Relative and Absolute Configuration of the 3,12-Dihydroxypalmitic Acids☆

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The relative and absolute configuration of (+)-3,12-dihydroxypalmitic acid, a constituent of the *Ipomea operculata* M. resin, has been determined by synthesis. Dimethyl L-malate was converted via (*S*)-(+)-**1** into the oxirane (*S*)-(−)-**2**. Reaction of (−)-**2** with the Grignard reagent of 8-benzyloxybromooctane provided (*S*)-(+)-**3** in 84% yield, and this was converted into the aldehyde (*S*)-(−)-**6** via (*S*)-(−)-**4** and (*S*)-(−)-**5**. Reaction with the lithium enolate of methyl acetate gave **7** and **8**, which could be converted via **9** and **10**, **11** and **12**, **13** and **14** into the lactones (4*S*,13*S*)-(+)-**15** and (4*R*,13*S*)-(+)-**16** and finally into the methyl esters (3*S*,12*S*)-(+)-**17** and (3*R*,12*S*)-(+)-**18** and acids (−)-**19** and (+)-**20**. The *erythro* configuration of (+)-**17** was established by a stereoselective synthesis starting from (*S*)-(−)-**2** via (*S*)-(+)-**21**, (+)-**22**, (+)-**23**, the Grignard reagent of (+)-**24** and (*R*)-(+)-2-(2-benzyloxyethyl)oxirane to give (3*S*,12*S*)-(−)-**25**, (−)-**26**, (+)-**27** and (+)-**28**, which could be oxidized to the diacetoxy acid (3*S*,12*S*)-(+)-**29**. Saponification and esterification gave (3*S*,12*S*)-(−)-**19** and (3*S*,12*S*)-(+)-**17**, with properties identical to those of (+)-**17** obtained from the resin glycoside.

The structure of operculinic acid, the main glycosidic acid of the ether-insoluble resin of *Ipomea operculata* Martin, was elucidated mainly by classical degradation work as that of a glucorhamnohexasaccharide of 3,12-dihydroxypalmitic acid. Partial solvolysis of the permethylated compound led to di- and trisaccharide derivatives and their structures could be determined. The accumulated results allowed Wagner and Kazmaier[1,2], and later on Graf and Bühle[3,4], to propose the structure of it to be a 12-[(*O*-6-deoxy-α-L-mannopyranosyl-(1→6)-*O*-[α-D-glucopyranosyl-(1→4))]-*O*-α-D-glucopyranosyl-(1→4)-*O*-6-deoxy-α-L-mannopyranosyl-(1→2)-*O*-[β-D-glucopyranosyl-(1→3)]-β-D-glucopyranosyl)oxy]-3-hydroxyhexadecanoic acid. Earlier investigations by Votocek and Prelog[5] had shown that the aglycone of operculinic acid (rhamnoconvolvulinic acid) is 3,12-dihydroxyhexadecanoic acid. But the relative and absolute configuration of this integral part of the naturally occurring resin glycoside is still unknown. Four structural possibilities have to be considered: One with *erythro* configuration of the hydroxy groups with either (3*S*,12*S*) or (3*R*,12*R*) chirality, and one with *threo* configuration and with (3*S*,12*R*) or (3*R*,12*S*) chirality. A mixture of these four compounds with the common constitution of a 3,12-dihydroxyhexadecanoic acid was prepared[3] and found to display properties very similar to those of the acid[5] isolated from the hydrolysis products of the natural compound, despite the fact that the synthetic product was a mixture of two racemic substances[6]. To determine the correct structure of the aglycone of operculinic acid we synthesized stereoselectively the 3,12-dihydroxyhexadecanoic acids with (3*S*,12*S*) and with (3*R*,12*S*) configuration[7]. The starting material for the synthesis was (*S*)-(−)-2-butyloxirane [(−)-**2**], which is easily available in a few steps[8] from L-dimethyl malate via the acetal (*S*)-(+)-**1**. By reaction of (−)-**2** with the Grignard reagent prepared from 8-benzyloxy-1-bromooctane[9] in the presence of 1,5-cyclooctadienecopper(I) chloride as catalyst[10], (*S*)-(+)-**3** was formed in 84% yield. Acetylation of the hydroxy group in (+)-**3** gave (*S*)-(−)-**4** and hydrogenolysis gave (*S*)-(−)-**5**, which was oxidized according to the Swern procedure to the aldehyde (*S*)-(−)-**6** in 81% overall yield. Reaction of (−)-**6** with the lithium enolate of methyl acetate afforded a mixture of (3*S*,12*S*)-**7** and (3*R*,12*S*)-**8**. Treatment of this mixture with *tert*-butylchlorodiphenylsilane and imidazole gave the corresponding silyl ethers (3*S*,12*S*)-**9** and (3*R*,12*S*)-**10**. Alkaline hydrolysis of these ethers furnished the hexadecanoic acids (3*S*,12*S*)-**11** and (3*R*,12*S*)-**12** with the 3-hydroxy group protected as the silyl ether and with a free 12-hydroxy group. The two compounds were isolated as a mixture after each reaction step. They could not be separated by chromatography and did not show different NMR spectra. This situation changed completely when a mixture of **11** and **12** was converted into the two macrocyclic lactones (4*S*,13*S*)-**13** and (4*R*,13*S*)-**14**. The cyclization[11] was achieved via the corresponding *S*-(2-pyridyl)carbothioates formed in situ and subsequently activated with silver perchlorate. The lactones (+)-**13** and (+)-**14** were formed in 82% yield, could easily be separated by chromatography, and showed different ^{1}H-NMR spectra. Desilylation of the individual lactones (+)-**13** and (+)-**14** with Bu_4NF gave the hydroxy lactones (4*S*,13*S*)-(+)-**15** and (4*R*,13*S*)-(+)-**16** with different R_f values and different ^{1}H-NMR and IR spectra. Heating of the lactones (+)-**15** and (+)-**16** individually with methanol and sodium methoxide as a catalyst furnished the methyl esters (3*S*,12*S*)-(+)-**17** with m.p. 79.7−80.2°C and (3*R*,12*S*)-(+)-**18** with m.p. 62.2−62.7°C. The chromatographic and spectral properties of the diastereoisomeric compounds (+)-**17** and (+)-**18** are practically indistinguishable. Saponification

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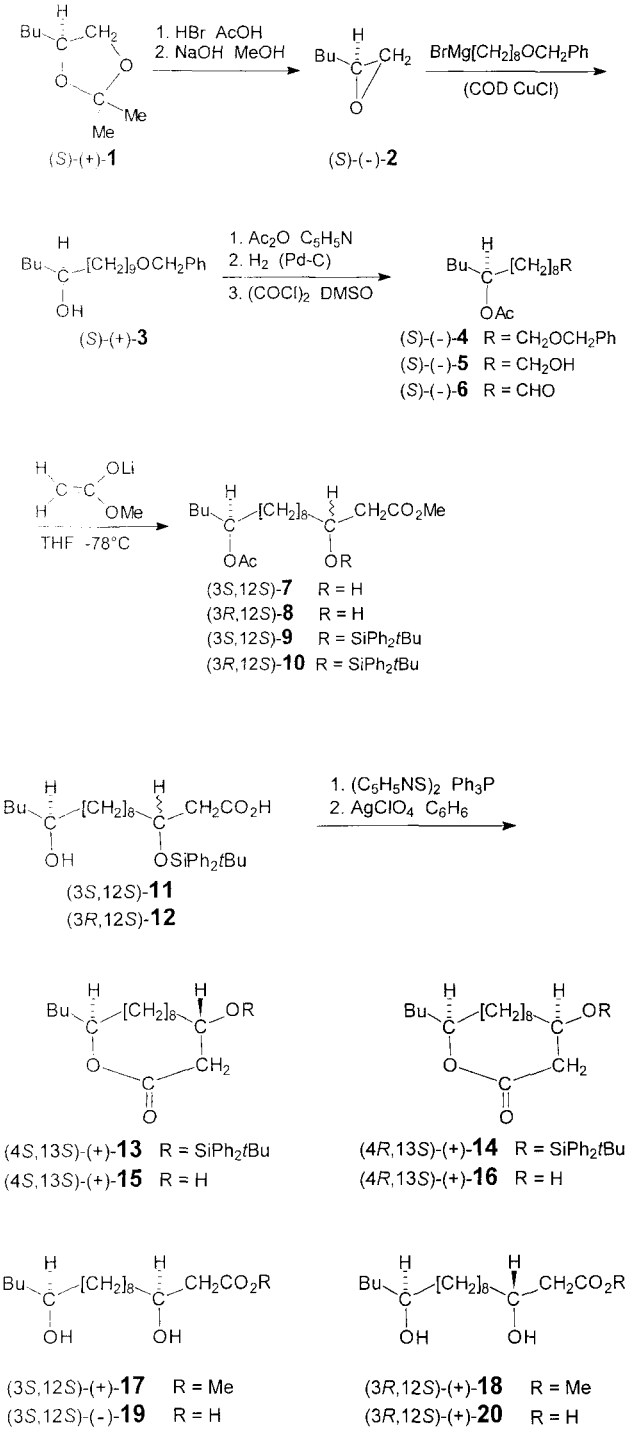
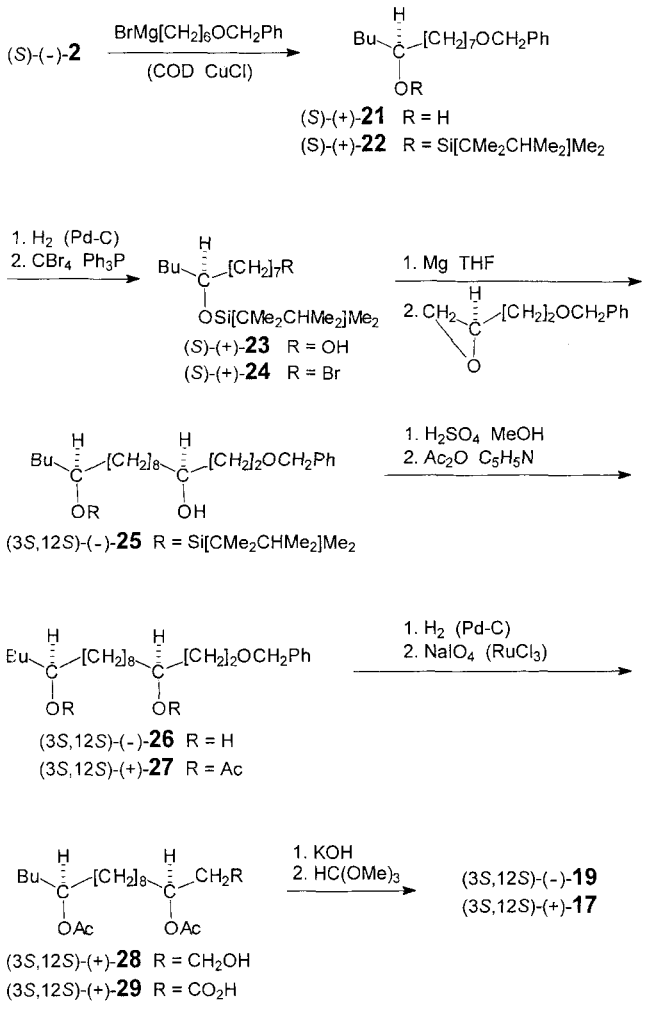
of (+)-**17** and (+)-**18** led to the 3,12-dihydroxyhexadecanoic acids (3*S*,12*S*)-(−)-**19** and (3*R*,12*S*)-(+)-**20**. The (3*S*,12*S*) configuration was assigned tentatively to the methyl ester (+)-**17**, derived from the less polar lactone (+)-**15**, because it shows a more positive optical rotation in methanol as solvent. Moreover, it was found that in trichloromethane as solvent (3*S*,12*S*)-**17** shows a positive optical rotation while (3*R*,12*S*)-**18** is levorotatory. The 3,12-dihydroxyhexadecanoic acid isolated from the resin of *Ipomea operculata* Martin was characterized by Votocek and Prelog[5] as its methyl ester with m.p. 80−81 °C and a small positive optical rotation. These properties are clearly identical with those of the synthesized methyl ester (3*S*,12*S*)-(+)-**17** and distinct from those of (3*R*,12*S*)-(+)-**18**. To prove the *erythro* configuration of (+)-**17** unequivocally, a selective synthesis of the (3*S*,12*S*) enantiomer was performed.

By reaction of the oxirane (*S*)-(−)-**2** with the Grignard reagent prepared from 6-benzyloxy-1-bromohexane[12] in the presence of 1,5-cyclooctadienecopper(I) chloride as catalyst[10] the alcohol (*S*)-(+)-**21** was formed in 80% yield. The hydroxy group in (+)-**21** was silylated with chlorodimethyl-*t*-hexylsilane to give (*S*)-(+)-**22**. Hydrogenolysis of the benzyl ether group in (+)-**22** produced the primary alcohol (*S*)-(+)-**23** which was converted into the primary bromide (*S*)-(+)-**24** by treatment with carbon tetrabromide and triphenylphosphane. Then (*R*)-(+)-2-(2-benzyloxyethyl)oxirane[13] was allowed to react with the Grignard reagent prepared from (*S*)-(+)-**24** to provide (3*S*,12*S*)-(−)-**25** in 88% yield. Treatment of (−)-**25** with H_2SO_4 in methanol caused cleavage of the silyl ether group, furnishing the diol (3*S*,12*S*)-(−)-**26** which was acetylated to the diacetate (3*S*,12*S*)-(+)-**27**. Hydrogenolysis of the benzyl ether group in (+)-**27** provided the primary alcohol (3*S*,12*S*)-(+)-**28**,





which was selectively oxidized with ruthenium(III) chloride and sodium periodate[14] to afford (3*S*,12*S*)-(+)-3,12-diacetoxyhexadecanoic acid [(+)-**29**] in 85% yield. Saponification of (+)-**29** provided (3*S*,12*S*)-(−)-**19**, which was transformed into methyl (3*S*,12*S*)-(+)-3,12-dihydroxyhexadecanoate [(+)-**17**] by treatment with trimethyl orthoformate. The properties of this methylester are identical with those of the methyl ester obtained by methanolysis of the resin glycoside (see Experimental and ref.[5]), thus establishing its *erythro* configuration and (3*S*,12*S*) chirality sense.

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Experimental

All solvents were distilled before use. THF was filtered through ICN Alumina B. – Column chromatography: Kieselgel 60 (from Merck). – TLC: Kieselgel 60 F_{254} glass plates (from Merck); the same solvent as for chromatography was used, and the compounds were visualized by treatment with concd. H_2SO_4 at 160°C for 5 min. – Optical rotations: Perkin-Elmer 241 polarimeter. – IR: Perkin-Elmer Paragon 1000 FT IR. – ^1H (270.17 MHz) and ^{13}C (67.94 MHz) NMR: Jeol JNM-EX 270 (δ values relative to residual solvent signal, internal standard TMS). – MS: spectrometer MAT 312 (Varian-MAT), 70 eV. – Elemental analyses: Microanalytical Laboratory of Ilse Beetz, D-96317 Kronach.

(S)-(+)-4-Butyl-2,2-dimethyl-1,3-dioxolane [(+)-**1**]: A solution of 260 ml (249 mmol) of 0.96 M methylmagnesium bromide in THF was added dropwise within 2 h under N_2 with stirring to a solution of 21.98 g (105 mmol) of (*S*)-(−)-2-(2,2-dimethyl-1,3-dioxolan-4-yl)ethyl bromide[8] in 500 ml of THF at −78°C. The resulting solution was stirred for 15 min at −78°C and then 12 ml (1.2 mmol) of a 0.1 M Li_2CuCl_4 solution in THF was added. The mixture was allowed to reach room temp. within 16 h. Then 80 ml of water was added and the solution was concentrated in vacuo. The residue was extracted twice with 450 ml of pentane/diethyl ether (1:1). The combined extracts were washed with water, dried (Na_2SO_4) and the solvent was evaporated through a Vigreux column. The residue was distilled in vacuo to give 10.68 g (64%) of (+)-**1** as a colorless liquid, b.p. 60−62°C/13 Torr [ref.[15] 62°C/15 Torr for (±)-**1**], $[\alpha]_D^{23}$ = +20.4 (*c* = 1.32, $CHCl_3$).

(S)-(−)-2-Butyloxirane [(−)-**2**]: A solution of 33% HBr in acetic acid (32 ml, 131 mmol) was added dropwise with stirring to 11.70 g (73.9 mmol) of (*S*)-(+)-**1** at 0°C. The resulting solution was stirred at room temp. for 90 min. Then it was poured into 250 ml of ice/water, 32.5 g of Na_2CO_3 was added and the resulting mixture was extracted twice with 250 ml of diethyl ether. The combined extracts were washed with 1 M Na_2CO_3, dried (Na_2SO_4), and the solvent was evaporated to give crude (*S*)-1-bromohex-2-yl acetate (18.9 g) which was used without purification for the next step. Twenty-eight milliliters (103 mmol) of 3.7 M KOH in MeOH was added dropwise with stirring at room temp. to this residue (18.9 g) in 20 ml of MeOH and the mixture was stirred for 2 h. Then 200 ml of H_2O was added and the mixture was extracted three times with 200 ml of pentane. The combined extracts were dried (Na_2SO_4), the solvent was evaporated through a Vigreux column, and the residue was distilled to give 6.17 g (83%) of (*S*)-(−)-**2** as a colorless liquid, b.p. 30−31°C/26 Torr, $[\alpha]_D^{23}$ = −9.3 (*c* = 1.29, $CHCl_3$) [ref.[16] −9.0 (*c* = 1, $CHCl_3$)]. – The IR and NMR data are identical with those reported in ref.[16].

(S)-(+)-1-Benzyloxy-10-tetradecanol [(+)-**3**]: A solution of 23.02 g (76.9 mmol) of 8-benzyloxy-1-bromooctane[9] and 0.4 ml of 1,2-dibromoethane in 200 ml of THF was added dropwise within 6 h under N_2 to a stirred suspension of 3.08 g (127 mmol) of magnesium turnings in 30 ml of boiling THF. The reaction mixture was heated at reflux for 60 min. Then the solution of the Grignard reagent was cooled to −10°C and 6.60 g (65.9 mmol) of (*S*)-(−)-**2** and 1.80 g (4.34 mmol) of 1,5-cyclooctadienecopper(I) chloride catalyst[10] were added. After stirring for 16 h at room temp. 250 ml of 0.5 N H_2SO_4 was added. THF was distilled off in vacuo and the residue was extracted twice with 500 ml of toluene/diethyl ether (1:1). The combined extracts were washed with 150 ml of 2 M $KHCO_3$, dried (Na_2SO_4), and the solvent was evaporated. The residue was chromatographed on 1000 g of silica gel (cyclohexane/AcOEt, 9:1) to yield 17.82 g (84%) of (+)-**3** as colorless crystals, R_f = 0.12, m.p. 35.0−35.8°C, $[\alpha]_D^{20}$ = +1.0 (*c* = 2.11, EtOH). – IR (CCl_4): $\tilde{\nu}$ = 3630 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 0.91 (t, *J* = 6.9 Hz, 3H, 14-H), 1.25−1.50 (21H, 2-H to 9-H, 11,12-H, OH), 1.61 (quint, *J* = 6.9 Hz, 2H, 2-H), 3.46 (t, *J* = 6.9 Hz, 2H, 1-H), 3.58 (m, 1H, 10-H), 4.50 (s, 2H, OCH_2Ph), 7.26−7.39 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = 13.8 (q, C-14), 22.5, 25.4, 25.9, 27.6, 29.2, 29.31, 29.34, 29.46, 29.49, 36.9, 37.2 (11 t, C-2 to C-9, C-11 to C-13), 70.1 (t, OCH_2Ph), 71.3 (d, C-10), 72.5 (t, C-1), 127.1, 127.2, 128.0, 138.3 (Ph). – $C_{21}H_{36}O_2$ (320.5): calcd. C 78.69, H 11.32; found C 78.62, H 11.29. – (+)-**3** was treated with (+)-MTPA to furnish the ester with a 14-Me signal at δ = 0.87 in the ^1H-NMR ($CDCl_3$) spectrum. The signal at δ = 0.81 of the diastereomeric ester could not be detected.

(S)-(+)-1-Benzyloxy-8-dodecanol [(+)-**21**]: Synthesized analogously as described above for (+)-**3** with the Grignard reagent [prepared from 7.71 g (28.5 mmol) of 6-benzyloxy-1-bromohexane[12], 1.12 g (46 mmol) of magnesium turnings in 75 ml of THF] and 2.01 g (20.0 mmol) of (*S*)-(−)-**2** in the presence of 580 mg (1.40 mmol) of 1,5-cyclooctadienecopper(I) chloride catalyst[10]. The residue (7.8 g) was chromatographed on 450 g of silica gel (cyclohexane/AcOEt, 9:1) to yield 4.65 g (80%) of (+)-**21** as colorless crystals, R_f = 0.14, m.p. 29−30°C, b.p. 131−132°C/0.001 Torr, $[\alpha]_D^{20}$ = +1.0 (*c* = 2.59, EtOH). – IR (CCl_4): $\tilde{\nu}$ = 3630, 3504 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 0.89 (t, *J* = 6.9 Hz, 3H, 12-H), 1.30−1.41 (15H, 2-H to 6-H, 10,11-H, OH), 1.50−1.70 (4H, 7,9-H), 3.44 (t, *J* = 6.6 Hz, 2H, 1-H), 3.56 (m, 1H, 8-H), 4.48 (s, 2H, OCH_2Ph), 7.23−7.33 (5H, Ph). – ^{13}C NMR($CDCl_3$): δ = 14.1 (q, C-12), 22.8, 25.6, 26.1, 27.8, 29.4, 29.6, 29.7, 37.2, 37.5 (9 t, C-2 to C-7, C-9 to C-11), 70.5 (t, OCH_2Ph), 72.0 (d, C-8), 72.9 (t, C-1), 127.5, 127.6, 128.3, 138.7 (Ph). – $C_{19}H_{32}O_2$ (292.5): calcd. C 78.03, H 11.03; found C 78.10, H 10.96. – (+)-**21** was treated with (+)-MTPA to furnish the ester with a 12-Me signal at δ = 0.87 in the ^1H-NMR ($CDCl_3$) spectrum. The signal at δ = 0.80 of the diastereomeric ester could not be detected.

(S)-(−)-1-Benzyloxytetradec-10-yl Acetate [(−)-**4**]: A mixture of 17.58 g (54.8 mmol) of (+)-**3**, 20 ml of acetic anhydride and 20 ml of pyridine was stirred at room temp. for 16 h. Toluene was added and the solvent and excess reagent were evaporated to afford 19.86 g (100%) of (−)-**4** as a pale yellow oil, R_f = 0.7 (cyclohexane/AcOEt, 4:1). An analytical sample of (−)-**4** was distilled, b.p. 142°C/0.001 Torr, $[\alpha]_D^{20}$ = −0.76 (*c* = 2.77, EtOH). – IR (CCl_4): $\tilde{\nu}$ = 1736 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.89 (t, *J* = 6.9 Hz, 3H, 14-H), 1.20−1.40 (16H, 3-H to 8-H, 12,13-H), 1.40−1.55 (4H, 9,11-H), 1.61 (quint, *J* = 6.9 Hz, 2-H), 2.04 (s, 3H, CH_3CO_2), 3.46 (t, *J* = 6.6 Hz, 2H, 1-H), 4.50 (s, 2H, OCH_2Ph), 4.85 (quint, *J* = 6.6 Hz, 1H, 10-H), 7.27−7.35 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-14), 21.3 (q, CH_3CO_2), 22.6, 25.3, 26.2, 27.5, 29.42, 29.44, 29.48, 29.50, 29.7, 33.8, 34.1 (11 t, C-2 to C-9, C-11 to C-13), 70.5 (t, OCH_2Ph), 72.8 (t, C-1), 74.4 (d, C-10), 127.4, 127.6,

128.3, 138.7 (Ph), 170.9 (s, $MeCO_2$). – $C_{23}H_{38}O_3$ (362.6): calcd. C 76.20, H 10.56; found C 76.29, H 10.61.

(S)-(+)-1-Benzyloxy-8-[dimethyl(1,1,2-trimethylpropyl)-silyloxy]dodecane [(+)-**22**]: To a solution of 5.55 ml (5.05 g, 28.3 mmol) of chlorodimethyl(1,1,2-trimethylpropyl)silane (Fluka) in 5 ml of DMF, 2.26 g (33.3 mmol) of imidazole (Fluka) and a solution of 4.11 g (14.05 mmol) of (+)-**21** in 10 ml of DMF were added. The mixture was stirred at room temp. for 16 h and then extracted twice with 250 ml of cyclohexane. The combined extracts were washed with water, dried (Na_2SO_4) and the solvent was evaporated. The residue was chromatographed on 800 g silica gel (cyclohexane/AcOEt, 19:1) to give 5.71 g (93%) of (+)-**22** as a colorless oil, R_f = 0.42. An analytical sample was distilled, b.p. 165°C/0.001 Torr, $[\alpha]_D^{20}$ = +1.6 (*c* = 2.36, EtOH). – ^{1}H NMR ($CDCl_3$): δ = 0.04 [s, 6H, $Si(CH_3)_2$], 0.80 [s, 6H, $SiC(CH_3)_2$], 0.86 [d, *J* = 6.6 Hz, 6H, $SiCC(CH_3)_2$], 0.84–0.89 (3H, 12-H), 1.25–1.70 (19H, 2-H to 7-H, 9-H to 11-H, SiCCH), 3.44 (t, *J* = 6.6 Hz, 2H, 1-H), 3.58 (quint, *J* = 5.6 Hz, 1H, 8-H), 4.48 (s, 2H, OCH_2Ph), 7.25–7.33 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = −2.4 [q, $Si(CH_3)_2$], 14.1 (q, C-12), 18.6 [q, $SiC(CH_3)_2$], 20.4 [q, $SiCC(CH_3)_2$], 24.8 [s, $SiC(CH_3)_2$], 22.9, 25.2, 26.2, 27.4, 29.5, 29.76, 29.84, 36.7, 36.9 (9 t, C-2 to C-7, C-9 to C-11), 34.2 (d, SiCCH), 70.5 (t, OCH_2Ph), 72.1 (d, C-8), 72.8 (t, C-1), 127.4, 127.6, 128.3, 138.7 (Ph). – $C_{27}H_{50}O_2Si$ (434.8): calcd. C 74.59, H 11.59; found C 74.62, H 11.55.

(S)-(−)-10-Acetoxy-1-tetradecanol [(−)-**5**]: A solution of 19.35 g (53.4 mmol) of (−)-**4** in 600 ml of MeOH was stirred with 1.50 g of Pd/C (5%, Fluka) under H_2 (1 bar) for 3 h. The mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue was chromatographed on 1000 g of silica gel (cyclohexane/AcOEt, 4:1) yielding 13.09 g (90%) of (−)-**5** as a colorless oil, R_f = 0.16. An analytical sample was distilled, b.p. 112–113°C/0.002 Torr, $[\alpha]_D^{20}$ = −1.1 (*c* = 2.33, EtOH). – IR (CCl_4): $\tilde{\nu}$ = 3638 cm^{-1} (OH), 1736 (C=O). – ^{1}H NMR ($CDCl_3$): δ = 0.87 (t, *J* = 6.9 Hz, 3H, 14-H), 1.20–1.40 (17H, 3-H to 8-H, 12,13-H, OH), 1.46–1.60 (6H, 2, 9, 11-H), 2.02 (s, 3H, CH_3CO_2), 3.62 (t, *J* = 6.6 Hz, 2H, 1-H), 4.84 (quint, *J* = 6.3 Hz, 1H, 10-H). – ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, C-14), 21.3 (q, CH_3CO_2), 22.6, 25.3, 25.7, 27.5, 29.32, 29.38, 29.43, 29.43, 32.8, 33.8, 34.1 (11 t, C-2 to C-9, C-11 to C-13), 63.0 (t, C-1), 74.4 (d, C-10), 171.0 (s, $MeCO_2$). – $C_{16}H_{32}O_3$ (272.4): calcd. C 70.54, H 11.84; found C 70.61, H 11.81.

(S)-(+)-8-[Dimethyl(1,1,2-trimethylpropyl)silyloxy]dodecan-1-ol [(+)-**23**]: A solution of 5.70 g (13.1 mmol) of (+)-**22** in 400 ml of MeOH, 50 ml of AcOEt and 20 ml of AcOH was stirred with 2.50 g of $Pd/BaSO_4$ (5%, Fluka) under H_2 (1 bar) for 2 h. The mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue was chromatographed on 480 g of silica gel (cyclohexane/AcOEt, 4:1) to give 4.38 g (97%) of (+)-**23** as a colorless oil, R_f = 0.30. An analytical sample was distilled, b.p. 126–128°C/0.001 Torr, $[\alpha]_D^{20}$ = +1.1 (*c* = 1.71, EtOH). – IR (CCl_4): $\tilde{\nu}$ = 3638 cm^{-1} (OH). – ^{1}H NMR ($CDCl_3$): δ = 0.04 [s, 6H, $Si(CH_3)_2$], 0.80 [s, 6H, $SiC(CH_3)_2$], 0.85 [d, *J* = 6.9 Hz, 6H, $SiCC(CH_3)_2$], 0.84–0.89 (3H, 12-H), 1.20–1.40 (17H, 3-H to 7-H, 9-H to 11-H, OH), 1.54 (m, 1H, SiCCH), 1.61 (quint, *J* = 6.9 Hz, 2H, 2-H), 3.58 (quint, *J* = 6.3 Hz, 1H, 8-H), 3.61 (t, *J* = 6.6 Hz, 2H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = −2.4 [q, $Si(CH_3)_2$], 14.1 (q, C-12), 18.6 [q, $SiC(CH_3)_2$], 20.3 [q, $SiCC(CH_3)_2$], 24.8 [s, $SiC(CH_3)_2$], 22.9, 25.1, 25.7, 27.4, 29.4, 29.8, 32.8, 36.6, 36.9 (9 t, C-2 to C-7, C-9 to C-11), 34.1 (d, SiCCH), 63.0 (t, 1 C, C-1), 72.1 (d, 1 C, C-8). – $C_{20}H_{44}O_2Si$ (344.7): calcd. C 69.70, H 12.87; found C 69.55, H 12.93.

(S)-(+)-1-Bromo-8-[dimethyl(1,1,2-trimethylpropyl)silyloxy]-dodecane [(+)-**24**]: Tetrabromomethane (6.26 g; 18.9 mmol) was added within 15 min to a solution of 4.37 g (12.7 mmol) of (+)-**23** and 5.55 g (21.2 mmol) of triphenylphosphane in 50 ml of dichloromethane. The mixture was stirred for 4 h at room temp. and then concentrated in vacuo. The residue was extracted five times with 80 ml of hexane. The combined extracts were filtered through ICN alumina N, the solvent was evaporated from the filtrate and the residue was distilled to give 4.65 g (90%) of (+)-**24** as a colorless oil, b.p. 136–137°C/0.005 Torr, R_f = 0.30 (cyclohexane), $[\alpha]_D^{20}$ = +1.8 (*c* = 1.75, EtOH). – ^{1}H NMR ($CDCl_3$): δ = 0.04 [s, 6H, $Si(CH_3)_2$], 0.80 [s, 6H, $SiC(CH_3)_2$], 0.86 [d, *J* = 6.9 Hz, 6H, $SiCC(CH_3)_2$], 0.83–0.89 (3H, 12-H), 1.20–1.50 (16H, 3-H to 7-H, 9-H to 11-H), 1.61 (sept, *J* = 6.9 Hz, 1H, SiCCH), 1.83 (quint, *J* = 6.9 Hz, 2H, 2-H), 3.39 (t, *J* = 6.6 Hz, 2H, 1-H), 3.59 (quint, *J* = 5.6 Hz, 1H, 8-H). – ^{13}C NMR ($CDCl_3$): δ = −2.42, −2.43 [2 q, $Si(CH_3)_2$], 14.1 (q, C-12), 18.6 [q, $SiC(CH_3)_2$], 20.4 [q, $SiCC(CH_3)_2$], 24.8 [s, $SiC(CH_3)_2$], 22.9, 25.1, 27.4, 28.1, 28.8, 29.7, 32.8, 34.0, 36.7, 36.9 (10 t, C-1 to C-7, C-9 to C-11), 34.2 (d, SiCCH), 72.1 (d, C-8). – $C_{20}H_{43}BrOSi$ (407.6): calcd. C 58.94, H 10.63, Br 19.61; found C 58.91, H 10.60, Br 19.72.

(S)-(−)-10-Acetoxytetradecanal [(−)-**6**]: A solution of 4.25 ml (4.68 g, 59.8 mmol) of DMSO in 20 ml of dichloromethane was added dropwise under N_2 at −75°C to a solution of 2.50 ml (3.69 g, 29.1 mmol) of oxalyl chloride in 55 ml of dichlormethane. Subsequently, a solution of 6.09 g (22.35 mmol) of (−)-**5** in 65 ml of dichloromethane was added dropwise within 2 h at −75°C, and the mixture was stirred for an additional 60 min. Then 25.0 ml of Et_3N was added all at once and the mixture was allowed to reach room temp. Then 80 ml of water was added and the mixture was extracted twice with 150 ml of dichloromethane. The combined extracts were washed with 120 ml of 1 M H_2SO_4 and 100 ml of 2 M $KHCO_3$, dried (Na_2SO_4) and the solvent was evaporated. The residue (6.7 g) was distilled to give 5.45 g (90%) of (−)-**6** as a yellowish oil, b.p. 129–130°C/0.03 Torr, $[\alpha]_D^{20}$ = −1.5 (*c* = 2.58, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 2714 (CHO), 1733 (C=O). – ^{1}H NMR ($CDCl_3$): δ = 0.84 (t, *J* = 6.6 Hz, 3H, 14-H), 1.10–1.39 (14H, 4-H to 8-H, 12,13-H), 1.40–1.65 (6H, 3,9,11-H), 1.99 (s, 3H, CH_3CO_2), 2.37 (td, *J* = 7.3, 1.7 Hz, 2H, 2-H), 4.81 (quint, *J* = 6.3 Hz, 1H, 10-H), 9.72 (t, *J* = 1.7 Hz, 1H, 1-H). – ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, C-14), 21.2 (q, CH_3CO_2), 22.0, 22.5, 25.2, 27.4, 29.0, 29.19, 29.22, 29.4, 33.8, 34.0, 43.8 (11 t, C-2 to C-9, C-11 to C-13), 74.2 (d, C-10), 170.9 (s, $MeCO_2$), 202.8 (d, CHO). – $C_{16}H_{30}O_3$ (270.4): calcd. C 71.07, H 11.18; found C 71.18, H 11.09.

Methyl (3R,12S)- and (3S,12S)-12-Acetoxy-3-hydroxyhexadecanoate (**8** and **7**): Thirty milliliters (48.0 mmol) of 1.6 M *n*BuLi in hexane (Merck) was dropped, within 20 min under N_2, into a solution of 4.20 ml (3.00 g, 29.6 mmol) of diisopropylamine (Fluka) in 42 ml of THF. The mixture was cooled to −78°C and a solution of 1.96 g (26.5 mmol) of methyl acetate in 28 ml of THF was added dropwise within 15 min. Then a solution of 5.40 g (19.97 mmol) of (−)-**6** in 60 ml of THF was added dropwise within 15 min and the mixture was stirred for an additional 90 min. Subsequently, 200 ml of 0.5 N H_2SO_4 was added and the mixture was extracted twice with 200 ml of cyclohexane/diethyl ether (1:1). The combined extracts were washed with 150 ml of 2 M $KHCO_3$, dried (Na_2SO_4), and the solvent was evaporated. The residue (7.24 g) was chromatographed on 1000 g of silica gel (cyclohexane/AcOEt, 4:1) yielding 4.72 g (69%) of **8** and **7** as a mixture of diastereoisomers, colorless oil, R_f = 0.22, b.p. 134–135°C/0.001 Torr, $[\alpha]_D^{20}$ = −1.3 (*c* = 2.14, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3554 cm^{-1} (OH), 1733 (C=O). – ^{1}H NMR ($CDCl_3$): δ = 0.85 (t, *J* = 6.6 Hz, 3H, 16-H), 1.20–1.35 (16H, 5-H to 10-H, 14,15-H), 1.35–1.55 (6H, 4,11,13-H), 2.00 (s, 3H, CH_3CO_2), 2.37 (dd, *J* = 16.3, 8.6 Hz, 1H, 2-H), 2.48 (dd, *J* = 16.3, 3.6 Hz, 1H, 2-H), 2.87 (d, *J* = 3.9 Hz, 1H,

OH), 3.68 (s, 3H, OCH_3), 3.96 (m, 1H, 3-H), 4.82 (quint, J = 6.3 Hz, 1H, 12-H). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-16), 21.3 (q, CH_3CO_2), 22.6, 25.3, 25.4, 27.5, 29.37, 29.40, 29.40, 29.43, 33.8, 34.1, 36.5, 41.1 (12 t, C-2, C-4 to C-11, C-13 to C-15), 51.7 (q, CO_2CH_3), 68.0 (d, C-3), 74.4 (d, C-12), 170.9 (s, $MeCO_2$), 173.4 (s, CO_2Me). – $C_{19}H_{36}O_5$ (344.5): calcd. C 66.25, H 10.53; found C 66.31, H 10.49.

Methyl (3R,12S)- and (3S,12S)-12-Acetoxy-3-(tert-butyldiphenylsilyloxy)hexadecanoate (**10** and **9**): To a solution of 5.00 ml (5.37 g, 19.5 mmol) of *tert*-butylchlorodiphenylsilane in 16 ml of DMF, 2.75 g (40.4 mmol) of imidazole and then 4.50 g (13.05 mmol) of each of **8** and **7** were added. The mixture was stirred at 65°C for 5 h. Subsequently, 50 ml of water was added and the mixture was extracted twice with 200 ml of cyclohexane/diethyl ether (1:1). The combined extracts were washed with water, dried (Na_2SO_4), and the solvent was evaporated. The residue (9.6 g) was chromatographed on 950 g silica gel (cyclohexane/AcOEt, 19:1) to give 7.38 g (97%) of **10** and **9** as a colorless oil, R_f = 0.20, b.p. 208–209°C/0.002 Torr, $[\alpha]_D^{20}$ = –1.4 (c = 2.23, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 1738 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3H, 16-H), 1.00 [s, 9H, $C(CH_3)_3$], 1.00–1.60 (22H, 4-H to 11-H, 13-H to 15-H), 2.02 (s, 3H, CH_3CO_2), 2.39 (dd, J = 14.8, 5.6 Hz, 1H, 2-H), 2.48 (dd, J = 14.8, 6.9 Hz, 1H, 2-H), 3.53 (s, 3H, OCH_3), 4.16 (quint, J = 6.6 Hz, 1H, 3-H), 4.83 (quint, J = 6.3 Hz, 1H, 12-H), 7.30–7.72 (10H, 2 Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-16), 19.3 [s, $C(CH_3)_3$], 21.3 (q, CH_3CO_2), 26.9 [q, $C(CH_3)_3$], 22.6, 24.7, 25.3, 26.6, 27.5, 29.4, 29.5, 33.4, 34.1, 36.5, 37.1, 41.9 (12 t, C-2,4 to C-11, C-13 to C-15), 51.4 (q, CO_2CH_3), 70.5 (d, C-3), 74.4 (d, C-12), 127.5, 127.7, 129.6, 129.7, 134.1, 134.2, 134.8, 135.9 (2 Ph), 170.9 (s, $MeCO_2$), 172.1 (s, CO_2Me). – $C_{35}H_{54}O_5Si$ (582.9). calcd. C 72.12, H 9.34; found C 72.03, H 9.32.

(3R,12S)- and (3S,12S)-3-(tert-Butyldiphenylsilyloxy)-12-hydroxyhexadecanoic Acid (**12** and **11**): A solution of 7.14 g (12.24 mmol) of **10** and **9** in a mixture of 15 ml of 10 N KOH and 15 ml of MeOH was stirred at 30°C for 7 h. Then 15 ml of 10 N H_2SO_4 and 100 ml of water were added and the mixture was extracted twice with 200 ml of cyclohexane/diethyl ether (1:1). The combined extracts were washed with 100 ml of water, dried (Na_2SO_4) and the solvent was evaporated. The residue (6.95 g) was chromatographed on 700 g of silica gel (cyclohexane/AcOEt/AcOH, 80:20:2) to give 6.38 g (99%) of **12** and **11** as a colorless oil, R_f = 0.28. An analytical sample was distilled, b.p. 225°C/0.002 Torr, $[\alpha]_D^{20}$ = +0.75 (c = 1.65, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3630 cm^{-1} (OH), 3500–2500 (CO_2H), 1712 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.87 (t, J = 6.6 Hz, 3H, 16-H), 1.00 [s, 9H, $C(CH_3)_3$], 1.13–1.40 (23H, 4-H to 11-H, 13-H to 15-H, OH), 2.41 (dd, J = 14.5, 5.9 Hz, 1H, 2-H), 2.47 (dd, J = 14.5, 6.3 Hz, 1H, 2-H), 3.55 (m, 1H, 12-H), 4.12 (quint, J = 5.9 Hz, 1H, 3-H), 6.28 (m, 1H, CO_2H), 7.24–7.67 (10H, 2 Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.1 (q, C-16), 19.3 [s, $C(CH_3)_3$], 26.9 [q, $C(CH_3)_3$], 22.7, 24.6, 25.5, 26.9, 27.8, 29.2, 29.3, 29.5, 36.7, 37.0, 37.3, 41.6 (12 t, C-2,4 to C-11, C-13 to C-15), 70.3 (d, C-3), 72.1 (d, C-12), 127.48, 127.49, 129.59, 129.60, 133.7, 134.0, 135.8, 135.9 (2 Ph), 176.7 (s, CO_2H). – $C_{32}H_{50}O_4Si$ (526.8): calcd. C 72.96, H 9.57; found C 73.02, H 9.55.

(4R,13S)-(+)- and (4S,13S)-(+)-13-Butyl-4-(tert-butyldiphenylsilyloxy)-1-oxacyclotridecan-2-one [(+)-**14** and (+)-**13**]: To a solution of 4.21 g (8.00 mmol) of **12** and **11** in 9.0 ml of benzene, 2.21 g (10.0 mmol) of 2,2′-dipyridyl disulfide and 2.63 g (10.0 mmol) of triphenylphosphane were added under N_2 and the mixture was stirred for 1 h at room temp. It was then dissolved in additional 12 ml of benzene and the resulting solution was added within 16 h with a motor-driven automatic syringe through the reflux condenser to a magnetically stirred, boiling solution of 30 ml (30 mmol) of 1 M $AgClO_4$ in toluene and 500 ml of benzene. The obtained mixture was cooled to room temp., washed with 200 ml of 0.5 M KCN and 80 ml of water. The organic layer was dried (Na_2SO_4), the solvent was evaporated and the residue was chromatographed on 900 g of silica gel (toluene) to give 1.59 (39%) of (+)-**14** as a colorless oil, R_f = 0.81, b.p. 200–202°C/0.001 Torr, $[\alpha]_D^{20}$ = +0.2, $[\alpha]_{365}^{20}$ = –2.72 (c = 1.73, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 1727 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 0.84 (t, 6.9 Hz, 3H, 4′-H), 1.04 [s, 9H, $C(CH_3)_3$], 1.10–1.60 (22H, 5-H to 12-H, 1′-H to 3′-H), 2.48 (dd, J = 13.8, 5.6 Hz, 1H, 3-H), 2.56 (dd, J = 13.8, 9.9 Hz, 1H, 3-H), 4.24 (m, 1H, 4-H), 4.78 (m, 1H, 13-H), 7.30–7.70 (10H, 2 Ph). – ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, C-4′), 19.2 [s, $C(CH_3)_3$], 27.0 [q, $C(CH_3)_3$], 20.5, 22.6, 22.7, 24.7, 24.9, 26.8, 27.0, 27.5, 32.5, 34.2, 34.9 (11 t, C-5 to C-12, C-1′ to C-3′), 42.3 (t, C-3), 70.4 (d, C-4), 74.3 (d, C-13), 127.55, 127.60, 129.61, 129.62, 134.0, 134.2, 135.74, 135.75 (2 Ph), 171.2 (s, C-2). – $C_{32}H_{48}O_3Si$ (508.8): calcd. C 75.54, H 9.51; found C 75.47, H 9.42.

The more polar fractions provided 1.75 g (43%) of (+)-**13** as a yellowish oil, R_f = 0.60, b.p. 180°C/0.002 Torr, $[\alpha]_D^{20}$ = +8.45 (c = 1.94, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 1731 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 0.83 (t, J = 7.3 Hz, 3H, 4′-H), 1.04 [s, 9H, $C(CH_3)_3$], 1.10–1.60 (22H, 5-H to 12-H, 1′-H to 3′-H), 2.31 (dd, J = 13.0, 10.3 Hz, 1H, 3-H), 2.52 (dd, J = 13.0, 3.3 Hz, 1H, 3-H), 4.06 (m, 1H, 4-H), 4.71 (m, 1H, 13-H), 7.32–7.71 (10H, 2 Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-4′), 19.4 [s, $C(CH_3)_3$], 27.0 [q, $C(CH_3)_3$], 21.5, 22.4, 22.6, 23.0, 23.1, 24.8, 26.3, 27.4, 33.5, 34.4, 34.5 (11 t, C-5 to C-12, C-1′ to C-3′), 45.1 (t, C-3), 69.5 (d, C-4), 74.5 (d, C-13), 127.5, 127.6, 129.6, 129.7, 133.6, 134.3, 135.9, 136.0 (2 Ph), 170.7 (s, C-2). – $C_{32}H_{48}O_3Si$ (508.8): calcd. C 75.54, H 9.51; found C 75.43, H 9.46.

(4R,13S)-(+)-13-Butyl-4-hydroxy-1-oxacyclotridecan-2-one [(+)-**16**]: A solution of 447 mg (0.88 mmol) of (+)-**14**, 832 mg (2.64 mmol) of tetrabutylammonium fluoride trihydrate (Fluka) and 167 mg (0.88 mmol) of *p*-toluenesulfonic acid hydrate in 25 ml of THF was stirred for 40 h at room temp. under N_2. Then 50 ml of water was added and the mixture was extracted twice with 100 ml of benzene. The combined extracts were dried (Na_2SO_4), the solvent was evaporated and the residue (475 mg) was chromatographed on 50 g of silica gel (toluene/AcOEt, 2:1) to give 224 mg (95%) of (+)-**16** as a colorless oil, R_f = 0.54, b.p. 132°C/0.002 Torr, $[\alpha]_D^{20}$ = +5.94 (c = 1.60, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3630, 3300–3500 cm^{-1} (OH), 1727 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3H, 4′-H), 1.25–1.70 (23H, 5-H to 12-H, 1′-H to 3′-H, OH), 2.53 (dd, J = 13.5, 8.9 Hz, 1H, 3-H), 2.60 (dd, J = 13.5, 4.3 Hz, 1H, 3-H), 4.09 (m, 1H, 4-H), 4.92 (tdd, J = 7.3, 5.9, 2.6 Hz, 1H, 13-H). – ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, C-4′), 21.8, 22.0, 22.5, 24.4, 24.8, 26.2, 26.4, 27.6, 32.3, 33.8, 34.9 (11 t, C-5 to C-12, C-1′ to C-3′), 43.2 (t, C-3), 69.4 (d, C-4), 74.7 (d, C-13), 171.5 (s, C-2). – $C_{16}H_{30}O_3$ (270.4): calcd. C 71.07, H 11.18; found C 71.18, H 11.13.

(4S,13S)-(+)-13-Butyl-4-hydroxy-1-oxacyclotridecan-2-one [(+)-**15**]: Analogously prepared as described above for (+)-**16** from 418 mg (0.82 mmol) of (+)-**13**, 778 mg (2.47 mmol) of tetrabutylammonium fluoride trihydrate (Fluka) and 156 mg (0.82 mmol) of *p*-toluenesulfonic acid in 25 ml of THF to give 221 mg (99%) of (+)-**15** as a colorless oil, R_f = 0.61 (toluene/AcOEt, 2:1), b.p. 121°C/0.001 Torr, $[\alpha]_D^{20}$ = +15.0 (c = 1.61, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3545 cm^{-1} (OH), 1731, 1712 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.87 (t, J = 6.9 Hz, 3H, 4′-H), 1.10–1.73 (23H, 5-H to 12-H, 1′-H to 3′-H, OH), 2.53 (dd, J = 14.5, 6.9 Hz, 1H, 3-H), 2.67 (dd, J = 14.5, 3.3 Hz, 1H, 3-H), 3.93 (m, 1H, 4-H), 4.93 (tdd, J = 7.3, 5.9, 2.6 Hz, 1H, 13-H). – ^{13}C NMR ($CDCl_3$): δ = 13.8 (q, C-4′), 22.4, 22.8, 23.0, 24.2, 24.9, 25.0, 26.7, 27.4, 33.4, 34.2, 34.6 (11 t,

C-5 to C-12, C-1′ to C-3′), 42.0 (t, C-3), 68.2 (d, C-4), 75.0 (d, C-13), 171.9 (s, C-2). – $C_{16}H_{30}O_3$ (270.4): calcd. C 71.07, H 11.18; found C 71.02, H 11.16.

(3S,12S)-(–)-1-Benzyloxy-12-[dimethyl(1,1,2-trimethylpropyl)-silyloxy]hexadecan-3-ol [(–)-**25**]: A solution of 3.18 g (7.80 mmol) of (+)-**24** and 0.3 ml of 1,2-dibromoethane in 80 ml of THF was added dropwise within 3.5 h under N_2 to a suspension of 1.50 g (61.7 mmol) of magnesium turnings in 30 ml of boiling THF. The reaction mixture was heated at reflux temp. for an additional 60 min. Then the solution of the Grignard reagent was cooled to 0 °C, a solution of 1.18 g (6.62 mmol) of (*R*)-(+)-2-benzyloxyethyloxirane[13] in 20 ml THF and 340 mg (0.82 mmol) of 1,5-cyclooctadienecopper(I) chloride catalyst[10] were added. After stirring of the mixture for 90 min at 20 °C, 50 ml of water was added and the THF was distilled off in vacuo. The residue was extracted twice with 300 ml of diethyl ether and the combined extracts were washed with 100 ml of 2 M $KHCO_3$, dried (Na_2SO_4), and the solvent was evaporated. The residue (3.99 g) was chromatographed on 480 g of silica gel (cyclohexane/AcOEt, 9:1) to give 2.95 g (88%) of (–)-**25** as a colorless oil, R_f = 0.14, b.p. 205 °C/0.001 Torr, $[\alpha]_D^{20}$ = –4.25 (*c* = 2.71, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3633, 3540 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 0.05 [s, 6H, $Si(CH_3)_2$], 0.81 [s, 6H, $SiC(CH_3)_2$], 0.87 [d, *J* = 6.6 Hz, 6H, $SiCC(CH_3)_2$], 0.84–0.91 (3H, 16-H), 1.20–1.50 (22H, 4-H to 11-H, 13-H to 15-H), 1.62 (sept, *J* = 6.9 Hz, 1H, SiCCH), 1.70 (dm, *J* = 5.6 Hz, 1H, 2-H), 1.75 (dm, *J* = 5.6 Hz, 1H, 2-H), 2.88 (m, 1H, OH), 3.59 (quint, *J* = 5.3 Hz, 1H, 12-H), 3.63 (dt, *J* = 9.2, 6.0 Hz, 1H, 1-H), 3.71 (dt, *J* = 9.2, 5.0 Hz, 1H, 1-H), 3.78 (m, 1H, 3-H), 4.51 (s, 2H, OCH_2Ph), 7.25–7.33 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = –2.5 [q, $Si(CH_3)_2$], 14.1 (q, C-16), 18.6 [q, $SiC(CH_3)_2$], 20.3 [q, $SiCC(CH_3)_2$], 24.8 [s, $SiC(CH_3)_2$], 22.9, 25.2, 25.6, 26.9, 27.4, 29.6, 29.7, 29.9, 36.4, 36.6, 37.0, 37.5 (12 t, C-2,4 to C-11, C-13 to C-15), 34.1 (d, SiCCH), 69.3 (t, C-1), 71.5 (d, C-3), 72.1 (d, C-12), 73.3 (t, OCH_2Ph), 127.6, 127.7, 128.4, 137.9 (Ph). – $C_{31}H_{58}O_3Si$ (506.9): calcd. C 73.46, H 11.53; found C 73.49, H 11.51.

(3S,12S)-(–)-1-(Benzyloxy)hexadecane-3,12-diol [(–)-**26**]: A solution of 2.677 g (5.28 mmol) of (–)-**25** in 48 ml of MeOH and 16.0 ml of 2 N H_2SO_4 was heated at reflux temp. for 50 min. After the reaction mixture had been cooled, it was concentrated in vacuo and the residue was extracted twice with 150 ml of AcOEt. The combined extracts were washed with water, dried (Na_2SO_4), and the solvent was evaporated. The residue (2.1 g) was chromatographed on silica gel (cyclohexane/AcOEt, 2:1) to give 1.81 g (94%) of (–)-**26** as colorless crystals, R_f = 0.26, m.p. 85.9–86.4 °C, $[\alpha]_D^{20}$ = –6.45 (*c* = 2.17, $CHCl_3$). – IR ($CHCl_3$): $\tilde{\nu}$ = 3621, 3500 cm^{-1} (OH). – ^1H NMR ($CDCl_3$): δ = 0.89 (t, *J* = 6.9 Hz, 3H, 16-H), 1.20–1.50 (22H, 4-H to 11-H, 13-H to 15-H), 1.70 (dm, *J* = 5.8 Hz, 1H, 2-H), 1.74 (dm, *J* = 5.8 Hz, 1H, 2-H), 2.86 (m, 2H, 2 OH), 3.56 (m, 1H, 12-H), 3.62 (dt, *J* = 9.3, 5.8 Hz, 1H, 1-H), 3.71 (dt, *J* = 9.3, 5.8 Hz, 1H, 1-H), 3.78 (m, 1H, 3-H), 4.50 (s, 2H, OCH_2Ph), 7.25–7.36 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.1 (q, C-16), 22.8, 25.57, 25.62, 27.8, 29.5, 29.5, 29.6, 29.7, 36.4, 37.2, 37.45, 37.46 (12 t, C-2,4 to C-11, C-13 to C-15), 69.3 (t, C-1), 71.5 (d, C-3), 72.0 (d, C-12), 73.3 (t, OCH_2Ph), 127.65, 127.72, 128.4, 137.9 (Ph). – $C_{23}H_{40}O_3$ (364.6): calcd. C 75.78, H 11.06; found C 75.83, H 11.00.

(3S,12S)-(+)-3,12-Diacetoxy-1-benzyloxyhexadecane [(+)-**27**]: A solution of 1.51 g (4.14 mmol) of (–)-**26** in 10 ml of acetic anhydride and 10 ml of pyridine was stirred at room temp. for 20 h. Toluene was added and the solvent and excess reagent were evaporated to afford 1.84 g (99%) of (+)-**27** as a colorless oil, R_f = 0.23 (cyclohexane/AcOEt, 9:1). An analytical sample of (+)-**27** was distilled, b.p. 175 °C/0.001 Torr, $[\alpha]_D^{20}$ = +10.1 (*c* = 2.68, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 1737 cm^{-1} (C=O). – ^1H NMR ($CDCl_3$): δ = 0.86 (t, *J* = 6.9 Hz, 3H, 16-H), 1.20–1.40 (16H, 5-H to 10-H, 14,15-H), 1.45–1.63 (6H, 4,11,13-H), 1.78 (ddd, *J* = 15.3, 6.6, 2.0 Hz, 1H, 2-H), 1.88 (ddm, *J* = 15.3, 6.6 Hz, 1H, 2-H), 1.97, 2.01 (2 s, 6H, 3-CH_3CO_2, 12-CH_3CO_2), 3.43 (dt, *J* = 16.2, 6.6 Hz, 1H, 1-H), 3.50 (dt, *J* = 16.2, 6.6 Hz, 1H, 1-H), 4.45 (s, 2H, OCH_2Ph), 4.83 (quint, *J* = 6.3 Hz, 1H, 12-H), 5.00 (tt, *J* = 6.6, 5.9 Hz, 1H, 3-H), 7.22–7.35 (5H, Ph). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-16), 21.2, 21.3 (2 q, 2 CH_3CO_2), 22.6, 25.2, 25.3, 26.9, 27.5, 29.41, 29.43, 29.5, 33.8, 34.1, 34.3, 34.4 (12 t, C-2,4 to C-11, C-13 to C-15), 66.8 (t, C-1), 71.8 (d, C-3), 73.0 (t, OCH_2Ph), 74.4 (d, C-12), 127.5, 127.7, 128.3, 138.3 (Ph), 170.8, 170.9 (2 s, 2 $MeCO_2$). – $C_{27}H_{44}O_5$ (448.6): calcd. C 72.28, H 9.88; found C 72.19, H 9.81.

(3S,12S)-(+)-3,12-Diacetoxyhexadecan-1-ol [(+)-**28**]: A solution of 1.45 g (3.23 mmol) of (+)-**27** in 100 ml of MeOH and 1 ml of acetic acid was stirred with 200 mg of Pd/C (5%, Fluka) under H_2 (1 bar) for 90 min. The mixture was filtered through Celite and the filtrate was concentrated in vacuo. The residue (1.25 g) was chromatographed on 125 g of silica gel (cyclohexane/AcOEt, 4:1) to give 1.16 g (100%) of (+)-**28** as a colorless oil, R_f = 0.25, b.p. 150 °C/0.001 Torr, $[\alpha]_D^{20}$ = +3 (*c* = 0.18, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3636, 3539 cm^{-1} (OH), 1735 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.85 (t, *J* = 6.9 Hz, 3H, 16-H), 1.10–1.40 (16H, 5-H to 10-H, 14,15-H), 1.43–1.60 (6H, 4,11,13-H), 1.61 (ddt, *J* = 14.5, 9.5, 4.3 Hz, 1H, 2-H), 1.80 (dddd, *J* = 14.5, 9.5, 6.0, 3.3 Hz, 1H, 2-H), 2.00, 2.05 (2 s, 6H, 2 CH_3CO_2), 2.43 (m, 1H, OH), 3.48–3.59 (2H, 1-H), 4.82 (quint, *J* = 6.3 Hz, 1H, 12-H), 4.98 (m, 1H, 3-H). – ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-16), 21.1, 21.3 (2 q, 2 CH_3CO_2), 22.6, 25.2, 25.4, 27.4, 29.28, 29.35, 29.35, 29.4, 33.8, 34.1, 34.6, 37.4 (12 t, C-2,4 to C-11, C-13 to C-15), 58.5 (t, C-1), 71.5 (d, C-3), 74.3 (d, C-12), 170.9, 172.0 (2 s, 2 $MeCO_2$). – $C_{20}H_{38}O_5$ (358.5): calcd. C 67.00, H 10.68; found C 66.98, H 10.70.

(3S,12S)-(+)-3,12-Diacetoxyhexadecanoic Acid [(+)-**29**]: A solution of 1.16 g (3.23 mmol) of (+)-**28** in 8 ml of CCl_4 was added within 8 h at 20 °C with stirring to a solution of 2.07 (9.70 mmol) of sodium periodate and 27 mg (0.10 mmol) of ruthenium(III) chloride hydrate in 16.0 ml of acetonitrile, 8.0 ml of CCl_4 and 24.0 ml of water. The mixture was stirred for an additional 16 h. It was then concentrated in vacuo, 100 ml of 2 N H_2SO_4 was added and the mixture was extracted twice with 250 ml of AcOEt. The combined extracts were dried (Na_2SO_4), the solvent was evaporated and the residue (1.24 g) was chromatographed on 280 g of silica gel (cyclohexane/AcOEt/AcOH, 90:10:2) to give 1.02 g (85%) of (+)-**29** as a colorless oil, R_f = 0.11, b.p. 175 °C/0.001 Torr, $[\alpha]_D^{20}$ = +0.9 (*c* = 1.22, $CHCl_3$). – IR (CCl_4): $\tilde{\nu}$ = 3500–2500 cm^{-1} (CO_2H), 1741 (C=O), 1716 (C=O). – ^1H NMR ($CDCl_3$): δ = 0.81 (t, *J* = 6.9 Hz, 3H, 16-H), 1.10–1.32 (16H, 5-H to 10-H, 14,15-H), 1.35–1.65 (6H, 4,11,13-H), 1.97 (s, 6H, 3-CH_3CO_2, 12-CH_3CO_2), 2.50 (dd, *J* = 15.8, 5.6 Hz, 1H, 2-H), 2.57 (dd, *J* = 15.8, 6.9 Hz, 1H, 2-H), 4.79 (quint, *J* = 6.3 Hz, 1H, 12-H), 5.14 (quint, *J* = 6.6 Hz, 1H, 3-H), 10.65 (m, 1H, CO_2H). – ^{13}C NMR ($CDCl_3$): δ = 13.9 (q, C-16), 20.9, 21.1 (2 q, 3-CH_3CO_2, 12-CH_3CO_2), 22.5, 24.9, 25.1, 27.3, 29.1, 29.20, 29.24, 29.3, 33.7, 33.8, 34.0, 38.7 (12 t, C-2,4 to C-11, C-13 to C-15), 70.2 (d, C-3), 74.4 (d, C-12), 170.5, 171.1 (2 s, 3-$MeCO_2$, 12-$MeCO_2$), 175.9 (s, CO_2H). – $C_{20}H_{36}O_6$ (372.5): calcd. C 64.49, H 9.74; found C 64.41, H 9.64.

(3S,12S)-(–)-3,12-Dihydroxyhexadecanoic Acid [(–)-**19**]: A solution of 790 mg (2.12 mmol) of (+)-**29** in 30 ml of methanol and 10 ml of 2 N KOH was heated at reflux for 1 h. After cooling to room temp. 100 ml of 1 N H_2SO_4 was added and the mixture was extracted twice with 250 ml of cyclohexane/diethyl ether (1:1).

The combined extracts were dried (Na_2SO_4), the solvent was evaporated and the residue (0.6 g) was chromatographed on 100 g of silica gel (cyclohexane/AcOEt/AcOH, 65:35:2) to give 589 mg (96%) of (−)-**19** as colorless crystals. An analytical sample was recrystallized from the tenfold amount of cyclohexane/AcOEt (4:1), m.p. 82.8−84.0 °C (ref.[5] 83−84 °C), $[\alpha]_D^{20} = -0.7$ (c = 1.98, MeOH) (ref.[5] no value given). − IR ($CHCl_3$): $\tilde{\nu}$ = 3608 cm^{-1}, 3510 (OH), 3300−2500 (CO_2H), 1710 (C=O). − ^1H NMR (CD_3OD): δ = 0.91 (t, J = 6.9 Hz, 3H, 16-H), 1.30−1.50 (24H, 4-H to 11-H, 13-H to 15-H, 2 OH), 2.35 (dd, J = 15.2, 7.9 Hz, 1H, 2-H), 2.44 (dd, J = 15.2, 4.6 Hz, 1H, 2-H), 3.49 (m, 1H, 12-H), 3.96 (m, 1H, 3-H), >8 (br, 1H, CO_2H). − ^{13}C NMR (CD_3OD): δ = 14.5 (q, C-16), 23.9, 26.6, 26.8, 29.1, 30.67, 30.68, 30.72, 30.9, 38.12, 38.15, 38.4, 43.3 (12 t, C-2,4 to C-11, C-13 to C-15), 69.3 (d, C-3), 72.4 (d, C-12), 175.7 (s, CO_2H). − $C_{16}H_{32}O_4$ (288.4): calcd. C 66.63, H 11.18; found C 66.55, H 11.13.

Methyl (3S,12S)-(+)-3,12-Dihydroxyhexadecanoate [(+)-**17**]: A solution of 323 mg (1.12 mmol) of (−)-**19**, 1.0 ml (0.97 g, 9.1 mmol) of trimethyl orthoformate and 190 mg (1 mmol) of *p*-toluenesulfonic acid in 10 ml of methanol was heated at reflux for 1 h. After cooling to room temp. the mixture was concentrated in vacuo and 10 ml of water was added to the residue. The mixture was extracted twice with 50 ml of cyclohexane/diethyl ether (1:1), the combined extracts were dried (Na_2SO_4) and the solvent was evaporated. The residue (0.4 g) was chromatographed on 50 g of silica gel (cyclohexane/AcOEt, 2:1) to give 340 mg (99%) of (+)-**17** as colorless crystals, R_f = 0.25. An analytical sample was recrystallized from the tenfold amount of cyclohexane/AcOEt (4:1), m.p. 79.0−79.8 °C, $[\alpha]_D^{20} = +12.1$ (c = 1.96, $CHCl_3$), +1.6 (c = 1.69, MeOH) [ref.[5] +0.91 (c = 8, MeOH)]. − IR (CCl_4): $\tilde{\nu}$ = 3629 cm^{-1}, 3600−3400 (OH), 1729 (C=O). − ^1H NMR ($CDCl_3$): δ = 0.86 (t, J = 6.9 Hz, 3H, 16-H), 1.20−1.50 (23H, 4-H to 11-H, 13-H to 15-H, OH), 2.36 (dd, J = 16.3, 8.6 Hz, 1H, 2-H), 2.47 (dd, J = 16.3, 3.3 Hz, 1H, 2-H), 2.95 (m, 1H, OH), 3.53 (m, 1H, 12-H), 3.67 (s, 3H, OCH_3), 3.96 (m, 1H, 3-H). − ^{13}C NMR ($CDCl_3$): δ = 14.0 (q, C-16), 22.7, 25.4, 25.6, 27.8, 29.40, 29.41, 29.45, 29.6, 36.5, 37.1, 37.4, 41.1 (12 t, C-2,4 to C-11, C-13 to C-15), 51.7 (q, OCH_3), 67.9 (d, C-3), 71.9 (d, C-12), 173.5 (s, CO_2Me). − $C_{17}H_{34}O_4$ (302.5): calcd. C 67.51, H 11.33; found C 67.59, H 11.30.

Methyl (3S,12S)-(+)-3,12-Dihydroxyhexadecanoate [(+)-**17**]: A solution of 142 mg (0.53 mmol) of (+)-**15** in 10.0 ml of 0.2 M NaOMe in methanol was heated at reflux temp. for 6 h. After cooling to room temp. 5 ml of 1 N HCl in methanol was added, the mixture was concentrated in vacuo and 20 ml of 1 M $KHCO_3$ was added. The mixture was extracted twice with 100 ml of cyclohexane/diethyl ether (1:1). The combined extracts were dried (Na_2SO_4), the solvent was evaporated and the residue (161 mg) was chromatographed on 50 g silica gel (cyclohexane/AcOEt, 2:1) to give 99 mg (62%) of (+)-**17** as colorless crystals, R_f = 0.25. An analytical sample (80 mg) was recrystallized from 1.3 ml of cyclohexane/AcOEt (4:1) to give 60 mg of (+)-**17**, m.p. 79.7−80.2 °C, $[\alpha]_D^{20} = +1.6$ (c = 1.86, MeOH), +13.2 (c = 1.87, $CHCl_3$). − The spectroscopic properties are identical with those described above. − $C_{17}H_{34}O_4$ (302.5): calcd. C 67.51, H 11.33; found C 67.52, H 11.21.

(+)-Methyl 3,12-Dihydroxyhexadecanoate [(+)-**17**] *from Resina Jalapae pulv. (Ipomea operculata):* A solution of 1.18 g of pulverized resin[17] in 50 ml of 0.5 M HCl in MeOH was heated at reflux temp. for 23 h. Then the solution was concentrated, 50 ml 0.5 M K_2CO_3 was added to the residue and the mixture was extracted twice with cyclohexane/diethyl ether (1:1). The combined extracts were dried (Na_2SO_4), the solvent was evaporated, and the residue (261 mg) was chromatographed on 120 g of silica gel (cyclohexane/AcOEt, 2:1) to give 161 mg of (+)-**17**, R_f = 0.21. Recrystallization of 128 mg from 1.50 ml of cyclohexane/AcOEt (4:1) gave 105 mg (+)-**17**, m.p. 79.5−80.0 °C, $[\alpha]_D^{20} = +13.6$ (c = 2.10, $CHCl_3$), +1.5 (c = 2.12, MeOH) [ref.[5] +0.91 (c = 8, MeOH)]. − The IR, ^1H and ^{13}C NMR spectra are identical with those of synthetic (+)-**17** described above. − MS (70 eV): *m/z* (%) = 245 (20), 227 (75), 195 (90), 103 (100), 69 (60). Treatment with MSTFA gave the bistrimethylsilyl derivative. MS (70 eV): *m/z* (%) = 446 (1) [M^+], 431 (6) [$M^+ - 15$], 389 (90) [$M^+ - (CH_2)_3Me$], 341 (90) [$M^+ - 15 - 90$ (Me_3SiOH)], 175 (20) [$Me_3SiO^+CHCH_2CO_2Me$], 159 (100) [$Me(CH_2)_3CHOSiMe_3^+$].

Methyl (3R,12S)-(+)-3,12-Dihydroxyhexadecanoate [(+)-**18**]: Analogously prepared as described above for (+)-**17** from 199 mg (0.74 mmol) of (+)-**16** in 10.0 ml of 0.2 M NaOMe in methanol to give 113 mg (51%) of (+)-**18** as colorless crystals, R_f = 0.25. An analytical sample (77 mg) was recrystallized from 1.0 ml cyclohexane/AcOEt (4:1) to give 45 mg of (+)-**18**, m.p. 62.2−62.7 °C, $[\alpha]_D^{20} = +0.7$ (c = 1.15, MeOH), −11.9 (c = 1.18, $CHCl_3$). − The IR, NMR and mass spectra were indistinguishable from those of (+)-**17**. − $C_{17}H_{34}O_4$ (302.5): calcd. C 67.51, H 11.33; found C 67.58, H 11.24.

(3R,12S)-(+)-3,12-Dihydroxyhexadecanoic Acid [(+)-**20**]: Prepared analogously as described above for (−)-**19** from 113 mg (0.37 mmol) of (+)-**18** in 10 ml of methanol and 10 ml of 2 N KOH to give 109 mg (100%) of (+)-**20** as colorless crystals. An analytical sample was recrystallized from the tenfold amount of cyclohexane/AcOEt (4:1), m.p. 70.5−71.3 °C, $[\alpha]_D^{20} = +3.2$ (c = 1.86, MeOH). − The IR, NMR and mass spectra are indistinguishable from those of (−)-**19**. − $C_{16}H_{32}O_4$ (288.4): calcd. C 66.63, H 11.18; found C 66.58, H 11.15.

☆ Dedicated to Prof. Dr. *Vladimir Prelog* on the occasion of his 90th birthday.

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