°C for 12 h. The reaction mixture was cooled and the crude product isolated by flash chromatography on 300 g of silica gel 60 (230–400 mesh) first with hexane as the eluant to remove excess phenyl vinyl sulfide followed by 4:1 hexane/ether to isolate the product.[9] The resulting pale yellow oil was subsequently distilled (170 °C, 1 mm Hg,) to give a colorless oil: 12 g (70%); IR (CCl_4) 3050, 2950, 2860, 1675, 1640, 1580, 1450, 1260, 1150 cm^{-1}; NMR (CCl_4) δ 1.6–2.1 (m, 1 H), 2.3–2.8 (m, 1 H); 3.2–4.0 (m, 3 H), 5.6–7.2 (m, 4 H), 7.2–7.6 (m, 5 H); MS, *m/e* (relative intensity) 242 (17), 219 (4), 137 (4), 136 (100), 135 (52), 133 (55). Anal. Calcd for $C_{15}H_{14}OS$: C, 74.35; H, 5.82. Found: C, 74.44; H, 5.79.

Preparation of Bicyclo[3.2.2]nona-3,6,8-trien-2-one(1). To a solution of 9-(phenylthio)bicyclo[3.2.2]nona-3,6-dien-2-one (4; 12 g, 0.05 mol) in 50 mL of methylene chloride at −78 °C was added 80% *m*-chloroperbenzoic acid (10.7 g, 0.05 mol) in 50 mL of methylene chloride. The resulting mixture was stirred at this temperature for 45 min at which time the mixture was diluted with chloroform and washed with three 60-mL portions of saturated aqueous sodium bicarbonate solution and one 60-mL portion of saturated aqueous sodium chloride solution. The organic layer was dried over anhydrous sodium sulfate, and the solvent was removed in vacuo to give 16 g of crude sulfoxide which was used without further purification. The sulfoxide was dissolved in 25 mL of dry toluene containing 1.5 equiv of pyridine (10 mL), and the mixture was heated at 95–100 °C for 48 h. The resulting reaction mixture was cooled and purified by flash column chromatography on 150 g of silica gel 60 (230–400 mesh) with 10:1 pentane/ether as the eluant. The product was recrystallized from pentane to provide 3.5 g (32% from 2,4,6-cycloheptatrien-1-one) of pure trienone **2**; mp 43–44 °C (lit.[3] mp 44 °C). Alternatively, trienone **2** could be isolated in pure form by fractional distillation (75–80 °C, 1.5 mmHg) of the reaction mixture. The spectral and analytical properties of this material were shown to be identical in every respect (^1H NMR, IR, TLC, mixture melting point, mass spectrum) with those of trienone **2** prepared by known methods.[3]

Acknowledgment. We thank the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Institutes of Health (Grant GM-30771-01) for their support of this research.

Registry No. 1, 6006-24-2; 3, 539-80-0; 4, 86900-37-0; 4 sulfoxide, 86854-65-1; phenyl vinyl sulfide, 1822-73-7.

(9) Alternatively, the material could be purified by distillative removal of the excess phenyl vinyl sulfide followed by flash column chromatography of the residue on silica gel 60 with 4:1 hexane/ether as the eluant.

Improved Synthesis and Absolute Configuration of (+)- and (−)-2,2,4-Trimethyl-1,3-dioxolane-4-carboxaldehyde

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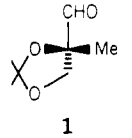
During the course of our ongoing investigations on the synthesis of bicyclomycin in optically active form,[1] it became necessary to prepare (*S*)-2,2,4-trimethyl-1,3-dioxolane-4-carboxaldehyde (**1**) as a means for introducing the C-1′–C-3′ polyoxo side chain with the correct absolute configuration. Preparation of (*R*)-**1** and racemic **1** has been



1

previously reported by two Hoffman-La Roche groups.[2,3] This protected aldehyde has been used in several total syntheses[4] and holds potential for being a useful chiral starting material for other synthetic targets.[5] Herein is reported a practical synthesis of both (+)- and (−)-**1**; the absolute configurations of which have been unambiguously confirmed by X-ray crystallographic analysis of a camphanyl ester derivative.

Results and Discussion

Our initial attempts to prepare useful quantities of both (*R*)- and (*S*)-**1** involved the resolution of the racemic alcohol precursor[6] **2**. Alcohol **2** was coupled with (−)-camphanyl chloride[7] (**3**) in pyridine to afford the diastereomeric esters **4** and **5** (Scheme I). These esters were separated by HPLC and hydrolyzed with $NaOCH_3$ in CH_3OH to afford the optically pure *R* and *S* alcohols **2**. Although large quantities of the esters **4** and **5** could be readily prepared, the separation proved to be feasible on a very small scale (HPLC) only; we were unable to find a practical large-scale chromatographic separation system.[8] Thus, for the purpose of preparing useful quantities of optically active **1**, we abandoned the resolution.

Both esters **4** and **5** were crystalline. A single-crystal X-ray structural determination was carried out on diastereomer **5**;[9] the structure thus established is exhibited in Figure 1. This structure unambiguously establishes the stereochemistry of the optically pure (−)-**2** as *S*.

We next turned our attention to an asymmetric synthesis of **1**. Sharpless'[10] asymmetric epoxidation of 2-methyl-2-propen-1-ol followed by the mercaptide ring opening/isopropylidination/oxidation sequence of Sharpless and Masamune[11] proceeded without incident to directly afford the optically pure aldehydes **1** (Scheme II). The aldehyde resulting from the (+)-tartrate-mediated epoxidation sequence possesses the expected *S*-configuration. Conversely, the (−)-tartrate-mediated epoxidation sequence provides (*R*)-**1**. The absolute configuration of the products was unambiguously correlated to the resolved alcohols **2** by $LiAlH_4$ reduction and comparison of optical rotation. From this data, it can be concluded that the

(1) (a) Williams, R. M.; Anderson, O. P.; Armstrong, R. W.; Josey, J.; Meyers, H.; Eriksson, C. *J. Am. Chem. Soc.* **1982**, *104*, 6092. (b) 183rd National Meeting of the American Chemical Society; Las Vegas, NV, March, 1982; American Chemical Society: Washington, DC, 1982; ORG 17. (c) Williams, R. M. *Tetrahedron Lett.* **1981**, *22*, 2341. (d) Williams, R. M.; Dung, J.-S.; Josey, J.; Armstrong, R. W.; Meyers, H. *J. Am. Chem. Soc.*, **1983**, *105*, 3214.

(2) Maag, H.; Blount, J. F.; Coffen, D. L.; Steppe, T. V.; Wong, F. *J. Am. Chem. Soc.* **1978**, *100*, 6786.

(3) Barner, R.; Schmid, M. *Helv. Chim. Acta* **1979**, *62*, 2384.

(4) (a) Vitamin E, see ref 3. (b) Bicyclomycin rearrangement product, see ref 2. (c) *N,N,O*-trimethylbicyclomycin: Nakatsuka, S.; Yoshida, K.; Goto, T. *Tetrahedron Lett.* **1981**, *22*, 4973. (d) *N,N′*-Dimethyl-4-desmethylenebicyclomycin, see ref. 1a,b,d.

(5) The corresponding (*R*)- and (*S*)-glyceraldehyde acetonides have often been used as chiral intermediates in synthesis and are readily available from natural sources, see: Jung, M. E.; Shaw, T. J. *J. Am. Chem. Soc.* **1980**, *102*, 6304 and references cited therein.

(6) Calinaud, P.; Gelas, J. *Bull. Soc. Chim. Fr.* **1975**, 1228.

(7) The procedure used for the preparation of camphanyl chloride was furnished by Dr. Juergen Martens.

(8) Silica gel chromatography on column and PTLC did not effect separation. Small quantities (up to 50 mg) could be separated on an analytical HPLC but proved to be impractical on a preparative scale (see Experimental Section).

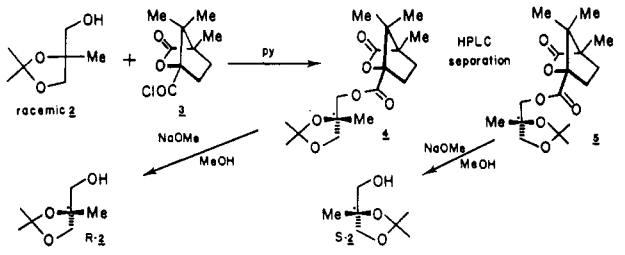
(9) A small (0.17 × 0.24 × 0.36 mm^3) crystal of **5** was orthorhombic (space group $p2_12_12_1$) with a = 7.458 (1) Å, b = 10.776 (2) Å, and c = 22.592 (5) Å. The 1015 observed ($I > 2\sigma(I)$) reflections (of 1408 unique reflections with 3.5° < 2θ < 45.0°) gave R = 0.047, R_w = 0.052, and the standard deviation in an observation of unit weight of 1.10 for a structural model that included anisotropic thermal parameters for all non-hydrogen atoms and hydrogen atoms included in idealized positions.

(10) Sharpless, K. B.; Katsuki, T. *J. Am. Chem. Soc.* **1980**, *102*, 5976.

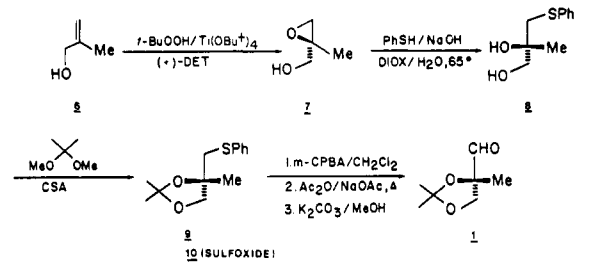
(11) Lee, A. W. M.; Martin, V. S.; Masamune, S.; Sharpless, K. B.; Walker, F. J. *J. Am. Chem. Soc.* **1982**, *104*, 3515.

0022-3263/83/1948-3592$01.50/0

Scheme I



Scheme II



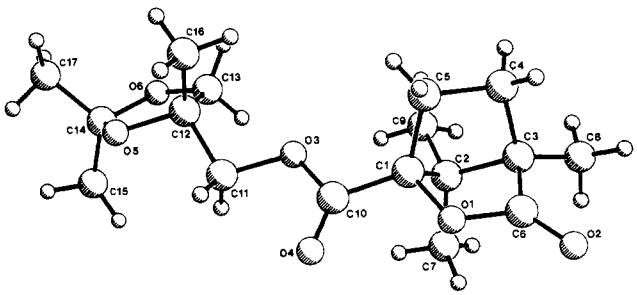


Figure 1. Molecular structure of **5**. Atoms are shown as spheres of fixed arbitrary radius.

epoxidation reaction in the case of (+)-DET and that from (−)-DET proceeds with 85% ee. Further confirmation of the % ee calculated on the optical rotations of the derived alcohols was obtained by coupling the alcohols synthesized via Scheme II to (−)-camphanyl chloride, which provided **4** and **5**; HPLC analysis of the percent of diastereomeric excess agreed with the percent enantiomeric excesses, calculated above (see Experimental Section).

One final comment regarding the asymmetric synthesis is important. When the epoxidation reaction was carried out with titanium tetraisopropoxide, it proved impossible to isolate and purify any of the intermediates prior to the sulfoxide **10**. In addition, the overall yield of this sequence turned out to be extremely low (ca. 2%). With titanium tetra-*tert*-butoxide,[12] on the other hand, the overall yield increased condiderably (10%) and the isolation and purification of all the intermediates became practicable.[13] The only chromatographic purification that was necessary was the purification of acetonide **9**; unfortunately, neither system permitted the isolation of any quantity of pure epoxide **7**.

Experimental Section[14]

Camphanyl Esters 4 and 5. To a stirred, room-temperature solution of racemic alcohol **2** (250 mg, 1.7 mmol, 1.0 equiv) (prepared as described in ref 6) in THF (5 mL) was added triethylamine (0.27 mL, 1.95 mmol, 1.1 equiv) and (−)-camphanyl chloride (**3**, 384 mg, 1.7 mmol, 1.0 equiv). The mixture was stirred for 1.5 h at room temperature, diluted with ether (20 mL), filtered, evaporated, and separated on PTLC silica gel (eluted with 50% ether in hexanes) to afford 531 mg (96%) of the diastereomeric esters **4** and **5**. These diastereomers were separated by HPLC (silica gel, 10% EtOAc in hexane).

Data for 4: $[\alpha]^{25}_D$ −8.2° (*c* 2.1, CH_2Cl_2); mp 81.5–82.5 °C (recrystallized from hexanes); ^1H NMR (360 MHz, $CDCl_3$) δ $CHCl_3$ 0.95 (3 H, s), 1.05 (3 H, s), 1.10 (3 H, s), 1.34 (3 H, s), 1.37 (3 H, s), 1.39 (3 H, s), 1.67 (1 H, m), 1.9 (1 H, m), 2.0 (1 H, m), 2.4 (1 H, m), 3.715 (1 H, $^1/_2$ ABq, *J* = 9.0 Hz), 3.95 (1 H, $^1/_2$ ABq, *J* = 9.0 Hz), 4.06 (1 H, $^1/_2$ ABq, *J* = 11 Hz), 4.14 (1 H, $^1/_2$ ABq, *J* = 11 Hz); IR (NaCl, neat) 1790, 1755, 1470, 1380, 1210, 1110, 1060 cm^{-1}.

Data for 5: $[\alpha]^{25}_D$ −14.4° (*c* 2.5, CH_2Cl_2); mp 100–101 °C (recrystallized from hexanes); ^1H NMR (360 MHz, $CDCl_3$) δ $CHCl_3$ 0.96 (3 H, s), 1.04 (3 H, s), 1.10 (3 H, s), 1.32 (3 H, s), 1.37 (3 H, s), 1.39 (3 H, s), 1.67 (1 H, m), 1.91 (1 H, m), 2.02 (1 H, m), 2.42 (1 H, m), 3.71 (1 H, $^1/_2$ ABq, *J* = 8.88 Hz), 3.97 (1 H, $^1/_2$ ABq, *J* = 8.88 Hz), 4.06 (1 H, $^1/_2$ ABq, *J* = 10.95 Hz), 4.16 (1 H, $^1/_2$ ABq, *J* = 10.95 Hz); IR (NaCl, neat) 1790, 1740, 1450, 1370, 1220, 1105, 1060 cm^{-1}; mass spectrum, *m/e* (relative intensity) 311 (39.3), 223 (3.7), 199 (6.8), 181 (11.3), 153 (15.6), 125 (23.6), 115 (100).

X-ray crystallographic data for this compound is provided in ref 9 and in the supplementary material.

(*R*)-(+)-2,2,4-Trimethyl-4-(hydroxymethyl)-1,3-dioxolane (2). A room-temperature solution of camphanyl ester **4** (17 mg, 0.052 mmol, 1.0 equiv) and 10% aqueous NaOH (0.05 mL, 0.114 mmol, 2.2 equiv) was stirred in MeOH (0.5 mL) for 3 h. Evaporation of the solvent and purification by a small silica gel column (eluted with 50% Et_2O in hexanes) afforded 6 mg (80%) of the optically pure (*R*)-acetonide alcohol **2** as a colorless oil: $[\alpha]^{25}_D$ +5.2° (*c* 0.5, CH_2Cl_2); ^1H NMR (100 MHz, $CDCl_3$) δ $CHCl_3$ 1.29 (3 H, s), 1.41 (6 H, s), 3.48 (3 H, br s), 3.72 (1 H, $^1/_2$ ABq, *J* = 8.5 Hz), 3.97 (1 H, $^1/_2$ ABq, *J* = 8.5 Hz); IR (NaCl, neat) 3480, 1470, 1370, 1260, 1210, 1060 cm^{-1}.

(*S*)-(−)-2,2,4-Trimethyl-4-(hydroxymethyl)-1,3-dioxolane (2). The same procedure used above on **4** for 17 mg of **5** furnished 6.3 mg (83%) of the corresponding (*S*)-acetonide alcohol **2** as a colorless oil, $[\alpha]^{25}_D$ −5.33° (*c* 0.3, CH_2Cl_2).

Epoxidation of 6 with (+)-Diethyl Tartrate. To a stirred solution of titanium *tert*-butoxide (1.5 g, 4.4 mmol, 1.0 equiv) in CH_2Cl_2 (22 mL) at −20 °C was added L-(+)-diethyl tartrate (0.77 mL, 4.4 mmol, 1.0 equiv) dropwise, and after 10 min, 2-methyl-2-propen-1-ol (0.38 mL, 4.4 mmol, 1.0 equiv) was added. The mixture was stirred for 1 h at −20 °C, and *tert*-butyl hydroperoxide (2.17 mL, 9.68 mmol, 2.2 equiv) was added. The solution was kept in the freezer at −20 °C for 3 days. The mixture was warmed to 0 °C, and saturated aqueous sodium sulfate (4.4 mL) was added followed by ether (20 mL). The mixture was allowed to come to room temperature, stirred for 5 h, and filtered through a pad of Celite. The filtrate was dried over anhydrous $MgSO_4$ and evaporated to afford the crude epoxide[15] (3.01 g), which was directly used for the next step without further purification.

Epoxidation of 6 with (−)-Diethyl Tartrate. The same procedure used above except (−)-DET was substituted; similarly, pure epoxide **7** was inseparable from the crude mixture and was used directly for the subsequent steps.

(*S*)-(+)-2-Methyl-1-(phenylthio)-2,3-propanediol (8). A solution of crude epoxide **7** (1.5 g, ca. 2.2 mmol, 1.0 equiv), thiophenol (1.12 mL, 11 mmol, 5 equiv), 1 N NaOH (5 mL), and dioxane (5 mL) was stirred at reflux for 3 h. After the mixture was allowed to cool to room temperature, CH_2Cl_2 (100 mL) was added, the organic layer was separated, dried over anhydrous sodium sulfate, filtered, and evaporated to afford the crude diol **8** (1.4 g, oil), which was directly used for the next step without further purification. An analytical sample was obtained on PTLC silica gel (eluted with 20% hexanes in Et_2O), (oil): $[\alpha]^{25}_D$ +2.593°

(12) We thank Professor K. B. Sharpless for suggesting this and also for providing an initial sample of titanium *tert*-butoxide.

(13) It should be noted that, to our knowledge, the specific rotations for **1** have not been reported in the literature.

(14) All compounds (except **7**) were obtained >99% pure by (as shown by ^1H NMR, MS, and homogeneity on TLC) preparative-layer chromatography; the analytical and spectroscopic data reported for each compound were obtained on analytically purified materials only.

(15) Note: All attempts to isolate this epoxide by numerous chromatographic and other conventional means such as distillation, etc., were uniformly unsuccessful. In no case was it possible to obtain any quantity of pure epoxide to record optical rotations.

(c 1.4, MeOH); ^{1}H NMR (100 MHz, $CDCl_3$) δ Me_4Si 1.24 (3 H, s), 3.13 (1 H, $^1/_2$ ABq, J = 14.6 Hz), 3.23 (1 H, $^1/_2$ ABq, J = 14.6 Hz), 3.53 (3 H, br s), 7.2–7.4 (5 H, m); IR (NaCl, neat) 3410, 3060, 1585, 1485, 1440, 1365, 1045, 735 cm^{-1}.

Utilizing exactly the same procedure above on the crude epoxide obtained from (-)-DET afforded (*R*)-(-)-**8**: $[\alpha]^{25}_D$ -2.631° (c 0.8, MeOH).

(*S*)-(+)-2,2,4-Trimethyl-4-[(phenylthio)methyl]-1,3-dioxolane (9). A solution of the crude diol **8** (1.4 g, ca. 2.2 mmol, 1.0 equiv) and D-camphorsulfonic acid (20 mg) was stirred in 2,2-dimethoxy propane (5 mL) at room temperature for 6 h. The mixture was diluted with CH_2Cl_2, poured into 0.1 N NaOH, and thoroughly extracted with CH_2Cl_2. The combined extracts were dried over anhydrous sodium sulfate, filtered, evaporated, and separated on silica gel (eluted with 5% Et_2O in hexanes and then 20% Et_2O in hexanes) to afford 181 mg (35% overall from **6**) of the acetonide **9** (oil): $[\alpha]^{25}_D$ +4.27° (c 1, $CHCl_3$); ^{1}H NMR (100 MHz, $CDCl_3$), δ Me_4Si 1.39 (9 H, s), 3.15 (2 H, s), 3.73 (1 H, $^1/_2$ ABq, J = 8.8 Hz), 4.00 (1 H, $^1/_2$ ABq, J = 8.8 Hz), 7.23–7.38 (5 H, m); IR (NaCl, neat) 3060, 1585, 1480, 1440, 1370, 1210, 1055, 980, 730, 685 cm^{-1}.

From (*R*)-(-)-**8**, (*R*)-(-)-**9** was obtained: $[\alpha]^{25}_D$ -4.545° (c 2.0, $CHCl_3$).

(*S*)-2,2,4-Trimethyl-4-[(phenylsulfinyl)methyl]-1,3-dioxolane (10). To a stirred solution of sulfide **9** (180 mg) in CH_2Cl_2 (5 mL) was added *m*-chloroperoxybenzoic acid (28 mg, 0.16 mmol) at room temperature. After 1.5 h, sequential addition of 10-mg portions of *m*-chloroperoxybenzoic acid was carried out every hour until the total amount added reached 93 mg. The mixture was diluted with CH_2Cl_2, poured into 0.1 N NaOH solution, and thoroughly extracted with CH_2Cl_2. The combined extracts were dried over anhydrous sodium sulfate, filtered, evaporated, and separated on PTLC silica gel (eluted with 25% hexanes in Et_2O) to afford a mixture of diastereomeric sulfoxides **10** (125 mg, 23% overall from **6**). A pure sample of each diastereomer could be obtained by repeated PTLC on silica gel (eluted with 25% hexanes in Et_2O).

One Isomer: ^{1}H NMR (100 MHz, $CDCl_3$) δ $CHCl_3$ 1.42 (6 H, s), 1.49 (3 H, s), 2.95 (2 H, d), 3.81 (1 H, $^1/_2$ ABq, J = 8.8 Hz), 4.40 (1 H, $^1/_2$ ABq, J = 8.8 Hz), 7.4–7.6 (5 H, m). **The Other isomer**: ^{1}H NMR (60 MHz, $CDCl_3$) δ $CHCl_3$ 1.36 (6 H, s), 1.62 (3 H, s), 2.96 (2 H, d), 3.80 (1 H, $^1/_2$ ABq, J = 9 Hz), 4.08 (1 H, $^1/_2$ ABq, J = 9 Hz), 7.3–7.7 (5 H, m). The mixture of diastereomers obtained from the initial reaction was used directly for the subsequent Pummerer reaction, without purification.

(*R*)-(+)-2,2,4-Trimethyl-4-(hydroxymethyl)-1,3-dioxolane (2). A stirred solution of the sulfoxide **10** (286 mg, 1.1 mmol, 1.0 equiv) and sodium acetate (550 mg, 6.6 mmol, 6.0 equiv) was heated to reflux in acetic anhydride (12 mL) for 11 h. The mixture was allowed to come to room temperature, diluted with CH_2Cl_2, poured into 1 N NaOH solution, and thoroughly extracted with CH_2Cl_2. The combined extracts were dried over anhydrous sodium sulfate, filtered, evaporated, and purified on PTLC silica gel (eluted with 25% Et_2O in hexanes) to afford 285 mg (88%) of the α-acetoxy sulfide, which was directly used for the subsequent reduction to **2** or hydrolysis to **1**.

Reduction to 2. To a stirred solution of the crude acetate obtained above (270 mg, 0.91 mmol, 1.0 equiv) in dry Et_2O (10 mL) at 0 °C was added lithium aluminum hydride (182 mg, 4.55 mmol, 5.0 equiv) in one portion. After 1 h, a saturated aqueous sodium sulfate solution was added dropwise to quench the excess hydride. The mixture was filtered and evaporated followed by a bulb-to-bulb distillation (ca. 1 mm) to afford the alcohol **2** (105 mg, 80%) as a colorless oil: $[\alpha]^{25}_D$ +4.42° (c 2.4, CH_2Cl_2) (85% ee based on resolved **2** $[\alpha]^{25}_D$ +5.2°).

From (*R*)-(-)-**9**, (*S*)-(-)-**2** was obtained: $[\alpha]^{25}_D$ -4.46° (c 1.3, CH_2Cl_2) (85% ee based on resolved **2** $[\alpha]^{25}_D$ -5.33°).

To verify the % ee calculated above, the (*S*)-acetonide alcohol **2** (16 mg, 0.11 mmol, 1.0 equiv) was treated with triethylamine (0.017 mL, 0.12 mmol, 1.11 equiv), and (-)-camphanyl chloride (**3**, 24 mg, 0.11 mmol, 1.0 equiv) in THF (0.8 mL) for 2 h at room temperature. The mixture was filtered and evaporated to afford 39 mg (100%) of the corresponding camphanyl esters; HPLC analysis (silica gel B10, eluted with 10% EtOAc in hexanes) indicated an 92.5:7.5 ratio of **5**:**4**, which corresponds to ca. 85% diastereomeric excess.

(*S*)-(-)-2,2,4-Trimethyl-1,3-dioxolane-4-carboxaldehyde (1). Procedure A: Swern Oxidation of 2. To a stirred solution of oxalyl chloride (0.24 mL, 2.75 mmol, 1.1 equiv) in CH_2Cl_2 (10 mL) at -78 °C was added Me_2SO (0.39 mL, 5.5 mmol, 2.2 equiv) over a 5-min period. After the suspension was stirred for 20 min, (*R*)-(+)-**2** (365 mg, 2.5 mmol, 1.0 equiv) in CH_2Cl_2 (3 mL) was added at -78 °C. After stirring for 55 min, Et_3N (1.75 mL, 12.5 mmol, 5.0 equiv) was added at -78 °C and the cooling bath was removed. The thick white suspension was stirred for 3.5 h at room temperature, diluted with Et_2O (70 mL), washed with water, dried over anhydrous sodium sulfate, filtered, evaporated, and carefully bulb-to-bulb distilled to afford 156 mg (43%) of the optically active (*S*)-aldehyde **1** as a clear, colorless oil: $[\alpha]^{25}_D$ -11.561° (c 5.0, CH_2Cl_2); ^{1}H NMR (100 MHz, $CDCl_3$) δ Me_4Si 1.37 (3 H, s), 1.40 (3 H, s), 1.43 (3 H, s), 3.72 (1 H, $^1/_2$ ABq, J = 9.0 Hz), 4.23 (1 H, $^1/_2$ ABq, J = 9.0 Hz), 9.63 (1 H, s).

Procedure B. To a stirred solution of the α-acetoxy sulfide (obtained above from the Pummerer reaction) (400 mg, 1.35 mmol, 1.0 equiv) in MeOH (5 mL) was added K_2CO_3 (100 mg), and the mixture was refluxed for 2 h. After being cooled to room temperature, Et_2O (25 mL) was added, and the mixture was filtered, carefully evaporated, and bulb-to-bulb distilled to afford 100 mg (51%) of the pure aldehyde as a clear, colorless oil.

The aldehyde **1** was obtained from the (-)-DET sequence: $[\alpha]^{25}_D$ +10.42° (c 0.2, CH_2Cl_2).

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, and to the National Institutes of Health Grant No. 1R01AIGM18957-01 for support of this work. The Nicolet R3-m/E diffractometer and computer system used in the determination of the structure of compound **5** were purchased with funds provided by the National Science Foundation under Grant No. CHE8103011. ^{1}H NMR measurements at 360 MHz were obtained at the Colorado State University Regional NMR Center, funded by the National Science Foundation Grant No. CHE78-18581.

Registry No. (*S*)-**1**, 79243-92-8; (±)-**2**, 86884-87-9; (*R*)-**2**, 86940-97-8; (*S*)-**2**, 86940-98-9; (-)-**3**, 39637-74-6; (-)-**4**, 86884-88-0; (-)-**5**, 86940-99-0; **6**, 513-42-8; (*R*)-**7**, 86884-89-1; (*S*)-**7**, 86884-90-4; (*S*)**8**, 86884-91-5; (*S*)-**9**, 86884-92-6; (*S*)-**10** (isomer 1), 86884-93-7; (*S*)-**10** (isomer 2), 86884-94-8; PhSH, 108-98-5; 2,2,4-trimethyl-4-[acetoxy(phenylthio)methyl]-1,3-dioxolane, 86884-95-9.

Supplementary Material Available: Table I, atomic coordinates for **5**; Table II, bond lengths for **5**; Table III, bond angles for **5**; Table IV, anisotropic thermal parameters for **5**; and Table V, hydrogen atom positions for **5** (5 pages). Ordering information is given on any current masterhead page.

Synthesis and Conformational Aspects of *cis*- and *trans*-3-Carbomethoxy-6-oxabicyclo[3.1.0]hexane

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It is recognized that 3-aminocyclopentanecarboxylic acid is a valuable probe for the study of the biological action of the neurotransmitter γ-aminobutyric acid (GABA). Striking differences in activity are noted for the cis and trans isomers in both neurotransmitter uptake[1] and action at the receptor.[2]

(1) (a) Pitzer, K. S. *Science* **1945**, *101*, 672. (b) Kilpatrick, J. E.; Pitzer, K. S.; Spitzer, R. *J. Am. Chem. Soc.* **1958**, *80*, 2486-7. (c) Pitzer, K.; Donath, W. E. *J. Am. Chem. Soc.* **1959**, *81*, 3213-8.

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