A Novel Electro-oxidative Methoxylation of Cyanomethyl Sulphides[1]

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Electrolysis of alkylthioacetonitriles (**1**) in the presence of toluene-*p*-sulphonic acid as an electrolyte in methanol readily affords synthetically useful α-methoxylated sulphides (**2**) possibly by way of a Pummerer-type intermediate.

Electrochemical oxidation of sulphur-containing compounds has been used in various synthetic reactions, most of which involve cleavage of C–S bonds as the key step.[2,3] Though the methoxylation of amino, olefinic, and alkylaromatic compounds at their α-positions is an important electro-oxidation method,[2] the analogous methoxylation of sulphides has rarely been developed, possibly because the electrolysis of simple sulphides usually results in the formation of sulphoxides and sulphones or cleavage of C–S bonds. We now report that alkylthioacetonitriles (**1**) give novel α-methoxylated sulphides (**2**) by simple electrolysis in methanol using toluene-*p*-sulphonic acid (TsOH) as the supporting electrolyte [reaction (1)].†

$$\underset{(\mathbf{1})}{\mathrm{RSCH_2CN}} \xrightarrow[\mathrm{TsOH{\cdot}H_2O}]{-\mathrm{e},\ \mathrm{MeOH}} \underset{(\mathbf{2})}{\mathrm{RSCH(OMe)CN}} \qquad (1)$$

In a typical procedure, a solution of the sulphide (**1**) (2 mmol) in methanol containing TsOH (2 mmol) was electrolysed at a constant current of 0.2 A in an undivided cell using platinum electrodes (1 × 3 cm^2). After an appropriate amount of electricity had been passed for the consumption of >95% of (**1**), the electrolysed solution was concentrated and the residue chromatographed on silica gel (eluant: hexane–CH_2Cl_2, 2 : 1) or distillated for large-scale experiments to provide (**2**) (Table 1).‡

Methoxylations of cyanomethyl sulphides (**1a**—**d**) proceeded in high yields without formation of sulphoxide or sulphone; only small amounts of C–S cleaved products such as diphenyl disulphide and methyl benzenesulphinate were detected. The electrolyte had a profound effect (Table 1). $TsOH{\cdot}H_2O$ effected successful methoxylation of (**1a**—**d**) in high yields; (**1d**) reacted with somewhat better current efficiency than (**1a**—**c**). Use of tetraethylammonium toluene-*p*-sulphonate (Et_4NOTs), a common neutral electrolyte, led to methoxylation of (**1c**) and (**1d**), whereas (**1a**) and (**1b**) remained intact. Halide ion electrolytes such as LiCl and Bu_4NBr were inadequate because they induced further reactions such as C–S bond cleavage. An analogous α-ethoxy-

Table 1. Electro-oxidation of (**1**) in methanol.

(1), R	Electrolyte	Electricity /F mol^{-1}	Yield of (2)/%[a]
(**1a**), Me	$TsOH{\cdot}H_2O$	8	70
	Et_4NOTs	10	0[b]
(**1b**), Et	$TsOH{\cdot}H_2O$	7	86
	Et_4NOTs	10	0[b]
(**1c**), Bu^t	$TsOH{\cdot}H_2O$	7	91
	Et_4NOTs	6	92
	Bu_4NBF_4	6	85
	$LiNO_3$	5	84
	MeONa	7	50
(**1d**), Ph	$TsOH{\cdot}H_2O$	4	89
	Et_4NOTs	7	76

[a] Yields were determined by g.l.c. [b] Starting (**1**) unchanged (>80%).

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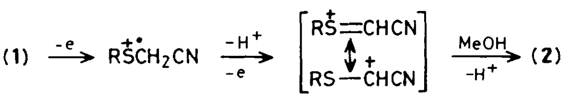
† Electrolysis of sulphides in acetic acid containing sodium acetate has been reported to give α-acetoxylated sulphides.[4] However, the same electrolysis of (**1a**—**c**) used here failed to give any α-acetoxylated sulphide.

‡ Satisfactory analytical and spectral data were obtained for new compounds.



Scheme 1

lation of (**1a**—**d**) in ethanol took place in comparable yields under these conditions.

Cyclic voltammetric measurements showed that cation radicals of the α-cyano sulphides (**1a**—**d**) are formed at potentials higher by *ca.* 0.5 V than those of the corresponding alkyl octyl sulphides RSC_8H_{17}. Electrolysis of the deuteriated sulphide Bu^tSCD_2CN under the typical conditions resulted in methoxylation without any deuterium exchange. Therefore, the present electro-oxidative methoxylation is suggested to proceed *via* a pathway involving Pummerer-type intermediates (Scheme 1).[5] Substitution with the electron-attracting CH_2CN group (Taft's σ^* +1.30) appears to facilitate deprotonation at the α-position.

The present electrochemical α-methoxylation of (**1**) can be performed by a simple procedure under mild conditions in the absence of any oxidizing or chlorinating agents such as t-butyl hypochlorite[6] or *N*-chlorosuccinimide.[7] Compounds (**2**) have a novel structure possessing three different functional groups on one carbon atom, so that various functional derivatizations of (**2**) are of interest in organic synthesis in providing a new one- and/or two-carbon-elongating agent.[8] For example, alkylation of (**2c**) with several primary alkyl bromides took place smoothly using sodium hydride as base in dimethylformamide at room temperature. Electrolysis of the alkylation products in methanol containing hydrochloric acid resulted in the formation of methyl esters of the homologous carboxylic acids in *ca.* 70% overall yields. Thus, (**2**) is a new ester synthon.[9]

Treatments of the alkylation products with di-isobutylaluminium hydride in benzene effected selective reduction of the cyano to aldehyde group giving derivatives of alkylated glyoxal quantitatively.

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