Use of ArSO 2 SR f reagents: an efficient tool for the introduction of SR f moieties

Xavier Pannecoucke, Tatiana Besset

Use of $ArSO_2SR_f$ Reagents: An Efficient Tool for the Introduction of SR_f Moieties

Xavier Pannecoucke and Tatiana Besset*

Normandie Univ, INSA Rouen, UNIROUEN, CNRS, COBRA (UMR 6014), 76000 Rouen, France. *E-mail: tatiana.besset@insa-rouen.fr*

Abstract: In recent years, a renewal of interest was showed to the quest of new synthetic solutions to directly introduce emergent fluorinated groups (SR_f) onto molecules. In this context, a new generation of reagents ($ArSO_2SR_f$) as efficient sources of SCF_3, SCF_2H and more generally SR_f groups, was designed. Hence, potent solutions was developed for the synthesis of SRf-containing molecules, compounds of interest for drug and agrochemical research. This review highlights the recent advances made in the synthesis and the use of this new class of reagents, considerably extending the portfolio of tools for the direct introduction of SR_f moieties.

Introduction

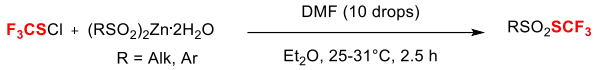
Omnipresent in the daily life, fluorinated molecules[1] are compounds of interest in both industry and pharmaceutical fields.[2] The importance of these compounds might be directly linked to the remarkable properties of the fluorine atom and the fluorinated groups.[3] Although key advances have been made over the years, limitations remain. To answer to the synthetic challenges of this very active research field, innovative methodologies and original reagents were developed. In particular, a strong interest was showed by the scientific community towards the SR_f groups. Indeed, merging the properties of sulfur-containing molecules with fluorinated groups, the corresponding functionalized fluorinated groups (SR_f) are of high interest. Therefore, several methods appeared to access these highly valuable SR_f-containing compounds. Indirect approaches from sulfur-containing molecules and complementary ones based on the direct introduction of the SR_f groups were designed.[4,5,6] Regarding the last strategy, a large panel of SR_f moieties are now available (R_f = CF_3, CF_2H, $CF_2C_nF_{2n+1}$, CF_2SO_2Ph, CF_2CO_2R, $CF_2PO(OEt)_2$) thanks to the efforts of key players of the field like Billard,[7] Goossen,[8] Shibata,[9] Shen[10] and our group,[11] among others. The design of original nucleophilic and electrophilic sources was successfully achieved, opening new avenues and unprecedented transformations.[5] However, these reagents suffer from multi-steps synthesis, difficulty to scale up their preparation and the generation of side products, which considerably hampered wide applications due to atom-economy concerns. Aiming at tackling new synthetic challenges, the generation of reagents, namely $ArSO_2SR_f$, was designed acting as efficient electrophilic or radical sources of SR_f moieties. In that review, the major recent advances made in that research field will be presented for the direct introduction of the SR_f moiety.

1. Recent advances in the trifluoromethylthiolation reactions using $ArSO_2SCF_3$ reagents

Although impressive progress has been made for the synthesis of SCF_3-containing molecules, several strategies based on radical pathways opened new avenues in this very active research field and the development of alternative transformations is still highly desirable. In this section, the recent reports dealing with the trifluoromethylthiolation of compounds using different $ArSO_2SCF_3$ reagents will be depicted.

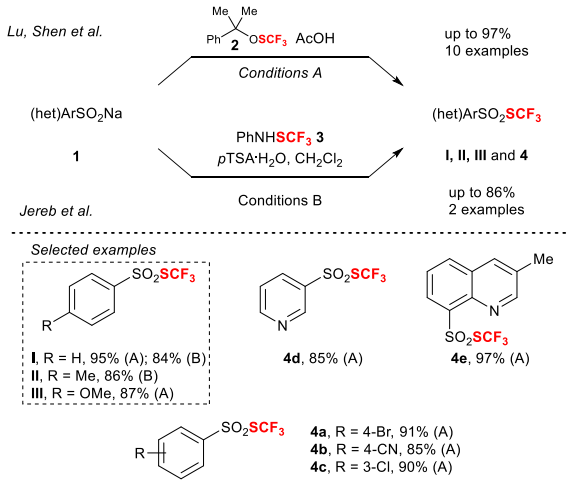
Synthesis and applications of $ArSO_2SCF_3$ reagents

Synthesis of the $PhSO_2SCF_3$ reagent I. A strong interest was demonstrated towards trifluoromethylthiolated sulfonate derivatives thanks to their antimicrobial activity.[12a,b] These derivatives were generally prepared by reacting the trifluoromethanesulfenyl chloride with zinc aryl sulfinate dihydrates. With this approach, a large variety of RSO_2SCF_3 derivatives was prepared (R = Alkyl and Aryl, 10 examples, Scheme 1) including the $PhSO_2SCF_3$ reagent **I**.[12c]



Scheme 1. Synthesis of reagent **I** and analogs from F_3CSCl.

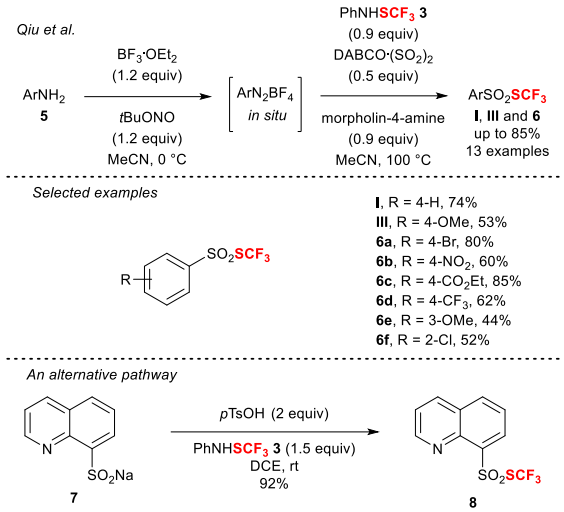
A common synthetic route to prepare trifluoromethylthiolated sulfonates relied on the reaction of sodium sulfinate derivatives with an electrophilic trifluoromethylthiolating reagent as independently reported in 2015 by the groups of Shen[13] and Jereb[14] (Scheme 2). Indeed, in 2015, Shen and co-workers reported the synthesis of an electrophilic trifluoromethylthiolating reagent and its use in several reactions with various nucleophiles. Among them, when sodium sulfinates reacted with the trifluorosulfenate **2** as the electrophilic SCF_3 source under acidic conditions, a panel of compounds (**I**, **II**, **III** and **4**) were synthesized in high yields (10 examples, up to 97% yield, Scheme 2, Conditions A). The transformation was tolerant with aromatic sodium sulfinates bearing halogens, electron donating and electron withdrawing groups (**II**, **III**, **4a-c**) as well as heteroaromatic derivatives (**4d** and **4e**). In the study from the Jereb's group, only two examples were depicted using the Billard-Langlois reagent **3** in the presence of *p*TSA·H_2O (Scheme 2, Conditions B). In particular, the reagent **I** was obtained in high yields with these approaches (95% (Conditions A) and 84% (Conditions B), respectively).



Scheme 2. Synthesis of the reagent **I** and analogs from (het)$ArSO_2Na$ and electrophilic SCF_3 sources (**2** and **3**).

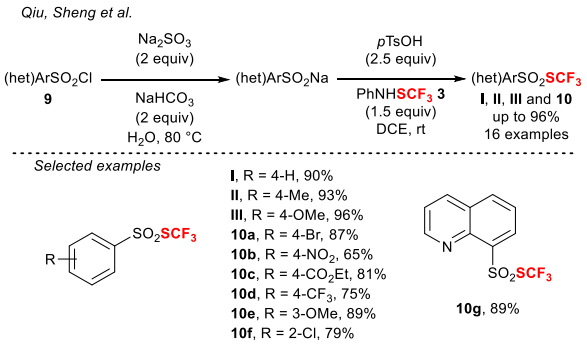
In 2017, the group of Qiu depicted a sequential tandem reaction to access trifluoromethylthiolated sulfonates (Scheme 3).[15] Starting from simple anilines, a panel of trifluoromethylthiolated sulfonates was prepared in moderate to high yields in the presence of DABCO·$(SO_2)_2$ as the sulphur dioxide source and the Billard-Langlois reagent **3**. The use of a Lewis acid such as bismuth(III) chloride was beneficial in this transformation, presumably activating the $PhNHSCF_3$ reagent. The reaction worked well with both anilines substituted with electron-donating and electron withdrawing groups (**III**, **6a-f**), the latter being the most

efficient. Note that heteroaromatic trifluoromethylthiolated sulfonates were not synthesized under these reaction conditions, which constituted the main limitation of this method. Alternatively, starting from a sodium sulfinate salt in the presence of the $PhNHSCF_3$ reagent **3** and *p*TsOH, the synthesis of an heteroaryl trifluoromethylthiolated sulfonate at room temperature was depicted.



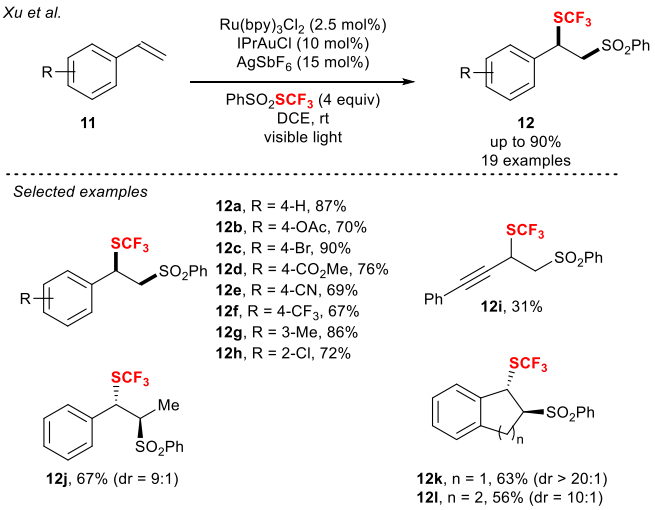
Scheme 3. Synthesis of reagent **I** and analogs from anilines, SO_2 source and $PhNHSCF_3$ reagent.

The same year, the group of Qiu and Sheng developed a complementary approach from sulfonyl chloride via a tandem process (Scheme 4).[16] Indeed, sulfonyl chloride derivatives were first converted into the corresponding sulfinates followed by a reaction with the Billard-Langlois reagent **3** to access the trifluoromethylthiolated sulfonates in the presence of *p*TsOH at room temperature. With this approach, various functional groups on aromatic derivatives were tolerated (CN, CO_2Et, NO_2, CF_3, I, Br, Cl) as well as naphthalene and heterocyclic compounds. Worth mentioning that the reagent **I** was furnished in a 90% yield.



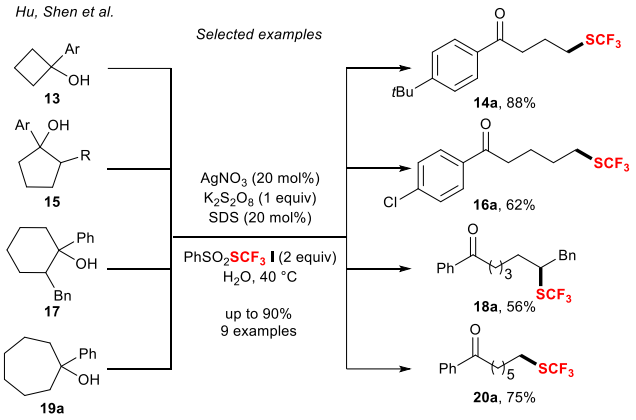
Scheme 4. A complementary approach to synthesize the reagent **I**.

Applications of the $PhSO_2SCF_3$ reagent I as a SCF_3 source. In 2017, the group of Xu reported the difunctionalization of alkenes **11** (Scheme 5).[17] By combining visible light photoredox catalysis with gold catalysis, the concomitant formation of a $C(sp^3)$-SCF_3 and $C(sp^3)$-SO_2Ph bonds was possible in a regioselective manner. The trifluoromethylthiosulfonylation reaction was successfully applied to styrene derivatives in moderate to good yields as well as to internal alkenes (cyclic and acyclic ones) with high diastereoselectivities.



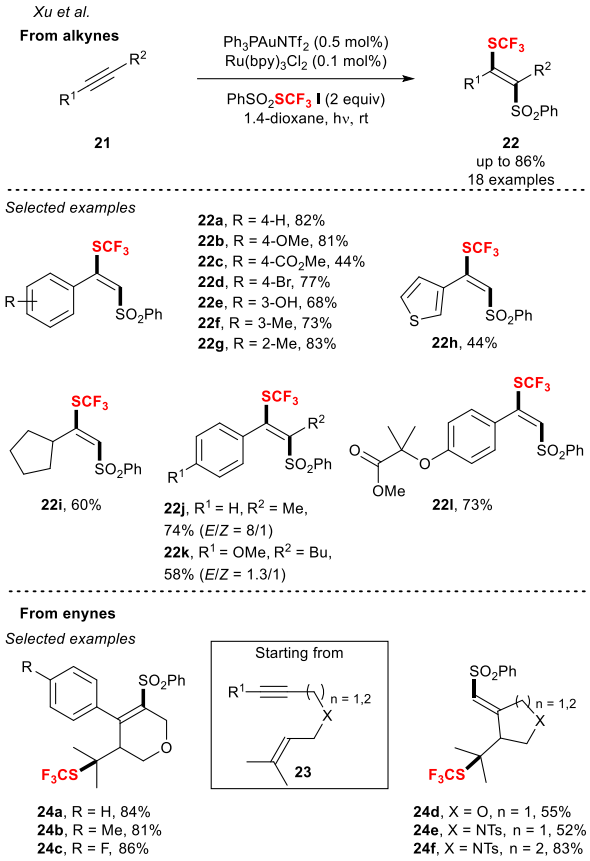
Scheme 5. Trifluoromethylthiosulfonylation reaction of alkenes.

In the course of their investigations for the Ag-catalysed ring-opening difluoromethylthiolation of cycloalkanols, Hu, Shen and co-workers showed that the transformation might also be extended to the trifluoromethylthiolation reaction.[18] Hence, under silver catalysis, the trifluoromethylthiolation of cyclobutanols **13**, cyclopentanols **15**, cyclohexanols **17** and the cycloheptanol **19** was possible in 56-90% yields, offering an access to the corresponding distally trifluoromethylthiolated ketones (Scheme 6).



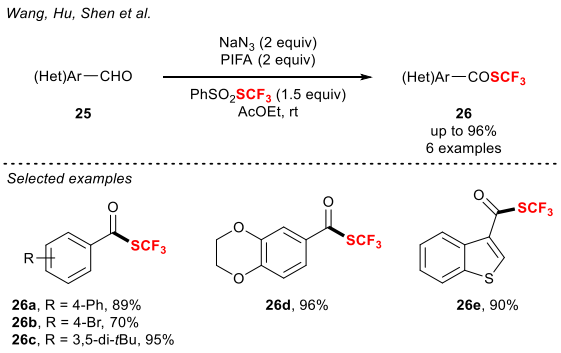
Scheme 6. Silver-catalysed trifluoromethylthiolation reaction of cycloalkanols. SDS = Sodium dodecyl sulfate.

The reagent **I** was successfully used for the trifluoromethylthiosulfonylation of alkynes via an atom-transfer addition reaction. Indeed, merging visible light photoredox catalysis and gold catalysis, the difunctionalization of alkynes **21** led to the trifluoromethylthiolated alkenes containing a sulfone residue (Scheme 7).[19] (Hetero)aromatic terminal alkynes and one aliphatic alkyne were functionalized, offering an access to the corresponding alkenes as single *E*-isomers. The reaction was not restricted to terminal alkynes, since several internal alkynes were used, yielding the corresponding *tetra*substituted alkenes, the *E* isomer being the major one. The synthetic utility of the approach was further demonstrated by the functionalization of bioactive compounds and drugs. When enynes **23** were used, a radical cascade cyclization occurred allowing the concomitant formation of C(sp^2)-SO_2Ph and C(sp^3)-SCF_3 bonds (Scheme 7). Thio-functionalized dihydropyrans, other heterocycles and carbocycles were obtained in good to high yields (up to 86%).[19]



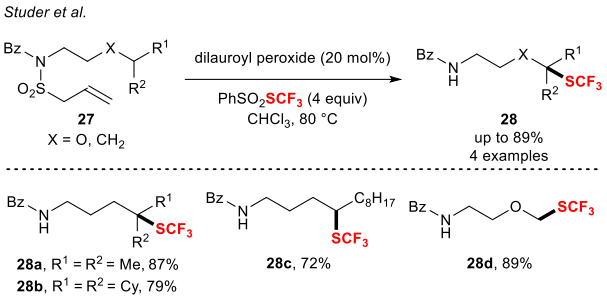
Scheme 7. Trifluoromethylthiosulfonylation reaction of alkyne and enyne derivatives.

Note that, in 2018, **I** was employed in the trifluoromethylthiolation of aldehydes **25** in the presence of PIDA and NaN_3 at room temperature (Scheme 8).[20] Six (hetero)aromatic aldehydes **25** were functionalized in high yields (70-96%).



Scheme 8. Trifluoromethylthiolation reaction of aldehydes.

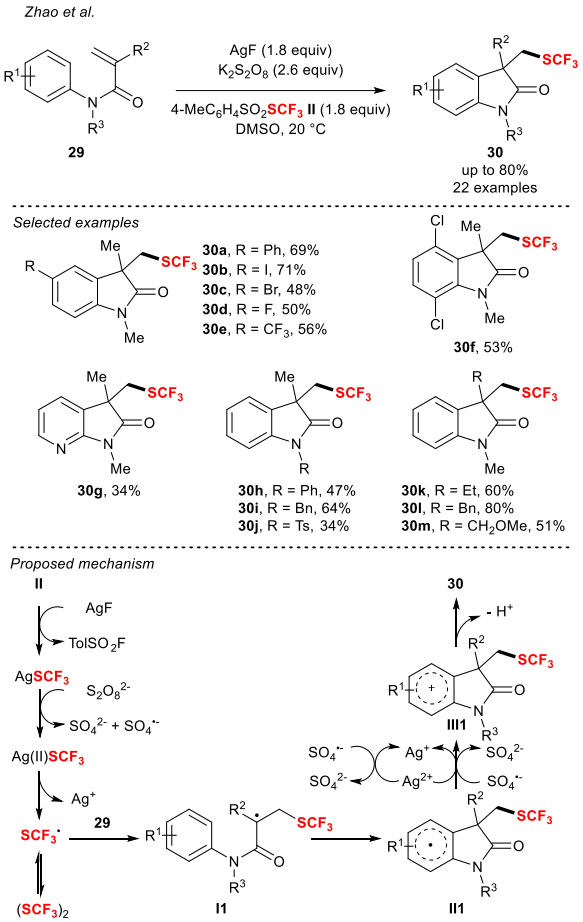
Recently, Studer and co-workers employed the reagent **I** in the amide directed remote trifluoromethylthiolation reaction *via* a 1,5-HAT process. Not only secondary and tertiary C(sp^3)-H bonds but also activated primary ones were efficiently and selectively trifluoromethylthiolated in good yields (Scheme 9).[21]



Scheme 9. Amide-mediated radical trifluoromethylthiolation reaction.

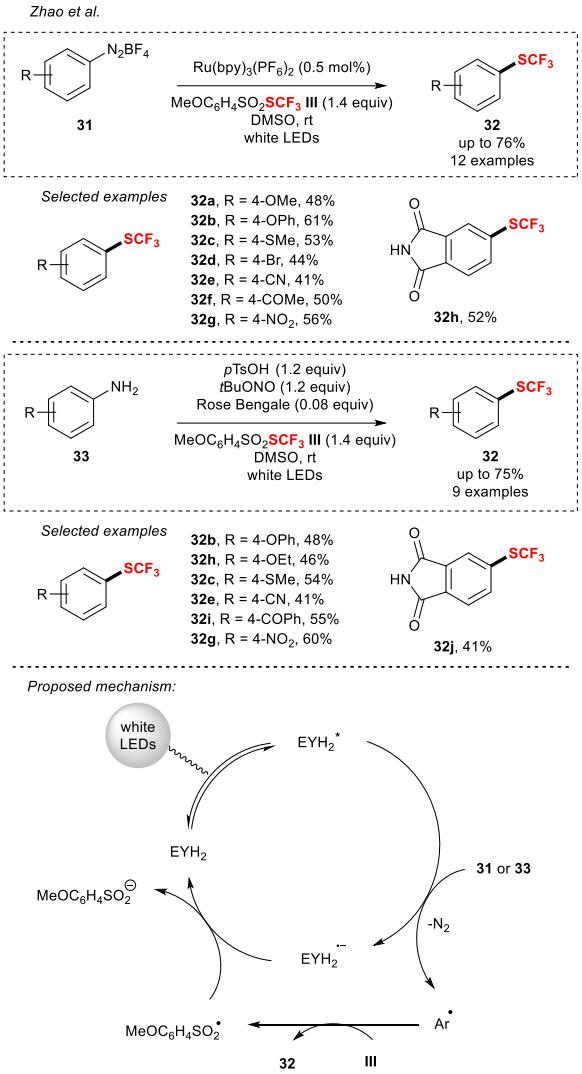
Synthesis and applications of 4-Me-$C_6H_4SO_2SCF_3$ II and 4-MeO-$C_6H_4SO_2SCF_3$ III reagents. As above-mentioned, the different approaches depicted were also applied to the synthesis of various $ArSO_2SCF_3$. Among them, access to the *S*-trifluoromethyl 4-methylbenzenesulfonothioate[12c,14,16] **II** (4-Me-$C_6H_4SO_2SCF_3$ or $TolSO_2SCF_3$, Scheme 1, 2 and 4) and the *S*-trifluoromethyl 4-methoxybenzenesulfonothioate[13,15,16] **III** (Scheme 2, 3 and 4) were reported and these reagents were also successfully applied as SCF_3 sources.

Indeed, Zhao and co-workers reported a complementary approach for the synthesis of trifluoromethylthiolated oxindole derivatives **30** (Scheme 10).[22] Using **II** as a coupling partner and in the presence of $K_2S_2O_8$, they depicted a silver mediated aryltrifluoromethylthiolation reaction of activated alkenes via a radical process.[23] Under mild conditions, the aryltrifluoromethylthiolation of a panel of activated alkenes **29** was possible with yields up to 80%. The transformation turned out to be tolerant to various functional groups such as nitro and halogens for instance. The authors proposed the following mechanism: *in situ* generation of $AgSCF_3$ after reaction of the reagent **II** and AgF, which then would be oxidized by $K_2S_2O_8$, leading to the corresponding $Ag(II)SCF_3$ and its decomposition into Ag(I) and the SCF_3 radical. After addition of the SCF_3 radical on the activated alkene, an alkyl radical **I1** would be formed, which would cyclise to provide the aryl radical **II1**. This later would undergo a final oxidation (intermediate **III1**) followed by a deprotonation step, which would furnish the trifluoromethylthiolated-substituted oxindole.



Scheme 10. Synthesis of trifluoromethylthiolated oxindole derivatives.

In addition, in 2018, the same group developed a methodology allowing the synthesis of aryl trifluoromethylthioether compounds **32** (Scheme 11)[24] via a visible light photocatalytic approach. The *S*-trifluoromethyl 4-methoxybenzenesulfonothioate **III** was employed as the SCF_3 reagent, which brought a clear added value to the process compared to the previously use of the toxic and volatile $(SCF_3)_2$.[25] The trifluoromethylthiolation reaction was conducted either on aryl diazonium tetrafluoroborate **31** or arylamines **33**. In the last case, the reaction conditions were slightly modified allowing the *in situ* generation of the diazonium salt. In both cases, the transformation turned out to be functional group tolerant (COMe, CN, Br, NO_2 for instance). The following mechanism was proposed by the authors: *in situ* generation of the diazonium salt followed by the formation of an aryl radical after a single radical transfer (SET) with the excited photocatalyst (EYH_2*). The later would react with the reagent **III** to afford the expected product and the sulfone radical. The photocatalyst would be regenerated after a SET with the sulfone radical. Note that very recently, a similar trifluoromethylthiolation reaction on diazonium salts was reported using the reagent **II** in the presence of a ruthenium-based photocatalyst.[26]



Scheme 11. Visible light photocatalytic approach for the trifluoromethylthiolation of *in situ* generated aryldiazonium salts or aryl amines.

2. Direct introduction of SR_f groups with $PhSO_2R_f$ reagents (R_f = CF_2H, CH_2F and C_2F_5)

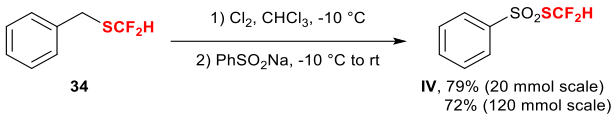
In contrast with the recent synthetic advances made using the $ArSO_2SCF_3$ reagents, the introduction of other SR_f groups remains limited. However, demonstrating interesting features, any advances made for the incorporation of the SCF_2H group and other SCF_2R_f ones will be undeniably impact this very active research field. In that context, the main breakthroughs that have been recently developed for the direct introduction of SCF_2H and SCF_2FG groups onto molecules using $ArSO_2SR_f$ as SR_f source will be summarized in the following section.

Synthesis and applications of the $PhSO_2SCF_2H$ reagent IV

Synthesis of the $PhSO_2SCF_2H$ reagent IV.

In 2016, the group of Lu and Shen investigated the radical difluoromethylthiolation of several classes of compounds.[27] In that purpose, the design of a new reagent was realized (Scheme 12). The *S*-(difluoromethyl)benzenesulfonothioate (**IV**, $PhSO_2SCF_2H$) was prepared in 79% yield in a 20 mmol scale, according to a one pot two-step sequence from benzyldifluoromethylsulfide

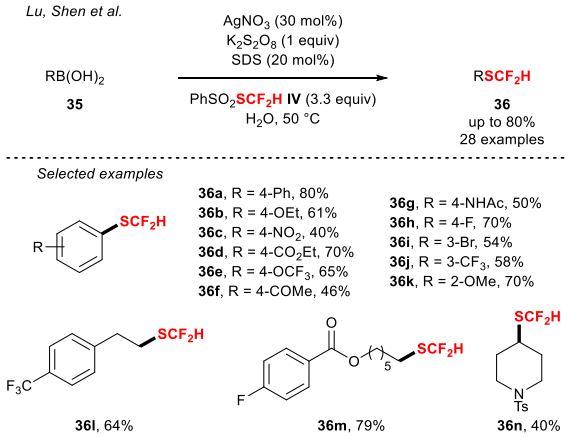
34. The *in situ* generation of HCF_2SCl was followed by a nucleophilic substitution with $PhSO_2Na$. Worth mentioning that the synthesis of **IV** was easily scaled up to a 20 grams' scale (120 mmol) and **IV** was obtained in a good 72% yield, showcasing the robustness of the synthesis.



Scheme 12. Synthesis of the $PhSO_2SCF_2H$ reagent **IV**.

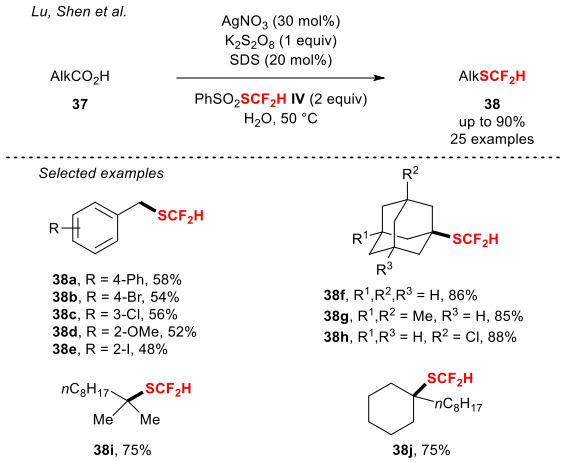
Applications of the $PhSO_2SCF_2H$ reagent IV. This reagent was successfully applied as a SCF_2H source, extending further the portfolio of tools for the direct introduction of this emergent moiety on various scaffolds.

First, the efficiency of the reagent was demonstrated in the silver-catalysed difluoromethylthiolating reaction of aryl and alkyl boronic acids **35** (Scheme 13).[27] Indeed, electron-rich and electron-poor arenes, as well as primary alkyl boronic acids were efficiently converted into the corresponding products **36**.[27] The reaction was carried out under mild reaction conditions, offering a large functional group tolerance such as halides, ester, ketone, nitro. Nevertheless, limitations remained as heteroaryl boronic acids like the pyridine-3-boronic acid was not suitable substrates. Moreover, secondary and tertiary alkyl boronic acids were less efficient compared to primary ones.

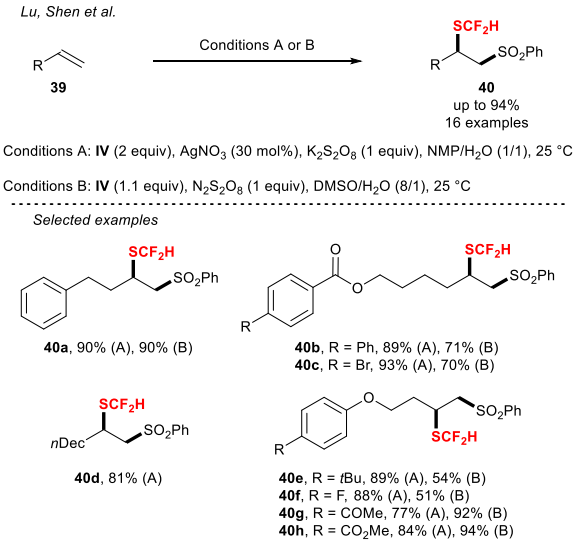


Scheme 13. Difluoromethylthiolation reaction of aryl and alkyl boronic acids with **IV** *via* Ag-catalysis.

To further demonstrate the versatility of the difluoromethylthiolating reagent, other transformations were evaluated. The direct introduction of the SCF_2H moiety thanks to a silver-catalysed decarboxylative difluoromethylthiolation reaction in the presence of **IV** was depicted (Scheme 14).[28] The transformation proceeded smoothly allowing the functionalization of tertiary, secondary ad even primary carboxylic acid derivatives **37**, the latter being less efficient. Finally, the Ag-catalysed difunctionalization of alkene derivatives **39** with the concomitant formation of a $C(sp^3)$-SCF_2H bond and $C(sp^3)$-SO_2Ph bond formation was reported (Scheme 15, conditions A). Note that the reaction also proceeded smoothly under silver-free conditions (Scheme 15, conditions B). A large variety of aliphatic alkenes bearing various functional groups (eg. sulfone, ester, aldehyde, halide) and even heterocyclic moiety were functionalized. Nevertheless, styrenes or □,□-unsaturated esters remain reluctant substrates. [27]

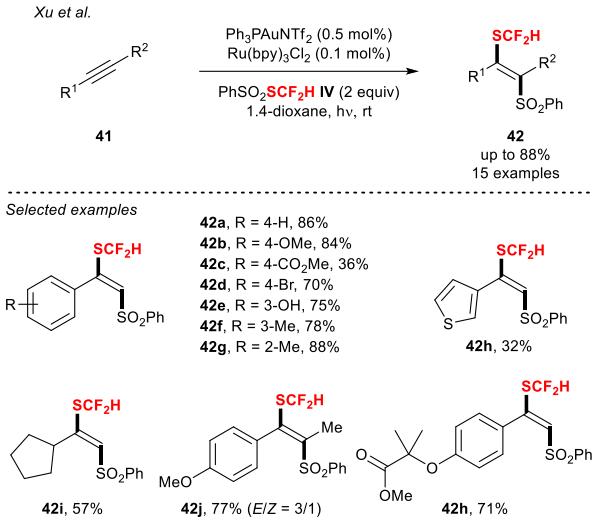


Scheme 14. Difluoromethylthiolation reaction of aliphatic carboxylic acids with **IV** *via* Ag-catalysis.



Scheme 15. Difunctionalization of alkenes using **IV**.

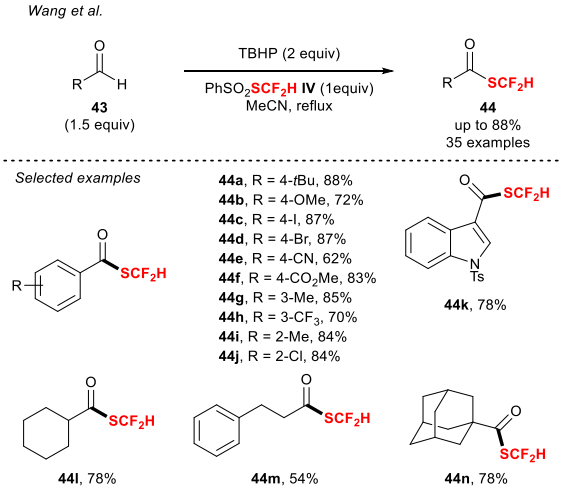
Then, two years later, during their investigations towards the difunctionalization of alkynes merging photoredox catalysis and gold catalysis, Xu and co-workers showed that the difluoromethylthiosulfonylation reaction was also possible.[19] A panel of terminal alkynes and an internal one **41** were functionalized in moderate to good yields leading to the corresponding SCF_2H-substituted alkenes **42** as *E*-isomers (Scheme 16).



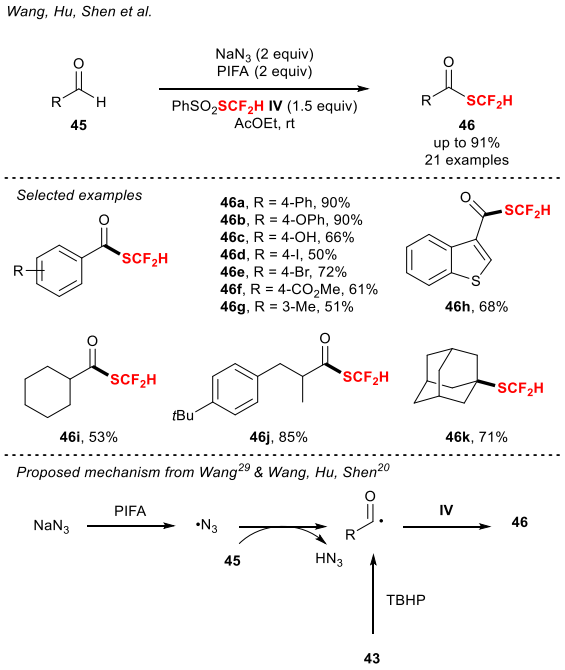
Scheme 16. Difluoromethylthiosulfonylation reaction via a gold/photoredox approach.

In 2018, Wang and co-workers reported the direct introduction of the SCF_2H group onto aldehydes *via* a metal free-approach.[29] Indeed, the combination of TBHP and the reagent **IV** allowed the functionalization of a large panel of (hetero)aromatic aldehydes **43** (Scheme 17). The methodology was also applied to the difluoromethylthiolation of aliphatic and α,β-unsaturated aldehydes, offering a straightforward access to difluoromethylthioethers. The reaction was turned out to be functional groups tolerant (cyano, ester, halides). The same year, Wang, Hu, Shen and co-workers, depicted a complementary approach using NaN_3 and PIFA to promote the difluoromethylthiolation of aldehydes **45** *via* a free radical process (Scheme 18).[20] The reaction occurred under mild conditions (room temperature). In addition the transformation was not restricted to the SCF_2H part (see other sections). Various aromatic and aliphatic aldehydes, except benzylic aldehydes, were suitable substrates including benzothiophene and thiophene (21 examples, up to 91% yield).

In both studies, a similar mechanism was proposed: 1) generation of an acyl radical with the abstraction of the H of the aldehyde either directly with TBHP or with in the *in situ* generated azide radical; then, 2) reaction with **IV** to afford the expected compound.



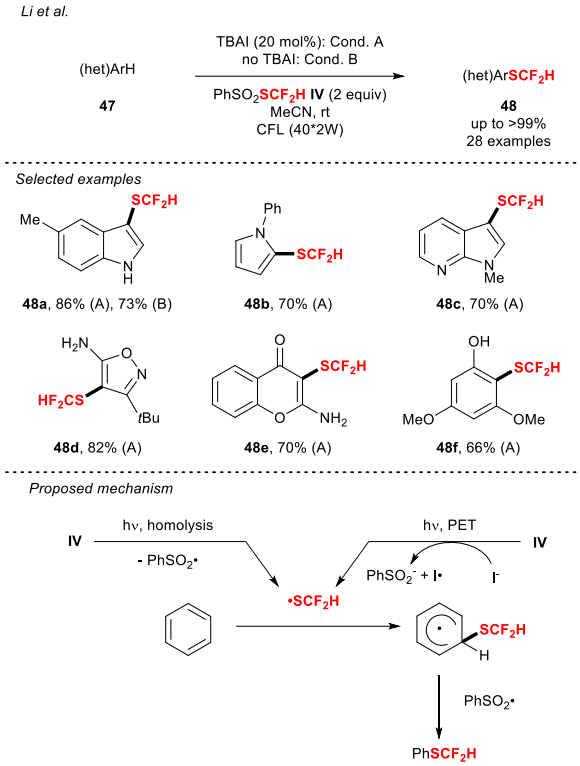
Scheme 17. Difluoromethylthiolation of aldehydes with the $PhSO_2SCF_2H$ reagent **IV**.



Scheme 18. Difluoromethylthiolation of aldehyde derivatives with the $PhSO_2SCF_2H$ reagent **IV**.

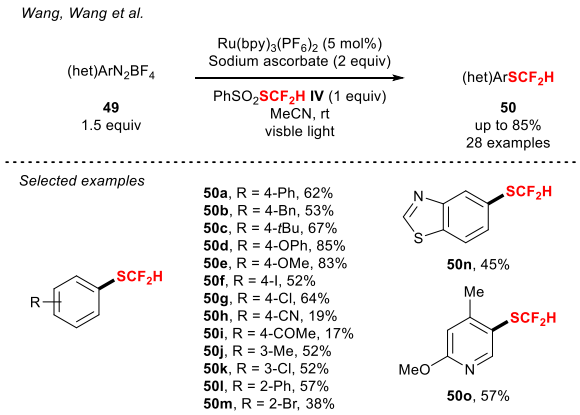
In course of the study towards the reactivity of the reagent **IV**, the group of Li demonstrated its successful use as a radical SCF_2H source in visible light promoted innate difluoromethylthiolation of aromatic derivatives **47** (Scheme 19).[30] Indeed, they anticipated that under light irradiation, the homolytic cleavage of the S-S bond would be possible and favoured by the release of the stabilized phenyl sulfonyl radical. Using this metal-free approach, various heteroaromatic derivatives such as indoles, pyrroles, azaindoles, pyrazoles, isoxazole, chromones and even thiophene were functionalized under mild conditions in the presence or not of a catalytic amount of *tetra*butylammonim iodide (TBAI). The innate introduction of the radical SCF_2H group on electron rich arenes was also realized, and the functionalization generally occurred at the most electron–rich and less sterically hindered positions.

The following mechanism was proposed: first, the generation of the SCF_2H radical upon light irradiation would occur, which would result from either the homolysis of $PhSO_2SCF_2H$ or the photo-induced electron transfer (PET) between the $PhSO_2SCF_2H$ and iodide. Then, after addition of the SCF_2H radical onto arenes, the phenyl sulfonium radical would abstract the hydrogen atom to afford the corresponding difluoromethylthiolated product **48**. Note that very recently the same group reported the generation of an aryl radical from potassium 4-biphenyl trifluoroborate through an S_H2 process. Its combination with $PhSO_2SCF_2H$ as a radical trapping reagent in the presence of diacetyl under hυ irradiation afforded the corresponding difluoromethylthiolated arene.[31]



Scheme 19. Radical difluoromethylthiolation reaction with (hetero)aromatics under visible light with the reagent **IV**.

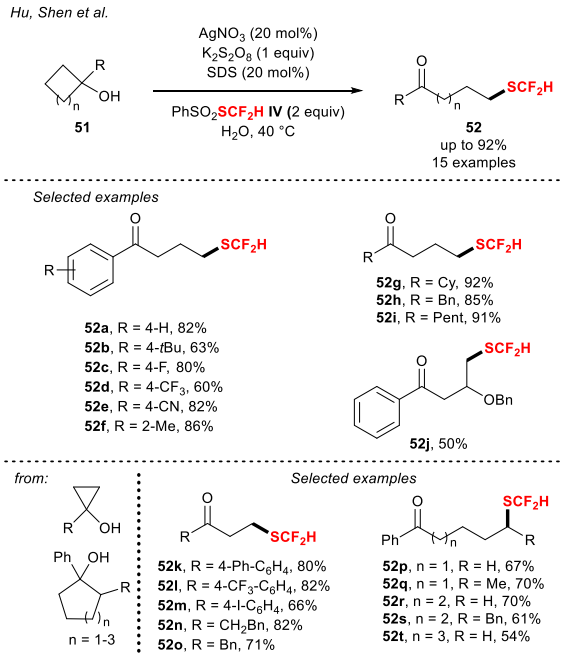
Very recently the visible light promoted difluoromethylthiolation of aryldiazonium salts **49** was reported (Scheme 20).[32] Using a catalytic amount of $Ru(bpy)_3(PF_6)_2$ in the presence of sodium ascorbate and the reagent **IV**, 28 (hetero)aryl diazonium salts were functionalized, offering a complementary synthetic route to the one developed by Li and co-workers.



Scheme 20. Radical difluoromethylthiolation reaction with (hetero)aromatics under visible light with the reagent **IV**.

The difluoromethylthiolation of alkyl ketone derivatives with $PhSO_2SCF_2H$ at a remote position was investigated by Hu, Shen and co-workers (Scheme 21).[18] In that purpose, the authors reported an efficient approach using cycloalkanols as precursors of functionalized alkyl ketones. Indeed, in 2018, they reported the silver-catalysed difluoromethylthiolation reaction of a variety of cycloalkanols. The construction of difluoromethylthioethers from cyclobutanol derivatives was carried in water in the presence of a surfactant sodium dodecyl sulfate (SDS), a catalytic amount of $AgNO_3$ and a stoichiometric amount of $K_2S_2O_8$ (15 examples, 50-95%). Not restricted to cyclobutanols, the transformation was extended to cyclopropanols (9 examples,

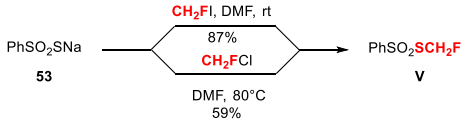
40-82%), cyclopentanols (3 examples, 60-70%), cyclohexanols (3 example, 61-70%) and cycloheptanol. The authors suggested that the reaction proceeded *via* the generation of a cycloalkoxy radical, which might lead to an alkyl radical after opening β-scission. Then, the intermediate could react with the reagent **IV** to afford the expected compounds.



Scheme 21. Silver-catalysed difluoromethylthiolation of cycloalkanol derivatives.

Synthesis and applications of the $PhSO_2SCH_2F$ reagent V

Synthesis of the $PhSO_2SCH_2F$ reagent V. Present in compounds of interest such as the Fluticasone drug, known for its anti-inflammatory properties, the development of efficient tools for the direct introduction of the SCH_2F residue onto molecules is of high importance. In that context, the group of Lu and Shen designed the first electrophilic *S*-(fluoromethyl) benzenesulfonothioate (**V**, $PhSO_2SCH_2F$). This robust reagent was prepared from the commercially $PhSO_2SNa$ **53** either with CH_2FI or with CH_2FCl (Scheme 22).[33]

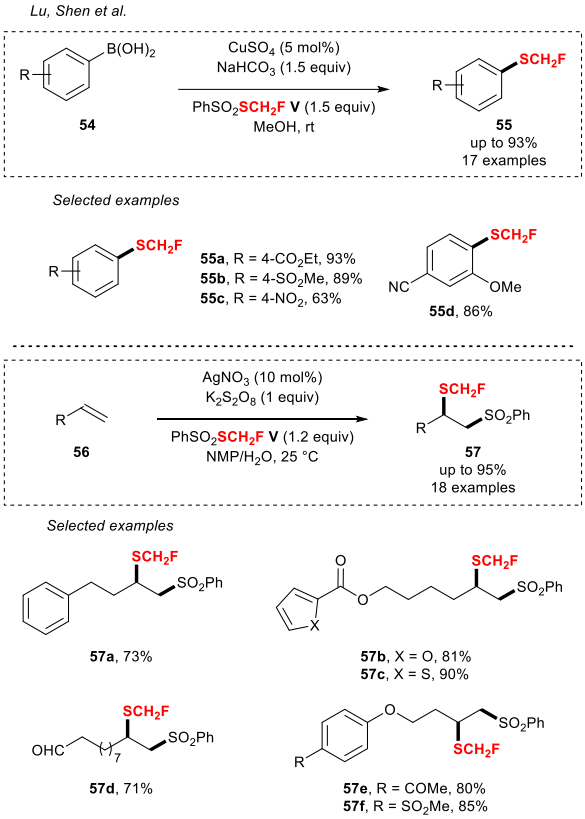


Scheme 22. Synthesis of the $PhSO_2SCH_2F$ reagent **V**.

Applications of the $PhSO_2SCH_2F$ reagent V. Although restricted so far to a limited number of examples, this reagent **V** has already showcased its potential in different reactions.

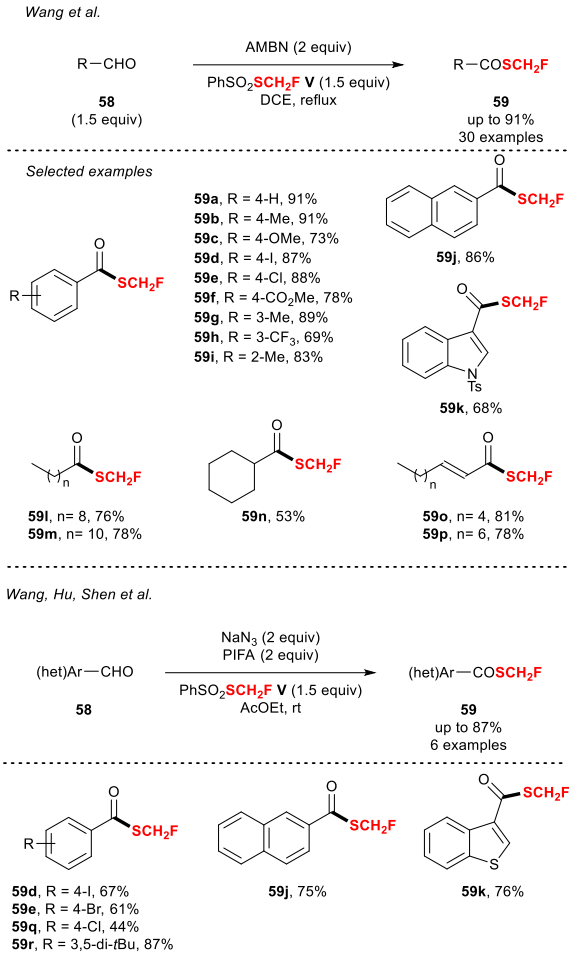
Lu, Shen and co-workers studied the formation of $C(sp^2)$-SCH_2F and $C(sp^3)$-SCH_2F bonds (Scheme 23).[33] Indeed, under copper catalysis, electron-rich and electron-poor aromatic boronic acids **54** were monofluoromethylated in an efficient manner. Note that in case of some products bearing electron-rich groups, an oxidation into the corresponding sulfoxide was necessary to prevent any defluorination of the products as a side reaction. In addition, the reagent **V** turned to be suitable for the difunctionalization of unactivated alkenes **56** leading to the corresponding monofluoromethylthioethers **57** with good yields, up to 95%. The

transformation was tolerant to various functional groups (halides, ketone, sulfonyl, …) as well as heteroaryl groups (indolyl, furyl, thienyl moieties).



Scheme 23. Monofluoromethylthiolation of aryl boronic acids and alkenes.

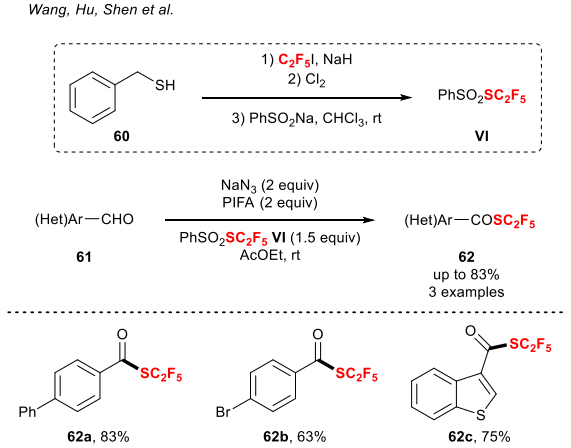
An additional example to showcase the efficiency of such reagent to introduce the SCH_2F group was recently reported by the groups of Wang,[34] as well as Wang, Hu and Shen (Scheme 24).[20] Indeed, Wang and co-workers studied the synthesis of monofluoromethylthioesters **59** from aldehydes **58** *via* a metal free approach. Using **V** as a SCH_2F radical source, a panel of (hereto)aromatic aldehydes as well as aliphatic and α,β-unsaturated aldehydes were functionalized (29 examples, 42-91%). The presence of 2,2'-azobisisovaleronitrile (AMBN) as radical initiator was necessary for the generation of the acyl radical from the aldehyde. In the case of Shen and co-workers, the authors demonstrated the versatility and generality of the $PhSO_2SR_f$ reagents to introduce a variety of emergent SR_f group on aldehydes including the SCH_2F moiety (6 examples, 44-87%).[20]



Scheme 24. Monofluoromethylthiolation of aldehydes with the $PhSO_2SCH_2F$ reagent. AMBN = 2,2'-azobisisovaleronitrile.

Synthesis and applications of the $PhSO_2SCF_2CF_3$ reagent VI

The reagent **VI** was prepared in three steps from the commercially available benzyl mercaptan **60**. The unique example of application of the $PhSO_2SCF_2CF_3$ reagent **VI** was recently depicted in the global study from Wang, Hu, Shen and co-workers about the functionalization of aldehydes with $PhSO_2SR_f$ reagents.[20] Encouraged by their success, the authors reported the synthesis of three unprecedented pentafluoroethylthioesters **62** (Scheme 25).



Scheme 25. Synthesis of the synthesis of pentafluoroethylthiothers using the the $PhSO_2SC_2F_5$ reagent **VI**.

Conclusion

Extending the portfolio of tools enabling the synthesis of original fluorinated compounds is of high importance. Consequently, over the last years, many efforts focused on the development of original approaches for the introduction of emergent fluorinated motifs. This review showcased and discussed the use of several $ArSO_2SR_f$ reagents as SR_f sources, a new emerging trend to access to SR_f-containing molecules. A myriad of transformations allowing the incorporation of the valuable SCF_3, SCF_2H, SCH_2F and SC_2F_5 groups were designed. We strongly believe that this review will bring considerable insights to the organofluorine chemistry community and would stimulate further developments for these promising emergent fluorinated groups.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

This work was partially supported by INSA Rouen, Rouen University, CNRS, EFRD, Labex SynOrg (ANR-11-LABX-0029), Région Normandie (Crunch Network).

Notes and references

1 a) T. Liang, C. N. Neumann and T. Ritter, *Angew. Chem. Int. Ed.,* 2013, **52**, 8214-8264; b) T. Besset, T. Poisson and X. Pannecoucke, *Chem. Eur. J.,* 2014, **20**, 16830-16845; c) C. Ni and J. Hu, *Chem. Soc. Rev.,* 2016, **45**, 5441-5454; d) G. Landelle, A. Panossian and F. R. Leroux, *Curr. Top. Med. Chem.,* 2014, **14**, 941-951; e) G. Landelle, A. Panossian, S. Pazenok, J.-P. Vors and F. R. Leroux, *Beilstein J. Org. Chem.,* 2013, **9**, 2476-2536; f) P. A. Champagne, J. Desroches, J.-D. Hamel, M. Vandamme and J.-F. Paquin, *Chem. Rev.,* 2015, **115**, 9073-9174; g) E. Merino and C. Nevado, *Chem. Soc. Rev.,* 2014, **43**, 6598-6608; h) H. Egami and M. Sodeoka, *Angew. Chem. Int. Ed.,* 2014, **53**, 8294-8308; i) M.-C. Belhomme, T. Besset, T. Poisson and X. Pannecoucke, *Chem. Eur. J.,* 2015, **21**, 12836-12865; j) T. Besset, P. Jubault, X. Pannecoucke and T. Poisson, *Org. Chem. Front.,* 2016, **3**, 1004–1010; k) Hai-Xia Song, Qiu-Yan Han, Cheng-Long Zhao and Cheng-Pan Zhang, *Green Chem.*, 2018, **20**, 1662-1731.

2 a) J. Wang, M. Sánchez-Roselló, J. L. Aceña, C. del Pozo, A. E. Sorochinsky, S. Fustero, V. A. Soloshonok and H. Liu, *Chem. Rev.,* 2014, **114**, 2432-2506; b) S. Purser, P. R. Moore, S. Swallow and V. Gouverneur, *Chem. Soc. Rev.,* 2008, **37**, 320-330; c) E. P. Gillis, K. J. Eastman, M. D. Hill, D. J. Donnelly and N. A. Meanwell, *J. Med. Chem.,* 2015, **58**, 8315-8359; d) E. A. Ilardi, E. Vitaku and J. T. Njardarson, *J. Med. Chem.,* 2014, **57**, 2832-2842.

3 D. O'Hagan, *Chem. Soc. Rev.,* 2008, **37**, 308-319.

4 For selective reviews on the SCF_3 group, see: a) F. Toulgoat, S. Alazet and T. Billard, *Eur. J. Org. Chem.,* 2014, 2415-2428; b) X.-H. Xu, K. Matsuzaki and N. Shibata, *Chem. Rev.,* 2015, **115**, 731-764; c) S. Barata-Vallejo, S. Bonesi and A. Postigo, *Org. Biomol. Chem.,* 2016, **14**, 7150-7182; d) M. Li, J. Guo, X.-S. Xue and J.-P. Cheng, *Org. Lett.,* 2016, **18**, 264-267; d) H. Zheng, Y. Huang and Z. Weng, *Tetrahedron,* 2016, **57**, 1397-1409.

5 For selective reviews on the SCF_2H and SCF_2FG group, see: a) H.-Y. Xiong, X. Pannecoucke and T. Besset, *Chem. Eur. J.*, 2016, **22**, 16734-16749 and references cited therein; a) B. Manteau, S. Pazenok, J.-P. Vors and F. R. Leroux, *J. Fluorine Chem.*, 2010, **131**, 140-158.

6 For selected examples, see: a) M. Hu, J. Rong, W. Miao, C. Ni, Y. Han, and J. Hu, *Org. Lett.,* 2014, **16**, 2030-2033; b J.-B. Liu, X.-H. Xu, Z.-H. Chen and F.-L. Qing, *Angew. Chem. Int. Ed.,* 2015, **54**, 897-900; c) K.-Y. Ye, X. Zhang, L.-X. Dai and S.-L. You, *J. Org. Chem.,* 2014, **79**, 12106-12110; d) K. Zhang, J.-B. Liu and F.-L. Qing, *Chem. Commun.,* 2014, **50**, 14157-14160; e) L. Jiang, J. Qian, W. Yi, G. Lu, C. Cai and W. Zhang, *Angew. Chem. Int. Ed*., 2015, **54,** 14965-14969; f) Y. Yang, L. Xu, S. Yu, X. Liu, Y. Zhang and D. A. Vicic, *Chem. Eur. J.,* 2016, **22**, 858-863; g) M. Bu, G. Lu and C. Cai, *Org. Chem. Front.*, 2017, **4**, 266-270; h) Q. Lefebvre, E. Fava, P. Nikolaienko and M. Rueping, *Chem. Commun.,* 2014, **50,** 6617-6619; i) M. Lübcke, W. Yuan and K. J. Szabó, *Org. Lett.,* 2017, **19**, 4548-4551; j) L. Jarrige, A. Carboni, G. Dagousset, G. Levitre, E. Magnier and G. Masson, *Org. Lett*., 2016, **18**, 2906−2909; k) X. Liu, R. An, X. Zhang, J. Luo and X. Zhao, *Angew. Chem. Int. Ed.,* 2016, **55**, 5846-5850; l) S. Pan, Y. Huang and F.-L. Qing, *Chem. Asian J.,* 2016, **11**, 2854-2858; m) J. Zhang, L. Wang, J.-H. Lin, J.-C. Xiao and S. H. Liang, *Angew. Chem. Int. Ed.,* 2015, **54,** 13236-

13240; n) Y. Li, T. Koike and M. Akita, *Asian J. Org. Chem.,* 2017*,* **6**, 445-448; o) F. Wang, L. Zhao, J. You and M.-X. Wang, *Org. Chem. Front.,* **2016**, **3**, 880-886; p) C. Ghiazza, L. Khrouz, C. Monnereau, T. Billard and A. Tlili, *Chem. Commun*., 2018, **54**, 9909-9912; q) P. Saravanan and P. Anbarasan, *Adv. Synth. Catal*., 2018, **360**, 2894-2899; r) C.-C. Xi, Z.-M. Chen, S.-Y. Zhang and Y.-Q. Tu, *Org. Lett.*, 2018, **20**, 4227-4230; s) G. Yin, I. Kalvet and F. Schoenebeck, *Angew. Chem. Int. Ed.,* 2015, **54**, 6809-6813; t) L. Candish, L. Pitzer, A. Gomez-Suarez and F. Glorius, *Chem. Eur. J.,* 2016, **22**, 4753-4756.

7 For selected examples, see: a) E. Ismalaj, D. Le Bars and T. Billard, *Angew. Chem. Int. Ed.,* 2016, **55**, 4790-4793. b) Q. Glenadel and T. Billard, *Chin. J. Chem.,* 2016, **34**, 455-458.

8 For selected examples, see: a) B. Bayarmagnai, C. Matheis, K. Jouvin and L. J. Goossen, *Angew. Chem. Int. Ed.,* 2015, **54**, 5753-5756; b) K. Jouvin, C. Matheis and L. J. Gooßen, *Chem. Eur. J.,* 2015, **21**, 14324-14327; c) B. Exner, B. Bayarmagnai, F. Jia and L. J. Goossen, *Chem. Eur. J.,* 2015, **21***,* 17220-17223.

9 a) S. Arimori, O. Matsubara, M. Takada, M. Shiro and N. Shibata, *R. Soc. Open Sci.,* 2016, **3**, 160102; b) Z. Huang, Y.-D. Yang, E. Tokunaga and N. Shibata, *Org. Lett.,* 2015, **17**, 1063-1065.

10 a) D. Zhu, Y. Gu, L. Lu and Q. Shen, *J. Am. Chem. Soc.,* 2015, **137**, 10547-10553; b) J. Wu, Y. Gu, X. Leng and Q. Shen, *Angew. Chem. Int. Ed.,* 2015, **54**, 7648-7652; c) J. Wu, Y. Liu, C. Lu and Q. Shen, *Chem. Sci.,* 2016, **7**, 3757-3762; d) F. Shen, P. Zhang, L. Lu and Q. Shen, *Org. Lett.*, 2017, **19**, 1032-1035; e) F. Hu, X.-X. Shao, D.-H. Zu, L. Lu and Q. Shen, *Angew. Chem. Int. Ed.,* 2014, **53**, 6105-6109; f) T. Yang, L. Lu, and Q. Shen, *Chem. Commun.,* 2015, **51**, 5479-5481.

11 a) H.-Y. Xiong, A. Bayle, X. Pannecoucke and T. Besset, *Angew. Chem. Int. Ed.*, 2016, **55**, 13490–13494; b) M. V. Ivanova, A. Bayle, T. Besset, X. Pannecoucke and T. Poisson, *Angew. Chem. Int. Ed.*, 2016, **55**, 14141–14145; c) M. V. Ivanova, A. Bayle, X. Pannecoucke, T. Besset and T. Poisson, *Eur. J. Org. Chem.*, 2017, 2475–2480; d) M. V. Ivanova, A. Bayle, T. Besset, X. Pannecoucke and T. Poisson, *Chem. Eur. J.*, 2017, **23**, 17318–17338.

12 a) S. S. Block and J. P. Weidner, *Nature*, 1967, **214**, 478-479; b) J. P. Weidner and S. S. Block, *J. Med. Chem.*, 1972, **15**, 564-567; c) J. P. Weidner and S. S. Block, *J. Med. Chem.*, 1967, **10**, 1167-1170.

13 X. Shao, C. Xu, L. Lu and Q. Shen, *J. Org. Chem*., 2015, **80**, 3012-3021.

14 M. Jereb and D. Dolenc*, RSC Adv.*, 2015, **5**, 58292-58306.

15 J. Sheng, Y. Li and G. Qiu, *Org. Chem. Front.*, 2017, **4**, 95-100.

16 Y. Li, G. Qiu, H. Wang and J. Sheng, *Tetrahedron Lett.*, 2017, **58**, 690-693.

17 H. Li, C. Shan, C.-H. Tung and Z. Xu, *Chem. Sci*., 2017, **8**, 2610-2615.

18 B. Xu, D. Wang, Y. Hu and Q. Shen, *Org. Chem. Front.*, 2018, **5**, 1462-1465.

19 H. Li, Z. Cheng, C.-H. Tung, Z. Xu, *ACS Catal*., 2018, **8**, 8237-8243.

20 B. Xu, D. Li, L. Lu, D. Wang, Y. Hu and Q. Shen, *Org. Chem. Front.*, 2018, **5**, 2163-2166.

21 Y. Xia, L. Wang and A. Studer, *Angew. Chem. Int. Ed.*, 2018, **57**, 12940-12944.

22 a) F. Yin and X.-S. Wang, *Org. Lett.*, 2014, **16**, 1128-1131; b) R. Honeker, R. A. Garza-Sanchez, M. N. Hopkinson and F. Glorius, *Chem. Eur. J.*, 2016, **22**, 4395-4399; c) G. Dagousset, C. Simon, E. Anselmi, B. Tuccio, T. Billard and E. Magnier, *Chem. Eur. J.*, 2017, **23**, 4282-4286.

23 X. Zhao, B. yang, A. Wei, J. Sheng, M. Tian, Q. Li and K. Lu, *Tetrahedron Lett*., 2018, **59**, 1719-1722.

24 X. Zhao, X. Zheng, M. Tian, Y. Tong, B. Yang, X. Wei, D. Qiu and K. Lu, *Org. Chem. Front.*, 2018, **5**, 2636-2640.

25 D. Koziakov, M. Majek and A. J. von Wangelin, *Eur. J. Org. Chem*., 2017, 6722-6725.

26 C. Ghiazza, C. Monnereau, L. Khrouz, T. Billard and A. Tlili, *Synthesis*, 2018, DOI: 10.1055/s-0037-1610322.

27 D. Zhu, X. Shao, X. Hong, L. Lu and Q. Shen, *Angew. Chem. Int. Ed.*, 2016, **55**, 15807-15811.

28 For an example of decarboxylative difluoromethylthiolation of carboxylic acid using an electrophilic SCF_2H source under visible light, see: L. Candish, L. Pitzer, A. Gómez-Suárez and F. Glorius, *Chem. Eur. J.*, 2016, **22**, 4753-4756.

29 S.-H. Guo, X.-L. Zhang, G.-F. Pan, X.-Q. Zhu, Y.-R. Gao and Y.-Q. Wang, *Angew. Chem. Int. Ed.*, 2018, **57**, 1663 –1667.

30 J. Li, D. Zhu, L. Lv and C.-J. Li, *Chem. Sci.*, 2018, **9**, 5781-5786 and references cited therein.

31 W. Liu, P. Liu, L. Lv and C.-J. Li, *Angew. Chem. Int. Ed.,* 2018, **57**, 13499-13503.

32 W. Wang, S. Zhang, H. Zhao and S. Wang, *Org. Biomol. Chem.*, 2018, **16**, 8565-8568.

33 Q. Zhao, L. Lu, and Q. Shen, *Angew. Chem. Int. Ed.,* 2017, **56**, 11575 –11578.

34 S.-H. Guo, M.-Y. Wang, G.-F. Pan, X.-Q. Zhu, Y.-R. Gao, and Y.-Q. Wang, *Adv. Synth. Catal.*, 2018, **360**, 1861-1869.