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Electrochemistry of Hypervalent Compounds. 6. Selective α-Fluorination of Sulfides Using Electrogenerated Hypervalent *p*-Methoxyiodobenzene Difluoride[1]

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Anodically generated hypervalent *p*-methoxyiodobenezene difluoride reacted with α-(arylthio)- and α-(benzylthio)acetates, and α-(phenylthio)acetophenone to provide the corresponding fluorinated compounds. In all cases, a fluorine atom was introduced exclusively α to the ester or benzoyl group.

INTRODUCTION

Organofluorine compounds are highly useful for the development of novel medicines, agrochemicals, and functional materials.[2] Therefore, selective fluorination of organic compounds has been increasingly important.[3] On the other hand, hypervalent iodobenzene difluorides have been reported to be useful fluorinating reagents by Zupan[4] and Motherwell.[5] However, such compounds are unstable in general, and their preparation requires hazardous fluorine gas[6-8] or costly XeF_2.[4]

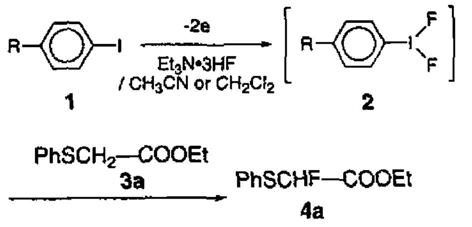
In view of this, we have recently developed an electrochemical method for the preparation of hypervalent iodobenzene difluorides.[9] This new method is safe and does not require any hazardous reagents. Although iodobenzene difluorides are useful, their synthetic applications have still been limited. The difluorides have been used for the fluorination of alkenes and alkynes, and for fluorodesulfurization so far.[4,5]

With these in mind, we have attempted fluorination of organo sulfur compounds such as α-(arylthio)-, α-(benzylthio)- and α-(alkylthio)acetates and α-(phenylthio)acetophenone using electrogenerated hypervalent iodobenzene difluorides.

RESULTS AND DISCUSSION

Fluorination of ethyl α-(phenylthio)acetate **3a** as a model compound was carried out using various *p*-substituted iodobenzene difluorides **2**[9] generated by anodic oxidation of *p*-substituted iodobenznenes **1** in acetonitrile or dichloromethane containing $Et_3N{\cdot}3HF$ as a supporting electrolyte and fluorine source. Since **2** is unstable to isolate, except for **2c** as reported previously,[9] the electrolytic solution containing **2** was subsequently used for the fluorination of **3a**. Two molar equiv of **2** was used for this fluorination because the fluorination was found to be slow.

As shown in Table 1, *p*-chloro- and *p*-nitroiodobenzene difluorides **2b** and **2c** gave only a trace amount of the desired α-fluorinated product **4a**, while *p*-methoxyiodobenzene difluoride **2a** provided **4a** in high yield based on the consumed starting material **3a** regardless of the solvents. From these results, fluorinating ability of **2** toward sulfides such as **3a** was greatly affected by the substituent R groups on the benzene ring of **2**. Thus, iodobenzene difluoride **2a** having an electron-donating methoxy group at the para position was found to be suitable for this fluorination.



(1)

Next, the fluorination using **2a** was extended to various α-(arylthio)-, α-(benzylthio)- and α-(alkylthio)acetates, and α-(phenylthio)acetophenone. As shown in Table 2, α-(arylthio)acetates **3a**-**3c** and α-(benzylthio)acetate **3d** underwent fluorination to provide the corresponding α-fluorinated products **4a**-**4d**, selectively, in reasonable absolute yields and in high yields based on the consumed **3**. Although α-(benzylthio)acetate **3d** has multiple positions susceptible to substitution by a fluorine, regioselective fluorination took place: a fluorine was introduced exclusively α to the ester group, and no benzylic fluorination was observed. Moreover, fluorination did not take place at the benzene ring

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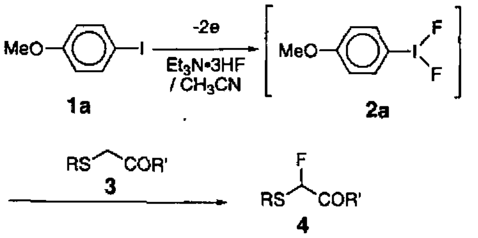
Dedicated to Professor Hsien-Ju Tien on the occasion of his 65th birthday.

Table 1. Fluorination of Ethyl α-(Phenylthio)acetate **3a** Using Anodically Generated Iodobenzene Difluorides

2 No.	2 R	Anodic Potential (V vs. SSCE)	Charge Passed (F/mol)	Solvent	Yield of **4a**[a] (%)
2a	CH_3O	1.9	4.9	CH_3CN	73 (37)
2a	CH_3O	1.9	4.9	CH_2Cl_2	78 (38)
2b	Cl	2.2	5.2	CH_2Cl_2	trace
2c	NO_2	2.3	5.1	CH_2Cl_2	trace

[a] Based on consumed **3**. The values in parentheses show absolute yields.

at all. Therefore, this fluorination is highly selective. In contrast to the cases of **3a-3d**, α-(alkylthio)acetate **3e** gave only trace amount of α-fluorinated product **4e**, and a large amount of starting **3e** was recovered. α-(Phenylthio)acetophenone **3f** also reacted with **2a** to provide the desired α-fluorinated product **4f**.



(2)

It was proposed that the sulfur atom of dithioacetals attacked nucleophilically the iodine atom of iodobenzene difluoride in the fluorodesulfurization to give the corresponding *gem*-difluoro compounds.[5b] As mentioned already, iodobenzene difluorides **2b** and **2c**, having electron-withdrawing groups at the para position, did not fluorinate α-(phenylthio)acetate. In consideration of these facts, a possible mechanism for the α-fluorination of organo sulfur compounds with **2a** can be illustrated as shown in Scheme I.

Scheme I

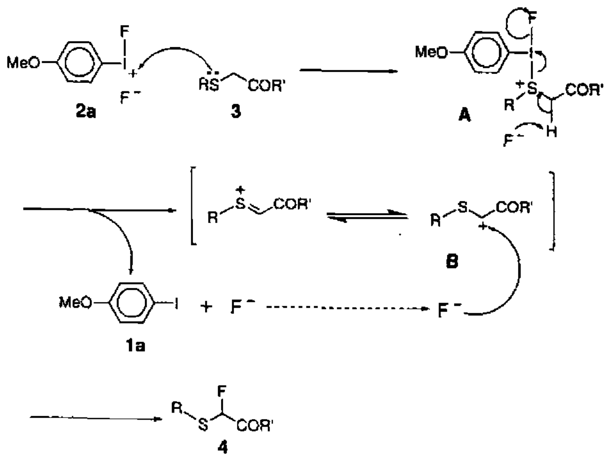


Table 2. α-Monofluorination of Sulfides Using Anodically Generated *p*-Methoxyiodobenzene Difluoride

3	Sulfide R	R′	Conversion (%)		Yield of **4**[a] (%)
3a	Ph	OEt	49	**4a**	78 (38)
3b	*p*-ClC_6H_4	OEt	35	**4b**	86 (30)
3c	*p*-$CH_3OC_6H_4$	OEt	48	**4c**	79 (38)
3d	$PhCH_2$	OEt	67	**4d**	66 (44)
3e	*n*-C_7H_{15}	OEt	-[b]	**4e**	trace
3f	Ph	Ph	-[b]	**4f**	- (25)

[a] Based on consumed **3**. The values in parentheses show absolute yields.

[b] A large amount of the starting material was recovered.

In this mechanism, the electron-donating methoxy group should promote the elimination of a fluoride ion of **2a** to form another type of a hypervalent compound **A** as the intermediate, followed by deprotonation and elimination of *p*-methoxyiodobenznene **1** to form the cationic intermediate **B**, which reacts with a fluoride ion from either **2** or supporting electrolyte $Et_3N \cdot 3HF$ to provide **4**. In fact, a large amount of **1** was recovered after the fluorination reaction. The intermediate similar to **A** was also proposed for the reaction of α-acylsulfides with iodobenzene bis(trifluoroacetate).[10]

Thus, we have demonstrated for the first time that electrogenerated hypervalent *p*-methoxyiodobenzne difluoride can be used for the selective fluorination of organo sulfur compounds.

EXPERIMENTAL SECTION

The electrolysis experiment was carried out using a Hokutodenko HA-501 potentiostat/Galvanostat equipped with a Hokutodenko HF-201 digital coulombmeter.

Fluorination of Organo Sulfur Compounds 3 Using Electrogenerated *p*-Methoxyiodobenezene Difluoride 2a

A typical procedure went as follows. Electrolysis was performed at a platinum anode and cathode (3 × 4 cm^2) in 0.67 M $Et_3N \cdot 3HF$/MeCN or CH_2Cl_2 (20 mL) containing 1.5 mmol of *p*-methoxyiodobenzene **1a** using a divided cell with an anion-exchange membrane (IE-DF34-5 TOSOH) under nitrogen atmosphere at ambient temperature. After the starting **1a** was completely consumed (TLC monitoring), the electrolytic solution containing electrogenerated **2a**[9] was mixed with a solution of 0.75 mmol of organosulfur compound **3** in 10 mL of MeCN or CH_2Cl_2. The resulting mixture was stirred overnight under nitrogen atmosphere at ambient temperature. After evaporation of the solvent under reduced pressure, the residue was dissolved in $CHCl_3$ and mixed with 50 mL of water. The organic layer was separated, the remaining aqueous solution was extracted repeatedly with $CHCl_3$ (50 mL × 3). The combined extracts were dried over anhydrous $MgSO_4$, and **4** was isolated by column chromatography on silica gel (CH_2Cl_2 for **4c**; $CHCl_3/CCl_4$, 1:1-7:3 for **4a**, **4b**, **4d-4f**). The spectral data (MS, ^{19}F NMR, ^1H NMR) of these products **4a-4f** are identical with the reported values.[11]

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Key Words

Direct fluorination; α-Fluorosulfide; α-Acylsulfide; Hypervalent compound; Iodobenzne difluoride; $Et_3N{\cdot}3HF$.

REFERENCES

1. Part 5: Fuchigami, T.; Miyazaki, M. *Electrochim. Acta* **1997**, *42*, 1979.
2. (a) *Biomedicinal Aspects of Fluorine Chemistry*; Filler, R., Kobayashi, Y., Eds.; Kodansha & Elsevier Biomibical: Tokyo, 1982. (b) Welch, J. T.; Eswarakrishnan, S. *Fluorine in Bioorganic Chemistry*; Wiley: New York, 1991. (c) Fuchigami, T. *Topics in Current Chemistry 170. Electrochemistry V*; Steckhan, E., Ed.; Springer-Verlag, Heideberg, 1994, p. 1.
3. (a) Fuchigami, T.; Konno, A. *J. Synth. Org. Chem. Jpn.* **1997**, *55*, 301. (b) Fuchigami, T.; Nishiyama, S. *J. Electrochem. Soc. Jpn.* **1997**, *65*, 626. (c) Fuchigami, T. *Rev. Heteroatom. Chem.* **1994**, *10*, 154. (d) *Selective Fluorination in Organic and Bioorganic Chemistry*; Welch, J. T., Ed.; American Chemical Society: Washington, DC, 1991.
4. (a) Zupan, M.; Pollak, A. *J. Fluorine Chem.* **1977**, *7*, 445. (b) Gregorcic, A.; Zupan, M. *Bull. Chem. Soc. Jpn.* **1976**, *50*, 517. (c) Gregorcic, A.; Zupan, M. *J. Chem. Soc., Perkin Trans. 1* **1977**, 1446.
5. (a) Edmunds, J. J.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1989**, 881. (b) Motherwell, W. B.; Wilkinson, J. A. *Synlett* **1991**, 191. (c) Caddick, S.; Motherwell, W. B.; Wilkinson, J. A. *J. Chem. Soc., Chem. Commun.* **1991**, 674. (d) Koen, M. J.; Guyader, F. L.; Motherwell, W. B. *J. Chem. Soc., Chem. Commun.* **1995**, 1241.
6. Malefina, I. I.; Orda, V. V.; Aleinikov, N. N.; Korsunskii, B. L.; Yagupolskii, I. M. *Zh. Org. Khim.* **1976**, *12*, 1371.
7. Ruppert, I. *J. Fluorine Chem.* **1980**, *15*, 173.
8. Naumann, D.; Ruther, G. *J. Fluorine Chem.* **1980**, *15*, 213.
9. Fuchigami, T.; Fujita, T. *J. Org. Chem.* **1994**, *59*, 7190.
10. Tamura, Y.; Yakura, T.; Shirouchi, Y.; Haruta, J. *Chem. Pharm. Bull.* **1986**, *34*, 1061.
11. Fuchigami, T.; Shimojo, M.; Konno, A. *J. Org. Chem.* **1995**, *60*, 3459.