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Electrolytic Partial Fluorination of Organic Compounds. 20.[1] Electrosynthesis of Novel Hypervalent Iodobenzene Chlorofluoride Derivatives and Its Application to Indirect Anodic *gem*-Difluorination

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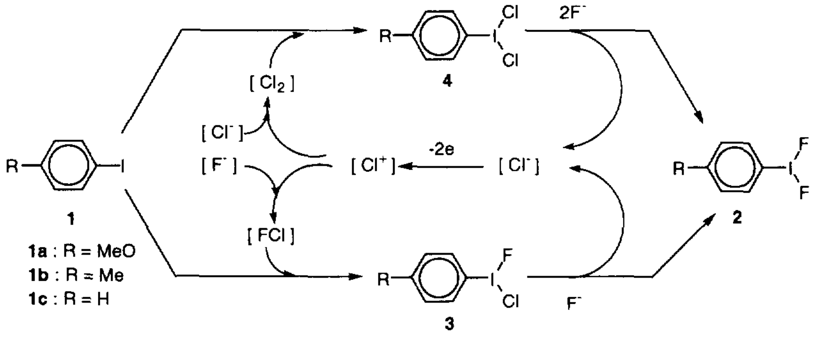
Abstract: Electrosynthesis of novel hypervalent iodobenzene chlorofluorides was successfully performed for the first time and it was demonstrated that *p*-methoxyiodobenzene chlorofluoride could be used as a mediator for indirect anodic *gem*-difluorination of dithioacetals.

Much attention has been paid to hypervalent organoiodine compounds from both synthetic and mechanistic aspects.[2] Hypervalent iodobenzene difluorides have been reported to be useful fluorinating reagents by Zupan[3] and Motherwell.[4] However, such compounds are generally unstable, moreover, their preparation requires hazardous fluorine gas[5] or costly XeF_2.[3]

Recently, we have reported that anodic oxidation of *p*-nitro- and *p*-methoxyiodobenzenes with $Et_3N{\bullet}3HF$ provided the corresponding hypervalent iodobenzene difluorides efficiently.[6] This electrochemical method is quite safe because hazardous reagents are not necessary. However, simple unsubstituted iodobenzene and *p*-iodotoluene did not give the desired difluorides because the former gave mainly a dimer and the latter gave a benzylic fluorinated product along with complex products.

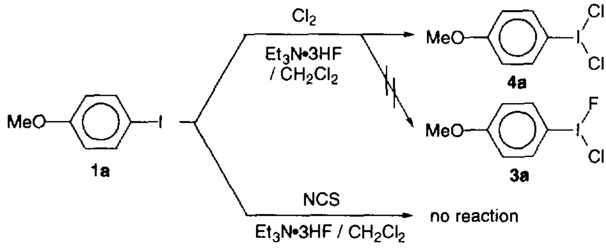
With these facts in mind, we have attempted to synthesize hypervalent iodobenzene difluorides **2** using indirect anodic oxidation of iodobenzenes with a chloride ion mediator as shown in Scheme 1.



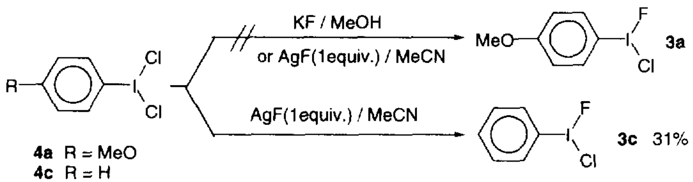
Scheme 1

Anodic oxidation of *p*-methoxyiodobenzene (**1a**) was performed in the presence of fluoride and chloride ions in anhydrous CH_2Cl_2.[7] The electrolytic fluorination proceeded smoothly. However, the product was not the expected difluoride **2a** but *p*-methoxyiodobenzene chlorofluoride (**3a**). Similarly, *p*-tolyliodobenzene (**1b**) and simple iodobenzene (**1c**) provided the corresponding chlorofluorides **3b** and **3c**, respectively. In these cases, side reactions such as benzylic fluorination and dimerization were not observed at all. Since isolation of **3** was difficult due to their instability, their structures were indirectly confirmed as follows. Although the mass spectrum of difluoride **2a** showed its molecular ion peak, m/e 272[6], such molecular ion peak was not observed in the mass spectrum of the electrolytic solution containing **3a**. Instead, only fragmentation ion peaks such as m/e 271, 269 (p-MeOC$_6$H$_4$ICl$^+$), and 253 (p-MeOC$_6$H$_4$IF$^+$) were observed. Therefore, it was concluded that difluoride **2a** was not formed in this electrolysis.

Next, the synthesis of **3a** was attempted independently as shown in Scheme 2. However, all attempts were unsuccessful. N-Chlorosuccinimide (NCS) did not react with **1a** at all. Treatment of **1a** with chlorine gas in the presence of fluoride ions gave dichloride **4a**[8] solely and **3a** was not formed. Then, halogen exchange of **4a** was attempted. However, the reaction of **4a** with KF did not proceed. Treatment of **4a** with AgF resulted in formation of complex products. On the other hand, halogen exchange of simple iodobenzene dichloride **4c** with AgF (one equiv.) proceeded to provide the desired chlorofluoride **3c** although the yield was low (31 % yield based on ^{19}F NMR) (Scheme 3). However, isolation and purification of **3c** were also unsuccessful because of its instability.



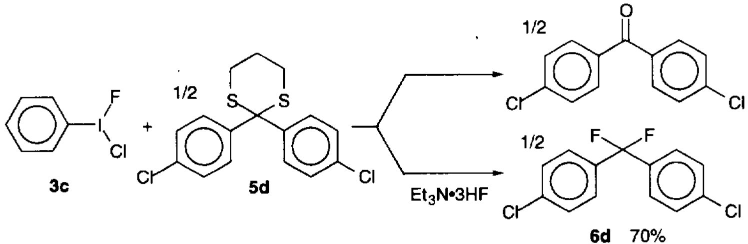
Scheme 2



Scheme 3

The product **3c** showed one singlet (δ=-73.58 ppm) in the ^{19}F NMR spectrum and also showed flagmentation ion peaks such as m/e 241, 239 (C$_6$H$_5$ICl$^+$), and 223 (C$_6$H$_5$IF$^+$) in the mass spectrum, but the molecular ion peak of **3c** was not observed at all.

Iodobenzene difluorides **2** are known to be useful fluorinating reagents. For example, the reaction of dithioacetals with **2** gives difluoromethylene compounds efficiently.[4b] Therefore, we were interested to know whether these novel hypervalent iodobenzene chlorofluorides **3** can be used as a fluorinating reagent or not. The reaction of dithioacetal **5d** as a model dithioacetal with chemically prepared crude **3c** was then carried out in dry MeCN. Desulfurization proceeded; however, fluorination did not take place and the formation of a large amount of 4,4'-dichlorodiphenylketone was detected. On the contrary, fluorination proceeded in the presence of a large amount of Et$_3$N•3HF to provide *gem*-difluoro product **6d** in relatively good yield (70 %) as shown in Scheme 4. In this case, chlorination did not take place at all. In sharp contrast to the case of **3c**, the dichlorides **4a** and **4c** did not react at all with dithioacetal **5d** in the presence of Et$_3$N•3HF and the starting **5d** was recovered. Thus, it was found that hypervalent iodobenzene chlorofluorides acted not as a fluorinating reagent but as an oxidizing reagent. The oxidizing power of **3** was found to be much stronger than that of the corresponding dichloride **4**.



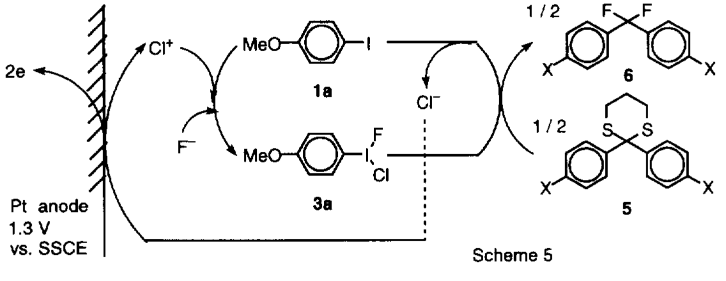
Scheme 4

Furthermore, it was confirmed that, without isolation of **3**, an electrolytic solution containing **3** (two equiv. to **5a**) was subsequently used for *gem*-difluorination of dithioacetals **5a**, and **6a** was obtained in moderate yields (**3a**: 51 %; **3b**: 55 %; **3c**: 53 %) regardless of substituents at the benzene ring. Thus, it was found that reactivity of **3** was not affected by the substituents.

Then, in order to decrease the required amount of starting iodobenzene, we attempted to use iodobenzene chlorofluoride **3** as a mediator for indirect anodic fluorination (Scheme 5). In this study, *p*-methoxyiodobenzene chlorofluoride (**3a**) was used as a model mediator.[9]

As shown in Table 1, this mediatory system worked nicely even at a low anodic potential as +1.3 V vs. SSCE, at which **1a** can not be oxidized at all. Even when a catalytic amount of iodobenzene **1a** was used, the reaction proceeded quite smoothly to give *gem*-difluoro products **6** in good yields (runs 2 and 3).

In contrast, in the case of electrolysis of **5** at 1.3V in the absence of iodobenzene **1a**, the electrolytic current became extremely small (*ca.* 3 mA) immediately after the electrolysis was started. Although it took a long time (*ca.* 35 h) to complete the electrolysis, fluorination took place but the yield was quite low (run 6).[11] Therefore, iodobenzene **1a** is essential to acieve efficient *gem*–difluorination.



Scheme 5

Table 1. Indirect Anodic *gem*–Difluorination of Dithioacetals

Run	**1a** equiv. to **5**	**5** X	Charge Passed (F / mol)	Yield of **6** (%)
1	0.2	H	3.8	**6a** (81)
2	0.05	H	3.7	**6a** (77)
3	0.05	MeO	3.8	**6b** (86)
4	0.05	F	3.7	**6c** (66)
5	0.05	Cl	3.7	**6d** (61)
6	—	Cl	3.7	**6d** (23)

It is known that severe passivation of an anode takes place generally during anodic partial fluorination.[10] In fact, pulse electrolysis was nessesary to avoid such passivation of the anode in the case of direct anodic *gem*–difluorination of dithioacetals.[13] In contrast to such direct fluorination, this indirect anodic fluorination did not cause the passivation at all. Furthermore, this anodic *gem*–difluorination does not require any oxidizing or dangerous reagents and can be carried out in normal glassware.

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7. The electrolysis was carried out at a platinum anode and cathode (3 x 4 cm^2) in 0.69 M Et_3N•3HF + 0.15 M Et_4NCl / 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.
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9. Anodic oxidation was carried out similarly at 1.3V vs SSCE in 0.46 M Et_3N•3HF + 0.05 M Et_4NCl / CH_2Cl_2 (20 ml) containing 1.0 mmol of dithioacetal **5** together with 0.2 or 0.05 mmol of **1a**. After **5** was completely consumed (TLC monitoring), the electrolytic solution was mixed with water and a CH_2Cl_2 layer was separated. The aqueous layer was extracted with CH_2Cl_2 repeatedly. The extracts were dried over anhydrous $MgSO_4$ and concentrated. The product **6** was isolated by column chromathography (silica gel, CH_2Cl_2 : Hexane = 1 : 2).
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11. In this case, FCl or its equivalent seems to be generated electrochemically in a manner similar to the case of the Br^-/F^- mixed system as reported previously.[12]
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