transferred to a separatory funnel and shaken vigorously with 5% H_2O_2 (44 mL) for 4 min. The organic layer was washed twice with 10% Na_2SO_3, dried ($MgSO_4$), and filtered. Removal of the solvent in vacuo left a residue that was dissolved in a small volume of 20% EtOAc/hexanes. Flash chromatography (1.8 × 20 cm, 20–50% EtOAc/hexanes) furnished, after concentration in vacuo and high-vacuum drying (P_2O_5), 422 mg of the phosphine oxide **8c**: 65%; ^{1}H NMR δ 7.4–7.8 (10 H, m, Ar), 5.42 (1 H, m, 1 H-2'), 4.90 (1 H, br s, H-7), 4.66 (1 H, br s, H-7), 3.1–3.8 (3 H, m, 2 H-1', H-5), 1.05 (18 H, s, Me_2CSi); MS m/e 495 (M + 1, 1), 494 (M^+, 4), 449 (100).

25,25-(Ethylenedioxy)-27-norvitamin D_3 Triisopropylsilyl Ether (9a). A solution of *n*-butyllithium in hexane (135 μL, 1.6 M, 0.21 mmol) was added dropwise to a −70 °C cooled solution of the phosphine oxide **8c** (104 mg, 0.21 mmol) in THF (4 mL). The resulting reddish solution was stirred for 30 min followed by the slow addition of the ketone **7d** (50 mg, 0.162 mmol) in THF (1 mL). The resulting solution was stirred for 1 h and then warmed to room temperature (at −35 °C the solution turns orange, at −30 °C yellow, and at 0 °C colorless). Dilution with hexanes and concentration in vacuo afforded a residue that was transferred to a separatory funnel by means of hexanes and EtOAc/hexanes. The organic phase was washed twice with a saturated solution of $NaHCO_3$, dried (Na_2SO_4), and filtered. Removal of solvents in vacuo left a residue that was flash chromatographed (1.5 × 5 cm, hexanes–5% EtOAc/hexanes) to give, after concentration in vacuo and high-vacuum drying, 88 mg of **9a**: 93%, viscous colorless oil; ^{1}H NMR δ 6.17 and 6.02 (2 H, AB, J = 11.3 Hz, H-6, H-7), 5.01 (1 H, br s, *Z* H-19), 4.79 (1 H, br d, J = 2.7 Hz, *E*-H-19), 3.95 (4 H, m, OCH_2CH_2O), 1.32 (3 H, s, $C_{26}CH_3$), 1.06 (18 H, d, J = 1.3 Hz), 0.93 (3 H, d, J = 6 Hz, $C_{21}CH_3$), 0.5 (3 H, s, $C_{18}CH_3$); MS, m/e 584 (M^+, 5), 569 (M − 15, 75), 398 (100).

25-Ketovitamin D_3 (9c). An aqueous solution of HF (48%, 4 drops) was added to a solution of the protected vitamin **9a** (38 mg, 0.065 mmol) in acetonitrile (10 mL). The resulting solution was stirred at room temperature in the dark for 3 h. Concentration in vacuo afforded a residue that was diluted with ether (20 mL), transferred to a separatory funnel, and washed with a saturated aqueous solution of $NaHCO_3$ (10 mL). The organic phase was dried ($MgSO_4$), filtered, and concentrated in vacuo. The crude residue was flash chromatographed (15% EtOAc/hexanes) to give, after concentration in vacuo and high-vacuum drying, 22 mg of ketal **9b** (81%): MS, m/e 428 (M^+, 3), 413 (M − 15, 2), 410 (M − 18), 43 (100); HRMS calcd for $C_{28}H_{44}O_3$ 428.3292, found 428.3237. A solution of the above hydroxy ketal **9b** (19 mg, 0.044 mmol) in MeOH (10 mL) was stirred with AG 50W-X4 200–400-mesh cation-exchange resin (1.3 g, prewashed with MeOH) at room temperature for 2.5 h in the dark. Filtration and concentration in vacuo afforded a residue that was diluted with $CHCl_3$ and transferred to a separatory funnel and shaken with water. The water phase was further extracted with $CHCl_3$, and the combined organic extracts were dried ($MgSO_4$), filtered, and concentrated under reduced pressure. Flash chromatography of the residue (20–40% Et_2O/hexanes) afforded, after removal of solvents under reduced pressure and high-vacuum drying, 16 mg of the desired 25-ketovitamin D_3 (**9c**), 93%. Alternatively, this compound was obtained as follows. A solution of **9a** (30 mg, 0.051 mmol) in MeOH (15 mL) was stirred with AG 50W-X4 resin (1.8 g) at room temperature for 20 h in the dark. Filtration, concentration in vacuo, dilution with EtOAc, washing twice with brine, drying ($MgSO_4$), and concentration in vacuo afforded a residue that was flash chromatographed (5–20% EtOAc/hexanes) to give, after concentration in vacuo and high-vacuum drying, 15 mg of 25-ketovitamin D_3 (**9c**)[15] in 79% yield: ^{1}H NMR δ 6.23 and 6.03 (2 H, AB, J = 11.35 Hz, H-6, H-7), 5.05 (1 H, d, J = 2.60 Hz, *Z*-H-19), 4.81 (1 H, d, J = 2.60 Hz, *E*-H-19), 3.95 (1 H, m, H-3), 2.14 (3 H, s, CH_3CO), 1.25 (s, OH), 0.95 (3 H, d, J = 6.22 Hz, $C_{21}CH_3$), 0.53 (3 H, s, $C_{18}CH_3$); UV (Et_2O) λ_{max} 266 nm (ϵ 18 300), λ_{min} 233 nm; MS, m/e 384 (M^+ 9), 366 (M − 18, 1), 351 (M − 18 − 15, 10), 325 (3), 271 (4), 253 (6), 171 (10), 159 (25), 158 (27), 157 (17), 145 (30), 143 (33), 136 (50), 135 (26), 133 (20), 131 (30), 129 (27), 121 (20), 119 (47), 118 (83), 117 (37), 115 (20), 113 (14), 111 (16), 109 (24), 107 (36), 105 (53), 97 (20), 95 (63), 94 (16), 93 (56), 92 (23), 91 (100).

25-Hydroxyvitamin D_3 (1b). A solution of methyllithium in diethyl ether (0.12 mL, 1.2 M) was added dropwise to a −80 °C cooled solution of 25-ketovitamin D_3 (15 mg, 0.039 mmol) in diethyl ether (4 mL). After stirring for 20 min, the reaction was quenched with water (2 mL). The ether was removed in vacuo, and the residue was diluted with $CHCl_3$ and transferred to a separatory funnel. Addition of water and shaking produced an organic phase that was dried ($MgSO_4$), filtered, and concentrated in vacuo. The resulting crude was flash chromatographed (25% EtOAc/hexanes) to give 14 mg of 25-hydroxyvitamin D_3 (**1b**)[16] in 90% yield.

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Synthesis of Enantiomerically Pure 24-Alkylsterol Side Chains, in Both Enantiomeric Forms, Starting from (*R*)-(+)-Limonene†

Francesco Nicotra, Luigi Panza, Fiamma Ronchetti, Giovanni Russo,* and Lucio Toma

Dipartimento di Chimica Organica e Industriale dell'Università and Centro di Studio per le Sostanze Organiche Naturali del CNR, 20133 Milano, Italy

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Three couples of enantiomeric synthons corresponding to six 24-alkylsterol side chains, (*R*)- and (*S*)-1-bromo-3,4-dimethylpentane, (*R*)- and (*S*)-1-bromo-3-ethyl-4-methylpentane, and (*R*)- and (*S*)-5-(acetyloxy)-1-bromo-3-(1-methylethyl)pentane, were synthesized from the same chiral intermediate, (*R*)-5-(acyloxy)-3-(1-methylethyl)pentan-1-ol, readily obtainable from (*R*)-(+)-limonene.

The stereospecificity of natural chemoreceptors requires that natural compounds obtained by synthesis have an optical purity as near as possible to 100%. As starting material for the synthesis of such optically pure compounds, natural products like carbohydrates,[1] terpenes,[2] hydroxy acids,[3] and amino acids,[4] which are easily available

† This paper is dedicated to the memory of the late Prof. L. Canonica.

(1) (a) Vasella, A. In "Modern Synthetic Methods"; Scheffold, R., Ed.; Salle and Sauerländer: Germany, 1980; p 173. (b) Hanessian, S. "Total Synthesis of Natural Products: the 'Chiron Approach'"; Pergamon Press: London, 1983.

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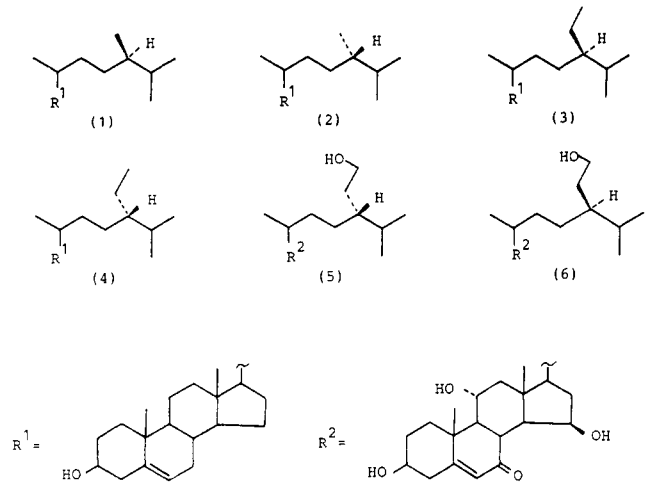
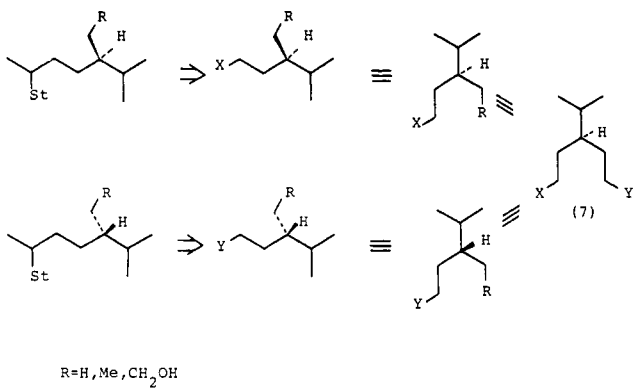
Scheme I



Scheme II



R=H,Me,CH_2OH

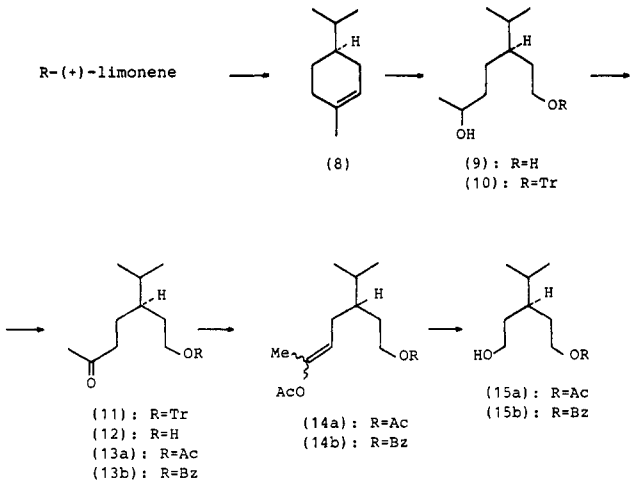
and cheap chiral molecules, can be used. However such molecules often exist only in one enantiomeric form so that if both enantiomers of a natural product are required two independent syntheses must be planned.

The problem could be solved more efficiently if methods for the synthesis of both enantiomers of a target molecule starting from the same chiral precursor could be developed. One such method consists in the elaboration of a chiral intermediate such as **7** in Scheme II, the chirality of which relies on the circumstance that two identical functions which are enantiotopic in the unprotected molecule are protected in different ways. The alternative elaboration of these two groups then leads to the two enantiomeric targets.

As an application of the above concept, we describe here the synthesis, from a chiral intermediate such as **7**, of couples of enantiomeric synthons which are equivalent to the C(22)–C(29) fragment of the 24-alkylsterols, campesterol (**1**), sitosterol (**3**), and oogoniol (**5**) and of their C-24 epimers dihydrobrassicasterol (**2**), clionasterol (**4**), and 24-*epi*-oogoniol (**6**) (Scheme I). The required configuration at the carbon atom which will become the C-24 of the sterols is obtained by selective elaboration of the two functionalized ends (X and Y).

In the case corresponding to **7** with X = OH and Y = OCOR, the key synthon was the hydroxy ester **15**, obtained

Scheme III



from the cheap, optically pure (*R*)-(+)-limonene according to Scheme III.

(*R*)-(+)-Limonene was converted[2a] to (*R*)-4-(1-methylethyl)-1-methylcyclohexene (**8**), which was submitted to ozonolysis at −78 °C followed by reduction with $NaBH_4$. The obtained diol **9** was selectively tritylated and oxidized with pyridinium dichromate to give the ketone **11**. Detritylation and subsequent acetylation (or benzoylation) afforded **13**, which was enolized under thermodynamic control yielding a mixture of *E* and *Z* isomers (**14**). Ozonolysis followed by $NaBH_4$ reduction gave (*R*)-5-(acetyloxy)-3-(1-methylethyl)pentan-1-ol (**15a**) [or (*R*)-5-(benzoyloxy)-3-(1-methylethyl)pentan-1-ol (**15b**)][5] from which, by elaboration either of the hydroxy or the acyloxy function, all the sterol side chains can be obtained.

(*R*)-1-Bromo-3,4-dimethylpentane (**21**) and (*S*)-1-bromo-3,4-dimethylpentane (**25**) were obtained from the compound **15b** according to Scheme IV. In the former case tritylation followed by alkaline hydrolysis and bromination with CBr_4/PPh_3 gave the bromo ether **18** which was detritylated, oxidized with pyridinium dichromate, and decarbonylated with Wilkinson catalyst to give the bromide **21**. In the latter case the compound **25** was obtained by bromination, ester cleavage, oxidation, and decarbonylation.

The couple (*R*)-1-bromo-3-ethyl-4-methylpentane (**27**) and (*S*)-1-bromo-3-ethyl-4-methylpentane (**32**) were obtained from **15b** with the procedure illustrated in Scheme V. Tosylation and reduction of compound **15b** gave the alcohol **26**, which on treatment with CBr_4/PPh_3 furnished the bromide **27**. In turn, protection of the alcoholic function of **15b** as tetrahydropyranyl ether followed by hydrolysis of the ester function, tosylation, $LiAlH_4$ reduction, cleavage of the THP protection, and bromination gave the enantiomeric synthon **32**.

The synthesis of (*S*)-5-(acetyloxy)-1-bromo-3-(1-methylethyl)pentane (**33**) and of (*R*)-5-(acetyloxy)-1-bromo-3-(1-methylethyl)pentane (**34**) is reported in scheme VI: the *S* isomer (**33**) was obtained in one step by bro-

(2) (a) White, J. D.; Ruppert, J. F.; Avery, M. A.; Torii, S.; Nokami, J. *J. Am. Chem. Soc.* **1981**, *103*, 1813. (b) Jackman, L. M.; Webb, R. L.; Yick, H. C. *J. Org. Chem.* **1982**, *47*, 1824. (c) Kitahara T.; Matsuoka, T., Katayama, M.; Marumo, S.; Mori, K. *Tetrahedron Lett.* **1984**, *25*, 4685.

(3) Seebach, D.; Hungerbüler, E. In "Modern Synthetic Methods"; Scheffold, R., Ed.; Salle and Sauerländer: Germany, 1980; p 91.

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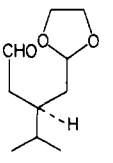
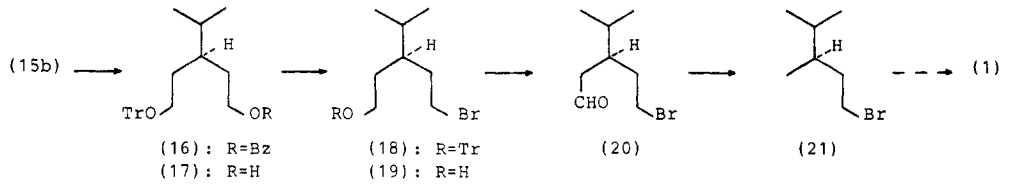
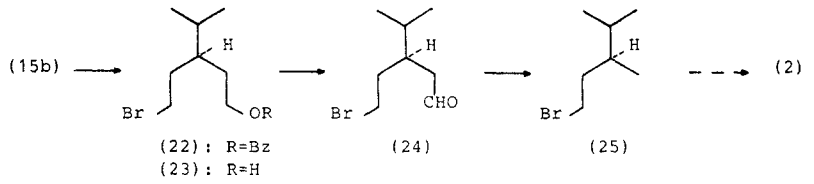
(5) A similar intermediate



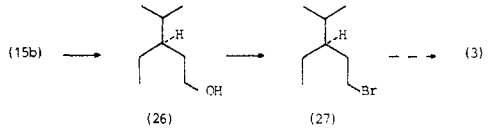
obtained from (*R*)-(−)-carvone, was utilized for the synthesis of both enantiomers of sclerosporin.[2c]

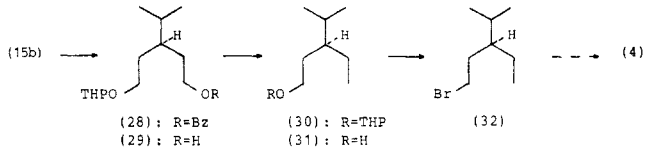
Scheme IV



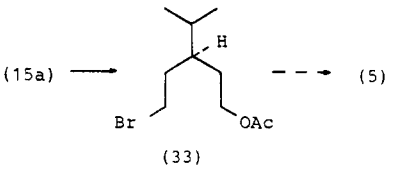


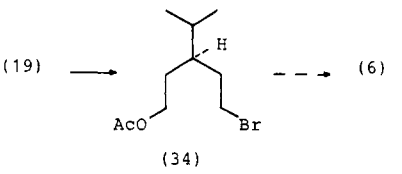
Scheme V





Scheme VI





mination of the intermediate **15a**, while acetylation of the compound **19** afforded the *R* enantiomer (**34**).

As several procedures are known[6] for coupling a bromide with a steroidal substrate, like pregnenolone, to give a sterol with the natural configuration at C-20, our six bromides can be utilized to afford the six desired sterols campesterol (**1**), dihydrobrassicasterol (**2**), sitosterol (**3**), clionasterol (**4**), and oogoniol (**5**) and its C-24 epimer (**6**).

Experimental Section

^{1}H NMR spectra were recorded in deuteriochloroform containing Me_4Si as an internal standard. Analytical TLC was carried out on Merck 60 F_{254} silica gel plates (0.25 mm thickness), and the spots were detected either by a UV lamp or by spraying with 50% aqueous H_2SO_4 and heating at 110 °C for 5 min. Column chromatography was performed with Merck 60 silica gel (70–230 mesh) and elution with mixtures of hexane–ethyl acetate of varying composition. Workup refers to dilution with water, extraction with an organic solvent, washing to neutrality, drying over Na_2SO_4, filtration, and evaporation under reduced pressure. All compounds gave satisfactory elemental analyses.

(3*R*,6*RS*)-3-(1-Methylethyl)heptane-1,6-diol (9). A solution of 26.0 g (188 mmol) of (4*R*)-1-methyl-4-(1-methylethyl)cyclohexene[2a] (**8**) in 200 mL of dry methanol and 50 mL of dry methylene chloride was submitted to ozonolysis at −78 °C until 1 mol equiv of O_3 was absorbed. Nitrogen was then passed through the solution, 7.15 g of $NaBH_4$ was added, and the mixture was stirred for 1 h at −78 °C. A second portion of $NaBH_4$ (7.15 g) was then added, and the temperature was slowly increased to room temperature. The mixture was stirred overnight, then treated with 5% HCl, and evaporated under reduced pressure. Workup afforded a crude product, which by chromatography on silica gel gave 26.2 g (80%) of the compound **9** as an oily product: $[\alpha]_D$ +4.5° (*c* 2.8, $CHCl_3$); ^{1}H NMR (80 MHz, $CDCl_3$) δ 0.87 and 0.88 (6 H, 2 d, J = 7 Hz, $CH(CH_3)_2$), 1.20 (3 H, d, J = 6 Hz, CH_3CHOH), 1.2–1.7 (8 H, m), 2.5 (2 H, s, OH), 3.66 (2 H, t, J = 7 Hz, CH_2OH), 3.7 (1 H, m, $CHOH$).

(3*R*,6*RS*)-5-(1-Methylethyl)-7-[(triphenylmethyl)oxy]-heptan-2-ol (10). Compound **9** (25.2 g, 145 mmol) was dissolved in 200 mL of dry pyridine, and 44.6 g of triphenylmethyl chloride was added. The mixture was left at room temperature overnight, and then workup afforded 58.4 g (97%) of the title compound as an oily product: $[\alpha]_D$ +4.3° (*c* 1.4, $CHCl_3$); ^{1}H NMR (80 MHz, $CDCl_3$) δ 0.83 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 1.15 (3 H, d, J = 7 Hz, CH_3CHOH), 1.1–1.7 (8 H, m), 2.5 (1 H, s, OH), 3.09 (2 H, t, J = 7 Hz, CH_2OTr), 3.7 (1 H, m, $CHOH$), 7.1–7.7 (15 H, m).

(*R*)-5-(1-Methylethyl)-7-[(triphenylmethyl)oxy]heptan-2-one (11). Compound **10** (54.1 g, 260 mequiv) was dissolved in 150 mL of dry methylene chloride, and 47.1 g (780 meq) of pyridinium dichromate was added. The mixture was stirred at room temperature for 48 h, then diluted with ethyl ether (300 mL), and filtered; the solvent was evaporated and the crude material passed through a short column of silica gel eluted with ethyl ether. The ketone **11** (52.2 g, 97%) was obtained as an oily product: $[\alpha]_D$ +20.0° (*c* 1.9, $CHCl_3$); ^{1}H NMR (80 MHz, $CDCl_3$) δ 0.80 (6 H, d, J = 7 Hz, $CH(CH_3)_2$), 1.1–1.7 (6 H, m), 2.08 (3 H, s, CH_3CO), 2.33 (2 H, t, J = 7 Hz, CH_2CO), 3.08 (2 H, t, J = 7 Hz, CH_2OTr), 7.1–7.7 (15 H, m).

(*R*)-5-(1-Methylethyl)-7-hydroxyheptan-2-one (12). Compound **11** (36.5 g, 88 mmol) was dissolved in 200 mL of methanol, and 335 mg of *p*-toluenesulfonic acid was added. The mixture was stirred for 24 h at room temperature while a white crystalline

(6) Piatak, D. M.; Wicha, J. *Chem. Rev.* **1978**, *78*, 199. (b) Redpath, J.; Zeelen, F. J. *Chem. Soc. Rev.* **1983**, *12*, 75. (c) Schmidt, J. P.; Piraux, M.; Pilette, J. F. *J. Org. Chem.* **1975**, *40*, 1586. (d) McMorris, T. C.; Schow, S. R. *Ibid.* **1976**, *41*, 3759. (e) Schow, S. R.; McMorris, T. C. *Ibid.* **1979**, *44*, 3760. (f) Fürst, A.; Labler, L.; Meier, W. *Helv. Chim. Acta* **1982**, *65*, 1499. (g) Ikan, R.; Markus, A.; Bergman, E. D. *Steroids* **1970**, *16*, 517. (h) Ikan, R.; Markus, A.; Bergman, E. D. *J. Org. Chem.* **1971**, *36*, 3944. (i) Joseph, J. M.; Nes, W. R. *J. Chem. Soc., Chem. Commun.* **1981**, 367.

product precipitated (methyl triphenylmethyl ether). The solid was filtered off, $NaHCO_3$ was added to neutralize the acidity of the catalyst, and workup afforded a crude mixture from which, by silica gel column, 4.38 g of unreacted material plus 11.4 g (85%) of the hydroxy ketone **12** as an oily product were obtained: $[\alpha]_D$ +14.1° (*c* 1.7, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 and 0.88 (6 H, 2 d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.7 (6 H, m), 2.14 (3 H, s, CH_3CO), 2.47 (1 H, s, O*H*), 2.44 (2 H, t, *J* = 7 Hz, CH_2CO), 3.68 (2 H, t, *J* = 7 Hz, CH_2OH).

(*R*)-7-(Acetyloxy)-5-(1-methylethyl)heptan-2-one (13a). Hydroxy ketone **12** (780 mg, 4.53 mmol) was dissolved into 8 mL of dry pyridine, and 0.8 mL of acetic anhydride was added. The mixture was heated at 50 °C for 3 h, and then 100 mL of H_2O was added. Workup gave 920 mg (95%) of the compound **13a** as an oily product: $[\alpha]_D$ +5.1° (*c* 1.8, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.1–1.9 (6 H, m), 2.06 (3 H, s, CH_3COO), 2.14 (3 H, s, CH_3CO), 2.47 (2 H, t, *J* = 7 Hz, CH_2CO), 4.09 (2 H, t, *J* = 7 Hz, CH_2OAc).

(*R*)-7-(Benzoyloxy)-5-(1-methylethyl)heptan-2-one (13b). Hydroxy ketone **12** (4.47 g, 26 mmol) was dissolved in 30 mL of dry pyridine, and 3.9 mL of freshly distilled benzoyl chloride was added. The mixture was left at room temperature overnight and then was diluted with 300 mL of H_2O. Workup gave 6.46 g (90%) of the compound **13b** as an oily product: $[\alpha]_D$ +6.5° (*c* 1.9, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.88 and 0.89 (6 H, 2 d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.9 (6 H, m), 2.14 (3 H, s, CH_3CO), 2.48 (2 H, t, *J* = 7 Hz, CH_2CO), 4.35 (2 H, t, *J* = 7 Hz, CH_2OBz), 7.3–8.2 (5 H, m).

(*R*)-2,7-Bis(acetyloxy)-5-(1-methylethyl)-2-heptene (14a). Ketone **13a** (920 mg, 4.30 mmol) was dissolved in 1 mL of acetic anhydride, 11 mg of *p*-toluenesulfonic acid was added, and the mixture was refluxed for 48 h.[7] The mixture was cooled (0 °C), neutralized with a saturated solution of $NaHCO_3$, and worked up. The crude product was a mixture of the starting material and the acetates **14a**. This mixture was separated by a silica gel column, giving 360 mg of unreacted starting material and 560 mg (84%) of the compound **14a** as a mixture of *E* and *Z* isomers: $[\alpha]_D$ +16.5° (*c* 2.1, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.7 (6 H, m), 1.88 (3 H, brs, $CH_3C{=}$), 2.03 (3 H, s, CH_3COOCH_2), 2.09 and 2.14 (3 H, 2 s, in a 1:2 ratio, $CH_3COOC{=}$), 4.08 (2 H, t, *J* = 7 Hz, CH_2OAc), 4.7–5.1 (1 H, m, $CH{=}C$).

(*R*)-2-(Acetyloxy)-7-(benzoyloxy)-5-(1-methylethyl)-2-heptene (14b). Ketone **13b** (6.32 g, 22.3 mmol) treated as above gave 2.90 g of unreacted starting material and 3.51 g (89%) of an *E*–*Z* mixture of the enol acetates **14b**: $[\alpha]_D$ +23.3° (*c* 1.9, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.88 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–2.0 (6 H, m), 1.89 (3 H, brs, $CH_3C{=}$), 2.08 and 2.13 (3 H, 2 s in a 1:2 ratio, $CH_3COOC{=}$), 4.34 (2 H, t, *J* = 7 Hz, CH_2OBz), 4.7–5.2 (1 H, m, $CH{=}C$), 7.3–8.2 (5 H, m).

(*R*)-5-(Acetyloxy)-3-(1-methylethyl)pentan-1-ol (15a). Enol acetates **14a** (460 mg, 1.80 mmol) were dissolved in 10 mL of dry methanol and 2.5 mL of dry methylene chloride. Ozone was bubbled into the solution until 1 mol equiv of O_3 was absorbed and the enol acetates disappeared (monitored by TLC). Nitrogen was then bubbled into the solution, and 68 mg of $NaBH_4$ was added at −78 °C. After 1 h a further addition of 68 mg of $NaBH_4$ was made, and the mixture was allowed to slowly reach room temperature and was stirred overnight. H_2O (15 mL) was then added, and workup afforded 310 mg (92%) of the hydroxy acetate **15a** as an oily product: $[\alpha]_D$ −0.1° (*c* 15.0, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.90 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.8 (7 H, m), 2.06 (3 H, s, CH_3COO), 3.69 (2 H, t, *J* = 7 Hz, CH_2OH), 4.10 (2 H, t, *J* = 7 Hz, CH_2OAc).

(*R*)-5-(Benzoyloxy)-3-(1-methylethyl)pentan-1-ol (15b). Enol acetates **14b** (3.50 g, 11.0 mmol), treated as above, gave 2.45 g (89%) of the compound **15b** as an oily product: $[\alpha]_D$ +0.9° (*c* 11.0, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.90 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.9 (6 H, m), 2.50 (1 H, s, O*H*), 3.69 (2 H, t, *J* = 7 Hz, CH_2OH), 4.35 (2 H, t, *J* = 7 Hz, CH_2OBz), 7.3–8.2 (5 H, m).

(*R*)-1-(Benzoyloxy)-3-(1-methylethyl)-5-[(triphenylmethyl)oxy]pentane (16). Compound **15b** (550 mg, 2.2 mol) was dissolved in 5 mL of dry pyridine, 674 mg of triphenylmethyl chloride was added, and the solution was kept at room temperature overnight. Usual workup afforded 1.01 g (93%) of the compound **16** as an oily product: $[\alpha]_D$ +1.0° (*c* 9.8, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.85 and 0.87 (6 H, 2 d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.8 (6 H, m), 3.12 (2 H, t, *J* = 7 Hz, CH_2OTr), 4.27 (2 H, t, *J* = 7 Hz, CH_2OBz), 7.2–8.2 (20 H, m).

(*S*)-3-(1-Methylethyl)-5-[(triphenylmethyl)oxy]pentan-1-ol (17). Compound **16** (980 mg, 2.0 mmol) was dissolved into 5% KOH/MeOH (5 mL), and the mixture was stirred at room temperature overnight. Usual workup afforded 734 mg (95%) of the title compound as an oily product: $[\alpha]_D$ +0.5° (*c* 7.0, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.80 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.1–1.8 (7 H, m), 3.10 (2 H, t, *J* = 7 Hz, CH_2OTr), 3.56 (2 H, t, *J* = 7 Hz, CH_2OH), 7.2–7.7 (15 H, m).

(*R*)-1-Bromo-3-(1-methylethyl)-5-[(triphenylmethyl)-oxy]pentane (18). Compound **17** (690 mg, 1.78 mmol) was dissolved in 10 mL of dry ethyl ether under nitrogen atmosphere, and 932 mg of triphenylphosphine and 1.18 g of tetrabromomethane were added.[8] The solution became pale yellow, and a white solid precipitated. After 90 min the white powder was filtered off and the solution evaporated. Pure compound **18** (530 mg, 66%) was obtained by column chromatography as an oily product: $[\alpha]_D$ +1.6° (*c* 0.8, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.80 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.2–1.9 (6 H, m), 3.10 (2 H, t, *J* = 7 Hz, CH_2OTr), 3.32 (2 H, t, *J* = 7 Hz, CH_2Br), 7.2–7.7 (15 H, m).

(*R*)-5-Bromo-3-(1-methylethyl)pentan-1-ol (19). Compound **18** (450 mg, 1 mmol) was dissolved in 5 mL of methanol, and 5 mg of *p*-toluenesulfonic acid was added. The solution was stirred at room temperature for 3 h, 10 mg of $NaHCO_3$ was added, the solid was filtered off, the solvent was evaporated, and the crude product was submitted to column chromatography. Bromo alcohol **19** (194 mg, 93%) was obtained as oily product: $[\alpha]_D$ +0.9° (*c* 8.0, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.85 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (7 H, m), 3.43 (2 H, t, *J* = 7 Hz, CH_2Br), 3.67 (2 H, t, *J* = 7 Hz, CH_2OH).

(*R*)-5-Bromo-3-(1-methylethyl)pentanal (20). Compound **19** (190 mg, 0.91 mmol) was dissolved in 2 mL of dry methylene chloride, and 680 mg of pyridinium dichromate was added. The solution was stirred overnight and then was filtered over a short silica gel column eluted with ethyl ether. Aldehyde **20** (169 mg, 89%) was obtained as an oily product: $[\alpha]_D$ +8.2° (*c* 7.8, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 and 0.88 (6 H, 2 d, *J* = 7 Hz, $CH(CH_3)_2$), 1.4–2.2 (4 H, m), 2.2–2.5 (2 H, m, CH_2CHO), 3.40 (2 H, brt, *J* = 7 Hz, CH_2Br), 9.77 (1 H, t, *J* = 2 Hz, C*H*O).

(*R*)-1-Bromo-3,4-dimethylpentane (21). Compound **20** (102 mg, 0.49 mmol) was dissolved in 5 mL of dry methylene chloride, and 456 mg of the Wilkinson catalyst was added. The mixture was stirred under nitrogen atmosphere for 48 h, then the solution was filtered, the solid material was washed with ethyl ether, the filtrate was lyophilized, and the crude product was submitted to column chromatography, yielding 31 mg (35%) of the bromide **21**: $[\alpha]_D$ +10.0° (*c* 2.4, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.82, 0.86, and 0.88 (9 H, 3 d, *J* = 7.0 Hz, CH_3), 1.2–2.0 (4 H, m), 3.36 (1 H, ddd, *J* = 9.5, 7.0, 5 Hz, CH_ABr), 3.48 (1 H, ddd, *J* = 9.5, 8.0, and 5.0 Hz, CH_BBr).

(*S*)-1-(Benzoyloxy)-5-bromo-3-(1-methylethyl)pentane (22). Compound **15b** (1.14 g, 4.56 mmol) was dissolved in 20 mL of dry ethyl ether under nitrogen atmosphere. Tetrabromomethane (3.03 g) and 2.39 g of triphenylphosphine (2 mol equiv each) were added. The mixture was stirred at room temperature for 15 min while a white powder formed. The solid was filtered off, the filtrate was evaporated under reduced pressure, and the crude product was chromatographed. The bromo derivative **22** (1.20 g, 84%) was obtained as an oily product: $[\alpha]_D$ −1.0° (*c* 9.9, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.89 (6 H, d, *J* = 7.0 Hz, $(CH_3)_2$), 1.4–2.0 (6 H, m), 3.44 (2 H, t, *J* = 7 Hz, CH_2Br), 4.35 (2 H, t, *J* = 7 Hz, CH_2OBz), 7.3–8.2 (5 H, m).

(*S*)-5-Bromo-3-(1-methylethyl)pentan-1-ol (23). Compound **22** (682 mg, 2.18 mmol) was dissolved in 10 mL of dry toluene, and the solution was cooled at −78 °C. A 1.2 M solution (2.72 mL) of diisopropylaluminium hydride was added, and the mixture

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was stirred for 2 h and then allowed to reach room temperature. A saturated solution (10 mL) of NH_4Cl was added; the workup afforded 328 mg (72%) of the bromo alcohol **23** as an oily product: $[\alpha]_D$ −0.8° (*c* 8.0, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (7 H, m), 3.42 (2 H, t, *J* = 7 Hz, CH_2Br), 3.66 (2 H, t, *J* = 7 Hz, CH_2OH).

(*S*)-5-Bromo-3-(1-methylethyl)pentanal (24). Compound **23** (297 mg, 1.42 mmol) treated as described for its enantiomer **19** yielded 265 mg (90%) of the bromo aldehyde **24** as an oily product: $[\alpha]_D$ −8.4° (*c* 8.5, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.86 and 0.88 (6 H, 2 d, *J* = 7 Hz, $CH(CH_3)_2$), 1.4–2.2 (4 H, m), 2.2–2.5 (2 H, m, CH_2CHO), 3.40 (2 H, brt, *J* = 7 Hz, CH_2Br), 9.78 (1 H, t, *J* = 2 Hz, CHO).

(*S*)-1-Bromo-3,4-dimethylpentane (25). Compound **24** (240 mg, 1.16 mmol) treated as described for the compound **20** gave 116 mg (45%) of the bromide **25**: $[\alpha]_D$ −10.1° (*c* 1.8, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.82, 0.86, and 0.88 (9 H, 3 d, *J* = 7.0 Hz, CH_3), 1.2–2.0 (4 H, m), 3.37 (1 H, ddd, *J* = 9.5, 8.0, and 7.5 Hz, CH_ABr), 3.48 (1 H, ddd, *J* = 9.5, 8.0, 5.0 Hz, CH_BBr).

(*R*)-3-Ethyl-4-methylpentan-1-ol (26). Compound **15b** (400 mg, 1.60 mmol) was dissolved in 4 mL of dry pyridine, and 460 mg of *p*-toluenesulfonyl chloride was added at 0 °C. The mixture was kept overnight in refrigerator, and then workup afforded 640 mg of crude tosylate, which was directly submitted to reduction with 24 mg of $LiAlH_4$ in 10 mL of dry ethyl ether. The mixture was stirred at room temperature for 1.5 h, then the excess of $LiAlH_4$ was destroyed by careful addition of 3% HCl, and the white powder was eliminated by filtration over a short column of Celite. The alcohol **26** (126 mg, 61%) was obtained: $[\alpha]_D$ +6.9° (*c* 5.2, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.85 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 0.89 (3 H, t, *J* = 7 Hz, CH_2CH_3), 1.1–1.5 (6 H, m), 1.6 (1 H, s, OH), 3.65 (2 H, t, *J* = 7 Hz, CH_2OH).

(*R*)-1-Bromo-3-ethyl-4-methylpentane (27). Compound **26** (108 mg, 0.83 mmol) was brominated according to the usual procedure. The bromide **27** (133 mg, 83%) was obtained: $[\alpha]_D$ +7.3° (*c* 5.4, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (3 H, d, *J* = 6.8 Hz, $CH(CH_3)_A$), 0.855 (3 H, d, *J* = 6.8 Hz, $CH(CH_3)_B$), 0.88 (3 H, t, *J* = 6.9 Hz, CH_2CH_3), 1.1–2.0 (6 H, m), 3.39 (1 H, ddd, *J* = 9.7, 8.1, 7.1 Hz, CH_ABr), 3.44 (1 H, ddd, *J* = 9.7, 8.4, 6.5 Hz, CH_BBr).

(*R*)-1-(Benzoyloxy)-3-(1-methylethyl)-5-(tetrahydropyranyloxy)pentane (28). Compound **15b** (1.47 g, 5.88 mmol) was dissolved in 30 mL of dry methylene chloride, and 2.1 mL of 3,4-dihydropyran and 10 mg of *p*-toluenesulfonic acid were added. The mixture was stirred for 1 h at room temperature, then 50 mL of a saturated solution of $NaHCO_3$ was added, and the solution was worked up. The crude product was chromatographed on a silica gel column, yielding 1.75 g (89%) of the compound (**28**) as an oily product: $[\alpha]_D$ +2.3° (*c* 11.2, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.89 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (12 H, m), 3.3–4.0 (4 H, m, CH_2O), 4.36 (2 H, t, *J* = 7 Hz, CH_2OBz), 4.55 (1 H, m, OCHO), 7.3–8.2 (5 H, m).

(*S*)-3-(1-Methylethyl)-5-(tetrahydropyranyloxy)pentan-1-ol (29). Compound **28** (1.53 g, 4.58 mmol) was dissolved in 50 mL of a solution of NaOH in methanol (1%). The mixture was left at room temperature overnight and then worked up. The alcohol **29** (980 mg, 93%) was obtained: $[\alpha]_D$ +5.0° (*c* 11.4, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.88 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (12 H, m), 2.00 (1 H, s, OH), 3.3–4.0 (6 H, m, CH_2O), 4.54 (1 H, m, OCHO).

(*S*)-3-Ethyl-4-methyl-1-(tetrahydropyranyloxy)pentane (30). Compound **29** (782 mg, 3.40 mmol) treated as described for the synthesis of the compound **26** gave 555 mg (75%) of the tetrahydropyranyl ether **30** as an oily product: $[\alpha]_D$ −3.8° (*c* 10.5, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.83 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 0.88 (3 H, t, *J* = 7 Hz, CH_2CH_3), 1.1–1.9 (12 H, m), 3.3–4.0 (4 H, m, CH_2O), 4.56 (1 H, m, OCHO).

(*S*)-3-Ethyl-4-methylpentan-1-ol (31). Compound **30** (440 mg, 2.06 mmol) was dissolved in 4 mL of methanol, and 400 mg of Dowex 50W-X8 was added.[9] The mixture was stirred for 1 h, the resin was filtered off, and 210 mg (79%) of the alcohol **31** was obtained: $[\alpha]_D$ −6.8° (*c* 12.8, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.85 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 0.90 (3 H, t, *J* = 7 Hz, CH_2CH_3), 1.1–1.5 (6 H, m), 1.6 (1 H, OH), 3.66 (2 H, t, *J* = 7 Hz, CH_2OH).

(*S*)-1-Bromo-3-ethyl-4-methylpentane (32). The compound **31** (160 mg, 1.23 mmol) was brominated with the usual procedure. Bromide **32** (195 mg, 82%) was obtained: $[\alpha]_D$ −7.2° (*c* 11.3, $CHCl_3$); ^1H NMR (200 MHz, $CDCl_3$) δ 0.84 (3 H, d, *J* = 6.8 Hz, $CH(CH_3)_A$), 0.85 (3 H, d, *J* = 6.8 Hz, $CH(CH_3)_B$), 0.88 (3 H, t, *J* = 6.9 Hz, CH_2CH_3), 1.1–2.0 (6 H, m), 3.39 (1 H, ddd, *J* = 9.6, 8.0, 7.1 Hz, CH_ABr), 3.44 (1 H, ddd, *J* = 9.6, 8.5, 6.4 Hz, CH_BBr).

(*S*)-1-(Acetyloxy)-5-bromo-3-(1-methylethyl)pentane (33). Compound **15a** (363 mg, 1.93 mmol) was brominated with the usual procedure to give 383 mg (79%) of the bromide **33**: $[\alpha]_D$ −5.8° (*c* 13.2, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.87 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (6 H, m), 2.03 (3 H, s, $OCOCH_3$), 3.42 (2 H, t, *J* = 7 Hz, CH_2Br), 4.10 (3 H, t, *J* = 7 Hz, CH_2OAc).

(*R*)-1-(Acetyloxy)-5-bromo-3-(1-methylethyl)pentane (34). Compound **19** (80 mg) was acetylated with acetic anhydride–pyridine, yielding 90 mg (94%) of the bromo acetate **34**: $[\alpha]_D$ +5.4° (*c* 4.2, $CHCl_3$); ^1H NMR (80 MHz, $CDCl_3$) δ 0.87 (6 H, d, *J* = 7 Hz, $CH(CH_3)_2$), 1.3–1.9 (6 H, m), 2.03 (3 H, s, $OCOCH_3$), 3.42 (2 H, t, *J* = 7 Hz, CH_2Br), 4.09 (3 H, t, *J* = 7 Hz, CH_2OAc).

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Registry No. **8**, 1195-31-9; **9** (isomer 1), 100431-64-9; **9** (isomer 2), 100431-90-1; **10** (isomer 1), 100431-65-0; **10** (isomer 2), 100431-91-2; **11**, 100431-66-1; **12**, 82425-87-4; **13a**, 91201-44-4; **13b**, 100431-67-2; (*E*)-**14a**, 100431-68-3; (*Z*)-**14a**, 100431-69-4; (*E*)-14b, 100431-70-7; (*Z*)-**14b**, 100431-71-8; **15a**, 100431-72-9; **15b**, 100431-73-0; **16**, 100431-74-1; **17**, 100431-75-2; **18**, 100431-76-3; **19**, 100431-77-4; **20**, 100431-78-5; **21**, 30656-65-6; **22**, 100431-79-6; **23**, 100431-80-9; **24**, 100431-81-0; **25**, 100568-99-8; **26**, 100431-82-1; **26** (tosylate), 100431-83-2; **27**, 32444-30-7; **28**, 100431-84-3; **29**, 100431-85-4; **30**, 100431-86-5; **31**, 100431-87-6; **32**, 32444-29-4; **33**, 100431-88-7; **34**, 100431-89-8.

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