Nuclear *vs.* Side-chain Reactivity in the Anodic Oxidation of 2-(4-Alkylphenoxy)ethanol Derivatives. An Interesting Effect of the 2-Hydroxyethyl Group

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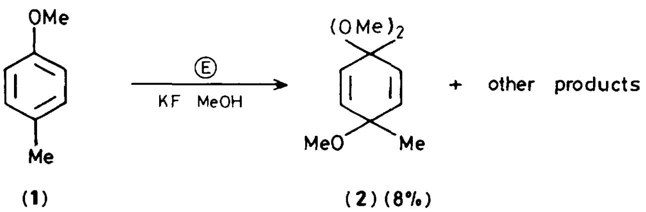
Anodic oxidation of 2-(4-alkylphenoxy)ethanol derivatives in methanol using potassium fluoride as electrolyte at constant current affords good yields of 4-alkyl-4-methoxycyclohexa-2,5-dienone acetals.

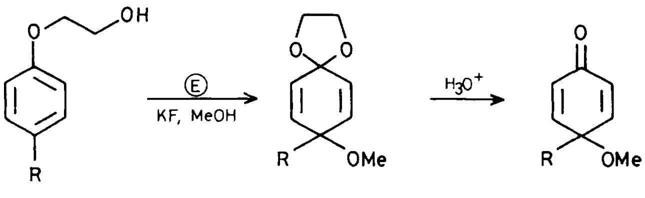
Anodic oxidation of 1,4-dialkoxy aromatic systems to afford the corresponding quinone bisacetals is an important synthetic process.[1] However, anodic oxidation of 1-methoxy-4-alkyl aromatic compounds, which would afford a facile route to the corresponding *p*-quinol (4-hydroxycyclohexa-2,5-dienone) ether acetals, often affords a mixture of nuclear and side-chain oxidation products.[2,3] The latter process has been employed as a method for the deprotection of benzyl ethers[4,5] and for the oxidation of aromatic methyl groups to aldehydes.[2,6] We report herein that the 2-hydroxyethyl side-chain dramatically favours nuclear oxidation of the 4-alkylphenyl and naphthyl ethers, (**3a**—**d**) and (**6**). These compounds afford high preparative yields of the respective acetals (**4**) and (**7**) when oxidized using platinum electrodes in a single cell apparatus at constant current (1 A).

Anodic oxidation of *p*-methoxytoluene, (**1**), in 1% methanolic potassium fluoride at 1 A and at a platinum anode afforded, at complete conversion, 4-methoxy-4-methylcyclohexa-2,5-dienone acetal (**2**) in only 8% yield (as determined by quantitative g.l.c.) in addition to other



(**1**) (**2**) (8%)

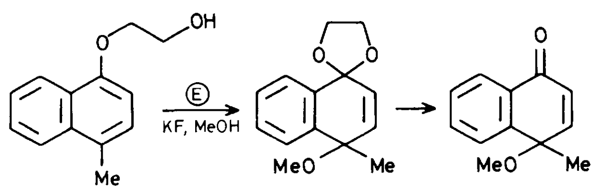
Table 1. Anodic oxidations of 2-(4-alkylphenoxy)ethanols.[a]



(**3**) (**4**) (**5**)

R^a	(4) % Yield[b]	% Current efficiency[d]	(5) % Yield
a; Me	79	28	96
b; Et	69	24	91
c; Pr^i	74	29	89
d; Bu^t	66	25	–[e]
e; $PhCH_2$	–[c]		

[a] All anodic oxidations were conducted in a single cell using a Pt sheet cathode (1.2 × 1.2 cm) and a Pt gauze anode (5 cm high × 3.5 cm diameter) at *ca.* 1 A. 2-Hydroxyethyl derivatives (**3a**—**e**) were prepared in 60—66% yields from the commercially available phenols.[8] [b] Yield of pure product for 2—5 g scale reactions after passage through neutral alumina (Activity III). [c] Complex product mixture. [d] Current efficiency at complete reaction of (**3**). [e] All attempts to hydrolyse (**4d**) with acid catalysis gave 2-(4-methoxyphenoxy)ethanol (85—90% yield).



(6) (7)(56%) (8)(90%)

products. In contrast, anodic oxidation of (**3a**) under the same conditions gave (**4a**) in 79% yield after purification of the reaction mixture on neutral alumina (Activity III). Initially, the electrolysis of (**4a**) was conducted using potassium hydroxide as electrolyte for which the current efficiency was only 7%; however, it was improved fourfold when the anodic oxidation was conducted with potassium fluoride[7] as electrolyte (see Table 1). Although the yield of (**4a**) increased to 85% if the reaction was conducted at a constant current of 0.1 A, it was more convenient for preparative purposes to use a current of 1 A. Table 1 shows that the use of the 2-hydroxyethyl side-chain with potassium fluoride as electrolyte resulted in good yields of nuclear oxidation products on a preparative scale with current efficiencies of 24—30%.

The effect of the 2-hydroxyethyl side-chain in the oxidation of a naphthalene derivative was equally dramatic. Anodic oxidation of 4-methyl-1-methoxynaphthalene in 1% methanolic potassium fluoride afforded a complex mixture of difficult-to-separate products, while anodic oxidation of (**6**) in 1% methanolic potassium fluoride gave (**7**) (56%) after a simple chromatographic separation. However, anodic oxidation of the benzyl ether (**3e**) in 1% methanolic potassium fluoride at 1 A gave a complicated mixture of products apparently arising from competing side-chain and nuclear oxidation processes.

The acetals (**4a—c**) and (**7**) can be hydrolysed to give the corresponding dienones (**5a—c**) and (**8**) in excellent yields using 10% aqueous HCl at 0 °C; no evidence for competing dienone–phenol rearrangements was detected. However, for the t-butyl derivative (**4d**), acid hydrolysis resulted in reduction to afford 2-(4-methoxyphenoxy)ethanol.

Electrode material, electrolyte, and solvent are all known to affect the ratio of side-chain to nuclear oxidation for both alkoxy and alkyl aromatic ether derivatives.[2,3] This work establishes that the 2-hydroxyethyl side-chain markedly favours a nuclear oxidation process, affording high preparative yields of protected quinol ethers.† In addition, the use of 1% methanolic potassium fluoride as a solvent–electrolyte system considerably enhances the current efficiency of the reaction, and this solvent–electrolyte system may prove useful for the anodic oxidations of other substrates.

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References

1 J. S. Swenton, *Acc. Chem. Res.*, 1983, **16**, 74, and references cited therein.
2 S. Torii and T. Siroi, *Yuki Gosei Kagaku Kyokaishi*, 1979, **37**, 914.
3 A. Nilsson, U. Palmquist, T. Pettersson, and A. Ronlán, *J. Chem. Soc., Perkin Trans. 1*, 1978, 708.
4 S. M. Weinreb, G. A. Epling, R. Comi, and M. Reitano, *J. Org. Chem.*, 1975, **40**, 1356.
5 R. F. Garwood, N.-Din, and B. C. L. Weedon, *J. Chem. Soc., Perkin Trans. 1*, 1975, 2471.
6 I. Nishiguchi and T. Hirashima, *J. Org. Chem.*, 1985, **50**, 539.
7 Methanolic potassium fluoride was one of the solvent–electrolyte systems employed in the anodic oxidation of benzene to form 3,3,6,6-tetramethoxycyclohexa-1,4-diene. R. Pistorius and H. Mallanuer, U.S. Patent 4,046,652.
8 M. G. Dolson and J. S. Swenton, *J. Org. Chem.*, 1981, **46**, 177.

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† All new compounds showed i.r. and ^1H n.m.r. spectra and exact mass measurements in agreement with the assigned structures. All compounds were colourless oils except: (**5a**), m.p. 60—62 °C; (**5b**), m.p. 32—34 °C; (**5c**), m.p. 41—43 °C; (**8**), m.p. 52—53 °C.