# Anodic Functionalisation in Synthesis. Part 1. Methoxylation of Methyl-substituted Benzene and Anisole Derivatives, and the Synthesis of Aromatic Aldehydes by Anodic Oxidation

By **Anders Nilsson, Ulf Palmquist, Tore Pettersson,** and **Alvin Ronlán,*** Organic Chemistry 2, Chemical Centre, University of Lund, P.O. Box 740, S-220 07 Lund 7, Sweden

The anodic oxidation in methanol of a series of alkylanisoles and hydroquinone ethers, and of p-xylene has been studied. It was established that the initial step in the product formation always involves direct anodic oxidation of the aromatic compound to the corresponding cation radical. If the electrolysis is conducted under conditions where formation of methoxyl radicals also takes place (platinum anode, supporting electrolyte NaOMe) nuclear methoxylation dominates. Substitution in the nucleus of the aromatic compound presumably occurs either by nucleophilic attack of a methoxide ion on the anodically generated cation radical or by a coupling reaction between the latter and an anodically generated methoxyl radical. If the electrolysis is conducted under conditions where formation of methoxyl radicals does not take place (carbon or platinum anode with supporting electrolyte LiBF$_4$) side-chain oxidation of p-alkylanisoles and p-xylene, with the formation of benzyl ethers, benzaldehyde dimethyl acetals, or ortho-esters of benzoic acids becomes important. This side-chain oxidation occurs via nucleophilic attack of methanol on a benzyl cation formed by deprotonation–anodic oxidation of the initially formed cation radical. Phenol ether cation radicals without p-alkyl substituents under these conditions either dimerise or undergo nuclear methoxylation via nucleophilic attack of methanol on the cation radical.

IN a previous publication[1] we described the anodic oxidation in methanol of a series of simple phenols. Both dimeric and methoxylated products were isolated. We presented evidence that the dimers were formed

all, for phenol ether cation radicals without a hydrogen-containing substituent, deprotonation is not likely to occur as this would lead to the formation of a very high energy carbene free-radical. Further anodic oxidation
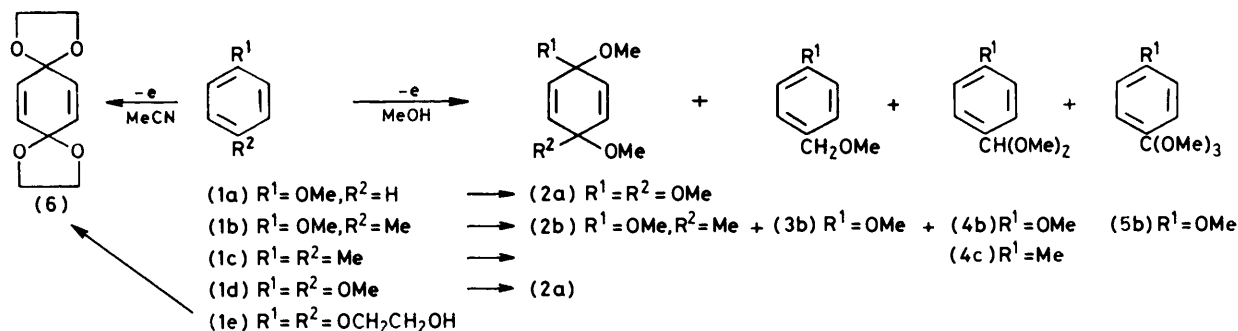
SCHEME 1

mainly by coupling of anodically generated phenoxy-radicals while methoxylation occurred by nucleophilic attack of methanol on a phenoxylium ion generated by anodic oxidation of the corresponding phenoxy-radical. Electronically, phenols and their methyl ethers differ little from each other, and this is reflected in the similarity of the *reversible* oxidation potentials[2] or gas-phase ionisation potentials[3] of phenols and phenol ethers. For both types of compound the initial step in the anodic oxidation must therefore be the formation of a cation radical. Phenol cation radicals are very rapidly deprotonated to the corresponding phenoxy-radicals.[2] However for the phenol ether cation radicals the situation is more complicated.[4,5] First of

is not likely to occur as long as the starting phenol ether is present, since phenol ether cation radicals are oxidised at an anodic potential *ca.* 0.5—1.0 V higher than the corresponding phenol ether.[6] For phenol ether cation radicals with an α-hydrogen-containing substituent, loss of a proton from the side chain with formation of an 'aromatic,' benzylic radical might occur. This benzylic radical in its turn is presumably more easily oxidised than the starting phenol ether and may be oxidised further as soon as it is formed giving a benzyl cation. Thus it should be possible to understand the reactivity of methoxy-substituted aromatic cation radicals and methoxy-substituted benzyl cations from a study of the

[1] A. Nilsson, U. Palmquist, T. Pettersson, and A. Ronlán, preceding paper.
[2] O. Hammerich, V. D. Parker, and A. Ronlán, *Acta Chem. Scand.,* 1976, **B30**, 891.
[3] T. Kobayashi and S. Negakura, *Bull. Chem. Soc. Japan,* 1974, **47**, 2563.
[4] For a review of previous work see N. L. Weinberg, ' Techniques of Electro-organic Synthesis,' Part I, p. 237; vol. V. of ' Techniques of Organic Chemistry,' ed. A. Weissberger, Wiley–Interscience, New York, 1974.
[5] A. J. Bard, A. Ledwith, and H. J. Shine, *Adv. Phys. Org. Chem.,* 1976, **13**, 155.
[6] A. Ronlán, J. Coleman, O. Hammerich, and V. D. Parker, *J. Amer. Chem. Soc.,* 1974, **96**, 845.

anodic oxidation of phenol ethers, and we therefore initiated the present study. In particular we wanted to know if it is possible (*a*) to use phenol ethers instead of

type of product obtained on anodic oxidation in methanol is shown in Schemes 1 and 2 and the actual yields and experimental conditions are given in Tables 1 and 2.
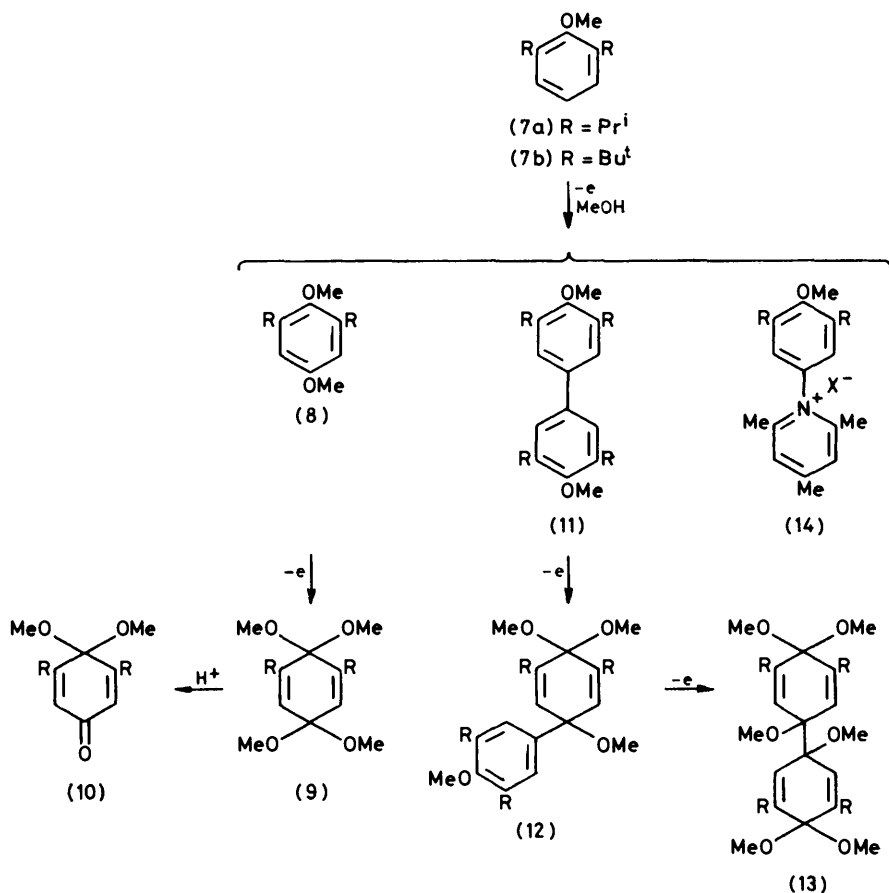
SCHEME 2

phenols[1] as substrates for synthesis of quinones or quinone acetals by anodic oxidation in methanol, and (*b*) to prepare aromatic aldehydes or carboxylic acids by anodic oxidation of alkyl-substituted phenol ethers. In order to compare the reactivity of methoxy-substituted with that of alkyl-substituted aromatic cation radicals, *p*-xylene was also included in this study. Previously a number of studies of the anodic oxidation of aromatic compounds have been carried out.[4,5] Of particular interest are the studies of the anodic oxidation of *p*-methylanisole[7] and of 1,4-dimethoxybenzene.[8]

RESULTS

Anisole (1a), *p*-methylanisole (1b), *p*-xylene (1c), 1,4-dimethoxybenzene (1d), hydroquinone bis-(2-hydroxyethyl) ether (1e), 2,6-di-isopropylanisole (7a), and 2,6-di-t-butylanisole (7b) were chosen as model compounds. The

Current–potential curves were measured for the various anode–electrolyte combinations used (see Tables 1 and 2). The results are given in the Figure.

DISCUSSION

Mechanisms of the Methoxylation Reactions.—The results in the Figure, the oxidation experiment no. 10 (Table 1), and similar results for the other anode–electrolyte combinations show clearly that direct anodic oxidation of the substrate is involved in product formation.* The results of our anodic methoxylations (Tables 1 and 2) can be rationalised in terms of the usual mechanisms,[4,5] *i.e.* nuclear-substituted products are formed *via* path A in Scheme 3 and side-chain-substituted products *via* path C. With *p*-methylanisole (1b) and *p*-xylene (1c) both nuclear [product (2)] and side-chain methoxylation [products (3)—(5)] occur. Nuclear methoxylation only occurs when methoxide ions are present in the electrolyte, in accordance with the

* The argument is the same as in the case of the anodic oxidation of phenols in methanol.[1]

[7] K. Yoshida, M. Shigi, and T. Feuno, *J. Org. Chem.*, 1975, **40**, 63.

[8] N. L. Weinberg, D. H. Marr, and N. Wu, *J. Amer. Chem. Soc.*, 1975, **97**, 1499.

observation, from previous studies of anodic acetoxylations [9] and cyanations,[10] that only strong nucleophiles react sufficiently fast with cation radicals to compete

B below. The cyclohexadienyl radical (16) which is shown as an intermediate in path A * is also believed to be an intermediate in the corresponding homolytic,

TABLE 1

Constant-current anodic oxidation of anisole (1a), 4-methylanisole (1b), p-xylene (1c), 1,4-dimethoxybenzene (1d), and hydroquinone bis(2-hydroxyethyl) ether (1e) [a]

Experiment no.	[Substrate]/ M	Anode–Cathode [b]	[Supporting electrolyte]/M	[Base]/ M	Current/ (mA cm⁻²)	Potential/ (V) [c]	Q/F mol⁻¹	Conversion (%)	Products, yields [%] [d]	(2)/ [(3) + (4)]
1	(1a), 0.15	Pt–W	NaOMe, 0.30		20	2.7—3.1	16	100	(2a), [34]	
2	(1b), 0.15	Pt–W	NaOMe, 0.15		6	2.1—2.3	4	79	(2b), [80]; (3b), (14)	5.7
3	(1b), 0.15	Pt–W	NaOMe, 0.15		20	3.0—3.4	3.8	87	(2b), [35]; (3b), [21]; (4b), [22]	0.8 0.8
4	(1b), 0.15	Pt–W	NaOMe, 0.60		20	2.5—2.9	3.8	71	(2b), [69]; (3b), [15]	4.6
5	(1b), 0.15	Pt–W	LiBF₄, 0.18	NaOMe, 0.15	6	1.6—2.1	4.0	100	(2b), [44]; (3b) [3]; (4b), [25]	1.6
6	(1b), 0.15	Pt–W	LiBF₄, 0.18	NaOMe, 0.15	6	1.6—1.8	3.0	87	(2b), [56]; (3b), [16]; (4b), [8]	2.3
7	(1b), 0.15	Pt–W	LiBF₄, 0.18	2,6-lutidine 0.15	6	1.9—2.0	1.6	65	(2b), [5]; (3b), [40]; (4b), [16]	0.09
8	(1b), 0.9	Pt–W	NaOMe 0.15		6	2.1—2.4	3.0	69	(2b), [66]; (3b), [15]	4.4
9	(1b), 0.16	Pt–W	NaOMe, 0.62		20	1.9—2.3	5.6	100	4-Methoxy-4-methylcyclohexa-2,5-dienone [52] [g,h]	
10	(1b) 0.15	C–Ni	NaOMe 0.15		6	1.4—1.5	2.0	5		
11	(1b), 0.15	C–Ni	NaOMe 0.15		45	4.3—4.5	2.0	62	(2b), [3]; (3b), [28]; (4b), [46]	0.04
12	(1b), 1.5	C–W	NaOMe, 0.2		45	3.9—4.1	4.5	100	(4b), [66] [g]	
13	(1c), 2.1	C–W	LiBF₄, 0.47	NaOMe 0.2	45	2.9—3.1	4.0	100	(4c), [57] [g]	
14	(1d), 0.15 [e]	Pt–C	LiBF₄, 0.1	2,6-lutidine, 0.17	6	1.3	3.5	100	(2a), [54] [g]	
15	(1e), 0.15 [f]	Pt–C	LiBF₄ 0.1	2,6-lutidine, 0.17	2		2.2	90	(6), [67] [g]	

[a] For more details see Experimental section. [b] Pt–W refers to a cylindrical platinum foil anode (50 cm²) and a tungsten wire cathode (1.6 cm²); C–Ni to a graphite (AUC-graphite) rod anode (22 cm²) and a nickel wire cathode (2.8 cm²); C–W to the same graphite anode and a tungsten wire (1.6 cm²) cathode; Pt–C to the above mentioned platinum anode in combination with a graphite (AUC) rod (7 cm²) cathode. [c] In all the experiments the anode potential was measured continuously relative to a s.c.e.-LiCl (see ref. 1). [d] The yields are based on converted starting material. The conventional chemical yield based on the total amount of starting material is obtained by multiplication of this yield by the conversion. The yields here refer to products actually isolated and purified. [e] The electrolysis was carried out in MeOH–MeNO₂ (1 : 1). [f] The electrolysis was conducted in MeNO₂. If the electrolysis is carried out without added base (2,6-lutidine) the monoethylene acetal of p-benzoquinone is obtained. If the electrolysis is conducted in MeOH–NaOMe the ethylene acetal of 4-(2-hydroxyethoxy)-4-methoxycyclohexa-2,5-dienone is obtained (see ref. 19). [g] This experiment is described in detail in the Experimental section. [h] (2b) was hydrolysed to 4-methoxy-4-methylcyclohexa-2,5-dienone during work-up.

with deprotonation (with the solvent or the nucleophile as base). The nucleophilic reaction of methanol, 2,6-lutidine, or sym-collidine with (1b)⁺˙ or (1c)⁺˙ is not sufficiently fast to compete with deprotonation to the benzyl radical. The effect of additives (LiBF₄) and electrode material (change from platinum to graphite) on the nuclear/side-chain methoxylation value is accounted for by their effect on [MeO]⁻ in the diffusion layer as described in detail in the discussion of mechanism

aromatic substitution of (1b) [or (1c)] with a methoxyl radical (MeO˙).† However, the exclusive formation of p-methoxylated products found in our anodic methoxylation experiments (Tables 1 and 2) and the ortho : meta : para ratios reported by other research groups [4-8] are the same as expected for the corresponding electrophilic, aromatic substitution with the methoxylium ion (MeO⁺) and quite different from the ortho : meta : para ratio expected for a homolytic, aromatic substitution with MeO˙.[12] The same is generally true for all the anodic substitutions of aromatic compounds which are believed to follow path A in Scheme 3.[4,5,9] This is by

* This is a formal presentation; the electron transfer giving the cation (17) could very well take place before the new C–O bond [and hence (16)] is fully formed.

† No such substitutions with MeO˙ have actually been reported. However, it seems reasonable that substitutions with methoxyl radicals should be quite similar to the corresponding hydroxylations with hydroxyl radicals, a reaction which has been studied in great detail.[11] The hydroxyl radical is more electrophilic than the methoxyl radical and polar effects therefore are expected to be more important in homolytic hydroxylations than in homolytic methoxylations.

[9] L. Eberson and K. Nyberg, Adv. Phys. Org. Chem., 1976, 12, 1.
[10] S. Andreades and E. W. Zahnow, J. Amer. Chem. Soc., 1969, 91, 4181.
[11] E. S. Fendler and J. H. Fendler, Progr. Phys. Org. Chem., 1970, 7, 229.
[12] M. J. Perkins in ' Free Radicals,' ed. J. K. Kochi, vol. II, p. 231, Wiley-Interscience, New York, 1973.

no means an argument against mechanism A, as polar effects should be much more important in a reaction between a cation radical and an anion (mechanism A) than

Anisole	Poten- tial V [b]	Q/F mol^{-1}	Conver- sion (%)	Products, [yields (%)]	D/M [c]
(7a)	1.73	5.0	100	(9a) [18]; (10a) [11]; (14a) [37]; (12a) [6]; [13a] [28]	0.5
(7a)	2.20	4.0	100	(9a) [10]; (10a) [6]; (14a) [33]; (12a) [12]; (13a) [39]	1.0
(7b)	2.2	4.0	100	(9b) [23]; (14b) [12]; (12b) [2]	0.06

[a] For further details see Experimental section. [b] Measured relative to a silver wire as described in ref. 1. [c] D is the sum of the yields of dimeric products and M is the sum of the yields of methoxylated, or base-substituted, monomeric products (see text).

in a reaction between a neutral, aromatic molecule and a free radical (homolytic substitution). That is, in mechanism A the ratio of the rates of *ortho*-, *meta*-, and

phile). The relative stability of the isomeric cyclo-hexadienyl radicals (16) is of no consequence as these radicals are oxidised further at the anode as soon as formed, so that there is no equilibration between these isomers. In a homolytic substitution the *ortho* : *meta* : *para* ratio is affected both by the rate of initial attack (maximum orbital overlap) and by the relative stability of the isomeric cyclohexadienyl radicals, as rapid equilibration can take place leading to increase of the amount of the most stable isomer.[13] Oxidation of the cyclohexadienyl radical (16) gives the cation (17). In general the relative stability of the *ortho*-, *meta*-, and *para*-isomers of this cation is reflected in the relative yields of the *ortho*-, *meta*-, and *para*-substituted product [9] and it is possible that a thermodynamic equilibrium is established between the various isomers through rapid carbocation rearrangements.

The variation in the ratio between nuclear and side-chain substitution observed for compound (1b) in this and other similar studies can also be rationalised in terms of mechanism B (Scheme 3) involving reaction between a cation radical (15) and a methoxyl radical formed by oxidation of the methoxide ion. The results
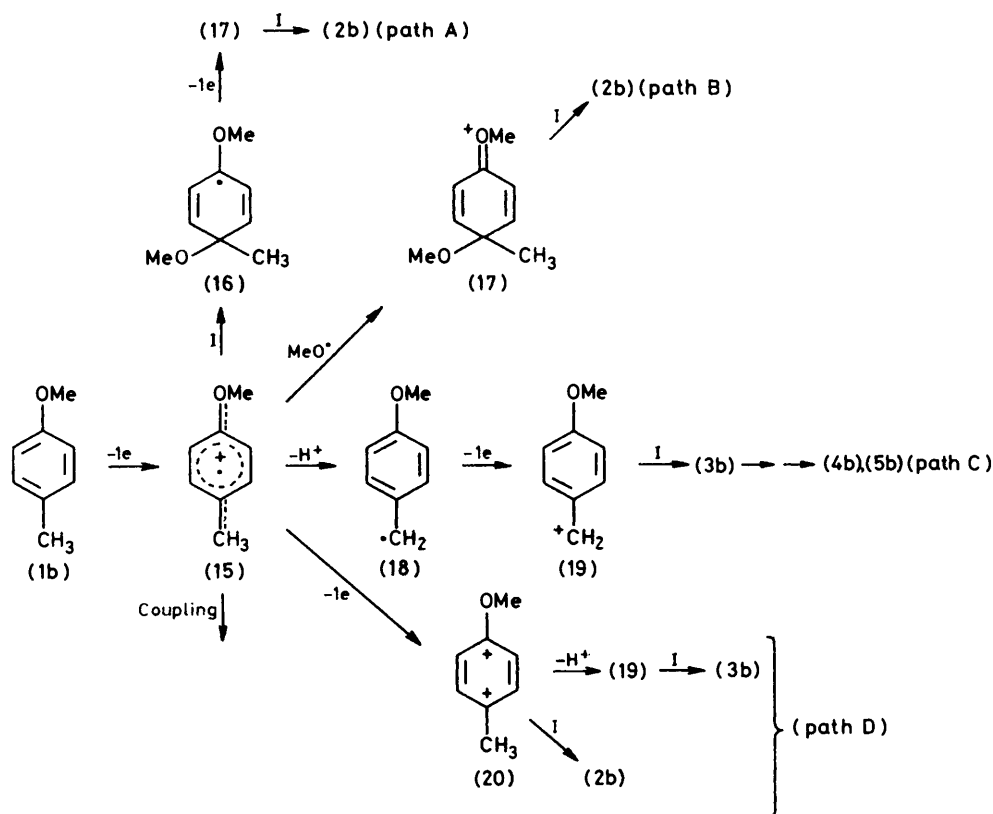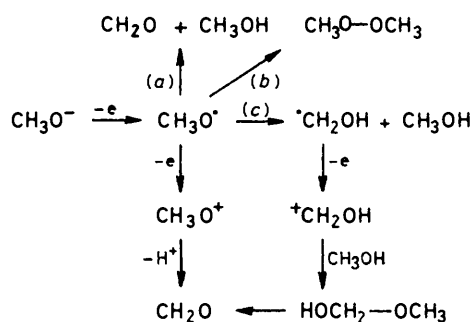

SCHEME 3

para-attack is mainly determined by the charge distribution in the cation radical (nucleophilic attack at the positions which give maximum overlap between the lowest unoccupied molecular orbital of the cation radical and the highest occupied molecular orbital of the nucleo-

in the Figure and Table 1 clearly show that a high nuclear/side-chain substitution value is only observed when oxidation of methoxide ions occurs. The initial

[13] M. K. Eberhardt and M. Yoshida, *J. Phys. Chem.*, 1973, **77**, 589.

electron transfer from the methoxide ion to the anode must involve one of the electrons of the non-bonding orbital and therefore the primary intermediate should be a methoxyl radical which can react further as shown in Scheme 4. Formaldehyde could be detected by n.m.r.

$$CH_2O + CH_3OH \quad CH_3O-OCH_3$$

$$CH_3O^- \xrightarrow{-e} CH_3O^{\bullet} \xrightarrow{(c)} {}^{\bullet}CH_2OH + CH_3OH$$

$$CH_3O^+ \quad {}^+CH_2OH$$

$$CH_2O \xleftarrow{} HOCH_2-OCH_3$$

SCHEME 4 (a) Disproportionation; (b) dimerisation; (c) proton abstraction

when oxidation of methoxide ion had occurred. In view of this it seems reasonable to invoke methoxyl radicals in the reaction leading to a nuclear-substituted product. The fact that no methoxylation of the aromatic substrate occurs when the oxidation is carried out at a potential where only the methoxide ion is discharged shows that the cation radical (15) must be involved in product formation. The activation energy for the reaction between a cation radical such as (15) and a methoxyl radical is expected to be very small and the reaction rate should be diffusion-controlled.[14] The transition state involved in the formation of (17), which is the same as for the corresponding electrophilic substitution with MeO^+ explains the isomer distribution very well. The formation of nuclear-substituted products can also be rationalised very well in terms of mechanism B. The spin density in a cation radical such as (15) is low at the side-chain carbon and high at the 1-, 2-, and 4-positions of the ring, i.e. coupling with another radical leads to substitution in the nucleus as observed in the oxidations on a platinum anode in the $MeOH-MeO^-$ electrolyte. The effects of adding $LiBF_4$ or changing the anode from platinum to graphite on the nuclear/side-chain substitution value [oxidation of (1b) and (1c)] can also be explained by mechanism B. In the presence of $LiBF_4$ a large part of the current to the anode is carried by the BF_4^- ions; i.e. less oxidation of MeO^- occurs, leading to a lower concentration of methoxyl radicals in the diffusion layer and hence more product formation via paths A and C.

Aromatic compounds are strongly adsorbed on graphite and displace $MeOH$ and MeO^- from the surface of a graphite anode, thus inhibiting the oxidation of MeO^- to methoxyl radicals. However, this effect is probably restricted to the surface and the concentration of MeO^- (and $MeOH$) outside the double layer should not be much affected. Therefore, we do not think that mechanism A explains satisfactorily the effects of going from a platinum to a graphite anode.

The homolytic hydroxylation of aromatic compounds with hydroxyl radicals is generally believed to be diffusion-controlled.[11] By analogy one might expect that the corresponding reaction with methoxyl radicals also should be diffusion-controlled. However, our finding that no methoxylation occurs below the discharge potential of the aromatic compound seems to indicate that this is not the case [even if the other possible reactions (Scheme 4) of the methoxyl radical are considered].

To summarise, we believe that when the anodic methoxylations are carried out under conditions where methoxide ions are oxidised to methoxyl radicals ($MeOH-MeO^-$ electrolyte, platinum anode) nuclear methoxylation products are formed via path B (Scheme 3). If the conditions are such (carbon anode and a supporting electrolyte other than a methoxide salt) that no or little formation of methoxide radicals occur,
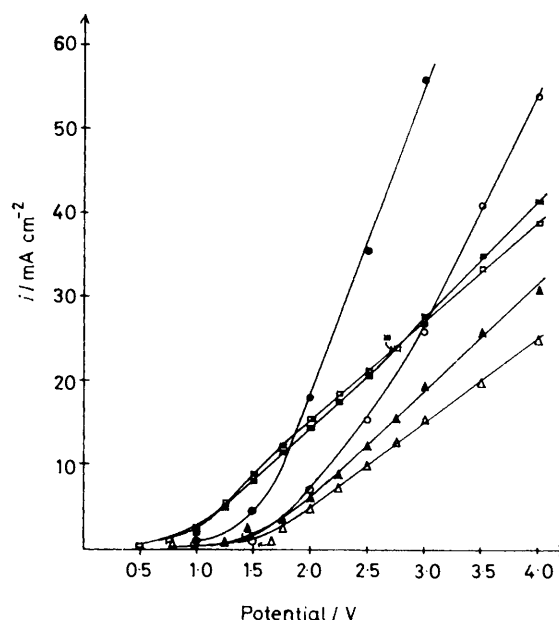
Current–potential curves for the various electrode–electrolyte combinations used in this study. All measurements at 10 °C, with $NaOMe-MeOH$ (0.15M) as solvent. The reference electrode was the standard calomel electrode and the cell used is as in experiments 1—8 in Table 1. ($\triangle$) Platinum anode (50 cm²), tungsten cathode (1.6 cm²). ($\blacktriangle$) As the previous experiment with p-methylanisole (0.15M) added. ($\bigcirc$) As the first experiment with $LiBF_4$ (0.18M) added. ($\bullet$) As the previous experiment with p-methylanisole (0.15M) added. ($\square$) Carbon anode (22 cm²), nickel cathode (2.8 cm²). ($\blacksquare$) As the previous experiment with p-methylanisole (0.15M) added. In all experiments the measurements were started at 4.0 V anodic potential and 30 s was allowed between each measurement

p-methylanisoles or methylaromatic compounds are mainly methoxylated in the side chain via path C.*

A similar effect of supporting electrolyte and electrode

* The oxidations of compounds (7a) and (7b) with no p-substituent were not carried out with MeO^- present. Therefore, the p-methoxylated products observed in these cases are probably formed via mechanism A.

14 L. Eberson, J.C.S. Chem. Comm., 1975, 826.

material on the nuclear : side chain acetoxylation ratio as observed in our methoxylations has been found in anodic acetoxylations of alkylbenzenes.[15,16] The fact that a path similar to C (leading to side-chain acetoxylation) dominates in the absence of acetate ions in the diffusion layer can be explained by assuming that only the radical-cation–radical coupling similar to B (Scheme 3) is fast enough to compete with path C. This is further supported by the finding that oxidation of alkylaromatic compounds with manganese(III) or cobalt(III) acetate in acetic acid gives side-chain acetoxylated products almost exclusively,[5] even in the presence of acetate ions. In the oxidation of alkylaromatic compounds with cobalt(III) trifluoroacetate in trifluoroacetic acid (TFA), little side-chain oxidation occurs (dimerisation appears

(see Table 2). It is therefore likely that the methoxylated products observed in these oxidations (Scheme 2) are formed by nucleophilic attack of MeOH on the anodically formed cation radicals and then further oxidation and methoxylation (as path A in Scheme 3). The lutidinium and collidinium salts (14) are probably formed in a similar way. The fact that high yields of the latter compounds are obtained shows that 2,6-lutidine and *sym*-collidine are either much better nucleophiles than methanol or are adsorbed on the anode surface, since the methanol concentration in these oxidations is far higher than the concentration of these bases.

Mechanism of Formation of Dimers.—The dimeric products (11), (12), and (13) must be formed by initial coupling of the cation radicals from (7a) and (7b).
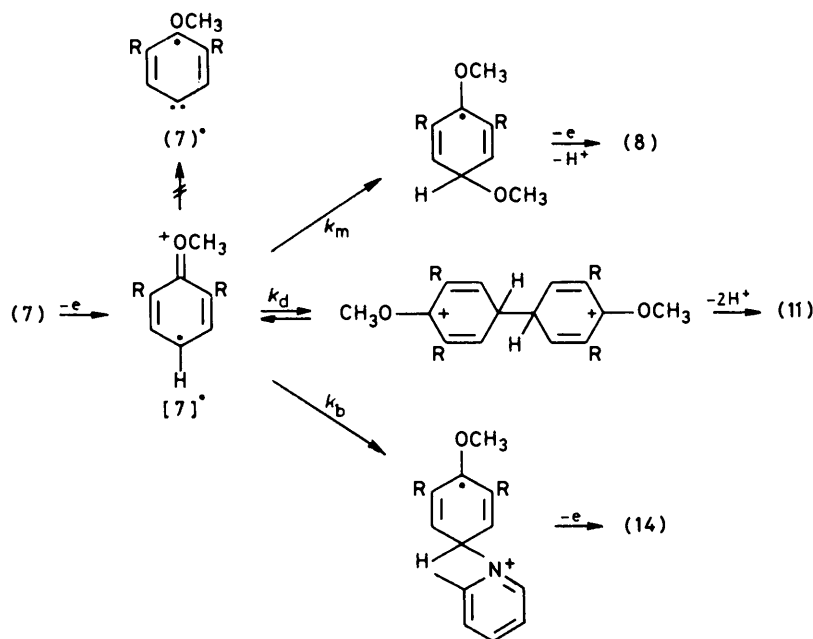
SCHEME 5

to be the principal reaction).[17] In this medium the deprotonation step in mechanism C is much slower than in acetic acid and various coupling reactions of the cation radical can occur.

So far the mechanisms D (Scheme 3) involving two consecutive one-electron transfers followed by nucleophilic attack (EEC mechanism) or by deprotonation and nucleophilic attack (EECC mechanism) have not been considered, since the oxidation potential of the cation radical (15) is 0.5—1.0 V more anodic than that of the starting material. These mechanisms therefore can only be of importance at high potential.*

The anodic oxidations of 2,6-substituted anisoles were carried out under conditions where little or no oxidation of methanol occurs and where no methoxide was present

---

* In some of the oxidations the measured potential was >2 V and formation of (20) might occur. For (20) both side-chain methoxylation (by deprotonation and substitution) and nuclear methoxylation (by substitution followed by deprotonation) should be possible.

Assuming that the value of D/M, where D is the sum of the yields of dimeric products [(11), (12), and (13)] and M the sum of base-substituted (14) and methoxylated, monomeric products [(8), (9), and (10)] is equal to the quotient of the rate of dimerisation of (7)[+] (rate constant k_d) and the sum of the rates of reaction of (7)[+] with methanol (rate constant k_m) and with the pyridinium base (rate constant k_b) we get:

$$D/M = (k_d[(7)^{+\cdot}]^2)/(k_m[MeOH][(7)^{+\cdot}] + k_b[Base][(7)^{+\cdot}])$$
$$D/M = (k_d[(7)^{+\cdot}])/(k_m[MeOH] + k_b[Base])$$

In this expression it is only the cation radical concentration $[(7)^{+\cdot}]$ that should be dependent on the oxidation potential. This is expected to increase with increasing

[15] C. Magnusson, B. Olofsson, and K. Nyberg, *Chemica Scripta*, 1971, **1**, 1.
[16] L. Eberson and K. Nyberg, *Acta Chem. Scand.*, 1975, **B29**, 168.
[17] J. K. Kochi, R. T. Tang, and T. Bernath, *J. Amer. Chem. Soc.*, 1973, **95**, 7114.

potential and the D/M value should also increase with increasing potential; this is found to be the case (Table 2). In our study[1] of the anodic oxidation of 2,6-disubstituted phenols in methanol the opposite dependence of the corresponding D/M value on the potential was observed. This further supports the formation of the phenolic dimers observed in that study by coupling of phenoxyl radicals formed by deprotonation of the phenol cation radicals.

Synthetic Applications.—From Table 1 it can be seen that the same products in approximately the same yields are obtained if the concentration of the starting material is increased ten-fold (experiments 2,8 and 11,12). All the experiments in Table 1 are therefore preparatively significant. Nuclear methoxylation converts anisole into *p*-benzoquinone bis(dimethyl acetal) (2a) in 34% yield (experiment no. 1). Compound (2a) can be converted into *p*-benzoquinone by acid catalysis, and into 1,2,4-trimethoxybenzene by treatment with boron tribromide in methanol.[8] The current yield is very low. However no attempts were made to optimise the yields and we believe that both the current yield and the chemical yield can be improved considerably. In the present experiment 66% of the starting material is not accounted for. There is probably some coupling with formation of 4,4'-dimethoxybiphenyl, and *ortho*-methoxylation with formation of catechol dimethyl ether. These products are further methoxylated to (13; R = H) and to the bis(dimethyl acetals) of *o*-benzoquinone and monomethoxybenzoquinone respectively.[8] However, no attempts were made to isolate these in the present study.

By simple change of anode material and supporting electrolyte, *p*-methylanisole can be methoxylated selectively in the nucleus or in the side chain. With a platinum anode and NaOMe as supporting electrolyte, (1b) is converted into methoxy-4-methylcyclohexa-2,5-dienone dimethyl acetal (2b) in 52% yield (isolated as 4-methoxy-4-methylcyclohexa-2,5-dienone). The yields given here are based on the total amount of starting material.

In our previous study of the anodic hydroxylation[18] and methoxylation[1] of phenols, phenol was oxidised (in sulphuric acid on a lead dioxide anode) to *p*-benzoquinone in 68% yield and (in methanol on a graphite anode) to *p*-benzoquinone dimethyl acetal in 46% yield. Hydroxylation of *p*-cresol[18] gave 4-hydroxy-4-methylcyclohexa-2,5-dienone in 51% yield and methoxylation[1] gave 4-methoxy-4-methylcyclohexa-2,5-dienone in 45% yield.

Synthetically the side-chain oxidations of the alkyl aromatic compounds are the most interesting and the procedure in experiments 12 and 13 (Table 1) appears to be generally useful for the conversion of alkylaromatic compounds or alkylmethoxyaromatic compounds into aldehydes or carboxylic acids.* Anodic side-chain

* The aldehyde acetals (4) on anodic oxidation in methanol give the orthoesters (5).

[18] A. Nilsson, A. Ronlán, and V. D. Parker, *J.C.S. Perkin I*, 1973, 2337.

oxidations are not observed in the electrolyses of the alkylphenols corresponding to the alkylanisoles studied here.[18] This illustrates a fundamental difference between cation radicals derived from phenols and those from phenol ethers. Another noteworthy difference between phenols and phenol ethers is the absence of *ortho*-methoxylated products in the anodic methoxylation of 2,6-substituted phenol ethers. The corresponding phenols give small amounts of *ortho*-methoxylated products.

EXPERIMENTAL

The analytical and electrochemical instrumentation and the electrolysis cells used in this study are described in the preceding paper.[1] Compounds (1a—d) were commercial samples and the phenol ethers (1e) and (7a, b) were prepared by alkylation of the corresponding phenols as described in the literature.[19, 20]

Anodic Oxidation of Anisole (1a). *Electrosynthesis of* p-*Benzoquinone Bis(dimethyl Acetal)* (2a) (*Experiment 1, Table 1*).—Anisole (1 g) was dissolved in methanol (60 ml) containing sodium methoxide (1 g) and subjected to constant-current electrolysis as described in Table 1. The temperature of the electrolyte was kept constant at 10 °C by external cooling. When 15 000 C had been passed through the cell the electrolysis was interrupted and the electrolysis mixture was poured into water containing CH_2Cl_2 (50 ml). The CH_2Cl_2 phase was separated. The aqueous phase was extracted a further four times with CH_2Cl_2 (40 ml). The combined extracts were washed once with water, dried (Na_2SO_4), and evaporated to dryness at reduced pressure. The yield of (2a) was determined from the n.m.r. spectrum of this crude product using nitromethane as internal, analytical standard. The product was identified by comparison with an authentic sample of (2a) prepared as described in the literature[21] (yield 34%).

Anodic Oxidation of p-*Methylanisole* (1b). *Electrosynthesis of* 4-*Methoxy*-4-*methylcyclohexa*-2,5-*dienone* (*Experiment 9, Table 1*).—*p*-Methylanisole (10 g) was dissolved in methanol (500 ml) containing sodium methoxide (16.8 g) and subjected to constant-current electrolysis at a platinum anode (see Table 1) (electrolysis temperature 10 °C). When 44 500 C had been passed the electrolysis was interrupted and water (350 ml) was added to the electrolyte, which was extracted with CH_2Cl_2 (1 × 150 ml and 3 × 50 ml). Saturated, aqueous sodium hydrogen sulphite (100 ml) was added to the combined CH_2Cl_2 extracts and after 15 min of stirring the organic phase was separated, washed with water, and evaporated to dryness at reduced pressure. Recrystallisation of the residue from light petroleum at −15 °C gave 4-methoxy-4-methylcyclohexa-2,5-dienone (5.3 g), m.p. 58—60 °C (lit.,[2] 62—63 °C). From the mother liquor a further 0.6 g of the dienone was isolated by chromatography on a carbon–Celite[1] column (total yield 5.9 g, 52% based on starting material).

Electrosynthesis of p-*Anisaldehyde Dimethyl Acetal* (4b) (*Experiment 12, Table 1*).—*p*-Methylanisole (10 g) was dissolved in methanol (45 ml) containing sodium methoxide (0.5 g) and subjected to constant-current electrolysis at a

[19] P. Margaretha and P. Tissot, *Helv. Chim. Acta*, 1975, **58**, 93.

[20] N. Kornblum and R. Seltzer, *J. Amer. Chem. Soc.*, 1961, **83**, 3668.

[21] B. Belleau and N. L. Weinberg, *J. Amer. Chem. Soc.*, 1963, **85**, 2525.

carbon anode (see Table 1) (electrolysis temperature 10 °C). When 35 200 C had been passed the electrolysis was interrupted and the electrolysis mixture was evaporated to dryness at reduced pressure. The residue was triturated with ether. The ether extract was filtered through neutral alumina. Evaporation of the filtrate followed by distillation gave (4b) (9.9 g, 66%), b.p. 129—129.5 °C (17 mmHg) [lit.,[22] 103 °C (3 mmHg)].

Anodic Oxidation of p-*Xylene* (1c). *Electrosynthesis of* p-*Methylbenzaldehyde Dimethyl Acetal* (4c) (*Experiment* 13, *Table* 1).—p-Xylene (10 g) was dissolved in methanol (45 ml) containing sodium methoxide (0.5 g) and lithium tetrafluoroborate (2 g) and subjected to constant-current electrolysis at a carbon anode (see Table 1) (electrolysis temperature 10 °C). When 37 000 C had been passed the electrolysis was interrupted and the mixture was poured into saturated, aqueous sodium hydrogen carbonate (150 ml). This solution was extracted four times with CH_2Cl_2. The combined CH_2Cl_2 extracts were washed once with saturated sodium hydrogen carbonate solution, and the CH_2Cl_2 was distilled off through a short column. Distillation of the residue through the same column afforded (4c) (9.0 g), b.p. 105—106 °C (20 mmHg) [lit.,[23] 99—100 °C, (15 mmHg)] (yield 57% based on starting material).

Anodic Oxidation of 1,4-*Dimethoxybenzene* (1d). *Electrosynthesis of* p-*Benzoquinone Bis(dimethyl Acetal)* (2a) (*Experiment* 14, *Table* 1).—1,4-Dimethoxybenzene (1.16 g) was dissolved in methanol–acetonitrile (1 : 1; 54 ml) containing lithium tetrafluoroborate (0.5 g) and 2,6-lutidine (1 ml) and subjected to constant-current electrolysis at a platinum anode (see Table 1) (electrolysis temperature 10 °C). When 2 460 C had been passed the electrolysis was interrupted and water (100 ml) was added. The solution was extracted with CH_2Cl_2 (5 × 50 ml). Evaporation of the CH_2Cl_2 and distillation of the residue gave (2a) (0.9 g, 54%), b.p. 60 °C (0.2 mmHg) (lit.,[21] m.p. 42.5 °C).

Anodic Oxidation of Hydroquinone Bis-(2-hydroxyethyl) Ether (1e). *Electrosynthesis of* (6) (*Experiment* 15, *Table* 1).—Compound (1e) (0.83 g) was dissolved in acetonitrile (5 ml) containing lithium tetrafluoroborate (0.5 g) and 2,6-lutidine (1 ml) and subjected to constant-current electrolysis at a platinum anode (see Table 1) (electrolysis temperature 10 °C). When 900 C had been passed the electrolysis was interrupted and the acetonitrile was evaporated off at reduced pressure. The residue was triturated with warm CH_2Cl_2. The CH_2Cl_2 extract was filtered and evaporated. Recrystallisation of the residue from CH_2Cl_2–MeOH gave (6) (0.54 g, 67%), m.p. 221—224 °C (lit.,[19] 232—235 °C).

Anodic Oxidation of 2,6-*Di-isopropylanisole* (7a).—Compound (7a) (2 g) was dissolved in acetonitrile–methanol (1 : 1, 60 ml) containing lithium tetrafluoroborate (2 g) and *sym*-collidine (1 ml), and subjected to constant-potential electrolysis at a platinum anode (50 cm²) with a tungsten wire cathode (1.6 cm²) (the same cell as in experiments 1—8, Table 1, was used). When the desired amount of current (see Table 2) had been passed the electrolysis mixture was poured into saturated, aqueous sodium hydrogen carbonate (100 ml) and extracted with CH_2Cl_2 (4 × 50 ml). The combined CH_2Cl_2 extracts were washed with sodium hydrogen carbonate solution and evaporated to dryness. The residue was analysed by n.m.r. spectroscopy (nitromethane as internal, analytical standard). The products were identified by comparison with the spectra of the pure compounds obtained or prepared as described below.

Isolation of products. The crude product from the elec-

trolysis was recrystallised from methanol affording (13a), m.p. 138—139 °C; δ (CDCl₃, internal SiMe₄) [24 H, d (*J* 7 Hz)], 2.72 (m, 4 H), 3.02 (s, 6 H), 3.10 (s, 12 H), and 5.97 (s, 4 H); $\nu_{max.}$ (KBr) 2 840, 2 825, and 1 460 cm⁻¹. The mother liquor from this recrystallisation was evaporated and the residue was filtered through neutral alumina (light petroleum–CH_2Cl_2, 4 : 1, as eluant). Recrystallisation of the crude product from methanol gave pure (10a), m.p. 102—104 °C; *m/e* 238 (*M*⁺); δ (CDCl₃) 1.20 [12 H, d (*J* 7 Hz)], 2.83 [2 H, m, (*J* 7 Hz)], 3.07 (s, 6 H), and 6.35 (s, 2 H); $\nu_{max.}$ (KBr) 2 840, 1 670, and 1 625 cm⁻¹.

Synthesis of (9a). 2,6-Di-isopropylphenol was oxidised electrochemically in methanol.[1] Distillation of the crude electrolysis product gave a mixture of 2,6-di-isopropylbenzoquinone and 2,6-di-isopropyl-4-methoxyphenol which by reduction with sodium dithionite and methylation with dimethyl sulphate was converted into (8a), b.p. 74—80 °C (0.2 mmHg). Anodic oxidation of (8a) under the same conditions as for (7a), gave, after work-up (evaporation of the electrolysis mixture followed by distillation), (9a), b.p. 96 °C (0.5 mmHg); m.p. 54.5—56 °C; δ (CDCl₃) 1.15. [12 H, d (*J* 7 Hz)], 2.72 [2 H, m (*J* 7 Hz)], 3.03 (s, 6 H), 3.32 (s, 6 H), and 6.15 (s, 2 H); no carbonyl i.r. absorption.

Synthesis of (12a). Methylation with dimethyl sulphate of 4,4′-dihydroxy-3,3′,5,5′-tetraisopropylbiphenyl (from 2,6-di-isopropylphenol by oxidation with lead dioxide in acetic acid) gave (11a), m.p. (MeOH) 190—192 °C; δ (CDCl₃) 1.30 [24 H, d (*J* 7 Hz)], 3.37 [4 H, m (*J* 7 Hz)], 3.75 (s, 6 H), and 7.17 (s, 4 H). Anodic oxidation of (11a) as for (7a) gave a crude product which was extracted with cold methanol. The methanol-insoluble residue was almost pure (11a). Evaporation of the methanol extract gave a residue which was recrystallised from light petroleum at −60 °C; m.p. 94.5—96 °C; *m/e* 444 (*M*⁺); δ (CDCl₃) 1.19 [24 H, d (*J* 7 Hz)], 2.77 [2 H, septet (*J* 7 Hz)], 3.30 [2 H, m (*J* 7 Hz)], 2.98 (s, 3 H), 3.16 (s, 3 H), 3.27 (s, 3 H), 3.71 (s, 3 H), 6.11 (s, 2 H), and 7.20 (s, 2 H). On the basis of these data the compound was assigned the structure (12a).

Anodic oxidation of 2,6-*di-t-butylanisole* (7b). The electrolysis and work-up were carried out exactly as for (7a). The crude electrolysis product was triturated with light petroleum–CHCl₃ (1 : 1). The residue was identified as (14b), X = BF₄⁻) by its mass spectrum, *m/e* 339. The molecular weight of the cation of (14b) is 340; the 339 peak corresponds to elimination of HBF₄. δ (CDCl₃) 1.43 (s, 18 H), 2.37 (s, 6 H), 2.62 (s, 3 H), 3.77 (s, 3 H), 7.22 (s, 2 H), and 7.70 (s, 2 H). The light petroleum–chloroform extract was evaporated to dryness and the residue was recrystallised from methanol giving (12b), m.p. 150—152 °C; $\nu_{max.}$ (KBr) 2 830 and 1 460 cm⁻¹; δ (CDCl₃) 1.33 (s, 18 H), 1.40 (s, 18 H), 3.02 (s, 3 H), 3.23 (s, 3 H), 3.27 (s, 3 H), 3.65 (s, 3 H), 6.27 (s, 2 H), and 7.37 (s, 2 H); *m/e* 500 (*M*⁺). The methanol mother liquor was evaporated and the residue was sublimated affording impure (9b), δ (CDCl₃) 1.30 (s, 18 H), 3.07 (s, 6 H), 3.30 (s, 6 H), and 6.23 (s, 2 H). On being left for a few days (9b) decomposed spontaneously to (10b), m.p. 143.5—145 °C; *m/e* 266 (*M*⁺); $\nu_{max.}$ (KBr) 3 060, 3 020, 2 840, 1 665, and 1 625 cm⁻¹; δ (CDCl₃) 1.35 (s, 18 H), 3.15 (s, 6 H), and 6.48 (s, 2 H).

[22] B. Wladislaw and H. Viertler, *J. Chem. Soc. (B)*, 1968, 576.
[23] F. Strauss and H.-J. Weber, *Annalen*, 1932, **498**, 101.