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# An auxiliary induced asymmetric synthesis of functionalized cyclobutanes by means of catalytic (2+2)-cycloaddition reaction

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**Abstract**—A new entry to optically active hydroxycyclobutanes is described. Treatment of silyl enol ether and (−)-8-phenylmenthyl acrylate in the presence of a catalytic amount of $EtAlCl_2$ affords enantiomerically enriched multi-substituted cyclobutane compounds in a good yield and diastereofacial selectivity.


## 1. Introduction

Previous work in our laboratory has demonstrated $EtAlCl_2$ catalyzed (2+2)-cycloaddition of silyl enol ether with α,β-unsaturated ester.[1] This process concisely provides siloxycyclobutane carboxylate in a high yield with an excellent stereoselectivity. Further studies revealed the reaction proceeds via a stepwise pathway, like a sequential Michael addition and aldol reaction. Chiral substances possessing a hydroxycyclobutane skeleton are found often in nature (Fig. 1)[2] and serve as key intermediates[3] in routes to biologically and medicinally important synthetic targets. However, stereocontrolled construction of the multi-substituted cyclobutanes remains a difficult task in preparative organic chemistry.[4–9] Recently we have demonstrated that chiral auxiliary such as phenylmenthol effectively induces new asymmetric centers with excellent diastereoselectivity in case of the intramolecular Michael–aldol reaction using a stoichiometric amount of trimethylsilyl iodide and hexamethyldisilazane.[5] Here we wish to report asymmetric catalytic intermolecular (2+2)-cycloaddition with 8-phenylmenthyl acrylate to afford enantiomerically enriched cyclobutanes.

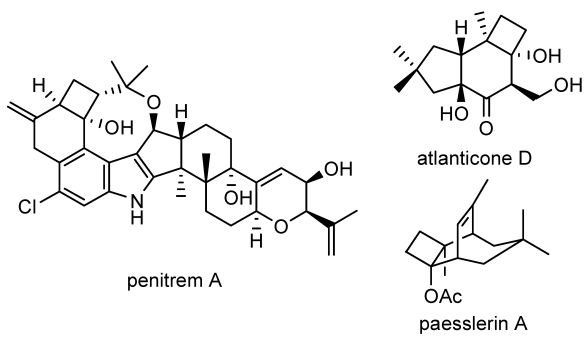


**Figure 1.** Examples of natural substances possessing functionalized cyclobutane ring.

## 2. Results and discussions

### 2.1. Asymmetric (2+2)-cycloaddition

Based on the results of our previous studies,[1] reaction was conducted using 1 equiv. of (−)-8-phenylmenthyl acrylate (**2a**) and 1.2 equiv. of silyl enol ether **1** in the presence of 20 mol% of $EtAlCl_2$ catalyst at −78 °C in $CH_2Cl_2$ (Scheme 1). Theoretically, eight disatereomeric isomers could be produced by this reaction since three stereogenic centers are generated on cyclobutane ring. The results of the (2+2)-cycloaddtion are summarized in Table 1. In the reaction of *t*-butyldimethylsiloxy-1-cyclohexene (**1a**) with **2a**, production of two diastereomers *trans*-**3a** and *cis*-**3a** in 51 and 33% yield, respectively, was observed (entry 1). These diastereomeic products can be separated by silica gel chromatography. Both *trans*-**3a** and *cis*-**3a** were analytically pure stereoisomeric compounds in $^1H$ and $^{13}C$ NMR spectroscopies. Except for siloxyethylene **1i** (entry 9), the resulting cyclobutane adducts were obtained in moderate to high yield from cyclic and acyclic substrates possessing TBS or TIPS moiety. However, only small amounts of cycloadducts were observed in the reaction of less stable TES enol ether **1c** (entry 3). The low yield of cycloadducts **3** was originated from decomposition of silyl enol ether into the corresponding ketone or dimeric aldol-adduct **4** (entries

*Keywords*: Hydroxycyclobutanes; (2+2)-Cycloadditions; Stereoselectivity; Chiral auxiliary; Asymmetric induction.
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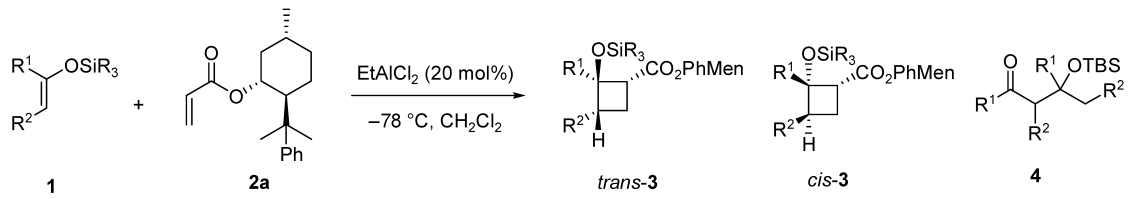



**Scheme 1.**

3, 4, 5 and 9). Interestingly, *trans*-**3** was exclusively furnished in an excellent yield using TBS enol ethers **1f** or **1k** as a substrate (entries 6 and 11).

To our surprise, it was observed a TIPS enol ether gives cyclobutane **3** with the higher *cis*-selectivity compared with the corresponding TBS enol ether (entry 1 vs. 2, 4 vs. 5, or 6 vs. 7). The selectivity in this asymmetric reaction is a complementary result against the one using achiral substrates.[1] We have reported that the *trans*-selectivity is enhanced in the reaction with achiral acrylate when more sterically bulky silyl enol ethers are employed as substrates. It has been proved no decomposition nor isomerization of cyclobutane products occurs under the (2+2)-cycloaddition conditions and work-up process. Although the detailed conformation of the transition state in this (2+2)-cycloaddition remains to be clarified, we assume an additional steric and/or stereoelectronic effect between triisopropylsilyl group and phenylmenthyl moiety causes the preferred production of *cis*-isomer.

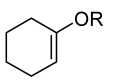
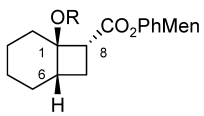
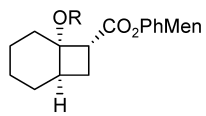
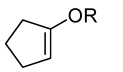
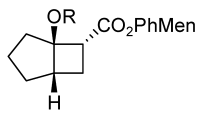
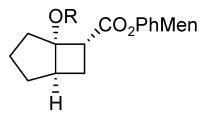
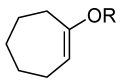
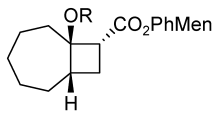
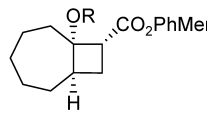
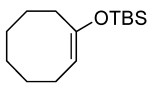
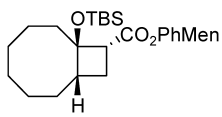
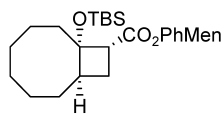
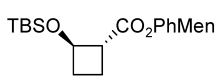
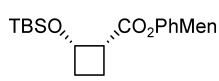
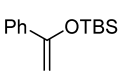
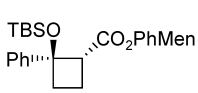
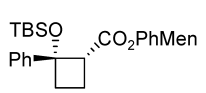
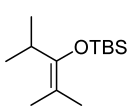
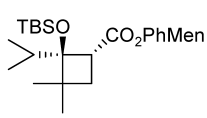
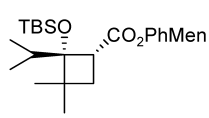
Phenylmenthyl methacrylate (**2b**) also affords (2+2)-adduct *trans*-**3l** in 42% yield along with *cis*-**3l** (3% yield) by the reaction with **1f** (Scheme 2). On the contrary, crotonate **2c** furnished cycloadducts in only 6% yield as a mixture of two diastereomers even using 100 mol% of a Lewis acid at the elevated temperature.

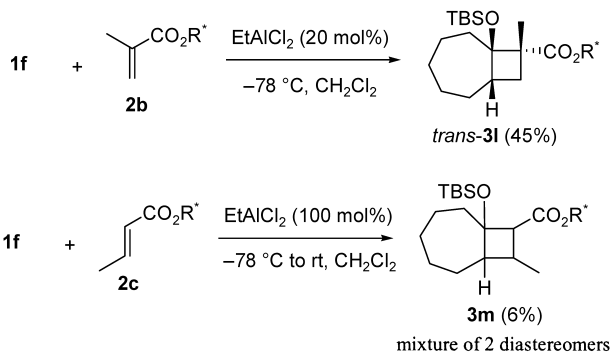
## 2.2. Stereochemical study of (2+2)-cycloaddition product

The absolute configuration of *trans*-**3a**, whose single crystals (colorless prisms) were prepared from a mixed solvent system of AcOH and MeOH, was determined by X-ray crystallography (Fig. 2). It reveals that *trans*-**3a** has the (1*R*,6*S*,8*R*)-bicyclo[4.2.0]octane skeleton.

The stereochemistry of *cis*-**3a** was determined by chemical transformation as shown in Scheme 3. Both diastereomers *trans*- and *cis*-**3a** were, separately, reduced with DIBAL-H into alcohols *trans*- and *cis*-**5a**, respectively. Since those

**Table 1**. Asymmetric (2+2)-cycloaddion reaction

| Entry | Silyl enol ether | | Product | | | |
|---|---|---|---|---|---|---|
| | | | *trans*-**3** | Yield (de) (%) | *cis*-**3** | Yield (de) (%) |
| 1 |  | **1a** (R=TBS) |  | 51 (>99) |  | 33 (>99) |
| 2 | | **1b** (R=TIPS) | | 23 (>99) | | 41 (>99) |
| 3 | | **1c** (R=TES) | | 5 (>99) | | 1 (>99) |
| 4 |  | **1d** (R=TBS) |  | 28 (>99) |  | 5 (>99) |
| 5 | | **1e** (R=TIPS) | | 26 (>99) | | 16 (>99) |
| 6 |  | **1f** (R=TBS) |  | 89 (>99) |  | 0 (—) |
| 7 | | **1g** (R=TIPS) | | 54 (>99) | | 16 (>99) |
| 8 |  | **1h** |  | 74 (>99) |  | 10 (>99) |
| 9 |  | **1i** |  | 0 (—) |  | 0 (—) |
| 10 |  | **1j** |  | 62 (>99) |  | 25 (>99) |
| 11 |  | **1k** |  | 91 (>99) |  | 0 (—) |




**Scheme 2.** R*=8-phenylmenthyl.

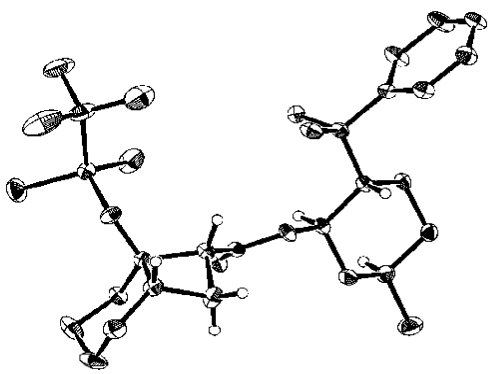
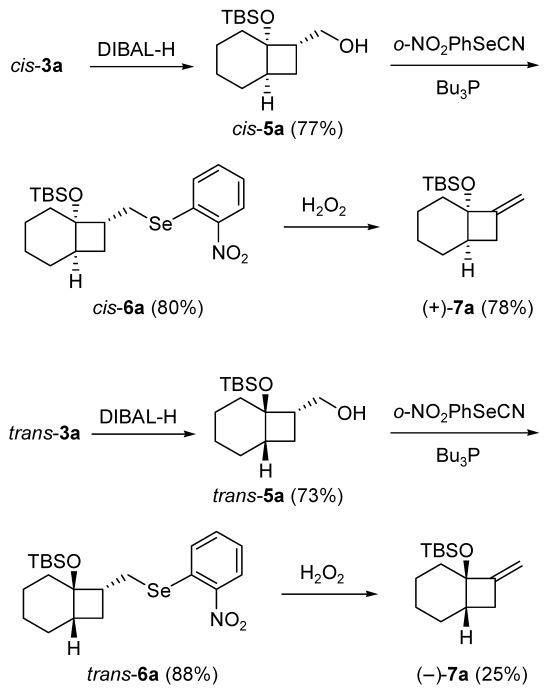


**Figure 2.** ORTEP drawing of *trans*-**3a**.




**Scheme 3.**

spectral data are not identical, the stereochemistry of cyclobutane skeleton of *cis*-**3a** corresponds to (1*R*,6*S*,8*S*) or its enantiomeric (1*S*,6*R*,8*R*). In order to remove the chirality at C(8) position, *cis*-**5a** was conducted to Grieco's dehydration reaction.[10] Namely, by treatment with *o*-nitrophenylselenyl cyanide in the presence of tributylphosphine *cis*-**5a** was transformed into selenoether *cis*-**6a**. Exposure of *cis*-**6a** under the oxidation conditions furnished *exo*-olefine (+)-**7a**, whose specific rotation ($[\alpha]_D$ in $CHCl_3$) is +10.4. In accordance with the above procedure, *trans*-**5a** was converted into (−)-**7a** ($[\alpha]_D$=−9.8 in $CHCl_3$), whose spectral data except for chiroptical sense were consistent with (+)-**7a**. Consequently, it has been made clear that *cis*-**3a** possesses the (1*S*,6*R*,8*R*)-bicyclo[4.2.0]octane framework.

The above stereochemical studies reveal that *trans*-**3a** and *cis*-**3a** possess the same (*R*)-configuration at the α-carbon of ester function. Thus, silyl enol ether **1a** would selectively approach to the enoate moiety from one side with complete diastereofacial recognition; the diastereofacial selection favoring **3a** is controlled by π-stacking interaction of the aromatic ring of phenylmenthol moiety (Fig. 3).[11] When TBS enol ether **3a** was reacted with phenylisomenthyl acrylate (**2d**),[12] which would not be expected for good conformational fixation by π-stacking interaction, under the same conditions, non-selective formation of four considerable diastereomers was observed (Scheme 4). It has been, thus, made clear that 8-phenylmenthyl moiety works as an effective chiral auxiliary in the $EtAlCl_2$ catalyzed (2+2)-cycloaddition of silyl enol ether with α,β-unsaturated ester.

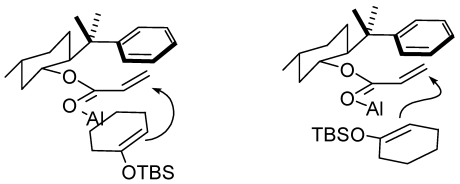
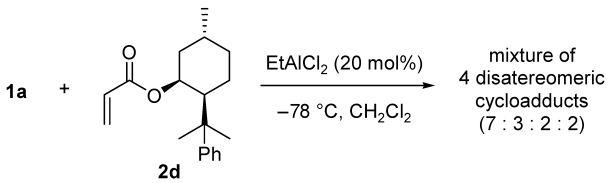



**Figure 3.** Proposed transition state models for the production of *trans*-**3a** (left) and *cis*-**3a** (right).




**Scheme 4.**

For the bicyclic compounds, *trans*- and *cis*-**3b**–**h**,**l**, their relative configurations around the cyclobutane ring were assigned based on analogy in $^1H$ and $^{13}C$ NMR spectroscopies. On the other hand, the relative stereochemistries of *trans*-**3j**, *cis*-**3j** and *trans*-**3k** were confirmed by NOESY experiment after transformation into the corresponding alcohols *trans*-**5j**, *cis*-**5j** and *trans*-**5k**, respectively (Fig. 4). The absolute configuration of all the product was presumed based on the mechanism described as above.

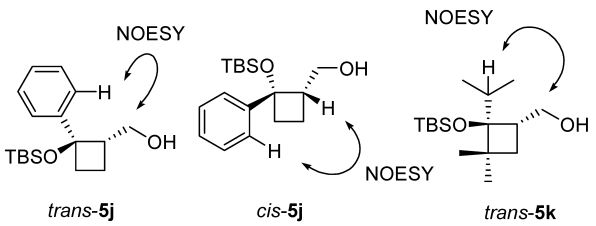



**Figure 4.**

## 3. Conclusion

In summary, we have developed a versatile, convenient and stereoselective method for the formation of optically active hydroxycyclobutanes using $EtAlCl_2$ catalyzed (2+2)-cycloaddition reaction. The reaction provides optically active multi-substituted cyclobutane compounds from readily available silyl enol ethers and 8-phenylmenthyl acrylate. The relative and absolute stereochemistries of cyclobutane products were assigned on the basis of X-ray crystallographic analysis and their chemical transformation.

## 4. Experimental

### 4.1. General

All reactions were carried out under an inert atmosphere. Anhydrous THF and $CH_2Cl_2$ were purchased from the Kanto Chemical Co., Inc. Unless otherwise described, other materials were obtained from commercial suppliers and used without further purification. Organic extracts were dried over $MgSO_4$ or $Na_2SO_4$, filtered and concentrated under reduced pressure using an evaporator. Column chromatography was performed on Merck silica gel 60 N (230–400 mesh), and flash column chromatography was performed on Cica silica gel 60 (spherical/40–100 μm). Reactions and chromatography fractions were analysed employing precoated silica gel plate (Merck silica gel $60F_{254}$). All melting points were determined on Yanaco micro melting point apparatus and are uncorrected. IR spectra were measured on JASCO IR Report-100 spectrophotometer or Shimadzu FTIR-8300 spectrometer. The $^1H$ and $^{13}C$ NMR spectra were recorded at Varian Gemini 2000 (300 and 75 MHz), JEOL AL 400 (400 and 100 MHz) as $CDCl_3$ solutions, respectively, and were reported in ppm downfield from TMS ($\delta$=0) for the $^1H$ NMR and relative to the central $CDCl_3$ resonance ($\delta$=77.00) for the $^{13}C$ NMR. Mass spectra were recorded on JEOL DX-303 or AX-500 spectrometer. Elemental analyses were performed on Yanagimoto MT-3 or YANACO CHN CORDER MT-6, and the results (C, H) were within±0.4% of theoretical values.

### 4.2. General procedure for (2+2)-cycloaddition reaction

To a solution of phenylmenthyl ester **2** (0.23 mmol) and silyl enol ether **1** (0.28 mmol) in $CH_2Cl_2$ (2 mL) was slowly added $EtAlCl_2$ (0. 46 μmol; 0.9 M solution in hexane) at −78 °C. After being stirred for 50 min, the resulting mixture was quenched with sat. $NaHCO_3$, and then was extracted with $Et_2O$ three times. The organic layer was washed with brine, dried and concentrated. The residue was purified by column chromatography on silica gel with 2% $Et_2O$/hexane to give **3**.

**4.2.1. (1*R*,6*S*,8*R*)-1-(*tert*-Butyldimethylsiloxy)-8-[(1*R*,2*S*,5*R*)-2-(1-methyl-1-phenylethyl)-5-methylcyclohexyloxycarbonyl]bicyclo[4.2.0]octane (*trans*-3a).** Colorless prisms, mp 108–110 °C (from AcOEt–MeOH); $[\alpha]_D^{27}$ (*c* 0.94, $CHCl_3$) −36.6; IR (KBr) 2927, 2856, 1717, 1249, 1184, 1101, 836, 768, 699, 668 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.37–7.22 (m, 4H), 7.21–7.12 (m, 1H), 4.83 (ddd, 1H, *J*=4.4, 10.7, 10.7 Hz), 2.77 (dd, 1H, *J*=8.8, 9.9 Hz), 2.18–1.82 (m, 3H), 1.76–1.16 (m, 10H), 1.32 (s, 3H), 1.22 (s, 3H), 1.08–0.72 (m, 9H), 0.17 (s, 3H), 0.14 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.1, 151.4, 128.0, 125.6, 125.2, 76.4, 74.3, 50.2, 41.9, 40.5, 39.9, 34.5, 32.1, 31.3, 27.2, 26.8, 26.0, 25.6, 23.4, 21.7, 21.4, 20.3, 19.2, 17.9, −2.92, −2.98; LRMS *m/z* 441 ($M^+$−57). Anal. calcd for $C_{31}H_{50}O_3Si$: C, 74.64; H, 10.10, found C, 74.60; H, 10.02.

**4.2.2. (1*S*,6*R*,8*R*)-1-(*tert*-Butyldimethylsiloxy)-8-[(1*R*,2*S*,5*R*)-2-(1-methyl-1-phenylethyl)-5-methylcyclohexyloxycarbonyl]bicyclo[4.2.0]octane (*cis*-3a).** Colorless oil; $[\alpha]_D^{28}$ (*c* 0.94, $CHCl_3$) −6.1; IR (neat) 2928, 2855, 1718, 1472, 1250, 1082, 835, 733, 699, 668 $cm^{-1}$; $^1H$ NMR (300 MHz, $CDCl_3$) $\delta$ 7.29–7.21 (m, 4H), 7.19–7.11 (m, 1H), 4.86 (ddd, 1H, *J*=4.4, 10.7, 10.7 Hz), 2.73 (dd, 1H, *J*=7.6, 7.6 Hz), 2.20 (m, 1H), 2.08–1.81 (m, 4H), 1.63–0.74 (m, 17H), 1.34 (s, 3H), 1.22 (s, 3H), 0.86 (s, 9H), 0.11 (s, 3H), 0.079 (s, 3H); $^{13}C$ NMR (75 MHz, $CDCl_3$) $\delta$ 171.1, 151.7, 127.9, 125.6, 125.1, 79.1, 74.0, 50.4, 46.9, 42.1, 39.9, 36.1, 34.5, 31.2, 28.9, 27.0, 26.8, 26.2, 25.9, 24.3, 22.8, 22.3, 21.6, 18.1, −2.28, −2.51; LRMS *m/z* 498 ($M^+$); HRMS calcd for $C_{31}H_{50}O_3Si$ 498.3529, found 498.3529.

**4.2.3. (1*R*,6*S*,8*R*)-1-Triisopropylsiloxy-8-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[4.2.0]octane (*trans*-3b).** Colorless prisms, mp 54–55 °C (from AcOEt–MeOH); $[\alpha]_D^{28}$ (*c* 0.50, $CHCl_3$) −38.0; IR (KBr) 2943, 2924, 2866, 1732, 1207, 1184, 1138, 1103 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.26–7.23 (m, 4H), 7.15–7.11 (m, 1H), 4.82 (ddd, 1H, *J*=10.7, 10.7, 4.4 Hz), 2.60 (dd, 1H, *J*=9.4, 9.4 Hz), 2.16–2.08 (m, 1H), 2.05–1.93 (m, 1H), 1.90–1.84 (m, 1H), 1.80–1.73 (m, 1H), 1.60–0.80 (m, 18H), 1.31 (s, 3H), 1.20 (s, 3H), 1.08–0.94 (m, 18H), 0.87–0.85 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.6, 151.3, 127.8, 125.4, 125.0, 76.0, 74.3, 50.8, 50.3, 42.0, 41.0, 40.0, 34.6, 32.9, 31.4, 27.1, 27.0, 26.4, 23.5, 21.9, 21.6, 20.6, 19.1, 18.4, 13.3; LRMS *m/z* 540 ($M^+$). Anal. calcd for $C_{34}H_{56}O_3Si$: C, 75.50; H, 10.44, found C, 75.40; H, 10.37.

**4.2.4. (1*S*,6*R*,8*R*)-1-Triisopropylsiloxy-8-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl] bicyclo[4.2.0]octane (*cis*-3b).** Colorless oil; $[\alpha]_D^{28}$ (*c* 0.53, $CHCl_3$) −1.0; IR (neat) 2943, 2866, 1724, 1462, 1242, 1115, 1088, 413 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.27–7.23 (m, 4H), 7.15–7.11 (m, 1H), 4.85 (ddd, 1H, *J*=10.7, 10.7, 4.4 Hz), 2.78 (dd, 1H, *J*=8.5, 8.5 Hz), 2.24–2.17 (m, 1H), 2.04–1.96 (m, 4H), 1.69–0.81 (m, 17H), 1.30 (s, 3H), 1.22 (s, 3H), 1.05 (d, 18H, *J*=7.6 Hz), 0.90–0.81 (m, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 151.5, 127.8, 125.4, 125.0, 80.7, 73.7, 50.4, 45.2, 42.2, 40.0, 35.3, 34.6, 31.3, 30.6, 27.1, 26.9, 26.8, 26.3, 23.5, 22.8, 21.8, 18.6, 18.2; LRMS *m/z* 540 ($M^+$). Anal. calcd for $C_{34}H_{56}O_3Si$: C, 75.50; H, 10.44, found C, 75.52; H, 10.39.

**4.2.5. (1*R*,6*S*,8*R*)-1-Triethylsiloxy-8-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[4.2.0]octane (*trans*-3c).** Pale yellow oil; $[\alpha]_D^{27}$ (*c* 0.54, $CHCl_3$) −47.1; IR (neat) 2953, 2928, 2874, 1715, 1238, 1186, 1101, 1078, 1018, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 7.28–7.24 (m, 4H), 7.17–7.12 (m, 1H), 4.80 (ddd, 1H, *J*=10.7, 10.7, 4.1 Hz), 2.59 (dd, 1H,

$J$=9.4, 9.4 Hz), 2.19–2.08 (m, 1H), 2.00–1.85 (m, 2H), 1.71–1.64 (m, 1H), 1.61–0.75 (m, 15H), 1.34 (s, 3H), 1.22 (s, 3H), 0.97 (t, 9H $J$=7.8 Hz), 0.64 (q, 6H, $J$=7.8 Hz); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.9, 151.2, 127.8, 125.4, 125.0, 76.3, 74.5, 50.5, 50.4, 42.0, 40.7, 40.1, 34.6, 32.4, 31.4, 28.0, 27.1, 25.7, 23.5, 21.9, 21.5, 20.5, 19.1, 7.1, 6.2; LRMS $m/z$ 498 ($M^+$); HRMS calcd for $C_{34}H_{56}O_3Si$, 498.3529, found 498.3564.

**4.2.6. (1*S*,6*R*,8*R*)-1-Triethylsiloxy-8-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[4.2.0]octane (*cis*-3c).** Colorless oil; $[\alpha]_D^{27}$ ($c$ 0.58, $CHCl_3$) −3.1; IR (neat) 2951, 2936, 2874, 1715, 1182, 1161, 1084, 741, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.30–7.18 (m, 4H), 7.15–7.09 (m, 1H), 4.88 (ddd, 1H, $J$=4.0, 10.6, 10.6 Hz), 2.72 (dd, 1H, $J$=7.0, 7.0 Hz), 2.24–2.20 (m, 1H), 2.03–1.92 (m, 4H), 1.90–1.73 (m, 3H), 1.66–0.82 (m, 16H), 1.33 (s, 3H), 1.22 (s, 3H), 0.93 (t, 9H $J$=7.6 Hz), 0.65–0.52 (m, 6H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.9, 151.5, 127.8, 125.4, 125.0, 78.4, 74.0, 50.5, 48.3, 42.1, 40.7, 40.0, 36.4, 34.7, 31.4, 28.0, 27.0, 26.4, 23.0, 22.7, 22.2, 21.8, 7.2, 6.6; LRMS $m/z$ 498 ($M^+$); HRMS calcd for $C_{34}H_{56}O_3Si$, 498.3529, found 498.3518.

**4.2.7. (1*R*,5*S*,7*R*)-1-*tert*-Butyldimethylsiloxy-7-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[3.2.0]heptane (*trans*-3d).** Pale yellow oil; $[\alpha]_D^{29}$ ($c$ 0.66, $CHCl_3$) −33.5; IR (neat) 2953, 2928, 2855, 1717, 1258, 1225, 1096, 837, 775, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27–7.20 (m, 4H), 7.18–7.10 (m, 1H), 4.83 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.93 (dd, 1H, $J$=10.1, 10.1 Hz), 2.44–2.36 (m, 1H), 2.05–1.88 (m, 4H), 1.82–1.65 (m, 5H), 1.60–0.70 (m, 10H), 1.33 (s, 3H), 1.23 (s, 3H), 0.86 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.4, 151.1, 127.8, 125.4, 125.1, 86.7, 74.5, 50.5, 49.0, 44.4, 42.0, 40.1, 37.6, 34.6, 31.4, 31.4, 27.9, 27.0, 25.8, 24.8, 21.9, 20.0, 17.9, −2.88, −2.95; LRMS $m/z$ 484 ($M^+$). Anal. calcd for $C_{30}H_{48}O_3Si$: C, 74.33; H, 9.98, found C, 74.32; H, 9.83.

**4.2.8. (1*S*,5*R*,7*R*)-1-*tert*-Butyldimethylsiloxy-7-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[3.2.0]heptane (*cis*-3d).** Pale yellow oil; $[\alpha]_D^{29}$ ($c$ 0.34, $CHCl_3$) −13.7; IR (neat) 2951, 2930, 2856, 1732, 1173, 1161, 1097, 905, 835, 775, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.29–7.23 (m, 4H), 7.18–7.10 (m, 1H), 4.78 (ddd, 1H, $J$=4.1, 10.5, 10.5 Hz), 2.77 (dd, 1H, $J$=8.3, 8.3 Hz), 2.54–2.46 (m, 1H), 2.45–2.34 (m, 1H), 2.18–2.08 (m, 1H), 1.87–1.75 (m, 5H), 1.60–0.70 (m, 12H), 1.38 (s, 3H), 1.25 (s, 3H), 0.90 (s, 9H), 0.11 (s, 3H), 0.03 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.0, 151.5, 127.8, 125.5, 125.0, 86.2, 74.9, 50.6, 48.3, 43.1, 42.0, 41.6, 40.4, 34.7, 31.5, 31.3, 29.5, 27.2, 25.9, 24.0, 21.8, 21.8, 18.2, −2.47, −2.87; LRMS $m/z$ 484 ($M^+$); HRMS calcd for $C_{30}H_{48}O_3Si$, 484.3373, found 484.3403.

**4.2.9. (1*R*,5*S*,7*R*)-1-Triisopropylsiloxy-7-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[3.2.0]heptane (*trans*-3e).** Pale yellow oil; $[\alpha]_D^{29}$ ($c$ 1.83, $CHCl_3$) −30.5; IR (neat) 2951, 2889, 2866, 1719, 1223, 1194, 1121, 1105, 881, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27–7.22 (m, 4H), 7.18–7.10 (m, 1H), 4.84 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.98 (dd, 1H, $J$=10.0, 10.0 Hz), 2.46–2.36 (m, 1H), 2.11–1.86 (m, 3H), 1.81–1.66 (m, 4H), 1.60–0.75 (m, 12H), 1.32 (s, 3H), 1.22 (s, 3H), 1.06 (s, 21H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 171.3, 151.2, 127.8, 125.4, 125.0, 86.7, 74.5, 50.5, 49.6, 44.8, 42.0, 40.1, 37.8, 34.6, 31.6, 31.4, 27.7, 25.9, 24.5, 21.9, 19.8, 18.3, 13.2; LRMS $m/z$ 526 ($M^+$). Anal. calcd for $C_{33}H_{54}O_3Si$: C, 75.23; H, 10.33, found C, 75.42; H, 10.27.

**4.2.10. (1*S*,5*R*,7*R*)-1-Triisopropylsiloxy-7-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[3.2.0]heptane (*cis*-3e).** Colorless oil; $[\alpha]_D^{28}$ ($c$ 1.01, $CHCl_3$) −11.1; IR (neat) 2947, 2866, 1732, 1231, 1163, 1103, 883, 700, 681 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28–7.22 (m, 4H), 7.16–7.08 (m, 1H), 4.84 (ddd, 1H, $J$=10.6, 10.6, 4.1 Hz), 2.75 (dd, 1H, $J$=8.5, 8.5 Hz), 2.48–2.38 (m, 1H), 2.35–2.20 (m, 1H), 2.11–2.02 (m, 1H), 2.00–1.90 (m, 1H), 1.90–1.67 (m, 4H), 1.67–0.74 (m, 12H), 1.34 (s, 3H), 1.22 (s, 3H), 1.05 (s, 21H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.3, 151.4, 127.8, 125.4, 125.0, 86.6, 74.5, 50.6, 48.7, 43.8, 42.0, 41.6, 40.2, 34.6, 31.3, 28.2, 27.1, 25.2, 24.3, 22.0, 21.8, 18.4, 18.3, 13.5; LRMS $m/z$ 526 ($M^+$); HRMS calcd for $C_{33}H_{54}O_3Si$, 526.3842, found 526.3888.

**4.2.11. (1*R*,7*S*,9*R*)-1-*tert*-Butyldimethylsiloxy-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[5.2.0]nonane (*trans*-3f).** Colorless prisms, mp 86–88 °C (from AcOEt–MeOH); $[\alpha]_D^{28}$ ($c$ 0.54, $CHCl_3$) −31.4; IR (KBr) 2924, 2855, 1728, 1254, 1150, 1126, 1065, 837, 775 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.25–7.24 (m, 4H), 7.15–7.13 (m, 1H), 4.83 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.73 (dd, 1H, $J$=9.8, 9.8 Hz), 2.14 (m, 1H), 1.99 (m, 1H), 1.91–1.84 (m, 2H), 1.79–0.81 (m, 20H), 1.30 (s, 3H), 1.20 (s, 3H), 0.90 (s, 9H), 0.20 (s, 3H), 0.16 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.7, 151.2, 127.8, 125.3, 125.0, 82.3, 74.4, 74.1, 50.3, 48.7, 46.7, 40.0, 34.7, 32.7, 31.4, 26.9, 26.7, 26.5, 26.1, 25.9, 23.7, 22.5, 22.0, 21.8, 18.2, −2.67, −2.84; LRMS $m/z$ 455 ($M^+$−57). Anal. calcd for $C_{32}H_{52}O_3Si$: C, 74.94; H, 10.22, found C, 75.00; H, 10.11.

**4.2.12. (1*R*,7*S*,9*R*)-1-Triisopropylsiloxy-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[5.2.0]nonane (*trans*-3g).** Colorless needles, mp 87–88 °C (from AcOEt–MeOH); $[\alpha]_D^{28}$ ($c$ 0.44, $CHCl_3$) −27.9; IR (KBr) 2926, 2866, 1728, 1460, 1252, 1225, 1205, 1192, 1130, 772, 700, 683 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.25–7.23 (m, 4H), 7.15–7.10 (m, 1H), 4.84 (ddd, 1H, $J$=4.1, 10.5, 10.5 Hz), 2.76 (dd, 1H, $J$=10.0, 10.0 Hz), 2.25–2.17 (m, 1H), 2.04–1.97 (m, 1H), 1.90–0.81 (m, 22H), 1.29 (s, 3H), 1.19 (s, 3H), 1.10 (s, 18H), 0.88–0.86 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.5, 151.3, 127.8, 125.3, 125.0, 82.3, 74.2, 50.3, 49.4, 47.1, 41.9, 40.0, 36.3, 34.6, 34.3, 33.6, 32.2, 31.4, 26.9, 26.7, 26.5, 23.7, 22.1, 21.9, 18.5, 13.4; LRMS $m/z$ 554 ($M^+$). Anal. calcd for $C_{32}H_{52}O_3Si$: C, 74.94; H, 10.22, found C, 75.00; H, 10.11.

**4.2.13. (1*S*,7*R*,9*R*)-1-Triisopropylsiloxy-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[5.2.0]nonane (*cis*-3g).** Colorless oil; $[\alpha]_D^{28}$ ($c$ 0.87, $CHCl_3$) −9.0; IR (neat) 2924, 2866, 1722, 1454, 1240, 1092, 762, 700, 677 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27–7.25 (m, 4H), 7.15–7.10 (m, 1H), 4.84 (ddd, 1H,

$J$=4.4, 10.5, 10.5 Hz), 2.87 (dd, 1H, $J$=8.8, 8.8 Hz), 2.41 (br, 1H), 2.12 (dd, 1H, $J$=10.5, 20.0 Hz), 2.04–1.94 (m, 1H), 1.92–1.85 (m, 1H), 1.80–1.71 (m, 1H), 1.70–0.80 (m, 19H), 1.32 (s, 3H), 1.20 (s, 3H), 1.05 (s, 18H), 0.86–0.80 (m, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.3, 151.5, 127.8, 125.4, 125.0, 84.3, 73.9, 50.5, 46.6, 45.9, 42.1, 40.9, 40.0, 34.6, 31.8, 31.3, 30.2, 26.9, 26.8, 26.6, 25.6, 24.9, 21.8, 21.5, 18.6, 13.8; LRMS $m/z$ 554 ($M^+$); HRMS calcd for $C_{32}H_{52}O_3Si$, 554.4155, found 554.4156.

**4.2.14. (1*R*,8*S*,10*R*)-1-*tert*-Butyldimethylsiloxy-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[6.2.0]decane (*trans*-3h).** Colorless oil; $[\alpha]_D^{27}$ ($c$ 0.76, $CHCl_3$) −14.2; IR (neat) 2927, 2855, 1713, 1240, 1165, 1136, 1005, 833, 812, 766, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.29–7.22 (m, 4H), 7.16–7.10 (m, 1H), 4.84 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.85 (dd, 1H, $J$=10.0, 10.0 Hz), 2.03–1.78 (m, 3H), 1.68–0.80 (m, 23H), 1.29 (s, 3H), 1.20 (s, 3H), 0.91 (s, 9H), 0.22 (s, 3H), 0.20 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.6, 151.2, 127.8, 125.3, 125.1, 81.7, 74.2, 50.3, 49.8, 46.5, 42.0, 40.0, 34.6, 31.4, 30.5, 28.9, 27.1, 26.9, 26.8, 26.7, 26.1, 24.9, 24.3, 24.1, 21.9, 21.4, 18.5, −2.34, −2.75; LRMS $m/z$ 526 ($M^+$); HRMS calcd for $C_{33}H_{54}O_3Si$: 526.3842, found 526.3854.

**4.2.15. (1*S*,8*R*,10*R*)-1-*tert*-Butyldimethylsiloxy-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[6.2.0]decane (*cis*-3h).** Colorless oil; $[\alpha]_D^{26}$ ($c$ 0.28, $CHCl_3$)+22.2; IR (neat) 2926, 2855, 1722, 1445, 1259, 1165, 1094, 1022, 835, 810, 764, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28–7.19 (m, 4H), 7.15–7.09 (m, 1H), 4.91 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.39 (dd, 1H, $J$=9.5, 9.5 Hz), 2.03–1.89 (m, 2H), 1.83–0.82 (m, 24H), 1.31 (s, 3H), 1.19 (s, 3H), 0.89 (s, 9H), 0.11 (s, 3H), 0.08 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$);$\delta$ 171.6, 151.3, 127.8, 125.3, 125.0, 81.2, 73.8, 50.6, 49.3, 47.2, 42.6, 39.8, 34.5, 31.9, 31.4, 29.1, 27.1, 26.7, 26.1, 26.0, 25.3, 24.9, 24.4, 24.3, 22.0, 21.0, 18.5, −2.10, −2.42; LRMS $m/z$ 526 ($M^+$); HRMS calcd for $C_{33}H_{54}O_3Si$: 526.3842, found 526.3854.

**4.2.16. (1*R*,2*R*)-1-*tert*-Butyldimethylsiloxy-2-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]-1-phenylcyclobutane (*trans*-3j).** Colorless oil; $[\alpha]_D^{27}$ ($c$ 1.17, $CHCl_3$) −48.0; IR (neat) 2928, 2856, 1715, 1256, 1005, 833, 698 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.44–7.39 (m, 2H), 7.30–7.15 (m, 7H), 7.15–7.09 (m, 1H), 4.49 (ddd, 1H, $J$=4.4, 10.6, 10.6 Hz), 3.22 (dd, 1H, $J$=9.4, 9.4 Hz), 2.64–2.56 (m, 1H), 2.25 (q, 4H, $J$=10.6 Hz), 1.79–1.62 (m, 3H), 1.47–1.35 (m, 2H), 1.24 (s, 3H), 1.11 (s, 3H), 0.90 (s, 9H), 0.94–0.55 (m, 7H), 0.15 (q, 1H, $J$=12.0 Hz), −0.02 (s, 3H), −0.23 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 169.7, 151.3, 142.2, 127.7, 127.6, 127.3, 126.3, 125.3, 125.0, 80.6, 73.9, 55.3, 50.1, 40.5, 39.9, 34.4, 33.9, 31.0, 26.8, 26.3, 25.9, 21.6, 18.1, 15.4, −2.83, −2.93; LRMS $m/z$ 520 ($M^+$). Anal. calcd for $C_{32}H_{48}O_3Si$: C, 76.10; H, 9.29, found C, 75.89; H, 8.97.

**4.2.17. (1*S*,2*R*)-1-*tert*-Butyldimethylsiloxy-2-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]-1-phenylcyclobutane (*cis*-3j).** Colorless oil; $[\alpha]_D^{27}$ ($c$ 1.17, $CHCl_3$) −37.3; IR (neat) 2928, 2856, 1722, 1229, 1124, 980, 835, 764, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.60–7.52 (m, 2H), 7.35–7.18 (m, 7H), 7.13–7.05 (m, 1H), 4.92 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.95 (dd, 1H, $J$=7.8, 7.8 Hz), 2.67–2.55 (m, 1H), 2.32 (ddd, 1H, $J$=5.4, 10.7, 10.7 Hz), 2.14–1.96 (m, 3H), 1.63–0.70 (m, 10H), 1.35 (s, 3H), 1.23 (s, 3H), 0.80 (s, 9H), −0.13 (s, 3H), −0.42 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 170.3, 151.4, 145.7, 127.9, 127.8, 127.2, 126.4, 125.4, 125.0, 80.7, 74.5, 53.3, 50.4, 42.3, 40.1, 34.6, 31.9, 31.4, 27.3, 27.0, 26.0, 21.8, 18.2, 17.7, −2.94, −3.37; LRMS $m/z$ 520 ($M^+$); HRMS calcd for $C_{32}H_{48}O_3Si$, 520.3373, found 520.3378.

**4.2.18. (1*S*,4*R*)-1-*tert*-Butyldimethylsiloxy-1-isopropyl-2,2-dimethyl-4-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]cyclobutane (*trans*-3k).** Colorless oil; $[\alpha]_D^{26}$ ($c$ 0.85, $CHCl_3$) −7.4; IR (neat) 2959, 2928, 2856, 1715, 1254, 1070, 764, 700, 669 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.27–7.23 (m, 4H), 7.16–7.11 (m, 1H), 4.85 (ddd, 1H, $J$=4.4, 10.7, 10.7 Hz), 2.78 (dd, 1H, $J$=6.4, 10.0 Hz), 2.31–2.20 (m, 1H), 2.05–1.95 (m, 1H), 1.94–1.84 (m, 1H), 1.62–0.78 (m, 17H), 1.32 (s, 3H), 1.21 (s, 3H), 1.13 (s, 3H), 0.98 (s, 3H), 0.93 (s, 9H,), 0.22 (s, 3H), 0.20 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 172.4, 151.3, 127.9, 125.4, 125.2, 74.3, 50.3, 47.4, 42.9, 41.4, 39.9, 34.5, 32.6, 31.4, 26.9, 26.2, 24.7, 21.8, 19.1, 17.7, 17.5, −2.28, −2.51; LRMS $m/z$ 457 ($M^+$−57); HRMS calcd for $C_{32}H_{48}O_3Si$: 457.3138, found 457.3156.

**4.2.19. (1*R*,7*S*,9*R*)-1-(*tert*-Butyldimethylsiloxy)-9-methyl-9-[(1*R*,2*S*,5*R*)-5-methyl-2-(1-methyl-1-phenylethyl)cyclohexyloxycarbonyl]bicyclo[5.2.0]nonane (*trans*-3l).** Colorless oil; $[\alpha]_D^{27}$ ($c$ 0.47, $CHCl_3$) −4.5; IR (neat) 2926, 2855, 1715, 1456, 1076, 835, 773, 700 cm$^{-1}$; $^1$H NMR (400 MHz, $CDCl_3$) $\delta$ 7.28–7.23 (m, 4H), 7.17–7.11 (m, 1H), 4.79 (ddd, 1H, $J$=4.1, 10.6, 10.6 Hz), 2.43–2.30 (m, 1H), 2.05–1.93 (m, 2H), 1.81–0.72 (m, 21H), 1.32 (s, 3H), 1.29 (s, 3H), 1.20 (s, 3H), 0.89 (s, 9H), 0.19 (s, 3H), 0.14 (s, 3H); $^{13}$C NMR (100 MHz, $CDCl_3$) $\delta$ 174.5, 151.1, 127.9, 125.4, 1251, 83.6, 75.1, 50.7, 50.3, 43.8, 41.8, 40.2, 34.7, 31.5, 31.4, 29.0, 28.2, 27.3, 26.2, 24.9, 23.4, 21.9, 21.9, 21.8, 18.8, 0.09, −1.63, −1.72; LRMS $m/z$ 526 ($M^+$); HRMS calcd for $C_{33}H_{54}O_3Si$, 526.3842, found 526.3861.

### 4.3. X-ray crystallography[13]

Prismatic crystals of *trans*-**3a** suitable for X-ray crystallography were grown by slow crystallization from AcOH–MeOH. A Colorless prism crystal of *trans*-**3a** having approximate dimensions of 0.20×0.20×0.20 mm was mounted on a glass fiber. All measurements were made on a Rigaku/MSC Mercury CCD diffractometer with graphite monochromated Mo Ka radiation. The data were collected at a temperature of −100±1 °C to a maximum $2\theta$ value of 55.0°. The structure was solved using the programs in teXsan; the compound *trans*-**3a** belongs to the monoclinic space group $P2_1$ (#4) with $a$=10.168(2) Å, $b$=11.027(2) Å, $c$=13.583(3) Å, $\beta$=91.139(4)°, $V$=1522.6(5) Å$^3$, $Z$=2, and $D$=1.088 g/cm$^3$. $R$=0.034, and $R_w$=0.036 for 3644 unique reflections. GOF=0.92.

### 4.4. General procedure for reduction of ester 3 into alcohol 5

To a solution of **3** (1.0 equiv.) in $CH_2Cl_2$ (0.1 M) was

gradually added DIBAL-H (7.0 equiv., 1 M hexane solution) at −78 °C. The mixture was stirred for 70 min at the same temperature, and then was quenched with MeOH. The resulting mixture was filtered through Celite® and the filtrate was concentrated in vacuo. The residue was chromatographed on silica gel (12% AcOEt/hexane) to afford alcohol **5**.

**4.4.1. (1*R*,6*S*,8*S*)-1-*tert*-Butyldimethylsiloxy-8-hydroxymethylbicyclo[4.2.0]octane (*trans*-5a).** *Compound trans*-**5a** was obtained from *trans*-**3a** (252 mg, 0.51 mmol) in 73% yield (100 mg). Colorless needles, mp 72–73 °C (from AcOEt–hexane); $[\alpha]_D^{28}$ (*c* 0.27, $CHCl_3$) −32.9; IR ($CHCl_3$) 3683, 3607, 3032, 3013, 1234, 1200, 802, 706, 679 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.78–3.73 (m, 1H), 3.60–3.54 (m, 1H), 2.30–2.17 (m, 2H), 1.73–1.22 (m, 9H), 1.08 (d, 1H, *J*=10.2 Hz), 1.03 (d, 1H, *J*=10.5 Hz), 0.85 (s, 9H), 0.12 (s, 3H), 0.10 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 100.5, 62.9, 48.6, 40.8, 31.1, 25.8, 23.7, 21.8, 20.4, 18.0, −2.36, −2.40; LRMS *m*/*z* 213 ($M^+$−57). Anal. calcd for $C_{15}H_{30}O_2Si$: C, 66.61; H, 11.18, found C, 66.43; H, 10.84.

**4.4.2. (1*S*,6*R*,8*S*)-1-*tert*-Butyldimethylsiloxy-8-hydroxymethylbicyclo[4.2.0]octane (*cis*-5a).** *Compound cis*-**5a** was obtained from *cis*-**3a** (35 mg, 0.070 mmol) in 77% yield (13 mg). Colorless oil; $[\alpha]_D^{27}$ (*c* 0.49, $CHCl_3$)+6.1; IR (neat) 3354, 2930, 2856, 1462, 1252, 1180, 1076, 881, 835, 772, 667 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 3.92–3.86 (m, 1H), 3.68–3.59 (m, 1H), 2.53–2.40 (m, 2H), 2.37–2.25 (m, 1H), 1.88–1.81 (m, 1H), 1.76–1.66 (m, 2H), 1.52–1.34 (m, 7H), 0.89 (s, 9H), 0.18 (s, 3H), 0.14 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 63.9, 45.7, 40.0, 37.6, 25.9, 25.6, 21.4, 21.1, 20.0, 18.1, −2.24, −2.40; LRMS *m*/*z* 213 ($M^+$−57); HRMS *m*/*z* calcd for $C_{15}H_{30}O_2Si$ ($M^+$−57): 213.1311, found 213.1321.

**4.4.3. (1*R*,2*S*)-1-*tert*-Butyldimethylsiloxy-2-hydroxymethyl-1-phenylcyclobutane (*trans*-5j).** *Compound trans*-**5j** was obtained from *trans*-**3j** (63 mg, 0.12 mmol) in 83% yield (29 mg). Colorless oil; $[\alpha]_D^{28}$ (*c* 1.17, $CHCl_3$) −24.6; IR (neat) 3329 2953, 2930, 2856, 1254, 775, 700 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.50–7.45 (m, 2H), 7.39–7.33 (m, 2H), 7.29–7.26 (m, 1H), 3.21 (ddd, 1H, *J*=6.3, 6.8, 11.4 Hz), 3.13 (ddd, 1H, *J*=5.8, 6.1, 11.6 Hz), 2.85–2.76 (m, 1H), 2.70 (ddd, 1H, *J*=2.7, 8.7, 11.6 Hz), 2.38–2.28 (m, 1H), 2.03–1.93 (m, 1H), 1.48–1.36 (m, 1H), 0.91 (s, 9H), 0.75 (dd, 1H, *J*=5.8, 6.3 Hz), −0.01 (s, 3H), −0.22 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 142.7, 128.1, 127.2, 126.2, 79.4, 63.3, 52.2, 33.3, 25.9, 18.0, 16.4, −2.86, −2.97; LRMS *m*/*z* 292 ($M^+$); HRMS calcd for $C_{17}H_{28}O_2Si$, 292.1859, found 292.1883.

**4.4.4. (1*S*,2*S*)-1-*tert*-Butyldimethylsiloxy-2-hydroxymethyl-1-phenylcyclobutane (*cis*-5j).** *Compound cis*-**5j** was obtained from *cis*-**3j** (26 mg, 0.050 mmol) in 66% yield (10 mg). Colorless oil; $[\alpha]_D^{27}$ (*c* 0.39, $CHCl_3$) −2.9; IR (neat) 3420, 2953, 2930, 2856, 1252, 1126, 835, 777, 669 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 7.51–7.47 (m, 2H), 7.39–7.34 (m, 2H), 7.30–7.25 (m, 1H), 4.15 (ddd, 1H, *J*=3.2, 11.2, 11.2 Hz), 3.79 (ddd, 1H, *J*=4.6, 9.8, 11.5 Hz), 3.22 (dd, 1H, *J*=3.2, 9.8 Hz), 2.88–2.80 (m, 1H), 2.70–2.60 (m, 1H), 2.49–2.39 (m, 1H), 1.73–1.62 (m, 1H), 1.55–1.46 (m, 1H), 0.87 (s, 9H), −0.01 (s, 3H), −0.45 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 145.7, 128.2, 127.3, 126.3, 79.7, 64.3, 50.2, 31.9, 25.8, 17.9, 14.9, −3.14, −3.69; LRMS *m*/*z* 292 ($M^+$); HRMS calcd for $C_{17}H_{28}O_2Si$, 292.1859, found 292.1871.

**4.4.5. (1*S*,4*S*)-1-*tert*-Butyldimethylsiloxy-4-hydroxymethyl-1-isopropyl-2,2-dimethylcyclobutane (*trans*-5k).** *Compound trans*-**5k** was obtained from *trans*-**3k** (65 mg, 0.13 mmol) in 61% yield (22 mg). Colorless needles, mp 60–61 °C (from AcOEt–hexane); $[\alpha]_D^{26}$ (*c* 0.78, $CHCl_3$)+6.4; IR (neat) 3317, 2934, 2860, 1462, 1256, 1067, 862, 835, 770 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.09–3.96 (m, 1H), 3.71 (dd, 1H, *J*=10.3, 10.3 Hz), 2.49–2.37 (m, 1H), 2.01–1.84 (m, 2H), 1.32 (dd, 1H, *J*=4.4, 11.7 Hz), 1.17 (s, 3H), 1.03 (s, 3H), 0.94 (s, 9H), 0.85 (d, 6H, *J*=7.1 Hz), 0.23 (s, 3H), 0.16 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 85.4, 64.4 45.5, 42.2, 34.0, 31.0, 26.8, 26.3, 25.8, 19.2, 17.3, −1.58, −1.85; LRMS *m*/*z* 228 ($M^+$−58); HRMS calcd for $C_{13}H_{28}OSi$: 228.1909, found 228.1889.

### 4.5. Transformation into *exo*-olefin 7a

**4.5.1. (1*S*,6*R*,8*R*)-1-*tert*-Butyldimethylsiloxy-8-*o*-nitrophenylselanylmethylbicyclo[4.2.0]octane (*cis*-6a).** To a solution of *cis*-**5a** (74 mg, 0.27 mmol) and *o*-nitrophenylselenocyanide (75 mg, 0.33 mmol) in THF (4.0 mL) was slowly added tributylphosphine (85 μL, 0.34 mmol) at ambient temperature, and the resulting solution was stirred for 22.5 h at 50–55 °C. After removal of solvent, the residue was purified by column chromatography on silica gel with 2% AcOEt/hexane to give *cis*-**6a** (100 mg, 80%) as yellowish prisms, mp 63–65 °C (from AcOEt–hexane); $[\alpha]_D^{28}$ (*c* 0.37, $CHCl_3$) −1.6; IR (KBr) 2928, 2855, 1512, 1329, 1304, 1067, 835, 733 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 8.30–8.25 (m, 1H), 7.56–7.46 (m, 2H), 7.31–7.25 (m, 1H), 3.22 (dd, 1H, *J*=5.5, 11.2 Hz), 2.98 (dd, 1H, *J*=10.6, 10.6 Hz), 2.52–2.33 (m, 2H), 1.84–1.21 (m, 10H), 0.93 (s, 9H), 0.16 (s, 3H), 0.14 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 134.5, 133.3, 129.1, 126.3, 125.0, 76.6, 41.6, 40.1, 36.7, 27.7, 27.2, 26.7, 26.0, 22.3, 22.1, 18.4, −2.23; LRMS *m*/*z* 398 ($M^+$−57). Anal. calcd for $C_{21}H_{33}NO_3SeSi$: C, 55.49; H, 7.32; N, 3.08, found C, 55.67; H, 7.15; N, 2.92.

**4.5.2. (1*S*,6*R*)-1-*tert*-Butyldimethylsiloxy-8-methylidenebicyclo[4.2.0]octane ((+)-7a).** To a solution of *cis*-**6a** (72 mg, 0.16 mmol) in THF (3.2 mL) was added $H_2O_2$ (31% v/v; 300 μL) at 0 °C, and the mixture was stirred for 17.5 h at ambient temperature. The resulting mixture was extracted with $Et_2O$ twice, dried, and concentrated. The residue was chromatographed on silica gel (hexane) to furnish (+)-**7a** (31 mg, 78%) as colorless oil, $[\alpha]_D^{27}$ (*c* 1.75, $CHCl_3$)+10.4; IR (neat) 2930, 2856, 1680, 1252, 1142, 1088, 835, 773 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) δ 4.91–4.86 (m, 1H), 4.69–4.63 (m, 1H), 2.42–2.25 (m, 2H), 2.20–2.10 (m, 1H), 1.78–1.18 (m, 8H), 0.88 (s, 9H), 0.09 (s, 6H); $^{13}C$ NMR (100 MHz, $CDCl_3$) δ 155.7, 101.2 77.6, 39.9, 35.8, 28.5 25.8, 24.2, 21.3 20.8 18.2, −2.40, −2.44; LRMS *m*/*z* 252 ($M^+$); HRMS *m*/*z* calcd for $C_{15}H_{28}OSi$ ($M^+$): 252.1909, found 252.1916.

**4.5.3. (1*R*,6*S*,8*R*)-1-*tert*-Butyldimethylsiloxy-8-*o*-nitrophenylselenylmethylbicyclo[4.2.0]octane (*trans*-6a).** To

a solution of *trans*-**5a** (95 mg, 0.35 mmol) and *o*-nitrophenylselenocyanide (96 mg, 0.42 mmol) in THF (4.0 mL) was slowly added tributylphosphine (105 μL, 0.42 mmol) at ambient temperature, and the resulting solution was stirred for 17 h at the same temperature and additional 5.5 h at 50 °C. After removal of solvent, the residue was purified by column chromatography on silica gel with 2% AcOEt/hexane to give *trans*-**6a**. (140 mg, 88%) as yellowish prisms, mp 91–93 °C (from AcOEt–hexane); $[\alpha]_D^{28}$ (*c* 0.36, $CHCl_3$) −54.8; IR (KBr) 2928, 2855, 1508, 1333, 1252, 1094, 773, 741 $cm^{-1}$; $^1H$ NMR (400 MHz, $CDCl_3$) $\delta$ 8.29 (d, 1H, *J*=7.8 Hz), 7.52–7.48 (m, 2H), 7.33–7.27 (m, 1H), 3.10 (dd, 1H, *J*=5.9, 11.0 Hz), 2.84 (dd, 1H, *J*=9.8, 9.8 Hz), 2.38–2.27 (m, 1H), 2.26–2.16 (m, 1H), 1.84 (dd, 1H, *J*=8.5, 8.5 Hz), 1.76–1.20 (m, 8H), 1.15 (d, 1H, *J*=10.3 Hz), 1.09 (d, 1H, *J*=10.5 Hz), 0.89 (s, 9H), 0.11 (s, 3H), 0.11 (s, 3H); $^{13}C$ NMR (100 MHz, $CDCl_3$) $\delta$ 134.2, 133.4, 128.9, 126.4, 125.1, 75.8, 44.7, 40.6, 31.1, 26.0, 25.8, 23.8, 23.6, 21.8, 20.4, 18.0, −2.24, −2.34; LRMS *m/z* 398 ($M^+$−57). Anal. calcd for $C_{21}H_{33}NO_3SeSi$: C, 55.49; H, 7.32; N, 3.08, found C, 55.34; H, 7.10; N, 2.92.

**4.5.4. (1*R*,6*S*)-1-*tert*-Butyldimethylsiloxy-8-methylidene-bicyclo[4.2.0]octane ((−)-7a).** To a solution of *trans*-**6a** (118 mg, 0.26 mmol) in THF (5.2 mL) was added $H_2O_2$ (31% v/v; 430 μL) at 0 °C, and the mixture was stirred for 21 h at ambient temperature. The resulting mixture was extracted with $Et_2O$ twice, dried, and concentrated. The residue was chromatographed on silica gel (hexane) to furnish (−)-**7a** (16 mg, 25%) as colorless oil, $[\alpha]_D^{26}$ (*c* 0.75, $CHCl_3$) −9.8. All spectral data were identical with (+)-**7**.

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