ELSEVIER

Journal of Fluorine Chemistry 111 (2001) 253–257

JOURNAL OF FLUORINE CHEMISTRY

www.elsevier.com/locate/jfluchem

Synthesis and comparison of *N*-fluorobis[(perfluoroalkyl)sulfonyl]imides with different perfluoroalkyl groups

Jie Zhang, Darryl D. DesMarteau*

Howard L. Hunter Chemistry Laboratory, Clemson University, Clemson, SC 29634-1905, USA

Received 9 May 2001; accepted 25 July 2001

Abstract

N-fluorobis[(perfluoroalkyl)sulfonyl]imides, $CF_3SO_2N(F)SO_2R_f$ ($R_f' = C_4F_9$, C_6F_{13}, C_8F_{17}) and $(C_4F_9SO_2)_2NF$, were prepared by direct fluorination of corresponding N–H compounds using elemental fluorine without a solvent in good to excellent yields. All of these N–F compounds are electrophilic fluorination agents and can easily deliver "F^+" to certain molecules. Their reactions with aromatic rings, beta-diketones, and alkenes were investigated to compare their fluorination power.

Keywords: Electrophilic fluorination; *N*-fluorosulfonimides

1. Introduction

In the past 20 years, a lot of effort has been directed towards discovering safer and more selective electrophilic fluorinating agents, which surmount some of the difficulties associated with perchloryl fluoride, elemental fluorine and hypofluorites. As a result of these efforts, a number of N–F compounds have been synthesized and found to be generally better sources of electrophilic fluorine for selective fluorinations [1,2]. While many other electrophilic N–F reagents have been developed and several are commercial, none of these possess the reactivity and utility of *N*-fluorobis[(perfluoroalkyl)sulfonyl]imide reagents [3].

The first and simplest compound of this type was *N*-fluorobis[(trifluoromethyl)sulfonyl]imide (**1a**) that was synthesized and shown to work as an efficient reagent for the selective fluorination of a variety of substrates [3]. It has excellent long-term stability, desirable physical properties and high reactivity [4–11].

In order to further study and evaluate the synthetic potential of *N*-fluorobis[(perfluoroalkyl)sulfonyl]imides, a variety of $R_fSO_2N(F)SO_2R_f'$ (**1b–e**) were synthesized. Their reactivities in several selective fluorinations were then compared.

2. Results and discussion

2.1. Synthesis of N–F compounds

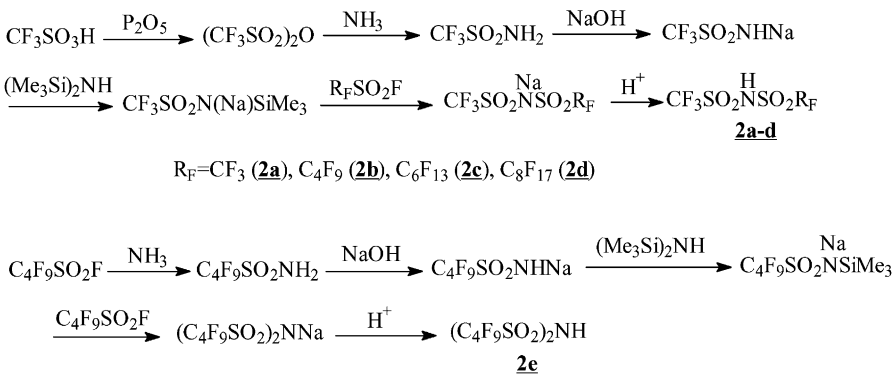
Bis[(perfluoroalkyl)sulfonyl]imides (**2**), the precursors of **1**, were prepared according to the synthetic route developed by us [12] as shown in Scheme 1. All steps except the preparation of triflic anhydride have excellent yields (95–98%). Recently $(CF_3SO_2N)_2Li$ is available from 3 M Co and both the acid and lithium salt are available from Aldrich. Bis[(perfluoroalkyl)sulfonyl]imides are extremely hygroscopic, and all procedures should be carried out under anhydrous conditions.

N-fluorobis[(perfluoroalkyl)sulfonyl]imides were prepared by the direct fluorination of corresponding N–H precursors (Scheme 2).

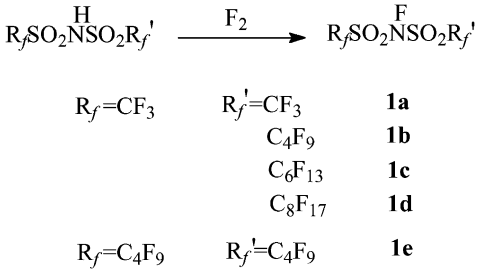
In earlier preparation of **1a–b**, Singh et al. [3] and Witz et al. [12] introduced F_2 in one portion into a stainless steel bomb containing the N–H compound at −196°C. But sometimes an uncontrolled overreaction occurred during warm-up, and led to low yields. An improved procedure in which fluorine gas is introduced in portions has replaced the older method. In the fluorination of 30 g (107 mmol) of **2a** 10% excess F_2 was introduced in portions according to Table 1 at −196°C. After each fluorine addition, the liquid nitrogen bath was removed and the bomb was allowed to warm to 22°C and remain at 22°C for several hours. After fluorination was complete, **1a–b** were purified by trap-to-trap distillation after the removal of co-product HF by forming $NaHF_2$ with NaF.

* Corresponding author. Tel.: +1-864-656-4705; fax: +1-864-656-0627.
E-mail address: fluorin@clemson.edu (D.D. DesMarteau).

0022-1139/01/$ – see front matter
PII: S0022-1139(01)00463-8



Scheme 1.



Scheme 2.

Table 1
Time table of fluorination of $(CF_3SO_2)_2NH$ (107 mmol)

Time (h)	Amount of F_2 introduced (mmol)
0	5
2	15
6	30
10	30
15	38 (118 total, 10% excess)[a]

[a] The bomb was allowed to stand at 22°C for 8 h after this addition.

The same method was used to prepare **1c–e**, and isolation of the pure compounds was possible by removal of the HF under vacuum at 0°C, followed vacuum distillation from any unreacted acid. The reaction of the N–H compounds becomes much slower with increasing size of the R_f group (Table 2). Heating at 50–60°C is necessary to obtain high conversion of the acids to the N–F derivatives. Surprisingly, the heating results in little or no degradation of the starting acid or the N–F product. The marked difference in reactivity could be due to a number of factors, including the structure of the solid acid, lower solubility of the acid in the product HF and perhaps low vapor pressure of the starting acid. Originally we had reported that **1e** could not be prepared at 22°C [3]. Higher reaction temperatures were not attempted based on the obviously incorrect assumption at that time that heating would lead to degradation. In fact, all the N–F compounds exhibit excellent thermal stability as determined by DSC measurements. The onset of decomposition was: **1b** 190°C; **1c** 200°C; **1d** 205°C; **1e** 150°C. Clearly the stability appears to be about the same as one R_f group increases in size, but is lower with two larger R_f groups. Differences in thermal stability may be due to the presence of a liquid phase for a longer time in the small, sealed, stainless steel DSC capsule for the larger R_f groups. For **1a**, we have not determined the decomposition under conditions where liquid **1a** would be present.

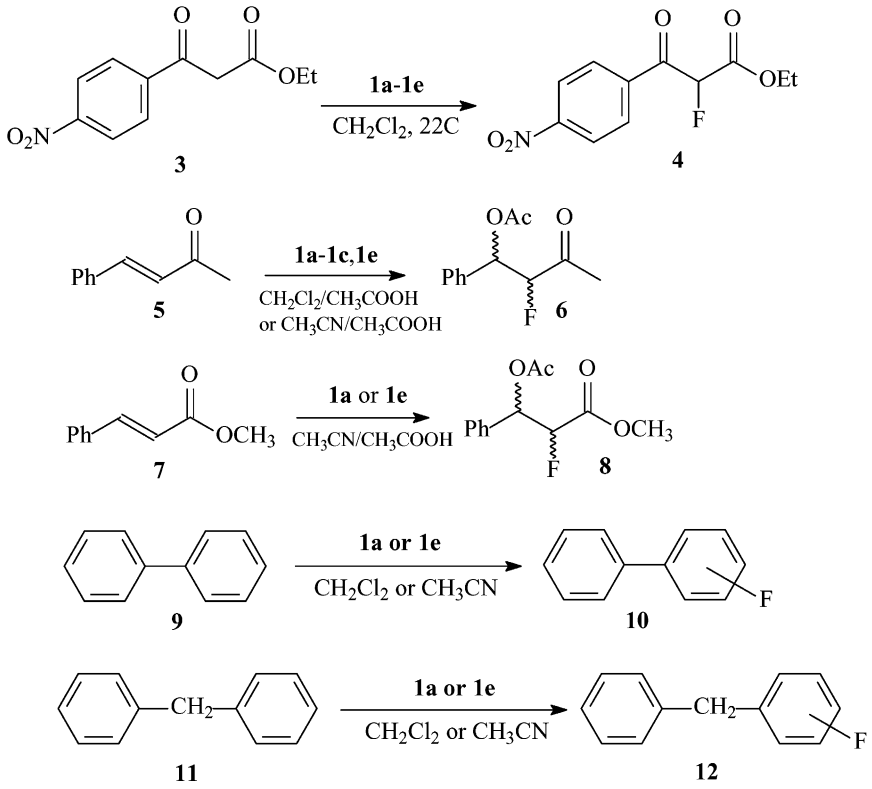
Table 2
Preparation of N–F compounds

N–F compound	Fluorination conditions	N–F (δ)	Yield (%)
1b	22°C, ~1 day	−32.4	81
1c	50–60°C, ~10 days	−32.3	80
1d	50–60°C, ~10 days	−32.3	92
1e	50–60°C, ~10 days	−31.3	98

2.2. Fluorination reactivity studies

N-fluorobis[(trifluoromethyl)sulfonyl]imide (**1a**) is the most reactive among known N–F compounds [13]. We believe its fluorination power comes from the extraordinary electron withdrawing ability of two CF_3SO_2 groups as related to the acidity of the parent sulfonimide $(CF_3SO_2)_2$-NH (**2a**). Koppel et al. [14] have measured the gas phase acidity of many perfluorinated sulfonimides and found that **2b–e** were more acidic than **2a** with $(C_4F_9SO_2)_2NH$ (**2e**) presently holding the record as the strongest measured gas phase superacid. We wondered if these acidity differences might be reflected in the fluorination power of the corresponding N–F compounds. Also of interest were the possible steric effects of the larger RF groups on reactivity. Based on the limited reactivity studies with these N–F agents with 1,3-dicarbonyl derivatives, α,β-unsaturated carbonyl compounds, and aromatic rings, we found no significant differences between the reactivity of **1a–e**.

All of these N–F agents can readily undergo reaction with neutral β-diketones and β-ketoesters in CH_2Cl_2 at 22°C to afford predominantly mono-fluorinated products (Scheme 3). The solubility of **1c–e** in CH_2Cl_2 was relatively



Scheme 3.

low, but reaction proceeded readily. But for other much slower reactions with α,β-unsaturated carbonyls, solubility appeared to be the rate-determining factor. If CH_2Cl_2/CH_3COOH was used as solvent, reaction of *trans*-4-phenyl-3-butene-2-one with **1e** was much slower than the same reaction with **1a**. But when the solvent was changed to dry CH_3CN/CH_3COOH, both reactions finished within 10 h.

All the reactions were carried out using one equivalent of the N–F reagents, so mono-fluorination was the major product, with small amounts of difluorinated product formed in the fluorination of substrate **3**. In the reactions of substrates **5** and **7**, two major isomers (*erythro*- and *threo*-) were obtained, but separation was not carried out.

Activated aromatics such as phenol, toluene, aniline, etc. can be smoothly fluorinated by **1a** at 22°C [3]. Here biphenyl and diphenylmethane were compared with **1a** and **1e** in dichloromethane and acetonitrile solvents. Again in acetonitrile the delivery of F to the aromatic ring is much faster than that in CH_2Cl_2. Preference for *o*-fluorination was observed in all cases with the *o*-/*p*- ratio ranging from 1.5 to 3.2.

3. Experimental section

IR spectra were taken as neat films on KCl using a Perkin-Elmer FT-IR spectrometer SPECTRUM 2000. ^1H 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 ^1H 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 ^1H NMR, unless otherwise noted. Mass spectra were measured with a Hewlett Packard 5985B GC/MS spectrometer. Column chromatography was performed on silica gel (100–200 mesh).

3.1. Materials

Bis[(perfluoroalkyl)sulfonyl]imides (**2a**–**e**) were prepared according to methods reported previously (Scheme 1). The solvents used for the reactions were dried by standard methods before use. Other commercially available compounds were used without further purification.

3.2. General procedure for preparation of *N*-fluorobis(perfluoroalkyl)sulfonimides (*1a–b*)

Inside a dry box, bis[(trifluoromethyl)sulfyl]imide (**2a**) (107 mmol) was placed into a 500 ml stainless steel bomb. The bomb was cooled to −196°C and evacuated. Excess fluorine gas (118 mmol) was then introduced in portions according to Table 1. After each addition of fluorine, the liquid nitrogen bath was removed and the bomb was allowed to warm to 22°C. After the final portion of F_2 was introduced, the bomb was kept at 22°C for 8 h. The reactor was then cooled to −196°C and excess F_2 was removed under dynamic vacuum through a soda-lime column. The remaining mixture was vacuum transferred into another stainless steel bomb containing 10 g of NaF and shaken at 22°C for ca. 5 min

to allow the complete absorption of HF by NaF. Then the pure product was obtained as a colorless liquid by trap-to-trap distillation (0, −70, −196°C; product in −70°C trap); **1a**: ^{19}F NMR δ −33.5 (N–F), −72.0 (6F); **1b**: IR ν (cm^{-1}) 1465(s), 1235(vs), 2150(s), 1022(w), 889(m), 849(m), 738(w), 703)w), 638(w), 584(w); ^{19}F NMR δ −32.4 (N–F), −72.3 (3F), −81.2 (3F), −106.0 (2F), −120.7 (2F), −126.1 (2F).

3.3. General procedure for preparation of N-fluoroperfluoroalkylsulfonimides (*1c–e*)

Inside a dry box, **2d** (7.1 mmol) was placed into an 80 ml stainless steel bomb. The bomb was cooled to −196°C and evacuated. Excess fluorine gas (12.1 mmol) was then introduced in one portion. After addition of fluorine, the liquid nitrogen bath was removed and the bomb was heated to 50–60°C for 10 days. The bomb was cooled to −196°C and excess fluorine was removed as above. The bomb was then warmed to 0° in an ice-water bath and connected to a dynamic vacuum through a FEP trap (−196°C) for about 10 min. All of the product HF was transferred into that FEP trap and pure N–F product remained inside the bomb as a colorless liquid. **1c**: IR ν (cm^{-1}) 1464(s), 1360(w), 1235(vs) 1150(s) 1022(w), 889(m), 849(m) 739(w), 703(w), 638(w), 585(w); ^{19}F NMR δ −32.3 (N–F), −72.0 (3F), −81.1 (3F), −105.8 (2F), −119.7 (2F), −121.8 (2F), −123.0 (2F), −126.5 (2F); **1d**: IR ν (cm^{-1}) 1465(s), 1233(vs), 1152(s), 986(w), 861(m), 733(w), 707(w), 659(w), 584(w); ^{19}F NMR δ −32.3 (N–F), −72.3 (3F), −81.0 (3F), −105.8 (2F), −119.7 (2F), −121.7 (4F), −122.2 (2F), −123.2 (2F), −126.6 (2F); **1e**: IR ν (cm^{-1}) 1464(s), 1351(s), 1208(vs), 1145(s), 1025(m), 845(m), 801(m), 739(m), 699(w), 651(w), 570(w); ^{19}F NMR δ −31.3 (N–F), −81.1 (3F), −106.0 (2F), −120.8 (2F), −126.2 (2F).

3.4. General procedure for fluorination of ethyl 4-nitrobenzoylacetate

Into a CH_2Cl_2 (15 ml) solution of ethyl 4-nitrobenzoylacetate (**3**, 2.0 mmol) was added 0.1 g of anhydrous Na_2CO_3 and 2.0 mmol of N–F at 22°C and the reaction mixture was stirred for 8 h. The reaction mixture was diluted with ethanol (10 ml) and water (50 ml), extracted by CH_2Cl_2 (10 ml × 2 ml), rinsed with brine and dried over Na_2SO_4. Pure ethyl 2-fluoro-3-(4′-nitrophenyl)-3-oxo-propanoate (**4**) was obtained by column chromatography on silica gel using hexane/ethyl acetate [9], **4**: ^{19}F NMR δ −190.86 (d, $^2J_{HF}$ = 48.4 Hz).

3.5. General procedure for fluorination of α,β-unsaturated carbonyl compound

The N–F reagent (1.0 mmol) was dissolved in 2 ml of solvent (Table 3) and added dropwise into the solution of α,β-unsaturated carbonyl compound. The mixture was then stirred at 22°C for the desired time. Simple column

Table 3
Selective fluorination using different N–F reagents

Substrate	N–F agent	Conditions (22°C)	Reaction time	Products (%, ratio)
3	**1a**	CH_2Cl_2, Na_2CO_3	8 h	**4** (80[a], 100/7[d])
3	**1b**	CH_2Cl_2, Na_2CO_3	8 h	**4** (83[a], 100/12[d])
3	**1c**	CH_2Cl_2, Na_2CO_3	8 h	**4** (77[a], 100/8[d])
3	**1d**	CH_2Cl_2, Na_2CO_3	8 h	**4** (80[a], 100/8[d])
3	**1e**	CH_2Cl_2, Na_2CO_3	8 h	**4** (80[a], 100/10[d])
5	**1a**	CH_2Cl_2/CH_3COOH	3 days	**6** (75[b], 61/100[e])
5	**1b**	CH_2Cl_2/CH_3COOH	3 days	**6** (81[b], 48/100[e])
5	**1c**	CH_2Cl_2/CH_3COOH	10 days (incomplete)	**6** (80[c], 50/100[e])
5	**1e**	CH_2Cl_2/CH_3COOH	10 days (incomplete)	**6** (75[b], 60/100[e])
5	**1a**	CH_3CN/CH_3COOH	<10 h	**6** (71[b], 50/100[e])
5	**1e**	CH_3CN/CH_3COOH	<10 h	**6** (74[b], 50/100[e])
7	**1a**	CH_3CN/CH_3COOH	2 days	**8** (79[b], 55/100[e])
7	**1e**	CH_3CN/CH_3COOH	2 days	**8** (80[b], 54/100[e])
9	**1a**	CH_2Cl_2	40 h	**10** (63[c], 1.5[f])
9	**1e**	CH_2Cl_2	40 h	**10** (28[c], 1.7[f])
9	**1a**	CH_3CN	40 h	**10** (90[c], 1.8[f])
9	**1e**	CH_3CN	40 h	**10** (97[c], 2.3[f])
11	**1a**	CH_2Cl_2	36 h	**12** (63[c], 2.4[f])
11	**1e**	CH_2Cl_2	36 h	**12** (34[c], 2.5[f])
11	**1a**	CH_3CN	36 h	**12** (95[c], 2.3[f])
11	**1e**	CH_3CN	36 h	**12** (94[c], 3.2[f])

[a] Isolated yields.
[b] Yields are based on NMR.
[c] NMR conversion as a ratio of fluorinated products to unreacted N–F.
[d] Ratio of mono-F/di-F based on NMR.
[e] Ratio of erythro-/threo- based on NMR.
[f] Ratio of *o*-/*p*- based on NMR.

chromatography gave the mixture of *erythro*- and *threo*-products [8]; **6**: *erythro*-form ^{19}F δ −200.1 (d-d-q, $^{2}J_{HF}$ = 51.2, $^{3}J_{HF}$ = 25, $^{4}J_{HF}$ = 5.3 Hz); *threo*-form ^{19}F δ −202.3 (d-d-q, $^{2}J_{HF}$ = 47.6, $^{3}J_{HF}$ = 26.9, $^{4}J_{HF}$ = 5.3 Hz); **8**: *erythro*-form ^{19}F δ −200.3 (d-d, $^{2}J_{HF}$ = 46.9, $^{3}J_{HF}$ = 25.2 Hz); *threo*-form ^{19}F δ −202.8 (d-d, $^{2}J_{HF}$ = 47.5, $^{2}J_{HF}$ = 24.7 Hz).

3.6. General procedure for fluorination of aromatic rings

The aromatic and the N–F reagent were dissolved into 10 ml of solvent and stirred at 22°C for desired time. ^{19}F NMR followed this reaction and the conversion of N–F was determined by ^{19}F NMR integration; **10**: 2-fluoro-^{19}F NMR δ −118.6, 4-fluoro-^{19}F NMR δ −116.1; **12**: 2-fluoro-^{19}F NMR δ −118.4, 4-fluoro-^{19}F NMR δ −118.0.

Acknowledgements

The financial support of this research by the National Science Foundation is gratefully acknowledged.

References

[1] S. Rozen, Chem. Rev. 96 (1996) 1717.
[2] S.D. Taylor, C.C. Kotoris, G. Hum, Tetrahedron 55 (1999) 12431.
[3] S. Singh, D.D. DesMarteau, S.S. Zuberi, M. Witz, H.-M. Huang, J. Am. Chem. Soc. 109 (1987) 7194.
[4] Z.-Q. Xu, D.D. DesMarteau, Y. Gotoh, J. Chem. Soc., Chem. Commun. (1991) 179.
[5] G. Resnati, D.D. DesMarteau, J. Org. Chem. 56 (1991) 4925.
[6] W.T. Pennington, G. Resnati, D.D. DesMarteau, J. Org. Chem. 57 (1992) 1536.
[7] Z.-Q. Xu, D.D. DesMarteau, J. Chem. Soc., Perkin Trans I (1992) 313.
[8] D.D. DesMarteau, Z.-Q. Xu, M. Witz, J. Org. Chem. 57 (1992) 629.
[9] Z.-Q. Xu, D.D. DesMarteau, Y. Gotoh, J. Fluorine Chem. 58 (1992) 71.
[10] G. Resnati, D.D. DesMarteau, J. Org. Chem. 57 (1992) 4281.
[11] W. Ying, D.D. DesMarteau, Y. Gotoh, Tetrahedron 52 (1996) 15.
[12] D.D. DesMarteau, M. Witz, J. Fluorine Chem. 52 (1991) 7.
[13] F.A. Davis, W. Han, C.K. Murphy, J. Org. Chem. 60 (1995) 4730.
[14] I.A. Koppel, R.W. Taft, F. Anvia, S.-Z. Zhu, L.-Q. Hu, K. Sung, D.D. DesMarteau, L.M. Yagupolski, Y.L. Yagupolski, N.V. Ignat'ev, N.V. Kondratenko, A.Y. Volkonskii, V.M. Vlasov, R. Natorio, P.-C. Maria, J. Am. Chem. Soc. 116 (1994) 3047.