Dihydro- and Tetrahydrofuran Building Blocks from 1,4:3,6-Dianhydrohexitols. 2. Synthesis of Acetal, Alcohol, Diol, Epoxide, Hydrocarbon, and Lactone Pheromones

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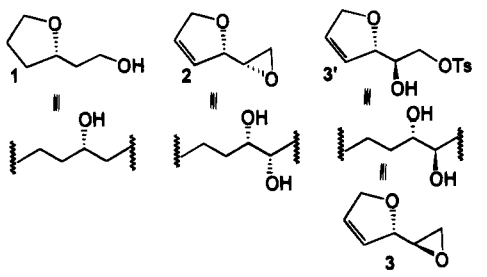
The potential of building blocks **1**–**3** for synthesis of enantiopure substances is illustrated by their transformation to various insect pheromones featuring functionalities specified in the title. A convenient synthesis of building block **3** from sorbitol is described.

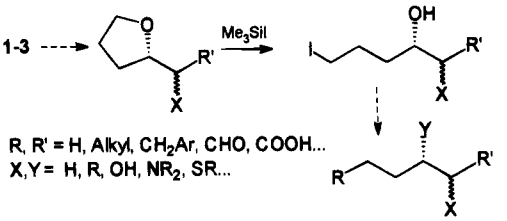
The preparation of building blocks **1**–**3′** from D-mannitol has been recently reported and their utility exemplified by the synthesis of a number of enantiopure insect pheromones (Scheme 1).[1] In this complementary paper we further illustrate the applications of the above building blocks and report the synthesis of several additional pheromones. Moreover, a procedure is described for the preparation of epoxide **3** from sorbitol, which is more economical and expeditious than that of the synthetically equivalent diol monotosylate **3′** from mannitol reported previously.[1]

In order to appreciate the synthetic scope and limits of building blocks **1**–**3**, it may be pointed out that they are equivalent to open-ended enantiomerically pure secondary alcohols (**1**) or diols (**2** and **3**) of at least six unbranched carbons. The operations which establish such equivalency are as follows (Scheme 2): (1) The side chain can be elaborated and extended by functional group transformation of the primary hydroxyl (for building block **1**) or the epoxide ring (for **2** and **3**). (2) After saturation of the double bond, the tetrahydrofuran ring may be regiospecifically cleaved at the primary ether linkage (Me_3SiI) to yield a γ-iodo alcohol or -diol which can be further manipulated at the halogenated chain terminal.

Scheme 1



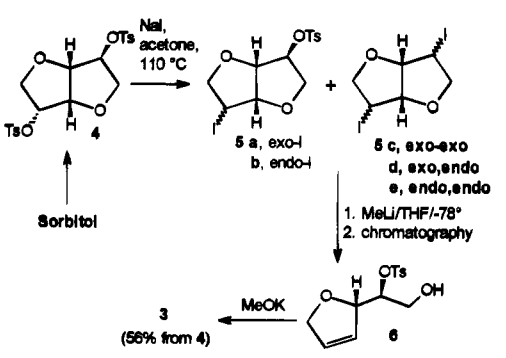
Scheme 2



Results and Discussion

Synthesis of Epoxide 3 from Sorbitol. In the reaction of 1,4:3.6-dianhydrosorbitol ditosylate (**4**) with iodide ion (Scheme 3), the endo tosylate is reported to react much more rapidly than the exo, such that a single (exo,exo) iodo tosylate (**5a**) is formed.[2] Under such circumstances a straightforward preparation of building block **3** could be envisioned where **5a** would be treated with methyllitium to give the diol monotosylate **6** from which epoxide **3** could be obtained by base treatment. This strategy (Scheme 3) was implemented, although it turned out to be less straightforward than expected. In fact, the rates of displacement of the endo and exo tosylates were not as different as anticipated; under all solvent and temperature conditions tested, nonnegligible proportions (2–7%) of diiodides **5c**–**e** were always formed even at relatively low conversions.[3] Since the endo,endo

Scheme 3



and endo,exo diiodides **5d** and **5e** would yield the epimeric epoxide **2**, some separation procedure was inevitable. Thus the crude mixture from iodide substitution (**5a**–**e** plus unreacted **4**) was treated with MeLi, and the product from this reaction was chromatographed to separate the halohydrin fractions from the diol monotosylate **6**. Base treatment of **6** gave the target epoxide **3** in 56% overall yield.

(*R*)-(+)-Hexanolide (9), (*R*)-(−)-3-Octanol (11), and (2*R*,5*S*;2*R*,5*R*)-Chalcogran (15a/15b). Scheme 4 summarizes the syntheses of the above pheromones starting from building block **1**.

The γ-lactone **9** is the main component of the natural pheromone of the dermestid and khapra beetles (*Trogo-*

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(3) The lower proportions were obtained with LiI in acetone at reflux; however, the conversion was too slow to be practicable.

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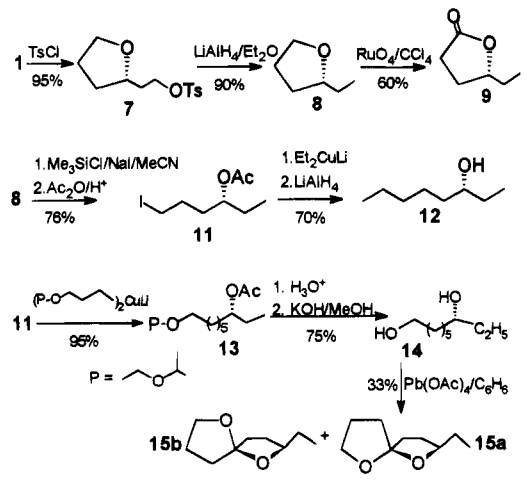
Scheme 4

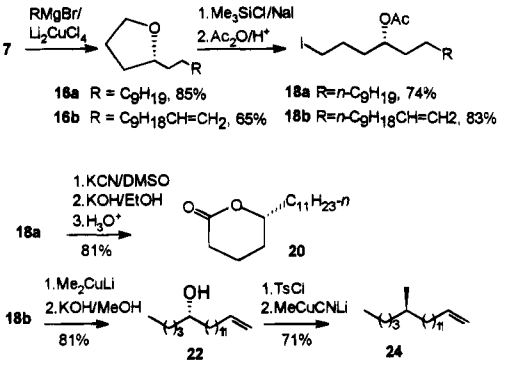


derma glabrum and T. granarium).[4] Its three-step synthesis was carried out via tosylation of **1** to **7**, followed by lithium aluminum hydride reduction to (*R*)-(−)-2-ethyltetrahydrofuran (**8**) and direct oxidation of the latter with ruthenium tetraoxide/$NaIO_4$ (51% from **1**).[5] Syntheses of **9** published up to 1989 have been reviewed by Mori.[6a] A few additional syntheses have since appeared.[7]

Alcohol **12** is a component of the pheromone mixture of several ant species, including *Crematogaster castanea* and *C. liegmei*, while other species are more susceptible to the *R* enantiomer or to mixtures thereof with the *S* enantiomer.[8] For its synthesis tetrahydrofuran **8** was cleaved with Me_3SiI. The iodo alcohol thus obtained (**10**, omitted from Scheme 4) was protected as the acetate **11.** The latter was coupled with lithium diethylcuprate. For easier recovery of the target alcohol **12**, deprotection was performed by $LiAlH_4$ reduction in Et_2O (43% from **1**). Previous syntheses of **12** have been discussed by Mori.[6b] One additional preparation has been recently reported.[9]

The 2*S*,5*R* form of 2-ethyl-1,6-dioxaspiro[4.4]nonane (chalcogran) is the principal component of the aggregation pheromone of the spruce bark beetle (*Pityogenes chalcographus*).[10] The unnatural diastereomeric mixture 2*R*,5*S*/2*R*,5*R* (**15a/15b**) is also active, however. A simple synthesis of the latter has been achieved (Scheme 4) from iodo acetate **11** by treatment with lithium (3-hydroxypropyl)cuprate (protected at the hydroxyl function by acetalation with ethyl vinyl ether).[11] Product **13** was deprotected by acid hydrolysis followed by saponification, and the resulting diol (**14**, omitted from Scheme 4) was directly oxidized to chacogran **15a/15b** according to a known procedure.[12] An alternative, simple route to **15a/15b** would be the reaction of (*R*)-hexanolide **9** with 3-(1-(ethoxyethoxy)propyl)lithium.[13] Syntheses of **15a/15b** published up to 1989 have been reviewed by Mori.[6c] A few additional syntheses have since appeared.[14]

Scheme 5



(*R*)-(+)-5-Hexadecanolide (20) and (*R*)-(+)-14-Methyloctadec-1-ene (24). Scheme 5 summarizes the syntheses of **20** and **24** from **7**, the tosylate from building block **1** (Scheme 5). The δ-lactone **20** is the natural pheromone of the oriental hornet (*Vespa orientalis*) where it performs the function of stimulating the workers to construct queen cells.[15] For its synthesis, tosylate **7** was coupled with nonylmagnesium bromide in THF in the presence of a catalytic amount of lithium tetrachlorocuprate. The tetrahydrofuran **16a** thus obtained was cleaved with trimethylsilyl iodide, and the resulting iodo alcohol (**17a**, omitted from the scheme) was acetylated to **18a**. Treatment of the latter with KCN gave a nitrile acetate (**19** omitted from Scheme 5) which, by saponification followed by acidification, gave the target pheromone **20** (48% overall from **1**). Syntheses of **20** published before 1989 have been reviewed by Mori.[6d] Several new syntheses have since been published.[16]

Alkene **24** is the unnatural enantiomer of the pheromone of *Lyonetia clerkella*, a destructive pest of Japanese peach orchards.[17] Its synthesis (27% fom **1**; Scheme 5) proceeds from **7** to **18b** in a manner similar to that described above for **18a** with the sole variation of the Grignard used in the side-chain homologation (10-undecenyl instead of nonyl). One-carbon homologation of iodo acetate **18b** followed by saponification gave alcohol **22**, the tosylate of which (**23**) was transformed to the hydrocarbon target **24** by reaction with a methylcuprate

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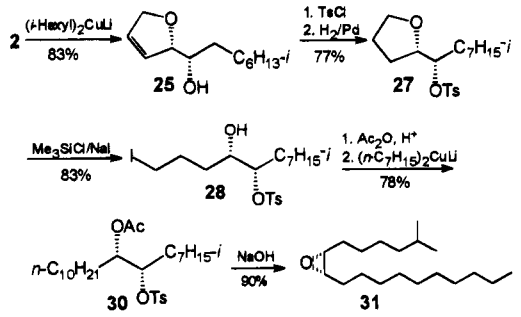
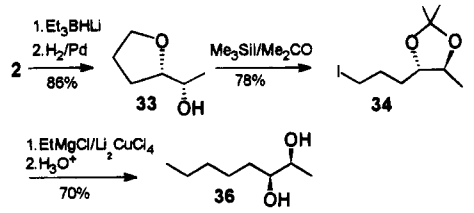
Scheme 6



Scheme 7



reagent. Of the cuprates tested (Me_2CuLi,[18] thienylmethylcuprate,[19] MeCuCNLi,[20] and $Me_2(CuCN)Li_2$,[20] the latter "high-order" cuprate gave the best results. Syntheses of **23** published up to 1989 have been reviewed by Mori.[6e] One additional preparations has appeared since.[21]

(7*S*,8*R*)-(+)-Disparlure (31). The 7*R*,8*S* enantiomer of (*Z*)-4-methyl-7-octadecene oxide is the natural pheromone of *Lymantria dispar* (the gypsy moth).[22] A *Z* epoxide could be obtained from either a threo or an erythro *vic*-diol, depending on the stereochemistry—inversion or, respectively, retention—of the overall process chosen for the transformation. Hence **31** could be obtained from either building block **2** or **3**. Our synthetic sequence is summarized in Scheme 6. Alcohol **25**, resulting from the reaction of epoxide **2** with lithium diisohexylcuprate in Et_2O, was tosylated and hydrogenated to give the tetrahydrofuran **27**, which was then subjected to Me_3SiI cleavage. The free hydroxyl of iodo alcohol **28** thus obtained was protected by acetylation under acidic conditions. The iodo acetate was treated with lithium diheptylcuprate to give **30**. The latter upon exposition to sodium hydroxide gave the target compound **31** (37% from **2**).

A remarkable feature of this sequence is that the secondary tosylate group of **27** appears to survive the ether cleaving conditions without undergoing appreciable substitution by iodide. It is also worth noting that the same synthetic sequence could be used for the preparation of the 7*S*,8*R* enantiomer of **31** by using dinonyl- and diisobutylcuprate, in the epoxide and the iodide homologations, respectively. Syntheses of **31** published up to 1989 have been discussed by Mori.[6f] Numerous additional syntheses have since appeared.[23]

(2*S*,3*S*)-Octanediol (36). This diol is the main component of the pheromone mixture of the grape borer (*Xylotrechus pyrroderus*).[24] Scheme 7 depicts its synthesis involving reductive opening of epoxide **2** with lithium triethylborohydride followed by hydrogenation to yield 2-(1-hydroxyethyl)tetrahydrofuran **33**. Treatment of **33** with Me_3SiI in acetone provided the isopropylidene derivative of 6-iodo-2,3-hexanol (**34**). The latter was treated with ethylmagnesium chloride in the presence of Li_2CuCl_4 to give, after acid hydrolysis, the target diol **36** (47% from **2**). Previous syntheses up to 1989 have been reviewed by Mori.[6g] Two additional preparations have since been published.[25]

Experimental Section

General. Melting points were obtained with a Buchi apparatus and are uncorrected. Unless specified otherwise, yields are for isolated compounds. Proton and ^{13}C NMR spectra were recorded at 200 and 50 MHz, respectively, usually in $CDCl_3$ solvent. Chemical shifts are in ppm downfield of TMS; signal multiplicities were established by DEPT experiments. Coupling constants are given in hertz. Electron impact mass spectra were obtained with a VG 7070 instrument at 70 eV, intensities being given (in parentheses) as percentages of the more intense signal. Optical rotations (Jasco polarimeter) were measured in $CHCl_3$ as well as in other solvents for comparison with literature values. Preparative flash chromatographic separations were performed using ICN Silica Adsorbienten 3263 60 A. For TLC precoated glass plates were used (Stratochrom SIF_{254}, 0.25 mm thick). Solvents and reagent were obtained as follows: THF was distilled from benzophenone ketyl; MeCN, CH_2Cl_2, and DMF were distilled from CaH_2, pyridine from KOH, acetone from K_2CO_3, Et_2O from $LiAlH_4$. Copper(I) iodide was purified by crystallization.[26] Chloroform used in the tosylation reaction was freed from ethanol by filtration over alumina. Noncommercial lithium reagents were prepared from the corresponding bromides with lithium metal in Et_2O.[27] Copper reagents were obtained from the corresponding alkyllithiums and CuI in Et_2O.[28] All reactions involving alkyllithium or -copper reagents were performed in freshly distilled Et_2O in an argon atmosphere.

Preparation of (2*S*,2′*R*)-(−)-2-(2′-Oxiranyl)-2,5-dihydrofuran (3) from Sorbitol. Commercial dianhydrosorbitol was reacted with tosyl chloride in pyridine to give the ditosylate **4** (94%); mp 108−109 °C (lit.[2] mp 98.3−99.6 °C)), $[\alpha]^{25.4}_D$ +57.2° (*c* 4.01, $CHCl_3$); (lit.[2] +57.4°).[29] The ditosylate (68.1 g, 150 mmol) dissolved in acetone (240 mL) was treated with NaI (45 g, 300 mmol) at 110 °C for 20 h in a sealed vessel. After cooling, the reaction mixture was diluted with Et_2O,

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(29) Ditosylate **4** had the following NMR spectra: ^{13}C: δ 145.95 (s), 145.78 (s), 133.75 (s, 2 C's), 130.60 (d), 130.43 (d), 128.35 (d), 128.26 (d), 86.00 (d), 83.74 (d), 80.77 (d), 78.81 (d), 73.48 (t), 70.13 (t); 21.7 (q, 2 C's). ^1H NMR: 7.78 and 7.35 (d's, 8.4 Hz, 4 H's each, *o* and *m* aromatic H), 4.84 (m, 2 H), 4.59 (m, 1 H), 4.47 (m, 1 H), 4.0−3.6 (m, 4 H), 2.45 (s, 6 H).

filtered, and evaporated to dryness. The residue dissolved in CH_2Cl_2 (500 mL) was washed successively with 5% aqueous $NaHSO_3$ and 3 × 100 mL of H_2O and dried over $MgSO_4$. The residue, after solvent evaporation, was dried overnight in a vacuum dessicator, dissolved in THF (1 L), and cooled to −78 °C, and MeLi was added via syringe (70 mL, 1.6 M in Et_2O, 122 mmol). The reaction mixture was allowed to stand at −78 °C for 15 min and then quenched with aqueous concd HCl (9.5 mL). The residue, after solvent evaporation, was, in sequence, dissolved in CH_2Cl_2 (500 mL), washed with 100 mL of 5% aqueous $NaHSO_3$ and 2 × 100 mL of H_2O, and dried over $MgSO_4$. The crude material was adsorbed on silica gel (40 g) and column chromatographed (100 g of SiO_2, height 5 cm, diameter 7 cm), eluting first with Et_2O/petroleum ether 1/1 (1 L) and then with Et_2O/MeOH 98/2 (1 L). The solid obtained from the latter fraction (29.5 g), consisting of **6** and unreacted **4** (8%), was dissolved in CH_2Cl_2/MeOH (15/1, 150 mL) and MeOK (8.8 g, 122 mmol) was added in portions over 20 min, the mixture being stirred at rt for an additional 30 min. After filtration and solvent evaporation, the residue was distilled, bp 84 °C, 40 mm, to give 9.4 g (56%) of epoxide **2**, $[\alpha]^{28.6}_D$ −176.7° (*c* 2.67, $CHCl_3$). ^{13}C NMR: 129.19 (d, C_3), 126.64 (d, C_4), 86.57 (d, C_2), 76.20 (t, C_5), 53.38, (d, $C_{2'}$), 45.59 (t, $C_{3'}$). ^1H NMR: 6.06, 5.92 (m's, 1 H each; irradiation at 4.7 changes the signals in to an AB q, $\Delta\nu$ = 28.5, J = 6.3); 4.65 (m, 2 H), 4.59 (m, 1 H), 2.93 (ddd, J = 2.6, 3.7, 5.0, 1 H), 2.81 (dd, J = 3.7, 5.0), 2.68 (dd, J = 2.6, 5.0, 1 H).

(1*R*,4*R*,5*R*,8*R*)-(+)-8-Iodo-4-(*p*-toluenesulfonyloxy)-2,6-dioxa[3.3.0]octane (5a). A sample of the product from the iodide displacement was chromatographed (sequentially with Et_2O/petrolueum ether 30/70 and 50/50) to give a mixture of the iodo tosylates **5a,b** from which the major component **5a** was separated by crystallization from MeOH, mp 94−94.5 °C (lit.[2] mp 90.8−91.3 °C); $[\alpha]^{30}_D$ +53.1° (*c* 4.75, $CHCl_3$), lit.[2] +52.7°. ^{13}C NMR: 145.45 (s), 133.24 (s), 130.15 (d), 127.84 (d), 90.20 (d), 85.11 (d), 82.84 (d), 76.95 (t), 73.70 (t), 25.37 (d), 21.70 (q). ^1H NMR: 7.80, 7.43 d's, J = 8.3 Hz, 2 H each), 4.96 (m, 1 H), 4.90 (m, 1H), 4.83 (m, 1 H), 4.33 (m, 1H), 4.16 (m, 3 H), 3.89 (m, 1 H), 2.45 (s, 3 H).

(2*S*,1'*S*)-(−)-2-[2-Hydroxy-1-(*p*-toluenesulfonyloxy)ethyl]-2,5-dihydrofuran (6). A sample of the crude from the MeLi reaction was purified by flash chromatography (sequentially with Et_2O/petroleum ether 50/50, and neat Et_2O), to obtain **6**; crystallized from MeOH/H_2O 1/1, mp 67−68 °C; $[\alpha]^{23.4}_D$ −88.0° (*c* 2.08, $CHCl_3$). ^{13}C NMR: 145.43 (s), 133,88 (s), 130.66 (d), 129.89 (d), 128.37 (d), 125.19 (d), 85.28 (d), 83.07 (d), 76.14 (t), 62.27 (t), 21.75 (q). ^1H NMR: 7.83, 7.43 (d's, J = 8.3 Hz, 2 H each), 5.96, 5.73, 4.95 (m's, 1 H each), 4.54 (m, 3 H), 3.76 (m, 2 H), 2.44 (s, 3 H), 2.35 (t, 1 H).

(*R*)-(−)-2-Ethyltetrahydrofuran (8) was obtained from tosylate **7**[1] (5.4 g, 20 mmol) by $LiAlH_4$ (1.52 g, 40 mmol) reduction in Et_2O (40 mL) at 0 °C. After standard workup, a clear liquid was obtained, bp 105−106 °C/760 mm (1.84 g, 92%); $[\alpha]^{25.4}_D$ −27.5° (*c* 7.2, $CHCl_3$). ^{13}C NMR: 80.75 (d), 67.44 (t), 30.99 (t), 28.59 (t), 25.51 (t), 10.44 (q). ^1H NMR: 3.65−390 (m, 3 H), 1.75−2.05 (m, 3 H), 1.35−1.70 (m, 3 H), 0.94 (t, 3 H).

(*R*)-(+)-4-Hexanolide (9) was obtained from **8** by oxidation with RuO_4 according to the procedure of Smith and Scarborough[5] as previously described for the preparation of (*R*)-4-dodecanolide.[1] From 0.20 g (2 mmol) of **8**, 0.138 g (60%) of **9** was obtained, bp 112 °C/18 mm, $[\alpha]^{24.2}_D$ +48.8° (*c* 1.72, MeOH) (lit.[7b] +50.0°). ^{13}C NMR: 177.55 (s), 82.12 (d), 28.75, 28.38, 27.35 (t's), 9.29 (q). ^1H NMR: 4.45 (m, 1 H), 2.55 (m, 2 H), 2.32 (m, 1 H), 1.96−1.55 (m, 3 H), 1.01 (t, 7.4 Hz, 3 H).[30,31] IR (KBr): 1765, lactone $\nu_{C=O}$.

(*R*)-(−)-6-Iodo-3-Hexanol (10). To dry NaI[32] (1.656 g, 11 mmol) in anhydrous MeCN (10 mL) were added sequentially Me_3SiCl (1.4 mL, 11 mmol) and tetrahydrofuran **8** (1.0 g, 10 mmol) dissolved in 5 mL of MeCN. The mixture was stirred at rt for 4 h and then poured in Et_2O (50 mL) and filtered through Celite. The residue after solvent evaporation was taken up in Et_2O (50 mL), washed with H_2O (2 × 5 mL) and brine, and dried over $MgSO_4$. After solvent evaporation, the residue was purified by flash chromatography (petroleum ether/ether 80/20) and distilled to give 1.73 g (76%) of a reddish liquid, bp 120 °C/1 mm; $[\alpha]^{34}_D$ −9.7° (*c* 1.12, $CHCl_3$). ^{13}C NMR: 73.78 (d), 36.89 (t), 29.61 (t, 2 C's), 10.00 (q), 6.98 (t). ^1H NMR: 5.50 (br s, 1 H), 3.72 (m, 1 H), 3.23 (t, J = 7.0, 2 H), 1.95 (m, 2H), 1.50−1.72 (m, 4 H), 0.98 (t, J = 7.5 Hz, 3 H).

(*R*)-(+)-6-Iodohex-3-yl Acetate (11). The iodo alcohol **10** (2.28 g, 10 mmol) was treated with Ac_2O (20 mL) in the presence of catalytic PTSA for 12 h at rt. The mixture was then poured onto ice (50 mL) and extracted with 2 × 50 mL of Et_2O. The organic phase was dried over $MgSO_4$ and the residue, after solvent evaporation, was purified by flash chromatography (petroleum ether/Et_2O 90/10) and distilled to give a clear liquid (2.57 g, 95%), bp 118 °C/1 mm; $[\alpha]^{27}_D$ +9.8° (*c* 3.69, $CHCl_3$). ^{13}C NMR: 170.78 (s), 74.24 (d), 34.48 (t), 29.35 (t), 27.07 (t), 21.22 (q), 9.64 (q), 6.36 (t). ^1H NMR: 4.83 (m, 1 H), 3.20 (t, J = 7.0 Hz, 2 H), 2.05 (s, 3 H), 1.83 (m, 2 H), 1.5−17 (m, 4 H), 0.90 (t, J = 7.4 Hz, 3 H). EIMS *m/z*: 241 (M − Et) (2), 210 (6), 143 (16), 83 (72), 55 (41), 43 (100), 41 (21).

(*R*)-(−)-3-Octanol (12). The iodo acetate **11** (1.35 g, 5 mmol) dissolved in Et_2O (5 mL) was added to a solution of lithium diethylcuprate in Et_2O (0.5 M, 40 mL) at −60 °C. After 2 h at −60 °C, the reaction mixture was first quenched with aqueous saturated NH_4Cl (10 mL) and then poured at rt onto saturated NH_4Cl (20 mL) and shaken for 1 h with Et_2O (50 mL). The aqueous phase was extracted with 3 × 20 mL of Et_2O, and the combined organic phases were washed, sequentially, with aqueous NH_4Cl (2 × 5 mL), H_2O, and brine. Since during these operations the acetate was partly saponified, the organic phase, dried over $MgSO_4$, was concentrated to about 20 mL, and then, at 0 °C, $LiAlH_4$ (0.115 g, 3 mmol, suspended in 6 mL Et_2O) was added. The mixture was stirred for 30 min at 0 °C and for 1.5 h at rt, quenched by dropwise addition of 1 mL of H_2O, filtered, dried over $MgSO_4$, and purified by flash chromatography (petroleum ether/ether 70/30). After distillation, a clear liquid was obtained (0.49 g, 77%), bp 82 °C/20 mm; $[\alpha]^{22}_D$ −9.3° (*c* 3.30, $CHCl_3$) (lit.[8b] −9.7°). ^{13}C NMR: 73.49 (d), 37.10 (t), 32.10 (t), 30.30 (t), 25.53 (t), 22.82 (t), 14.22 (q), 10.05 (q). ^1H NMR: 3.50 (m, 1 H), 1.35 (m, 11H), 0.90 (m, 6 H).

(1*R*)-(+)-7-(1-Ethoxyethoxy)-1-ethylheptyl Acetate (13). The iodo acetate **11** (0.81 g, 3 mmol) was added to 11 mL of a 0.73 M Et_2O solution of lithium bis(3-(1-ethoxyethoxy)propyl)-cuprate at −40 °C, stirred for 2 h at −40 °C and for 1 h at rt, and worked up as described above for the cuprate reaction to give **12**. After flash chromatography (sequentially with petroleum ether/Et_2O 80/20 and 50/50), 0.782 g (95%) of a liquid was obtained, bp 133 °C/1 mm; $[\alpha]^{28.6}_D$ +5.7° (*c* 4.86, $CHCl_3$). Although **13** most likely is a mixture of diastereomers, its ^{13}C NMR spectrum displays gives just one set of signals: 170.83 (s), 99.48 (d), 75.39 (d), 65.15 (t), 60.59 (t), 33.52 (t), 29.78 (t), 29.31 (t), 26.94 (t), 26.13 (t), 25.24 (t), 21.08 (q), 19.80 (q), 15.26 (q), 9.49 (q). ^1H NMR: 4.68 (m, 1 H), 4.55 (q, J = 7.0, 1 H), 3.42 (m, 4 H), 1.90 (s, 3 H), 1.42 (m, 6 H), 1.19 (m superimposed to a d, J = 7.5, 9 H overall), 1.08 (t, J = 7.4, 3 H), 0.75 (t, J = 7.4, 3 H).

The cuprate reagent used in the above homologation had been prepared from (3-(1-ethoxyethoxy)propyl)lithium, prepared in turn from commercial 3-bromopropan-1-ol according to a known procedure.[11]

(*R*)-(−)-Nonane-1,7-diol (14) was obtained from **13** (0.70 g, 2.55 mmol) by acid hydrolysis (THF/concd HCl 3/1, 3 mL, 4 h, rt) followed, after evaporation of THF, by saponification (3 M KOH in MeOH, 0.5 h, rt). Purification by flash chromatography (eluent Et_2O) and distillation gave the title compound (0.305 g, 75%), bp 138 °C/1 mm; $[\alpha]^{25}_D$ −9.5° (*c* 1.8, $CHCl_3$). ^{13}C NMR: 73.26 (d), 62.70 (t), 36.76 (t), 32.60 (t), 30.09, 29.47 (C_2), 25.73, 25.58 (t's), 9.86 (q). The ^1H NMR spectrum is consistent with that reported for the racemic material.[12]

(30) Although there is some discrepancy between these NMR spectra and those reported in recent papers,[4b,7c] they coincide with those of the racemic material as reported in the Aldrich catalog.[31] In particular the resonance at δ 66.01 reported by Nunez and Martin[7c] is absent in our ^{13}C spectrum.

(31) Pouchet, C. J.; Behnke, J. *The Aldrich Library of ^{13}C and ^1H NMR spectra*, 1st ed.; 1993; Vol. 1, spectrum #1128c.

(32) Amoroux, R.; Jatczak, M.; Chastrette, M. *Bull. Chem. Soc. Fr.* **1987**, 506.

(2*R*,5*RS*)-Chalcogran (15a/15b). The diol **14** (1.45 g, 9 mmol) in benzene (36 mL) was reacted with 95% $Pb(OAc)_4$ (9.28 g, 19.9 mmol) in the presence of $CaCO_3$ (2 g) following the procedure of Cekovic and Bosnjak.[12] The title product was isolated by flash chromatography and distilled, 0.47 g (33%), bp 183–186 °C, $[\alpha]^{29}_D$ +13.4° (*c* 1.71, $CHCl_3$).[33] By GC (capillary column, methyl phenyl silicone) and ^{13}C analyses, the product appears to consist of a diastereomeric mixture of composition very similar to that reported by Seebach et al.[34] Our ^{13}C chemical shifts are essentially identical to those reported by the latter authors.[34]

(*R*)-(−)-2-(*n*-Undecyl)tetrahydrofuran (16a) was prepared from tosylate **7** (2.82 g, 10 mmol) by reaction with nonylmagnesium bromide according to the procedure previously described for the preparation of the corresponding 2-octyl derivative.[1] The crude product was purified by flash chromatography (petroleum ether/ether 98/2) and distilled, bp 138 °C/1.5 mm, to give 1.92 g of a liquid; $[\alpha]^{29.4}_D$ −4.6° (*c* 3.26, $CHCl_3$). ^{13}C NMR: 79.40 (d), 67.47 (t), 35.60 (t), 31.75 (t), 31.22 (t), 29.59 (t), 29.45, (t, 3 C's), 29.16 (t), 26.21 (t), 25.52 (t), 22.47 (t), 13.82 (q). ^1H NMR: 3.60–3.90 (m, 3 H), 1.90 (m, 3 H), 1.3–1.6 (m, 21 H), 0.88 (t, 3 H). EIMS *m/z*: 208 (M − H_2O) (1), 71 (100), 43 (19).

(*R*)-(−)-1-(3-Iodopropyl)dodecan-1-ol (17a) was prepared by Me_3SiI cleavage of **16a** (2.26 g, 10 mmol) as described for the preparation of **10** above. After purification by flash chromatography, 2.76 g (78%) of a white solid was obtained, mp 42–43 °C; $[\alpha]^{26.6}_D$ −5.0° (*c* 2.1, $CHCl_3$). ^{13}C NMR: 70.84 (d), 37.84 (t), 37.41 (t), 31.67 (t), 29.56 (t), 29.42 (t, 2 C's), 29.39 (t, 3 C's), 29.10 (t), 25.39 (t), 22.41 (t), 13.83 (q), 6.82 (t). ^1H NMR: 3.68 (m, 1 H), 3.27 (t, *J* = 6.8, 2 H), 2.1–1.8 (m, 2 H), 1.7–1.2 (m, 23 H), 0.90, t, *J* = 6.4, 3 H). EIMS *m/z*: 227 (M − I) (26), 199 (11), 155 (6), 97 (46), 83 (59), 71 (100), 43 (68).

(*R*)-(+)-1-(3-Iodopropyl)dodecyl acetate (18a) was prepared from **17a** as described for **11** above. From 3.54 g (10 mmol) after flash chromatography (petroleum ether/ether 90/10) and distillation, 3.76 g (95%) of a clear liquid was obtained, bp 125 °C/0.001 mm (Kugelrhor); $[\alpha]^{31.8}_D$ +1.6° (*c* 3.04, $CHCl_3$). ^{13}C NMR: 171.19 (s), 73.25 (d), 34.98 (t), 34.18 (t), 31.95 (t), 29.65 (t, 4 C's), 29.51 (t, 2 C's), 29.4 (t), 25.30 (t), 22.69 (t), 21.21 (q), 14.10 (q), 6.21 (t). ^1H NMR: 4.89 (m, 1 H), 3.20 (t, J 6.7, 2 H), 2.04 (s, 3 H), 1.84 (m, 2 H), 1.7–1.4 (m, 5 H), 1.26 (m, 17 H), 0.89 (t, 6.5 Hz, 3 H). EIMS *m/z*: 336 (M − CH_3-COOH) (5), 269 (7), 209 (6), 154 (3), 97 (41), 83 (43)), 69 (36), 55 (31), 43 (100), 41 (24).

(*R*)-(−)-1-(3-Cyanopropyl)dodecyl acetate (19) was prepared from **18a** (1.98 g, 5 mmol) by reaction with KCN (0.50 g, 7.7 mmol) in 15 mL of DMSO. At completion (TLC monitoring, 4 h at rt), the reaction mixture was poured onto Et_2O (50 mL) and washed with H_2O. The aqueous phase was twice extracted with 10 mL of Et_2O. The combined organic phases were evaporated under reduced pressure, and the residue was flash chromatographed (petroleum ether/ether 65/35) to give 1.33 g (90%) of a colorless liquid; $[\alpha]^{23.8}_D$ −5.6° (*c* 3.23, $CHCl_3$). ^{13}C NMR: 171.05 (s), 119.47 (s), 72.95 (d), 34.07 (t), 32.95 (t), 31.79 (t), 29.49 (t, 3 C's), 29.32 (t, 2 C's), 29.21 (t), 25.13 (t), 22.54 (t), 21.32 (t), 20.95 (q), 16.82 (t), 13.92 (q). ^1H NMR: 4.89 (m, 1 H), 2.38 (m, 2 H), 2.02 (s, 3 H), 1.67 (m, 4 H), 1.52 (m, 2 H), 1.27 (m, 18 H), 0.88 (t, 6.4 Hz, 3 H).

(R)-(+)-5-Hexadecanolide (20). The nitrile acetate **19** (1.18 g, 4 mmol) was treated with KOH (1 M in EtOH/H_2O 2/1, 20 mL) at rt for 24 h under stirring. The solution was neutralized with 2 M HCl (phenolphthalein), concentrated under reduced pressure, and refluxed for 12 h in benzene in the presence of a few milligrams of PTSA. The crude product after solvent evaporation was flash chromatographed (petroleum ether/ether 65/35) to give 0.89 g (90%) of a white solid, mp 39–40 °C (lit.[35] mp 37.0 °C); $[\alpha]^{25.8}_D$ +38.6° (*c* 2.36, THF) (lit.[16e] +39.8°). The ^1H NMR spectrum was identical to that previously reported.[35] ^{13}C NMR: 172.22 (s), 80.71 (d), 35.79 (t), 31.82 (t), 29.52 (t, 2 C's), 29.40 (t, 2 C's), 29.33 (t, 2 C's), 29.23 (t), 27.72 (t), 24.82 (t), 22.55 (t), 18.37 (t), 13.93 (q). IR: 1727 $\nu_{C=O}$. EIMS *m/z*: 255 (M + 1) (4), 254 (M) (3), 236 (16), 99 (100), 71 (29).

(*R*)-(−)-2-(Tridec-12-enyl)tetrahydrofuran (16b) was prepared from tosylate **7** (2.70 g, 10 mmol) and undec-10-en-1-ylmagnesium bromide (prepared from commercial undec-10-en-1-ol via the bromide) in the presence of catalytic Li_2CuCl_4 as previously described for the corresponding 2-octyl derivative.[1] The crude product was purified by flash chromatography (successively petroleum ether and petroleum ether/ether 50/50) and distilled (bp 149 °C/1 mm) to yield 2.10 g (83%) of a clear liquid; $[\alpha]^{23.4}_D$ −4.4° (*c* 2.55, $CHCl_3$). ^{13}C NMR: 139.34 (d), 114.23 (t), 79.63 (d), 67.72 (t), 35.96 (t), 33.97 (t), 31.60 (t), 29.94 (t), 29.79 (t, 4 C's), 29.68 (t), 29.34 (t), 29.16 (t), 26.56 (t), 25.92 (t). ^1H NMR: 5.75 (m, 1 H), 4.90 (m, 2 H), 3.89–3.59 (m, 3 H), 2.07–1.62 (m, 4 H), 1.2 (m, 22 H).

(*R*)-(−)-1-Iodoheptadec-16-en-4-ol (17b) was prepared by cleavage of **16b** (2.52 g, 10 mmol) with excess Me_3SiI (25 mmol). Due to insufficient solubility of **16a** in MeCN, CCl_4 (50 mL) was used as the solvent. After 5.5 h at rt, 100 mL of Et_2O was added to the reaction mixture, which was filtered through Celite and evaporated under reduced pressure. The residue was taken up in Et_2O, washed in succession with aqueous $NaHSO_3$, H_2O, and brine, and dried over $CaSO_4$. The crude product appeared to consist of the title compound and a byproduct (ca 10%) which is likely to be the diiodide (as evinced in the ^{13}C spectrum by a doublet at 37.5). Purification by flash chromatography (in succession, petroleum ether/ether 97/3 and 50/50) yielded 3.16 g (83%) of a waxy white solid, mp 36–37 °C (crystallizd from *n*-hexane); $[\alpha]^{23.0}_D$ −5.27° (*c* 1.87, $CHCl_3$). ^{13}C NMR: 139.32 (d), 114.20 (t), 71.25 (d), 38.08 (t), 37.64 (t), 33.79 (t), 29.82 (t), 29.60 (t, 5 C's), 29.49 (t), 29.14 (t), 28.98 (t), 25.61 (t), 7.06 (t). ^1H NMR: 5.83 (m, 1 H), 4.96 (m, 2 H), 3.65 (m, 1 H), 3.23 (t, *J* = 6.8, 3 H), 2.1–1.7 (m, 6 H), 1.5–1.2 (m, 21 H).

(*R*)-(+)-1-Iodoheptadec-16-en-4-yl acetate (18b) was prepared from **17b** (3.8 g, 10 mmol) as described for **11** above. After flash chromatography (petroleum ether/ether 97/3) a liquid was obtained, 3.12 g (74%), $[\alpha]^{25.4}_D$ +1.16° (*c* 4.53, $CHCl_3$). ^{13}C NMR: 172.23 (s), 139.40 (d), 114.32 (t), 73.19 (d), 35.02 (t), 34.19 (t), 33.76 (t), 29.46 (t, 5 C's), 29.12 (t), 28.97, (t), 28.76 (t), 25.26 (t), 21.03 (q), 5.72 (t). ^1H NMR: 5.80 (m, 1 H), 4.91 (m, 2 H), 4.83 (m, 1 H), 3.15 (t, *J* = 6.7, 2 H), 2.1–1.15 (m, superimposed to a 2.01 s, 29 H overall).

(*S*)-(−)-Octadec-17-en-5-yl acetate (21). Iodo acetate **18b** (4.67 g, 11 mmol) was treated with a 3-fold excess of lithium dimethylcuprate at −35 °C for 4 h in Et_2O. After a saturated aqueous NH_4Cl quench, the aqueous phase was extracted with Et_2O (3 × 100 mL) and the combined organic extracts were washed with H_2O and brine and dried over $CaSO_4$. The crude product was purified by flash chromatography (petroleum ether/ether 98/2) and distilled, bp 169–171 °C/1 mm, to yield 3.05 g (89%) of **21**; $[\alpha]^{25.4}_D$ −1.92° (*c* 3.65, $CHCl_3$). ^{13}C NMR: 171.26 (s), 139.65 (d), 114.42 (t), 74.74 (d), 34.35 (t), 34.02 (t), 33.91 (t), 29.69 (t, 5 C's), 29.27 (t), 29.12 (t), 27.65 (t), 25.44 (t), 22.70 (t), 21.55 (q), 13.96 (q). ^1H NMR: 5.83 (m, 1H), 4.95 (m, 2 H), 4.86 (m, 1 H), 2.03 (s superimposed to a m, 5 H overall), 1.65–1.15 (m, 26 H), 0.90 (t, 3 H).

(*S*)-(+)-Octadec-17-en-5-ol (22). To the acetate **21** (3.0 g, 9.67 mmol) dissolved in MeOH (10 mL) was added, portionwise over 1 h, KOH (0.81 g, 14.5 mmol). The reaction mixture, monitored by TLC, was quenched after 16 h by pouring the mixture into Et_2O (70 mL). After filtration and solvent evaporation, the residue was purified by flash chromatography (petroleum ether/ether 85/15) to yield 2.37 g (92%) of a solid (crystallized from pentane), mp 39–40 °C; $[\alpha]^{23.6}_D$ +0.89° (*c* 2.59, $CHCl_3$). ^{13}C NMR: 139.42 (d), 114.33 (t), 71.98 (d), 37.52 (t), 37.21 (t), 33.84 (t), 29.66 (t, 5 C's), 29.54 (t), 29.18 (t), 28.96 (t), 27.87 (t), 25.68 (t), 22.77 (t), 14.03 (q). ^1H NMR: 5.80 (m,

(33) In our hands the procedure of Cekovic and Bosnjak failed to reproduce the yield (GC, 61%) reported by the authors.[12] Our product always contained large proportions of partial oxidation products (tetrahydrofuranyl derivatives of both the primary and the secondary alkyl acetates).

(34) Hungerbuehler, E.; Naef, R.; Wasmuth, D.; Seebach, D.; Loosli, H.-R.; Wehrli, A. *Helv. Chim. Acta* **1980**, *63*, 1960.

(35) Mori, K.; Otsuka, T. *Tetrahedron* **1985**, *41*, 547.

1 H), 4.95 (m, 2 H), 3.55 (m, 1 H), 2.03 (m, 2 H), 1.92 (br s, 1 H, OH), 1.53–1.15 (m 26 H), 0.91 (t, 3 H).

(*S*)-(+)-Octadec-17-en-5-yl *p*-toluenesulfonate (23) was prepared from **22** (0.955 g, 3.56 mmol) according to the standard procedure ($CHCl_3$–pyridine) to give, after purification by flash chromatography (petroleum ether/ether 98/2), 1.35 g (99%) of a liquid, $[\alpha]^{20}_D$ +3.80° (*c* 11, $CHCl_3$). ^{13}C NMR: 144.80 (s), 139.71 (d), 135.33 (s), 130.1 (d), 128.20 (d), 114.55 (t), 84.92 (d), 34.30 (t), 34.03 (t), 29.78 (t, 3 C's), 29.68 (t, 2 C's), 29.58 (t), 29.47 (t), 29.35 (t), 29.13 (t), 27.00 (t), 24.87 (t), 22.57 (t), 21.74 (q), 14.00 (q). ^1H NMR: 7.80 and 7.30 (d's, J = 8.3, 2 H each), 5.80 (m, 1 H), 4.94 (m, 2 H), 6.62 (m, 1 H), 2.42 (s, 3 H), 2.05 (m, 2 H), 1.65–1.04 (m, 26 H), 0.81 (t, 3 H).

(*R*)-(−)-14-Methyloctadecene (24). Tosylate **23** (1.32 g, 3.1 mmol) in 5 mL of THF at −10 °C was added to a THF/Et_2O solution containing a 10-fold excess of dilithium dimethylcyanocuprate at −10 °C. The reaction mixture was maintained for 3 d at −10 °C and for 3 more d at 0 °C and then quenched with saturated aqueous NH_4Cl (first 10 mL was added slowly, then poured onto 50 more mL). The aqueous phase was washed with Et_2O, and the combined organic extracts were washed with H_2O and dried over $CaSO_4$. The residue after solvent removal was flash chromatographed (pentane). The first fraction (0.166 g, 20.4%) consisted of a mixture of at least three isomeric dienes (elimination products). The second fraction (0.595 g, 71.3%) was the title compound, bp 150 °C/1 mm; $[\alpha]^{26.6}_D$ −1.16° (*c* 4.55, *n*-hexane) (lit.[36] −1.24°). ^{13}C NMR: 139.56 (d), 114.38 (t), 37.27 (t), 36.93 (t), 33.91 (t), 32.89 (d), 30.16 (t), 29.80 (t, 4 C's), 29.63 (t), 29.47 (t), 29.28 (t), 29.10 (t), 27.21 (t), 23.12 (t), 19.78 (q), 14.13 (q). ^1H NMR: 5.82 (m, 1 H), 4.95 (m, 2 H), 2.05 (m, 2 H), 1.5–1.0 (m, 27 H), 0.86 (d, superimposed to a t, 6 H overall).

(2*S*,1′*S*)-(−)-2-(1-Hydroxy-6-methylheptyl)-2,5-dihydrofuran (25). Epoxide **2** (1.12 g, 10 mmol, in 20 mL of Et_2O) was added dropwise to a 0.3 M Et_2O solution (70 mL, 20 mmol) of lithium diisohexylcuprate at −70 °C. The mixture was stirred for 1 h at −70 °C and for 2 more h at −30 °C, the reaction being monitored by GC and TLC. The mixture was then quenched with saturated aqueous NH_4Cl and extracted with Et_2O. The combined organic phases were dried over $MgSO_4$ and evaporated under reduced pressure. The residue was purified by flash chromatography (petroleum ether/ether 75/25) and distilled. A liquid was obtained (1.74 g, 87%), bp 125 °C/1 mm; $[\alpha]^{23.8}_D$ −26.7° (*c* 6.72, $CHCl_3$). ^{13}C NMR: 128.29 (d), 126.75 (d), 89.54 (d), 75.16 (t), 73.53 (d), 32.70 (t), 32.88 (t), 27.65 (d), 25.18 (t), 25.66 (t), 22.34 (q, 2 C's). ^1H NMR: 5.92 (m, 1 H), 5.73 (m, 1 H), 4.61 (m, 3 H), 3.44 (br s, 1 H), 2.60 (br s, 1 H), 1.6–1.0 (m, 9 H), 0.79 (d, J = 7.5, 6 H). EIMS *m/z*: 197 (M − 1) (1), 111 (2), 71 (6), 70 (100), 69 (61), 41 (17).

(2*S*,1′*S*)-(−)-2-(1-Hydroxy-6-methylheptyl)tetrahydrofuran (26) was obtained from **25** (9.9 g, 50 mmol in 50 mL of Et_2O) by hydrogenation (H_2, 2 atm, Pd/C 10%, 4 h). After filtration through Celite and solvent evaporation, the residue was purified by flash chromatography (petroleum ether/ether 80/20) and distilled, 9.1 g (91%); bp 124 °C/2 mm; $[\alpha]^{26.6}_D$ −16.5° (*c* 5.10, $CHCl_3$). ^{13}C NMR: 82.64 (d), 74.09 (d), 68.23 (t), 38.98 (t), 33.79 (t), 27.98 (d), 27.98 (t), 27.48 (t), 26.30 (t), 25.94 (t), 22.64 (q, 2 C's). ^1H NMR: 3.9–3.6 (m, 3 H), 3.40 (m, 1 H), 2.50 (br s, 1 H), 1.90 (m, 3 H), 1.7–1.1 (m, 10 H), 0.86 (d, J = 7.5, 6 H).

(2*S*,1′*S*)-(−)-2-[1-(*p*-Toluenesulfonyloxy)-6-methylheptyl]tetrahydrofuran (27). To **26** (2.03 g, 10 mmol) dissolved in $CHCl_3$ (10 mL) were added at 0 °C 1.7 mL (20 mmol) of pyridine and, portionwise, 2.85 g (15 mmol) of TsCl. After 18 h at 0 °C (TLC monitoring), the mixture was quenched with ice (2 mL), poured onto H_2O (10 mL) and stirred with 50 mL of Et_2O for 1 h. The separated organic phase was washed with 2 N HCl (2 × 5 mL), saturated aqueous $NaHCO_3$, and brine, and dried over $MgSO_4$. The solution was filtered and the residue, after solvent evaporation under reduced pressure, was flash chromatographed (petroleum ether/ether 80/20) to give 3.19 g (90%) of an oil; $[\alpha]^{28.6}_D$ −4.4° (*c* 7.4, $CHCl_3$). ^{13}C NMR: 144.67 (s), 135.04 (s), 129.83 (d), 128.08 (d), 85.02 (d), 78.72 (d), 68.53 (t), 38.66 (t), 30.83 (t), 27.74 (d), 27.41 (t), 27.08 (t), 25.92 (t), 25.26 (t), 22.53 (q, 2 C's), 21.58 q). ^1H NMR: 7.80, 7.34 (d's, J = 8.4, 2 H each), 4.55 (m, 1 H), 3.99 (m, 1 H), 3.72 (m, 2 H), 2.44 (s, 3 H), 1.95–1.35 (m, 7 H), 1.30–0.95 (m, 6 H), 0.83 (d, J = 7.5, 6 H). EIMS *m/z*: 355 (M + 1) (2), 226 (8), 182 (9), 155 (9), 71 (100), 43 (33).

(4*S*,5*S*)-(−)-1-Iodo-4-hydroxy-10-methyl-5-(*p*-toluenesulfonyloxy)undecane (28). Trimethylsilyl iodide cleavage of the tetrahydrofuran ring of **27** was performed on 3.74 g (10 mmol) as described for the preparation of **10** above, except that the reaction was carried out at rt for 18 h. After workup, flash chromatography (petroleum ether/ether 80/20), and crystallization (hexane), 4.24 g (88%) of a solid was obtained, mp 46–47 °C; $[\alpha]^{27.0}_D$ −16.0° (*c* 8.85, $CHCl_3$). ^{13}C NMR: 145.22 (s), 134.32 (s), 130.14 (d), 128.06 (d), 86.63 (d), 70.96 (d), 38.61 (t), 33.49 (t), 30.41 (t), 29.51 (t), 27.72 (d), 26.99 (t), 25.04 (t), 22.54 (q, 2 C's), 21.64 (q), 6.56 (t). ^1H NMR: 7.82, 7.36 (d's, J = 8.4, 2 H each), 4.50 (m, 1 H), 3.67 (m, 1 H), 3.18 (t, J = 6.5, 2 H), 2.45 (s, 3 H), 2.10 (br s, 1 H), 2.05–1.35 (m, 7 H), 1.25–1.0 (m, 6 H), 0.83 (d, J = 7.5, 6 H).

(4*S*,5*S*)-(−)-1-Iodo-4-acetoxy-10-methyl-5-(*p*-toluenesulfonyloxy)undecane (29). Acetylation of **28** was carried out as described for **11** above. From 4.82 g (10 mmol) of **28**, after purification by flash chromatography (ether/petroleum ether 50/50), 5.20 g (100%) of **29** was obtained as a clear oil; $[\alpha]^{30.3}_D$ −14.7° (*c* 5.15, $CHCl_3$). ^{13}C NMR: 170.78 (s), 145.10 (s), 134.65 (s), 130.11 (d), 128.06 (d), 82.85 (d), 71.65 (d), 38.56 (t), 31.07 (t), 30.54 (t), 29.04 (t), 27.73 (d), 26.92 (t), 24.86 (t), 22.53 (q, 2 C's), 21.64 (q), 20.78 (q), 5.44 (t). ^1H NMR: 7.81, 735 (d's, J = 8.3, 2 H each), 4.97, 4.60 (m's, 1 H each), 3.10 (t, J = 6.5, 2 H), 2.44, 2.03 (s's, 3 H each), 1.90–1.35 (m, 7 H), 0.98–1.26 (m, 6 H), 0.82 (d, J = 7.5, 6 H).

(7*S*,8*S*)-(−)-2-Methyl-7-(*p*-toluenesulfonyloxy)-8-acetoxyoctadecane (30). The seven-carbon elongation of the unbranched chain of iodide **29** was carried out by reaction with lithium diheptylcuprate as described for **12** above, except the reaction was carried out at −30 °C for 3 h. From 5.24 g (10 mmol) of **29**, 3.72 g (75%) of **30** was obtained after flash chromatographic purification (petroleum ether/ether 90/10) as a clear oil; $[\alpha]^{27.0}_D$ −12.8° (*c* 6.1, $CHCl_3$). ^{13}C NMR: 170.72 (s), 144.83 (s), 134.90 (s), 129.96 (d), 127.97 (d), 83.14 (d), 72.74 (d), 38.54 (t), 31.86 (t), 30.61 (t), 30.07 (t), 29.51 (t, 2 C's), 29.35 (t), 29.25 (t, 2 C's), 27.69 (d), 26.91 (t), 25.06 (t), 24.84 (t), 22.62 (t), 22.48 (q, 2 C's), 21.48 (q), 20.73 (q), 14.02 (q). ^1H NMR: 7.80, 7.33 (d's, J = 8.3, 2 H each), 4.95, 4.62 (m, 1 H each), 2.43, 2.00 (s's, 3 H each), 1.65–1.35 (m, 6 H), 1.35–1.0 (m, 21 H), 0.86, 0.83, (t overlapping a d, 9 H overall).

(7*R*,8*S*)-(+)-Disparlure (31). The acetate tosylate **30** (1.02 g, 2 mmol) dissolved in MeOH (4 mL) was treated at 0 °C with 0.25 g of solid KOH. After 1 h at 0 °C and 0.5 h at rt, the mixture was poured onto 50 mL of Et_2O, washed with 2 × 10 mL of H_2O, dried over $MgSO_4$, filtered, and evaporated under reduced pressure. The crude product was purified by flash chromatography (petroleum ether/ether 95/5) and distilled, bp 180 °C/1 mm, to give 0.51 g (90%) of the title compound as a colorless liquid, $[\alpha]^{26.6}_D$ +0.54° (*c* 8.5, CCl_4) (lit.[37] +0.54°). ^1H NMR: 2.94 (m, 2 H), 1.70–1.15 (m, 27 H), 0.85, 0.82 (t overlapping a d, 9 H overall). The ^{13}C NMR spectrum was identical to that reported previously.[38]

(*S*,*S*)-(−)-2-(1-Hydroxyethyl)-2,5-dihydrofuran (32). To a solution of lithium diethylborohydride (45 mL, 1 M in THF) was added dropwise a solution of epoxide **2** (3.36 g, 30 mmol) in THF (10 mL). After 5 min at rt, the reaction was quenched with 2 mL of H_2O. The solvent was evaporated at 0 °C under reduced pressure; the residue was taken up in Et_2O (50 mL) and washed with brine (2 × 5 mL). After solvent evaporation and flash chromatography (petroleum ether/ether 65/35), the crude product was distilled (bp 82.0 °C/15 mm) to yield a colorless liquid (3.25 g, 95%); $[\alpha]^{27.8}_D$ −193.6° (*c* 3.28, $CHCl_3$). ^{13}C NMR: 128.86 (d), 126.95 (d), 91.16 (d), 75.62 (t), 70.17 (d), 18.44 (q). ^1H NMR (acetone-d_6): 6.02, 5.83 (m, 1 H each), 4.55 (m, 3 H), 3.66, 3.04 (m's, 2 H each), 1.03 (d, J = 7.0, 3 H).

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EIMS *m/z*: 113 (M − 1) (6), 97 (14), 84 (44), 69 (100), 55 (20), 45 (76), 41 (35).

(*S,S*)-(−)-2-(1-Hydroxyethyl)tetrahydrofuran (33). Dihydrofuran **32** (5.70 g, 50 mmol) in Et_2O (50 mL) was hydrogenated (H_2, 2 atm, rt, 4 h, 150 mg 10% Pd/C). The reaction mixture was filtered through Celite and, after solvent evaporation under reduced pressure, purified by flash chromatography (petroleum ether/ether 65/35) and distilled to yield 5.15 g (90%) of a colorless liquid, bp 87.0 °C/25 mm; $[\alpha]^{27.8}_D$ −5.8° (*c* 1.01, $CHCl_3$). ^{13}C NMR: 83.85 (d), 70.09 (d), 67.94 (t), 27.72 (t), 25.98 (t), 16.69 (q). ^1H NMR: 3.83 (m, 2 H), 3.7–3.5 (m, 2 H), 2.8 (br s, 1 H), 1.90 (m, 3 H), 1.55 (m, 1 H), 1.15 (d, J = 6.0, 3 H).

(*S,S*)-(−)-4-(3-Iodopropyl)-2,2,5-trimethyldioxolane (34) was prepared by cleavage of **33** (1.16 g, 10 mmol) as described above for the preparation of **10** except that acetone was used as the solvent. The crude product was purified by flash chromatography (petroleum ether/ether 95/5) and distilled to yield a clear liquid (2.21 g, 78%), bp 87 °C/1 mm; $[\alpha]^{30.6}_D$ −11.9° (*c* 2.32, $CHCl_3$). ^{13}C NMR: 108.03 (s), 81.54 (d), 76.73 (d), 33.06 (t), 39.17 (t), 27.41 (q), 27.30 (q), 17.56 (q), 6.68 (t). ^1H NMR: 3.75, 3.53 (m's, 1 H each), 3.25 (t, J = 6.5, 2 H), 1.98, 1.73 (m's, 2 H each), 1.40, 1.39 (s's, 6 H overall), 1.25 (d, J = 7.5, 3 H).

(*S,S*)-(−)-4-Pentyl-2,2,5-trimethyldioxolane (35) was prepared by reaction of **34** (0.38 g, 1.3 mmol, in 5 mL of THF) with ethylmagnesium chloride (2 mL, 2 M in THF) in the presence of catalytic Li_2CuCl_4 as described above for the homologation of **7** to **16a** or **16b**. The product was distilled, bp 103 °C/10 mm (Kugelrhor), to give 0.187 g (75%) of a liquid; $[\alpha]^{29.4}_D$ −18.8° (*c* 1.02, $CHCl_3$). ^{13}C NMR: 107.75 (s), 82.73 (d), 77.02 (d), 32.51 (t), 32.21 (t), 27.52 (q), 27.45 (q), 25.99 (t), 22.75 (t), 17.87 (q), 14.23 (q). ^1H NMR: 3.68 (m, 1 H), 3.50 (m, 1 H), 1.55–1.20 (m superimposed to s's at 1.37 and 1.36 and a d, J = 6.0, at 1.23; overall 17 H), 0.88 (deformed t, 3 H).

(*S,S*)-(−)-2,3-Octanediol (36). Acetonide **35** (0.187 g, 1.0 mmol) was deprotected in MeOH in the presence of catalytic PTSA for 4 h at reflux. The residue after solvent evaporation was taken up in C_2H_2 (5 mL), neutralized with $NaHCO_3$ (0.2 g), filtered over SiO_2, and distilled (Kugelrhor) to a liquid, 0.128 g (87%), bp 60 °C/1 mm; $[\alpha]^{27.8}_D$ −19.8° (*c* 1.11, $CHCl_3$) (lit.[39] −18.5°). ^1H NMR: 3.59 (apparent quintet, J = 6.3, 1 H), 3.32 (m, 1 H), 2.63 (br s, 2 H), 1.60–1.25 (m, 8 H), 1.19 (d, 6.3 Hz, 3 H), 0.89 (deformed t, 3 H). By irradiation at δ 1.19, the low-field quintet changes to a d, J = 6.3 Hz. The ^{13}C NMR spectrum agrees with those previously published.[39,40]

Supplementary Material Available: Analytical data for new compounds (2 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

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