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Synthesis of Polyhydroxycyclohexanes and Relatives from (−)-Quinic Acid†

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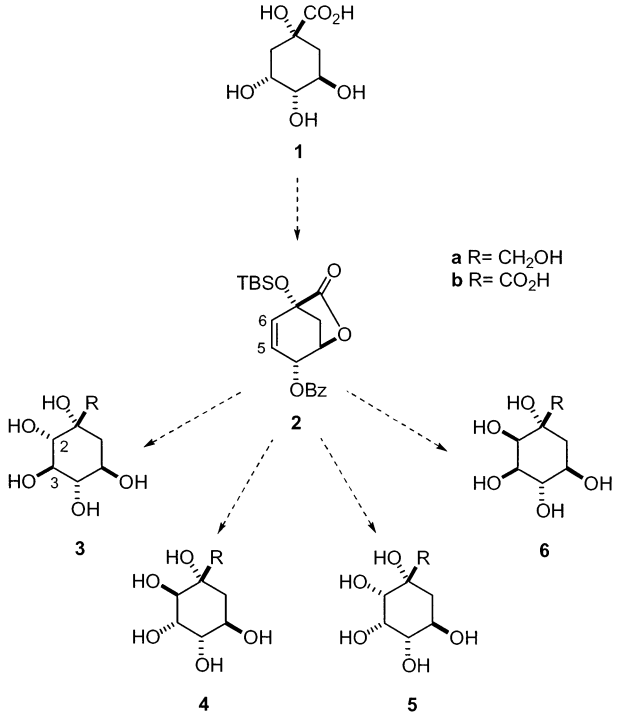
An efficient and versatile strategy for the synthesis of polyhydroxycyclohexanes and related compounds **3**−**6** is reported. The successful synthesis of these analogues has been achieved from a common intermediate, quinic acid derived lactone **2**, rapidly accessible from cheap and commercially available (−)-quinic acid (**1**) as a chiral template. A practical route involving stereocontrolled epoxide formation and hydrolysis has been developed for the synthesis of 2,3-trans analogues **3** and **4**. The preparation of the 2,3-cis analogues **5** and **6** has been realized by diasteroselective oxidation of a 5,6-double bond.

Introduction

Structural entities having polyhydroxylated cyclohexanoid cores are found in many biologically important molecules and natural products.[1] This fact has aroused widespread synthetic interest because of the diverse biological activity exhibited by them ranging from glycosidase inhibition to mediation of cellular communitation.[2] In addition, these compounds may have therapeutic application for the treatment of, among others, viral infections, HIV, cancer, and hyperglycemias and disorders related to these conditions, such as obesity and diabetes mellitus.[3] Carba-sugars (or pseudo-sugars) are an important type of polyhydroxylated cyclohexanoids that have been proved to be potent glycomimics. Carba-sugars are carbocyclic analogues of naturally occurring carbohydrates.[4] As a consequence of this substitution, carba-sugars are hydrolytically stable analogues of their parent sugars toward degradation of glycosidases.

SCHEME 1



As part of our ongoing research directed toward the synthesis of structurally diverse carba-sugar entities, we became interested in the synthesis of a variety of polyhydroxylated analogues. Herein, we disclose the synthesis of four carba-sugars, **3a**, **4a**, **5a**, and **6a**, as well as their corresponding acids, **3b**, **4b**, **5b**, and **6b** (Scheme 1). Our approach involves modification of a common key intermediate, the 5-cyclohexene derivative **2**, to access a wide range of polyhydroxylated derivatives. This intermediate can be obtained in three steps from (−)-quinic

† In memory of the late Prof. Antonio González, a great organic chemist pioneer in Spain.

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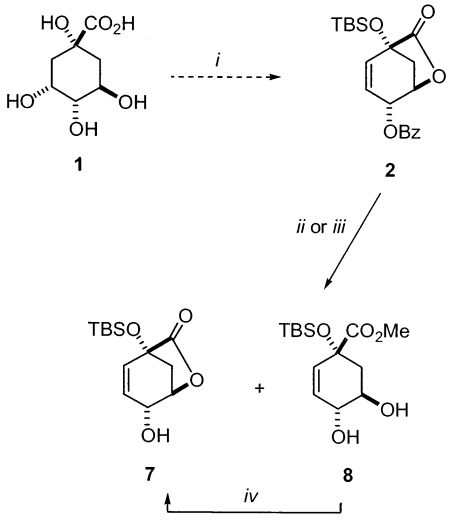
SCHEME 2[a]



[a] Reagents and conditions: (i) ref 6; (ii) K_2CO_3, MeOH, 60 °C [**7** (65%) and **8** (17%)] or rt [**7** (39%) and **8** (55%)]; (iii) KCN, MeOH, rt [**7** (8%) and **8** (89%)]; (iv) NaH, THF, 0 °C (83%).

acid (**1**). The rich functionality present in (−)-quinic acid, as well as its relatively low cost, make it an attractive optically active precursor for the synthesis of substituted cyclohexane skeletons.[5]

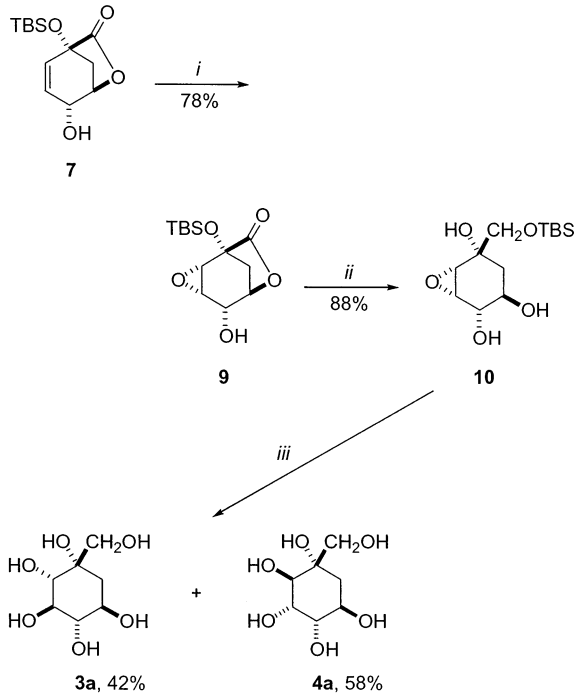
Compounds 3 and **4** with *trans*-hydroxyl groups in positions 2 and 3 were synthesized by disateroselective epoxidation of a double bond and subsequent hydrolysis. The synthesis of compounds **5** and **6**, which have *cis*-hydroxyl groups in C2 and C3, was achieved by *cis*-hydroxylation of the allyl alcohol derivative of **2**.

Results and Discussion

The strategy used for making compounds **3**−**6** involved the initial preparation of the allyl alcohol **7** (Scheme 2). This was made from benzoate **2**, which was synthesized in three steps from (−)-quinic acid (**1**) using previously reported protocols.[6] Treatment of benzoate **2** with potassium carbonate in methanol afforded a chromatographically separable mixture of the hydroxycarbolactone **7** and the methyl ester **8**, which can be converted into **7** with sodium hydride. The relative ratio of compounds **7** and **8** depends on the reaction temperature. At room temperature the ratio **7**:**8** is approximately 1:1.4, but at 60 °C the proportion of hydroxycarbolactone **7** increases to be approximately a 3.8:1 mixture. The reaction can be also carried out with potassium cyanide in methanol, and under these conditions the relative ratio between compounds **7**:**8** at room temperature is approximately 1:11.1.

Synthesis of *trans*-2,3-Dihydroxy Analogues 3 and 4. The introduction of the *trans*-2,3-dihydroxy group into the cyclohexane ring was achieved by a ring-opening hydrolysis of an epoxide. The treatment of allylic alcohol **7** with *m*-chloroperbenzoic acid and sodium bicarbonate afforded the epoxy alcohol **9** as the sole diastereoisomer (Scheme 3). The sterochemistry of the epoxidation was

SCHEME 3[a]



[a] Reagents and conditions: (i) MCPBA, $NaHCO_3$, DCM, Δ; (ii) $LiBH_4$, MeOH, THF, Δ; (iii) TFA (aq, 50%), 80 °C.

confirmed by NOE experiments. Irradiation of H-4 led to enhancement of the signal for H-3 (5%). The epoxidation occurs from the less hindered face, opposite to the lactone, also due to the orientating effect of the allylic hydroxyl group.[7]

The desired polyhydroxycyclohexanes **3a** and **4a** were obtained by a two-step reaction sequence. First, reduction of the carbolactone **9** with lithium borohydride in methanol afforded alcohol **10** in 88% yield, which underwent a 1,2-migration of the silyl group from the tertiary to the primary hydroxyl group. This fact was confirmed by NOE experiments. Irradiation of methyl groups led to enhancement of the methylene group in C1 (2%). This migration process was not surprinsing, since it is known that silyl ethers with a *cis* vicinal hydroxyl group, specially under basic conditions, can undergo migration to the most stable compound.[8] The reduction reaction was attempted using other reducing agents such as sodium borohydride and lithium aluminum hydride, but a lower yield or decomposition was obtained. Finally, ring-opening hydrolysis of the epoxide **10** with concomitant deprotection of the primary hydroxyl group was achieved by reflux in aqueous trifluoroacetic acid to afford a chromatographically separable mixture of diastereoisomers **3a** (42%) and **4a** (58%). The hydrolysis reaction was also attempted using Nafion-H, but lower yield and longer reaction times were required.

A similar strategy was used for making acids **3b** and **4b**. Whereas almost no diasteroselectivity was obtained

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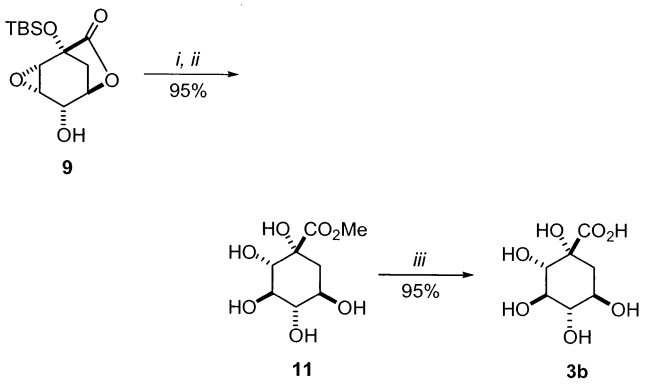
SCHEME 4[a]



[a] Reagents and conditions: (i) TFA (aq, 50%), 80 °C; (ii) MeOH, HCl(c) cat., Δ; (iii) (1) LiOH, rt, (2) Amberlite IR-120.

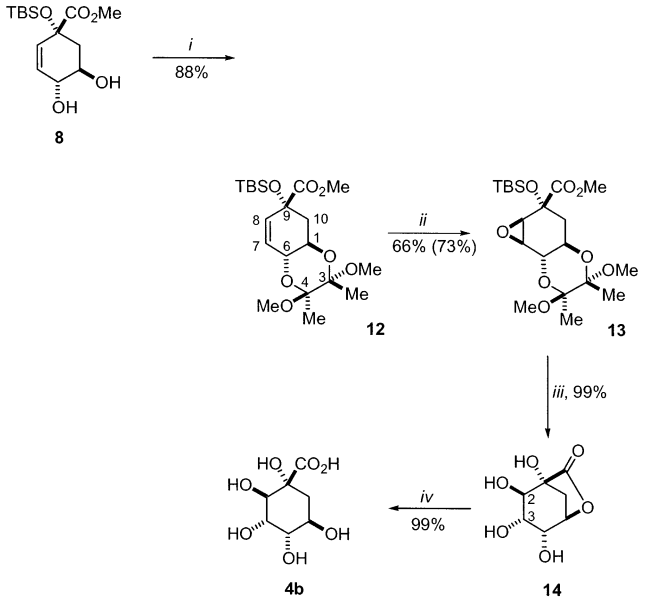
in the hydrolytic ring-opening step of epoxide **10** to analogues **3a** and **4a**, the results proved to be completely opposite when C1 has a carboxyl group. We have found that treatment of epoxycarbolactone **9** with aqueous trifluoroacetic acid at 80 °C afforded mainly acid **3b** (Scheme 4). Traces of acid **4b** were only detected by NMR.

Although acid **3b** can be directly obtained from epoxydecarbolactone **9**, as was indicated above, product purification proved to be difficult, even by ion-exchange chromatography. To avoid this problem, conversion of crude acid **3b** to the methyl ester **11** was achieved by reflux in methanol in the presence of catalytic amount of concentrated hydrochloric acid to afford a chromatographically purifiable methyl ester **11** in 95% overall yield from **9**. The ^{1}H NMR spectrum of **11** shows that H-2 and H-3 are now at the axial position ($J_{2,3}$ = 9.6 Hz, $J_{3,4}$ = 9.2 Hz). X-ray diffraction confirmed the structure of methyl ester **11**.[9] Finally, basic hydrolysis, followed by treatment with Amberlite IR-120 (H) ion-exchange resin and lyophilization, gave the desired acid **3b** in excellent yield.

Having in mind the fact that hydrolysis of epoxycarbolatone **9** occurs diasteroselectively from the less hindered side of the epoxide, C-3, to afford the 2*R*,3*S* isomer, the opposite 2,3-epoxide would afford the desired 2*S*,3*R* isomer. Indeed, treatment of epoxide **13** with aqueous trifluoroacetic acid at 80 °C afforded exclusively carbolactone **14** in excellent yield (Scheme 5). The sterochemistry of the ring-opening hydrolysis was confirmed by NOE experiments. Irradiation of H-4 led to enhancement of the signal for H-3 (9%). Irradiation of H-6$_{axial}$ led to enhancement of the signal for H-2 (6%). The structure of carbolactone **14** is also consistent with a diaxial constant coupling between H-2 and H-3 ($J_{2,3}$ = 8.8 Hz). The synthesis of epoxide **13** was carried out by protection of the *trans*-diol in **8** to give 1,2-dimethoxyacetal **12** in 88% yield, which then by treatment with MCPBA and sodium bicarbonate in dichloromethane under reflux afforded epoxide **13** in 66% yield (73% considering the recovered starting material). This transformation was particularly difficult due to the low reactivity of the alkene. We found that in order to get successful results it is crucial, first, to use fresh recrystallizated MCPBA and, second, to add after 24 h more fresh MCPBA and

(9) See Supporting Information.

SCHEME 5[a]



[a] Reagents and conditions: (i) MeCOCOMe, CH(OMe)$_3$, MeOH, CSA cat., Δ; (ii) MCPBA, NaHCO$_3$, DCM, Δ; (iii) TFA (aq, 50%), 80 °C; (iv) (1) LiOH, rt, (2) Amberlite IR-120.

sodium bicarbonate. The stereochemistry of the epoxide **13** was confirmed by NOE experiments. Irradiation of H-5 led to enhancement of H-3 (1%), and irradiation of H-2 led to enhacement of methyl groups in TBS group in C1 (2%). Finally, treatment of carbolactone **14** with lithium hydroxide, followed by ion exchange, gave the desired acid **4b** in excellent yield.

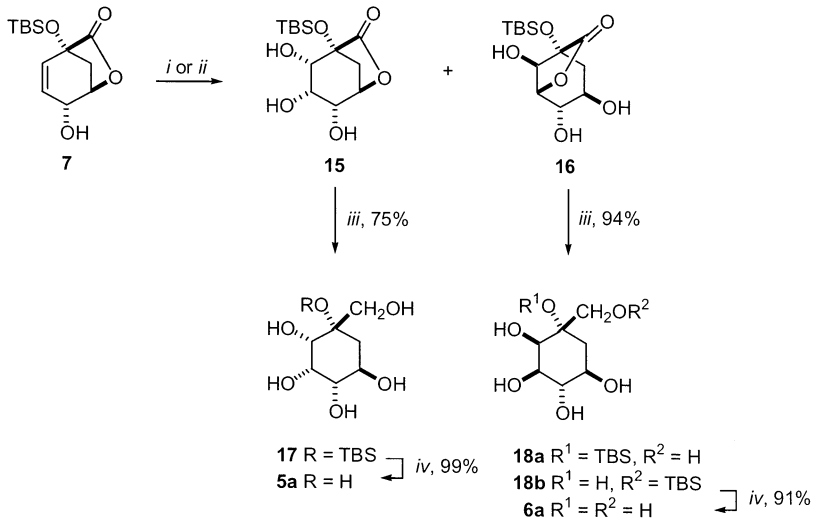
Synthesis of *cis*-2,3-Dihydroxy Analogues 5 and 6. The synthesis of analogues **5** and **6** was achieved by *cis*-hydroxylation of the 5-cyclohexene derivative **7** using catalytic osmium tetroxide (Scheme 6). Hydroxylation of the allylic alcohol **7** gave a mixture of two hydroxylated products, **15** and **16**, resulting from reaction from the *si* and *re* faces, respectively, as we have reported before.[10] When the addition occurs from the *re* face, migration of the carbolactone from the 1,5- to the 1,3-position was also observed. Hydroxylated lactone **15** was the major diastereoisomer in the OsO_4/NMO oxidation. In contrast, hydroxylated lactone **16** was the major diastereoisomer in the OsO_4/$NaIO_4$ oxidation.

Osmylation of alkene **8** takes place diasteroselectively on the olefin face opposite to the allylic oxygen, giving a sole diastereoisomer **19** in high yield (Scheme 7).

The desired polyhydroxycyclohexane **5a** was obtained from lactone **15**, by a two-step reaction sequence (Scheme 6). First, reduction of the carbolactone **15** with lithium borohydride in methanol afforded alcohol **17** in 75% yield, which by treatment with aqueous acetic acid at 40 °C gave quantitatively polyhydroxycyclohexane **5a**. Similar strategy was used for the synthesis of acid **6a**. Then, the reduction of carbolactone **16** gave a mixture of difficult to separate alcohols, the expected alcohols **18a** and **18b**, resulting from the migration of the silyl group from the tertiary to the primary hydroxyl group in C1. The relative ratio of alcohols **18a** and **18b** depends on the reaction

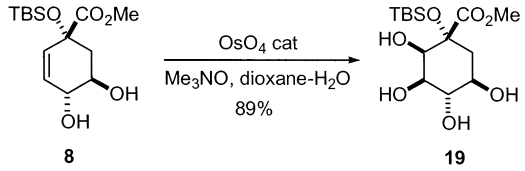
(10) Carballido, M.; Castedo, L.; González, C. *Tetrahedron Lett.* **2001**, *42*, 3973.

SCHEME 6[a]

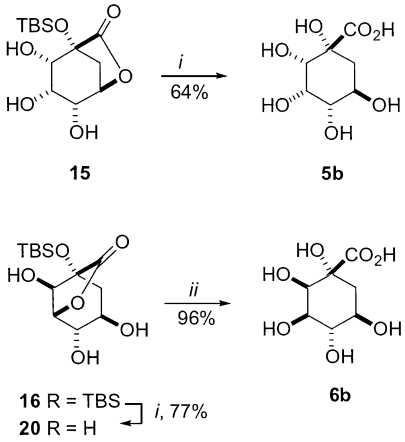


[a] Reagents and conditions: (i) OsO_4 cat., NMO, dioxane−H_2O, rt [**15** (61%) and **16** (18%)]; (ii) OsO_4 cat., $NaIO_4$, dioxane−H_2O, rt [**15** (12%) and **16** (55%)]; (iii) $LiBH_4$, MeOH, THF, Δ; (iv) AcOH (80%), 40 °C.

SCHEME 7



SCHEME 8[a]



[a] Reagents and conditions: (i) AcOH−THF−H_2O (4:1:1), 40 °C; (ii) (1) LiOH, rt, (2) Amberlite IR-120.

time. Longer reaction time favors the proportion of **18b**. Both silyl ethers **18a** or **18b** were deprotected individually or as mixture to the desired polyhydroxycyclohexane **6a** in excellent yield.

Finally, the desired acids **5b** and **6b** were obtained from lactones **15** and **16**, respectively (Scheme 8). Treatment of carbolactone **15** with aqueous acetic acid at 80 °C gave directly the acid **5b** in 64% yield. The acid **5b** was purified by extraction into water and washing with diethyl ether to remove impurities, followed by lyophilization. Under the same reaction conditions, lactone **16** afforded lactone **20**[11] in 91% yield. Hydrolysis of lactone **20** under basic conditions produced the derivative **6b** in quantitative yield.

In conclusion, quinic acid derived lactone **2** can be used as the starting point for the efficient synthesis of polyhydroxycyclohexanes and related compounds **3**−**6**. Functionalities at C1 and C4 positions have been successfully utilized to control the facial selectivity in the formation of diols and the epoxides as well as to direct the regioselectivity in the opening epoxides.

Experimental Section

General Procedures. All organic solvents were purified and freshly distilled prior to use according to the methods of Armarego et al.[12] FT-IR spectra were measured as NaCl plates, Nujol mulls, or KBr disks. $[\alpha]_D$ values are given in 10^{-1} deg cm^2 g^{-1}. ^{1}H NMR spectra (250, 300, and 500 mHz) and ^{13}C NMR spectra (63, 75, and 500 MHz) were measured in deuterated solvents. *J* values are given in hertz. NMR assignments were made by a combination of 1 D, COSY, DEPT-135, and NOE experiments. All procedures involving the use of ion-exchange resins were carried out at room temperature and used Mili-Q deionized water. Amberlite IR-120 (H) (cation exchanger) was washed alternately with water, 10% HCl, water, 10% sodium hydroxide, water, 10% HCl, and finally water before use.

(1*R*,3*R*,4*R*)-1-(*tert*-Butyldimethylsilyloxy)-4-hydroxycyclohex-5-en-1,3-carbolactone (7) and Methyl (1*R*,3*R*,4*R*)-1-(*tert*-Butyldimethylsilyloxy)-3,4-dihydroxycyclohex-5-en-1-carboxylate (8). K_2CO_3/MeOH Method. A stirred suspention of the benzoate **2**[6] (2.12 g, 5.67 mmol) and anhydrous K_2CO_3 (118 mg, 0.85 mmol) in dry methanol (20 mL) was heated at 60 °C for 1 h. The solvent was removed under reduced pressure and the crude reaction was purified by flash chromatography eluting with a gradient of diethyl ether−hexane (50:50 to 100:0) to yield carbolactone **7** (988 mg, 65%) and diol **8** (295 mg, 17%), both as white needles.

KCN/MeOH Method. To a stirred suspention of the benzoate **2**[6] (2.30 g, 6.15 mmol) in dry methanol (65 mL) was added potassium cyanide (439 mg, 6.76 mmol). The resultant

(11) Crystallographic data have been deposited in the Cambridge Crystallographic Data Centre (CCDC no. 157890).

(12) Armarego, W. L. F.; Perrin, D. D. *Purification of Laboratory Chemicals*; Butterworth Heinemann: Oxford, 1996.

solution was stirred at room temperature for 1 h. Dichloromethane was added and then water. The organic layer was separated and the aqueous layer was extracted twice with dichloromethane. All the combined organic extracts were dried (anhydrous Na_2SO_4), filtered, and evaporated. The obtained residue was purified by flash chromatography eluting with a gradient of diethyl ether−hexane (50:50 to 100:0) to yield carbolactone **7** (140 mg, 8%) and diol **8** (1.65 g, 89%).

Data for carbolactone **7**: mp 89−90 °C (hexane); $[\alpha]^{20}_D$ −170° (*c* 1.7 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) 6.09 (d, 1H, *J* 9.7), 5.72 (ddd, 1H, *J* 9.7, 3.3 and 2.2), 4.61 (q, 1H, *J* 2.7), 4.25 (t, 1H, *J* 3.0), 2.76 (br. s, 1H), 2.40−2.31 (m, 2H), 0.91 (s, 9H), 0.16 (s, 3H), and 0.14 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ (ppm) 176.1, 138.1, 126.8, 76.1, 75.2, 64.9, 37.2, 25.6, 18.0, −3.0, and −3.1; υ_{max} (NaCl)/cm^{-1} 3430 (O−H) and 1760 (C═O); MS (FAB$^+$) *m*/*z* (%) 271 (MH$^+$); HRMS calcd for $C_{13}H_{23}O_4Si$, MH$^+$, 271.1366; found, MH$^+$, 271.1365. Anal. Calcd for $C_{13}H_{22}O_4Si$: C, 57.75; H, 8.21. Found: C, 57.64; H, 8.16.

Data for methyl ester **8**: mp 50−51 °C (hexane); $[\alpha]^{20}_D$ −4° (*c* 1.5 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) 5.78 (d, 1H, *J* 14.8), 5.76 (d, 1H, *J* 14.8), 4.04 (m, 1H), 3.89 (m, 1H), 3.72 (s, 3H), 3.49 (d, 1H, *J* 4.9), 3.43 (d, 1H, *J* 3.8), 2.16 (ddd, 1H, *J* 11.9, 3.6 and 1.2), 1.95 (t, 1 H, *J* 12.5), 0.85 (s, 9H), 0.08 (s, 3H), and 0.04 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 174.0, 132.4, 128.7, 75.8, 73.4, 70.3, 52.4, 40.9, 25.7, 18.2, −2.9, and −3.3; υ_{max} (NaCl)/cm^{-1} 3392 (O−H) and 1741 (C═O); MS (CI) *m*/*z* (%) 287 (MH$^+$); HRMS calcd for $C_{13}H_{23}O_5Si$, MH$^+$, 287.1315; found, MH$^+$, 287.1316.

Lactonization of 8. To a stirred solution of the diol **8** (4.25 g, 14.07 mmol) in dry THF (50 mL) at 0 °C and under argon was added sodium hydride (280 mg, 7.10 mmol, ca. 60% in mineral oil). The resultant suspention was stirred for 15 min. Diethyl ether and then water were added. The organic layer was separated and the aqueous layer was extracted with diethyl ether (3 × 30 mL). All combined organic layers were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure. The crude residue was purified by flash chromatography eluting with 50% diethyl ether−hexane to afford carbolactone **7** (3.17 g, 83%).

(1*R*,2*S*,3*S*,4*S*,5*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3-epoxy-4-hydroxycyclohexan-1,5-carbolactone (9). A stirred suspention of the alkene **7** (50 mg, 0.19 mmol), sodium bicarbonate (40 mg, 0.48 mmol), and *m*-chloroperbenzoic acid (50 mg, 0.28 mmol) in dry dichloromethane (4 mL) and under argon was heated under reflux for 24 h. The reaction mixture was cooled to room temperature and diluted with diethyl ether and water. The aqueous layer was separated and the organic layer was washed with water (2 × 3 mL), saturated $NaHCO_3$ (3 × 3 mL), and brine (2 × 3 mL). The organic extract was dried (anhydrous Na_2SO_4) and concentrated under reduced pressure. The crude reaction was purified by flash cromatography eluting with 60% diethyl ether−hexane and recrystallizalled from hexane to yield the epoxide **9** as white needles (41 mg, 78%): mp 85−86 °C (hexane); $[\alpha]^{20}_D$ −92° (*c* 3.5 in $CHCl_3$); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) 4.38 (dt, 1H, *J* 6.4 and 2.9), 4.02 (br. t, 1H, *J* 2.9), 3.51 (dd, 1H, *J* 4.2 and 1.1), 3.40 (ddd, 1H, *J* 4.2, 2.1, and 0.5), 2.55 (d, 1H, *J* 11.8), 2.10 (d, 1H, *J* 11.8 and 6.4), 0.90 (s, 9H), 0.17 (s, 3H), and 0.16 (s, 3H); ^{13}C NMR (63 MHz, $CDCl_3$) δ (ppm) 174.0, 75.7, 75.0, 64.1, 57.7, 52.0, 32.2, 25.4, 17.8, and −3.3; υ_{max} (KBr)/cm^{-1} 3432 (O−H) and 1767 (C═O); MS (FAB$^+$) *m*/*z* (%) 287 (MH$^+$); HRMS calcd for $C_{13}H_{23}O_5Si$, MH$^+$, 287.1315; found, MH$^+$, 287.1322. Anal. Calcd for $C_{13}H_{22}O_5Si$: C, 54.52; H, 7.74. Found: C, 54.13; H, 7.65.

(1*S*,2*S*,3*S*,4*S*,5*R*)-2,3-Epoxy-1,4,5-trihydroxy-1-[(*tert*-butyldimethylsilyloxy)methyl]cyclohexane (10). To a stirred solution of the lactone **9** (140 mg, 0.49 mmol), under argon and at 0 °C, in 5 mL of a dry solution of methanol in tetrahydrofuran (1/20 v/v), was added lithium borohydride (20 mg, 0.42 mmol). The reaction mixture was stirred at room temperature for 20 min, and then ethyl acetate (1 mL) and water (3 mL) were added. The organic layer was separated and the aqueous layer was extracted with ethyl acetate (4 × 3 mL). The combined organic extracts were dried (anhydrous Na_2SO_4) and concentrated under reduced pressure. The crude reaction was purified by flash cromatography eluting with ethyl acetate to yield the triol **10** as white needles (125 mg, 88%): mp 102−104 °C; $[\alpha]^{20}_D$ −23° (*c* 1.6 in $CHCl_3$); ^{1}H NMR (500 MHz, $(CD_3)_3CO$) δ (ppm) 4.35 (d, 1H, *J* 5.1), 3.97 (d, 1H, *J* 4.5), 3.93 (s, 1H), 3.75 (m, 1H), 3.56 (d, 1H, *J* 9.7), 3.54 (m, 1H), 3.45 (d, 1H, *J* 9.7), 3.27 (dd, 1H, *J* 4.0 and 1.6), 3.08 (m, 1H), 1.59 (d, 1H, *J* 10.5), 1.57 (m, 1H), 0.85 (s, 9H), and 0.04 (s, 6H); ^{13}C NMR (125 MHz, $(CD_3)_3CO$) δ (ppm) 75.2, 72.1, 70.4, 67.5, 59.9, 59.3, 41.7, 26.5, 19.1, −5.0, and −5.0; υ_{max} (Nujol)/cm^{-1} 3540 (O−H) and 3389 (O−H); MS (CI) *m*/*z* (%) 273 (MH$^+$ − H_2O); HRMS calcd for $C_{13}H_{25}O_4Si$, MH$^+$, 273.1522; found, MH$^+$, 273.1520. Anal. Calcd for $C_{13}H_{26}O_5Si$: C, 53.76; H, 9.02. Found: C, 54.14; H, 9.31.

(1*S*,2*S*,3*R*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxy-1-hydroxymethylcyclohexane (3a) and (1*S*,2*R*,3*S*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxy-1-hydroxymethylcyclohexane (4a). A solution of the epoxide **10** (57 mg, 0.20 mmol) in 2 mL of aqueous TFA (50%) was stirred under reflux for 11 h. After cooling to room temperature, the solvent was evaporated. The crude reaction was purified by flash cromatography [eluent: (1) ethyl acetate, (2) acetone−methanol−acetic acid (83:15:2)] to yield 16 mg of **3a** (42%) and 22 mg of **4a** (58%) both as colorless oils.

Data for **3a**: $[\alpha]^{20}_D$ −19° (*c* 1.2 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 3.79 (m, 1H), 3.61 (d, 1H, *J* 11.0), 3.58 (t, 1H, *J* 9.8 and 9.0), 3.44 (d, 1H, *J* 9.8), 3.40 (d, 1H, *J* 11.0), 3.19 (t, 1H, *J* 9.7 and 9.0), 1.94 (dd, 1H, *J* 13.8 and 5.1), and 1.57 (t, 1H, *J* 11.9 and 13.8); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 79.3, 75.6, 74.7, 74.6, 70.1, 67.5, and 38.6; υ_{max} (Nujol)/cm^{-1} 3446 (O−H); MS (CI) *m*/*z* (%) 195 (MH$^+$); HRMS calcd for $C_7H_{15}O_6$, MH$^+$, 195.0869; found, MH$^+$, 195.0875.

Data for **4a**: $[\alpha]^{20}_D$ −41° (*c* 1.1 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 3.85 (m, 1H), 3.47 (d, 1H, *J* 11.0), 3.40 (dd, 1H, *J* 3.9 and 1.7), 3.66 (dd, 1H, *J* 8.2 and 1.7), 3.56 (d, 1H, *J* 11.0), 3.26 (dd, 1H, *J* 3.9 and 1.3), 1.68 (ddd, 1H, *J* 13.8, 4.2 and 1.3), and 1.61 (dd, 1H, *J* 13.8 and 11.6); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 74.9, 72.2, 69.2, 67.7, 59.5, 59.4, and 41.5; υ_{max} (Nujol)/cm^{-1} 3420 (O−H); MS (CI) *m*/*z* (%) 195 (MH$^+$); HRMS calcd for $C_7H_{15}O_6$, MH$^+$, 195.0869; found, MH$^+$, 195.0865.

Methyl (1*R*,2*S*,3*R*,4*S*,5*R*)-1,2,3,4-Tetrahydroxycyclohexan-1-carboxylate (11). A stirred solution of the epoxide **9** (100 mg, 0.35 mmol) in 3.5 mL of aqueous TFA (50%) was heated under reflux for 18 h. After cooling at room temperature, the solvent was evaporated. The obtained residue was redisolved in 4 mL of dry methanol with a catalytic amount of concentrated hydrochloric acid (2 drops). The resultant mixture was heated under reflux for 6 h. After cooling at room temperature, the solvent was removed at reduced pressure and the residue was purified by flash cromatography eluting with acetone−methanol−acetic acid (87:12:1) to yield methyl ester **11** (74 mg, 95%) as a colorless oil, which solidifies on standing: $[\alpha]^{20}_D$ −20° (*c* 1.2 in CH_3OH); ^{1}H NMR (250 MHz, CD_3OD) δ (ppm) 3.81 (s, 3H), 3.79−3.72 (m, 1H), 3.72 (d, 1H, *J* 9.6), 3.54 (t, 1H, *J* 9.6 and 9.2), 3.26 (t, 1H, *J* 9.2), 2.01 (dd, 1H, *J* 13.4 and 5.0), and 1.79 (dd, 1H, *J* 11.7 and 13.4); ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm) 175.9, 79.1, 78.0, 76.6, 75.0, 70.0, 53.1, and 39.5; υ_{max} (Nujol)/cm^{-1} 3446 (O−H) and 1734 (C═O); MS (CI) *m*/*z* (%) 205 (MH$^+$ − H_2O); HRMS calcd for $C_8H_{13}O_6$, MH$^+$, 205.0712; found, MH$^+$, 205.0712.

(1*R*,2*S*,3*R*,4*S*,5*R*)-1,2,3,4-Tetrahydroxycyclohexan-1-carboxylic Acid (3b). A solution of the methyl ester **11** (9 mg, 0.04 mmol) in aqueous lithium hydroxide (0.2 mL, 0.5M) was stirred at room temperature for 1 h. The resultant solution was washed with diethyl ether. The aqueous extract was diluted with water and treated with Amberlite IR-120 until pH 6. The resin was filtered and washed with water. The filtrate was lyophilized to afford acid **3b** (8 mg, 95%) as a

colorless oil: $[\alpha]^{20}_D$ −25° (*c* 0.8 in H_2O); ^{1}H NMR (250 MHz, D_2O) δ (ppm) 3.90 (d, 1H, *J* 7.1), 3.86 (m, 1H), 3.70 (t, 1H, *J* 6.9), 3.58 (t, 1H, *J* 6.8), 2.62 (dd, 1H, *J* 10.1 and 3.6), and 2.47 (t, 1H, *J* 9.3); ^{13}C NMR (75 MHz, D_2O) δ (ppm) 177.8, 77.1, 76.9, 74.8, 73.6, 68.8, and 37.9; υ_{max} (NaCl)/cm^{-1} 3432 (O−H) and 1728 (C═O); MS (CI) *m*/*z* (%) 209 (MH^+); HRMS calcd for $C_7H_{13}O_7$, MH^+, 209.0661; found, MH^+, 209.0652.

Methyl (1*R*,3*S*,4*S*,6*R*,9*R*)-9-(*tert*-Butyldimethylsilyloxy)-3,4-dimethoxy-3,4-dimethyl-2,5-dioxabicyclo[4.4.0]dec-7-ene-9-carboxylate (12). A stirred solution of the diol **8** (1.65 g, 5.45 mmol), camphorsulfonic acid (63 mg, 0.27 mmol), trimethyl orthoformate (3 mL, 27.27 mmol), and 2,3-butadione (0.72 mL, 8.18 mmol) in dry methanol (50 mL) was heated under reflux for 12 h. After cooling at room temperature, powdered sodium bicarbonate was added and the solvent was removed under reduced pressure. The crude product was redisolved in a mixture of water and diethyl ether. The organic layer was separated and the aqueous layer was extracted twice with diethyl ether. All the combined organic extracts were dried (anhydrous Na_2SO_4), filtered, and evaporated to give an oil, which was purified by flash cromatography eluting with diethyl ether−hexane (20:80) to yield diacetal 12 (2 g, 88%) as a colorless oil, which solidifies on standing: mp 68−69 °C; $[\alpha]^{20}_D$ +67° (*c* 1.8 in $CHCl_3$); ^{1}H NMR (500 MHz, $CDCl_3$) δ (ppm) 5.80 (dd, 1H, *J* 10.0 and 1.5), 5.67 (ddd, 1H, *J* 10.0, 2.5 and 1.6), 4.16 (ddd, 1H, *J* 9.2, 1.6 and 2.5), 3.96 (ddd, 1H, *J* 9.2, 2.9 and 4.2), 3.72 (s, 3H), 3.26 (s, 3H), 3.25 (s, 3H), 2.11 (d, 1H, *J* 13.0), 2.06 (ddd, 1H, *J* 13.0, 4.2 and 1.6), 1.33 (s, 3H), 1.31 (s, 3H), 0.87 (s, 9H), 0.09 (s, 3H), and 0.08 (s, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm) 168.0, 130.2, 129.0, 100.4, 100.0, 76.4, 69.4, 65.7, 52.4, 47.9, 47.9, 38.3, 25.7, 18.3, 17.9, −2.9, and −3.3; υ_{max} ($CHCl_3$)/cm^{-1} 1735 (C═O); MS (ESI) *m*/*z* (%) 439 (MNa^+); HRMS calcd for $C_{20}H_{36}O_7SiNa$, MNa^+, 439.2122; found, MNa^+, 439.2108.

Methyl (1*R*,3*S*,4*S*,6*R*,7*R*,8*R*,9*R*)-9-(*tert*-Butyldimethylsilyloxy)-7,8-epoxy-3,4-dimethoxy-3,4-dimethyl-2,5-dioxabicyclo[4.4.0]decane-9-carboxylate (13). To a stirred solution of the alkene **12** (82 mg, 0.20 mmol) in dry dichloromethane (2 mL) were added sodium bicarbonate (42 mg, 0.50 mmol) and freshly recrystallized MCPBA (51 mg, 0.30 mmol). The resultant solution was heated under reflux. After 24 h, more sodium bicarbonate (42 mg, 0.50 mmol) and MCPBA (51 mg, 0.30 mmol) were added, and the reaction mixture was heated under reflux for an additional 24 h. After cooling to room temperature, saturated sodium bicarbonate was added and the organic layer was separated. The organic extract was washed twice with saturated sodium bicarbonate. The organic extract was dried (anhydrous Na_2SO_4), filtered, and evaporated to give a white solid, which was purified by flash cromatography eluting with acetone−hexane (10:90) to yield 57 mg of epoxide **13** (66%) as a colorless oil, which solidifies on standing, and 10 mg of starting material (12%): mp 82−83 °C; $[\alpha]^{20}_D$ +89° (*c* 2.1 in $CHCl_3$); ^{1}H NMR (250 MHz, $(CD_3)_2CO$) δ (ppm) 3.85 (ddd, 1H, *J* 11.7, 10.0 and 4.1), 3.78 (s, 3H), 3.53 (dd, 1H, *J* 0.6 and 10.0), 3.28 (dt, 1H, *J* 3.3 and 1.1), 3.25 (s, 3H), 3.20 (s, 3H), 3.15 (d, 1H, *J* 3.3), 1.76 (ddd, 1H, *J* 11.7, 1.1 and 4.1), 1.70 (d, 1H, *J* 11.7) 1.27 (s, 3H), 1.21 (s, 3H), 0.92 (s, 9H), and 0.14 (s, 6H); ^{13}C NMR (63 MHz, $CDCl_3$) δ (ppm) 171.6, 100.3, 99.9, 76.3, 69.0, 64.4, 56.5, 55.7, 52.4, 48.2, 48.0, 33.4, 25.6, 18.2, 17.7, 17.7, −3.4, and −3.9; υ_{max} ($CHCl_3$)/ cm^{-1} 1745 (C═O); MS (CI) *m*/*z* (%) 433 (MH^+); HRMS calcd for $C_{20}H_{37}O_8Si$, MH^+, 433.2258; found, MH^+, 433.2276.

(1*R*,2*R*,3*S*,4*S*,5*R*)-1,2,3,4-Tetrahydroxycyclohexan-1,5-carbolactone (14). A stirred solution of the epoxide **13** (84 mg, 0.19 mmol) in 2 mL of aqueous TFA (50%) was stirred under reflux for 6 h. After cooling at room temperature the solvent was evaporated. The crude reaction was purified by flash cromatography eluting with methanol−ethyl acetate (15:85) to yield lactone **13** (36 mg, 99%) as colorless oil, which solidifies on standing: $[\alpha]^{20}_D$ −2° (*c* 1.7 in CH_3OH); ^{1}H NMR (250 MHz, $CDCl_3$) δ (ppm) 4.70 (t, 1H, *J* 5.3), 4.16 (t, 1H, *J* 4.7), 3.77 (d, 1H, *J* 8.8), 3.52 (dd, 1H, *J* 8.8 and 4.9), 2.51 (d, 1H, *J* 11.9), and 2.35 (dd, 1H, *J* 11.9 and 5.9); ^{13}C NMR (62.5 MHz, $CDCl_3$) δ (ppm) 177.5, 77.4, 76.8, 75.7, 73.9, 68.7, and 36.2; υ_{max} (Nujol)/cm^{-1} 3446 (O−H) and 1772 (C═O); MS (CI) *m*/*z* (%) 191 (MH^+); HRMS calcd for $C_7H_{11}O_6$, MH^+, 191.0556; found, MH^+, 191.0556.

(1*R*,2*R*,3*S*,4*S*,5*R*)-1,2,3,4-Tetrahydroxycyclohexan-1-carboxylate (4b). To a solution of the lactone **14** (22 mg, 0.12 mmol) in 1 mL of water was added aqueous lithium hydroxide (0.6 mL, 0.5 M). The resultant solution was stirred at room temperature for 1 h. Water was added and the solution was treated with Amberlite IR-120 until pH 6. The resin was filtered and washed with water. The filtrate was lyophilized to afford acid **4b** (25 mg, 99%) as a colorless oil: $[\alpha]^{20}_D$ +16° (*c* 1.1 in H_2O); ^{1}H NMR (250 MHz, D_2O) δ (ppm) 4.09 (dd, 1H, *J* 5.4 and 2.3), 4.00−3.91 (m, 3H), and 2.61 (m, 2H); ^{13}C NMR (62.5 MHz, D_2O) δ (ppm) 178.0, 77.8, 73.5, 72.5, 71.0, 67.4, and 35.0; υ_{max} (NaCl)/cm^{-1} 3417 (O−H) and 1724 (C═O); MS (CI) *m*/*z* (%) 191 ($MH^+ - H_2O$); HRMS calcd for $C_7H_{11}O_6$, MH^+, 191.0556; found, MH^+, 195.0558.

General Procedure of *Cis*-Hydroxylation. To a stirred solution of the alkene **7** (1 equiv) and the cooxidant (1.2 equiv) in 1:1 dioxane−water at room temperature was added 0.15 equiv of a freshly made aqueous solution of osmium tetroxide (0.12 M). After stirring for between 4 and 6 h, ethyl acetate was added and then saturated Na_2SO_3. The reaction mixture was stirred for 20 min. The organic layer was separated and the aqueous layer was extracted with ethyl acetate. All combined organic layers were dried (anhydrous Na_2SO_4) and concentrated in vacuo. The crude residue was crystallized and/or purified by flash cromatography.

Method A. The reaction was carried out as described above with alkene **7** (400 mg, 1.48 mmol), sodium periodate (380 mg, 1.78 mmol), osmium tetroxide (1.9 mL), and dioxane−water (14 mL) and a reaction time of 6 h. The crude residue was purified by crystallization from 25% ethyl acetate−hexane to yield (1*R*,2*R*,3*R*,4*S*,5*R*)-1-(*tert*-butyldimethylsilyloxy)-2,4,5-trihydroxycyclohexan-1,3-carbolactone (**16**) as white needles (203 mg, 45%). The mother waters were purified by flash cromatography eluting with 60% dichloromethane−diethyl ether to yield (1*R*,2*S*,3*S*,4*S*,5*R*)-1-(*tert*-butyldimethylsilyloxy)-2,3,4-trihydroxycyclohexan-1,5-carbolactone (**15**) as white needles (52 mg, 12%).

Method B. The reaction was carried out as described above with alkene **7** (1 g, 3.70 mmol), *N*-methylmorpholine oxide (560 mg, 4.81 mmol), osmium tetroxide (5.7 mL), and dioxane−water (30 mL) and a reaction time of 4 h. The crude residue was purified by crystallization from 25% ethyl acetate−hexane to yield alcohol **16** (203 mg, 18%). The mother waters were purified by flash cromatography eluting with 60% dichloromethane−diethyl ether to yield diol **15** (687 mg, 61%).

Data for 1,3-carbolactone **15**: mp 176−178 °C (25% ethyl acetate−hexane); $[\alpha]^{20}_D$ −329° (*c* 2.0 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 4.47 (d, 1H, *J* 4.5), 4.41 (s, 1H), 4.10 (dd, 1H, *J* 4.5 and 1.0), 3.98 (dd, 1H, *J* 5.0 and 1.0), 2.31 (dd, 1H, *J* 14.0 and 5.0), 2.10 (d, 1H, *J* 14.0), 0.96 (s, 9H), 0.18 (s, 3H), and 0.18 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 179.6, 84.8, 78.1, 76.1, 71.7, 71.5, 41.6, 26.3, 19.2, −4.4, and −4.8; υ_{max} (Nujol)/cm^{-1} 3413 (O−H), 3282 (O−H), and 1775 (C═O); MS (CI) *m*/*z* (%) 305 (MH^+); HRMS calcd for $C_{13}H_{25}O_6Si$, MH^+, 305.1420; found, MH^+, 305.1414.

Data for 1,5-carbolactone **16**: mp 110−112 °C (hexane); $[\alpha]^{20}_D$ +42° (*c* 1.25 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 4.75 (t, 1H, *J* 6.0 and 5.0), 4.04 (t, 1H, *J* 5.0), 3.85 (dd, 1H, *J* 4.15 and 1.5), 3.61 (t, 1H, *J* 5 and 4.15), 3.04 (d, 1H, *J* 11.7), 2.14 (ddd, 1H, *J* 11.7, 1.5, and 6.0), 0.95 (s, 9H), 0.21 (s, 3H), and 0.19 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 178.3, 80.0, 77.4, 74.9, 67.8, 67.7, 32.4, 26.2, 19.1, −3.0, and −3.0; υ_{max} (Nujol)/cm^{-1} 3521 (O−H), 3390 (O−H), and 1779 (C═O); MS (CI) *m*/*z* (%) 305 (MH^+); HRMS calcd for $C_{13}H_{25}O_6Si$, MH^+, 305.1420; found, MH^+, 305.1411.

Methyl (1*R*,2*R*,3*R*,4*S*,5*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3,4,5-tetrahydroxycyclohexane-1-carboxylate (19). The

reaction was carried out as described above with alkene **8** (50 mg, 0.17 mmol), trimethylamine *N*-oxide (23 mg, 0.20 mmol), osmium tetroxide (0.21 mL), and dioxane−water (2 mL) and a reaction time of 20 h. The crude residue was purified by recrystallization from dichloromethane to yield 38 mg of methyl ester **19** as white prisms, and the mother waters were purified by flash cromatography eluting with methanol−ethyl acetate (5:95) to afford 13 mg of alcohol **19** (89%): mp 177−178 °C (DCM); $[\alpha]^{20}_D$ +6° (*c* 1.9 in CH_3OH);^{1}H NMR (250 MHz, CD_3OD) δ 3.77 (dd, 1H, *J* 3.0 and 1.1), 3.53 (s, 3H), 3.52−3.42 (m, 2H), 3.32 (t, 1H, *J* 9.3), 1.97−1.80 (m, 2H), 0.71 (s, 9H), −0.10 (s, 3H), and −0.13 (s, 3H); ^{13}C NMR (63 MHz, CD_3OD) δ 173.8, 80.1, 76.2, 75.8, 72.8, 70.6, 52.5, 37.0, 26.3, 19.2, −3.2, and −4.0; υ_{max} (KBr)/cm^{-1} 3377 (O−H) and 1738 (C═O); MS (CI) *m*/*z* (%) 337 (MH^+); HRMS calcd for $C_{14}H_{29}O_7Si$, MH^+, 337.1683; found, MH^+, 337.1690.

(1*S*,2*S*,3*S*,4*S*,5*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3,4,5-tetrahydroxy-1-hydroxymethylcyclohexane (17). To a stirred solution of the lactone **15** (100 mg, 0.33 mmol), under argon and at 0 °C, in 4.2 mL of a dry solution of methanol in tetrahydrofuran (1/20 v/v), was added lithium borohydride (22 mg, 1.01 mmol). The resultant reaction mixture was refluxed for 10 h. After cooling to room temperature, ethyl acetate (1 mL) and then water (3 mL) were added. The solvent was evaporated and the crude reaction was purified by flash cromatography [eluent: (1) ethyl acetate, (2) methanol−ethyl acetate−acetic acid (14:85:1)] to yield the alcohol **17** as white needles (70 mg, 75%): mp 126−128 °C; $[\alpha]^{20}_D$ −22° (*c* 1.1 in CH_3OH); ^{1}H NMR (250 MHz, CD_3OD) δ (ppm) 4.10 (t, 1H, *J* 3.0), 4.09−3.99 (m, 1H), 3.80 (d, 1H, *J* 9.3), 3.63 (d, 1H, *J* 3.0), 3.29 (dd, 1H, *J* 9.5 and 3.0), 3.27 (d, 1H, *J* 9.3), 1.90 (dd, 1H, *J* 13.7 and 5.1), 1.67 (dd, 1H, *J* 13.7 and 11.8), 0.97 (s, 9H), 0.16 (s, 3H), and 0.15 (s, 3H); ^{13}C NMR (62.5 MHz, CD_3OD) δ (ppm) 77.9, 77.0, 76.5, 69.2, 67.9, 67.3, 39.9, 26.3, 19.1, and −5.4; υ_{max} (NaCl)/cm^{-1} 3454 (O−H); MS (CI) *m*/*z* (%) 309 (MH^+); HRMS calcd for $C_{13}H_{29}O_6Si$, MH^+, 309.1733; found, MH^+, 309.1744.

(1*S*,2*S*,3*S*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxy-1-hydroxymethylcyclohexane (5a). A stirred solution of the silyl ether **17** (43 mg, 0.14 mmol) in 1.5 mL of aqueous acetic acid (80%) was heated at 40 °C for 5 h. The crude mixture was diluted with water and diethyl ether. The organic layer was separated and the aqueous layer was washed with diethyl ether (2 × 2 mL). The aqueous extract was freeze-dried to afford polyhydroxycyclohexane **5a** as colorless oil (30 mg, 99%): $[\alpha]^{20}_D$ −20° (*c* 1.1 in CH_3OH); ^{1}H NMR (250 MHz, CD_3OD) δ (ppm) 4.12 (t, 1H, *J* 3.0), 4.05 (m, 1H), 3.66 (m, 2H), 3.64 (s, 2H), 3.32 (m, 1H), 1.98 (dd, 1H, *J* 13.6 and 4.9), and 1.56 (dd, 1H, *J* 13.6 and 11.7); ^{13}C NMR (63 MHz, CD_3OD) δ (ppm) 78.1, 77.1, 76.8, 70.4, 68.2, 67.5, and 39.8; υ_{max} (Nujol)/cm^{-1} 3423 (O−H); MS (+FAB) *m*/*z* (%) 195 (MH^+); HRMS calcd for $C_7H_{15}O_6$, MH^+, 195.0869; found, MH^+, 195.0875.

(1*S*,2*R*,3*R*,4*S*,5*R*)-1-(*tert*-Butyldimethylsilyloxy)-2,3,4,5-tetrahydroxy-1-hydroxymethylcyclohexane (18a) and (1*S*,2*R*,3*R*,4*S*,5*R*)-1-[(*tert*-Butyldimethylsilyloxy)methyl]-1,2,3,4,5-pentahydroxycyclohexane (18b). To a stirred solution of the lactone **16** (55 mg, 0.18 mmol), under argon and at 0 °C, in 0.8 mL of a dry solution of methanol in tetrahydrofuran (1/20 v/v), was added lithium borohydride (10 mg, 0.46 mmol). The resultant reaction mixture was refluxed for 7 h. After cooling at room temperature, ethyl acetate (0.7 mL) and then water (1.5 mL) were added. The solvent was evaporated and the crude reaction was purified by flash cromatography [eluent: (1) ethyl acetate, (2) methanol−ethyl acetate (15:85), and (3) methanol−ethyl acetate−acetic acid (14:85:1)] to yield 31 mg (55%) of **18a** and 22 mg (39%) of **18b** both as white needles.

Data for **18a**: mp 131−132 °C; $[\alpha]^{20}_D$ −2° (*c* 1.5 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 3.82 (dd, 1H, *J* 3.0 and 9.6), 3.78 (m, 1H), 3.76 (d, 1H, *J* 1.3), 3.67 (d, 1H, *J* 11.3), 3.59 (d, 1H, *J* 11.3), 3.57 (m, 1H), 1.79 (ddd, 1H, *J* 13.0, 4.8 and 1.3), 1.66 (dd, 1H, *J* 13.0 and 11.6), 0.96 (s, 9H), 0.21 (s, 3H) and 0.19 (s, 3H); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 79.4, 76.9, 74.6, 73.3, 71.0, 67.7, 37.2, 26.7, 19.5, −2.4, and −2.4; υ_{max} (NaCl)/cm^{-1} 3417 and 3215; MS (CI) *m*/*z* (%) 309 (MH^+); HRMS calcd for $C_{13}H_{29}O_6Si$, MH^+, 309.1733; found, MH^+, 309.1729; Anal. Calcd for $C_{13}H_{28}O_6Si$: C, 50.62; H, 9.15. Found: C, 50.95; H, 9.26.

Data for **18b**: mp 133−134 °C; $[\alpha]^{20}_D$ +1° (*c* 1.2 in CH_3OH); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 3.79 (m, 3H), 3.74 (d, 1H, *J* 10.0), 3.59 (t, 1H, *J* 9.3 and 10.9), 3.55 (d, 1H, *J* 10.0), 1.80 (m, 1H), 1.65 (dd, 1H, *J* 13.1 and 11.8), 0.96 (s, 9H), and 0.08 (s, 6H); ^{13}C NMR (125 MHz, CD_3OD) δ (ppm) 77.0, 75.1, 73.9, 73.4, 70.8, 69.5, 36.2, 26.5, 19.3, −5.4, and −5.4; υ_{max} (NaCl)/cm^{-1} 3417 and 3209; MS (CI) *m*/*z* (%) 309 (MH^+); HRMS calcd for $C_{13}H_{29}O_6Si$, MH^+, 309.1733; found, MH^+, 309.1735

(1*S*,2*R*,3*R*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxy-1-hydroxymethylcyclohexane (6a). A stirred solution of the silyl ethers **18a** and **18b** (14 mg, 0.05 mmol) in 0.5 mL of aqueous acetic acid (80%) was heated at 40 °C for 17 h. The crude mixture was diluted with water and diethyl ether. The organic layer was separated and the aqueous layer was washed with diethyl ether (2 × 2 mL). The aqueous extract was freeze-dried to afford polyhydroxycyclohexane **6a** as colorless oil (8 mg, 91%): $[\alpha]^{20}_D$ −2° (*c* 0.7 in CH_3OH); ^{1}H NMR (500 MHz, CH_3OD) δ (ppm) 3.76 (m, 3H), 3.64 (s, 2H), 3.45 (d, 1H, *J* 11.2), 1.77 (dd, 1H, *J* 13.1 and 4.7) and 1.66 (dd, 1H, *J* 13.1 and 11.8); ^{13}C NMR (125 MHz, CH_3OD) δ (ppm) 86.8, 84.2, 82.6, 81.7, 78.4, 75.1, and 31.7; υ_{max} (Nujol)/cm^{-1} 3423 (O−H); MS (+FAB) *m*/*z* (%) 195 (MH^+); HRMS calcd for $C_7H_{15}O_6$, MH^+, 195.0869; found, MH^+, 195.0875.

(1*R*,2*S*,3*S*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxycyclohexan-1-carboxylic Acid (5b). A stirred solution of the carbolactone **15** (150 mg, 0.49 mmol) in 5 mL of aqueous acetic acid (80%) was heated at 40 °C for 5.5 days. The crude mixture was diluted with water and ethyl acetate. The organic layer was separated and the aqueous layer was washed with ethyl acetate (5 × 1 mL). The aqueous extract was freeze-dried and crystallized from 20% ethyl acetate−methanol to afford acid **5b** as an amorphous solid (69 mg, 64%): mp 210−212 °C [20% ethyl acetate−methanol (lit.[13] mp 221 °C, 25% aqueous ethanol)]; $[\alpha]^{20}_D$ −17° (*c* 2.6 in H_2O) [lit.[13] $[\alpha]^{20}_D$ −16° (*c* 1.0 in 50% aqueous ethanol)]; ^{1}H NMR (300 MHz, CD_3OD) δ (ppm) 4.07 (t, 1H, *J* 3.0), 3.97 (m, 2H), 3.41 (dd, 1H, *J* 3.0 and 9.9), 2.10 (dd, 1H, *J* 13.1 and 4.9), and 1.81 (t, 1H, *J* 13.1); υ_{max} (KBr)/cm^{-1} 3430 (O−H), 3313 (O−H), and 1734 (C═O); MS (CI) *m*/*z* (%) 209 (MH^+).

(1*R*,2*R*,3*R*,4*S*,5*R*)-1,2,4,5-Tetrahydroxycyclohexan-1,3-carbolactone (20). A stirred solution of the silyl ether **16** (140 mg, 0.46 mmol) in 5 mL of aqueous acetic acid (80%) was heated at 40 °C for 76 h. The crude mixture was diluted with water and ethyl acetate. The organic layer was separated and the aqueous layer was washed with ethyl acetate (5 × 1 mL). The aqueous extract was freeze-dried and crystallizated from water to afford carbolactone **20** as white prisms (67 mg, 77%): mp 286 °C (dec) (H_2O); $[\alpha]^{20}_D$ −21° (*c* 2.2 in H_2O); ^{1}H NMR (500 MHz, CD_3OD) δ (ppm) 4.52 (dd, 1H, *J* 4.5 and 1.0), 4.29 (br. s, 1H), 4.09 (m, 1H), 3.98 (m, 1H), 2.61 (dd, 1H, *J* 13.9 and 5.1), and 2.09 (dt, 1H, *J* 13.9 and 1.6); ^{13}C NMR (63 MHz, D_2O) δ (ppm) 181.0, 84.3, 76.7, 75.8, 71.1, 70.6, and 40.7; υ_{max} (KBr)/cm^{-1} 3360 (O−H) and 1761 (C═O); MS (CI) *m*/*z* (%) 191 (MH^+); HRMS calcd for $C_7H_{11}O_6$, MH^+, 191.0556; found, MH^+, 191.0554.

(1*R*,2*R*,3*R*,4*S*,5*R*)-1,2,3,4,5-Pentahydroxycyclohexan-1-carboxylic Acid (6b). A solution of the lactone **20** (19 mg, 0.10 mmol) in aqueous lithium hydroxide (0.2 mL, 0.2 M) was stirred at room temperature for 2 h. The resultant solution was diluted with water and treated with Amberlite IR-120

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until pH 6. The resin was filtered and washed with water. The filtrate was concentrated to afford acid **6b** (20 mg, 96%) as a colorless oil: $[\alpha]^{20}_{D}$ −12° (*c* 0.7 in H_2O); ^{1}H NMR (250 MHz, D_2O) δ (ppm) 3.59 (d, 1H, *J* 3.0), 3.41 (dd, 1H, *J* 3.0 and 9.5), 3.33 (m, 1H), 3.22 (t, 1H, *J* 9.5), and 1.70 (m, 2H); ^{13}C NMR (63 MHz, D_2O) δ (ppm) 177.5, 76.0, 74.5, 73.2, 71.2, 69.1, and 34.7; υ_{max} (Nujol)/cm^{-1} 3351 (O−H) and 1721 (C═O); MS (CI) *m*/*z* (%) 209 (MH^+); HRMS calcd for $C_7H_{13}O_7$, MH^+, 209.0661; found, MH^+, 209.0658.

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Supporting Information Available: Crystallographic data for compound **11**. This material is available free of charge via the Internet at http://pubs.acs.org.

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