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A Systematic Study of the Hydride Reduction of Cyclopropyl Ketones with Structurally Simplified Substrates. Highly Stereoselective Reductions of *Trans*-Substituted Cyclopropyl Ketones via the Bisected *s-Cis* Conformation

Yuji Kazuta,[†] Hiroshi Abe,[†] Tamotsu Yamamoto,[‡] Akira Matsuda,[†] and Satoshi Shuto*[,†]

Graduate School of Pharmaceutical Sciences, Hokkaido University, Kita-12, Nishi-6, Kita-ku, Sapporo 060-0812, Japan, and Institute for Life Science Research, Asahi Kasei Co., Ltd., Ohito-cho, Shizuoka 410-2321, Japan

shu@pharm.hokudai.ac.jp

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The stereoselective hydride reduction of the *cis*- and *trans*-substituted cyclopropyl ketones was systematically investigated using a series of structurally simplified substrates, *trans*-[*tert*-butyldiphenylsilyloxymethyl]cyclopropyl ketones **1a**−**e** and *trans*-(benzyloxymethyl)cyclopropyl methyl ketone (**2**), and the corresponding *cis* congeners **3a**,**b**,**e** and **4**. The results showed that, not only in the reduction of the *cis*-substituted cyclopropyl ketones but also in that of the *trans*-substituted ketones, high stereoselectivity can be realized when the substrate has a bulky substituent on the cyclopropane ring, even though it is attached to the position *trans* to the acyl moiety. Ab initio calculations based on the density functional theory (DFT) of cyclopropyl ketones showed that (1) the bisected *s-cis* and *s-trans* conformers were the only two minimum energy conformers, while the *s-cis* conformer was more stable than the *s-trans* and (2) a bulky alkyl group in the acyl moiety and a *cis* substituent on the cyclopropane ring made the bisected *s-cis* conformer much more stable. On the basis of these calculations and experimental results, it is likely that the more stable the bisected *s-cis* conformer of the substrate, the more stereoselective the hydride reduction. Thus, the stereochemistry can be explained by hydride attack on the bisected *s-cis* conformation of the substrate from the less-hindered face. The predictability of the stereochemical results is predicated on the bisected *s-cis* transition-state model, which is very important from the viewpoint of synthetic organic chemistry.

Introduction

Cyclopropanes are important as key fragments in many natural products and as synthetic key intermediates due to the ease of their ring-opening.[1−4] The cyclopropane ring is also very useful for restricting the conformation of biologically active compounds to improve the activity.[5] Therefore, considerable effort has been devoted to developing efficient methods for preparing cyclopropane derivatives.[1−6]

We recently devised a new method for restricting the conformation of cyclopropane derivatives based on the fact that adjacent substituents on the ring exert significant mutual steric repulsion because of their eclipsed conformation to each other, which has been successfully used in the design of NMDA (*N*-methyl-D-aspartic acid) receptor antagonists.[6] In the course of these continuous studies, we have needed a highly stereoselective method for the reduction of cyclopropyl ketones.

It is known that cyclopropanes adjacent to an unsaturated bond, such as vinylcyclopropanes, cyclopropyl ketones, or cyclopropanecarbaldehydes, preferentially exist in the bisected *s-trans* and *s-cis* conformations, as shown

* To whom correspondence and reprint requests should be addressed. Phone: +81-11-706-3228. Fax: +81-11-706-498.

[†] Hokkaido University.

[‡] Asahi Kasei Co., Ltd.

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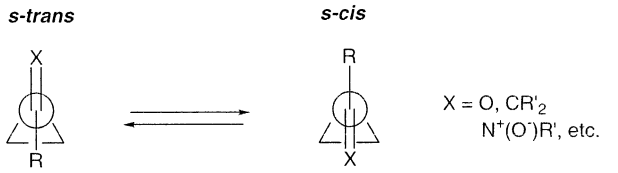

FIGURE 1. *s-Cis*- and *s-trans*-bisected conformations of α,β-unsaturated cyclopropanes.

in Figure 1, due to the characteristic stereoelectronic effects of the cyclopropane ring.[1a,7,8] We recently found that a *C*-cyclopropylnitrone was also stable in the bisected conformation.[6e,f] Several groups including ours have reported that reduction of cyclopropyl ketones by nucleophilic hydride reagents is possible to proceed stereoselectively, which has been considered to occur via the stereoelectronically stable bisected conformation.[8] These reactions are very useful for the stereoselective synthesis of cyclopropane derivatives having a stereogenic carbon center at the position adjacent to the cyclopropane ring. However, only limited examples of such stereoselective reductions of cyclopropyl ketones are known, and these are summarized in Tables 1 and 2.[8,9]

The cyclopropyl ketones having a substituent at the position *cis* to the acyl group on the cyclopropane ring, i.e., the *cis*-substituted cyclopropyl ketones **I**, are often stereoselectively reduced to form the corresponding *anti*-alcohols as the major product (Table 1).[8] On the other hand, the hydride reduction of cyclopropyl ketones without a substituent attached to the position *cis* to the acyl group on the cyclopropane ring, i.e., the *trans*-substituted cyclopropyl ketones **II**, usually occur with low to moderate stereoselectivity,[8b,10] except for an example using a *trans*-(phosphorylfluoromethyl)cyclopropyl ketone,[8f] and the stereochemical results do not seem readily predictable.[11] The previous examples of the *trans*-substituted cyclopropyl ketones are summarized in Table 2.

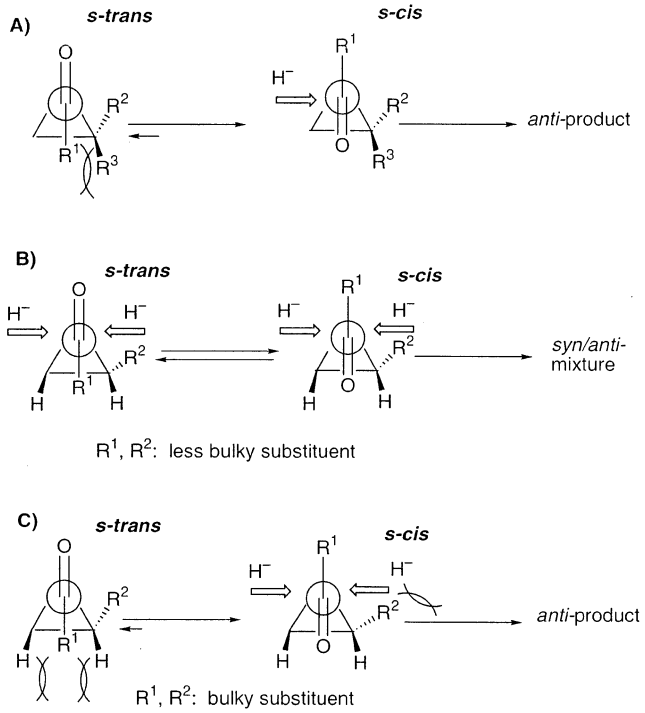

FIGURE 2. Conceivable reaction pathways of the hydride reductions of cyclopropyl ketones.

Our consideration on the hydride reduction of the cyclopropyl ketones is summarized in Figure 2. As described above, cyclopropyl ketones are conformationally stable in their bisected *s-cis* and *s-trans* conformations:[7] theoretical calculations[7f] and experimental[7b,c] studies indicate that the *s-cis* conformation seems to be favored over the *s-trans*. The preference for the *s-cis* conformer, as shown in Figure 2A, can be understood because in the *s-trans* conformer the alkyl group (R^1) in the acyl moiety is oriented toward the cyclopropyl moiety leading to increased steric repulsion for the *cis* substituent (R^3). In the *s-cis* conformation, the substituent (R^3) attached to the position *cis* to the acyl moiety would effectively hinder one side of the carbonyl to result in the stereoselective hydride attack from the less hindered side (Figure 2A).

On the other hand, as shown in Figure 2B, in the *s-cis* conformation of the *trans*-substituted cyclopropyl ketones, the steric repulsion due to the alkyl group (R1) would be less, because of the absence of the *cis* substituent on the cyclopropane ring, than in that of the corresponding *cis*-substituted ketones. Accordingly, the *s-cis* and the *s-trans* conformers might be similarly stable in the *trans*-cyclopropyl ketones, which may be why their

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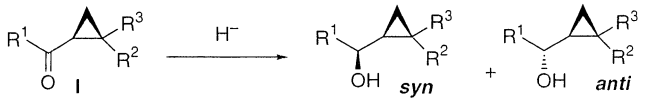
(11) Stereocontrol in carbon−nucleophile additions to *trans*-cyclopropyl carbonyls is also known to be exceedingly difficult, see: Critcher, D. J.; Connolly, S.; Wills, M. *J. Org. Chem*. **1997**, *62*, 6638−6657.

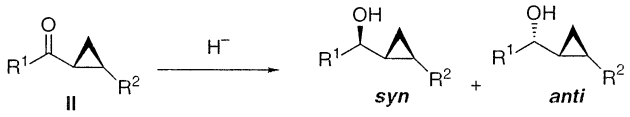
TABLE 1. Hydride Reductions of the *Cis*-Substituted Cyclopropyl Ketones Reported Previously



substrate	R^1	R^2	R^3	conditions	yield (%)	*syn*/*anti*	ref
I	Me	$CH{=}CH_2$	H	$LiAlH_4$ (0.5 equiv), 35 °C	80	1:16	8a
I	Me	CO_2Me	CO_2Me	$NaBH_4/CeCl_3$[a]	99	only *anti*	8b
I	*n*-Pr	TMS	H	$LiAlH_4$ (1.1−1.5 equiv), 0 °C	48	1:15	8c
I	*c*-hexyl	Bu_3Sn	*n*-Bu	$LiAlH_4$ (1.1−1.5 equiv), 0 °C	88	1:15	8c
I	Et	$CONEt_2$	Ph	$NaBH_4$ (0.9 equiv), −20 °C	70	1:4	8d
I	Et	$CONEt_2$	Ph	L-Selectride (2.5 equiv), −78 °C	91	1:49	8d
I	Me	Me	$CF_2PO_3Et_2$	K-Selectride (1.1 equiv), −78 °C	57	1:99	8f

[a] The detailed reaction conditions were not reported in ref 8b.

TABLE 2. Hydride Reduction of the *Trans*-Substituted Cyclopropyl Ketones Reported Previously



substrate	R^1	R^2	conditions	yield (%)	*syn*/*anti*	ref
II	*c*-hexyl	TMS	$LiAlH_4$(1.1−1.5 equiv), 0 °C	60	1:2.5	8c
II	*c*-hexyl	*n*-Bu	$LiAlH_4$ (1.1−1.5 equiv), 0 °C	92	1:1	8c
II	*i*-Pr	*n*-Bu	$LiAlH_4$ (1.1−1.5 equiv), 0 °C	62	1:1	8c
II	allyl	CH_2OTBS	K-Selectride (2 equiv), −78 °C	92	1:9	9
II	Me	$CF_2PO_3Et_2$	K-Selectride (1.1 equiv), −78 °C	77	1:33	8f

hydride reductions are less stereoselective. However, when the alkyl group (R^1) in the acyl moiety is rather bulky, steric repulsion for the protons at the position cis to the acyl moiety in the *s-trans* conformation should increase to restrict the conformation to the *s-cis* form, as shown in Figure 2C, which may allow the reduction to proceed stereoselectively. We speculated that if the substituent (R^2) on the cyclopropane ring was significantly bulky, despite being trans to the acyl moiety, the hydride access to the stable bisected *s-cis* conformer from one side of the carbonyl could be sterically hampered due to the bulky R^2 substituent, as shown in Figure 2C. If this indeed occurs, the stereoselective hydride reduction of the *trans*-substituted cyclopropyl ketones can be realized, particularly by employing a bulky hydride reagent.

Based on these considerations, to develop a versatile stereoselective method for the reduction of cyclopropyl ketones, especially the *trans*-substituted cyclopropyl ketones, we performed a systematic study of the hydride reduction of cyclopropyl ketones, using the structurally simplified *trans*-substituted substrates **1** and **2** as well as their diastereomeric *cis*-substituted congeners **3** and **4** (Figure 3). Conformational analysis of the substrates was also studied to clarify the mode of the nucleophilic hydride reduction of the cyclopropyl ketones. In this paper, we describe the results of these studies.

Results and Discussion

Design and Synthesis of the Structurally Simplified Substrates. The cyclopropyl ketones used in the previous studies as the substrates bore sterically and stereoelectronically different functional groups affecting the stereochemical outcome, which might make the reaction mechanism somewhat difficult to understand.

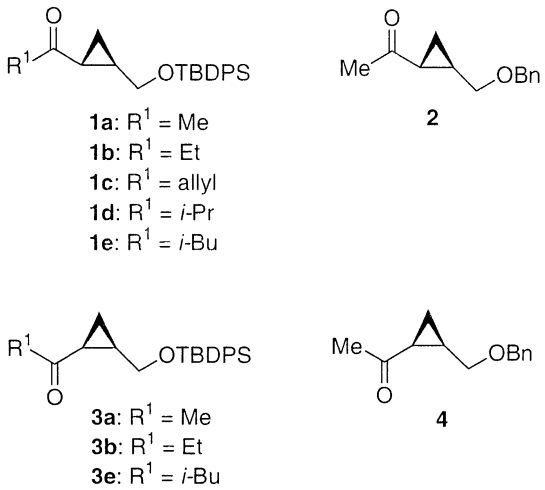
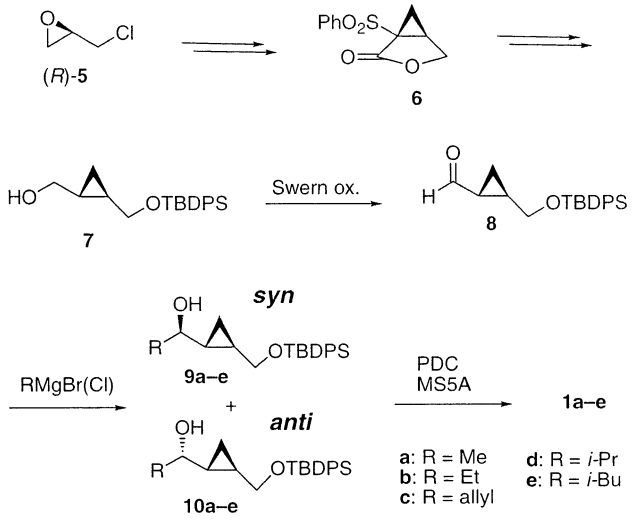


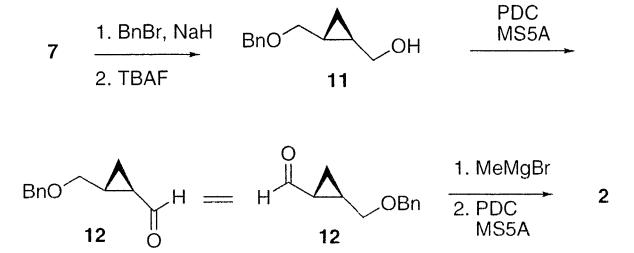
FIGURE 3. Structurally simplified cyclopropyl ketones as the reaction substrates.

Therefore, we designed structurally simplified cyclopropyl ketones as the reaction substrates, namely *trans*-[*tert*-butyldiphenylsilyl (TBDPS) oxymethyl]cyclopropyl ketones **1a**−**e** and *trans*-(benzyloxymethyl)cyclopropyl methyl ketone (**2**) (Figure 3) to investigate the above-mentioned hypothesis and also to realize the highly stereoselective hydride reduction of the *trans*-substituted cyclopropyl ketones. The hydride reduction of the corresponding *cis* substrates, **3a**,**b**,**e** and **4** (Figure 3), was likewise planned to compare the results with those of the *trans* substrates. Use of these simplified substrates would make the experimental stereochemical results readily understood. We decided to use these substrates in an optically active form since the stereochemistries of the

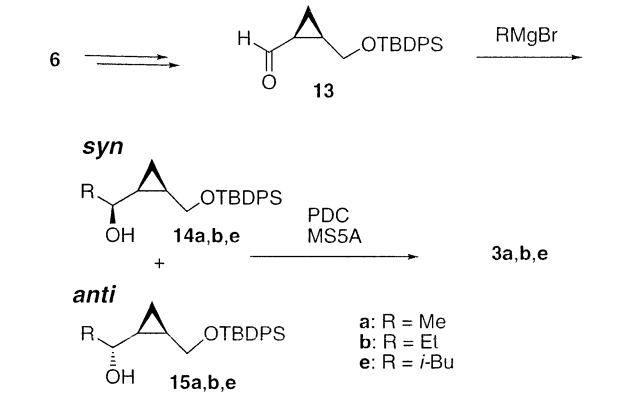
SCHEME 1



SCHEME 2



SCHEME 3



resulting secondary alcoholic products should be easily determined by employing the modified Mosher method.[12]

Syntheses of the substrates are shown in Schemes 1−4. We recently developed the versatile chiral cyclopropane intermediates **6** and its enantiomer ***ent*-6**, which were readily synthesized from (*R*)- or (*S*)-epichlorohydrin [(*R*)-**5** or (*S*)-**5**], respectively, and were effectively used for the synthesis of conformationally restricted analogues of histamine.[5] After conversion of the intermediate **6** into the *trans*-silyloxymethyl-substituted cyclopropanecarbaldehyde **8**, Grignard additions to it gave a mixture of the *syn*- and *anti*-alcohol products, **9a**−**e** and **10a**−**e**, PDC oxidations of which produced the corresponding cyclopropyl ketones **1a**−**e** having the *trans*-silyloxymethyl substituent (Scheme 1). The *trans*-1,2-bis(hydroxymethyl)cyclopropane derivative **7**[5] was converted to aldehyde **12**, from which the *trans*-methyl ketone **2** having a benzyloxymethyl substituent was prepared via successive Grignard addition and oxidation (Scheme 2). The *cis*-silyloxymethylcyclopropyl ketone substrates **3a**,**b**,**e** were prepared from aldehyde **13**[5] by the successive Grignard addition/oxidation procedure (Scheme 3). The *cis*-benzyloxymethyl-substituted cyclopropyl methyl ketone **4** was synthesized from ***ent*-13**, which was readily prepared from *S*-epichlorohydrin,[5] as shown in Scheme 4.

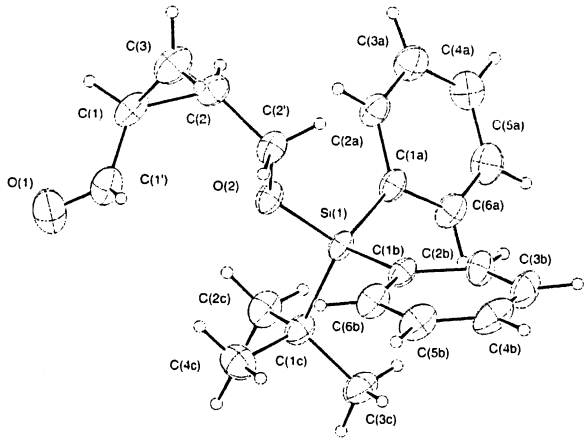


FIGURE 4. X-ray crystallographic structure of **3a**.

SCHEME 4

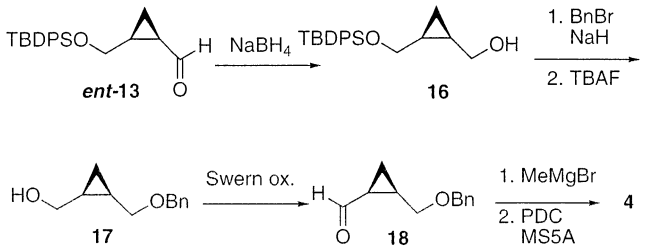


Figure 4 shows the X-ray crystallographic structure of the *O*-TBDPS-protected *cis*-cyclopropyl methyl ketone **3a**, which demonstrates that it exists in the bisected *s-cis*-conformation in the solid state.[13]

Conformation Analysis by DFT Calculations. We wanted to know whether the bisected *s-trans* and/or *s-cis* conformations would predominate in the substrates. Therefore, we examined the conformations of the model compounds of the substrates, i.e., cyclopropyl methyl ketone (**i**), the corresponding ethyl ketone (**ii**), *cis*-methylcyclopropyl methyl ketone (**iii**), and *trans*-methylcyclopropyl methyl ketone (**iv**), the structures of which are shown in Figure 5, by ab initio calculations based on the density functional theory (DFT) using the Gaussian 98 program.[14] The final optimizations were carried out at RB3LYP/6-31G(d). As a result, only two minimum energy conformers, which were in the *s-cis*- and *s-trans*-bisected conformations, were obtained for the each cyclopropyl ketone. The structures of the minimum energy

(12) The stereochemistries of the reduction products were determined by the modified Mosher's method (Ohtani, I.; Kusumi, T.; Kashman, Y.; Kakisawa, H. *J. Am. Chem. Soc.* **1991**, *113*, 4092−4096); see the Supporting Information.

(13) NOE experiments of the *trans*-ketone **1a** in $CDCl_3$ did not suggest a stable conformation in solution, and crystals of the *trans*-substituted ketones **1a**−**e** and **2** suitable for X-ray crystallographic analysis were not obtained.

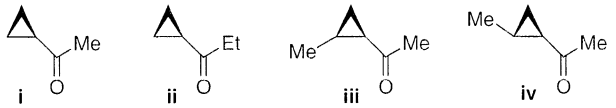


FIGURE 5. Model cyclopropyl ketones for ab initio calculations.

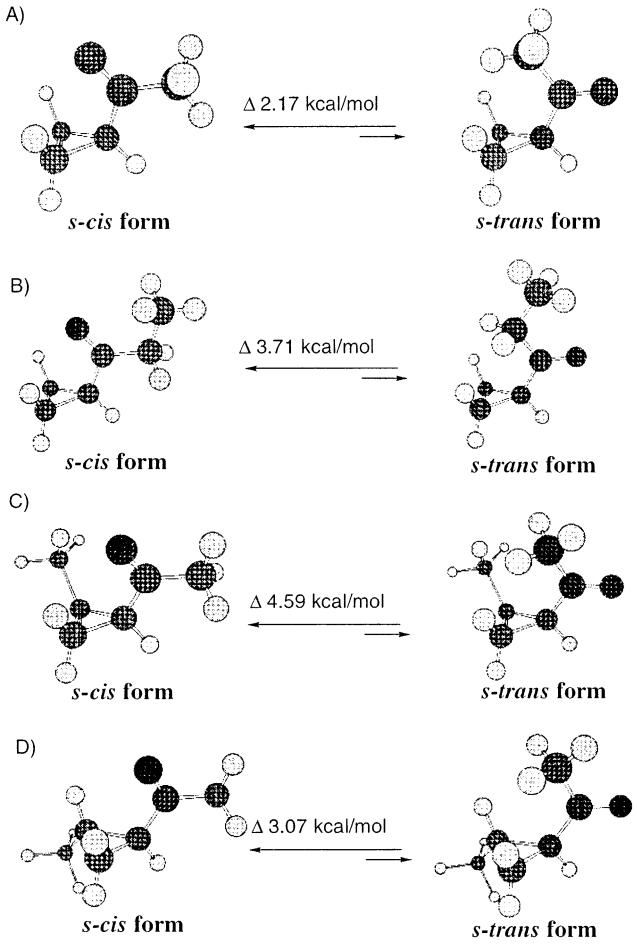
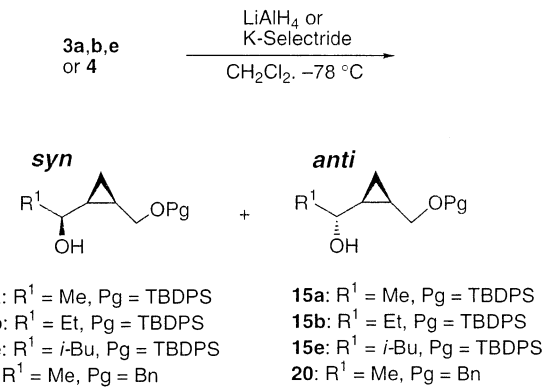


FIGURE 6. Minimum energy *s-cis* and *s-trans*conformers obtained by the ab initio calculations of the model cyclopropyl ketones **i** (A), **ii** (B), **iii** (C), and **vi** (D).

s-cis and *trans* conformers are shown in Figure 6. While the *s-cis* conformer was more stable than the corresponding *s-trans* conformer in all the four model ketones, the relative stability was rather different: the energy differences were 2.17 kcal/mol (**i**), 3.71 kcal/mol (**ii**), 4.59 kcal/mol (**iii**), and 3.07 kcal/mol (**iv**), respectively. These calculations showed that a bulky alkyl group in the acyl moiety plus a *cis* substituent on the cyclopropane ring make the *s-cis*-bisected conformer much more stable, as we expected. It may also be important that a substituent on the cyclopropane ring is able to stabilize the *s-cis* conformer even though it is attached to the position *trans* to the acyl moiety, based on the results of **i** and **iv**.

SCHEME 5



Hydride Reduction of the *Cis*-Substituted Cyclopropyl Ketones. Hydride reductions of the *cis*-substituted substrates **3a**,**b**,**e** and **4** were examined (Scheme 5). The reactions were performed with $LiAlH_4$ or K-Selectride (2.0 equiv) as the reducing reagent at −78 °C in CH_2Cl_2 (entries 1, 2, and 4−8) or THF (entry 3), and the results are summarized in Table 3.[12] All of the reductions of the cyclopropyl ketones **3a**,**b**,**e** having an *O*-TBDPS protecting group occurred highly stereoselectively to give the corresponding *anti* products (entries 1−7). However, when K-Selectride was used for the reduction of the ethyl or isobutyl ketones **3b** or **3e**, the reaction rate was quite slow and the yield was insufficient (entries 5 and 7). The reduction of the *O*-benzyl-protected methyl ketone **4** with K-Selectride also proceeded stereoselectively to give the *anti* product (entry 8); however, the stereoselectivity was somewhat decreased compared with that with the corresponding bulky *O*-silyl-protected methyl ketone **3a** (entry 2). These results with the structurally simplified *cis*-substituted substrates were similar to those of the previously reported hydride reductions of the cyclopropyl ketones having a *cis* substituent as summarized in Table 1.

Hydride Reduction of the *Trans*-Substituted Cyclopropyl Ketones. The hydride reductions of the *trans*-substituted cyclopropyl ketones **1a**−**e** and **2**, lacking the *cis* substituent on the cyclopropane ring, were next investigated, as shown in Scheme 6. The reactions were carried out with 2.0 equiv of a hydride reagent at −78 °C in CH_2Cl_2 (entries 1−4 and 6−14) or THF (entry 5), and the results are summarized in Table 4.[12] If the hydride attack on the substrate in the bisected *s-cis* conformation from its less hindered side indeed occurs, as shown in Figure 2C, the corresponding *anti* product should be selectively produced. First, the reaction was examined with the methyl ketone **1a** having an *O*-TBDPS protecting group by using several hydride reagents, i.e., $LiBH_4$, DIBAL-H, N-Selectride, K-Selectride, and KS-Selectride (entries 1−6). The reactions with $LiBH_4$, DIBAL-H, N-Selectride, or K-Selectride gave a diastereomeric mixture of the reduction products, i.e., the *syn*-alcohol **9a** and the *anti*-alcohol **10a**, in high yield (entries

(14) Gaussian 98, Revision A.6: Frisch, M. J.; Trucks, G. W.; Schlegel, H. B.; Scuseria, G. E.; Robb, M. A.; Cheeseman, J. R.; Zakrzewski, V. G.; Montgomery, Jr., J. A.; Stratmann, R. E.; Burant, J. C.; Dapprich, S.; Millam, J. M.; Daniels, A. D.; Kudin, K. N.; Strain, M. C.; Farkas, O.; Tomasi, J.; Barone, V.; Cossi, M.; Cammi, R.; Mennucci, B.; Pomelli, C.; Adamo, C.; Clifford, S.; Ochterski, J.; Petersson, G. A.; Ayala, P. Y.; Cui, Q.; Morokuma, K.; Malick, D. K.; Rabuck, A. D.; Raghavachari, K.; Foresman, J. B.; Cioslowski, J.; Ortiz, J. V.; Stefanov, B. B.; Liu, G.; Liashenko, A.; Piskorz, P.; Komaromi, I.; Gomperts, R.; Martin, R. L.; Fox, D. J.; Keith, T.; Al-Laham, M. A.; Peng, C. Y.; Nanayakkara, A.; Gonzalez, C.; Challacombe, M.; Gill, P. M. W.; Johnson, B.; Chen, W.; Wong, M. W.; Andres, J. L.; Gonzalez, C.; Head-Gordon, M.; Replogle, E. S.; Pople, J. A. Gaussian, Inc., Pittsburgh, PA, 1998.

TABLE 3. Hydride Reduction of the *Cis*-Substituted Cyclopropyl Ketones 3a,b,e and 4[a]

entry	substrate	R^1	Pg	reagent	time (h)	product	yield (%)	*syn*/*anti*[b]
1	**3a**	Me	TBDPS	$LiAlH_4$	1	**14a**, **15a**	90	1:31
2	**3a**	Me	TBDPS	K-Selectride	1	**15a**	99	only *anti*
3[c]	**3a**	Me	TBDPS	K-Selectride	1	**15a**	99	only *anti*
4	**3b**	Et	TBDPS	$LiAlH_4$	24	**14b**, **15b**	90 (8)[d]	1:35
5	**3b**	Et	TBDPS	K-Selectride	12	**15b**	51 (44)[d]	only *anti*
6	**3e**	*i*-Bu	TBDPS	$LiAlH_4$	24	**15e**	84 (8)[d]	only *anti*
7	**3e**	*i*-Bu	TBDPS	K-Selectride	30	**15e**	15 (85)[d]	only *anti*
8	**4**	Me	Bn	K-Selectride	1	**19**, **20**[e]	97	1:9.5

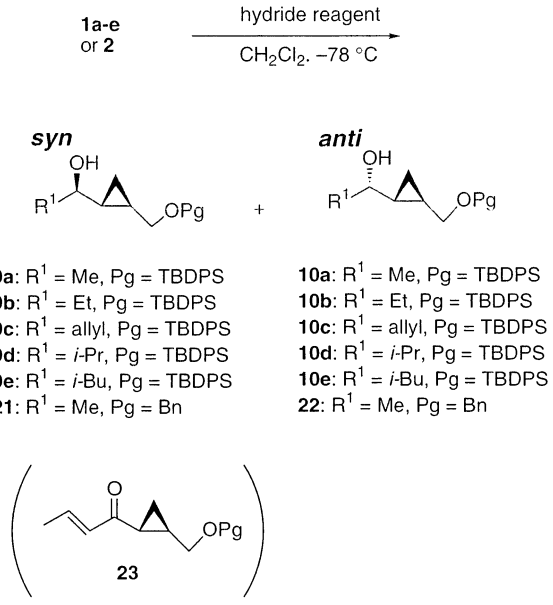
[a] Reaction was performed with 2.0 equiv of a hydride reagent in CH_2Cl_2 at −78 °C. [b] Determined by ^1H NMR. [c] Reaction was performed in THF. [d] Number in parentheses is yield of the substrate recovered. [e] The mixture of **19** and **20** was successively treated with H_2/Pd−C in MeOH and TBDPSCl/imidazole in DMF to give a mixture of **14a** and **15a**, which confirmed the structure of the major product **20** as the *anti*-alcohol.

TABLE 4. Hydride Reduction of the *Trans*-Substituted Cyclopropyl Ketones 1a−e and 2[a]

entry	substrate	R^1	Pg	reagent	time (h)	products	yield (%)	*syn*/*anti*[b]
1	**1a**	Me	TBDPS	$LiBH_4$	5	**9a**, **10a**	90	1:1.4
2	**1a**	Me	TBDPS	DIBAL-H	0.5	**9a**, **10a**	87	1:2.2
3	**1a**	Me	TBDPS	N-Selectride	0.5	**9a**, **10a**	85	1:3.5
4	**1a**	Me	TBDPS	K-Selectride	1	**9a**, **10a**	93	1:3.4
5[c]	**1a**	Me	TBDPS	K-Selectride	0.5	**9a**, **10a**	91	1:3.6
6	**1a**	Me	TBDPS	KS-Selectride	8	**10a**	88 (3)[d]	only *anti*
7	**1b**	Et	TBDPS	K-Selectride	1	**9b**, **10b**	98	1:4.3
8	**1b**	Et	TBDPS	KS-Selectride	8	**10b**	8 (90)[d]	only *anti*
9	**1c**	allyl	TBDPS	K-Selectride	8	**9c**, **10c**	89	1:4.6
10	**1c**	allyl	TBDPS	KS-Selectride	8	**23**	69[e]	−
11	**1d**	*i*-Pr	TBDPS	K-Selectride	1	**9d**, **10d**	92	1:19
12	**1e**	*i*-Bu	TBDPS	K-Selectride	5	**9e**, **10e**	81 (13)[d]	1:49
13	**2**	Me	Bn	K-Selectride	1	**21**, **22**[f]	92	1:1.6
14	**2**	Me	Bn	KS-Selectride	5	**21**, **22**[f]	80 (7)[d]	1:2.3

[a] Reaction was performed with 2.0 equiv of a hydride reagent in CH_2Cl_2 at −78 °C. [b] Determined by ^1H NMR. [c] Reaction was performed in THF. [d] Number in parentheses is yield of the substrate recovered. [e] The yield of enone **23**. [f] The mixture of **21** and **22** was successively treated with H_2/Pd−C in MeOH and TBDPSCl/imidazole in DMF to give a mixture of **9a** and **10a**, which confirmed the structure of the major product **22** as the *anti*-alcohol.

SCHEME 6



1−5). Although reduction by $LiBH_4$ was almost nonstereoselective (entry 1), reductions with DIBAL-H, N-Selectride, and K-Selectride produced the expected *anti* product **10a** with some stereoselectivity (entries 2−5, *syn*/*anti* = 1:2.2−1.3:5). When KS-Selectride was used, the reduction of **1a** proceeded with high stereoselectivity to give the *anti*-alcohol **10a** as the sole product in high yield (entry 6). The reduction by KS-Selectride proceeded slowly and a trace of the substrate was recovered, probably due to the significant bulkiness of the reagent. The reduction of the corresponding ethyl ketone **1b** by KS-Selectride hardly occurred to give the *anti* product in only 8% yield along with 90% yield of the recovered substrate (entry 8). Similarly the reduction of the allyl ketone **1c** by KS-Selectride did not proceed and the *endo* double bond of the substrate migrated to give the corresponding enone **23** in 69% yield (entry 10). However, K-Selectride rather effectively reduced the ethyl ketone **1b** and the allyl ketone **1c** to give the corresponding *anti*-alcohols **10b** and **10c** as the major products (entries 7 and 9). The K-Selectride reductions of the isopropyl ketone **1d** and the isobutyl ketone **1e** occurred with high stereoselectivity to give the expected *anti* products **10d** and **10e** (entries 11 and 12, *syn*/*anti* = 1:19 and 1:49, respectively). On the other hand, when the *O*-silyl-protecting group of the substrate was replaced with an *O*-benzyl group, i.e., substrate **3**, the stereoselectivity was significantly lowered (entries 13 and 14). Thus, we proved that highly stereoselective reduction of the *trans*-substituted ketones occurs when the substrate has a bulky *O*-silyl protecting group.

Discussion

This is the first study to investigate experimentally stereoselectivity in the hydride reduction of the *cis*- and *trans*-substituted cyclopropyl ketones in a systematic manner. The conformations of the substrates, which are very important to understand the mechanism of the

reactions, were also analyzed. Therefore, the results obtained from this study can be useful for discussing and understanding the reaction pathways.

The experimental results showed that: (1) the *cis*-substituted cyclopropyl ketones are reduced with high stereoselectivity to give the corresponding *anti* products and (2) the *trans*-substituted ketones give the corresponding *anti* products also with high stereoselectivity when the substrate has a bulky *O*-silyl protecting group even though it is attached to the position *trans* to the acyl moiety. The DFT calculations of the model cyclopropyl ketones suggested that: (1) the bisected *s-cis* and *s-trans* conformers are the only two minimum energy conformers, while the *s-cis* conformer is more stable than the *s-trans*; (2) a bulky alkyl group in the acyl moiety and a *cis* substituent on the cyclopropane ring make the *s-cis*-bisected conformer much more stable; and (3) a *trans* substituent also stabilizes the *s-cis*-bisected conformer, while the effect is smaller than that by the corresponding *cis* substituent. On the basis of these experimental and calculated results, it is likely that the more stable the bisected *s-cis* conformer in the substrate, the more stereoselective the hydride reduction, as we hypothesized. Accordingly, the stereoselective hydride reduction of cyclopropyl ketones would be explained by the hydride attack on the less hindered side of the bisected *s-cis* conformation.[15]

On the other hand, the stereochemistry of reduction of cyclopropyl ketones by nucleophilic hydride agents is also in accord with that predicted by the Felkin−Anh model as previously described by Reiser in an excellent review on the Felkin−Anh model.[16] However, the present experimental and theoretical studies employing structurally simplified substrates as well as the previous studies showing the significant stability of the bisected conformations[7] suggest that the reductions are likely to proceed via the bisected conformation-like transition state effectively stabilized by the characteristic stereoelectronic feature of the cyclopropane ring.[15] Further studies are needed to confirm the reaction mechanism.

In summary, this study shows that the highly stereoselective reduction of the *trans*-substituted cyclopropyl ketones can be realized when the substrate has a bulky substituent on the cyclopropane ring, even though it is attached to the position trans to the acyl moiety. The stereochemistry can be explained by the hydride attack on the bisected *s-cis* conformation of the substrate from the less-hindered face. The predictability of the stereochemical results based on the bisected *s-cis* transition-state model is very important from the viewpoint of synthetic organic chemistry.

Experimental Section

Melting points are uncorrected. NMR spectra were recorded at 400, 500 MHz (^{1}H) and at 125 MHz (^{13}C) and are reported in ppm downfield from Me_4Si. Mass spectra were obtained by electron ionization (EI) or the fast atom bombardment (FAB) or electrospray ionization (ESI) method. Thin-layer chromatography was performed on Merck coated plate $60F_{254}$. Silica gel chromatography (gravity) was performed with Merck silica gel 5715 or 9385 (neutral). Reactions were carried out under an argon atmosphere otherwise noted.

(1*R*,2*R*)-2-Benzyloxymethyl-1-hydroxymethylcyclopropane (11). After a mixture of **7** (2.38 g, 7.00 mmol) and NaH (60% in paraffin liquid, 336 mg, 8.40 mmol) in THF (10 mL) was stirred at 0 °C for 1 h, BnBr (1.67 mL, 14.0 mmol) was added, and the resulting mixture was further stirred at room temperature for 2 days. After addition of MeOH, the mixture was partitioned between AcOEt and H_2O, and the organic layer was washed with brine, dried (Na_2SO_4), and evaporated to give a residual oil. A mixture of the oil and TBAF (1.0 M in THF, 10.5 mL, 10.5 mmol) in THF (10 mL) was stirred at room temperature for 3 h, and the resulting mixture was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), evaporated, and purified by column chromatography (silica gel; AcOEt/hexane 1:9) to give **11** (737 mg, 55%) as a colorless liquid: $[\alpha]^{23}_D$ −15.24 (*c* 1.930, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.44 (2 H, m), 0.97−1.04 (2 H, m), 2.19 (1 H, br s), 3.26 (1 H, dd, J = 7.0, 10.0 Hz), 3.38 (1 H, m), 3.41 (1 H, dd, J = 6.0, 10.0 Hz), 3.49 (1 H, m), 4.52 (2 H, s), 7.26−7.36 (5 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.0, 16.7, 19.8, 66.2, 72.6, 73.5, 127.6, 127.7, 128.4, 138.3; LR-MS (EI) *m*/*z* 215 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.87; H, 8.37.

(1*R*,2*R*)-2-Benzyloxymethyl-1-formylcyclopropane (12). To a solution of oxalyl chloride (0.52 mL, 6.0 mmol) in CH_2Cl_2 (5 mL) was added slowly a solution of DMSO (0.85 mL, 24 mmol) in CH_2Cl_2 (10 mL) at −78 °C over 30 min. To the resulting mixture was added dropwise a solution of **11** (577 mg, 3.00 mmol) in CH_2Cl_2 (5 mL) at −78 °C, the mixture was stirred at the same temperature for 1 h, and then Et_3N (3.37 mL, 24.0 mmol) was added. The mixture was further stirred at the same temperature for 30 min, and then saturated NH_4Cl and CH_2Cl_2 was added. The organic layer separated was washed with brine, dried (Na_2SO_4), evaporated, and purified by column chromatography (silica gel; AcOEt/hexane 1:15) to give **12** as a colorless liquid (503 mg, 88%): $[\alpha]^{23}_D$ +43.37 (*c* 0.520, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.07 (1 H, m), 1.32 (1 H, m), 1.79−1.86 (2 H, m), 3.41 (1 H, dd, J = 6.0, 10.5 Hz), 3.49 (1 H, dd, J = 5.5, 10.5 Hz), 4.52 (2 H, s), 7.26−7.36 (5 H, m), 9.10 (1 H, d, J = 4.9 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4, 21.5, 28.0, 70.9, 72.8, 127.6, 127.7, 128.4, 137.9, 200.2; LR-MS (ESI) *m*/*z* 213 ((M + Na)$^+$, 5.0). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 75.57; H, 7.54.

(1*S*,2*R*)-1-[(*tert*-Butyldiphenylsilyloxy)methyl]-2-hydroxymethylcyclopropane (16). A mixture of ***ent*-13**[5] (1.02 g, 3.00 mmol) and $NaBH_4$ (226 mg, 6.00 mmol) in THF (10 mL) was stirred at room temperature for 1 h, and then the mixture was neutralized with AcOH. The solvent was evaporated, and the residue was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), evaporated, and purified by column chromatography (silica gel; AcOEt/hexane 1:9) to give **16** as a colorless oil (1.00 g, 98%): $[\alpha]^{24}_D$ −12.04 (*c* 1.280, $CHCl_3$); LR-MS (EI) *m*/*z* 283 ((M − *t*-Bu)$^+$, 3.5%). Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 73.76; H, 8.34. The ^{1}H NMR spectrum of **16** was in accord with that of the enantiomer of **16** reported previously.[5]

(1*S*,2*R*)-2-Benzyloxymethyl-1-hydroxymethylcyclopropane (17). Compound **17** was prepared from **16** (681 mg, 2.00 mmol) as described for **11**. After purification by column chromatography (silica gel; AcOEt/hexane 1:9), **17** was obtained as a colorless liquid (246 mg, 64%): $[\alpha]^{23}_D$ −83.56 (*c* 1.450, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.21 (1 H, m), 0.81 (1 H, m), 1.28−1.40 (2 H, m), 3.13−3,20 (3 H, m), 3.92 (1 H, dd, J = 5.4, 10.6 Hz), 3.94 (1 H, m), 4.51 (1 H, d, J = 11.7 Hz), 4.58 (1 H, d, J = 11.7 Hz), 7.28−7.37 (5 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.6, 14.7, 18.4, 63.0, 70.7, 73.1, 127.9,

(15) The conformation of the transition state and the intermediate can be strongly influenced by conformational effects which stabilize the ground state conformation, for examples see: (a) Pothier, N.; Goldstein, S.; Deslongchamps, P. *Helv. Chim Acta* **1992**, 75, 604−620. (b) Romero, J. A. C.; Tabacco, S. A.; Woerpel, K. A. *J. Am. Chem. Soc.* **2000**, *122*, 168−189. (c) Abe, H.; Shuto, S.; Matsuda, A. *J. Am. Chem. Soc.* **2001**, *123*, 11870−11882. (d) Tamura, A.; Abe, H.; Matsuda, A. Shuto, S. *Angew. Chem., Int. Ed.* **2003**, *42*, 1021−1023.

(16) Mengel, A.; Reiser O. *Chem. Rev.* **1999**, *99*, 1191−1223.

127.9, 128.5, 137.4; LR-MS (EI) *m*/*z* 215 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{12}H_{16}O_2$: C, 74.97; H, 8.39. Found: C, 74.66; H, 8.23.

(1*S*,2*R*)-2-Benzyloxymethyl-1-formylcyclopropane (18). Compound **18** was prepared from **17** (192 mg, 1.00 mmol) as described for **12**. After purification by column chromatography (silica gel; AcOEt/hexane 1:15), **18** was obtained as a colorless liquid (132 mg, 69%): $[\alpha]^{23}_D$ +26.01 (*c* 1.020, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.24 (1 H, m), 1.33 (1 H, m), 1.85 (1 H, m), 2.04 (1 H, m), 3.43 (1 H, dd, J = 8.6, J = 10.4 Hz), 3.81 (1 H, dd, J = 5.7, J = 10.4 Hz), 4.45 (1 H, d, J = 11.8 Hz), 4.49 (1 H, d, J = 11.8 Hz), 7.26−7.36 (5 H, m), 9.47 (1 H, d, J = 4.5 Hz); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.4, 23.7, 26.8, 67.9, 73.0, 127.7, 127.8, 128.4, 138.0, 200.4; LR-MS (ESI) *m*/*z* 213 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{12}H_{14}O_2$: C, 75.76; H, 7.42. Found: C, 76.12; H, 7.56.

General Procedure for the Grignard Reaction of Aldehyde 8, 12, 13, or 18. A mixture of an aldehyde (1.0 mmol) and a Grignard reagent (2.0 equiv) in THF (10 mL) was stirred at room temperature for 5 h, and then MeOH was added. The mixture was evaporated, and the residue was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), evaporated, and purified by column chromatography (silica gel; AcOEt/hexane 1:9) to give a *syn*/*anti* mixture of the corresponding Grignard addition products. A part of the mixtures obtained from *O*-TBDPS aldehydes **8** and **13** was separated by column chromatography (silica gel; AcOEt/hexane 1:19) to give the *syn* and the *anti* product in a pure form, respectively. However, the mixture obtained form *O*-benzyl aldehydes **12** and **18** could not be separated into the pure diastereomers. The *syn*/*anti* mixture was used for the next PDC oxidation.

General Procedure for the PDC Oxidation. A mixture of the *syn*/*anti* mixture of the Grignard reaction products (1.0 mmol), PDC (752 mg, 2.0 mmol), and molecular sieves 5A (200 mg) in CH_2Cl_2 (20 mL) was stirred at room temperature for 5 h, and the resulting mixture was filtered through a pad of Florisil and Celite. The filtrate was evaporated, and the residue was purified by column chromatography (silica gel; AcOEt/hexane 1:19−1:9) to give the corresponding ketone.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxyethyl]cyclopropane (9a) and (1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxyethyl)-cyclopropane (10a). From the mixture of **9a** and **10a** (380 mg), **9a** (213 mg), and **10a** (157 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **9a**: $[\alpha]^{18}_D$ −11.77 (*c* 1.220, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.40 (1 H, m), 0.57 (1 H, m), 0.81 (1 H, m), 0.94 (1 H, m), 1.05 (9 H, s), 1.27 (3 H, d, J = 6.2 Hz), 1.45 (1 H, br s), 3.17 (1 H, dq, J = 4.4 Hz, $J_{1',2'}$ = 6.2 Hz), 3.41 (1 H, dd, J = 6.6, 10.5 Hz), 3.68 (1 H, dd, J = 5.5, 10.5 Hz), 7.36−7.46 (6 H, m), 7.66−7.67 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.12, 18.64, 19.26, 22.63, 25.02, 26.88, 66.40, 71.97, 127.53, 129.51, 133.75, 133.77, 135.49; LR-MS (EI) *m*/*z* 297 ((M − *t*-Bu)$^+$, 19.0%). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.46; H, 8.41. **10a**: $[\alpha]^{19}_D$ −9.00 (*c* 0.660, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.39 (2 H, m), 0.76 (1 H, m), 1.01 (1 H, m), 1.05 (9 H, s), 1.23 (3 H, d, J = 6.2 Hz), 1.54 (1 H, br s), 3.15 (1 H, dq, J = 6.2, 7.8 Hz), 3.37 (1 H, dd, J = 6.2, 10.6 Hz), 3.71 (1 H, dd, J = 5.6, 10.6 Hz), 7.37−7.44 (6 H, m), 7.66−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.4, 19.3, 19.4, 22.2, 25.4, 26.9, 66.7, 71.7, 127.6, 129.5, 133.7, 135.5; LR-MS (EI) *m*/*z* 297 ((M − *t*-Bu)$^+$, 6.0). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.47; H, 8.51.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxypropyl]cyclopropane (9b) and (1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxypropyl]-cyclopropane (10b). From the mixture of **9b** and **10b** (290 mg), **9b** (150 mg) and **10b** (129 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **9b**: $[\alpha]^{21}_D$ −16.50 (*c* 1.350, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.39 (1 H, m), 0.45 (1 H, m), 0.81 (1 H, m), 0.98 (3 H, t, J = 7.5 Hz), 0.99 (1 H, m), 1.05 (9 H, s), 1.46 (1 H, br s), 1.62 (2 H, m), 2.87 (1 H, m), 3.44 (1 H, dd, J = 6.7, 10.7 Hz), 3.68 (1 H, dd, J = 6.6, 10.7 Hz), 7.36−7.43 (6 H, m), 7.65−7.67 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.30, 10.05, 18.94, 19.19, 23.27, 26.84, 30.13, 66.45, 77.15, 127.60, 129.57, 133.88, 135.59; LR-MS (ESI) *m*/*z* 391 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 75.95; H, 8.75. Found: C, 75.70; H, 8.54. **10b**: $[\alpha]^{22}_D$ −10.52 (*c* 1.330, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.43 (2 H, m), 0.75 (1 H, m), 0.96 (3 H, t, J = 7.5 Hz), 1.01 (1 H, m), 1.05 (9 H, s), 1.51 (1 H, br s), 1.59 (2 H, m), 2.88 (1 H, m), 3.35 (1 H, dd, J = 7.4, 10.7 Hz), 3.73 (1 H, dd, J = 5.6, 10.7 Hz), 7.37−7.44 (6 H, m), 7.66−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.8, 10.0, 18.6, 19.2, 23.7, 26.9, 29.7, 66.8, 76.8, 127.6, 129.6, 133.9, 135.6; LR-MS (ESI) *m*/*z* 391 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.78; H, 8.99.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxy-3-butenyl]cyclopropane (9c) and (1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxy-3-butenyl]cyclopropane (10c). From the mixture of **9c** and **10c** (130 mg), **9c** (66 mg) and **10c** (56 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **9c**: $[\alpha]^{25}_D$ −17.88 (*c* 1.560, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.44 (1 H, m), 0.54 (1 H, m), 0.84 (1 H, m), 0.96 (1 H, m), 1.05 (9 H, s), 1.62 (1 H, br s), 2.32 (1 H, m), 2.42 (1 H, m), 3.01 (1 H, m), 3.46 (1 H, dd, J = 6.5, 10.7 Hz), 3.66 (1 H, dd, J = 5.6, 10.7 Hz), 5.11 (2 H, m), 5.89 (1 H, m), 7.36−7.44 (6 H, m), 7.65−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.8, 18.7, 19.2, 22.9, 26.9, 41.9, 66.2, 75.0, 117.6, 127.6, 129.6, 133.9, 134.9, 135.6; LR-MS (EI) *m*/*z* 323 ((M − *t*-Bu)$^+$, 2.5). Anal. Calcd for $C_{24}H_{32}O_2Si$: C, 75.74; H, 8.47. Found: C, 75.52; H, 8.54. **10c**: $[\alpha]^{24}_D$ −12.66 (*c* 1.090, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.43 (2 H, m), 0.77 (1 H, m), 1.04 (1 H, m), 1.05 (9 H, s), 1.59 (1 H, br s), 2.29 (1 H, m), 2.37 (1 H, m), 3.05 (1 H, m), 3.41 (1 H, dd, J = 6.9, 10.6 Hz), 3.70 (1 H, dd, J = 5.7, 10.6 Hz), 5.08−5.14 (2 H, m), 5.18 (1 H, m), 7.36−7.43 (6 H, m), 7.66−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.6, 18.8, 19.2, 23.2, 26.9, 41.4, 66.7, 74.4, 117.0, 127.6, 129.6, 133.9, 134.9, 135.6; LR-MS (EI) *m*/*z* 323 ((M − *t*-Bu)$^+$, 7.0). Anal. Calcd for $C_{24}H_{32}O_2Si$: C, 75.74; H, 8.47. Found: C, 75.65; H, 8.52.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxy-2-methylpropyl]cyclopropane (9d) and (1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxy-2-methylpropyl]cyclopropane (10d). From the mixture of **9d** and **10d** (120 mg), **9d** (59 mg) and **10d** (52 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **9d**: $[\alpha]^{26}_D$ −22.28 (*c* 1.850, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.39 (1 H, m), 0.43 (1 H, m), 0.86 (1 H, m), 0.99 (3 H, d, J = 6.8 Hz), 1.00 (3 H, d, J = 6.8 Hz), 1.01 (1 H, m), 1.04 (9 H, s), 1.40 (1 H, br s), 1.81 (1 H, m), 2.66 (1 H, dd, J = 6.0, 8.8 Hz), 3.48 (1 H, dd, J = 6.6, 10.7 Hz), 3.68 (1 H, dd, J = 5.6, 10.7 Hz), 7.36−7.44 (6 H, m), 7.65−7.67 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.0, 18.4, 18.7, 19.2, 19.7, 21.3, 26.8, 34.5, 66.4, 80.9, 127.6, 129.6, 133.8, 133.8, 135.6, 135.6; LR-MS (EI) *m*/*z* 364 ((M − H_2O)$^+$, 4.0). Anal. Calcd for $C_{24}H_{34}O_2Si$: C, 75.34; H, 8.96. Found: C, 75.25; H, 9.10. **10d**: $[\alpha]^{24}_D$ −8.03 (*c* 1.170, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.47 (2 H, m), 0.77 (1 H, m), 0.96 (3 H, d, J = 6.8 Hz), 0.97 (3 H, d, J = 6.8 Hz), 1.00 (1 H, m), 1.05 (9 H, s), 1.47 (1 H, br s), 1.78 (2 H, m), 2.67 (1 H, dd, J' = 5.9, 8.5 Hz), 3.30 (1 H, dd, J = 7.6, 10.6 Hz), 3.77 (1 H, dd, J = 5.4, 10.6 Hz), 7.35−7.44 (6 H, m), 7.66−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.7, 18.2, 18.4, 18.6, 19.2, 21.9, 27.0, 34.2, 66.9, 80.5, 127.7, 129.6, 133.9, 135.6; LR-MS (EI) *m*/*z* 364 ((M − H_2O)$^+$, 2.0). Anal. Calcd for $C_{24}H_{34}O_2Si$: C, 75.34; H, 8.96. Found: C, 75.21; H, 9.01.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxy-3-methylbutyl]cyclopropane (9e) and (1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxy-3-methylbutyl]cyclopropane (10e). From the mixture of **9e** and **10e** (197 mg), **9e** (122 mg) and **10e** (61 mg) were obtained

in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **9e**: $[\alpha]^{24}_D$ −8.15 (*c* 1.260, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.39 (1 H, m), 0.46 (1 H, m), 0.78 (1 H, m), 0.88 (3 H, d, J = 6.6 Hz), 0.91 (3 H, d, J = 6.6 Hz), 0.96 (1 H, m), 1.05 (9 H, s), 1.40 (1 H, br s), 1.43 (1 H, m), 1.54 (1 H, m), 1.86 (1 H, m), 3.00 (1 H, m), 3.40 (1 H, dd, J = 6.9, 10.6 Hz), 3.68 (1 H, dd, J = 5.4, 10.6 Hz), 7.36−7.44 (6 H, m), 7.65−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.5, 18.9, 19.2, 22.2, 23.3, 24.3, 24.5, 26.8, 46.6, 66.5, 73.8, 127.6, 129.6, 133.9, 135.6; LR-MS (FAB) *m*/*z* 419 ((M − *t*-Bu)$^+$, 10.0). Anal. Calcd for $C_{25}H_{36}O_2Si$: C, 75.70; H, 9.15. Found: C, 75.58; H, 9.21. **10e**: $[\alpha]^{24}_D$ −19.08 (*c* 1.280, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.42 (2 H, m), 0.75 (1 H, m), 0.89 (3 H, d, J = 6.6 Hz), 0.97 (3 H, d, J = 6.6 Hz), 1.04 (1 H, m), 1.07 (9 H, s), 1.34 (1 H, m), 1.45 (1 H, br s), 1.52 (1 H, m), 1.82 (1 H, m), 3.02 (1 H, m), 3.34 (1 H, dd, J = 7.2, 10.7 Hz), 3.77 (1 H, dd, J = 5.6, 10.7 Hz), 7.37−7.44 (6 H, m), 7.65−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.7, 18.9, 19.2, 22.2, 23.5, 24.5, 24.6, 26.9, 46.2, 66.8, 73.5, 127.6, 129.6, 133.9, 135.6; LR-MS (FAB) *m*/*z* 419 ((M − *t*-Bu)$^+$, 3.0%). Anal. Calcd for $C_{25}H_{36}O_2Si$: C, 75.70; H, 9.15. Found: C, 75.55; H, 9.14.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxyethyl]cyclopropane (14a) and (1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxyethyl]-cyclopropane (15a). From the mixture of **14a** and **15a** (160 mg), **14a** (105 mg) and **15a** (52 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **14a**: $[\alpha]^{20}_D$ +5.04 (*c* 1.010, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.21 (1 H, m), 0.69 (1 H, m), 1.03 (1 H, m), 1.06 (9 H, s), 1.24 (1 H, m), 1.39 (3 H, d, J = 6.2 Hz), 3.52 (1 H, dd, J = 8.8, 11.2 Hz), 3.53 (1 H, m), 3.85 (1 H, dd, J = 6.9, J = 11.2 Hz), 7.37−7.44 (6 H, m), 7.65−7.70 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.68, 18.50, 19.17, 23.74, 24.57, 26.82, 64.22, 68.48, 127.63, 127.66, 129.63, 133.70, 133.74, 135.54, 135.60; LR-MS (ESI) *m*/*z* 297 ((M − *t*-Bu)$^+$, 1.5). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.64; H, 8.62. **15a**: $[\alpha]^{19}_D$ +12.66 (*c* 0.820, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.10 (1 H, m), 0.68 (1 H, m), 1.06 (9 H, s), 1.13−1.26 (2 H, m), 1.37 (3 H, d, J = 6.1 Hz), 3.35 (1 H, dd, J = 11.0, 11.4 Hz), 3.51 (1 H, m), 3.99 (1 H, br s), 4.10 (1 H, dd, J = 5.0, 11.4 Hz), 7.35−7.46 (6 H, m), 7.68−7.74 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.2, 17.5, 19.0, 21.9, 24.8, 26.8, 63.7, 68.9, 127.8, 127.8, 129.8, 129.9, 132.9, 132.9, 135.5, 135.6; LR-MS (ESI) *m*/*z* 297 ((M − *t*-Bu)$^+$, 1.0). Anal. Calcd for $C_{22}H_{30}O_2Si$: C, 74.53; H, 8.53. Found: C, 74.42; H, 8.45.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxypropyl]cyclopropane (14b) and (1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxypropyl]-cyclopropane (15b). From the mixture of **14b** and **15b** (160 mg), **14b** (114 mg) and **15b** (40 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **14b**: $[\alpha]^{20}_D$ +2.60 (*c* 1.370, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.22 (1 H, m), 0.69 (1 H, m), 0.99 (3 H, t, J = 7.4 Hz), 1.05 (9 H, s), 1.06 (1 H, m), 1.24 (1 H, m), 1.54−1.66 (2 H, m), 1.83 (1 H, m), 3.27 (1 H, m), 3.55 (1 H, dd, J = 8.6, 11.2 Hz), 3.85 (1 H, dd, J = 6.0, 11.2 Hz), 7.37−7.44 (6 H, m), 7.65−7.71 (4 H, m);^{13}C NMR (125 MHz, $CDCl_3$) δ 7.31, 10.05, 18.65, 19.14, 23.02, 26.80, 30.60, 64.26, 73.20 (C-1′), 127.62, 127.65, 129.61, 133.73, 133.76, 135.53, 135.59; LR-MS (FAB) *m*/*z* 369 ((M + H)$^+$, 4.0). Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.70; H, 8.77. **15b**: $[\alpha]^{21}_D$ +12.64 (*c* 1.130, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.13 (1 H, m), 0.72 (1 H, m), 1.02 (3 H, t, J = 7.5 Hz), 1.06 (9 H, s), 1.10−1.26 (2 H, m), 1.68 (1 H, m), 1.77 (1 H, m), 3.26 (1 H, m), 3.35 (1 H, dd, J = 11.2, 11.2 Hz), 3.91 (1 H, br s), 4.10 (1 H, dd, J = 5.0, 11.2 Hz), 7.39−7.46 (6 H, m), 7.68−7.74 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.5, 10.3, 16.5, 19.1, 23.1, 26.8, 29.7, 65.5, 74.0, 127.8, 127.8, 129.8, 129.9, 133.0, 133.0, 135.5, 135.7; LR-MS (FAB) *m*/*z* 369 ((M + H)$^+$, 7.0). Anal. Calcd for $C_{23}H_{32}O_2Si$: C, 74.95; H, 8.75. Found: C, 74.64; H, 8.79.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*S*)-1-hydroxy-3-methylbutyl]cyclopropane (14e) and (1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-[(*R*)-1-hydroxy-3-methylbutyl]cyclopropane (15e). From the mixture **14e** and **15e** (190 mg), **14e** (136 mg) and **15e** (46 mg) were obtained in a pure form, after column chromatography (silica gel; AcOEt/hexane 1:19). **14e**: $[\alpha]^{17}_D$ −3.46 (*c* 1.350, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.22 (1 H, m), 0.69 (1 H, m), 0.87 (3 H, d, J = 6.6 Hz), 0.92 (3 H, d, J = 6.6 Hz), 1.02 (1 H, m), 1.06 (9 H, s), 1.19 (1 H, m), 1.55−1.58 (2 H, m), 1.64 (1 H, br s), 1.83 (1 H, m, H-3′), 3.40 (1 H, m), 3.58 (1 H, dd, J = 8.5, 11.2 Hz), 3.80 (1 H, dd, J = 6.2, 11.2 Hz), 7.36−7.44 (6 H, m), 7.66−7.70 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 7.47, 18.62, 19.16, 21.48, 23.82, 23.92, 24.52, 26.86, 46.84, 64.20, 70.05, 127.60, 127.63, 129.60, 129.61, 133.78, 133.79, 135.53, 135.60; LR-MS (FAB) *m*/*z* 397 ((M + H)$^+$, 2.0). Anal. Calcd for $C_{25}H_{36}O_2Si$: C, 75.70; H, 9.15. Found: C, 75.60; H, 9.03. **15e**: $[\alpha]^{20}_D$ +16.97 (*c* 1.080, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.11 (1 H, m), 0.69 (1 H, m), 0.94 (6 H, d, $J_{4',3'}$ = 6.6 Hz), 1.06 (9 H, s), 1.12 (2 H, m), 1.18 (1 H, m), 1.44 (1 H, m), 1.67 (1 H, m), 1.91 (1 H, m), 3.35 (1 H, dd, J = 11.4, 11.4 Hz), 3.39 (1 H, m), 3.83 (1 H, br s), 4.10 (1 H, dd, J = 5.2, 11.4 Hz), 7.37−7.46 (6 H, m), 7.67−7.74 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.4, 16.5, 19.1, 22.5, 23.4, 24.0, 24.6, 26.8, 65.5, 70.6, 127.8, 127.8, 129.8, 129.9, 133.0, 133.0, 135.5, 135.7; LR-MS (FAB) *m*/*z* 397 ((M + H)$^+$, 5.0). Anal. Calcd for $C_{25}H_{36}O_2Si$: C, 75.70; H, 9.15. Found: C, 75.68; H, 9.30.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(1-ethanoyl)cyclopropane (1a). Compound **1a** was obtained in 89% yield from **8** as an oil: $[\alpha]^{19}_D$ −55.15 (*c* 1.490, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.88 (1 H, m, H-3a), 1.05 (9 H, s, −C(CH_3)$_3$), 1.20 (1 H, m, H-3b), 1.67 (1 H, m, H-2), 1.85 (1 H, m, H-1), 2.19 (3 H, s, H-2′), 3.51 (1 H, dd, H-1″a, J = 6.0, J = 11.0 Hz), 3.77 (1 H, dd, H-1″b, J = 4.8, 11.0 Hz), 7.37−7.45 (6 H, m, aromatic), 7.64−7.66 (4 H, m, aromatic), the ^1H NMR assignments indicated were in agreement with the COSY spectra; NOE (400 MHz, CD_2Cl_2, 32 °C) H-2 → H-3b (4.0%), H-2→ H-2′ (1.0%), H-2→ H-1″a (1.9%), H-2 → H-1″b (2.4%), H-3b → H-2 (6.2%), H-3b → H-3a (23.0%), H-2′ → H-1 (1.6%), H-2′ → H-2 (0.5%), H-2′ → H-3b (0.3%); NOE (400 MHz, CD_2Cl_2, −78 °C) H-2 → H-3b (3.7%), H-2 → H-1″a (1.4%), H-2 → H-1″b (2.0%), H-3b → H-2 (5.9%), H-3b → H-3a (12.9%), H-2′ → H-1 (1.5%), H-2′ → H-2 (0.3%);^{13}C NMR (125 MHz, $CDCl_3$) δ 14.6, 19.2, 26.4, 26.8, 26.9, 30.4, 64.7, 127.7, 129.7, 129.7, 133.5, 133.6, 135.6, 208.0. LR-MS (EI) *m*/*z* 295 ((M − *t*-Bu)$^+$, 100.0). Anal. Calcd for $C_{22}H_{28}O_2Si$: C, 74.95; H, 8.01. Found: C, 74.99; H, 8.04.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(1-propanoyl)cyclopropane (1b). Compound **1b** was obtained in 79% from **8** yield as an oil: $[\alpha]^{20}_D$ −77.96 (*c* 1.020, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.85 (1 H, m), 1.04 (9 H, s), 1.07 (3 H, t, J = 7.4 Hz), 1.18 (1 H, m), 1.66 (1 H, m), 1.84 (1 H, m), 2.46−2.57 (2 H, m), 3.50 (1 H, dd, J = 6.1, 11.0 Hz), 3.77 (1 H, dd, J = 4.8, 11.0 Hz), 7.37−7.44 (6 H, m), 7.64−7.66 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.0, 14.3, 19.2, 25.3, 26.1, 26.8, 36.7, 64.8, 127.7, 129.7, 129.7, 133.6, 133.6, 135.6, 135.6, 210.6; LR-MS (FAB) *m*/*z* 367 ((M + H)$^+$, 8.0). Anal. Calcd for $C_{23}H_{30}O_2Si$: C, 75.36; H, 8.25. Found: C, 75.30; H, 8.21.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(3-butenoyl)cyclopropane (1c). Compound **2c** was obtained in 48% yield from **8** as an oil: $[\alpha]^{22}_D$ −63.92 (*c* 0.400, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.90 (1 H, m), 1.04 (9 H, s), 1.22 (1 H, m), 1.70 (1 H, m), 1.91 (1 H, m), 3.25 (2 H, dd, J = 1.1, 6.9 Hz), 3.51 (1 H, dd, J = 6.0, 11.0 Hz), 3.77 (1 H, dd, J = 4.6, 11.0 Hz), 5.16 (2 H, m), 5.94 (1 H, m), 7.35−7.45 (6 H, m), 7.64−7.65 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.7, 19.2, 25.3, 26.8, 27.1, 48.5, 64.5, 118.6,127.7, 129.7, 129.7, 130.7, 133.5, 133.5, 135.5, 135.6, 207.7; LR-MS (ESI) *m*/*z* 401 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{24}H_{30}O_2Si$: C, 76.14; H, 7.99. Found: C, 75.94; H, 8.12.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(2-methyl-1-propanoyl)cyclopropane (1d). Compound **1d** was obtained in 82% yield from **8** as an oil: $[\alpha]^{22}_D$ −62.38 (*c* 1.360, $CHCl_3$); ^1H NMR (500 MHz, $CDCl_3$) δ 0.85 (1 H, m), 1.04 (9 H,

s), 1.12 (3 H, d, J = 6.9 Hz), 1.15 (3 H, t, J = 6.9 Hz), 1.18 (1 H, m), 1.63 (1 H, m), 1.94 (1 H, m), 2.70 (1 H, m), 3.49 (1 H, dd, J = 6.3, 11.0 Hz), 3.79 (1 H, dd, J = 5.6, 11.0 Hz), 7.37−7.45 (6 H, m), 7.64−7.66 (4 H, m);[1] ^{3}C NMR (125 MHz, $CDCl_3$) δ 14.3, 18.1, 18.3, 19.2, 24.0, 26.8, 26.9, 41.7, 64.9, 127.7, 129.7, 129.7, 133.5, 133.6, 135.5, 135.6, 213.6; LR-MS (ESI) m/z 403 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{24}H_{32}O_2Si$: C, 75.74; H, 8.47. Found: C, 75.71; H, 8.59.

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(3-methyl-1-buthanoyl)cyclopropane (1e). Compound **1e** was obtained in 74% from **8** as an oil: $[\alpha]^{21}_D$ −66.54 (c 1.120, $CHCl_3$);^{1}H NMR (500 MHz, $CDCl_3$) δ 0.84 (1 H, m, H-3a), 0.92 (3 H, d, H-4′a, $J_{4'a,3'}$ = 6.6 Hz), 0.93 (3 H, d, H-4′b, $J_{4'b,3'}$ = 6.6 Hz), 1.04 (9 H, s, −C(CH_3)$_3$), 1.19 (1 H, m, H-3b), 1.65 (1 H, m, H-2), 1.85 (1 H, m, H-1), 2.16 (1 H, m, H-3′), 2.36 (2 H, m, H-2′), 3.48 (1 H, dd, H-1″a, $J_{1''a,2}$ = 6.2 Hz, $J_{1''a,1''b}$ = 11.0 Hz), 3.78 (1 H, dd, H-1″b, $J_{1''b,2}$ = 4.6 Hz, $J_{1''b,1''a}$ = 11.0 Hz), 7.37−7.45 (6 H, m, aromatic), 7.62−7.65 (4 H, m, aromatic), the ^{1}H NMR assignments indicated were in agreement with the COSY spectra; NOE (400 MHz, CD_2Cl_2, −78 °C) H-2 → H-3b (3.3%), H-2 → H-1″a (1.2%), H-2 → H-1″b (1.9%), H-3b → H-2 (2.2%), H-3b → H-3a (18.9%), H-2′a → H-1 (1.3%), H-2′a → H-2′b (22.8%), H-2″b → H-1 (2.0%), H-2″b → H-2 a (22.8%); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.3, 19.2, 22.6, 22.7, 24.9, 26.0, 26.8, 26.8, 52.9, 64.8, 127.7, 129.7, 129.7, 133.6, 133.6, 135.6, 135.6, 210.0; LR-MS (ESI) m/z 417 ((M + Na)$^+$, 100.0). Anal. Calcd for $C_{25}H_{34}O_2Si$: C, 76.09; H, 8.68. Found: C, 75.98; H, 8.80.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl])-1-(1-ethanoyl)cyclopropane (3a). Compound **3a** was obtained in 84% yield from **13** as white crystals: mp (hexane/AcOEt) 73−74 °C; $[\alpha]^{20}_D$ +35.42 (c 1.030, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.90 (1 H, m), 1.04 (9 H, s), 1.13 (1 H, m), 1.68 (1 H, m), 2.16 (1 H, m), 2.35 (3 H, s), 3.51 (1 H, dd, J = 9.7, 11.1 Hz), 3.87 (1 H, dd, J = 5.1, 11.1 Hz), 7.36−7.44 (6 H, m), 7.61−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 19.2, 25.5, 26.6, 26.8, 31.8, 61.5, 127.6, 129.6, 133.7, 134.0, 135.5, 206.2; LR-MS (EI) m/z 295 ((M − t-Bu)$^+$, 80.0). Anal. Calcd for $C_{22}H_{28}O_2Si$: C, 74.95; H, 8.01. Found: C, 74.74; H, 8.06.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(1-propanoyl)cyclopropane (3b). Compound **3b** was obtained in 72% yield from **13** as white crystals: mp (hexane/AcOEt) 72−74 °C; $[\alpha]^{20}_D$ +33.26 (c 1.010, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (1 H, m), 1.01 (9 H, s), 1.11 (3 H, t, J = 7.5 Hz), 1.13 (1 H, m), 1.65 (1 H, m), 2.13 (1 H, m), 2.60−2.77 (2 H, m), 3.53 (1 H, dd, J = 9.7, 11.2 Hz), 3.87 (1 H, dd, J = 5.0, 11.2 Hz), 7.36−7.42 (6 H, m), 7.60−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 8.0, 11.4, 19.2, 25.5, 26.3, 26.8, 37.2, 61.5, 127.6, 127.6, 129.5, 133.8, 134.1, 135.5, 208.8; LR-MS (FAB) m/z 367 ((M + H)$^+$, 25.0). Anal. Calcd for $C_{23}H_{30}O_2Si$: C, 75.36; H, 8.25. Found: C, 75.36; H, 8.38.

(1*S*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(3-methyl-1-buthanoyl)cyclopropane (3e). Compound **3e** was obtained from **13** in 79% yield as an oil: $[\alpha]^{25}_D$ +33.59 (c 1.380, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (1 H, m), 0.94 (3 H, d, J = 6.6 Hz), 0.96 (3 H, d, J = 6.6 Hz), 1.02 (9 H, s), 1.10 (1 H, m), 1.62 (1 H, m), 2.10 (1 H, m), 2.20 (1 H, m), 2.53 (2 H, d, J = 6.8 Hz), 3.59 (1 H, dd, J = 9.4, 11.2 Hz), 3.85 (1 H, dd, J = 5.3, 11.2 Hz), 7.36−7.43 (6 H, m), 7.61−7.68 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 11.7, 19.2, 22.7, 22.8, 24.6, 25.1, 26.5, 26.8, 53.7, 61.4, 127.6, 129.5, 129.5, 133.8, 134.1, 135.5, 135.5, 208.3; LR-MS (FAB) m/z 395 ((M + H)$^+$, 26.0). Anal. Calcd for $C_{25}H_{34}O_2Si$: C, 76.09; H, 8.68. Found: C, 76.00; H, 8.58.

(1*R*,2*R*)-2-Benzyloxymethyl-1-ethanoylcyclopropane (2). Compound **12** (192 mg, 1.0 mmol) was successively treated by the above general procedures for the Grignard reaction with MeMgBr and the PDC oxidation to give **2** (173 mg, 85%) as a colorless oil: $[\alpha]^{20}_D$ −115.38 (c 2.130, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.89 (1 H, m), 1.25 (1 H, m), 1.76 (1 H, m), 1.90 (1 H, m), 2.23 (3 H, s), 3.32 (1 H, dd, J = 6.8, 10.5 Hz), 3.49 (1 H, dd, J = 5.6, 10.5 Hz), 4.50 (1 H, s, J = 12.0 Hz), 4.53 (1 H, s, J = 12.0 Hz), 7.26−7.36 (5 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 15.1, 24.1, 26.9, 30.3, 71.6, 72.6, 127.6, 127.7, 128.4, 138.1, 207.5; LR-MS (FAB) m/z 205 ((M + H)$^+$), 53.0). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.11; H, 7.89.

(1*S*,2*R*)-2-Benzyloxymethyl-1-ethanoylcyclopropane (4). Compound **18** (192 mg, 1.0 mmol) was successively treated by the above general procedures of the Grignard reaction with MeMgBr and the PDC oxidation to give **4** (159 mg, 78%) as a colorless oil: $[\alpha]^{18}_D$ +85.51 (c 1.110, $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ 1.00 (1 H, m), 1.21 (1 H, m), 1.74 (1 H, m), 2.16 (1 H, m), 2.31 (3 H, s), 3.30 (1 H, dd, J = 10.2, 10.2 Hz), 3.74 (1 H, dd, J = 5.2, 10.2 Hz), 4.40 (2 H, s), 7.25−7.34 (5 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 12.1, 23.8, 25.3, 31.8, 67.6, 73.0, 127.6, 127.8, 128.3, 138.3, 206.3; LR-MS (FAB) m/z 205 ((M + H)$^+$, 64.0). Anal. Calcd for $C_{13}H_{16}O_2$: C, 76.44; H, 7.90. Found: C, 76.21; H, 7.96.

General Procedure for the Hydride Reduction of Ketones 1, 2, 3, or 4 (Tables 3 and 4). To a solution of a ketone **1**, **2**, **3**, or **4** (0.10 mmol) in CH_2Cl_2 (2 mL) was added a solution of a hydride reagent ($LiAlH_4$, 1.0 M in THF; $LiBH_4$, 2.0 M in THF; DIBAL-H, 1.0 M in n-hexane; N-Selectride, 1.0 M in THF; K-sElectride, 1.0 M in THF; KS-Selectride, 1.0 M in THF), and the mixture was stirred at −78 °C for 0.5−30 h. The resulting mixture was evaporated, and the residue was partitioned between AcOEt and H_2O. The organic layer was washed with brine, dried (Na_2SO_4), and evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:9) to give a *syn*/*anti* mixture of the product, the ratio of which was determined by ^{1}H NMR analysis. The results are summarized in Tables 3 and 4.

(1*S*,2*R*)-2-Benzyloxymethyl-1-[(*S*)-1-hydroxyethyl]cyclopropane (19) and (1*S*,2*R*)-2-Benzyloxymethyl-1-[(*R*)-1-hydroxyethyl]cyclopropane (20). The K-Selectride reduction of **4** gave a mixture of **19** and **20** (Table 3, entry 7), the structures of which were confirmed after its conversion into the corresponding *O*-TBDPS-protected derivatives **14a** and **15a** as described below: ^{1}H NMR (500 MHz, $CDCl_3$) for major product **20**, δ 0.18 (1 H, m), 0.80 (1 H, m), 1.09 (1 H, m), 1.28 (1 H, m), 1.30 (3 H, d, H-2′, J = 6.2 Hz), 3.18 (1 H, dd, J = 10.3, 10.8 Hz), 3.33 (1 H, m), 3.69 (1 H, br s), 3.96 (1 H, dd, J = 5.5, 10.3 Hz), 4.53 (1 H, d, J = 11.6 Hz), 4.57 (1 H, d, J = 11.6 Hz), 7.26−7.35 (5 H, m), for minor product **19**, δ 0.32 (1 H, m), 0.80 (1 H, m), 1.04 (1 H, m), 1.28 (1 H, m), 1.31 (3 H, d, J = 6.2 Hz), 3.33 (1 H, dd, J = 8.6, 10.4 Hz), 3.46 (1 H, m), 3.62 (1 H, dd, J = 6.7, 10.4 Hz), 4.47 (1 H, d, J = 11.6 Hz), 4.55 (1 H, d, J = 11.6 Hz), 7.26−7.35 (5 H, m); HR-MS (EI) calcd for $C_{13}H_{18}O_2$ 206.2808, found 206.2797 (M$^+$).

(1*R*,2*R*)-2-Benzyloxymethyl-1-[(*R*)-1-hydroxyethyl]cyclopropane (21) and (1*R*,2*R*)-2-Benzyloxymethyl-1-[(*S*)-1-hydroxyethyl]cyclopropane (22). The K-Selectride or KS-Selectride reduction of **2** gave a mixture of **21** and **22** (Table 4, entries 12 and 13), the structures of which were confirmed after its conversion into the corresponding *O*-TBDPS-protected derivatives **9a** and **10** as described below: ^{1}H NMR (500 MHz, $CDCl_3$) for major product **22**, δ 0.46 (2 H, m), 0.83 (1 H, m), 1.09 (1 H, m), 1.25 (3 H, d, J = 6.2 Hz), 3.12 (1 H, m), 3.18 (1 H, dd, J = 7.6, 10.0 Hz), 3.44 (1 H, dd, J = 6.2, 10.0 Hz), 4.52 (2 H, s), 7.26−7.36 (5 H, m), for minor product **21**, δ 0.46 (1 H, m), 0.58 (1 H, m), 0.83 (1 H, m), 1.03 (1 H, m), 1.27 (3 H, d, J = 6.3 Hz), 3.23 (1 H, m), 3.33 (2 H, m), 4.53 (2 H, s), 7.26−7.36 (5 H, m); HR-MS (EI) calcd for $C_{13}H_{18}O_2$ 206.2808, found 206.2804 (M$^+$).

(1*R*,2*R*)-2-[(*tert*-Butyldiphenylsilyloxy)methyl]-1-(2-butenoyl)cyclopropane (23). Compound **23** was obtained in 69% yield as an oil by the treatment of **1c** with KS-Selectride (Table 4, entry 9), after column chromatography (silica gel; AcOEt/hexane 1:19): ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.91 (1 H, m), 1.04 (9 H, s), 1.26 (1 H, m), 1.70 (1 H, m), 1.91 (3 H, dd, J' = 1.6, 6.8 Hz), 2.06 (1 H, m), 3.56 (1 H, dd, J = 6.0, 11.0 Hz), 3.79 (1 H, dd, J = 4.8, 11.0 Hz), 6.20 (1 H, dq, J = 1.6, 5.6 Hz), 6.87 (1 H, dq, J = 5.6, 6.8 Hz), 7.37−7.45 (6 H, m), 7.64−

7.66 (4 H, m); ^{13}C NMR (125 MHz, $CDCl_3$) δ 14.5, 18.3, 19.3, 23.8, 26.9, 27.0, 64.8, 127.7, 129.7, 129.7, 132.3, 133.6, 135.6, 135.6, 142.1, 207.7; HR-MS (FAB) calcd for $C_{24}H_{31}O_2Si$ 379.2093, found 379.2107 ($(M + H)^+$).

Conversion of 19/20 Mixture into 14a/15a Mixture. A mixture of **19** and **20** (17 mg, 80 μmol) and 10% Pd-charcoal (5 mg) in MeOH (1 mL) was stirred under atmospheric pressure hydrogen gas at room temperature for 1 h, and then the catalyst was filtered off. The filtrate was evaporated, and a mixture of the residue, TBDPSCl (21 μL, 0.80 μmol), and imidazole (5 mg, 0.80 μmol) in DMF (1 mL) was stirred at room temperature for 5 h. After addition of MeOH, the resulting mixture was partitioned between AcOEt and H_2O, and the organic layer separated was washed with brine, dried (Na_2SO_4), evaporated. The residue was purified by column chromatography (silica gel; AcOEt/hexane 1:9) to give a mixture of **14a** and **15a** (26 mg, 90%) as an oil.

Conversion of 21/22 Mixture into 9a/10a Mixture. A mixture of **21** and **22** (20 mg, 100 μmol) was converted into a mixture of **9a** and **10a** (29 mg, 85%) as described above for the mixture of **19a** and **20a**.

X-ray crystallographic data of 3a: $C_{22}H_{28}O_2Si$, M = 352.55, monoclinic, $P2_1$, a = 10.289 (3) Å, b = 9.002 (2) Å, c = 12.155 (2) Å, β = 113.39(2)°, V = 1033.4(4) Å^3, Z = 2, D_{calc} = 1.133 Mg cm^{-3}. Cell parameters were determined and refined from 26 reflections in the range 26.5° < θ < 30.0°. A colorless crystal (0.40 × 0.30 × 0.25 mm) was mounted on a Mac Science MXC18 diffractometer with graphite-monochromated Cu Kα radiation (λ = 1.541 78 Å). Data collection using the $\omega/2\theta$ scan technique gave 1744 reflections at room temperature, 1644 unique, of which 1612 with $I > 3.00\sigma(I)$ reflections were used in calculations. The intensities were corrected for the Lorentz, polarization, and the extinction effect, but not for the absorption. The structure was solved by the direct method and refined by full-matrix least squares technique using maXus (version 4.3) as the computer program. The non-hydrogen atoms were refined anisotropically. The hydrogen atoms were included by calculation, but these positions were not refined. The R values were 0.038.

Calculations. All ab initio and DFT (density functional theory) calculations were performed using the Gaussian 98 program[14] on an SGI O2 workstation. The preoptimized geometries by RHF/6-31G(d) were taken to be the input geometries for final optimization by RB3LYP/6-31G(d). Finally, single-point energies were calculated by RB3LYP/6-31G(d).

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Supporting Information Available: Experimental details for determination of the stereochemistry of the *syn* and *anti* products by the modified Mosher method. This material is available free of charge via the Internet at http://pubs.acs.org.

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