, 21.2. (minor isomer): $^1$H NMR (500 MHz, C$_6$D$_6$) δ 3.40–3.30 (m, 1H), 1.90–1.84
Chapter 3

(m, 1H), 1.79–1.73 (m, 2H), 1.70–1.61 (m, 2H), 1.59–1.51 (m, 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$_6$D$_6$) 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 C$_9$H$_{16}$O$_2$ [M]$^+$: 156.1150.

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

(major isomer): $^1$H NMR (500 MHz, C$_6$D$_6$) 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$_6$D$_6$) 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 C$_{16}$H$_{30}$O$_2$: C, 67.57; H, 9.92%. Found: C, 67.13; H, 9.92%.

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

$^1$H 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$_6$D$_6$) 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 C$_{11}$H$_{14}$O$_2$: C, 74.13; H, 7.92%. Found: C, 74.07; H, 7.90%.

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

$^1$H NMR (300 MHz, CDCl$_3$) δ 5.02 (s, 1H), 4.99 (s, 1H), 3.99 (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 C$_9$H$_{14}$O [M]$^+$: 138.1045.
4-Methyl-1-phenyl-3-penten-1-one (5a)

\[ \text{Ph} \quad \text{O} \quad \text{C} \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH} \quad \text{Ph} \]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{12}$H$_{15}$O [MH]$^+$: 175.1123.

The spectral data of the product 5a are in agreement with those published.$^{26}$

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

\[ \text{Ph} \quad \text{O} \quad \text{C} \quad \text{CH}_2 \quad \text{CH} \quad \text{C} \quad \text{Ph} \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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, 1H); $^{13}$C NMR (125 MHz, CDCl$_3$) $\delta$ 198.0, 136.5, 133.2, 131.0, 128.6, 128.3, 118.7, 43.4. HRMS (m/z) Found: 145.0648. Calcd for C$_{10}$H$_9$O [M−H]$^+$: 145.0653.

The spectral data of the product 5b are in agreement with those published.$^{26}$

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

\[ \text{Ph} \quad \text{O} \quad \text{C} \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH}_2 \quad \text{CH} \quad \text{Ph} \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{11}$H$_{12}$O [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)

\[ \text{Ph} \quad \text{O} \quad \text{C} \quad \text{CH}_2 \quad \text{CH} \quad \text{C} \quad \text{CH}_3 \]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 198.1, 139.7, 136.8, 133.1, 128.5, 128.4, 115.0, 47.7, 22.8;
The spectral data of the product \textbf{5d} are in agreement with those published.\textsuperscript{27}

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

\[ \text{Ph} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \]

\( ^1\text{H NMR (500 MHz, CDCl}_3\) \delta 7.99–7.97 (m, 2H), 7.57–7.53 (m, 1H), 7.47–7.43 (m, 2H), 5.39 (qqt, \( J = 7.0, 1.5, 1.5 \text{ Hz, 1H}\)), 3.47 (t, \( J = 1.0 \text{ Hz, 2H}\)), 1.69 (dt, \( J = 1.0, 1.0 \text{ Hz, 3H}\)), 1.64 (dtq, \( J = 7.0, 1.5, 1.5 \text{ Hz, 3H}\)); \( ^{13}\text{C NMR (125 MHz, CDCl}_3\) \delta 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 \( \text{C}_{12}\text{H}_{14}\text{O} \): C, 82.72; H, 8.10%. Found: C, 82.75; H, 8.13%; HRMS (m/z) Found: 174.1045. Calcd for \( \text{C}_{12}\text{H}_{14}\text{O} [M]^+ \): 174.1045.

\( \text{1-nonen-4-one (5f)} \)

\[ \text{\textit{P}en} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \]

\( ^1\text{H NMR (500 MHz, CDCl}_3\) \delta 5.92 (ddt, \( J = 17.0, 10.5, 7.0 \text{ Hz, 1H}\)), 5.18 (ddt, \( J = 10.0, 1.5, 1.5 \text{ Hz, 2H}\)), 5.13 (ddt, \( J = 17.0, 1.5, 1.5 \text{ Hz, 1H}\)), 3.17 (ddt, \( J = 7.0, 1.5, 1.5 \text{ Hz, 1H}\)), 2.43 (t, \( J = 7.5 \text{ Hz, 2H}\)), 1.57 (tt, \( J = 7.5, 7.5 \text{ Hz, 2H}\)), 1.33–1.24 (m, 4H), 0.88 (t, \( J = 7.0 \text{ Hz, 3H}\)); \( ^{13}\text{C NMR (125 MHz, CDCl}_3\) \delta 209.1, 130.7, 118.7, 47.7, 42.3, 31.3, 23.4, 22.4, 13.9;

The spectral data of the product \textbf{5f} are in agreement with those published.\textsuperscript{28}

\( \text{1-(4-Acetylphenyl)-3-buten-1-one (5g)} \)

\[ \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \quad \begin{array}{c}
\text{O} \\
\text{O}
\end{array} \]

\( ^1\text{H NMR (500 MHz, CDCl}_3\) \delta 8.04 (s, 4H), 6.08 (ddt, \( J = 17.0, 10.0, 7.0 \text{ Hz, 1H}\)), 5.26 (ddt, \( J = 10.0, 1.5, 1.5 \text{ Hz, 1H}\)), 5.23 (ddt, \( J = 17.0, 1.5, 1.5 \text{ Hz, 1H}\)), 3.79 (ddd, \( J = 7.0, 1.5, 1.5 \text{ Hz, 2H}\)), 2.66 (s, 3H); \( ^{13}\text{C NMR (125 MHz, C}_6\text{D}_6\) \delta 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 \( \text{C}_{12}\text{H}_{12}\text{O}_2 \): C, 76.57; H, 6.43%. Found: C, 76.31, H, 6.56%; HRMS (m/z) Found: 188.0832. Calcd for \( \text{C}_{12}\text{H}_{12}\text{O}_2 [M]^+ \): 188.0837.
(E)-3-cyclohexadecen-1-one (5j)

\[
\begin{array}{c}
\text{H} \\
\text{O} \\
\text{16}
\end{array}
\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{16}$H$_{28}$O: C, 81.29; H, 11.94%. Found: C, 81.06; H, 11.99%; HRMS (m/z) Found: 236.2136. Calcd for C$_{16}$H$_{28}$O [M]$^+$: 236.2140.

1-Cyclohexenylpropanone (5m)

\[
\begin{array}{c}
\text{H} \\
\text{O} \\
\end{array}
\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_9$H$_{14}$O [M]$^+$: 138.1045.

The spectral data of the product 5m are in agreement with those published.$^{29}$

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

\[
\begin{array}{c}
\text{O} \\
\text{Ph} \\
\end{array}
\]

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{11}$H$_{12}$O [M]$^+$: 160.0888.

The spectral data of the product 5o are in agreement with those published.$^{30}$
References and Notes


6. Crystal structure data: Monoclinic, a = 5.9500(9), b = 22.439(3), c = 17.496(3) Å, β = 90.536(3)°, V = 2335.9(6) Å³, Z = 4, \( \rho_{\text{calc}} = 1.508 \text{ Mgm}^{-3} \), \( \lambda(\text{Mo}_\lambda) = 0.71073 \text{ Å} \), \( T = 293(2) \text{ K} \), \( \theta_{\text{max}} = 54.0° \), \( R = 0.0838 \) for 5098 reflections (\( I > 2\sigma(I) \)).


9. Crystal structure data: Orthorhombic, a = 6.1690(7), b = 16.0965(17), c = 22.395(2) Å, β =
90°, $V = 2223.8(4) \, \text{Å}^3$, $Z = 9$, $\rho_{\text{calc.}} = 1.148 \, \text{Mg/m}^3$, $\lambda(\text{Mo Kα}) = 0.71073 \, \text{Å}$, $T = 293(2) \, \text{K}$, $\theta_{\text{max}} = 54.0°$, $R = 0.0640$ for 4852 reflections ($I > 2\sigma(I)$).


13. Treatment of diastereomeric mixture of 3c with 5 equiv. of TFA at room temperature for 6 h did not change the E/Z ratio. An addition of 1 equiv. of H$_2$O to this system did not also change the ratio. These experiments mean that the diastereoselectivity does not come from isomerization of the initial product.


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.
Chapter 4

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)). When the latter reaction was examined using the labeled reagent, CD₂(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”.

87
Results and Discussion

The author speculated that the reaction proceeded via a zinicate 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 zinicate $A$ may fragment into aldehyde and carbonium as $B$ through a strong electron-donating effect of the zinicate. The two fragments, aldehyde and carbonium, will form a tight pair through zinc ($C$), and yield $5a'$ via nucleophilic addition.\(^\text{11}\)

![Scheme 4](image_url)

Scheme 4. The working hypothesis of the rearrangement.

Considering the role of zinicate-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 zinicate-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 zinicate-complex such as
(RO)₂BuZnLi. The stoichiometric amount of zincate, 'Bu₃ZnLi¹², which can be prepared easily from ZnCl₂ and 'BuLi, was also effective for this rearrangement (entry 7). Treatment of the prepared lithium alkoxide of 3b with a catalytic amount of 'Bu₃ZnLi also gave 5b (entries 8 and 9).

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

<table>
<thead>
<tr>
<th>Entry</th>
<th>reagent</th>
<th>time (h)</th>
<th>yield (%)ᵇ</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>CH₂(ZnI)₂ (1.0 equiv.)</td>
<td>3</td>
<td>18</td>
</tr>
<tr>
<td>2</td>
<td>Me₂Zn (2.0 equiv.)</td>
<td>3</td>
<td>0ᶜ</td>
</tr>
<tr>
<td>3</td>
<td>BuLi (3.0 equiv.)</td>
<td>3</td>
<td>0ᶜ</td>
</tr>
<tr>
<td>4</td>
<td>BuLi (3.0 equiv.) / ZnCl₂ (1.0 equiv.)</td>
<td>3</td>
<td>88</td>
</tr>
<tr>
<td>5</td>
<td>BuLi (3.0 equiv.) / ZnCl₂ (2.0 equiv.)</td>
<td>3</td>
<td>53</td>
</tr>
<tr>
<td>6</td>
<td>BuLi (2.0 equiv.) / ZnCl₂ (1.0 equiv.)</td>
<td>3</td>
<td>0ᵈ</td>
</tr>
<tr>
<td>7</td>
<td>tBu₃ZnLi (1.0 equiv.)</td>
<td>3</td>
<td>70</td>
</tr>
<tr>
<td>8</td>
<td>BuLi (2.0 equiv.) / 'Bu₃ZnLi (0.2 equiv.)</td>
<td>6</td>
<td>88</td>
</tr>
<tr>
<td>9</td>
<td>BuLi (2.0 equiv.) / 'Bu₃ZnLi (0.1 equiv.)</td>
<td>12</td>
<td>65</td>
</tr>
</tbody>
</table>

ᵃ The substrate 3b (0.5 mmol) was used.ᵇ Yield was determined by 'H 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.
In order to determine the generality of the rearrangement, we treated various lithium alkoxides of 2-(1-hydoxyalkyl)-1-alkyclopropanol 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.\textsuperscript{11}
Table 2. Examples of the rearrangement of 3 into 5.

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>time (h)</th>
<th>yield (%)&lt;sup&gt;b&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>3&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5&lt;sup&gt;e&lt;/sup&gt;</td>
<td>24</td>
<td>89</td>
</tr>
<tr>
<td>2</td>
<td>3&lt;sup&gt;d&lt;/sup&gt;</td>
<td>5&lt;sup&gt;d&lt;/sup&gt;</td>
<td>24</td>
<td>89</td>
</tr>
<tr>
<td>3</td>
<td>3&lt;sup&gt;a&lt;/sup&gt;</td>
<td>5&lt;sup&gt;a&lt;/sup&gt;</td>
<td>24</td>
<td>78</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>dr = 3/2&lt;sup&gt;c,d&lt;/sup&gt;</td>
</tr>
<tr>
<td>4</td>
<td>3&lt;sup&gt;e&lt;/sup&gt;</td>
<td>5&lt;sup&gt;e&lt;/sup&gt;</td>
<td>24</td>
<td>98</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>dr = 2/1&lt;sup&gt;c,e&lt;/sup&gt;</td>
</tr>
<tr>
<td>5</td>
<td>3&lt;sup&gt;f&lt;/sup&gt;</td>
<td>5&lt;sup&gt;f&lt;/sup&gt;</td>
<td>24</td>
<td>86</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td>dr = 3/1&lt;sup&gt;c,f&lt;/sup&gt;</td>
</tr>
<tr>
<td>6&lt;sup&gt;g&lt;/sup&gt;</td>
<td>3&lt;sup&gt;g&lt;/sup&gt;</td>
<td>5&lt;sup&gt;g&lt;/sup&gt;</td>
<td>1</td>
<td>57&lt;sup&gt;h&lt;/sup&gt;</td>
</tr>
<tr>
<td>7&lt;sup&gt;i&lt;/sup&gt;</td>
<td>3&lt;sup&gt;h&lt;/sup&gt;</td>
<td>5&lt;sup&gt;h&lt;/sup&gt;</td>
<td>1</td>
<td>n.d.&lt;sup&gt;j&lt;/sup&gt;</td>
</tr>
</tbody>
</table>

<sup>a</sup> Substrate 3 (0.5 mmol), BuLi (1.0 mmol), Bu<sub>3</sub>ZnLi (0.1 mmol) were used. <sup>b</sup> Isolated yields. <sup>c</sup> The diastereomeric ratios were determined by <sup>1</sup>H NMR. <sup>d</sup> The stereochemistry of major product was (2S*,3R*). <sup>e</sup> The stereochemistry of major product was (2S*,3S*). <sup>f</sup> The stereochemistry of major product was (2S*,3R*). <sup>g</sup> Reaction was carried out at 47 °C. <sup>h</sup> Propiophenone was also obtained in 30% yield. <sup>i</sup> Reaction was carried out at 60 °C. <sup>j</sup> 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), the zincate-catalyzed reaction gave 14-membered diol (5i, 1-vinylcyclooctadecan-1,2-diol) (Scheme 6). The stereochemistry of the major product is (IR*,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 'Bu₂ZnLi 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. 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).
Chapter 4

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 \((JR,2R)-3b\) 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. The zinc alkoxide, \((1R,2R)-3b'\), is converted into \(\beta\)-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, \((1S,2S)-3b'\).

![Scheme 11. Proposed mechanism of isomerization of 3b' under the reaction condition.](image)

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. 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), \(^7\)BuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C. The mixture was heated to reflux. Then saturated aqueous solution of NH\(_4\)Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na\(_2\)SO\(_4\). The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding \textit{vic}-diol 5.

General procedure of the rearrangement (method B): \(^7\)Bu\(_3\)ZnLi was prepared by liberated procedure.\(^{13a}\) To a solution of 2-(1-hydroxyalkyl)-1-alkylcyclopropanol (3, 1.0 mmol) in THF (8 mL), \(^7\)BuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C, and stirred for 10 min. To the solution, the prepared \(^7\)Bu\(_3\)ZnLi (THF solution, 0.2 mmol) was added at 0 °C. The mixture was heated to reflux. Then saturated aqueous solution of NH\(_4\)Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na\(_2\)SO\(_4\). The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding \textit{vic}-diol 5.

The rearrangement using the labeled reagent, CD\(_2\)(ZnI)\(_2\): To a solution of 2a (1.0 mmol) in THF (4 mL), CD\(_2\)(ZnI)\(_2\) (I’, 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 NH\(_4\)Cl was added to quench the reaction and
extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na$_2$SO$_4$. 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):** To a solution of 3i (1.0 mmol) in CH$_2$Cl$_2$ (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 NH$_4$Cl was added to quench the reaction and the saturated aqueous solution of NaHCO$_3$ was added to neutralize. Then the organic layer was extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na$_2$SO$_4$. 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 Dimrotho 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), iBuLi (1.6 M in pentane, 3.0 mmol) was added at 0 °C, and stirred for 10 min. To the solution, the prepared iBu$_3$ZnLi (THF solution, 0.2 mmol) was added at 0 °C. The mixture was heated to reflux. The ReactIR™ 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.
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 \((\text{IR,2R})\)-3b and (S)-5b during the reaction

**Procedure for tracking of ee of \((\text{IR,2R})\)-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), \(^t\)BuLi (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 NH\(_4\)Cl, and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na\(_2\)SO\(_4\). 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 \((\text{IR,2R})\)-3b was determined by \(^1\)HNMR after converting into the corresponding (S)-(−)-\(\alpha\)-methoxy-\(\alpha\)-(trifluoromethyl)phenylacetate. To the solution of 3b (0.1 mmol), dichloromethane (0.5 mL) and pyridine (0.24 mmol), (R)-(+)\(-\alpha\)-methoxy-\(\alpha\)-(trifluoromethyl)phenylacetyl chloride (0.12 mmol) was added at 0 °C and stirred for 1 h. Then the solution was poured into sat. Na\(_2\)CO\(_3\)aq, and the organic layer was extracted with dichloromethane. The combined organic layers were dried over Na\(_2\)SO\(_4\). The solvent was removed under reduced pressure, and the residue was purified with silica gel column chromatography to give the corresponding (S)-\(\alpha\)-methoxy-\(\alpha\)-(trifluoromethyl)phenylacetate. The enantiomeric excess of the product was determined by \(^1\)H NMR focused on cyclopropyl carbinol group (the chemical shift at 4.67 ppm corresponds to \((\text{IR,2R})\)-isomer and that at 4.66 ppm, \((\text{IS,2S})\)-isomer).

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)) \(\delta\) 89.7 (s)

Meanwhile, the enantiomeric purity of (S)-5b was determined by \(^1\)H 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, 0.66H), 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

(IR*,2R*)-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, 2934, 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)

\[ \text{Ph} \quad \text{OH} \quad \text{OH} \]

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 7.52–7.23 (m, 5H), 6.34 (dd, $J = 17.1, 10.5$ Hz), 6.27 (dd, $J = 17.1, 10.5$ Hz), 5.47 (dd, $J = 17.1, 1.5$ Hz), 5.46 (dd, $J = 17.1, 1.5$ Hz), 5.30 (dd, $J = 10.5, 1.5$ Hz), 5.29 (dd, $J = 10.5, 1.5$ Hz), 4.14 (q, $J = 6.3$ Hz), 4.10 (q, $J = 6.3$ Hz), 1.18 (d, $J = 6.3$ Hz), 0.97 (d, $J = 6.3$ Hz); $^{13}$C NMR (75 MHz, CDCl$_3$) $\delta$ 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 C$_{11}$H$_{14}$O$_2$: C, 74.13; H, 7.92%. Found: C, 73.84; H, 8.03%; HRMS (m/z) Found: 178.0993. Calcd for C$_{11}$H$_{14}$O$_2$ [M]$^+$: 178.0994.

To confirm the stereochemistry of the rearranged product 5a, we synthesized an authentic sample of (2S*,3R*)-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, CH$_2$Cl$_2$; (b) vinylmagnesium bromide, THF; (c) TBAF, THF.

The ORTEP figure of the authentic sample was shown in Figure 5. Compared with $^1$H NMR spectrum of the authentic (2S*,3R*)-5a, it was found that the major isomer of the rearranged product 5a was (2S*,3S*)-isomer.
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 MoKα radiation. Crystal data: $M = 178.22$, Orthorhombic, Pbcn, $a = 25.693(7), b = 7.699(2), c = 10.478(3) \text{ Å}$, $\beta= 90^\circ$, $V = 2072.6(10) \text{ Å}^3$, $Z = 9$, $\rho_{\text{calc}} = 1.285 \text{ Mg/m}^3$, $\lambda(\text{MoKα}) = 0.71073 \text{ Å}$, $T = 293(2) \text{ K}$, $2\theta_{\text{max}} = 54.0^\circ$, $R = 0.1075$ for 2276 reflections ($I > 2\sigma(I)$).

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

$\begin{align*}
\text{D}_2\text{C} & \equiv \text{OH} \\
\text{Ph} & \text{OH}
\end{align*}$

$^1\text{H NMR (300 MHz, CDCl}_3\text{)} \delta 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)

$\begin{align*}
\equiv & \text{OH} \\
\text{Ph} & \text{OH}
\end{align*}$

$^1\text{H NMR (300 MHz, CDCl}_3\text{)} \delta 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); $^{13}\text{C NMR (75 MHz, CDCl}_3\text{)} \delta 142.7, 140.8, 128.7, 127.7, 125.9, 115.8, 77.8, 69.8$. HRMS (m/z) Found:164.0833. Caled for C$_{10}$H$_{12}$O$_2$ [M]$^+$ :164.0837.

The spectral data are in agreement with those published.$^{21}$
1,2-Dihydroxy-3-methyl-2-phenyl-3-butene (5c)

\[
\begin{align*}
\text{H NMR (300 MHz, CDCl}_3) & \quad \delta 7.47–7.25 \text{ (m, 5H)}, 5.16 \text{ (dq, 1H, } J = 0.9, 0.9 \text{ Hz),} \\
& \quad 5.08 \text{ (dq, 1H, } J = 1.2, 0.9 \text{ Hz),} 4.05 \text{ (d, 1H, } J = 11.1 \text{ Hz),} 3.89 \text{ (d, 1H, } J = 11.1 \text{ Hz),} \\
& \quad 1.64 \text{ (dd, 3H, } J = 1.2, 0.9 \text{ Hz);} \\
\text{13C NMR (75 MHz, CDCl}_3) & \quad \delta 147.1, 142.2, 128.6, 127.8, 126.0, \\
& \quad 112.2, 79.5, 68.4, 19.8; \text{ IR (neat) 3278, 1448, 1191, 1066, 1035 cm}^{-1}; \text{ mp 30.0–30.5 °C.}
\end{align*}
\]

Anal. Calcd for C\text{11}H\text{14}O\text{2}: C, 74.13; H, 7.92%. Found: C, 74.41; H, 7.94%; HRMS (m/z) Found: \text{178.0993. Calcd for C}\text{11}H\text{14}O\text{2}[\text{M}^+]\text{:178.0994.}

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

\[
\begin{align*}
\text{H NMR (300 MHz, CDCl}_3) & \quad \delta 5.80 \text{ (ddd, 1H, } J = 17.4, 10.8, 0.6 \text{ Hz),} \\
& \quad 5.34 \text{ (ddd, 1H, } J = 17.4, 1.5, 0.6 \text{ Hz),} 5.25 \text{ (ddd, 1H, } J = 10.8, 1.5, 0.6 \text{ Hz),} 3.49 \text{ (s, 2H),} \\
& \quad 2.28 \text{ (bs, 1H),} 1.97 \text{ (bs, 1H),} 1.58–1.42 \text{ (m, 2H),} 1.36–1.24 \text{ (m, 6H),} 0.87 \text{ (t, 3H, } J = 6.6 \text{ Hz);} \\
\text{13C NMR (125 MHz, CDCl}_3) & \quad \delta 140.8, 115.0, 76.0, 68.7, 37.0, 32.2, 22.8, 22.5, 14.0; \text{ IR (neat) 3382,} \\
& \quad 2933, 2359, 1460, 1379, 1060 \text{ cm}^{-1}. \text{ Anal. Calcd for C}\text{9}H\text{18}O\text{2}: C, 68.31; H, 11.47%. \text{ Found: C,} \\
& \quad 68.04; H, 11.54%; \text{ HRMS (m/z) Found: 157.1233. Calcd for C}\text{9}H\text{17}O\text{2}[\text{M–H}^+]\text{:157.1229.}
\end{align*}
\]

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

\[
\begin{align*}
\text{H NMR (500 MHz, CDCl}_3) & \quad \delta 7.57–7.20 \text{ (m, 5H),} 5.28 \text{ (dq, 0.72H, } J = 1.0, 1.0 \text{ Hz),} \\
& \quad 5.24 \text{ (dq, 0.28H, } J = 1.0, 1.0 \text{ Hz),} 5.07 \text{ (dq, 0.28H, } J = 1.5, 1.0 \text{ Hz),} 4.89 \text{ (dq,} \\
& \quad 0.72H, J = 1.5, 1.0 \text{ Hz),} 4.61 \text{ (q, 0.72H, } J = 6.0 \text{ Hz),} 4.49 \text{ (q, 0.28H, } J = 6.0 \text{ Hz),} \\
& \quad 1.65 \text{ (dd, 0.84H, } J = 1.5, 1.0 \text{ Hz),} 1.56 \text{ (dd, 2.16H, } J = 1.5, 1.0 \text{ Hz),} 1.24 \text{ (d, 2.16H, } J = 6.0 \text{ Hz),} \\
& \quad 0.93 \text{ (d, 0.84H, } J = 6.0 \text{ Hz);} \\
\text{13C NMR (125 MHz, CDCl}_3) & \quad \delta 149.1, 146.5, 143.7, 141.4, 128.3, \\
& \quad 127.9, 127.2, 126.9, 126.1, 125.3, 110.8, 110.7, 80.9, 80.8, 70.0, 69.2, 19.4, 19.3, 16.5, 16.4; \text{ IR} \\
& \quad \text{ (neat) 3458 cm}^{-1}. \text{ Anal. Calcd for C}\text{9}H\text{18}O\text{2}: C, 74.97; H, 8.39%. \text{ Found: C,} \\
& \quad 74.91; H, 8.56%.
\end{align*}
\]

To confirm the stereochemistry of the rearranged product 5e, we synthesized an authentic sample
of (2R*,3S*)-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.](image)

Compared with ¹H NMR spectrum of the authentic (2R*,3S*)-5e, it was found that the major isomer of the rearranged product 5e was (2S*,3S*)-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 (2R*,3R*)-5f as shown in Scheme 14. Nucleophilic addition of vinylmagnesium bromide to the α-siloxyketone afforded a single isomer because of the chelation control.
2,3-Dihydroxy-2-methyl-3-phenyl-4-pentene (5g)

\[ \text{Ph} \] \[ \text{OH} \] \[ \text{OH} \] 

\(^1\text{H NMR} (300 \text{ MHz, CDCl}_3) \delta 7.57–7.53 (m, 2H), 7.37–7.23 (m, 3H), 6.74 (dd, \( J = 17.1, 10.8 \text{ Hz}, 1\text{H} \)), 5.47 (dd, \( J = 17.1, 1.5 \text{ Hz}, 1\text{H} \)), 5.34 (dd, \( J = 10.8, 1.5 \text{ Hz}, 1\text{H} \)), 1.27 (d, \( J = 0.3 \text{ Hz}, 3\text{H} \)), 1.10 (d, \( J = 0.3 \text{ Hz}, 3\text{H} \)); \(^{13}\text{C NMR} (75 \text{ MHz, CDCl}_3) \delta 142.7, 140.5, 128.0, 127.4, 127.3, 115.8, 80.9, 75.9, 25.8, 25.0; \) IR (neat) 3462, 3326, 1446, 1360, 1161, 1008 cm\(^{-1}\); mp 45.3–46.0 °C. Anal. Calcd for C\(_{12}\)H\(_{16}\)O\(_2\): C, 74.97; H, 8.39%. Found: C, 74.70; H, 8.38%.

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

\[ \text{Ph} \] \[ \text{OH} \] \[ \text{OH} \] 

\(^1\text{H NMR} (500 \text{ MHz, CDCl}_3) \delta 5.92 (dd, 1\text{H}, \( J = 17.5, 10.5 \text{ Hz} \)), 5.37 (dd, 1\text{H}, \( J = 17.5, 1.5 \text{ Hz} \)), 5.23 (dd, 1\text{H}, \( J = 10.5, 1.5 \text{ Hz} \)), 3.72 (d, 1\text{H}, \( J = 10.0 \text{ Hz} \)), 1.71–1.04 (m, 24H); \(^{13}\text{C NMR} (125 \text{ MHz, CDCl}_3) \delta 140.5, 115.0, 77.5, 74.4, 36.9, 28.6, 26.43, 26.35, 25.8, 24.5, 23.7, 23.6, 23.5, 23.4, 19.2; \) IR (neat) 3325, 2922, 2359, 1456, 1377, 1043 cm\(^{-1}\); mp 107.5–108.5 °C. Anal. Calcd for C\(_{16}\)H\(_{30}\)O\(_2\): C, 75.54; H, 11.89%. Found: C, 75.26; H, 11.98%; HRMS (m/z) Found: 254.2247. Calcd for C\(_{16}\)H\(_{30}\)O\(_2\) [M]^+: 254.2246.

To confirm the stereochemistry of the rearranged product 5f, we synthesized an authentic sample
of \((IR^*, 2R^*)\)-1,2-dihydroxy-1-vinylcyclopentadecane as shown in Scheme 15. Nucleophilic addition of vinylmagnesium bromide to the \(\alpha\)-siloxylketone 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\(_2\)Cl\(_2\); (b) vinylmagnesium bromide, THF; (c) TBAF, THF.

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

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

**major isomer (syn):** \(^1\)H NMR (500 MHz, C\(_6\)D\(_6\)) \(\delta\) 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\(_6\)D\(_6\)) \(\delta\) 151.7, 108.9, 76.0, 74.5, 32.7, 30.3, 24.1, 22.5; IR (nujol) 3307, 2363, 1456, 1377, 1108, 1057 cm\(^{-1}\); mp 64.8–66.0 °C. Anal. Calcd for C\(_8\)H\(_{14}\)O\(_2\): C, 67.57; H, 9.92%. Found: C, 67.32; H, 9.64%; HRMS (m/z) Found: 142.0994. Calcd for C\(_8\)H\(_{14}\)O\(_2\) [M\(^+\)]: 142.0994.

**minor isomer (anti):** \(^1\)H NMR (500 MHz, C\(_6\)D\(_6\)) \(\delta\) 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\(_3\)) \(\delta\) 152.9, 107.4, 77.8, 77.4, 33.1, 31.5, 24.6, 20.0; HRMS (m/z) Found: 142.0994. Calcd for C\(_8\)H\(_{14}\)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, \( \beta = 102.343(4)^\circ \), \( V = 3235.5(11) \) Å\(^3\), \( Z = 8 \), \( \rho_{\text{calc}} = 1.381 \) Mg/m\(^3\), \( \lambda (\text{Mo}\kappa\alpha) = 0.71073 \) Å, \( T = 296 \) K, \( 2\theta_{\text{max}} = 54.0^\circ \), \( R = 0.0569 \) for 7050 reflections \( (I > 2\sigma(I)) \)

**(IR*,2R*)-2-Methoxymethyl-1-phenycyclopropanol (6)**

\[
\begin{align*}
\text{Ph} & \quad \overset{\text{HO}}{\text{OMe}} \\
\end{align*}
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \( \delta \) 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-methycyclopropanol (11)**

\[
\begin{align*}
\text{Ph} & \quad \overset{\text{HO}}{\text{NHTs}} \\
\end{align*}
\]

\(^1\)H NMR (300 MHz, C\(_6\)D\(_6\)) \( \delta \) 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-\textit{p}-toluenesulfonamino-3-butene (12)

\[
\begin{align*}
&\text{HNHS} \quad \text{Ph} \quad \text{CH}_2\text{CH} = \text{CH}_2
\end{align*}
\]

\( ^1\text{H NMR} (500 \text{ MHz, C}_6\text{D}_6) \delta 7.51–7.49 \text{ (m, 2H)}, 6.85–6.79 \text{ (m, 3H)}, 6.72–6.70 \text{ (m, 2H)}, 6.54–6.53 \text{ (m, 2H)}, 5.46 \text{ (dd, 1H, } J = 17.5, 11.0 \text{ Hz)}, 5.39 \text{ (d, 1H, } J = 8.5 \text{ Hz)}, 5.00 \text{ (dd, 1H, } J = 17.5, 1.5 \text{ Hz)}, 4.78 \text{ (dd, 1H, } J = 11.0, 1.5 \text{ Hz)}, 4.36 \text{ (d, 1H, } J = 8.5 \text{ Hz)}, 1.78 \text{ (s, 3H)}, 1.17 \text{ (s, 3H)}, 0.45 \text{ (s, 1H)}; ^{13}\text{C NMR (125 MHz, C}_6\text{D}_6) \delta 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; \text{IR (nujol) 3480, 3245, 1377, 1318, 1158, 1089 cm}^{-1}; \text{mp 98.7–99.5 °C. Anal. Calcd for C}_{18}\text{H}_{21}\text{NO}_3\text{S: C, 65.23%; H, 6.39%. Found: C, 65.27; H, 6.42%; HRMS (m/z) Found: 332.1320. Calcd for C}_{18}\text{H}_{22}\text{NO}_3\text{S [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 \(\alpha\)-aminoketone proceeded via the chelation control, and \((2R^*,3R^*)\)-isomer was obtained.

\[
\begin{align*}
\text{Ph} \quad \text{NHTs} & \quad \text{O} \quad \text{vinylmagnesium bromide} \quad \text{THF, 0 °C, 0.5 h} \quad \text{Ph} \quad \text{NHTs} \quad \text{OH}
\end{align*}
\]

\textbf{Scheme 16. Synthesis of an authentic sample of 12.}

Compared with \(^1\text{H NMR} \text{ spectrum of the authentic (2R^*,3R^*)-12, it was found that the obtained product 12 was (2R^*,3R^*)-isomer as a single diastereomer.}
References and Notes


11. Still and Macdonald have been reported that α-alkoxyallyl carbanion undergoes preferential protonation and alkylation at the unsubstituted terminus and reaction with carbonyl compounds at the alkoxy-substituted terminus. See, W. C. Still, T. L. Macdonald, J. Org. Chem. 1976, 41, 3620.


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.


18. Although we tried to trap D or E with allyl bromide and methyl iodide, the corresponding β-allylated ketone and β-methylated ketone was not obtained.

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)’Bu₂). 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,


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 homoenoolate, 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. 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 $\text{S}_2\text{N}_2$ 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 $\text{S}_2\text{N}_2$ reaction does not proceed. However, in cases of intramolecular reactions, an $\text{S}_2\text{N}_2$ 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. 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 ($1$), which possesses a couple of carbon–zinc bonds on a carbon atom, to a carbonyl group of a ketone carrying an enantiomer enriched stereogenic center containing a leaving group at $\alpha$-position, such as $\alpha,\beta$-epoxy ketone or $\alpha$-sulfonyloxy ketone.

The author have already reported an efficient route for cyclopropane ring formation by a sequential nucleophilic reaction of bis(iodozincio)methane ($1$): As shown in Scheme 1, when $\alpha,\beta$-epoxy ketone or $\alpha$-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 $\text{S}_2\text{N}_2$ 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 by a ring opening. Treatment of an electrophile with the homoenolate would afford an optically active α-tertiary or -quaternary ketone 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 bisthiozincio)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 bisthiozincio)methane (1). a

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

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 ³H 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 NH₄Cl, 1-phenyl-1-trimethylsiloxyxycyclopropane (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 SN2 reaction of the existing iodozinciomethyl group to the adjacent stereogenic center that has a tosyloxy group will proceed in stereospecific SN2 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. 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.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>product</th>
<th>t (h)</th>
<th>yield (%)(^b)</th>
<th>d.r.(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph(\text{O})(\text{OtS}) 7a</td>
<td>Ph(\text{HO}) (11a)</td>
<td>2</td>
<td>56(^d)</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>(\text{Oct} \text{yl})(\text{O})(\text{OtS}) 7b</td>
<td>(\text{Oct} \text{yl})(\text{HO}) (11b)</td>
<td>15</td>
<td>31(^e)</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(\text{Furyl})(\text{O})(\text{OtS}) 7c</td>
<td>(\text{Furyl})(\text{HO}) (11c)</td>
<td>12</td>
<td>38(^f)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>(\text{F}_{3}\text{C} \text{Ph} \text{O} \text{OtS}) 7d</td>
<td>(\text{F}_{3}\text{C} \text{Ph} \text{HO}) (11d)</td>
<td>2</td>
<td>95</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>(\text{Ph} \text{O} \text{OtS}) Me 7e</td>
<td>(\text{Ph} \text{HO}) Me (11e)</td>
<td>10</td>
<td>86</td>
<td>76/24(^g)</td>
</tr>
<tr>
<td>6</td>
<td>(\text{Naphthyl} \text{O} \text{OtS}) Me 7f</td>
<td>(\text{Naphthyl} \text{HO}) Me (11f)</td>
<td>15</td>
<td>99</td>
<td>67/33(^g)</td>
</tr>
<tr>
<td>7</td>
<td>(\text{MeO} \text{Ph} \text{O} \text{OtS}) Me 7g</td>
<td>(\text{MeO} \text{Ph} \text{HO}) Me (11g)</td>
<td>20</td>
<td>81</td>
<td>67/33(^g)</td>
</tr>
<tr>
<td>8</td>
<td>(\text{F}_{3}\text{C} \text{MeO} \text{O} \text{OtS}) Me 7h</td>
<td>(\text{F}_{3}\text{C} \text{MeO} \text{HO}) Me (11h)</td>
<td>4</td>
<td>88</td>
<td>72/28(^g)</td>
</tr>
</tbody>
</table>

\(^a\) 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 \(^1\text{H}\) 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). 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. 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) 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 (t2) 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.$^a$

\[
\begin{array}{cccccc}
\text{entry} & \text{substrate} & \text{Product} & t^1 (h) & t^2 (h) & \text{yield (%)$^b$} \\
1 & \text{Ph} & \text{15a} & 4 & 4 & 85 \\
2 & \text{nOctyl} & \text{15b} & 24 & 3 & 84 \\
3 & \text{F} & \text{15c} & 15 & 6 & 79 \\
4 & \text{F} & \text{15d} & 3 & 5 & 88 \\
5 & \text{Me} & \text{15e} & 4 & 4 & 76 \\
6 & \text{Me} & \text{15f} & 18 & 20 & 78 \\
7 & \text{MeO} & \text{15g} & 24 & 12 & 55 \\
\end{array}
\]
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, 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. 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 CuCN•2LiCl 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.](image)

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 CuCN•2LiCl (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

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>$E^1^+$</th>
<th>product</th>
<th>Yield (%)^b</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Ph(\text{O})</td>
<td>(\text{CH}_2\text{Br})</td>
<td>Ph(\text{H})(\text{OH})(\text{CH})(\text{Br})</td>
<td>69</td>
</tr>
<tr>
<td>2(^c)</td>
<td>Ph(\text{O}) Me(\text{O})</td>
<td>(\text{CH}_2\text{Br})</td>
<td>Ph(\text{Me})(\text{H})(\text{OH})(\text{CH})(\text{Br})</td>
<td>52</td>
</tr>
<tr>
<td>3(^c)</td>
<td>(\text{nBu})(\text{O}) Me(\text{O})</td>
<td>(\text{CH}_2\text{Br})</td>
<td>(\text{nBu})(\text{Me})(\text{H})(\text{OH})(\text{CH})(\text{Br})</td>
<td>27</td>
</tr>
</tbody>
</table>
An α,β-epoxy ketone 19 (1.0 mmol), the dizinc 1 (1.2 mmol, 0.5 M in THF), CuCN•2LiCl (2.4 mmol, 1 M in THF), electrophile (2.4 mmol), and THF (4 mL) were used. Isolated yields. The reaction of allyl bromide with the prepared homoenolate 20 were carried out at 40 °C.
An optically active $\alpha,\beta$-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 $\alpha$-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 $\alpha$-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.\textsuperscript{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 CuCN•2LiCl 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 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 NH$_4$Cl was added to quench the reaction and extracted with ethyl acetate. The combined organic layers were washed with brine, and dried over Na$_2$SO$_4$. 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 Na$_2$SO$_4$. 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, 7b, 7c, 7e, 10, 12, 19a, 19b, 19c, 19d, and 19e were found in
Chapter 5

the literature.

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

\[
\begin{align*}
\text{F}_3\text{C} & \quad \text{O} \quad \text{OTs} \\
& \quad \text{H} \quad \text{NMR (500 MHz, CDCl}_3\text{)} \: \delta \, 7.95 \, (d, \, J = 8.1 \, \text{Hz}, \, 2\text{H}), \, 7.83 \, (d, \, J = 8.1 \, \text{Hz}, \, 2\text{H}), \, 7.73 \, (d, \, J = 8.4 \, \text{Hz}, \, 2\text{H}), \, 7.35 \, (d, \, J = 8.4 \, \text{Hz}, \, 2\text{H}), \, 5.24 \, (s, \, 2\text{H}), \, 2.45 \, (s, \, 3\text{H}); \quad ^{13}\text{C} \text{ NMR (125 MHz, CDCl}_3\text{)}: \, \delta \, 190.0, \, 145.5, \, 136.5, \, 135.3 \\
& \quad \text{q,} \, J = 33.0 \, \text{Hz}, \, 132.5, \, 129.9, \, 128.5, \, 128.1, \, 125.9 (q, \, J = 3.9 \, \text{Hz}), \, 123.3 (q, \, J = 271.5 \, \text{Hz}), \, 69.9, \, 21.6; \, ^{19}\text{F} \text{ NMR (282 MHz, CDCl}_3\text{)} \: \delta \, 97.84; \quad \text{IR (nujor)} \, 1709, \, 1364, \, 1327, \, 1175, \, 1130, \, 1057, \, 966, \, 910, \, 739 \, \text{cm}^{-1}, \, \text{mp 117.5–118.0 °C.} \quad \text{Anal. Calcd for } \text{C}_{16}\text{H}_{13}\text{O}_{4}\text{F}_{3}\text{S}: \, \text{C, 53.63; H, 3.66%.} \quad \text{Found: C, 53.56; H, 3.80%; HRMS (m/z) Found: 358.0490. Calcd for } \text{C}_{16}\text{H}_{13}\text{O}_{4}\text{F}_{3}\text{S [M] }^+: \, 358.0487.
\end{align*}
\]

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

\[
\begin{align*}
\text{Me} & \quad \text{O} \quad \text{OTs} \\
& \quad \text{H} \quad \text{NMR (300 MHz, CDCl}_3\text{)} \: \delta \, 8.40 \, (s, \, 1\text{H}), \, 7.96–7.86 \, (m, \, 4\text{H}), \, 7.75 \, (d, \, J = 8.4 \, \text{Hz}, \, 2\text{H}), \, 7.66–7.55 \, (m, \, 2\text{H}), \, 7.20 \, (d, \, J = 7.8 \, \text{Hz}, \, 2\text{H}), \, 5.94 \, (q, \, J = 6.9 \, \text{Hz}, \, 1\text{H}), \, 2.35 \, (s, \, 3\text{H}), \, 1.67 \, (d, \, J = 6.9 \, \text{Hz}, \, 3\text{H}); \quad ^{13}\text{C} \text{ NMR (125 MHz, CDCl}_3\text{)}: \, \delta \, 194.7, \, 145.0, \, 135.8, \, 133.5 \, (\text{co-incident}), \, 132.3, \, 131.0, \, 130.7, \, 129.7, \, 129.9, \, 129.0, \, 128.7, \, 127.9, \, 127.8, \, 124.0, \, 77.4, \, 21.5, \, 18.9; \quad \text{IR (nujor) 1694, 1626, 1597, 1470, 1362, 1190, 1177, 1071, 1017, 920, 816 cm}^{-1}, \, \text{mp 98.2–98.6 °C.} \quad \text{Anal. Calcd for } \text{C}_{20}\text{H}_{18}\text{O}_{4}\text{S}: \, \text{C, 67.78; H, 5.12%.} \quad \text{Found: C, 67.81; H, 5.30%; HRMS (m/z) Found: 354.0920. Calcd for } \text{C}_{20}\text{H}_{18}\text{O}_{4}\text{S [M] }^+: \, 354.0926.
\end{align*}
\]

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

\[
\begin{align*}
\text{MeO} & \quad \text{O} \quad \text{OTs} \\
& \quad \text{H} \quad \text{NMR (300 MHz, CDCl}_3\text{)} \: \delta \, 7.88 \, (d, \, J = 9.0 \, \text{Hz}, \, 2\text{H}), \, 7.75 \, (d, \, J = 8.4 \, \text{Hz}, \, 2\text{H}), \, 7.26 \, (d, \, J = 8.4 \, \text{Hz}, \, 2\text{H}), \, 6.92 \, (d, \, J = 9.0 \, \text{Hz}, \, 2\text{H}), \, 5.73 \, (q, \, J = 6.9 \, \text{Hz}, \, 1\text{H}), \, 3.87 \, (s, \, 3\text{H}), \, 2.40 \, (s, \, 3\text{H}), \, 1.57 \, (d, \, J = 6.9 \, \text{Hz}, \, 3\text{H}); \quad ^{13}\text{C} \text{ NMR (125 MHz, CDCl}_3\text{)}: \, \delta \, 193.0, \, 164.1, \, 144.9, \, 133.6, \, 131.2, \, 129.7, \, 127.9, \, 126.5, \, 114.0, \, 77.3, \, 55.5, \, 21.6, \, 18.8; \quad \text{IR (nujor) 1694, 1601, 1514, 1354, 1267, 1234, 1177, 1030, 1009, 928, 843, 820,}
\end{align*}
\]
735 cm\(^{-1}\), mp 87.0–87.5 °C. Anal. Calcd for C\(_{17}H_{18}O_5\)S: C, 61.06; H, 5.43%. Found: C, 61.00; H, 5.44%; HRMS (m/z) Found: 334.0875. Calcd for C\(_{17}H_{18}O_5S\) [M]\(^+\): 334.0875.

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

\(\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 8.00 (d, J = 8.4 \text{ Hz, 2H}, 7.73 (d, J = 8.1 \text{ Hz, 2H}), 7.71 (d, J = 8.1 \text{ Hz, 2H}), 7.27 (d, J = 8.4 \text{ Hz, 2H}), 5.71 (q, J = 6.9 \text{ Hz, 1H}), 2.42 (s, 3H), 1.61 (d, J = 6.9 \text{ Hz, 3H}); \text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 194.4, 145.3, 136.6, 134.9 (q, J = 32.4 \text{ Hz}), 133.3, 129.8, 129.2, 127.9, 125.7 (q, J = 3.75 \text{ Hz}), 123.4 (q, J = 271.5 \text{ Hz}), 77.6, 21.6, 18.4; \text{F NMR (282MHz, CDCl}_3\text{)} \delta 97.84; \text{IR (nujol) 1703, 1597, 1360, 1323, 1176, 1142, 1067, 1011, 924, 665 cm}^{-1}, \text{mp 92.5–93.0 °C. Anal. Calcd for C}_{17}H_{15}O_4F_3S: C, 54.83; H, 4.06%. Found: C, 54.86; H, 4.16%; HRMS (m/z) Found: 372.0641. Calcd for C\(_{17}H_{15}O_4F_3S\) [M]\(^+\): 372.0643.

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

\(\text{H NMR (300 MHz, CDCl}_3\text{)} \delta 8.03 (d, J = 8.4 \text{ Hz, 2H}, 7.93 (d, J = 8.4 \text{ Hz, 2H}), 7.85 (d, J = 8.4 \text{ Hz, 2H}), 7.36 (d, J = 8.4 \text{ Hz, 2H}), 5.25 (s, 2H), 2.65 (s, 3H), 2.46 (s, 3H); \text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 197.1, 190.2, 145.5, 140.9, 136.9, 132.6, 130.0, 128.7, 128.4, 128.2, 70.0, 26.8, 21.7; \text{IR (nujol) 1717, 1690, 1362, 1263, 1179, 968, 910, 735 cm}^{-1}, \text{mp 116.0–117.0 °C. HRMS (m/z) Found: 332.0722. Calcd for C}_{17}H_{16}O_5S\) [M]\(^+\): 332.0718.

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

\(\text{H NMR (300 MHz, CDCl}_3\text{)} \delta 8.12 (d, J = 8.1 \text{ Hz, 2H}, 7.89 (d, J = 8.1 \text{ Hz, 2H}), 7.84 (d, J = 8.1 \text{ Hz, 2H}), 7.35 (d, J = 8.1 \text{ Hz, 2H}), 5.26 (s, 2H), 3.96 (s, 3H), 2.45 (s, 3H); \text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 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; \text{IR (nujol) 1720, 1715, 1373, 1283, 1179, 1111, 1065, 968, 910, 733 cm}^{-1}, \text{mp 109.5–110.2 °C. Anal. Calcd for}
C\textsubscript{17}H\textsubscript{16}O\textsubscript{6}S: C, 58.61%; H, 4.63%. Found: C, 58.48%; H, 4.68%; HRMS (m/z) Found: 348.0673. Calcd for C\textsubscript{17}H\textsubscript{16}O\textsubscript{6}S [M]+: 348.0668.

1-phenylcyclopropanol (11a)

\[
\begin{align*}
\text{\textit{H}} \text{NMR (500 MHz, CDCl}_3\text{)} \delta &\ 7.36-7.30 \text{ (m, 4H), 7.25-7.21 \text{ (m, 1H)}, 2.17 \text{ (bs, 1H)}, \\
&\ 1.27 \text{ (ddd, } J = 7.5, 5.5, 0.5 \text{ Hz, 2H}), 1.05 \text{ (ddd, } J = 7.5, 5.5, 0.5 \text{ Hz, 2H}); \text{ } \textit{C} \text{ NMR} \text{ (125 MHz, CDCl}_3\text{)} \delta 144.2, 128.3, 126.4, 124.4, 56.6, 17.9.
\end{align*}
\]

The spectral data of the product 11a are in agreement with those published.\textsuperscript{21}

1-octylcyclopropanol (11b)

\[
\begin{align*}
\text{\textit{H}} \text{NMR (500 MHz, CDCl}_3\text{)} \delta &\ 1.77 \text{ (bs, 1H), 1.56-1.27 \text{ (m, 14H), 0.88 \text{ (t, } J = 6.5 \text{ Hz, 3H), 0.72 \text{ (dd, } J = 7.0, 5.5 \text{ Hz, 2H), 0.43 \text{ (dd, } J = 7.0, 5.5 \text{ Hz, 2H}); } \textit{C} \text{ NMR} \text{ (125 MHz, CDCl}_3\text{)} \delta 55.9, 38.3, 31.9, 29.7, 29.6, 29.3, 25.9, 22.7, 14.1, 13.5; \text{ IR (neat) 3321, 2926, 1466, 1377, 1258, 1101, 1007 cm}^{-1}. \text{ Anal. Calcd for C}_{11}H_{22}O: C, 77.58; H, 13.02%. Found: C, 77.69; H, 13.01%; HRMS (m/z) Found: 170.1665. Calcd for C_{11}H_{22}O [M+]\textsuperscript{+}: 170.1671.
\end{align*}
\]

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

\[
\begin{align*}
\text{\textit{H}} \text{NMR (500 MHz, CDCl}_3\text{)} \delta &\ 7.32 \text{ (dd, } J = 2.0, 1.0 \text{ Hz, 1H), 6.32 \text{ (dd, } J = 3.5, 2.0 \text{ Hz, 1H), 6.22 \text{ (dd, } J = 3.5, 1.0 \text{ Hz, 1H), 1.18-1.15 \text{ (m, 2H), 1.09-1.06 \text{ (m, 2H); } } \textit{C} \text{ NMR} \text{ (125 MHz, CDCl}_3\text{)} \delta 156.5, 141.4, 110.3, 104.7, 52.3, 15.2. \end{align*}
\]

The spectral data of the product 11c are in agreement with those published.\textsuperscript{22}

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

\[
\begin{align*}
\text{\textit{H}} \text{NMR (500 MHz, CDCl}_3\text{)} \delta &\ 7.56 \text{ (d, } J = 8.0 \text{ Hz, 2H), 7.36 \text{ (d, } J = 8.0 \text{ Hz, 2H), 2.35 \text{ (bs, 1H), 1.35 \text{ (ddd, } J = 7.5, 5.5, 0.5 \text{ Hz, 2H), 1.10 \text{ (ddd, } J = 7.5, 5.5, 0.5 \text{ Hz, 2H); } \textit{C} \text{ NMR} \text{ (125 MHz, CDCl}_3\text{)} \delta 148.7, 128.4 \text{ (q, } J = 31.9 \text{ Hz), 125.2 \text{ (q, } J = 3.3 \text{ Hz), 124.2 \text{ (q, } J = 270.1 \text{ Hz), 124.1, 56.1, 19.1; } \textit{F} \text{ NMR (282MHz, CDCl}_3\text{) } \delta}
\end{align*}
\]
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 °C for 30 min. The obtained siloxycyclopropane was treated with trifluoroacetic acid to give cis-2-methyl-1-phenycyclopropanol A (Scheme 8).

![Scheme 8. Synthesis of an authentic sample of 11e.](image)

Compared with $^1$H 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-naphtyl)cyclopropanol (11f)

(major isomer): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 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 °C. Anal. Calcd for C\(_{14}\)H\(_{14}\)O: C, 84.81; H, 7.12%. Found: C, 84.63; H, 7.17%; HRMS (m/z) Found: 198.1040. Calcd for C\(_{14}\)H\(_{14}\)O [M]: 198.1045. (minor isomer): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 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 °C.

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

(major isomer): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 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 C\(_{11}\)H\(_{14}\)O\(_2\) [M]: 178.0994. (minor isomer): \(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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); \(^1^3\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 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): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$) $\delta$ 97.89. HRMS (m/z) Found: 216.0760. Calcd for C$_{11}$H$_{11}$OF$_3$: 216.0762.

(minor isomer): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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$_3$) $\delta$ 98.12; IR (nujor) 3338, 2923, 1456, 1377, 1328, 1167, 1111, 1072 cm$^{-1}$; mp 66.8–67.4 °C.

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

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 197.7, 150.5, 135.1, 128.5, 123.6, 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 C$_{11}$H$_{12}$O$_2$: C, 74.98; H, 6.86%. Found: C, 75.12; H, 6.93%; HRMS (m/z) Found: 176.0836. Calcd for C$_{11}$H$_{12}$O$_2$ [M]$^+$: 176.0837.

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

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 167.1, 150.3, 129.6, 127.7, 123.6, 56.1, 52.0, 19.4; IR (nujor) 3450, 2925, 1456, 1377, 1288, 1240, 1183, 1119 cm$^{-1}$; mp 78.0–78.8 °C. Anal. Calcd for C$_{11}$H$_{12}$O$_3$: C, 68.74; H, 6.29%. Found: C, 68.79; H, 6.32%;
HRMS (m/z) Found: 193.0857. Calcd for C\textsubscript{11}H\textsubscript{13}O\textsubscript{3} [MH\textsuperscript{+}]: 193.0865.

1-Phenyl-1-trimethylsiloxy cyclopropane (13)

```
\[
\text{Me}_3\text{SiO} \\
\text{Ph}
\]
```

\(^1\)H NMR (300 MHz, CDCl\textsubscript{3}) \(\delta\) 7.35–7.20 (m, 5H), 1.19 (ddd, \(J = 7.5, 5.1, 0.6\) Hz, 2H), 0.99 (ddd, \(J = 7.5, 5.1, 0.6\) Hz, 2H), 0.05 (s, 9H).

The spectral data of the product 13 are in agreement with those published.\(^{24}\)

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

```
\[
\text{Ph} \quad \text{O} \quad \text{Ph} \\
\text{O} \\
\text{Ph}
\]
```

\(^1\)H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.06–8.04 (m, 4H), 7.60–7.57 (m, 2H), 7.51–7.47 (m, 4H), 3.48 (s, 4H); \(^1\)C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 198.7, 136.7, 133.2, 128.6, 128.1, 32.6.

The spectral data of the product 14a are in agreement with those published.\(^{25}\)

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

```
\[
\text{Ph} \\
\text{O} \quad \text{O} \\
\text{Ph}
\]
```

\(^1\)H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 8.03–8.01 (m, 2H), 7.60 (dd, \(J = 2.0, 0.5\) Hz, 1H), 7.57 (tt, \(J = 7.0, 1.5\) Hz, 1H), 7.49–7.46 (m, 2H), 7.26 (dd, \(J = 3.5, 0.5\) Hz, 1H), 6.55 (dd, \(J = 3.5, 1.5\) Hz, 1H), 3.46–3.44 (m, 2H), 3.33–3.30 (m, 2H); \(^1\)C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 198.4, 187.9, 152.5, 146.3, 136.6, 133.2, 128.6, 128.1, 117.1, 112.2, 32.24, 32.20.

The spectral data of the product 14c are in agreement with those published.\(^{26}\)

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

```
\[
\text{Ph} \quad \text{O} \\
\text{Ph}
\]
```

\(^1\)H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 7.97–7.95 (m, 2H), 7.57–7.54 (m, 1H), 7.48–7.44 (m, 2H), 5.82 (ddt, \(J = 17.0, 10.0, 6.5\) Hz, 1H), 5.05 (ddt, \(J = 17.0, 2.0, 1.5\) Hz, 1H), 5.00 (ddt, \(J = 10.0, 2.0, 1.5\) Hz, 1H), 2.98 (t, \(J = 7.5\) Hz, 2H), 2.16 (qt, \(J = 7.5, 1.5\) Hz, 2H), 1.86 (tt, \(J = 7.5, 7.5\) Hz, 2H); \(^1\)C NMR (125 MHz, CDCl\textsubscript{3}) \(\delta\) 200.2, 138.0, 137.0, 132.9, 128.5, 128.0, 115.3, 37.7, 33.2, 23.3.
The spectral data of the product 15a are in agreement with those published.27

1-tetradecen-6-one (15b)

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_{3}\text{)} & \delta 5.76 (ddt, J = 17.0, 10.0, 6.5 Hz, 1H), 5.01 (ddt, J = 17.0, 2.0, 1.5 Hz, 1H), 4.96 (ddt, J = 10.0, 2.0, 1.5 Hz, 1H), 2.42–2.36 (m, 4H), 2.05 (qt, J = 7.5, 1.5 Hz, 2H), 1.67 (tt, J = 7.5, 7.5 Hz, 2H), 1.56–1.53 (m, 2H), 1.30–1.25 (m, 10H), 0.87 (t, J = 6.5 Hz, 3H); \\
\text{\textsuperscript{13}C NMR (125 MHz, CDCl}_{3}\text{)} & \delta 211.3, 138.0, 115.1, 42.9, 41.8, 33.1, 31.8, 29.3, 29.2, 29.1, 23.9, 22.8, 22.6, 14.1; IR (neat) 2928, 1713, 1674, 1641, 1605, 1454, 1410, 1371, 1273, 1130, 1074 cm\textsuperscript{-1}. Anal. Calcd for C\textsubscript{14}H\textsubscript{26}O: C, 79.94; H, 12.46%. Found: C, 80.21; H, 12.53%; HRMS (m/z) Found: 210.1990. Calcd for C\textsubscript{14}H\textsubscript{26}O [M\textsuperscript{+}]: 210.1984.
\end{align*}
\]

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

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_{3}\text{)} & \delta 7.57 (dd, J = 2.0, 1.0 Hz, 1H), 7.17 (dd, J = 4.0, 1.0 Hz, 1H), 6.52 (dd, J = 4.0, 2.0 Hz, 1H), 5.80 (ddt, J = 17.0, 10.0, 6.5 Hz, 1H), 5.04 (ddt, J = 17.0, 2.0, 1.5 Hz, 1H), 4.99 (ddt, J = 10.0, 2.0, 1.5 Hz, 1H), 2.82 (t, J = 7.5 Hz, 2H), 2.14 (qt, J = 7.5, 1.5 Hz, 2H), 1.83 (tt, J = 7.5, 7.5 Hz, 2H); \\
\text{\textsuperscript{13}C NMR (125 MHz, CDCl}_{3}\text{)} & \delta 189.5, 152.8, 146.2, 137.9, 116.8, 115.3, 112.1, 37.6, 33.1, 23.2. \\
The spectral data of the product 15c are in agreement with those published.28
\end{align*}
\]

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

\[
\begin{align*}
\text{\textsuperscript{1}H NMR (500 MHz, CDCl}_{3}\text{)} & \delta 8.04 (d, J = 8.0 Hz, 2H), 7.71 (d, J = 8.0 Hz, 2H), 5.81 (ddt, J = 17.0, 10.0, 6.5 Hz, 1H), 5.04 (ddt, J = 17.0, 2.0, 1.5 Hz, 1H), 5.00 (ddt, J = 10.0, 2.0, 1.5 Hz, 1H), 2.99 (t, J = 7.5 Hz, 2H), 2.16 (qt, J = 7.0, 1.5 Hz, 2H), 1.86 (tt, J = 7.5, 7.5 Hz, 2H); \\
\text{\textsuperscript{13}C NMR (125 MHz, CDCl}_{3}\text{)} & \delta 199.1, 139.6, 137.8, 134.2 (q, J = 32.9 Hz), 128.3, 125.6 (q, J = 3.8 Hz), 123.6 (q, J = 271.1 Hz), 115.5, 37.9, 33.0, 23.0; \\
\text{\textsuperscript{19}F NMR (282MHz, CDCl}_{3}\text{)} & \delta 98.06; IR (neat) 2938, 2359,
\end{align*}
\]
Chapter 5

1694, 1410, 1327, 1170, 1132, 1067, 1016 cm\(^{-1}\). Anal. Calcd for C\(_{13}\)H\(_{12}\)OF\(_3\): C, 64.46; H, 5.41%. Found: C, 64.21; H, 5.43%; HRMS (m/z) Found: 242.0918. Calcd for C\(_{13}\)H\(_{12}\)OF\(_3\) [M\(^+\)]: 242.0918.

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

\[^1\text{H} \text{NMR (500 MHz, CDCl}_3\)] \text{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, 2.0, 1.5 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}\text{C NMR (125 MHz, CDCl}_3\)] \text{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-naphtyl)-5-hexen-1-one (15f)

\[^1\text{H NMR (500 MHz, CDCl}_3\)] \text{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}\text{C NMR (125 MHz, CDCl}_3\)] \text{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 C\(_{17}\)H\(_{18}\)O: C, 85.67; H, 7.61%. Found: C, 85.52; H, 7.64%; HRMS (m/z) Found: 238.1362. Calcd for C\(_{17}\)H\(_{18}\)O [M\(^+\)]: 238.1358.

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

\[^1\text{H NMR (500 MHz, CDCl}_3\)] \text{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}\text{C NMR (125 MHz, CDCl}_3\)] \text{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,
161, 1510, 1460, 1420, 1371, 1308, 1260, 1173, 103 1 cm\(^{-1}\). Anal. Calcd for C\(_{14}\)H\(_{18}\)O\(_2\): C, 77.03%; H, 8.31%. Found: C, 76.95; H, 8.27%; HRMS (m/z) Found: 218.1306. Calcd for C\(_{14}\)H\(_{18}\)O\(_2\) [M]\(^+\): 218.1307.

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

\[\text{**1H NMR (500 MHz, CDCl}_3\text{)} \delta 8.04 (d, J = 8.0 \text{ Hz}, 2H), 7.73 (d, J = 8.0 \text{ Hz}, 2H), 5.77 (ddt, J = 17.0, 10.0, 6.5 \text{ Hz}, 1H), 5.00–4.96 (m, 2H), 3.49 (dq, J = 14.0, 6.5 \text{ 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 \text{ Hz}, 3H); \text{^13C NMR (125 MHz, CDCl}_3\text{)} \delta 203.3, 139.3 (d, J = 0.9 \text{ Hz}), 137.8, 134.2 (q, J = 32.9 \text{ Hz}), 128.6, 125.7 (q, J = 3.8 \text{ Hz}), 123.6 (q, J = 271.5 \text{ Hz}), 115.4, 40.1, 32.3, 31.4, 17.0; \text{^19F NMR (282 MHz, CDCl}_3\text{)} \delta 97.96; \text{IR (neat)} 2935, 1690, 1410, 1326, 1172, 1132, 1068, 1017 \text{ cm}^{-1}. \text{Anal. Calcd for 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 C\(_{14}\)H\(_{15}\)OF\(_3\) [M]\(^+\): 256.1075.

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

\[\text{**1H NMR (500 MHz, CDCl}_3\text{)} \delta 8.03 (s, 4H), 5.82 (ddt, J = 17.0, 10.0, 6.5 \text{ Hz}, 1H), 5.05 (ddt, J = 17.0, 2.0, 1.5 \text{ Hz}, 1H), 5.01 (ddt, J = 10.0, 2.0, 1.5 \text{ Hz}, 1H), 3.01 (t, J = 7.5 \text{ Hz}, 2H), 2.65 (s, 3H), 2.17 (qt, J = 7.0, 1.5 \text{ Hz}, 2H), 1.86 (tt, J = 7.0, 7.0 \text{ Hz}, 2H); \text{^13C NMR (125 MHz, CDCl}_3\text{)} \delta 199.7, 197.5, 140.1, 140.0, 137.9, 128.5, 128.2, 115.5, 38.1, 33.1, 26.9, 23.0; \text{IR (neat)} 2923, 2360, 1679, 1456, 1404, 1312, 1268 \text{ cm}^{-1}; \text{mp 49.5–51.0 }^\circ\text{C. Anal. Calcd for 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 C\(_{14}\)H\(_{16}\)O\(_2\) [M]\(^+\): 216.1150.

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

\[\text{**1H NMR (500 MHz, CDCl}_3\text{)} \delta 8.12 (d, J = 9.0 \text{ Hz}, 2H), 8.00 (d, J = 9.0 \text{ Hz}, 2H), 5.82 (ddt, J = 17.0, 10.0, 6.5 \text{ Hz}, 1H), 5.05 (ddt, J = 17.0, 2.0, 2.0 \text{ Hz}, 1H), 5.00 (ddt, J = 10.0, 2.0, 1.5 \text{ Hz}, 1H), 2.08 (s, 3H), 1.96 (t, J = 7.5 \text{ Hz}, 2H), 2.65 (s, 3H), 2.17 (qt, J = 7.0, 1.5 \text{ Hz}, 2H), 1.86 (tt, J = 7.0, 7.0 \text{ Hz}, 2H); \text{^13C NMR (125 MHz, CDCl}_3\text{)} \delta 199.7, 197.5, 140.1, 140.0, 137.9, 128.5, 128.2, 115.5, 38.1, 33.1, 26.9, 23.0; \text{IR (neat)} 2923, 2360, 1679, 1456, 1404, 1312, 1268 \text{ cm}^{-1}; \text{mp 49.5–51.0 }^\circ\text{C. Anal. Calcd for 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 C\(_{14}\)H\(_{16}\)O\(_2\) [M]\(^+\): 216.1150.
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 (nujor) 2924, 1722, 1677, 1457, 1407, 1378, 1284, 1112 cm$^{-1}$; mp 55.5–57.0 °C. HRMS (m/z) Found: 232.1097. Calcd for C$_{14}$H$_{16}$O$_3$ [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 (nujor) 1709, 1352, 1221, 1179, 976, 910, 735 cm$^{-1}$. Anal. Calcd for C$_{14}$H$_{11}$O$_4$: C, 78.84; H, 7.09%. Found: C, 79.06; H, 7.20%; HRMS (m/z) Found: 253.0413. Calcd for C$_{14}$H$_{11}$O$_4$NS [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 C$_{14}$H$_{15}$ON: C, 78.84; H, 7.09%. Found: C, 79.06; H, 7.20%; HRMS (m/z) Found: 213.1156. Calcd for C$_{14}$H$_{15}$ON $[M]^+$: 213.1154. $[\alpha]_{D}^{25}$ = −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), 2.16–2.08 (m, 2H), 1.86–1.79 (m, 1H), 1.77–1.69 (m, 1H); \(^{13}\)C NMR (125 MHz, C\(_{6}D_{6}\)) \(\delta\) 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 C\(_{13}\)H\(_{16}\)O\(_{2}\): C, 76.44; H, 7.90%. Found: C, 76.69; H, 8.02%; HRMS (m/z) Found: 204.1154. Calcd for C\(_{13}\)H\(_{16}\)O\(_{2}\) [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)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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, \(J = 17.0, 2.0, 1.5\) 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), 1.33 (s, 3H); \(^{13}\)C NMR (125 MHz, CDCl\(_3\)) \(\delta\) 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 C\(_{14}\)H\(_{18}\)O\(_2\): C, 77.03; H, 8.31%. Found: C, 77.11; H, 8.24%; HRMS (m/z) Found: 218.1305. Calcd for C\(_{14}\)H\(_{18}\)O\(_2\) [M]: 218.1307.

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

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 5.77 (ddt, \(J = 17.0, 10.0, 6.5\) 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), 3.74 (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\(_3\)) \(\delta\) 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 C\(_{12}\)H\(_{23}\)O\(_2\) [MH]: 199.1698.
(IR,2R)-2-acetyl-2-(3-butenyl)cyclohexanol (22da)

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_6$D$_6$) $\delta$ 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, 1695, 1450, 1355, 1263, 1232, 1170, 1046 cm$^{-1}$. HRMS (m/z) Found: 197.1540. Calcd for C$_{12}$H$_{21}$O$_2$ [MH]$^+$: 197.1542. [α]$_D^{25}$ = +16 (c = 0.0188 g/mL, benzene).

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

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

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

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

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$) $\delta$ 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 C$_{13}$H$_{22}$O$_2$: C, 74.24; H, 10.54%. Found: C, 74.34; H, 10.31%; HRMS (m/z) Found: 210.1621. Calcd for
\( \text{C}_{13}\text{H}_{22}\text{O}_2 [\text{M}]^+ : 210.1620. \)

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

\(^1\text{H} \text{NMR} \ (500 \text{ MHz, CDCl}_3 ) \ \delta \ 5.07–5.03 \ (m, 1H), \ 3.70 \ (\text{ddd}, \ J = 8.0, 8.0, 4.0 \text{ Hz, } 1H), \ 3.05 \ (d, \ J = 8.0 \text{ Hz, } 1H), \ 2.15 \ (s, 3H), \ 1.99–1.78 \ (m, 4H), \ 1.70–1.46 \ (m, 6H), \ 1.67 \ (d, \ 3 \ J = 1.0 \text{ Hz, } 3H), \ 1.58 \ (d, \ J = 1.0 \text{ Hz, } 3H), \ 1.39–1.26 \ (m, 2H); \ \ ^{13}\text{C} \ \text{NMR} \ (125 \text{ MHz, CDCl}_3) \ \delta \ 216.4, \ 132.3, \ 123.7, \ 73.3, \ 55.7, \ 35.4, \ 30.9, \ 30.1, \ 26.3, \ 25.6, \ 22.8, \ 22.5, \ 22.2, \ 17.6; \ \text{IR (neat)} \ 3458, \ 2934, \ 2344, \ 1697, \ 1449, \ 1375, \ 1354, \ 1265, \ 1236, \ 1217, \ 1167, \ 1138, \ 1064 \text{ cm}^{-1}. \ \text{HRMS (m/z) Found: 224.1774. Calcd for C}_{14}\text{H}_{24}\text{O}_2 [\text{M}]^+: 224.1776. \)

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

\(^1\text{H} \text{NMR} \ (500 \text{ MHz, CDCl}_3) \ \delta \ 5.10 \ (m, 1H), \ 4.67 \ (\text{dt}, \ J = 6.5, 2.5 \text{ Hz, } 2H), \ 3.62 \ (\text{ddd}, \ J = 9.0, 9.0, 4.0 \text{ Hz, } 1H), \ 3.21 \ (d, \ J = 9.0 \text{ Hz, } 1H), \ 2.44–2.31 \ (m, 2H), \ 2.16 \ (s, 3H), \ 2.02 \ (\text{dddd}, \ J = 14.0, 6.5, 3.5, 1.5 \text{ Hz, } 1H), \ 1.86–1.80 \ (m, 1H), \ 1.72–1.54 \ (m, 3H), \ 1.47 \ (\text{ddd}, \ J = 14.0, 10.0, 3.5 \text{ Hz, } 1H), \ 1.38–1.22 \ (m, 2H); \ \ ^{13}\text{C} \ \text{NMR} \ (125 \text{ MHz, CDCl}_3) \ \delta \ 216.2, \ 209.7, \ 84.8, \ 74.5, \ 74.0, \ 56.1, \ 35.1, \ 31.2, \ 30.8, \ 26.8, \ 23.1, \ 22.4; \ \text{IR (neat)} \ 3389, \ 2936, \ 2359, \ 1954, \ 1693, \ 1604, \ 1447, \ 1408, \ 1360, \ 1273, \ 1244, \ 1177, \ 1123 \text{ cm}^{-1}. \ \text{HRMS (m/z) Found: 195.1382. Calcd for C}_{12}\text{H}_{19}\text{O}_2 [\text{MH}]^+: 195.1385. \)

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

\(^1\text{H} \text{NMR} \ (500 \text{ MHz, CDCl}_3) \ \delta \ 4.60–4.57 \ (m, 2H), \ 3.74 \ (\text{ddd}, \ J = 7.5, 7.5, 3.5 \text{ Hz, } 1H), \ 3.19 \ (d, \ J = 7.5 \text{ Hz, } 1H), \ 2.34 \ (\text{dd}, \ J = 2.5, 2.5 \text{ Hz, } 2H), \ 2.18 \ (s, 3H), \ 2.06–2.01 \ (m, 1H), \ 1.84–1.79 \ (m, 1H), \ 1.70 \ (t, \ J = 3.0 \text{ Hz, } 3H), \ 1.69–1.52 \ (m, 4H), \ 1.40–1.30 \ (m, 2H); \ \ ^{13}\text{C} \ \text{NMR} \ (125 \text{ MHz, CDCl}_3) \ \delta \ 216.4, \ 208.0, \ 93.8, \ 74.3, \ 72.9, \ 56.0, \ 38.1, \ 30.7, \ 29.9, \ 27.2, \ 22.2, \ 22.1, \ 20.8; \ \text{IR (neat)} \ 3460, \ 2938, \ 2360, \ 1958, \ 1697, \ 1449, \ 1424, \ 1354, \ 1136, \ 1078, \ 1060 \text{ cm}^{-1}. \ \text{Anal. Calcd for C}_{13}\text{H}_{20}\text{O}_2: \ C, 74.96; \ H, 9.68\% . \ \text{Found: C, 74.71; H, 9.56.} \)
Chapter 5

9.78%; HRMS (m/z) Found: 208.1471. Calcd for C_{13}H_{20}O_{2} [M]^+: 208.1463.

\( (1R^*,2R^*)-2\text{-acetyl-2-(3-butenyl)cyclopentanol (22ea)} \)

\[ \begin{align*}
^1\text{H NMR (500 MHz, CDCl}_3) & \delta 5.75 \text{ (ddt, } J = 17.0, 10.0, 6.5 \text{ Hz, 1H), 5.00 (ddt, } J = \\
& 17.0, 2.0, 1.5 \text{ Hz, 1H), 4.95 (ddt, } J = 10.0, 2.0, 1.5 \text{ Hz, 1H), 4.15 (ddd, } J = 5.0, 5.0, \\
& 3.0 \text{ Hz, 1H), 2.74 (dd, } J = 5.0, 0.5 \text{ Hz, 1H), 2.20–2.14 \text{ (m, 1H), 2.18 (s, 3H),} \\
& 2.05–1.82 \text{ (m, 4H), 1.72–1.52 (m, 5H)}; ^{13}\text{C NMR (125 MHz, CDCl}_3) \delta 214.1, 137.7, \\
& 115.0, 78.7, 63.8, 35.1, 32.6, 30.8, 29.1, 27.8, 20.5; IR (neat) 3420, 2936, 1695, 1448, 1355, 1232, \\
& 1170, 1046 \text{ cm}^{-1}. \text{ Anal. Calcd for C}_{11}\text{H}_{18}\text{O}_{2}: \text{C}, 72.49; \text{H}, 9.95%. \text{ Found: C, 72.31; H, 9.87%;} \\
& \text{HRMS (m/z) Found: 183.1380. Calcd for C}_{11}\text{H}_{19}\text{O}_{2} [\text{MH}]^+: 183.1385.}
\end{align*} \]

\( (1R^*,2R^*)-2\text{-acetyl-2-(3-methyl-3-butenyl)cyclopentanol (22eb)} \)

\[ \begin{align*}
^1\text{H NMR (500 MHz, CDCl}_3) & \delta 4.71–4.70 \text{ (m, 1H), 4.66–4.65 \text{ (m, 1H), 4.16 (ddd, } J = \\
& 5.0, 5.0, 2.5 \text{ Hz, 1H), 2.74 (d, } J = 5.0 \text{ Hz, 1H), 2.21–2.15 \text{ (m, 1H), 2.18 (s, 3H),} \\
& 2.06–1.56 \text{ (m, 9H), 1.70 (s, 3H)}; ^{13}\text{C NMR (125 MHz, CDCl}_3) \delta 214.1, 145.1, 110.0, \\
& 78.8, 63.9, 34.1, 32.8, 32.6, 30.8, 27.7, 22.6, 20.5; IR (neat) 3461, 2936, 1694, 1447, \\
& 1357, 1167, 1052 \text{ cm}^{-1}. \text{ HRMS (m/z) Found: 197.1542. Calcd for C}_{12}\text{H}_{21}\text{O}_{2} [\text{MH}]^+: 197.1542.}
\end{align*} \]
References and Notes


10. $M = 390.39$, Monoclinic, $a = 9.758(8)$, $b = 5.772(5)$, $c = 16.977(13)$ Å, $b = 96.702^\circ$, $V = 949.7(13)$ Å$^3$, $Z = 2$, $\rho_{\text{calc}} = 1.365$ g / cm$^3$, $\lambda(\text{Mo}\lambda\kappa) = 0.71073$ Å, $T = 293$ K, $2\theta_{\text{max}} = 54.0^\circ$, $R = 0.050$ for 3638 reflections ($I > 2\sigma(I)$).


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-trimethylsiloxy-cyclopropane 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.
Chapter 6

Introduction

Many examples of 1,4-addition of organozinc reagent to $\alpha,\beta$-unsaturated ketones have been reported.\(^1\) Matsubara et al. had also reported that the gem-dizinc reagent undergoes 1,4-addition to $\alpha,\beta$-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 $\beta$-iodozinciomethylketone 3 via 1,4-addition (Scheme 1).\(^3\) The sequential coupling reaction at the introduced zincothyl 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, $\alpha,\beta$-epoxy ketone 6, or $\alpha$-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 \( \text{gem-dizinc} \) to produce \( \beta \)-cyclopropyl substituted silyl enol ether. As shown in Scheme 3, the author examined the treatment of \( \alpha,\beta \)-unsaturated ketone carrying an electrophilic site at \( \gamma \)-position with bis(iodozincio)methane (1) in the presence of silylation reagent (\( R_3\text{SiX} \)).

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

Results and Discussion

A mixture of \( \gamma \)-acetoxy-\( \alpha,\beta \)-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).

![Scheme 4](image)

**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-eneone 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 °C did not improve the diastereomeric ratio (entry 5). In these cases, the diastereofacial selectivity of 1,4-addition to α,β-eneone 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. In general, the diastereoselectivity can be explained by the modified Felkin–Anh model when 1,4-additions proceed through the Bürgi–Dunitz trajectory (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-eneone 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.\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>conditions</th>
<th>product</th>
<th>yield (%)(^b)</th>
<th>dr(^c)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>25 °C, 3 h</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>86</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>25 °C, 3 h</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>83</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>25 °C, 3 h</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>51(^d)</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>0 to 25 °C</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>80</td>
<td>59/41(^e)</td>
</tr>
<tr>
<td>5</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>(-40) to 25 °C</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>80</td>
<td>60/40</td>
</tr>
<tr>
<td>6</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>0 to 25 °C</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>75</td>
<td>66/34</td>
</tr>
<tr>
<td>7</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>0 to 25 °C</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>82</td>
<td>79/21(^f)</td>
</tr>
<tr>
<td>8</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>0 to 25 °C</td>
<td>(\text{R}^1\text{O} = \text{OCH}<em>{3}) (\text{R}^2\text{O} = \text{OCH}</em>{3})</td>
<td>27(^g)</td>
<td>85/15</td>
</tr>
</tbody>
</table>

\(^a\) Ketone 14 (1.0 mmol), the dizinc 1 (1.2 mmol, 0.5 M in THF), triethylamine (2.5 mmol), \(\text{R}^1\text{SiX}\) (2.2 mmol), and THF (4 mL) were used. \(^b\) Isolated yields. \(^c\) The diastereomeric ratios were determined by \(^1\)H 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-trimethylsiloxy cyclopropane 17a was obtained in 99% yield (Scheme 5). The configuration of enolate was (Z)-form without any diastereoselectivity of cyclopropanation formation reaction.

![Cyclopropanation of ketoester 16a with bis(iodozincio)methane (1).](image)

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).\(^a\)

<table>
<thead>
<tr>
<th>entry</th>
<th>substrate</th>
<th>R’(_3)SiX</th>
<th>product</th>
<th>yield (%)(^b)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>16b</td>
<td>Me(_3)SiCN</td>
<td>17b</td>
<td>99</td>
</tr>
<tr>
<td>2</td>
<td>16c</td>
<td>Me(_3)SiCN</td>
<td>17c</td>
<td>73</td>
</tr>
<tr>
<td>3</td>
<td>16d</td>
<td>Me(_3)SiCN</td>
<td>17d</td>
<td>99</td>
</tr>
<tr>
<td>4</td>
<td>16e</td>
<td>Me(_3)SiCN</td>
<td>17e</td>
<td>83</td>
</tr>
<tr>
<td>5</td>
<td>16a</td>
<td>PhMe(_2)SiCl</td>
<td>17a’</td>
<td>93</td>
</tr>
<tr>
<td>6</td>
<td>16b</td>
<td>PhMe(_2)SiCl</td>
<td>17b’</td>
<td>90</td>
</tr>
<tr>
<td>7</td>
<td>16c</td>
<td>PhMe(_2)SiCl</td>
<td>17c’</td>
<td>65</td>
</tr>
<tr>
<td>8</td>
<td>16d</td>
<td>PhMe(_2)SiCl</td>
<td>17d’</td>
<td>97</td>
</tr>
</tbody>
</table>

\(^a\) (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’\(_3\)SiX (2.2 mmol), and THF (4 mL) were used. \(^b\) Isolated yields.
The product \textbf{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, which can be applied for the C–C bond forming reactions. When \textbf{17} was activated by Lewis acid, the homoenolate \textbf{19} would be generated via cyclopropane ring opening (Scheme 7); the homoenolate \textbf{19} is considered to be as 3-siloxyallylmetal species. This reagent might have an allylmetal form \textbf{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 \textbf{19} as 3-siloxyallylmetal reagent was expected to proceed regio- and diastereoselectively.

\begin{center}
\textbf{Scheme 6.} Formation of cyclopropane \textbf{17} via 1,4-addition.
\end{center}

\begin{center}
\textbf{Scheme 7.} Strategy of migration of iodozincio group from homoallyl metal into allyl metal.
\end{center}
Treatment of tosylimine of benzaldehyde with 17a in the presence of zinc(II) iodide gave the \( \beta \)-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 homenolate 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 homenolate. So we tried the cyclopropantion 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, \( \beta \)-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](image)

Scheme 9. Reaction of various imines with the homoenoate 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 diastereomeric mixture (Scheme 10 (a)). The reaction of acid anhydrides with 17a afforded α-(E)-alkenyl-α-siloxyketones 22 in good yields with high (E)-selectivity (Scheme 10 (b)).
Scheme 10. Reaction of propanal or acid anhydride with the homoenoate from 16a.

The author proposes the explanation for the high diastereoselectivites in the reaction of imines with the homoenoate, 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.
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 $\gamma$-acyloxy-$\alpha,\beta$-unsaturated ketone (14): $\gamma$-Hydroxy-$\alpha,\beta$-unsaturated ketone was prepared according to the literature. To a solution of $\gamma$-hydroxy-$\alpha,\beta$-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 Na$_2$CO$_3$ 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 $\gamma$-acyloxy-$\alpha,\beta$-unsaturated ketone 14.

General procedure for the nucleophilic cyclopropanation of $\gamma$-acyloxy-$\alpha,\beta$-unsaturated ketone (14): A mixture of $\gamma$-acyloxy-$\alpha,\beta$-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 Na$_2$SO$_4$. 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$_4$Cl 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$_2$SO$_4$. 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$_2$SO$_4$. 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 Na$_2$SO$_4$. 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 Na$_2$SO$_4$. The solvent was removed under reduced pressure, and the residue was purified by silica gel column chromatography to give the corresponding α-siloxynketone 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)**

$^{1}$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 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 C$_{12}$H$_{12}$O$_3$ [M]$^+$: 204.0786.

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

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 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 C$_{13}$H$_{14}$O$_3$ [M]$^+$: 218.0943.

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

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 188.8, 170.3, 141.7, 136.1, 131.9, 130.1, 128.2, 125.4, 63.1, 20.7; IR (nujor) 1742, 1674, 1630, 1586, 1285, 1233, 1072, 1034, 1011, 910, 733 cm$^{-1}$, mp 52.5–53.5 °C. Anal. Calcd for C$_{12}$H$_{11}$O$_3$Br: C, 50.91; H, 3.92%. Found: C, 51.03; H, 3.88%; HRMS (m/z) Found: 281.9891. Calcd for C$_{12}$H$_{11}$O$_3$Br [M]$^+$: 281.9892.

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

$^1$H NMR (300 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 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, 1088, 1034, 976, 731 cm\(^{-1}\). Anal. Calcd for C\(_{11}\)H\(_{18}\)O\(_3\): C, 66.64; H, 9.15%. Found: C, 66.84; H, 9.36%. HRMS (m/z) Found: 198.1249. Calcd for C\(_{11}\)H\(_{18}\)O\(_3\)[M\(^+\)]: 198.1256.

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

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)): \(\delta\) 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 C\(_{13}\)H\(_{14}\)O\(_3\)[M\(^+\)]: 218.0943.

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

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)): \(\delta\) 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 C\(_{18}\)H\(_{16}\)O\(_3\): C, 77.12; H, 5.75%. Found: C, 77.09; H, 5.93%. HRMS (m/z) Found: 280.1103. Calcd for C\(_{18}\)H\(_{16}\)O\(_3\)[M\(^+\)]: 280.1099.

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

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta\) 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 (dd, \(J = 5.4, 5.4, 0.9\) 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\(_3\)): \(\delta\) 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, 1449, 1371, 1292, 1236, 1022, 986 cm\(^{-1}\). Anal. Calcd for C\(_{15}\)H\(_{18}\)O\(_3\): C, 73.15; H, 7.37%. Found: C, 73.20; H, 7.46%; HRMS (m/z) Found: 246.1264. Calcd for C\(_{15}\)H\(_{18}\)O\(_3\) [M]\(^+\): 246.1256.

\([\text{Z}-2\text{-trimethysiloxy-2-phenylethenyl}]\text{cyclopropane (15a)}\)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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 (dtt, \(J = 9.5, 8.0, 4.5\) 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\(_3\)): \(\delta\) 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 C\(_{14}\)H\(_{20}\)OSi: C, 72.36; H, 8.67%. Found: C, 72.22; H, 8.94%; HRMS (m/z) Found: 232.1284. Calcd for C\(_{14}\)H\(_{20}\)OSi [M]\(^+\): 232.1283.

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

\([\text{Z}-2\text{-trimethysiloxy-2-(4-tolyl)ethenyl}]\text{cyclopropane (15b)}\)

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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 (dtt, \(J = 9.5, 8.0, 4.5\) 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\(_3\)): \(\delta\) 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 C\(_{15}\)H\(_{22}\)OSi: C, 73.11; H, 9.00%. Found: C, 72.87; H, 8.89%; HRMS (m/z) Found: 246.1445. Calcd for C\(_{15}\)H\(_{22}\)OSi [M]\(^+\): 246.1440.
[(Z)-2-trimethysiloxy-2-(4-bromophenyl)ethenyl)cyclopropane (15c)]

\[\text{OSiMe}_3\]

\[\text{Br}\]

\[\text{CH}_3\]

\[^{1}H\text{ NMR (500 MHz, CDCl}_3\delta 7.39 (d, J = 8.5 \text{ Hz, 2H}), 7.30 (d, J = 8.5 \text{ Hz, 2H}), 4.76 (d, J = 9.5 \text{ Hz, 1H}), 1.74 (dtt, J = 9.5, 8.0, 4.5 \text{ Hz, 1H}), 0.82 (dd, J = 8.0, 6.0, 4.5 \text{ Hz, 2H}), 0.42 (dd, J = 6.0, 4.5, 4.5 \text{ Hz, 2H}), 0.17 (s, 9H);}

\[^{13}C\text{ NMR (125 MHz, CDCl}_3\delta 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, 1252, 1065, 1008 \text{ cm}^{-1}. \text{Anal. Calcd for C}_{14}H_{19}BrOSi: C, 54.02; H, 6.15%. Found: C, 54.08; H, 6.11%; HRMS (m/z) Found: 310.0385. Calcd for C}_{14}H_{19}BrOSi [M]^+: 310.0389.]

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

\[\text{OSiMe}_3\]

\[^{1}H\text{ NMR (500 MHz, CDCl}_3\delta 4.16 (d, J = 8.5 \text{ Hz, 0.5H}), 3.95 (d, J = 9.5 \text{ Hz, 0.5 H}), 2.16 (t, J = 7.5 \text{ Hz, 1H}), 1.97 (t, J = 7.5 \text{ Hz, 1H}), 1.56–1.41 (m, 3H), 1.35–1.23 (m, 4H), 0.90 (t, J = 7.0 \text{ Hz, 1.5H}), 0.88 (t, J = 7.0 \text{ 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\text{ NMR (125 MHz, CDCl}_3\delta 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 \text{ cm}^{-1}. \text{HRMS (m/z) Found: 226.1759. Calcd for C}_{13}H_{26}OSi [M]^+: 226.1753.]

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

\[\text{OSiMe}_3\]

\[\text{Ph}\]

\[\text{CH}_3\]

\[^{1}H\text{ NMR (500 MHz, CDCl}_3\delta 7.47–7.42 (m, 2H), 7.30–7.25 (m, 2H), 7.22–7.18 (m, 1H), 5.02 (d, J = 9.5 \text{ Hz, 0.35H}), 4.79 (d, J = 10.0 \text{ 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\text{ NMR (125 MHz, CDCl}_3\delta 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 \text{ cm}^{-1}. \text{HRMS (m/z) Found: 246.1434. Calcd for C}_{13}H_{22}OSi [M]^+: 246.1440.]

169
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.](image)

2-(2-methycyclopropyl)-1-phenylethanone (A): $^1$H 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.](image)
Compared with $^1$H NMR spectrum of the authentic sample A, it was found that the stereochemistry of cyclopropane ring in major isomer was \textit{trans}.

\begin{center}
\textbf{1-[2-trimethylsiloxy-2-phenylethenyl]-2-phenylcyclopropane (15g)}
\end{center}

$^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 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 C$_{20}$H$_{26}$OSi [M]$^+$: 308.1596.

\begin{center}
\textbf{1-[2-trimethylsiloxy-2-phenylethenyl]-2-isopropylcyclopropane (15h)}
\end{center}

(major isomer): $^1$H NMR (500 MHz, CDCl$_3$) $\delta$ 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$_3$): $\delta$ 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 C$_{17}$H$_{26}$OSi [M]$^+$: 274.1753.
(E)-Ethyl 4-(2-naphthyl)-4-oxobut-2-enoate (16d)

\( ^1H \) NMR (300 MHz, CDCl\textsubscript{3}) \( \delta 8.52 \) (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\textsubscript{3}): \( \delta 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 (nujol) 2982, 1717, 1667, 1622, 1470, 1368, 1300, 1171, 1125, 974, 862, 775 cm\textsuperscript{-1}, mp 62.0–62.7 °C. Anal. Calcd for C\textsubscript{16}H\textsubscript{14}O\textsubscript{3}: C, 75.57; H, 5.55%. Found: C, 75.54; H, 5.66%; HRMS (m/z) Found: 254.0948. Calcd for C\textsubscript{16}H\textsubscript{14}O\textsubscript{3}[M]\textsuperscript{+}: 254.0943.

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

\( ^1H \) NMR (500 MHz, CDCl\textsubscript{3}) \( \delta 7.76 \) (d, \( J = 15.5 \) 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\textsubscript{3}): \( \delta 176.2, 165.2, 152.6, 147.6, 135.3, 132.0, 119.4, 112.8, 61.4, 14.2; IR (nujol) 2984, 2255, 1721, 1667, 1630, 1568, 1464, 1397, 1302, 1182, 1028, 910, 733 cm\textsuperscript{-1}, mp 49.8–50.5 °C. HRMS (m/z) Found: 194.0575. Calcd for C\textsubscript{10}H\textsubscript{10}O\textsubscript{4}[M]\textsuperscript{+}: 194.0579.

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

\( ^1H \) NMR (500 MHz, CDCl\textsubscript{3}) \( \delta 7.48–7.42 \) (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\textsubscript{3}): \( \delta 149.6, 149.5, 139.10, 139.08, 128.24, 128.23, 127.44, 127.42, 125.21, 125.17, 110.0, 109.7,

172
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 C\(_{19}\)H\(_{32}\)O\(_3\)Si\(_2\): C, 62.59; H, 8.85%. Found: C, 62.52; H, 8.63%; HRMS (m/z) Found: 364.1883. Calcd for C\(_{19}\)H\(_{32}\)O\(_3\)Si\(_2\) [M\(^+\)]: 364.1890.

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

![Structure of 17a](image)

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

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta\) 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\(_3\)): \(\delta\) 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 C\(_{19}\)H\(_{31}\)BrO\(_3\)Si\(_2\) [M\(^+\)]: 442.0995.

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

\(^1\)H NMR (500 MHz, C\(_6\)D\(_6\)) \(\delta\) 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); 13C NMR (125 MHz, CDCl\textsubscript{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\textsuperscript{-1}. HRMS (m/z) Found: 394.1997. Calcd for C\textsubscript{20}H\textsubscript{34}O\textsubscript{4}Si\textsubscript{2}[M]\textsuperscript{+}: 394.1996.

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

\[
\begin{align*}
&O\text{SiMe}_3 \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3}
\end{align*}
\]

\(^1\text{H} \text{NMR (500 MHz, CDCl\textsubscript{3})} \delta 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}\text{C} \text{NMR (125 MHz, CDCl\textsubscript{3})}: \delta 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\textsuperscript{-1}. HRMS (m/z) Found: 414.2044. Calcd for C\textsubscript{23}H\textsubscript{34}O\textsubscript{3}Si\textsubscript{2}[M]\textsuperscript{+}: 414.2046.

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

\[
\begin{align*}
&O\text{SiMe}_3 \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3} \\
&\text{OEt} \\
&\text{O\text{SiMe}_3}
\end{align*}
\]

\(^1\text{H} \text{NMR (500 MHz, CDCl\textsubscript{3})} \delta 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, 141.1, 111.94, 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 C$_{17}$H$_{30}$O$_4$Si$_2$: C, 57.58; H, 8.53%. Found: C, 57.46; H, 8.31%; HRMS (m/z) Found: 354.1685. Calcd for C$_{17}$H$_{30}$O$_4$Si$_2$ [M$^+$]: 354.1683.

2-[(Z)-2-dimethylphenylsiloxy-2-phenylethenyl]-1-ethoxy-1-dimethylphenylsiloxy cyclopropane (17a$^*$)

$^1$H 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, 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 C$_{29}$H$_{36}$O$_3$Si$_2$ [M$^+$]: 488.2203.

2-[(Z)-2-dimethylphenylsiloxy-2-(4-bromophenyl)ethenyl]-1-ethoxy-1-dimethylphenylsiloxy cyclopropane (17b$^*$)

$^1$H 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); ¹³C NMR (125 MHz, CDCl₃): 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 C₉₂H₃₈BrO₃Si₂[M]⁺: 566.1308.

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

\[\text{OSiPhMe}_2\text{OEt} \quad \text{OSiPhMe}_2\]

¹H NMR (300 MHz, CDCl₃) 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); ¹³C NMR (125 MHz, CDCl₃): 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 C₃₉H₃₈O₄Si₂[M]⁺: 518.2309.
2-[(Z)-2-dimethylphenylsiloxo-2-(2-naphthyl)ethenyl]-1-ethoxy-1-dimethylphenylsiloxycyclopropane (17d’)

1H NMR (300 MHz, CDCl₃) 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); 13C NMR (125 MHz, CDCl₃): 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 C₃₃H₃₈O₃Si₂[M]⁺: 538.2359.

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

1H NMR (500 MHz, CDCl₃) 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); 13C NMR (125 MHz, CDCl₃): 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 (nujor) 3279, 2855, 1733, 1599, 1447, 1377, 1328, 1250, 1162, 1073, 1022 cm⁻¹; mp 143.5–144.5 °C. Anal. Calcd for C₃₀H₃₇NO₃SSi: C, 65.30; H, 6.76%. Found: C, 65.21; H, 6.50%; HRMS (m/z) Found: 552.2245. Calcd for C₃₀H₃₈NO₃SSi [MH]⁺: 552.2240.
Ethyl (5S*,6S*)-(E)-5-phenyl-6-tosylamino-5-trimethylsiloxy-3-nonenate (20b)

\[
\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.69 (d, J = 6.5 \text{ Hz}, 2\text{H}), 7.33 (d, J = 6.5 \text{ Hz}, 2\text{H}), 7.30–7.20 (m, 5\text{H}), 5.99 (d, J = 15.5 \text{ Hz}, 1\text{H}), 5.76 (dt, J = 15.5, 7.0 \text{ Hz}, 1\text{H}), 4.55 (d, J = 9.0 \text{ Hz}, 1\text{H}), 4.14 (q, J = 7.5 \text{ Hz}, 2\text{H}), 3.76 (dd, J = 9.0, 9.0, 2.5 \text{ Hz}, 1\text{H}), 3.08 (d, J = 7.0 \text{ Hz}, 2\text{H}), 2.39 (s, 3\text{H}), 1.42-1.20 (m, 2\text{H}), 1.27 (t, J = 7.5 \text{ Hz}, 3\text{H}), 1.19–1.06 (m, 1\text{H}), 0.95–0.85 (m, 1\text{H}), 0.71 (t, J = 7.0 \text{ Hz}, 3\text{H}), 0.16 (s, 9\text{H}); ^{13}\text{C NMR (125 MHz, CDCl}_3\text{)}: \delta 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; \text{IR (nujol) 3298, 2928, 1733, 1599, 1448, 1325, 1251, 1160 cm}^{-1}. \text{Anal. Calcd for C}_{27}\text{H}_{39}\text{NO}_3\text{SSi: 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) \text{ Å}, \beta = 110.316(15)\text{"}, V = 1489(2) \text{ Å}^3, Z = 2, \rho_{\text{calc}} = 1.154 \text{ Mgm}^{-3}, \lambda(\text{Mo}_\text{K}\alpha) = 0.71073 \text{ Å}, T = 293(2) \text{K}, \theta_{\text{max}} = 54.0\text{"}, R = 0.0514 for 6267 reflections (I > 2\sigma(I)).

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

\[
\text{H NMR (500 MHz, CDCl}_3\text{)} \delta 7.65 (d, J = 8.5 \text{ Hz}, 2\text{H}), 7.31–7.21 (m, 7\text{H}), 5.95 (d, J = 16.0 \text{ Hz}, 1\text{H}), 5.71 (dt, J = 16.0, 7.0 \text{ Hz}, 1\text{H}), 4.59 (d, J = 9.5 \text{ Hz}, 1\text{H}), 4.14 (q, J = 7.0 \text{ Hz}, 2\text{H}), 3.49 (d, J = 9.5 \text{ Hz}, 1\text{H}), 3.07 (d, J = 7.0 \text{ Hz}, 2\text{H}), 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, 1275, 1154, 1061, 1024 cm$^{-1}$. Anal. Calcd for C$_{30}$H$_{43}$NO$_3$Si: 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, β = 69.7620(10)$^\circ$, V = 1578.31(18) Å$^3$, Z = 2, $\rho_{\text{calc}} = 1.174$ Mgm$^{-3}$, $\lambda$(Mo$\kappa\alpha$) = 0.71073 Å, $T = 293(2)$ K, $\theta_{\text{max}} = 54.0^\circ$, $R = 0.0573$ for 6726 reflections ($I > 2\sigma(I)$).

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

$^1$H 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_{3}Si: 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_{3}Sس [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, β = 97.4430(10)^°, V = 1498.38(15) Å^3, Z = 2, ρ_{calc} = 1.176 Mgm^{-3}, λ(MoKα) = 0.71073 Å, T = 293(2) K, θ_{max} = 54.0^°, R = 0.0506 for 5493 reflections (I > 2σ(I)).

Ethyl (5S*,6S*)-(3E,7E)-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 (nujor) 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_{3}SSi: 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_{3}SSi [M]^+: 577.2318.
Ethyl (5S*,6S*)-(E)-5,6-diphenyl-6-phenylamino-5-trimethylsiloxy-3-hexenoate (20f)

\[
\text{Ph} \quad \overset{\text{O}}{\overset{\text{SiMe}_3}{\text{O}}} \quad \text{Ph} \\
\text{Et} \quad \text{Et}
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.43\) (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\(_3\)) \(\delta 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 C\(_{29}\)H\(_{34}\)NO\(_3\)Si [M–H]\(^+\): 472.2308.

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

\[
\text{C}_2\text{H}_5 \quad \overset{\text{O}}{\overset{\text{SiMe}_3}{\text{O}}} \quad \text{Et} \\
\text{OH}
\]

\(^1\)H NMR (300 MHz, CDCl\(_3\)) \(\delta 7.45–7.42\) (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\(_3\)) \(\delta 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 C\(_{19}\)H\(_{29}\)O\(_4\)Si [M–H]\(^+\): 349.1835.

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

\[
\text{H}_3\text{C} \quad \overset{\text{O}}{\overset{\text{SiMe}_3}{\text{O}}} \quad \text{Et} \\
\text{O}
\]

\(^1\)H NMR (500 MHz, CDCl\(_3\)) \(\delta 7.37–7.27\) (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\(_3\)) \(\delta 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 C\(_{18}\)H\(_{26}\)O\(_4\)Si [M\(^+\): 334.1600.
Ethyl (E)-5,6-diphenyl-6-oxo-5-trimethylsiloxy-3-hexenoate (22b)

^1^H NMR (500 MHz, CDCl\textsubscript{3}) \(\delta\) 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); ^1^C NMR (125 MHz, CDCl\textsubscript{3}): \(\delta\) 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\textsuperscript{-1}. Anal. Calcd for C\textsubscript{23}H\textsubscript{28}O\textsubscript{4}Si: C, 69.66; H, 7.12%. Found: C, 69.54; H, 7.11%; HRMS (m/z) Found: 396.1758. Calcd for C\textsubscript{23}H\textsubscript{28}O\textsubscript{4}Si [M]^+: 396.1757.
References and Notes


5. The stereochemistry of **15a** was determined by NOE experiments of $^1$HNMR. The same selectivity of (Z)-silyl enol ether formations were also observed when simple $\alpha,\beta$-unsaturated ketone such as chalcone was treated with bis(iodozincio)methane in the presence of silylation reagent.


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


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 Seijiro Matsubara

Diastereoselective Nucleophilic Cyclopropanation of 1,2-Diketones and α-Ketoimines with Bis(iodozincio)methane
Kenichi Nomura, Keisuke Asano, Takuya Kurahashi, and Seijiro 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 Seijiro Matsubara

Stereoselective Synthesis of β,γ-Unsaturated Ketones by Acid-Mediated Julia-Type Transformation from 2-(1-Hydroxyalkyl)-1-alkylcyclopropanols
Kenichi Nomura and Seijiro Matsubara
*Synlett* **2008**, 1412–1414.
Chapter 4  Zincate-Mediated Rearrangement Reaction of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanol
Kenichi Nomura and Seijiro Matsubara

A New Zincate-Mediated Rearrangement Reaction of 2-(1-Hydroxyalkyl)-1-alkylcyclopropanol
Kenichi Nomura and Seijiro Matsubara

Chapter 5  Preparation of Zinc–Homoenolate from α-Sulfonyloxy Ketone and Bis(iodozincio)methane
Kenichi Nomura and Seijiro Matsubara

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

Chapter 6  Nucleophilic cyclopropanation Reaction with Bis(iodozincio)methane by 1,4-Addition to α,β-Unsaturated Carbonyl Compounds
Kenichi Nomura, Takaharu Hirayama, and Seijiro Matsubara
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)\textsubscript{2,3})
Hideaki Yoshino, Kenichi Nomura, Seijiro Matsubara, Koichiro Oshima, Kazuhiko Matsumoto, Rika Hagiwara, and Yasuhiko Ito

(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

(3) Stereoselective Preparation of 3-Alkanoylprop-2-en-1-ol Derivatives
Mutsumi Sada, Shizue Ueno, Keisuke Asano, Kenichi Nomura, Seijiro Matsubara
Acknowledgment

The studies described in this thesis have been carried out under the direction of Professor Seijiro Matsubara at the Department of Material Chemistry, Graduate School of Engineering, Kyoto University, during April 2003 to March 2006 and during October 2007 to March 2010.

Professor Matsubara always encouraged the author with a warm and gentle heart. The author wishes to express his most grateful acknowledgment to Professor Matsubara for his kind guidance, constant support, and valuable discussion throughout the course of this work. He would like to express his gratitude to Professor Tamejiro Hiyama for his fruitful advice. He is deeply grateful to Professor Koichiro Oshima for helpful discussion, suggestions and encouragement.

The author is indebted to Associate Professor Masaki Shimizu for the instruction of X-ray analysis and helpful discussions. He is grateful to Associate Professor Hideki Yorimitsu and Dr. Takuya Kurahashi for helpful discussions and accurate advice. He is thankful to Dr. Yoshiaki Nakao for generous help. He is grateful to Dr. Keiko Kuwata for the measurement of mass spectra.

The author would like to express his appreciation to the members of Professor Matsubara’s research group and the members of Professor Oshima’s research group for their active and helpful discussions. He tenders his acknowledgment to Dr. Hideaki Yoshino and Mr. Takaharu Hirayama for teaching him the fundamentals of organic chemistry and experimental techniques. He is also thankful to Dr. Shin-ichi Usugi, Dr. Kazuya Fujita, Dr. Hidenori Kinoshita, Dr. Hirohisa Ohmiya, Dr. Koji Hirano, Dr. Minoru Uemura, Dr. Akinori Sato, Dr. Yasuhiro Hirata, Mr. Kazunari Yagi, Mr. Yutaka Yokota, Mr. Masaaki Takahashi, Mr. Zenichi Ikeda, Mr. Kenichi Ishibashi, Mr. Yuichi Kajita, Mr. Keisuke Asano and Mr. Hiroaki Horie for their kind support and generous suggestions.

The author would like to thank Professor Barry M. Trost, Professor Reinhard W. Hoffmann and Professor Masanobu Uchiyama for their fruitful discussions and helpful advices.

The author is thanking deeply to Professor Bernhard Breit for giving him a chance to join the exciting and stimulating research group at the University of Freiburg from November 2009 to February 2010. He is also grateful to all members of Professor Breit’s research group for kind assistance during his stay at Freiburg.
The author is thankful to Matsubara group’s secretary, Ms. Kyoko Kumamoto, for her various supports.

Financial support from JSPS, Research Fellowship of the Japan Society for the Promotion of Science for Young Scientists, was indispensable, and the author would like to express his gratitude.

Special thanks are due to the former colleagues of Pfizer Nagoya Laboratories and all of the author’s friends. Without their encouragement, this thesis would not be completed.

Finally, the author would like to express his sincere appreciation to his family, especially to his father, Hiromi and his mother, Terumi for their constant assistance and encouragement.

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