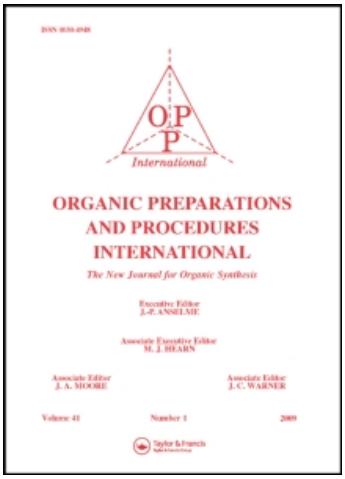

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SYNTHESIS OF 1,3,6,8-TETRAMETHOXY-*cis*-4b,5,9b,10-TETRAHYDROINDENO[2,1-a]INDENE-5,10-DIONE

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SYNTHESIS OF 1,3,6,8-TETRAMETHOXY-*cis*-4b,5,9b,10-TETRAHYDROINDENO[2,1-a]INDENE-5,10-DIONE

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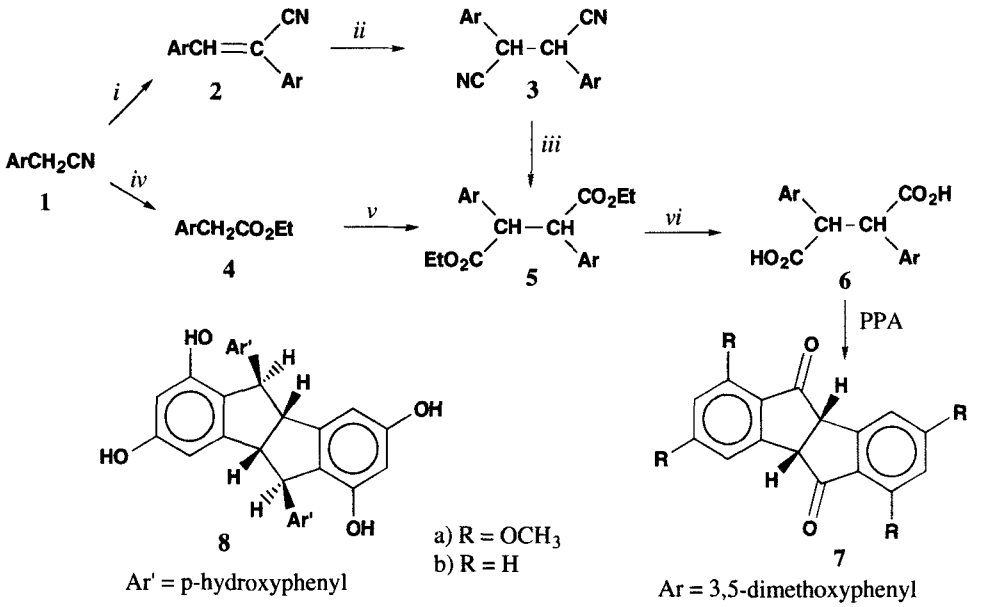
For use in an investigation of the synthesis of pallidol **8**,[1] an unambiguous synthesis of **7a** was required, and we now describe a synthetic sequence for its preparation.



i) ArCHO, NaOEt *ii*) KCN, NH_4Cl, DMF *iii*) $EtOH/H^+$ *iv*) aq. NaOH; then $EtOH/H^+$
v) I_2/NaOMe/THF *vi*) Aq. NaOH; then H_3O^+

Our inability to hydrolyze the stereoisomeric mixture of **3** efficiently under either acid or basic conditions and the low yield obtained from ethanolysis of **3** led us prepare **5** as a *meso*-dl in one step from **4**.[2] Since both *meso* and *d,l*-stereoisomers of the 2,3-diphenylsuccinic acid give **7b** after cyclization,[3-5] no attempt was made to separate the mixtures.

The ^1H NMR spectrum of the diastereoisomeric mixture **6** shows one signal for the methoxy groups (3.64) while compound **7a** exhibits two signals, one for each methoxy group (3.85 and 3.95) because of the different magnetic surroundings. The ^{13}C NMR spectrum of **7a** displays a characteristic ketone carbonyl signal (197.6), markedly shifted to lower field compared to carboxylic carbonyl signals shown in the mixture **6**. The molecular weight (*m/e* 354) for compound **7a** was determined by mass spectrometry.

EXPERIMENTAL SECTION

Melting points are uncorrected and were obtained on a Thomas Hoover apparatus. The NMR spectra were recorded on a Bruker AW 80 or Varian FT 80 A spectrometer using TMS as internal reference. IR spectra were determined as KBr pellets on a Jasco A-200 spectrophotometer. Elemental analyses were performed on a Coleman Analyzer. The MS were recorded in a Shimadzu QP 1000 operating at 20 eV. Polyphosphoric acid was purchased from Riedel de Haen.

3,5-Dimethoxyphenylacetonitrile (1).- Compound **1** was synthesized by a modification of a published procedure.[6] Commercial 3,5-dimethoxybenzyl chloride (2g, 11 mmol) in DMSO (9mL)

was added dropwise (1 hr) to a stirred solution of NaCN (0.9 g, 18 mmol) in DMSO (35mL). Stirring was continued for 4 hrs, then water (50 mL) was added and the mixture cooled in the refrigerator. The crystals were collected and washed with water to afford after recrystallization from cyclohexane 1.8 g (95%) of **1**, mp. 50-51°, lit.[6] mp. 53°. ^{1}H NMR ($CDCl_3$): δ 3.10 (2H, s), 3.25 (6H, s), 6.30-6.45 (3H, m).

***Z*-2,3-bis(3,5-Dimethoxyphenyl)propenonitrile (2)**.- A solution of **1** (2 g, 11.3 mmol) and 3,5-dimethoxybenzaldehyde (1.88 g, 11.3 mmol) in absolute ethanol (8 mL) was treated with sodium ethoxide (0.08 g) in absolute ethanol (1 mL) with stirring at room temperature until a white solid precipitated (1 hr). The suspension was cooled and the solid was collected and recrystallized from ethanol to afford 1.8 g (76 %) of **2** as white crystals, mp. 120-121°. IR: 2240 (CN), 840 and 680 (Ar) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 3.80 (12H, s), 6.35 - 6.60 (2H, m), 6.75 (2H, d, J = 2.5Hz), 7.00 (2H, d, J = 2.5Hz), 7.40 (1H, s); ^{13}C NMR ($CDCl_3$): δ 52.9 (OCH_3), 98.0, 100.9, 101.9, 104.7 (Ar), 116.6 (CN), 132.7, 133.8 (Ar), 109.9 (C-2), 139.8 (C-3), 158.5, 158.8 (Ar).

Anal. Calcd. for $C_{19}H_{19}NO_4$: C, 70.15; H, 5.85; N, 4.31. Found: C, 70.18; H, 5.82; N, 4.31

2,3-bis(3,5-Dimethoxyphenyl)succinodinitrile (3).- In a round-bottomed flask fitted with a reflux condenser was placed **2** (1.2 g, 3.7 mmol), distilled DMF (100 mL), a solution of KCN (0.5g, 7.7 mmol), and NH_4Cl (0.3 g, 5.6 mmol) in water (15 mL). The reaction mixture was refluxed for 6 hrs; then a further amount of NH_4Cl (0.15 g) was added and the red colored solution cooled to room temperature. The reaction mixture was concentrated to half its volume and water (50 mL) was added. The solid form was collected and recrystallized from ethanol giving 0.9 g (69%) of **3** as a mixture of *meso* and *d,l*-stereoisomers, mp. 175-180°. IR: 2260 (CN), 840 and 710 (Ar) cm^{-1}; ^{1}H NMR (DMSO d_6): δ 3.88 (12H, s), 5.18 (2H, br.s), 6.70 (6H, m).

Anal. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.18; H, 5.68; N, 7.95. Found: C, 68.20; H, 5.67; N, 7.97

Ethyl 3,5-Dimethoxyphenylacetate (4).- A mixture of **1** (2 g, 11.3 mmol) and NaOH (0.8 g, 20 mmol) in ethanol:water (1:1, 10 mL) was refluxed for 6 hrs. The reaction mixture was cooled, filtered, and acidified with 2 N HCl. The white solid was collected, washed with water, and dried to give 2.1 g (95%) of acid, mp. 100-102°; lit.[7] mp. 100-101°. The crude acid was esterified under standard conditions[8] to give 2.16 g (90%) of **4** as an oil.[9] ^{1}H NMR ($CDCl_3$): δ 1.25 (3H, t, J = 7.6 Hz), 3.50 (2H, s), 3.80 (6H, s), 4.15 (2H, q, J = 7.6 Hz), 6.30-6.45 (3H, m).

Diethyl 2,3-bis(3,5 Dimethoxyphenyl)succinate (5).- To a suspension of NaOH (0.25g, 4.6 mmol) in dry THF (10 mL) at - 78 was added **3** (1 g, 4.4 mmol) and the reaction mixture was stirred for 30 min. The cooling bath was removed followed immediately by dropwise addition of iodine (0.56 g, 2.3 mmol) in dry THF (5 mL). The resulting clear solution was stirred at room temperature for additional 10 min and 5% $NaHSO_3$ (10 mL) was added. The solvent was removed *in vacuo* and the organic residue was extracted with methylene chloride (2 x 20 mL) The organic extract was dried over Na_2SO_4 and evaporated *in vacuo* to give 0.8 g of a yellow solid which was crystallized twice from ethanol to give 0.71 g (71%) of white crystals of **5** as a mixture of *d,l* and *meso* stereoisomers, mp. 131-135°. IR: 1730 (CO) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ 0.99 (t, J = 7.4 Hz, CH_3), 1.21 (t, J = 7.4 Hz,

CH_3), 3.64 and 3.77 (s, OCH_3), 3.85-4.50 (m, CH, CH_2), 6.23 (s, Ar), 6.36 (t, Ar), 6.64 (d, J = 2.5 Hz, Ar); ^{13}C NMR ($CDCl_3$): δ 13.7 (CH_3), 13.9 (CH_3), 54.9 (OCH_3), 55.3 (OCH_3), 60.6 (CH_2), 61.0 (CH_2), 99.5, 99.9, 106.4, 137.8, 138.4, 160.5, 160.7 (Ar), 170.9 (CO), 172.6 (CO).

Anal. Calcd. for $C_{24}H_{30}O_8$: C, 64.57; H, 6.73, Found: C, 64.59; H, 6.71

Compound **5** was also obtained by hydrolysis of dinitrile **3** (0.28 g) with a mixture of ethanol (17 mL) and sulfuric acid (3 mL) at 80 for 4 hrs. Water (30 mL) was added followed by extraction with $CHCl_3$. The solvent was removed *in vacuo* and the resulting gum was purified by preparative silica gel chromatography (eluted with dichloroethane) to give a solid (0.04 g, 12%), mp. softens at 145°.

2,3-bis(3,5-Dimethoxyphenyl)succinic Acid (6).- Diesters **5** (0.62 g, 1.4 mmol) were hydrolyzed with KOH (0.6 g) in water (20 mL) and ethanol (4 mL) under reflux for 7 hrs. The mixture was cooled to room temperature, filtered, and after acidification with 10% HCl rendered the diacid **6** as a mixture of *d,l* and *meso* diasteroisomers. Recrystallization from ethanol gave 0.42 g (80 %): mp. of the mixture 237-240° (dec.); IR: 1710 (CO) cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.64 (12H, s), 4.12 (2H, br s), 6.20-6.60 (6H Ar); ^{13}C NMR (DMSO-d_6): δ 53.8 (CH), 54.5 (CH), 55.2 (OCH_3), 55.3 (OCH_3), 98.9 (Ar), 99.1 (Ar), 107.0 (Ar), 107.6 (Ar), 138.9 (Ar). 139.7 (Ar), 160.2 (Ar), 160.4 (Ar), 172.3 (CO), 174.0 (CO). MS (*m/e*) 390 (M^+) (12.8 %), 372 (100 %).

Anal. Calcd. for $C_{20}H_{22}O_8$: C, 61.54; H, 5.64; . Found: C, 61.55; H, 5.66

1,3,6,8-Tetramethoxy-cis-4b,5,9b,10-tetrahydroindeno[2,1-a]indene-5,10-dione (7a).- A mixture of **6** (0.50 g, 1.28 mmol), and commercial polyphosphoric acid (PPA) (10 g) was heated at 70° (oil bath) for 4 hrs in a tube fitted with a mercury seal and a mechanical stirrer. The resulting brown mixture was cooled externally with an ice bath for 30 min. The mixture was extracted with $CHCl_3$ (3 x 20 mL), the organic layer was washed with 5% $NaHCO_3$ and water, dried with Na_2SO_4 and concentrated *in vacuo* gave a brown solid which was crystallized from benzene to afford 0.25 g (55 %) of **7a** as a white solid: mp. (aluminium block) 303-305° (dec.); IR: 1720 (CO) cm^{-1}; ^1H NMR ($CDCl_3$): δ 3.85 and 3.95 (12H, s, OCH_3), 4.17 (2H, s, CH), 6.30 (2H, s, Ar); ^{13}C NMR ($CDCl_3$): δ 52.7 (CH), 55.6, 55.8 (OCH_3), 99.2, 101.4, 116.4, 155.6, 159.7, 167.6 (Ar), 197.6 (CO). MS (*m/e*) 354 (M^+) (100%).

Anal. Calcd. for $C_{20}H_{18}O_6$: C, 67.79; H, 5.08. Found: C, 67.81; H, 5.09

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RAPID OXIDATION OF SULFIDES AND SULFOXIDES WITH SODIUM HYPOCHLORITE

Submitted by (07/14/95)

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Sulfones are important in organic synthesis. A number of reagents have been reported to oxidize sulfides and sulfoxides to the corresponding sulfones.[1] Sodium hypochlorite has been reported as an inexpensive and convenient oxidizing reagent for a variety of functional groups.[2] Sodium hypochlorite has also been used to oxidize sulfides and disulfides to sulfoxides and disulfoxides selectively[3] and in other cases it yields a mixture of sulfoxides and sulfones.[1b,c] While working on oxidations with hypochlorite,[4] we observed that dibenzyl sulfide was rapidly oxidized to the corresponding sulfone with sodium hypochlorite in acetonitrile at ambient temperature; prolonged oxidation resulted in a mixture of the products. Therefore, we decided to investigate the oxidation of different sulfides and sulfoxides with sodium hypochlorite in acetonitrile at ambient temperature. This paper reports a simple, rapid and convenient procedure for the oxidation of a variety of sulfides and sulfoxides to the corresponding sulfones with aqueous sodium hypochlorite at ambient temperature.

The oxidations were quite rapid and high yields of the sulfones were obtained by a simple work up. Most of the known reagents including hydrogen peroxide require more vigorous conditions (higher temperatures and long reaction times). This procedure is applicable to dibenzyl, dialkyl, diaryl, benzyl alkyl, benzyl aryl and aryl alkyl sulfides and sulfoxides; even a fatty sulfide such as benzyl n-dodecyl sulfide was easily oxidized using a somewhat higher molar ratio of substrate to NaOCl (Tables 1 and 2). In a separate reaction of **1a** with sodium hypochlorite at room temperature, aliquots were removed after 2 min, 10 min, 20 min and 30 min, quenched and analyzed. All these