

0040-4039(95)00654-0

## Anodic Fluorination of Aromatic Thioethers Substituted by Strongly Electron-Withdrawing Groups

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<u>Abstract</u>: Arylalkylthioethers (aryl substituted by efficiently withdrawing groups) were anodically oxidized in the presence of Et<sub>3</sub>N, 3HF. Monofluorinations occuring often in good yield were found to be regiospecific onto the  $\alpha$ -carbon of the aliphatic chain branched to the sulfur atom.

In the course of the two last decades, large efforts for developping new fluorination methods for organic molecules were made. The driving force of such a challenge was principally the interest of (mono and poly) fluorinated molecules in the field of chemistry, biophysics, biology and pharmacology<sup>1</sup>. However, the synthesis of organofluorinated compounds still remains difficult and all new modes of formation are still being received by chemists working in this field with a indeniable attention<sup>2</sup>. Within the whole palette of possible synthetic methods, the direct anodic fluorination is of interest since fluorine atom(s) can be inserted in one step from amine hydrofluoride. In particular, Et<sub>3</sub>N, 3HF is now considered as a mild fluorination agent, of easy handling, of low toxicity and also widely available<sup>3</sup>.

As the matter of fact, litterature data<sup>4, 5</sup> show that electrochemical fluorination was first used in the case of thioethers 1 all possessing a strongly electron withdrawing group (EWG = CF<sub>3</sub>, CO<sub>2</sub>R, CN, PhCO, CHF<sub>2</sub>, CH<sub>2</sub>F...) grafted onto the central methylene :

PhSCH<sub>2</sub>-EWG 
$$\xrightarrow{-2e, -H^+}$$
 PhSCH-EWG  
 $\stackrel{l}{\xrightarrow{}}$  I PhSCH-EWG  
 $\stackrel{l}{\xrightarrow{}}$  PhSCH-EWG  
 $\stackrel{l}{\xrightarrow{}}$  PhSCH-EWG

Especially, it has been underlined that the presence of EWG in 1 was a necessary condition to achieve such anodic fluorination in good or high yields. Nevertheless, it has to be quoted that anodic conversion of thioanisole could also be obtained in tetrahydrofuran but in much lower yields.

In the present paper, we describe (see table 1) the fluorination of substrates 3 possessing an EWG as a substituent onto the aromatic moiety. The interest of transient 4 would be to afford by cleavage monofluorinated chains 5. The reaction was found to be regioselective. Fixed potential electrolyses (first oxidation step of 3) led only to the monofluorinated product.



			Working	Isolated	m.p.	Products 4
compound	EWG	R	Potential	Yields	(°C)	<sup>19</sup> F NMR
				~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~~		160.0 (1F, t)
<b>3a</b>	p-NO <sub>2</sub>	н	1.65	55*	84-85	$^{2}J_{HF} = 52 \text{ Hz}$
						147.5 (1F, ddd)
3b	p-NO <sub>2</sub>	(CH <sub>2</sub> ) <sub>2</sub> CH <sub>3</sub>	1.50	50*	liq	${}^{2}J_{HF} = 56 \text{ Hz} ; {}^{3}J_{HF} = 20 \text{ Hz}$
						$^{3}J_{\rm HF} = 16$ Hz
3 c	p—CN	Н	1.50	50*	liq	$159.5 (^{1}F, t); ^{2}J_{HF} = 52 Hz$
	[					147.0 (1F, ddd);
3d	p-CN	(CH <sub>2</sub> ) <sub>6</sub> CH <sub>3</sub>	1.50	20	liq	$^{2}J_{HF} = 56 \text{ Hz} ; ^{3}J_{HF} = 20 \text{ Hz})$
						$^{3}J_{\text{HF}} = 16 \text{ Hz}$
						147.5 (1F, ddd);
3e	p-SO <sub>2</sub> Me	$(CH_2)_2CH_3$	1.45	60	57-58	$^{2}J_{HF} = 56 \text{ Hz} ; ^{3}J_{HF} = 20 \text{ Hz})$
						$^{3}J_{HF} = 16 \text{ Hz}$
					50.50	147.0 (1F, ddd);
3f	p-SO <sub>2</sub> Me	(CH <sub>2</sub> ) <sub>6</sub> CH <sub>3</sub>	1.40	65	58-59	$^{2}J_{HF} = 56 \text{ Hz}$ ; $^{3}J_{HF} = 20 \text{ Hz}$ )
						$^{3}J_{HF} = 16 \text{ Hz}$
			1.45	*	14 46	147.0 (1F, ddd);
3g	p-SO2Oct	(CH <sub>2</sub> ) <sub>6</sub> CH <sub>3</sub>	1.45	67*	44-40	$^{2}J_{HF} = 56 \text{ Hz}; ^{3}J_{HF} = 20 \text{ Hz})$
				ļ		$^{3}J_{HF} = 16 \text{ Hz}$
21	- SO-Dh	CH-) CH-	1 45	55	52 54	146.9 (1F, ddd)
511	p-sogra	(Сп2)6СП3	1.45	55	55-54	$^{2}J_{HF} = 56 Hz$
						$^{3}J_{HF} = 20 \text{ Hz}$
				ļ		$^{3}$ <sub>HF</sub> = 16 Hz
21	SOLD	(CHA) CHA	1.55	63	lia	147.2 (IF, ddd, CHF)
51	0	(Ch2)6Ch3	1.55	05	пq	$^{2}J_{HF} = 50 HZ$
1						$^{3}J_{\text{HF}} = 20 \text{ Hz}$
						1.2 Jurg = 16 Hz

Table 1: Fluorination relevant to the  $3 \rightarrow 4$  transition with sulfide amounts of 2 mmoles in acetonitrile containing Et<sub>3</sub>N, 3HF at the concentration  $10^{-2}$  M. (Working anode : platinum sheet, area : 5 cm<sup>2</sup>). Current density at the electrolysis start : 20 mA.cm<sup>2</sup>. All experiments were carried out in a one compartment cell except with compounds **3a**, **3b**, **3c**, and **3g** for which<sup>\*</sup> a cell equipped with a glass separator was used. Potentials are referred to Ag/Ag<sup>+</sup> NO<sub>3</sub><sup>-</sup> 0.1 M electrode in acetonitrile.

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