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Large-scalc Laboratory Electrolysis in Organic Systems. IV. Anodic Methoxylation and Acetoxylation

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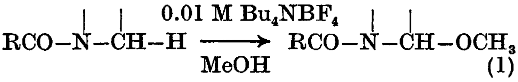
Further examples on the use of a concentric capillary gap cell in large-scale laboratory anodic synthesis are presented. These include methoxylation of *N*,*N*-dialkylamides and 1,4-dimethoxybenzene, bisacetoxylation of *N*,*N*,*N*′,*N*′-tetramethyloxamide, and side-chain acetoxylation of 4-substituted toluenes.

An optimal use of organic electrosynthesis depends not only on the possibility to synthesize compounds that are inaccessible by other routes or more easily available by electrolytic methods but also to a great extent on the availability of electrochemical cells that can produce relatively large quantities in a short period of time. In previous parts of this series [1–3] we have reported on the construction and performance of a concentric capillary gap cell for electrolysis on a large laboratory scale. Our cell consists of a graphite rod anode (surface area *ca.* 800 cm^2) surrounded by a stainless steel cathode and with a 1 mm gap between the electrodes. The small distance between the electrodes reduces the ohmic resistance in comparison to conventional laboratory cells and therefore allows the use of low-conducting solvents, such as acetic acid, at fairly high currents. In addition, lesser amounts of expensive supporting electrolytes are needed. The cell is connected to a flow system made up of a reservoir, a pump, and a heat exchanger (a normal water condenser). In our work the cell has been used for anodic reactions with currents up to 50 A. This allows for the electrolysis of approximately 1 mol of substrate in 1 h for a 2*e* reaction. We have earlier [1–7] demonstrated the use of the cell for a number of anodic acyloxylation, alkoxylation, and dehydrodimerization reactions. It has also been used by others [8] for carrying out anodic syntheses in trifluoroacetic acid.

In this paper we present further results of the use of the concentric capillary gap cell in anodic methoxylation of *N*,*N*-dialkylamides [3] yielding products that are useful for amidoalkylation reactions [9] and enamide synthesis, [10] as well as anodic side-chain acetoxylation, and anodic methoxylation of 1,4-dimethoxybenzene.

RESULTS

Anodic methoxylation of N,N-*dialkylamides.* Anodic oxidation of an *N*,*N*-dialkylamide in methanol produces an *N*-acyl-*O*,*N*-acetal [3] as shown in eqn. 1. The results from four experiments are shown in Table 1. In the oxidation of the pyrrolidine derivative the methoxylated product is not stable during work-up but is converted into the enamide.[10]



$$\mathrm{RCO{-}\overset{|}{N}{-}\overset{|}{C}H{-}H} \xrightarrow[\mathrm{MeOH}]{0.01\ \mathrm{M\ Bu_4NBF_4}} \mathrm{RCO{-}\overset{|}{N}{-}\overset{|}{C}H{-}OCH_3} \qquad (1)$$

Anodic bisacetoxylation of N,N,N′,N′-*tetramethyloxamide.* This reaction, (eqn. 2), represents the first example of the anodic oxidative substitution of a diamide. The monoacetate is first formed and then transformed into the diacetate on prolonged electrolysis.

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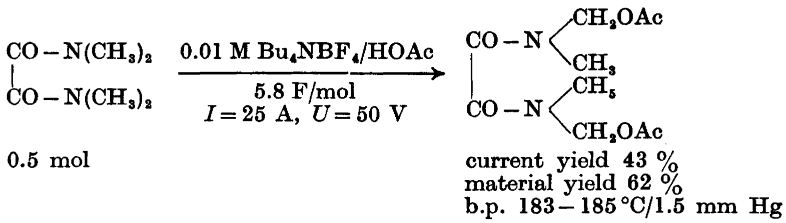


$$(CO-N(CH_3)_2)_2 \xrightarrow[\text{5.8 F/mol, } I = 25 \text{ A, } U = 50 \text{ V}]{\text{0.01 M } Bu_4NBF_4/HOAc} (CO-N(CH_2OAc)(CH_3))-(CO-N(CH_3)(CH_2OAc)) \quad (2)$$

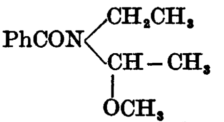
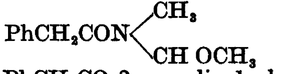
0.5 mol

current yield 43 %
material yield 62 %
b.p. 183–185 °C/1.5 mm Hg

Anodic side-chain acetoxylation of 4-substituted toluenes. The reaction gives a simple direct route to benzyl acetates[11] and is performed in HOAc containing Bu_4NBF_4, eqn. 3. The absence of acetate ion in the electrolyte prevents nuclear acetoxylation. The results are shown in Table 2. Since HOAc is a poorly conducting solvent a considerable amount of heat is evolved during the oxidation and therefore the temperature is allowed to increase to 50–60 °C. We would like to draw attention to the bisacetoxylation of *p*-xylene, where the selectivity for formation of

$$ArCH_3 \xrightarrow{\text{0.05 M } Bu_4NBF_4/HOAc} ArCH_2OAc \quad (3)$$

Table 1. Anodic methoxylation in 0.01 M Bu_4NBF_4/CH_3OH ($I = 50$ A, $U = 20-26$ V).

Substrate (mol)	Product	CH_3OH (mol)	F/mol	Yield/% curr.	Yield/% mat.	B.p./°C at mm Hg (M.p./°C)
$PhCON(CH_2CH_3)_2$ (1)	 $PhCON(CH_2CH_3)(CH(OCH_3)-CH_3)$	1000	2.4	63	76	114–115/0.3
$PhCH_2CON(CH_3)_2$ (0.62)	 $PhCH_2CON(CH_3)(CH_2OCH_3)$	800	2.5	68	85	131–132/1
$PhCH_2CO$-1-pyrrolidinyl (0.5)	$PhCH_2CO$-2-pyrrolin-1-yl	800	2.14	58	62	140–150/0.5 (83–85)[a]
$PhCH_2CO$-1-piperidyl (0.5)	$PhCH_2CO$-2-methoxy-1-piperidyl	800	2.1	81	85	130–132/0.4

[a] The enamide is formed by decomposition of the methoxy compound during distillation and solidifies in the condenser.

Table 2. Anodic acetoxylation in 0.05 M $Bu_4NBF_4/HOAc$ ($I = 20$ A, $U = 55-60$ V).

Substrate (mol)		Product	HOAc (ml)	F/mol	Yield/% curr.	B.p./°C at mm Hg (M.p./°C)
$4-BrC_6H_4CH_3$	(0.5)	$4-BrC_6H_4CH_2OAc$	500	2	35	65–70/14
$4-ClC_6H_4CH_3$	(0.5)	$4-ClC_6H_4CH_2OAc$	500	2	32	110–115/15
$4-FC_6H_4CH_3$	(0.5)	$4-FC_6H_4CH_2OAc$	500	2	36	94–96/13
$4-CH_3C_6H_4CH_3$	(1)	$4-AcOCH_2C_6H_4CH_2OAc$[a]	1000	3.5	19	(49–50)
$4-AcOCH_2C_6H_4CH_3$	(1)	$4-AcOCH_2C_6H_4CH_2OAc$	1000	2	25	(49–50)

[a] The unsymmetrical bisacetoxylation product was formed in *ca.* 2 % yield.

the α,α′ isomer is 10:1 over the α,α isomer. The symmetrical diacetate is an interesting bifunctional product with potential use as a polymer starting material. No attempt was made to optimize the yield.

Oxidative addition of 1,4-dimethoxybenzene. This compound is converted into 1,1,4,4-tetramethoxycyclohexa-2,5-diene in methanol containing 1 % KOH, as has been shown previously.[12,13] The electrochemical method is the only practical route to this compound. Since it had earlier been carried out in a conventional apparatus with Pt electrodes, we were interested to see if it was possible to perform the reaction in the capillary gap cell with a graphite anode. We carried out the oxidation of 1,4-dimethoxybenzene (1 mol) in 1 % KOH/CH_3OH (1000 ml) at a current of 25 A and an applied voltage of 6 − 7 V. Without any attempts to optimize the procedure we obtained a material yield of 44 % (current yield 29 %), showing that graphite indeed supports this type of reaction, although not as well as platinum (material yield 70 − 71 %[13]).

We now believe that we have amply demonstrated that the use of a simple concentric capillary gap cell is feasible in laboratory routine work.

EXPERIMENTAL

Details of the operation of the cell[14] have been given in Part II of this series.[2] The work-up procedure in the methoxylation of *N*,*N*-dialkylamides and the bisacetoxylation of *N*,*N*,*N′*,*N′*-tetramethyloxamide involves evaporation of the solvent *in vacuo* followed by distillation of the product. All products were satisfactorily characterized by spectral methods. The work-up procedure in the side-chain acetoxylation of 4-substituted toluenes consists of addition of water to the electrolyte, extraction with dichloromethane, followed by washing successively with water, dilute sodium bicarbonate solution, and water. After drying the dichloromethane solution the solvent was removed by evaporation *in vacuo* and the product was isolated by distillation at reduced pressure. The products were characterized by spectral data and/or conversion to the alcohols by hydrolysis.

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14. The cell is available for sale from this Department. For details, write to L. Eberson.

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