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Electrosynthesis in systems of two immiscible liquids and a phase transfer catalyst. II. Aromatic nuclear acyloxylation

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The anodic acetoxylation of 1,4-dimethoxybenzene in a methylene chloride/water emulsion and using a phase transfer catalyst to supply the acetate ion to the organic medium is discussed. The yield of 2,5-dimethoxyphenylacetate is shown to vary with the electrolysis conditions but this product can be obtained with an organic yield of 85% and current yield, 60%. Similar conditions are used to introduce other carboxylates; with the longer chain, branched chain and unsaturated acids the yields of the esters are good. Finally the acetoxylation of some other aromatic molecules is shown to lead to variable yields of the acetates.

1. Introduction

The previous paper in this series [1] described further studies of the anodic cyanation of aromatic molecules in water/methylenedichloride emulsions containing a phase transfer agent. The corresponding carboxylation processes have received very little attention; one paper [2] discusses the acetoxylation of anisole, naphthalene and some alkyl benzenes and a patent [3] claims the substitution of anisole by longer chain carboxylic acids. The yields are, however, always low compared to cyanation. Hence in the study reported here, the acetoxylation of 1,4-dimethoxybenzene has been examined in some detail in order to define the conditions for a high yield. These conditions have then been used for attempting the substitution of 1,4-dimethoxybenzene by a range of carboxylates and the acetoxylation of several aromatic substrates. 1,4-dimethoxybenzene was selected as the model compound both because its monosubstitution leads to a single isomer and because its cation radical [4] is a well defined species with a half life of 10–100s in methylenechloride at − 70° C allowing the possibility of a parallel mechanistic study (see later paper).

2. Experimental procedure

All electrolyses were carried out in closed beaker cells with a 15.4 cm^2 Pt gauze anode and Cu gauze cathode and the emulsion was formed and maintained with a magnetic bar stirrer. In fact two cells, capacities 80 cm^3 and 200 cm^3 were used interchangeabily during the study. The source of the constant current was a modified Chemical Electronics Transistorised Potentiostat and charge was monitored with a laboratory built integrator. The cyclic voltammetry was carried out in a three electrode, two compartment cell. The Pt wire working electrode and Pt spiral counter electrode were in the same compartment but the Ag reference electrode was separated by a Luggin capillary and sinter. For the low temperature study, the cell was immersed in a chloroform slush bath. The experiments used in a Hi-Tek potentiostat DT 2101 and function generator PPR 1 and I–E curves were recorded on a Hewlett Packard 7014 A recorder.

The electrolyses were carried out with the cell in an ice/water bath and in the presence of hexadecane as an internal standard for the analysis. At the end of the electrolyses the phases were

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allowed to separate and the organic phase was evaporated at reduced pressure. The residue was partitioned between ether and water (to remove the phase transfer agent) and the ether phase was dried with Na_2SO_4 and made up to a known volume. The resulting solution was analysed by glc using a Pye Unicam GCD chromatograph and a 5% C20M column at a temperature selected for the particular analysis. Where possible, the products were identified and estimated using standard solutions of an authentic sample. In several cases, however, authentic samples were not available and the products were then identified by glc-mass spectroscopy and yields were estimated using a standard solution of the substrate and an estimated response factor.

A pure sample of 2,5-dimethoxyphenol was prepared by combining the product from a number of electrolyses of 1,4-dimethoxybenzene and hydrolysing the extract with NaOH. The purity of the phenol was checked by IR spectroscopy and glc. A pure sample of the 2,5-dimethoxyphenylacetate was then prepared by refluxing some of the phenol with acetyl chloride and recrystallising from petroleum ether. The methylene chloride was distilled from CaH_2 and the acetonitrile was purified by refluxing with (a) C_6H_5COCl (b) $KMnO_4$ and then distillation. Bu_4NBF_4 was prepared by double decomposition from $NaBF_4$ and Bu_4NHSO_4 in water and recrystallisation from water. The other chemicals were purchased in the purest form available from commercial sources and used without further purification.

3. Results and discussion

3.1. *The acetoxylation of 1,4-dimethoxybenzene*

In view of the results in the previous paper [1] on the cyanation of naphthalene, all the electrolyses for the acetoxylation of 1,4-dimethoxybenzene was carried out with a Pt anode in a methylene chloride/water (saturated with Na_2SO_4) emulsion containing tetrabutylammonium ions as the phase transfer agent.

An early paper [5] has reported that acetate ions are only poorly extracted by tetrabutylammonium ions into methylene chloride but that when acetic acid is present, the solvated species, $Bu_4N^+OAc^-.HOAc$, transfers more readily. The observations are essentially confirmed by the data in Table 1 where it can be seen that an equimolar concentration of acetic acid increases the extraction efficiency by 250%. It should be noted, however, that even with a high concentration of both acetic acid and acetate and the aqueous phase saturated with Na_2SO_4, only 60% of the tetrabutylammonium ion is able to transfer to the methylene chloride as $Bu_4N^+OAc^-$. This figure is very low compared to many diverse anions e.g., I^-, Cl^-, $Cr_2O_7^{2-}$. It may further be observed that a large excess of acetic acid enters the methylene chloride so that the electrode reaction occurs in an environment where the acetic acid: acetate ratio is 4.7 : 1. This has an important effect on the I–E curves. Fig. 1 shows the I–E curves for the organic medium resulting from equilibrating methylene chloride with an equal volume of an aqueous solution containing sodium acetate (1.5 mol dm^{-3}), acetic acid (1.5 mol dm^{-3}), tetrabutylammonium bisulphate (0.1 mol dm^{-3}) and saturated sodium sulphate before and after the addition of 1,4-dimethoxybenzene. The main feature of interest is the well formed oxidation wave for the substrate at a potential less positive than that for acetate oxidation in this system, i.e., the nucleophile in the synthesis is less readily oxidised than the 1,4-dimethoxybenzene. The acetic acid is necessary for this advantageous situation; cyclic voltammograms for Na^+ OAc^- and 1,4-dimethoxybenzene in methylene chloride/Bu_4NBF_4 (0.1 mol dm^{-3}) show their oxidation potentials to be + 1.15 V and + 1.42 V respectively. Hence the addition of acetic acid

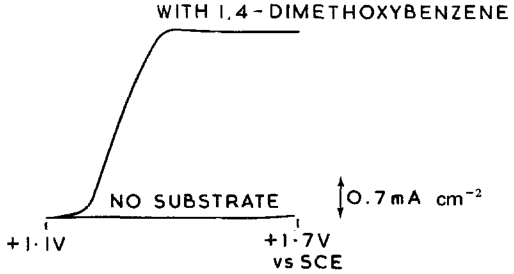


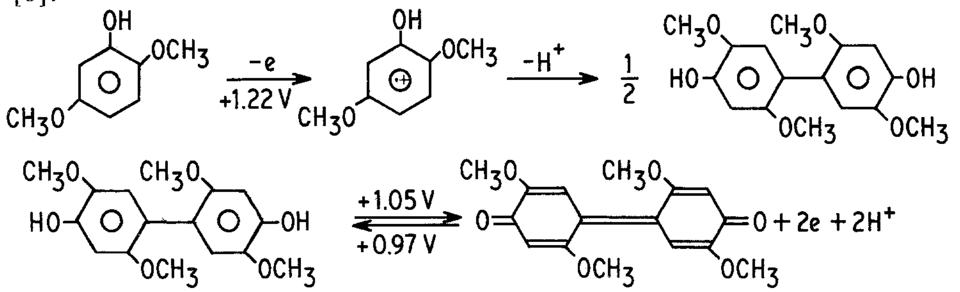
Fig. 1. I–E curves for the solution resulting from the extraction of an aqueous solution of CH_3COONa (1.5 mol dm^{-3}) + CH_3COOH (1.5 mol dm^{-3}) + Bu_4NHSO_4 (0.1 mol dm^{-3}) saturated with Na_2SO_4 by methylene chloride before and after the addition of 1,4-dimethoxybenzene (0.1 mol dm^{-3}). Pt electrode. Potential scan rate 1 mV s^{-1}.

Table 1. 50 cm³ of saturated aqueous Na_2SO_4 *+ 50 cm³* CH_2Cl_2. Bu_4NHSO_4 *neutralized with NaOH prior to addition of NaOAc or HOAc*

NaOAc (mmol)	*HOAc* (mmol)	Bu_4N^+ (mmol)	*Transfer to* CH_2Cl_2 (mmol)
75	75	0	HOAc (13.5)
75	0	5	Bu_4NOAc (1.2)
75	75	5	Bu_4NOAc (3) + HOAc (14)

makes the acetate ion more difficult to oxidize confirming the interaction between the acetate and the acid in methylene chloride.

Cyclic voltammetry in methylene chloride/ Bu_4NBF_4 (0.1 mol dm^{-3}) was also used to compare the oxidation behaviour of 1,4-dimethoxybenzene and likely electrolysis products, namely, 2,5-dimethoxyphenylacetate and 2,5-dimethoxyphenol. The latter would most likely arise by hydrolysis of the initially formed acetate although it could also form by direct interaction of the cation radical of 1,4-dimethoxybenzene with water. At room temperature, cyclic voltammograms at Pt for both 1,4-dimethoxybenzene and 2,5-dimethoxyphenylacetate show irreversible oxidation peaks and at very similar potentials + 1.42 V and + 1.44 V respectively. On reducing the temperature to − 60° C, the processes become reversible above 0.1 V s^{-1}. At very slow sweep rates I_p^C/I_p^A becomes less than one and the half lives of the cation radicals may be estimated. The values found were 14s and 16s for the cation radicals of 1,4-dimethoxybenzene and 2,5-dimethoxyphenyl acetate. The phenol is more readily oxidised, see Fig. 2. On the first scan to positive potentials, an irreversible oxidation peak is observed at + 1.22 V but there is a reduction peak at + 0.97 V on the reverse peak. On the second scan a new peak appears at + 1.05 V. Such cyclic voltammetry is common for substituted phenols and may be explained by the reaction scheme [6]:



There is also a further oxidation process at more positive potentials, at about + 1.5 V so that any phenol formed during the preparative electrolyses will undergo several further oxidation steps.

Table 2 reports the effect of current density and reactant concentrations on the 1,4-dimethoxybenzene and 2,5-dimethoxyphenylacetate recovered from the organic phase of electrolyses terminated after the passage of 2.33 F mol^{-1}. The data is also recalculated to report the organic yield and current efficiency for the acetate formation. In all electrolyses a few percent of the phenol was also isolated. The data shows that under all conditions the organic yield is above 50% but it can be as high as 87%. The current yield is more susceptible to the conditions ranging from 14–61%. The current density did not have a large effect on the product efficiency but since there was evidence of a decrease at the highest value used, 35 mA cm^{-2} was chosen for most experiments. The concentrations of acetate ion (and acetic acid since $CH_3COOH:CH_3COO^-$ was maintained at 1 : 1) and the phase transfer agent had the largest effect on both current and organic yields and this indicates that it is advantageous to have a high concentration of acetate in the methylene chloride phase during oxidation. In the absence of the nucleophile in excess, the cation radical of the 1,4-dimethoxybenzene will decompose by unwanted reaction pathways such as reaction with water or polymerisation; the phenol will not be

Table 2. Effect of electrolysis conditions on the oxidation of 1,4-dimethyoxybenzene. The cell always contained 40 cm^3 CH_2Cl_2 + 40 cm^3 saturated Na_2SO_4. Pt gauze anode. Temperature 278 K. Solution stirred with magnetic bar. Electrolysis terminated after 2.33 F mol^{-1} of 1,4-dimethoxybenzene.

Electrolysis conditions				*Analysis organic phase after 2.33 F mol^{-1}*		*Yields of ester*	
1,4-dimethoxybenzene (mmol)	Bu_4N^+ (mmol)	*Total* CH_3COO^- (mmol)	I (mA cm^{-2})	*1,4-dimethoxybenzene* (mmol)	*2,5-dimethoxyphenylacetate* (mmol)	*Organic** *yield* (%)	*Current yield* (%)
40	0.8	120	35	27	7	53	14
20	–	–	–	12	6	73	25
4	–	–	–	1.55	1.45	59	31
4	0.8	120	7	1.7	1.3	56	28
–	–	–	18	1.6	1.6	67	35
–	–	–	35	1.55	1.45	59	31
–	–	–	52	2.3	1.05	55	22
4	0.8	120	35	1.55	1.45	59	31
–	4	–	–	1.1	2.1	73	45
–	20	–	–	1.4	1.6	62	34
4	0.8	120	35	1.55	1.45	59	31
–	–	180	–	1.5	1.6	64	35
–	–	360	–	1.65	1.65	74	36
4	4	120	35	1.1	2.1	73	45
–	–	240	–	1.0	2.2	72	46
–	–	360	–	0.7	2.8	87	61

*based on substrate consumed

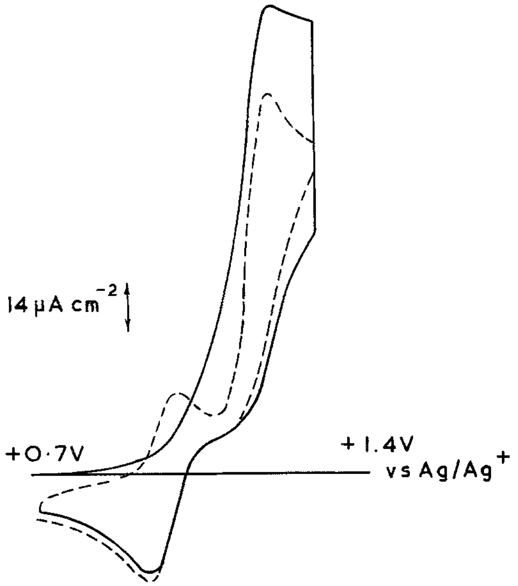


Fig. 2. Cyclic voltammogram of 2,5-dimethoxyphenol (2 mmole) in methylene chloride + Bu_4NBF_4 (0.1 mol dm^{-3}) at Pt. Temperature — 60° C. Potential scan rate 0.4 V s^{-1}. —— first scan, – – – second scan.

stable at the anode potential prevailing during this electrolysis.

Fig. 3 shows the course of an electrolysis followed by periodic analysis of the organic phase; this electrolysis used rather less than the optimum concentration of acetate and Bu_4N^+.

Table 3. The acyloxylation of 1,4-dimethoxybenzene by two phase electrolysis. Electrolysis conditions; methlenechloride (100 cm³), 1,4-dimethoxybenzene (0.01 mol), water (100 cm³) saturated with Na_2SO_4, carboxylic acid (0.3 mol) half neutralized with NaOH, $Bu_4N\,HSO_4$ (0.01 mol). Pt gauze anode. Current density 32 mA cm^{-2}. Electrolyses terminated after 2.33 F mol^{-1} of 1,4-dimethoxybenzene. Temperature 278 K. Emulsion formed with magnetic bar stirrer

Carboxylic acid	*2,5-dimethoxyphenyl ester*	
	Current yield (%)	*Organic yield (%)*
HCOOH	4	33
CH_3COOH	45	69
C_2H_5COOH	49	78
C_3H_7COOH	58	80
$C_5H_{11}COOH$	54	80
$(CH_3)_2CHCOOH$	33	50
$(CH_3)_3CCOOH$	31	52
$CH_3CH{=}CHCOOH$	41	61
$CH_2{=}CHCH_2COOH$	10	17

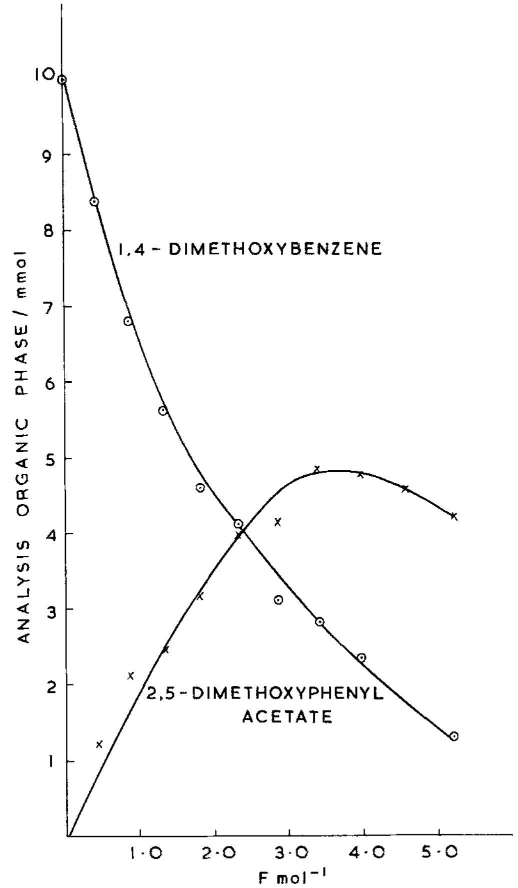


Fig. 3. Analysis of methylene chloride phase as a function of charge passed during an oxidation of 1,4-dimethoxybenzene. Electrolysis conditions: 100 cm³ of water containing CH_3COONa (1.5 mol dm^{-3}) + CH_3COOH (1.5 mol dm^{-3}) + $Bu_4N\,HSO_4$ (0.1 mol dm^{-3}) saturated with Na_2SO_4 + 100 cm³ of methylene chloride containing 1,4-dimethoxybenzene (0.1 mol dm^{-3}). I = 32.5 mA cm^{-2}.

It can be seen that early in the electrolysis, the 1,4-dimethoxybenzene converts to the ester in good organic and reasonable current yield. After about 50% conversion which occurs at about 2–3 F mol^{-1}, however, the concentration of product peaks and even falls slightly even though the substrate continues to be consumed. This would suggest strongly that the 2,5-dimethoxyphenylacetate is oxidised further and this would not be surprising in view of the proximity of its oxidation potential to that of 1,4-dimethoxybenzene.

Hence it is the conclusion of this study that the concentration of acetate ion and the phase transfer catalyst should be as high as possible, the current density should be 35 mA cm^{-2} and the electrolyses should not be continued beyond 2 F mol^{-1}. Indeed these are the expected conditions for a reaction where the nucleophile is more stable than the substrate but the product of the electrolysis is oxidised at a potential only slightly positive to that for the starting material.

3.2. *Other acyloxylations of 1,4-dimethoxybenzene*

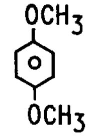
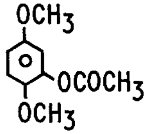
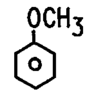
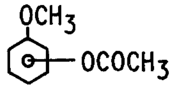
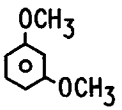
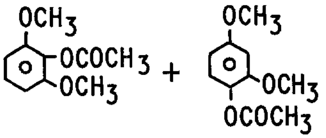
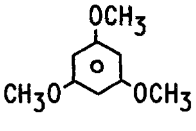
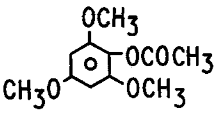
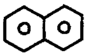
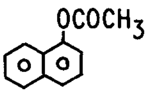
A series of two phase electrolyses were carried out to define whether the procedure could be extended to the synthesis of other carboxylate esters. Uniform conditions were used and the carboxylic acid in the aqueous phase was always half neutralised with caustic soda. The results for nine acids are reported in Table 3.

With straight chain acids, there is some tendency for the current and organic yields of the ester to increase with the size of the alkyl group. Certainly the yields of formate ester are particularly poor and the yields for the substitution of propionate, butyrate and hexanoate are all better than for the acetate. This largely results from a more favourable extraction coefficient for the ion pair RCOO$^-$ Bu$_4$N$^+$ and hence higher concentrations of the nucleophiles in the methylene chloride phase. With formate, however, direct oxidation of the formate will also contribute to the very low current yield. The yields of esters from branch chain and unsaturated carboxylic acids are all lower but only in the case of vinylacetic acid was a very poor yield isolated.

3.3. *Acetoxylation of other substrates*

The two phase acetoxylation procedure was also extended to some other aromatic substrates which would oxidise below + 2.0 V where acetate

Table 4. Anodic acetoxylations in two phase systems. Electrolysis conditions: methylene chloride (40 cm^3), substrate (4 mmole), water (40 cm^3) saturated with Na$_2$SO$_4$, acetic acid (0.12 mole) half neutralized with NaOH, Bu$_4$NHSO$_4$ (4 mmole). Pt gauze anode. Current density 32 mA cm^{-2}. Electrolysis terminated after 2.33 F mol^{-1} substrate. Temperature 278 K. Emulsion formed with magnetic bar stirrer

Substrate	*Products*	*Current yield (%)*	*Organic yield (%)*
		44	67
	 o:m:p ≡ 65:3:32	27	41
		15	40
		11	23
		27	40

decomposition was observed to commence. The yields of acetate esters are reported in Table 4. With the conditions employed for these electrolyses the yields of substitution products were reasonable and comparable to those reported by Eberson and Helgee [2]. On the basis of the experiments with 1,4-dimethoxybenzene, however, these should be capable of improvement by increasing the concentration of phase transfer agent and the acetate ion in the aqueous phase.

4. Conclusions

It has been demonstrated that good yields (organic 85%, current 60%) of 2,5-dimethoxyphenyl acetate may be isolated from the two phase acetoxylation of 1,4-dimethoxybenzene despite the problem that the oxidation potential for the monosubstituted product is very similar to that for the substrate. Moreover the method can be extended to other acyloxylations and the acetoxylation of different substrates.

All the evidence would suggest the reactions proceed by direct oxidation of the substrates in the methylene chloride phase and that the products arise by reaction of the cation radicals with an electroinactive nucleophile. The cation radicals of all substrates used in this study are, however, quite unstable at room temperature even in the absence of carboxylate and hence a high yield of the desired product is dependent on a high concentration of the carboxylate ion in the organic phase (note that there is a rough correlation between cation radical stability and yield of acetate ester in Table 4). Hence the most favourable electrolysis conditions are those which promote transfer of carboxylate into the methylene chloride, i.e., high Bu_4N^+ and $RCOO^-$ concentrations. Moreover since transfer is higher for long chain acids, if the objective of the electrolysis was to synthesise the corresponding phenols, hexanoic acid would be better than acetic acid.

Acknowledgements

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