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Synthesis of Aza-S(VI) Fluorides and Primary Sulfonimidamides from Sulfinylamines

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Abstract: Aza-S(VI) fluorides are crucial compounds in the synthesis of various S(VI) derivatives, which find broad applications in drug discovery. However, the synthesis of sulfonimidoyl and sulfondiimidoyl fluorides have been relatively underexplored, often requiring lengthy reaction sequences and/or the use of hazardous gaseous reagents. In this study, we present a rapid one-pot method for producing sulfonimidoyl fluorides from sulfinylamines via a nucleophilic addition/electrophilic fluorination sequence. Similarly, sulfondiimidoyl fluorides can be synthesized using the same sequence, preceded by the formation of unsymmetrical sulfurdiimides readily generated in situ from sulfinylamines. Whereas isolation of sulfondiimidoyl fluorides was not feasible, they could be efficiently converted into primary sulfonimidamides by base hydrolysis in a one-pot process. Furthermore, we explored the reactivity of aza-S(VI) fluorides with various nucleophiles, demonstrating a versatile synthetic platform for the synthesis of aza-S(VI) compounds.

Keywords: Sulfonimidoyl fluorides; Sulfondiimidoyl fluorides; Sulfonimidamides; Sulfinylamines; SuFEx

Introduction

Organosulfur motifs serve as pivotal building blocks in the development of innovative drugs and agrochemicals.[1] Whereas sulfonamides and sulfones are well-established in medicinal chemistry, their aza-analogues have recently emerged as promising alternatives.[2] Notably, substituting the oxygen atom with an NH group can significantly modify physicochemical properties, as demonstrated by recent advancements in sulfoximines and sulfonimidamides.[3] Additionally, introducing a nitrogen atom facilitates linking additional groups, thereby enabling further exploration of structural modifications and access to new chemical space.[4] Thus, the pursuit of novel synthetic methods for accessing aza-S(VI) motifs remains imperative.[5]

In synthetic contexts, various S(VI) fluorides have proven valuable as precursors for diverse S(VI) motifs, involving the formation of S–O, S–C, and S–N bonds.[6] Since the introduction of SuFEx (sulfur-fluoride exchange) chemistry by Sharpless and colleagues in 2014, it has become a strategic tool for synthesizing sulfur-containing compounds, finding numerous applications in medicinal chemistry.[7] Whereas the chemistry of sulfonyl fluorides, sulfamoyl fluorides, and organosulfates is well-documented, information regarding the preparation and derivatization of sulfonimidoyl and sulfondiimidoyl fluorides is relatively scarce. Moreover, most methods for obtaining sulfonimidoyl fluorides involve multistep synthetic routes starting from preformed sulfinamides or hazardous gaseous reagents.[6a] For example, sulfonimidoyl fluorides can be prepared via fluorine-chlorine exchange on unstable sulfonimidoyl chlorides, which are generated *in situ* using strong oxidants such as chlorine or *tert*-butyl hypochlorite.[8] In this context, Liu and colleagues recently detailed the synthesis of *N*-trityl sulfonimidoyl fluorides via copper-catalyzed reactions involving arendiazonium compounds and *N*-trityl sulfinylamine, with sulfonimidoyl chlorides serving as intermediates (Figure 1, A).[9] Alternatively, Sharpless and co-workers demonstrated a one-pot multistep method for accessing sulfonimidoyl fluorides by derivatizing gaseous thionyl tetrafluoride with amines and organolithium compounds (Figure 1, B).[10] More recently, Cornella et al. disclosed a procedure for preparing sulfonimidoyl fluorides through the reaction of highly moisture-sensitive aryl sulfur(VI) trifluoridoxides with amines.[11] Notably, Bull and Lopchuk's recent findings showcased the facile and stereoselective synthesis of sulfonimidoyl fluorides via the electrophilic fluorination of sulfinamide sodium salts bearing electron-withdrawing groups on the nitrogen atom (Figure 1, C).[12] Similarly, Willis and Zeng very recently disclosed the preparation of sulfondiimidamides via electrophilic fluorination of sulfinamidine salts (Figure 1, D).[13]

Motivated by the advancements reported by Bull and Lopchuk, we endeavored to develop a rapid approach for synthesizing aza-S(VI) fluorides, aiming to circumvent lengthy synthetic routes and the involvement of chlorinated intermediates. In this study, we present a multistep one-pot strategy for the preparation and derivatization of sulfonimidoyl and sulfondiimidoyl fluorides utilizing sulfinylamines as shared synthetic precursors.

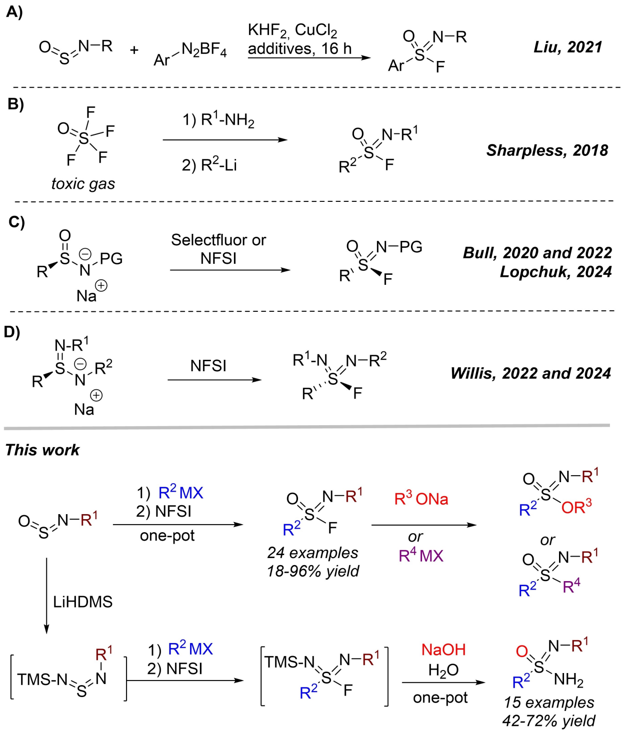
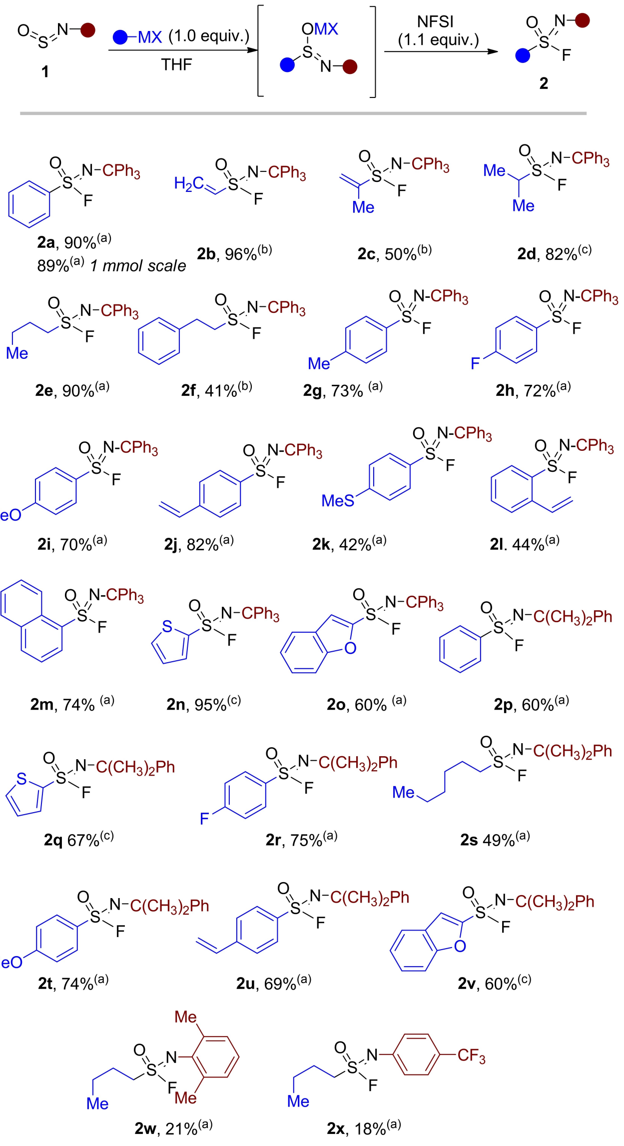


Figure 1. (A–D) Synthesis of sulfonimidoyl and sulfondiimidoyl fluorides; bottom: this work.

Results and Discussion

In the initial phase of our research, we conceived a one-pot sequence involving the nucleophilic addition of organometallics to sulfinylamines, followed by electrophilic fluorination with an electrophilic fluorine source of the intermediate sulfinamide salts.[14] This approach aimed to directly yield the corresponding sulfonimidoyl fluorides without the need for isolating the intermediate sulfinamide salt. Remarkably, the reaction of bench-stable *N*-trityl sulfinylamine **1 a** with phenyllithium at room temperature, followed by the addition of a slight excess of NFSI (*N*-fluorobenzenesulfonimide), produced the desired product **2 a** in 90% yield within just 6 minutes of reaction time across 2 steps (Scheme 1). Notably, the reaction worked efficiently on 1 mmol scale without any loss in yield. Encouraged by this promising initial outcome, we investigated the feasibility of employing various organometallic reagents to access diversified *S*-aryl and *S*-alkyl sulfinimidoyl fluorides (Scheme 1). The utilization of Grignard reagents such as vinyl magnesium bromide and isopropenyl magnesium bromide proved effective, yielding the corresponding products **2 b** and **2 c** in 96% and 50% isolated yield, respectively. Similarly, reactions with isopropyl magnesium chloride lithium chloride complex (**2 d**, 82%) and *n*-butyllithium (**2 e**, 90%) demonstrated that Turbo-Grignard reagents and alkyllithiums were competent nucleophiles in this transformation.

Expanding the scope, commercially available phenethyl magnesium bromide furnished **2 f** with a 41% yield, alongside various freshly prepared organometallic reagents. Consequently, *N*-trityl sulfonimidoyl fluorides bearing *p*-tolyl (**2 g**), *p*-fluorophenyl (**2 h**), *p*-methoxyphenyl (**2 i**), *p*-styrenyl (**2 j**), and *p*-methylthiophenyl (**2 k**) substituents were obtained with yields ranging from 42% to 82%. Notably, *ortho*-substituted sulfonimidoyl fluoride **2 l** was accessible when 2-vinylphenyllithium was utilized, yielding the product in 44% yield. Furthermore, 1-naphthyl and 2-thienyl derivatives **2 m** and **2 n** were efficiently synthesized with yields of 74% and 95%, respectively. Additionally, 2-benzofuranyllithium revealed to be a competent nucleophile for this transformation, furnishing benzofuran-substituted sulfonimidoyl fluoride **2 o** in 60% yield. Having explored the reactivity of *N*-trityl sulfinylamines, attention shifted towards diverse *N*-functionalized sulfinylamines for accessing corre-



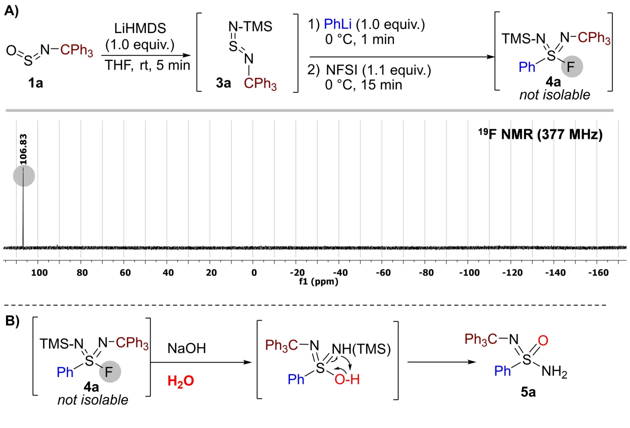
Scheme 1. One-pot synthesis of *N*-protected sulfonimidoyl fluorides from sulfinylamines. a) From organolithium; b) from Grignard reagent; c) From Turbo-Grignard reagent. Preparation of *N*-trityl sulfonimidoyl fluorides: R–Li or R-MgX (1.0 equiv.), 0.25 M in dry THF, rt, 1 min, then NFSI (1.1 equiv.), rt, 5 min. Preparation of *N*-cumyl sulfonimidoyl fluorides: R–Li or R-MgX (1.0 equiv.), 0.25 M in dry THF, 0 °C, 15 min, then NFSI (1.1 equiv.), 0 °C to rt, 5 min. Preparation of *N*-aryl sulfonimidoyl fluorides: R–Li or R-MgX (1.0 equiv.), 0.25 M in dry THF, −78 °C, 15 min, then NFSI (1.1 equiv.), −78 °C to rt, 15 min.

sponding sulfonimidoyl fluorides. Remarkably, efficient preparation of *N*-cumyl sulfinylamine (see Supporting Information) allowed for the synthesis of unprecedented sulfonimidoyl fluorides as depicted in Scheme 1. The reaction of *N*-cumyl sulfinylamine with organometallics proceeded at 0 °C in THF for 15 minutes before the addition of NFSI, yielding the desired compounds in generally good yields. Specifically, a range of organometallic reagents furnished *N*-cumyl sulfonimidoyl fluorides **2 p–v** bearing alkyl, aryl, and heteroaryl *S*-substituents with yields ranging from 25% to 75% (Scheme 1). Moreover, extending the methodology to unstable *N*-aryl sulfinylamines yielded the desired *N*-aryl sulfonimidoyl fluorides **2 w** and **x** albeit with low yields.

Delighted by our success in sulfonimidoyl fluoride synthesis, we sought to expand the methodology to sulfurdiimides, the aza-analogues of sulfinilamines. Building upon our recent work on the preparation and derivatization of an unsymmetric sulfurdiimide, we performed the synthesis of *N*-TMS,*N'*-trityl sulfurdiimide **3 a** through the straightforward treatment of *N*-trityl sulfinilamine **1 a** with lithium bis trimethylsilylamide (LiHMDS) in dry THF.[15] Subsequently, the resulting solution of sulfurdiimide **3 a** in THF was subjected to treatment with phenyllithium, followed by the addition of NFSI (1.1 equivalents) in one portion. Analysis via ^{19}F NMR of the reaction mixture unveiled the emergence of a peak at +106.8 ppm after 15 minutes, indicative of the rapid formation of a sulfondiimidoyl fluoride **4 a** (Scheme 2A).[13]

Although our attempts to isolate **4 a** were unsuccessful, we hypothesized that treating such a transient aza-S(VI) fluoride with water under basic conditions would furnish NH_2-free sulfonimidamides, analogous to the reported reactivity of sulfonimidoyl fluorides.[9] Hence, we hypothesized that this transformation might proceed through nucleophilic substitution by the hydroxy group at sulfur, followed by an intramolecular rearrangement to yield the NH_2-free sulfonimidamides **5** (Scheme 2, B).

As a result, NH_2-free *N*-trityl sulfonimidamides **5 a and c–e** were readily obtained from phenyllithium, isopropylmagnesium chloride lithium chloride complex, butyl- and hexyllithium, respectively, in moderate



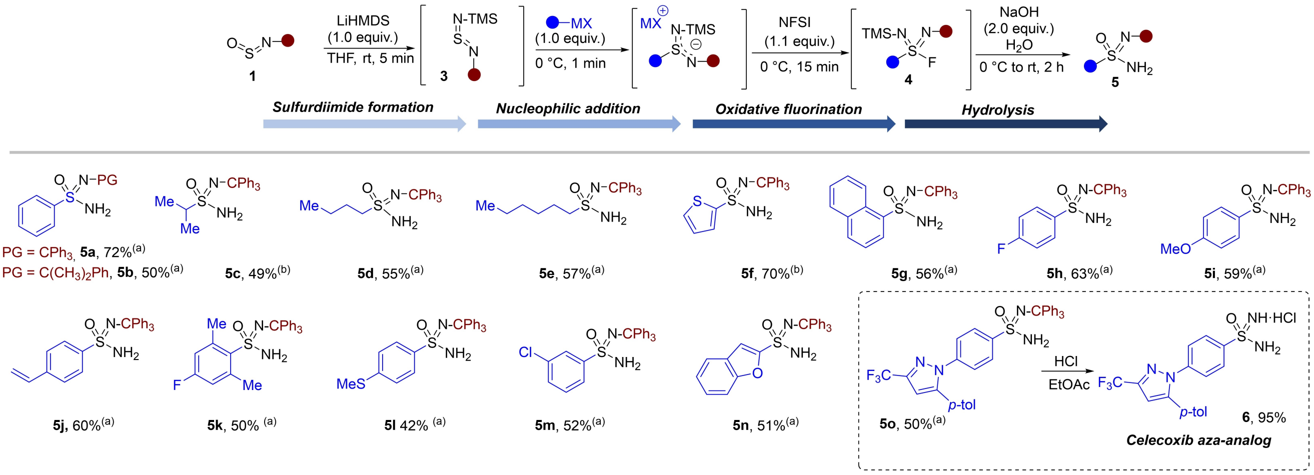
Scheme 2. A) Synthesis of sulfondiimidoyl fluoride **4 a** and ^{19}F NMR spectrum of the reaction crude. B) Proposed mechanism towards the formation of primary sulfonimidamides **5**.

yields (49–72%, Scheme 3). In addition, *N*-cumylsulfinylamine could be successfully employed releasing compound **5b** in 50% yield. The reaction proceeded efficiently when freshly prepared 2-thienylmagnesium chloride lithium chloride complex was employed, yielding product **5f** in 70% yield. Various freshly prepared (hetero)aryllithiums were also utilized, facilitating the synthesis of sulfonimidamides **5g–n** in yields ranging from 42% to 63%. Notably, the use of aryllithiums bearing electron-donating (**5i**) and electron-withdrawing groups (**5h**) was well tolerated, as well as the use of the more sterically demanding 2,6-dimethyl-4-fluorophenyllithium, which yielded compound **5k** in 50% yield. Moreover, the methodology enabled the facile preparation of N-protected sulfonimidamide **5o** from the corresponding aryllithium in 50% yield. Treatment of **5o** with an excess of HCl in EtOAc furnished *N*-unprotected sulfonimidamide salt **6**, representing the mono-aza-analogue of the sulfonamide nonsteroidal anti-inflammatory drug Celecoxib (Scheme 3).

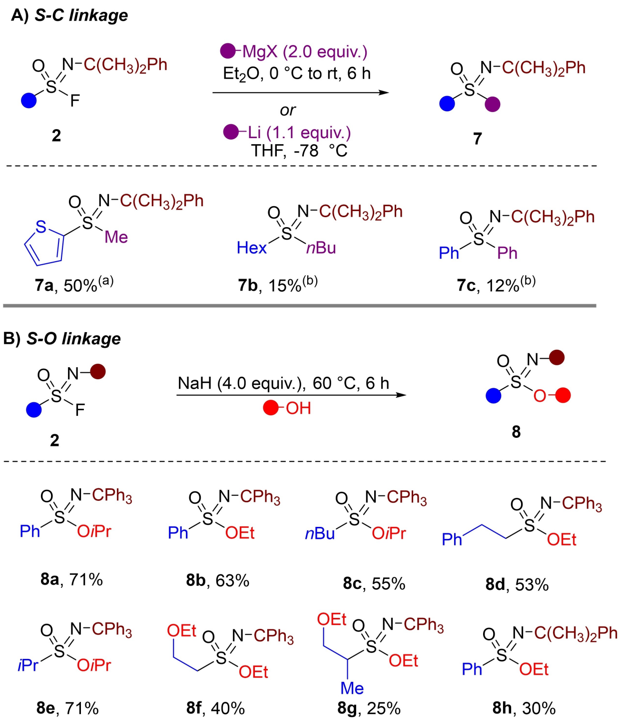
After investigating the one-pot preparation of aza-S(VI) fluorides from sulfinylamines, we shifted our focus to assessing the synthetic utility of such SuFEx hubs. Whereas the reactivity of *N*-aryl sulfonimidoyl fluorides has been extensively documented, limited information is available regarding the reactivity of *N*-trityl derivatives, and *N*-cumyl sulfonimidoyl fluorides represent a novel class of SuFEx linkers.[6,10] In detail, recent reports disclosed the transformation of *N*-trityl sulfonimidoyl fluorides with isotopically labeled water (^{18}O) towards labeled sulfonamides, and with amines towards sulfonimidamides.[9] However, to our knowledge, the transformation of *N*-trityl sulfonimidoyl fluorides with carbon nucleophiles and aliphatic alcohols remains unexplored. To fill this gap, we initially investigated the reaction of *N*-trityl sulfonimidoyl fluorides with lithium and magnesium organometallics. Unfortunately, we were unable to identify efficient reaction conditions for the S–C linkage (see Supporting Information), and *N*-trityl sulfonimidoyl fluorides proved to be unsuccessful substrates for the formation of sulfoximines. In contrast, we were pleased to observe the effective SuFEx reaction of the less sterically demanding *N*-cumyl sulfonimidoyl fluoride **2q** with methylmagnesium bromide, yielding sulfoximine **7a** in 50% yield (Scheme 4, A). The extension of the transformation to other substrates led to the formation of sulfoximines **7b** and **c** abeit in low yields. Having assessed the reactivity of *N*-protected sulfonimidoyl fluorides with carbon nucleophiles, we turned our attention to the S–O linkage with alkoxides.[16] In the first instance, the treatment of sulfonimidoyl fluoride **2a** with phenol under the conditions reported by Zuilhof et al. proved unsuccessful in yielding the desired sulfonimidate, and unreacted compound **2a** was recovered from the mixture.[17] Differently, the reaction of *N*-trityl sulfonimidoyl fluorides in alcohol with NaH upon heating proved efficient for the preparation of the corresponding sulfonimidates **8a–g** in moderate yields (Scheme 4, B). However, in the case of *S*-alkenyl sulfonimidoyl fluorides **2b–c**, we were unable to obtain the corresponding *S*-alkenyl sulfonimidates; instead, a Michael-type addition reactivity was observed, yielding products **8f** and **g** derived from the incorporation of two alkoxide units.[18] Additionally, *N*-cumylsulfonimidoyl fluoride **2p** could be transformed with ethanol and sodium hydride, yielding product **8h** in 30% yield.

Conclusions

In summary, this study presents a rapid one-pot method for preparing sulfonimidoyl fluorides from sulfinyl-



Scheme 3. Multistep one-pot synthesis of *N*-protected primary sulfonimidamides from sulfinylamines. a) From organolithium; b) From Turbo-Grignard reagent.



Scheme 4. A) Sulfoximine formation from sulfonimidoyl fluorides; a) from MeMgBr, b) from organolithiums. B) Sulfonimidate synthesis from sulfonimidoyl flourides.

amine through a nucleophilic addition/electrophilic fluorination sequence. Similarly, sulfondiimidoyl fluorides can be synthesized using the same procedure, preceded by the formation of an unsymmetrical sulfurdiimide easily generated in situ from *N*-tritylsulfinylamine. Although isolating sulfondiimidoyl fluorides was not feasible, they could be efficiently converted into NH_2-free sulfonimidamides through basic hydrolysis in a one-pot process, which was also effectively applied to prepare the mono-aza-analogue of the pharmaceutically relevant Celecoxib. In general, our methodology offers a synthetically improved route to previously reported compounds with at least comparable yields. In addition, this methodology is characterized by a range of practical benefits, including short reaction durations, use of shelf-stable precursors, absence of highly toxic or gaseous reagents, or the preclusion of photochemical equipment, making this route scalable and easily transferable to any synthetic laboratory. Additionally, we explored the reactivity of aza-S(VI) fluorides with various nucleophiles, demonstrating a versatile synthetic platform for producing aza-S(VI) compounds. Specifically, *N*-cumyl sulfonimidoyl fluorides released sulfoximines when treated with organometallics. Conversely, *N*-trityl sulfonimidoyl fluorides could be successfully transformed into sulfonimidates when treated with sodium alkoxides under mild heating. Further investigations on the synthesis and reactivity of aza-S(VI) fluorides are currently underway in our laboratory and will be reported in due course.

Experimental Section

Synthesis of *N*-Trityl Sulfonimidoyl Fluorides

To a solution of *N*-sulfinyltritylamine (50 mg, 0.16 mmol, 1.0 equiv.) in dry THF (0.25 M) under nitrogen atmosphere, organometallic solution (0.16 mmol, 1.0 equiv.) was added dropwise, and the mixture was stirred at room temperature for 1 minute. Subsequently, NFSI (0.18 mmol, 57 mg, 1.1 equiv.) was added in one portion and the reaction was stirred for additional 5 minutes (complete conversion was checked by TLC plate analysis). The solution directly concentrated under reduced pressure, and the crude was purified by column chromatography to afford the desired sulfonimidoyl fluoride.

Synthesis of *N*-cumyl Sulfonimidoyl Fluorides

To a cooled solution of *N*-sulfinylcumylamine (100 mg, 0.55 mmol, 1.0 equiv.) in dry THF (0.25 M) at 0 °C, under nitrogen atmosphere, organometallic solution (0.55 mmol, 1.0 equiv.) was added dropwise, and the mixture was stirred at 0 °C for 15 minutes. Subsequently, NFSI (0.6 mmol, 191 mg, 1.1 equiv.) was added in one portion and the reaction was stirred for additional 5 minutes at room temperature (complete conversion was checked by TLC plate analysis). The solution directly concentrated under reduced pressure, and the crude was purified by column chromatography to afford the desired sulfonimidoyl fluoride.

Synthesis of *N*-aryl Sulfonimidoyl Fluorides

To a cooled solution of *N*-sulfinylarylamine (1.0 mmol, 1.0 equiv.) in dry THF (0.25 M) at −78 °C, under nitrogen atmosphere, organometallic solution (1.0 mmol, 1.0 equiv.) was added dropwise, and the mixture was stirred at 0 °C for 15 minutes. Subsequently, NFSI (1.1 mmol, 347 mg, 1.1 equiv.) was added in one portion and the reaction was stirred for additional 15 minutes at room temperature. The solution directly concentrated under reduced pressure, and the crude was purified by column chromatography as indicated for each entry, to afford the desired sulfonimidoyl fluoride.

Synthesis of Sulfonimidamides

To a solution of *N*-sulfinylamine (0.33 mmol, 1.0 equiv.) in dry THF (0.25 M) under nitrogen atmosphere, LiHMDS (1.0 M inTHF, 1.0 equiv., 330 µL) was added dropwise and the mixture was stirred for 5 minutes at room temperature. Subsequently, the solution was cooled to 0 °C and the organometallic solution (0.33 mmol, 1.0 equiv.) was added dropwise, and the mixture was stirred at 0 °C for 1 minute. NFSI (0.36 mmol, 114 mg, 1.1 equiv.) was added in one portion and the reaction was stirred for additional 15 minutes at 0 °C, before adding NaOH (2.0 equiv., 26 mg) and water (250 µl). The solution was stirred for 2 h at room temperature. The crude was poured into water (15 mL) and extracted with EtOAc (3×15 mL). The organic layers were collected, dried over anhydrous sodium sulfate, and the solvent was evaporated at reduced pressure. The compounds were purified by column chromatography to afford the desired sulfonimidamide.

Synthesis of Sulfoximines

To a solution of *N*-cumyl sulfonimidoyl fluoride (0.2 mmol, 1.0 equiv, 0.2 M), organometallic compound (0.4 mmo, 2.0 equiv.) was added dropwise and the mixture was stirred for 6 h. The crude was poured into water (15 mL) and extracted with EtOAc (3×15 mL). The organic layers were collected, dried over anhydrous sodium sulfate, and the solvent was evaporated at reduced pressure. The compounds were purified by column chromatography to afford the desired sulfoximine.

Synthesis of Sulfonimidates

To a solution of sulfonimidoyl fluoride (0.1 mmol, 1.0 equiv.) in alchohol (0.2 M) NaH (0.4 mmol, 16 mg, 4 equiv.) was added and the mixture was stirred at 60 °C for 6 h. The crude was poured into water (15 mL) and extracted with EtOAc (3×15 mL). The organic layers were collected, dried over anhydrous sodium sulfate, and the solvent was evaporated at reduced pressure. The compounds were purified by column chromatography to afford the desired sulfonimidate.

Supporting Information Summary

Supporting information for this article is available on the WWW under https://doi.org/10.1002/adsc.202400908.

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References

[1] a) J. Yu, X. Jiang, *Adv. Agrochem.* **2023**, *2*, 3–14; b) C. Lamberth, H. Walter, F. M. Kessabi, L. Quaranta, R. Beaudegnies, S. Trah, A. Jeanguenat, F. Cederbaum, *Phosphorus Sulfur Relat. Elem.* **2015**, *190*, 1225–1235; c) M. Mustafa, J.-Y. Winum, *Expert Opin. Drug Discov.* **2022**, *17*, 501–512; d) K. A. Scott, J. T. Njardarson, *Top. Curr. Chem. (Z)* **2018**, *376*, DOI: 10.1007/s41061-018-0184-5.

[2] a) U. Lücking, *Org. Chem. Front.* **2019**, *6*, 1319–1324; b) C. Zhao, K. P. Rakesh, L. Ravidar, W.-Y. Fang, H.-L. Qin, *Eur. J. Med. Chem.* **2019**, *162*, 679–734; c) M. J. Tilby, M. C. Willis, *Expert Opin. Drug Discov.* **2021**, *16*, 1227–1231.

[3] a) P. Mäder, L. Kattner, *J. Med. Chem.* **2020**, *63*, 14243–14275; b) P. K. Chinthakindi, T. Naicker, N. Thota, T. Govender, H. G. Kruger, P. I. Arvidsson, *Angew. Chem. Int. Ed.* **2017**, *56*, 4100–4109.

[4] a) Z.-X. Zhang, M. C. Willis, *Trends Chem.* **2023**, *5*, 3–6; b) M. Andresini, M. Colella, L. Degennaro, R. Luisi, *Org. Biomol. Chem.* **2023**, *21*, 7681–7690; c) M. Andresini, M. Spennacchio, G. Romanazzi, F. Ciriaco, G. Clarkson, L. Degennaro, R. Luisi, *Org. Lett.* **2020**, *22*, 7129–7134; d) M. Andresini, M. Spennacchio, M. Colella, G. Losito, A. Aramini, L. Degennaro, R. Luisi, *Org. Lett.* **2021**, *23*, 6850–6854; e) P. Wu, J. Demaerel, B. J. Statham, C. Bolm, *Chem. Sci.* **2024**, *15*, 5333–5339.

[5] M. Andresini, A. Tota, L. Degennaro, J. A. Bull, R. Luisi, *Chem. Eur. J.* **2021**, *27*, 17293–17321.

[6] a) S. N. Carneiro, S. R. Khasnavis, J. Lee, T. W. Butler, J. D. Majmudar, C. W. am Ende, N. D. Ball, *Org. Biomol. Chem.* **2023**, *21*, 1356–1372; b) A. S. Barrow, C. J. Smedley, Q. Zheng, S. Li, J. Dong, J. E. Moses, *Chem. Soc. Rev.* **2019**, *48*, 4731–4758; c) S. Wilson Lucas, R. Zijian Qin, K. P. Rakesh, K. S. Sharath Kumar, H.-L. Qin, *Bioorg. Chem.* **2023**, *130*, 106227; d) T. S.-B. Lou, M. C. Willis, *Nat. Rev. Chem.* **2022**, *6*, 146–162.

[7] a) Z. Zhang, S.-L. Zhang, C. Wu, H.-H. Li, L. Zha, J. Shi, X. Liu, H.-L. Qin, W. Tang, *Eur. J. Med. Chem.* **2023**, *257*, 115502; b) 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, D. W. Wolan, *J. Am. Chem. Soc.* **2020**, *142*, 10899–10904; c) Z. Qin, K. Zhang, P. He, X. Zhang, M. Xie, Y. Fu, C. Gu, Y. Zhu, A. Tong, H. Wei, C. Zhang, Y. Xiang, *Nat. Chem.* **2023**, *15*, 1705–1714.

[8] C. R. Johnson, A. Wambsgans, *J. Org. Chem.* **1979**, *44*, 2278–2280.

[9] Y. Liu, Q. Pan, X. Hu, Y. Guo, Q.-Y. Chen, C. Liu, *Org. Lett.* **2021**, *23*, 3975–3980.

[10] B. Gao, S. Li, P. Wu, J. E. Moses, K. B. Sharpless, *Angew. Chem. Int. Ed.* **2018**, *57*, 1939–1943.

[11] L. Wang, J. Cornella, *Angew. Chem. Int. Ed.* **2020**, *59*, 23510–23515.

[12] a) S. Greed, E. L. Briggs, F. I. M. Idiris, A. J. P. White, U. Lücking, J. A. Bull, *Chem. Eur. J.* **2020**, *26*, 12533–12538; b) S. Greed, O. Symes, J. A. Bull, *Chem.*

Commun. **2022**, *58*, 5387–5390; c) S. Teng, Z. P. Shultz, C. Shan, L. Wojtas, J. M. Lopchuk, *Nat. Chem.* **2024**, *16*, 183–192.

[13] a) Z.-X. Zhang, M. C. Willis, *Chem.* **2022**, *8*, 1137–1146; b) M. Ding, C. Bell, M. C. Willis, *Angew. Chem. Int. Ed.* **2024**, DOI: 10.1002/anie.202409240.

[14] For the nucleophilic addition of organometallics to sulfinylamines see: a) T. Q. Davies, M. J. Tilby, J. Ren, N. A. Parker, D. Skolc, A. Hall, F. Duarte, M. C. Willis, *J. Am. Chem. Soc.* **2020**, *142*, 15445–15453; b) T. Q. Davies, M. C. Willis, *Chem. Eur. J.* **2021**, *27*, 8918–8927; c) M. Ding, Z.-X. Zhang, T. Q. Davies, M. C. Willis, *Org. Lett.* **2022**, *24*, 1711–1715; d) T. Q. Davies, M. J. Tilby, D. Skolc, A. Hall, M. C. Willis, *Org. Lett.* **2020**, *22*, 9495–9499; e) M. Malik, R. Senatore, D. Castiglione, A. Roller-Prado, V. Pace, *Chem. Commun.* **2023**, *59*, 11065–11068.

[15] M. Andresini, S. Carret, L. Degennaro, F. Ciriaco, J. Poisson, R. Luisi, *Chem. Eur. J.* **2022**, *28*, DOI: 10.1002/chem.202202066.

[16] a) D. Zeng, W. Deng, X. Jiang, *Chem. Eur. J.* **2023**, *29*, DOI: 10.1002/chem.202300536; b) D. Liang, D. E. Streefkerk, D. Jordaan, J. Wagemakers, J. Baggerman, H. Zuilhof, *Angew. Chem. Int. Ed.* **2020**, *59*, 7494–7500.

[17] D. Liang, D. E. Streefkerk, D. Jordaan, J. Wagemakers, J. Baggerman, H. Zuilhof, *Angew. Chem. Int. Ed.* **2020**, *59*, 7494–7500.

[18] S. Strasser, C. Slugovc, *Catal. Sci. Technol.* **2015**, *5*, 5091–5094.