Synthetic Studies on Macropyrrolizidine Alkaloid, Monocrotaline: Enantioselective Synthesis of a Necic Acid Moiety, Monocrotalic Acid Methylene Acetal

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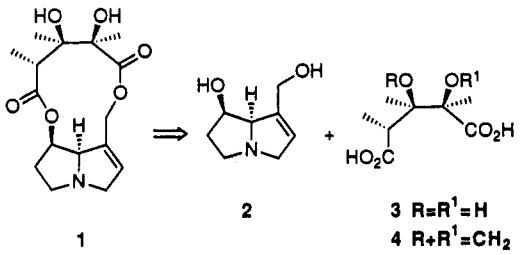
A methylene acetal derivative **4** of the necic acid, monocrotalic acid, part of the macropyrrolizidine alkaloid, monocrotaline, was enantioselectively synthesized from 2-furylmethanol derivative **6**. Oxidation of **6**, followed by silylation of the resulting lactol **9**, gave silyl ether **19** as a major product. Introduction of the di-*tert*-hydroxy groups to **22** was achieved by stereoselective dihydroxylation with osmium tetroxide. After protection of the vicinal diol as a methylenedioxy derivative, acetal **26** was successfully converted into the desired product **4**.

Introduction

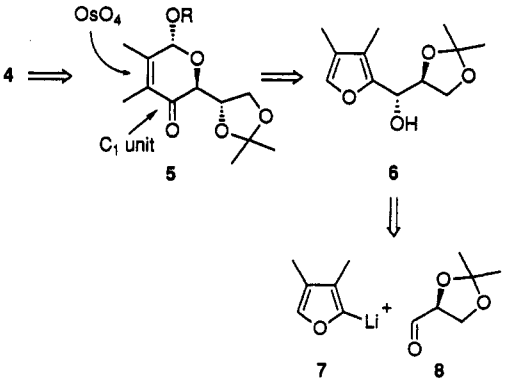
Monocrotaline (**1**), isolated from *Crotalaria* species as a hepatotoxic carcinogen, is a 11-membered macrocyclic pyrrolizidine alkaloid in which the necine base, retronecine (**2**), is esterified with monocrotalic acid (**3**).[1] Owing to the interesting physiological activities and the characteristic chemical structures, macrocyclic pyrrolizidine alkaloids continue to provide challenging synthetic targets.[2] The total synthesis of monocrotaline (**1**) has been reported by Vedejs[3] in racemic form and by Niwa[4] in optically active form. In both syntheses a methylenedioxy derivative of monocrotalic acid **4** was used for the coupling reaction with retronecine (Scheme I). Recently we reported a chiral synthesis of the necine base, retronecine (**2**), by means of a stereoselective carbenoid displacement reaction.[5] We have investigated a novel synthetic route to the necic acid, monocrotalic acid, in an optically active form and in this paper we report an enantioselective synthesis of **4**.

Scheme I



1 2 3 R=R¹=H 4 R+R¹=CH₂

Scheme II



Results and Discussion

Monocrotalic acid bears three contiguous chiral centers with vicinal *tert*-hydroxy groups, whose stereoselective construction seems to be a central problem of the synthesis. The strategy for the synthesis of **4** was envisaged to employ a chiral pyranone (or equivalent) **5**, readily accessible from a 2-furylmethanol derivative **6** by oxidative treatment.[6] Osmylation for **5** would be expected to occur from the sterically more favored face to provide the vicinal diol with the desired stereochemistry, and also the secondary methyl group can be introduced by manipulation of the carbonyl function, on the basis of previous results[6-8] related to the exploitation of nonracemic pyranones in the synthesis of natural products (Scheme II).

Synthesis of the chiral pyranone **10** was investigated as shown in Scheme III. Chelation-controlled addition

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(2) For some examples of the syntheses of macrolactone pyrrolizidine alkaloids, (a) (+)-Dicrotaline: Devlin, J. A.; Robins, D. J. *J. Chem. Soc., Chem. Commun.* **1981**, 1272. (b) (+)-Dicrotalin: Niwa, H.; Okamoto, O.; Ishiwata, H.; Kuroda, A.; Uosaki, Y.; Ymada, K. *Bull. Chem. Soc. Jpn.* **1988**, *61*, 3017. (c) (±)-Fulvine and (±)-crispatine: Vedejs, E.; Larsen, S. D. *J. Am. Chem. Soc.* **1984**, *106*, 3030. (d) (±)-Integerrimine: Narasaka, K.; Sakakura, T.; Uchimaru, T.; Güedin-Vuong, D. *Ibid.* **1984**, *106*, 2954. (e) (−)-Integerrimine and (+)-usaramine: White, J. D.; Amedio, J. C., Jr.; Gut, S.; Ohira, S.; Jayasinghe, L. R. *J. Org. Chem.* **1992**, *57*, 2270. (f) (−)-Integerrimine: Niwa, H.; Machiya, Y.; Okamoto, O.; Uosaki, Y.; Kuroda, A.; Ishiwata, H.; Yamada, K. *Tetrahedron* **1992**, *48*, 393.

(3) Vedejs, E.; Ahmad, S.; Larsen, S. D.; Westwood, S. *J. Org. Chem.* **1987**, *52*, 3937.

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(6) For some representative examples of the uses of furylmethanols as key intermediates in the syntheses of natural products, see (a) Achmatowiczs, O., Jr.; Bukowski, P.; Szechner, B.; Zwierzchowska, Z.; Zamojski, A. *Tetrahedron* **1971**, *27*, 1973. (b) Achmatowiczs, O., Jr.; Bielski, R. *Carbohydr. Res.* **1977**, *55*, 165. (c) Jaworska, A.; Zamojski, A. *Ibid.*, **1984**, *126*, 191. (d) DeShong, P.; Ramesh, S.; Perez, J. J. *J. Org. Chem.* **1983**, *48*, 2117. (e) Ziegler, F. E.; Wester, R. T. *Tetrahedron Lett.* **1984**, *25*, 617. (f) Martin, S. F.; Gluchowski, C.; Campbell, C. L.; Chapman, R. C. *J. Org. Chem.* **1984**, *49*, 2512. (g) Martin, S. F.; Guinn, D. E. *Ibid.* **1987**, *52*, 5588. (h) Sammes, P. G.; Thetford, D. *J. Chem. Soc., Perkin Trans. 1* **1988**, 111. (i) Bates, M. A.; Sammes, P. G.; Thomson, G. A. *Ibid* **1988**, 3037. (j) Hauser, F. M.; Chakrapani, S.; Ellenberger, W. P. *J. Org. Chem.* **1991**, *56*, 5284. (k) Martin, S. F.; Zinke, P. W. *Ibid.* **1991**, *56*, 6600. (l) De Haan, R. A.; Heeg, M. J.; Albizati, K. F. *Ibid.* **1993**, *58*, 291.

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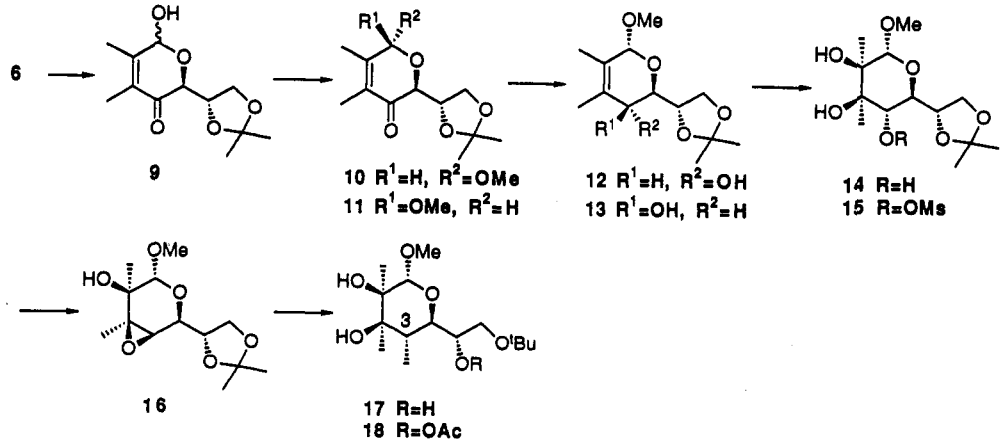
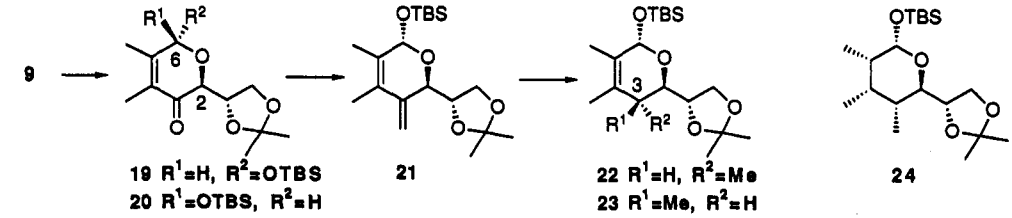
Scheme III



Scheme IV



reaction of 2-lithio-3,4-dimethylfuran (**7**)[9] to (*S*)-2,3-*O*-isopropylideneglyceraldehyde (**8**)[10,11] in the presence of zinc bromide afforded glycerol derivative **6** in 95% yield with >90% diastereomeric excess. Treatment of **6** with *N*-bromosuccinimide in aqueous tetrahydrofuran[12] brought about ring transformation to furnish lactol **9** in 84% yield, which on methylation with methyl iodide in the presence of silver(I) oxide[6i] gave methyl ethers **10** and **11** in 62 and 23% yields. Reduction of the major α-anomer **10** with sodium borohydride in the presence of cerium chloride[13] afforded alcohols **12** and **13**, in 82 and 11% yields. Osmylation[7] of α-alcohol **12** in ether containing a catalytic amount of pyridine gave rise to triol **14** as the only isolated product in 96% yield. Since introduction of the vicinal *tert*-hydroxy groups was thus accomplished with the desired stereochemistry, the construction of the secondary methyl group at C_3 was investigated. As protection of the vicinal *tert*-diol of **14** proved unfeasible, the secondary hydroxy group was treated with mesyl chloride in the presence of triethylamine to provide mesylate **15** in 94% yield. On exposure to sodium methoxide, **15** yielded epoxide **16** in quantitative yield. Epoxide opening with trimethylaluminum[14] afforded triol **17**, which was acetylated with acetic anhydride in pyridine to give acetate **18** in 24% yield. The ^{1}H-NMR spectrum of **18** showed the presence of one doublet methyl signal at δ 0.99 with the coupling constant of $J = 6.7$ Hz and two singlet *tert*-methyl signals at δ 1.12 and 1.21. Since the above procedure requires relatively multistep operation and the overall yield was rather poor, we turned our attention on searching an alternative route involving the proper choice of the protecting group for lactol **9**.

Thus, lactol **9** was treated with *tert*-butyldimethylsilyl chloride in the presence of silver(I) oxide to afford silyl ethers **19** and **20** in 68 and 25% yields (Scheme IV). The C_6 stereochemistry of these ethers was determined based on ^{1}H-NMR analysis. A 13% NOE enhancement was observed between the protons at the 2- and 6-positions for **19**; no enhancement was observed for **20**. The minor ether **20** can be recycled by successive desilylation with tetrabutylammonium fluoride and silylation of the resulting lactol under the same reaction condition as above to give the desired ether **19** in 85% yield after one cycle. The introduction of the secondary methyl group was then attempted prior to the osmylation. The Wittig reaction of **19** with methyltriphenylphosphonium bromide and potassium *tert*-butoxide gave the *exo*-olefin **21** in 68% yield, which on hydrogenation[6g] over 5% palladium–charcoal in ethyl acetate under an atmospheric pressure of hydrogen afforded the desired product **22** together with the stereoisomer **23** and over-reduction product **24**, in 95% yield, in a ratio of 12:4:3. The results for the catalytic hydrogenation attempted were summarized in Table I, in which the best stereoselectivity was obtained by employing the Wilkinson catalyst in benzene furnishing **22** and **23** in 98% yield in a ratio of 24:1.

The stereochemistry of the C_3 methyl group of **22** was confirmed as α based on its ^{1}H-NMR spectrum exhibiting the coupling constant of $J = 9.2$ Hz between the diaxial protons at the 2 and 3 positions. These NMR study suggested that the stable conformation for **22** would be **A** as depicted in Figure 1, hence its osmylation would be expected to occur from the less-hindered side of the molecule affording diol **25** with the desired stereochemistry. In fact, dihydroxylation of **22** with osmium tetroxide in the presence of a catalytic amount of pyridine provided diol **25**, in 97% yield, as the only product.

Since all the chiral centers for monocrotalic acid were thus constructed stereoselectively, preparation of the diacid function was then investigated. Protection of the diol in **25** with dimethoxymethane and phosphorus pen-

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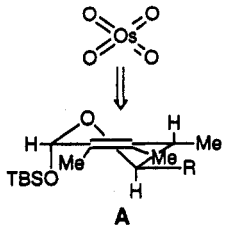
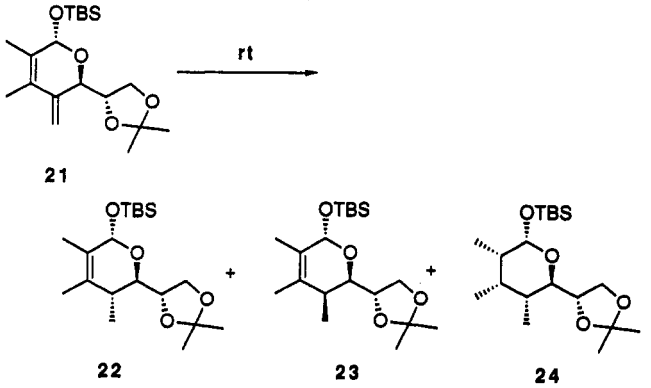


A

Figure 1.

Table I. Hydrogenation of Diene 21



catalyst or reducing agent	solvent	time	yield (%)	products 22/23/24
5% Pd–C, H_2 (1 atm)	AcOEt	1.5 h	95	12:4:3
5% Pd–C, H_2 (1 atm)	EtOH	1.5 h	69	2:1:3
10% Pd–C, H_2 (1 atm)	AcOEt	1.5 h	71	6:2:3
Rh on alumina, H_2 (1 atm)	AcOEt	1.5 h	90	4:1:4
Ir brack, H_2 (1 atm)	EtOH	1 h	0	–
PtO_2, H_2 (1 atm)	AcOEt	15 min	0	–
$N_2H_4{\cdot}H_2O$, AcOH, $CuSO_4$, $NaIO_4$	MeOH	7 days	37	2:1:0
$N_2H_4{\cdot}H_2O$, H_2O_2	EtOH	3 days	87	2:1:0
$(Ph_3P)_3RhCl$, H_2 (1 atm)	benzene	12 h	98	24:1:0

toxide[15] gave the bis(methylenedioxy) compound **26**, involving the exchange reaction of the acetonide protecting group in 96% yield. Silyl ether **26** was converted into lactone **28** by sequential desilylation with tetrabutylammonium fluoride and oxidation of the resulting lactol **27** with pyridinium chlorochromate in 83% overall yield. Selective deprotection of the methylenedioxy group of **28** by treatment with a catalytic amount of concentrated sulfuric acid in a mixture of acetic acid and acetic anhydride[16] gave rise to diacetate **29** in 78% yield, which on hydrolysis with sodium methoxide, followed by ruthenium tetraoxide oxidation,[17] afforded the diacid **4**, mp 127–128 °C (lit.[4] 127–129 °C). The spectroscopic data of **4** including specific optical rotation $[\alpha]_D$ +41.3° (C = 0.54, $CHCl_3$) {lit.[4] $[\alpha]_D$ +41.7° (c = 0.57, $CHCl_3$)} were identical with those reported[4] (Scheme V).

In summary , this paper reports the enantioselective synthesis of the methylenedioxy derivative of monocrotalic acid. Since we have already succeeded in the synthesis of retronecine, this synthesis constitutes formal total synthesis of the macropyrrolizidine alkaloid, monocrotaline.

Experimental Section

Melting points were measured with a Yanagimoto MP apparatus and are uncorrected. IR spectra were measured for solutions in $CHCl_3$ on a Hitachi 260-10 spectrophotometer. ^{1}H NMR spectra were obtained for solutions in $CDCl_3$ on a JEOL GSX-270 instrument, and chemical shifts are reported on the δ scale from internal TMS. Mass spectra were measured with a JEOL JMS D-300 spectrometer. Optical rotations were taken with a JASCO DIP-360 polarimeter.

(2*S*,3*S*)-3-[2-(3,4-Dimethylfuryl)]-1,2-*O*-isopropylideneglycerol (6). To a stirred solution of 2-lithio-3,4-dimethylfuran (**7**) [prepared from 3,4-dimethylfuran (3.99 g, 41.6 mmol) and *n*-butyllithium (25 mL, 1.66 M/L in hexane, 41.4 mmol)] in THF (25 mL) in the presence of zinc(II) bromide (5.6 g, 24.9 mmol) was added a solution of (*S*)-2,3-*O*-isopropylideneglyceraldehyde (**8**)(2.7 g, 20.8 mmol) in THF (20 mL) at 0 °C under argon, and the resulting mixture was further stirred at the same temperature for 1 h. Saturated ammonium chloride solution was added to the solution and the mixture was extracted with ethyl acetate. The organic layer was washed with water and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (5:1) afforded a mixture of (2*S*,3*S*)-glycerol **6** and (2*S*,3*R*)-glycerol (95:5) as a colorless oil (4.45 g, 95%). (2*S*,3*S*)-Isomer: $[\alpha]^{25}_D$ −11.36° (c = 1.25, $CHCl_3$); IR (cm^{-1}) 3550 (OH); ^{1}H-NMR δ 1.35 (3H, s, CMe), 1.43 (3H, s, CMe), 1.92 and 1.96 (each 3H, each br s, 3′-Me and 4′-Me), 2.41 (1H, br s, OH), 4.09 and 4.22 (each 1H, each dd, J = 6.5 and 8.5 Hz, 1-H_2), 4.32 (1H, distorted q, J = 6.5 Hz, 2-H), 4.75 (1H, br d, J = 5.5 Hz, 3-H), 7.11 (1H, br s, 5′-H); MS m/z, calcd for $C_{12}H_{18}O_4$ (M^+) 226.1205, found 226.1205. Anal. Calcd for $C_{12}H_{18}O_4$: C, 63.70, H; 8.02. Found: C; 63.60, H; 8.24. (2*S*,3*R*)-Isomer: ^{1}H-NMR δ 1.38 and 1.47 (each 3H, each s, CMe_2), 1.92 and 1.98 (each 3H, each br s, 3′-Me and 4′-Me), 2.73 (1H, br s, OH), 3.54 (1H, dd, J = 4.9 and 8.5 Hz, half of 1-H_2), 3.87 (1H, dd, J = 6.5 and 8.5 Hz, half of the 1-H_2), 4.52 (1H, ddd, J = 4.9 and 6.5 and 8.5 Hz, 2-H), 4.57 (1H, br d, J = 8.5 Hz, 3-H), 7.11 (1H, br s, 5′-H).

(2*S*)-6-Hydroxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dimethyl-6*H*-pyran-3(2*H*)-one (9). To a stirred solution of glycerol derivative **6** (1.8 g, 7.96 mmol) and sodium acetate (653 mg, 7.96 mmol) in aqueous THF (20 mL, H_2O–THF = 1:4) was added portionwise NBS (1.42 g, 7.96 mmol) at 0 °C, and the resulting mixture was further stirred for 30 min at the same temperature. The solution was successively treated with an excess of the 10% KI solution and with saturated sodium thiosulfite solution. After removal of the solvent, the aqueous residue was extracted with ethyl acetate and the extract was washed with water and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded lactol **9** (1.62 g, 84%) as a colorless oil: IR (cm^{-1}) 3450 (OH), 1680 (CO); ^{1}H-NMR δ 1.27 (0.6H, s, CMe), 1.37 (0.6H, s, CMe), 1.38 (2.4H, s, CMe), 1.44 (2.4H, s, CMe), 1.77 and 1.88 (each 2.4H, each s, 4-Me and 5-Me) 1.80 and 1.98 (each 0.6H, each s, 4-Me and 5-Me), 3.95 (1.6H, ddd, J = 2.4, 6.7, and 7.9 Hz, 5′-H_2), 4.14 (0.4H, m, 5′-H_2), 4.23 (0.2H, d, J = 2.4 Hz, 2-H), 4.34 (0.8H, br s, OH), 4.52 (0.2H, dt, J = 2.4 and 7.3 Hz, 4′-H), 4.73 (0.8H, dt, J = 2.4 and 6.7 Hz, 4′-H), 4.81 (0.8H, d J = 2.4 Hz, 2-H), 4.97 (0.2H, d, J = 10.4 Hz, OH), 5.32 (0.2H, d, J = 10.4 Hz, 6-H), 5.51 (0.8H, br s, 6-H); MS m/z, calcd for $C_{12}H_{18}O_5$ (M^+) 242.1154, found 242.1159. Anal. Calcd for $C_{12}H_{18}O_5$: C; 59.49, H; 7.49. Found: C; 59.25, H; 7.69.

(2*S*,6*R*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dimethyl-6*H*-pyran-3(2*H*)-one (10) and (2*S*,6*S*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dimethyl-6*H*-pyran-3(2*H*)-one (11). Methyl iodide (2.9 mL, 46.6 mmol) was added to a solution of lactol **9** (1.62 g, 6.69 mmol) in acetone (16 mL) containing silver(I) oxide (10.8 g, 46.6 mmol) at ambient temperature, and the resulting mixture was further stirred at the same temperature for 12 h. The insoluble material was filtered off through a Celite pad and the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (8:1) afforded α-anomer **10** (1.06 g, 62%) as a colorless oil: $[\alpha]^{25}_D$ −1.22° (c = 1.28, $CHCl_3$); IR (cm^{-1}) 1670 (CO); ^{1}H-NMR δ 1.38 (3H, s, CMe), 1.46 (3H, s, CMe), 1.76 and 1.94 (each 3H, each s, 4-Me and 5-Me), 3.53 (3H, s, OMe), 4.01 (2H, dd, J = 3.1 and 6.7 Hz, 5′-H_2), 4.58 (1H, d, J = 3.1 Hz, 2-H), 4.74 (1H, dt, J = 3.1 and 6.7 Hz, 4′-H), 4.96 (1H, s, 6-H). MS m/z, calcd for $C_{12}H_{17}O_5$ (M^+ − 15) 241.1074, found 241.1073. Anal. Calcd for $C_{13}H_{20}O_5$: C; 60.92,

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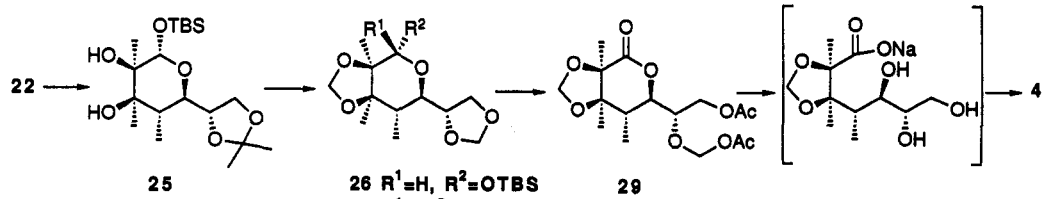
Scheme V



H; 7.87. Found: C; 60.65, H; 8.07. Further elution with the same solvent system gave β-anomer **11** (395 mg, 23%) as a colorless oil: $[\alpha]^{25}_D$ +17.83° (*c* = 0.12, $CHCl_3$); IR (cm^{-1}) 1680 (CO); ^{1}H-NMR δ 1.37 (3H, s, CMe), 1.45 (3H, s, CMe), 1.80 and 1.92 (each 3H, each s, 4-Me and 5-Me), 3.54 (3H, s, OMe), 4.07(2H, d, *J* = 6.1 Hz, 5′-H_2), 4.15 (1H, d, *J* = 6.1 Hz, 2-H), 4.67 (1H, q, *J* = 6.1 Hz, 4′-H), 5.02 (1H, s, 6-H), MS *m/z* calcd for $C_{12}H_{17}O_5$ (M^+ − 15) 241.1074, found 241.1073.

(2*R*,3*R*,6*R*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydro-4,5-dimethyl-6*H*-pyran-3-ol (12) and (2*R*,3*S*,-6*R*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydro-4,5-dimethyl-6*H*-pyran-3-ol (13). To a stirred solution of ketone **10** (700 mg, 2.73 mmol) in THF (10 mL) in the presence of cerium chloride (8.2 mL of 0.4 M methanol solution, 3.28 mmol) was added sodium borohydride (120 mg, 3.01 mmol) portionwise at −78 °C, and the mixture was further stirred at the same temperature for 2 h. After addition of saturated ammonium chloride solution, most of the organic solvent was evaporated to leave a residue, which was extracted with ethyl acetate. The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (4:1) afforded α-alcohol **12** (580 mg, 82%) as a colorless oil: $[\alpha]^{25}_D$ −16.33° (*c* = 1.23, $CHCl_3$); IR (cm^{-1}) 3550 (OH); ^{1}H-NMR δ 1.38 (3H, s, CMe), 1.46 (3H, s, CMe), 1.66 (3H, s, 5-Me), 1.74 (3H, d, *J* = 1.2 Hz, 4-Me), 3.15 (1H, br s, OH), 3.42 (3H, s, OMe), 3.61 (1H, br t, *J* = 8.6 Hz, 2-H), 3.99 (1H, dt, *J* = 6.1 and 7.3 Hz, half of 5′-H_2), 4.08 (1H, br d, *J* = 8.6 Hz, 3-H), 4.14–4.22 (2H, m, 4′-H and half of 5′-H_2), 4.54 (1H, s, 6-H). MS *m/z* calcd for $C_{13}H_{22}O_5$ (M^+) 258.1466, found 258.1466. Anal. Calcd for $C_{13}H_{22}O_5$: C, 60.44, H; 8.59. Found: C; 60.56, H; 8.88. Further elution with hexane–ethyl acetate (2:2) afforded β-alcohol **13** (80 mg, 11%) as a colorless oil: $[\alpha]^{25}_D$ +44.22° (*c* = 0.09, $CHCl_3$); IR (cm^{-1}) 3550 (OH); ^{1}H-NMR δ 1.38 (3H, s, CMe), 1.42 (3H, s, CMe), 1.69 and 1.83 (each 3H, each s, 4-Me and 5-Me), 3.43 (3H, s, OMe), 3.71 (1H, br s, 3-H), 3.81 (1H, dd, *J* = 2.4 and 8.6 Hz, 2-H), 3.97 (1H, dd, *J* = 4.9 and 8.6 Hz, half of 5′-H_2), 4.18 (1H, dd, *J* = 6.1 and 8.6 Hz, half of 5′-H_2), 4.34 (1H, ddd, *J* = 4.9, 6.1, and 8.6 Hz, 4′-H), 4.62 (1H, s, 6-H); MS *m/z*, calcd for $C_{13}H_{22}O_5$ (M^+) 258.1466, found 258.1465.

(2*R*,3*S*,4*R*,5*R*,6*R*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3,4,5,6-tetrahydro-4,5-dimethyl-2*H*-pyran-3,4,5-triol (14). A solution of α-alcohol **12** (835 mg, 3.24 mmol) and osmium tetraoxide (1.23 g, 4.84 mmol) in ether (45 mL) and pyridine (1.05 mL, 13 mmol) was stirred at room temperature for 12 h. After removal of the solvent, the residue was dissolved in pyridine (60 mL). To this solution was added a solution of sodium hydrogen sulfite (4.4 g, 42.3 mmol) in water (45 mL), and the resulting mixture was stirred for 4 h at ambient temperature. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with ethyl acetate afforded triol **14** (903 mg, 96%) as colorless needles: mp 112 °C (hexane); $[\alpha]^{25}_D$ −69.52° (*c* = 1.22, $CHCl_3$); IR (cm^{-1}) 3550 (OH); ^{1}H-NMR δ 1.22 and 1.30 (each 3H, each s, 4-Me and 5-Me), 1.37 (3H, s, CMe), 1.47 (3H, s, CMe), 3.10 (3H, br s, 3 × OH), 3.36 (3H, s, OMe), 3.42 (1H, dd, *J* = 6.7 and 9.8 Hz, 2-H), 3.92 (1H, d, *J* = 9.8 Hz, 3-H), 4.01 (1H, dd, *J* = 4.9 and 8.5 Hz, half of 5′-H_2), 4.14 (1H, dd, *J* = 6.1, and 8.5 Hz, half of 5′-H_2), 4.31 (1H, ddd, *J* = 4.9, 6.1, and 6.7 Hz, 4′-H), 4.41 (1H, s, 6-H); MS *m/z* calcd for $C_{12}H_{21}O_7$ (M^+ −15) 277.1286, found 277.1280. Anal. Calcd for $C_{13}H_{24}O_7$: C; 53.41, H; 8.28. Found: C; 53.37, H; 8.56.

(2*S*,3*S*,4*R*,5*R*,6*R*)-3-(Mesyloxy)-6-methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3,4,5-tetrahydro-4,5-dimethyl-6*H*-pyran-4,5-diol (15). To a stirred solution of triol **14** (900 mg, 3.08 mmol) in dichloromethane (9 mL) containing triethylamine (0.86 mL, 6.15 mmol) was added mesyl chloride (0.36 mL, 4.65 mmol) at −20 °C, and the mixture was stirred for 30 min at the same temperature. The solution was treated with saturated ammonium chloride solution and extracted with dichloromethane. The organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (1:1) afforded mesylate **15** (1.08 g, 94%) as a colorless oil: $[\alpha]^{25}_D$ −185.61° (*c* = 1.32, $CHCl_3$); IR (cm^{-1}) 3500 (OH); ^{1}H-NMR δ 1.26 and 1.33 (each 3H, each s, 4-Me and 5-Me), 1.36 (3H, s, CMe), 1.45 (3H, s, CMe), 2.62 and 3.05 (each 1H, br, s, 2 × OH), 3.19 (3H, s, OSO_2Me), 3.39 (3H, s, OMe), 3.84 (1H, dd, *J* = 3.7 and 10.4 Hz, 2-H), 4.06 (1H, dd, *J* = 6.1 and 8.6 Hz, half of 5′-H_2), 4.13 (1H, dd, *J* = 6.7 and 8.6 Hz, half of 5′-H_2), 4.41 (1H, ddd, *J* = 3.7, 6.1, and 6.7 Hz, 4′-H), 4.48 (1H, s, 6-H), 4.66 (1H, d, *J* = 10.4 Hz, 3-H). Anal. Calcd for $C_{14}H_{26}O_9S$: C; 45.39, H; 7.08. Found: C; 44.91, H; 7.26.

(2*S*,3*R*,4*R*,5*R*,6*R*)-6-Methoxy-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3,4,5-tetrahydro-4,5-dimethyl-3,4-epoxy-6*H*-pyran-5-ol 16. A solution of sodium methoxide (1.5 mL, 3.5 mmol/L in MeOH, 5.22 mmol) was added to a solution of mesylate **15** (97 mg, 0.26 mmol) in MeOH (1 mL) at 0 °C, and the mixture was stirred at the same temperature for 20 min. The solution was diluted with water and extracted with ethyl acetate. The extract was washed with saturated ammonium chloride solution and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded epoxide **16** (71 mg, 99%) as a colorless oil: $[\alpha]^{25}_D$ −55.5° (*c* = 1.98, $CHCl_3$); IR (cm^{-1}) 3550 (OH); ^{1}H-NMR δ 1.27 and 1.41 (each 3H, each s, 4-Me and 5-Me), 1.38 (3H, s, CMe), 1.46 (3H, s, CMe), 2.91 (1H, br s, OH), 3.31 (1H, d, *J* = 1.2 Hz, 3-H), 3.37 (3H, s, OMe), 3.75 (1H, br d, *J* = 8.5 Hz, 2-H), 3.97 (1H, dd, *J* = 4.9 and 8.6 Hz, half of 5′-H_2), 4.13 (1H, dd, *J* = 6.1 and 8.6 Hz, half of 5′-H_2), 4.15 (1H, s, 6-H), 4.21 (1H, ddd, *J* = 4.9, 6.1, and 8.5 Hz, 4′-H); MS *m/z* calcd for $C_{12}H_{19}O_6$ (M^+ − 15) 259.1180, found 259.1179. Anal. Calcd for $C_{13}H_{22}O_6$: C; 56.92, H; 8.08. Found: C; 56.83, H; 8.34.

(2*R*,3*S*,4*R*,5*S*,6*R*)-6-Methoxy-2-[(1*S*)-1-acetoxy-2-*tert*-butoxyethyl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-2*H*-pyran-4,5-diol (18). To a stirred solution of trimethylaluminum (0.99 mL, 0.99 M/L in hexane, 1 mmol) was added dropwise a solution of epoxide **16** (55 mg, 0.2 mmol) in dry dichloromethane (0.5 mL) at 0 °C, and the reaction mixture was stirred at 60 °C for 2 h. The mixture was diluted with dichloromethane (5 mL), sodium fluoride (0.21 g, 5 mmol) was added, and stirring was continued at ambient temperature for 30 min. After insoluble material was filtered off through a Celite pad, the filtrate was concentrated to afford the crude alcohol **17**, which without purification was acetylated as follows. A solution of alcohol **17** in acetic anhydride (19 μL, 0.2 mmol), pyridine (16 μL, 0.2 mmol), and dry dichloromethane (0.5 mL) containing a catalytic amount of 4-(dimethylamino)pyridine was stirred at 0 °C for 30 min. The solution was diluted with water and extracted with ethyl acetate. The extract was washed with saturated ammonium chloride solution and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded acetate **18** (17 mg, 24%) as a colorless oil: $[\alpha]^{25}_D$ −42.02° (*c* = 0.296, $CHCl_3$); IR (cm^{-1}) 3400 (OH), 1720 (CO); ^{1}H-NMR δ 0.99 (3H, d, *J* = 6.7 Hz, CH*Me*), 1.19 (9H, s, CMe_3), 1.12 and 1.21 (each 3H, each s, 4-Me and 5-Me), 2.08 (3H, s, OAc), 2.07 (1H, dq, J = 6.7 and 11.6 Hz, 3-H), 2.26 and 2.47 (2H, br s, 2 × OH), 3.34 (3H, s, OMe), 3.54 (1H, dd, *J* = 6.7 and 9.7 Hz, half of 2′-H_2), 3.61 (1H, dd, *J*

= 1.8 and 11.6 Hz, 2-H), 3.70 (1H, dd, J = 6.1 and 9.7 Hz, half of 2′-H_2), 4.49 (1H, s, 6-H), 5.11 (1H, ddd, J = 1.8, 6.1, and 6.7 Hz, 1′-H); FABMS m/z 313 (M^+). Anal. Calcd for $C_{17}H_{32}O_7 \cdot 0.5H_2O$: C 57.12; H; 9.31. Found: C; 57.29, H; 9.41.

(2*S*,6*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dimethyl-6*H*-pyran-3(2H)-one (19) and (2*S*,6*R*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-4,5-dimethyl-6*H*-pyran-3(2*H*)-one (20). A mixture of lactol **9** (1 g, 4.13 mmol), silver(I) oxide (6.7 g, 28.9 mmol), *tert*-butyldimethylchlorosilane (1.87 g), and DMF (15 mL) was stirred at −30 °C for 3 h. After the insoluble material was filtered off through a Celite pad, the filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (9:1) afforded α-silyl ether **19** (1.01 g, 68%) as a colorless oil: $[\alpha]^{25}_D$ +24.75° (c = 1.02, $CHCl_3$); IR (cm^{-1}) 1670 (CO); ^{1}H-NMR δ 0.19 (3H, s, SiMe), 0.20 (3H, s, SiMe), 0.92 (9H, s, CMe_3), 1.37 (3H, s, CMe), 1.43 (3H, s, CMe), 1.76 and 1.90 (each 3H, each s, 4-Me and 5-Me), 3.93 and 3.99 (each 1H, each dd, J = 6.7 and 8.5 Hz, 5′-H_2), 4.67 (1H, d, J = 3.1 Hz, 2-H), 4.74 (1H, dt, J = 3.1 and 6.7 Hz, 4′-H), 5.38 (1H, s, 6-H); MS m/z calcd for $C_{18}H_{32}O_5Si$ (M^+) 356.2017, found 356.2014. Anal. Calcd for $C_{18}H_{32}O_5Si$: C, 60.64, H; 9.05. Found: C; 60.84, H; 9.26. Further elution with the same solvent system afforded β-silyl ether **20** (360 mg, 25%) as a colorless oil: $[\alpha]^{25}_D$ +19.20° (c = 1.21, $CHCl_3$); IR (cm^{-1}) 1690 (CO); ^{1}H-NMR δ 0.20 (6H, s, $SiMe_2$), 0.93 (9H, s, CMe_3), 1.38 (3H, s, CMe), 1.41 (3H, s, CMe), 1.78 and 1.91 (each 3H, each s, 4-Me and 5-Me), 3.94 (1H, dd, J = 7.3 and 8.5 Hz, half of 5′-H_2), 4.24 (1H, dd, J = 6.1 and 8.5 Hz, half of 5′-H_2), 4.39 (1H, d, J = 6.1 Hz, 2-H), 4.50 (1H, dt, J = 6.1 and 7.3 Hz, 4′-H), 5.41 (1H, s, 6-H); MS m/z calcd for $C_{18}H_{32}O_5Si$ (M^+) 356.2017, found 356.2014. Anal. Calcd for $C_{18}H_{32}O_5Si$: C; 60.64, H; 9.05. Found: C; 60.79, H; 9.29.

Desilylation of β-Silyl Ether 20. A solution of β-silyl ether **20** (190 mg, 0.53 mmol) and tetrabutylammonium fluoride (0.54 mL, 1 M THF solution, 0.54 mmol) in THF (5 mL) was stirred at 0 °C for 30 min. The solution was then treated with saturated ammonium chloride solution and extracted with ethyl acetate. The organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded lactol **9** (127 mg, 98%) as a colorless oil, which was identical with the authentic specimen.

(2*R*,6*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydro-4,5-dimethyl-3-methylene-6*H*-pyran (21). To a suspension of methyltriphenylphosphonium bromide (4.91 g, 13.8 mmol) in THF (15 mL) was added potassium *tert*-butoxide (1.51 g, 13.5 mmol) at ambient temperature under argon, and the resulting yellow solution was heated at 70 °C for 30 min. A solution of ketone **19** (980 mg, 2.75 mmol) in THF (10 mL) was added to this solution and the mixture was further heated at the same temperature for 30 min. After cooled to room temperature, this solution was treated with saturated ammonium chloride solution and extracted with ether. The ethereal layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–benzene–ether (38:1:1) afforded diene **21** (667 mg, 68%) as a colorless oil: $[\alpha]^{25}_D$ +67.25° (c = 2.19, $CHCl_3$); 1H-NMR δ 0.08 (3H, s, SiMe), 0.10 (3H, s, SiMe), 0.85 (9H, s, CMe_3), 1.33 (3H, s, CMe), 1.34 (3H, s, CMe), 1.67 and 1.74 (each 3H, each s, 4-Me, and 5-Me), 3.88 (1H, dd, J = 7.3 and 8.5 Hz, half of 5′-H_2) 4.03 (1H, dd, J = 6.1 and 8.5 Hz, half of 5′-H_2), 4.27 (1H, dt, J = 6.1 and 7.3 Hz, 4′-H), 4.42 (1H, d, J = 6.1 Hz, 2-H), 5.05 (1H, s, 6-H), 5.05 and 5.18 (2H, each br s, $CHCH_2$); MS m/z calcd for $C_{19}H_{34}O_4Si$ (M^+) 354.2227, found 354.2234. Anal. Calcd for $C_{19}H_{34}O_4Si$: C; 64.42, H; 9.97. Found: C; 64.36, H; 9.67.

Catalytic Hydrogenation of Diene 21. General Procedure. A solution of diene **21** (10 mg, 0.028 mmol) in an appropriate solvent (0.5 mL) containing a catalyst (3 mg) was stirred at ambient temperature under an atmospheric pressure of hydrogen. The reaction was performed under the condition described in Table I. An insoluble material was filtered off. The filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel (Fuji-Davison BW-300 X). Elution with hexane–ether (10:1) afforded **(2*R*,3*R*,6*S*)-6-[(*tert*-butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydro-3,4,5-trimethyl-6*H*-pyran (22)** as a colorless oil: $[\alpha]^{25}_D$ +8.45° (c = 1.67, benzene); ^{1}H-NMR δ 0.14 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.92 (9H, s, CMe_3), 1.09 (3H, d, J = 6.7 Hz, CH*Me*), 1.38 and 1.42 (each 3H, each s, 4-Me and 5-Me), 1.63 (6H, s, CMe_2), 1.99 (1H, dt, J = 6.7 and 9.2 Hz, 3-H), 3.74 (1H, dd, J = 6.1 and 9.2 Hz, 2-H), 3.94 (1H, dd, J = 7.3 and 7.9 Hz, half of 5′-H_2), 4.05 (1H, dd, J = 6.1 and 7.9 Hz, half of 5′-H_2), 4.16 (1H, dt, J = 6.1 and 7.3 Hz, 4′-H), 5.02 (1H, s, 6-H); ^{1}H-NMR (benzene-d_6) δ 0.16 (3H, s, SiMe), 0.26 (3H, s, SiMe), 0.98 (3H, d, J = 6.7 Hz, CH*Me*), 0.10 (9H, s, CMe_3), 1.39 (3H, s, CMe), 1.50 (3H, s, CMe), 1.43 and 1.59 (each 3H, each s, 4-Me and 5-Me), 1.92 (1H, m, 3-H), 3.96 (1H, dd, J = 4.9 and 9.1 Hz, 2-H), 4.05–4.20 (3H, m, 4′-H and 5′-H_2), 5.09 (1H, s, 6-H); MS m/z calcd for $C_{19}H_{36}O_4Si$ (M^+) 356.2383, found 356.2389. Anal. Calcd for $C_{19}H_{36}O_4Si$: C; 64.01, H; 10.18. Found: C; 64.11, H; 10.38; **(2*R*,3*S*,6*S*)-6-[(*tert*-butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3-dihydro-3,4,5-trimethyl-6*H*-pyran (23)** as a colorless oil: $[\alpha]^{25}_D$ −33.3° (c = 0.01, benzene; ^{1}H-NMR (benzene-d_6) δ 0.10 (3H, s, SiMe), 0.17 (3H, s, SiMe), 0.98 (9H, s, CMe_3), 1.13 (3H, d, J = 6.7 Hz, CH*Me*), 1.33 (3H, s, CMe), 1.39 (3H, s, CMe), 1.50 and 1.55 (each 3H, each s, 4-Me and 5-Me), 2.12 (1H, br q, J = 6.7 Hz, 3-H), 4.12–4.28 (4H, m, 2H and 4′-H and 5′-H_2), 5.04 (1H, s, 6-H); MS m/z calcd for $C_{19}H_{36}O_4Si$ (M^+) 356.2383, found 356.2374; and **(2*R*,3*R*,4*S*,5*S*,6*S*)-6-[(*tert*-butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-2,3,4,5-tetrahydro-3,4,5-trimethyl-6*H*-pyran (24)**: $[\alpha]^{25}_D$ −132.7° (c = 0.02, benzene); ^{1}H-NMR (benzene-d_6) δ 0.07 (3H, s, SiMe), 0.21 (3H, s, SiMe), 0.84, 0.89, and 1.00 (each 3H, each d, J = 7.3 Hz, 3-Me and 4-Me and 5-Me), 0.98 (9H, s, CMe_3), 1.12–1.65 (3H, m, 3-H, 4-H, and 5-H), 1.42 (3H, s, CMe), 1.51 (3H, s, CMe), 3.87–4.18 (4-H, m, 2-H, 4′-H, and 5′-H_2), 4.88 (1H, d, J = 3.0 Hz, 6-H); FABMS m/z 343 (M^+ − 16), in a ratio described in Table I. These compounds **22–24** tend to decompose on exposure to acid.

Diimide Reduction of Diene 21. (a) To a stirred solution of diene **21** (40 mg, 0.13 mmol), hydrazine monohydrate (0.9 mL, 18.6 mmol), acetic acid (10 μL, 0.18 mmol), and saturated aqueous copper(II) sulfate solution (10 μL) in MeOH (3.4 mL) was added dropwise a solution of sodium periodate (0.36 g, 1.68 mmol) in H_2O (2 mL) at 0 °C, and stirring was continued at ambient temperature for 7 days. The reaction mixture was poured into water and the product was extracted with ether. The organic layer was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel (Fuji-Davison BW-300 X). Elution with hexane–ether (10:1) afforded the α-methyl compound **22** (10 mg, 25%) and the β-methyl compound **23** (5 mg, 12%), respectively. (b) To a stirred solution of hydrazine monohydrate (0.8 mL, 16.5 mmol) in EtOH (2 mL) was added dropwise 35% hydrogen peroxide (1 mL, 8.82 mmol) at 0 °C, and the reaction mixture was stirred at the same temperature for 10 min. A solution of diene **21** (429 mg, 1.69 mmol) in EtOH (6 mL) was added to this mixture at 0 °C and stirring was continued at ambient temperature for 3 days. The same workup as above was carried out to afford the α-methyl compound **22** (247 mg, 58%) and the β-methyl compound **23** (125 mg, 29%), respectively.

Hydrogenation of Diene 21 with Wilkinson Catalyst. To a stirred solution of tris(triphenylphosphine)rhodium(I) chloride (Wilkinson catalyst) (100 mg, 0.11 mmol) in benzene (10 mL) was added a solution of diene **21** (950 mg, 2.68 mmol) in benzene (5 mL) at ambient temperature under an atmospheric pressure of hydrogen and stirring was continued for 12 h. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel (Fuji-Davison MB-5D). Elution with hexane–benzene–ether (38:1:1) afforded the α-methyl compound **22** (909 mg, 95%) and the β-methyl compound **23** (30 mg, 3%), respectively.

(2*R*,3*S*,4*R*,5*R*,6*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4*S*)-2,2-dimethyl-1,3-dioxolan-4-yl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-2*H*-pyran-4,5-diol (25). To a solution of olefin **22** (625 mg, 1.76 mmol) in ether (25 mL) was added pyridine (0.57 mL, 7.04 mmol) and osmium tetraoxide (670 mg, 2.63 mmol) at 0 °C and the resulting mixture was further stirred at room temperature for 12 h. After removal of the solvent, the residue was dissolved in pyridine (30 mL). To this solution was added a solution of

sodium hydrogen sulfite (2.38 g, 22.9 mmol) in water (25 mL), and the resulting mixture was stirred for 4 h at ambient temperature. Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded diol **25** (662 mg, 97%) as colorless needles: mp 104–106 °C (hexane); $[\alpha]^{25}_D$ −71.55° (*c* = 1.14, $CHCl_3$); IR (cm^{-1}) 3350 (OH); ^{1}H-NMR δ 0.12 (3H, s, SiMe), 0.16 (3H, s, SiMe), 0.92 (9H, s, CMe_3), 0.98 (3H, d, *J* = 6.7 Hz, CH*Me*), 1.19 and 1.20 (each 3H, each s, 4-Me and 5-Me), 1.36 (3H, s, CMe), 1.39 (3H, s, CMe), 1.75 (1H, dq, *J* = 6.7 and 10.9 Hz, 3-H), 2.31 and 2.45 (each 1H, each br s, OH), 3.69 (1H, dd, *J* = 4.9 and 10.9 Hz, 2-H), 3.98 (2H, ddd, *J* = 6.7, 7.1, and 7.9 Hz, 5′-H_2), 4.12–4.19 (1H, m, 4′-H), 4.89 (1H, s, 6-H); MS *m/z* calcd for $C_{18}H_{35}O_6Si$ (M^+ − 15) 375.2201, found 375.2195. Anal. Calcd for $C_{19}H_{38}O_6Si$: C; 58.52, H; 10.05. Found: C 58.43, H; 9.81.

(2*R*,3*S*,4*R*,5*R*,6*S*)-6-[(*tert*-Butyldimethylsilyl)oxy]-2-[(4*S*)-1,3-dioxolan-4-yl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-4,5-(methylenedioxy)-2*H*-pyran (26). A solution of diol **25** (660 mg, 1.69 mmol) in dichloromethane (7 mL) was added to a suspension of phosphorus pentoxide (480 mg, 3.38 mmol) and dimethoxymethane (0.3 mL, 3.38 mmol) in dichloromethane (5 mL) at 0 °C. The resulting mixture was stirred at the same temperature for 30 min and neutralized with 2 N NaOH solution and extracted with ethyl acetate. The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (9:1) afforded the bis(methylenedioxy) derivative **26** (605 mg, 96%) as a colorless oil: $[\alpha]^{25}_D$ −51.49° (*c* = 1.29, $CHCl_3$); ^{1}H-NMR δ 0.12 (3H, s, SiMe), 0.15 (3H, s, SiMe), 0.92 (9H, s, CMe_3), 0.99 (3H, d, *J* = 7.3 Hz, CH*Me*), 1.15 and 1.12 (each 3H, each s, 4-Me and 5-Me), 1.88 (1H, dq, *J* = 7.3 and 10.4 Hz, 3-H), 3.76 (1H, dd, *J* = 4.9 and 10.4 Hz, 2-H), 3.88–4.10 (3H, m, 4′-H and 5′-H_2), 4.94, 5.04, and 5.13 (5H, each s, 6-H and 2 × OCH_2O). Anal. Calcd for $C_{18}H_{34}O_6Si$: C; 57.83, H; 9.37. Found: C; 57.72, H; 9.15.

(2*R*,3*S*,4*R*,5*R*)-2-[(4*S*)-1,3-Dioxolan-4-yl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-4,5-(methylenedioxy)-2*H*-pyran-6-ol (27). To a stirred solution of silyl ether **26** (575 mg, 1.54 mmol) in THF (6 mL) was added tetrabutylammonium fluoride (1.54 mL, 1 M THF solution, 1.54 mmol) at 0 °C, and the mixture was further stirred at the same temperature for 1 h and treated with saturated ammonium chloride solution. After removal of the solvent, the residue was extracted with ethyl acetate and the extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:2) afforded lactol **27** (400 mg, 100%) as a colorless oil: IR (cm^{-1}) 3450 (OH); ^{1}H-NMR δ 0.98 (3H, d, *J* = 7.3 Hz, CH*Me*), 1.20 and 1.23 (each 3H, each s, 4-Me and 5-Me), 1.86 (1H, dq, *J* = 7.3 and 11.0 Hz, 3-H), 3.88–4.16 (5H, m, 2-H, 4′-H, 5′-H_2, and OH), 4.89, 5.01, 5.04, and 5.05 (each 1H, each s, 2 × OCH_2O), 5.22 (1H, s, 6-H); FABMS (negative) *m/z* $C_{12}H_{19}O_6$ (M^+ − 1) 259.

(2*R*,3*S*,4*R*,5*R*)-2-[(4*S*)-1,3-Dioxolan-4-yl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-4,5-(methylenedioxy)-2*H*-pyran-6-one (28). To a suspension of pyridinium chlorochromate (2.58 g, 12.0 mmol), sodium acetate (985 mg, 12.0 mmol), and molecular sieves 4A in dichloromethane (5 mL) was added a solution of lactol **27** (430 mg, 2.40 mmol) in dichloromethane (4 mL) at 0 °C, and the resulting mixture was stirred for 4 h. An excess amount of ether was added to the mixture and the insoluble material was filtered off. The filtrate was concentrated to leave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (3:1) afforded lactone **28** (354 mg, 83%) as a colorless oil: $[\alpha]^{25}_D$ −67.47° (*c* = 0.95, $CHCl_3$); IR (cm^{-1}) 1740 (CO); ^{1}H-NMR δ 1.18 (3H, d, *J* = 6.7 Hz, CH*Me*), 1.26 and 1.53 (each 3H, each s, 4-Me and 5-Me), 2.02 (1H, dq, *J* = 6.7 and 9.2 Hz, 3-H), 3.94 (1H, dd, *J* = 6.7 and 9.2 Hz, 2-H), 4.03-4.18 (3H, m, 4′-H and 5′-H_2), 4.83, 4.93, 5.04, and 5.06 (each 1H, each s, 2 × OCH_2O); MS *m/z* calcd for $C_{12}H_{18}O_6$ (M^+) 258.1103, found 258.1111. Anal. Calcd for $C_{12}H_{18}O_6$: C; 55.58, H; 7.16. Found: C; 55.80, H; 7.03.

(2*R*,3*S*,4*R*,5*R*)-2-[(1*S*)-(2-Acetoxy-1-[(acetoxymethyl)ethyl]-3,4,5,6-tetrahydro-3,4,5-trimethyl-4,5-(methylenedioxy)-2*H*-pyran-6-one (29). A solution of lactone **28** (220 mg, 0.853 mmol) in acetic anhydride (0.56 mL, 5.94 mmol), acetic acid (0.5 mL, 8.73 mmol), and concd sulfuric acid (8 mL, 0.15 mmol) was stirred at 0 °C for 30 min. The mixture was poured into ice–water, neutralized with saturated sodium hydrogen carbonate solution, and extracted with ethyl acetate. The extract was washed with brine and dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with hexane–ethyl acetate (2:1) afforded diacetate **29** (238 mg, 78%) as a colorless oil: $[\alpha]^{25}_D$ −50.49° (*c* = 1.35, $CHCl_3$); IR (cm^{-1}) 1740 (CO); ^{1}H-NMR δ 1.16 (3H, d, *J* = 6.7 Hz, CH*Me*), 1.25 and 1.51 (each 3H, each s, 4-Me and 5-Me), 2.10 and 2.11 (each 3H, each s, 2 × OAc), 2.07–2.22 (1H, m, 3-H), 4.15–4.25 (3H, m, 1′-H and 2′-H_2), 4.40 (1H, dd, *J* = 3.0 and 11.6 Hz, 2-H), 4.84 and 5.05 (each 1H, each s, OCH_2O), 5.36 (2H, dd, *J* = 6.7 and 8.5 Hz, O*CH*$_2$OAc); MS *m/z* calcd for $C_{13}H_{19}O_7$ (M^+ − 73) 287.1131, found 287.1132. Anal. Calcd for $C_{16}H_{24}O_9$: C; 53.33, H; 6.71. Found: C; 53.31, H; 6.99.

(2*R*,3*R*,4*R*)-2,3,4-Trimethyl-2,3-(methylenedioxy)pentanedioic Acid (4). A solution of sodium methoxide (0.3 mL, 5 M in MeOH, 1.56 mmol) was added to the solution of lactone **29** (90 mg, 0.25 mmol) in MeOH (1 mL) at 0 °C, and the mixture was stirred at the same temperature for 30 min. After removal of the solvent at 20 °C, the residue was subjected to column chromatography on silica gel. Elution with methanol afforded the triol as a colorless solid, which, without further purification, was taken up into a mixture of CCl_4 (0.5 mL), acetonitrile (0.5 mL), and water (0.75 mL). To this solution was added sodium periodate (320 mg, 1.5 mmol) and ruthenium chloride (5 mg, 0.025 mmol), and the resulting mixture was stirred at ambient temperature for 2 h. After acidified with 6 N HCl to pH 1, the mixture was extracted twice with chloroform and three times with ethyl acetate. The combined extracts were dried (Na_2SO_4). Evaporation of the solvent gave a residue, which was subjected to column chromatography on silica gel. Elution with ether afforded the methylenedioxy derivative **4**, which was recrystallized from benzene to give the pure compound (42 mg, 77%) as colorless crystals: mp 127–128 °C (benzene) {lit.[4] mp 127–129 °C (benzene)}; $[\alpha]^{25}_D$ +41.33° (*c* = 0.54, $CHCl_3$) {lit.,[4] $[\alpha]^{16}_D$ +41.7° (*c* = 0.57, $CHCl_3$)}; IR (cm^{-1}) 3050 (OH), 1730 (CO); ^{1}H-NMR δ 1.37 (3H, d, *J* = 7.3 Hz, CH*Me*), 1.50 and 1.53 (each 3H, each s, 4-Me and 5-Me), 3.14 (1H, q, *J* = 7.3 Hz, 4-H), 5.07 and 5.12 (each 1H, each s, OCH_2O) 9.90 (2H, br s, 2 × COOH).

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