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[3+2] Cycloaddition of Azomethyne Ylide and Vinyl Sulfonyl Fluorides – an Approach to Pyrrolidine-3-sulfonyl Fluorides

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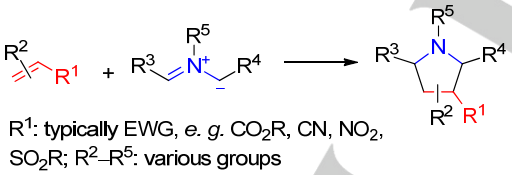
Abstract: [3+2] cycloaddition of vinyl sulfonyl fluorides and generated *in situ* non-stabilized azomethine ylide is described for the first time. The resulting pyrrolidine-3-sulfonyl fluorides were obtained in 50–83% yields on up to 25 g scale. Their utility as reagents for sulphur (VI) fluoride exchange (SuFEx) and some other transformations was also demonstrated.

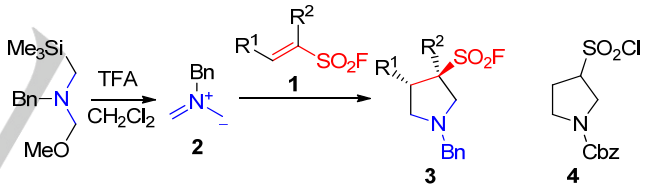
Introduction

[3+2] cycloaddition with azomethine ylides (Scheme 1) is an important synthetic method which have attracted much attention in the last two decades.[1–11] The main reason behind this is that the products of this reaction – pyrrolidines – are important class of compounds widespread among both natural products[12–14] and synthetic drugs.[15] Typically, cycloaddition with azomethine ylides requires participation of electron-poor dipolarophile; various alkenes with electron-withdrawing groups (EWGs) were studied comprehensively in the reaction including α,β-unsaturated carboxylic acid derivatives, nitro compounds and sulfones.[5] Vinyl sulfonamides were also introduced in this transformation.[16–22]



Scheme 1. [3+2] cycloaddition with azomethine ylides

In both above-mentioned cases, the resulting sulfur-containing pyrrolidines provide limited possibilities for further functionalization. In this work, we report [3+2] cycloaddition of azomethine ylides with novel organosulfur substrates for this particular type of transformation – vinyl sulfonyl fluorides (**1**). It should be noted that sulfonyl fluorides have given rise to significant interest in recent years; they are widely used in design of covalent inhibitors,[23] as well as reagents for sulfur (VI) fluoride exchange (SuFEx), which was proposed by Sharpless and co-workers as "another good reaction for the click chemistry".[24] Moreover, the parent vinyl sulfonyl fluoride (**1a**) was referred to as "the most perfect Michael acceptor ever found".[24,25] To date, [3+2] cycloaddition with nitrones,[26] as well as Diels – Alder reactions[27,28] of **1** were reported in the literature. Herein, we describe reactions of **1** with non-stabilized azomethine ylide **2**, as well as some further transformations of the products **3** obtained (Scheme 2). It should be outlined that pyrrolidines of the type **3** or their analogues have been virtually unknown to date; only Cbz-protected sulfonyl chloride **4** was described in the literature previously.[29,30] Meanwhile, these conformationally restricted derivatives of β-amino sulfonic acids are of special interest to organic and medicinal chemistry,[31] in particular as building blocks in synthesis of sulfonopeptides.[32–34]



Scheme 2. Synthesis of sulfonyl fluorides **3** *via* [3+2] cycloaddition (relative configuration is shown)

Results and Discussion

First of all, we have checked if the standard protocol for generation of azomethine ylide **2** (*N*-benzyl-1-methoxy-*N*-((trimethylsilyl)methyl)methanamine, CH_2Cl_2, cat. TFA, rt), which was originally developed by Achiwa and co-workers[35,36] and has been widely used by us[37–40] and others[41–44] in recent years, works for the parent commercially available vinyl sulfonyl fluoride **1a** (Scheme 2, $R^1 = R^2 = H$). It was found that under these typical conditions, the target adduct **3a** was obtained in 75% yield (Table 1). Notably, the reaction could be scaled up to 25 g without significant change in its outcome.

Being encouraged by this result, we have prepared a series of β-aryl-substituted vinyl sulfonyl fluorides **1b–j** using a variation of the previously reported method,[45,46] *i.e.* chlorosulfonation of the corresponding styrenes **5b–h** with varied electronic and steric properties (42–71% yield), followed by reaction of the sulfonyl chlorides **6b–h** with KHF_2 (92–99% yield, Scheme 3). In

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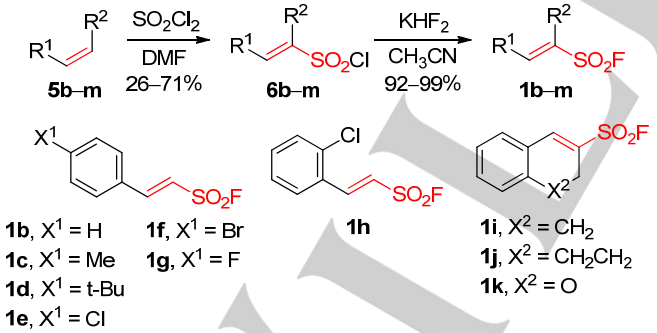
addition to that, bicyclic α,β-unsaturated sulfonyl fluorides **1i–k** were also prepared in 26–60% overall yield using the same reaction sequence. It was found that all the substrates **1b–k** reacted smoothly under the conditions shown in Scheme 2, and the corresponding adducts **3b–k** were obtained in 50–83% yields.

Table 1. Reaction of vinyl sulfonyl fluorides **1** and generated *in situ* azomethine ylide **2** (according to Scheme 2)

#	Substrate	Product	R^1	R^2	Yield, %
1	**1a**	**3a**	H	H	80
2	**1b**	**3b**	Ph	H	82
3	**1c**	**3c**	4-MeC_6H_4	H	83
4	**1d**	**3d**	4-*t*-BuC_6H_4	H	60
5	**1e**	**3e**	4-ClC_6H_4	H	80
6	**1f**	**3f**	4-BrC_6H_4	H	87
7	**1g**	**3g**	4-FC_6H_4	H	80
8	**1h**	**3h**	2-ClC_6H_4	H	77
9	**1i**	**3i**	–*o*-$C_6H_4CH_2CH_2$–		81
10	**1j**	**3j**	–*o*-$C_6H_4CH_2CH_2CH_2$–		50
11	**1k**	**3k**	–*o*-$C_6H_4CH_2O$–		70



Scheme 3. Synthesis of vinyl sulfonyl fluorides **1** (for R^1/R^2, see also Table 1)

As it might be expected for the synchronous process, single diastereomers of the products **3b–n** were formed in the reaction, with *trans* relative configuration of the R^1 and SO_2F groups. This was confirmed using NOESY experiments with adducts **3e** and **3g** (Figure 1).

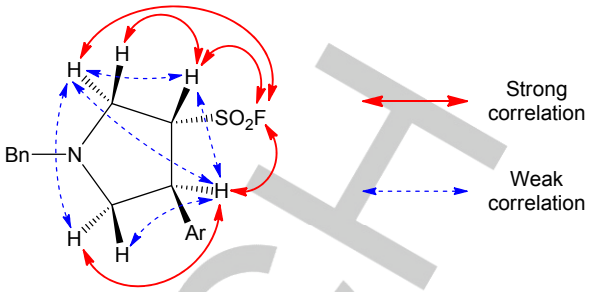
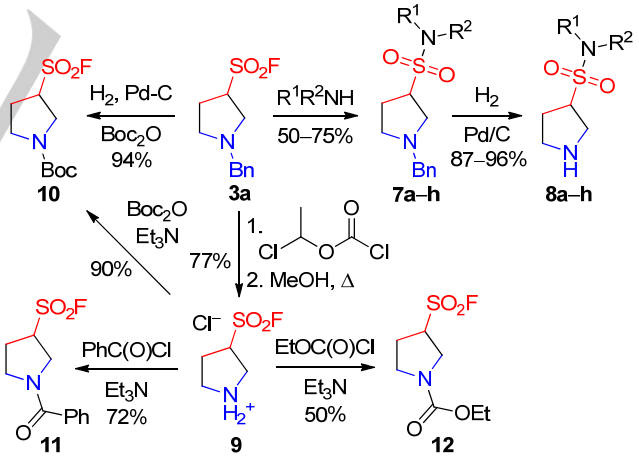


Figure 1. Significant ^1H-^1H and ^1H-^{19}F NOESY correlations observed for **3e** (Ar = 4-ClC_6H_4) and/or **3g** (Ar = 4-FC_6H_4)

To demonstrate utility of adducts **3** as (potentially) bifunctional building blocks for organic synthesis and drug discovery, we have performed some transformations at both protected amino and sulfonyl fluoride functions. In particular, the parent compound **3a** smoothly underwent the SuFEx click reaction, so that sulfonamides **7a–f** were obtained (Scheme 4). In turn, catalytic debenzylation of **7a–f** gave free pyrrolidines **8a–f** (87–96% yield for two steps). Direct debenzylation was also possible with **3a** either upon action of chloroethyl formate, followed by methanolysis, or catalytic hydrogenolysis in the presence of Boc_2O. Thus, sulfonyl fluorides **9** and **10** were obtained in 77% and 94% yields, respectively. It was also shown that **9** can form amides (*e. g.* **11**, 72% yield) or carbamates (**10** or **12**, 90% and 50% yield, respectively) without the sulfonyl fluoride function being affected.



R^1/R^2 = H/H (**7a**, **8a**); Me/H (**7b**, **8b**); Et/H (**7c**, **8c**); *i*-Pr/H (**7d**, **8d**); *c*-Pr/H (**7e**, **8e**); $(CH_2)_4$ (**7f**, **8f**)

Scheme 4. Chemical properties of amino sulfonyl fluoride **3a**

Conclusions

[3+2] cycloaddition of vinyl sulfonyl fluorides and generated *in situ* non-stabilized azomethine ylide **2** is an efficient method for the multigram diastereoselective synthesis of 3-substituted, 3,4-

disubstituted, or 3,3,4-trisubstituted pyrrolidine-derived sulfonyl fluorides. These adducts can be considered as monoprotected bifunctional conformationally restricted building blocks, which have great potential for application in drug discovery and organic synthesis. This statement was illustrated by some common chemical transformations, including sulphur (VI) fluoride exchange (SuFEx) which has been recently referred to as another click reaction;[24] in all cases, either the (protected) amino function or the sulfonyl fluoride moiety participated in the reaction selectively.

Experimental Section

General. The solvents were purified according to the standard procedures.[47] Sulfonyl halides **1**[45,46] and **6**[48,49] were obtained using the reported procedures. All other starting materials were purchased from commercial sources. Melting points were measured on MPA100 OptiMelt automated melting point system. Analytical TLC was performed using Polychrom SI F254 plates. Column chromatography was performed using Kieselgel Merck 60 (230–400 mesh) as the stationary phase. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker 170 Avance 500 spectrometer (at 499.9 MHz for Protons and 124.9 MHz for Carbon-13) and Varian Unity Plus 400 spectrometer (at 400.4 MHz for protons and 100.7 MHz for Carbon-13). Chemical shifts are reported in downfield from TMS as an internal standard. Elemental analyses were performed at the Laboratory of Organic Analysis, Department of Chemistry, National Taras Shevchenko University of Kyiv. Mass spectra were recorded on an Agilent 1100 LCMSD SL instrument (chemical ionization (APCI), electrospray ionization (EI)) and Agilent 5890 Series II 5972 GCMS instrument (electron impact ionization (EI)).

General procedure for the preparation of sulfonyl chlorides 6. Sulfuryl chloride (41.6 g, 0.308 mol) was added dropwise to anhydrous DMF (25 mL) at 0 °C with stirring under argon atmosphere. After the addition was completed, the mixture was warmed to rt and stirred for additional 0.5 h. Styrene **5** (0.154 mol) was then added in three portions, and the reaction mixture was heated to 90 °C over 3 h. The reaction mixture was cooled and poured onto the crushed ice, the resulting precipitate was filtered, washed with cold H_2O and dissolved in *t*-BuOMe (300 mL). If the precipitate was not formed, the mixture obtained after pouring on ice was extracted with *t*-BuOMe (3×150 mL). The organic phase was washed with brine (150 mL), dried over Na_2SO_4 and evaporated under reduced pressure. The crude product was recrystallized from *t*-BuOMe.

3,4-Dihydronaphthalene-2-sulfonyl chloride (6i).[48] Yield 22.1 g, 63%. Colorless solid. Mp 61–62 °C. Anal. calcd. for $C_{10}H_9ClO_2S$: C 52.52; H 3.97; S 14.02; Cl 15.50. Found: C 52.64; H 3.58; S 13.82; Cl 15.63. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.55 (s, 1H), 7.41 – 7.32 (m, 1H), 7.32 – 7.18 (m, 3H), 3.07 (t, *J* = 8.3 Hz, 2H), 2.88 (t, *J* = 8.3 Hz, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 141.3, 137.4, 135.9, 131.8, 130.2, 129.5, 128.1, 127.5, 27.6, 22.1.

6,7-Dihydro-5*H*-benzo[7]annulene-8-sulfonyl chloride (6j). Yield 19.4 g, 52%. Colorless solid. Mp 63–64 °C. Anal. calcd. for $C_{11}H_{11}ClO_2S$: C 54.43; H 4.57; S 13.21; Cl 14.61. Found: C 54.09; H 4.23; S 13.08; Cl 14.7. ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.73 (s, 1H), 7.42 – 7.14 (m, 4H), 2.99 (t, *J* = 6.5 Hz, 2H), 2.96 – 2.90 (m, 2H), 2.21 – 2.10 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 145.3, 143.4, 140.5, 134.7, 131.1, 130.3, 130.1, 126.9, 35.3, 30.2, 25.1.

2*H*-Chromene-3-sulfonyl chloride (6k). Yield 9.2 g, 26 %. Colorless solid. Mp 58–59 °C. Anal. calcd. for $C_9H_7ClO_3S$: C 46.87; H 3.06; S 13.9; Cl 15.37. Found: C 46.61; H 3.23; S 14.01; Cl 15.62. ^{1}H NMR (400 MHz, $CDCl_3$) *δ* = 7.51 (s, 1H), 7.41 – 7.32 (m, 1H), 7.28 – 7.20 (m, 1H), 7.02 (d, *J* = 7.5, 1H), 6.93 (d, *J* = 8.2 Hz, 1H), 5.13 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) *δ* = 154.7, 134.9, 134.4, 132.8, 130.4, 122.9, 118.6, 116.8, 62.6.

General procedure for the preparation of sulfonyl fluorides 1. To a solution of sulfonyl chloride **6** (0.092 mol) in MeCN (320 mL), 28% aq KHF_2 (0.188 mol, 360 mL) was added, and the mixture was stirred at rt overnight. After the reaction was completed, the upper layer of the biphasic mixture was concentrated in *vacuo*, diluted with H_2O (300 mL) and extracted with EtOAc (3×200 mL). The aqueous phase was extracted with EtOAc (300 mL), and the combined organic extracts were washed with 10% aq NaCl (2×100 mL), brine (2×50 mL), dried over Na_2SO_4, and concentrated under reduced pressure.

(*E*)-2-(*p*-Tolyl)ethenesulfonyl fluoride (1c).[45] Yield 17.7 g, 96%. Colorless solid. Mp 132–133 °C. Anal. calcd. for $C_9H_9FO_2S$: C 53.99; H 4.53; S 16.01. Found: C 54.11; H 4.45; S 16.02. MS (EI): 200 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.76 (d, *J* = 15.5 Hz, 1H), 7.43 (d, *J* = 8.0 Hz, 2H), 7.26 (d, *J* = 8.0 Hz, 2H), 6.79 (d, *J* = 15.5 Hz, 1H), 2.40 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 148.9 (d, *J* = 2.7 Hz), 143.6, 130.1, 129.1, 128.3, 116.6 (d, *J* = 27.8 Hz), 21.7. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* = 62.1.

(*E*)-2-(4-(*tert*-Butyl)phenyl)ethenesulfonyl fluoride (1d). Yield 21.8 g, 98%. Colorless solid. Mp 54–56 °C. Anal. calcd. for $C_{12}H_{15}FO_2S$: C 59.48; H 6.24; S 13.23. Found: C 59.64; H 6.29; S 13.28. MS (EI): 242 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.79 (d, *J* = 15.5 Hz, 1H), 7.49 (s, 4H), 6.82 (dd, *J* = 15.5, 2.6 Hz, 1H), 1.34 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 156.7, 148.8 (d, *J* = 2.7 Hz), 129.0, 128.2, 126.4, 116.7 (d, *J* = 27.8 Hz), 35.2, 31.0. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* = 62.1.

(*E*)-2-(4-Chlorophenyl)ethenesulfonyl fluoride (1e).[45] Yield 18.7 g, 93%. Colorless solid. Mp 127–128 °C. Anal. calcd. for $C_8H_6ClFO_2S$: C 43.55; H 2.74; S 14.53; Cl 16.07. Found: C 43.49; H 2.85; S 14.24; Cl 16.28. MS (EI): 220/222 ([M]$^+$, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.75 (d, *J* = 15.5 Hz, 1H), 7.52 – 7.39 (m, 4H), 6.83 (dd, *J* = 15.5, 2.6 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 147.3 (d, *J* = 2.6 Hz), 138.9, 130.2, 129.8, 129.4, 118.5 (d, *J* = 28.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): *δ* = 53.68.

(*E*)-2-(4-Bromophenyl)ethenesulfonyl fluoride (1f).[50] Yield 22.9 g, 95%. Colorless solid. Mp 143–146 °C. Anal. calcd. for $C_8H_6BrFO_2S$: C 36.25; H 2.28; S 12.09; Br 30.14. Found: C 36.34; H 2.65; S 11.95; Br 30.28. MS (EI): 264/266 ([M]$^+$, 1:1). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.76 (d, *J* = 15.5 Hz, 1H), 7.62 (d, *J* = 8.5 Hz, 1H), 7.43 (d, *J* = 8.5 Hz, 1H), 6.88 (dd, *J* = 15.5, 2.5 Hz, 1H). ^{13}C NMR (126 MHz, CDCl3): *δ* 147.5 (d, *J* = 2.8 Hz), 132.9, 130.4, 130.0, 127.5, 118.8 (d, *J* = 28.7 Hz). ^{19}F NMR (376 MHz, CDCl3): *δ* = 61.80.

(*E*)-2-(4-Fluorophenyl)ethenesulfonyl fluoride (1g).[51] Yield 18.2 g, 97%. Colorless solid. Mp 92–94 °C. Anal. calcd. for $C_8H_6F_2O_2S$: C 47.06; H 2.96; S 15.70. Found: C 46.92; H 3.02; S 16.03. MS (EI): 204 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 7.78 (d, *J* = 15.5 Hz, 1H), 7.57 (dd, *J* = 8.5, 5.3 Hz, 2H), 7.17 (t, *J* = 8.5 Hz, 2H), 6.81 (dd, *J* = 15.5, 2.5 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 165.2 (d, *J* = 255.5 Hz), 147.5 (d, *J* = 2.7 Hz), 131.3 (d, *J* = 9.7 Hz), 127.3 (d, *J* = 2.9 Hz), 117.6 (dd, *J* = 28.3, 2.5 Hz), 116.8 (d, *J* = 22.3 Hz). ^{19}F NMR (376 MHz, $CDCl_3$): δ = 61.9 (s), –105.56 – –105.48 (m).

(*E*)-2-(2-Chlorophenyl)ethenesulfonyl fluoride (1h).[52] Yield 18.6 g, 92%. Colorless oil. Anal. calcd. for $C_8H_6ClFO_2S$: C 43.55; H 2.74; S 14.53; Cl 16.07. Found: C 43.67; H 2.69; S 14.48; Cl 15.94. MS (EI):

220/222 ([M]$^+$, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.22 (dd, J = 15.7, 2.4 Hz, 1H), 7.59 (dt, J = 7.7, 2.0 Hz, 1H), 7.53 – 7.41 (m, 2H), 7.35 (t, J = 7.4 Hz, 1H), 6.92 (dt, J = 15.6, 2.2 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$) δ 144.6, 135.9, 133.3, 130.8, 129.3, 128.6, 127.5, 120.6 (d, J = 28.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ 61.50.

3,4-Dihydronaphthalene-2-sulfonyl fluoride (1i). Yield 18.7 g, 96%. Colorless oil. Anal. calcd. for $C_{10}H_9FO_2S$: C 56.59; H 4.27; S 15.11. Found: C 56.33; H 4.46; S 15.02. MS (EI): 212 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.60 (s, 1H), 7.42 – 7.32 (m, 1H), 7.31 – 7.17 (m, 3H), 3.03 (t, J = 8.3 Hz, 2H), 2.77 (t, J = 8.3 Hz, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.3, 136.1, 131.9, 130.4 (d, J = 25.1 Hz), 129.9, 129.8, 128.2, 127.6, 27.3, 22.1. ^{19}F NMR (376 MHz, $CDCl_3$) δ 53.68.

6,7-Dihydro-5*H*-benzo[7]annulene-8-sulfonyl fluoride (1j). Yield 20.4 g, 98%. Colorless solid. Mp 61–63 °C. Anal. calcd. for $C_{11}H_{11}FO_2S$: C 58.39; H 4.90; S 14.17. Found: C 58.17; H 4.84; S 14.45. MS (EI): 226 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.72 (s, 1H), 7.41 – 7.13 (m, 3H), 2.97 – 2.89 (m, 2H), 2.84 (t, J = 6.5 Hz, 2H), 2.18 – 2.07 (m, 2H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 143.4, 142.6, 134.4, 134.2 (d, J = 20.5 Hz), 131.1, 130.6 (d, J = 1.4 Hz), 130.0, 126.8, 35.3, 30.3, 25.4. ^{19}F NMR (376 MHz, $CDCl_3$) δ 51.95.

2*H*-Chromene-3-sulfonyl fluoride (1k). Yield 19.5 g, 99%. Colorless oil. Anal. calcd. for $C_9H_7FO_3S$: C 50.46; H 3.29; S 14.97. Found: C 50.84; H 3.69; S 15.14. MS (EI): 214 ([M]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$) δ = 7.57 (s, 1H), 7.36 (d, J = 7.9 Hz, 1H), 7.29 – 7.18 (m, 1H), 7.09 – 6.99 (m, 1H), 6.92 (d, J = 8.2 Hz, 1H), 5.03 (s, 2H). ^{13}C NMR (101 MHz, $CDCl_3$) δ = 154.8, 138.1 (d, J = 2.8 Hz), 134.4, 130.1, 122.8, 122.5, 122.2, 118.8, 116.8, 62.5. ^{19}F NMR (376 MHz, $CDCl_3$) δ 57.45.

General procedure for the preparation of sulfonyl fluorides 3. A solution of the sulfonyl fluoride **1** (50.0 mmol) in CH_2Cl_2 (75 mL) was cooled to 0 °C under argon. *N*-benzyl-1-methoxy-*N*-((trimethylsilyl)-methyl)methanamine (12.1 g, 5.5 mmol) was added in one portion, and then dropwise addition of trifluoroacetic acid (0.38 mL, 5.0 mmol) in CH_2Cl_2 (5 mL) followed at 0 °C. After the reaction was complete (monitored by ^{1}H NMR), the mixture was diluted with H_2O (50 mL), the organic layer was separated, washed with saturated aq $NaHCO_3$ (2×25 mL) and brine (25 mL), dried over Na_2SO_4, and evaporated under reduced pressure. The residue was purified by recrystallization (Hexanes – *t*-BuOMe) or column chromatography.

1-Benzylpyrrolidine-3-sulfonyl fluoride (3a). Yield 25.1 g, 80%. Colorless oil. Anal. calcd. for $C_{11}H_{14}FNO_2S$: C 54.30; H 5.80; N 5.76; S 13.18. Found: C 54.61; H 5.99; N 5.42; S 13.02. MS (APCI) *m/z*: 244 ([M+H]$^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.38 – 7.25 (m, 5H), 3.98 (p, J = 7.7 Hz, 1H), 3.70 (d, J = 12.9 Hz, 1H), 3.67 (d, J = 12.9 Hz, 1H), 3.16 – 3.08 (m, 1H), 2.95 (dd, J = 10.6, 6.3 Hz, 1H), 2.84 – 2.75 (m, 1H), 2.71 (q, J = 7.2 Hz, 1H), 2.43 – 2.34 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 137.9, 128.7, 128.6, 127.6, 59.3, 59.0 (d, J = 14.8 Hz), 54.1, 52.9, 26.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ 46.30.

(3*R,4*S**)-1-Benzyl-4-phenylpyrrolidine-3-sulfonyl fluoride (3b).** Yield 13.1 g, 82%. Colorless oil. Anal. calcd. for $C_{17}H_{18}FNO_2S$: C 63.93; H 5.68; N 4.39; S 10.04. Found: C 63.83; H 5.70; N 4.31; S 9.71. MS (APCI) *m/z*: 320 ([M+H]$^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.42 – 7.27 (m, 10H), 4.05 – 3.95 (m, 1H), 3.90 – 3.84 (m, 1H), 3.78 (d, J = 12.8 Hz, 1H), 3.75 (d, J = 12.8 Hz, 1H), 3.30 (t, J = 9.5 Hz, 1H), 3.20 – 3.12 (m, 2H), 2.91 (dd, J = 9.5, 5.4 Hz, 1H). ^{13}C NMR (126 MHz, $CDCl_3$): δ 140.7, 137.3, 128.6, 128.1, 127.3, 127.1, 127.0, 67.0 (d, J = 13.0 Hz), 60.7, 58.7, 54.3, 45.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ 47.9.

(3*R,4*S**)-1-Benzyl-4-(*p*-tolyl)pyrrolidine-3-sulfonyl fluoride (3c).** Yield 13.8 g, 83%. Colorless oil. Anal. calcd. for $C_{18}H_{20}FNO_2S$: C 64.84; H 6.05; N 4.20; S 9.62. Found: C 64.72; H 6.08; N 4.47; S 9.52. MS (APCI) *m/z*: 334 ([M+H]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.40 – 7.20 (m, 7H), 7.14 (d, J = 7.8 Hz, 2H), 3.99 – 3.88 (m, 1H), 3.85 – 3.77 (m, 1H), 3.74 (d, J = 13.0 Hz, 1H), 3.69 (d, J = 13.0 Hz, 1H), 3.28 – 3.18 (m, 1H), 3.17 – 3.06 (m, 2H), 2.83 (dd, J = 9.5, 5.5 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 138.1, 137.7, 137.4, 129.6, 128.5, 127.5, 127.2, 67.5 (d, J = 12.9 Hz), 61.2, 59.1, 54.6, 45.6, 21.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ 47.80.

(3*R,4*S**)-1-Benzyl-4-(4-(*tert*-butyl)phenyl)pyrrolidine-3-sulfonyl fluoride (3d).** Yield 11.2 g, 60%. Colorless solid. Mp 99–101 °C. Anal. calcd. for $C_{21}H_{26}FNO_2S$: C 67.17; H 6.98; N 3.73; S 8.54. Found: C 66.85; H 6.61; N 3.39; S 8.57. MS (APCI) *m/z*: 376 ([M+H]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.39 – 7.21 (m, 9H), 4.00 – 3.89 (m, 1H), 3.85 – 3.79 (m, 1H), 3.74 (d, J = 16.0 Hz, 1H), 3.70 (d, J = 16.0 Hz, 1H), 3.28 – 3.18 (m, 1H), 3.11 (m, 2H), 2.92 – 2.80 (m, 1H), 1.30 (s, 9H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 150.6, 138.1, 137.7, 128.7 – 128.3 (2C), 127.5, 127.0, 125.9, 67.4 (d, J = 13.0 Hz), 61.1, 59.2, 54.6, 45.4, 34.5, 31.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ = 47.7.

(3*R,4*S**)-1-Benzyl-4-(4-chlorophenyl)pyrrolidine-3-sulfonyl fluoride (3e).** Yield 14.1 g, 80%. Colorless solid. Mp 73–74 °C. Anal. calcd. for $C_{17}H_{17}ClFNO_2S$: C 57.71; H 4.84; N 3.96; S 9.06; Cl 10.02. Found: C 57.45; H 4.57; N 4.22; S 9.13; Cl 9.72. MS (APCI) *m/z*: 354/356 ([M+H]$^+$, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.43 – 7.18 (m, 9H), 3.89 (dd, J = 14.0, 7.0 Hz, 1H, 3-C*H*), 3.81–3.76 (m, 1H, 4-C*H*), 3.74 (d, J = 13.2 Hz, 1H, C*H*HPh), 3.70 (d, J = 13.2 Hz, 1H, CH*H*Ph), 3.29 (t, J = 9.5 Hz, 1H, 2-C*H*H), 3.10 – 3.03 (m, 2H, 2-CH*H* and 5-C*H*H), 2.86 (dd, J = 9.5, 4.8 Hz, 1H, 5-CH*H*). ^{13}C NMR (101 MHz, $CDCl_3$): δ 139.8, 137.5, 133.5, 129.2, 128.8, 128.6, 128.5, 127.6, 67.3 (d, J = 13.2 Hz, 3-*C*H), 60.8 (5-*C*H$_2$), 59.1 (*C*H$_2$Ph), 54.6 (2-*C*H$_2$), 45.3 (4-*C*H). ^{19}F NMR (376 MHz, $CDCl_3$): δ 47.9.

(3*R,4*S**)-1-Benzyl-4-(4-bromophenyl)pyrrolidine-3-sulfonyl fluoride (3f).** Yield 17.3 g, 87%. Colorless solid. Mp 61–62 °C. Anal. calcd. for $C_{17}H_{17}BrFNO_2S$: C 51.27; H 4.30; N 3.52; S 8.05; Br 20.06. Found: C 51.41; H 4.69; N 3.68; S 7.68; Br 19.67. MS (APCI) *m/z*: 398/400 ([M+H]$^+$, 1:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.50 – 7.42 (m, 2H), 7.39 – 7.21 (m, 7H), 3.89 (q, J = 6.5 Hz, 1H), 3.83 – 3.65 (m, 3H), 3.29 (t, J = 9.4 Hz, 1H), 3.11 – 3.02 (m, 2H), 2.91 – 2.81 (m, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): δ 140.3, 137.5, 132.1, 129.1, 128.6, 128.5, 127.6, 121.6, 67.2 (d, J = 13.3 Hz), 60.8, 59.1, 54.6, 45.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ 48.0.

(3*R,4*S**)-1-Benzyl-4-(4-fluorophenyl)pyrrolidine-3-sulfonyl fluoride (3g).** Yield 13.5 g, 80%. Colorless solid. Mp 59–60 °C. Anal. calcd. for $C_{17}H_{17}F_2NO_2S$: C 60.52; H 5.08; N 4.15; S 9.50. Found: C 60.18; H 5.43; N 4.07; S 9.51.MS (APCI): 338 ([M+H]$^+$). ^{1}H NMR (500 MHz, $CDCl_3$): δ 7.39 – 7.26 (m, 7H), 7.04 (t, J = 8.6 Hz, 2H), 3.92 (dd, J = 14.0 and 6.9 Hz, 1H, 3-C*H*), 3.87 – 3.79 (m, 1H. 4-C*H*), 3.76 (d, 12.9 Hz, 1H, C*H*HPh) , 3.73 (d, 12.9 Hz, 1H, CH*H*Ph), 3.30 (t, J = 9.5 Hz, 1H, 2-C*H*H), 3.11 – 3.04 (m, 2H, 2-CH*H* and 5-C*H*H), 2.88 (dd, J = 9.5, 4.9 Hz, 1H, 5-CH*H*). ^{13}C NMR (126 MHz, $CDCl_3$): δ 163.2, 161.3, 137.7, 137.2 (d, J = 3.3 Hz), 129.1 (d, J = 8.1 Hz), 128.6 (d, J = 5.9 Hz), 127.7, 116.0 (d, J = 21.4 Hz), 67.6 (d, J = 13.2 Hz), 61.1, 59.2, 54.7, 45.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ 47.87, –115.14.

(3*R,4*S**)-1-Benzyl-4-(2-chlorophenyl)pyrrolidine-3-sulfonyl fluoride (3h).** Yield 13.6 g, 77%. Colorless oil. Anal. calcd. for $C_{17}H_{17}ClFNO_2S$: C 57.71; H 4.84; N 3.96; S 9.06; Cl 10.02. Found: C 57.70; H 4.67; N 4.12; S 9.21; Cl 10.39. MS (APCI): 354/356 ([M+H]$^+$, 3:1). ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.49 (dd, J = 7.8, 1.7 Hz, 1H), 7.41 – 7.16 (m, 8H), 4.46 –

4.36 (m, 1H), 4.16 – 4.06 (m, 1H), 3.76 (d, *J* = 13.0 Hz, 1H), 3.71 (d, *J* = 13.0 Hz, 1H), 3.31 (t, *J* = 9.4 Hz, 1H), 3.24 – 3.12 (m, 2H), 2.82 (dd, *J* = 9.4, 5.7 Hz, 1H). ^{13}C NMR (101 MHz, $CDCl_3$): *δ* 138.1, 137.6, 133.5, 130.0, 128.9 (2C), 128.5, 127.6, 127.5, 66.0 (d, *J* = 13.9 Hz), 60.4, 59.0, 54.4, 42.6. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* 48.30.

2-Benzyl-2,3,3a,4,5,9*b*-hexahydro-1*H*-benzo[*e*]isoindole-3*a*-sulfonyl fluoride (3i). Yield 13.9 g, 81%. Colorless solid. Mp 77–78 °C. Anal. calcd. for $C_{19}H_{20}FNO_2S$: C 66.07; H 5.84; N 4.05; S 9.28. Found: C 65.81; H 5.48; N 3.86; S 8.97. MS (APCI) *m/z*: 345 ([M+H]$^+$). ^{1}H NMR (500 MHz, $CDCl_3$): *δ* 7.39 – 7.10 (m, 4H), 4.07 – 4.00 (m, 1H), 3.70 – 3.60 (m, 3H), 3.36 (t, *J* = 8.5 Hz, 1H), 2.90 – 2.82 (m, 2H), 2.77 (dd, *J* = 11.4, 2.4 Hz, 1H), 2.38 (t, *J* = 8.5 Hz, 1H), 2.29 – 2.18 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$): *δ* 137.8, 136.1, 135.3, 128.8, 128.6, 128.5, 128.3, 127.5, 127.2, 127.1, 70.9 (d, *J* = 10.5 Hz), 62.9, 60.9, 58.9, 44.0, 29.9, 25.8. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* 35.99.

2-Benzyl-1,2,3,3a,4,5,6,10*b*-octahydrobenzo[3,4]cyclohepta[1,2-*c*]-pyrrole-3a-sulfonyl fluoride (3j). Yield 8.98 g, 50%. Colorless oil. Anal. calcd. for $C_{20}H_{22}FNO_2S$: C 66.83; H 6.17; N 3.90; S 8.92. Found: C 66.86; H 5.98; N 4.29; S 8.74. MS (APCI) *m/z*: 360 ([M+H]$^+$). ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 4H), 7.33 – 7.20 (m, 4H), 7.14 (d, *J* = 7.2 Hz, 1H), 4.13 (t, *J* = 6.3 Hz, 1H), 3.78 (s, 2H), 3.35 (d, *J* = 11.4 Hz, 1H), 3.29 – 3.14 (m, 2H), 3.08 (d, *J* = 11.4 Hz, 1H), 2.87 – 2.76 (m, 1H), 2.02 - 1.94 (m, 3H), 1.90 – 1.77 (m, 1H). ^{13}C NMR (126 MHz, $CDCl_3$) *δ* 138.4, 138.2, 135.7, 129.7, 128.5, 128.5, 128.3, 127.4, 126.9, 59.4, 58.7, 57.7, 48.2, 29.7, 28.6, 21.1. ^{19}F NMR (470 MHz, $CDCl_3$) *δ* 39.42.

2-Benzyl-1,2,3,3a,4,9*b*-hexahydrochromeno[3,4-*c*]pyrrole-3*a*-sulfonyl fluoride (3k). Yield 12.1 g, 70%. Colorless solid. Mp 105–108 °C. Anal. calcd. for $C_{18}H_{18}FNO_3S$: C 62.23; H 5.22; N 4.03; S 9.23. Found: C 62.51; H 5.11; N 3.81; S 9.05. MS (APCI): m/z = 348 ([M+H]$^+$). ^{1}H NMR (400 MHz, $CDCl_3$) *δ* = 7.41 – 7.25 (m, 5H), 7.25 – 7.16 (m, 1H), 7.17 – 7.08 (m, 1H), 7.07 – 6.93 (m, 1H), 4.64 (d, *J* = 12.3 Hz, 1H), 4.08 (dd, *J* = 12.3, 3.8 Hz, 1H), 4.00 (t, *J* = 7.5 Hz, 1H), 3.82 – 3.63 (m, 2H), 3.52 (d, *J* = 11.1 Hz, 1H), 3.46 (t, *J* = 8.6 Hz, 1H), 2.83 – 2.57 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 153.3, 136.9, 128.5, 128.1, 127.9, 127.8, 127.1, 122.2, 121.7, 117.2, 68.4 (d, *J* = 11.0 Hz), 66.3, 60.8, 58.1, 57.5, 39.1. ^{19}F NMR (376 MHz, $CDCl_3$): *δ* 43.7.

General procedure for the preparation of sulfonamides 8. To a solution of sulfonyl fluoride (**3a**) (15.0 mmol) in 1,4-dioxane (30 mL), the corresponding amine (45.0 mol) was added (in the case **8a–c**, 25–40% aqueous amines were used), and the mixture was heated at 50 °C. After the reaction was complete (monitored by ^{1}H NMR), the solvent was evaporated in *vacuo*, the residue was diluted with water (50 mL) and extracted with EtOAc (3×50 mL). The combined organic extracts were washed with brine (25 mL), dried over Na_2SO_4 and evaporated under reduced pressure to give sulfonamide **7**, which was used in the next step without purification. The residue was dissolved in anhydrous MeOH (60 mL) and 10% Pd-C (0.3 g) was added. This mixture was hydrogenated under 300 psi of H_2 at rt for *ca.* 10 h. After the reaction was complete (monitored by ^{1}H NMR), the catalyst was filtered off, and the filtrate was evaporated in *vacuo*. The crude product was triturated with *t*-BuOMe (10–20 mL) and filtered.

Pyrrolidine-3-sulfonamide (8a). Yield 20.2 g, 90%. Colorless solid. Mp 124–125 °C. Anal. calcd. for $C_4H_{10}N_2O_2S$: C 31.99; H 6.71; N 18.65; S 21.34. Found: C 32.25; H 6.32; N 18.34; S 21.66. MS (APCI): 151 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 6.75 (s, 2H), 3.47 (p, *J*=7.1 Hz, 1H), 3.10 – 2.40 (br. s, 1H), 3.07 – 2.93 (m, 2H), 2.87 – 2.78 (m, 1H), 2.77 – 2.66 (m, 1H), 1.93 (q, *J* = 7.1 Hz, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 63.2, 49.4, 47.6, 29.3.

3-(*N*-Methylsulfamoyl)pyrrolidine hydrochloride (8b·HCl). Yield 7.94 g, 86%. Colorless solid. Mp 167–168 °C. Anal. calcd. for $C_5H_{13}ClN_2O_2S$: C 29.93; H 6.53; N 13.96; S 15.98; Cl 17.66. Found: C 30.11; H 6.67; N 14.08; S 16.15; Cl 17.76.MS (APCI): 165 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 9.75 (s, 2H), 7.48 (q, *J* = 4.8 Hz, 1H), 4.11 – 3.99 (m, 1H), 3.58 – 3.48 (m, 1H), 3.38 – 3.28 (m, 1H), 3.30 – 3.13 (m, 2H), 2.61 (d, *J*=4.8 Hz, 3H), 2.32 – 2.13 (m, 2H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 56.7, 45.1 (2C), 29.1, 26.8.

***N*-Ethylpyrrolidine-3-sulfonamide (8c).** Yield 22.4 g, 94%. Colorless solid. Mp 69–70 °C. Anal. calcd. for $C_6H_{14}N_2O_2S$: C 40.43; H 7.92; N 15.72; S 17.99. Found: C 40.06; H 7.61; N 15.43; S 17.69. MS (APCI): 179 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 7.01 (s, 1H), 3.63 – 3.53 (m, 1H), 3.20 – 2.80 (br. s, 1H), 3.06 – 2.93 (m, 6H), 2.88 – 2.77 (m, 1H), 2.78 – 2.67 (m, 1H), 2.01 – 1.82 (m, 2H), 1.07 (t, *J*=7.2 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 60.6, 49.1, 47.6, 37.8, 29.0, 16.2.

***N*-Isopropylpyrrolidine-3-sulfonamide (8d).** Yield 4.09 g, 96%. Colorless solid. Mp 105–106 °C. Anal. calcd. for $C_7H_{16}N_2O_2S$: C 43.73; H 8.39; N 14.57; S 16.67. Found: C 43.36; H 8.65; N 14.67; S 16.49. MS (APCI): 193 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* 7.03 (d, *J* = 7.8 Hz, 1H), 3.76 – 3.49 (m, 1H), 3.49 – 3.38 (m, 1H), 3.05 – 2.90 (m, 2H), 3.05 – 2.93 (m, 1H), 2.77 – 2.70 (m, 1H), 2.70 – 2.54 (m, 2H), 2.01 – 1.82 (m, 2H), 1.31 – 0.83 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* 61.46, 49.30, 47.67, 45.59, 29.19, 24.56 (d, *J* = 3.1 Hz).

3-(*N*-Cyclopropylsulfamoyl)pyrrolidine hydrochloride (8e·HCl). Yield 14.2 g, 87%. Colorless solid. Mp 165–166 °C. Anal. calcd. for $C_7H_{15}ClN_2O_2S$: C 37.08; H 6.67; N 12.36; S 14.14; Cl 15.64. Found: C 36.87; H 7.03; N 12.67; S 13.89; Cl 15.41. MS (APCI): 191 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 10.37 – 9.26 (m, 2H), 7.97 – 7.91 (m, 1H), 4.09 (p, *J*=6.9 Hz, 1H), 3.62 – 3.51 (m, 1H), 3.41 – 3.31 (m, 1H), 3.28 – 3.13 (m, 2H), 2.55 – 2.44 (m, 1H), 2.35 – 2.16 (m, 2H), 0.66 – 0.51 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 57.4, 45.1, 26.7, 24.4, 6.2, 6.1.

3-(Pyrrolidin-1-ylsulfonyl)pyrrolidine hydrochloride (8f·HCl). Yield 5.12 g, 92%. Colorless solid. Mp 178–179 °C. Anal. calcd. for $C_8H_{17}ClN_2O_2S$: C 39.91; H 7.12; N 11.64; S 13.32; Cl 14.72. Found: C 40.11; H 7.02; N 11.26; S 13.54; Cl 14.52. MS (APCI): 205 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6) *δ* = 9.81 (s, 2H), 4.18 (p, *J*=7.6 Hz, 1H), 3.61 – 3.51 (m, 1H), 3.44 – 3.02 (m, 7H), 2.36 – 2.22 (m, 1H), 2.24 – 2.10 (m, 1H), 1.91 – 1.79 (m, 4H). ^{13}C NMR (101 MHz, DMSO-d_6) *δ* = 57.1, 48.2, 45.1, 45.0, 27.0, 25.8.

3-(Fluorosulfonyl)pyrrolidine hydrochloride (9). To a solution of **3a** (45.0 g, 0.185 mol) in CH_2Cl_2 (500 mL), 1-chloroethyl chloroformate (33.9 g, 0.241 mol) was added dropwise at 0 °C. The reaction mixture was refluxed for 8 h and then evaporated in *vacuo*. The residue was dissolved in MeOH (500 mL) heated to reflux for 2 h, and then cooled to rt. The solvent was evaporated in *vacuo* and the residue was triturated with acetone (250 mL). The resulting solid was filtered and dried on air. Yield 26.3 g, 77%. White powder. Mp 140–141 °C. Anal. calcd. for $C_4H_9ClFNO_2S$: C 25.34; H 4.78; N 7.39; S 16.91; Cl 18.69. Found: C 25.49; H 4.65; N 7.19; S 17.12; Cl 18.63. MS (APCI): m/z = 154 ([M+H]$^+$). ^{1}H NMR (400 MHz, DMSO-d_6): *δ* 10.15 (s, 2H), 5.07 – 4.94 (m, 1H), 3.79 (dd, *J* = 13.4, 9.0 Hz, 1H), 3.59 (dd, *J* = 13.4, 5.6 Hz, 1H), 3.38 – 3.22 (m, 2H), 2.61 – 2.48 (m, 1H), 2.47 – 2.34 (m, 1H). ^{13}C NMR (101 MHz, DMSO-d_6): *δ* 58.5 (d, *J* = 15.7 Hz), 45.1, 44.8, 27.1. ^{19}F NMR (376 MHz, DMSO-d_6): *δ* 48.0.

***tert*-Butyl 3-(fluorosulfonyl)pyrrolidine-1-carboxylate (10).**

From 9: To a solution of **9** (14.8 g, 78.1 mmol) and di-*tert*-butyl dicarbonate (17.0 g, 78.1 mmol) in THF (250 mL), a solution of Et_3N (11.0 mL, 78.9 mmol) in THF (50 mL) was added dropwise. The resulting mixture was stirred at rt for 24 h, and the solvent was evaporated under reduced pressure. The residue was dissolved in *t*-BuOMe (100 mL), washed with H_2O (2×50 mL), 10% aq citric acid (2×50 mL), saturated aq $NaHCO_3$ (2×50 mL), and brine (50 mL). The organic layer was dried over Na_2SO_4 and evaporated in *vacuo*. Yield 17.8 g, 90%. Anal. calcd. for $C_9H_{16}FNO_4S$: C 42.68; H 6.37; N 5.53; S 12.66. Found: C 42.61; H 6.59; N 5.15; S 12.79. MS (EI): m/z = 253 ($[M]^+$). ^{1}H NMR (400 MHz, $CDCl_3$): *δ* 4.07 – 3.97 (m, 1H), 3.97 – 3.70 (m, 3H), 3.68 – 3.53 (m, 1H), 3.53 – 3.39 (m, 1H), 2.55 – 2.33 (m, 2H), 1.42 (s, 9H). ^{13}C NMR (126 MHz, $CDCl_3$): *δ* 153.0, 80.0, 58.8 (d, *J* = 80.6 Hz), 45.6, 43.8, 27.8, 26.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ 47.3 (d, *J* = 11.6 Hz).

From 3a: Compound **3a** (3.51 g, 14.4 mmol) was dissolved in anhydrous MeOH (50 mL), and $Pd(OH)_2$-C (0.710 g) was added, followed by di-*tert*-butyl dicarbonate (3.22 g, 15.1 mmol). This mixture was hydrogenated under 75 psi of H_2 at rt for 10 h. After completion of the reaction (monitored by ^{1}H NMR), the catalyst was filtered off, and the filtrate was evaporated in *vacuo*. Yield 3.42 g, 94%.

1-Benzoylpyrrolidine-3-sulfonyl fluoride (11). To a suspension of **9** (0.381 g, 2.05 mmol) in CH_2Cl_2 (5 mL), benzoyl chloride (0.23 mL, 2.10 mmol) was added, followed by Et_3N (0.61 mL, 4.05 mmol). The resulting mixture was stirred at rt overnight. The resulting mixture diluted with H_2O (5 mL), the organic layer was washed with saturated aq $NaHCO_3$ (2×5 mL) and brine (2×5 mL), dried over Na_2SO_4, and evaporated under reduced pressure. Yield 0.379 g, 72%. Anal. calcd. for $C_{11}H_{12}FNO_3S$: C 51.35; H 4.70; N 5.44; S 12.46. Found: C 51.19; H 4.66; N 5.71; S 12.42. MS (APCI): 258 ($[M+H]^+$). ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 7.58 – 7.34 (m, 5H), 4.45 – 3.51 (m, 5H), 2.69 – 2.38 (m, 2H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 169.3, 135.0, 130.2, 128.1, 126.6, 59.2 and 58.1, 48.7 and 47.0, 45.9 and 44.1, 27.4 and 25.5. ^{19}F NMR (376 MHz, $CDCl_3$) *δ* 48.33 and 47.74.

Ethyl 3-(fluorosulfonyl)pyrrolidine-1-carboxylate (12). Compound **12** was prepared from **9** analogously to **11**, using ethyl chloroformate instead of benzoyl chloride. Yield 0.228 g, 50%. Anal. calcd. for $C_7H_{12}FNO_4S$: C 37.33; H 5.37; N 6.22; S 14.23. Found: C 37.35; H 5.22; N 6.42; S 14.54. MS (EI): 225 ($[M]^+$). ^{1}H NMR (500 MHz, $CDCl_3$) *δ* 4.25 – 4.12 (m, 2H), 4.14 – 3.85 (m, 3H), 3.77 – 3.64 (m, 1H), 3.59 (s, 1H), 2.55 (s, 1H), 2.49 (s, 1H), 1.25–1.30 (m, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.0 and 153.8, 61.2, 59.2 (d, *J* = 15.8 Hz) and 58.4 (d, *J* = 15.2 Hz), 45.9 and 45.5, 44.1 and 43.7, 26.8 and 26.0, 14.14.^{19}F NMR (470 MHz, $CDCl_3$) *δ* 48.07 and 48.02.

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Keywords: Organosulfur compounds • Pyrrolidines • Click chemistry • Cycloaddition • Azomethine ylides

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FULL PAPER

[3+2] cycloaddition of various vinyl sulfonyl fluorides and unsubstituted azomethine ylide results in the formation of pyrrolidine-3-sulfonyl fluorides. The method is scalable, and the products are suitable building blocks for sulphur (VI) fluoride exchange (SuFEx), which has been referred to as another click reaction.

Sulfonyl Fluorides

*Volodymyr L. Mykhalchuk, Vladimir S. Yarmolchuk, Andrey A. Tolmachev, Roman O. Doroschuk, Oleksandr O. Grygorenko**

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[3+2] Cycloaddition of Azomethyne Ylide and Vinyl Sulfonyl Fluorides – an Approach to Pyrrolidine-3-sulfonyl Fluorides