

A FACILE OXIDATION OF 3,4-DIPHENYLTHIOPHENE-2,5-DIMETHANOL AND FURAN-2,5-DIMETHANOL TO 3,4-DIPHENYLTHIOPHENE-2,5-DICARBOXALDEHYDE AND FURAN-2,5-DICARBOXYLIC ACID USING BIS(PYRIDINE) SILVER PERMANGANATE

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3,4-Diphenylthiophene-2,5-dicarboxaldehyde **4** has been obtained in 90% yield by oxidation of the corresponding dimethanol **3** with bis(pyridine)silver permanganate (BPSP). However, similar oxidation of furan-2,5-dimethanol **8** gave furan-2,5-dicarboxylic acid **9** only in 56% yield. This appears to be the first instance of oxidation of an aromatic dimethanol to the corresponding dicarboxylic acid with BPSP.

Key Words: 3,4-Diphenylthiophene-2,5-dicarboxaldehyde; 2-formyl-3,4-diphenylthiophene-5-methanol, bis(pyridine)silver permanganate; Oxidation; 3,4-diphenylthiophene-2,5-dimethanol, 3,4-diphenyl-2,5-thiophenedicarbonyl chloride; Furan-2,5-dicarboxylic acid

Introduction

In connection with our studies on the anticancer activities of metal complexes of macrocyclic ligands¹, we required 3,4-diphenylthiophene-2,5-dicarboxaldehyde **4** and furan-2,5-dicarboxaldehyde **10**. The thiophenedicarboxaldehyde **4** is unknown, while a number of methods^{2,3} are available in the literature for the preparation of **10**. Recently, Firouzabadi *et al.*⁴ have reported that oxidation of 2,5-diphenylthiophene-3,4-dimethanol, 2,5-diphenylfuran-3,4-dimethanol and benzene-1,2-dimethanol with bis(pyridine)silver permanganate yielded the corresponding dicarboxaldehydes in excellent yields, but the yields dropped to about 20% when BPSP was replaced by manganese dioxide. We decided to use BPSP for the synthesis of **4** and **10** and our results are presented herein.

The thiophene dimethanol **3** was obtained in 65% yield by reduction of the corresponding ester acid **2** with lithium aluminium hydride (LAH) (Scheme I). Reduction of the dimethyl ester **1** to **3** with LAH is recorded in the literature without mentioning the yield⁵. We obtained **3** in 89.8% yield by reduction of **1** with LAH in refluxing tetrahydrofuran (THF), and **3** in 60% yield by reduction of the dicarbonylchloride **6** with sodium borohydride following the literature procedure⁶.

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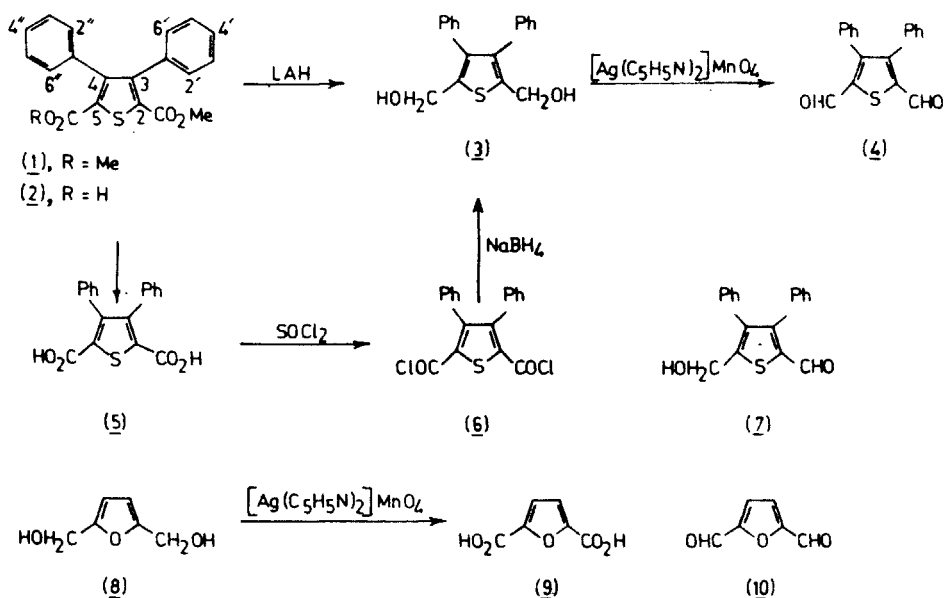
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The dimethanol **3** gave the dicarboxaldehyde **4** in 90% yield on oxidation with 1.5 molar equivalent of BPSP. The poor solubility of **3** in benzene posed a problem and for completion of the reaction. BPSP had to be added in two instalments and the reaction mixture required a total of six hours refluxing. When all the oxidant was added at a time, the reaction remained incomplete. When equimolar proportion of **3** and BPSP was employed, 40% of **3** remained unchanged and the yield of **4** dropped down to 10.3%. A small amount (10.9%) of the partially oxidised product **7** was also isolated from the reaction using equimolar proportion of **3** and BPSP. **7** could be further oxidised readily to **4** in 90% yield with excess BPSP.

The oxidation of the furandimethanol **8** required the addition of 2.26 molar equivalent of BPSP in four instalments and a total of 16.5 hours' refluxing. Only the dicarboxylic acid **9** was obtained in 56% yield. This appears to be the first observation of the oxidation of an aromatic dimethanol to the corresponding dicarboxylic acid with BPSP.

Experimental Procedure

Melting points are uncorrected. IR spectra were recorded in KBr on a Beckman IR 20, Pye Unicam SP 1025 or Perkin-Elmer 782 spectrophotometer. PMR and CMR spectra were run on a Bruker AM-300L (300.133 MHz on proton and 75.5 MHz on carbon) NMR machine in CDCl_3 , if not otherwise mentioned, using TMS as the internal standard. The carbon chemical shifts are reported in δ (ppm) downfield from TMS: $\delta_{\text{TMS}} = \delta_{\text{CDCl}_3} + 76.9$ ppm. The degree of protonation of the carbon was determined by DEPT 135° experiments. Water distilled twice from potassium permanganate and guaranteed reagent grade potassium permanganate, silver nitrate and pyridine were used for



the preparation of BPSP. Furan-2,5-dimethanol was procured from Aldrich Chemical Company, U.S.A. Petroleum ether refers to the fraction boiling at 60-80°. The progress of the oxidation reactions was followed by observing the disappearance of the dimethanols **3** and **8** by thin layer chromatography using silica gel plates (ACME) and chloroform-ethyl acetate (4:1).

3,4-Diphenyl-2,5-thiophenedicarbonyl chloride **6**

Following the published procedures^{7,8} a mixture of redistilled thionyl chloride (20 ml, 274 mmol) and the dicarboxylic acid **5**^{9,10} (10 g, 30 mmol) was refluxed with stirring for 13 hr and then evaporated to dryness under reduced pressure. The residue was extracted with dry petroleum ether, the extract treated with charcoal, concentrated and cooled to yield yellow needles, which after recrystallisation from carbon tetrachloride-petroleum ether afforded the dicarbonyl chloride **6** as long yellow needles (9.00 g, 81%), m.p. 122-123° [lit. m.p. (i)⁷ 121-122°, (ii)⁸ 123-124°]. (Found: C, 59.55; H, 2.98. C₁₈H₁₀Cl₂O₂S requires C, 59.84; H, 2.79%).

3,4-Diphenylthiophene-2,5-dimethanol **3**

Method (i):

Following the literature method⁹, a mixture of the dicarbonyl chloride **6** (2.5 g, 6.92 mmol), sodium borohydride (0.5 g, 13.22 mmol) and dry diglyme (50 ml) was allowed to stand for 15 hr. After addition of crushed ice, the reaction mixture was acidified with hydrochloric acid (1:1), evaporated to dryness under reduced pressure and the residue extracted with ethyl acetate (5 × 50 ml). The extract was dried (Na₂SO₄), evaporated to dryness and the residue crystallised thrice from benzene to furnish the dimethanol **3** as colourless shining needles (1.231 g, 60%), m.p. softened from 174° and melted at 185-187° [lit. m.p. (i)⁵ 167-167.5°, (ii)⁶ 162-165°]. (Found: C, 72.64; H, 5.47. C₁₈H₁₆O₂S requires C, 72.94; H, 5.44%). IR(KBr): 3220-3380 (O-H), 3000-3060, 1510, 1060, 1470, 1315, 1030, 800, 770, 720, 700 cm⁻¹

Method (ii):

Essentially following the method of Dann and Hauck⁵, a solution of dimethyl 3,4-diphenylthiophene-2,5-dicarboxylate¹¹ **1** (3.5 g, 9.932 mmol) in anhydrous tetrahydrofuran (50 ml) was added dropwise with stirring to a suspension of lithium aluminium hydride (1.9 g, 50.076 mmol) in anhydrous tetrahydrofuran (100 ml) and then refluxed for 4.5 hr. Excess lithium aluminium hydride was destroyed carefully by dropwise addition of cold ethyl acetate (50 ml) with stirring and then cold water (100 ml). Most of the liquids was removed under reduced pressure and the white residue extracted with refluxing ethyl acetate (6 × 75 ml), the extract dried (Na₂SO₄) and evaporated to dryness. The pale yellow crystalline residue was crystallised twice from benzene to give the dimethanol **3** as colourless shining needles (2.645 g, 89.8%), identical in all respects with the material prepared by Method (i).

Method (iii):

A solution of 2-carbomethoxy-3,4-diphenylthiophene-5-carboxylic acid¹² **2** (3.0 g, 8.86 mmol) in anhydrous tetrahydrofuran (50 ml) was added as in Method (ii) to a suspension of lithium aluminium hydride (1.9 g, 50.07 mmol) in dry tetrahydrofuran (100 ml) and refluxed for 5 hr and then worked up as in Method (ii) to afford the dimethanol **3** (1.708 g, 65%).

Bis(pyridine)silver permanganate (BPSP)

This was prepared essentially following the method of Firouzabadi *et al.*⁴ Pyridine (9.7 ml, 9.492 g, 120 mmol) was added with stirring to a solution of potassium permanganate (6.32 g, 40 mmol) in distilled water (50 ml) at 10°. A cold solution of silver nitrate (6.795 g, 40 mmol) in distilled water (68 ml) was then added slowly keeping the internal temperature at 10°. Stirring was continued for another 30 min at 10° and the mixture kept overnight in a refrigerator for crystallisation and ease in filtration. The product was collected, washed with cold water (5 × 50 ml), followed by sodium-dried benzene (4 × 50 ml), protected from light and dried in vacuo over fused calcium chloride at 5-10° to give BPSP (13.86 g, 90%). A small fraction was crystallised from acetone-benzene as purple micro-needles, m.p. 103-105° (decompn.) [lit.⁴ m.p. 104-105° (decompn.)].

Oxidation of 3,4-diphenylthiophene-2,5-dimethanol **3 with BPSP***Method (a):*

3,4-Diphenylthiophene-2,5-dimethanol **3** (5.928 g, 20 mmol) was introduced in a three-necked R.B. flask equipped with a Dean and Stark water separator followed by sodium-dried benzene (1400 ml). The mixture was stirred magnetically and refluxed until a clear solution resulted. It was cooled to about 60° [a considerable amount of **3** crystallised out], freshly prepared BPSP (7.2 g, 20 mmol) was added in portions with stirring over 3 min and the mixture refluxed with stirring for 3 hr. The reaction mixture was cooled to about 60° and BPSP (3.6 g, 10 mmol) was added and the mixture refluxed for 3 hr. The reaction mixture was filtered while hot and the residue washed with hot benzene (6 × 250 ml). The combined filtrate and the washings were evaporated to dryness under reduced pressure and the pale yellow crystalline residue was crystallised first from ethanol and then from benzene to furnish 3,4-diphenylthiophene-2,5-dicarboxaldehyde **4** (5.263 g, 90%) as pale yellow needles, m.p. 210° (Found: C, 73.88; H, 4.34. C₁₈H₁₂O₂S requires C, 73.95; H, 4.14%). IR: 3060 (m) (aromatic C-H), 2850(w) (aldehydic C-H), 1655(s) (C=O), 1525(m) and 1025(s) (C=C of thiophene ring), 1380(s) (aldehydic C-H), 795(s), 765(s) and 725(s) (aromatic out of plane C-H), 690 cm⁻¹(s) (thiophene ring vibration); PMR: δ 9.79 (2H, s, 2 × HC=O), 7.26-7.31 (6H, m, 2'-H, 2"-H, 4'-H, 4"-H, 6'-H and 6"-H), 7.12-7.15 (4H, m, 3'-H, 3"-H, 5'-H and 5"-H); ¹³C NMR: δ 184.94 (d, 2 × HC=O), 150.69 (s, C-2 and C-5), 144.03 (s, C-3 and C-4), 131.69 (s, C-1' and C-1"), 130.41 (d, C-2', C-2", C-6' and C-6"), 128.73 (d, C-4' and C-4"), 128.34 ppm (d, C-3', C-3", C-5' and C-5"); MS: *m/z*

(rel. abundance %) 292 (100, M^+), 263 (22, $M - CHO$), 234 (21, $M - 2 \times CHO$), 202 (15, $M - 2 \times CHO$ and S), 137 (8, $M - 2 \times C_6H_5$ and H).

Method (b):

Following the foregoing procedure, a mixture of the dimethanol **3** (1.482 g, 5 mmol), sodium-dried benzene (250 ml) and freshly prepared BPSP (1.925 g, 5 mmol) was refluxed with stirring for 1 hr and worked up as in the previous case. The residue left after evaporation of the benzene filtrate and washings were chromatographed on a silica gel column. Elution with benzene-petroleum ether gave the dicarboxaldehyde **4** (150 mg, 10.3%). Further elution of the column with benzene resulted in the isolation of 2-formyl-3,4-diphenylthiophene-5-methanol **7** (160 mg, 10.9%) as colourless needles (from benzene-petroleum ether), m.p. 153° (Found: C, 73.54; H, 4.69. $C_{18}H_{14}O_2S$ requires C, 73.44; H, 4.79%); IR: 3250-3400(m) (OH), 1660 cm^{-1} (C=O); PMR (Varian EM 390, 90 MHz): δ 9.70 (1H, s, HC=O), 7.0-7.5 (10H, m, Ar-H), 4.50 (2H, s, CH_2), 3.3 (H, b.s., OH). Continued elution of the column with chloroform-ethyl acetate (9:1) yielded the starting material **3** (593 mg, 40%).

Oxidation of 2-formyl-3,4-diphenylthiophene-5-methanol **7**

A mixture of **7** (147 mg, 0.5 mmol), BPSP (97 mg, 0.25 mmol) and sodium-dried benzene (30 ml) was refluxed for 3 hr, cooled to about 60°, BPSP (97 mg, 0.25 mmol) added, refluxed for 3 hr and worked up following the foregoing procedures to give the dicarboxaldehyde **4** (131 mg, 90%).

Furan-2,5-dicarboxylic acid **9**

Following the foregoing procedure a mixture of furan-2,5-dimethanol (3.85 g, 30 mmol), sodium-dried benzene (750 ml) and freshly prepared BPSP (11.55 g, 30 mmol) was refluxed with stirring for 3 hr. Further 6 g (15.6 mmol), 6 g and 2.5 g (6.5 mmol) of BPSP were added in three instalments after refluxing for 4.5 hr after each addition (total 16.5 hr). The reaction mixture was worked up as in the previous cases, but the combined benzene filtrate and washings did not afford any pure product. The residual oxidant was extracted repeatedly with hot ethyl acetate which also did not yield any pure product. The residue was finally extracted exhaustively with boiling water, the extract concentrated under reduced pressure, cooled, acidified with conc. hydrochloric acid and extracted with ethyl acetate (5 \times 300 ml), the extract dried (Na_2SO_4), evaporated to dryness and the residue crystallised from water to give furan-2,5-dicarboxylic acid **9** (2.63 g, 56%) as white flakes, m.p. above 320° (lit.¹³ m.p. above 320°); IR: 2520-3150(b) (OH) (intermolecular hydrogen bonding and furan ring vibration), 1710(s) (C=O), 1520(s) (furan ring distortion), 1270(s), 1040(s) (C-O for COOH and furan ring), 870(s) (characteristic absorption band for furan ring), 760 cm^{-1} (s) (out-of-plane C-H). It was converted to dimethyl furan 2,5-dicarboxylate by the literature method¹³ and obtained as white flakes, m.p. 112°; IR: 3020(w), and 3120(m) (aromatic C-H for furan ring), 1720 (C=O), 1580(w) (C=C), 1515(m) (furan ring distortion), 1435(s) (as- CH_3),

1380(m) (sym-CH₃), 1280(s) (C-CO-O), 1030(s) (C-O for ester and furan ring), 880 cm⁻¹ (s) (characteristic absorption band of furan ring); PMR: δ 3.92 (6H, s, 2 \times CO₂CH₃), 7.22 (2H, s, 3-H and 4-H).

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