Anodic Cyanation of Benzo[*b*]thiophenes

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The electrooxidation of benzo[*b*]thiophene and 2-methyl- and 3-methyl-benzo[*b*]thiophene was carried out in methanol containing sodium cyanide at a Pt anode in a divided cell. In all instances, heterocyclic ring-substitution products were obtained, together with minor amounts of addition products. With methylbenzo[*b*]thiophene, a small amount of side-chain-methoxylation product was also formed as a by-product.

Previously we showed that 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.[1,2] As part of our programme of electrochemical functionalization of five-membered heterocyclic aromatic compounds, the present paper describes the electrooxidation of benzo[*b*]thiophenes in methanol containing sodium cyanide. Prior to this work, the reports dealing with electrooxidation of benzo[*b*]thiophene and its derivatives have been restricted to the reaction in a methanolic solution of potassium hydroxide, where unsubstituted and methyl-substituted benzo[*b*]thiophenes gave addition products of two methoxy groups to an olefinic double bond in modest yield together with a considerable quantity of tarry residue.[3] On the other hand, electrooxidation of 4-methoxybenzo[*b*]thiophenes results in addition of methoxy groups across the 1,4-positions of the benzene moiety of the molecule, which gives benzo[*b*]thiophene-4,7-quinone bis-acetals.[4]

Results and Discussion

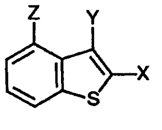
Cyclic voltammograms were recorded in the anodic direction, using a solution of 0.4 mol dm^{-3} NaCN in MeOH. The peak current for benzo[*b*]thiophene (BT) overlapped with the background current for this solvent–electrolyte system. Cyclic voltammetric peak potentials (E_ps) for BT, 2-methylbenzo-[*b*]thiophene (2-MBT), and 3-methylbenzo[*b*]thiophene (3-MBT) were ~1.55, 1.43, and 1.40 V *vs.* SCE (saturated calomel electrode) (at v 0.1 V s^{-1}), respectively.

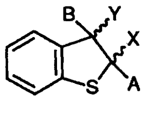
The reaction of BT was conducted at a constant current of 0.1 A in a divided cell with a Pt anode, at room temperature. The oxidation was terminated after passage of 4.5 F mol^{-1} of added substrate. After usual work-up, the products were separated by column chromatography. Benzo[*b*]thiophene-2-carbonitrile **1** and -3-carbonitrile **2** were produced in yields of 2 and 7%, respectively (based on unrecovered starting material). The conversion was 63%. GLC analysis showed the existence of several minor peaks near the peaks of the above isomeric products.

Electrooxidation of 3-MBT were carried out potentiostatically as well as galvanostatically. The replacement of an aromatic hydrogen by a cyano group was achieved at a position lacking any substituent on the thiophene portion of the molecule. Both addition of methoxy and/or cyano groups to the double bonds and side-chain substitution occurred to only a slight extent.

2-MBT produced the 3-cyanation product predominantly. Minor products were not investigated.

Table 1 summarizes the results of the electroreaction.





1 X = CN, Y = Z = H
2 X = Z = H, Y = CN
3 X = Me, Y = CN, Z = H
4 X = CN, Y = Me, Z = H
5 X = H, Y = Me, Z = CN
6 X = Z = H, Y = CH_2OMe
7 A = H, B = Me, X = CN, Y = OMe
8 A = H, B = Me, X = Y = OMe
9 A = CN, B = Me, X = Y = OMe

The products were isolated by column chromatography and preparative GLC and were identified by elemental and ^{1}H NMR, IR and mass spectroscopic analyses (Table 2).

^{1}H NMR spectroscopy was used to assign structure to compound **5**. The chemical-shift difference between the substituent methyl group of compound **5** and that of the parent 3-MBT was 0.31 ppm. Such a large difference was previously observed on anodic cyanation of 1-methyl-, 1,4-dimethyl- and 1,5-dimethyl-naphthalene at the *peri* position, where aromatic substitution at the *peri* position raised the δ-value of the methyl group compared with the values obtained for substitution at other positions.[11] Thus, structure **5** is assignable to the pertinent product.

NMR spectroscopy was also used to assign structure to isomeric pairs of compound **8**. The chemical shift of a group in the 3-position of the thiophene portion is affected both by the other group at the 3-position and by the magnetic influence exerted by the group at the 2-position that is *cis* to it. Thus, if a 3-methyl group is *cis* to a 2-methoxy group it will resonate at lower field and raise the δ-value compared with the values obtained if it is *cis* to a 2-protium group. The same reasoning can be applied to the methoxy peaks and permits the indicated structural assignments for the two isomers to be undertaken. Previously, Srogl *et al.* isolated the 2,3-dimethoxy adduct through the electrooxidation of 3-MBT.[3] In the light of reported ^{1}H NMR spectral data, their product had the *cis* configuration.

The structures of the minor addition products, **7** and **9**, were presumed from the spectroscopic data. They were isolated in amounts too small for elemental analyses.

One major advantage of the present anodic reaction lies in its high selectivity with regard to the type of product obtained. Unlike methoxylation, which gives rise to addition products,[3] cyanide anion as a nucleophile gives predominantly aromatic substitution products. When a methyl group as the substituent is introduced into the thiophene portion, substitution occurs

Table 1 Products and yields of electrooxidation of BT, 2-MBT, and 3-MBT in NaCN–MeOH[a]

Substrate	E_p (V *vs.* SCE)[b]	E (V *vs.* SCE)[c]	Electrical current (F mol^{-1})	Conversion (%)	Product	Yield (%)[e]
BT	~1.55	*d*	4.5	63	**1**	2
					2	7
2-MBT	1.43	1.5	2.0	71	**3**	75
3-MBT	1.40	1.4	2.0	68	**4**	73 (50)[d]
					5	3
					6	1
					7	4
					8	1
					9	trace

[a] Pt anode; SCE reference; divided cell. [b] NaCN–MeOH (0.4 mol dm^{-3}); at v 0.1 V s^{-1}. [c] Potential for controlled-potential electroreaction. [d] Constant-current electrooxidation at 0.1 A. [e] Based on unrecovered starting material.

Table 2 Physical characteristics of electrooxidation products

Product	M.p. (°C)	^{1}H NMR [δ(J/Hz)][k]	Mass m/z (M$^+$)	IR (ν_{max}/cm^{-1})[m]
1[a]	Oil	7.30–7.64 (2 H, m), 7.72–7.98 (3 H, m)	159	2220 (CN)
2[b–d]	70.0–71.0 (from $CHCl_3$–hexane)	7.34–7.68 (2 H, m), 7.76–8.04 (2 H, m) 8.08 (1 H, s)	159	2220 (CN)
3[e]	85.0–86.0 (from hexane)	2.77 (3 H, s), 7.24–7.53 (2 H, m), 7.62–7.90 (2 H, m)	173	2200 (CN)
4[e,f]	76.0–76.5 (from hexane)	2.63 (3 H, s), 7.32–7.60 (2 H, m), 7.60–7.84 (2 H, m)	173	2200 (CN)
5[g]	122.5–123.5 (from hexane)	2.74 (3 H, s),[l] 7.26 (1 H, s), 7.36 (1 H, d, J 8.1), 7.70 (1 H, dd, J 7.1, 1.4), 8.00 (1 H, dd, J 8.1, 1.4)	173	2200 (CN)
6[h]	Oil	3.40 (3 H, s), 4.68 (2 H, s),[l] 7.06–7.46 (3 H, m), 7.60–7.90 (2 H, s)	178	2800 (OMe), 1100 (C–O–C)
7	Oil	1.66 (3 H, s), 3.44 (3 H, s), 5.04 (1 H, s), 7.04–7.52 (4 H, m)	205	2820 (OMe), 2220 (CN), 1095 (C–O–C)
8[i,j]	Oil	(*cis*) 1.54 (3 H, s), 3.42 (6 H, s), 5.08 (1 H, s), 6.9–7.3 (4 H, m) (*trans*) 1.62 (3 H, s), 3.08 (3 H, s), 3.43 (3 H, s), 5.16 (1 H, s), 6.9–7.3 (4 H, m)	210	2850 (OMe), 1100 (C–O–C)
9	Oil	1.70 (3 H, s), 3.14 (3 H, s), 3.58 (3 H, s), 7.0–7.4 (4 H, m)	235	2830 (OMe), 2220 (CN), 1100 (C–O–C)

[a] Ref. 5. [b] Ref. 6. [c] Ref. 7. [d] Ref. 8. [e] Ref. 9. [f] Ref. 10. [g] Found: C, 69.4; H, 4.4; N, 7.9. $C_{10}H_7NS$ requires C, 69.3; H, 4.1; N, 8.1%. [h] Found: C, 67.2; H, C, 67.2; H, 5.8; S, 17.8. $C_{10}H_{10}OS$ requires C, 67.4; H, 5.7; S, 18.0%. [i] Ref. 3. [j] *cis*:*trans* = 2.5. [k] 100 MHz; $CDCl_3$ solution; standard Me_4Si. [l] A split head. [m] Mull for solid sample.

at the other vacant heterocyclic ring position. In that case, the oxidation potential of substrates goes down, and the yields of resultant carbonitriles is increased.

Experimental

General.—Spectrometers and electrochemical equipment have been described previously.[12]

Materials.—Methanol and reagent-grade sodium cyanide were used without purification. BT was obtained commercially. 2-MBT was prepared by the method of Hansch and Blondon:[13] δ(100 MHz; $CDCl_3$) 2.57 (3 H, s),* 6.93 (1 H, s),* 7.04–7.36 (2 H, m) and 7.44–7.80 (2 H, m). 3-MBT was obtained according to the literature:[14] δ(100 MHz; $CDCl_3$) 2.43 (3 H, s),* 7.02 (1 H, s),* 7.20–7.44 (2 H, m) and 7.56–7.88 (2 H, m).

Benzo[*b*]thiophene-2-carbonitrile was prepared according to the method of Brown and Meth-Cohn.[5]

Cyclic Voltammetry.—Voltammograms were recorded as described previously.[12] E_ps for BT, 2-MBT, and 3-MBT were ~1.55, 1.43, and 1.40 V *vs.* SCE in methanol at a sweep rate v of 0.1 V s^{-1} (Pt anode; NaCN electrolyte).

Constant-current Electroreaction of BT.—The electroreaction was carried out in a two-compartment H-type cell with a glass frit separating the compartments fitted with Pt foil electrode (2 × 4 cm). The anolyte was made up of BT (5.4 g, 0.04 mol), NaCN (7.8 g, 0.16 mol), and MeOH (200 cm^3). The catholyte was the same medium in the absence of the substrate. The anode and cathode compartments were kept under nitrogen and the anolyte was stirred magnetically. The reaction was performed at 0.1 A of constant current by using a direct-current power supply at room temperature until 4.5 F mol^{-1} of added BT had passed through the solution, which took *ca.* 46 h.

After completion of the oxidation, the anolyte was treated with brine and extracted with diethyl ether. The extract was concentrated and analysed by GLC using a PEG 6000 column at 190 °C. Each product was separated in pure form by column chromatography on a silica-gel column with light petroleum

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* A split head.

(b.p. range 30–70 °C) containing chloroform (15%) as eluent. Unchanged starting material was eluted first, followed by cyanated products. Identification was made by comparison of physical characteristics with literature results (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.

Controlled-potential Electroreaction of MBT.—A three-compartment cell which has been previously described was used.[12] The reference electrode was an SCE. Oxidation of MBT (0.30 g, 0.002 mol) in MeOH (50 cm^3) containing NaCN (1.0 g, 0.02 mol) was performed at the peak potential of the substrate. The reaction was termined after passage of 2 F mol^{-1} of added MBT. The method of work-up and product analysis was identical with that described for BT. The products were separated in pure form by either column chromatography or preparative GLC. They were identified by elemental and ^1H NMR, IR, and mass spectroscopic analyses as well as by comparison with literature data (Table 2).

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