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ENANTIOSELECTIVE SYNTHESIS OF 2-BENZYLOXY ALCOHOLS AND 1,2-DIOLS VIA ALKYLATION OF CHIRAL GLYCOLATE IMIDES. A CONVENIENT APPROACH TO OPTICALLY ACTIVE GLYCEROL DERIVATIVES

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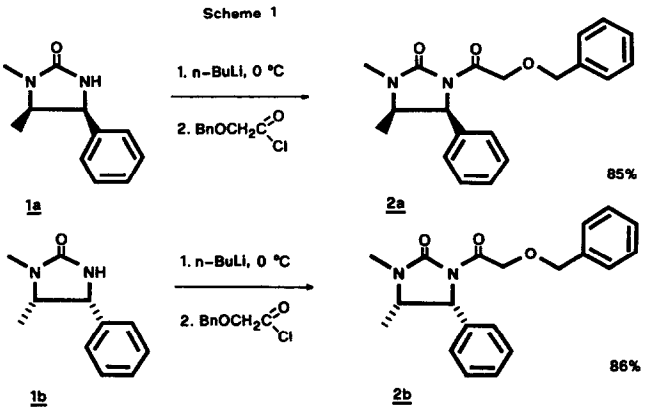
Abstract The alkylation of the chiral enolates of glycolate imides 2a and 2b proceedes in highly diastereoselective manner to give 2'-substituted products in good yield. Reductive cleavage with $LiBH_4$ affords the corresponding 2-benzyloxyalcohols 3a-c and 11a-b which are successively converted to 1,2-diols in high optical purity. By this method (R)-1-propanoyloxy-2,3-propanediol 9 and (S)-1-tridecyloxy-2,3-propanediol 14, a glyceride extracted from sponges Plocamiidae, have been synthesized, starting from 2a and 2b, respectively.

In a previous paper we have outlined a general synthesis of optically active alcohols starting from chiral imide enolates. [1] Both the enantiomers have been prepared by simply changing the chiral auxiliaries, the imidazolidin-2-ones 1a and 1b easily obtained from (+)- or (-)-ephedrine, respectively, [2] and the method has been applied to the synthesis of natural products, such as (R)- and (S)-lavandulol. [1]

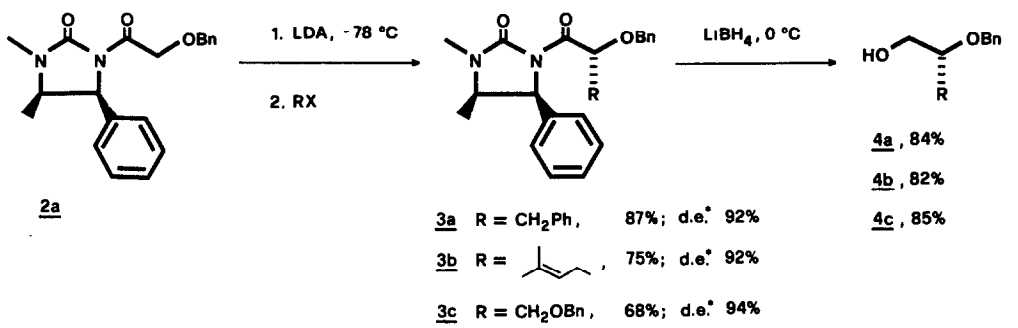
We wish to report here an efficient approach to the synthesis of either 2-benzyloxyalcohols or 1,2-diols having a stereogenic center at the C-2, with the aim to prepare natural, biologically active compounds. As shown in the Scheme 1, the imidazolidin-2-ones 1a and 1b have been converted into the glycolate imides 2a and 2b, respectively, simply reacting the corresponding lithium anion in THF with an equimolar amount of benzyloxyacetyl chloride (Scheme 1). [3]

Scheme 1



1a 2a 1b 2b

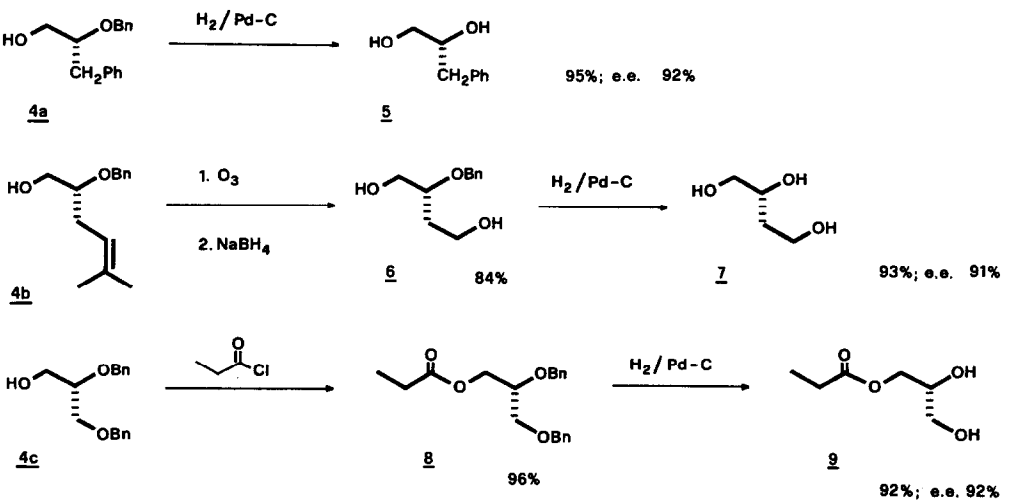
Scheme 2



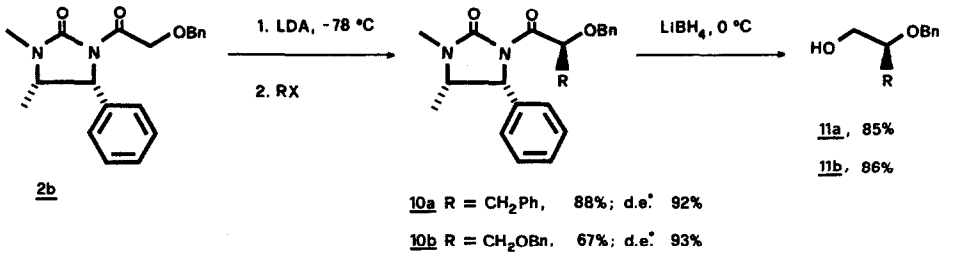
*determined by ^{13}C NMR of the diastereomeric mixture

After deprotonation of 2a with LDA in THF at -78 °C, the resulting chiral enolate undergoes alkylation by treatment with the appropriate alkyl halide at the same temperature. [4] The diastereomeric ratios of 2'-substituted glycolate imides 3a, 3b and 3c are easily determined by ^{13}C NMR spectroscopy (Scheme 2). The imides are cleaved with $LiBH_4$ in THF at 0 °C, to give 2-benzyloxy-alcohols 4a-c in good yield. The configurations [1] and the enantiomeric excess are determined by conversion to known compounds (Scheme 3). In fact, after hydrogenolysis on Pd-C, 4a affords (R)-3-phenyl-1,2-propanediol 5. [5] The alcohol 4b, on the contrary, a potential intermediate to chiral terpenic compounds, undergoes oxidative cleavage with ozone, followed by reduction with $NaBH_4$ and hydrogenolysis, to yield (R)-1,2,4-butanetriol 7. [6] The dibenzyloxyalcohol 4c [7] can be eventually considered a key intermediate to chiral monoacylglycerols: [8] after acylation with propanoyl chloride and successive hydrogenolysis, (R)-1-propanoyloxy-2,3-propanediol 9 has been obtained in good yield and high e.e. [9]

Scheme 3



Scheme 4



2b

10a R = CH_2Ph, 88%; d.e.* 92%

10b R = CH_2OBn, 67%; d.e.* 93%

11a, 85%

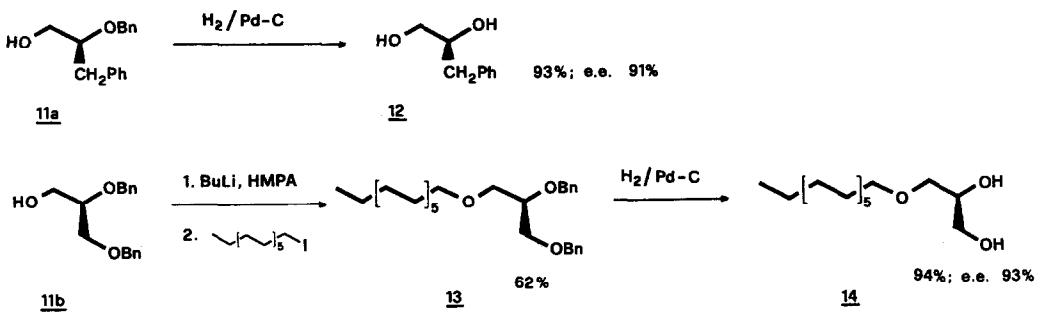
11b, 86%

* determined by ^{13}C NMR of the diastereomeric mixture

In the synthesis of biologically active compounds it is oftentimes necessary to synthesize both enantiomers with high optical purity, especially for exploring the relationship of biological activity with structure. Thus the attention was turned to the chiral synthon 2b, in order to obtain products with the opposite configuration in respect to those synthesized starting from 2a. The enolate of 2b, generated as above reported, has been alkylated to give i good yield the imides 10a and 10b as diastereomeric mixtures whose ratios are reported in the Scheme 4. The reductive cleavage affords the corresponding 2-benzyloxyalcohols 11a and 11b. After hydrogenolysis of 11a, (S)-3-phenyl-1,2-propanediol 12 [5] is obtained in high e.e. (Scheme 5). The alcohol 11b, on the other hand, has been employed for the synthesis of (S)-1-tridecyloxy-2,3-propanediol 14, a glyceride extracted from marine sponges Plocamiidae, [10] which displays toxicity to goldfish. The ether 13 is obtained simply by treating the lithium alkoxide of 11b with 1-iodotridecane in THF/HMPA (Scheme 5). The successive catalytic debenzylation affords the natural product 14 in good yield and high e.e.

According to these results, a new enantioselective route to either enantiomer of 2-benzyloxyalcohols or 1,2-diols has been devised. Further, the chiral auxiliary is efficiently recycled without loss in activity.

Scheme 5



11a

12 93%; e.e. 91%

11b

13 62%

14 94%; e.e. 93%

EXPERIMENTAL SECTION

General Reactions involving carbanions were carried out under argon. Tetrahydrofuran (THF) was freshly distilled from sodium benzophenone ketyl; diisopropylamine and HMPA were distilled from CaH_2. Butyllithium (2.5 M in hexanes) was purchased from Janssen and titrated against 2-propanol to the 1,10-phenanthroline end point. Melting points were taken on a Buchi 510 melting point apparatus and are uncorrected. ^1H NMR (90 and 200 MHz) spectra were recorded on a Varian EM 390 or on a Varian Gemini 200 instrument, respectively, using $CDCl_3$ as solvent, unless otherwise stated. ^{13}C NMR (20 MHz) spectra were recorded on a Varian FT 80-A Fourier transform spectrometer. Chemical shifts are given in δ with respect to Me_4Si used as internal standard. Mass spectra were taken with Varian MAT 112 (direct injection, 70 eV). Optical rotations were measured on a Perkin-Elmer 241 digital polarimeter. Infrared spectra (IR) were recorded on a Perkin-Elmer 682 spectrophotometer.

General Procedure for Preparation of 3-Acylimidazolidin-2-ones 2a,b

A solution of 9.5 g (50 mmol) of 1a or 1b [2] in dry THF (100 ml) is treated with an equimolar amount of n-BuLi at 0 °C. After the solids are dissolved, the clear solution is stirred for 0.5 h at 0 °C and then benzyloxyacetyl chloride [3] (9.2 g; 50 mmol) dissolved in THF (50 ml) is added and the mixture stirred for 1 h at 0 °C. Work-up with saturated ammonium chloride solution and CH_2Cl_2, followed by flash chromatography (cyclohexane:CH_2Cl_2 1:1) affords the pure products 2a or 2b in good yield.

(4S,5R)-1,5-Dimethyl-4-phenyl-3-benzyloxyacetylimidazolidin-2-one 2a

Reaction from 1a and benzyloxyacetyl chloride affords 14.4 g (85%) of 2a as white crystals: m.p. 84 - 86 °C; IR (nujol): 1740, 1690 cm^{-1}; ^1H NMR: 0.8 (d, 3H, J = 6 Hz), 2.8 (s, 3H), 3.9 (dq, 1H, J = 6, J = 7 Hz), 4.65 (s, 2H), 4.8 (s, 2H), 5.3 (d, 1H, J = 7 Hz), 7.2 (m, $10H_{arom}$); ^{13}C NMR: 14.8, 27.9, 54.6, 58.7, 69.9, 73.1, 126.9, 127.2, 127.6, 127.9, 128.3, 128.4, 136.3, 169.5; $[\alpha]_D$ +60.1° (c 1, CH_2Cl_2); m/e 338 (M^+), 261, 244, 231, 217, 189. Anal. calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.85; H, 6.54; N, 8.29.

(4R,5S)-1,5-Dimethyl-4-phenyl-3-benzyloxyacetylimidazolidin-2-one 2b

Reaction from 1b and benzyloxyacetyl chloride affords 14.5 g (86%) of 2b as white crystals: m.p. 85 - 86 °C; $[\alpha]_D$ -60.5° (c 1, CH_2Cl_2). Anal. calcd for $C_{20}H_{22}N_2O_3$: C, 70.99; H, 6.55; N, 8.28. Found: C, 70.85; C, 71.09; H, 6.54; N, 8.27.

General Procedure for the Alkylation of 3-Benzyloxyacetylimidazolidin-2-ones 2a or 2b

To a solution of 3-benzyloxyacetylimidazolidin-2-one 2a or 2b (30 mmol) in THF (50 ml) at -78 °C, are added 30 mmol of LDA in THF (20 ml). After 1 h a solution of the appropriate alkyl halide (30 mmol) in THF (20 ml) is slowly dropped and the mixture is allowed to warm to 0 °C in 12 h. Work-up with 2M HCl and CH_2Cl_2, followed by flash chromatography on silica gel (cyclohexane:CH_2Cl_2 6:4) yields the products 3a,b,c or 10a,b as diastereomeric mixtures, whose ratios are determined on the basis of the ^{13}C NMR spectra.

(4S,5R,2'R)-1,5-Dimethyl-4-phenyl-3-(2'-benzyloxy-3'-phenylpropanoyl)imidazolidin-2-one 3a

Reaction from 2a and benzyl bromide affords 11.2 g (87%) of 3a as a yiellow oil; diastereomeric ratio 96:4; IR (nujol): 1730, 1680 cm^{-1}, ^1H NMR: 0.7 (d, 3H, J = 6 Hz), 2.6 - 2.9 (m, 3H), 2.75 (s, 3H), 3.25 (dd, 1H, J = 12, J = 3 Hz), 3.75 (dq, 1H, J = 6, J = 9 Hz), 4.45 (ABq, 2H, J = 12 Hz), 5.26 (d, 1H, J = 9 Hz), 5.55 (dd, 1H, J = 9, J = 3 Hz), 7.0 - 7.4 (m, $15H_{arom}$); ^{13}C NMR: 15.0, 28.2, 39.2, 54.2, 59.0, 72.3, 78.9, 126.2, 127.0, 127.3, 127.7, 128.0, 128.1, 128.5, 129.7, 136.3, 137.9, 138.1, 155.3, 171.7; $[\alpha]_D$ +147.1° (c 1, CH_2Cl_2); m/e 428 (M^+), 336, 321, 307, 291, 261, 253, 223, 217, 210, 190, 91. Anal. calcd for $C_{27}H_{28}N_2O_3$: C, 75.68; H, 6.59; N, 6.54. Found:

C, 75.53; H, 6.57; N, 6.55.

(4S,5R,2'R)-1,5-Dimethyl-4-phenyl-3-(2'-benzyloxy-5'-methyl-5'-hexenoyl)imidazolidin-2-one 3b

Reaction from 2a and 1-bromo-3-methyl-2-butene affords 8.1 g (75%) of 3b as white crystals: m.p. 108 - 109 °C; diastereomeric ratio 96:4; IR (nujol): 1720, 1690 cm^{-1}; ^1H NMR: 0.8 (d, 3H, J = 6 Hz), 1.5 (s, 3H), 1.65 (s, 3H), 2.45 (m, 2H), 2.75 (s, 3H), 3.8 (dq, 1H, J = 6, J = 9 Hz), 4.55 (ABq, 2H, J = 9 Hz), 5.3 (m, 3H), 7.2 (m, $10H_{arom}$); ^{13}C NMR: 14.0, 17.9, 25.7, 28.1, 31.7, 54.2, 59.0, 72.2, 77.5, 119.2, 127.1, 127.4, 127.9, 128.3, 134.1, 136.4, 138.4, 155.3, 172.0; $[\alpha]_D$ +83.0° (c 1, CH_2Cl_2); m/e 406 (M^+), 388, 337, 315, 308, 298, 283, 258, 232, 217, 191, 107, 91. Anal. calcd for $C_{25}H_{30}N_2O_3$: C, 73.86; H, 7.44; N, 6.89. Found, C, 73.97; H, 7.43; N, 6.88.

(4S,5R,2'R)-1,5-Dimethyl-4-phenyl-3-(2',3'-dibenzyloxypropanoyl)imidazolidin-2-one 3c

Reaction from 2a and benzyl chloromethyl ether affords 9.3 g (68%) of 3c as a colorless oil; diastereomeric ratio 97:3; IR (neat): 1725, 1690 cm^{-1}; ^1H NMR: 0.6 (d, 3H, J = 6 Hz), 2.65 (s, 3H), 3.6 (dq, 1H, J = 6, J = 7 Hz), 3.8 (ABq, 2H, J = 11 Hz), 4.5 (s, 2H), 4.6 (ABq, 2H, J = 10 Hz), 5.2 (d, 1H, J = 7 Hz), 5.7 (t, 1H, J = 6 Hz), 7.2 (m, $15H_{arom}$); ^{13}C NMR: 15.0, 28.1, 54.1, 59.0, 71.0, 72.5, 73.2, 77.5, 126.1, 126.3, 127.1, 128.0, 128.1, 128.3, 136.1, 138.2, 138.3, 155.1, 170.0; $[\alpha]_D$ +81.2° (c 1, CH_2Cl_2); m/e 458 (M^+), 415, 367, 352, 337, 259, 246, 231, 217, 189, 91. Anal. calcd for $C_{28}H_{30}N_2O_4$: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.34; H, 6.59; N, 6.11. Found: C, 73.47; H, 6.60; N, 6.12.

(4R,5S,2'S)-1,5-Dimethyl-4-phenyl-3-(2'-benzyloxy-3'-phenylpropanoyl)imidazolidin-2-one 10a

Reaction from 2b and benzyl bromide affords 11.3 g (88) of 10a as a yiellow oil; diastereomeric ratio: 96.4; $[\alpha]_D$ -146.8° (c 1, CH_2Cl_2). Anal. calcd for $C_{27}H_{28}N_2O_3$: C, 75.68; H, 6.59; N, 6.54. Found: C, 75.80; H, 6.60; N, 6.53.

(4S,5R,2'R)-1,5-Dimethyl-4-phenyl-2-(2',3'-dibenzyloxypropanoyl)imidazolidin-2-one 10b

Reaction from 2b and benzyl chloromethyl ether affords 9.2 g (67%) of 10b as a colorless oil; diastereomeric ratio 97:3; $[\alpha]_D$ -81.7° (c 1, CH_2Cl_2. Anal. calcd for $C_{28}H_{30}N_2O_4$: C, 73.34; H, 6.59; N, 6.11. Found:C; 73.26; H, 6.58; N, 6.12.

General Procedure for the Reductive Cleavage of 3-Acylimidazolidin-2-ones 3a,b,c and 10a,b

A solution of 3-acylimidazolidin-2-ones 3a,b,c or 10a,b (20 mmol) in THF (20 ml) is slowly added under argon at 0 °C to a stirred solution of $LiBH_4$ (2M in THF; 20 mmol) and the mixture is stirred at 0 °C for 1 h. Afterwards the reaction is quenched by addition of 100 ml of saturated NH_4Cl solution and extracted with CH_2Cl_2. The residue is chromatographed on silica gel (cyclohexane:ethyl acetate 75:25) to yield the alcohols 4a,b,c or 11a,b. Further elution with ethyl acetate provides the imidazolidin-2-ones 1a or 1b in good yield.

(R)-2-Benzyloxy-3-phenylpropan-1-ol 4a

Reductive cleavage of 3a gives 4.0 g (84%) of 4a as a colorless oil; IR (neat): 3400 cm^{-1}; ^1H NMR: 2.46 (bs, 1H, OH), 2.75 (dd, 2H, J = 6, J = 3 Hz), 3.60 (m, 3H), 4.50 (s, 2H), 7.1 - 7.4 (m, $10H_{arom}$); ^{13}C NMR: 37.6, 63.7, 71.9, 80.9, 126.3, 127.8, 128.1, 128.4, 129.5, 129.8, 138.3; $[\alpha]_D$ +22.2° (c 1; CH_2Cl_2); m/e 242 (M^+), 211, 182, 151, 118, 105, 103, 91. Anal. calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.47; H, 7.47.

(R)-2-Benzyloxy-5-methyl-4-hexen-1-ol 4b

Reductive cleavage of 3b gives 3.6 g (82%) of 4b as a colorless oil; IR (neat): 3420 cm^{-1}; ^1H NMR: 1.6 (s, 3H), 1.7 (s, 3H), 2.25 (m, 2H), 2.65 (bs, 1H, OH), 3.5 (m, 3H), 4.56 (ABq, 2H, J = 9 Hz), 5.16 (t, 1H), 7.2 (m, $5H_{arom}$); ^{13}C NMR: 17.8, 25.8, 29.6, 64.2, 71.5, 79.9, 119.6, 127.8, 128.4, 134.0, 138.6; $[\alpha]_D$ -20.8° (c 1; CH_2Cl_2); m/e 220 (M^+), 202, 189, 181, 172, 161, 129, 105, 91. Anal. calcd for $C_{14}H_{20}O_2$: C, 76.33; H, 9.15. Found: C, 76.43; H, 9.16.

(S)-2,3-Dibenzyloxypropan-1-ol 4c

Reductive cleavage of 3c gives 4.6 g (85%) of 4c as an oil; IR (neat): 3440 cm^{-1}; ^1H NMR: 2.76 (bs, 1H, OH), 3.55 (m, 5H), 4.45 (s, 2H), 4.6 (s, 2H), 7.3 (m, $10H_{arom}$); ^{13}C NMR: 62.8, 70.2, 72.1, 73.5, 78.2, 127.7, 128.0, 128.4; $[\alpha]_D$ -15.8° (c 1, $CHCl_3$)(Lit.[7] -17.2° (c 1; $CHCl_3$)); m/e 181 (M^+ - 91), 107, 91, 79, 51. Anal. calcd for $C_{17}H_{20}O_3$: C, 74.97; H, 7.40. Found: C, 74.85; H, 7.39.

(S)-2-Benzyloxy-3-phenylpropan-1-ol 11a

Reductive cleavage of 10a gives 4.1 g (85%) of 11a as a colorless oil: $[\alpha]_D$ -22.6° (c 1; CH_2Cl_2). Anal. calcd for $C_{16}H_{18}O_2$: C, 79.31; H, 7.49. Found: C, 79.16; H, 7.47.

(R)-2,3-Dibenzyloxypropan-1-ol 11b

Reductive cleavage of 10b gives 4.7 g (86%) of 11b as a colorless oil; $[\alpha]_D$ +15.7° (c 1; $CHCl_3$)(Lit.[7] for S-isomer -17.2° (C 1; $CHCl_3$)). Anal. calcd for $C_{17}H_{20}O_2$: C, 74.97; H, 7.40. Found: C, 74.88; H, 7.41.

(R)-3-Phenyl-1,2-propanediol 5

A solution of 4a (2.4 g; 10 mmol) in methanol (40 ml) is degassed with nitrogen for 1 h; then 0.3 g of 10% Pd-C is added and hydrogen is introduced via a gas dispersion tube with stirring for 5 h. The catalyst is removed by filtration through Celite and the solvent is evaporated to give 1.4 g (95%) of 5 as a colorless oil: IR (neat): 3380 cm^{-1}; ^1H NMR: 2.7 (d, 2H, J = 6 Hz), 3.4 (bs, 2H, OH), 3.55 (m, 2H), 3.8 (m, 1H), 7.2 (m, $5H_{arom}$); ^{13}C NMR: 40.0, 66.2, 73.5, 126.9, 129.0, 129.8; $[\alpha]_D$ +33.2° (c 1; EtOH) (Lit.[5] for S-isomer -36° (c 1; EtOH)); m/e 138 (M^+ - H_2O), 121, 103, 91, 77. Anal. calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.10; H, 7.96.

(R)-2-Benzyloxy-1,4-butanediol 6

A solution of 4b (4.4 g; 20 mmol) in CH_2Cl_2 (60 ml) is cooled to -78 °C and then O_3 is introduced until starting material disappears. To the mixture Me_2S (5 ml) is added and the solvent is removed under reduced pressure. The residue is dissolved in dry ethanol (60 ml), $NaBH_4$ (3.8 g; 10 mmol) is added in small portions at 0 °C and the solution is stirred at 0 °C for 3 h and at room temperature for 1 h. The mixture is then diluted with water (30 ml) and continuously extracted with chloroform. The organic extract is dried and evaporated and the residue is chromatographed on silica gel (cyclohexane:ethyl acetate 2:8) to give 3.3 g (84%) of 6 as a colorless oil; IR (neat): 3350 cm^{-1}; ^1H NMR: 1.75 (m, 2H), 3.6 (bs, 2H, OH), 3.8 (m, 5H), 4.55 (s, 2H), 7.25 (m, $5H_{arom}$); ^{13}C NMR: 34.0, 59.3, 63.9, 71.6, 77.8, 127.9, 128.5, 129.6; $[\alpha]_D$ +20.6° (c 0.8; $CHCl_3$); m/e 196 (M^+), 107, 105, 91, 77. Anal. calcd for $C_{11}H_{16}O_3$: C, 67.32; H, 8.22. Found: C, 67.41; H, 8.21.

(R)-1,2,4-Butanetriol 7

By the same procedure above described for 5, this compound is obtained, starting from 6 (1.6 g; 8 mmol) in 93% yield (0.79 g) as a colorless oil: IR (neat): 3350 cm^{-1}; ^1H NMR (D_2O): 1.65 (m, 2H), 3.2 - 3.8 (m, 5H); ^{13}C NMR (CD_3OD): 36.9, 59.8, 67.3, 70.6; $[\alpha]_D$ +26.7° (c 1; MeOH)(Lit.[6] for S-isomer -29°(c 1.03; MeOH)); m/e 90 (M^+- H_2O), 78, 56, 54. Anal. calcd for $C_4H_{10}O_3$: C, 45.27; H, 9.50. Found: C, 45.34; H, 9.51.

(R)-1-Propanoyloxy-2,3-dibenzyloxypropane 8

A solution of the alcohol 4c (5.4 g; 20 mmol) in CH_2Cl_2 (40 ml) is cooled to 0 °C under nitrogen, triethylamine (2.0 g; 20 mmol) and N,N-dimethylaminopyridine (0.24 g; 2 mmol) are added and then propanoyl chloride (1.8 g; 20 mmol) in CH_2Cl_2 is dropped over a period of 30 min. The solution is allowed to warm to room temperature and then washed with water. The organic layer is evaporated and the residue chromatographed on silica gel (cyclohexane:ethyl acetate 9:1) to give 8 (6.0 g)

in 96% yield as a colorless oil: IR (neat): 1740 cm^{-1}; ^1H NMR: 1.05 (t, 3H, J = 6 Hz), 2.25 (q, 2H, J = 6 Hz), 3.5 - 4.3 (m, 5H), 4.5 (s, 2H), 4.65 (s, 2H), 7.25 (m, $10H_{arom}$); ^{13}C NMR: 9.1, 27.5, 63.7, 69.7, 72.2, 73.4, 75.9, 127.6, 128.3; $[\alpha]_D$ -14.8° (c 1.4; $CHCl_3$); m/e 237 (M^+-91), 207, 181, 131, 91. Anal. calcd. for $C_{20}H_{24}O_4$: C, 73.14; H, 7.37. Found: C, 73.07; H, 7.36.

(R)-1-Propanoyloxy-2,3-propanediol 9

By the same procedure above described for 5, this compound is obtained, starting from 8 (2.4 g; 10 mmol) in 92% yield (1.3 g) as a colorless oil: IR (neat): 3400, 1740 cm^{-1}; ^1H NMR: 1.2 (t, 3H, J = 6 Hz), 2.4 (q, 2H, J = 6 Hz), 3.65 (bs, 2H, OH), 3.8 (m, 3H), 4.2 (m, 2H); ^{13}C NMR: 9.1, 27.6, 63.7, 65.4, 70.5; $[\alpha]_D$ +14.9° (c 1; EtOH)(Lit.[9] for S-isomer -15.9° (c 10; EtOH)); m/e 148 (M^+), 130, 117, 75. Anal. calcd for $C_6H_{12}O_4$: C, 48.64; H, 8.16. Found: C, 48.69; H, 8.15.

(S)-3-Phenyl-1,2-propanediol 12

By the same procedure above described for 5, this compound is obtained, starting from 11a (2.4 g; 10 mmol) in 93% yield (1.4 g) as a colorless oil: $[\alpha]_D$ -33.1° (c 1; EtOH)(Lit.[5] -36° (c 1; EtOH)). Anal. calcd for $C_9H_{12}O_2$: C, 71.03; H, 7.95. Found: C, 71.11; H, 7.96.

(R)-1-Tridecyloxy-2,3-dibenzyloxypropane 13

To a solution of 11b (2.7 g; 10 mmol) in dry THF (20 ml) under argon, 4 ml of a solution of n-BuLi in hexanes (2.5 M; 10 mmol) is added dropwise at 0 °C for 10 min, the mixture is stirred at 0 °C for 1 h and dry HMPA (4 ml) is added at once. A solution of 1-iodotridecane (2.9 g; 10 mmol) in dry THF (20 ml) is slowly dropped in 30 min at 0 °C and then the reaction mixture is refluxed for 3 h. The mixture is diluted with water (15 ml) and extracted with ether. The organic extract is washed with water, dried and evaporated and the residue is chromatographed on silica gel (cyclohexane:ether 95:5) to give 13 (2.6 g) in 62% yield as a colorless oil; ^1H NMR: 0.95 (t, 3H), 1.35 (m, 22H), 1.7 (m, 2H), 3.3 - 3.9 (m, 7H), 4.55 (s, 2H), 4.75 (s, 2H), 7.3 (m, $10H_{arom}$); ^{13}C NMR: 14.1, 22.7, 26.2, 29.7, 32.0, 70.1, 71.0, 71.8, 72.3, 73.5, 77.4, 127.7, 127.8, 128.0, 128.3; $[\alpha]_D$ -1.1° (c 0.3; $CHCl_3$); m/e 454 (M^+), 363, 257, 181, 149, 105, 91. Anal. calcd for $C_{30}H_{46}O_3$: C, 79.24; H, 10.20. Found: C, 79.14; H, 10.18.

(S)-1-Tridecyloxy-2,3-propanediol 14

By the same procedure above described for 5, this compound is obtained, starting from 13 (2.05 g; 5 mmol) in 94% yield (1.3 g) as a white solid: m.p. 54 - 55 °C (Lit.[10] 57 °C); IR (nujol): 3370 cm^{-1}; ^1H NMR: 0.85 (t, 3H), 1.25 (m, 22H), 1.45 (m, 2H), 3.2 (m, 2H), 3.3 (m, 4H, 2 H + 2 OH), 3.5 (m, 2H), 3.75 (m, 1H); ^{13}C NMR: 14.2, 22.8, 26.2, 29.5, 29.7, 29.8, 32.1, 64.2, 71.1, 72.0, 72.4; $[\alpha]_D$ +2.28° (c 0.3; $CHCl_3$) (Lit.[10] +2.4° (c 0.02; $CHCl_3$)); m/e 274 (M^+), 256, 224, 213, 163, 122, 105, 83. Anal. calcd for $C_{16}H_{34}O_3$: C, 70.02; H, 12.50. Found, C, 69.91; H, 12.50.

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