Regiospecific Anodic Pyridination of 2-Hydroxy-3-methoxy-5-methylbenzaldehyde Schiff Bases

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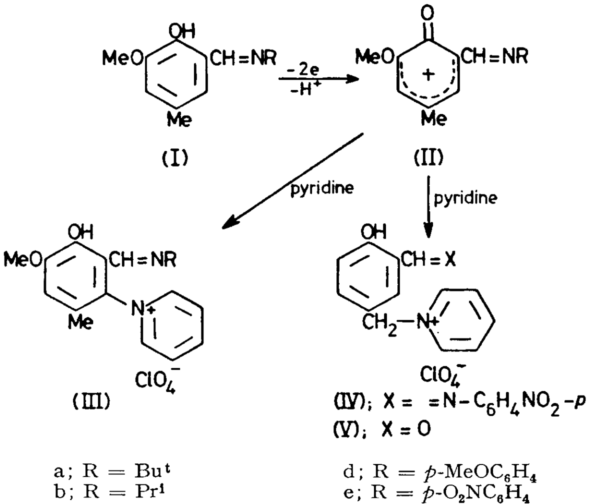
Summary Anodic oxidation of 2-hydroxy-3-methoxy-5-methylbenzaldehyde Schiff bases in acetonitrile containing an excess of pyridine results in the formation of pyridinated Schiff bases in which the pyridinium group is *meta* to the hydroxy group.

The attack of nucleophiles on anodically-generated phenoxonium ions takes place exclusively at positions *ortho* or *para* to the original hydroxy group, or at the side chain attached to these positions.[1] Even in the anodic pyridination of the highly hindered 2,4,6-tri-t-butylphenol, the nucleophile attacks at 2- and 4-positions.[2]

We report here anodic pyridination of a phenol in which pyridine attacks at a position *meta* to the hydroxy group. On cyclic voltammetry in acetonitrile (0·1 M $NaClO_4$), the first anodic peak of the title compounds (I)† was irreversible and corresponded to an apparent one-electron oxidation. Peak potentials were as follows (glassy carbon electrode, sweep rate 50 mV s^{-1}): (Ia), 0·66; (Ib), 0·67; (Ic), 0·78; (Id), 0·78; and (Ie), 0·88 V *vs.* S.C.E. In the presence of 1% pyridine, the peak current of (I) was almost doubled, and the peak potentials shifted toward less positive potentials: (Ia), 0·61; (Ib), 0·63; (Ic), 0·66; (Id), 0·73; and (Ie), 0·60 V *vs.* S.C.E. Controlled potential electrolysis of (I) was carried out in acetonitrile containing 0·1 M sodium perchlorate and 1% pyridine at a potential 50 mV more anodic than the corresponding peak potential, in a divided cell at a glassy carbon plate. A coulometric *n*-value of *ca.* 2 was obtained in every case. Compounds (IIIa—d) were the only pyridinated products isolated (yield 40—60%)‡ from the electrolysis of (Ia—d). On the other hand, electrolysis of (Ie) gave one of the expected products (IV) (30%); attack of nucleophiles on the side chain has been reported in the anodic substitution of 2,6-di-t-butyl-*p*-cresol.[3] Formation of other stable product was not detected. Electrolysis of 2-hydroxy-3-methoxy-5-methylbenzaldehyde (V), m.p. 50 °C, under the same conditions gave only (VI) (80%). Some of the physical data for the products are given in the Table. In the n.m.r. spectra of (III) the upfield shift of the azomethine



a; R = Bu^t
b; R = Pr^i
c; R = Ph
d; R = *p*-$MeOC_6H_4$
e; R = *p*-$O_2NC_6H_4$

Table. M.p.s and ^1H n.m.r. chemical shifts of the azomethine proton for the pyridinated products.

Compound	M.p./°C[a]	δ(–CH=N–)[b]
(IIIa)	230 (decomp.)	7·58 (8·44)[c]
(IIIb)	235 (decomp.)	7·85 (8·49)[c]
(IIIc)	210 (decomp.)	8·41 (8·90)[c]
(IIId)	273 (decomp.)	8·30 (8·90)[c]
(IV)	180—182	d (8·92)[c]
(VI)	158	10·32[e] (10·24)[c]

[a] Uncorrected. [b] In $(CD_3)_2SO$ with Me_4Si as internal standard; singlet. [c] The value in the parentheses represents the chemical shift of the corresponding proton in compound (I) or (V). [d] The signal is hidden under the signals due to the pyridinium group. Upon hydrolysis of compound (IV) in 10% HCl, compound (VI) was obtained. [e] Aldehyde proton.

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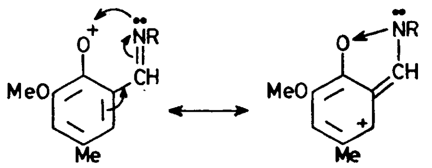
† M.p. or b.p. of compounds (I) (in °C): (Ia), 120 at 0·02 mm Hg; (Ib), 98 at 0·02 mmHg; (Ic), 67; (Id), 70; and (Ie), 173.

‡ All products were isolated by means of column chromatography on neutral alumina, and were satisfactorily characterized by i.r. and n.m.r. spectroscopy and by elemental analysis (*cf.* Table).

proton (by *ca.* 0·9 p.p.m.) compared to the chemical shift of that in (I) supports the position of the pyridinium group.

It has been shown that the anodic oxidation of Schiff bases with a hydroxy group on the *C*-phenyl ring can be regarded as a phenolic oxidation,[4,5] and hence the intermediacy of the phenoxonium ion (II) seems reasonable in the present case. The assumption that the methoxy group in (I) exerts little directing effect is supported by the fact that the anodic dimerization of Schiff bases derived from 2-hydroxy-3-methoxybenzaldehyde occurs exclusively at the position *para* to the hydroxy group.[4] Although the exact mechanism for the formation of (III) is not yet clear, participation of the lone pair of electrons on the azomethine nitrogen atom, *e.g.* in (VII), seems plausible. In the case of (Ie), the strong electron-withdrawing effect of the nitro-group reduces the basicity of the azomethine nitrogen, and the contribution of resonance such as (VII) will be diminished as in the case of (V).



(VII)

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