RESEARCH ARTICLE

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Photocatalytic fluorosulfonylation of aliphatic carboxylic acid NHPI esters†

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Sulfonyl fluorides have been increasingly favored by medicinal chemists and chemical biologists because of their unique reactivity and stability, but their synthetic methods still have certain limitations. Based on the SO_2 radical insertion/fluorination strategy, we have developed a novel method for photocatalytic induced synthesis of alkylsulfonyl fluorides (low to 1 mol% P.C. and up to 92% yield), which covers primary, secondary and tertiary aliphatic carboxylic acid NHPI esters, providing a facile method for the late-stage fluorosulfonylation of natural products and drugs. This method provides an efficient and reliable approach for the synthesis and application of alkylsulfonyl fluorides.

Introduction

The discovery of sulfonyl fluorides can be traced back to 1921, when Steinkopf treated toluene with fluorosulfonic acid.[1] However, sulfonyl fluorides did not get enough attention until 2014, when Sharpless and colleagues proposed the concept of sulfur(VI) fluoride exchange (SuFEx),[2] which became known as an excellent reaction for click chemistry and came to be widely used in organic synthesis,[3] chemical biology,[4] drug discovery,[5] materials science,[6] *etc.*[7] Then, a new chapter opened up for the syntheses and applications of sulfonyl fluorides. The growing demand for sulfonyl fluorides has led to an increasing emphasis on the development of novel and efficient synthetic methods.

In recent years, the synthesis methods of sulfonyl fluorides have developed rapidly.[8] Typical methods mainly include: (1) accessing the fluorosulfonyl group *via* the chloride–fluoride exchange[9] and alternative methods;[10] (2) introducing sulfonyl fluoride fragments into the target molecules *via* sulfonyl fluoride hubs;[11] and (3) direct fluorosulfonylation *via* FSO_2 reagents or FSO_2 synthons.[12] Due to decades of development, the classic approaches to access the fluorosulfonyl group have proven to be a straightforward and efficient way.

DABSO was developed by Santos *et al.* in 1988[13] and was first applied as a novel SO_2 source by Willis and co-workers to deliver aryl aminosulfonamides in 2010.[14] Since then, DABSO has frequently been used as a solid precursor of SO_2 gas in the synthesis of various sulfonyl products,[15] especially arylsulfonyl fluorides in recent years (Scheme 1, I).[16] Unsurprisingly, it can also be used to synthesize aliphatic sulfonyl fluorides.[17] For example, the Willis group reported a radical approach toward

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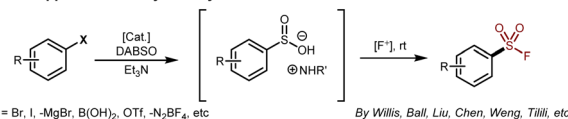*E-mail: shliao@fzu.edu.cn, nxl646036@163.com*
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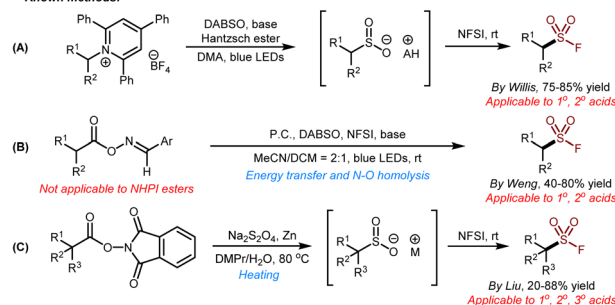†Electronic supplementary information (ESI) available: Experimental procedures, data for all the products. See DOI: https://doi.org/10.1039/d2qo00861k

Scheme 1 Approaches for fluorosulfonyl group installation *via* SO_2 radical insertion/fluorination.
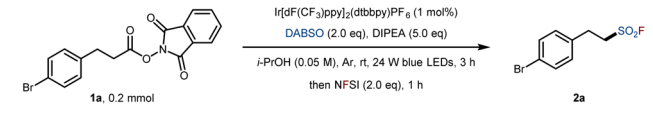
primary and secondary alkylsulfonyl derivatives *via* donor–acceptor activation of pyridinium salts which were trapped by DABSO to generate sulfonyl radicals (Scheme 1, II, A).[18] Hence, the SO$_2$ radical insertion/fluorination strategy became a popular method for the construction of the fluorosulfonyl group, with special synthetic advantages in the direct synthesis of sulfonyl fluorides *via* C–SO$_2$F bond formation.[8] Very recently, the Weng group reported a photocatalytic decarboxylative fluorosulfonylation approach for converting aldoxime esters to the corresponding sulfonyl fluorides,[17f] which was enabled by energy-transfer-mediated photocatalysis and N–O bond homolysis. However, this protocol delivers the corresponding sulfonyl fluorides usually in modest yields and is not applicable to tertiary carboxylic acids (Scheme 1, II, B). Moreover, SO$_2$ sources including SO$_2$ gas and its surrogates,[15a–c] such as inorganic hypervalent sulfur sources like sodium/potassium metabisulfite, are the key factors for the introduction of sulfone groups.[19]

Aliphatic carboxylic acids, as a type of cheap and easily available organic compound, are widely used in the synthesis of various organic compounds. In particular, redox-active *N*-hydroxyphthalimide (NHPI) esters, readily prepared from abundant and widely available carboxylic acids, are considered to be reliable precursors of alkyl radicals, which are widely used in the synthesis of various C–X bonds.[20] This year, the Liu group developed an efficient method for obtaining alkylsulfonyl fluorides from aliphatic carboxylic acid NHPI esters using sodium dithionite as the SO$_2$ source.[19i] However, limited by the equivalent amount of zinc powder to be used and high temperature conditions, this method afforded the corresponding alkylsulfonyl fluoride products in moderate yields (Scheme 1, II, C). Our group is dedicated to the synthesis of various types of sulfonyl fluorides by the photocatalytic redox strategy. Based on the SO$_2$ radical insertion/fluorination strategy, we envisaged a facile method to synthesize alkylsulfonyl fluorides through photocatalytic redox active ester decarboxylation with carboxylic acids as the alkyl radical source, DABSO as the SO$_2$ source and NFSI as the fluorine source. Herein, we wish to report our efforts toward this goal and the establishment of a facile method to access aliphatic sulfonyl fluorides based on visible light-mediated decarboxylative radical fluorosulfonylation *via* SO$_2$ radical insertion/fluorination of alkyl NHPI esters (low to 1 mol% P.C. and up to 92% yield). This method is characterized by the rapid synthesis of a broad range of alkylsulfonyl fluorides from primary, secondary, and tertiary acids, late-stage modification of natural products and drugs, and mild conditions (Scheme 1, II).

Results and discussion

To achieve the photocatalytic decarboxylated fluorosulfonylation of aliphatic carboxylic acid NHPI esters, an initial study was conducted with 4-bromophenylpropionic acid-derived NHPI ester **1a** as the model substrate (Table 1). Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ was first tested as the photocatalyst in combi-

Table 1 Optimization of the reaction conditions[a]

Entry	Variation from the standard conditions	Yield[b] (%)
1	None	91 (85)[c]
2	Addition of Hantzsch esters (2.0 eq.)	85
3	Eosin Y-Na$_2$ instead of Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$	6
4	*fac*-Ir(ppy)$_3$ instead of Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$	17
5	Ru(bpy)$_3$Cl$_2$ instead of Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$	5
6	MeCN instead of i-PrOH	13
7	DMF instead of i-PrOH	17
8	THF instead of i-PrOH	N.P.
9	DCM instead of i-PrOH	N.P.
10	Et$_3$N instead of DIPEA	13
11	DABSO (1.5 eq.)	84
12	DIPEA (3.0 eq.)	61
13	Selectfluor™ instead of NFSI	18
14	NFSI (3.0 eq.)	90
15	Without P.C.	N.P.
16	No light	Trace
17	In air	Trace

[a] Reaction conditions: **1a** (0.2 mmol), DABSO (0.4 mmol), DIPEA (1.0 mmol), Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (1 mol%), *i*-PrOH (4.0 mL), 24 W blue LEDs (λ_{max} = 460 nm), rt, argon, 3 h; then NFSI (0.4 mmol), 1 h; N.P. = no product was detected. [b] Yields were determined by ^{19}F NMR analysis with 4-iodofluorobenzene as the internal standard. [c] Isolated yield is shown in parentheses.

nation with DIPEA as the reductant and DABSO as the SO$_2$ source. After 3 h of stirring, NFSI was added as the F source and the reactions proceeded for an additional 1 h. The desired product **2a** was obtained in 91% yield (85% isolated yield, Table 1, entry 1). The addition of Hantzsch ester (HE) as the additional reductant slightly reduced the yield (entry 2 *vs.* entry 1). This is probably due to the formation of a cloudy mixture upon the addition of HE, which negatively affects the light absorption of the photocatalyst. Next, changing the photocatalyst to eosin Y (disodium salt), *fac*-Ir(ppy)$_3$, or Ru(bpy)$_3$Cl$_2$ would dramatically reduce the yields (entries 3–5). Furthermore, varying the solvent proved that MeCN, DMF, THF or DCM are all not suitable for the reaction (entries 6–9). Replacing the sacrificial agent DIPEA with Et$_3$N also significantly reduced the yield to 13% (entry 10). When reducing the equivalents of DABSO or DIPEA, the yield of **2a** also decreased accordingly (entries 11 and 12). In contrast, Selectfluor™ gave a reduced reaction yield of 18% compared to NFSI (entry 13). Also, more equivalents of NFSI did not result in a better yield for this reaction (entry 14). Finally, control experiments showed that photocatalyst, light source and inert gas protection were necessary (entries 15–17).

Having established the optimized reaction conditions, we turned our attention to investigate the reaction scope. A variety of primary, secondary and tertiary carboxylic acid-derived NHPI esters were examined, and the results are shown in Table 2. In the case of primary carboxylic acids, we could observe good compatibility toward phenyl (**2b**, 86%), 4-methoxybenzene (**2c**, 79%), thienyl (**2d**, 78%), chloride (**2e**, 73%), C–C
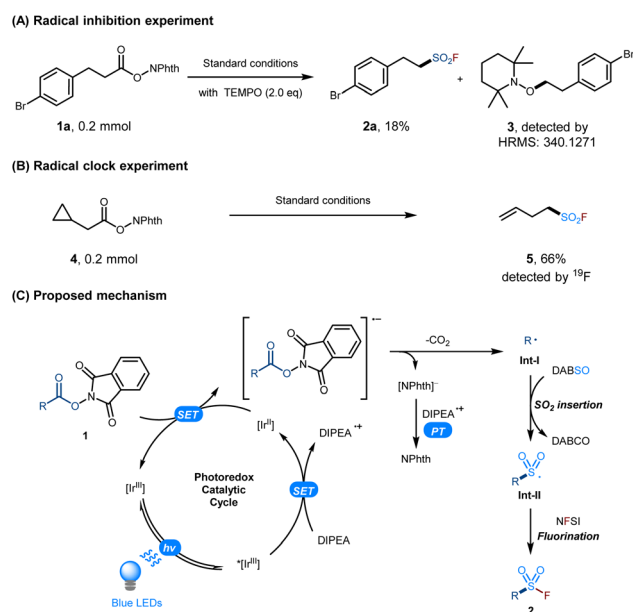
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Table 2 Substrate scope[a]

(A) Primary aliphatic carboxylic acid NHPI ester

2a, 85%   **2b**, 86%   **2c**, 79%   **2d**, 78%

2e, 73%   **2f**, 70%   **2g**, 71%

(B) Secondary aliphatic carboxylic acid NHPI ester

2h, 85%   **2i**, 90%   **2j**, 92%   **2k**, 88%

(C) Tertiary aliphatic carboxylic acid NHPI ester

2l, 78%   **2m**, 81%   **2n**, 93%   **2o**, 67%

(D) Late-stage modification of natural products and drugs

2p, 77%
from Myristic acid

2q, 83%
from Palmitic acid

2r, 80%
from stearic acid

2s, 81%
from Oleic acid

2t, 79%
from Oxaprozin

2u, 86%
from Flubiprofen

2v, 84%
from Abietic acid

[a] Standard conditions: at the 0.2 mmol scale, isolated yields.

In order to gain a better understanding of the reaction mechanism, 2,2,6,6-tetramethylpiperidinooxy (TEMPO) was added to the reactions under the standard conditions. It was found that the yield of the expected product **2a** was dramatically reduced and the TEMPO-trapped product **3** was detected by HRMS analysis (Scheme 2A). In addition, we obtained the corresponding ring-opened fluorosulfonylation product **5**[19i] in 66% [19]F yield when cyclopropionate was used as the radical probe under the standard conditions (Scheme 2B). The above results showed that the reaction proceeds through an alkyl radical mechanism. According to the above studies and previous work,[21] a plausible mechanism for this visible light-mediated decarboxylative radical fluorosulfonylation via SO₂ insertion/fluorination is proposed, as shown in Scheme 2C.

Initially, the single electron transfer (SET) between the excited photocatalyst Ir[dF(CF₃)ppy]₂(dtbbpy)PF₆ (P.C., [Ir]) and DIPEA produces DIPEA•+ and the reductive [Ir^II] species. Subsequently, the reduction of NHPI esters **1** by the resulting [Ir^II] species leads to the formation of the alkyl radical **Int-I** and the regeneration of the photocatalyst [Ir^III]. The insertion of SO₂ into the alkyl radical **Int-I** then gives rise to the sulfonyl radical **Int-II**, which is captured by NFSI through fluorine atom transfer[17e,f] to afford the final fluorosulfonylation product **2**.

To demonstrate the synthetic value of our products, we carried out the derivatization of the obtained product **2b** (Scheme 3). We investigated the multifunctional synthesis of various sulfonyl-containing derivatives based on the fluorosulfonyl group. For example, sulfonyl azide **6** was obtained through SuFEx click reactions with trimethylsilyl azide (TMSN₃). On the other hand, sulfonate ester **7** was achieved through the reaction of **2b** with naphthol. Moreover, the sulfonate derivatives of estrone **8** can also be obtained in 77% yield by the SuFEx click reaction.

triple bond (**2f**, 70%) and benzyl (**2g**, 71%). Secondary acids could also be efficiently converted into the corresponding alkylsulfonyl fluorides in high yields (**2h–2l**, 78%–92%), including norbornylane (**2i**, 90%), cyclohexene (**2j**, 92%), cycloheptane (**2k**, 88%) and α-methylbenzyl (**2l**, 78%) substrates. Delightfully, compared with the existing synthetic methods of tertiary alkylsulfonyl fluorides which suffer from synthetic difficulties or moderate yields,[17f,19i] the most prominent feature of this novel method is that it allows for direct fluorosulfonylation of tertiary aliphatic carboxylic acid NHPI ester to access tertiary alkylsulfonyl fluorides in high yields, including adamantane (**2n**, 93%). Remarkably, due to mild conditions and excellent compatibility, this method can also be used in the late-stage modification of natural products or drugs to obtain the corresponding fluorosulfonylation products in good to high yields, including **2q** (83%, from palmitic acid), **2t** (79%, from oxaprozin), **2u** (86%, from flubiprofen) and **2v** (84%, from abietic acid). As shown in Table 2, primary, secondary and tertiary alkyl carboxylic acid-derived NHPI esters can all be well accommodated under the reaction conditions, providing rapid access to alkyl boronic esters with considerable structural diversity.

Scheme 2 Mechanistic study and proposed mechanism.

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Scheme 3 Derivatization reactions of 2-phenylethane-1-sulfonyl fluoride (**2b**).

Conclusions

In conclusion, by combining photoredox catalysis and SO_2 radical insertion, a visible light-mediated decarboxylative radical fluorosulfonylation *via* SO_2 insertion/fluorination of aliphatic carboxylic acid NHPI esters has been successfully developed for the first time. This method is applicable to a variety of alkyl carboxylic acids, including primary, secondary, and tertiary ones, as well as several natural products and drugs, allowing for facile access to various alkylsulfonyl fluorides, which are important compounds in multiple fields of chemistry, biology and materials science. Moreover, the value of the products has been demonstrated once again with a direct transformation of sulfonyl fluorides to sulfonyl azides and sulfonate esters. We anticipate that this radical photocatalytic decarboxylative fluorosulfonylation will provide a useful and complementary new approach for the synthesis of sulfonyl fluorides.

Author contributions

X. Nie conceived this study, developed the reactions, performed the reaction optimization and completed this manuscript; H. Zhang and S. Li completed the scope investigation, mechanistic study and product diversification; and H. Zheng, G. Zhu and S. Liao helped complete this manuscript with feedback from X. Nie. In addition, S. Liao provided financial and experimental material support. We thank the members of the NMR and HRMS departments for their excellent service.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

1 (*a*) W. Steinkopf, Über Aromatische Sulfofluoride, *J. Prakt. Chem.*, 1927, **117**, 1–82; (*b*) W. Steinkopf and P. Jaeger, Über Aromatische Sulfofluoride. II. Mitteilung, *J. Prakt. Chem.*, 1930, **128**, 63–88.

2 J. Dong, L. Krasnova, M. G. Finn and K. B. Sharpless, Sulfur(VI) Fluoride Exchange (SuFEx): Another Good Reaction for Click Chemistry, *Angew. Chem., Int. Ed.*, 2014, **53**, 9430–9448.

3 For selected reviews, see: (*a*) P. K. Chinthakindi and P. I. Arvidsson, Sulfonyl Fluorides (SFs): More Than Click Reagents?, *Eur. J. Org. Chem.*, 2018, 3648–3666; (*b*) A. S. Barrow, C. J. Smedley, Q. Zheng, S. Li, J. Dong and J. E. Moses, The Growing Applications of SuFEx Click Chemistry, *Chem. Soc. Rev.*, 2019, **48**, 4731–4758; (*c*) L. Xu and J. Dong, Click Chemistry: Evolving on the Fringe, *Chin. J. Chem.*, 2020, **38**, 414–419; (*d*) C. Lee, A. J. Cook, J. E. Elisabeth, N. C. Friede, G. M. Sammis and N. D. Ball, The Emerging Applications of Sulfur(VI) Fluorides in Catalysis, *ACS Catal.*, 2021, **11**, 6578–6589; (*e*) T. Zhong, Z. Chen, J. Yi, G. Lu and J. Weng, Recent Progress in the Synthesis of Sulfonyl Fluorides for SuFEx Click Chemistry, *Chin. Chem. Lett.*, 2021, **32**, 2736–2750.

4 For selected reviews, see: (*a*) A. Narayanan and L. H. Jones, Sulfonyl Fluorides as Privileged Warheads in Chemical Biology, *Chem. Sci.*, 2015, **6**, 2650–2659; (*b*) L. H. Jones, Emerging Utility of Fluorosulfate Chemical Probes, *ACS Med. Chem. Lett.*, 2018, **9**, 584–586; (*c*) P. Martin-Gago and C. A. Olsen, Arylfluorosulfate-Based Electrophiles for Covalent Protein Labeling: A New Addition to the Arsenal, *Angew. Chem., Int. Ed.*, 2019, **58**, 957–966; (*d*) S. E. Dalton and S. Campos, Covalent Small Molecules as Enabling Platforms for Drug Discovery, *ChemBioChem*, 2020, **21**, 1080–1100; (*e*) L. H. Jones and J. W. Kelly, Structure-Based Design and Analysis of SuFEx Chemical Probes, *RSC Med. Chem.*, 2020, **11**, 10–17.

5 (*a*) R. Artschwager, D. J. Ward, S. Gannon, A. J. Brouwer, H. van de Langemheen, H. Kowalski and R. M. J. Liskamp, Potent and Highly Selective Inhibitors of the Proteasome Trypsin-Like Site by Incorporation of Basic Side Chain Containing Amino Acid Derived Sulfonyl Fluorides, *J. Med. Chem.*, 2018, **61**, 5395–5411; (*b*) Z. Liu, J. Li, S. Li, G. Li, K. B. Sharpless and P. Wu, SufEx Click Chemistry Enabled Late-Stage Drug Functionalization, *J. Am. Chem. Soc.*, 2018, **140**, 2919–2925; (*c*) X. Yang, T. J. M. Michiels, C. de Jong, M. Soethoudt, N. Dekker, E. Gordon, M. van der Stelt, L. H. Heitman, D. van der Es and I. J. AP, An Affinity-Based Probe for the Human Adenosine A_{2A} Receptor, *J. Med. Chem.*, 2018, **61**, 7892–7901; (*d*) C. Baggio, P. Udompholkul, L. Gambini, A. F. Salem, J. Jossart, J. J. P. Perry and M. Pellecchia, Aryl-Fluorosulfate-Based Lysine Covalent Pan-Inhibitors of Apoptosis Protein (Iap) Antagonists with Cellular Efficacy, *J. Med. Chem.*, 2019, **62**, 9188–9200; (*e*) H. Xu, F. Ma, N. Wang, W. Hou, H. Xiong, F. Lu, J. Li, S. Wang, P. Ma, G. Yang and R. A. Lerner,

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Org. Chem. Front., 2022, **9**, 4854–4860 | **4857**

DNA-Encoded Libraries: Aryl Fluorosulfonates as Versatile Electrophiles Enabling Facile on-DNA Suzuki, Sonogashira, and Buchwald Reactions, *Adv. Sci.*, 2019, **6**, 1901551; (*f*) S. Kitamura, Q. Zheng, J. L. Woehl, A. Solania, E. Chen, N. Dillon, M. V. Hull, M. Kotaniguchi, J. R. Cappiello, S. Kitamura, V. Nizet, K. B. Sharpless and D. W. Wolan, Sulfur(VI) Fluoride Exchange (SuFEx)-Enabled High-Throughput Medicinal Chemistry, *J. Am. Chem. Soc.*, 2020, **142**, 10899–10904; (*g*) Q. Li, Q. Chen, P. C. Klauser, M. Li, F. Zheng, N. Wang, X. Li, Q. Zhang, X. Fu, Q. Wang, Y. Xu and L. Wang, Developing Covalent Protein Drugs via Proximity-Enabled Reactive Therapeutics, *Cell*, 2020, **182**, 85–97; (*h*) C. Liu, Q. Zhou, Y. Li, L. V. Garner, S. P. Watkins, L. J. Carter, J. Smoot, A. C. Gregg, A. D. Daniels, S. Jervey and D. Albaiu, Research and Development on Therapeutic Agents and Vaccines for COVID-19 and Related Human Coronavirus Diseases, *ACS Cent. Sci.*, 2020, **6**, 315–331; (*i*) M. Teng, S. B. Ficarro, H. Yoon, J. Che, J. Zhou, E. S. Fischer, J. A. Marto, T. Zhang and N. S. Gray, Rationally Designed Covalent BCL6 Inhibitor That Targets a Tyrosine Residue in the Homodimer Interface, *ACS Med. Chem. Lett.*, 2020, **11**, 1269–1273.

6 (*a*) J. Dong, K. B. Sharpless, L. Kwisnek, J. S. Oakdale and V. V. Fokin, SuFEx-Based Synthesis of Polysulfates, *Angew. Chem., Int. Ed.*, 2014, **53**, 9466–9470; (*b*) B. Gao, L. Zhang, Q. Zheng, F. Zhou, L. M. Klivansky, J. Lu, Y. Liu, J. Dong, P. Wu and K. B. Sharpless, Bifluoride-Catalysed Sulfur(VI) Fluoride Exchange Reaction for the Synthesis of Polysulfates and Polysulfonates, *Nat. Chem.*, 2017, **9**, 1083–1088; (*c*) K. Durie, J. Yatvin, M. Kovaliov, G. H. Crane, J. Horn, S. Averick and J. Locklin, SuFEx Postpolymerization Modification Kinetics and Reactivity in Polymer Brushes, *Macromolecules*, 2018, **51**, 297–305; (*d*) T. Hmissa, X. Zhang, N. R. Dhumal, G. J. McManus, X. Zhou, H. B. Nulwala and A. Mirjafari, Autocatalytic Synthesis of Bifluoride Ionic Liquids by SuFEx Click Chemistry, *Angew. Chem., Int. Ed.*, 2018, **57**, 16005–16009; (*e*) C. Yang, J. P. Flynn and J. Niu, Facile Synthesis of Sequence-Regulated Synthetic Polymers Using Orthogonal SuFEx and CuAAc Click Reactions, *Angew. Chem., Int. Ed.*, 2018, **57**, 16194–16199; (*f*) Z. Cao, F. Zhou, P.-Y. Gu, D. Chen, J. He, J. R. Cappiello, P. Wu, Q. Xu and J. Lu, Preparation of Aryl Polysulfonates via a Highly Efficient SuFEx Click Reaction, Their Controllable Degradation and Functionalized Behavior, *Polym. Chem.*, 2020, **11**, 3120–3124; (*g*) H. Wan, S. Zhou, P. Gu, F. Zhou, D. Lyu, Q. Xu, A. Wang, H. Shi, Q. Xu and J. Lu, Aie-Active Polysulfates via a Sulfur(VI) Fluoride Exchange (SuFEx) Click Reaction and Investigation of Their Two-photon Fluorescence and Cyanide Detection in Water and in Living Cells, *Polym. Chem.*, 2020, **11**, 1033–1042.

7 (*a*) G. F. Zha, W. Y. Fang, Y. G. Li, J. Leng, X. Chen and H. L. Qin, SO$_2$F$_2$ Mediated Oxidative Dehydrogenation and Dehydration of Alcohols to Alkynes, *J. Am. Chem. Soc.*, 2018, **140**, 17666–17673; (*b*) P. J. Foth, F. Gu, T. G. Bolduc, S. S. Kanani and G. M. Sammis, New Sulfuryl Fluoride-

Derived Alkylating Reagents for the 1,1-Dihydrofluoroalkylation of Thiols, *Chem. Sci.*, 2019, **10**, 10331–10335; (*c*) G. Meng, T. Guo, T. Ma, J. Zhang, Y. Shen, K. B. Sharpless and J. Dong, Modular Click Chemistry Libraries for Functional Screens Using a Diazotizing Reagent, *Nature*, 2019, **574**, 86–89; (*d*) C. J. Smedley, Q. Zheng, B. Gao, S. Li, A. Molino, H. M. Duivenvoorden, B. S. Parker, D. J. D. Wilson, K. B. Sharpless and J. E. Moses, Bifluoride Ion Mediated SuFEx Trifluoromethylation of Sulfonyl Fluorides and Iminosulfur Oxydifluorides, *Angew. Chem., Int. Ed.*, 2019, **58**, 4552–4556; (*e*) M. C. Giel, C. J. Smedley, E. R. R. Mackie, T. Guo, J. Dong, T. P. Soares da Costa and J. E. Moses, Metal-Free Synthesis of Functional 1-Substituted-1,2,3-Triazoles from Ethenesulfonyl Fluoride and Organic Azides, *Angew. Chem., Int. Ed.*, 2020, **59**, 1181–1186; (*f*) D. D. Liang, D. E. Streefkerk, D. Jordaan, J. Wagemakers, J. Baggerman and H. Zuilhof, Silicon-Free SuFEx Reactions of Sulfonimidoyl Fluorides: Scope, Enantioselectivity, and Mechanism, *Angew. Chem., Int. Ed.*, 2020, **59**, 7494–7500; (*g*) S. Mahapatra, C. P. Woroch, T. W. Butler, S. N. Carneiro, S. C. Kwan, S. R. Khasnavis, J. Gu, J. K. Dutra, B. C. Vetelino, J. Bellenger, C. W. Am Ende and N. D. Ball, SuFEx Activation with Ca(NTf$_2$)$_2$: A Unified Strategy to Access Sulfamides, Sulfamates, and Sulfonamides from S(VI) Fluorides, *Org. Lett.*, 2020, **22**, 4389–4394; (*h*) M. Mendel, I. Kalvet, D. Hupperich, G. Magnin and F. Schoenebeck, Site-Selective, Modular Diversification of Polyhalogenated Aryl Fluorosulfates (ArOSO$_2$F) Enabled by an Air-Stable Pd(I) Dimer, *Angew. Chem., Int. Ed.*, 2020, **59**, 2115–2119.

8 T. S.-B. Lou and M. C. Willis, Sulfonyl Fluorides as Targets and Substrates in the Development of New Synthetic Methods, *Nat. Rev. Chem.*, 2022, **6**, 146–162.

9 (*a*) T. A. Bianchi and L. A. Cate, Phase Transfer Catalysis. Preparation of Aliphatic and Aromatic Sulfonyl Fluorides, *J. Org. Chem.*, 1977, **42**, 2031–2032; (*b*) J. J. Krutak, R. D. Burpitt, W. H. Moore and J. A. Hyatt, Chemistry of Ethenesulfonyl Fluoride. Fluorosulfonylethylation of Organic Compounds, *J. Org. Chem.*, 1979, **44**, 3847–3858.

10 (*a*) A. Shavnya, S. B. Coffey, K. D. Hesp, S. C. Ross and A. S. Tsai, Reaction of Alkyl Halides with Rongalite: One-Pot and Telescoped Syntheses of Aliphatic Sulfonamides, Sulfonyl Fluorides, and Unsymmetrical Sulfones, *Org. Lett.*, 2016, **18**, 5848–5851; (*b*) L. Tang, Y. Yang, L. Wen, X. Yang and Z. Wang, Catalyst-Free Radical Fluorination of Sulfonyl Hydrazides in Water, *Green Chem.*, 2016, **18**, 1224–1228; (*c*) G. Laudadio, A. A. Bartolomeu, L. Verwijlen, Y. Cao, K. T. de Oliveira and T. Noel, Sulfonyl Fluoride Synthesis through Electrochemical Oxidative Coupling of Thiols and Potassium Fluoride, *J. Am. Chem. Soc.*, 2019, **141**, 11832–11836; (*d*) P. K. T. Lo, Y. Chen and M. C. Willis, Nickel(II)-Catalyzed Synthesis of Sulfinates from Aryl and Heteroaryl Boronic Acids and the Sulfur Dioxide Surrogate Dabso, *ACS Catal.*, 2019, **9**, 10668–10673; (*e*) L. Wang and J. Cornella, A Unified Strategy for Arylsulfur(VI) Fluorides from Aryl

4858 | *Org. Chem. Front.*, 2022, **9**, 4854–4860

This journal is © the Partner Organisations 2022

Halides: Access to Ar-SOF$_3$ Compounds, *Angew. Chem., Int. Ed.*, 2020, **59**, 23510–23515.

11 (*a*) P. K. Chinthakindi, H. G. Kruger, T. Govender, T. Naicker and P. I. Arvidsson, On-Water Synthesis of Biaryl Sulfonyl Fluorides, *J. Org. Chem.*, 2016, **81**, 2618–2623; (*b*) J. Leng and H. L. Qin, 1-Bromoethene-1-Sulfonyl Fluoride (1-Br-ESF), a New Sufex Clickable Reagent, and Its Application for Regioselective Construction of 5-Sulfonylfluoro Isoxazoles, *Chem. Commun.*, 2018, **54**, 4477–4480; (*c*) C. J. Smedley, M. C. Giel, A. Molino, A. S. Barrow, D. J. D. Wilson and J. E. Moses, 1-Bromoethene-1-Sulfonyl Fluoride (BESF) Is Another Good Connective Hub for Sufex Click Chemistry, *Chem. Commun.*, 2018, **54**, 6020–6023; (*d*) J. Thomas and V. V. Fokin, Regioselective Synthesis of Fluorosulfonyl 1,2,3-Triazoles from Bromovinylsulfonyl Fluoride, *Org. Lett.*, 2018, **20**, 3749–3752; (*e*) Y.-P. Meng, S.-M. Wang, W.-Y. Fang, Z.-Z. Xie, J. Leng, H. Alsulami and H.-L. Qin, Ethenesulfonyl Fluoride (ESF) and Its Derivatives in Sufex Click Chemistry and More, *Synthesis*, 2019, **52**, 673–687; (*f*) X. Zhang, B. Moku, J. Leng, K. P. Rakesh and H.-L. Qin, 2-Azidoethane-1-Sulfonylfluoride (ASF): A Versatile Bis-Clickable Reagent for SuFEx and CuAAC Click Reactions, *Eur. J. Org. Chem.*, 2019, 1763–1769; (*g*) C. J. Smedley, G. Li, A. S. Barrow, T. L. Gialelis, M. C. Giel, A. Ottonello, Y. Cheng, S. Kitamura, D. W. Wolan, K. B. Sharpless and J. E. Moses, Diversity Oriented Clicking (DOC): Divergent Synthesis of Sufexable Pharmacophores from 2-Substituted-Alkynyl-1-Sulfonyl Fluoride (SASF) Hubs, *Angew. Chem., Int. Ed.*, 2020, **59**, 12460–12469.

12 (*a*) G. P. Roth and C. Sapino, Palladium in Cephalosporin Chemistry: An Inexpensive Triflate Replacement for Palladium Acetate Mediated Coupling Reactions, *Tetrahedron Lett.*, 1991, **32**, 4073–4076; (*b*) T. Guo, G. Meng, X. Zhan, Q. Yang, T. Ma, L. Xu, K. B. Sharpless and J. Dong, A New Portal to Sufex Click Chemistry: A Stable Fluorosulfuryl Imidazolium Salt Emerging as an "F-SO$_2$+" Donor of Unprecedented Reactivity, Selectivity, and Scope, *Angew. Chem., Int. Ed.*, 2018, **57**, 2605–2610; (*c*) H. Zhou, P. Mukherjee, R. Liu, E. Evrard, D. Wang, J. M. Humphrey, T. W. Butler, L. R. Hoth, J. B. Sperry, S. K. Sakata, C. J. Helal and C. W. Am Ende, Introduction of a Crystalline, Shelf-Stable Reagent for the Synthesis of Sulfur(VI) Fluorides, *Org. Lett.*, 2018, **20**, 812–815; (*d*) R. Lekkala, R. Lekkala, B. Moku, K. P. Rakesh and H.-L. Qin, Applications of Sulfuryl Fluoride (SO$_2$F$_2$) in Chemical Transformations, *Org. Chem. Front.*, 2019, **6**, 3490–3516; (*e*) X. Nie, T. Xu, Y. Hong, H. Zhang, C. Mao and S. Liao, Introducing a New Class of Sulfonyl Fluoride Hubs via Radical Chloro-Fluorosulfonylation of Alkynes, *Angew. Chem., Int. Ed.*, 2021, **60**, 22035–22042; (*f*) X. Nie, T. Xu, J. Song, A. Devaraj, B. Zhang, Y. Chen and S. Liao, Radical Fluorosulfonylation: Accessing Alkenyl Sulfonyl Fluorides from Alkenes, *Angew. Chem., Int. Ed.*, 2021, **60**, 3956–3960; (*g*) N. L. Frye, C. G. Daniliuc and A. Studer, Radical 1-Fluorosulfonyl-2-Alkynylation of Unactivated Alkenes, *Angew. Chem., Int. Ed.*, 2022, **61**, e202115593.

13 P. S. Santos and M. T. S. Mello, The Raman Spectra of Some Molecular Complexes of 1-Azabicyclo[2.2.2]Octane and 1,4-Diazabicyclo[2.2.2]Octane, *J. Mol. Struct.*, 1988, **178**, 121–133.

14 B. Nguyen, E. J. Emmett and M. C. Willis, Palladium-Catalyzed Aminosulfonylation of Aryl Halides, *J. Am. Chem. Soc.*, 2010, **132**, 16372–16373.

15 For selected reviews on DABSO, see: (*a*) E. J. Emmett and M. C. Willis, The Development and Application of Sulfur Dioxide Surrogates in Synthetic Organic Chemistry, *Asian J. Org. Chem.*, 2015, **4**, 602–611; (*b*) Y. Q. Li and Y. H. Fan, Recent Advances in C-S Bond Construction to Synthesize Sulfone, *Synth. Commun.*, 2019, **49**, 3227–3264; (*c*) S. Liang, K. Hofman, M. Friedrich and G. Manolikakes, Recent Advances in the Synthesis and Direct Application of Sulfinate Salts, *Eur. J. Org. Chem.*, 2020, 4664–4676; (*d*) D. Zeng, M. Wang, W.-P. Deng and X. Jiang, The Same Oxygenation-State Introduction of Hypervalent Sulfur under Transition-Metal-Free Conditions, *Org. Chem. Front.*, 2020, **7**, 3956–3966; (*e*) J. A. Andrews and M. C. Willis, DABSO – a Reagent to Revolutionize Organosulfur Chemistry, *Synthesis*, 2022, **54**, 1695–1707; (*f*) M. Seyed Hashtroudi, V. Fathi Vavsari and S. Balalaie, DABSO as a SO$_2$ Gas Surrogate in the Synthesis of Organic Structures, *Org. Biomol. Chem.*, 2022, **20**, 2149–2163.

16 (*a*) A. T. Davies, J. M. Curto, S. W. Bagley and M. C. Willis, One-Pot Palladium-Catalyzed Synthesis of Sulfonyl Fluorides from Aryl Bromides, *Chem. Sci.*, 2017, **8**, 1233–1237; (*b*) A. L. Tribby, I. Rodriguez, S. Shariffudin and N. D. Ball, Pd-Catalyzed Conversion of Aryl Iodides to Sulfonyl Fluorides Using SO$_2$ Surrogate DABSO and Selectfluor, *J. Org. Chem.*, 2017, **82**, 2294–2299; (*c*) T. S. Lou, S. W. Bagley and M. C. Willis, Cyclic Alkenylsulfonyl Fluorides: Palladium-Catalyzed Synthesis and Functionalization of Compact Multifunctional Reagents, *Angew. Chem., Int. Ed.*, 2019, **58**, 18859–18863; (*d*) Y. Liu, D. Yu, Y. Guo, J. C. Xiao, Q. Y. Chen and C. Liu, Arenesulfonyl Fluoride Synthesis via Copper-Catalyzed Fluorosulfonylation of Arenediazonium Salts, *Org. Lett.*, 2020, **22**, 2281–2286; (*e*) D. Louvel, A. Chelagha, J. Rouillon, P. A. Payard, L. Khrouz, C. Monnereau and A. Tlili, Metal-Free Visible-Light Synthesis of Arylsulfonyl Fluorides: Scope and Mechanism, *Chem. – Eur. J.*, 2021, **27**, 8704–8708.

17 (*a*) Y. Liu, H. Wu, Y. Guo, J. C. Xiao, Q. Y. Chen and C. Liu, Trifluoromethylfluorosulfonylation of Unactivated Alkenes Using Readily Available Ag(O$_2$CCF$_2$SO$_2$F) and N-Fluorobenzenesulfonimide, *Angew. Chem., Int. Ed.*, 2017, **56**, 15432–15435; (*b*) Q. Lin, Y. Liu, Z. Xiao, L. Zheng, X. Zhou, Y. Guo, Q.-Y. Chen, C. Zheng and C. Liu, Intermolecular Oxidative Radical Fluoroalkylfluorosulfonylation of Unactivated Alkenes with (Fluoroalkyl)Trimethylsilane, Silver Fluoride, Sulfur Dioxide and N-fluorobenzenesulfonimide, *Org. Chem. Front.*, 2019, **6**, 447–450; (*c*) Y. Liu, Q. Lin, Z. Xiao, C. Zheng, Y. Guo, Q. Y. Chen and C. Liu, Zinc-Mediated

This journal is © the Partner Organisations 2022

Org. Chem. Front., 2022, **9**, 4854–4860 | **4859**

Intermolecular Reductive Radical Fluoroalkylsulfination of Unsaturated Carbon-Carbon Bonds with Fluoroalkyl Bromides and Sulfur Dioxide, *Chem. – Eur. J.*, 2019, **25**, 1824–1828; (*d*) P. J. Sarver, N. B. Bissonnette and D. W. C. MacMillan, Decatungstate-Catalyzed C(sp³)-H Sulfinylation: Rapid Access to Diverse Organosulfur Functionality, *J. Am. Chem. Soc.*, 2021, **143**, 9737–9743; (*e*) T. Zhong, J. T. Yi, Z. D. Chen, Q. C. Zhuang, Y. Z. Li, G. Lu and J. Weng, Photoredox-Catalyzed Aminofluorosulfonylation of Unactivated Olefins, *Chem. Sci.*, 2021, **12**, 9359–9365; (*f*) Z. D. Chen, X. Zhou, J. T. Yi, H. J. Diao, Q. L. Chen, G. Lu and J. Weng, Catalytic Decarboxylative Fluorosulfonylation Enabled by Energy-Transfer-Mediated Photocatalysis, *Org. Lett.*, 2022, **24**, 2474–2478.

18 J. A. Andrews, L. R. E. Pantaine, C. F. Palmer, D. L. Poole and M. C. Willis, Sulfinates from Amines: A Radical Approach to Alkyl Sulfonyl Derivatives via Donor-Acceptor Activation of Pyridinium Salts, *Org. Lett.*, 2021, **23**, 8488–8493.

19 (*a*) G. Qiu, L. Lai, J. Cheng and J. Wu, Recent Advances in the Sulfonylation of Alkenes with the Insertion of Sulfur Dioxide via Radical Reactions, *Chem. Commun.*, 2018, **54**, 10405–10414; (*b*) G. Qiu, K. Zhou, L. Gao and J. Wu, Insertion of Sulfur Dioxide via a Radical Process: An Efficient Route to Sulfonyl Compounds, *Org. Chem. Front.*, 2018, **5**, 691–705; (*c*) G. Qiu, K. Zhou and J. Wu, Recent Advances in the Sulfonylation of C-H Bonds with the Insertion of Sulfur Dioxide, *Chem. Commun.*, 2018, **54**, 12561–12569; (*d*) S. Ye, G. Qiu and J. Wu, Inorganic Sulfites as the Sulfur Dioxide Surrogates in Sulfonylation Reactions, *Chem. Commun.*, 2019, **55**, 1013–1019; (*e*) S. Ye, M. Yang and J. Wu, Recent Advances in Sulfonylation Reactions Using Potassium/Sodium Metabisulfite, *Chem. Commun.*, 2020, **56**, 4145–4155; (*f*) Q. Lin, Z. Ma, C. Zheng, X. J. Hu, Y. Guo, Q. Y. Chen and C. Liu, Arenesulfonyl Fluoride Synthesis via Copper–Free Sandmeyer–Type Fluorosulfonylation of Arenediazonium Salts, *Chin. J. Chem.*, 2020, **38**, 1107–1110; (*g*) S. Liu, Y. Huang, X.-H. Xu and F.-L. Qing, Fluorosulfonylation of Arenediazonium Tetrafluoroborates with Na₂S₂O₅ and *N*-fluorobenzenesulfonimide, *J. Fluor. Chem.*, 2020, **240**, 109653; (*h*) T. Zhong, M. K. Pang, Z. D. Chen, B. Zhang,

J. Weng and G. Lu, Copper-Free Sandmeyer-Type Reaction for the Synthesis of Sulfonyl Fluorides, *Org. Lett.*, 2020, **22**, 3072–3078; (*i*) Z. Ma, Y. Liu, X. Ma, X. Hu, Y. Guo, Q.-Y. Chen and C. Liu, Aliphatic Sulfonyl Fluoride Synthesis via Reductive Decarboxylative Fluorosulfonylation of Aliphatic Carboxylic Acid NHPI Esters, *Org. Chem. Front.*, 2022, **9**, 1115–1120.

20 For selected reviews and articles on NHPI esters, see: (*a*) J. Xuan, Z. G. Zhang and W. J. Xiao, Visible-Light-Induced Decarboxylative Functionalization of Carboxylic Acids and Their Derivatives, *Angew. Chem., Int. Ed.*, 2015, **54**, 15632–15641; (*b*) Y. Jin and H. Fu, Visible–Light Photoredox Decarboxylative Couplings, *Asian J. Org. Chem.*, 2017, **6**, 368–385; (*c*) S. Murarka, *N*-(Acyloxy)Phthalimides as Redox-Active Esters in Cross-Coupling Reactions, *Adv. Synth. Catal.*, 2018, **360**, 1735–1753; (*d*) J. Schwarz and B. König, Decarboxylative Reactions with and without Light – a Comparison, *Green Chem.*, 2018, **20**, 323–361; (*e*) J. He, G. Chen, B. Zhang, Y. Li, J.-R. Chen, W.-J. Xiao, F. Liu and C. Li, Catalytic Decarboxylative Radical Sulfonylation, *Chem*, 2020, **6**, 1149–1159; (*f*) S. Karmakar, A. Silamkoti, N. A. Meanwell, A. Mathur and A. K. Gupta, Utilization of C(sp³)–Carboxylic Acids and Their Redox–Active Esters in Decarboxylative Carbon–Carbon Bond Formation, *Adv. Synth. Catal.*, 2021, **363**, 3693–3736; (*g*) S. K. Parida, S. K. Hota, R. Kumar and S. Murarka, Late-Stage Alkylation of Heterocycles Using *N*-(Acyloxy)Phthalimides, *Chem. – Asian J.*, 2021, **16**, 879–889; (*h*) S. K. Parida, T. Mandal, S. Das, S. K. Hota, S. De Sarkar and S. Murarka, Single Electron Transfer-Induced Redox Processes Involving N-(Acyloxy)Phthalimides, *ACS Catal.*, 2021, **11**, 1640–1683.

21 (*a*) R. Xu, T. Xu, M. Yang, T. Cao and S. Liao, A Rapid Access to Aliphatic Sulfonyl Fluorides, *Nat. Commun.*, 2019, **10**, 3752–3758; (*b*) T. Cao, T. Xu, R. Xu, X. Shu and S. Liao, Decarboxylative Thiolation of Redox-Active Esters to Free Thiols and Further Diversification, *Nat. Commun.*, 2020, **11**, 5340–5347; (*c*) X. Shu, R. Xu, Q. Ma and S. Liao, Accessing Alkyl Boronic Esters via Visible Light-Mediated Decarboxylative Addition Reactions of Redox-Active Esters, *Org. Chem. Front.*, 2020, **7**, 2003–2007; (*d*) X. Shu, R. Xu and S. Liao, Photocatalytic Divergent Decarboxylative Amination: A Metal-Free Access to Aliphatic Amines and Hydrazines, *Sci. China: Chem.*, 2021, **64**, 1756–1762.