Anodic Oxidation of Carboxamides. Part II.[1] Anodic Oxidation and Pyridination of *N*-Methyl-4′-methoxybenzanilide in Acetonitrile

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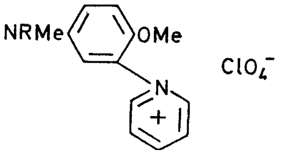
Anodic oxidation of *N*-methyl-4′-methoxybenzanilide (*N*-methyl-MBA) was investigated by cyclic voltammetry and controlled potential electrolysis at a glassy-carbon electrode in acetonitrile in the presence and absence of water or pyridine. In acetonitrile *N*-methyl-MBA showed a single anodic peak at 1.27 V *versus* the saturated calomel electrode with a peak height corresponding to that of a two-electron process. Added pyridine and/or water had no effect on the peak potential or peak height. On electrolysis of *N*-methyl-MBA in acetonitrile, *p*-benzoquinone, and *N*-methylbenzamide were mainly formed. Essentially the same results were obtained on electrolysis in the presence of added water. In the presence of excess of pyridine, electrolysis of *N*-methyl-MBA resulted in the formation of pyridinated *N*-methyl-MBA in which the pyridinium group was *meta* to the anilide nitrogen atom on the *N*-methylanisidine ring. The results were compared with those obtained on anodic oxidation of 4′-methoxybenzanilide.

We have previously reported a mechanism for the anodic oxidation of 4′-methoxybenzanilide (MBA) at a glassy-carbon electrode.[1] Studies on *N*-methyl-4′-methoxybenzanilide (*N*-methyl-MBA), which lacks a hydrogen atom on the nitrogen, were expected to afford further evidence for this mechanism. Controlled potential electrolysis of *N*-methyl-MBA in acetonitrile containing an excess of pyridine gave pyridinated *N*-methyl-MBA in which the pyridinium group was attached to a different position in the ring from that in pyridinated MBA,[1] *i.e.* 1-(3-*N*-methylbenzamido-6-methoxyphenyl)pyridinium perchlorate (I) was the sole pyridinated product identified.



(I) R = Bz
(II) R = H

We report the results of cyclic voltammetry and controlled potential electrolysis of *N*-methyl-MBA in acetonitrile with and without added water or pyridine.

RESULTS

Cyclic Voltammetry.—In acetonitrile containing 0.1M-sodium perchlorate, *N*-methyl-MBA showed a single anodic peak at 1.27 V and a small cathodic peak near 0.07 V in the reverse scan. All potentials were measured against an aqueous saturated calomel electrode (s.c.e.). The height of the anodic peak was essentially the same as that obtained with MBA under the same conditions, and corresponded to a two-electron process.[1] Typical voltammograms are shown in the Figure.† The peak potential of the anodic peak of MBA shifted gradually towards a less positive potential on addition of water, and underwent a *ca.* 100 mV

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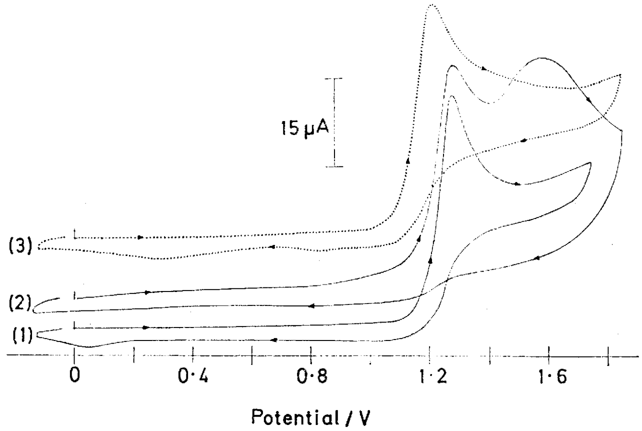
† The peak heights, especially those of the cathodic peaks, seemed sensitive to the nature of the electrode surface. A series of measurements with a particular working electrode was required to compare the results.

[1] Part I, S. Ikenoya, M. Masui, H. Ohmori, and H. Sayo, *J.C.S. Perkin II*, 1974, 571.

shift in the presence of 10% water. The effects of pyridine on the anodic peak of MBA have been reported.[1] On the other hand, the peak potential and peak height of the anodic peak of *N*-methyl-MBA were not affected by added pyridine (~1%) or water (~20%). The broad peak near 1.5 V seen in the cyclic voltammogram of *N*-methyl-MBA in the presence of pyridine (Figure) must be due to the oxidation of the pyridinated *N*-methyl-MBA (see below). The origin of the cathodic peak of *N*-methyl-MBA near 0 V is not clear, but may be ascribed to the reduction of *p*-benzoquinone (see below). Free hydrogen ion did not show a reduction wave at this potential under the experimental conditions.



Cyclic voltammogram of (1) *N*-methyl-MBA (1mM) in acetonitrile, (2) *N*-methyl-MBA (1mM) in acetonitrile containing 1% pyridine, and (3) MBA (1mM) in acetonitrile; 0.1M-$NaClO_4$, 50 mV s^{-1}

Controlled Potential Electrolysis.—The coulometric *n* value obtained on electrolysis of *N*-methyl-MBA in acetonitrile at 1.25 V varied from 2.1 to 2.8. In all cases, however, *p*-benzoquinone (>60%), *N*-methylbenzamide (>70%), a trace of benzoic acid, and methanol (>90%) were identified as the final products. No formation of protonated *N*-methyl-MBA * or benzamide was detected. The results were the same in the presence and absence of oxygen. Electrolysis of *N*-methyl-MBA in acetonitrile with added water (1—5%) gave essentially the same results but the coulometric *n* value was 2.0—2.5. An *n* value >2 may be ascribed to slow follow-up reactions of an initial oxidation product or of *p*-benzoquinone with small amounts of impurities other than water in the acetonitrile to produce an electroactive species at the applied potential. In fact the yield of *p*-benzoquinone decreased with increase in the *n* value. The current–time curve during the electrolysis was drawn out when a high *n* value was obtained. However, even when an *n* value of *ca.* 2 was obtained, the yields of *p*-benzoquinone and *N*-methylbenzamide were considerably lower than the theoretical amounts, indicating the occurrence of other reactions of the initial oxidation product to give unidentified products. *N*-Methylbenzamide itself showed no oxidation wave at up to 1.6 V in acetonitrile containing 0.1M-sodium perchlorate.

Electrolysis of *N*-methyl-MBA in acetonitrile containing 1% pyridine at 1.25 V gave an *n* value of 2.2—2.5, and pyridinated *N*-methyl-MBA (I) was identified as the final product. A cyclic voltammogram of the solution after completion of electrolysis showed a peak corresponding to the second peak of the starting *N*-methyl-MBA (*cf.* Figure). The same cyclic voltammogram was obtained when purified (I) was subjected to cyclic voltammetry under the same conditions. When (I) was hydrolysed in concentrated hydrochloric acid, 1-(3-methylamino-6-methoxyphenyl)-pyridinium perchlorate (II) and benzoic acid were produced. Details of the procedures and identification of the products are described in the Experimental section.

DISCUSSION

The formations of *p*-benzoquinone and *N*-methylbenzamide on oxidation of *N*-methyl-MBA in acetonitrile without added water may be due to hydrolysis of initial oxidation products by water unavoidably contaminating the medium, since essentially the same results were obtained on oxidation with added water. Though the exact process of anodic oxidation of *N*-methyl-MBA under these conditions is uncertain, by analogy with that suggested for the oxidation of MBA,[1] the Scheme can be proposed for the reaction. Pyridinated *N*-methyl-MBA (I) is thought to be produced *via* attack of pyridine on the dication (III). Molecular models suggest that in the dication (III) the position in the anisidine ring *ortho* to the nitrogen atom is considerably hindered by the *N*-methyl group compared with the corresponding intermediate[1] derived from MBA. This is probably why the nucleophilic attack of pyridine took place *meta* to the nitrogen atom, though the *ortho*-position should have a higher positive charge density.

$$\mathrm{BzNMe.C_6H_4OMe} \xrightarrow{-2e} \underset{\text{(III)}}{[\mathrm{BzNMe.C_6H_4OMe}]^{2+}}$$

$$\text{(III)} \overset{2H_2O}{\rightsquigarrow} \mathrm{BzNHMe} + \mathrm{O:C_6H_4:O} + \mathrm{MeOH} + 2\mathrm{H}^+$$

$$\text{(III)} \rightsquigarrow \text{unidentified products}$$

SCHEME

The peak potential of MBA shifted towards a less positive potential on addition of water, whereas that of *N*-methyl-MBA remained unchanged. Water is not a strong enough base to deprotonate the NH group in MBA under these conditions, so these results support the idea suggested previously[1] that a general base-type assistance of water at the electrode is operative in the anodic oxidation of MBA.

It is interesting to compare the present results with those reported on the anodic oxidation of aliphatic amides.[2] *NN*-Dimethylacetamide (a tertiary amide) is oxidized more easily than *N*-methylacetamide (a secondary amide) in acetonitrile, whereas in the present case the order is reversed (see Figure). In the oxidation of aliphatic amides, an electrochemical dealkylation in acetonitrile with added water has been reported, *i.e.* one-electron transfer from the lone pair of the amide nitrogen, followed by loss of a second electron and a

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* On oxidation of aliphatic amides under similar conditions, almost quantitative amounts of the starting amides were recovered in their protonated form.[2]

[2] J. F. O'Donnell and C. K. Mann, *J. Electroanalyt. Chem.*, 1967, **13**, 157.

proton from the α-carbon atom to form a carbonium ion which is hydrolysed to give the corresponding aldehyde and lower amide. *N*-Methyl-MBA however, seems to produce exclusively *N*-methylbenzamide following an initial two-electron transfer. The absence of benzamide in the solution after controlled potential electrolysis supports this view. It is difficult to explain these observations at this stage because the exact nature of the proposed dication (III) is still uncertain. Oxidation of *N*-methyl-MBA in aqueous solution seems to give different products and should provide further information on the nature of the dication. Detailed studies are in progress.

EXPERIMENTAL

Materials.—*N*-Methyl-MBA was prepared from benzoyl chloride and *N*-methylanisidine by a known method.[3] The product was subjected to column chromatography on silica gel with chloroform as eluant, and recrystallized from ethanol–water, m.p. 79—80°. MBA was from previous work.[1] Pyridine was obtained commercially and purified by distillation. Sodium perchlorate was purified as described previously.[4] Acetonitrile was distilled first from calcium hydride and then from phosphorus pentoxide after treatment by the method of Mann *et al.*[5]

Physical and spectroscopic data of compound (I) and (II)

			Elemental analysis (%)					
Compound	M.p. (°C)		C	H	N	N.m.r.[a] [δ]		I.r.[b] (ν/cm^{-1})
(I)	177—178	Found	57.3	4.6	6.6	3.42 (3 H, s)		3 120, 3 060,
		Required	57.35	4.5	6.7	3.77 (3 H, s)		1 640, 1 512
						6.8—7.6 (8 H, m)		
						8.0—8.8 (5 H, m) [c]		
(II)	174—176	Found	49.5	5.0	9.0	3.75 (3 H, s) [d]	(1)	3 430, 3 140,
		Required	49.6	4.8	8.9	6.7—7.0 (2 H, m)		3 090, 1 630,
						7.13 (1 H, d, *J* 9 Hz)		1 522
						8.0—8.9 (5 H, m) [c]		
						3.22 (3 H, s)	(2)	
						3.97 (3 H, s)		
						7.52 (1 H, d, *J* 10 Hz)		
						7.8—8.0 (2 H, m)		
						8.2—9.1 (5 H, m) [c]		

[a] The n.m.r. spectra (90 MHz) of (I) and (II)(1) were recorded in $CDCl_3$ and in MeCN, respectively, with Me_4Si as internal standard, and that of (II)(2) in D_2O–DCl (20%) with sodium 4,4-dimethyl-4-silapentanesulphonate as standard. [b] For KBr discs. [c] These signals were assigned to the pyridinium group. [d] The other signal of the methyl proton at δ *ca.* 3.4 is hidden by the strong signal of MeCN.

Apparatus.—Cyclic voltammetry and controlled potential electrolysis were carried out as described previously.[6] All voltammetric measurements were carried out at 25 ± 0.05°. U.v., i.r., and n.m.r. spectra were obtained using Hitachi 124, EPI-2, and R-20A spectrometers, respectively. Methanol formed in controlled potential electrolysis was detected as described previously using a JEOL JGC-750 gas chromatograph.[1] Analyses of *p*-benzoquinone, *N*-methylbenzamide, benzamide, and benzoic acid were carried out by liquid chromatography (l.c.) using a Waters 6000-A solvent delivery system with a U6K universal injector and a JASCO UVIDEC-1 spectrophotometer. The conditions were as follows: Bondapack C_{18}–Corasil (37—50 μ); 1/8 in × 2 ft column; water–methanol–acetic acid 87 : 10 : 3 (v/v); 1 ml min^{-1}; at 235 nm.

Controlled Potential Electrolysis.—Typical examples of the procedure are described.

(a) *Electrolysis in acetonitrile*. *N*-Methyl-MBA (24.4 mg, *ca.* 10^{-4} mol) was subjected to electrolysis in acetonitrile (50 ml) containing 0.1M-$NaClO_4$ at 1.25 V at room temperature until the current became <2% of the initial value (*ca.* 70 min). From the current–time curve 21.2 C, which corresponded to *n* 2.2, was found to be consumed. The resulting pale yellow solution was subjected to g.l.c. and l.c. Methanol (93%), *p*-benzoquinone (73%), *N*-methylbenzamide (76%), and benzoic acid (trace) were found. Benzoic acid may be produced *via* acid catalysed hydrolysis of *N*-methylbenzamide within the time scale of electrolysis.

(b) *Electrolysis in acetonitrile containing excess of pyridine*. *N*-Methyl-MBA (485.4 mg) was subjected to electrolysis in acetonitrile (100 ml) containing 1% pyridine and 0.1M-$NaClO_4$ at 1.25 V. The resulting solution was evaporated to dryness under reduced pressure and the residue was extracted with chloroform (50 ml). The chloroform was removed under reduced pressure and the residue was subjected to column chromatography on neutral alumina with acetonitrile as eluant. The yellow crystals obtained (595 mg) from the first effluent were recrystallized from ethanol to give pale yellow needles which were identified as 1-(3-*N*-methylbenzamido-6-methoxyphenyl)pyridinium perchlorate (I) by elemental analysis and i.r. and n.m.r. spectra (Table). Compound (I) was hydrolysed in concentrated HCl (*ca.* 3 h). The resulting solution was evaporated to dryness under reduced pressure and the residue was washed with ether to remove benzoic acid. The yellow crystals obtained were subjected to column chromatography on neutral alumina with acetonitrile as eluant. The orange needles obtained from the first effluent were identified as (II) (Table). When acetonitrile was added to the solution of (II) in a small amount of concentrated HCl, colourless, very hygroscopic crystals were deposited, which were identified as the dihydrochloride form of (II) from i.r. and n.m.r. spectra. The p$K_{a'}$ value of (II) (3.52 ± 0.16), determined spectrophotometrically by

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[3] E. Fröhlich and E. Wedekind, *Ber.*, 1907, **40**, 1009; T. W. Bentley and R. A. W. Johnstone, *J. Chem. Soc.* (*B*), 1971, 1804.

[4] M. Masui and H. Ohmori, *J.C.S. Perkin II*, 1972, 1882.

[5] J. F. O'Donnell, J. T. Ayres, and C. K. Mann, *Analyt. Chem.*, 1965, **37**, 1161.

[6] H. Sayo and M. Masui, *J.C.S. Perkin II*, 1973, 1640.

the method of Reeves,[7,*] supports the suggested structure. When pyridinated MBA,[1] 1-(2-benzamido-5-methoxyphenyl)pyridinium perchlorate, was similarly hydrolysed in concentrated HCl, 4-methoxy-2-pyridiniumanilinium dichloride[8] and benzoic acid were produced. The $\mathrm{p}K_{\mathrm{a}'}$ value of the former compound was found to be 1.32 ± 0.02.[8]

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[*] Compound (II) exhibited absorption maxima at 219 and 261 nm in strong acid solution, and at 241 nm in neutral or alkaline solution. Its $\mathrm{p}K_{\mathrm{a}'}$ value was determined by measuring the change in absorbance at 241 nm with change in pH.

[7] R. L. Reeves, *J. Amer. Chem. Soc.*, 1962, **84**, 3332.
[8] M. Masui and H. Ohmori, *J.C.S. Perkin II*, **1973**, 1112.