Synthesis and Absolute Configuration of (-)-Meridinol and (-)-3-Epimeridinol

Daisuke Takano [a], Matsumi Doe [a], Yoshiki Morimoto [a], Kazuo Yoshihara [b] and Takamasa Kinoshita* [a]

[a] Department of Chemistry, Graduate School of Science, Osaka City University, Sumiyoshi-ku, Osaka 558-8585, Japan
[b] Suntory Institute for Bioorganic Research, Shimamoto-cho, Osaka 618-0024, Japan

Received August 17, 1998

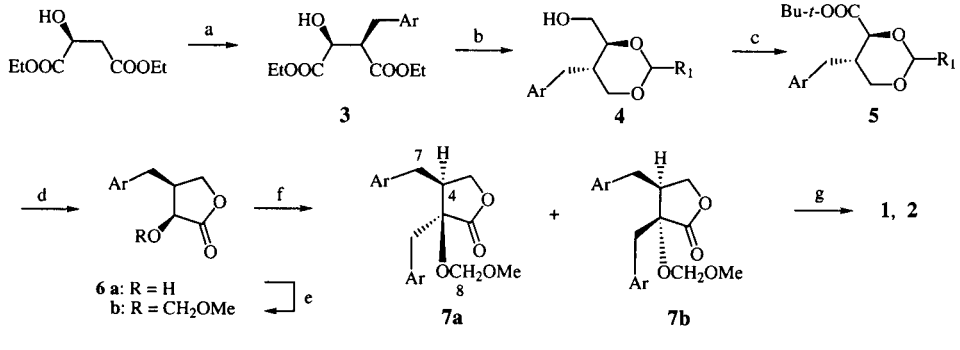
The first synthesis of (-)-meridinol and (-)-3-epimeridinol was accomplished from (*S*)-malic acid. This synthesis unambiguously established the absolute stereochemistry of meridinol.

J. Heterocyclic Chem., **36**, 221 (1999).

Lignans of the 3,4-dibenzyl-γ-butyrolactone series [1] having a hydroxyl group at the 3-position [2] are widely distributed in plants and have attracted considerable interest since the discovery of their intriguing biological properties such as cytotoxic, antibiotic and other activities.

The structure of a novel lignan, meridinol (-)-**1**, isolated from *Zanthoxylum fagara* (a shrub widely distributed over Central and South America, which has been used in indigenous medical systems as a sudorific and as a sedative) was determined by the evidence of its spectroscopic data and X-ray single crystal structure as (3*S*,4*S*)-3,4-bis(3,4-methylenedioxybenzyl)-3-hydroxybutyrolactone [3]. The total synthesis of (±)-meridinol and (±)-3-epimeridinol has been reported [4]. We now describe herein the first synthesis of (-)-**1** and (-)-**2** from (*S*)-malic acid in a stereoselective fashion.

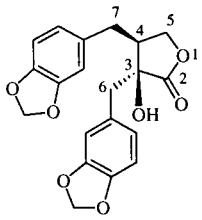
Scheme



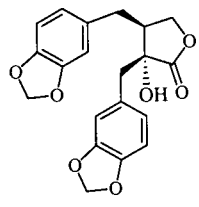
Ar = piperonyl, R_1 = *p*-$MeOC_6H_4$

Reagents and conditions: (a) 2 equivalents of lithium diisopropylamide, tetrahydrofuran, -78°C, 5.5 hours then rt, overnight, $ArCH_2I$, 78%; (b) 1) $LiAlH_4$, ether, 85% 2) *p*-anisaldehyde, *p*-TsOH, benzene, reflux, 59%; (c) CrO_3, pyridine, CH_2Cl_2, Ac_2O, *t*-BuOH, 55%; (d) 3*N* HCl, dioxane, 94%; (e) methoxymethyl chloride, CH_2Cl_2, $(i\text{-}Pr)_2EtN$, 88%; (f) lithium diisopropylamide, tetrahydrofuran, -78°C, $ArCH_2I$, hexamethylphosphoric triamide, 40%; (g) Me_3SiBr, CH_2Cl_2, 81% for **7a**, 87% for **7b**.

As the starting chiral template we chose (*S*)-malic acid to adopt its stereogenic center to that of **1** bearing an β-orientated piperonylmethyl group. Alkylation of diethyl (*S*)-malate with 3,4-methylenedioxybenzyl iodide was carried out according to the procedure by Seebach [5] and afforded **3** [6] in 78% yield. Reduction of **3** with lithium aluminium hydride in ether followed by protection with *p*-anisaldehyde in the presence of *p*-toluenesulfonic acid in boiling benzene gave crystalline acetal **4** in 59% yield. Neither a diastereo-isomer of the acetal nor a 1,2-acetal of the regio-isomer of **4** was detected. Oxidation of the acetal **4** by the Corey method [7] gave the ester **5** in 55% yield. Acid-catalyzed deprotection with hydrochloric acid followed by cyclization in one pot afforded crystalline hydroxy lactone **6a** in 94% yield, which would be a versatile compound for the synthesis of some natural products. The coupling reaction of the lithium enolate of lactone **6b** [8], after methoxymethylation of **6a** in the usual manner, with 3,4-methylenedioxybenzyl iodide afforded the lactone **7** as a separable mixture of two diastereomers (4:3). The stereochemistry of the newly introduced stereogenic center in **7** was confirmed by ^1H nmr analysis and NOE experiments. The lower chemical shifts of H-7 (δ 2.65 and 2.82) in **7a** compared with those of H-7 (δ 2.51) in **7b** by the anisotropic effect of the methoxymethyloxy group indicates that the two piperonylmethyl groups are located *anti* relationship. A NOE between H-4 and H-8 in **7b** was observed, but not in **7a**. From these results the



1 Meridinol



2 3-Epimeridinol

stereochernistry of **7a** and **7b** were determined to be (3*S*,4*S*)- and (3*R*,4*S*)- configuration, respectively.

Removal of methoxymethyl protection [9] in **7a** and **7b** with bromotrimethylsilane gave crystalline **1** (81% yield) and **2** (87% yield), respectively. Compound **1** was found to be identical with the natural product by comparing its mp, $[\alpha]_D$, hrms, elemental analysis, ^1H and ^{13}C nmr spectra with those reported [3], while the physical data of the compound **2** were all different except hrms and elemental analysis.

As it is apparent that the stereochemistry of the 4-position in **6a** is *s*-configuration, the absolute configuration of the synthetic **1** [(-)-meridinol] is determined as (3*S*,4*S*)-(-)-3,4-bis[(3,4-methylenedioxy)benzyl]-3-hydroxy-γ-butyrolactone and its isomer **2** [3-epimeridinol] is (3*R*,4*S*)-(-)-3,4-bis[(3,4-methylenedioxy)benzyl]-3-hydroxy-γ-butyrolactone.

In conclusion, this chiral synthesis from (*S*)-malic acid unambiguously established the absolute configuration of (-)-meridinol.

EXPERIMENTAL

All melting points were determined on a hot-stage microscope and are uncorrected. The ir spectra were taken on a JASCO A-102 IR spectrophotometer. The ^1H and ^{13}C nmr spectra were recorded on a JEOL LA-300 (300 MHz) in deuteriochloroform solution, unless stated otherwise. Chemical shifts (ppm) are given downfield of tetramethylsilane. Electron impact mass spectra were determined on a JEOL AX-500 spectrometer at an ionization energy of 70 eV. Optical rotations were determined with a JASCO Model DIP-370 polarimeter. Elemental analyses were performed with a JMS-AX 500 elemental analyzer. Column chromatography was performed with silica gel (Merck NO, 7734; 63-200 μm), and thin-layer chromatography (tlc) was performed on a glass plate coated with Kieselgel 60 GF_{254} (Merck).

Diethyl (2*S*,3*R*)-(+)-3-(3,4-Methylenedioxy)benzyl-2-hydroxysuccinate **3**.

A solution of lithium diisopropylamide was prepared by the addition of *n*-butyllithium (1.6 *N* in *n*-hexane, 62.5 ml, 0.1 mole) to a stirred and cooled solution of diisopropylamine (16.8 ml, 0.12 mole) in dry tetrahydrofuran (100 ml) at -78° under nitrogen. To this was added with stirring and cooling at -78° a solution of diethyl (*S*)-malate (9.50 g, 0.05 mole) in dry tetrahydrofuran (50 ml). The solution was stirred at -78° for 30 minutes, then the solution was warmed to -20° within 30 minutes. The solution was stirred at -20° for 30 minutes and then was cooled to -78°. Then 3,4-methylenedioxybenzyl iodide (15.7 g, 0.06 mole) in tetrahydrofuran (30 ml) was added dropwise during 10 minutes. After stirring for 5.5 hours at -78° and then overnight at 5°, the mixture was quenched by the addition of glacial acetic acid (11.4 ml) at -50°, and extracted with ether. The organic layer was washed with saturated sodium bicarbonate and brine, dried with sodium sulfate, and concentrated *in vacuo* to give an oil. The residue was chromatographed on silica gel (300 g) with hexane-ethyl acetate (3:1) to give **3** as a viscous oil (12.6 g, 78%); $[\alpha]_D^{20}$ +4.1° (c 1.03, ethanol); ir (film): 3510, 1725, 1370, 1035, 930, 860, 810 cm^{-1}; ^1H nmr: δ 6.73-6.77 (m, 3H), 5.93 (s, 2H), 4.23 (t, 1H, J = 7.5 Hz), 4.13 (q, 4H, J = 7.2 Hz), 3.20 (d, 1H, J = 7.5 Hz), 3.10 (m, 1H), 3.09 (m, 1H), 2.90 (m, 1H), 1.28 (t, 3H, J = 7.2 Hz), 1.22 (t, 3H, J = 7.2 Hz); ^{13}C nmr: δ 173.6 (s), 172.0 (s), 147.7 (s), 146.3 (s), 132.1 (s), 122.3 (d), 109.5 (d), 108.3 (d), 100.9 (t), 69.5 (d), 61.8 (t), 61.0 (t), 50.3 (d), 33.6 (t), 14.1 (q) x 2; hrms: Calcd. for $C_{16}H_{20}O_7$: (M^+) 324.1209. Found: m/z 324.1197.

(2*S*,3*S*)-(+)-3-(3,4-Methylenedioxy)benzylbutan-1,2,4-triol 2,4-(4-Methoxybenzylidene)acetal **4**.

To a stirred suspension of lithium aluminium hydride (1.59 g, 41.8 mmoles) in dry ether (80 ml) was added a solution of **3** (6.78 g, 20.9 mmoles) in dry ether (20 ml). After refluxing for 16 hours, a small amount of water was dropwise added to decompose excess lithium aluminium hydride, and the precipitate was filtered off through celite and washed with ethyl acetate. The combined organic layer was dried with sodium sulfate and concentrated *in vacuo* to give triol as a syrup (4.27 g, 85%).

A solution of the triol (5.06 g, 21.1 mmoles), *p*-anisaldehyde (2.82 ml, 23.2 mmoles) and a catalytic amount of *p*-toluenesulfonic acid in benzene (100 ml) was boiled at reflux overnight. The reaction mixture was washed with saturated sodium bicarbonate and brine, and dried with sodium sulfate. The resulting residue was chromatographed on silica gel (200 g) with hexane-ethyl acetate (2:1) to give **4** (4.46 g, 59%), mp 117°; $[\alpha]_D^{20}$ + 15.7° (c 0.90, ethanol); ir (nujol): 3475, 1610, 1375, 1245, 1030, 830 cm^{-1}; ^1H nmr: δ 7.39 (d, 2H, J = 8.7 Hz), 6.88 (d, 2H, J = 8.7 Hz), 6.72 (d, 1H, J = 7.8 Hz), 6.59 (dd, 1H, J = 7.8 Hz, J = 1.6 Hz), 6.45 (d, 1H, J = 1.6 Hz), 5.92 (s, 2H), 5.45 (s, 1H), 4.02 (dd, 1H, J = 11.4 Hz, J = 4.3 Hz), 3.85-3.88 (m, 1H), 3.68-3.83 (m, 2H), 3.79 (s, 3H), 3.53 (t, 1H, J = 11.4 Hz), 2.70 (dd, 1H, J = 12.7 Hz, J = 3.5 Hz), 2.13-2.33 (m, 2H); ^{13}C nmr: δ 160.0 (s), 147.8 (s), 146.1 (s), 131.7 (s), 130.7 (s), 127.4 (d) x 2, 121.6 (d), 113.6 (d) x 2, 109.0 (d), 108.2 (d), 101.0 (d), 100.9 (t), 81.9 (d), 70.9 (t), 63.2 (t), 55.3 (q), 36.1 (d), 34.0 (t); hrms: Calcd. for $C_{20}H_{22}O_6$: (M^+) 358.1416. Found: m/z 358.1433.

Anal. Calcd. for $C_{20}H_{22}O_6$. C, 67.03; H, 6.19. Found: C, 67.08; H, 6.19.

tert-Butyl (2*S*,3*S*)-(-)-3-(3,4-Methylenedioxy)benzyl-2,4-dihydroxybutylate 2,4-(4-methoxybenzylidene)acetal **5**.

Chromium(VI) oxide (2.56 g, 25.6 mmoles) and pyridine (4.14 ml, 51.2 mmoles) in dichloromethane-dimethyl formamide (4:1, v/v, 37.5 ml) was stirred for 15 minutes at room temperature. A solution of **4** (2.29 g, 6.40 mmoles) in dichloromethane-dimethyl formamide (10 ml) was added, followed by acetic anhydride (4.83 ml, 51.2 mmoles) and *tert*-butyl alcohol (12.2 ml, 128 mmoles). The mixture was stirred for 16 hours at room temperature. Ethanol (3.5 ml) was added, and the reaction mixture was stirred for an additional 10 minutes and diluted with ether. The resulting mixture was filtered

with gentle suction through a column with silica in ether (8 cm). Elution with ether, removal of the solvent *in vacuo*, and column chromatography on silica gel (100 g) using hexane-ethyl acetate (6:1) as eluent yielded **5** (1.51 g, 55%), mp 146°; $[\alpha]_D^{20}$ -6.6° (c 0.13, ethanol); ir (nujol): 1735, 1610, 1370, 1255, 1155, 1075, 1030, 815 cm^{-1}; ^1H nmr: δ 7.40 (d, 2H, J = 6.8 Hz), 6.87 (d, 2H, J = 6.8 Hz), 6.73 (d, 1H, J = 7.9 Hz), 6.66 (d, 1H, J = 1.7 Hz), 6.59 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 5.93 (s, 2H), 5.41 (s, 1H), 4.09 (d, 1H, J = 10.4 Hz), 4.04 (dd, 1H, J = 11.2 Hz, J = 4.8 Hz), 3.79 (s, 3H), 3.55 (t, 1H, J = 11.2 Hz), 2.77 (dd, 1H, J = 11.2 Hz, J = 3.7 Hz), 2.44 (m, 1H), 2.24 (dd, 1H, J = 11.2 Hz, J = 3.7 Hz), 1.53 (s, 9H); ^{13}C nmr: δ 168.2 (s), 160.1 (s), 147.8 (s), 146.2 (s), 131.4 (s), 130.3 (s), 127.6 (d) x 2, 121.7 (d), 113.6 (d) x 2, 109.2 (d), 108.2 (d), 101.0 (d), 100.9 (t), 82.1. (s), 81.7 (d), 70.8 (t), 55.3 (q), 37.6 (d), 33.8 (t) and 28.1 (q) x 3; hrms: Calcd. for $C_{24}H_{28}O_7$: (M^+) 428.1835. Found: m/z 428.1853.

Anal. Calcd. for $C_{24}H_{28}O_7$. C, 67.28; H, 6.59. Found: C, 67.34; H, 6.62.

(3*S*,4*S*)-(+)-3-Hydroxy-4-(3,4-methylenedioxy)benzyl-γ-butyrolactone **6a**.

To a stirred solution of **5** (428 mg, 1 mmole) in 1,4-dioxane (10 ml) was added 3 *N* hydrochloric acid (1 ml) at room temperature. After stirring for 24 hours, the reaction mixture was extracted with ethyl acetate and washed with saturated sodium bicarbonate and brine, dried with sodium sulfate, and concentrated to dryness. The residue was chromatographed on silica gel (15 g) with hexane-ethyl acetate (2:1) to give **6a** (222 mg, 94%), mp 86°, $[\alpha]_D^{20}$ + 41.6° (c 1.03, ethanol); ir (nujol): 3375, 1735, 1605, 1370, 1035, 970, 925, 870, 805, 775, 735 cm^{-1}; ^1H nmr: δ 6.75 (d, 1H, J = 7.9 Hz), 6.69 (d, 1H, J = 1.5 Hz), 6.64 (dd, 1H, J = 7.9 Hz, J = 1.5 Hz), 5.94 (s, 2H), 4.57 (dd, 1H, J = 7.1 Hz, J = 3.4 Hz), 4.16 (d, 2H, J = 3.8 Hz), 3.18 (d, 1H, J = 3.4 Hz, OH), 3.07 (dd, 1H, J = 14.1 Hz, J = 4.7 Hz), 2.83 (m, 1H), 2.35 (dd, 1H, J = 14.1 Hz, J = 11.0 Hz); ^{13}C nmr: δ 177.4 (s), 147.9 (s), 146.3 (s), 132.0 (s), 122.0 (d), 109.2 (d), 108.4 (d), 101.0 (t), 69.6 (d), 68.7 (t), 42.2 (d), 30.8 (t); hrms: Calcd. for $C_{12}H_{12}O_5$: (M^+) 236.0684. Found: m/z 236.0667.

Anal. Calcd. for $C_{12}H_{12}O_5$. C, 61.02; H, 5.12. Found: C, 61.10; H, 5.08.

(3*S*,4*S*)-(-)-3-(Methoxymethyl)oxy-4-(3,4-methylenedioxy)benzyl-γ-butyrolactone **6b**.

To a stirred solution of **6a** (600 mg, 2.54 mmoles) and ethyl diisopropylamine (1.33 ml, 3.81 mmoles) in dichloromethane (20 ml) was added methoxymethyl chloride (0.29 ml, 3.81 mmoles) at room temperature, and the mixture was heated under reflux overnight. The reaction mixture was neutralized with dilute hydrochloric acid and extracted with dichloromethane. The resulting residue, after removal of the solvent, was chromatographed on silica gel (25 g) with hexane-ethyl acetate (2:1) to give **6b** (499 mg, 88%) and recovered **6a** (123 mg), mp 103°; $[\alpha]_D^{20}$ -0.82° (c 0.30, ethanol); ir (nujol): 1770, 1375, 1245, 1150, 1060, 980, 925 cm^{-1}; ^1H nmr: δ 6.75 (d, 1H, J = 7.9 Hz), 6.67 (d, 1H, J = 1.7 Hz), 6.63 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 5.94 (s, 2H), 4.98 (d, 1H, J = 6.7 Hz), 4.73 (d, 1H, J = 6.7 Hz), 4.46 (d, 1H, J = 6.8 Hz), 4.14 (m, 2H), 3.46 (s, 3H), 2.98 (dd, 1H, J = 14.1 Hz, J = 5.1 Hz), 2.80 (m, 1H), 2.49 (dd, 1H, J = 14.1 Hz, J = 10.4 Hz); ^{13}C nmr: δ 174.4 (s), 147.9 (s), 146.3 (s), 131.9 (s), 121.8 (d), 109.0 (d), 108.4 (d), 101.0 (t), 95.9 (t), 72.1 (d), 68.8 (t), 56.2 (q), 41.6 (d), 31.3 (t); hrms: Calcd. for $C_{14}H_{16}O_6$: (M^+) 280.0947. Found: m/z 280.0945.

Anal. Calcd. for $C_{14}H_{16}O_6$. C, 60.00; H, 5.75. Found: C, 59.93; H, 5.77.

(3*S*,4*S*)-(-)-3-(Methoxymethyl)oxy-3,4-bis[(3,4-methylenedioxy)benzyl]-γ-butyrolactone **7a** and its 3-Epimer **7b**.

A solution of lithium diisopropylamide was prepared by the addition of *n*-butyllithiurn (1.6 *N* in hexane, 0.74 ml, 1.18 mmoles) to a stirred and cooled solution of diisopropylamine (0.194 ml, 1.39 mmoles) in dry tetrahydrofuran (10 ml) at -78° under nitrogen. To this was added a solution of **6b** (300 mg, 1.07 mmoles) in dry tetrahydrofuran and hexamethylphosphoric triamide (1:1, v/v, 5.6 ml) and stirred for 1 hour at -78°. A solution of 3,4-methylenedioxybenzyl iodide (355 mg, 1.18 mmoles) in dry tetrahydrofuran (2 ml) was added to the enolate and stirred for 5 hours. After kept standing overnight at 5°, the reaction mixture was quenched by the addition of saturated ammonium chloride and extracted with ether. The combined extracts were washed with water and brine, dried with sodium sulfate, and concentrated to dryness. The residue was chromatographed on silica gel (15 g) with hexane-ethyl acetate (4:1) to give **7a** (101 mg, 23%) and **7b** (75 mg, 17%) as a viscous oil, respectively.

Compound **7a** had $[\alpha]_D^{20}$ -36.2° (c 0.58, ethanol); ir (film): 1765, 1730, 1605, 1355, 915, 805 cm^{-1}; ^1H nmr: δ 6.74 (d, 1H, J = 7.9 Hz), 6.72 (d, 1H, J = 8.4 Hz), 6.65 (d, 1H, J = 1.7 Hz), 6.61 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 6.55 (d, 1H, J = 1.7 Hz), 6.54 (dd, 1H, J = 8.4 Hz, J = 1.7 Hz), 5.93 (bs, 4H), 5.01 (d, 1H, J = 7.0 Hz), 4.90 (d, 1H, J = 7.0 Hz), 3.97 (m, 2H), 3.46 (s, 3H), 3.40 (d, 1H, J = 13.9 Hz), 2.89 (d, 1H, J = 13.9 Hz), 2.82 (dd, 1H, J = 14.0 Hz, J = 4.9 Hz), 2.65 (dd, 1H, J = 14.0 Hz, J = 10.1 Hz), 2.42 (m, 1H); ^{13}C nmr: δ 175.2 (s), 147.9 (s) x 2, 146.7 (s), 146.3 (s), 132.0 (s), 128.4 (s), 123.4 (d), 121.4 (d), 110.5 (d), 108.9 (d), 108.4 (d), 108.3 (d), 101.0 (t) x 2, 92.2 (t), 79.7 (s), 70.5 (t), 56.1 (q), 44.2 (d), 37.3 (t), 30.7 (t); hrms: Calcd. for $C_{22}H_{22}O_8$: (M^+) 414.1314. Found: m/z 414.1324.

Compound **7b** had $[\alpha]_D^{20}$ -32.5° (c 0.28, ethanol); ir (film): 1780, 1735, 1610, 1360, 1245, 1100, 1035, 920, 810 cm^{-1}; ^1H nmr: δ 6.80-6.72 (m, 4H), 6.59 (d, 1H, J = 1.7 Hz), 6.56 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 5.93 (bs, 4H), 4.86 (d, 1H, J = 7.7 Hz), 4.77 (d, 1H, J = 7.7 Hz), 4.16 (dd, 1H, J = 8.8 Hz, J = 7.0 Hz), 3.81 (t, 1H, J = 8.8 Hz), 3.49 (s, 3H), 3.13-2.95 (m, 2H), 3.06 (d, 1H, J = 15.0 Hz), 2.97 (d, 1H, J = 15.0 Hz), 2.51 (dd, 1H, J = 13.2 Hz, J = 12.0 Hz); ^{13}C nmr: δ 175.0 (s), 148.0 (s), 147.5 (s), 146.7 (s), 146.4 (s), 131.8 (s), 128.0 (s), 123.3 (d), 121.3 (d), 110.6 (d), 108.9 (d), 108.5 (d), 108.0 (d), 101.0 (t) x 2, 93.1 (t), 82.2 (s), 69.0 (t), 56.2 (q), 45.9 (d), 36.5 (t), 31.8 (t); hrms: Calcd. for $C_{22}H_{22}O_8$: (M^+) 414.1314. Found: m/z 414.1333.

(3*S*,4*S*)-(-)-3,4-Bis[(3,4-methylenedioxy)benzyl]-3-hydroxy-γ-butyrolactone **1**, Meridinol.

To a cooled solution (-30°) of **7a** (82 mg, 0.28 mmole) in 3 ml of dichloromethane containing molecular sieves (4 A) was added a trimethylsilyl bromide (0.105 ml, 0.792 mmole), and the solution was stirred for 1 hour at -30°, then 7 hours at 0°. The reaction mixture was poured into a solution of saturated sodium bicarbonate, extracted with ether, dried with sodium sulfate, and evaporated to dryness. The residue was chromatographed on silica gel (7 g) with hexane-ethyl acetate (4:1) to give **1** (59 mg, 81%), mp 126.5°, [lit [3] 122-123°]; $[\alpha]_D^{20}$ -38.6° (c 0.095, chloroform), [lit [3] -30° (c 0.1, chloroform)]; ir (nujol): 3475, 1755, 1375, 1240, 1040 cm^{-1}; ^1H nmr: δ 6.75 (d, 1H, J = 7.9 Hz), 6.73 (d, 1H, J = 7.9 Hz), 6.69 (d, 1H, J = 1.7 Hz), 6.62 (dd, 1H, J = 7.9 Hz, J = 1.7

Hz), 6.60 (d, 1H, J = 1.7 Hz), 6.57 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 5.93 (s, 4H), 4.06-3.96 (m, 2H), 3.07 (d, 1H, J = 13.9 Hz), 3.04 (s, 1H, OH), 2.93 (d, 1H, J = 13.9 Hz), 2.87 (m, 1H), 2.54-2.45 (m, 2H); ^{13}C nmr: δ 178.7 (s), 148.2 (s), 148.1 (s), 147.2 (s), 146.6 (s), 132.5 (s), 128.2 (s), 123.7 (d), 122.1 (d), 110.9 (d), 109.5 (d), 108.7 (d), 108.6 (d), 101.4 (t), 101.3 (t), 76.6 (s), 70.3 (t), 44.2 (d), 42.4 (t), 32.0 (t); hrms: Calcd. for $C_{20}H_{18}O_7$: (M^+) 370.1052. Found: m/z 370.1031.

Anal. Calcd. for $C_{20}H_{18}O_7$. C, 64.86; H, 4,90. Found: C, 64.69; H, 4.86.

(3*R*,4*S*)-(-)-3,4-Bis[(3,4-methylenedioxy)benzyl]-3-hydroxy-γ-butyrolactone **2**, 3-Epimeridinol.

Compound **7b** (53 mg, 0.13 mmole) was treated as described for the preparation of **1**. Column chromatography was performed on a small column of silica gel (5 g) with hexane-ethyl acetate (4:1) to give **2** (41 mg, 87%), mp 130°, [lit [4] waxy solid for (±)-form]; $[\alpha]_D^{20}$ -16.6° (c 0.100, chloroform); ir (nujol): 3510, 1780, 1370, 1240, 1030, 920 cm^{-1}; ^{1}H nmr: δ 6.77 (d, 1H, J = 7.9 Hz), 6.75 (d, 1H, J = 7.9 Hz), 6.72 (d, 1H, J = 1.7 Hz), 6.66 (dd, 1H, J = 7.9 Hz, J = 1.7 Hz), 6.67 (d, 1H, J = 1.7 Hz), 6.62 (dd, 1H, J = 7.8 Hz, J = 1.7 Hz), 5.95 (s, 4H), 4.19 (dd, 1H, J = 9.2 Hz, J = 7.7 Hz), 3.89 (t, 1H, J = 9.2 Hz), 3.09 (dd, 1H, J = 13.4 Hz, J = 4.0 Hz), 2.95 (d, 1H, J = 14.0 Hz), 2.93-2.84 (m, 1H), 2.89 (d, 1H, J = 14.0 Hz), 2.75 (s, 1H, OH), 2.61 (dd, 1H, J = 13.4 Hz, J = 11.4 Hz); ^{13}C nmr: δ 177.5 (s), 148.0 (s), 147.7 (s), 147.1 (s), 146.4 (s), 131.4 (s), 126.7 (s), 123.5 (d), 121.3 (s), 110.6 (d), 108.7 (d), 108.5 (d), 108.3 (d), 101.0 (t) x 2, 75.8 (s), 69.3 (t), 48.1 (d), 38.1 (t) 32.0 (t); hrms: Calcd. for $C_{20}H_{18}O_7$: (M^+) 370.1052. Found: m/z 370.1058.

Anal. Calcd. for $C_{20}H_{18}O_7$. C, 64.86; H, 4,90. Found: C, 64.80; H, 4.95.

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