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Synthesis of the first difunctional *N*-fluoro perfluoroalkylsulfonylimides, $CF_3SO_2NFSO_2(CF_2)_nSO_2NFSO_2CF_3$

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Dedicated to Professor D.W.A. Sharp in recognition of his contribution to Journal of Flourine Chemistry

Abstract

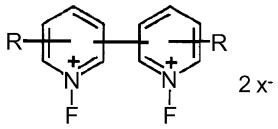
Synthesis of difunctional *N*,*N*′-difluoro perfluoroalkylsulfonamides, $CF_3SO_2NFSO_2(CF_2)_nSO_2NFSO_2CF_3$, where $n = 4, 6$ is reported. A related compound with an oxygen linkage $CF_3SO_2NFSO_2(CF_2)_2O(CF_2)_2SO_2NFSO_2CF_3$ has also been prepared. These reagents showed good activity for electrophilic fluorination.

Keywords: Selective fluorination; *N*-Fluorosulfonyl imides; Difunctional fluorination reagents

1. Introduction

During the past decade, many compounds with an NF moiety have been made available as easy-to-handle and highly reactive electrophilic fluorinating reagents [1–3]. Among more than 30 different kinds of NF compounds developed, *N*-fluoro bis((perfluoroalkyl)sulfonyl)imide, first introduced in 1987 [4], possesses the most powerful fluorinating activity.

N,*N*′-Difluoro-1,4-diazoniabicyclo[2,2,2]octane salts were the first fluorination reagents containing two NF moieties in one molecule [5,6]. In these compounds, only one NF function is effective for fluorination and the other promotes the fluorination reactivity. The first true difunctional NF compounds reported in the literature [7] were the *N*,*N*′-difluoro dipyridine derivatives.



These NF reagents exhibited fluorinating power similar to the monofunctional compounds and both fluorine atoms could be utilized in the fluorination of certain carbanions.

During the past several years, our research group has developed a new series of difunctional perfluorosulfinimides [8,9], $R_FSO_2NHSO_2R_F'SO_2NHSO_2R_F''$. Both –NH-protons are strongly acidic and should be easily converted to respective *N*-fluoro compounds. Initial attempts to prepare the NF derivatives of these difunctional compounds under conditions similar to that used for preparation of $(CF_3SO_2)_2NF$ led to no reaction with fluorine. We now report the successful synthesis of the difunctional *N*-fluoro compounds and examples of their reactivity in selective fluorination.

2. Results and discussion

Starting from commercially available $I(CF_2)_nI$ ($n = 4, 6$) and $I(CF_2)_2O(CF_2)_2SO_2F$, α,ω-disulfonyl fluoride compounds (**2a–c**) were prepared in overall yields of more than 65%. (Scheme 1).

In the formation of $CF_3SO_2N(Na)SO_2R_FSO_2N(Na)SO_2CF_3$ (**3a–c**), acetonitrile was initially used as solvent and the reaction was carried out at 1 atm under nitrogen. Due to the relatively low boiling point of this solvent, the desilylation reaction in refluxing acetonitrile required several days for complete conversion. When a higher boiling point solvent 1,4-dioxane was used instead, the reaction was complete in <8 h, but dioxane was strongly complexed to the sodium salts and complete removal by prolonged heating under vacuum was difficult [10]. Finally, a closed system

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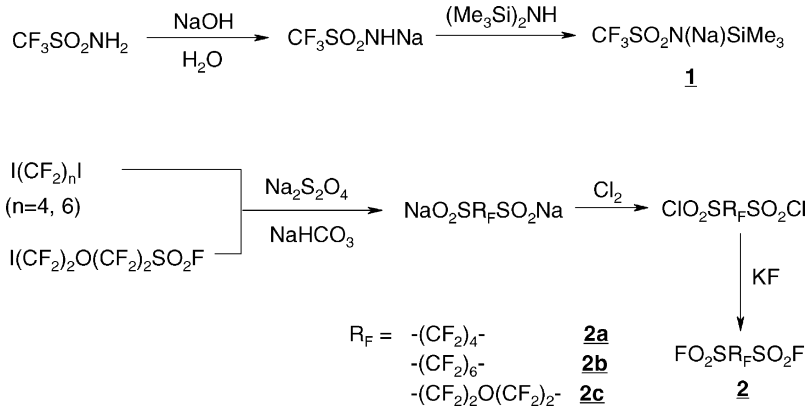
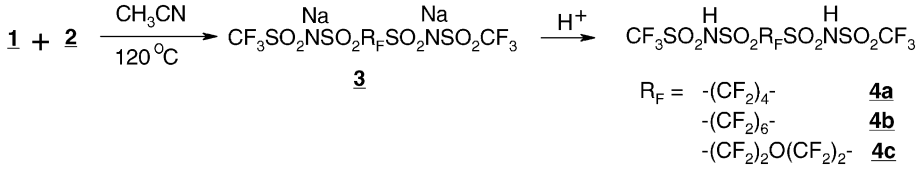


Scheme 1. Preparation of starting materials.



Scheme 2. Preparation of parental di-NH compounds.

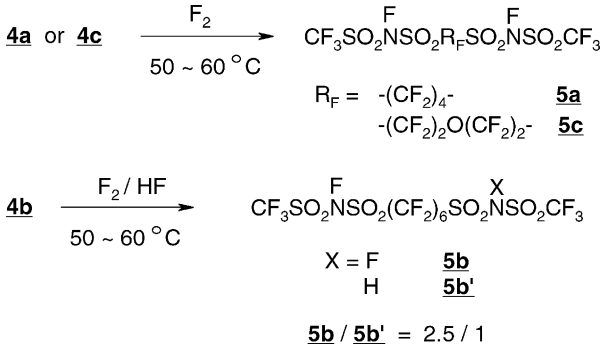
with acetonitrile as solvent was chosen. Reactions were carried out in a stainless steel bomb at 120 °C for 6 h to achieve more than 95% yields of **3** (Scheme 2).

Concentrated sulfuric acid is often used to convert the salt form to its acid form in simple sulfonimides such as $R_FSO_2NHSO_2R_F'$ (R_F, $R_F' = CF_3$, C_4F_9, C_6F_{13}, C_8F_{17}). These can be easily sublimed from the mixture of the salt with H_2SO_4 under high vacuum. For the difunctional sodium salts (**3**), only **4c** was readily sublimed from H_2SO_4 at 70 °C. Increasing the temperature to >100 °C fails to give **4a** or **4b** and the 96–98% sulfuric acid begins to volatilize under high vacuum. Therefore ion exchange using Nafion-H beads was used to acidify **3a** and **3b**.

Fluorination of these difunctional NH compounds (**4a–c**) with elemental fluorine required much longer reaction times and higher temperatures than the related monofunctional derivatives [11]. Heating **4a** and **4c** with excess fluorine at 50–60 °C for 7–14 days gave good yields of corresponding *N*-fluoro derivatives **5a** and **5c**. For compound **4b** with a longer perfluorocarbon chain, the same conditions did not give any **5b**. Increasing the reaction temperature to 80 °C led to the destructive fluorination of **4b**. Finally, it was realized that the presence of a liquid phase HF during the fluorination could serve as a solvent and promote the fluorination. Heating **4b** at 50–60 °C with a large excess of F_2 and HF in a reaction bomb for 10 days gave **5b** as the major product along with a partially fluorinated minor product **5b′** (Scheme 3 and Table 1). All of these NF compounds are stable and non-hydroscopic. The compound **5a** is a colorless solid melting at 28–29 °C and **5c** is a high boiling colorless liquid. The thermal stability of **5a** and **5c** were examined by DSC using 10 mg samples in sealed stainless steel sample pans. The onset of decomposition for **5c** was at 225 °C. Compound **5a** underwent a sudden decomposition at 260 °C, distorting the sample pan. By contrast, the sodium salts **3** are stable to near 450 °C and the acids **4** are stable to near 400 °C.

Due to the very similar physical properties of **5b** and **5b′**, separation was not successful and they were identified from a mixture by ^{19}F NMR. The signals for three of the six CF_2 groups in **5b′** are clearly distinguished from **5b** and do not fit a mixture of **5b** and **4b**. With the correct integrations and the different chemical shifts of the NF fluorines in **5b** and **5b′**, the identify of both **5b** and **5b′** is clear.

The existence of the analogues of **5b′** for **5a** and **5c** were observed by ^{19}F NMR while monitoring reactions of the latter with dicarbonyl compounds. One could clearly



Scheme 3. Synthesis of difunctional NF compounds.

Table 1
Direct fluorination of **4**

NH compound	Reaction conditions	NF product (yield, %)	δ_F of NF (ppm)
4a	50–60 °C, 14 days	**5a** (88%)[a]	−32.0
4b	50–60 °C, 10 days, HF	**5b** (50%)[b]; **5b′** (20%)[b]	−32.2 (**5b**); −32.3 (**5b′**)
4c	50–60 °C, 7 days	**5c** (63%)[a]	−32.2

[a] Isolated yield based on **4**.
[b] ^{19}F NMR estimated yield based on **4**.

observe the formation and subsequent disappearance of **5a′** and **5c′**, indicating as expected that the compounds react in stepwise manner.

The effect of HF and the size of the fluorocarbon groups on the rate of fluorination is interesting. We have observed the same effect for monofunctional compounds where the rate of fluorination of $CF_3SO_2NHSO_2R_F$ ($R_F = C_4F_9, C_6F_{13}, C_8F_{17}$) under the same condition is progressively slower with the increasing size of R_F [11]. The fluorination of $(C_4F_9SO_2)_2NH$ is considerably more difficult than the aforementioned example with $R_F = C_4F_9$. Hydrogen fluoride is formed in the reaction with fluorine and one might assume that if some HF is required, the generated HF would be sufficient. But clearly, the example of **4b** indicates the situation is more complicated and we do not have a good explanation for the variation in reactivity of the parent sulfonimides.

Compounds **5a–c** exhibited good electrophilic fluorinating activity similar to $(CF_3SO_2)_2NF$. When reacted with a 1,3-dicarbonyl compound, 0.5 eq. of NF gave a very clean monofluorination utilizing both NF functions (Scheme 4). Qualitatively, there was little difference in reactivity between **5a** and **5c**.

In conclusion, although they require longer reaction times and higher temperatures to prepare than the monofunctional bis((perfluoroalkyl)sulfonyl)imides, difunctional α,ω-*N*-fluoro bis((perfluoroalkyl)sulfonyl)imides have been successfully prepared and shown to have fluorinating ability similar to the related monofunctional *N*-fluoro sulfonimides.

3. Experimental

IR spectra were taken as neat films on KCl using Perkin-Elmer FT-IR spectrometer SPECTRUM 2000. DSC was performed on a Perkin-Elmer series 7 instrument. ^{1}H and ^{19}F NMR spectra were obtained on a Bruker AC-200 instrument at 200.13 and 188.31 MHz, respectively. Chemical shifts are given in ppm from internal TMS for ^{1}H NMR spectra and from internal $CFCl_3$ for ^{19}F NMR spectra. $CDCl_3$ was the solvent for ^{19}F NMR as well as for ^{1}H NMR, unless otherwise noted. $^nJ_{FF}$ couplings were observed in all sulfonimide compounds but values could not readily be determined from the unresolved multiplets. Column chromatography was performed on silica gel (100–200 mesh).

3.1. Materials

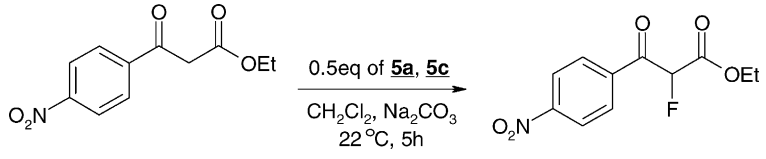
Disodium salts of perfluoroalkylsulfonimides (**3a–c**) were prepared by a modified literature method [10,12] (see Section 2, Schemes 1 and 2). The solvents used for the reactions were dried by standard methods before use. Other commercially available compounds were used without further purification.

3.2. Preparation of perfluoroalkylsulfinimides *4a* and *4b*

General procedure: Nafion-H beads (10–30 mesh), freshly regenerated by standard methods (heated with concentrated HNO_3, followed by washing with H_2O until neutral), were packed into a short column. Then aqueous solution of **3a** and **3b** was passed through above column slowly (one to two drops per second). After washing the column with water until neutral, the combined aqueous fractions were evaporated to dryness. Vacuum sublimation (150 °C/10 μmHg) of the residue gave a hydroscopic white solid **4a** (92%) and **4b** (95%). $(CF_3{}^aSO_2N(H)SO_2CF_2{}^bCF_2{}^c)_2$ **4a** (dry CD_3CN) ^{19}F NMR δ −78.0 (a, 6F, s), −111.0 (b, 4F, m), −119.1 (c, 4F, m); ^{1}H NMR δ 11.2 (s). $(CF_3{}^aSO_2N(H)SO_2CF_2{}^bCF_2{}^cCF_2{}^d)_2$ **4b** (dry CD_3CN) ^{19}F NMR δ −78.8 (a, 6F, s), −112.3 (b, 4F, m), −119.4 (c, 4F, m), −120.8 (d, 4F, m); ^{1}H NMR δ 10.2 (s).

3.3. Preparation of perfluoroalkylsulfinimides *4c*

Into a small sublimator was added dry **3b** (7.8 g, 11.4 mmol) and 10 ml of 96% sulfuric acid. After stirring for 3 h, the mixture was heated to 70 °C under high vacuum



Scheme 4. Flourination of 1,3-dicarbonyl compound.

(10 μmHg). A hydroscopic white solid (**4c**, 7.1 g, 11.1 mmol, 97%) was sublimed out. $(CF_3{}^aSO_2N(H)SO_2CF_2{}^bCF_2{}^c)_2O$ **4c** (dry CD_3CN) ^{19}F NMR δ −76.6 (a, 6F, s), −80.0 (c, 4F, m), −113.2 (b, 4F, m); ^1H NMR δ 11.5 (s).

3.4. Preparation of $CF_3SO_2NFSO_2R_FSO_2NFSO_2CF_3$, $R_F = (CF_2)_4$ **5a**, $(CF_2)_2O(CF_2)_2$ **5c**

In a typical reaction, **4a** (1.0 g, 1.6 mmol) was placed into an 80 ml stainless steel bomb reactor and evacuated. Fluorine (6.0 mmol) was condensed into the reactor at −196 °C and the reactor was allowed to slowly warm to 22 °C, and then kept in a 50–60 °C water bath for 14 days. After pumping out excess unreacted F_2 through a soda-lime column, a colorless solid (0.9 g, 1.4 mmol, 88%) was recovered from the bomb. $(CF_3{}^aSO_2N(F)^bSO_2CF_2{}^cCF_2{}^d)_2$ **5a** (m.p. 28–29 °C) ^{19}F NMR δ −32.0 (b, 2F, br, s), −71.9 (a, 6F, s), −105.9 (c, 4F, m), −119.4 (d, 4F, m); IR (KCl, cm^{-1}) 1462 (s), 1222 (vs), 1145–1126 (s), 1031 (w), 856 (s), 769 (w), 726 (w), 637 (w). $(CF_3{}^aSO_2N(F^b)SO_2CF_2{}^cCF_2{}^d)_2O$ 5c (colorless liquid) ^{19}F NMR δ −32.2 (b, 2F, br, s), −72.0 (a, 6F, m), −80.6 (d, 4F, m), −110.0 (c, 4F, m); IR (KCl, cm^{-1}) 1464 (s), 1344 (s), 1219 (vs), 1146 (s), 1075 (w), 993 (w), 96 (w), 852 (m), 771 (w), 646 (w).

3.5. Preparation of $CF_3SO_2NFSO_2R_FSO_2NFSO_2CF_3$, $R_F = (CF_2)_6$ **5b**

Into an 80 ml stainless steel bomb containing **4b** (1.2 g, 1.7 mmol) were condensed HF (16 mmol) and F_2 (6 mmol) at −196 °C. The reactor was allowed to slowly warm to 22 °C and then kept in a 50–60 °C water bath for 10 days. After pumping out excess HF and F_2 through a soda-lime column, a white solid mixture (0.9g, **5b/5b′** = 2.5/1, 50% for **5b**, 20% for **5b′**) was obtained. The NMR was obtained on this mixture. $(CF_3{}^aSO_2N(F)^bSO_2CF_2{}^cCF_2{}^dCF_2{}^e)_2$ **5b** ^{19}F NMR δ −32.2 (b, 2F, br, s), −70.7 (a, 6F, m), −104.5 (c, 4F, m), −118.4 (d, 4F), −120.1 (e, 4F, m); $(CF_3{}^aSO_2N(F^b)$-$SO_2CF_2{}^cCF_2{}^dCF_2{}^eCF_2{}^fCF_2{}^gCF_2{}^hSO_2N(H)SO_2CF_3{}^i)$ **5b′** ^{19}F NMR δ −32.3 (b, 1F, br, s), −71.9 (a and i, 6F, m), −104.5 (c, 2F, m), −106.8 (h, 2F, m), −118.4 (d, 2F, m), −119.1 (g, 2F, m), −120.1 (e or f, 2F, m), −121.7 (e or f, 2F, m); ^1H NMR δ 11.1 (s).

3.6. Fluorination of ethyl 4-nitrobenzoyl acetate using **5a** and **5c**

Into a CH_2Cl_2 (10 ml) solution of ethyl 4-nitrobenzoylacetate (0.3 mmol) was added 5 mg of anhydrous Na_2CO_3 and 0.15 mmol **5a** at 22 °C and the reaction mixture was stirred for 5 h. The reaction mixture was diluted with ethanol (5 ml) and water (20 ml), extracted by CH_2Cl_2 (2 × 10 ml), rinsed with brine and dried over Na_2SO_4. Pure ethyl 2-fluoro-3-(4′-nitrophenyl)-3-oxo-propanate (91%) was obtained by column chromatography on silica gel using hexane/ethyl acetate (3/1) as the eluent. Reaction with **5c** was carried out in the same way (90% yield). ^{19}F NMR δ −190.8 (d, $^2J_{HF}$ = 48 Hz); ^1H NMR δ 1.3 (3H, t), 4.7 (2H, q), 6.0 (^1H, d, $^2J_{HF}$ = 48 Hz), 8.27, 8.38 (4H, AB-type).

Acknowledgements

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