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A Chiral Building Block with Bicyclo[2.2.2]octanone Skeleton by the Reduction with Baker's Yeast.†

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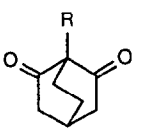
Abstract: Preparation of functionalized bicyclo[2.2.2]octan-2-one with high optical purity is described. Reduction of a bridged diketone **2** with baker's yeast gave an *endo*-hydroxyketone (+)-**12** of 98.5~99.5 %*e.e.* in 91 % yield. X-ray crystallography of its (*S*)-MTPA ester **13a** determined the absolute configuration of (+)-**12** as (1*S*,4*S*,6*S*).

INTRODUCTION

During the course of our continuing interest in the chiral synthesis of bioactive natural products, we have been looking for versatile building blocks with high optical purity.[1] Asymmetric reduction by fermenting baker's yeast is generally known as one of the efficient procedure to afford those chiral materials.[2,3] In our group, it was found that the asymmetric reduction of simple bicyclo[2.2.2]octane-2,6-dione analogs gave mainly *endo*-hydroxyketones with acceptable diastereoselectivity and optical purity.[4] Among them, 1-methylbicyclo[2.2.2]-octane-2,6-dione **1** gave the best result. Since bicyclo[2.2.2]octane system is very popular in the world of natural products and would also be nice precursor for various carbon skeleta *via* chemical transformation, we became interested in preparing the bicyclo[2.2.2]octanone with additional functionality, which would be convertible to complex molecules. Thus, we selected 1-acetoxyethylbicyclo[2.2.2]octane-2,6-dione **2** as a candidate for biochemical transformation.



1 R = Me
2 R = CH_2CH_2OAc

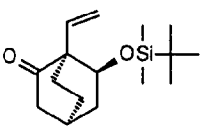


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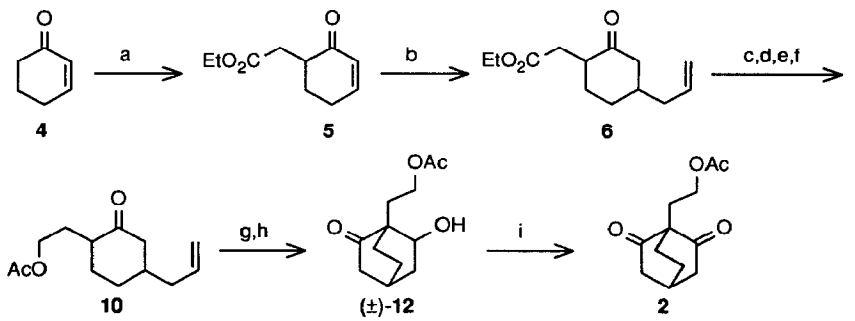
Fig. I

†Preparative Bioorganic Chemistry Part 13. For part 12, see Mori, K.; Bernotas, R. *Tetrahedron: Asymmetry*, 1990, *1*, 87.

Below we wish to describe the efficient synthesis of the substrate **2**, asymmetric reduction with baker's yeast and finally transformation to the desired chiral building block, 6-*t*-butyldimethylsilyloxy-1-vinylbicyclo-[2.2.2]octan-2-one **3**.

PREPARATION OF THE SUBSTRATE

Although direct methylation of cyclohexenone **4** failed and it was only possible by indirect method *via* metalation of its dimethylhydrazone,[5] we found that alkylation of **4** with ethyl bromoacetate in the presence of LDA under carefully controlled condition (see experimental) gave the desired product **5** in 72 % yield. Reaction of **5** with allyltrimethylsilane and $TiCl_4$[6] gave 5-allyl-2-ethoxycarbonylmethylcyclohexanone **6** (93 %), which was converted to 5-allyl-2-(2-acetoxyethyl)cyclohexanone **10** through 4 steps procedure (acetal formation, reduction with $LiAlH_4$, acetylation and acetal cleavage; 91 %). Ozonization of **10** and reductive work-up followed by acid treatment to give mainly an *endo*-hydroxyketone (±)-**12** (83 %). PDC oxidation of (±)-**12** afforded the symmetrical substrate, 1-acetoxyethylbicyclo[2.2.2]octane-2,6-dione **2** (91 %). Overall yield of **2** from cyclohexenone **4** was very good,46 %,through 9 steps.



a) LDA,$BrCH_2CO_2Et$/THF,-70°C. b) CH_2=$CHCH_2TMS$,$TiCl_4$/CH_2Cl_2,-70°C. c) $HOCH_2CH_2OH$,*p*-TsOH/benzene. d) $LiAlH_4$/ether. e) Ac_2O/pyridine. f) *p*-TsOH/acetone. g) O_3/CH_2Cl_2-MeOH; Me_2S. h) HCl aq/acetone. i) PDC,MS-4A/CH_2Cl_2.

Fig. II

ASYMMETRIC REDUCTION AND ABSOLUTE CONFIGURATION

Asymmetric reduction of **2** with dry baker's yeast was executed under similar condition as reported,[4,7,8] except for reaction scale and concentration of the substrate. It seemed to be better to stir the reaction mixture efficiently to prevent hydrolysis of acetoxy group. Thus, a mixture of **2** (3.5 g), baker's yeast (50 g) and sugar

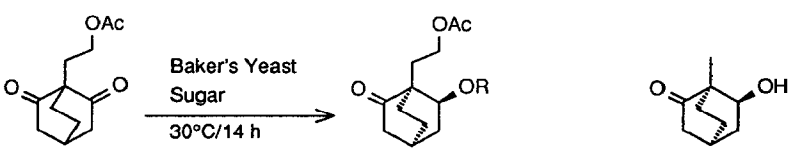


Fig. III

(80 g) in water (700 ml) was placed in 5 l Erlenmeyer flask and shaken vigorously at 30°C for 14 h. This was proved to be the procedure of choice to give (+)-1-acetoxyethyl-6-hydroxybicyclo[2.2.2]octan-2-one **12** in the highest yield (91 % based on the unrecovered **2**, 71 % efficiency), $[\alpha]_D^{22}$ +6.5 (MeOH). Essentially, the sole product with *endo*-OH was obtained. Diastereoselectivity (~100 %*d.e.*) was improved as compared with that of the methyl analog **14** (98.8 %*d.e.*),[4] probably because the substrate **2** contains bulkier substituent at bridgehead position (C-1). Optical purity of **12** determined *via* its MTPA esters **13** to be 98.8 %*e.e.* As the absolute configuration of **14** was determined by chemical correlation to the known sample and CD spectral comparison,[4,9] our product **12** might have the same configuration as **14** in accord with Prelog's prediction,[10] but it was not concluded. Fortunately, we noticed that the (*S*)-MTPA ester **13a** of **12** was nicely crystalline compound. X-ray crystallography of **13a** revealed that the absolute configuration of (+)-**12** is (1*S*,4*S*,6*S*). Fig. IV shows a perspective view of **13a**.

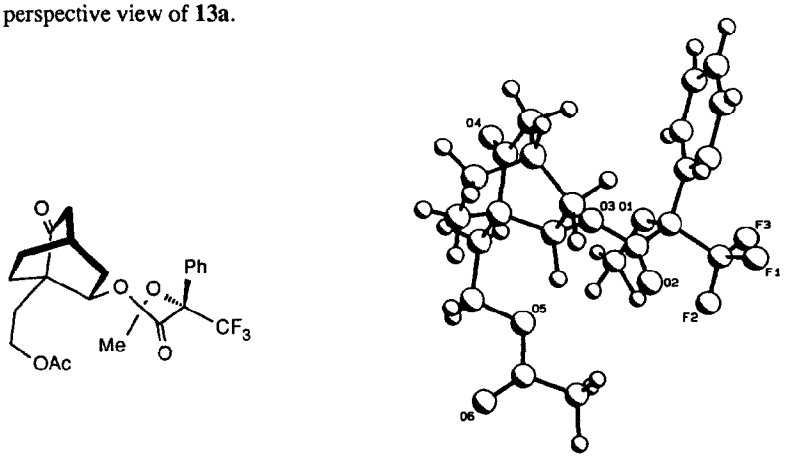
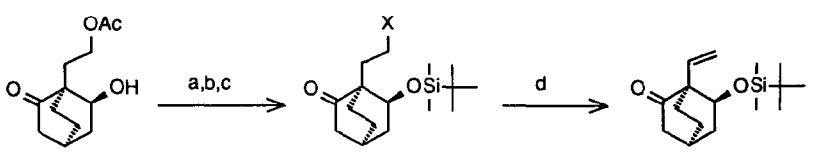


Fig. IV A perspective view of (*S*)-MTPA ester **13a**

CONVERSION TO THE CHIRAL BUILDING BLOCK

Silylation of *endo*-OH in **12**, followed by methanolysis of acetate with MeOH-K_2CO_3 gave a primary hydroxyketone **16** (93 %). Phenylselenenylation with *N*-(phenylseleno)phthalimide[11] gave the phenylselenide **17**, which on oxidative elimination afforded the desired (+)-6-*t*-butyldimethylsilyloxy-1-vinylbicyclo[2.2.2]-octan-2-one **3** (91 %), $[\alpha]_D^{21}$ +42.0 (hexane). Overall yield of **3** starting from cyclohexenone **4** was satisfactorily high 36 % through 14 steps.



12 **16** X = OH, **17** X = SePh, **3**

a) *t*-BuSi(Me)$_2$Cl,imidazole/DMF. b) K_2CO_3/MeOH. c) NPSP,(*n*-Bu)$_3$P/THF. d) O_3/CH_2Cl_2; Et_3N/CCl_4

Fig. V

In conclusion, preparative scale synthesis of functionalized bicyclo[2.2.2]octan-2-one **3** was achieved in optically active form using asymmetric reduction with dry baker's yeast. Absolute configuration of **3** was determined unambiguously by X-ray analysis. As the procedure is simple and efficient, large scale preparation of **3** is now possible. Chiral synthesis of complex natural products from **3** is in progress and will be reported in due course.

EXPERIMENTAL

All b.ps and m.ps were uncorrected. IR spectra were measured as CCl_4 soln on a Jasco IRA-102 spectrometer unless otherwise stated. ^1H NMR spectra were measured in $CDCl_3$ with TMS or $CHCl_3$ as an internal standard at 90 MHz on a JEOL JNM EX-90 spectrometer unless otherwise stated. Optical rotations were recorded on a Jasco DIP 140 polarimeter. Merck Kieselgel 60 Art. 7734 was used for a column chromatography.

Ethyl 2-oxo-3-cyclohexeneacetate **5**. A soln of 2-cyclohexen-1-one 4 (96.13 g, 1.00 mol) in dry THF (100 ml) was added dropwise through a cooling jacket to a stirred and cooled soln of LDA [prepared from $(i\text{-Pr})_2NH$ (150 ml, 108 g, 1.07 mol) and *n*-BuLi (1.53 N in hexane, 700 ml, 1.07 mol) in dry THF (800 ml)] at -70°C. After stirring for 30 min at -70°C, a soln of ethyl bromoacetate (122 ml, 184 g, 1.10 mol) in dry THF (100 ml) was added dropwise through a cooling jacket to the mixture and the stirring was continued for 1 h. 6 N HCl aq was added, and the mixture was extracted with ether. The organic soln was washed with 2 N HCl aq, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was diluted with hexane (2 l) and filtered through SiO_2. The filtrate was concentrated *in vacuo* to give 131 g (71.8 %) of **5**. An analytical sample was obtained by distillation, b.p. 99°C/0.6 Torr; n_D^{21} 1.4752; IR vmax 3050 (m), 1738 (s), 1686 (s), 1622 (m), 1220 (s), 1170 (s), 1030 (s), 900 (m) cm^{-1}; ^1H NMR δ 1.27 (3H, t, *J*=7.1 Hz), 1.6-2.6 (5H, m), 2.7-3.1 (2H, m), 4.16 (2H, q, *J*=7.1 Hz), 6.03 (1H, dt, *J*=9.9, 2.0 Hz), 6.97 (1H, dddd, *J*=9.9, 4.6, 3.3, 1.3 Hz). (Found: C, 65.65; H, 7.79. Calc. for $C_{10}H_{14}O_3$: C, 65.92; H, 7.74 %).

Ethyl 4-allyl-2-oxocyclohexaneacetate **6**. A soln of $TiCl_4$ (190 g, 1.00 mol) in CH_2Cl_2 (800 ml) was added dropwise through a cooling jacket to a stirred and cooled soln of **5** (91.1 g, 0.50 mol) in CH_2Cl_2 (400 ml) at -70°C. After stirring for 30 min at -70°C, a soln of allyltrimethylsilane (68.6 g, 0.60 mol) in CH_2Cl_2 (100 ml) was added dropwise through a cooling jacket to the mixture and the temp was raised to -40°C for 1 h. Water was added and the mixture was extracted with CH_2Cl_2. The organic soln was filtered through SiO_2 and concentrated *in vacuo* at 0°C. The residue was purified by SiO_2 column chromatography (1 kg) followed by distillation to give 103.7 g (92.5 %) of **6**, b.p. 101-115°C/0.4 Torr; n_D^{21} 1.4695; IR vmax 3090 (w), 1742 (s), 1720 (s), 1643 (m), 1190 (s), 1165 (s), 920 (s) cm^{-1}; ^1H NMR δ 1.27 (3H, t, *J*=7.2 Hz), 1.3-3.0 (12H, m), 4.14 (2H, q, *J*=7.2 Hz), 4.9-5.2 (2H, m), 5.5-6.0 (1H, m). (Found: C, 69.47; H, 8.97. Calc. for $C_{13}H_{20}O_3$: C, 69.61; H, 8.99 %).

Ethyl 4-allyl-2,2-ethylenedioxycyclohexaneacetate **7**. A mixture of **6** (102.3 g, 0.456 mol), ethylene glycol (37.24 g, 0.60 mol), *p*-TsOH·H_2O (1.9 g, 10 mmol) and C_6H_6 (1 l) was refluxed for 4 h with azeotropic removal of water. After cooling, the mixture was filtered through SiO_2 (300 g). The filtrate was concentrated *in vacuo* to give 122.9 g (100 %) of **7**. An analytical sample was obtained by distillation, n_D^{21} 1.4732; IR vmax 3090 (w), 1740 (s), 1640 (s), 1175 (s), 1155 (s), 1040 (s), 916 (s) cm^{-1}; ^1H NMR δ 1.24 (3H, t, *J*=7.2 Hz), 0.8-2.7 (12H, m), 3.95 (4H, br.s), 4.12 (2H, q, *J*=7.2 Hz), 4.8-5.1 (2H, m), 5.5-6.0 (1H, m). (Found: C, 67.30; H, 8.98. Calc. for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01 %).

4-Allyl-2,2-ethylenedioxycyclohexaneethanol **8**. A soln of **7** (94.8 g, 0.353 mol) in dry ether (100 ml) was added dropwise to a stirred and ice-cooled suspension of $LiAlH_4$ (9.1 g, 0.24 mol) in dry ether (1 l) and the mixture was stirred for 1 h. The usual alkaline work-up gave 80.0 g (100 %) of **8**. An analytical sample was obtained by distillation, n_D^{21} 1.4891; IR vmax 3480 (m), 3080 (m), 1640 (m), 1090 (s), 1065 (s), 915 (s) cm^{-1}; ^1H NMR δ 0.8-2.5 (13H, m), 3.3-4.1 (6H, m), 4.8-5.2 (2H, m), 5.5-6.0 (1H, m). (Found: C, 68.68; H, 9.81. Calc. for $C_{13}H_{22}O_3$: C, 68.99; H, 9.80 %).

4-Allyl-2,2-ethylenedioxycyclohexaneethyl acetate **9**. A soln of **8** (80.0 g, 0.353 mol) and Ac_2O (37.7 ml, 40.8 g, 0.40 mol) in pyridine (182 ml, 178 g, 2.25 mol) was stirred overnight at 4°C. Water (9 ml, 0.5 mol) was added and the mixture was stirred at room temp for 1 h. The mixture was poured into cold 6 N HCl aq (300 ml) and extracted with ether. The organic soln was washed with 1 N HCl aq, water, 2 N NaOH aq, sat $NaHCO_3$ aq and brine, dried ($MgSO_4$) and concentrated *in vacuo* to give 92.9 g (98.0 %) of **9**. An analytical sample was obtained by distillation, n_D^{21} 1.4766; IR νmax 3080 (w), 1742 (s), 1640 (m), 1242 (s), 1095 (m), 1060 (m), 915 (m) cm^{-1}; ^1H NMR δ 0.8-2.2 (12H, m), 2.05 (3H, s), 3.94 (4H, m), 4.12 (2H, br.t, *J*=6.8 Hz), 4.8-5.1 (2H, m), 5.77 (1H, ddt, *J*=17.7, 9.3, 7.0 Hz). (Found: C, 67.08; H, 9.07. Calc. for $C_{15}H_{24}O_4$: C, 67.14; H, 9.01 %).

4-Allyl-2-oxocyclohexaneethyl acetate **10**. A soln of **9** (92.9 g, 0.346 mol), *p*-TsOH·H_2O (1.9 g, 10 mmol) and MeOH (20 ml) in acetone (700 ml) was refluxed for 4 h. After cooling, a soln of $NaHCO_3$ (0.84 g) in water (10 ml) was added and the mixture was concentrated *in vacuo*. The residue was filtered through SiO_2 (700 g). The filtrate was concentrated *in vacuo* to give 72.2 g (93.0 %) of **10**, IR νmax 3090 (w), 1745 (s), 1718 (s), 1642 (m), 1240 (s), 920 (m) cm^{-1}. This included a starting material, but this was employed in the next step without further purification.

2-Oxo-4-(2-oxoethyl)cyclohexaneethyl acetate **11**. Ozone was bubbled into a mixture of **10** obtained above (67.7 g, 0.30 mol), $NaHCO_3$ (0.84 g, 10 mmol), CH_2Cl_2 (350 ml) and MeOH (350 ml) at -70°C until blue color developed. Then, N_2 was bubbled to remove excess ozone. To this was added Me_2S (36.7 ml, 31.1 g, 0.50 mol), and the mixture was stirred overnight at room temp. The mixture was concentrated *in vacuo* and filtered through SiO_2 to give crude **11** (81.7 g), IR νmax (film) 3450 (m), 2740 (m), 1720 (s), 1240 (s), 1040 (s) cm^{-1}. This was employed in the next step without further purification.

(1S,4S*,6S*)-1-(2-Acetoxyethyl)-6-hydroxybicyclo[2.2.2]octan-2-one* (±)-**12**. A mixture of **11** obtained above (81.7 g), 2 N HCl aq (70 ml) and acetone (1.4 l) was refluxed for 10 min. After cooling, a suspension of $NaHCO_3$ (11.8 g, 0.14 mol) in water (20 ml) was added and the mixture was concentrated *in vacuo*. The residue was extracted with ether, washed with sat $NaHCO_3$ aq and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (500 g) to give 56.4 g (82.5 % from **10**) of (±)-**12**, n_D^{21} 1.4993; IR νmax 3500 (m), 1740 (sh), 1728 (s), 1240 (s), 1035 (m) cm^{-1}; ^1H NMR δ 1.4-1.8 (6H, m), 1.92 (1H, t, *J*=6.0 Hz), 1.96 (1H, t, *J*=6.4 Hz), 2.05 (3H, s), 2.0-2.4 (4H, m), 4.08 (1H, br.d, *J*=9.0 Hz), 4.21 (1H, t, *J*=6.0 Hz), 4.22 (1H, t, *J*=6.4 Hz). (Found: C, 63.52; H, 7.98. Calc. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02 %).

1-(2-Acetoxyethyl)bicyclo[2.2.2]octane-2,6-dione **2**. PDC (137 g, 0.364 mol) was added to a stirred and ice-cooled mixture of (±)-**12** (55.0 g, 0.243 mol), MS-4A (140 g) and CH_2Cl_2 (500 ml) and the mixture was stirred at room temp for 3 h. Ether (500 ml) was added and the mixture was filtered through Florisil. The filter cake was washed with EtOAc. Combined Organic soln was concentrated *in vacuo* to give 49.5 g (90.8 %) of **2**. An analytical sample was obtained by recrystallization (Et_2O), m.p. 50-52°C; IR νmax (KBr) 1730 (s), 1710 (s), 1240 (s), 1030 (s), 750 (m) cm^{-1}; ^1H NMR δ (300 MHz) 1.9-2.0 (4H, m), 2.03 (3H,s), 2.05 (2H, t, *J*=6.9 Hz), 2.40 (2H, br.d, *J*=18.5 Hz), 2.55 (2H, br.d, *J*=18.5 Hz), 2.64 (1H, m), 4.18 (2H, t, *J*=6.9 Hz). (Found: C, 64.31; H, 7.21. Calc. for $C_{12}H_{16}O_4$: C, 64.27; H, 7.19 %).

(1S,4S,6S)-1-(2-Acetoxyethyl)-6-hydroxybicyclo[2.2.2]octan-2-one **12**. A mixture of dry yeast (50 g), sugar (80 g) and water (700 ml) was incubated in a 5 l Erlenmeyer flask for 30 min at 30°C. A soln of **2** (3.5 g, 15.6 mmol) in EtOH (25 ml) was added and the incubation was continued for 14 h with rotary shaker. Ether (150 ml), EtOAc (150 ml) and Celite was added and the mixture was allowed to stand for 3 h at 4°C. The mixture was filtered and the filter cake was washed thoroughly with ether. The filtrate was extracted with ether. The organic soln was washed with sat $NaHCO_3$ aq and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (35 g).

Fractions eluted earlier gave 0.74 g (21 % recovery) of **2**.

Fractions eluted later gave 2.50 g (71.4 %) of **12**, n_D^{20} 1.4998; $[\alpha]_D^{20}$ +6.5 (c=0.99, MeOH). Its IR and ^1H NMR spectra were identical with those of (±)-**12**. (Found: C, 63.63; H, 7.93. Calc. for $C_{12}H_{18}O_4$: C, 63.70; H, 8.02 %).

Determination of the enantiomeric purity of **12**. **12** was converted to the corresponding (*S*)- and (*R*)-MTPA esters (**13a** and **13b**). These were employed in the HPLC analysis. HPLC (Column; Senshu Pak Silica-1251-N; 4.6 mmϕ×25 cm; *n*-hexane:THF = 8:1; 1.2

ml/min; detected at 254 nm): Mixture of **13a** and **13b**: Rt 30.2 (23 %) and 37.6 (57 %) min. **13b**: Rt 30.9 (0.55 %) and 36.5 (97.7 %) min. Therefore, the enantiomeric purity of **12** was determined to be 98.8 %*e.e.*

(1S,4S,6S)-1-(2-Acetoxyethyl)-6-t-butyldimethylsilyloxybicyclo[2.2.2]octan-2-one **15**. A soln of **12** (25.90 g, 0.114 mol), *t*-butylchlorodimethylsilane (19.6 g, 0.13 mol) and imidazole (17.7 g, 0.26 mol) in DMF (120 ml) was stirred overnight at room temp. The mixture was poured into water and extracted with ether. The organic soln was washed with 1 N HCl aq, water and brine, dried ($MgSO_4$) and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (400 g) to give 36.1 g (92.6 %) of **15**, n_D^{21} 1.4752; $[\alpha]_D^{21}$ +19.0 (c=1.01, hexane); IR νmax 1735 (s), 1245 (s), 1100 (s), 1045 (m) cm^{-1}; ^1H NMR δ 0.03 (3H, s), 0.05 (3H, s), 0.84 (9H, s), 1.4-1.9 (7H, m), 2.03 (3H, s), 1.9-2.3 (4H, m), 3.96 (1H, dd, *J*=8.3, 1.2 Hz), 4.13 (1H, t, *J*=7.2 Hz), 4.14 (1H, t, *J*=7.3 Hz). (Found: C, 63.57; H, 9.50. Calc. for $C_{18}H_{32}O_4Si$: C, 63.49; H, 9.47 %).

(1S,4S,6S)-6-t-Butyldimethylsilyloxy-1-(2-hydroxyethyl)bicyclo[2.2.2]octan-2-one **16**. A mixture of **15** (34.05 g, 0.10 mol), K_2CO_3 (0.69 g, 5 mmol) and MeOH (400 ml) was stirred overnight at room temp. To this was added 2 N HCl aq (2.5 ml), and the mixture was concentrated *in vacuo*. The residue was diluted with ether, filtered through Florisil and concentrated *in vacuo* to give 29.9 g (100 %) of **16**, n_D^{21} 1.4863; $[\alpha]_D^{21}$ +22.3 (c=0.99, hexane); IR νmax 3500 (m), 1720 (s), 1258 (s), 1105 (s), 1090 (s), 1045 (s) cm^{-1}; ^1H NMR δ 0.05 (6H, s), 0.85 (9H, s), 1.1-2.5 (11H, m), 3.00 (1H, OH), 3.84 (1H, dd, *J*=1.4, 8.0 Hz), 3.68 (2H, dd, *J*=4.9, 7.3 Hz). (Found: C, 64.26; H, 10.10. Calc. for $C_{16}H_{30}O_3Si$: C, 64.38; H, 10.13 %).

(1S,4S,6S)-6-t-Butyldimethylsilyloxy-1-(2-phenylselenenylethyl)bicyclo[2.2.2]octan-2-one **17**. A mixture of PhSeCl (26.8 g, 0.14 mol), potassium phthalimide (29.6 g, 0.16 mol) and dry THF (200 ml) was stirred at room temp for 2 h. A soln of **16** (28.95 g, 97 mmol) in dry THF (100 ml) was added and the mixture was cooled to 0°C. To this was added dropwise $(n\text{-Bu})_3P$ (29.9 ml, 24.3 g, 0.12 mol), and the mixture was stirred at room temp for 3 h. Water (0.2 ml) was added and the mixture was concentrated *in vacuo*. The residue was diluted with hexane (600 ml), filtered through Celite and concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (500 g) to give 38.4 g (90.4 %) of **17**. An analytical sample was obtained by recrystallization (hexane), m.p. 53.2-53.5°C; $[\alpha]_D^{21}$ -3.9 (c=1.03, hexane); IR νmax 3070 (w), 1728 (s), 1255 (m), 1105 (s) cm^{-1}; ^1H NMR δ -0.06 (3H, s), 0.00 (3H, s), 0.79 (9H, s), 1.4-1.8 (7H, m), 1.9-2.5 (4H, m), 2.5-3.2 (2H, m), 3.88 (1H, dd, *J*=9.2, 1.5 Hz), 7.1-7.3 (3H, m), 7.4-7.6 (2H, m). (Found: C, 60.74; H, 7.90. Calc. for $C_{22}H_{34}O_2SeSi$: C, 60.39; H, 7.83 %).

(1S,4S,6S)-6-t-Butyldimethylsilyloxy-1-vinylbicyclo[2.2.2]octan-2-one **3**. Ozone was bubbled into a soln of **17** (37.6 g, 86 mmol) in CH_2Cl_2 (700 ml) at -70°C until blue color developed. Then, N_2 was bubbled to remove excess ozone. To this was added Et_3N (42 ml, 30.5 g, 0.30 mol) and CCl_4 (500 ml), and the mixture was heated for 2 h at 70°C with removal of CH_2Cl_2 by distillation. After cooling, the mixture was filtered through Florisil and the filtrate was concentrated *in vacuo*. The residue was purified by SiO_2 column chromatography (320 g) to give 24.1 g (100 %) of **3**, n_D^{21} 1.4798; $[\alpha]_D^{21}$ +42.0 (c=1.02, hexane); IR νmax 3090 (w), 1730 (s), 1638 (m), 1255 (s), 1105 (s), 908 (s) cm^{-1}; ^1H NMR δ 0.00 (3H, s), 0.02 (3H, s), 0.83 (9H, s), 1.4-2.6 (9H, m), 3.90 (1H, dd, *J*=0.95, 8.0 Hz), 5.02 (1H, dd, *J*=1.7, 18 Hz), 5.20 (1H, dd, *J*=1.7, 11 Hz), 6.39 (1H, dd, *J*=11, 18 Hz). (Found: C, 68.59; H, 10.09. Calc. for $C_{16}H_{28}O_2Si$: C, 68.52; H, 10.06 %).

X-ray crystallographic analysis of **13a**.[12] A colorless rod-like crystal having approximate dimensions of 0.3 × 0.3 × 0.3 mm was mounted on a glass fiber. All measurements were made on a Rigaku AFC5S diffractometer with graphite monochromated MoKα radiation and a 50 KV 30 mA sealed tube X-ray generator.

The data were collected using the ω-2θ scan technique to a maximum 2θ value of 50.0°. A total of 2194 independent reflections was collected. The liner absorption coefficient for MoKα is 1.1 cm^{-1}. Azimuthal scans of several reflections indicated no need for an absorption correction. The data were corrected for Lorentz and polarization effects.

The structure was solved by direct methods.[13] The resulting E map revealed the position of all non-H atoms. All H atoms positions were found on a difference Fourier map. The refinement of atomic parameters was carried out by a full-matrix least-squares refinement. Thermal parameters were refined anisotropically for all non-H atoms and isotropically for the H atoms. The final refinement was based on 1266 observed reflections ($I>3.00\sigma(I)$) and 380 variable parameters and converged (largest parameter shift was 1.67 times its e.s.d.) with unweighted and weighted agreement factors of:

$R = \Sigma||Fo|-|Fc||/\Sigma|Fo| = 0.046$

$Rw = [(\Sigma w(|Fo|-|Fc|)^2/\Sigma wFo^2)]^{1/2} = 0.059$

The standard deviation of an observation of unit weight was 1.46. The weighting scheme was based on counting statistics and included a factor (p=0.03) to downweight the intense reflections. Plots of $\Sigma w(|Fo|-|Fc|)$ versus |Fo|, reflection order in data collection, $\sin\theta/\lambda$, and various classes of indices showed no usual trends. The maximum and minimum peaks on the final difference Fourier map corresponded to 0.18 and -0.21 $e^-/Å^3$, respectively.

Neutral atom scattering factors were taken from Cromer and Waber.[14] All calculations were performed using the TEXSAN[15] crystallographic software package of Molecular Structure Corporation.

Table 1. Crystal Data

Empirical Formula	$C_{22}H_{25}O_6F_3$
Formula Weight	442.43
Crystal System	orthorhombic
Lattice Parameters:	a = 10.687 (2) Å
	b = 23.612 (2) Å
	c = 8.488 (2) Å
	V = 2142.1 (5) $Å^3$
Space Group	$P2_12_12_1$(#19)
Z value	4
D calc	1.372 g/cm^3

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