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One-pot synthesis of arylfluoroalkylsulfoxides and study of their anomalous ^{19}F NMR behavior

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ABSTRACT

Arylfluoroalkylsulfoxides were successfully synthesized in one-pot when fluoroalkylsulfinate reacted with benzene and triflic anhydride in triflic acid and dichloromethane as the medium. The characteristics of their ^{19}F NMR spectra were examined and analyzed for these structures. Electronic and steric effects of substituents at α- or β-position were revealed to be the main cause of the anomalous behavior of their chemical shifts and coupling constants. Interactions between arylfluoroalkylsulfoxides and solvents were also investigated and discussed.

1. Introduction

Introducing fluorine-containing groups into organic compounds and materials has attracted great interest in different fields of chemistry such as material science, biochemistry, pharmaceuticals and coordination chemistry. The fluorine-containing substituents often conferred unusual physical properties and enhanced chemical reactivities [1–4]. For example, the introduction of trifluoromethanesulfinyl group into benzene resulted in *S*-(trifluoromethyl)-diphenylsulfonium triflates with significantly different properties and applications from its precursor [5–9]. Little work on arylfluoroalkylsulfoxides has been available in the literature, however. These fluorinated sulfoxides were usually synthesized by the oxidation of corresponding sulfides with peracids, a process that is hard to control because a mixture of sulfoxide and sulfone compounds plus the initial sulfide was often obtained. In 2001, Wakselman et al. reported that aryltrifluoromethyl sulfoxides could directly be yielded from substituted benzenes and triflinates in the triflic acid medium [10]. Nevertheless, the preparation of other kinds of arylfluoroalkyl sulfoxides by this method is still undocumented. Aryl(iododifluoromethyl)sulfoxides, the first optically active compounds with polyfluoroalkyliodo groups, synthesized by Yagupolskii and Matsnev exhibited characteristic ^{19}F NMR spectra [11]. Chirality of the S=O group causes marked differences in chemical shift between the two gem-fluorine atoms. We report herein an improved procedure for the synthesis of arylfluoroalkylsulfoxides and examine the ^{19}F NMR spectra of the variously substituted fluoroalkylsulfoxides.

2. Results and discussion

The introduction of a trifluoromethanesulfinyl group into organic compounds using trifluoromethanesulfinyl chloride, or sodium trifluoromethanesulfinate and phosphoryl chloride, suffers from a low conversion efficiency problem due to the poor stability and low reactivity of these reagents [12–14]. Wakselman et al. consequently improved the method through the preparation of aryltrifluoromethyl sulfoxides from substituted benzenes and triflinates in the triflic acid medium [10]. Triflic anhydride and triflic acid were employed as activated reagents instead of commonly used acyl chloride or phosphoryl chloride. According to the literature, this method was effective for trifluoromethanesulfinylation of substituted aromatic compounds [10]. Application of this method to benzene itself, however, resulted in polymeric reactions. It was found that when sodium 2-chloro-1,1,2,2-tetrafluoroethanesulfinate reacted with benzene and triflic anhydride in triflic acid at room temperature, the system became ineffectual. ^{19}F NMR analyses of the reaction mixture showed the formation of undesired polyarylenesulfonium salts [15–17]. The yield of 1-(2-chloro-1,1,2,2-tetrafluoroethylsulfinyl)benzene (**1d**) was only 20% after 23 h, although the polyfluoroalkylsulfinate salt

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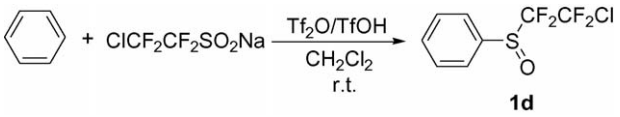
Table 1
Preparation of 1-(2-chloro-1,1,2,2-tetrafluoroethylsulfinyl)benzene (**1d**)



Entry	R_fSO_2Na:Tf_2O:TfOH	Time (h)	Solvent	Yield[a] (%)
1	1:1.1:10	23	–	20
2	1:1.1:10	38	CH_2Cl_2	30
3	1:0:10	67	CH_2Cl_2	Trace
4	1:1.0:2.2	67	CH_2Cl_2	0

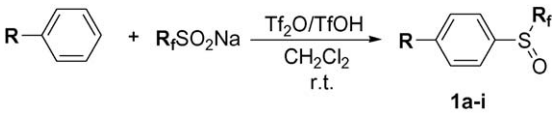
[a] Isolated yield.

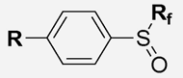
was completely consumed (entry 1, Table 1). To optimize the reaction system, dichloromethane was added as part of the medium. It was found that the polymerization reaction was efficiently inhibited, giving **1d** in 30% yield (entry 2, Table 1). However, longer reaction time was needed under this reaction condition. The polyfluoroalkylsulfinylation was also tremendously influenced by the amount of Tf_2O and TfOH. Only trace of **1d** was detected if no triflic anhydride was added at room temperature (entry 3, Table 1). Sufficient TfOH was necessary for the formation of **1d** (entry 4, Table 1).

In order to investigate the applicability of this method, we extended the reaction to the synthesis of other arylfluoroalkylsulfoxides. 1-(difluoromethylsulfinyl)benzene (**1a**) was prepared in 44% yield after 19 h from sodium difluoromethanesulfinate and benzene using triflic acid and dichloromethane as medium (entry 1, Table 2). Similar results were obtained in the case of sodium bromodifluoromethanesulfinate and sodium perfluoroethylsulfinate (entries 2 and 3, Table 2). With increased length of the polyfluoroalkyl chain, polyfluoroalkylsulfinylation reactions between benzene and polyfluoroalkylsulfinate were also successful, giving the desired sulfoxides **1e**, **1f** and **1g** in moderate yield (entries 5–7, Table 2). When diphenyl was employed as the substrate, the reaction stopped at the monofluoroalkylsulfinylation stage, giving para-substituted **1h** and **1i** as the only product (entries 8 and 9, Table 2). However, no sulfinylated product was observed in the case of terphenyl (entry 10, Table 2), as confirmed by ^{19}F NMR.

The chemical shift and coupling constant of CF_2 adjacent to the S=O group were dramatically influenced by its substituents. For example, the two fluorine nuclei of the CF_2 group in **1a** both appeared upfield at −119.1 ppm and the ones in **1b** shifted to downfield at −52.9 and −54.9 ppm, respectively (Fig. 1), indicating that the fluorine nuclei were sharply deshielded by the bromine atom at α-position in **1b** [18]. Further investigations showed that geminal coupling constants between the two fluorine atoms in **1a** and **1b** are markedly different. The chiral nature of the S=O group makes a favorable diastereotopic environment for the two fluorine atoms to differentiate, leading to that the two diastereotopic fluorines in **1b** possess larger observed geminal coupling constants

Table 2
Polyfluoroalkylsulfination of aromatic compounds



Entry	R	R_fSO_2Na		Time (h)	Yield[a] (%)
1	H	HCF_2	**1a**	19	44
2	H	$BrCF_2$	**1b**	19	28
3	H	CF_3CF_2	**1c**	36	37
4	H	$ClCF_2CF_2$	**1d**	38	30
5	H	$C_3H_3N_2CF_2CF_2$[b]	**1e**	41	60
6	H	$PhOCF_2CF_2$	**1f**	41	35
7	H	$ClCF_2CF_2CF_2CF_2$	**1g**	25	41
8	Ph	HCF_2	**1h**	10	21
9	Ph	$ClCF_2CF_2$	**1i**	30	34
10[c]	4-PhC_6H_4	$ClCF_2CF_2$	–	23	–

[a] Isolated yield.
[b] Sodium 1,1,2,2-tetrafluoro-2-(1H-imidazol-1-yl)ethanesulfinate.
[c] Determined by ^{19}F NMR.

than those in **1a** (Fig. 1). The bromine atom attached directly to CF_2 makes the two gem-fluorine atoms so different that the $^2J_{FF}$ coupling constant is raised to 145.3 Hz for **1b** compared to $^2J_{FF}$ = 5.1 Hz for **1a**. This is also the reason that the chemical shift of one fluorine atom in **1b** is −52.9 ppm and the other −54.9 ppm.

As shown in Fig. 2, when the fluorinated carbon was attached to the α-CF_2 group, large differences up to 11 ppm in chemical shift between the two diastereotopic fluorines at the α-position adjacent to the S=O group were observed in **1c–f**. For example, in **1c**, the chemical shifts for the two α-CF_2 fluorine nuclei were −115.6 and −126.1 ppm, respectively. Substitution with a weaker electronegative species relative to fluorine atoms at the β-position has a mild deshielding impact on the α-CF_2 group. For example, when the $ClCF_2$ group instead of CF_3 was employed to bond to α-CF_2, the chemical shift of α-CF_2 moved to the lower field (−109.7 and −121.9 ppm). Similar results were also found in **1e** and **1f**. As was the case in **1b**, stronger electronegative substituents at the β-position greatly deshielded the two β-CF_2 fluorine nuclei, leading to lower field in chemical shift (**1d–f** in Fig. 2). Chlorine displayed the largest deshielding effect compared to phenoxyl and imidazolyl function groups in these systems. But unnoticeable difference was observed in chemical shift between the two fluorine nuclei at the β-position in **1d–f**. This may be resulted from the longer distance between the fluorine nuclei and the optically active S=O group. A sulfinyl group was difficult to create diastereotopic environments for the two fluorine nuclei at β-position (**1d**). The steric effect which strengthens the diastereotopic environments of the fluorine nuclei by phenoxyl group and imidazolyl function was also substantially weakened by the increased spacious separation between the fluorine nuclei and the S=O group. As a result, only

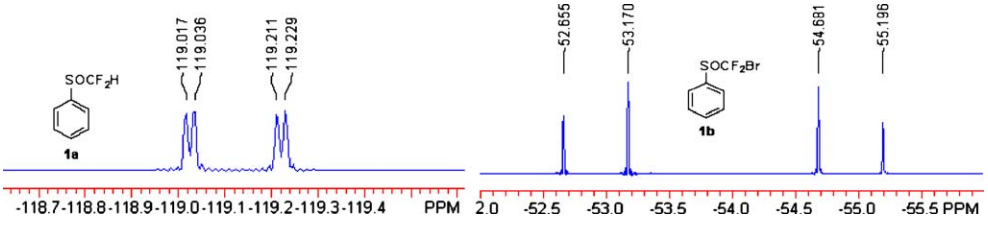


Fig. 1. ^{19}F NMR spectra of the CF_2 group in **1a** and **1b** in $CDCl_3$ (282 MHz).