Direct monofluoromethylation of *O*-, *S*-, *N*-, and *P*-nucleophiles with PhSO(NTs)CH$_2$F: the accelerating effect of α-fluorine substitution†

Xiao Shen, Min Zhou, Chuanfa Ni, Wei Zhang and Jinbo Hu*

An efficient and direct monofluoromethylation of *O*-, *S*-, *N*-, and *P*-nucleophiles with PhSO(NTs)CH$_2$F **1** has been developed. In contrast to the previously known detrimental effect of α-fluorine substitution on S$_N$2 reactions, the current monofluoromethylation is accelerated by the α-fluorine substitution. Based on a mechanistic study, a new reactivity of sulfoximine (as a radical monofluoromethylation reagent) is disclosed.

Recently, fluorine-containing compounds have attracted increasing attention in pharmaceutical and agrochemical fields, because the incorporation of fluorine atom(s) or fluoroalkyl group(s) (such as CF$_3$, CF$_2$H, and CH$_2$F) into bioactive molecules can often result in profound changes in their chemical and biological properties.[1] In this context, monofluoromethyl compounds are particularly valuable, as the CH$_2$F functionality can mimic CH$_3$ and CH$_2$OH groups, which are often encountered in biologically active molecules.[2] Nucleophilic monofluoromethylation has been well developed with fluoromethyl phenyl sulfone, fluorobis(phenylsulfonyl) methane, fluoromalonates and other reagents as a powerful strategy for the introduction of the CH$_2$F moiety into organic molecules.[3] Direct electrophilic monofluoromethylation has also been reported by using FCH$_2$X (X = I, Br, Cl, OSO$_2$R (R = methyl, tolyl, trifluoromethyl)) and other reagents.[3a,4] Our previous study revealed that the reactions of a variety of *O*-, *S*-, and *N*-nucleophiles with FCH$_2$Cl were not sensitive to the presence of a radical scavenger such as nitrobenzene, which supports the operation of an S$_N$2 mechanism rather than a radical mechanism in these reactions.[4a] Although nucleophilic and electrophilic (*via* S$_N$2 mechanism) monofluoromethylations have been well established, reports of radical monofluoromethylation are scarce.[5,6] In 1971, Raymond and Andrews reported the characterization of the monofluoromethyl radical (CH$_2$F) by the matrix reaction of bromofluoromethane with alkali metals, but its synthetic application was not demonstrated.[5] Very recently, Baran and co-workers elegantly reported a C–H radical monofluoromethylation using (FCH$_2$SO$_2$)$_2$Zn; however, the method was only applied to *N*-heteroaromatic

compounds.[6] Therefore, new radical monofluoromethylation methods are highly desirable.

Given their important physiological and diverse chemical properties, sulfoximines and sulfoximinium salts have been widely used in organic synthesis.[7] Recently, the use of fluorinated sulfoximines and sulfoximinium salts as fluoroalkylating agents has attracted much attention.[8,9] In our previous work, we found that the carbanion derived from PhSO(NTs)CF$_2$H was highly unstable and readily decomposed to difluorocarbene, which could be captured by a variety of *C*-, *S*-, and *N*-nucleophiles (Scheme 1a).[8d] In contrast, the carbanion derived from (*R*)-PhSO(NTs)CH$_2$F [(*R*)-**1**] was found to possess good thermal stability and nucleophilicity, and we were therefore able to achieve a highly enantioselective fluorocyclopropanation reaction *via* a Michael addition–elimination process (Scheme 1b).[8b] Although both fluorinated and non-fluorinated sulfoximines have been successfully used in nucleophilic or electrophilic (fluoro)alkylation reactions, a reaction involving the production of the (fluoro)alkyl radical *via* the C–S bond homolysis of a neutral sulfoximine has never been reported.[10] Herein, we report a direct monofluoromethylation of *O*-, *S*-, *N*-, and *P*-nucleophiles using PhSO(NTs)CH$_2$F (**1**) as a novel monofluoromethylating agent (Scheme 1c). We also disclose a preliminary study into the mechanism which supports the operation of a radical (S$_{RN}$1) mechanism in this reaction. The accelerating effect of α-fluorine substitution in sulfoximine **1** on the current monofluoromethylation provides additional intriguing insight into the unusual reactivities of fluorinated sulfoximines.[8,9]

Firstly, we developed a new and efficient synthesis of *N*-tosyl-*S*-fluoromethyl-*S*-phenylsulfoximine (**1**) on a relatively large scale (Scheme 2). PhSCH$_2$F was prepared according to the reported procedure.[11] *N*-Tosyl-*S*-fluoromethyl-*S*-phenyl-sulfilimine (**2**) was readily prepared by imidation of PhSCH$_2$F with chloramine-T·3H$_2$O in 71% yield. Oxidation of **2** (on 300 mmol scale) with H$_2$O$_2$ gave **1** (73.5 g) in 75% yield. It is noteworthy

Key Laboratory of Organofluorine Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 345 Ling-Ling Road, Shanghai, 200032, China. E-mail: jinbohu@sioc.ac.cn; Fax: +86 21-64166128
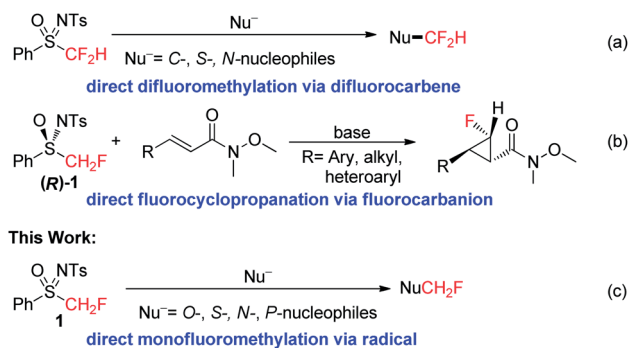
Scheme 1 Fluoroalkylations with PhSO(NTs)CF$_2$H and PhSO(NTs)CH$_2$F reagents.
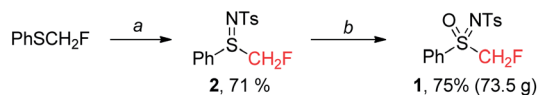
^{a} Chloramine-T·3H$_2$O, CH$_2$Cl$_2$, N-benzyl-N,N-diethylethanaminium chloride, reflux, 3 d; ^{b} NaOH, H$_2$O$_2$, MeOH–H$_2$O, reflux, 2 h.

Scheme 2 Preparation of N-tosyl-S-fluoromethyl-S-phenyl-sulfoximine (**1**).

Table 1 Survey of reaction conditions^a

Entry	Sol	**3a** : **1** : NaH	T (°C)	t (h)	Yield^b (%)
1	THF	1 : 1 : 1.2	60	35	Trace
2	CH$_3$CN	1 : 1 : 1.2	60	35	<10
3	NMP	1 : 1 : 1.25	60	35	74
4	DMF	1 : 1 : 1.25	60	35	81
5	DMSO	1 : 1 : 1.25	60	35	89
6	DMSO	1 : 1.2 : 1.3	60	36	94^c
7	DMSO	1 : 1.3 : 1.25	80	4	95^c
8	DMSO	1 : 1.2 : 1.3	rt	36	3

^{a} Under N$_2$, NaH (60% purity) was added to the solution of **3a** (51 mg, 0.3 mmol) in solvent (2 mL) at rt; 30 min later, **1** in solvent (1 mL) was added and the solution was stirred at the conditions shown. ^{b} Yield determined by ^{19}F NMR spectroscopy. ^{c} Isolated yield.

that **1** is a stable white solid, which does not decompose even after being stored under air for a year.

With compound **1** in hand, we investigated the direct monofluoromethylation of O-, S-, and N-nucleophiles by using (1,1′-biphenyl)-4-ol (**3a**) as a model substrate, and sodium hydride (NaH) as a base. Typically, **3a** was stirred with NaH at room temperature (rt) for 30 min, after which **1** was added and the solution was stirred at a specified temperature for a specified time, as shown in Table 1. It was found that the choice of solvent was important for the reaction (Table 1, entries 1–6). Polar solvents such as DMSO and DMF are beneficial for the reaction. The optimal yield (95%) of **4a** was obtained when the

reaction was performed in DMSO at 80 °C for 4 h, with the ratio of **3a**, **1**, and NaH being 1 : 1.3 : 1.25 (Table 1, entry 7).

We chose entry 7 shown in Table 1 as the standard conditions under which to study the scope of the reactions between the O-, S-, and N-nucleophiles **3** and PhSO(NTs)CH$_2$F (**1**). The results are summarized in Scheme 3. The reaction proved to be general and a variety of structurally diverse phenols were successfully monofluoromethylated by **1** to give the corresponding monofluoromethyl ethers **4** in good to excellent yields (71–95%). The reaction is tolerant of chloro, bromo, and iodo substituents that are useful in transition metal-catalyzed cross-coupling reactions, enabling the subsequent synthesis of more useful CH$_2$F-containing compounds. However, the current reaction conditions were not amenable to the reaction with 2-phenylethanol (**3j**), and only trace amounts of **4j** were formed, with 75% of compound **1** being recovered.[12] Moreover, the direct transfer of CH$_2$F to sulfur-nucleophiles under similar reaction conditions (**1**, NaH, 80 °C, 4 h) was also found to be successful, and a variety of thiophenol and its derivatives were successfully monofluoromethylated by reagent **1**, affording the corresponding monofluoromethyl sulfides in high yields (82–98%). Heteroaryl thiols such as benzo-[d]thiazole-2-thiol (**3o**), 1-($tert$-butyl)-1H-tetrazole-5-thiol (**3p**), and pyridine-2-thiol (**3q**) were also suitable substrates for the current monofluoromethylation reaction, resulting in the corresponding products **4o** (92% yield), **4p** (76% yield), and **4q** (85% yield), respectively. In contrast to the reaction of **3o** with PhSO(NTs)CF$_2$H where both N-difluoromethylation and S-difluoromethylation occurred,[8d] only S-monofluoromethylation was observed in the current monofluoromethylation reaction, which might indicate the different mechanism of the two reactions. The current reaction conditions were also amenable to the monofluoromethylation of phenylmethanethiol (**3r**), and the resulting product **4r** was obtained in 97% yield. Bicyclic heteroaryl compounds featuring a 1-(fluoromethyl)-1H-benzo[d]imidazyl group have previously been reported to be effective phosphodiesterase 10 (PDE 10) inhibitors.[13] Therefore, we carried out the direct monofluoromethylation of some N-heterocyclic secondary amines. As shown in Scheme 3, 2-phenyl-1H-imidazole (**3s**), 2-phenyl-1H-benzo[d]imidazole (**3t**), and 5,6-dimethyl-1H-benzo-[d]imida-zole (**3u**) were successfully monofluoromethylated to give the corresponding products **4s** (71% yield), **4t** (62% yield), and **4u** (86% yield), respectively. When 5-nitro-1H-benzo[d]imid-azole (**3v**) was used as a substrate, a mixture of **4va** and **4vb** was obtained in 71% yield. It is worth noting that the current method was also applicable to the direct monofluoromethylation of 1H-benzo[d][1,2,3]triazole (**3w**), affording **4wa** (50% yield) and **4wb** (24% yield), which could be separated by silica gel column chromatography.

To further broaden the scope of this new monofluoromethylation protocol, we applied this method to other nucleophiles (Scheme 4). It was found that diphenylphosphine **5** could also react with sulfoximine **1** under similar conditions to give product **6** in 92% yield, after the addition of hydrogen peroxide to quench the reaction (Scheme 4a). Compound **6** was reported to be an effective reagent for the synthesis of monofluoroalkenes.[14] To our delight, even 4-methoxybenzoic acid **7** was also a suitable substrate for the monofluoromethylation
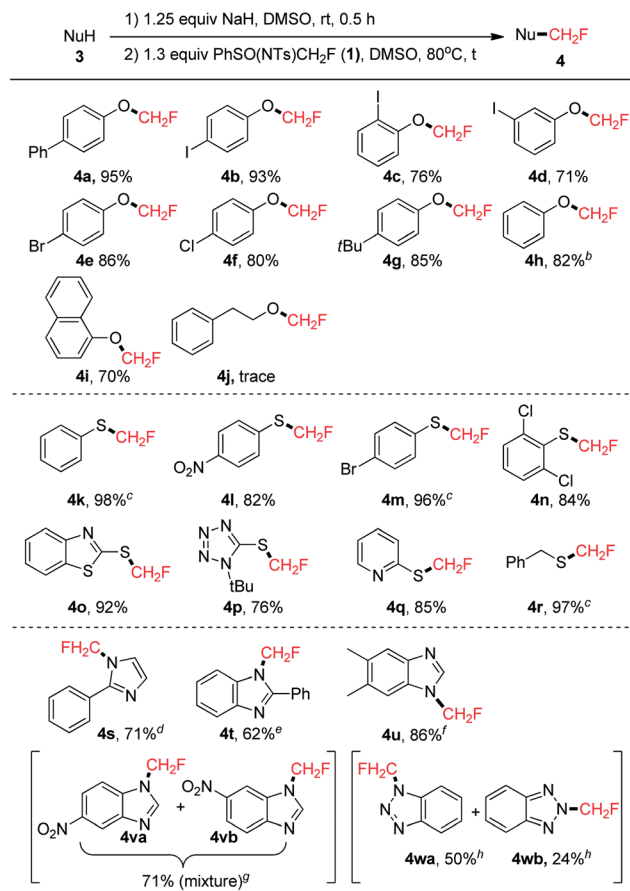
Scheme 3 Monofluoromethylation of *O*-, *S*-, and *N*-Nucleophiles with PhSO(NTs)CH$_2$F **1**.[a] All reactions were performed at 80 °C for 4 h, and values indicate isolated yields unless otherwise noted. [b] Low bp, yield was determined by ^{19}F NMR. [c] Unstable, yield was determined by ^{19}F NMR. [d] 8 h. [e] 9.5 h. [f] 8.5 h. [g] 71 h. [h] 18 h.
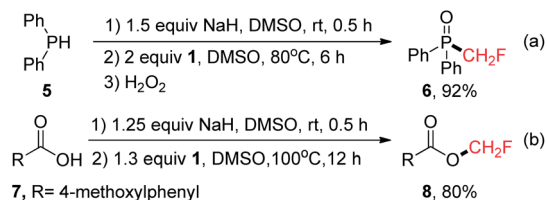
Scheme 4 Monofluoromethylation of diphenylphosphine (**5**) and 4-methoxybenzoic acid (**7**).

reaction, and product **8** was produced in 80% yield when the reaction temperature was raised to 100 °C (Scheme 4b).

Although Johnson and co-workers reported the nucleophilic methylidene transfer reaction with the anion of *N*-tosyl-*S*-methyl-*S*-phenylsulfoximine (**9**) in 1970,[15] there has been no report on the direct methylation of phenols by using **9** as a methylation reagent. Encouraged by our aforementioned success with the direct monofluoromethylation using sulfoximine **1**, we carried out the reaction of **3a** with non-fluorinated sulfoximine **9** under similar conditions (80 °C, 4 h). To our surprise, product **10a** was only obtained in 3% yield (Table 2,

entry 2). When the temperature was raised to 120 °C, **10a** was formed in 75% yield (Table 2, entry 3). When **3a** was treated with 1.3 equivalents of **1** and 1.3 equivalents of **9** in one pot, the total yield of product **4a** and **10a** was 89%, with the ratio of **4a**/**10a** being 145/1 (Table 2, entry 4). We also tested the competitive reactions of **1** and **9** with thiol **3o**, imidazole **3u**, diphenyl-phosphine **5**, and acid **7** as substrates (see ESI†). In all cases, the monofluoromethylation product was obtained as the major product and the methylation product was formed as the minor product. These results suggest that α-fluoro sulfoximine **1** possesses a higher reactivity than the non-fluorinated sulfox-imine **9** under the current reaction conditions.

It is known that α-fluorine substitution can *decrease* the reactivity of methylene halides in S$_N$2 reactions.[16] In 1955, Hine and co-workers reported that the S$_N$2 reactivity of FCH$_2$Br proved to be about 350 times less reactive than CH$_3$Br in its reaction with iodide ions in acetone at 20 °C.[16a] Very recently, Dolbier and co-workers reported that the substitution of 1-bromononane by azide ions at 50 °C in DMSO was 7.0 times faster than its α-fluorinated analog.[16b] Therefore, the unusual *accelerating effect* of α-fluorine substitution in our current monofluoromethylation reaction (Table 2) suggests that the monofluoromethylation reaction proceeds through a different reaction mechanism as opposed to an S$_N$2 pathway.

In our previous work, a difluorocarbene mechanism was proposed for the difluoromethylation of PhSNa with PhSO(NTs)CF$_2$H, based on deuterium-labeling experiments.[8d] It was found that PhSCF$_2$D was obtained as the major product (PhSCF$_2$D/PhSCF$_2$H = 6/1) in the presence of 10 equivalents of D$_2$O.[8d] We subsequently investigated the reaction of PhONa with sulfox-imine **1** in the presence of 10 equivalents of D$_2$O (Scheme 5). Since an excess amount of D$_2$O was present in the reaction mixture, the deuterated monofluoromethylation product should be the major product, if the monofluorocarbene pathway was dominant in the monofluoromethylation reaction. However, the monofluoromethylation yielded non-deuterated PhOCH$_2$F as the major product (PhOCH$_2$F, 45% yield; PhOCHDF, 31% yield; PhOCD$_2$F, 10% yield). Note that the deuterated products might result from the reactions of the deuterated sulfoximines, because substantial amounts of PhSO(NTs)CHDF (11% yield) and PhSO(NTs)CD$_2$F (1% yield) were detected in the reaction mixture. Furthermore, we also attempted to trap monofluorocarbene with 2,3-dimethylbut-2-ene in the presence of a phenolate. It was reported that mon-ofluorocarbene could readily react with 2,3-dimethylbut-2-ene to form 3-fluoro-1,1,2,2-tetramethylcyclopropane.[17] However, no 3-fluoro-1,1,2,2-tetramethylcyclopropane was obtained when 2,3-dimethylbut-2-ene was added into the monfluor-omethylation reaction of **3a**, and product **4a** was obtained in 96% yield (Scheme 6). These results indicate that the mono-fluorocarbene mechanism is not likely to be the major pathway for the current monofluoromethylation reaction.

In 1969, Sangster and Thynne reported that CH$_2$F is six times more reactive towards ethylene than CH$_3$,[18] which is somewhat consistent with the accelerating effect of α-fluorine substitution in our monofluoromethylation reaction. In order to probe the possibility of a radical mechanism in our monofluoromethylation

Table 2 Accelerating effect of α-fluorine substitution[a]

Entry	NuH	Reagent	T (°C)	t (h)	Product	Yield (%)	**4/10**
1		**1**	80	4	**4a**	95	
2		**9**	80	4	**10a**	3	
3		**9**	120	6	**10a**	75	
4		**1 + 9**	120	6	**4a + 10a**	89	145/1

[a] NaH (1.25 equiv.) and reagent (1.3 equiv.) were used.
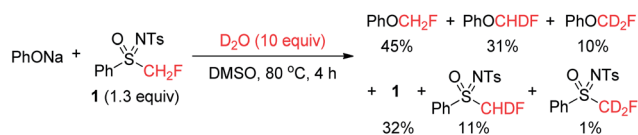
Scheme 5 Monofluoromethylation of PhONa in the presence of D$_2$O.
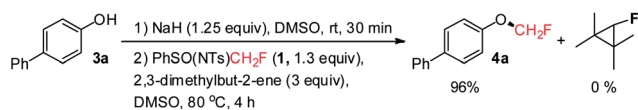
Scheme 6 Monofluoromethylation of **3a** in the presence of 2,3-dimethylbut-2-ene.

reaction, we added radical scavengers into the reaction mixtures.[19] The results are shown in Table 3. When nitrobenzene was added as an additive, the yield of **4a** was decreased to 72%, and compound **1** was recovered in 47% yield (Table 3, entry 1). When the better electron acceptor, 1,4-dinitrobenzene, was employed, the monofluoromethylation was totally inhibited and 4-(4-nitrophenoxy)-1,1′-biphenyl (probably resulting from the reaction of ArO⁻ with 1,4-dinitrobenzene) was obtained in 78% yield, while compound **1** was recovered in 120% yield (Table 3, entry 2).[20] When benzoquinone was added, **4a** was obtained in only 5% yield, and **3a** was recovered in 87% yield (Table 3, entry 3). It is worth noting that a similar inhibitory effect was observed when PhONa was directly used as the substrate instead of using the **3a**/NaH system (for details, see ESI†). Moreover, the yield of **4a** was increased from 5% to 35% when the reaction time was extended from 4 to 8 hours (Table 3, entries 3 and 4), which is in accordance with the inhibiting effect of benzoquinone in S$_{RN}$1 reactions. Further study showed that the yields of the reactions of **3o**, **3u**, **5**, and **7** with **1** were also largely decreased in the presence of benzoquinone (Table 3, entries 5–8). It is noteworthy that the reaction of **3a** with **9** could also be suppressed by benzoquinone, as the yield of product **10** decreased to 25% (Table 3, entry 9).

Based on the aforementioned experimental results, an S$_{RN}$1 mechanism[19] was proposed as shown in Scheme 7, though further mechanistic investigation is necessary to gain more details. An SET (single electron transfer) from the nucleophile to **1** afforded a radical anion **A**,[21] followed by the elimination of **B**[8d,15] (concerted or stepwise) to afford the monofluoromethyl radical, which combined with another nucleophile to form radical anion intermediate **C**. The product NuCH$_2$F was formed after the SET from **C** to **1** with the formation of intermediate **A**.

Subsequently, we tested the possibility of direct tri-fluoromethylation of **3a** with PhSO(NTs)CF$_3$ **11** (Scheme 8a). It is interesting that the expected product, 4-(trifluoromethoxy)-1,1′-biphenyl (**12**), was not formed, while a large amount of CF$_3$H was afforded, and the starting material **3a** was isolated in 88% yield. It was found that when **11** was treated with PhONa in the presence of 4-bromobenzaldehyde (**13**), the nucleophilic trifluoromethylation product **14** was obtained in 50% yield, and CF$_3$H was afforded in no less than 19% yield accompanied by the recovery of sulfoximine **11** in 65% yield (Scheme 8b).[22] To the best of our knowledge, [CF$_3$] is a typical electrophilic radical and there has been no report on the free radical

Table 3 Reactions of selected nucleophiles with **1** and **9** in the presence of radical scavengers[a]

| Entry	NuH	Additive	T (°C)	t (h)	Yield (%)	Unreacted[e] **1** (%)
1	**3a**	Nitrobenzene	80	4	72	47
2[b]	**3a**	1,4-Dinitrobenzene	80	4	0	120
3[c]	**3a**	Benzoquinone	80	4	5	110
4	**3a**	Benzoquinone	80	8	35	94
5	**3o**	Benzoquinone	80	4	7	120
6	**3u**	Benzoquinone	80	8.5	0	71
7	**5**	Benzoquinone	80	6	20	60
8	**7**	Benzoquinone	100	12	52	54
9[d]	**3a**	Benzoquinone	120	6	25	ND

[a] Yield was determined by ¹⁹F NMR. [b] 4-(4-Nitrophenoxy)-1,1′-biphenyl was isolated in 78% yield. [c] **3a** was recovered in 87% yield. [d] **9** was used instead of **1**, the yield of methylation product refers to the isolated yield, and the yield of residual **9** was not determined (ND). [e] 130% of **1** (based on the amount of NuH) was added as starting material.
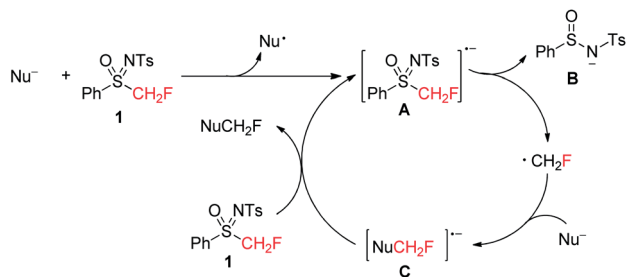
Scheme 7 Proposed reaction mechanism.
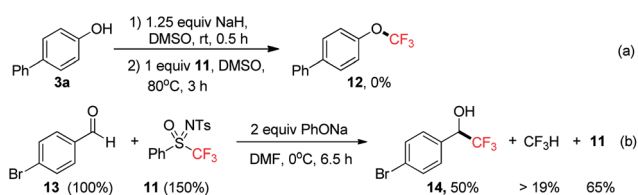
Scheme 8 Reactions with reagent **11**.
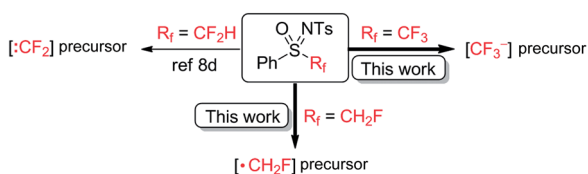
Scheme 9 Diversified reactivities of fluoroalkyl sulfoximines.

trifluoromethylation of electrophilic aldehydes.[23] Therefore, a trifluoromethyl anion ("CF_3^-") could possibly be involved in the reaction. The process of $[CF_3^-]$ production from $PhSO(NTs)CF_3$ is somewhat similar to the reaction of $PhSO_2CF_3$ with alkoxides.[24] Therefore, it can be concluded that the number of fluorine substituents significantly affects the reactivity of mono-, di-,[8d] and trifluoromethyl sulfoximines. In contrast to direct electrophilic monofluoromethylation with $PhSO(NTs)CH_2F$ *via* $[CH_2F]$ and direct electrophilic difluoromethylation with $PhSO(NTs)CF_2H$ *via* $[:CF_2]$,[8d] $PhSO(NTs)CF_3$ was found to be a potential direct nucleophilic trifluoromethylation reagent *via* a $[CF_3^-]$ intermediate (Scheme 9).

In conclusion, *N*-tosyl-*S*-fluoromethyl-*S*-phenylsulfoximine (**1**) was conveniently prepared and used as a new efficient monofluoromethylating agent for *O*-, *S*-, *N*-, and *P*-nucleophiles. In contrast to the previously known detrimental effect of α-fluorine substitution on S_N2 reactions, the current monofluoromethylation with **1** was accelerated by the α-fluorine substitution. The preliminary mechanistic study suggests a radical mechanism involving an SET process. To the best of our knowledge, this is the first example of a fluoroalkylation reaction using a sulfoximine as a fluoroalkyl radical precursor. Moreover, $PhSO(NTs)CF_3$ was found to be a nucleophilic trifluoromethylating agent *via* $[CF_3^-]$ which further highlights the diverse reactivities of fluoroalkyl sulfoximines.

Acknowledgements

Notes and references

1 (*a*) H. J. Böhm, D. Banner, S. Bendels, M. Kansy, B. Kuhn, K. Müller, U. Obst-Sander and M. Stahl, *ChemBioChem*, 2004, **5**, 637; (*b*) M. Sani, A. Volonterio and M. Zanda, *ChemMedChem*, 2007, **2**, 1693; (*c*) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.*, 2008, **37**, 320; (*d*) C. Fäh, R. Mathys, L. A. Hardegger, S. Meyer, D. Bur and F. Diederich, *Eur. J. Org. Chem.*, 2010, 4617.

2 For selected examples, see (*a*) J. Kollonitsch, A. A. Patchett, S. Marburg, A. L. Maycock, L. M. Perkins, G. A. Doldouras, D. E. Duggan and S. D. Aster, *Nature*, 1978, **274**, 906; (*b*) K. Mckeage and S. J. Keam, *Drugs*, 2009, **69**, 1799; (*c*) R. A. Rojas, I. Paluga, C. H. Goldfrad, M. T. Duggan and N. Barnes, *J. Asthma*, 2007, **44**, 437.

3 For a feature article, see: (*a*) J. Hu, W. Zhang and F. Wang, *Chem. Commun.*, 2009, 7465; for selected examples, see (*b*) Y. Li, C. Ni, J. Liu, L. Zhang, J. Zheng, L. Zhu and J. Hu, *Org. Lett.*, 2006, **8**, 1693; (*c*) C. Ni, Y. Li and J. Hu, *J. Org. Chem.*, 2006, **71**, 6829; (*d*) T. Fukuzumi, N. Shibata, M. Sugiura, H. Yasui, S. Nakamura and T. Toru, *Angew. Chem., Int. Ed.*, 2006, **45**, 4973; (*e*) J. T. Palmer, Eur. Patent Appl. 0442754A2, 1991; (*f*) T. Koizumi, T. Hagi, Y. Horie and Y. Takeuchi, *Chem. Pharm. Bull.*, 1987, **35**, 3959.

4 (*a*) W. Zhang, L. Zhu and J. Hu, *Tetrahedron*, 2007, **63**, 10569; and the references therein; (*b*) G. K. S. Prakash, S. C. Istvan and G. A. Olah, *Org. Lett.*, 2008, **10**, 557; (*c*) G. A. Olah and A. Pavlath, *Acta Chim. Acad. Sci. Hung.*, 1953, **3**, 425; (*d*) Y. Nomura, E. Tokunaga and N. Shibata, *Angew. Chem., Int. Ed.*, 2011, **50**, 1885.

5 J. I. Raymond and L. Andews, *J. Phys. Chem.*, 1971, **75**, 3235.

6 Y. Fujiwara, J. A. Dixon, F. O'Hara, E. D. Funder, D. D. Dixon, R. A. Rodriguez, R. D. Baxter, B. Herle, N. Sach, M. R. Collins, Y. Ishihara and P. S. Baran, *Nature*, 2012, **492**, 95.

7 For reviews, see: (*a*) M. Reggelin and C. Zur, *Synthesis*, 2000, 1; (*b*) H. Okamura and C. Bolm, *Chem. Lett.*, 2004, **33**, 482; (*c*) M. Harmata, *Chemtracts: Org. Chem.*, 2003, **16**, 660; (*d*) C. R. Johnson, *Acc. Chem. Res.*, 1973, **6**, 341.

8 (*a*) X. Shen, W. Zhang, C. Ni, Y. Gu and J. Hu, *J. Am. Chem. Soc.*, 2012, **134**, 16999; (*b*) X. Shen, W. Zhang, L. Zhang, T. Luo, X. Wan, Y. Gu and J. Hu, *Angew. Chem., Int. Ed.*, 2012, **51**, 6966; (*c*) W. Zhang, W. Huang and J. Hu, *Angew. Chem., Int. Ed.*, 2009, **48**, 9858; (*d*) W. Zhang, F. Wang and J. Hu, *Org. Lett.*, 2009, **11**, 2109; (*e*) W. Zhang and J. Hu, *Adv. Synth. Catal.*, 2010, **352**, 2799.

9 (*a*) Y. Mace and E. Magnier, *Eur. J. Org. Chem.*, 2012, 2479; (*b*) R. Kowalczyk, A. J. F. Edmunds, R. G. Hall and C. Bolm, *Org. Lett.*, 2011, **13**, 768; (*c*) G. K. S. Prakash, Z. Zhang, F. Wang, C. Ni and G. A. Olah, *J. Fluorine Chem.*, 2011, **132**, 792; (*d*)

C. Urban, F. Cadoret, J.-C. Blazejewski and E. Magnier, *Eur. J. Org. Chem.*, 2011, 4862; (*e*) S. Noritake, N. Shibata, S. Nakamura, T. Toru and M. Shiro, *Eur. J. Org. Chem.*, 2008, 3465.

10 A computational study on the reaction of β-ketoesters with a sulfoximinium salt without experimental evidence suggests a radical-like species, see Y.-D. Yang, X. Lu, G. Liu, E. Tokunaga, S. Tsuzuki and N. Shibata, *ChemistryOpen*, 2012, **1**, 221.

11 (*a*) P. G. Theobald and W. H. Okamura, *J. Org. Chem.*, 1990, **55**, 741; (*b*) K. M. More and J. Wemple, *Synthesis*, 1977, 791.

12 The failure of the reaction between 2-phenylethanol and **1** might be explained by the following two points: (1) the relatively poorer electron donating ability of 2-phenylethanolate than phenolate; (2) the deprotonation and subsequent decomposition of **1** resulting from the strong basicity of 2-phenylethanolate.

13 P. R. Verhoest and C. J. Helal, *US Pat.*, 0155779 A1, 2007.

14 J. H. van Steenis and A. van der Gen, *Eur. J. Org. Chem.*, 2001, 897.

15 C. R. Johnson and G. F. Katekar, *J. Am. Chem. Soc.*, 1970, **92**, 5753.

16 (*a*) J. Hine, C. H. Thomas and S. J. Ehrenson, *J. Am. Chem. Soc.*, 1955, **77**, 3886; (*b*) H. Martinez, A. Rebeyrol, T. B. Nelms and W. R. Dolbier, Jr, *J. Fluorine Chem.*, 2012, **135**, 167.

17 (*a*) J. L. Hahnfeld and D. J. Burton, *Tetrahedron Lett.*, 1975, 1819; (*b*) D. L. S. Brahms and W. P. Dailey, *Chem. Rev.*, 1996, **96**, 1585.

18 We thank one of the referees for providing the report that we did not notice when we were preparing the paper, see

J. M. Sangster and J. C. J. Thynne, *Trans. Faraday Soc.*, 1969, **65**, 2110.

19 R. A. Rossi, A. B. Pierini and A. B. Penenory, *Chem. Rev.*, 2003, **103**, 71.

20 Previously, the reaction of PhSNa with 1,4-dinitrobenzene in DMSO to form (4-nitrophenyl)(phenyl)sulfane was proposed to proceed *via* a $S_{RN}1$ mechanism; see: (*a*) Y. Liu and W. Zhao, *Acta Chim. Sin.*, 1991, **49**, 615; (*b*) I. H. Leaver and G. C. Ramsay, *Tetrahedron*, 1969, **25**, 5669.

21 We tested the possibility of the homolytic thermal decomposition of **1** generating the CH_2F radical. After the heating of PhSO(NTs)CH_2F in DMSO at 80 °C for 4 hours, 99% of **1** was recovered. After heating sulfoximine **1** and benzoquinone in DMSO at 80 °C for 4 hours, 96% of **1** and 50% of benzoquinone were recovered. The above results indicate that the homolytic thermal decomposition of **1** generating the CH_2F radical is less likely, though it can not be completely ruled out. We thank one of the referees for suggesting this possible mechanistic pathway.

22 We performedthe similar reactions (as shown in Scheme 8a) with PhSO(NTs)CH_2F and PhSO(NTs)CF_2H reagents, and no 1-(4-bromophenyl)-2-fluoroethanol or 1-(4-bromophenyl)-2,2-difluoroethanol was obtained.

23 (*a*) W. R. Dolbier Jr, *Chem. Rev.*, 1996, **96**, 1557; (*b*) W. R. Dolbier Jr, in *Topics in Current Chemistry*, ed. R. D. Chambers, Springer, Heidelberg, 1997, vol. 192, pp. 97–163; (*c*) S. Barata-Vallejo and A. Postigo, *Eur. J. Org. Chem.*, 2012, 1889; (*d*) A. Studer, *Angew. Chem., Int. Ed.*, 2012, **51**, 8950.

24 G. K. S. Prakash, J. Hu and G. A. Olah, *Org. Lett.*, 2003, **5**, 3253.