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EFFICIENT ASYMMETRIC SYNTHESIS OF *CIS*-2-METHYLCYCLOPROPANECARBOXYLIC ACID

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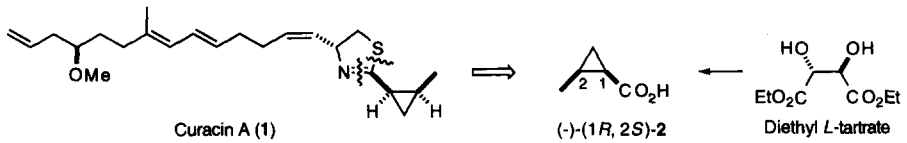
Abstract: We have developed a versatile method for the synthesis of enantiomerically pure *cis*-2-methylcyclopropanecarboxylic acid (-)-**2**, a component of curacin A, and its enantiomer, (+)-**2**. Double-asymmetric Simmons-Smith cyclopropanation of the dienes **5** and **9** derived from diethyl *L*-tartrate proceeded with excellent diastereofacial selectivity (>99% de) to give the dicyclopropanes **6** and **10**, which were converted to both enantiomers of **2**. Copyright © 1996 Published by Elsevier Science Ltd

The cyclopropane subunit is found as a basic structural element in a number of natural and non-natural products of biological interest.[1] The biological and biochemical importance of optically active cyclopropanes has led to the development of numerous methods for their construction.[2] The Simmons-Smith reaction is the most widely used method for conversion of an alkene to the corresponding cyclopropane.[3] In this reaction, the oxygen function proximal to the alkene can, *via* chelation to zinc, direct the stereoselective attack of the reagent[4], allowing application of the reaction to asymmetric synthesis. The Simmons-Smith reactions of olefins with chiral auxiliaries[5] and of achiral allylic alcohols using chiral ligands[6] were reported to give cyclopropanes with high stereoselectivity.

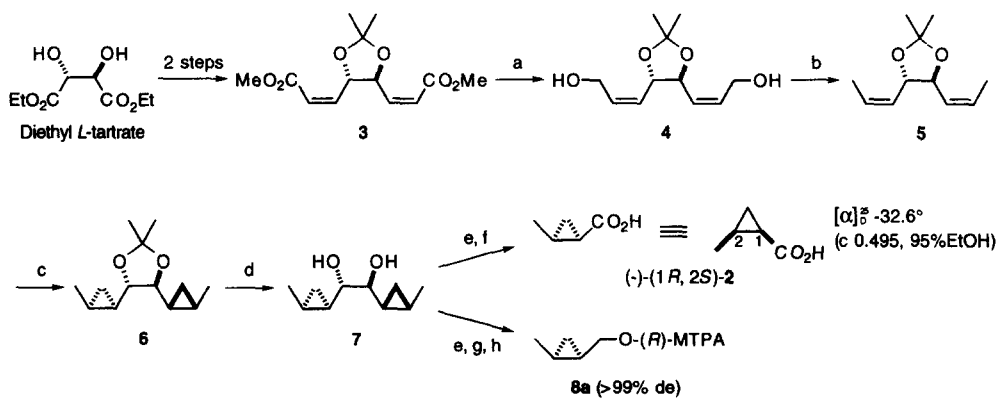
Curacin A (**1**)[7] is a novel antimitotic agent recently isolated from a Caribbean cyanobacterium, *Lyngbya majuscula*, and contains a chiral cyclopropane substructure. Several groups have reported synthetic approaches to curacin A.[8] In a previous paper[8a], we reported on the synthesis of 2-(2-methyl)cyclopropyl-4-(1-propenyl)thiazolines as a partial structure of curacin A, using racemic or resolved (+)-(1*S*, 2*R*)-2-methylcyclopropanecarboxylic acid to construct the cyclopropyl moiety. Here we describe an efficient stereoselective synthesis of *cis*-2-methylcyclopropanecarboxylic acid (-)-(1*R*, 2*S*)-**2**, a component of natural curacin A, and its enantiomer, (+)-(1*S*, 2*R*)-**2**, using double-asymmetric Simmons-Smith reaction of the dienes **5** and **9** derived from diethyl *L*-tartrate (**Scheme 1**).

Scheme 1



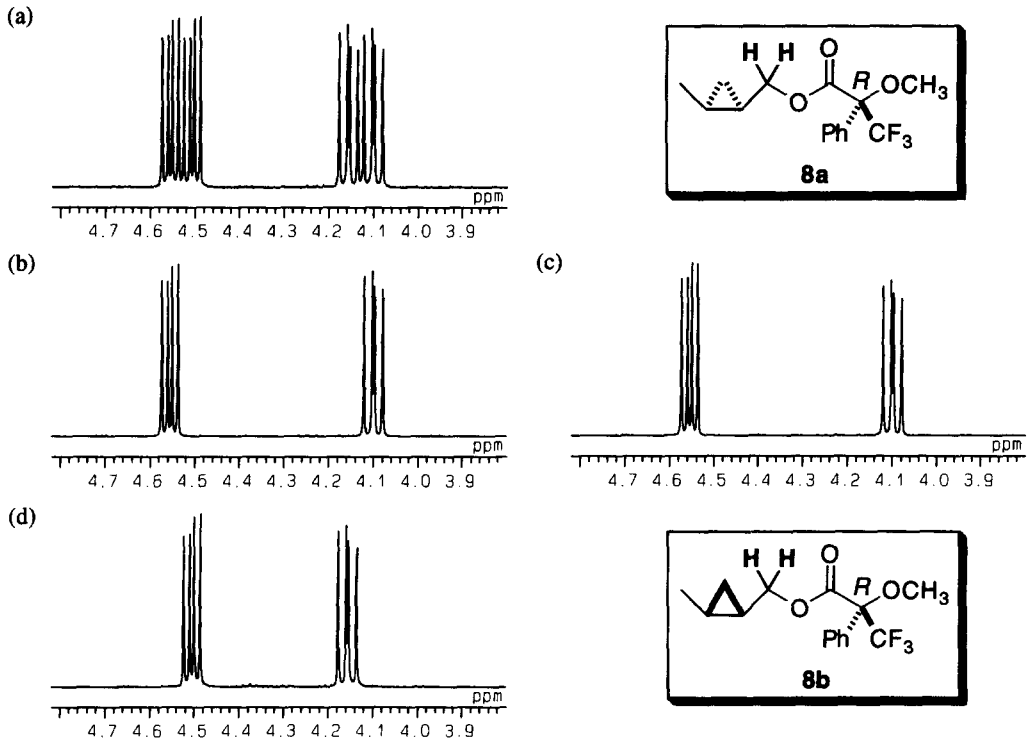
The synthetic scheme of (-)-**2** is shown in **Scheme 2**. We intended to transform the two functional groups of diethyl *L*-tartrate simultaneously[9] and to introduce the desired stereochemistry by a substrate-controlled diastereofacial cyclopropanation process. The (*Z*, *Z*)-diester **3** was easily prepared from diethyl *L*-tartrate in two steps.[10] Reduction of the (*Z*, *Z*)-diester **3** with DIBAL-H gave the corresponding bisallyl alcohol **4** in 58% yield. Bromination of **4** with CBr_4 and Ph_3P gave the bisallyl bromide, which was reduced with $LiAlH_4$ to give the (*Z*, *Z*)-diene **5** in 69% yield. Double Simmons-Smith reaction of **5** with Et_2Zn-CH_2I_2 or Zn-Cu -CH_2I_2 gave the desired dicyclopropane **6** as the sole product in 63% or 60% yield, respectively. The ^1H- and ^{13}C-NMR spectra of **6** were consistent with its C_2 symmetric structure. Compound **6** was converted, *via* the diol **7**, to the corresponding aldehyde, which was further oxidized *in situ* with $KMnO_4$[11] to give the known and desired (-)-(1*R*, 2*S*)-2-methylcyclopropanecarboxylic acid **2** in 81% yield. The optical purity (>99% ee) and absolute configuration of **2** were determined from its optical rotation[12] and the ^1H- and ^{13}C-NMR spectra of the Mosher ester **8a** of the 2-methylcyclopropanemethanol derived from **7** (**Figure 1** (b) and (c)). It is clear that the stereoselectivity in the double cyclopropanation reaction was the result of coordination of the zinc methylene-transfer reagent by each of the Lewis basic dioxolane ring oxygens prior to each cyclopropanation process. Related reactions with high diastereoselectivity in the mono- and dicyclopropanation of 1, 3-dioxolanyl-alkenes have precedent, for example, in the recent studies by Taguchi *et al.* and Barrett *et al.*[13]

Scheme 2



Reagents and conditions: (a) DIBAL-H, CH_2Cl_2, -78-0°C, 1.5 h (58%); (b) CBr_4, Ph_3P, CH_2Cl_2, 0°C, 0.5 h, then $LiAlH_4$, ether, 35°C, 1 h (69%); (c) Et_2Zn, CH_2I_2, CH_2Cl_2, -25°C, 2.5 h (63%) or Zn-Cu, CH_2I_2, ether, 35°C, 6 h (60%); (d) PTSA, aq. MeOH, 20°C, 2.5 h (92%); (e) $NaIO_4$, CH_2Cl_2-H_2O, 20°C, 1.5 h; (f) $KMnO_4$, *t*-BuOH-aq. KH_2PO_4, 20°C, 2 h (89% from 7); (g) $NaBH_4$, CH_2Cl_2-MeOH, 0°C, 0.5 h; (h) (*S*)-(+)-MTPACl, pyridine, CH_2Cl_2, 20°C, 1 h (57% from 7)

Figure 1

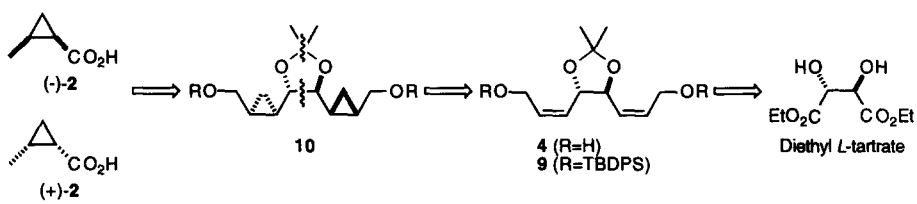


^{1}H-NMR spectra of the Mosher ester **8a** and **8b** (500 MHz, $CDCl_3$): (a) from racemic *cis*-2-methylcyclopropanemethanol (b) **8a** from **6** (Et_2Zn-CH_2I_2) (c) **8a** from **6** (Zn-Cu couple-CH_2I_2) (d) **8b** from **14** (Et_2Zn-CH_2I_2)

Since the structural requirements for the antimitotic activity of curacin A are not clear, the significance of the stereochemistry of the methylcyclopropyl moiety remains unknown. The availability of the enantiomer (+)-**2** should, therefore, aid study of the structure-activity relationships of curacin A. Though the enantiomer can be prepared by the same procedure as shown in **Scheme 2**, starting from diethyl *D*-tartrate, we planned to develop an efficient method for the enantioselective synthesis of both enantiomers of **2** from the same readily available source, *L*-tartrate.

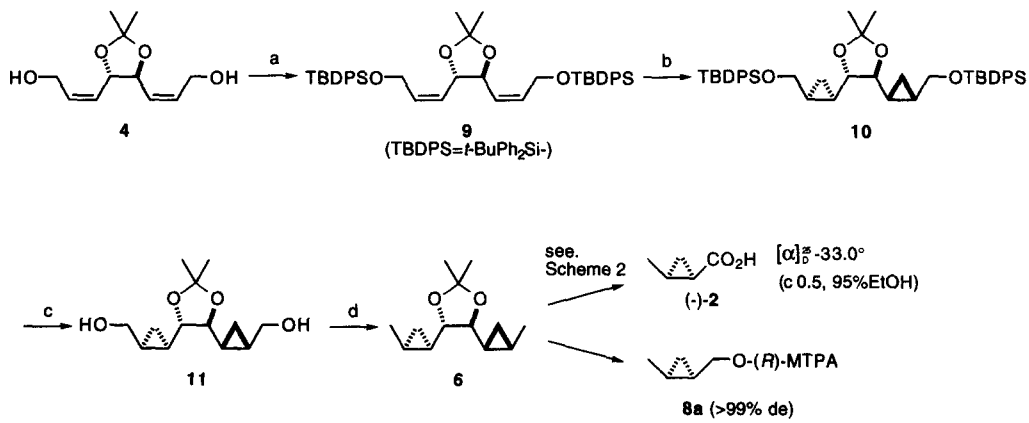
The retrosynthetic analysis is shown in **Scheme 3**. The key intermediate is the dicyclopropane **10**, which should be obtainable by the double-asymmetric Simmons-Smith reaction of the diene **9** derived from diethyl *L*-tartrate. We expected to obtain both enantiomers of **2** by differential transformations of the two functional groups in **10**, the terminal protected hydroxyl groups and the dioxolane, which can be regarded as a synthetic equivalent of aldehyde, to methyl and carboxyl groups, respectively. Taguchi *et al.*[13a] reported that the diastereoselectivity in the mono-cyclopropanation of 1, 3-dioxolanyl alkenes was dependent on the protecting group on the terminal allylic oxygen, and high diastereoselectivities were observed with bulky *tert*-butyldiphenylsilyl (TBDPS) ethers. So, we chose the TBDPS group as the protecting group of the bisallyl alcohol **4**.

Scheme 3



First, asymmetric synthesis of (-)-**2** is shown in **Scheme 4**. Silylation of the foregoing bisallyl alcohol **4** gave the bissilyl ether **9** in 82% yield. Double Simmons-Smith reaction of **9** with Et_2Zn-CH_2I_2 or Zn-Cu -CH_2I_2 proceeded slowly compared with that of the diene **5** and gave the desired dicyclopropane **10** as the sole product in 75% or 61% yield, respectively. Desilylation of **10** with Bu_4NF gave the corresponding diol **11** in 95% yield. Mesylation of the terminal hydroxyl groups in **11** gave the bismesylate, which was reduced with $LiAlH_4$ to give the known dicyclopropane **6**. Compound **6** was converted to the desired (-)-(1*R*, 2*S*)-2-methylcyclopropanecarboxylic acid **2** and the Mosher ester **8a** by the same procedure as shown in **Scheme 2**. The optical purity (>99% ee) and absolute configuration of the newly obtained **2** were also determined from its optical rotation and the ^1H- and ^{13}C-NMR spectra of the Mosher ester **8a**.

Scheme 4

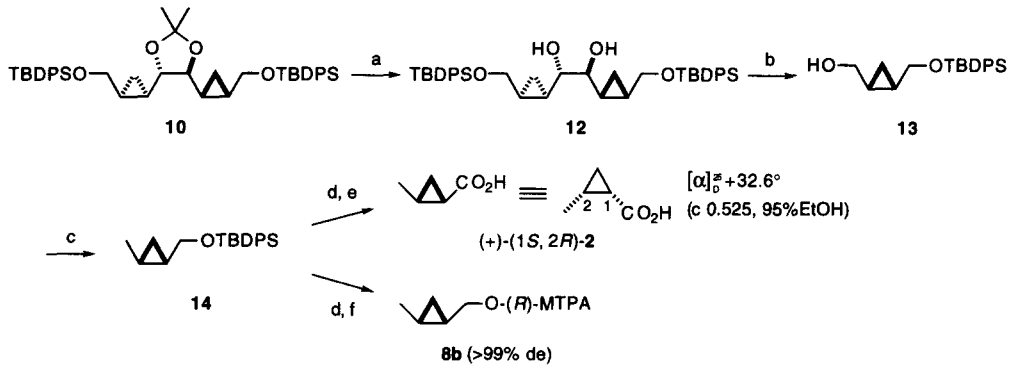


Reagents and conditions: (a) TBDPSCl, imidazole, CH_2Cl_2, 20 °C, 3 h (82%); (b)Et_2Zn, CH_2I_2, CH_2Cl_2, -25-0°C, 8 h (75%) or Zn-Cu, CH_2I_2, ether, 35°C, 30 h (61%); (c) Bu_4NF, THF, 20 °C, 2 h (95%); (d) MsCl, Et_3N, CH_2Cl_2, 0 °C, 2 h, then $LiAlH_4$, ether, 20°C, 1 h (56%)

The asymmetric synthesis of (+)-**2** is shown in **Scheme 5**. In deprotection of the acetal group in **10**, acidic hydrolysis with PPTS or PTSA afforded a complex mixture containing the starting material **10**, the desired diol **12** and decomposition products. However, $FeCl_3$-SiO_2 treatment[14] proceeded selectively to give the desired diol **12** in 31% yield (plus 62% recovery of the starting material **10**). Oxidative cleavage of the diol **12** with $NaIO_4$, followed by reduction with $NaBH_4$, gave the alcohol **13** in 85% yield. Mesylation of **13** gave the mesylate, which was reduced with $LiAlH_4$ to give the cyclopropane **14** in 84% yield. After desilylation of **14** with Bu_4NF, the resulting alcohol was oxidized to the desired (+)-(1*S*, 2*R*)-2-methylcyclopropanecarboxylic acid **2** with $NaIO_4$ in the presence of a catalytic amount of $RuCl_3 \cdot H_2O$[15] in 62%

yield. The optical purity (>99% ee) and absolute configuration of the obtained **2** were determined from its optical rotation and the ^{1}H- and ^{13}C-NMR spectra of the Mosher ester **8b** derived from **14** (**Figure 1** (d)).

Scheme 5



Reagents and conditions: (a) $FeCl_3$-SiO_2, $CHCl_3$, 20 °C, 3 h (31% and recovery of **10**, 62%); (b) $NaIO_4$, THF-H_2O, 20°C, 1 h, then $NaBH_4$, MeOH, 0°C, 0.5 h (85%); (c) MsCl, Et_3N, CH_2Cl_2, 0 °C, 1 h, then $LiAlH_4$, ether, 20°C, 0.5 h (84%); (d) Bu_4NF, THF, 20 °C, 1 h; (e) $NaIO_4$, cat. $RuCl_3$-H_2O, CCl_4-MeCN-H_2O, 20°C, 12 h (62% from **14**); (f) (*S*)-(+)-MTPACl, pyridine, CH_2Cl_2, 20°C, 1 h (68% from **14**)

Asymmetric cyclopropanations of the diester **3** and the bisallyl alcohol **4** using Et_2Zn-CH_2I_2 reagent were also attempted. The cyclopropanation of the diester **3** resulted in complete recovery of the starting material, and that of the bisallyl alcohol **4** gave a mixture of the desired dicyclopropane **11** and the monocyclopropane, as indicated by the ^{1}H- and ^{13}C-NMR analyses. The desired dicyclopropane **11** could not be separated from the mixture by silica gel column chromatography. Treatment of the mixture with TBDPS followed by chromatography on silica gel afforded the desired dicyclopropane **10** in 24% overall yield. The ^{1}H- and ^{13}C-NMR spectra and the optical rotation of purified **10** indicated that it was a single stereoisomer.[16]

In conclusion, we have developed a versatile method for the synthesis of enantiomerically pure *cis*-2-methylcyclopropanecarboxylic acids, showing that the readily available dienes **5** and **9** are efficient substrates in the enantioselective Simmons-Smith cyclopropanation reaction. This methodology could be extended for the synthesis of *cis*-alkylcyclopropanecarboxylic acids in general.

Acknowledgement

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Experimental Section

All ^{1}H- and ^{13}C-NMR spectra were measured in $CDCl_3$ with TMS and the solvent peak as internal standards, and recorded on a JEOL JMN-A500 spectrometer. IR spectra were recorded on a JASCO A-102 infrared spectrophotometer. Mass spectra (MS) were obtained on a JEOL JMS-HX110 spectrometer. Optical rotations were measured on a JASCO DIP-100 digital polarimeter. All reactions were carried out in an

atmosphere of dry argon at room temperature unless otherwise stated. Column chromatography was carried out on Wakogel C-200. Analytical thin-layer chromatography (TLC) was performed on Merck precoated silica gel 60 F_{254} plates, and compounds were visualized by UV illumination (254 nm) or by heating to 150 °C after spraying phosphomolybdic acid in ethanol. Dry diethyl ether (Et_2O) and tetrahydrofuran (THF) were distilled from sodium-benzophenone ketyl and dry toluene (PhMe) and dichloromethane (CH_2Cl_2) were distilled from phosphorus pentoxide and calcium hydride, respectively under an inert atmosphere. Zinc-copper couple was prepared according to the methed of Shank and Shechter[17] immediately before use. All other organic solvents and reagents were obtained from commercial sources and used without further purification. Organic extracts were dried over magnesium sulfate ($MgSO_4$), filtered, and concentrated using a rotary evaporator at < 40 °C bath temperature. Nonvolatile oils and solids were vacuum dried at < 2 mmHg.

(4*S*, 5*S*)-4, 5-Bis[3-methoxycarbonyl-1(*Z*)-propenyl]-2, 2-dimethyl-1, 3-dioxolane (3).

The title compound was prepared according to the following procedure[10] from diethyl *L*-tartrate. A solution of diethyl *L*-tartrate (25.30 g, 0.123 mol), 2, 2-dimethoxypropane (17.89 g, 0.172 mol) and cat. PTSA (94.0 mg, 0.494 mmol) in benzene (150 mL) was refluxed, while the benzene-methanol azeotrope (20 mL) was removed from the reaction mixture, repeatedly. After 8 h, the mixture was neutralized with K_2CO_3 (68.0 mg, 0.492 mmol) and the solvent and unreacted 2, 2-dimethoxypropane were removed under reduced pressure. The residue was passed through a short-pad column (silica gel, 100 g, 10/1 hexane/EtOAc), followed by Kugelrohr distillation (150-170 °C, 1-2 mmHg) to give diethyl 2, 3-*O*-isopropylidene-*L*-tartrate (29.60 g, 98% yield): pale yellow oil as a mixture of ester ketal homologs. DIBAL-H (260 mL, 0.93 M in hexane, 0.242 mol) was added dropwise to a solution of the foregoing diester (29.38 g, 0.119 mol) in dry toluene (590 mL) at -78 °C. The reaction mixture was stirred for 2 h at -78 °C, then a solution of methyl triphenylphosphoranilidene acetate (99.44 g, 0.297 mol) in distilled methanol (1760 mL) was added at the same temperature. The resulting mixture was allowed to warm slowly to 20 °C for 16 h and quenched by the addition of H_2O (600 mL). The methanol was evaporated under reduced pressure and the resulting mixture was extracted with EtOAc (3x600 mL). The combined organic phases were washed with saturated aqueous NaCl (600 mL), dried and concentrated. Chromatography of the residue on silica gel (2 times, 440 g and 330 g, 20/1 to 10/1 hexane/EtOAc), followed by crystallization in hexane gave **3** (15.47 g, 48% yield) as colorless crystals: mp 50-51 °C, lit. mp 51-52 °C[10a]; $[\alpha]_D^{25}$ +306.5° (c=1.01, $CHCl_3$), lit. $[\alpha]_D^{23}$ +307.7° (c=12, $CHCl_3$)[10a]; IR ($CHCl_3$) 3000, 2950, 1720, 1660, 1440, 1410, 1370, 1180, 1160, 1090, 1050, 880 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.48 (s, 6H, $(CH_3)_2$-2), 3.68 (s, 6H, (CO_2CH_3)x2), 5.44 (m, 2H, H-4 and H-5), 5.94 (d, 2H, J=11.5 Hz, H-2'), 6.29 (m, 2H, H-1'); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 27.07 (x2), 51.40 (x2), 75.75 (x2), 110.43, 122.68 (x2), 144.50 (x2), 165.86 (x2); FABMS (m/z): 271 $(M+H)^+$; HRFABMS calcd. for $C_{13}H_{19}O_6$ $(M+H)^+$ 271.1182, found 271.1201; Anal. Calcd for $C_{13}H_{18}O_6$: C, 57.77; H, 6.71. Found: C, 57.49; H, 6.72.

(4*S*, 5*S*)-4, 5-Bis[3-hydroxy-1(*Z*)-propenyl]-2, 2-dimethyl-1, 3-dioxolane (4).

DIBAL-H (109 mL, 0.93 M in hexane, 0.101 mol) was added dropwise to a solution of **3** (5.94 g, 22.0 mmol) in dry CH_2Cl_2 (60 mL) at -78 °C. The reaction mixture was allowed to warm slowly to 0 °C over 1.5 h and quenched by the addition of saturated aqueous NH_4Cl (8 mL). The resulting thick slurry was filtered through Celite. The residue was triturated repeatedly with EtOAc (3x300 mL) and filtered through Celite. The combined filtrates were dried and concentrated. Chromatography of the residue on silica gel (180 g, 1/2 hexane/EtOAc to EtOAc) gave **4** (2.74 g, 58% yield) as a pale yellow oil: $[\alpha]_D^{25}$ +85.4° (c=1.025, $CHCl_3$); IR ($CHCl_3$) 3430 (broad), 3000, 2950, 2900, 1730, 1380, 1230, 1160, 1030, 940, 870 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.45 (s, 6H, $(CH_3)_2$-2), 1.77 (br, 2H, OHx2), 4.14 (d, 4H, J=7.0 Hz, H-3'), 4.48 (m, 2H, H-4 and H-5), 5.56 (m, 2H, H-1'), 5.88 (dtd, 2H, J=11.0, 7.0, 0.5 Hz, H-2'); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 27.00 (x2), 58.34 (x2), 76.93 (x2), 109.77, 128.41 (x2), 133.38 (x2); FABMS (m/z): 215 $(M+H)^+$; HRFABMS calcd. for $C_{11}H_{19}O_4$ $(M+H)^+$ 215.1283, found 215.1306; Anal. Calcd for $C_{11}H_{18}O_4$: C, 61.66; H, 8.47. Found: C, 61.79; H, 8.53.

(4*S*, 5*S*)-2, 2-Dimethyl-4, 5-di[1(*Z*)-propenyl]-1, 3-dioxolane (5).

CBr_4 (20.88 g, 63.0 mmol) and PPh_3 (16.51 g, 63.0 mmol) were added to a solution of **4** (5.62 g, 26.2 mmol) in dry CH_2Cl_2 (112 mL) at 0 °C, and the reaction mixture was stirred for 0.5 h at 0 °C. After

evaporation of the solvent, the residue was chromatographed on silica gel (170 g, 10/1 hexane/EtOAc) to give the corresponding bisallyl bromide (8.12 g, 91% yield) as a pale yellow oil. $LiAlH_4$ (3.95 g 0.104 mol) was added in small portions to a solution of the foregoing bisallyl bromide (8.12 g 23.9 mmol) in dry Et_2O (265 mL), and the reaction mixture was heated to reflux for 1 h. The reaction mixture was cooled to 0 °C and quenched by the slow addition of saturated aqueous NH_4Cl (11 mL). The resulting slurry was filtered through Celite and the precipitate was washed well with Et_2O. The combined filtrates were washed with saturated aqueous NaCl (265 mL), dried and concentrated. Chromatography of the residue on silica gel (170 g, 3/1 to 2/1 hexane/CH_2Cl_2), followed by Kugelrohr distillation (130-150 °C, 18-19 mmHg) gave **5** (3.29 g, 69% yield from **4**) as a colorless oil: $[\alpha]_D^{25}$ +130.0° (c=1.06, $CHCl_3$); IR ($CHCl_3$) 3000, 2930, 1670, 1440, 1370, 1230, 1160, 1040, 1000, 910, 870 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.45 (s, 6H, $(CH_3)_2$-2), 1.68 (dd, 6H, J=7.0, 2.0 Hz, CH_3-2'), 4.49 (m, 2H, H-4 and H-5), 5.43 (ddq, 2H, J=11.0, 8.3, 2.0 Hz, H-1'), 5.75 (dq, 2H, J=11.0, 7.0 Hz, H-2'); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 13.56 (x2), 27.12 (x2), 76.29 (x2), 108.74, 126.62 (x2), 130.36 (x2); Anal. Calcd for $C_{11}H_{18}O_2$: C, 72.49; H, 9.95. Found: C, 72.05; H, 9.83.

(4*S*, 5*S*)-4, 5-Bis[(1*R*, 2*S*)-2-methylcyclopropyl]-2, 2-dimethyl-1, 3-dioxolane (6).

(a) Et_2Zn-CH_2I_2 method: A solution of **5** (1.50 g, 8.23 mmol) in dry CH_2Cl_2 (90 mL) was cooled to -25 °C, and Et_2Zn (82 mL, 1.0 M in hexane, 82.0 mmol) and CH_2I_2 (13.26 mL, 0.165 mol) were added slowly. The reaction mixture was stirred vigorously for 2.5 h at -25 °C and quenched by slowly pouring it into saturated aqueous NH_4Cl (150 mL). The aqueous phase was extracted with CH_2Cl_2 (90 mL), and the combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (90 mL), dried and concentrated. Chromatography of the residue on silica gel (3 times, 300 g, 65 g and 64 g, 40/1 hexane/EtOAc), followed by Kugelrohr distillation (170-180 °C, 20 mmHg) gave **6** (1.09 g, 63% yield) as a pale yellow oil: $[\alpha]_D^{25}$ +14.5° (c=0.965, $CHCl_3$); IR ($CHCl_3$) 3060, 2980, 1450, 1370, 1170, 1040, 1000, 950, 910, 830 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.21 (q, 2H, J=5.0 Hz, H-3'), 0.71-0.81 (m, 2H, H-1'), 0.85 (td, 2H, J=8.5, 5.0 Hz, H-3'), 0.91-1.00 (m, 2H, H-2'), 1.15 (d, 6H, J=6.5 Hz, CH_3-2'), 1.40 (s, 6H, $(CH_3)_2$-2), 3.39 (m, 2H, H-4 and H-5); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.42 (x2), 10.98 (x2), 14.40 (x2), 16.63 (x2), 27.22 (x2), 82.40 (x2), 106.84; Anal. Calcd for $C_{13}H_{22}O_2$: C, 74.24; H, 10.54. Found: C, 74.12; H, 10.43.

(b) Zn-Cu couple-CH_2I_2 method: Zn-Cu couple (1.00 g) was added to a solution of **5** (100.0 mg, 0.549 mmol) and CH_2I_2 (442 μL, 5.49 mmol) in dry Et_2O (10 mL). The reaction mixture was heated to reflux for 6 h and filtered through Celite. The precipitate was washed well with Et_2O, and the combined filtrates were washed with saturated aqueous NH_4Cl, $NaHCO_3$ and NaCl (5 mL), dried and concentrated. Chromatography of the residue on silica gel (2 times, 50 g and 20 g, 40/1 hexane/EtOAc), followed by Kugelrohr distillation (170-180 °C, 20 mmHg) gave **6** (69.4 mg, 60% yield) as a pale yellow oil: $[\alpha]_D^{25}$ +14.3° (c=1.10, $CHCl_3$)

(1*S*, 2*S*)-1, 2-Bis[(1*R*, 2*S*)-2-methylcyclopropyl]-1, 2-ethanediol (7).

A solution of **6** (984.6 mg, 4.68 mmol) and TsOH·H_2O (1.78 g, 9.36 mmol) in MeOH (19.7 mL) and H_2O (3.9 mL) was stirred for 2.5 h. The reaction mixture was neutralized with $NaHCO_3$ (1.18 g, 14.0 mmol) and concentrated. After the addition of saturated aqueous NaCl (10 mL), the resulting mixture was extracted with EtOAc (2x25 mL) and the combined organic phases were dried and concentrated. Chromatography of the residue on silica gel (40 g, 2/1 hexane/EtOAc to EtOAc) gave **7** (666.0 mg, 84% yield) as a white solid, with recovery of **6** (157.0 mg, 16%). The same procedure was repeated two more times to afford **7** (730.1 mg) in 92% yield from **6** . Recrystallization from hexane-CH_2Cl_2 gave pure clear, colorless crystals: mp 103-104 °C; $[\alpha]_D^{25}$ -5.4° (c=1.05, $CHCl_3$); IR ($CHCl_3$) 3600, 3450, 3000, 2950, 1450, 1380, 1230, 1070, 1030, 990, 900, 860 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.15 (q, 2H, J=5.0 Hz, H-3'), 0.80 (td, 2H, J=8.0, 5.0 Hz, H-3'), 0.93-1.07 (m, 4H, H-1' and H-2'), 1.11 (d, 6H, J=6.5 Hz, CH_3-2'), 2.14 (br, 2H, OHx2), 3.23 (m, 2H, H-1 and H-2); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.44 (x2), 11.00 (x2), 14.66 (x2), 19.56 (x2), 75.54 (x2); FABMS (m/z): 193 $(M+Na)^+$; HRFABMS calcd. for $C_{10}H_{18}O_2Na$ $(M+Na)^+$ 193.1204, found 193.1271; Anal. Calcd for $C_{10}H_{18}O_2$: C, 70.55; H, 10.66. Found: C, 70.26; H, 10.56.

(-)-(1*R*, 2*S*)-2-Methylcyclopropanecarboxylic acid (-)-2.

(a) From **6**, *via* **7**: $NaIO_4$ (1.36 g, 6.36 mmol) was added to a solution of **7** (719.3 mg, 4.22 mmol) in CH_2Cl_2 (21.6 mL) and H_2O (2.16 mL). The mixture was stirred for 1.5 h, then $MgSO_4$ was added to it. The

resulting mixture was filtered and the precipitate was washed well with CH_2Cl_2. The combined organic phases containing the corresponding aldehyde were used for the next oxidation without concentration. *tert*-BuOH (42.7 mL) and aqueous KH_2PO_4 (1.25 M, 35.5 mL) were added to the foregoing CH_2Cl_2 solution, and aqueous $KMnO_4$ (50.7 mL, 1 M, 50.7 mmol) was added. The reaction mixture was stirred vigorously for 2 h, cooled to 0 °C and quenched by the slow addition of aqueous Na_2SO_3 (15.81 g/85 mL) and aqueous HCl (10%, 60 mL). The aqueous phase was extracted with CH_2Cl_2 (4x60 mL) and the combined organic phases were washed with saturated aqueous NaCl (100 mL), dried and concentrated. Kugelrohr distillation of the residue (130-150 °C, 21-22 mmHg) gave (-)-**2** (750.8 mg, 89% yield from **7**) as a colorless oil: $[\alpha]_D^{25}$ -32.6° (c=0.495, 95% EtOH); IR ($CHCl_3$) 3600-2750 (broad), 2700, 2560, 1690, 1430, 1350, 1300, 1170, 1120, 1070, 930, 890 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.94 (ddd, 1H, J=7.0, 5.5, 4.5 Hz, H-3, observed as dt signal), 1.09 (td, 1H, J=8.0, 4.5 Hz, H-3), 1.24 (d, 3H, J=6.0 Hz, CH_3-2), 1.33-1.43 (m, 1H, H-2), 1.67 (ddd, 1H, J=9.0, 8.0, 5.5 Hz, H-1); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 12.06, 15.25, 17.09, 18.51, 179.89; Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 59.70; H, 8.08.

(b) From **11**, *via* **6** and **7**: $[\alpha]_D^{25}$ -33.0° (c=0.5, 95% EtOH)

(1*R*, 2*S*)-(2-Methylcyclopropyl)methyl (*R*)-α-methoxy-α-(trifluoromethyl)phenyl acetate (8a).

By a procedure similar to that used to prepare (-)-**2**, **7** (22.4 mg, 0.132 mmol) was converted to the corresponding aldehyde in CH_2Cl_2, and this solution was used for the next step without concentration. After the addition of MeOH (0.2 mL), the mixture containing the foregoing aldehyde was cooled to 0 °C, and $NaBH_4$ (11.0 mg, 0.291 mmol) was added portionwise. The reaction mixture was stirred for 0.5 h at 0 °C, quenched by the addition of saturated aqueous NH_4Cl (2 mL) and extracted with CH_2Cl_2 (2x3 mL). The combined organic phases were washed with saturated aqueous NaCl (2 mL), dried and concentrated. Pyridine (50 μL, 0.618 mmol) and (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (43 μL, 0.230 mmol) were added to a solution of the obtained alcohol in dry CH_2Cl_2 (0.2 mL). The reaction mixture was stirred for 1 h, quenched by the addition of aqueous HCl (5%, 1 mL) and extracted with EtOAc (2x3 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (2 mL), dried and concentrated. Preparative TLC purification of the residue (1/1 hexane/CH_2Cl_2) gave **8a** (45.0 mg, 57% yield from **7**) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.05 (q, 1H, J=5.0 Hz, H-3), 0.78 (td, 1H, J=8.5, 5.0 Hz, H-3), 0.90-1.00 (m, 1H, H-2), 1.03 (d, 3H, J=6.0 Hz, CH_3-2), 1.16-1.27 (m, 1H, H-1), 3.58 (m, 3H, OCH_3), 4.10 (dd, 1H, J=11.5, 9.5 Hz, OCH_2-1), 4.56 (dd, 1H, J=11.5, 7.0 Hz, OCH_2-1), 7.38-7.42 and 7.53-7.58 (m, 5H, C_6H_5); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.20, 11.17, 13.06, 13.92, 55.40, 67.47, 84.55 (q), 123.34 (q, J=288.2 Hz), 127.31 (x2), 128.33 (x2), 129.52, 132.47, 166.62; FABMS (m/z): 303 $(M+H)^+$

(4*S*, 5*S*)-4, 5-Bis[3-[(*tert*-butyldiphenylsilyl)oxy]-1(*Z*)-propenyl]-2, 2-dimethyl-1, 3-dioxolane (9).

TBDPSCl (19.2 mL, 74.7 mmol) and imidazole (6.80 g, 99.9 mmol) were added to a solution of **4** (5.35 g, 25.0 mmol) in dry CH_2Cl_2 (107 mL). The reaction mixture was stirred for 3 h and quenched by the addition of H_2O (200 mL). The organic phase was washed repeatedly with H_2O (200 mL), dried and concentrated. Chromatography of the residue on silica gel (2 times, 400 g and 178 g, 70/1 hexane/EtOAc) gave **9** (14.15 g, 82% yield) as a gummy white solid: $[\alpha]_D^{25}$ +76.0° (c=1.005, $CHCl_3$); IR ($CHCl_3$) 3060, 2950, 2860, 1730, 1590, 1460, 1430, 1370, 1230, 1160, 1110, 1010, 960, 870 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 1.03 (s, 18H, $(CH_3)_3Cx2$), 1.31 (s, 6H, $(CH_3)_2$-2), 4.10 (ddd, 2H, J=13.5, 5.5, 1.5 Hz, H-3'), 4.11 (m, 2H, H-4 and H-5), 4.23 (ddd, 2H, J=13.5, 7.0, 1.5 Hz, H-3'), 5.24 (m, 2H, H-1'), 5.74 (ddd, 2H, J=11.0, 7.0, 5.5 Hz, H-2'), 7.34-7.44 and 7.62-7.67 (m, 20H, C_6H_5x4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 19.10 (x2), 26.75 (x4), 26.94, 27.20, 27.03 (x2), 60.34 (x2), 76.65 (x2), 109.13, 125.81 (x2), 127.69 (x8), 129.68 (x4), 133.40 (x2), 133.53 (x2), 134.93 (x2), 135.53 (x8); FABMS (m/z): 677 $(M-CH_3+2H)^+$, 631 $(M-C_4H_9-2H)^+$, 615 $(M-C_6H_5+2H)^+$, 575 $(M-2xC_4H_9-H)^+$; Anal. Calcd for $C_{43}H_{54}O_4Si_2$: C, 74.73; H, 7.88. Found: C, 74.65; H, 7.99.

(4*S*, 5*S*)-4, 5-Bis[(1*R*, 2*S*)-2-[(*tert*-butyldiphenylsilyl)oxy]methylcyclopropyl]-2, 2-dimethyl-1, 3-dioxolane (10)

(a) Et_2Zn-CH_2I_2 method: A solution of **9** (10.66 g, 15.4 mmol) in dry CH_2Cl_2 (530 mL) was cooled to -25 °C, and Et_2Zn (154 mL, 1.0 M in hexane, 0.154 mol) and CH_2I_2 (24.93 mL, 0.309 mol) were added slowly. The reaction mixture was stirred vigorously, allowed to warm slowly to 0 °C for 8 h and quenched by

slowly pouring it into saturated aqueous NH_4Cl (530 mL). The aqueous phase was extracted with CH_2Cl_2 (530 mL), and the combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (530 mL), dried and concentrated. Chromatography of the residue on silica gel (2 times, 405 g and 350 g, 50/1 to 20/1 hexane/EtOAc) gave **10** (8.36 g, 75% yield) as a colorless oil: $[\alpha]_D^{25}$ +18.1° (c=1.70, $CHCl_3$); IR ($CHCl_3$) 3080, 3000, 2950, 2860, 1590, 1460, 1430, 1380, 1370, 1230, 1170, 1110, 1050, 1010, 930 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.49 (q, 2H, J=5.0 Hz, H-3'), 0.70 (td, 2H, J=8.5, 5.0 Hz, H-3'), 0.82 (m, 2H, H-1'), 0.96 (m, 2H, H-2'), 1.04 (s, 18H, $(CH_3)_3Cx2$), 1.31 (s, 6H, $(CH_3)_2$-2), 3.51 (m, 2H, H-4 and H-5), 3.59 (dd, 2H, J=11.0, 6.5 Hz, OCH_2-2'), 3.81 (dd, 2H, J=11.0, 6.0 Hz, OCH_2-2'), 7.32-7.42 and 7.62-7.67 (m, 20H, C_6H_5x4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 6.87 (x2), 16.48 (x2), 18.13 (x2), 19.18 (x2), 26.87 (x6), 27.16 (x2), 63.22 (x2), 80.94 (x2), 107.18, 127.59 (x8), 129.58 (x2), 129.61 (x2), 133.75 (x4), 135.58 (x8); FABMS (m/z): 703 $(M-CH_3)^+$, 661 $(M-C_4H_9)^+$, 643 $(M-C_6H_5+2H)^+$, 603 $(M-2xC_4H_9-H)^+$, 583 $(M-C_4H_9-C_6H_5-H)^+$; Anal. Calcd for $C_{45}H_{58}O_4Si_2$: C, 75.17; H, 8.13. Found: C, 75.14; H, 8.11.

(b) Zn-Cu couple-CH_2I_2 method: Zn-Cu couple (75 g) was added to a solution of **9** (2.50 g, 3.62 mmol) and CH_2I_2 (8.75 mL, 0.109 mol) in dry Et_2O (250 mL). The reaction mixture was heated to reflux for 30 h and filtered through Celite. The precipitate was washed well with Et_2O, and the combined filtrates were washed with saturated aqueous NH_4Cl, $NaHCO_3$ and NaCl (125 mL), dried and concentrated. Chromatography of the residue on silica gel (250 g, 50/1 to 20/1 hexane/EtOAc) gave **10** (1.60 g, 61% yield) as a colorless oil: $[\alpha]_D^{25}$ +18.0° (c=1.885, $CHCl_3$)

(4*S*, 5*S*)-4, 5-Bis[(1*R*, 2*S*)-2-hydroxymethylcyclopropyl]-2, 2-dimethyl-1, 3-dioxolane (11).

A solution of **10** (2.55 g, 3.55 mmol) and Bu_4NF (7.09 mL, 1.0 M in THF, 7.09 mmol) in dry THF (50 mL) was stirred for 2 h and the reaction mixture was concentrated. Chromatography of the residue on silica gel (2 times, 128 g and 77 g, 3/1 hexane/acetone) gave **11** (0.82 g, 95% yield) as a white gummy solid: $[\alpha]_D^{25}$ -55.1° (c=1.105, $CHCl_3$); IR ($CHCl_3$) 3400 (broad), 3000, 2900, 1720, 1450, 1410, 1370, 1230, 1170, 1020, 920, 900, 840 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.44 (q, 2H, J=5.0 Hz, H-3'), 0.91 (td, 2H, J=8.5, 5.0 Hz, H-3'), 1.08 (m, 2H, H-1'), 1.33 (m, 2H, H-2'), 1.43 (s, 6H, $(CH_3)_2$-2), 3.05 (br, 2H, OHx2), 3.48 (dd, 2H, J=11.5, 9.5 Hz, OCH_2-2'), 3.63 (m, 2H, H-4 and H-5), 3.95 (dd, 2H, J=11.5, 5.5 Hz, OCH_2-2'); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 7.01 (x2), 18.12 (x2), 19.18 (x2), 27.23 (x2), 62.47 (x2), 81.49 (x2), 107.30; FABMS (m/z): 243 $(M+H)^+$, 241 $(M-H)^+$; HRFABMS calcd. for $C_{13}H_{23}O_4$ $(M+H)^+$ 243.1596, found 243.1611, calcd. for $C_{13}H_{21}O_4$ $(M-H)^+$ 241.1440, found 241.1480; Anal. Calcd for $C_{13}H_{22}O_4$: C, 64.44; H, 9.15. Found: C, 64.46; H, 9.27.

(4*S*, 5*S*)-4, 5-Bis[(1*R*, 2*S*)-2-methylcyclopropyl]-2, 2-dimethyl-1, 3-dioxolane (6).

(a) From **11** (dicyclopropanation using the Et_2Zn-CH_2I_2 method): A solution of **11** (300.0 mg, 1.24 mmol) in dry CH_2Cl_2 (6 mL) was cooled to 0 °C, and Et_3N (1.04 mL, 7.46 mmol) and methanesulfonyl chloride (383 μL, 4.95 mmol) were added. The reaction mixture was stirred for 2 h at 0 °C and quenched by the addition of saturated aqueous NH_4Cl (9 mL). The aqueous phase was extracted with CH_2Cl_2 (30 mL) and the combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (30 mL), dried and concentrated. Chromatography of the residue on silica gel (18 g, 3/1 hexane/EtOAc) gave the corresponding bismesylate (448.8 mg, 99% yield) as a pale yellow oil. $LiAlH_4$ (188.0 mg 4.95 mmol) was added in small portions to a solution of the foregoing bismesylate (448.8 mg 1.22 mmol) in dry Et_2O (15 mL) and the reaction mixture was stirred for 1 h. It was then cooled to 0 °C and quenched by the slow addition of saturated aqueous NH_4Cl (1.5 mL). The resulting slurry was filtered through Celite and the precipitate was washed well with Et_2O. The combined filtrates were washed with saturated aqueous NaCl (15 mL), dried and concentrated. Chromatography of the residue on silica gel (45 g, 40/1 hexane/EtOAc), followed by Kugelrohr distillation (170-180 °C, 20 mmHg) gave **6** (145.8 mg, 56% yield from **11**) as a pale yellow oil: $[\alpha]_D^{25}$ +15.5° (c=1.005, $CHCl_3$)

(b) From **11** (dicyclopropanation using the Zn-Cu couple-CH_2I_2 method): $[\alpha]_D^{25}$ +15.7° (c=1.00, $CHCl_3$)

(1*S*, 2*S*)-1, 2-Bis[(1*R*, 2*S*)-2-[(*tert*-butyldiphenylsilyl)oxy]methylcyclopropyl]-1, 2-ethanediol (12).

$FeCl_3$-SiO_2 was prepared according to the methed of Kim *et al.*[14] A mixture of $FeCl_3$-SiO_2 (1.00 g) and **10** (1.00 g, 1.39 mmol) was stirred for 3 h and the reaction mixture was filtered. The precipitate was washed

well with EtOAc and the combined organic phases were concentrated. Chromatography of the residue on silica gel (100 g, 5/1 to 1/1 hexane/EtOAc) gave **12** (294.0 mg, 31% yield) as a gummy white solid, with recovery of **10** (617.0 mg, 62%): $[\alpha]_D^{25}$ -25.8° (c=0.965, $CHCl_3$); IR ($CHCl_3$) 3420, 3060, 3000, 2950, 2860, 1730, 1590, 1460, 1430, 1390, 1250, 1110, 1050, 940 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.33 (q, 2H, J=5.0 Hz, H-3'), 0.73 (td, 2H, J=8.5, 5.0 Hz, H-3'), 1.06 (s, 18H, $(CH_3)_3Cx2$), 1.15-1.30 (m, 4H, H-1' and H-2'), 3.51 (m, 2H, H-1 and H-2), 3.56 (dd, 2H, J=11.5, 9.5 Hz, OCH_2-2'), 3.96 (dd, 2H, J=11.5, 5.0 Hz, OCH_2-2'), 7.36-7.45 and 7.65-7.73 (m, 20H, C_6H_5x4); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 6.67 (x2), 18.60 (x2), 19.00 (x2), 19.07 (x2), 26.78 (x6), 64.78 (x2), 75.52 (x2), 127.69 (x4), 127.72 (x4), 129.75 (x2), 129.78 (x2), 133.15 (x2), 133.31 (x2), 135.55 (x4), 135.65 (x4); FABMS (m/z): 701 $(M+Na)^+$; HRFABMS calcd. for $C_{42}H_{54}O_4Si_2Na$ $(M+Na)^+$ 701.3458, found 701.3482; Anal. Calcd for $C_{42}H_{54}O_4Si_2 \cdot 1/2H_2O$: C, 73.32; H, 8.06. Found: C, 73.71; H, 8.00.

(1*S*, 2*R*)-1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-2-(hydroxymethyl)cyclopropane (13).

$NaIO_4$ (2.25 g, 10.5 mmol) was added to a solution of **12** (1.59 g, 2.34 mmol) in THF (48 mL) and H_2O (16 mL). The reaction mixture was stirred vigorously for 1 h and quenched by the addition of saturated aqueous NaCl (150 mL). The resulting mixture was extracted with EtOAc (4x100 mL) and the combined organic phases were washed with saturated aqueous NaCl (100 mL), dried and concentrated. After the addition of MeOH (16 mL), a solution containing the aldehyde obtained above was cooled to 0 °C, and $NaBH_4$ (177.0 mg, 4.68 mmol) was added portionwise. The reaction mixture was stirred for 0.5 h at 0 °C, quenched by the addition of saturated aqueous NH_4Cl (150 mL) and extracted with EtOAc (4x100 mL). The combined organic phases were washed with saturated aqueous NaCl (100 mL), dried and concentrated. Chromatography of the residue on silica gel (110 g, 20/1 to 10/1 hexane/EtOAc) gave **13** (1.35 g, 85% yield from **12**) as a gummy white solid: $[\alpha]_D^{25}$ -10.1° (c=1.02, $CHCl_3$); IR ($CHCl_3$) 3470, 3050, 3000, 2950, 2860, 1590, 1460, 1420, 1390, 1360, 1260, 1140, 1110, 1030, 1000, 940 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.13 (td, 1H, J=5.5, 5.0 Hz, H-3, observed as q signal), 0.71 (td, 1H, J=8.5, 5.0 Hz, H-3), 1.06 (s, 9H, $(CH_3)_3C$), 1.23 (dtt, 1H, J=11.5, 8.5, 5.5 Hz, H-1), 1.44 (dtt, 1H, J=11.5, 8.5, 5.5 Hz, H-2), 3.34 (t, 2H, J=11.5 Hz, OCH_2-1 and OCH_2-2), 4.01 (td, 1H, J=11.5, 5.5 Hz, OCH_2-2), 4.08 (dd, 1H, J=11.5, 5.5 Hz, OCH_2-1), 7.38-7.47 and 7.66-7.74 (m, 10H, C_6H_5x2); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 8.29, 17.15, 18.41, 19.06, 26.79 (x3), 63.26, 64.93, 127.78 (x2), 127.81 (x2), 129.84, 129.87, 132.99 (x2), 135.49 (x2), 135.61 (x2); FABMS (m/z): 341 $(M+H)^+$; HRFABMS calcd. for $C_{21}H_{29}O_2Si$ $(M+H)^+$ 341.1939, found 341.1955; Anal. Calcd for $C_{21}H_{28}O_2Si$: C, 74.07; H, 8.29. Found: C, 74.34; H, 8.20.

(1*S*, 2*R*)-1-[[(*tert*-Butyldiphenylsilyl)oxy]methyl]-2-methylcyclopropane (14).

A solution of **13** (1.14 g, 3.35 mmol) in dry CH_2Cl_2 (17.1 mL) was cooled to 0 °C, and Et_3N (1.40 mL, 10.0 mmol) and methanesulfonyl chloride (518 μL, 6.69 mmol) were added. The reaction mixture was stirred for 1 h at 0 °C and quenched by the addition of saturated aqueous NH_4Cl (34 mL). The aqueous phase was extracted with CH_2Cl_2 (114 mL) and the combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (34 mL), dried and concentrated. $LiAlH_4$ (254.0 mg 6.69 mmol) was added in small portions to a solution of the foregoing mesylate in dry Et_2O (57 mL) and the reaction mixture was stirred for 0.5 h. Then it was cooled to 0 °C and quenched by the slow addition of saturated aqueous NH_4Cl (2.9 mL). The resulting slurry was filtered through Celite and the precipitate was washed well with Et_2O. The combined filtrates were washed with saturated aqueous NaCl (57 mL), dried and concentrated. Chromatography of the residue on silica gel (114 g, 100/1 to 50/1 hexane/EtOAc) gave **14** (916.0 mg, 84% yield from **13**) as a colorless oil: $[\alpha]_D^{25}$ -9.4° (c=1.035, $CHCl_3$); IR ($CHCl_3$) 3070, 3010, 2950, 2870, 1590, 1465, 1430, 1390, 1360, 1265, 1160, 1110, 1070, 1010, 940 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: -0.19 (q, 1H, J=5.0 Hz, H-3), 0.60 (td, 1H, J=8.5, 5.0 Hz, H-3), 0.86 (m, 1H, H-2), 1.00-1.07 (m, 1H, H-1), 1.03 (d, 3H, J=6.0 Hz, CH_3-2), 1.06 (s, 9H, $(CH_3)_3C$), 3.53 (dd, 1H, J=11.0, 8.0 Hz, OCH_2-1), 3.80 (dd, 1H, J=11.0, 6.0 Hz, OCH_2-1), 7.35-7.43 and 7.67-7.72 (m, 10H, C_6H_5x2); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 9.78, 10.42, 13.28, 17.84, 19.23, 26.88 (x3), 64.25, 127.53 (x4), 129.44 (x2), 134.22, 134.27, 135.63 (x4); FABMS (m/z): 323 $(M-H)^+$; HRFABMS calcd. for $C_{21}H_{27}OSi$ $(M-H)^+$ 323.1831, found 323.1830; Anal. Calcd for $C_{21}H_{28}OSi$: C, 77.72; H, 8.70. Found: C, 77.44; H, 8.62.

(+)-(1*S*, 2*R*)-2-Methylcyclopropanecarboxylic acid (+)-2.

A solution of **14** (625.3 mg, 1.93 mmol) and Bu_4NF (1.93 mL, 1.0 M in THF, 1.93 mmol) in dry THF (1.2 mL) was stirred for 1 h and the reaction mixture was quenched by the addition of saturated aqueous NaCl (9 mL). The aqueous phase was extracted with Et_2O (4x9 mL), and the combined organic phases were dried and concentrated. Kugelrohr distillation (170 °C, 20 mmHg) gave the corresponding alcohol (123.6 mg, 75% yield) as a pale yellow oil. The foregoing alcohol was dissolved in CCl_4 (3.0 mL), acetonitrile (3 mL) and H_2O (4.5 mL), and $NaIO_4$ (1.23 g, 5.75 mmol) was added. After the addition of the catalyst, $RuCl_3 \cdot H_2O$ (9.7 mg, 0.043 mmol), the reaction mixture was stirred vigorously for 12 h. The resulting mixture was extracted with CH_2Cl_2 (4x12 mL), and the combined organic phases were dried and concentrated. Kugelrohr distillation of the residue (130-150 °C, 20 mmHg) gave (+)-**2** (118.9 mg, 62% yield from **14**) as a colorless oil: $[\alpha]_D^{25}$ +32.6° (c=0.525, 95% EtOH); IR ($CHCl_3$) 3600-2750 (broad), 2700, 2560, 1690, 1430, 1350, 1300, 1170, 1120, 1070, 930, 890 cm^{-1}; ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.94 (ddd, 1H, J=7.0, 5.5, 4.5 Hz, H-3, observed as dt signal), 1.09 (td, 1H, J=8.0, 4.5 Hz, H-3), 1.24 (d, 3H, J=6.0 Hz, CH_3-2), 1.33-1.43 (m, 1H, H-2), 1.67 (ddd, 1H, J=9.0, 8.0, 5.5 Hz, H-1); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 12.06, 15.23, 17.04, 18.48, 179.64; Anal. Calcd for $C_5H_8O_2$: C, 59.98; H, 8.05. Found: C, 59.95; H, 8.14.

(1*S*, 2*R*)-(2-Methylcyclopropyl)methyl (*R*)-α-methoxy-α-(trifluoromethyl)phenyl acetate (8b).

A solution of **14** (30.0 mg, 0.092 mmol) and Bu_4NF (93 μL, 1.0 M in THF, 0.093 mmol) in dry THF (90 μL) was stirred for 1 h and the reaction mixture was quenched by the addition of saturated aqueous NaCl (1 mL). The aqueous phase was extracted with Et_2O (4x2 mL), and the combined organic phases were dried and concentrated. Pyridine (37 μL, 0.457 mmol) and (*S*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetyl chloride (18 μL, 0.096 mmol) were added to a solution of the obtained alcohol in dry CH_2Cl_2 (0.2 mL). The reaction mixture was stirred for 1 h, quenched by the addition of aqueous HCl (5%, 1 mL) and extracted with EtOAc (2x3 mL). The combined organic phases were washed with saturated aqueous $NaHCO_3$ and NaCl (2 mL), dried and concentrated. Preparative TLC purification of the residue (1/1 hexane/CH_2Cl_2) gave **8b** (19.0 mg, 68% yield from **14**) as a colorless oil: ^{1}H-NMR (500 MHz, $CDCl_3$) δ: 0.06 (q, 1H, J=5.0 Hz, H-3), 0.78 (td, 1H, J=8.5, 5.0 Hz, H-3), 0.90-1.00 (m, 1H, H-2), 1.04 (d, 3H, J=6.5 Hz, CH_3-2), 1.16-1.27 (m, 1H, H-1), 3.58 (m, 3H, OCH_3), 4.16 (dd, 1H, J=11.5, 9.0 Hz, OCH_2-1), 4.51 (dd, 1H, J=11.5, 7.0 Hz, OCH_2-1), 7.37-7.42 and 7.53-7.58 (m, 5H, C_6H_5); ^{13}C-NMR (125 MHz, $CDCl_3$) δ: 10.22, 11.12, 13.13, 13.95, 55.41, 67.44, 84.61 (q), 123.34 (q, J=288.2 Hz), 127.36 (x2), 128.33 (x2), 129.52, 132.47, 166.61; FABMS (m/z): 303 $(M+H)^+$

(4*S*, 5*S*)-4, 5-Bis[(1*R*, 2*S*)-2-[(*tert*-butyldiphenylsilyl)oxy]methylcyclopropyl]-2, 2-dimethyl-1, 3-dioxolane (10).

From **4**, *via* **11**: A solution of **4** (100.0 mg, 0.467 mmol) in dry CH_2Cl_2 (5 mL) was cooled to -25 °C, and Et_2Zn (4.7 mL, 1.0 M in hexane, 4.70 mmol) and CH_2I_2 (0.75 mL, 9.31 mmol) were added slowly. The reaction mixture was stirred vigorously, allowed to warm slowly to 0 °C for 7.5 h and quenched by slowly pouring it into saturated aqueous NH_4Cl (4 mL). The aqueous phase was extracted with EtOAc (3x10 mL), and the combined organic phases were dried and concentrated. The residue was chromatographed on silica gel (10 g, 3/1 hexane/acetone). TBDPSCl (143 μL, 0.557 mmol) and imidazole (63.0 mg, 0.925 mmol) were added to a solution of the resulting product (89.7 mg), containing the desired dicyclopropane **11**, in dry CH_2Cl_2 (1.8 mL). The reaction mixture was stirred for 5 h and quenched by the addition of H_2O (2 mL). After the addition of CH_2Cl_2 (10 mL), the organic phase was washed repeatedly with H_2O (2 mL), dried and concentrated. Chromatography of the residue on silica gel (10 g, 50/1 hexane/EtOAc) and preparative TLC (10/1 hexane/EtOAc) gave **10** (80.2 mg, 24% yield from **4**) as a gummy white solid: $[\alpha]_D^{25}$ +17.4° (c=1.14, $CHCl_3$)

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