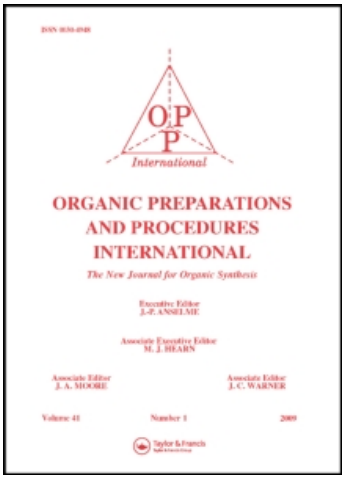

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AN IMPROVED SYNTHESIS OF NAPHTHO[2,3-d]-1,3-DIOXOLE-5-METHOXY-6-CARBOXYLIC ACID

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AN IMPROVED SYNTHESIS OF NAPHTHO[2,3-d]-1,3-DIOXOLE-5-METHOXY-6-CARBOXYLIC ACID

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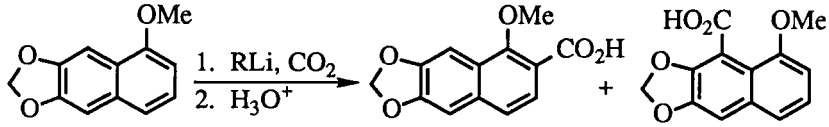
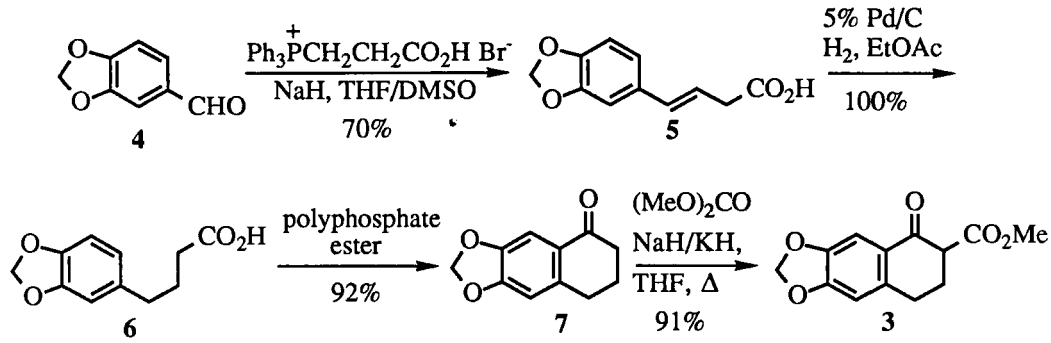
The potential use of naphtho[2,3-d]-1,3-dioxole-5-methoxy-6-carboxylic acid (1) in the synthesis of taiwanin C was demonstrated by Meyers and Avila.[1] We found need for large quantities of 1 in a synthesis of an extended-aromatic epipodophyllotoxin analog.[2] The only prior synthesis of 1 yielded it as a minor product from the metalation/carbonylation of 5-methoxynaphtho[2,3-d]-1,3-dioxole (2).[1] Compound 2 was prepared in 10% overall yield from piperonal.[3]

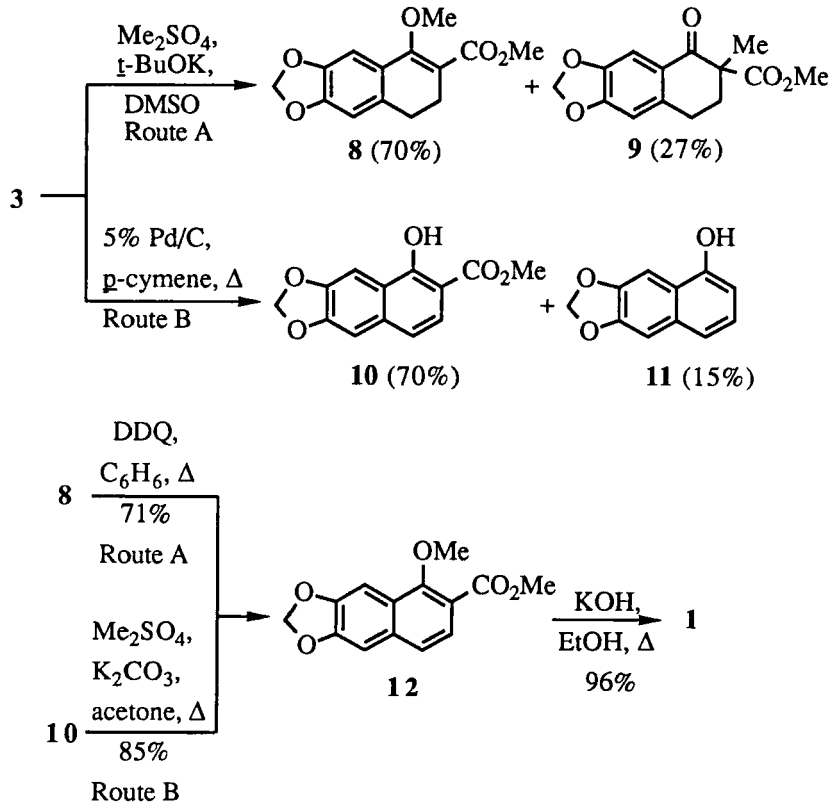


2 1 (10%) (65%)

We now report an efficient route to 1 through the highly functionalized keto ester 3. The latter compound was prepared from piperonal (4) in 59% overall yield via a modification of the literature procedures.[4-9] In particular, the yield of 5 was enhanced from 41% to 70% by use of a stoichiometric amount of sodium hydride in the Wittig reaction. The material obtained upon acidic workup was sufficiently pure for immediate catalytic hydrogenation. The resulting acid 6 was cyclized to tetralone 7 by treatment with polyphosphate ester.[5] α-Carboxymethylation of 7 with dimethyl carbonate and a sodium hydride/potassium hydride base system[7] afforded the keto ester 3 in 91% yield. The previously reported method for preparing 3 from 7 involved two steps that were more laborious and gave a lower overall yield in our hands.[8,9]



Two routes were explored for the conversion of 3 to the naphthoic acid 1. Route A involved the consecutive introduction of two double bonds into the tetralone ring, while Route B utilized a one-step aromatization.



In Route A, 3 was converted first to 8 with dimethyl sulfate and potassium t-butoxide. Enol ether 8 was separated easily from the isomeric C-alkylation[10,11] product 9 by crystallization. Oxidation of 8 with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) provided 12. In Route B, catalytic dehydrogenation of 3 over 5% palladium on carbon[12,13]

gave the hydroxynaphthoic ester 10 along with a small amount of naphthol 11.[14,15] The mechanistic pathway leading to 11 is projected to proceed through hydrolysis of 3 or 10, followed by decarboxylation and aromatization in the case of 3. Keto ester 3 was stable in refluxing p-cymene, however, small quantities of water were observed shortly after addition of the dry palladium catalyst to the reaction. The formation of water in this system is probably caused by a competitive deoxygenation of 3. Catalytic reductions of a carbonyl function have been well documented in palladium dehydrogenation reactions of polycyclic aromatic ketones.[13] O-Methylation of 10 with dimethyl sulfate converged the synthesis to 12. The saponification of 12 obtained from either route led to naphtho[2,3-d]-1,3-dioxole-5-methoxy-6-carboxylic acid (1) in high yield (96%). A comparison of Routes A and B shows that latter is not only higher yielding (57% vs 47% of 1), but also more convenient on a large scale. In contrast to Route A, the side-product 11 of Route B could be utilized in a preparation of 1 by an ortho-carboxylation procedure,[16] which would make the process even more efficient.

EXPERIMENTAL SECTION

All reagents were purchased from the Aldrich Chemical Co. THF and DMSO were dried by standard laboratory procedures prior to use. Melting points were determined with a Thomas-Hoover capillary melting point apparatus and are corrected. Infrared spectra were recorded on a Perkin-Elmer 281B spectrophotometer. The NMR spectra were obtained on a Varian VXR-300 FT spectrometer operating at 300 MHz for hydrogen and 75 MHz for carbon. Chemical shifts are recorded as parts per million down field relative to tetramethylsilane. Multiplicities are given as singlet (s), doublet (d), triplet (t), quartet (q) and multiplet (m). High resolution mass spectra were obtained using an electron impact source at the Mass Spectrometry Laboratory, Department of Chemistry, University of Kansas, Lawrence, KS. Low resolution electron impact mass spectra were obtained on a Finnigan 3200 GC/MS spectrometer. Elemental analyses were performed by Ms. Paulannne Rider at the Northern Illinois University Chemical Instrumentation Laboratory (DeKalb, IL) using a Perkin-Elmer Model 240 analyzer.

(E)-4-(1,3-Benzodioxol-5-yl)but-3-enoic Acid (5).- A solution of piperonal (4) (45.0 g, 0.30 mol) and (3-carboxypropyl)triphenylphosphonium bromide[17] (124.6 g, 0.30 mol) in a 1:1 mixture (600 mL) of dry, freshly distilled THF and DMSO was added dropwise to a slurry of freshly washed (n-pentane) sodium hydride (24.0 g, 60% dispersion in mineral oil, 0.60 mol) in dry THF (200 mL) at 0°. The mixture was mechanically stirred for 20 hrs at ambient temperature, and then cautiously quenched with H_2O (400 mL) and washed with Et_2O (3 x 200 mL). The aqueous mixture was acidified to pH 1-2 with concentrated hydrochloric acid and extracted with Et_2O (3 x 200 mL). The latter extracts were washed with H_2O (2 x 200

mL), dried ($MgSO_4$), and concentrated to dryness. Trituration of the residue with CH_2Cl_2 provided 43.3 g (70%) of 5 that was sufficiently pure (mp. 114-116°) for the next step. An analytical sample, mp. 116-117°, lit.[4] 116-117°, was obtained by crystallization from CH_2Cl_2. IR (KBr) 2980 (br) 1685, 1605, 1505, 1490, 1450, 1260, 1230, 1040, 930 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.93 (d, 1 H, J = 1.6 Hz, H_{arom}), 6.80 (dd, 1 H, J = 7.9, 1.6 Hz, H_{arom}), 6.74 (d, 1 H, J = 7.9 Hz, H_{arom}), 6.42 (br d, 1 H, J = 15.8 Hz, ArC<u>H</u>=CH-), 6.10 (dt, 1 H, J = 15.8, 7.1 Hz, ArCH=C<u>H</u>-), 5.95 (s, 2 H, -OC<u>H</u>$_2$O-), 3.27 (dd, 2 H, J = 7.1, 1.4 Hz, =CHC<u>H</u>$_2$-); ^{13}C NMR ($CDCl_3$):[18] δ 178.0 (0), 148.0 (0), 147.3 (0), 133.5 (1), 131.1 (0), 121.0 (1), 119.0 (1), 108.2 (1), 105.7 (1), 101.1 (2), 37.9 (2).

4-(1,3-Benzodioxol-5-yl)butanoic Acid (6).- An ethyl acetate (750 mL) solution of butenoic acid 5 (41.2 g, 0.20 mol) was hydrogenated over 5% palladium on carbon (3 g) for 1 hr in a Paar hydrogenator at 25°. The catalyst was removed by filtration through a bed of Celite, and the solvent evaporated in vacuo to provide 41.6 g (100%) of pure 6: mp. 79-80°, lit.[4] 79-80°. IR (KBr) 2910 (br), 1710, 1600, 1510, 1495, 1450, 1260, 1040, 930 cm^{-1}; ^1H NMR ($CDCl_3$): δ 6.73 (d, 1 H, J = 7.9 Hz, H_{arom}), 6.68 (d, 1 H, J = 1.7 Hz, H_{arom}), 6.62 (dd, 1 H, J = 7.9, 1.7 Hz, H_{arom}), 5.92 (s, 2 H, -OC<u>H</u>$_2$O-), 2.60 (t, 2 H, J = 7.4 Hz, -C<u>H</u>$_2$-), 2.36 (t, 2 H, J = 7.4 Hz, -C<u>H</u>$_2$-), 1.92 (quintet, 2 H, J = 7.4 Hz, -CH$_2$C<u>H</u>$_2$CH$_2$-); ^{13}C NMR ($CDCl_3$):[18] δ 179.8 (0), 147.6 (0), 147.8 (0), 135.0 (0), 121.2 (1), 108.9 (1), 108.1 (1), 100.8 (2), 34.7 (2), 33.1 (2), 26.39 (2).

Naphtho[2,3-d]-1,3-dioxole-7,8-dihydro-5(6H)-one (7).- A mixture of phosphorous pentoxide (250 g), dry Et_2O (250 mL) and dry $CHCl_3$ (500 mL) was refluxed with mechanical stirring for 48 hrs. Polyphosphate ester[19] (ca. 350 mL) was obtained as a thick oil upon evaporation of the solvents. Carboxylic acid 6 (62.4 g, 0.3 mol) was added slowly to the polyphosphate ester and the mixture stirred for 2 hr at 20°. This mixture was subsequently cooled in an ice-water bath and the reaction cautiously (exothermic!) quenched with H_2O (1250 mL). The resulting solution was stirred overnight before extracting with Et_2O (3 x 300 mL). The combined extracts were washed with saturated $NaHCO_3$ solution (3 x 200 mL) and H_2O (3 x 200 mL). Concentration following drying ($MgSO_4$) provided a residue that crystallized, mp. 75-76°, lit.[4] 75-76°, lit.[5] 74-76°, lit.[6] 75°, from EtOH to give 52.5 g (92%) of 7. IR

(KBr) 2960, 1675, 1665, 1620, 1495, 1270, 1030, 935 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.39 (s, 1 H, H_{arom}), 6.60 (s, 1 H, H_{arom}), 5.94 (s, 2 H, -OC$\underline{H_2}$O-), 2.81 (t, 2 H, J = 6.2 Hz, -CO-C$\underline{H_2}CH_2$-), 2.53 (t, 2 H, J = 6.5 Hz, ArC$\underline{H_2}$-), 2.08-2.00 (m, 2 H, -$CH_2C\underline{H_2}CH_2$-); ^{13}C NMR ($CDCl_3$):[18] δ 196.5 (0), 151.9 (0), 146.8 (0), 141.3 (0), 127.3 (0), 107.8 (1), 106.0 (1), 101.5 (2), 38.5 (2), 29.9 (2), 23.4 (2).

Methyl Naphtho[2,3-d]-1,3-dioxole-5,6,7,8-tetrahydro-5-oxo-6-carboxylate (3).- Dimethyl carbonate (67.6 g, 64.0 mL, 0.75 mol) was added to a suspension of freshly washed (n-pentane) sodium hydride (37.5 g, 60% dispersion in oil, 0.94 mol) and the mixture brought to reflux. A few milliliters of a solution of tetralone 7 (57.0 g, 0.30 mol) in dry THF (200 mL) was added to the mixture, followed by addition of a THF (50 mL) suspension of freshly washed (n-pentane) potassium hydride (3.4 g, 35% mineral oil dispersion, 0.03 mol). The addition of the tetralone solution was then continued, and the mixture stirred and refluxed for an additional 2 hr before cooling in an ice-water bath. The reaction was carefully acidified with 30% aqueous HOAc (200 mL), the excess THF removed by evaporation, H_2O (300 mL) added, and the product extracted with Et_2O (3 x 300 mL). The combined extracts were washed with saturated $NaHCO_3$ solution (2 x 200 mL), H_2O (3 x 200 mL) and dried ($MgSO_4$). The residue after solvent evaporation crystallized, mp. 84-86°, lit.[8] mp. - not reported, from MeOH to give 67.7 g (91%) of 3. IR (KBr) 2960, 2940, 1740, 1665, 1610, 1500, 1480, 1260, 1030, 930 cm^{-1}; ^1H NMR ($CDCl_3$, 4:1 keto/enol mixture): δ 12.41 (s, 0.2 H, enol -O$\underline{H}$), 7.32 (s, 0.8 H, keto H_{arom}), 7.15 (s, 0.2 H, enol H_{arom}), 6.55 (s, 1 H, H_{arom}), 5.92 (s, 1.6 H, keto -OC$\underline{H_2}$O-), 5.89 (s, 0.4 H, enol -OC$\underline{H_2}$O-), 3.73 (s, 0.6 H, enol -$CO_2C\underline{H_3}$), 3.70 (s, 2.4 H, keto -$CO_2C\underline{H_3}$), 3.53-3.42 (m, 0.8 H, keto -C$\underline{H}CO_2Me$), 2.94-2.74 (m, 1.6 H, keto Ar-C$\underline{H_2}$-), 2.65-2.58 (m, 0.4 H, enol Ar-C$\underline{H_2}$-), 2.47-2.16 (m, 2 H, -$CH_2C\underline{H_2}CH_2$-); ^{13}C NMR ($CDCl_3$, signals for keto form only):[18] δ 191.1 (0), 170.6 (0), 152.3 (0), 146.9 (0), 140.6 (0), 126.0 (0), 107.6 (1), 106.1 (1), 101.6 (2), 53.7 (1 or 3), 52.0 (1 or 3), 27.7 (2), 26.3 (2); MS, *m/z* (relative intensity): 248 (100, M+), 216 (70), 188 (100), 162 (28), 159 (14), 134 (70), 103 (36), 76 (46), 63 (19), 59 (15), 51 (35); high resolution MS: calcd. for $C_{13}H_{12}O_5$ 248.0685 (M+), found 248.0689.

Anal. Calcd. for $C_{13}H_{12}O_5$: C, 62.90; H, 4.87. Found: C, 62.89; H, 4.80

Methyl Naphtho[2,3-d]-1,3-dioxole-7,8-dihydro-5-methoxy-6-carboxylate (8) and Methyl Naphtho[2,3-d]-1,3-dioxole-5,6,7,8-tetrahydro-5-oxo-6-methyl-6-carboxylate (9), Route A.- A solution of keto ester 3 (12.41 g, 0.050 mol) in dry DMSO (50 mL) was added to a mixture of freshly sublimed potassium t-butoxide (8.42 g, 0.075 mol) in dry DMSO (25 mL). Dimethyl sulfate (9.46 g, 7.1 mL, 0.075 mol) was added to the reaction after 15 min and the mixture stirred for 0.5 hr at 20°. The reaction was quenched by adding H_2O (100 mL), and the products extracted with $CHCl_3$ (3 x 100 mL). The combined extracts were washed with saturated $NaHCO_3$ solution (2 x 100 mL), H_2O (5 x 100 mL) and dried ($MgSO_4$). After solvent removal, the residue crystallized, mp. 112-113°, from MeOH to provide 9.17 g (70%) of 8. IR (KBr) 2970, 1740, 1720, 1630, 1590, 1510, 1500, 1485, 1290, 1040, 930 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.05 (s, 1 H, H_{arom}), 6.66 (s, 1 H, H_{arom}), 5.95 (s, 2 H, -OCH_2O-), 3.79 (s, 3 H, -OCH_3), 3.77 (s, 3 H, -OCH_3), 2.72-2.64 (m, 2 H, -CH_2-), 2.60-2.53 (m, 2 H, -CH_2-); ^{13}C NMR ($CDCl_3$):[18] δ 167.4 (0), 160.6 (0), 148.5 (0), 146.5 (0), 134.4 (0), 124.9 (0), 111.7 (0), 108.2 (1), 104.7 (1), 101.2 (2), 61.1 (3), 51.5 (3), 27.9 (2), 24.2 (2); MS, *m/z* (relative intensity): 262 (100, M+), 247 (26), 231 (31), 215 (53), 203 (51), 188 (38), 173 (19), 159 (17), 145 (19), 130 (12), 115 (29), 102 (30), 89 (8), 76 (16), 63 (10); high resolution MS: calcd. for $C_{14}H_{14}O_5$ 262.0841 (M+), found 262.0832. Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.41; H, 5.39

From the mother liquor, the C-alkylation product 9 (3.5 g, 27%) was separated by crystallization, mp. 100-101°, from MeOH. IR (KBr) 2920, 1730, 1680, 1620, 1495, 1480, 1250, 1030, 935 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.45 (s, 1 H, H_{arom}), 6.60 (s, 1 H, H_{arom}), 5.98 (s, 2 H, -OCH_2O-), 3.66 (s, 3 H, -CO_2CH_3), 2.92 (ddd, 1 H, J = 17.3, 9.4, 4.9 Hz, one of ArCH_2-), 2.81 (br dt, 1 H, J = 17.3, 5.4 Hz, one of ArCH_2-), 2.54 (ddd, 1 H, J = 13.5, 5.8, 4.8 Hz, one of -CH_2C(Me)(CO_2Me)), 1.99 (ddd, 1 H, J = 13.5, 9.4, 4.9 Hz, one of -CH_2-C(Me)(CO_2Me)), 1.46 (s, 3 H, -CH_3); ^{13}C NMR ($CDCl_3$):[18] δ 194.4 (0), 173.5 (0), 152.3 (0), 147.1 (0), 140.1 (0), 126.2 (0), 107.8 (1), 106.9 (1), 101.7 (2), 53.4 (0), 52.5 (3), 34.1 (2), 26.3 (2), 20.8 (3); MS, *m/z* (relative intensity): 262 (60, M+), 247 (4), 231 (2), 215 (4), 202 (100), 188 (5), 175 (23), 162 (20), 145 (22), 134 (87), 115 (28), 104 (21), 91 (12), 76 (34), 63 (12), 50 (16); high resolution MS: calcd. for $C_{14}H_{14}O_5$ 262.0841 (M+), found

262.0842.

Anal. Calcd. for $C_{14}H_{14}O_5$: C, 64.12; H, 5.38. Found: C, 64.28; H, 5.51

Methyl Naphtho[2,3-d]-1,3-dioxole-5-hydroxy-6-carboxylate (10) and Naphtho[2,3-d]-1,3-dioxole-5-ol (11), Route B.- A solution of the keto ester 3 (74.4 g, 0.30 mol) in dry p-cymene (900 mL) was refluxed in the presence of 5% palladium on carbon (37.2 g) with mechanical stirring for a period of 2 hr while removing any H_2O (ca. 1.5 mL) formed via a Dean-Stark adapter. The spent catalyst was removed by filtration through Celite and washed well with acetone. The filtrate was concentrated and then subjected to steam distillation to remove the p-cymene. The pot residue was extracted with ethyl acetate (3 x 200 mL) and the extract dried over $MgSO_4$. The residue obtained upon evaporation crystallized, mp. 136-138°, from MeOH to provide 51.7 g (70%) of 10. IR (KBr) 3020, 2960, 2910, 1660, 1620, 1500, 1460, 1270, 1040, 940 cm^{-1}; ^1H NMR ($CDCl_3$): δ 11.79 (s, 1 H, -OH), 7.63 (s, 1 H, H_{arom}), 7.60 (d, 1 H, J = 8.8 Hz, H_{arom}), 7.06 (d, 1 H, J = 8.8 Hz, H_{arom}), 7.00 (s, 1 H, H_{arom}), 6.05 (s, 2 H, -OCH_2O-), 3.96 (s, 3 H, -CO_2CH_3); ^{13}C NMR ($CDCl_3$):[18] δ 171.4 (0), 159.7 (0), 150.2 (0), 147.5 (0), 135.1 (0), 123.1 (1), 120.8 (0), 117.8 (1), 104.9 (0), 103.9 (1), 101.4 (2), 100.4 (1), 52.1 (3); MS, *m/z* (relative intensity) 246 (100, M+), 214 (98), 158 (26), 101 (13), 75 (19), 51 (14); high resolution MS: calcd. for $C_{13}H_{10}O_5$ 246.0528 (M+), found 246.0531.

Anal. Calcd. for $C_{13}H_{10}O_5$: C, 63.42; H, 4.09. Found: C, 63.63; H, 4.16

From the mother liquor, 11.1 g (15%) of 11, mp. 124-126°, was isolated by column chromatography. An analytical sample, mp. 133-134°, lit.[14] mp. - not reported, lit.[15] 124°, was obtained by crystallization from petroleum ether/ethyl acetate. IR (KBr) 3260 (br), 2910, 1640, 1620, 1530, 1490, 1240, 1040, 950 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.51 (s, 1 H, H_{arom}), 7.26 (br d, 1 H, J = 8.2 Hz, H_{arom}), 7.15 (dd, 1 H, J = 8.2, 7.5 Hz, H_{arom}), 7.10 (s, 1 H, H_{arom}), 6.70 (dd, 1 H, J = 7.5, 1.1 Hz, H_{arom}), 6.03 (s, 2 H, -OCH_2O-), 5.62 (br s, 1 H, -OH); ^{13}C NMR ($CDCl_3$):[18] δ 151.0 (0), 148.0 (0), 147.2 (0), 132.0 (0), 124.4 (1), 120.8 (0), 119.8 (1), 107.8 (1), 103.8 (1), 101.0 (2), 98.6 (1); MS, *m/z* (relative intensity) 188 (100, M+), 130 (26), 102 (53), 75 (19), 51 (24); high resolution MS: calcd. for $C_{11}H_8O_3$ 188.04733 (M+), found 188.0477.

Anal. Calcd. for $C_{11}H_8O_3$: C, 70.21; H, 4.29. Found: C, 70.32; H, 4.32

Methyl Naphtho[2,3-d]-1,3-dioxole-5-methoxy-6-carboxylate (12). Route A - From Methyl Naphtho[2,3-d]-1,3-dioxole-7,8-dihydro-5-methoxy-6-carboxylate (8). - A mixture of 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) (8.74 g, 0.039 mol) and 8 (9.17 g, 0.035 mol) in dry benzene (100 mL) was refluxed for 5 hrs. The hydroquinone was removed by filtration and washed with benzene (20 mL), and the combined filtrates washed with 10% NaOH solution until the washings were colorless. The organic phase was then washed with H_2O (5 x 50 mL), dried ($MgSO_4$) and evaporated. The residue crystallized, mp. 110-111°, from MeOH to give 6.50 g (71%) of 12.

Route B - From Methyl Naphtho[2,3-d]-1,3-dioxole-5-hydroxy-6-carboxylate (10). - A mixture of 10 (24.6 g, 0.10 mol), acetone (1000 mL), anhydrous potassium carbonate (69.1 g, 0.50 mol) and dimethyl sulfate (37.8 g, 28.4 mL, 0.30 mol) was stirred and heated for 3 hrs at reflux. The inorganic salts were separated from the reaction by filtration and washed with with acetone (200 mL), and the solvent removed in vacuo. The resultant residue was triturated with MeOH to give 22.1 g (85%) of 12, mp. 110-111°. IR (KBr) 2960, 2910, 1745, 1645, 1595, 1500, 1470, 1260, 1040, 940 cm^{-1}; ^1H NMR ($CDCl_3$): δ 7.70 (d, 1 H, J = 8.8 Hz, H_{arom}), 7.49 (s, 1 H, H_{arom}), 7.36 (d, 1 H, J = 8.8 Hz, H_{arom}), 7.04 (s, 1 H, H_{arom}), 6.02 (s, 2 H, -OCH_2O-), 3.98 (s, 3 H, -OCH_3), 3.94 (s, 3 H, -OCH_3); ^{13}C NMR ($CDCl_3$):[18] δ 166.5 (0), 157.3 (0), 149.4 (0), 148.3 (0), 134.5 (0), 125.5 (1), 125.3 (0), 122.5 (1), 117.8 (0), 103.8 (1), 101.4 (2), 99.8 (1), 62.8 (3), 51.9 (3); MS, *m/z* (relative intensity): 260 (100, M^+), 245 (17), 229 (99), 214 (39), 199 (22), 189 (31), 174 (26), 158 (20), 141 (13), 128 (12), 113 (18), 100 (20), 86 (8), 74 (21), 63 (12); high resolution MS: calcd. for $C_{14}H_{12}O_5$ 260.0684 (M^+), found 260.0688.

Anal. Calcd. for $C_{14}H_{12}O_5$: C, 64.61; H, 4.65. Found: C, 64.61; H, 4.61

Naphtho[2,3-d]-1,3-dioxole-5-methoxy-6-carboxylic Acid (1). - A mixture of the 12 (26.0 g, 0.10 mol) and a 16% aqueous-ethanolic solution of KOH (ca. 400 mL, prepared from 66 g of KOH and 160 mL of H_2O and 180 mL of EtOH) was refluxed with stirring for 3 hrs. After cooling, the mixture was diluted with H_2O to 800 mL total volume and then acidified with concentrated hydrochloric acid to pH 1-2. The product was isolated by filtration,

washed with H_2O, and dried in the funnel to give 23.6 g (96%) of 1, mp. 182-183°, lit.[1] mp. - not reported. IR (KBr) 2910 (br), 2640 (br), 1680, 1600, 1510, 1500, 1460, 1260, 1040, 950 cm^{-1}; ^1H NMR (DMSO-d_6): δ 12.84 (s, 1 H, -CO_2H), 7.63 (d, 1 H, J = 8.7 Hz, H_{arom}), 7.52 (d, 1 H, J = 8.7 Hz, H_{arom}), 7.46 (s, 1 H, H_{arom}), 7.36 (s, 1 H, H_{arom}), 6.18 (s, 2 H, -OCH_2O-), 3.91 (s, 3 H, -OCH_3); ^{13}C NMR (DMSO-d_6):[18] δ 167.2 (0), 156.2 (0), 149.2 (0), 148.3 (0), 133.9 (0), 125.4 (1), 124.7 (0), 122.4 (1), 119.1 (0), 103.8 (1), 101.7 (2), 99.0 (1), 62.5 (3); MS, *m/z* (relative intensity): 246 (100, M^+), 229 (16), 214 (14), 199 (19), 187 (24), 173 (25), 159 (42), 143 (11), 129 (12), 115 (13), 101 (31), 89 (15), 74 (27), 63 (19), 51 (12); high resolution MS: calcd. for $C_{13}H_{10}O_5$ 246.0528 (M^+), found 246.0538.

Anal. Calcd. for $C_{13}H_{10}O_5$: C, 63.42; H, 4.09. Found: C, 63.41; H, 4.08

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REFERENCES

1. A. I. Meyers and W. B. Avila, J. Org. Chem., 46, 3881 (1981).
2. J. Zjawiony and J. R. Peterson, 23rd Great Lakes Regional Meeting of the American Chemical Society, DeKalb, Illinois, May 30 - June 1, 1990.
3. L. S. El-Assal and S. A. M. El-Wahhab, J. Chem. Soc., 849 (1960).
4. W. J. Begley and J. Grimshaw, J. Chem. Soc., Perkin Trans. 1, 2324 (1977).
5. J. Smidrkal, Coll. Czech. Chem. Comm., 49, 1412 (1984).
6. R. Beugelmans, J. Chastanet, H. Ginsburg, L. Quintero-Cortes and G. Roussi, J. Org. Chem., 50, 4933 (1985).
7. L. Ruest, G. Blouin and P. Deslongchamps, Syn. Comm., 6, 169 (1976).
8. I. Ninomiya, O. Yamamoto and T. Naito, J. Chem. Soc., Perkin Trans. 1, 212 (1980).
9. S. Hirosada, I. Katsumi, N. Kohei (Takeda Chemical Industries Ltd.), Eur. Pat. Appl. EP 318,235; Chem. Abstr., 111, P225318v (1989).
10. G. J. Heiszwolf and H. Kloosterziel, J. Chem. Soc., Chem. Comm., 51 (1966).
11. H. O. House, "Modern Synthetic Reactions", 2nd Ed., p. 492, W.A. Benjamin, Menlo Park, CA, 1972.
12. M. S. Newman and J. Blum, J. Am. Chem. Soc., 86, 503 (1964).
13. P. P. Fu and R. G. Harvey, Chem. Rev., 78, 317 (1978).

14. N. Takas, M. Kamigauchi, M. Sugiuta, I. Ninomiya, O. Miyato and T. Naito, Heterocycles, 16, 221 (1981).

15. F. Dallacker and P. Schneider, Chem.-Ztg., 110, 455 (1986).

16. G. Wurm, J. Geres and H. Schmidt, Arch. Pharm., 314, 861 (1981).

17. J. A. Findlay and D. Kwan, Can. J. Chem., 51, 3299 (1973).

18. The numbers in parentheses refer to the number of attached hydrogens on that carbon as determined by the attached proton test (APT).

19. W. Pollmann and G. Schramm, Biochem. Biophys. Acta, 80, 1 (1964).

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