

SHORT COMMUNICATION

Electrolytic partial fluorination of organic compounds.**Part XI Regioselective anodic monofluorination of phenylsulfenylacetate using a flow-cell system**

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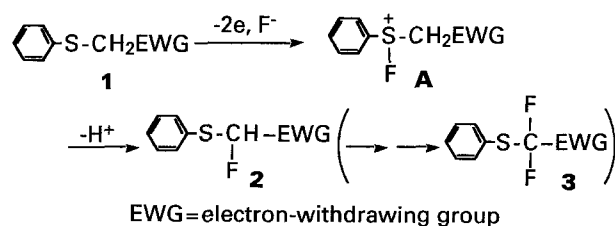
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1. Introduction

Organofluorine compounds have attracted much interest on account of their potential biological activity [1–3]. The synthesis of these compounds, however, is limited in many cases because of the strong electron-withdrawing ability of the fluorine atom (for example, [4]). Although direct fluorinations are the most simple way for the synthesis of such compounds, methods are not always straightforward and have to use troublesome reagents (explosive, sensitive to air or moisture, expensive) (for example, [5]). Thus, electrochemical fluorination is an ideal method for direct fluorination. Although electrochemical perfluorinations (Simons process) are familiar, electrochemical partial fluorination has been seen in few cases. In electrochemical fluorinations it is difficult to control the chemo and regioselectivity. Indeed, reported electrochemical partial fluorinations of organic compounds were not successful (low yields and product selectivity) [6–9], and there have been no reports on electrochemical partial fluorination on a large scale.

Recently, the present authors [10, 11] and Laurent *et al.* [12] reported highly regioselective electrochemical monofluorination at α -position to the sulfur atom of sulfides using $\text{Et}_3\text{N} \cdot 3\text{HF}$ as a supporting electrolyte and a fluorine source. It was pointed out that this reaction proceeds by a Pummerer like mechanism via a unique fluorosulfonium cation intermediate (A) (Scheme 1) [13]. Preliminary results have shown that the anodic monofluorination could be conducted, not only in controlled potential electrolysis, but also in galvanostatic electrolysis.



Scheme 1

We, therefore, extend this reaction to a flow-cell system which may be scaled-up. This is the first example of anodic partial fluorination using a flow cell.

2. Experimental details**2.1. Chemicals and electrode materials**

Ethyl phenylthioacetate (1) was purchased from Tokyo Kasei Chemical Co. and was used without further purification. Acetonitrile was purified by distillation with CaH_2 . A DSA (ruthenium oxide-coated titanium anode) and a carbon sheet were obtained from Electrocell AB, Sweden and Nippon Carbon Co., respectively. $\text{Et}_3\text{N} \cdot 3\text{HF}$ was purchased from Aldrich Co. $\text{Et}_4\text{NF} \cdot 3\text{HF}$ was a gift from Morita Chemical Co.

2.2. Electrolytic conditions

The electrolysis was carried out using a filter-press type microflow-cell (Electrocell AB, Sweden) modified for the present purpose. A schematic illustration of the microflow cell system is shown in Figs 1 and 2. Platinum sheets (3.3 cm \times 3.3 cm) were mainly used as anode and cathode and a DSA (3.3 cm \times 3.3 cm) and a carbon sheet (3.3 cm \times 3.3 cm) were used in some cases. The following two conditions were chosen unless otherwise noted. (a) Conditions A (using acetonitrile as a solvent): 1 (5 mmol) was dissolved in 0.39 M $\text{Et}_4\text{NF} \cdot 3\text{HF}$ or $\text{Et}_3\text{N} \cdot 3\text{HF}/\text{MeCN}$ solution (50 ml). (b) Conditions B (no solvent (neat)): 1 (40 mmol) was dissolved in $\text{Et}_3\text{N} \cdot 3\text{HF}$ (40 ml: 111 mmol). When the concentration of 1 was varied (Section 3.2), the concentration of supporting electrolyte was adjusted to the amount corresponding to 10 equivalents to 1 (based on F^-). The reactions were monitored by GC (Yanaco GC-1800: Polyester FF, 2 m, 180°C). The electrolytic solution was passed through a short column (Silica gel) in order to remove supporting electrolyte. The yields of fluorinated products were determined by ^{19}F NMR (Jeol EX-270) using $\text{C}_6\text{H}_5\text{F}$ as an internal standard.

3. Results and discussion

Ethyl phenylsulfenylacetate (1) was chosen as a model compound for anodic fluorination. When the electrolysis was conducted in $\text{Et}_4\text{NF} \cdot 3\text{HF}$ as a supporting electrolyte and fluorine source instead of

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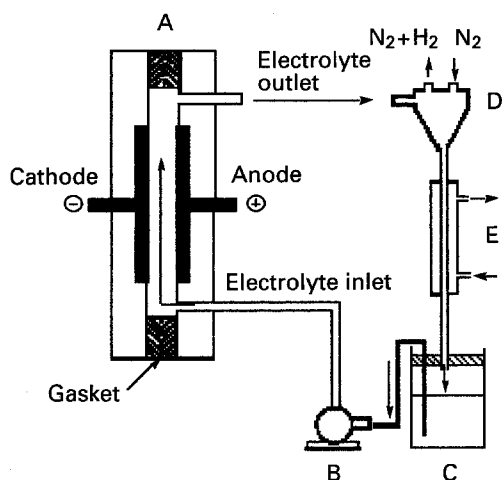


Fig. 1. Micro flow-cell system. (A) Microflow-cell (Electrosyn AB), (B) pump, (C) electrolyte reservoir, (D) hydrocyclone, (E) heat exchanger.

$\text{Et}_3\text{N} \cdot 3\text{HF}$, the yield of monofluorinated product **2** was slightly improved (58 \rightarrow 61%), but no significant difference was observed between the electrolytes. If the anodic fluorination was carried out under air, the yields of **2** decreased significantly and diphenyl disulfide (a product from C–S bond cleavage) was detected as a byproduct. Therefore, the following electrolyses were carried out under a nitrogen atmosphere.

3.1. Influence of electrode material

Three anode materials used are listed in Table 1. Anodic fluorination produced the desired monofluorinated product **2** in reasonable yield, with platinum giving the best result. DSA was also effective and carbon may be used for this fluorination, although both the yield and the current efficiency were somewhat lower. This is in contrast to other well-known electrochemical perfluorinations, where materials other than nickel are unsuitable.

3.2. Influence of initial concentration of **1**

Little effect was found of the concentration of **1** on the yield of **2**. Even in the case of neat (no solvent) conditions (conditions B), the yields of fluorination were almost constant (see Section 3.3) regardless of the concentrations of **1**.

3.3. Influence of current density

Under conditions A, the influence of current density is

Table 1. Effects of electrode materials on anodic monofluorination of **1**

Run	Anode material	Charge passed /F mol ⁻¹	Yield of 2 /%	Current efficiency for 2 /%
1	Pt	2.4	61	51
2	DSA	2.2	51	46
3	Carbon sheet	2.4	49	41

Conditions A: 5 mmol of **1** was dissolved in 0.39 M $\text{Et}_3\text{N} \cdot 3\text{HF}/\text{MeCN}$ (50 ml). Current density: 15 mA cm⁻², flow rate: 200 ml min⁻¹.

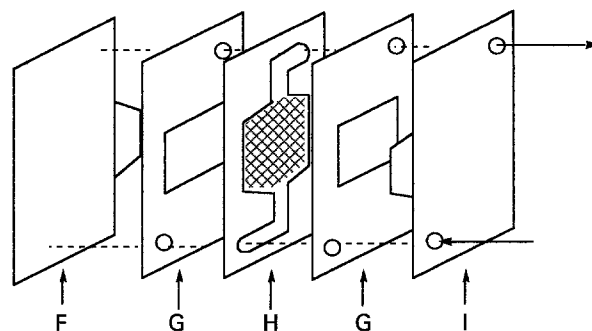


Fig. 2. Internal structure of microflow-cell system. (F) Anode, (G) gasket, (H) fluid distributor, (I) cathode.

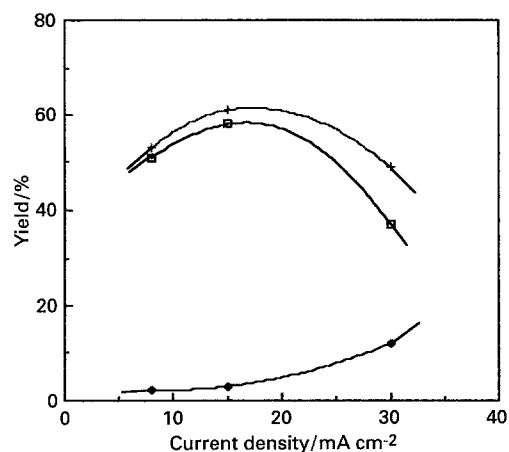
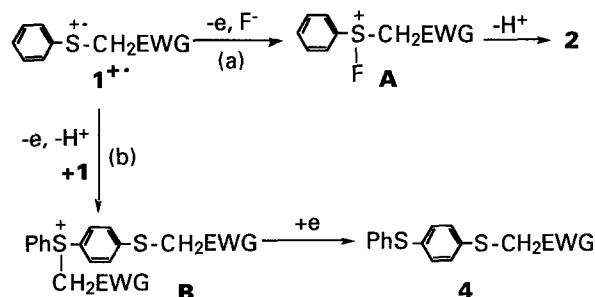


Fig. 3. Influence of current density on the yields of **2** (□), **3** (◆) and total yield of **2+3** (+) (conditions A, flow rate: 200 ml min⁻¹, charge passed: 2.2 F mol⁻¹).

illustrated in Fig. 3. At low current densities, monofluorinated product was obtained in good yields. At higher current densities, the yield of **2** decreased and the yield of difluorinated product **3** increased. Under conditions B, the influence of current density (Fig. 4) was different. As current density increased, the monofluorination yield decreased, whereas that of difluorination increased. However, at higher current density (80 mA cm⁻²), the yields of both decreased. In this case, an appreciable amount of phenylsulfenylated product **4** was detected from the MS spectrum of the electrolytic solution. The byproduct **4** is probably formed from a dimeric cation intermediate of **1**, (**B**) as shown in Scheme 2. The initially formed cation radical (**1**^{•+}) is trapped by neutral **1** (path b) competitively with fluoride ions (path a), due to high concentration of **1**. It is known that, even at low concentrations, simple alkyl phenyl sulfides devoid of electron-withdrawing groups undergo such anodic dimerization [14].



Scheme 2

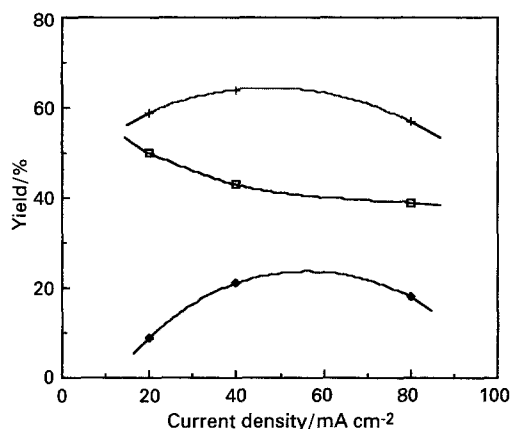


Fig. 4. Influence of current density on the yields of **2** (□), **3** (◆) and total yield of **2** + **3** (+) (condition B, flow rate: 200 ml min⁻¹, charge passed: 2.2 F mol⁻¹).

The total yield of **2** and **3** was almost constant although each yield was greatly affected by current density. Figure 5 shows the cell voltage-time relationship in the course of each electrolysis. At the final stage of the electrolytic fluorination (2.0 ~ 2.4 F mol⁻¹), an increase in cell voltage was observed in a constant current (800 mA) electrolysis. This suggests that the second stage of fluorination, namely difluorination begins. This is a useful indication that the reaction should be stopped because difluorinated product **3** is very difficult to separate from monofluorinated product **2**.

3.4. Influence of flow rate

Flow rates had almost no influence on the yields of monofluorinated product **2**.

Acknowledgement

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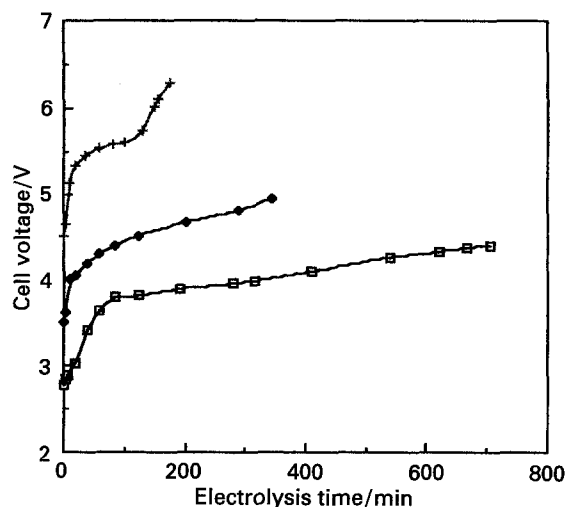


Fig. 5. Dependency of electrolysis time on the cell voltage during electrolysis (conditions B, flow rate: 200 ml min⁻¹). Constant current electrolysis: 200 mA (□), 400 mA (◆), 800 mA (+).

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