solvent gradient of petroleum ether/ether (20:1 and 10:1) to leave pure cycized **3a**-α-*cis* (64%), **3a**-α-*trans* (17%), and **3a**-β-*trans* (19%). **3a**-α-*cis* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.53 (1 H, m), 5.31 (1 H, m), 3.51 (1 H, d, J = 14.1 Hz), 3.15 (1 H, dq, J = 14.1, 1.1 Hz), 2.81 (1 H, m, $J_{3/8}$ = 5.9 Hz), 2.45 (1 H, m), 2.34 (1 H, m), 1.86 (3 H, d, J = 1.1 Hz), 0.97 (3 H, s). **3a**-β-*trans* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.49 (1 H, m), 5.45 (1 H, m), 3.29 (1 H, d, J = 14.7 Hz), 3.00 (1 H, d, J = 14.7 Hz), 2.69 (1 H, ddd, J = 14.0, 11.0, 3.7 Hz), 2.39 (1 H, m, $J_{3/8}$ = 13.9 Hz), 2.36 (1 H, quint), 1.85 (3 H, s), 1.00 (3 H, s). **3a**-α-*trans* (300-MHz) ^{1}H NMR ($CDCl_3$): 5.56 (1 H, m), 5.18 (1 H, m), 3.50 (1 H, d, J = 14.9 Hz), 3.13 (1 H, d, J = 14.9 Hz), 3.13 (1 H, ddq, J = 14.9, 1.7, 1.2 Hz), 2.55 (1 H, m, $J_{3/8}$ = 9.7 Hz), 2.42 (1 H, dddd, J = 11.4, 9.7, 3.6, 1.7 Hz), 2.31 (1 H, m), 1.80 (3 H, d, J = 1.2 Hz), 1.09 (3 H, s).

Thermal Cycloaddition of Tetraene 2b. By use of the procedure outlined previously, **2b** gave **3b**-α-*cis* (49%), **3b**-α-*trans* (36%), and **3b**-α-*trans* (15%) after purification by column chromatography on silica. **3b**-α-*cis* (300-MHz) ^{1}H NMR ($CDCl_3$): 5.25 (1 H, bs), 3.50 (1 H, d, J = 14.6 Hz), 3.15 (1 H, dq, J = 14.6, 1.3 Hz), 2.61 (1 H, m, $J_{3/8}$ = 4.9 Hz), 2.32 (1 H, dddd, J = 11.9, 4.9, 2.4 Hz), 2.31 (1 H, m), 1.81 (3 H, d, J = 1.3 Hz), 1.59 (3 H, bs), 0.93 (3 H, s). **3b**-β-*trans* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.36 (1 H, bs), 3.30 (1 H, d, J = 15.1 Hz), 3.01 (1 H, d, J = 15.1 Hz), 2.79 (1 H, ddd, J = 14.0, 10.6, 3.7 Hz), 2.37 (1 H, quint), 2.33 (1 H, m, $J_{3/8}$ = 14.0 Hz), 1.84 (3 H, s), 1.66 (3 H, b s), 1.04 (3 H, s). **3b**-α-*trans* (300-MHz) ^{1}H NMR ($CDCl_3$): 5.48 (1 H, bd, J = 6.4 Hz), 3.30 (1 H, d, J = 13.1 Hz), 3.19 (1 H, d, J = 13.1 Hz), 2.78 (1 H, b quint), 2.27 (1 H, m), 1.72 (3 H, s), 1.50 (3 H, b s), 1.31 (3 H, s).

Thermal Cycloaddition of Tetraene 2c. In an analogous manner to that above, thermal cycloaddition of **2c** yielded after purification **3c**-α-*cis* (27%), **3c**-α-*trans* (38%), **3c**-β-*cis* (13.5%), and **3c**-β-*trans* (12%). **3c**-β-*cis* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.55 (1 H, m), 5.48 (1 H, m), 3.54 (1 H, d, J = 13.2 Hz), 3.22 (1 H, d, J = 13.6 Hz), 2.82 (1 H, b s), 2.22 (1 H, bs), 1.80 (3 H, s), 1.40 (3 H, s), 1.17 (3 H, s). **3c**-α-*cis* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.40 (1 H, m), 5.29 (1 H, m), 3.85 (1 H, d, J = 14.3 Hz), 3.05 (1 H, dq, J = 14.3, 1.1 Hz), 2.37 (1 H, b t), 2.34 (1 H, b q), 1.92 (3 H, d, J = 1.1 Hz), 1.12 (3 H, s), 0.99 (3 H, s). **3c**-β-*trans* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.55 (1 H, m), 5.17 (1 H, m), 3.58 (1 H, d, J = 15.1 Hz), 3.15 (1 H, dq, J = 15.1, 1.5 Hz), 2.65 (1 H, m), 2.28 (1 H, m), 1.85 (3 H, d, J = 1.5 Hz), 1.08 (3 H, s), 1.03 (3 H, s). **3c**-α-*trans* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.47 (1 H, m), 5.15 (1 H, m), 3.68 (1 H, d, J = 16.2 Hz), 3.15 (1 H, m), 3.09 (1 H, dq, J = 16.2, 1.8 Hz), 2.31 (1 H, quint, J = 2.9 Hz), 1.82 (3 H, d, J = 1.8 Hz), 1.10 (3 H, s), 0.94 (3 H, s).

Thermal Cycloaddition of Tetraene 2d. In a similar fashion to that above, **2d** afforded **3d**-α-*trans* (70%) after purification. **3d**-α-*trans* (300-MHz) ^{1}H NMR ($CDCl_3$): 5.16 (1 H, m), 3.85 (1 H, d, J = 14.4 Hz), 3.05 (1 H, dq, J = 14.4, 1.4 Hz), 2.33 (1 H, q, J = 2.9 Hz), 2.14 (1 H, b d, J = 6.0 Hz), 1.90 (3 H, d, J = 1.4 Hz), 1.60 (3 H, b s), 1.06 (3 H, s), 0.98 (3 H, s).

Method B. Lewis Acid Cycloaddition of Tetraene 2d. A solution of **2d** (40 mg, 0.145 mmol) in dry benzene (25 mL) was treated slowly with dimethylammonium chloride (1.0 M, 0.15 mL, 0.145 mmol) at room temperature. After the addition was complete, TLC (80:7 petroleum ether/ether) indicated complete consumption, and the reaction was quenched with saturated $NaHCO_3$ (5 mL). After 30 min, the reaction was diluted with petroleum ether (ca. 15 mL) and transferred into a separatory funnel. The organic layer was separated and the aqueous portion further extracted with petroleum ether (5 × 5 mL). The combined organic layers were then washed with brine, dried over Na_2SO_4, filtered, and concentrated. Flash chromatography on silica gel (80:7 petroleum ether/ether) provided pure **3d**-α-*cis* (85%). **3d**-α-*cis* (600-MHz) ^{1}H NMR ($CDCl_3$): 5.33 (1 H, b s), 3.70 (1 H, d), 3.09 (1 H, dq), 3.04 (1 H, b s), 2.31 (1 H, quint), 1.82 (3 H, d), 1.64 (3 H, m), 1.11 (3 H, s), 0.97 (3 H, s).

Epimerization Studies on Cycloadducts 3a-α-*cis* and 3a-α-*trans*. A methanolic solution of pure or enriched mixtures of **3a**-α-*cis* or **3a**-α-*trans* were treated with 1 M NaOMe at 58 °C for 18 h. The reaction was cooled to ambient temperature and diluted with petroleum ether (20 mL). The organic mixture was quenched with saturated $NaHCO_3$ and the layers separated. The organic phase was then washed with brine, dried over Na_2SO_4, and concentrated. The crude reaction was examined by proton NMR to determine the product ratios.

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Supplementary Material Available: X-ray experimental procedures and coordinates for hydrogen and non-hydrogen atoms, anisotropic thermal parameters, bond distances and angles, and torsion angles for **3a**-α-*cis* and **3a**-β-*trans*; approximate coordinates for the ordered molecular **3b**-β-*trans* (16 pages). Ordering information is given on any current masthead page.

Asymmetric Synthesis of (*S*)-Zearalenone Dimethyl Ether, an Orsellinic Acid Type Macrolide

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The synthesis of (*S*)-zearalenone dimethyl ether is described. The chiral part of the molecule was obtained by asymmetric synthesis monitored by a chiral sulfoxide group and introduced in the very last steps of the synthesis.

Zearalenone (**1a**) is a naturally occuring 14-membered orsellinic acid type macrolide[1] with anabolic and uterotropic activity. Several total syntheses of racemic zearalenone were carried out during the last 20 years,[2] and a chiral synthesis from a natural product was recently published.[2j]

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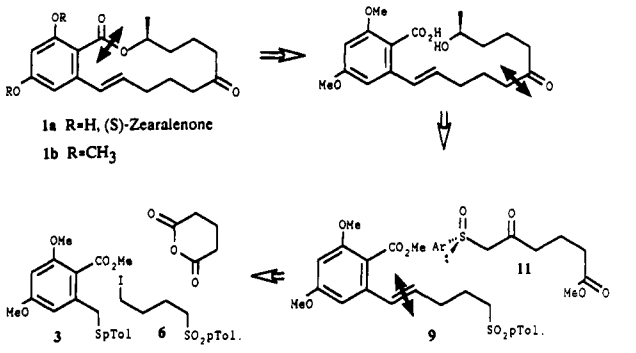
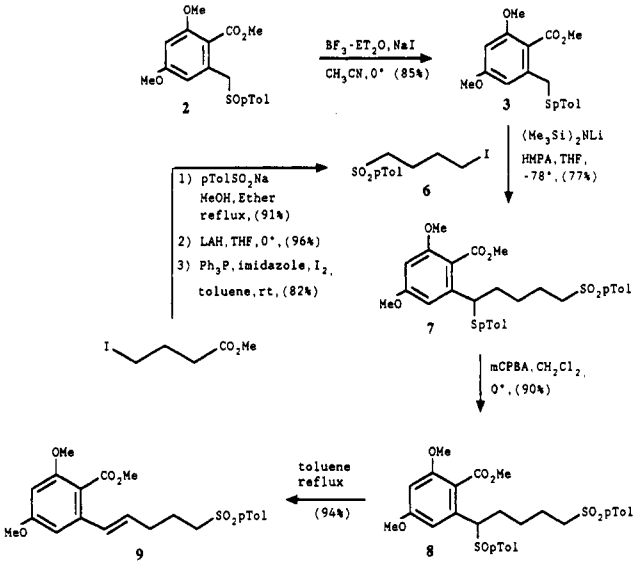
0022-3263/91/1956-2317$02.50/0

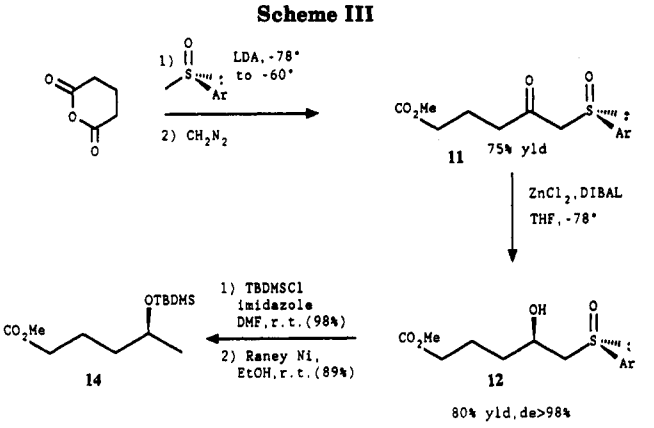
Scheme I



Scheme II



Scheme III



We report in this paper the first asymmetric synthesis of (*S*)-zearalenone dimethyl ether (**1b**) using a general strategy that was already applied to prepare optically active lasiodiplodin, one member of this macrolide family.[3] The advantage of our methodology is to allow the preparation of both antipodes of the natural product from methylcarbinols readily made from esters via the stereoselective reduction of β-keto sulfoxides.[4]

As shown on the retrosynthetic scheme of (*S*)-zearalenone dimethyl ether (Scheme I), it is possible to prepare the chiral methylcarbinol moiety from the β-keto sulfoxide **11** by stereoselective reduction of the carbonyl group followed by reductive desulfurization, the compound **11** being readily made from glutaric anhydride and optically active methyl *p*-tolyl sulfoxide. Therefore, the total synthesis of the macrolide can be divided, first of all, in the synthesis of the achiral sulfone ester **9** and then introduction of the chiral methylcarbinol part via a β-keto sulfoxide functionality in the very last steps of the synthesis, allowing, if necessary, the preparation of both configurations of the macrolide by choosing the reduction conditions of the chiral β-keto sulfoxide.[4]

The synthesis of the sulfone ester **9** started from the racemic sulfoxide **2** readily available from orcinol.[3] The corresponding sulfide **3**, prepared by sulfoxide deoxygenation with boron trifluoride–sodium iodide[5], was alkylated in HMPA with 4-iodobutyl *p*-tolylsulfone **6** in 77% yield to give compound **7** (Scheme II). This alkylation was unsuccessful from the corresponding sulfoxide **2** in the same conditions.

The sulfone **6** was obtained from methyl 4-iodobutanoate through iodine displacement with sodium *p*-toluenesulfinate, lithium aluminum hydride reduction of the ester group, and iodine substitution.[6]

Finally, the sulfoxide **8**, prepared by sulfide oxidation with *m*-CPBA, was submitted to a sulfoxide pyrolytic elimination leading to the sulfone ester **9** in 94% yield.

The β-keto sulfoxide **11** was obtained in 75% overall yield from glutaric anhydride, which was opened with the carbanion of (+)(*R*)-methyl *p*-tolylsulfoxide and the resulting carboxylic acid esterified with diazomethane (Scheme III). Reduction of the β-keto sulfoxide **11** with DIBAL in the presence of zinc chloride yielded the [2*R*,(*S*)*R*]-β-hydroxy sulfoxide **12** in 80% yield.

The *R* configuration of the hydroxylic carbon can be deduced from the reaction mechanism already published[4] and also from the NMR characteristics of the product. From the numerous examples of the reduction of β-keto sulfoxides we reported, we noticed that the nonequivalence of the methylene hydrogens α to the sulfoxide group is quite different in the two diastereoisomers:[4b-d] in the *RR* configuration the $\bar{\nu}$ value between these two hydrogens is ~40 Hz (39 Hz in **11**) and ~80 Hz in the *RS* configuration (the coupling constants J_{AX} and J_{BX} are also in agreement with this assignment[4d]). The final correlation with natural zearalenone will indeed confirm this absolute configuration. The diastereoselectivity for the reduction was higher than 98%; only one diastereoisomer was observed in the NMR spectrum of the crude reduction mixture.

The final hydroxy ester **14** was obtained after protection of the hydroxyl group with TBDMS and desulfurization with Raney nickel. The carbanion α to sulfone in compound **9** was made with lithium hexamethyldisilazide, and

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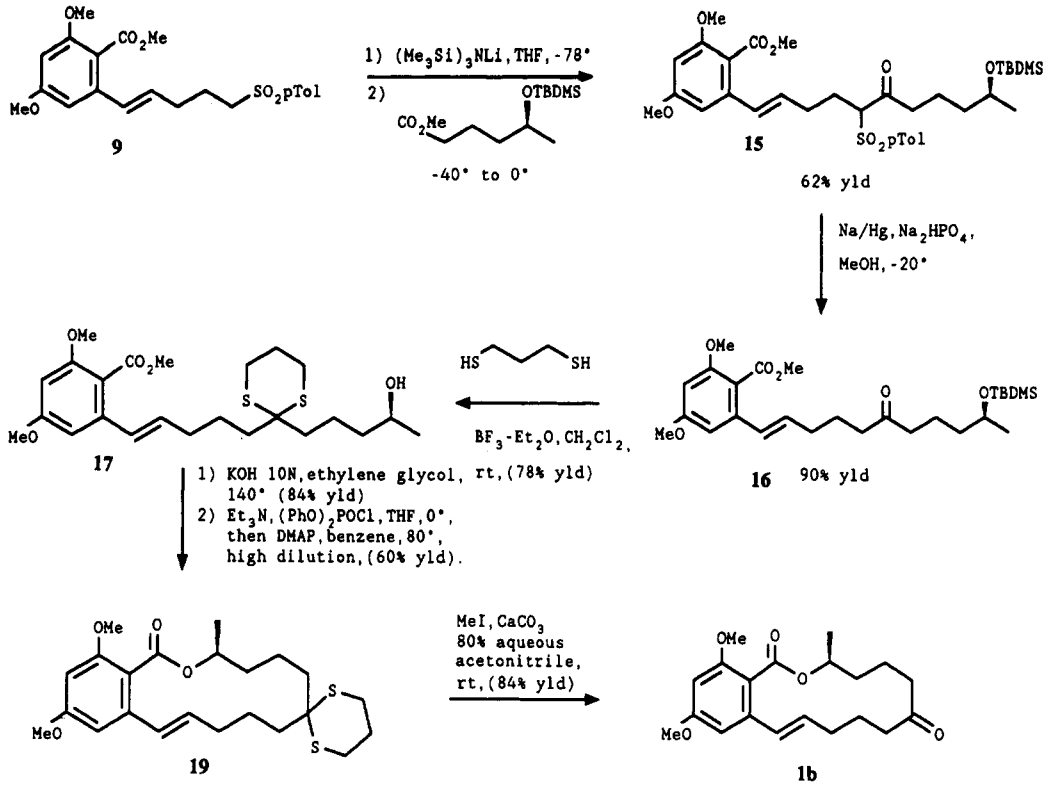
Scheme IV



the chiral ester **14** was added to give the keto sulfone **15** in 62% yield (Scheme IV). After desulfurization with sodium amalgam and carbonyl protection with propane dithiol, the resulting secoester **17** was saponified and cyclized in 60% yield by the phosphoric acid mixed-anhydride method developed by Masamune.[2h] (*S*)-Zearalenone dimethyl ether **1b** was finally obtained after carbonyl deprotection with methyl iodide–calcium carbonate in acetonitrile in 84% yield.

All the characteristics of the product are consistent with those described in the literature.[2a,e] The optical rotation of **1b** is consistent with that reported for the dimethyl ether of the natural *S* enantiomer,[2a] showing the absolute configuration and the high enantiomeric purity of **1b** (ee > 95%). The hydrolysis of the methyl ether groups is already described in the first synthesis of racemic zearalenone reported by the Merck group.[2a]

Further application of this method to the asymmetric synthesis of more complex macrolide is in progress.

Experimental Section

Melting points have been determined in open capillary tubes on a Gallenkamp apparatus and are uncorrected. IR spectra were recorded in $CHCl_3$ solution, unless otherwise indicated, on a Philips PU-9716 spectrophotometer, values in cm^{-1}. ^1H and ^{13}C NMR spectra were recorded at 200.1 and 50.3 MHz in $CDCl_3$ on a Bruker WM 200 SY spectrometer. Signals are reported in δ units. Mass spectra were recorded at 70 eV on a Hewlett-Packard 5985 mass spectrometer, relative intensities in brackets. Optical rotations were recorded with a Perkin-Elmer 141 polarimeter at 25 °C. Thin-layer chromatography (TLC) was performed by using precoated sheets of silica gel 60, and flash column chromatography was carried out with silica gel 60 (230–400 mesh) of Macherey-Nagel. Eluting solvents are indicated in the text. Dry THF was distilled from sodium/benzophenone ketyl, and dichloromethane and chloroform were dried over phosphorus pentoxide. Diisopropylamine and hexamethyldisilazane were freshly distilled over potassium hydroxide and hexamethylphosphoric triamide (HMPA) over calcium hydride. Butyllithium used to form lithium hexamethyldisilazide (LHMDS), and lithium diisopropylamide (LDA) was titrated with diphenylacetic acid. Apparatus for all experiments carried out under inert atmosphere was dried by flaming in a stream of dry argon. All reactions were monitored by TLC.

Methyl 2,4-Dimethyl-6-[(*p*-tolylsulfenyl)methyl]benzoate (3). To a stirred solution of sulfoxide **2** (1.39 g, 4 mmol) and sodium iodide (2.10 g, 14 mmol) in dry acetonitrile (15 mL) at 0 °C was dropwise added a solution of freshly distilled BF_3-Et_2O (1.80 mL, 12 mmol) in acetonitrile (4 mL). After being stirred for 30 min at 0 °C, the reaction mixture was poured into ice–water (40 mL), treated with a 15% aqueous sodium thiosulfate solution, and extracted with ethyl acetate. The organic layer was washed with water (2 × 10 mL) and brine (25 mL), dried (Na_2SO_4), and evaporated in vacuum to yield 1.29 g of crude sulfide, which was purified by column chromatography (hexane:ethyl acetate = 2:1) giving 1.13 g (85%) of pure **3** as an oil. IR: 1720, 1610, 1590, 1340, 1280, 1160. ^1H NMR: 7.22, 7.05 (AA'BB' system, 4 H, *p*-tol); 6.35 (d, 1 H, Ar, J = 2.3 Hz); 6.31 (d, 1 H, Ar, J = 2.3 Hz); 4.07 (s, 2 H, CH_2); 3.87, 3.80, 3.71 (3 s, 9 H, OCH_3); 2.30 (s, 3 H, CH_3, *p*-tol). ^{13}C NMR: 168.0 ($COOCH_3$); 161.3, 158.5 (C-2, C-4); 138.7, 136.8, 131.9 (C-6; C-S, *p*-tol; CCH_3, *p*-tol); 131.3, 129.5 (4 CH, *p*-tol); 115.5 (C-1); 106.2 (C-5); 97.7 (C-3); 55.9, 55.3, 52.1 (3-OCH_3); 38.0 (CH_2S); 21.0 (CH_3, *p*-tol). MS *m/z*: 332 (M1+, 14), 209 (100), 179 (13), 178 (8), 91 (9).

Methyl 4-(*p*-Tolylsulfonyl)butanoate (4). To a solution of dry sodium *p*-toluenesulfinate (12.0 g, 67 mmol) in anhydrous methanol (150 mL) was added with stirring a solution of methyl 4-iodobutanoate (15.4 g, 67 mmol) in dry ether (100 mL), and the resulting mixture was refluxed for 48 h. After solvent removal and water addition (100 mL), the crude product was extracted with dichloromethane (4 × 40 mL). The combined extracts were dried (Na_2SO_4), and after solvent evaporation in vacuo, the crude sulfone **4** (15.76 g, oil, 91%) was used without further purification. IR (film): 1730, 1600, 1300, 1150. ^1H NMR: 7.80, 7.37 (AA'BB' system, 4 H, *p*-tol); 3.65 (s, 3 H, OCH_3); 3.16 (m, 2 H, H-4); 2.46 (s, 3 H, CH_3, *p*-tol); 2.46 (t, 2 H, H-2, J = 7.1 Hz); 2.02 (m, 2 H, H-3). ^{13}C NMR: 172.3 ($COOCH_3$); 144.6 (CSO_2, *p*-tol); 135.7 (CCH_3, *p*-tol); 129.7, 127.8 (4 CH, *p*-tol); 54.9 (C-4); 51.5 (OCH_3); 31.7 (C-2); 21.4 (CH_3, *p*-tol); 18.1 (C-3). MS *m/z*: 256 (M^+, 4), 225 (18), 197 (6), 183 (7), 155 (11), 139 (13), 101 (100), 91 (48), 59 (48).

4-Hydroxybutyl *p*-Tolyl Sulfone (5). To a suspension of lithium aluminum hydride (1.21 g, 32 mmol) in THF (100 mL) under argon was added dropwise a solution of ester **4** (8.21 g, 32

mmol) in THF (200 mL) at 0 °C. The reaction mixture was stirred 15 min at 0 °C (TLC, hexane:ethyl acetate = 1:1). Usual hydrolysis with water (1.2 mL), 15% aqueous sodium hydroxide solution (1.2 mL), and water (3.6 mL), precipitate filtration, and in vacuum removal of solvent yielded alcohol **5** (7.0 g, 96%) as an oil. IR (film): 3500, 1600, 1300, 1150. ^{1}H NMR: 7.78, 7.36 (AA'BB' system, 4 H, *p*-tol); 3.62 (m, 2 H, H-4); 3.13 (m, 2 H, H-1); 2.44 (s, 3 H, CH_3, *p*-tol); 2.00 (broad s, 1 H, OH); 1.82, 1.65 (2 m, 4 H, CH_2). ^{13}C NMR: 144.6 (CSO_2, *p*-tol); 135.6 (CCH_3, *p*-tol); 129.9, 128.0 (4 CH, *p*-tol); 61.8 (C-4); 56.0 (C-1); 30.9 (C-3); 21.6 (CH_3, *p*-tol); 19.5 (C-2). MS *m/z*: 228 (M^+, 1), 198 (36), 156 (29), 139 (21), 121 (31), 105 (22), 92 (100), 91 (86).

4-Iodobutyl *p*-Tolyl Sulfone (6). To a stirred mixture of alcohol **5** (1.14 g, 5 mmol), triphenylphosphine (4.59 g, 17.5 mmol), and imidazole (1.19 g, 17.5 mmol) in toluene (75 mL) was portionwise added solid iodine (5.07 g, 20 mmol). After 10 min at room temperature, the reaction was shown to be completed (TLC, hexane:ethyl acetate = 2:1). The mixture was then treated with saturated aqueous sodium bicarbonate solution (15 mL) and stirred for 10 min. Toluene (20 mL) was added, and the red organic layer was washed with an aqueous thiosulfate solution, water, and brine. The organic layer was dried (Na_2SO_4) and evaporated, and the crude residue was purified by column chromatography (hexane:ethyl acetate = 5:2) to yield iodide **6** (1.38 g, 82%) as a yellow solid. Mp: 58–60 °C (ether). IR: 1600, 1320, 1300, 1150, 1090. ^{1}H NMR: 7.79, 7.38 (AA'BB' system, 4 H, *p*-tol); 3.14 (t, 2 H, H-4, J = 6.5 Hz); 3.09 (m, 2 H, H-1); 2.46 (s, 3 H, CH_3, *p*-tol); 1.87 (m, 4 H, H-2, H-3). ^{13}C NMR: 144.7 (COS_2, *p*-tol); 135.8 (CCH_3, *p*-tol); 129.9, 127.9 (4 CH, *p*-tol); 54.9 (C-1); 31.5, 23.7 (C-2, C-3); 21.5 (CH_3, *p*-tol); 4.8 (C-4). MS *m/z* 211 [$(M - 127)^+$, 100], 183 (16), 157 (65), 155 (37), 139 (27), 127 (4), 91 (76). Anal. Calcd for $C_{11}H_{15}IO_2S$: C, 39.07; H, 4.47; S, 9.48. Found: C, 39.15; H, 4.53; S, 9.34.

Methyl 2,4-Dimethoxy-6-[1'-(*p*-tolylsulfenyl)-5'-(*p*-tolylsulfonyl)pentyl]benzoate (7). The sulfenyl ester **3** (664 mg, 2 mmol) in THF (15 mL) was added to a stirred solution of LHMDS (4.12 mmol) in THF (15 mL) at −78 °C under argon, and the resulting red solution was stirred for 15 min before addition of HMPA (950 μL, 5.45 mmol). Five minutes after HMPA addition, a solution of iodo sulfone **6** (711 mg, 2.10 mmol) in THF (15 mL) at −78 °C was added, resulting in a solution decoloration. TLC (hexane:ethyl acetate = 2:1) showed iodide disappearance after 15 min at −78 °C. Hydrolysis was performed by addition of a 5% aqueous sodium bicarbonate solution. Ethyl acetate extraction, followed by washing (brine) and drying (Na_2SO_4) of the organic layer, gave a crude residue that was purified by column chromatography (hexane:ethyl acetate = 2.5:1) to yield pure sulfonyl ester **7** (836 mg, 77%) as an oil. IR: 1720, 1610, 1590, 1320, 1160, 1150. ^{1}H NMR: 7.74, 7.33 (AA'BB' system, 4 H, *p*-tolSO_2); 7.15, 7.02 (AA'BB' system, 4 H, *p*-tolS); 6.55 (d, 1 H, Ar, J = 2.2 Hz); 6.31 (d, 1 H, Ar, J = 2.2 Hz); 4.08 (t, 1 H, H-1', J = 7.3 Hz); 3.78 (s, 6 H, OCH_3); 3.77 (s, 3 H, OCH_3); 2.98 (m, 2 H, H-5'); 2.44 (s, 3 H, CH_3, *p*-tolSO_2); 2.29 (s, 3 H, CH_3, *p*-tolS); 1.82 (m, 2 H, H-2'); 1.63 (m, 2 H, H-4'); 1.35 (m, 2 H, H-3'). ^{13}C NMR: 168.1 ($COOCH_3$); 161.5, 157.6 (C-2, C-4); 144.4, 142.2 (COS_2, *p*-tol; C-S, *p*-tol); 137.2, 136.0, 130.7 (C-6; 2CCH_3, *p*-tol); 132.5, 129.7, 129.4, 127.9 (8 CH, *p*-tol); 116.2 (C-1); 103.2, 97.3 (C-3, C-5); 55.9 (C-5'); 55.8 55.3, 52.0 (3 OCH_3); 49.9 (C-1'); 36.1, 25.9, 22.3 (C-2', C-3', C-4'); 21.5, 20.9 (2 CH_3, *p*-tol). MS *m/z*: 542 (M^+, 8), 419 (38), 387 (64), 232 (14), 231 (89), 203 (21), 155 (8), 139 (19), 123 (100), 91 (50).

Methyl 2,4-Dimethoxy-6-[1'-(*p*-tolylsulfinyl)-5'-(*p*-tolylsulfonyl)pentyl]benzoate (8). A 0.06 M solution of *m*-chloroperbenzoic acid in methylene chloride (16.83 mL) was slowly added to a stirred solution of the preceeding sulfenyl ester (550 mg, 1.01 mmol) at 0 °C. TLC analysis (hexane:ethyl acetate = 1:1) during addition is essential to prevent sulfone formation. The reaction mixture was treated with a saturated sodium bicarbonate solution (2 × 20 mL), washed with brine and dried (Na_2OS_4) and the solvent evaporated to yield sulfinyl ester **8** (510 mg, 90%) as a 3:1 mixture of diastereomers. Crude oily product was used in the next step without further purification. ^{1}H NMR: 7.80–7.05 (AA'BB' system, 8 H, *p*-tol); 6.55–6.32 (m, 2 H, Ar); 4.05–3.60 (m, 1 H, H-1'); 3.85, 3.77, 3.76, 3.73, 3.68, 3.63 (6 s, 9 H, OCH_3); 3.07–2.88 (m, 2 H, H-5'); 2.45, 2.38, 2.35 (3 s, 6 H, CH_3, *p*-tol); 2.20–1.10 (m, 6 H, H-2', H-3', H-4'). MS *m/z*: 543 [$(M - 15)^+$, 1], 419 (39), 387 (48), 231 (100), 209 (13), 155 (8), 139 (13), 91 (61).

Methyl (1'*E*)-2,4-Dimethoxy-6-[5'-(*p*-tolylsulfonyl)-1'-pentenyl]benzoate (9). A solution of sulfinyl ester **8** (487 mg, 0.87 mmol) in toluene (50 mL) was refluxed 2 h (TLC, hexane:ethyl acetate = 1:1). Evaporation and purification by column chromatography (hexane:ethyl acetate = 10:8) afforded the alkene **9** (343 mg, 94%) as an oil. IR: 1720, 1600, 1580, 1320, 1270, 1160, 1150. ^{1}H NMR: 7.79, 7.35 (AA'BB' system, 4 H, *p*-tol); 6.53 (d, 1 H, Ar, J = 2.1 Hz); 6.36 (d, 1 H, Ar, J = 2.1 Hz); 6.34 (dt, 1 H, H-1', J = 15.6 and 1.3 Hz); 6.01 (dt, 1 H, H-2', J = 15.6 and 6.9 Hz); 3.86, 3.83, 3.80 (3 s, 9 H, OCH_3), 3.09 (m, 2 H, H-5'); 2.45 (s, 3 H, CH_3, *p*-tol); 2.28 (m, 2 H, H-3'); 1.88 (m, 2 H, H-4'). ^{13}C NMR: 168.3 ($COOCH_3$); 161.4, 158.0 (C-2, C-4); 144.6 (CSO_2, *p*-tol); 137.3, 136.1 (C-6; CCH_3, *p*-tol); 131.4, 129.8, 128.6, 128.0 (C-1', C-2', 4 CH, *p*-tol); 115.3 (C-1); 101.7 (C-5); 97.6 (C-3); 55.9, 55.4, 52.2 (2 OCH_3, C-5'); 31.3 (C-3); 22.0 (C-4'); 21.5 (CH_3, *p*-tol). MS *m/z*: 418 (M^+, 1), 387 (5), 231 (33), 230 (100), 155 (2), 91 (23). Anal. Calcd for $C_{22}H_{26}O_6S$: C, 63.14; H, 6.26; S, 7.66. Found: C, 62.90; H, 6.37; S, 7.46.

(+)-Methyl [(*S*)*R*]-5-Oxo-6-(*p*-tolylsulfinyl)hexanoate (11). (*R*)-Methyl *p*-tolyl sulfoxide (1.54 g, 10 mmol) in THF (20 mL) was added to a LDA (23 mmol) solution in THF (20 mL) at −78 °C under argon. After stirring for 30 min at −40 °C, the mixture was cooled to −78 °C and glutaric anhydride (1.25 g, 11 mmol) in THF (20 mL) was added at −78 °C with a double-tipped needle. The reaction mixture was stirred at −78 → −60 °C for 1 h and monitored by TLC (hexane:ethyl acetate:isopropanol = 10:10:2). Hydrolysis with a saturated ammonium chloride solution (40 mL) was followed by ethyl acetate extraction of the basic reaction mixture (378 mg of methyl *p*-tolyl sulfoxide were recovered). The aqueous layer was acidified to pH 3 with a 10% sulfuric acid solution and extracted with ethyl acetate (2 × 50 mL). Organic extracts obtained from acid solution were washed with brine, dried (Na_2OS_4), and evaporated to yield 2.40 g of crude 5-oxo-6-(*p*-tolylsulfinyl)hexanoic acid. ^{1}H NMR: 7.53, 7.34 (AA'BB' system, 4 H, *p*-tol); 3.89 (AB system, 2 H, H-6, J = 13 Hz); 2.63 (t, 1 H, H-4, J = 7.1 Hz); 2.61 (t, 1 H, H-4, J = 6.9 Hz); 2.42 (s, 3 H, CH_3, *p*-tol); 2.35 (t, 2 H, H-2, J = 7.0 Hz); 1.88 (q, 2 H, H-3, J = 7.0 Hz).

Acid was esterified with diazomethane. Over a stirred solution of crude acid (2.40 g, 8.9 mmol) in ether–methanol at 0 °C, a cold diazomethane (~0.8 g, 19 mmol) solution in ether was dropwise added. The reaction proceeded instantaneously with the usual liberation of nitrogen. Excess diazomethane was destroyed with a 50% acetic acid solution in ether. Solvent evaporation in vacuum and column chromatography purification (hexane:acetone = 2:1) yielded pure solid ester **11** (1.60 g, 57, 75% from methyl *p*-tolyl sulfoxide consumed, two steps). Mp 45–47 °C (ether–hexane). $[\alpha]_D$ = +195° (c = 1, acetone). IR: 1730, 1600, 1220, 1090, 1050, 1020. ^{1}H NMR: 7.53, 7.34 (AA'BB' system, 4 H, *p*-tol); 3.81 (AB system, 2 H, H-6, J = 13.4 Hz); 3.66 (s, 3 H, OCH_3); 2.59 (t, 1 H, H-4, J = 7.1 Hz); 2.58 (t, 1 H, H-4, J = 6.9 Hz); 2.42 (s, 3 H, CH_3, *p*-tol); 2.30 (t, 2 H, H-2, J = 7.2 Hz); 1.85 (q, 2 H, H-3, J = 7.1 Hz). ^{13}C NMR: 200.6 (CO); 173.0 ($COOCH_3$); 141.8, 139.2 (CSO, *p*-tol; CH_3, *p*-tol); 129.7, 123.6 (4 CH, *p*-tol); 67.4 (C-6); 51.2 (OCH_3); 43.4 (C-4); 32.2 (C-2); 21.04 (CH_3, *p*-tol); 17.8 (C-3). MS *m/z*: 282 (M^+, 2), 143 (18), 139 (100), 91 (9), 59 (8). Anal. Calcd for $C_{14}H_{18}O_4S$: C, 59.55; H, 6.43. Found: C, 59.50; H, 6.52.

(+)-Methyl [5*R*,(*S*)*R*]-5-Hydroxy-6-(*p*-tolylsulfinyl)-hexanoate (12). A solution of the keto sulfoxide **11** (2.75 g, 9.77 mmol) and anhydrous zinc chloride (2 g, 14.65 mmol) in THF (100 mL) was stirred under argon for 20 min at room temperature. The reaction mixture was cooled at −78 °C, and a 1 M solution of DIBAL (21.5 mL, 21.5 mmol) was dropwise added in two portions (TLC, ethyl acetate). After 30 min, the mixture was decomposed at −78 °C with 100 mL of methanol and the solvents were evaporated. The residue was stirred for 15 min with ethyl acetate (100 mL) and saturated sodium tartrate solution (100 mL) and extracted with ethyl acetate (2 × 100 mL). The combined extracts were washed with brine, dried (Na_2SO_4), and evaporated to yield alcohol **12** (2 g, 80%, de = 98%). Purification was achieved by column chromatography (ethyl acetate) to yield a white solid. Mp = 46–47 °C. $[\alpha]_D$ = +178.5° (c = 1, $CHCl_3$). IR: 3300, 1730, 1220, 1180, 1090, 1040, 1020. ^{1}H NMR: 7.55, 7.34 (AA'BB' system, 4 H, *p*-tol); 4.26 (ABX system, part X, 1 H, H-5, J = 9.0 and 2.7 Hz, $\Delta\bar{\nu}$ = 38.8 Hz); 3.66 (s, 3 H, OCH_3); 2.88 (ABX system, part

AB, 2 H, H-6, J = 13.1 Hz); 2.43 (s, 3 H, CH_3, p-tol); 2.36 (t, 2 H, H-2, J = 7.1 Hz); 1.92–1.53 (m, 4 H, H-3, H-4). ^{13}C NMR: 173.2 ($COOCH_3$); 141.2, 139.7 (CSO, p-tol; CCH_3, p-tol); 129.4, 123.6 (4 CH, p-tol); 66.6 (C-5); 63.2 (C-6); 50.8 (OCH_3); 35.6, 32.9 (C-2, C-4); 20.8 (CH_3, p-tol); 20.0 (C-3). MS m/z: 284 (M^+, 1), 267 (5); 145 (27), 140 (100), 139 (97), 113 (93), 91 (40).

(+)-Methyl [5*R*,(*S*)*R*]-5-[(*tert*-Butyldimethylsilyl)oxy]-6-(*p*-tolylsulfinyl)hexanoate (13). To a solution of hydroxy sulfoxide **12** (420 mg, 1.48 mmol) in dry DMF (3 mL) under argon was added 251 mg (3.69 mmol) of imidazole followed by slow addition of *tert*-butyldimethylsilyl chloride (267 mg, 1.77 mmol). The reaction mixture was stirred overnight at room temperature and then diluted with ether, washed with water and brine, dried (Na_2SO_4), and evaporated to yield crude silyl derivative **13** (574 mg, 98%), used in the next step without further purification. Pure compound was obtained by column chromatography (hexane:ethyl acetate = 1:1) as an oil. $[\alpha]_D$ = +136.4° (c = 1, $CHCl_3$). IR: 1730, 1600, 1260, 1090, 1030, 1020, 840. ^1H NMR: 7.53, 7.33 (AA'BB' system, 4 H, p-tol); 4.08 (ABX system, part X, 1 H, H-5, J = 4.2 and 7.6 Hz); 3.68 (s, 3 H, OCH_3); 2.90 (ABX system, part AB, 2 H, H-6, J = 13.2 Hz); 2.42 (s, 3 H, CH_3, p-tol); 2.34 (t, 2 H, H-2, J = 6.7 Hz); 1.75 (m, 4 H, H-3, H-4); 0.88 (s, 9 H, t-Bu); 0.07, 0.05 (2 s, 6 H, CH_3Si). ^{13}C NMR: 173.3 ($COOCH_3$); 141.2, 140.9 (CSO, p-tol; CCH_3, p-tol); 129.7, 123.6 (4 CH, p-tol); 67.2 (C-5); 65.1 (C-6); 51.1 (OCH_3); 35.6, 33.4 (C-2, C-5); 25.4 (3 CH_3, t-Bu); 21.0 (CH_3, p-tol); 20.1 (C-3); 17.6 (CSi, t-Bu); -4.8 (2 CH_3Si). MS m/z: 383 [(M - 15)$^+$, 2], 367 (1), 341 (100), 139 (46), 115 (7), 101 (7), 91 (14).

(+)-Methyl (5*S*)-5-[(*tert*-Butyldimethylsilyl)oxy]hexanoate (14). A solution of the silylated sulfoxide **13** (489 mg, 1.23 mmol) in ethanol (16 mL) was added on a Raney nickel suspension in the same solvent. TLC (hexane:ethyl acetate = 1:1) of the reaction mixture showed starting compound consumption after 1 h with stirring at room temperature. Nickel was filtered and washed with ethanol (3 × 10 mL). Solvent removal under reduced pressure yielded desulfinylated compound **14** (284 mg, 89%) as an oil. $[\alpha]_D$ = +12.5° (c = 0.84, $CHCl_3$). IR: 1730, 1260, 1170, 1140, 1100, 1030, 1010, 840. ^1H NMR: 3.80 (m, 1 H, H-5); 3.67 (s, 3 H, OCH_3); 2.31 (t, 2 H, H-2, J = 7.5 Hz); 1.80–1.18 (m, 4 H, H-3, H-4); 1.13 (d, 3 H, H-6, J = 6.0 Hz); 0.88 (s, 9 H, 3 CH_3, t-Bu); 0.07 (s, 6 H, CH_3Si). ^{13}C NMR: 173.9 ($COOCH_3$); 68.0 (C-5); 51.2 (OCH_3); 38.8, 33.9 (C-2, C-4); 25.7 (3 CH_3, t-Bu); 23.6 (C-6); 21.0 (C-3); 17.9 (CSi, t-Bu), -4.6, -4.9 (2 CH_3Si). MS m/z: 245 [(M - 15)$^+$, 6], 229 (11), 203 (37), 171 (100), 149 (35), 115 (14).

Methyl (1'*E*,10'*S*)-2,4-Dimethoxy-6-[10'-[(*tert*-butyldimethylsilyl)oxy]-6'-oxo-5'-(*p*-tolylsulfonyl)-1'-undecenyl]benzoate (15). To a solution of LHMDS (2.2 mmol) in THF (15 mL) at -78 °C under argon was added sulfone **9** (414 mg, 1 mmol) in THF (10 mL) at -78 °C, and the mixture was stirred at -78 °C for 30 min. A solution of silylated ester **14** (257 mg, 1 mmol) in THF (10 mL) at -40 °C was added with a double-tipped needle over the resulting orange solution at -40 °C, and the reaction was left 2 h to attain 0 °C (TLC, hexane:ethyl acetate = 1:1). A concentrated ammonium chloride solution (20 mL) was then added, and the resulting mixture was extracted with ethyl acetate (3 × 40 mL). The organic extracts were washed with brine, dried (Na_2SO_4), and evaporated to yield, after column chromatography (hexane:ethyl acetate = 5:2), pure **15** (400 mg, 62%) as a 50:50 diastereomeric mixture in the form of an oil. IR: 1720, 1600, 1580, 1320, 1260, 1160, 840. ^1H NMR: 7.63, 7.34 (AA'BB' system, p-tol); 6.50 (d, 1 H, Ar, J = 2.2 Hz); 6.36 (d, 1 H, Ar, J = 2.2 Hz); 6.31 (d, 1 H, H-1', J = 15.6 Hz); 5.92 (m, 1 H, H-2'); 4.14 (t, 1 H, H-5', J = 6.7 Hz); 3.88, 3.82, 3.80 (3 s, 9 H, OCH_3); 3.90–3.65 (m, 1 H, H-10'); 3.00–2.77 (m, 1 H, H-7'); 2.63–2.43 (m, 1 H, H-7'); 2.45 (s, 3 H, CH_3, p-tol); 2.25–1.95 (m, 4 H, H-3', H-4'); 1.70–1.15 (m, 4 H, H-8', H-9'); 1.09, 1.08 (2 d, 3 H, H-11', two diastereomers, J = 6.1 Hz), 0.88 (s, 9 H, CH_3, t-Bu); 0.04 (s, 6 H, CH_3Si). ^{13}C NMR: 198.5 (CO); 168.2 ($COOCH_3$); 161.3, 158.0 (C-2, C-4); 145.3 (C-SO_2, p-tol); 136.9, 133.1 (C-6; CCH_3, p-tol); 131.0, 129.6, 129.3, 128.6 (C-1', C-2'; 4 CH, p-tol); 115.3 (C-1), 101.4 (C-5); 97.7 (C-3); 73.8 (C-5'); 68.1 (C-10'); 55.8, 55.3, 52.2 (3 OCH_3); 45.4, 38.5 (C-7', C-9'); 30.3 (C-3'); 26.3, 19.3 (C-4', C-8'); 25.7 (CH_3, t-Bu); 23.6 (C-11'); 21.5 (CH_3, p-tol); 18.0 (CSi, t-Bu); -4.5, -4.9 (2 CH_3Si). MS m/z: 589 [(M - 57)$^+$, 26]; 557 (23), 401 (57), 327 (87), 257 (19), 235 (41), 217 (34), 215 (42), 213 (71), 189 (76), 115 (22), 91 (31), 75 (100).

(+)-Methyl (1'*E*,10'*S*)-2,4-Dimethoxy-6-[10'-[(*tert*-butyldimethylsilyl)oxy]-6'-oxo-1'-undecenyl]benzoate (16). Sodium amalgam (6%, 2 g) was portionwise added under argon to a stirred mixture of keto sulfone **15** (357 mg, 0.55 mmol) and anhydrous disodium hydrogen phosphate (314 mg, 2.21 mmol) in methanol (10 mL) at -20 °C. After being stirred for 18 h (TLC, hexane:ethyl acetate = 5:2), the reaction mixture was poured on ice and extracted with ethyl acetate (3 × 50 mL). Combined extracts were washed with brine, dried (Na_2SO_4), and evaporated to yield crude **16** (254 mg, 93%). Purification by column chromatography (hexane:ethyl acetate = 5:2) yielded pure **16** (245 mg, 90%) as an oil. $[\alpha]_D$ = 6.2° (c = 1.06, $CHCl_3$). IR: 1720, 1600, 1580, 1260, 1160, 840. ^1H NMR: 6.58 (d, 1 H, Ar, J = 2.2 Hz); 6.35 (d, 1 H, Ar, J = 2.2 Hz); 6.35 (d, 1 H, H-1', J = 15.6 Hz); 6.12 (dt, 1 H, H-2', J = 15.6 and 6.7 Hz); 3.89, 3.83, 3.80 (3 s, 9 H, OCH_3); 2.41 (c, 4 H, H-5', H-7'); 2.19 (c, 2 H, H-3', J = 7.1 Hz); 1.74 (q, 2 H, C-4', J = 7.2 Hz); 1.65–1.25 (m, 4 H, H-8', H-9'); 1.11 (d, 3 H, H-11', J = 6.1 Hz); 0.88 (s, 9 H, CH_3, t-Bu); 0.04 (s, 6 H, CH_3Si). ^{13}C NMR: 210.5 (CO); 168.3 ($COOCH_3$); 161.3, 158.0 (C-2, C-4); 137.6 (C-6); 133.2, 127.3 (C-1', C-2'); 115.3 (C-1); 101.6 (C-5); 97.4 (C-3); 68.2 (C-10'); 55.8, 55.2, 52.0 (3 OCH_3); 42.8, 41.6, 39.0 (C-5', C-7', C-9'); 32.3 (C-3'), 25.8 (3 CH_3, t-Bu); 23.6 (C-11'); 22.9, 19.9 (C-4', C-8'); 17.9 (CSi, t-Bu); -4.5, -4.8 (2 CH_3Si). MS m/z: [(M - 57)$^+$, 47], 403 (51), 361 (7), 329 (57), 231 (17), 217 (85), 215 (83), 189 (100), 159 (31), 145 (58), 115 (25), 75 (99). Anal. Calcd for $C_{27}H_{44}O_6Si$: C, 65.81; H, 9.00. Found: C, 66.01; H, 9.30.

(+)-Methyl (1'*E*,10'*S*)-2,4-Dimethoxy-6-[10'-hydroxy-6',6'-(trimethylenedithio)-1'-undecenyl]benzoate (17). To a stirred solution of ketone **16** (127 mg, 0.26 mmol) in dichloromethane (3 mL) at room temperature were successively added propanedithiol (28 mg, 0.26 mmol) and BF_3·Et_2O (19 μL, 0.15 mmol). Reaction was completed in 1 h (TLC, hexane:ethyl acetate = 5:2). Dichloromethane was added to the resulting mixture, and the solution was washed with water, 30% Na_2CO_3 solution, and brine. The organic layer was dried (Na_2SO_4), evaporated, and purified by column chromatography to yield **17** (95 mg, 78%) as an oil. $[\alpha]_D$ = +3.2° (c = 2.6, $CHCl_3$). IR: 1720, 1600, 1580, 1270, 1205, 1160. ^1H NMR: 6.59 (d, 1 H, Ar, J = 2.2 Hz); 6.38 (d, 1 H, H-1', J = 15.5 Hz); 6.35 (d, 1 H, Ar, J = 2.2 Hz); 6.16 (dt, J = 15.5 and 6.7 Hz); 3.90, 3.83, 3.80 (3 s, 9 H, OCH_3); 2.80 (m, 4 H, CH_2S); 2.22 (m, 3 H, H-3', OH); 2.05–1.40 (m, 12 H, CH_2); 1.20 (d, 3 H, H-11', J = 6.2 Hz). ^{13}C NMR: 168.5 ($COOCH_3$); 161.2, 157.9 (C-2, C-4), 137.7 (C-6), 133.6, 127.1 (C-1', C-2'); 115.1 (C-1), 101.4 (C-5); 97.2 (C-3); 67.6 (C-10'); 55.8, 55.3, 53.0, 52.2 (3 OCH_3, C-6'); 39.1, 38.1, 37.4, 32.9, 25.8 (2 C), 25.3, 23.6, 23.5, 20.3 (C-3', C-4', C-5', C-7', C-8', C-9', C-11', 3 CH_2 dithiane). MS m/z: 468 (M^+, 3), 361 (14), 248 (28), 217 (12), 215 (7), 189 (100), 145 (13).

(+)-(1'*E*,10'*S*)-2,4-Dimethoxy-6-[10'-hydroxy-6',6'-(trimethylenedithio)-1'-undecenyl]benzoic Acid (18). A mixture of ester **17** (37 mg, 0.079 mmol), ethylene glycol (0.8 mL), and 10 N potassium hydroxide solution (0.08 mL) was heated 2 h at 140 °C. Then, the solution was cooled and diluted with toluene (10 mL) and a 2 N potassium hydroxide solution (5 mL). The aqueous phase was acidified at 0 °C with concentrated hydrochloric acid and extracted with toluene (3 × 10 mL). The combined extracts were washed with water and dried (Na_2SO_4). After solvent removal, acid **18** (30 mg, 84%) was obtained. IR: 3400, 1720, 1595, 1155, 1090. ^1H NMR: 6.76 (d, 1 H, H-1', J = 15.8 Hz); 6.58 (d, 1 H, Ar, J = 2.2 Hz); 6.39 (d, 1 H, Ar, J = 2.2 Hz); 6.12 (dt, 1 H, J = 15.8 and 6.7 Hz); 5.55 (broad s, 1 H, OH); 4.0–3.8 (m, 1 H, H-10'); 3.87, 3.84 (2 s, 6 H, OCH_3); 2.80 (m, 4 H, CH_2S); 2.26 (m, 2 H, H-3'; 2.05–1.40 (m, 12 H, CH_2); 1.23 (d, 3 H, CH_3, J = 6.3 Hz). ^{13}C NMR: 169.2 (COOH); 161.7, 158.4 (C-2, C-4); 140.1 (C-6); 133.3, 128.8 (C-1', C-2'); 113.8 (C-1), 103.2 (C-5); 97.3 (C-3); 68.2 (C-10'); 56.1, 55.4, 53.1 (2 OCH_3, C-6'); 38.9, 38.3, 37.3, 32.6, 25.9 (2 C), 25.4, 23.5, 23.2, 20.3 (C-3', C-4', C-5', C-7', C-8', C-9', C-11', 3 CH_2 dithiane). MS m/z: 454 (M^+, 1), 437 (1), 347 (10), 346 (15), 234 (17), 217 (16), 215 (11), 205 (23), 189 (100), 151 (42), 145 (18), 107 (10), 106 (17).

(+)-(*S*)-Dimethylzearalenone Trimethylene Dithioketal (19). Triethylamine (11 μL, 0.077 mmol) was added to a solution of seco acid **18** (35 mg, 0.077 mmol) in THF (0.8 mL), and the mixture was stirred for 10 min under argon. Diphenylphosphochloridate (16 mL, 0.077 mmol) was then added at 0 °C, and a white precipitate was formed. After 30 min, the precipitate was filtered under argon, and the filtrate was diluted with benzene

(30 mL) and added, over a period of 8 h, to a solution of 4-(dimethylamino)pyridine (28 mg, 0.231 mmol) in benzene (50 mL) heated at 80 °C. After complete addition, the solution refluxed for 15 h. The reaction mixture was washed with 5% hydrochloric acid solution, water, 5% sodium bicarbonate solution, and brine. The organic layer was dried (Na_2SO_4) and evaporated. The residue was purified by column chromatography (hexane:ether = 2:1) to yield pure solid lactone **19** (20 mg, 60%). Mp = 169-170 °C (hexane-ether). $[\alpha]_D$ = +97.7° (c = 1.2, $CHCl_3$). IR: 1710, 1600, 1160, 1090. ^1H NMR: 6.56 (d, 1 H, Ar, J = 2.2 Hz); 6.44 (d, 1 H, C=C, J = 16.4 Hz); 6.35 (d, 1 H, Ar, J = 2.2 Hz); 6.33 (dt, 1 H, J = 16.4 and 4.1 Hz); 5.20 (m, 1 H, CHOCO); 3.82, 3.79 (2 s, 6 H, OCH_3); 2.80 (m, 4 H, CH_2S), 2.50-1.50 (m, 14 H, CH_2); 1.36 (d, 3 H, CH_3, J = 6.3 Hz). ^{13}C NMR: 168.2 (CO); 161.0, 157.4 (C-2, C-3); 136 (C-6); 133.0, 125.7 (2 CH=); 116.7 (C-1); 101.2 (C-5); 97.4 (C-3); 70.9 (CHO); 55.9, 55.4, 52.7 (2 OCH_3, SCS); 36.4 35.4, 35.0, 29.7, 26.1 (2 C), 25.7, 21.1, 20.1, 18.3 (9 CH_2, CH_3). MS m/z: 436 (M^+, 53), 361 (27), 330 (23); 234 (21), 217 (36), 215 (20), 205 (47), 203 (50), 189 (100), 145 (56), 107 (21).

(+)-(S)-Dimethylzearalenone (1b). To a stirred solution of lactone **19** (9 mg, 0.02 mmol) in aqueous 80% acetonitrile (1 mL) were successively added calcium carbonate (2.5 mg) and iodomethane (9 mL, 0.1 mmol). The mixture was maintained at room temperature, and additional portions (3 × 0.1 mmol) of iodomethane were added (4 days; TLC, hexane:ethyl acetate = 1:1). Dichloromethane addition and filtration by a short silica gel column to retain sulfonium salts yielded pure **1b** (6 mg, 84%) as a white solid. Mp = 110-111 °C (hexane-ether). $[\alpha]_D$ = +23.7° (c = 0.35, MeOH) [lit.[2a] mp = 108-110 °C; $[\alpha]_D$ = +25 (MeOH)]. IR: 1720, 1710, 1600, 1580, 1270, 1210, 1160. ^1H NMR: 6.60 (d, 1 H, Ar, J = 2.1 Hz); 6.39 (dd, 1 H, C=C, J = 15.5 and 1.9 Hz); 6.38 (d, 1 H, Ar, J = 2.1 Hz); 5.99 (ddd, 1 H, C=C, J = 15.5, 4.4 and 10.0 Hz); 5.32 (m, 1 H, HCOCO); 3.83, 3.80 (2 s, 6 H, OCH_3); 2.85-1.45 (m, 12 H, CH_2); 1.34 (d, 3 H, CH_3, J = 6.3 Hz). MS m/z: 346 (M^+, 22), 235 (19), 217 (100), 207 (31), 204 (30), 189 (86), 151 (37).[2e]

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Supplementary Material Available: ^1H NMR spectra of **1b**, **3-19**, ^{13}C NMR spectra of **3-7** and **9-19**, and mass spectra of **1b**, **3-5**, and **7-19** (59 pages). Ordering information is given on any current masthead page.

Optically Active Amines. 36.[1] Application of the Benzene Chirality Rule to Ring-Substituted Mandelic Acids

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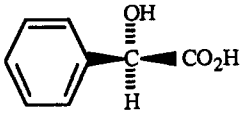
The positive sign of the ^1L_b Cotton effects (CEs) from about 250 to 270 nm in the circular dichroism (CD) spectrum of (R)-mandelic acid and its sodium salt is determined by vibronic borrowing from allowed transitions at shorter wavelength. On ring substitution, transition moments are induced in the benzene ring bonds adjacent to the attachment bond of the chiral group, resulting in enhanced coupling of the ^1L_b transition with the chiral group. The sign of the ^1L_b CEs for a ring-substituted (R)-mandelic acid may be the same or opposite to that of (R)-mandelic acid, but the sign of its ^1L_b CEs can often be correlated with its absolute configuration provided the ring position of the substituent and its spectroscopic moment is taken into account.

Among the many structural variations that have been examined to obtain β-lactam antibiotics with higher levels and wider breadth of antimicrobial activity have been those involving the acylamino side chain.[2] Some studies have focused on semisynthetic penicillins[2] and cephalosporins[3,4] and totally synthetic 1-oxacephens[5] and tricyclic β-lactams[6] in which the acyl group on the side chain was derived from mandelic acid (**1a**). For the cephalosporins,



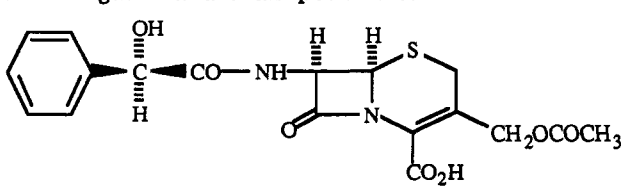
(R)-**1a**

also included were studies of the in vitro and in vivo activity of benzene ring-substituted derivatives of (7R)-7-((R)-mandelamido)cephalosporanic acid (**2**) against Gram-negative and Gram-positive bacteria.[3] Since **2** is

Table I. Mandelic Acids Used

compd	name	$[\alpha]^{23-25}_D$,[a] deg	% ee
(R)-**1a**	(R)-mandelic acid	-152[b]	99[c]
(S)-**1b**	(S)-p-methylmandelic acid	+145[b]	95[d]
(S)-**1f**	(S)-m-methylmandelic acid	+137[e]	95[d]
(R)-**1g**	(R)-m-chloromandelic acid	-113[e]	97[d]
(R)-**1h**	(R)-m-fluoromandelic acid	-119[f]	92[g]
(R)-**1i**	(R)-o-methylmandelic acid	-171[e]	98[d]
(R)-**3c**	(R)-p-(aminomethyl)mandelic acid	-116[h]	94[d]

[a] c 0.333-4.40 g/100 mL of solvent. [b] Methanol as solvent. [c] On the basis that the rotatory power of this compound in ref 8 corresponds to 100% ee. [d] On the basis that the rotatory power of this compound or its enantiomer in ref 3 corresponds to 100% ee. [e] Ethanol as solvent. [f] Acetone as solvent. [g] On the basis that the rotory power of this compound in ref 9 corresponds to 100% ee. [h] 1 N hydrochloric acid as solvent.



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