peak was 58/42.

Data for 1-Phenyl-2,3-butadien-1-ol (Table III, Entry 1). TLC analysis (cyclohexane–ether, 8:2) of the crude reaction mixture shows two spots, the first with R_f 0.30, which takes up an orange color upon spraying with 2,4-dinitrophenylhydrazine and corresponding to the title dienol, the second with R_f 0.24 corresponding to 1-phenyl-3-butyn-1-ol as established by its spectra: IR (neat) 3400, 3300, 2120, 865, 755, 700; ^{1}H NMR (CCl_4) 1.2 (s, 1 H, OH), 1.9 (t, J = 2.6 Hz, 1 H), 2.5 (dd, J = 2.6 Hz, J = 7 Hz, 2 H), 4.75 (t, J = 7 Hz, 1 H), 7.3 (m, 5 H). GLC analysis of the same mixture (Carbowax, 150 °C) shows two peaks having retention times 3.9 and 4.6 min in 12/88 area ratio, the latter corresponding to the title dienol. 1-Phenyl-2,3-butadien-1-ol was purified by flash chromatography using cyclohexane–ether (9:1; two elutions): IR (neat) 3360, 3090, 3060, 3025, 1955, 1020, 920, 850, 760, 700; ^{1}H NMR (CCl_4) 3.6 (s, 1 H, OH), 4.6–4.85 (dd, J = 2.5 Hz, J = 5.5 Hz, 2 H), 4.85–5.5 (m, 2 H), 7.25 (pseudo s, 5 H); MS, m/e (relative intensity) 146 (M^+, 4), 128 (7), 108 (35), 107 (100), 105 (21), 79 (91), 77 (82), 51 (34), 39 (49). In order to establish the absolute configuration and the ee, the title dienol (150 mg) was hydrogenated in methanol in the presence of 5% Pd on carbon to 1-phenyl-1-butanol having $[\alpha]^{25}_D$ −21.5° (c 10, benzene) (lit.[34] $[\alpha]^{22}_D$ −31.6° (c 10, benzene) for a sample reported to be 69% ee).

Data for 1-Cyclohexyl-2,3-butadien-1-ol (Table III, Entry 2). GLC analysis (Carbowax, temperature program starting from 80 to 220 °C at 10 °C/min) shows the homopropargylic alcohol peak at 8.3 min and the dienol peak at 9.0 min in 7.7/92.3 area ratio. The title dienol has R_f 0.32 (cyclohexane–ether, 8:2) and was isolated by flash chromatography (cyclohexane–ether, 9:1; two elutions): IR (neat) 3350, 1950, 1450, 1020, 895, 865, 840; ^{1}H NMR 0.9–1.5 (m, 6 H), 1.5–2.0 (m, 4 H), 1.95 (s, 1 H, OH), 3.85 (m, 1 H), 4.75 (m, 2 H), 5.15 (dd, J = 13.5 Hz, J = 6.5 Hz, 1 H); MS, m/e (relative abundance) 113 ($M^+ - C_3H_3$, 37), 95 (100), 70 (23), 69 (59), 67 (32), 55 (56), 41 (61), 39 (28). The ee of the title dienol was established according to the Feringa's procedure:[35] the alcohol (110 mg) was dissolved in $CDCl_3$ (2 mL) and pyridine (60 mg) and treated at 0 °C with PCl_3 (34 mg) dissolved in $CDCl_3$ (2 mL) to give three diastereomeric phosphonates. The ^{31}P NMR spectrum showed three peaks at δ 6.4, 6.0, and 5.6 in the 14:71:15 area ratio.

Data for 1,2-Dodecadien-4-ol (Table III, Entry 3). GLC analysis of the reaction mixture (Carbowax, temperature program starting from 80 to 220 °C at 10 °C/min) shows the homopropargylic alcohol peak at 10.9 min and the dienol peak at 11.6 min in the 15/85 area ratio. The dienol has R_f 0.38 (cyclohexane–ether, 8:2) and is isolated by flash chromatography (cyclohexane–ether, 9:1; two elutions): IR (neat) 3430, 1950, 840; ^{1}H NMR 0.9 (t, 3 H), 1.1–1.9 (14 H), 2.2 (s, 1 H, OH), 4.2 (m, 1 H), 4.8 (m, 2 H), 5.2 (dd, J = 6.0 Hz, J = 12.9 Hz, 1 H); MS, m/e (relative intensity) 143 ($M^+ - C_3H_3$, 9), 107 (100), 79 (69), 69 (64), 55 (24), 41 (53), 43 (15), 39 (22). The ee was established by conversion of the dienol into diastereomeric phosphonates as in the case of 1-cyclohexyl-2,3-butadien-1-ol: the ^{31}P NMR contains three peaks at δ 5.6, 5.3, and 5.0 in the 16:69.5:14.5 ratio.

Acknowledgment. This research was supported by a grant from the Ministero della Pubblica Istruzione (Roma).

Registry No. (+)-**3**, 109958-05-6; (−)-**3**, 109907-86-0; **5**, 109958-04-5; **6**, 79364-35-5; **7**, 87604-46-4; (±)-**8**, 63553-62-8; **9**, 103882-39-9; (*R,R*)-*i*-PrOC(O)CH(OH)CH(OH)C(O)O-*i*-Pr, 2217-15-4; (*R,R*)-[$(CH_3)_2CH]_2$CHOC(O)CH(OH)CH(OH)C(O)-OCH[$(CH(CH_3)_2]_2$, 99686-56-3; CH_2=C(CH_3)CH_2Br, 1458-98-6; EtOC(O)C(=CH_2)CH_2Br, 17435-72-2; $(CH_3)_2$C=CHCH_2Br, 870-63-3; c-C_6H_{11}CHO, 2043-61-0; $CH_3(CH_2)_7$CHO, 124-19-6; $(CH_3)_3$CCHO, 630-19-3; $(CH_3)_2$C=CHCHO, 107-86-8; PhCHO, 100-52-7; (*R*)-$CH_3(CH_2)_7$CH(OH)CH_2CH=CH_2, 85029-09-0; (*S*)-$(CH_3)_3$CCH(OH)CH_2CH=CH_2, 67760-86-5; (*S*)-PhCH-(OH)CH_2C(CH_3)=CH_2, 77127-91-4; (*S*)-c-C_6H_{11}CH(OH)CH_2C-(CH_3)=CH_2, 94340-24-6; (*S*)-PhCH(OH)CH_2C(=CH_2)c(O)OEt, 109907-81-5; (*R*)-$CH_3(CH_2)_7$CH(OH)C(CH_3)CH=CH_2, 109927-25-5; (*R*)-$(CH_3)_2$C=CHCH(OH)C$(CH_3)_2$CH=CH_2, 77363-66-7; (*S*)-CH_3CH(Ph)N=C=O, 14649-03-7; (*R,S*)-$CH_3(CH_2)_7$CH[OC-(O)NHCH(Ph)CH_3]C$(CH_3)_2$CH=CH_2, 109907-82-6; (*S,S*)-CH_3-$(CH_2)_7$CH[OC(O)NHCH(Ph)CH_3]C$(CH_3)_2$CH=CH_2, 109907-83-7; (*S*)-c-C_6H_{11}CH(OH)CH_2CH=CH_2, 94340-22-4; (*S*)-CH_2=C=CHCH(OH)Ph, 104516-09-8; (*R*)-CH_2=C=CHCH(OH)-c-C_6H_{11}, 109907-84-8; (*R*)-CH_2=C=CHCH(OH)$(CH_2)_7CH_3$, 109907-85-9; (*S*)-CH_2=CHCH_2CH(OH)Ph, 77118-87-7; (*S*)-$CH_3(CH_2)_2$CH-(OH)Ph, 22135-49-5; (+)-diethyl tartrate, 87-91-2; (−)-diethyl tartrate, 13811-71-7; allyl bromide, 106-95-6; propargyl bromide, 106-96-7; (*R*)-glyceraldehyde acetonide, 15186-48-8; (*E*)-crotyl bromide, 29576-14-5; (*Z*)-crotyl bromide, 39616-19-8.

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Absolute Configuration of A-32′287 [Conocandin] and Total Synthesis of Its Methyl and *tert*-Butyl Esters

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The first total synthesis of *ent*-conocandin *tert*-butyl ester and conocandin methyl ester is described. The synthetic route involves initial stereoselective construction of the unsaturated aldehyde **3**, its homologation into the enantiomerically pure 2-alkoxy aldehyde **19**, and subsequent addition of an α-acrylate anion equivalent. Further functional group modifications afforded the desired targets. A chemical correlation with the natural product allowed absolute configuration assignment.

In 1976 J. M. Muller and co-workers[1] isolated a new compound from *Hormococcus conorum* cultures which exhibited a marked activity against yeasts and fungi. This new and interesting antibiotic, named conocandin (A-32′287), was assigned structure **1** (R = H), the absolute configuration remaining unknown; Figure 1.

A total synthesis of such a compound involves the achievement of three main goals: (a) A stereoselective synthesis of the C-9/C-10 trisubstituted double bond. (B)

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(1) Muller J. M.; Fuhrer, H.; Gruner, J.; Voser, W. *Helv. Chim. Acta* **1976**, *59*, 2506.

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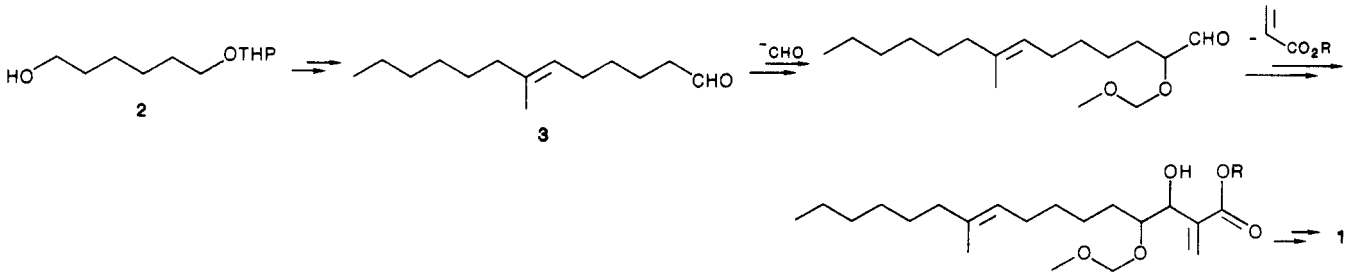
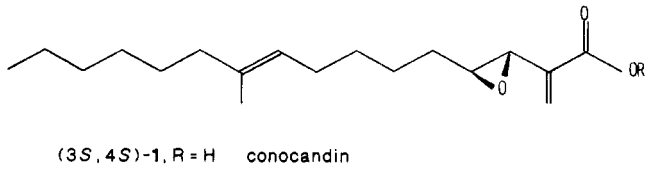
Scheme I. Synthetic Approach to Conocandin





(3S,4S)-1, R = H conocandin

Figure 1.

A stereoselective synthesis of the trans α-methylene-β,γ-epoxy moiety. (C) The obtaining of the target in enantiomerically pure form.

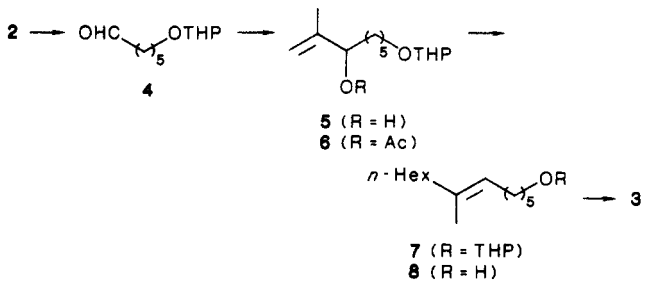
Our route toward the target entails the initial construction of the C-4/C-16 intermediate **3**. Subsequent sequential reaction with a chiral formyl anion equivalent and an α-acrylate anion equivalent provides the correct skeleton whose last functional group modifications eventually lead to the desired target (Scheme I).

Results and Discussion

C-4/C-16 Segment. Several methods are available to stereoselectively synthesize trisubstituted double bonds.[2] Among these, we chose a cuprate addition to a suitable allylic system.[3] Accordingly, PCC oxidation of 1,6-hexanediol monopyranyl ether (**2**)[4] afforded aldehyde **4** in 88% yield. Subsequent reaction with the Grignard reagent of 2-bromopropene[5] gave the allylic alcohol **5** which was acetylated under standard conditions to give the allylic acetate **6** in 80% yield starting from **4**. Di-*n*-pentyllithiocuprate, prepared from *n*-pentyllithium and CuI in ether at −25 °C,[6] reacted in SN_2' fashion at the less substituted allylic terminus of **6**, affording **7**. Depyranylation of **7** with methanol and catalytic *p*-toluenesulfonic acid gave the alcohol **8** in 84% yield from **6**. Capillary gas chromatographic analysis and ^{13}C spectroscopy[7] of **8** showed an *E*:*Z* ratio of 20:1. No branched product could be detected, in agreement with similar findings in this area.[3a] Intermediate **3** was obtained in 86% yield by PCC oxidation of **8** (Scheme II).

Enantiomerically Pure α-Alkoxy Aldehydes [(*R*)- and (*S*)-19]. (a) Aldol-Type Route. Reaction of the

Scheme II. Stereoselective Synthesis of the Key Intermediate 3



lithium anion of (+)-(*S*)-*p*-tolyl (*p*-tolylthio)methyl sulfoxide (**9**)[8] with **3** in THF at −85 °C gave, in 84% yield, the four possible diastereomeric β-hydroxy sulfoxides **10a–d** in a ratio of 53:9:23:15, shown in order of chromatographic elution (CH_2Cl_2/*i*-Pr_2O 9:1, HPLC).

(b) Acylation–Reduction Route. Reaction of a twofold molar excess of the lithium anion of **9** with the imidazolide **12**, obtained from **3** through the acid **11**, afforded the β-keto sulfoxides **13a,b** as a 55:45 inseparable mixture in 30% yield. $NaBH_4$ reduction of this mixture under equilibrating conditions[9] gave **10a–d** in a 7:60:15:18 ratio in virtually quantitative yield. The configurational assignment of stereoisomers **10a–d** relies upon earlier studies on a model compound.[9] Accordingly, $NaBH_4$ reduction of a 6:4 mixture of the β-keto sulfoxides **14a,b**, under equilibrating conditions, afforded **15b** as the only isomer. The typical J_{H3-H4} value (conocandin numbering) of **15b** coupled with its conversion into optically pure (−)-(*S*)-2-(methoxyphenyl)octan-2-ol (**16**)[10] revealed the 3*R*,4*R* absolute configuration of **15b**. Since LAH/$TiCl_4$-promoted sulfoxide to sulfide reduction of both **10a** and **10b** led to the same enantiomerically pure dithioacetal (vide infra), whereas the antipodal one was obtained from the reduction of both **10c** and **10d**, we confidently assigned to **10a–d** the 3*S*,4*R*, 3*R*,4*R*, 3*S*,4*S*, and 3*R*,4*S* configurations, respectively. The known preference for the si side addition of the lithium anion of **9** to benzaldehyde under similar conditions[11] further supports this assignment.

Chromatographic purification and subsequent collection of **10a** and **10b**, followed by LAH/$TiCl_4$-promoted sulfoxide reduction, afforded the enantiomerically pure[12] di-

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(6) The temperature of the cuprate formation must be carefully controlled. Indeed temperatures below −35 °C do not allow its formation.

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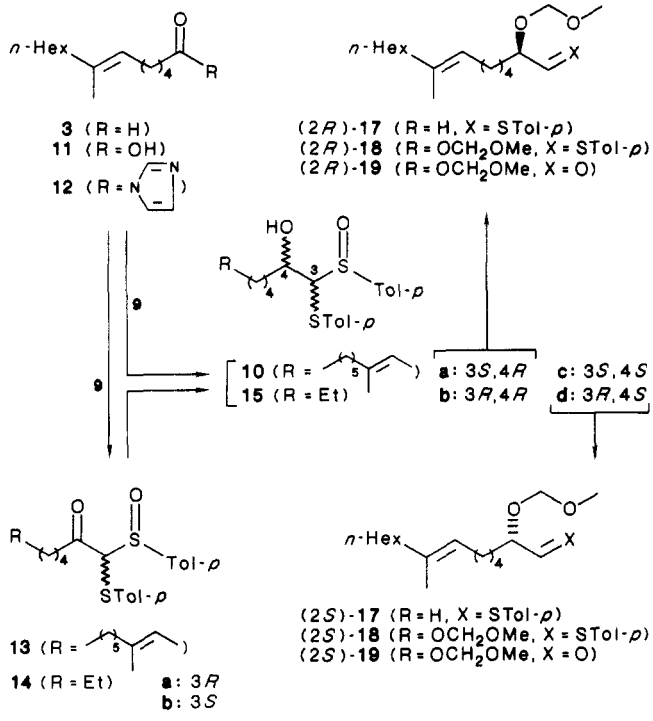
(10) (−)-(*S*)-**16** was obtained in six steps (20% overall yield) starting from **15b** via sulfoxide to sulfide reduction, *O*-methoxymethyl protection, dithioacetal to aldehyde conversion, reduction to primary alcohol, and iodide and hydride sequential displacements. This compound and that obtained via *O*-methoxymethylation of the commercially available (−)-(*R*)-octan-2-ol showed different lanthanide induced shift (LIS) at ^1H NMR [Eu(hfc)$_3$].

(11) Colombo, L.; Gennari, C.; Scolastico, C.; Guanti, G.; Narisano, E. *J. Chem. Soc., Perkin Trans. 1* **1981**, 1278.

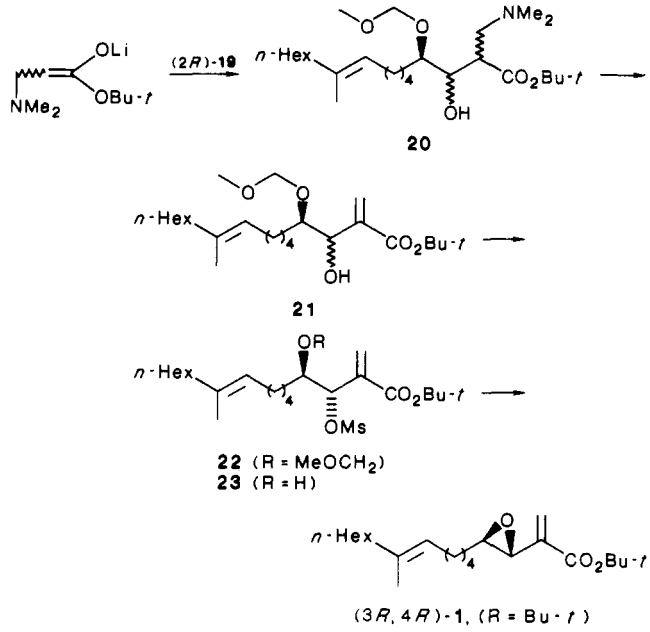
Scheme III. Conversion of 3 into Enantiomerically Pure (2*R*)-19 and (2*S*)-19



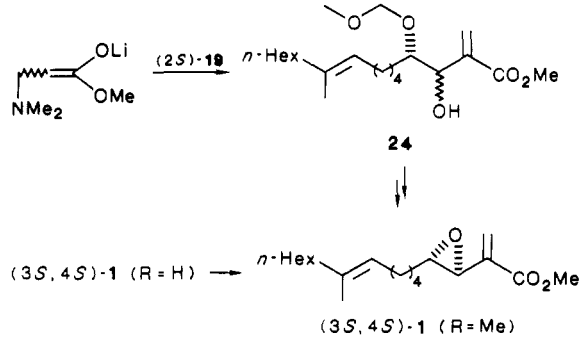
thioacetal (2*R*)-**17** in 70% yield. Protection of the hydroxyl group as a methoxymethyl ether and subsequent HgO dithioacetal hydrolysis gave the α-alkoxy aldehyde (2*R*)-**19** in 80% yield. An identical sequence starting from **10c** and **10d** similarly afforded the antipodal aldehyde (2*S*)-**19** (Scheme III).

Trans α-Methylene-β,γ-epoxy Acid Framework. The last part of the synthesis exploits our previous findings in the stereoselective additions of an α-acrylate anion equivalent[13] to chiral α-alkoxy aldehydes.[14] Accordingly, excess *tert*-butyl β-(dimethylamino)propionate, upon LDA metalation in Et_2O at 0 °C and treatment with (2*R*)-**19**, afforded after aqueous workup the adducts **20** as a diasteromeric mixture. Treatment of the crude material with excess MeI and K_2CO_3 in MeOH gave the two diastereomeric allylic alcohols **21** in 60% yield starting from **18**. The 4.5:1 anti:syn ratio observed in the ^1H NMR spectrum of crude **21**, although poorer than the one found in the model study,[12] reflects the preferred Felkin-type mode of addition of such enolates to chiral α-alkoxy aldehydes. Additional evidence for the present relative configuration assignment comes from the typical C-2 upfield shift of the anti isomer in the ^{13}C spectrum.[15] Treatment of the isomeric mixture **21** with mesyl chloride and triethylamine in CH_2Cl_2 gave the two corresponding mesylates in 60% yield, which could be easily separated by chromatography. Acetal hydrolysis of the major anti mesylate **22** by means of 37% HCl in THF afforded the alcohol **23**, which upon exposure to *n*-Bu_4NOH underwent

Scheme IV. Elaboration of (2*R*)-19 into *ent*-Conocandin *tert*-Butyl Ester



Scheme V. Elaboration of (2*S*)-19 into Conocandin Methyl Ester



the desired intramolecular mesylate displacement to give *ent*-conocandin *tert*-butyl ester (3*R*,4*R*)-**1** (R = *t*-Bu) in 60% yield from **22** (Scheme IV).

Alternatively, the lithium enolate of methyl β-(dimethylamino)propionate, generated from LDA at −78 °C, upon reaction with (2*S*)-**19**, followed by methylation and elimination, afforded the allylic alcohol **24** as a 3.6:1 anti:syn mixture in 40% yield. Subsequent mesylation, chromatographic anti isomer isolation, acetal hydrolysis, and epoxide formation similarly gave the expected (3*S*,4*S*)-**1** (R = Me). The chiroptical comparison of this material with the product derived from CH_2N_2 treatment of natural conocandin (see Experimental Section) eventually revealed the 3*S*,4*S* absolute configuration of the natural antibiotic (Scheme V).

Conclusions

The first total synthesis of enantiomerically pure conocandin and *ent*-conocandin as their respective methyl and *tert*-butyl esters is described. The synthesis, consisting of 15 sequential steps, builds up the conocandin skeleton from 1,6-hexanediol monopyranyl ether, an alkyl β-(dimethylamino)propionate, and (+)-(*S*)-*p*-tolyl (*p*-tolylthio)methyl sulfoxide; all readily available materials. The present synthesis, which establishes for the first time the absolute configuration of the natural product, shows the value of three main methods: (1) The cuprate addition to allylic acetates to achieve high *E* selectivity in the

(12) The enantiomeric purity of this compound was checked by ^1H NMR [Eu(hfc)$_3$].

(13) For recent papers dealing with other acrylate anion equivalents, see: (a) Baraldi, P. G.; Guarneri, M.; Pollini, G. P.; Simoni, D.; Barco, A.; Benetti, S. *J. Chem. Soc., Perkin Trans. 1* **1984**, 2501. (b) Hoffman, H. M. R.; Rabe, J. *Angew. Chem., Int. Ed. Engl.* **1983**, *22*, 795 and references therein.

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(15) Banfi, L.; Potenza, D.; Ricca, S. G. *Org. Magn. Reson.* **1984**, *22*, 224.

construction of trisubstituted olefins. (2) The use of chiral nonracemic sulfoxides to obtain enantiomerically pure compounds via carbonyl umpolung. (3) The addition of alkyl β-(dimethylamino)propionate enolates to chiral α-alkoxy aldehydes to control the relative stereochemistry of α-methylene-β,γ-dihydroxy esters.

Experimental Section

^1H NMR spectra were recorded with a XL-200 or a Bruker WP-80 spectrophotometer; ^{13}C NMR spectra were recorded with a Varian XL-200 or a Varian XL-100 instrument in the FT mode with tetramethylsilane as internal standard. Optical rotations were measured in 1-dm cells of 1-mL capacity by using a Perkin-Elmer 241 polarimeter. Elemental analyses were performed with a Perkin-Elmer 240 instrument. Silica gel 60 F_{254} plates (Merck) were used for analytical TLC and 270–400-mesh silica gel (Merck) for flash chromatography. GC analyses were performed on a Dani 3900 instrument with a capillary OV-1 column using a Hewlett-Packard 3390A integrator. HPLC analyses were performed on a Varian 5000 with a LiChrosorb column and a UV (254 nm) detector using a Hewlett-Packard 3390A integrator. Organic extracts were dried over Na_2SO_4 and filtered before removal of the solvent under reduced pressure. "Dry" solvents were distilled under dry N_2 just before use: tetrahydrofuran (THF) was distilled from sodium in the presence of a blue solution of benzophenone ketyl and CH_2Cl_2 and diisopropylamine were distilled from CaH_2. All reactions employing dry solvents were run under a nitrogen atmosphere.

6-[(Tetrahydro-2*H*-pyran-2-yl)oxy]hexanal (4). To a stirred suspension of pyridinium chlorochromate (PCC) (32.15 g, 148.5 mmol) and AcONa (2.4 g, 29.7 mmol) in anhydrous CH_2Cl_2 (280 mL) was added **2** (20 g, 99 mmol) in CH_2Cl_2 (20 mL). After 2 h anhydrous Et_2O (100 mL) was added, and the mixture was filtered through a pad of Celite, washing repeatedly the chromium salts. After solvent evaporation the crude product was purified by flash chromatography (*n*-hexane/AcOEt 80–20) (17.4 g, 88%). Anal. Found: C, 65.4; H, 10.00. Calcd for $C_{11}H_{20}O_3$: C, 65.97; H, 10.07. IR ($CHCl_3$): 2980, 2940, 2860, 2720, 1730, cm^{-1}. ^1H NMR ($CDCl_3$): 1.20–2.20 (m, 12 H), 2.2–2.6 (dt, 2 H), 3.20–4.0 (m, 4 H), 4.55 (s, 1 H), 9.75 (t, J = 2.0 Hz, 1 H).

2-Methyl-8-[(tetrahydro-2*H*-pyran-2-yl)oxy]octen-3-ol (5). To a stirred suspension of activated Mg turnings (2.78 g, 115.7 mmol) in dry THF (168 mL) was dropwise added 2-bromopropene (4.6 g, 38.56 mmol) and the mixture was gently warmed at 45 °C to start the organomagnesium formation. Further bromide was then added (9.4 g, 77.14 mmol) at such a rate so as to maintain controlled refluxing. After 30 min the mixture was cooled to −15 °C and **4** (7.70 g, 38.6 mmol) in dry THF (10 mL) was slowly added. The mixture was allowed to reach 25 °C in 30 min and then treated with saturated aqueous NH_4Cl. Extraction with AcOEt followed by Na_2SO_4 drying and solvent evaporation afforded crude **5** that was purified by flash chromatography (*n*-hexane/AcOEt 70/30) (7.84 g, 84%). Anal. Found: C, 69.45; H, 10.70. Calcd for $C_{14}H_{26}O_3$: C, 69.38; H, 10.81. IR ($CHCl_3$): 3425, 2940, 2860, 1650, 1460, 1450, 1440, cm^{-1}. ^1H NMR ($CDCl_3$): 1.20–2.0 (m, 17 H), 3.20–4.20 (m, 5 H), 4.55 (bs, 1 H), 4.82 and 4.92 (m, 2 H).

3-Acetoxy-2-methyl-8-[(tetrahydro-2*H*-pyran-2-yl)oxy]-oct-1-ene (6). To a stirred solution of **5** (22 g, 90.91 mmol) in dry CH_2Cl_2 (315 mL) were added in order triethylamine (18.9 mL, 136.4 mmol), Ac_2O (9.45 mL, 100 mmol), and 4-(dimethylamino)pyridine (1.1 g, 9.1 mmol). After 1 h the mixture was treated with water and diluted with Et_2O. Extraction with Et_2O followed by Na_2SO_4 drying and solvent evaporation gave crude **6** that was purified by flash chromatography (*n*-hexane/AcOEt 80/20) (24.51 g, 95%). Anal. Found: C, 67.85; H, 9.80. Calcd for $C_{16}H_{28}O_4$: C, 67.57; H, 9.92. IR ($CHCl_3$) 2940, 2860, 1725, 1650, 1530, 1450, 1370, cm^{-1}. ^1H NMR ($CDCl_3$): 1.10–2.0 (m, 17 H), 2.10 (s, 3 H), 3.20–4.0 (m, 4 H), 4.55 (bs, 1 H), 4.9 (m, 2 H), 5.15 (t, J = 6.6 Hz, 1 H).

(*E*)-[(Tetrahydro-2*H*-pyran-2-yl)oxy]-7-methyltridec-6-ene (7) and (*E*)-7-Methyltridec-6-en-1-ol (8). To a stirred suspension of CuI (36.9 g) in dry Et_2O (980 mL) under nitrogen atmosphere was added a 1.28 M pentyllithium solution in Et_2O (302 mL, 387.3 mmol) dropwise at −25 °C. The yellowish precipitate initially formed turned into a blue-black solution at the end of the addition. After 10 min **6** (22 g, 77.5 mmol) in dry Et_2O (220 mL) was added. After a further 5 min water was added and the salts were filtered off and washed with Et_2O. The organic phase was separated, dried, and evaporated under reduced pressure to give a crude product which was directly submitted to depyranylation.

An analytical sample was obtained by flash chromatography of crude **7**. IR ($CHCl_3$): 2990, 2920, 2840, 1595, 1460, 1450, 1435, 1390, 1345, 1025, 1015 cm^{-1}. ^1H NMR ($CDCl_3$): 0.88 (bt, 3 H), 1.1–2.2 (m, 27 H), 3.20–4.10 (m, 4 H), 4.59 (bs, 1 H), 5.12 (bt, J = 6 Hz, 1 H). ^{13}C NMR (selected values, $CDCl_3$) 135.31, 124.27, 98.81, 67.66, and 62.3.

To a solution of crude **7** in dry methanol (550 mL) was added *p*-toluenesulfonic acid until pH 1–2 was obtained. After 2 h the mixture was evaporated to dryness and purified by flash chromatography (*n*-hexane/AcOEt 80/20) (13.8 g, 84%). Anal. Found: C, 79.10; H, 13.35. Calcd for $C_{14}H_{28}O$: C, 79.18; H, 13.29. IR ($CHCl_3$): 3450, 2980, 2940, 2910, 2840, 1600, 1450, 1370, 1035 cm^{-1}. ^1H NMR ($CDCl_3$): 0.86 (bt, 3 H), 1.0–2.3 (m, 21 H), 3.62 (bt, J = 5.3 Hz, 2 H), 5.1 (bt, J = 6.7 Hz, 1 H). ^{13}C NMR ($CDCl_3$): 14.08, 15.9 (C-7'*E*), 22.7, 23.4 (C-7'*Z*), 25.4, 27.8, 27.9, 28.9, 29.7, 31.8, 32.7, 39.7, 63.0, 124.1 (C-6*E*), 124.9 (C-6*Z*), 135.4.

(*E*)-7-Methyltridec-6-en-1-al (3). To a stirred suspension of PCC (12.37 g, 57.1 mmol) in dry CH_2Cl_2 (100 mL) was added **8** (8 g, 37.74 mmol) in dry CH_2Cl_2 (12 mL). After 2 h dry Et_2O (100 mL) was added and the mixture was worked up as described for **4**. The crude product was purified by flash chromatography (*n*-hexane/AcOEt 94/6) (6.81 g, 86%). Anal. Found: C, 80.0, H, 12.5. Calcd for $C_{14}H_{26}O$: C, 79.94, H, 12.46. IR ($CHCl_3$): 2920, 2842, 2720, 1720, 1455, 1370, 1240, 1040 cm^{-1}. ^1H NMR ($CDCl_3$): 0.7–1.1 (bt, 3 H), 1.1–1.95 (m, 16 H), 1.6 (bs, 3 H), 2.4 (bt, 2 H), 5.10 (bt, J = 6.7 Hz, 1 H), 9.75 (t, J = 1.3 Hz, 1 H). ^{13}C NMR ($CDCl_3$) 14.1, 15.9, 21.8, 22.7, 27.6, 28.1, 29.1, 29.5, 31.9, 39.8, 43.8, 123.6, 135.7.

Aldol Route. (*E*)-1-((*S*)-*p*-Tolylsulfinyl)-1-(*p*-tolylthio)-8-methyltetradec-7-en-2-ol 10a–d. To a solution of **9** (7.22 g, 26.18 mmol) in dry THF (65 mL) was added a 1.55 M hexane solution of *n*-BuLi (17.4 mL, 26.18 mmol) dropwise at −40 °C. After 45 min **3** (5 g, 23.8 mmol) in dry THF (19 mL) was added at −85 °C. After 15 min the mixture was treated with saturated aqueous NH_4Cl and diluted with Et_2O (60 mL). Et_2O extraction followed by washing with brine, Na_2SO_4 drying, and solvent evaporation gave crude **10** (9.7 g, 84%). Pure **10a + 10b** could be obtained by flash chromatography (CH_2Cl_2/*i*-Pr_2O 85/15). Anal. Found: C, 71.65; H, 8.55. Calcd for $C_{29}H_{42}S_2O_2$: C, 71.56; H, 8.70. IR ($CHCl_3$): 3360, 2910, 2840, 1590, 1480, 1450, 1070, 1010, 1000, cm^{-1}. ^1H NMR ($CDCl_3$): 0.81–1.1 (m, 3 H), 1.1–2.15 (m, 21 H), 2.27 (s, 3 H), 2.38 (s, 3 H), 3.82–4.05 (m, J_{3-4} = 8 Hz (for **10a**), J_{3-4} = 2.8 Hz (for **10b**)), 4.25 (m, 2 H), 5.10 (bt, J = 6.7 Hz, 1 H), 6.85–7.80 (m, 8 H). HPLC diastereomeric ratio of crude **10** (CH_2Cl_2/*i*-Pr_2O 90/10): **10a**/**10b**/**10c**/**10d** = 53/9/23/15 in the order of elution.

Acylation–Reduction Route. (*E*)-7-Methyltridec-6-enoic Acid (11). To a stirred suspension of **3** (58 mg, 0.276 mmol) in dioxane/H_2O 1/1 (2.1 mL) were added $AgNO_3$ (93.8 mg, 0.522 mmol) and KOH (185 mg, 3.31 mmol) in water (0.43 mL). After 1 h the mixture was filtered through a Celite cake and the eluted solution was gently acidified until pH 4 with 1 N H_2SO_4. Extraction with AcOEt, brine washing, Na_2SO_4 drying, and solvent evaporation gave crude **11** that was purified by flash chromatography (CH_2Cl_2/AcOEt/AcOH 8/2/0.5) (57.4 mg, 92%). Anal. Found: C, 74.35; H, 11.60. Calcd for $C_{14}H_{26}O_2$: C, 74.29; H, 11.58. ^1H NMR ($CDCl_3$): 0.70–1.05 (bt, 3 H), 1.1–2.2 (m, 19 H), 2.35 (t, J = 6.6 Hz, 2 H), 5.10 (bt, J = 6.7 Hz, 1 H), 9.72 (bs, exchangeable, 1 H).

(1*S*)- and (1*R*)-(*E*)-1-((*S*)-*p*-Tolylsulfinyl)-1-(*p*-tolylthio)-8-methyltetradec-7-en-2-one (13). To a solution of **11** (284 mg, 1.25 mmol) in dry THF (6.4 mL) was added 1,1'-carbonyldiimidazole (305 mg, 1.88 mmol) at 25 °C. The disappearance of **11** and the formation of imidazolide **12** was detected by TLC. After 1 h the mixture was syringed into a solution of the lithium anion of **9** (3.12 mmol) in THF (6 mL) at −78 °C, previously prepared as described in the aldol route. After 15 min the mixture was treated with saturated NH_4Cl and diluted with Et_2O (10 mL). After the usual workup crude **13** was purified by flash chroma-

tography (*n*-hexane/AcOEt 70/30) (181 mg, 30%). Anal. Found: C, 71.80; H, 8.40. Calcd for $C_{29}H_{40}S_2O_2$: C, 71.85; H, 8.32. IR ($CHCl_3$): 3010, 2920, 2860, 1710, 1600, 1490, 1440, 1080, 1040, cm^{-1}. ^1H NMR ($CDCl_3$): 0.85 (bt, 3 H), 1.02–2.18 (m, 16 H), 1.53 (s, 3 H), 2.28–2.35 (2 s, 3 H), 2.56 (AB system, J = 7.9 Hz, 2 H), 4.45 (s, 0.43 H (1*S* isomer)), 4.66 (s, 0.57 H, (1*R* isomer)), 5.08 (bt, J = 6.7 Hz, 1 H), 6.95–7.80 (m, 10 H).

(*E*)-1-((*S*)-*p*-Tolylsulfinyl)-1-(*p*-tolylthio)-8-methyltetradec-7-en-2-ol 10a–d. To a solutioin of **13** (50 mg, 0.103 mmol) in dry EtOH (3.6 mL) at 25 °C and in the presence of a catalytic amount (0.05 molar equiv) of EtONa was added $NaBH_4$ (8 mg, 0.206 mmol). After 1 h 5% HCl was added until pH 4, and the mixture was concentrated in vacuo and extracted with Et_2O. After a usual workup crude **10** was purified by flash chromatography as described in the aldol route (49.0 mg, 98%). HPLC diastereomeric ratio of crude **10** (CH_2Cl_2/*i*-Pr_2O 90/10): **10a/10b/10c/10d** = 7/60/15/18.

(+)-(2*R*)-(*E*)-1,1-Bis(*p*-tolylthio)-8-methyltetradec-7-en-2-ol ((2*R*)-17). To a solution of **10a + 10b** (89:11) (6.017 g, 13.28 mmol) in dry Et_2O (241 mL), at −20 °C, were in order slowly added $LiAlH_4$ (1.411 g, 37.14 mmol) and a 1 M CH_2Cl_2 solution of $TiCl_4$ (37.14 mL, 37.14 mmol). After 10 min the mixture was treated with water (60 mL) and extracted with Et_2O. The organic phases were collected, washed with 5% $NaHCO_3$ and then with water, dried, and evaporated to dryness. The crude product was purified by flash chromatography (*n*-hexane/AcOEt 93/7). Oil (4.08 g, 70%). Anal. Found: C, 74.05; H, 8.90. Calcd for $C_{29}H_{42}S_2O$: C, 73.99; H, 8,99. $[\alpha]^{20}_D$ +72° (*c* 1.0; acetone). IR ($CHCl_3$): 3540, 3020, 3000, 2940, 2920, 1450, 1370, 1290, 1170, 1080, 1010 cm^{-1}. ^1H NMR ($CDCl_3$) 0.88 (bt, 3 H), 1.10–2.10 (m, 18 H), 1.55 (bs, 3 H), 2.30 (s, 6 H), 2.60 (d, J = 5.3 Hz exchangeable, 1 H), 3.60–3.90 (m, 1 H), 4.32 (d, J = 4.0 Hz, 1 H), 5.10 (bt, J = 6.7 Hz, 1 H), 7.0–7.50 (m, 8 H). ^{13}C NMR ($CDCl_3$): 14.1, 15.9, 21.1, 22.7, 25.5, 27.8, 27.9, 28.9, 29.7, 31.8, 33.6, 39.7, 67.8, 72.5, 124.1, 129.6, 130.4, 133.0, 135.1, 137.7, 137.8.

(−)-(2*S*)-(*E*)-1,1-Bis(*p*-tolylthio)-8-methyltetradec-7-en-2-ol ((2*S*)-17). This was synthesized starting from **10c + 10d** (60:40) as reported above for the 2*R* enantiomer.

(+)-(2*R*)-(*E*)-1,1-Bis(*p*-tolylthio)-8-methyl-2-(methoxymethoxy)tetradec-7-ene ((2*R*)-18). To a solution of (2*R*)-17 (3 g, 6.38 mmol) in dry CH_2Cl_2 (26 mL) were in order added $NEtPr_2$ (4.44 mL, 25.5 mmol) and $MeOCH_2Cl$ (1.95 mL, 25.5 mmol). After 15 h at 25 °C further amine (2.22 mL, 12.8 mmol) and chloride (0.97 mL, 12.8 mmol) were added. After 2 h the reaction mixture was treated with water (6 mL) and extracted with Et_2O. After the usual workup crude (2*R*)-18 was purified by flash chromatography (*n*-hexane/AcOEt 92/8). Oil (3.18 g, 97%). Anal. Found: C, 72.30; H, 9.05. Calcd for $C_{31}H_{46}S_2O_2$: C, 72.32; H, 9.00. $[\alpha]^{20}_D$ +3.9° (*c* 1, $CHCl_3$). IR ($CHCl_3$) 2910, 2840, 1040, 800 cm^{-1}. ^1H NMR ($CDCl_3$): 0.75–1.1 (bt, 3 H), 1.10–2.20 (m, 18 H), 1.55 (s, 3 H), 2.30 (s, 3 H), 3.36 (s, 3 H), 3.70–3.95 (m, 1 H), 4.53 (d, J = 2.7 Hz, 1 H), 4.67 (AB system, J = 6.7 Hz, 2 H), 5.10 (bt, J = 6.7 Hz, 1 H), 6.95–7.45 (m, 8 H). ^{13}C NMR ($CDCl_3$): 14.1, 15.8, 21.1, 22.7, 25.7, 27.8, 28.0, 29.0, 29.6, 31.4, 31.9, 39.8, 55.8, 64.7, 80.1, 96.7, 124.1, 129.5, 131.6, 132.3, 132.7, 135.1, 137.3.

(+)-(2*R*)-(*E*)-8-Methyl-2-(methoxymethoxy)tetradec-7-en-1-al ((2*R*)-19). To a stirred suspension of HgO (0.632 g, 2.92 mmol) in 85/15 THF/H_2O (11.6 mL) were added in order $BF_3{\cdot}Et_2O$ (0.372 mL, 2.92 mmol) and (2*R*)-18 (1 g, 1.94 mmol) in THF (2 mL). After 1 h *n*-hexane (30 mL) was added and the two phases were separated. After Et_2O extraction and Na_2SO_4 drying, evaporation to dryness gave crude (2*R*)-19 (0.552 g) that was used without further purification for the subsequent reaction. An analytical sample was obtained by repeated decantations from cold *n*-hexane. Anal. Found: C, 71.75; H, 11.30. Calcd for $C_{17}H_{32}O_3$: C, 71.79; H, 11.34. $[\alpha]^{20}_D$ +22° (*c* 1, $CHCl_3$). IR ($CHCl_3$) 2930, 2850, 1730, 1460, 1375, 1145, 1110, 1035 cm^{-1}. ^1H NMR ($CDCl_3$): 0.85 (bt, 3 H), 1.10–2.10 (m, 18 H), 1.55 (s, 3 H), 3.40 (s, 3 H), 3.75–4.0 (m, 1 H), 4.70 (s, 2 H), 5.10 (bt, J = 6.7 Hz, 1 H), 9.60 (d, J = 1.9 Hz, 1 H).

(−)-(2*S*)-(*E*)-1,1-Bis(*p*-tolylthio)-8-methyl-2-(methoxymethoxy)tetradec-7-ene ((2*S*)-18) and (−)-(2*S*)-(*E*)-8-Methyl-2-(methoxymethoxy)tetradec-7-en-1-al ((2*S*)-19). These compounds were synthesized starting from (2*S*)-17 as reported above for the 2*R* enantiomer.

(3*S*,4*R*)- and (3*R*,4*R*)-(*E*)-*tert*-Butyl 3-Hydroxy-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (21). To a solution of diisopropylamine (0.706 mL, 5.04 mmol) in dry Et_2O (3.55 mL) was added a 1 M solution of BuLi (3.23 mL, 4.85 mmol) dropwise at 0 °C. After 20 min *tert*-butyl β-(dimethylamino)propionate (0.928 mL, 4.85 mmol) was added by a syringe. After 3 h at 0 °C the mixture was brought to −78 °C and (2*R*)-19 (0.552 g) in the minimum amount of dry THF was added. After 10 min the mixture was treated with saturated aqueous NH_4Cl (1 mL), diluted with Et_2O, and extracted. The organic phases were dried and evaporated under reduced pressure to give crude **20**. K_2CO_3 (1.34 g, 9.7 mmol) and MeI (2.4 g, 15.5 mmol) were in order added to a methanolic (7.3 mL) solution of crude **20** (0.552 g). After 3 h the mixture was filtered on a Buchner funnel and the filtrate washed first with 0.1 N sodium thiosulfate solution and then with water. The solution was dried and evaporated under reduced pressure to afford crude **21** that was purified by flash chromatography (*n*-hexane/AcOEt 85/15). Oil (479.4 mg, 60% starting from **18**). Anal. Found: C, 69.80; H, 10.8. Calcd for $C_{24}H_{44}O_5$: C, 69.84; H, 10.78%. IR $CHCl_3$): 3390, 2920, 2845, 1705, 1620, 1450, 1385, 1360, 1280, 1215, 1140, 1030 cm^{-1}. ^1H NMR ($CDCl_3$): 0.86 (t, J = 9 Hz, 3 H), 1.23–1.60 (m, 18 H), 1.45 (s, 9 H), 1.55 (s, 3 H), 2.10 (bt, J = 8.0 Hz, 4 H), 3.0 (d, J = 5.3 Hz, exchangeable, 1 H), 3.32 (s, 0.18 H, syn), 3.40 (s, 0.81 H, anti), 3.60–3.95 (m, 1 H), 4.50–4.80 (m, 3 H), 5.10 (bt, J = 6.7 Hz, 1 H), 5.81 (m, 0.18 H, syn), 5.85 (m, 0.81 H, anti), 6.30 (m, 1 H). ^{13}C NMR ($CDCl_3$): 14.1, 15.9, 22.6–31.8 (aliphatic C), 39.7, 55.8, 72.4, 80.0 (anti), 81.3 (C-4 syn and C-19), 96.3 (anti), 96.9 (syn), 124.1, 125.3 (syn), 125.9 (anti), 134.9 (anti), 135.4 (syn), 140.4 (anti), 142.4 (syn).

(+)-(3*S*,4*R*)-(*E*)-*tert*-Butyl 3-[(Methylsulfonyl)oxy]-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (22). To a solution of **21** (348.2 mg, 0.093 mmol) in CH_2Cl_2 (0.373 mL) was added triethylamine (0.0174 mL, 0.186 mmol) and mesyl chloride (0.0145 mL, 0.186 mmol). After 10 min the mixture was treated with saturated aqueous NH_4Cl and extracted with Et_2O. The organic phases were collected, dried, and evaporated under reduced pressure. Crude **22** was purified by flash chromatography (*n*-hexane/AcOEt 80/20). Oil (60%). Anal. Found: C, 61.10; H, 9.50. Calcd for $C_{25}H_{46}SO_7$: C, 61.19; H, 9.45. $[\alpha]^{20}_D$ +28° (*c* 1, $CHCl_3$). IR ($CHCl_3$) 2915, 2860, 1720, 1355 cm^{-1}. ^1H NMR ($CDCl_3$): 0.85 (bt, 3 H), 1.10–2.10 (m, 18 H), 1.45 (s, 9 H), 1.55 (s, 3 H), 3.06 (s, 3 H), 3.42 (s, 3 H), 3.80–4.0 (m, 1 H), 4.75 (AB system, J = 7.4 Hz, 2 H), 5.09 (bt, J = 6.7 Hz, 1 H), 5.60 (m, 1 H), 5.97 (m, 1 H), 6.40 (m, 1 H).

(+)-(3*S*,4*R*)-(*E*)-*tert*-Butyl 4-Hydroxy-10-methyl-2-methylene-3-[(methylsulfonyl)oxy]hexadec-9-enoate (23). To a solution of **22** (52 mg, 0.11 mmol) in THF (2.1 mL) was added 37.5% HCl (0.71 mL). After 2 h of stirring the mixture was treated with 5% aqueous $NaHCO_3$ to pH 8–9 and diluted with ether. After extraction, Na_2SO_4 drying, and solvent evaporation crude **23** was purified by flash chromatography (*n*-hexane/AcOEt 63/35). Oil (23.5 mg, 63%). Anal. Found: C, 61.80; H, 9.45. Calcd for $C_{23}H_{42}SO_6$: C, 61.85; H, 9.48. $[\alpha]^{20}_D$ +10° (*c* 1, $CHCl_3$). IR ($CHCl_3$) 3400, 2935, 2845, 1715, 1350 cm^{-1}. ^1H NMR ($CDCl_3$) 0.85 (bt, 3 H), 1.0–2.20 (m, 21 H), 1.50 (s, 9 H), 2.32 (d, J = 6.4 Hz, exchangeable, 1 H), 3.10 (s, 3 H), 3.85–4.10 (m, 1 H), 5.07 (bt, J = 6.7 Hz, 1 H), 5.45 (d, J = 3.9 Hz, 1 H), 6.0 (s, 1 H), 6.40 (s, 1 H).

(3*R*,4*R*)-(*E*)-*tert*-Butyl 3,4-Epoxy-10-methyl-2-methylenehexadec-9-enoate (1, R = *t*-Bu) (*ent*-Conocandin *tert*-butyl ester). To a stirred solution of NaOH (132 mg, 3.3 mmol) in H_2O (0.750 mL) was added *n*-Bu_4NHSO_4 (68 mg, 0.2 mmol) at 0 °C. After 30 min **23** (54 mg, 0.12 mmol) in CH_2Cl_2 (0.750 mL) was added. After a further 10 min the two layers were separated and the water phase was extracted with Et_2O. The organic layers were collected, dried, and evaporated under reduced pressure. The crude product was purified by flash chromatography (*n*-hexane/AcOEt 95/5). Oil (37.8 mg, 95%). Anal. Found: C, 75.30; H, 10.50. Calcd for $C_{22}H_{38}O_3$: C, 75.38; H, 10.93. $[\alpha]^{20}_D$ −4° (*c* 1, $CHCl_3$); +2.7° (*c* 0.55, EtOH 96%). IR ($CHCl_3$): 2998, 2900, 2820, 2400, 2370, 1690, 1500, 1460, 1410, 1200, 1000, 910, cm^{-1}. ^1H NMR ($CDCl_3$): 0.89 (bt, 3 H), 1.10–2.20 (m, 21 H), 1.54 (s, 9 H), 2.55–2.78 (m, 1 H), 3.45 (bd, J_{3-4} = 2.2 Hz, 1 H), 5.10 (bt, J = 6.7 Hz, 1 H), 5.64 (m, 1 H), 6.10 (d, J = 2.0 Hz, 1 H); ^{13}C NMR ($CDCl_3$) 14.0, 22.6, 25.5, 27.8, 28.1, 29.0, 29.6, 31.8, 32.1,

39.7, 55.3, 62.7, 81.1, 122.7, 123.9.

(3*R*,4*S*)- and (3*S*,4*S*)-(*E*)-Methyl 3-Hydroxy-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (24). To a solution of diisopropylamine (2.78 mL, 7.07 mmol) in Et_2O (5 mL) was dropwise added a 1 M *n*-hexane solution of *n*-BuLi (4.53 mL, 6.8 mmol) at 0 °C. After 20 min the reaction was cooled to −78 °C and methyl β-(dimethylamino) propionate (0.736 mL, 6.8 mmol) was added. After 30 min (2*S*)-**19** (0.772 g, 2.72 mmol) was added. After a further 10 min the reaction was treated with saturated aqueous NH_4Cl, extracted with Et_2O, dried, and evaporated to dryness. The crude product was dissolved in MeOH (10 mL) and K_2CO_3 (1.87 g, 13.6 mmol) and MeI (1.5 mL, 21.7 mmol) were added. After 3 h the mixture was filtered and the filtrate was worked up as described for **20**. The crude was purified by chromatography (*n*-hexane/AcOEt 9/1). Oil, 40%. IR ($CHCl_3$): 3500, 2910, 2830, 1705, 1430 cm^{-1}. ^1H NMR ($CDCl_3$): 0.87 (t, J = 9 Hz, 3 H), 1.15–1.68 (m, 1 H), 1.57 (s, 3 H), 1.9 (bt, J = 9 Hz, 4 H), 3.04 (bs, exchangeable, 1 H), 3.35 (s, 0.22 H, syn), 3.4 (s, 0.78 H, anti), 3.69–3.86 (m, 4 H), 4.6–4.8 (m, 3 H), 5.09 (bt, J = 7 Hz, 1 H), 5.84 (s, 0.22 H), 5.96 (s, 0.78 H), 6.64 (s, 0.22 H), 6.7 (s, 0.78 H).

The following compounds were synthesized analogously to the above reported corresponding *tert*-butyl ester derivatives.

(+)-(3*R*,4*S*)-(*E*)-Methyl 3-[(Methylsulfonyl)oxy]-10-methyl-2-methylene-4-(methoxymethoxy)hexadec-9-enoate (25). Oil, (58% anti + syn, 45% anti). IR ($CHCl_3$): 2900, 2820, 1705, 1340, 1155. ^1H NMR ($CDCl_3$): 0.87 (bt, 3 H), 1.03–2.1 (m, 18 H), 1.55 (s, 3 H), 3.08 (s, 3 H), 3.42 (s, 3 H), 3.7–3.98 (m, 4 H), 4.75 (AB system, J = 6.7 Hz, 2 H), 5.07 (bt, J = 7 Hz, 1 H), 5.65 (m, 1 H), 6.10 (m, 1 H), 6.40 (m, 1 H). $[\alpha]^{20}_D$ +24° (c 1.025, $CHCl_3$).

(+)-(3*R*,4*S*)-(*E*)-Methyl 4-Hydroxy-10-methyl-2-methylene-3-[(methylsulfonyl)oxy]hexadec-9-enoate (26). Oil (30%). Anal. Found: C, 59.35; H, 9.0. Calcd for $C_{20}H_{36}SO_6$: C, 59.38; H, 9.0. IR ($CHCl_3$): 3400, 2920, 2840, 1720, 1350, 1170, 960 cm^{-1}. ^1H NMR ($CDCl_3$): 0.86 (bs, 3 H), 1.05–2.15 (m, 22 H), 3.03 (s, 3 H), 3.80 (s, 3 H), 3.85–4.10 (m, 1 H), 5.07 (bt, J = 6.7 Hz, 1 H), 5.45 (d, J = 4 Hz, 1 H), 6.1 (s, 1 H), 6.52 (s, 1 H). $[\alpha]^{20}_D$ +12° (c 0.53, $CHCl_3$).

(+)-(3*S*,4*S*)-(*E*)-Methyl 3,4-Epoxy-10-methyl-2-methylenehexadec-9-enoate (1, R = Me) (Conocandin methyl ester). Oil (25%). Anal. Found: C, 74.00; H, 10.40. Calcd for $C_{19}H_{32}O_3$: C, 73.98; H, 10.46. IR ($CHCl_3$): 2900, 2820, 1710, 1420, 1265, 1130 cm^{-1}. ^1H NMR ($CDCl_3$): 0.88 (bt, 3 H), 1.0–2.1 (m, 21 H), 2.57–2.80 (m, 1 H), 3.4–3.52 (m, 1 H), 3.8 (s, 3 H), 5.1 (bt, J = 6.9 Hz, 1 H), 5.75 (dd, J_{3-4} = 1.6 Hz, 1 H), 6.2 (d, J = 1.6 Hz, 1 H). $[\alpha]^{20}_D$ +4.2° (c 0.3, $CHCl_3$).

Preparation of (+)-(3*S*,4*S*)-1 (R = Me) Starting from Natural Conocandin. To a solution of (+)-(3*S*,4*S*)-1 (R = H) (10 mg, 0.034 mmol) in $CHCl_3$ (1 mL) was added a 1 M CH_2N_2 ethereal solution at −70 °C until the reaction remained pale yellow. Evaporation under reducd pressure gave pure (+)-(3*S*,4*S*)-1 (R = Me); quantitative. Spectroscopical data as well as sign and value of rotation were identical with those obtained from the previous preparation.

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Registry No. (+)-(3*S*,4*S*)-1 (R = H), 61371-61-7; (3*S*,4*S*)-1 (R = Me), 61417-68-3; (3*R*,4*R*)-1 (R = *t*-Bu), 109639-31-8; **2**, 28659-22-5; **3**, 109669-14-9; **4**, 33803-62-2; **5**, 103021-89-2; **6**, 103021-88-1; **7**, 103021-80-3; **8**, 103021-92-7; **9**, 109639-16-9; **10a**, 109639-17-0; **10b**, 109717-16-0; **10c**, 109717-17-1; **10d**, 109717-18-2; **11**, 109639-18-1; **12**, 109639-19-2; **13a**, 109639-20-5; **13b**, 109639-32-9; (2*R*)-**17**, 109639-21-6; (2*S*)-**17**, 109639-33-0; (2*R*)-**18**, 109639-22-7; (2*S*)-**18**, 109639-34-1; (2*R*)-**19**, 109639-23-8; (2*S*)-**19**, 109639-35-2; **20**, 109639-24-9; (3*S*,4*R*)-**21**, 109639-25-0; (3*R*,4*R*)-**21**, 109639-36-3; (3*S*,4*R*)-**22**, 109639-26-1; (3*R*,4*R*)-**22**, 109639-44-3; **23**, 109639-27-2; (3*R*,4*S*)-**24**, 109639-28-3; (3*S*,4*S*)-**24**, 109639-37-4; (3*R*,4*S*)-**25**, 109639-29-4; (3*S*,4*S*)-**25**, 109639-45-4; **26**, 109639-30-7; $CH_3(CH_2)_5C(CH_3)=CH(CH_2)_4CH(OCH_2OCH_3)CH(OH)C(=CH_2)CO_2H$, 109639-38-5; $CH_3(CH_2)_5CH(OH)CH(S\text{-}p\text{-}C_6H_4Me)S(O)\text{-}p\text{-}C_6H_4Me$, 86544-35-6; methyl β-(dimethylamino)propionate, 3853-06-3; 2-bromopropene, 75-26-3; *tert*-butyl β-(dimethylamino)propionate, 88722-74-1; (+)-(*R*)-1,1-bis(*p*-tolylthio)octan-2-ol, 109717-19-3; (−)-(*R*)-1,1-bis(*p*-tolylthio)-2-(methoxymethoxy)octane, 109717-20-6; (+)-(*R*)-2-(methoxymethoxy)octanal, 109717-21-7; (*R*)-2-(methoxymethoxy)octan-1-ol, 109639-39-6; (*R*)-1-[(methylsulfonyl)oxy]-2-(methoxymethoxy)octane, 109639-40-9; (*R*)-1-iodo-2-(methoxymethoxy)octane, 109639-41-0; (*S*)-2-(methoxymethoxy)octane, 109639-42-1; (*R*)-2-(methoxymethoxy)octane, 109639-43-2; (*R*)-octan-2-ol, 5978-70-1; (±)-2-(methoxymethoxy)octane, 109717-22-8; (±)-octan-2-ol, 4128-31-8; phenyllithium, 3525-31-3.

Supplementary Material Available: Experimental section describing the preparation of (−)-(*S*)-**16** from **15b** and related spectral data (5 pages). Ordering information is given on any current masthead page.

Synthesis of Analogues of Neplanocin A: Utilization of Optically Active Dihydroxycyclopentenones Derived from Carbohydrates

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The dihydroxycyclopentenones **1** and **2** were synthesized enantiomerically pure from D-ribonolactone and D-mannose, respectively. The synthesis involves the conversion of these carbohydrates to erythruronolactones, which are subsequently converted to the desired dihydroxycyclopentenones in good yields. The dihydroxycyclopentenone **1** was then used to synthesize analogues of neplanocin A.

Neplanocin A (NpcA, (−)-9-[*trans*-2′,*trans*-3′-dihydroxy-4′-(hydroxymethyl)cyclopent-4′-enyl]adenine) is a carbocyclic analogue of adenosine, which has been shown to possess both antitumor and antiviral activity.[1-3] The antitumor activity (cytotoxicity) of NpcA is believed to be mediated through the formation of NpcA nucleotides, catalyzed by adenosine kinase, which selectively inhibit RNA synthesis.[4] NpcA's antiviral activity has been cor-

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