

Anodic Cyanation of Tetramethylthiophene

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The electrooxidation of tetramethylthiophene in methanol containing sodium cyanide produced 2,5-dihydro-2,3,4,5-tetramethylthiophene-2,5-dicarbonitrile **1** (*cis/trans* = 0.7) and 2,5-dihydro-5-methoxy-2,3,4,5-tetramethylthiophene-2-carbonitrile **2** (*cis/trans* = 2.2) in 21 and 25% yields respectively, together with a small amount of 2-methoxymethyl-3,4,5-trimethylthiophene **3**. Treatment of the resultant 2,5-mixed adduct **2** with a small amount of acid induced elimination of a methanol molecule to give 2,5-dihydro-2,3,4-trimethyl-5-methylenethiophene-2-carbonitrile **4a**.

Electrooxidative reactions that generate cation radicals make it possible to direct the introduction of a functional nucleophile such as a cyanide ion onto a nucleophilic centre of the starting material.¹ Previously we have investigated the electrooxidation of 2,5-dimethylthiophene (DMT) in methanol containing various electrolytes.² With sodium cyanide as the electrolyte, the product arising from a mixed 2,5-addition of one cyano and one methoxy group was formed, together with comparable amounts of the ring cyanation and side-chain methoxylation product.

The conversion of thiophenes into 2,5-dihydrothiophenes is unusual and was peculiar to the cyanide electrolyte. In view of the results obtained on anodic oxidation of a series of sequentially methyl-substituted furans,³ the formation of dihydrothiophene from the tetramethyl compound may well exceed that from the 2,5-dimethyl one.

Results

Cyclic Voltammetry (CV).—Cyclic voltammograms were recorded using a solution of 0.4 mol dm⁻³ NaCN in MeOH. The voltammogram for tetramethylthiophene (TMT) has several features in common with those for other aromatic compounds which are consistent with a fast chemical reaction following electron transfer.³⁻⁵ On this voltammogram the current function, $i_p/v^{1/2}$, where i_p is the peak current and v is the sweep rate, decreased, and E_p was shifted to a more positive value with increasing sweep rate. There was no evidence of a cathodic peak on reversal.

Controlled-potential Electroreaction (CPE).—The reaction was carried out at a controlled anode potential in a divided cell with a Pt anode, at room temperature. The reference electrode was an SCE (saturated calomel electrode). The potential was set at the peak potential of the substrate. At the potential adopted, background current is negligible. The oxidation was terminated after the passage of 2 F mol⁻¹ of added TMT. The products were isolated by preparative GLC and were identified by the elemental analysis and ¹H NMR, IR and mass spectroscopy. Coulometry showed that $n = 2$.

The 2,5-addition of two cyano groups to the thiophene ring was achieved, and a mixed addition of one cyano and one methoxy group occurred concurrently. A small amount of side-chain methoxylation product was also formed. The *cis:trans* ratios of the stereoisomers **1** and **2** were estimated by GLC analyses.

The NMR spectroscopic studies on geometrical isomerism in 2,5-dihydrofurans^{3,6} could be applied to the structural assignments of isomeric pairs of the relevant 2,5-dihydrothiophenes. The chemical shift of a group in the 2 position of the thiophene

Table 1 Cyclic voltammetric data for the electrooxidation of TMT in 0.4 mol dm⁻³ NaCN–MeOH^a

Sweep rate, mV s ⁻¹	i_p , mA	$i_p/v^{1/2}$, mA s ^{1/2} /V ^{1/2}	E_p , V vs. SCE
25	0.43	2.98	1.23
100	0.87	2.75	1.25
400	1.48	2.34	1.31

^a Pt wire electrode, 0.322 cm². 4 × 10⁻³ mol dm⁻³ TMT.



1; X = CN; 21% yield
(*cis/trans* = 0.7)
2; X = OMe; 25% yield
(*cis/trans* = 2.2)

3 3% yield

ring is affected both by the other group at the 2 position and the magnetic influence exerted by the group at the 5 position that is *cis* to it. Thus, if a 2-methyl is *cis* to a 5-methoxy (or a 5-cyano) group it will resonate at a lower field and raise the δ value more than if it is *cis* to another 5-methyl group (Table 2).

Acid-catalysed Transformation of the 2,5-Mixed Addition Product 2.—The stereoisomeric 2,5-mixed adduct is thermally stable. Each isomer remained intact on GLC. In CDCl₃ solution in an NMR tube or with a trace of a strong acid in CHCl₃, they lost MeOH to give compound **4**. Two possible structures, **4a** and **4b**, are conceivable for **4**. The ¹H NMR spectrum of **4** shows all three methyl groups with δ values maximally at 1.96. If the acid-catalysed hydromethoxy-elimination product **4** has the structure **4b**, the chemical shift of



4a X = CN
5a X = OMe

4b X = CN
5b X = OMe

the methyl group at the 5 position would show a higher δ value. For reference, the methyl groups at the 2 and 5 positions of DMT and TMT show δ values of 2.40 and 2.25, respectively.

In the case of anodic oxidation of TMT in methanol containing sodium methoxide as the electrolyte,⁷ the same type of compound was isolated and assigned the structure **5a**. The latter was established by treating the compound with a trace of

Table 2 Physical characteristics of electrooxidation products

Product	m.p. (°C)	¹ H NMR, ^c δ (J in Hz)	Mass m/z (M ⁺)	IR, ^g ν _{max} /cm ⁻¹
<i>cis</i> -1 ^a	110.0–111.0 (from EtOH–hexane)	1.80 (6 H, s), 1.87 (6 H, s)	192	2230 (CN)
<i>trans</i> -1 ^a	64.5–65.5 (from hexane)	1.84 (6 H, s), 1.87 (6 H, s)	192	2230 (CN)
<i>cis</i> -2 ^b	68.5–70.0 (from hexane)	1.62 (3 H, m), 1.67 (3 H, s), 1.72 (3 H, s), 1.85 (3 H, m), 3.11 (3 H, s) ^f	197	2220 (CN) 1108 (C–O–C)
<i>trans</i> -2 ^b	Oil	1.61 (3 H, m), 1.72 (3 H, s), 1.76 (3 H, s), 1.84 (3 H, m), 3.00 (3 H, s) ^f	197	2220 (CN) 1112 (C–O–C)
3 ^c	Oil	2.00 (3 H, m), 2.08 (3 H, s), 2.31 (3 H, m), 3.33 (3 H, s), 4.46 (2 H, s)	170	1095 (C–O–C)
4 ^d	Oil	1.81 (3 H, s), 1.85 (3 H, m), 1.96 (3 H, m), 4.94 (1 H, d, <i>J</i> = 1.5), 5.07 (1 H, d, <i>J</i> = 1.5)	165	2220 (CN) 1592 (conj. C=C)

^a Found (for *cis* and *trans* mixture): C, 62.7; H, 6.3; N, 14.5; S, 16.6. Calc. for C₁₀H₁₂N₂S: C, 62.5; H, 6.3; N, 14.6; S, 16.7%. ^b Found (for *cis* and *trans* mixture): C, 60.9; H, 7.6; N, 7.1; S, 16.1. Calc. for C₁₀H₁₅NOS: C, 60.9; H, 7.7; N, 7.1; S, 16.3%. ^c Found: C, 63.7; H, 8.3; S, 18.4. Calc. for C₉H₁₄OS: C, 63.5; H, 8.3; S, 18.8%. ^d Found: C, 65.0; H, 6.7; N, 8.3; S, 19.1. Calc. for C₉H₁₁NS: C, 65.4; H, 6.7; N, 8.5; S, 19.4%. ^e 100 MHz; CDCl₃ solution unless otherwise noted; standard Me₄Si. ^f CCl₄ solution. ^g Mull for solid sample.

acid, to give the 2-methoxymethyl compound 3. Structure 5b must therefore give the 3-methoxymethyl compound.

Discussion

The voltammetric characteristics (Table 1) indicate that oxidation is initiated by electron transfer from the substrate molecule, followed by a fast chemical reaction. By analogy with anodic cyanation and methoxylation of other aromatic compounds, the ECEC mechanism^{1–6} involving a cation radical intermediate would be reasonable.

Comparisons of the effect of the methyl substituent on product distributions show a considerable analogy between methylated thiophenes and furans. Dimethylfuran (DMF) gave a mixed adduct together with a small amount of 2,5-dimethoxy adduct, while tetramethylfuran (TMF) produced a 2,5-dicyano adduct as well as a mixed one.^{3,6} TMT resembles TMF in giving both the 2,5-dicyano and mixed adducts (2,5-dihydrothiophenes), while DMT is like DMF affording exclusively the corresponding mixed adduct, along with comparable amounts of the ring and side-chain substitution products.²

GLC analyses of product mixtures indicate the existence of several minor products. Those might result from further electrooxidation of primarily generated 3.

Experimental

General.—Spectrometers and electrochemical equipment have been described previously.³

Materials.—MeOH and reagent grade NaCN were used without purification.

TMT was prepared by lithium aluminium hydride reduction of 3,4-bis(chloromethyl)-2,5-dimethylthiophene, which was obtained by chloromethylation of DMT:⁸ b.p. 100 °C/37 mmHg; δ(100 MHz; CDCl₃) 1.96 (6 H, s) and 2.25 (6 H, s).

CV.—Voltammograms were recorded as described previously.³ The *E*_p value was 1.25 V vs. SCE at sweep rate of 0.1 V s⁻¹ (Table 1).

CPE.—A three-compartment cell which has been previously

described³ was employed. The reference electrode was an SCE. Oxidation of TMT (0.28 g, 2 mmol) in MeOH (50 cm³) containing 0.4 mol dm⁻³ NaCN was performed at the peak potential of the substrate. During the run the current dropped with time and was terminated after the passage of 2 F mol⁻¹ of substrate, which took ca. 24 h. An internal standard for GLC analysis was added to the product mixture which was then treated with brine and extracted with ether. The ethereal solution was concentrated and analysed by GLC using a PEG 6000 column at 180 °C. Each product was separated in pure form by preparative GLC. Identification was made on the basis of elemental and ¹H NMR, IR and mass spectroscopic analyses (Table 2). **CAUTION:** a cyanide salt in MeOH must be handled in a fume hood since it contains HCN as a result of the equilibrium between CN⁻ and the solvent MeOH.

Acid-catalysed Transformation of 2 to 4.—The adduct 2 was dissolved in chloroform containing 1% CF₃CO₂H at room temperature. After several hours, saturated aqueous sodium carbonate was added and the mixture was extracted into chloroform. The solution was dried (MgSO₄), filtered and concentrated. A sample for elemental analysis was purified by preparative GLC using a Silicone GE SE-30 at 65 °C.

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