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OXIDATIVE FLUORINATION OF SULFIDES IN PRESENCE OF $Et_3N.3HF$

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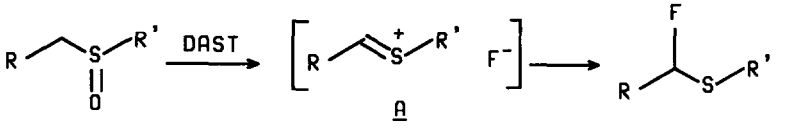
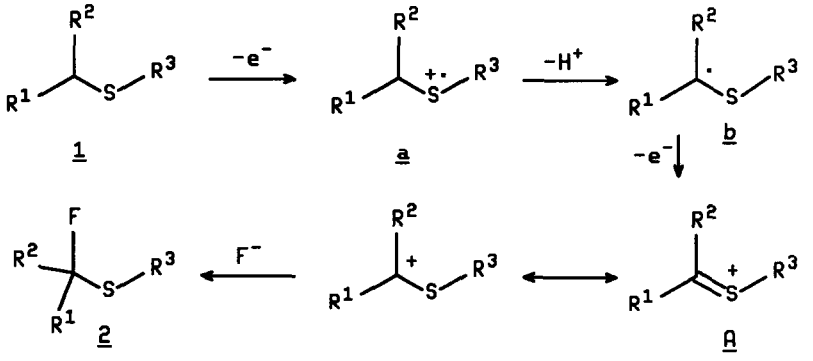
Summary : The synthesis of fluorocompounds by sulfide electrochemical oxidation using $Et_3N.3HF$ as fluorinating agent is described. Chemical oxidation (DBH) is less efficient.

Novel methods of introduction of fluorine in organic molecules are useful because of the biological potentiality of fluorinated molecules[1]. It is particularly interesting to use amine hydrofluorides as fluorinating agents as they are not very toxic and are easy to handle ; this justifies our use of $Et_3N.3HF$ to synthesize α-fluorothioethers. Previously these compounds were synthesized by the reaction of diethylaminosulfur trifluoride (DAST) on sulfoxides[2]. This reaction proceeds by the addition of a fluoride ion on the sulfonium ion **A** which results from a Pummerer rearrangement :



A

Sulfonium ions such as **A** can also be obtained by the oxidation of sulfides[3]. If this reaction is carried out in the presence of fluoride ions, the preparation of α-fluorothioethers can be expected as follows :

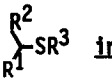


1 **a** **b** **2** **A**

We wish to report our results on the electrochemical and chemical oxidation of sulfides 1 in $CH_3CN/Et_3N.3HF$.

Electrochemical oxidation

Constant potential electrolysis of sulfides 1a-d (2.25 mmole) was carried out on a platinum electrode in acetonitrile (30 ml) containing $Et_3N.3HF$ (4.5 ml) at room temperature,with the results shown in the table.

Table : Anodic oxidation of sulfide  **in the presence of $Et_3N.3HF$**

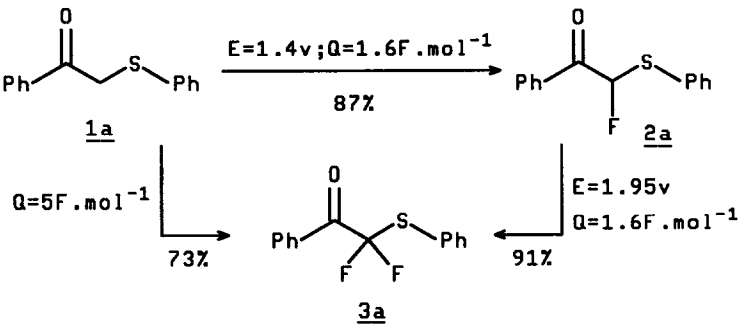
1		E(v)[a]	Coulometry ($F.mol^{-1}$)	PRODUCTS 2 %	other products %
				yields in isolated products	
1a	R^1=PhCO, R^2=H, R^3=Ph	1.10	1.6[b]	2a 87	
1b	R^1=Ph, R^2=CO_2Et, R^3=Ph	1.10	6.9[c]	2b 84	
1c	R^1=CO_2Et, R^2=H, R^3=CH_2CO_2Et	1.46	4.0[c]	2c 50	$Et_2OC-CH_2-\overset{\overset{O}{\|}}{S}-CH_2CO_2Et$ 19
1d	R^1=$CH_3(CH_2)_6$, R^2=H, R^3=Ph	1.02	1.8[b]		$CH_3-(CH_2)_7-\overset{\overset{O}{\|}}{S}-Ph$ 73
		1.60	3.4[b]		$CH_3-(CH_2)_7-SO_2Ph$ 51
					$CH_3-(CH_2)_5-\underset{\underset{\diagdown COCH_3}{\|}}{\overset{\overset{HN}{\diagup}}{CH}}-CH_3$ 12

[a] vs Ag/0.01M $AgNO_3$; [b] divided cell ; [c] undivided cell.

The formation of the sulfonium ion is conditioned by the deprotonation of the intermediate radical cation a. Under our experimental conditions $F_3H_2^-$ was not basic enough to deprotonate the radical cation of aliphatic sulfides such as 1d. For this particular substrate, the nucleophilic attack on sulfur, which provides the sulfoxide is faster than the deprotonation. On the other hand, substrates 1a, 1b and 1c with an electron-withdrawing group in the β position of sulfur yielded a captodative radical b which provides the sulfonium ion A and the corresponding fluorinated derivatives. These

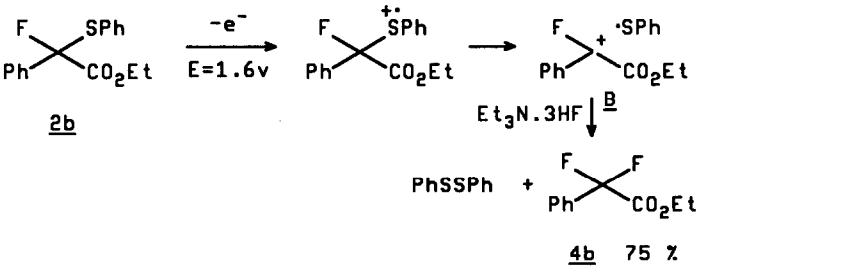
observations agree with literature results. In practice, methoxylation and acetoxylation occur in the α position of nitriles[3], carbonyls[5] and CF_3 group[6]. However, only acetoxylation can be carried out on substrates without the electron-withdrawing group[5].

Compound **2a** contains another proton susceptible of being substituted by a fluorine atom. Therefore, by increasing the potential during the electrolysis, the difluorocompound **3a** was obtained. This product **3a** can also be synthesized in a one pot reaction from the starting sulfide **1a**.



1a 2a 3a

By continuing the oxidation of **2b**, the C-S bond is broken affording ethylphenyldifluoroacetate **4b**.



2b 4b 75 %

(for 100 % conversion of 2b)

The cleavage of the C-S bond seems to be related to the stability of the carbocation **B**[7]. This can explain the fact that trifluoroacetophenone was obtained only in a low yield from the oxidation of **3a**.

Chemical oxidation

In order to compare our electrochemical results with chemical oxidations, the sulfides **1b** and **1d** were oxidized by 1,3-dibromo-5,5'-dimethylhydantoin (DBH)[8] with $Et_3N.3HF$. **1b** only yields the monofluorocompound **2b** in a lower yield than by the electrochemical route, but not the sulfone. In every case, no C-S bond breaking products

are observed. The oxidative power of DBH seems to be weaker than the electrooxidation. In conclusion, the oxidation of sulfides **1** substituted by an electron-withdrawing group in the presence of $Et_3N.3HF$ provides α-fluorothioethers. Furthermore, electrochemical oxidation allows fluorination to be continued which affords, depending on the structure of the sulfide, either difluorothioethers or compounds corresponding to the substitution of the SPh group by a fluoride.

References and Notes

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4 - Products purified by chromatography on silica gel. Spectral data :

2a - ^1H NMR (60 MHz, $CDCl_3$) : 6.70 (1H, d, $^2J_{HF}$=53, CHF) ; 7.1-7.6 (8H, m, H arom.) ; 7.8-8.1 (2H, m, H_o PhCO).
^{19}F NMR (60 MHz, $CDCl_3$) : -159.3 (1F, d, $^2J_{HF}$=53).
MS (70 eV) m/z : 246 ($M^{\cdot +}$).

2b - ^1H NMR (60 MHz, $CDCl_3$) : 1.05 (3H, t, J=8, CH_3) ; 3.99 (2H, q, J=8, CH_2) ; 7.1-7.8 (10H, m, H arom.).
^{19}F NMR (60 MHz, $CDCl_3$) : -132.0 (1F, s).

2c - ^1H NMR (300 MHz, $CDCl_3$) : 1.29 (3H, t, J=7, $CH_2CO_2CH_2CH_3$) ; 1.34 (3H, t, J=7, $CHFCO_2CH_2CH_3$) ; 3.50 and 3.53 (2H, ABX system, $^2J_{HH}$=17, $^4J_{HF}$=2, CH_2CO_2Et) ; 4.21 (2H, q, $CH_2CO_2CH_2CH_3$) ; 4.17-4.35 (2H, m, $CHFCO_2CH_2CH_3$) ; 6.03 (1H, d, $^2J_{HF}$=51, CHF).
^{19}F NMR (80 MHz, $CDCl_3$) : -166.2 (1F, d, $^2J_{HF}$=51).

3a - ^1H NMR (60 MHz, $CDCl_3$) : 7.1-7.8 (8H, m, H arom.) ; 8.0-8.4 (2H, m, H_o PhCO).
^{19}F NMR (60 MHz, $CDCl_3$) ; -77.3 (2F, s, CF_2).
MS (70 eV) m/z : 264 ($M^{\cdot +}$).

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