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Stereoselective Cyclopropylmethylation Reactions of Homoallylstannanes with Carbon Electrophiles

Masanobu Sugawara and Jun-ichi Yoshida*

Department of Synthetic Chemistry & Biological Chemistry, Graduate School of Engineering, Kyoto University, Sakyo-ku, Kyoto 606-8501, Japan

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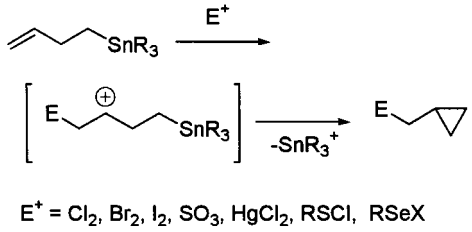
Abstract—The reactions of homoallylstannanes with acetals, aldehydes, and acyl chlorides in the presence of a Lewis acid proceeded smoothly to give the corresponding cyclopropylmethylated products. The reactions of *E*-3-pentenylstannane with aldehydes were stereoselective and gave the *erythro* products predominantly. A mechanism involving antiperiplanar attack is suggested. The stereoselectivity of the *Z* isomer was, however, not high. © 2000 Elsevier Science Ltd. All rights reserved.

Introduction

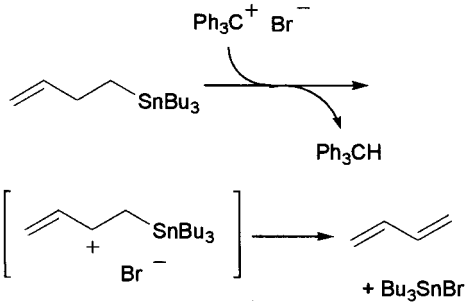
Allylstannanes are useful synthetic reagents for the construction of carbon–carbon bonds, because they undergo regio- and stereoselective allylation reactions with carbonyl compounds in the presence of Lewis acids or under thermal conditions.[1] Moreover, they react with organic halides to give the corresponding allylated products under radical conditions.[2] The reactions of homoallylstannanes, however, are less popular in organic synthesis. Peterson and Robbins[3a] reported a pioneering work on the reactions of homoallylstannanes with various heteroatom electrophiles, such as Cl_2, Br_2, I_2, SO_3, $HgCl_2$, RSCl and RSeX, which lead to the formation of the corresponding cyclopropylmethyl compounds. A mechanism involving the initial addition of an electrophile to the carbon–carbon double bond of homoallylstannane followed by facile γ-elimination of the formal stannyl cation[4] to form the cyclopropane ring seems to be the most plausible (Scheme 1).

To our knowledge, however, there had been no successful example of the reaction of homoallylstannanes with carbon electrophiles to achieve intermolecular carbon–carbon bond formation.[5] In fact, it was reported that the reaction of homoallylstannane with triphenylmethyl cation led to the hydride abstraction followed by β-elimination of the stannyl bromide (Scheme 2).[3b] Hydride losses at carbon atoms β to tin are known to occur rapidly and quantitatively.[6]

We have been interested in the reaction of homoallylstannanes with carbon electrophiles and found that the reaction of homoallylstannanes with carbon electrophiles such as acetals, aldehydes, and acyl halides could be accomplished in the presence of a suitable Lewis acid.[7] In addition to a mechanistic interest, synthetic utility of this reaction is noteworthy. This reaction serves as an efficient and convenient method for cyclopropylmethylation of carbonyl compounds. This type of tranformation is rather difficult to accomplish with the homoallyl Grignard reagent because of a ring-opening side reaction.[8] Use of the tin reagent, however, enables the direct cyclopropylmethylation of



Scheme 1.



Scheme 2.

Keywords: cyclopropylmethylation; homoallylstannane; stereoselective; γ-elimination; γ-effect.

* Corresponding author. Tel.: +81-75-753-5651, fax: +81-75-753-5911; e-mail: yoshida@sbchem.kyoto-u.ac.jp

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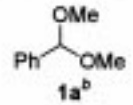
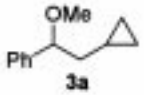
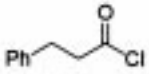
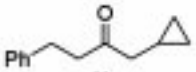
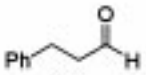
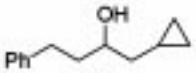
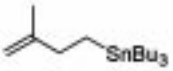
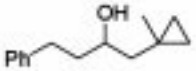
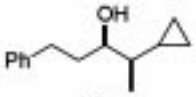
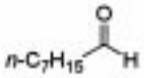
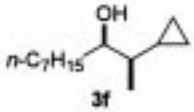
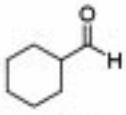
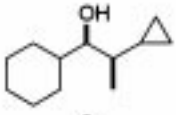
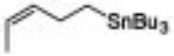
Table 1. Reactions of homoallylstannanes with carbon electrophiles in the presence of Lewis acids[a]

entry	electrophile	homoallylstannane	Lewis acid	major product	yield(%) of 3 (*erythro*/*threo*)[c]	yield(%) of **4**
1	 **1a**[b]	 **2a** (1.3 equiv)	$TMSOTf$	 **3a**	83	<1[d]
2	 **1b**	**2a** (1.0 equiv)	$TiCl_4$	 **3b**	87	12
3	 **1c**	**2a** (1.2 equiv)	$TiCl_4$	 **3c**	76	7
4	**1c**	 **2b** (1.3 equiv)	$TiCl_4$	 **3d**	86	10[d]
5	**1c**	 **2c** (E/Z = 88/12) (1.1 equiv)	$TiCl_4$	 **3e**	87 (97/3)	7[d]
6	 **1d**	**2c** (1.1 equiv)	$TiCl_4$	 **3f**	83 (>99/1)	3[d]
7	 **1e**	**2c** (1.1 equiv)	$TiCl_4$	 **3g**	87 (97/3)	5[d]
8	**1e**	 **2d** (E/Z = 1/>99) (1.2 equiv)	$TiCl_4$	**3g**	78 (68/32)	<1[d]

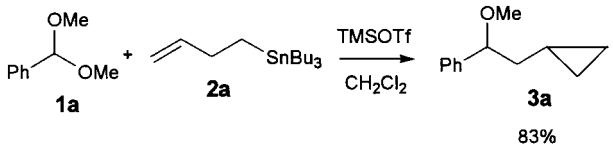
[a] Reaction conditions: 1.0 equiv. of **1**, 1.0–1.3 equiv. of **2** and 1.1 equiv. of $TiCl_4$ in CH_2Cl_2 (1.8 mL) at −78°C for 3–3.5 h.
[b] TMSOTf (1.1 equiv.) was used instead of $TiCl_4$, at −40°C, 3 h.
[c] Determined by GLC.
[d] The homoallylated product **4** was not fully characterized.

carbonyl compounds and related compounds. In this paper, we report on full details of this study.

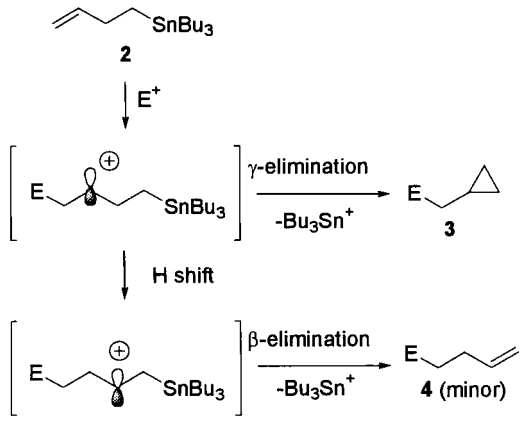
Results and Discussion

The reaction of benzaldehyde dimethyl acetal (**1a**) with 3-butenyltributylstannane (**2a**, 1.3 equiv.)[9] in the presence of TMSOTf (1.1 equiv.) in CH_2Cl_2 at −40°C for 3 h gave the corresponding cyclopropylmethylated product **3a** in 83% yield (Table 1, entry 1). This result indicates that carbon electrophiles[10] are also effective for the reactions toward homoallylstannanes to form cyclopropane derivatives, if we choose a suitable precursor and a Lewis acid. The use of $BF_3{\cdot}OEt_2$ as a Lewis acid caused decrease of the yield of the product (**3a**). The use of $TiCl_4$ gave rise to a very low yield of **3a**; presumably the methoxy group in **3a** was eliminated by the action of $TiCl_4$, although the product was not fully characterized (Scheme 3).

Acyl halides and aldehydes were also found to be effective as carbon electrophiles (Table 1, entries 2–8). The corresponding cyclopropylmethylated products **3** were obtained in good yields together with small amounts of homoallylated by-products **4**. It was reported that similar by-products were obtained in the reaction of homoallylsilanes.[5a] In these



Scheme 3.



Scheme 4.

cases, $TiCl_4$ was found to be more effective than TMSOTf. Presumably TMSOTf is not strong enough to generate cationic species from acyl halides and aldehydes.

These reactions seem to proceed by the initial electrophilic attack of a carbocation (E^+) generated from acetals, acyl halides, or aldehydes to the carbon–carbon double bond of the homoallylstannane to give the carbocation γ to the tin atom, which undergoes γ-elimination of the formal stannyl cation to form a cyclopropane ring (Scheme 4). The homoallylated product **4** seems to be produced by the isomerization of the carbocation via hydride shift to form β-stannyl carbocation followed by β-elimination of tin.

In order to get an insight into the isomerization of the γ-stannyl carbocation to the β-stannyl carbocation, their relative stabilities were determined by molecular orbital calculations of the model compounds. It is worth noting that in the optimized structure of γ-stannyl carboation (**A**), the cyclopropane ring is almost formed, indicating a strong percaudal interaction between the empty p orbital of the carbocation and the C–Sn σ orbital. The calculations indicated that the β-stannyl carbocation **B** (Fig. 1) is 15 kcal/mol more stable than the γ-stannyl carbocation **A**. This result is consistent with the general tendency that the β-effect is stronger than the γ-effect.[11] Therefore, the isomerization of the γ-stannyl carbocation to the β-stannyl carbocation is exothermic, although the activation energy for this isomerization is not clear at present.

The reaction of substituted homoallylstannanes such as **2b** and **2c** with aldehydes in the presence of $TiCl_4$ also proceeded smoothly to give the corresponding cyclopropylmethylated products in good yields. Especially, diastereoselectivity of the present reaction using homoallylstannane having an internal double bond was remarkable. For example, the *erythro* product was obtained selectively (97/3) starting from **1c** and *E*-3-pentenyltributylstannane (**2c**: *E*/*Z*=88/12) (entry 5).[12] The reaction of **2c** with other aldehydes such as **1d** and **1e** also took place stereoselectively to give the corresponding *erythro* products (entries 6 and 7).

Highly *erythro*-selective addition of crotyltrialkyltins to aldehydes has been reported by Y. Yamamoto and a mechanism involving an acyclic transition state is proposed.[13] The stereoselectivity of the present reaction can also be explained by an acyclic transition state model. The addition of *E* homoallylstannane to the carbonyl group seems to take place in antiperiplanar fashion to give the *erythro* product selectively (Fig. 2).

The reaction of **1e** and (*Z*)-3-pentenyltributylstannane (*E*/*Z*=1/>99), however, resulted in the decrease of the selectivity (68/32) (entry 8). This result sharply contrasts to high *erythro* selectivity regardless of the geometry of the crotyl unit reported for crotylstannane reported by Yamamoto,[13] although Keck reported the lower selectivity for the *Z*-crotylstannane than the *E* isomer.[14,15] Low selectivity of the *Z* isomer in the present case might be explained in terms of the competition between the antiperiplanar transition state and the synclinal transition

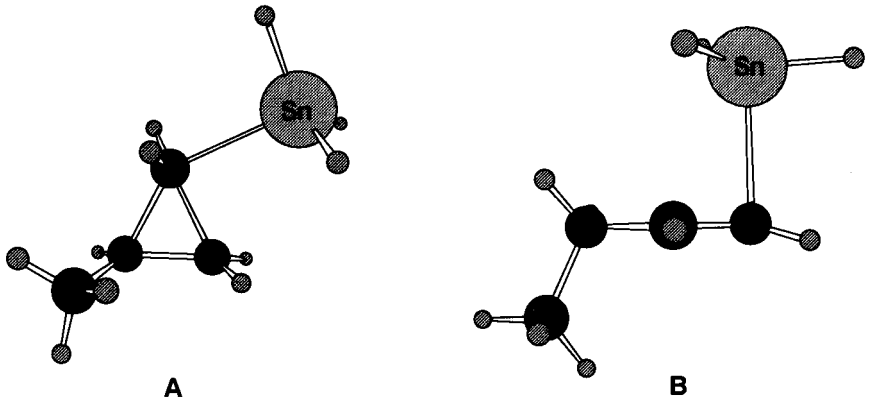


Figure 1. The optimized structures of: (A) $CH_3CHCH_2CH_2SnH_3$ cation; and (B) $CH_3CH_2CHCH_2SnH_3$ cation obtained by molecular orbital calculations (MP2/LANL2DZ).

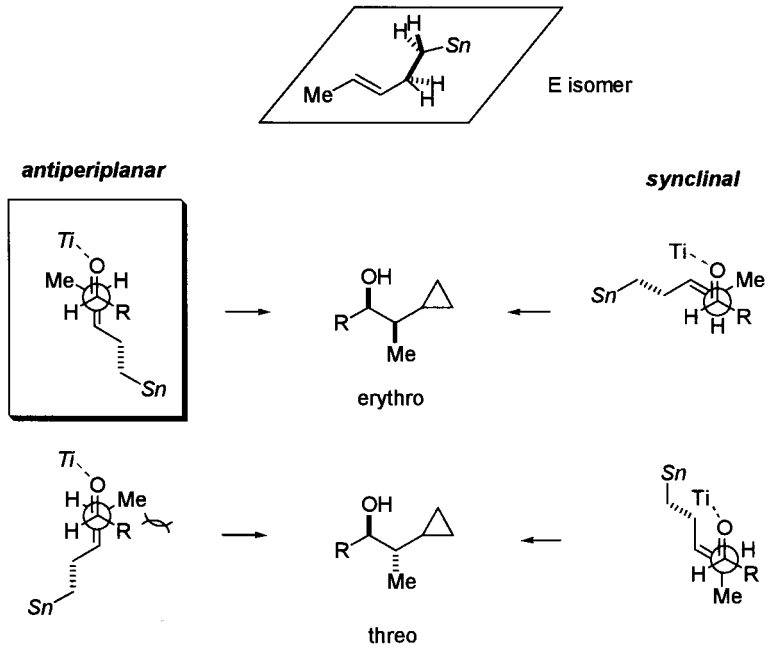


Figure 2. Proposed transition state of cyclopropylmethylation by the *E*-homoallylstannane.

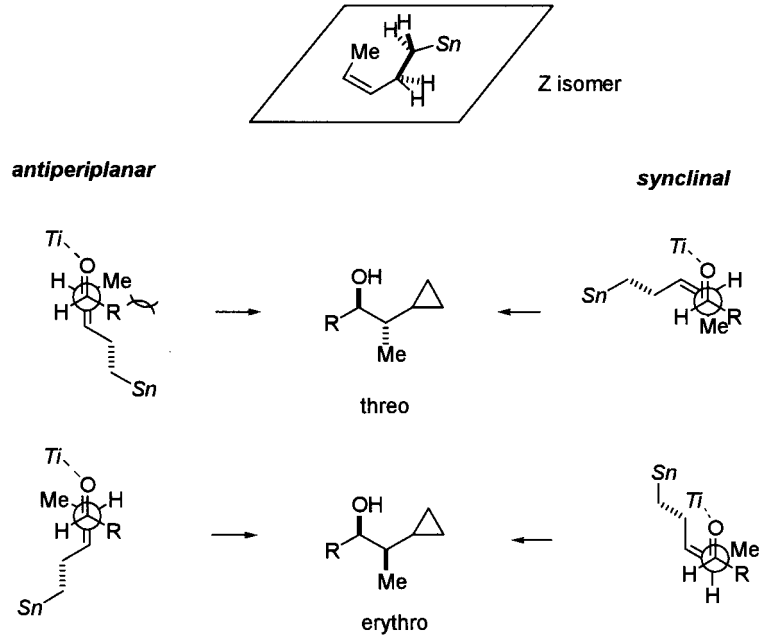


Figure 3. Proposed transition state of cyclopropylmethylation by the *Z*-homoallylstannane.

state, although the detailed mechanism is not clear at present (Fig. 3).

Conclusion

The reactions of homoallylstannanes with carbon electrophiles such as acetals, aldehydes, and acid halides have been achieved in the presence of a suitable Lewis acid, such as TMSOTf and $TiCl_4$. Especially, the reaction with *E*-3-pentenylstannane has been found to be highly stereoselective giving the *erythro* products predominantly. These reactions serve as a convenient method for the cyclopropylmethylation of carbonyl compounds.

Experimental

General remarks

Glass-support pre-coated (Merk silica gel 60 F254, 0.25 mm) plates were employed for analytical TLC. Flash

chromatography was carried out using Wako-Gel C-300. Proton (300 MHz) and carbon (75 MHz) NMR spectra were determined on a Varian Gemini 2000 spectrometer. Mass spectra were obtained on a JEOL JMS SX-102A mass spectrometer (EI, 70 eV). Isomer and diastereomer ratios were determined by capillary GLC analyses (Simadzu GC-14A, equipped with an OV-1 column, 0.25 mm×25 m) and proton NMR analyses. Preparative gel permeation chromatography (GPC) was carried out with a Japan Analytical Industry LC908 with GPC columns (JAIGEL 1H and 2H) using $CHCl_3$ as eluent. Thin-layer chromatography (TLC) was carried out by using Merck precoated silica gel 60 F_{254} plates (thickness 0.25 mm).

3-Methyl-3-butenyltributylstannane (2b). To a lithium diisopropylamide (LDA) solution (2.2 mmol) in THF (5.0 mL) was added tributhyltin hydride (568 mg, 1.95 mmol) over 5 min at −78°C. After being stirred for 30 min at 0°C, the resulting tributylstannyl lithium solution was cooled to −78°C. 3-Methyl-3-butenyl tosylate (556 mg, 2.3 mmol) was added to the reaction mixture at −78°C and the solution was stirred for 7 h at −5°C. Water was added, and the organic materials were extracted with ether. The organic phase was washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography to obtain the title compound (660 mg, 94%, 83% purity by GC), which was further purified with GPC. TLC R_f 0.85 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.70–1.0 (m, 17H), 1.20–1.40 (m, 6H), 1.42–1.52 (m, 6H), 1.75 (s, 3H), 2.75 (t, J=8.1 Hz, 2H), 4.67 (s, 1H), 4.70 (t, J=1.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 6.85, 8.64, 13.60, 21.98, 27.31, 29.15, 34.75, 108.40, 149.51; IR (neat) 2920, 1649, 882 cm^{-1}; Anal. Calcd for $C_{17}H_{36}Sn$: C, 56.85; H, 10.10. Found: C, 56.72; H, 9.87.

(*E*)-3-Pentenyltributylstannane (2c). To a mixture of Mg (436 mg, 17.9 mmol) and THF (2.0 mL) was added a small piece of iodine at room temperature, and the mixture was stirred until a brown color disappeared. Two drops of the solution of 1-bromo-3-pentene (*E*/*Z*=88/12) (2.21 g, 14.8 mmol) in THF (2.0 mL) was added to the mixture. After the reaction was initiated, THF (20 mL) was added to the reaction mixture. Then the remained solution of 1-bromo-3-pentene was added dropwise to the reaction mixture at room temperature over 15 min. After being refluxed for 1 h, the reaction mixture was cooled to 0°C. Tributyltin chloride (2.9 mL, 10.7 mmol) was added slowly to the Grignard solution and the reaction mixture was stirred for 2 h at room temperature. Saturated aq NH_4Cl (1.5 mL) was added and solid materials were removed by filtration. The solvent was evaporated and the residue was purified by distillation (135°C, 1.0 mmHg) to obtain the title compound (3.92 g, quantitative). The *E*/*Z* ratio (88/12) was determined by GLC analysis. TLC R_f 0.85 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.70–1.0 (m, 17H), 1.20–1.40 (m, 6H), 1.42–1.52 (m, 6H), 1.64 (d, J=4.8 Hz, 3H), 2.10–2.35 (m, 2H), 5.30–5.50 (m, 2H); ^{13}C NMR($CDCl_3$) δ 8.77, 13.60, 17.76, 27.33, 29.03, 29.16, 29.66, 123.41, 134.92; IR (neat) 2921, 1464, 962 cm^{-1}; Anal. Calcd for $C_{17}H_{36}Sn$: C, 56.85; H, 10.10. Found: C, 56.57; H, 9.80. The *E* stereochemistry is consistent with the strong IR absorption at 963 cm^{-1} which is absent in **2d**.

(*Z*)-3-Pentenyltributylstannane (2d). To an LDA solution (1.1 mmol) in THF (2.0 mL) was added tributhyltin hydride (0.30 mL, 1.1 mmol) over 5 min at −78°C. After being stirred for 30 min at 0°C, the resulting tributylstannyllithium solution was cooled to −78°C. (*Z*)-3-Pentenyl tosylate (234.2 mg, 0.98 mmol) was added to the reaction mixture at −78°C and the solution was stirred overnight at room temperature. Water was added and the organic materials were extracted with ether. The organic phase was washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography to obtain the title compound (394 mg, 99%). The *E*/*Z* ratio (1/>99) was determined by ^{1}H NMR. TLC R_f 0.85 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.70–1.0 (m, 17H), 1.20–1.40 (m, 6H), 1.42–1.52 (m, 6H), 1.60 (d, J=4.5 Hz, 3H), 2.10–2.35 (m, 2H), 5.30–5.45 (m, 2H); ^{13}C NMR ($CDCl_3$) δ 8.73, 12.57, 13.60, 23.83, 27.31, 29.16, 29.30, 122.35, 134.25; IR (neat) 2924, 1464, 1071 cm^{-1}; MS (EI) *m*/*e* (%) 303 (M^+-Bu, 100), 235 (30), 177 (51); HRMS (EI) calcd for $C_{17}H_{36}Sn-C_4H_9$ 303.1135, found 303.1148.

2-Cyclopropyl-1-phenyl-1-methoxyethane (3a). To a solution of benzaldehyde dimethyl acetal (75 μL, 0.50 mmol) and 3-butenyltributylstannane (219.5 mg, 0.64 mmol) in CH_2Cl_2 (1.8 mL) was added TMSOTf (100 μL, 0.55 mmol) at −40°C. The reaction mixture was stirred at the same temperature for 3 h. The reaction was quenched by the addition of sat. aq. $NaHCO_3$. The mixture was warmed to room temperature. The organic materials were extracted with ether, and the organic phase was washed with brine, and dried over $MgSO_4$. After removal of the solvent, the residue was purified by flash chromatography to obtain the title compound (73.1 mg, 83%). TLC R_f 0.27 (hexane/EtOAc=20/1); ^{1}H NMR ($CDCl_3$) δ −0.02 (ddd, J=14.4, 9.0, 5.1 Hz, 1H), 0.06 (ddd, J=14.4, 9.6, 5.4 Hz, 1H), 0.30–0.50 (m, 2H), 0.60–0.70 (m, 1H), 1.47 (ddd, J=13.8, 6.9, 6.9 Hz, 1H), 1.77 (ddd, J=13.8, 6.9, 6.9 Hz, 1H), 3.23 (s, 3H), 4.18 (t, J=6.9 Hz, 1H), 7.20–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 4.26, 7.56, 43.10, 56.53, 84.44, 126.89, 127.51, 128.35, 142.47; IR (neat) 3090 (cyclopropane C–H) cm^{-1}; Anal. Calcd for $C_{12}H_{16}O$: C, 81.77; H, 9.15. Found: C, 81.33; H, 9.10.

1-Cyclopropyl-4-phenylbutan-2-one (3b). *A typical procedure for $TiCl_4$ promoted cyclopropylmethylation with homoallylstannane (**2**).* To a solution of 3-phenylpropionyl chloride (35.0 mg, 0.21 mmol) and 3-butenyltributylstannane (70.0 mg, 0.20 mmol) in CH_2Cl_2 (0.60 mL) was added slowly a solution of $TiCl_4$ in CH_2Cl_2 (1.0 M, 0.22 mL, 0.22 mmol) at −78°C. The reaction mixture was stirred at the same temperature for 3 h. After most of the acid chloride was consumed, the reaction was quenched by the addition of sat. aq. $NaHCO_3$ (ca. 5 mL) at the same temperature. The mixture was warmed to room temperature. The organic materials were extracted with ether, and the organic phase was washed with brine. After removal of the solvent, the residue was treated with sat. KF/MeOH solution (ca. 0.5 mL) for 1.5 h at room temperature. The resulted suspension was diluted with ether and water. The organic phase was separated and dried over $MgSO_4$. After the solvent was removed, the residue was purified by flash chromatography to obtain the title compound (32.7 mg,

87%). TLC R_f 0.31 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.09 (dd, J=10.2, 4.5 Hz, 2H), 0.54 (ddd, J=10.5, 5.7, 4.5 Hz, 2H), 0.90–1.00 (m, 1H), 2.27 (d, J=7.2 Hz, 2H), 2.70–2.84 (m, 2H), 2.85–2.95 (m, 2H), 7.10–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 4.33, 6.15, 29.57, 43.78, 48.20, 126.11, 128.39, 128.53, 141.28, 210.28; IR (neat) 3090 (cyclopropane C–H), 1716 (C=H) cm^{-1}; MS (EI) *m/e* (%) 188 (M^+, 60), 159 (30), 133 (85); HRMS (EI) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1204; Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.74; H, 8.53.

1-Cyclopropyl-4-phenylbutan-2-ol (3c). TLC R_f 0.11 (hexane/EtOAc=10/1), ^{1}H NMR ($CDCl_3$) δ 0.00–0.20 (m, 2H), 0.40–0.60 (m, 2H), 0.68–0.81 (m, 1H), 1.35–1.45 (m, 2H), 1.71–1.85 (m, 2H), 2.68 (ddd, J=13.8, 9.9, 6.9 Hz, 1H), 2.80 (ddd, J=13.8, 9.6, 6.9 Hz, 1H), 3.70–3.80 (m, 1H), 7.15–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 3.54, 4.36, 7.21, 31.97, 38.68, 42.23, 71.85, 125.82, 128.44, 128.50, 142.34; IR (neat) 3350 (br, OH), 3090 (cyclopropane C–H) cm^{-1}; MS (EI) *m/e* (%) 190 (M^+, 12), 172 (65), 143 (30); HRMS (EI) calcd for $C_{13}H_{18}O$–H_2O 172.1252, found 172.1243.; Anal. Calcd for $C_{13}H_{18}O$: C, 82.06; H, 9.53. Found: C, 81.82; H, 9.66.

1-(1-Methylcyclopropyl)-4-phenylbutan-2-ol (3d). TLC R_f 0.17 (hexane/EtOAc=10/1), ^{1}H NMR ($CDCl_3$) δ 0.20–0.38 (m, 3H), 0.39–0.45 (m, 1H), 1.06 (s, 3H), 1.22 (dd, J=13.8, 9.0 Hz, 1H), 1.63 (ddd, J=14.1, 3.9, 1.2 Hz, 1H), 1.70–1.90 (m, 2H), 2.69 (ddd, J=13.8, 9.6, 6.6 Hz, 1H), 2.81 (ddd, J=13.8, 9.6, 6.6 Hz, 1H), 3.85–3.93 (m, 1H), 7.20–7.35 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 11.93, 12.62, 12.84, 22.65, 31.96, 39.17, 46.53, 69.80, 125.81, 128.44, 128.50, 142.39; IR (neat) 3370 (br, OH), 3067 (cyclopropane C–H) cm^{-1}; MS (EI) *m/e* (%) 204 (M^+, 2), 186 (38), 157 (25); HRMS (EI) calcd for $C_{14}H_{20}O$–H_2O 186.1408, found 186.1404.

***erythro*-4-Cyclopropyl-1-phenylpentan-3-ol (3e).** TLC R_f 0.17 (hexane/EtOAc=10/1), ^{1}H NMR ($CDCl_3$) δ 0.02–0.10 (m, 1H), 0.12–0.22 (m, 1H), 0.45 (dd, J=8.7, 2.1 Hz, 2H), 0.58–0.70 (m, 1H), 0.72–0.84 (m, 1H), 0.97 (d, J=6.6 Hz, 3H), 1.70–1.95 (m, 2H), 2.65 (ddd, J=13.8, 9.9, 6.6 Hz, 1H), 2.86 (ddd, J=13.8, 9.9, 6.6 Hz, 1H), 3.62 (dt, J=9.0, 3.9 Hz, 1H), 7.15–7.30 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 3.01, 4.31, 14.04, 14.47, 32.58, 36.33, 44.03, 75.48, 125.82, 128.44, 128.50, 142.45; IR (neat) 3370 (br, OH), 3085 (cyclopropane C–H) cm^{-1}; Anal. Calcd for $C_{14}H_{20}O$: C, 82.30; H, 9.87. Found: C, 82.16; H, 9.75.

***erythro*-2-Cyclopropyldecan-3-ol (3f).** TLC R_f 0.25 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.02–0.10 (m, 1H), 0.14–0.20 (m, 1H), 0.47 (dd, J=8.4, 2.1 Hz, 2H), 0.60–0.80 (m, 2H), 0.87 (t, J=8.4 Hz, 3H), 0.97 (d, J=6.6 Hz, 3H), 1.20–1.60 (m, 12H), 3.55–3.65 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 3.10, 4.21, 13.77, 13.97, 14.63, 22.54, 26.17, 29.22, 29.60, 31.76, 34.60, 43.84, 75.97; IR (neat) 3360 (br, OH), 3075 (cyclopropane C–H) cm^{-1}; MS (EI) *m/e* (%) 180 (M^+−H_2O, 2), 169 (10), 151 (2); HRMS (EI) calcd for $C_{13}H_{26}O$–C_2H_5 169.1592, found 169.1591; Anal. Calcd for $C_{13}H_{26}O$: C, 78.72; H, 13.21. Found: C, 78.51; H, 12.95.

***erythro*-2-Cyclopropyl-1-cyclohexylpropan-1-ol (*erythro*-3g).** TLC R_f 0.25 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.06–0.12 (m, 2H), 0.40–0.52 (m, 2H), 0.68–0.77 (m, 1H), 0.81–0.91 (m, 1H), 0.94 (d, J=6.3 Hz, 3H), 0.95–1.05 (m, 2H), 1.10–1.35 (m, 3H), 1.40–1.58 (m, 3H), 1.60–1.80 (m, 3H), 1.98 (d, J=12.6 Hz, 1H), 3.30 (dd, J=7.8, 3.6 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 3.76, 3.87, 12.74, 15.42, 25.88, 26.14, 26.40, 29.00, 29.41, 40.19, 40.29, 79.92; IR (neat) 3360 (br, OH), 3075 (cyclopropane C–H) cm^{-1}; MS (EI) *m/e* (%) 153 (M^+−C_2H_5, 2), 135 (10), 113 (42); HRMS (EI) calcd for $C_{12}H_{22}O$–C_2H_5 153.1279, found 153.1277; Anal. Calcd for $C_{12}H_{22}O$: C, 79.06; H, 12.16. Found: C, 79.23; H, 11.91.

***threo*-2-Cyclopropyl-1-cyclohexylpropan-1-ol (*threo*-3g).** TLC R_f 0.27 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 0.04 (dt, J=9.3, 5.4 Hz, 1H), 0.29 (dt, J=5.4, 3.6 Hz, 1H), 0.38–0.50 (m, 1H), 0.50–0.65 (m, 2H), 0.82–0.95 (m, 1H), 0.96 (d, J=0.9 Hz, 3H), 1.00–1.40 (m, 6H), 1.45–1.80 (m, 6H), 3.20–3.30 (m, 1H); ^{13}C NMR ($CDCl_3$) δ 1.29, 4.96, 13.97, 16.93, 26.11, 26.20, 26.52 (probably a signal of another carbon is buried), 30.50, 40.06, 40.26, 81.36; MS (EI) *m/e* (%) 182 (M^+, 1), 164 (3), 153 (10); HRMS (EI) calcd for $C_{12}H_{22}O$–C_2H_5 153.1279, found 153.1284.

1-Phenylhept-6-en-3-one (4b). TLC R_f 0.33 (hexane/EtOAc=10/1); ^{1}H NMR ($CDCl_3$) δ 2.31 (dt, J=6.6 and 6.9 Hz, 2H), 2.49 (t, J=6.9 Hz, 2H), 2.74 (t, J=7.2 Hz, 2H), 2.91 (t, J=7.2 Hz, 2H), 4.98 (dt, J=10.2, 1.8 Hz, 1H), 5.01 (dq, J=16.8, 1.8 Hz, 1H), 5.84 (ddd, J=16.8, 10.2, 6.6 Hz, 1H), 7.15–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 27.61, 29.62, 41.95, 44.30, 115.32, 126.17, 128.39, 128.57, 137.13, 141.17, 209.47; IR (neat) 2926, 1717 (C=H), 1455 cm^{-1}; MS (EI) *m/e* (%) 188 (M^+, 30), 133 (65), 105 (100); HRMS (EI) calcd for $C_{13}H_{16}O$ 188.1201, found 188.1205. Anal. Calcd for $C_{13}H_{16}O$: C, 82.94; H, 8.57. Found: C, 82.74; H, 8.53.

1-Phenylhept-6-en-3-ol (4c). TLC R_f 0.11 (hexane/EtOAc=10/1), ^{1}H NMR ($CDCl_3$) δ 1.42 (d, J=5.1 Hz, 1H), 1.54–1.64 (m, 2H), 1.70–1.82 (m, 2H), 2.05–2.24 (m, 2H), 2.68 (ddd, J=13.8, 9.3, 6.9 Hz, 1H), 2.81 (ddd, J=13.8, 9.3, 6.9 Hz, 1H), 3.62–3.72 (m, 1H), 4.96 (dt, J=10.2, 1.8 Hz, 1H), 5.04 (dq, J=17.7, 1.8 Hz, 1H), 5.84 (ddd, J=17.7, 10.2, 6.9 Hz, 1H), 7.15–7.40 (m, 5H); ^{13}C NMR ($CDCl_3$) δ 29.97, 31.96, 36.51, 39.12, 70.94, 114.92, 125.90, 128.50 (2 carbons), 138.59, 142.21; IR (neat) 3400 (OH), 1641, 1454 cm^{-1}; MS (EI) *m/e* (%) 190 (M^+, 3), 172 (40), 130 (65); HRMS (EI) calcd for $C_{13}H_{18}O$–H_2O 172.1252, found 172.1251.

Molecular orbital calculations

The ab initio calculations were carried out using the GAUSSIAN 98 program[16] at the MP2/LANL2DZ level. All geometries were fully optimized and all the optimized structures were local minima according to the vibration frequency analyses. Relative energies were corrected for ZPE (zero point energy) calculated at MP2/LANL2DZ.

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