methylsilane (^{1}H, δ 0.0) or $CDCl_3$ (^{13}C, δ 77.0) as internal standards. Optical rotations were measured on a Jasco DIP-360 digital polarimeter. Mass spectra were recorded on a MAT CH7 mass spectrometer. THF was distilled from sodium/benzophenone ketyl, and CH_2Cl_2 was distilled from CaH_2. Anhydrous TBHP in CH_2Cl_2 was prepared and titrated by the method of Hanson and Sharpless.[6] (*R*)-(+)-α-Methoxy-α-(trifluoromethyl)phenylacetyl chloride (MTPA-Cl) was prepared (99% yield) from (*R*)-(+)-α-methoxy-α-(trifluoromethyl)phenylacetic acid (Aldrich) by treatment with oxalyl chloride (5 equiv, catalytic DMF, reflux 1 h) followed by Kugelrohr distillation [air bath temperature 80–90 °C (9 torr)]. Other chemicals were used as received from Aldrich Chemical Co. Elemental analyses were performed by M-H-W Laboratories, Phoenix, AZ.

(*Z*)-4-[(4-Bromobenzyl)oxy]-2-buten-1-ol (3b). To a cold (0 °C) stirred suspension of NaH (4.8 g, 0.12 mol of a 60% dispersion in oil previously washed with 3 × 70 mL of dry petroleum ether) in dry THF (400 mL) under an atmosphere of argon was added *cis*-2-butene-1,4-diol (49 mL, 53 g, 0.6 mol) over 10 min. The ice bath was removed and the resulting tan solution was stirred at room temperature for 30 min. Tetrabutylammonium iodide (300 mg) and 4-bromobenzyl bromide (25.0 g, 0.100 mol) were then added, and the reaction mixture was stirred at room temperature for 15 h. Water (5 mL) was added, and the THF was removed by rotary evaporation. The residue was taken up in Et_2O (250 mL) and washed with 5 × 100 mL of water. Drying ($MgSO_4$), followed by concentration and Kugelrohr distillation [air bath temperature 120–130 °C (0.2 torr)] afforded the monoprotected diol **3b** as a light yellow oil [23.8 g (93%)]. It was homogeneous by TLC (petroleum ether:ether 1:1): IR (film) 3380 (br), 3020, 2860, 1590, 1485, 1070, 1010, 840, 800 cm^{-1}; ^{1}H NMR δ 4.04 (d, 2 H, J = 5.8 Hz), 4.09 (d, 2 H, J = 5.8 Hz), 4.42 (s, 2 H), 5.71 (AB of ABX_2Y_2 system, 2 H, Δδ 0.08, J_{AB} = 11.3, J_{AX} = J_{VY} = 5.8 Hz), 7.18, 7.44 (AA′BB′ system, 4 H, J_{AB} = 8.3 Hz); ^{13}C NMR (δ 57.8, 65.4, 71.1, 121.2, 127.1, 129.0, 131.1, 132.2, 136.6; MS, m/z 258 (1.0, M$^+$, ^{81}Br), 256 (2.0, M$^+$, ^{79}Br), 188 (45), 187 (100), 186 (94), 185 (100), 184 (57), 183 (100), 172 (81), 171 (100), 170 (78), 169 (100), 159 (26), 157 (33), 107 (71).

The stillpot residue (1.0 g) was chromatographed on 35 g of silica with petroleum ether–ether (20:1) as eluant to furnish the corresponding diprotected diol as a thick oil (0.5 g): IR (film) 3020, 2860, 1590, 1485, 1090, 1070, 1010, 840, 800 cm^{-1}; ^{1}H NMR δ 4.03 (m, 4 H), 4.42 (s, 4 H), 5.75–5.79 (sym m, 2 H), 7.18, 7.45 (AA′BB′ system, J_{AB} = 8.5 Hz). ^{13}C NMR δ 65.7, 71.2, 121.3, 129.1, 129.2, 131.3, 137.0; MS, m/z 428 (0.3, M$^+$, ^{81}Br – ^{81}Br), 426 (0.7, M$^+$, ^{79}Br – ^{81}Br), 424 (0.3, M$^+$, ^{79}Br – 79 Br), 257 (18), 255 (18), 247 (16), 245 (19), 240 (14), 238 (14), 189 (24), 188 (100), 187 (100), 186 (100), 185 (100), 183 (54), 172 (78), 171 (100), 170 (79), 169 (100), 107 (60).

(2*R*,3*S*)-3-[[(4-Bromobenzyl)oxy]methyl]oxirane-2-methanol (1b). To a cold (–20 °C) stirred suspension of powdered 4-Å molecular sieves (6.2 g) in dry CH_2Cl_2 (400 mL) under an atmosphere of argon was added titanium isopropoxide (4.54 g, 16 mmol), D-(–)-diisopropyl tartrate (5.12 g, 22 mmol) and *tert*-butyl hydroperoxide (36 mL of a 4.4 M solution in CH_2Cl_2, 160 mmol). The slurry was stirred at –20 °C for 30 min. Allylic alcohol **3b** (20.7 g, 80 mmol) was then added as a solution in CH_2Cl_2 (30 mL), and the reaction mixture was stirred at –20 °C for 2 h and then stored in a –20 °C freezer overnight (actual temperature –20 to –12 °C). After 24 h, TLC (petroleum ether:ether 1:2) indicated no remaining allylic alcohol and a single lower R_f product. The reaction was vigorously stirred and quenched with water (90 mL). The mixture was allowed to warm to room temperature and stirred for 60 min. A solution of 30% NaOH in brine (20 mL) was then added. After 30 min of vigorous stirring, the phases were separated and the aqueous layer was extracted with CH_2Cl_2 (2 × 40 mL). The combined organic layer was dried ($MgSO_4$) and filtered through a pad of Celite. Concentration afforded a TBHP-containing colorless oil; removal of excess TBHP in vacuo (0.1 torr) gave a white solid that still contained traces of TBHP.

Purification of a small amount (200 mg) of this material by flash chromatography (petroleum ether:ether = 1:2) gave chemically pure epoxy alcohol, $[\alpha]^{22}_D$ + 14.7° (*c* 1.5, $CHCl_3$, 85% ee). Acetylation of some (20 mg) of this alcohol (excess Ac_2O, pyridine, catalytic DMAP) gave the corresponding acetate. Analysis using the chiral shift reagent Eu(hfc)$_3$ (250-MHz ^{1}H NMR in benzene-d_6, hfc = 3-[(heptafluoropropyl)hydroxymethylene]-*d*-camphorate) indicated an optical purity of 86%.

The bulk solid was suspended in petroleum ether (100 mL), and sufficient ether was added to form a solution at ambient temperature. The solution was slowly cooled to –20 °C (freezer) and left for a few hours. The white needles were collected by suction filtration, washed with petroleum ether (2 × 10 mL), and dried in vacuo to afford epoxy alcohol **1b** [15.3 g (70%)]. This material was homogeneous by TLC: mp 52–52.5 °C; IR ($CHCl_3$) 3600, 3430, 3000, 2860, 1600, 1490, 1090 cm^{-1}; ^{1}H NMR ($CDCl_3$, D_2O) δ 3.22 (1 H, dt, H_2, J = 4.4, 5.3 Hz), 3.29 (1 H, dt, H_3, J = 4.4, 5.3 Hz), 3.68 (d, 2 H, H_4, J = 5.3 Hz), 3.73 (d, 2 H, H_1, J = 5.3 Hz), 4.52 (2 H, AB q, Δδ 0.10, J_{AB} = 12.0 Hz), 7.21, 7.48 (AA′BB′ system, 4 H, J_{AB} = 8.3 Hz); ^{13}C NMR δ 54.8, 55.7, 60.5, 68.1, 72.5, 121.7, 129.3, 131.5, 136.4; MS, m/z 274 (5.8, M$^+$, ^{81}Br), 272 (5.2, M$^+$, ^{79}Br), 213 (21), 211 (22), 188 (73), 187 (100), 186 (100), 185 (100), 184 (90), 183 (84), 172 (59), 171 (100), 170 (63), 169 (100), 159 (34), 157 (46), 132 (14), 119 (15), 107 (53), 106 (25); $[\alpha]^{22}_D$ +17.4° (*c* 1.5, $CHCl_3$). Anal. Calcd for $C_{11}H_{13}BrO_3$: C, 48.37; H, 4.80; Br, 29.25. Found: C, 48.35; H, 5.00; Br, 29.41.

Analysis (250 MHz, ^{1}H NMR, C_6D_6) of the Mosher ester (excess (+)-MTPA-Cl, Et_3N, catalytic DMAP in CH_2Cl_2) from the crystalline epoxy alcohol indicated the presence of only one diastereomer. Peaks due to the other diastereomer (obtained from **2b**) were not detected; in particular, the signals due to the epoxide protons (δ 2.79 for **1b**-OMTPA and δ 2.75 for **2b**-OMTPA) for each diastereomer were quite distinctive.

Further recrystallization did not affect the specific rotation of the epoxy alcohol.

(2*S*,3*R*)-3-[[(4-Bromobenzyl)oxy]methyl]oxirane-2-methanol (2b). Essentially the same procedure as for **1b** was followed with the obvious exception that L-(+)-diisopropyl tartrate was used in place of (–)-DIPT. The following materials were used: 4-Å molecular sieves (2 g), CH_2Cl_2 (150 mL), titanium isopropoxide (1.7 g, 6 mmol), (+)-DIPT (1.9 g, 8.2 mmol), TBHP (4.4 M in CH_2Cl_2, 13.7 mL, 60 mmol), and allylic alcohol **3b** (7.77 g, 30 mmol). Reaction at –20 °C for 24 h subsequent workup afforded a white solid (crude ee 86%). Recrystallization from petroleum ether–ether gave epoxy alcohol **2b** as white needles: (6.02 g (73%); $[\alpha]^{22}_D$–17.3° (*c* 1.5, $CHCl_3$); spectral data identical with those for **1b**.

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A Convenient Synthesis of Sulfinate Esters from Sulfonyl Chlorides

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The reaction of an organometallic reagent with a diastereomerically pure sulfinate ester of menthol[1] continues to be the method most often employed for the preparation of optically active sulfoxides, despite recent advances in the asymmetric oxidation of sulfides.[2] These sulfoxides have proven to be valuable intermediates for asymmetric synthesis.[3] The requisite sulfinate esters are generally

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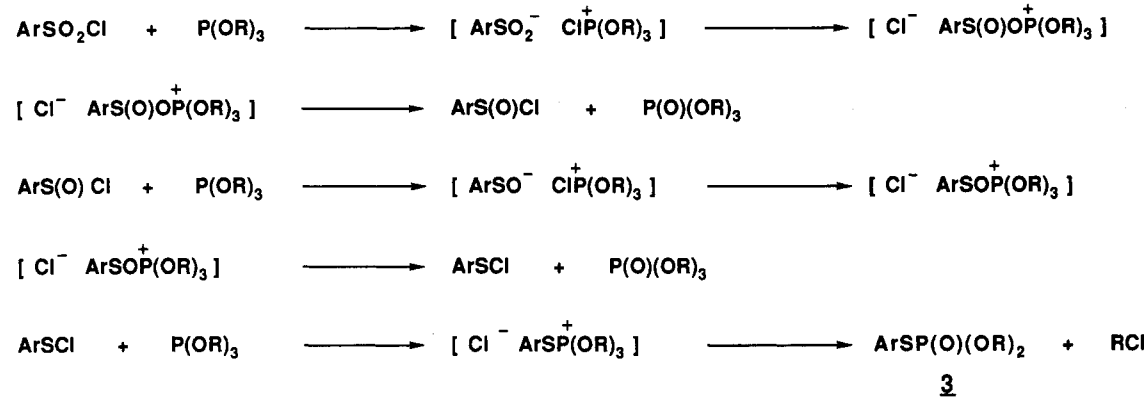
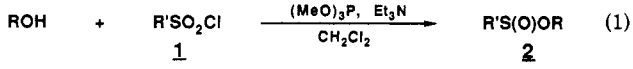
0022-3263/87/1952-2598$01.50/0

Scheme I



prepared from the corresponding sulfinic acids, either directly[4] or via the sulfinyl chlorides.[5] However, an additional synthetic step is often necessitated by the lack of commercially available sulfinic acids. Alternatively, the sulfinyl chloride may be directly prepared from a more available precursor, the disulfide, by reaction with chlorine[6] or sulfuryl chloride[7] in the presence of acetic acid. When the former reaction is carried out in alcohol solvent, the sulfinate ester is obtained directly.[8] We describe herein an extremely convenient, one-step synthesis of sulfinate esters (2) from readily available sulfonyl chlorides, proceeding in this case by in situ reduction (eq 1).



The discovery of this procedure stems from our observation that in situ sulfonylations of epoxy alcohols following asymmetric epoxidation persistently afforded the undesired sulfinate ester as a significant byproduct.[9] Isolation of *O,O*-dimethyl *S*-*p*-tolyl phosphorothiolate (**3**; Ar = *p*-Tol, R = Me)[10] as an additional byproduct aided in tracing the source of the problem to the presence of excess trimethyl phosphite in the reaction mixture after reduction of the hydroperoxide. The reaction between triethyl phosphite and a sulfonyl chloride to afford the corresponding phosphorothiolate and triethyl phosphate was reported by Hoffmann and co-workers[11] in 1956 and involves sequential deoxygenation of the sulfonyl chloride, presumably via quasi-phosphonium intermediates, followed by a Michaelis–Arbusov reaction (Scheme I, R = Et). In the presence of alcohol, the intermediate sulfinyl chloride is apparently intercepted to produce the sulfinate ester.[12] While a number of similar reductions of organic sulfur compounds by tervalent phosphorus have been reported,[10,13] this appears to be the first example of the trapping of an intermediate in such a reduction sequence by an external nucleophile.

Table I. Preparation of Menthyl Sulfinate Esters

entry	1: R′	time, h	yield,[a] %	recovered menthol, %	diastereoselectivity[b]
1	*p*-$CH_3C_6H_4$	8	90	6	1.4:1
2	2-naphthalenyl	5	96	4	1.4:1
3	*p*-$OCH_3C_6H_4$	20	89		1.3:1
4	*p*-ClC_6H_4	1.5	92		1.6:1
5	2,4,6-(*i*-Pr)$_3C_6H_2$	27	36	52	
6	*p*-(*t*-Bu)C_6H_4	6.5	87		1.5:1
7	*o*-$MeO_2CC_6H_4$	6.5	48		1.6:1[c]
8	2,4,5-$Cl_3C_6H_2$	3	75[d]	25	2.1:1
9	2,4,6-$Me_3C_6H_2$	15	70	21	1.5:1[e]
10	8-quinolinyl	4	52	41	1.9:1[c]
11	2-thiophenyl	1.5	92		1.8:1
12	CCl_3	1	76[f]	19	2.9:1
13	CH_3	4	22		1.7:1

[a] Yields are isolated yields after chromatographic purification and in most cases are not optimized. Yields are based on menthol and are not corrected for recovered starting material. [b] Ratios were determined by ^1H NMR (250 MHz, $CDCl_3$), usually examining the sulfinate methine. Except where noted, peak separation was not complete and the numbers given should be regarded as approximate values. In all cases the major diastereomer is that with the more upfield methine, and when separation was possible, the major diastereomer in all cases proved to have a negative sign of rotation, indicating the *S* configuration at sulfur.[19] [c] Base-line separation was attained. [d] Reaction was performed at room temperature. [e] Ratio was determined by ^1H NMR (C_6D_6) in the presence of an achiral shift reagent [Eu(fod)$_3$], examining the aromatic protons. [f] Only 1 equiv of sulfonyl chloride was used.

In optimizing the reaction as a preparatively useful synthesis of sulfinate esters, we concentrated initially on the preparation of menthyl sulfinates, due to their estab-

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(11) Hoffmann, R. W.; Moore, T. R.; Kagan, B. *J. Am. Chem. Soc.* **1956**, *78*, 6413.

(12) We have shown in control experiments that the sulfonate ester is not reduced under the reaction conditions. Intermediates other than sulfinyl chloride may also be capable of capture by menthol, however, and it is possible that the product sulfinate ester is formed by the concurrent operation of more than one pathway (vide infra). We are not presently able to distinguish between these possibilities, however, and for convenience we will refer only to the sulfinyl chloride as the reactive intermediate.

(13) (a) Cadogan, J. I. G. *Q. Rev. Chem. Soc.* **1962**, *16*, 208 and references cited therein. (b) Poshkus, A. C.; Herweh, J. E. *J. Am. Chem. Soc.* **1957**, *79*, 4245. (c) Michalski, J.; Modro, T.; Wieczorkowski, J. *J. Chem. Soc.* **1960**, 1665. (d) Edmundson, R. S.; Forth, C. I. *Phosphorus Sulfur* **1980**, *8*, 315. (e) Harpp, D. N.; Smith, R. A. *J. Am. Chem. Soc.* **1982**, *104*, 6045. (f) Adlington, R. M.; Barrett, A. G. M. *J. Chem. Soc., Perkin Trans. 1* **1980**, 1076.

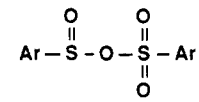
lished utility as synthetic intermediates.[1] The results of these efforts are presented in Table I. Although incomplete conversion was typical, the desired product was usually isolated in good to excellent yield. Attempts to drive the reaction to completion by using the higher boiling solvent 1,2-dichloroethane, or by performing the reaction at higher concentration (0.5 M), were unsuccessful. In both cases, more rapid consumption of sulfonyl chloride was observed, but at the expense of lower menthol conversion. The use of other phosphorus reagents was explored briefly. Tributylphosphine afforded *p*-tolyl disulfide as the only product, and a complex mixture resulted from the reaction employing triphenyl phosphite.

As described, the reaction is not suitable for sulfonyl chlorides possessing α-hydrogens. In those cases, deprotonation to a sulfene intermediate favors formation of the sulfonate ester and protects the sulfonyl chloride from reduction by phosphite. Thus, when *l*-menthol was treated with (+)-camphorsulfonyl chloride and trimethyl phosphite under standard conditions, a very rapid reaction ensued to afford the sulfonate ester in 92% yield. Attempts to prevent deprotonation by the use of weaker bases, or by performing the reaction in the absence of base, met with only limited success. The best result was obtained when *l*-menthol was treated with methanesulfonyl chloride (1.5 equiv), pyridine (1.5 equiv), and trimethyl phosphite (2.0 equiv) at reflux for 4 h (entry 13). A 22% isolated yield of the desired methane sulfinate was obtained, but conversion was low and the sulfonate ester was also formed.

With the exceptions noted above, the corresponding sulfonate ester was not detected in any reaction employing menthol as the trapping nucleophile. Similarly, the reaction of cyclohexanol with tosyl chloride afforded the *p*-toluenesulfinate in 78% yield, with no trace of cyclohexyl tosylate. Relative rates were somewhat less favorable in the reactions of primary alcohols. Thus, reaction of 1-decanol with tosyl chloride under standard conditions afforded a 6.1:1 mixture of the sulfinate and sulfonate esters, while the more sterically encumbered 2,4,6-triisopropylbenzenesulfonyl chloride gave a ratio of 11.5:1. At lower temperatures, reduction of the sulfonyl chloride ceased to compete effectively with direct sulfonylation of the alcohol, and at −20 °C, the reaction of 1-decanol with tosyl chloride produced the sulfinate and sulfonate esters in a 1:1.8 ratio. Sulfinamides were not successfully prepared by this procedure, the corresponding sulfonamide being the predominant product from the reaction of tosyl chloride with either phenethylamine or ephedrine at all reaction temperatures examined.

As expected, formation of the phosphorothiolate **3** was a consistent side reaction in all cases examined, resulting in a significant reduction in product yield when nucleophilic trapping of the sulfinyl chloride by alcohol was slow (entry 5). *p*-Tolyl disulfone was also isolated as a byproduct from reactions employing tosyl chloride, and similar products, while not isolated or characterized, were observed in most other reactions as well. These byproducts were easily removed by chromatography on silica gel, or by recrystallization of the product from acetone.

The mechanism for the formation of disulfones in this reaction is not entirely clear. Although one might postulate that these products result from attack by sulfinate anion on the sulfonyl chloride, this reaction reportedly does not occur.[14] Recently, however, Grossert and co-workers[15] observed the formation of disulfone as a minor contaminant in the preparation of sulfinate esters by reaction of the sulfinate salt with a sulfonyl chloride in the presence of alcohol. They proposed the intermediacy of mixed anhydride **4**, which could suffer nucleophilic attack by alcohol to afford the sulfinate ester or undergo thermal rearrangement to the disulfone. It is possible that the current reaction is operating at least partially by a similar mechanism. Because of the reported[16] preparation of α-disulfones by means of a radical coupling mechanism, the effects of the radical inhibitors 4,4′-thiobis(6-*tert*-butyl-*m*-cresol)[17] (5 mol %) and γ-terpinene (0.5 equiv) on this reaction were examined, but neither appeared to reduce the formation of disulfone.



4

The method described here promises to find widespread application in the preparation of sulfinate esters for which the corresponding sulfinic acid is not commercially available and should allow a more rapid and complete screening of sulfur substituent effects in chiral sulfoxide chemistry than has previously been possible. Given the experimental simplicity of the reaction and the low cost of the reagents, it may even find some use where both the sulfonyl chloride and the sulfinic acid are available. A 0.2-mol-scale preparation of (−)-menthyl *p*-toluenesulfinate compared favorably (66% yield of the pure diastereomer) with previously reported methods,[3b,18] further illustrating the practicality of the reaction.

Experimental Section

General. All reagents were commercially available and were used as received. Except as noted, all reactions were performed on a 2.0-mmol-scale as described in Table I. In all reactions involving menthol, the *l*-(−)-isomer was used. As noted in Table I, when separation of isomers was possible, the major diastereomer in all cases proved to have a negative sign of rotation. Literature precedent[19] suggests that these compounds have the *S* configuration at sulfur. However, *R* and *S* descriptors are given only where the absolute configuration has been unambiguously determined.

General Procedure. A dry 25-mL two-necked pear-shaped flask equipped with a reflux condenser is charged with the alcohol (2.0 mmol), sulfonyl chloride (3.0 mmol), and CH_2Cl_2 (10 mL) under nitrogen. Triethylamine (3.0 mmol) and trimethyl phosphite (4.0 mmol) are introduced via syringe through a rubber septum in the sidearm. The rubber septum is replaced by a glass stopper, and the reaction mixture is heated to reflux. When TLC shows no remaining sulfonyl chloride, the reaction mixture is allowed to cool and then is poured into a mixture of ether (20 mL) and 1 N HCl (10 mL). The ethereal layer is washed with saturated $NaHCO_3$ and saturated NaCl, dried ($MgSO_4$), and concentrated. Purification by flash chromatography affords the pure product as a mixture of diastereomers, which in many cases can be separated by recrystallization from acetone.

Menthyl 2-Naphthalenesulfinate. Reaction was performed on a 5.0-mmol scale to afford after chromatography an oily white solid (1.593 g, 96%): ^{1}H NMR ($CDCl_3$) δ 7.54–8.26 (m, 7 H), 4.27 (dt, J = 4, 11 Hz, 0.42 H); 4.19 (dt, J = 4, 11 Hz, 0.58 H), 0.70–2.38 (m, 18 H). Two recrystallizations from acetone afforded pure (+)-[(−)-menthyl 2-naphthalenesulfinate][20,24] (0.469 g, 28%): mp

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(18) Hulce, M.; Mallamo, J. P.; Frye, L. L.; Kogan, T. P.; Posner, G. H. *Org. Synth.* **1986**, *64*, 196. These authors report a 63–65% yield for a 0.20-mol-scale preparation of (*S*)-(−)-menthyl *p*-toluenesulfinate.
(19) Axelrod, M.; Bickart, P.; Jacobus, J.; Green, M. M.; Mislow, K. *J. Am. Chem. Soc.* **1968**, *90*, 4835.

133–136 °C; $[\alpha]^{25}_D$ +41.03° (*c* 1.36, acetone); IR (KBr) 3060, 2955, 2920, 2870, 1590, 1455, 1130, 955, 918, 852, 785, 770, 653 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.57–8.27 (m, 7 H), 4.27 (dt, *J* = 4.5, 10.6 Hz), 0.75–2.22 (m, 18 H). Anal. Calcd for $C_{20}H_{26}O_2S$: C, 72.68; H, 7.93. Found: C, 72.39; H, 7.90.

Menthyl *p*-Methoxybenzenesulfinate. Reaction afforded 0.550 g (89%) of a white solid: ^1H NMR ($CDCl_3$) δ 7.62–7.67 (m, 2 H), 6.99–7.04 (m, 2 H), 4.19 (dt, *J* = 4.5, 11 Hz, 0.43 H), 4.11 (dt, *J* = 4.5, 11 Hz, 0.57 H), 0.70–2.29 (m, 18 H). Recrystallization from acetone afforded pure (*S*)-(−)-menthyl *p*-methoxybenzenesulfinate (0.250 g, 40%): mp 111–115 °C (lit.[21] mp 110–110.5 °C); $[\alpha]^{25}_D$ −191.2° (*c* 1.21, acetone) (lit.[21] $[\alpha]^{25}_D$ −188.9° (*c* 1.19, acetone)).

Menthyl *p*-Chlorobenzenesulfinate. Reaction afforded a white solid (0.574 g, 92%): ^1H NMR ($CDCl_3$) δ 7.63–7.68 (m, 2 H), 7.48–7.53 (m, 2 H), 4.21 (dt, *J* = 4, 11 Hz, 0.38 H), 4.14 (dt, *J* = 4, 11 Hz, 0.62 H), 0.67–2.33 (m, 18 H). Recrystallization from acetone afforded pure (*S*)-(−)-menthyl *p*-chlorobenzensulfinate: mp 83.5–86.5 °C (lit.[22] mp 87–88 °C); $[\alpha]^{25}_D$ −180.0° (*c* 0.65, acetone) (lit.[22] $[\alpha]^{25}_D$ −181.1° (*c* 0.66, acetone)).

O,O-Dimethyl *S*-*p*-chlorophenyl phosphorothiolate[23] was also isolated as a colorless oil: IR (thin film) 3045, 2960, 2880, 1615, 1480, 1265, 1030, 830, 770 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.47–7.52 (m, 2 H), 7.31–7.36 (m, 2 H), 3.83 (d, *J* = 12 Hz, 6 H).

Menthyl 2,4,6-Triisopropylbenzenesulfinate. Reaction afforded a colorless oil (0.290 g, 36%): ^1H NMR ($CDCl_3$) δ 7.08 (s, 2 H), 4.03–4.15 (m, 3 H), 2.88 (heptet, *J* = 6.9 Hz, 1 H), 0.84–2.37 (m, 36 H); IR (thin film) 2940, 2880, 1600, 1460, 1128, 960, 750 cm^{-1}. Anal. Calcd for $C_{25}H_{42}O_2S$: C, 73.83; H, 10.41. Found: C, 73.57; H, 10.70.

Also isolated was *O,O*-dimethyl *S*-2,4,6-triisopropylphenyl phosphorothiolate (0.207 g, 0.55 mmol) as a colorless oil: IR (thin film) 2965, 2850, 1600, 1465, 1260, 1040, 830, 770, 608 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.04 (s, 2 H), 3.90 (heptet, *J* = 7 Hz, 2 H), 3.75 (d, *J* = 12 Hz, 6 H), 2.88 (heptet, *J* = 7 Hz, 18 H).

Menthyl 4-*tert*-Butylbenzenesulfinate. Reaction afforded a white solid (0.587 g, 87%): ^1H NMR ($CDCl_3$) δ 7.65 (d, *J* = 8 Hz, 2 H), 7.54 (d, *J* = 8 Hz, 2 H), 4.21 (dt, *J* = 4, 11 Hz, 0.4 H), 4.13 (dt, *J* = 4, 11 Hz, 0.6 H), 0.66–2.31 (m, 27 H). Pure (−)-[(−)-menthyl 4-*tert*-butylbenzenesulfinate][24] (0.131 g, 19%) was obtained after three recrystallizations from acetone: mp 102.5–103.5 °C; $[\alpha]^{25}_D$ −172.8° (*c* 1.38, acetone); IR (KBr) 2960, 2925, 2870, 1598, 1455, 1390, 1370, 1270, 1140, 965, 955, 920, 785, 770, 612 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.64 (d, *J* = 8 Hz, 2 H), 7.54 (d, *J* = 8 Hz, 2 H), 4.13 (dt, *J* = 4.5, 11 Hz, 1 H), 2.06–2.31 (m, 2 H), 0.84–1.71 (m, 7 H), 1.34 (s, 9 H), 0.96 (d, *J* = 6.5 Hz, 3 H), 0.86 (d, *J* = 7 Hz, 3 H). Anal. Calcd for $C_{20}H_{32}O_2S$: C, 71.38; H, 9.59. Found: C, 71.57; H, 9.99.

Menthyl 2-Carbomethoxybenzenesulfinate. Reaction afforded 0.320 g (48%): ^1H NMR ($CDCl_3$) δ 7.56–8.33 (m, 4 H), 4.25 (dt, *J* = 5, 11 Hz, 0.38 H), 4.12 (dt, *J* = 4, 11 Hz, 0.62 H), 3.96 (s, 1.14 H), 3.95 (s, 1.86 H), 0.67–2.36 (m, 18 H). Two recrystallizations from acetone afforded pure (−)-[(−)-menthyl 2-carbomethoxybenzenesulfinate][24] as white needles (0.140 g, 21%): mp 139–141.5 °C; $[\alpha]^{25}_D$ −348.6° (*c* 1.18, acetone); IR (KBr) 2960, 2938, 2865, 1720, 1280, 1122, 1110, 955, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.31 (dd, *J* = 1, 8 Hz, 1 H), 8.04 (dd, *J* = 1, 8 Hz, 1 H), 7.77 (dt, *J* = 1, 8 Hz, 1 H), 7.59 (dt, *J* = 1, 8 Hz, 1 H), 4.12 (dt, *J* = 4.4, 10.7 Hz, 1 H), 3.96 (s, 3 H), 2.28–2.39 (m, 1 H), 2.0–2.15 (m, 1 H), 0.75–1.73 (m, 7 H), 0.95 (d, *J* = 7 Hz, 3 H). Anal. Calcd for $C_{18}H_{26}O_4S$: C, 63.87; H, 7.74. Found: C, 64.00; H, 7.84.

Also isolated was *O,O*-dimethyl *S*-2-carbomethoxyphenyl phosphorothiolate (0.127 g, 0.41 mmol): IR (thin film) 3070, 3000, 2960, 2860, 1725, 1435, 1260 (br), 1030 (br), 830, 795, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.82 (m, 2 H), 7.48 (dt, *J* = 2, 8 Hz, 1 H), 7.40 (tt, *J* = 1, 8 Hz, 1 H), 3.95 (s, 3 H), 3.82 (d, *J* = 12.8 Hz, 6 H).

Menthyl 2,4,5-Trichlorobenzenesulfinate. Reaction was performed at room temperature and was exothermic. A colorless oil (0.5731 g, 75%) was obtained after the usual chromatography: IR (thin film) 3085, 3060, 2960, 2930, 2875, 1482, 1145, 1064, 950, 914, 868, 852, 780, 765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.05 (d, *J* = 3 Hz, 1 H), 7.53 (s, 1 H), 4.23 (dt, *J* = 4, 11 Hz, 0.32 H), 4.13 (dt, *J* = 4, 11 Hz, 0.68 H), 0.69–2.53 (m, 18 H). Anal. Calcd for $C_{16}H_{21}Cl_3O_2S$: C, 50.07; H, 5.52. Found: C, 49.96; H, 5.55.

Menthyl 2,4,6-Trimethylbenzenesulfinate.[25] Reaction afforded a colorless oil (0.447 g, 70%): IR (thin film) 2960, 2930, 2878, 1602, 1452, 1130, 960, 850, 755, 632 cm^{-1}; ^1H NMR ($CDCl_3$) δ 6.85 (s, 2 H), 4.01–4.14 (m, 1 H), 2.59 (s, 6 H), 2.28 (s, 3 H), 0.78–2.35 (m, 18 H). Shift-study analysis (C_6D_6, Eu(fod)$_3$; ratio was determined from the relative integrations of the aromatic peaks for the two diastereomers) indicated a diastereomeric ratio of 1.5:1. Attempts to recrystallize this material were unsuccessful.

Menthyl 8-Quinolinesulfinate. Reaction was begun at room temperature and was somewhat exothermic. Heat was applied after 1 h, and the reaction was worked up after 4 h to afford 0.346 g (52%) of a white solid: ^1H NMR ($CDCl_3$) δ 8.94 (m, 1 H), 8.39–8.44 (m, 1 H), 8.23 (dd, *J* = 1.5, 8 Hz, 1 H), 8.01 (dd, *J* = 1, 8 Hz, 1 H), 7.70–7.77 (m, 1 H), 7.47–7.53 (m, 1 H), 4.39 (dt, *J* = 4.5, 11 Hz, 0.34 H), 4.23 (dt, *J* = 4.5, 11 Hz, 0.66 H), 0.49–2.54 (m, 18 H). Recrystallization from acetone afforded (−)-[(−)-menthyl 8-quinolinesulfinate] as white cubic crystals (0.177 g, 27%): mp 160–162 °C; $[\alpha]^{25}_D$ −447.5° (*c* 1.23, acetone); IR (KBr) 3035, 3000, 2980, 2930, 2880, 2860, 1560, 1492, 1460, 1385, 1120, 955, 915, 852, 785, 760 cm^{-1}; ^1H NMR ($CDCl_3$) δ 8.99 (dd, *J* = 1.8, 4.3 Hz, 1 H), 8.43 (dd, *J* = 1.5, 7 Hz, 1 H), 8.24 (dd, *J* = 1.5, 8 Hz, 1 H), 8.01 (dd, *J* = 1.8, 8 Hz, 1 H), 7.74 (dd, *J* = 7 Hz, 1 H), 7.51 (dd, *J* = 4.3, 8 Hz, 1 H), 4.23 (dt, *J* = 4.5, 11 Hz, 1 H), 2.55–2.60 (m, 1 H), 1.99–2.10 (m, 1 H), 0.75–1.73 (m, 7 H), 0.94 (d, *J* = 6 Hz, 3 H), 0.79 (d, *J* = 7 Hz, 3 H), 0.51 (d, *J* = 7 Hz, 3 H). Anal. Calcd for $C_{19}H_{25}NO_2S$: C, 68.84; H, 7.60. Found: C, 68.65; H, 7.84.

Also isolated as a yellow-orange semisolid was *O,O*-dimethyl *S*-8-quinolinyl phosphorothiolate: ^1H NMR ($CDCl_3$) δ 8.21 (dt, *J* = 2, 8 Hz, 1 H), 7.71 (d, *J* = 8 Hz, 1 H), 7.54 (t, *J* = 8 Hz, 1 H), 7.48 (dd, *J* = 4, 8 Hz, 1 H), 3.89 (d, *J* = 13 Hz, 6 H).

Menthyl 2-Thiophenesulfinate. Reaction afforded a colorless oil (0.530 g, 92%): IR (thin film) 3090, 2960, 2930, 2880, 1455, 1406, 1140, 955, 928, 854, 765 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.61 (dd, *J* = 1, 5 Hz, 1 H), 7.49 (dt, *J* = 4, 1 Hz, 1 H), 7.13 (dd, *J* = 4, 5 Hz, 1 H), 4.24 (dt, *J* = 4, 11 Hz, 0.36 H), 4.18 (dt, *J* = 4, 11 Hz, 0.64 H), 2.08–2.27 (m, 2 H), 0.66–1.78 (m, 16 H). Anal. Calcd for $C_{14}H_{22}O_2S_2$: C, 58.70; H, 7.74. Found: C, 58.97; H, 7.83.

Also isolated as a yellow oil was *O,O*-dimethyl *S*-2-thiopheneyl phosphorothiolate (0.125 g, 0.56 mmol): IR (thin film) 3095, 3000, 2960, 2860, 1445, 1265, 1030, 835, 795, 778, 710, 563 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.43–7.49 (m, 1 H), 7.22–7.28 (m, 1 H), 7.04 (dd, *J* = 4, 5 Hz, 1 H), 3.86 (d, *J* = 12 Hz, 6 H). Anal. Calcd for $C_6H_9O_3S_2P$: C, 32.14; H, 4.05. Found: C, 31.98; H, 4.12.

Menthyl Trichloromethanesulfinate. Only 1 equiv of sulfonyl chloride was employed. Reaction was begun at 0 °C and allowed to warm to room temperature after 10 min. Workup after 1 h afforded 0.4876 g (76%) of colorless oil: IR (thin film) 2965, 2935, 2880, 1458, 1392, 1375, 1190, 948, 910, 858, 820, 798 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.35 (dt, *J* = 5, 10.5 Hz, 0.26 H), 4.31 (dt, *J* = 4.5, 11 Hz, 0.74 H), 0.72–1.79 (m, 18 H). Anal. Calcd for $C_{11}H_{19}Cl_3O_2S$: C, 41.07; H, 5.95. Found: C, 41.36; H, 6.24.

Menthyl Methanesulfinate. Methanesulfonyl chloride (0.23 mL, 3.0 mmol) was added to a solution of *l*-menthol (0.3148 g, 2.0 mmol), pyridine (0.24 mL, 3.0 mmol), and trimethyl phosphite (0.47 mL, 4.0 mmol) in CH_2Cl_2 (10 mL) at 0 °C under nitrogen. After 4 h, standard workup and purification afforded 0.095 g (22%) of menthyl methanesulfinate[26] as a colorless oil: IR (thin film) 2960, 2930, 2880, 1460, 1140, 990, 940, 915, 855, 760, 700 cm^{-1}; ^1H NMR ($CDCl_3$) δ 3.91–4.04 (m, 1 H), 2.62 (s, 1.11 H), 2.60 (s, 1.89 H), 0.75–2.22 (m, 18 H).

Menthyl Camphorsulfonate. Reaction of *l*-menthol (0.3125 g, 2.0 mmol), (+)-camphorsulfonyl chloride (0.7518 g, 3.0 mmol), triethylamine (0.42 mL, 3.0 mmol), and trimethyl phosphite (0.47 mL, 4.0 mmol) under standard conditions for 1 h afforded, after workup and purification, 0.6525 g (92%) of the sulfonate ester

(20) Note: This is the minor diastereomer produced in the reaction.
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as a white solid: mp 119–121 °C; IR (KBr) 2980, 2880, 1745, 1345, 1170, 1160, 950, 925, 910, 892, 878 cm^{-1}; ^1H NMR ($CDCl_3$) δ 4.60 (dt, J = 5, 11 Hz, 1 H), 3.61 (d, J = 15 Hz, 1 H), 3.01 (d, J = 15 Hz, 1 H), 0.80–2.54 (m, 31 H).

Cyclohexyl *p*-Toluenesulfinate. Reaction of cyclohexanol (0.21 mL, 2.0 mmol) with *p*-toluenesulfonyl chloride (0.572 g, 3.0 mmol), triethylamine (0.42 mL, 3.0 mmol), and trimethyl phosphite (0.47 mL, 4.0 mmol) under standard conditions afforded, after workup and purification, 0.373 g (78%) of cyclohexyl *p*-toluenesulfinate as a colorless oil: IR (thin film) 3040, 2940, 2865, 1598, 1450, 1138, 945, 850, 763 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.60 (d, J = 8 Hz, 2 H), 7.32 (d, J = 2 Hz, 2 H), 4.33 (tt, J = 4, 9 Hz, 1 H), 2.42 (s, 3 H), 1.13–2.05 (m, 10 H).

1-Decanyl *p*-Toluenesulfinate. A 25-mL two-necked pear-shaped flask was charged with *p*-toluenesulfonyl chloride (0.460 g, 2.4 mmol), triethylamine (0.33 mL, 2.4 mmol), trimethyl phosphite (0.47 mL, 4.0 mmol), and dichloromethane (7 mL) under nitrogen, and the resulting solution was warmed to reflux. After 10 min, 1-decanol (0.323 g, 2.0 mmol) was added via cannula as a solution in 3 mL of dichloromethane. After 6 h at reflux, standard workup afforded 0.61 g of an oil. Purification by flash chromatography (elution with 25% CH_2Cl_2–hexane) afforded 0.481 g (79%) of a mixture of sulfinate and sulfonate esters, in a ratio of 86:14 (as determined by ^1H NMR). An analytical sample of the sulfinate ester was obtained by a second chromatography. Data for 1-decanyl *p*-toluenesulfinate: IR (thin film) 3060, 3030, 2940, 2860, 1600, 1465, 1140, 945 (br), 815, 630 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.59 (d, J = 8 Hz, 2 H), 7.33 (d, J = 8 Hz, 2 H), 3.97–4.06 (m, 1 H), 3.55–3.64 (m, 1 H), 2.43 (s, 3 H), 1.24–1.64 (m, 18 H), 0.88 (t, J = 6.5 Hz, 3 H). Anal. Calcd for $C_{17}H_{28}O_2$: C, 68.87; H, 9.52. Found: C, 69.15; H, 9.80.

1-Decanyl 2,4,5-Triisopropylbenzenesulfinate. Reaction of 2,4,5-triisopropylbenzenesulfonyl chloride (0.731 g, 2.4 mmol), triethylamine (0.33 mL, 2.4 mmol), trimethyl phosphite (0.47 mL, 4.0 mmol), and 1-decanol (0.324 g, 2.0 mmol) for 6 h as described in the preceding paragraph afforded, after workup and purification (chromatography on silica gel, eluting with 5% EtOAc–hexane), 0.637 g (78%) of a colorless oil. ^1H NMR ($CDCl_3$) analysis indicated a 92:8 mixture of sulfinate and sulfonate esters. An analytical sample of the sulfinate ester was obtained by a second chromatography (elution with 20% CH_2Cl_2–hexane). Data for 1-decanyl 2,4,5-triisopropylbenzenesulfinate: IR (thin film) 2965, 2935, 2860, 1600, 1465, 1130 cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.08 (s, 2 H), 3.98–4.22 (m, 4 H), 2.88 (heptet, J = 7 Hz, 1 H), 1.18–1.73 (m, 34 H), 0.87 (t, J = 7 Hz, 3 H). Anal. Calcd for $C_{25}H_{44}O_2S$: C, 73.47; H, 10.85. Found: C, 73.22; H, 11.03.

Large-Scale Preparation of (*S*)-(−)-Menthyl *p*-Toluenesulfinate. A dry 2-L three-necked round-bottomed flask equipped with a reflux condenser and nitrogen inlet was charged with *l*-menthol (31.25 g, 0.20 mol), *p*-toluenesulfonyl chloride (45.76 g, 0.24 mol), triethylamine (33.5 mL, 0.24 mol), and CH_2Cl_2 (1000 mL). Trimethyl phosphite (35.5 mL, 0.30 mol) was added, and the reaction mixture was heated to reflux. After 10 h the reaction mixture was allowed to cool to room temperature, washed with 1 N HCl (2 × 100 mL), saturated $NaHCO_3$ (100 mL), and saturated NaCl (2 × 100 mL), dried ($MgSO_4$), and concentrated. Kugelrohr distillation (45–50 °C (0.2 mm)) effected removal of trimethyl phosphate and some remaining menthol to afford a yellow oil (61.3 g), which solidified upon standing. This was dissolved in ether–petroleum ether (ca. 1:2, 300 mL) and filtered. *p*-Tolyl disulfone (1.32 g) was collected: mp 215 °C dec (lit.[27] mp 212 °C). The residue after removal of solvent was crystallized from acetone at −20 °C to afford 29.5 g of white crystals in four crops, with concentration after each filtration. HCl(g) was then bubbled through the neat mother liquor for 10 min to effect epimerization at sulfur. A white solid separated out and was recrystallized from acetone to give an additional 12.2 g of product. The combined crops were recrystallized from acetone to yield 39.11 g (66%) of pure (*S*)-(−)-menthyl *p*-toluenesulfinate in two crops: mp 103–105 °C (lit.[28] mp 106–107 °C); $[\alpha]^{25}_D$ −200.2° (*c* 1.23, acetone) (lit.[28] $[\alpha]^{25}_D$ −199° (*c* 2, acetone)).

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Regiospecific Synthesis of β-Thujaplicin (Hinokitiol) from 2-Isopropylphenol

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α-, β-, and γ-thujaplicins (3-, 4-, and 5-isopropyltropolones), isolated from *Chamaecyparis taiwanensis* Masamune et Suzuki[1] and *Thuja plicata* D. Don,[2] were the first naturally occurring monocyclic tropolones, and the unique character of these nonbenzenoid aromatic compounds has attracted considerable synthetic, biogenetic, and theoretical attention.[3] Particularly, their antibacterial and antifungal activities, which evidently confer on the heart-wood its resistance to decay, have aroused interest. A variety of synthetic approaches to these compounds, inter alia to β-thujaplicin (hinokitiol) (1), have been devised so far.[4] In view of the biological significance of 1, however, only the cycloaddition process of 1-isopropylcyclopentadiene with dichloroketene, which was reported from our laboratory,[4f] has been applied practically for industrial purposes.[5]

We now present another expedient synthesis of β-thujaplicin (1) starting from commercially available 2-isopropylphenol (2).[6] The new synthetic process consists of the site-specific ring expansion of 2-isopropylcyclohexanone (3) to 3-isopropylcycloheptanone (5) followed by the regiospecific conversion of the latter into 1 as illustrated in Scheme I.

2-Isopropylcyclohexanone (3)[7] was conveniently prepared from 1 by catalytic hydrogenation on Raney nickel (W-2) followed by sodium hypochlorite oxidation[8] of the resulting cyclohexanols in excellent yield.

Subsequent one-carbon homologation of 3 to the cycloheptanone 5, a key intermediate in this synthesis, was accomplished by the Tiffeneau–Demjanov ring expansion[9] by way of the cyanohydrin isomers 4. For the preparation of cyanohydrins 4, we observed that the reaction of 3 with alcoholic potassium cyanide under the usual conditions was not satisfactory because it proceeded only sluggishly. We found, however, that this transformation was readily performed by exchange with acetone cyanohydrin.[10] Thus the treatment of 3 with acetone cyanohydrin in basic media produced 4 as an isomeric mixture (**4a**/**4b** = 85:15) in 93% yield. The major isomer was assigned as *trans*-**4a** on the basis of application of Julia's method.[11] Although these isomers could be separated by column chromatography, the mixture was, without separation, subjected to the following ring expansion since we assumed that both cyanohydrins 4 would yield predominantly the same cycloheptanone 5 by the Tiffeneau–Demjanov rearrangement.[12]

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