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Regioselective ring-opening reaction of 2-trifluoromethyl-*N*-tosylaziridine with some nucleophiles under basic conditions

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ABSTRACT

The ring-opening reaction of 2-trifluoromethyl-*N*-tosylaziridine with a variety of heteroatom- and carbon-centered nucleophiles was achieved under basic conditions in good to high yield with excellent regioselectivity. These findings enabled an easy access to useful α-trifluoromethyl-*N*-tosylmethylamine derivatives, such as 1,2-aminoalcohol, 1,2-diamine, 1,2-aminothiol, and distant secondary amine.

1. Introduction

Medicinal modifications in biologically active molecules are frequently related to replacing hydrogen with fluorine at the specific position.[1] Lipitor bearing one fluorine on the benzene ring is the most popular fluorinated drug for a cholesterol-reducer. On the other hand, trifluoromethyl group (CF_3) also plays an important role due to its unique stereoelectronic property. Celecoxib possessing CF_3 group on the pyrazole ring is well-accepted as an anti-inflammatory drug. Accordingly, the facile preparation of selectively trifluoromethylated molecules has become a great challenging task in the areas of pharmaceuticals and agrochemicals.[2] In conjunction with this area, we have been interested in an easy preparation of a wide range of α-(trifluoromethyl)methylamine derivatives. In spite of the versatile potential of these molecules, their expeditious preparation remains unexplored. We considered that these molecules should be directly accessible from the regio-controlled ring-opening reaction of 2-(trifluoromethyl)aziridine. Aziridines are important synthetic intermediates for the synthesis of biologically active compounds due to their inherent ring strain. Reports on the ring-opening reaction of 2-(trifluoromethyl)aziridine derivatives under acidic conditions are available in the literature.[3] However, the corresponding ring-opening reaction under basic conditions is scarce.[4] The reason seems to be electrostatic repulsion between one pair of fluorine on the trifluoromethyl group and the negative charge of nucleophiles.[4c]

We recently reported the easily prepared 2-trifluoromethyl-*N*-tosylaziridine **1** would be a useful precursor for the synthesis of the corresponding *cis*-4-trifluoromethyl-2-substituted-*N*-tosyl-1,3-oxazolidines.[5] The CF_3–aziridine **1** would be also a fascinating electrophile for the ring-opening reaction due to the small steric hindrance (no substituents on the ring except for CF_3 group). We report herein the first effective ring-opening reaction of **1** with a variety of nucleophiles, such as alcohols, phenols, amides, imides, thiols, and active methylene compounds under basic conditions, providing the corresponding α-trifluoromethyl-*N*-tosylmethylamine derivatives.

2. Results and discussion

2.1. Ring-opening reaction of 2-trifluoromethyl-*N*-tosylaziridine 1 with O-nucleophiles

Literature search for the ring-opening reaction of non-fluorinated aziridines under basic conditions revealed that the protocol by Zhou and co-workers was essentially suitable for our purpose. They actually reported the tandem ring-opening/closing reactions of 2-alkyl-*N*-tosylaziridines and aryl propargyl alcohols in the presence of ^{t}BuOK in DMSO.[6] Our investigation started by

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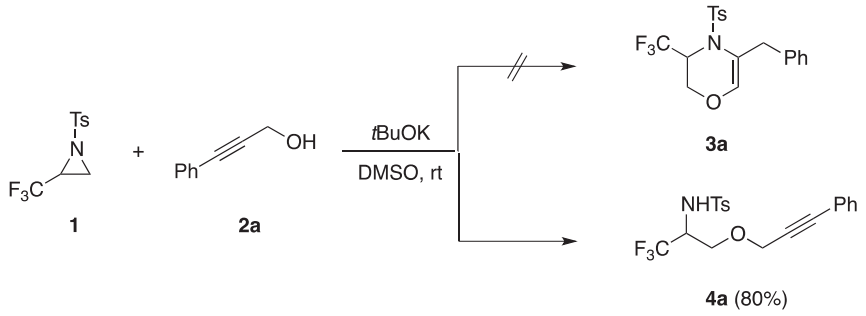
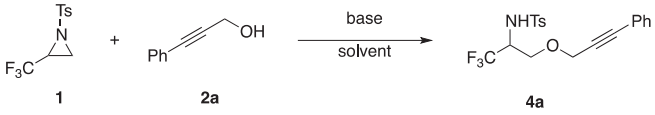
using **1** and phenyl propargyl alcohol **2a** as a model compound. When the reaction of **1** was conducted with **2a** using ^{t}BuOK in DMSO at room temperature, the reaction smoothly proceeded giving not the anticipated cyclized product **3a** but the simple ring-opening product **4a** as a single isomer in 80% yield (Scheme 1).



Scheme 1. Ring-opening reaction of **1** and **2a**.

The reaction was highly regioselective such that other isomers were not detected in the crude reaction mixture. Although we did not obtain the corresponding CF_3—morphorine derivative, considering the simplicity of the reaction under mild conditions, the result in Scheme 1 appeared to be meaningful synthetic transformation. To build on this result, we screened another base and solvents shown in Table 1.

Table 1
Screening of reaction conditions.



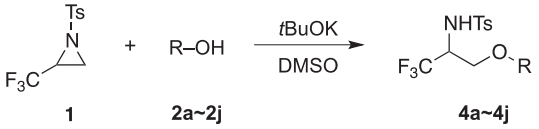
Entry	Base	Solv.	Time/h	Yield/%[a]
1	^{t}BuOK	DMSO	1	80
2	^{t}BuOK	DMF	4.5	78
3	^{t}BuOK	THF	4	32
4	NaH	DMSO	1	54
5	NaH	THF	16	70

[a] Isolated yield.

The suitable base from this screening was ^{t}BuOK in DMSO. With the aim of preparing the cyclic product **3a** (see Scheme 1), the elevated reaction temperature (up to 80 °C) and the longer reaction time (24 h) caused **4a** to partially decompose. Accordingly, room temperature in DMSO (entry 1) was suitable for the optimal reaction conditions of this ring-opening reaction. Once again, it is noteworthy that this reaction proceeded affording the single regioisomer under mild conditions. We deduced that both steric and electronic effects of the trifluoromethyl group resulted in the excellent regioselectivity and the high reactivity resulted from the strong electron-withdrawing effect of tosyl group.[7]

With the optimal reaction conditions in hand, we examined the substrate scope. Table 2 summarized the results of the ring-opening reaction of **1** and a wide range of alcohols and phenol (**2**). In most cases, the reaction smoothly proceeded giving the corresponding product as a single regioisomer. When we conducted the reaction of **2d**, a mixture of diastereomers was obtained in 92% combined yield (entry 4). This mixture could not be separated to its components. When we carried out the reaction using **1** (1.0 equiv) and **2e** (1.1 equiv) as a bi-functional nucleophile under the optimized reaction conditions, the 1:1 ring-opening product (**4e**) and the additional 1:2 ring-opening product (**4ee**) were obtained in 46% and 52% yields, respectively (entry 5 and Scheme 2). With the aim of gaining **4e** exclusively, the use of **2e** (2.2 equiv) resulted in the formation of **4e** (66% yield) along with **4ee** (32% yield) under the identical reaction conditions.

Table 2
Ring-opening reaction of **1** and various O-nucleophiles.[a]

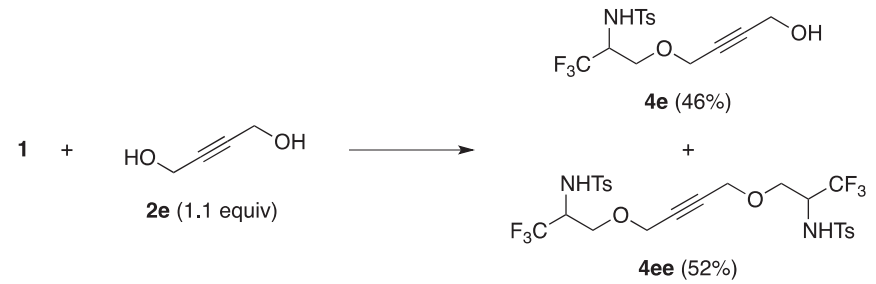


Entry	Product (Yield)[b]	Entry	Product (Yield)[b]
1	**4a** (80%)	6	**4f** (74%)
2	**4b** (97%)	7[e]	**4g** (50%)
3	**4c** (93%)	8[f]	**4h** (82%)
4[c]	**4d** (92%)	9[f]	**4i** (74%)
5[d]	**4e** (46%)	10[g]	**4j** (88%)

[a] The reaction were carried out using **1** (1.0 equiv) and **2** (1.1 equiv) in the presence of ^{t}BuOK (1.1 equiv) in DMSO at rt for 1 h unless otherwise noted.
[b] Isolated yield.
[c] An inseparable mixture of diastereomers was produced.
[d] The corresponding bis-adduct was also produced (52%). See the text.
[e] Reaction was run for 2 h.
[f] Reaction was run in DMF at 0 °C for 2 h.
[g] Reaction was run in DMSO/THF=1/1 at −20 °C for 2 h.

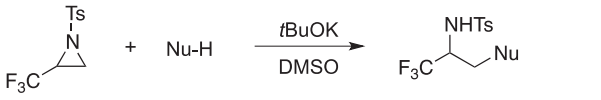
2.2. Ring-opening reaction of 2-trifluoromethyl-*N*-tosylaziridine 1 with N-, S-, C-nucleophiles

We next investigated replacing the O-nucleophiles with other nucleophiles. Table 3 shows the additional results of the ring-opening reaction of **1** and N-, S-, and C-nucleophiles. In some cases, we needed slightly modified reaction conditions in order to

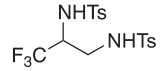
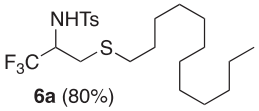
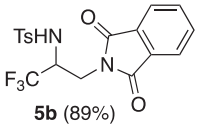
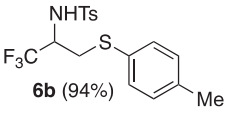
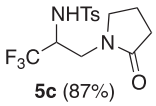
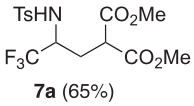
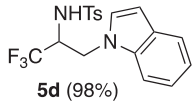
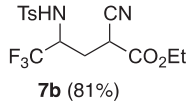
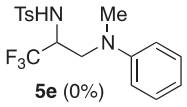
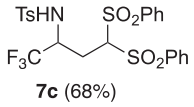


Scheme 2. Reaction of **1** with 2-butyn-1,4-diol.

Table 3
Ring-opening reaction of **1** and various N-, S-, C-nucleophiles.[a]



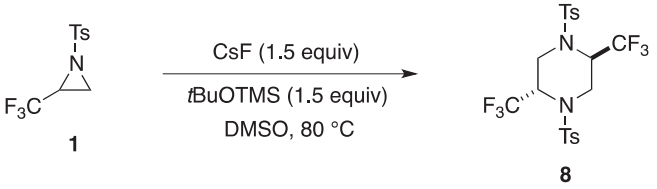
1 **5, 6, 7**

Entry	Product (Yield)[b]	Entry	Product (Yield)[b]
1	 **5a** (91%)	6	 **6a** (80%)
2[c]	 **5b** (89%)	7	 **6b** (94%)
3[c]	 **5c** (87%)	8	 **7a** (65%)
4[c]	 **5d** (98%)	9	 **7b** (81%)
5[d]	 **5e** (0%)	10[e]	 **7c** (68%)

[a] The reaction were carried out using **1** (1.0 equiv) and NaH (1.1 equiv) in the presence of ^{t}BuOK (1.1 equiv) in DMSO at rt for 1 h unless otherwise stated.
[b] Isolated yield.
[c] Reaction was run for 1.5 h.
[d] Reaction was conducted using NaH (1.1 equiv).
[e] Reaction was run for 4 h.

obtain the corresponding products in good yields. As shown in entries 1–4, N-nucleophiles smoothly reacted with **1** to afford the corresponding adducts as a single regioisomer in high to excellent yields. However, the reaction of **1** and *N*-methylaniline in the presence of NaH in DMSO did not proceed as both starting materials were recovered intact (entry 5). The next reactions using S-nucleophiles, such as an aliphatic thiol and an aromatic thiol (entries 6 and 7) also gave the corresponding regioisomers in good and high yields, respectively. Compared with O-, N-, and S-nucleophiles, C-nucleophiles afforded the products in reasonable yields (entries 8–10). In addition, the useable C-nucleophiles had some limitations. When we carried out the reaction using other C-nucleophiles, such as *tert*-butyl acetoacetate, pentane-2,4-dione, 1,3-dimethylbarbituric acid, phenylacetylene, the reactions resulted in complex mixtures. In other words, the reactions did not afford a detectable quantity of the ring-opening products. The reason for these unsuccessful reactions is not clear at present. Although the useable nucleophiles have some limitations for this reaction, the ring-opening products produced here should be transformed into the corresponding trifluoromethylated 1,2-aminoalcohols, 1,2-diamines, 1,2-amino thiols, and distant secondary amines by exposure of appropriate reaction conditions.

Finally, in addition to above findings, we happened to encounter the formation of acceptable-yielding 2,5-bis(trifluoromethyl)-1,4-bis(tosyl)piperazine **8** during the optimization of ring-opening reaction.[8] Thus, the reaction of **1** using each amount of ^{t}BuOTMS (1.5 equiv) and CsF (1.5 equiv) in DMSO at 80 °C for 24 h furnished several products from which fortunately we separated **8** as a single isomer in 33% yield after decantation repeated several times (Scheme 3).



Scheme 3. Formation of 2,5-bis(CF_3)-1,4-bis(Ts) piperazine under basic conditions.

The structure of **8** was tentatively assigned on the basis of ^{1}H NMR, ^{13}C NMR, ^{19}F NMR, and GC–MS. The final structural determination was established by its X-ray analysis. The ORTEP drawing of **8** is shown in Fig. 1. The X-ray analysis reveals unambiguous proof of the structure and stereochemistry of *trans*-**8**.

We again monitored this interesting reaction process by TLC and GC–MS analysis, which resulted in detection and isolation of the corresponding slightly contaminated acyclic product **9** as a precursor for **8** by column chromatography. The structure of **9** was assigned on the basis of ^{1}H and ^{19}F NMR, and GC–MS analysis.[9] These results let us to propose the following cyclization mechanism in Scheme 4. The deprotonation of **1** with cesium *tert*-butoxide (^{t}BuOCs) generated probably in situ resulted in the transformation to the corresponding anion intermediate **A**. This anion attacks the less hindered carbon of the remaining **1** to generate the corresponding anion intermediate **B**. This intermediate **B** undergoes intramolecular cyclization in a 6-*endo*-*trig* fashion yielding the *trans*-**8**.

3. Conclusion

We have developed the efficient and completely regioselective ring-opening reaction of 2-CF_3-*N*-Ts-aziridine **1** with a wide range of O-, N-, S-, and C-nucleophiles in good to excellent yields under mild conditions, affording α-trifluoromethyl-*N*-tosylmethylamine derivatives, such as 1,2-aminoalcohol, 1,2-diamine, 1,2-aminothiol, and distant secondary amine. We also found the formation of

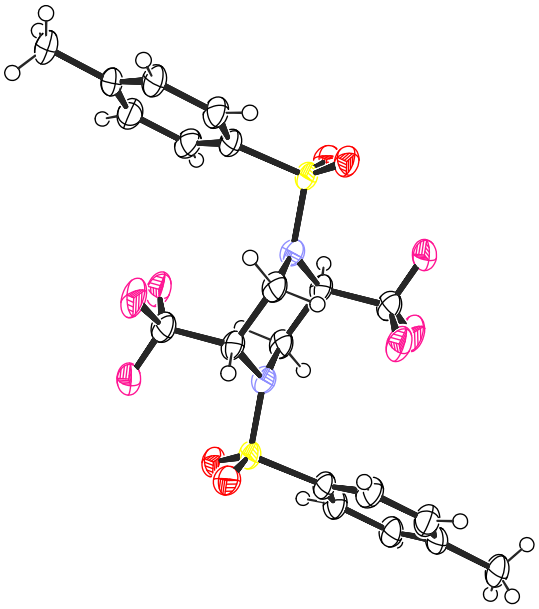


Fig. 1. X-ray crystal structure of **8** with thermal ellipsoids shown at the 50% probability level.

a novel *trans*-2,5-bis(trifluoromethyl)-1,4-bis(tosyl)piperazine **8**. Various α-(trifluoromethyl)methylamine derivatives and **8** would provide additional opportunities for valuable synthetic strategies in the field of organofluorine chemistry.

4. Experimental section

4.1. General information

^{1}H, ^{13}C, and ^{19}F NMR spectra were measured in $CDCl_3$ solutions. Chemical shifts are reported in parts per million using an internal Me_4Si (TMS) for ^{1}H NMR and ^{13}C NMR spectra. Chemical shifts are reported in ppm relative to that of $CFCl_3$ for ^{19}F NMR spectra using an internal $CF_3C_6H_5$ (benzotrifluoride) or C_6F_6. Infrared (IR) spectra are reported in cm^{-1}. Melting points are uncorrected.

4.2. *N*-(1,1,1-Trifluoro-3-(phenylprop-2-ynyloxy)propan-2-yl) toluenesulfonamide (4a)

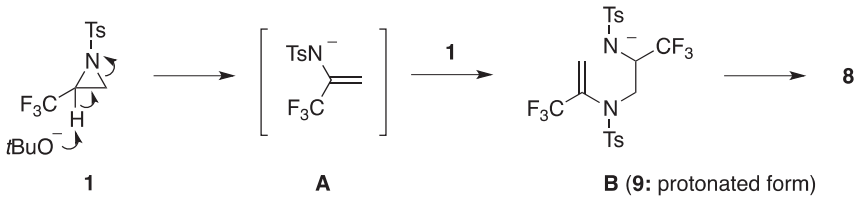
A 25 mL two-necked flask equipped with a magnetic stir bar, a stopcock, and a three-way stopcock, was charged with 3-phenyl-2-propyn-1-ol **2a** (26.0 mL, 0.21 mmol) and ^{t}BuOK (23.4 mg, 0.21 mmol) in DMSO (1 mL). After stirring for 10 min, to this mixture was added 2-CF_3-*N*-Ts-aziridine **1** (50.8 mg, 0.19 mmol) and the mixture was stirred for 1 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The aqueous layer was extracted with hexane/EtOAc=3/1. An additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting oily residue was purified by column chromatography (silica gel, hexane/EtOAc=3/1) to give **4a** as a white solid (61.1 mg, 80%): mp: 84.5–85.9 °C; IR (KBr) 3268, 2970, 2879, 1599, 1333, 1288, 1233, 1036, 968, 694 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76 (d, J=8.8 Hz, 2H), 7.46–7.41 (m, 2H), 7.37–7.32 (m, 3H), 7.26 (s, 2H), 5.34 (d, J=9.5 Hz, 1H), 4.34 (d, J=0.92 Hz, 2H), 4.12–3.98 (m, 1H), 3.83 (dd, J=10.3, 3.1 Hz, 1H), 3.69–3.62 (dm, J=10.3 Hz, 1H), 2.37 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.8, 137.4, 131.8, 129.6, 128.7, 128.3, 127.0, 123.9 (q, J=282.1 Hz), 122.1, 87.4, 83.4, 65.7 (q, J=1.9 Hz), 59.4, 54.4 (q, J=31.1 Hz), 21.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −75.1 (d, J=7.3 Hz); GC–MS m/z 333 (1), 258 (3), 242 (100), 155 (18), 131 (6), 115 (53), 112 (28), 91 (25), 65 (6); Anal. Calcd for $C_{19}H_{18}F_3NO_3S$: C, 57.42; H, 4.57; N, 3.52. Found: C, 57.41; H, 4.52; N, 3.51%.

4.3. *N*-(1,1,1-Trifluoro-3-(prop-2-ynyloxy)propan-2-yl)toluenesulfonamide (4b)

White solid; yield 97%; mp: 122.8–124.5 °C; IR (KBr) 3319, 2970, 2125, 1598, 1384, 1337, 1262, 1146, 1090, 817, 662, 565 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.76 (d, J=8.1 Hz, 2H), 7.30 (d, J=8.1 Hz, 2H), 5.29 (d, J=9.4 Hz, 1H), 4.10 (d, J=2.4 Hz, 2H), 4.12–3.97 (m, 1H), 3.78 (dd, J=10.3, 3.1 Hz, 1H), 3.61 (dd, J=10.3, 2.9 Hz, 1H), 2.45 (d, J=2.4 Hz, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.9, 137.5, 129.6, 127.0, 123.8 (q, J=282.7 Hz), 78.1, 75.7, 65.8 (q, J=1.8 Hz), 58.6, 54.4 (q, J=31.1 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −75.1 (d, J=9.5 Hz); GC–MS m/z 302 (1), 282 (1), 257 (5), 242 (1), 166 (81), 155 (57), 139 (16), 112 (21), 91 (100), 69 (46); Anal. Calcd for $C_{13}H_{14}F_3NO_3S$: C, 48.59; H, 4.39; N, 4.36. Found: C, 48.72; H, 4.35; N, 4.36%.

4.4. *N*-(1,1,1-Trifluoro-3-(but-2-ynyloxy)propan-2-yl)toluenesulfonamide (4c)

White solid; yield 93%; mp: 106.3–107.3 °C; IR (KBr) 3336, 2978, 2925, 2225, 1599, 1377, 1341, 1179, 1142, 1090, 820, 661, 567 cm^{-1}; ^{1}H NMR ($CDCl_3$, 300 MHz) δ 7.78 (d, J=7.9 Hz, 2H), 7.31 (d, J=7.9 Hz, 2H), 5.31 (d, J=9.2 Hz, 1H), 4.14–3.93 (m, 3H), 3.76 (dd, J=10.3, 3.1 Hz, 1H), 3.58 (dm, J=10.3 Hz, 1H), 2.44 (s, 3H), 1.86 (t, J=2.4 Hz, 3H); ^{13}C NMR ($CDCl_3$, 75 MHz) δ 143.8, 137.4, 129.5, 127.0, 123.8 (q, J=282.7 Hz), 83.8, 73.7, 65.4, 59.1, 54.37 (q, J=29.9 Hz), 21.5, 3.4; ^{19}F NMR ($CDCl_3$, 283 MHz) δ −74.8 (d, J=7.1 Hz); GC–MS m/z 271 (11), 252 (3), 207 (4), 180 (93), 155 (91), 139 (29), 112 (39), 91 (100), 65 (22), 53 (41); Anal. Calcd for $C_{14}H_{16}F_3NO_3S$: C, 50.14; H, 4.81; N, 4.18. Found: C, 50.25; H, 4.76; N, 4.15%.



Scheme 4. . Plausible reaction mechanism of formulation of **8**.

4.5. *N*-(1,1,1-Trifluoro-3-(but-3-yn-2-yloxy)propan-2-yl)toluenesulfonamide (4d)

Mixture of diastereomers; white solid; yield 92%; mp: 73.5–75.0 °C; IR (KBr) 3276, 2924, 2113, 1599, 1445, 1330, 1280, 1186, 1153, 813, 675, 563 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79–7.77 (m, 4H), 7.32–7.25 (m, 4H), 5.30 (d, *J*=9.0 Hz, 1H), 5.20 (d, *J*=8.8 Hz, 1H), 4.14–3.98 (m, 4H), 3.93 (dd, *J*=10.1, 3.7 Hz, 1H), 3.81–3.76 (m, 1H), 3.62 (dd, *J*=10.2, 2.8 Hz, 1H), 3.53–3.47 (m, 1H), 2.45–2.40 (m, 8H), 1.39–1.34 (m, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.9, 143.8, 129.7, 129.6, 127.1, 123.9 (q, *J*=282.6 Hz), 123.8 (q, *J*=282.6 Hz), 82.2, 82.1, 74.2, 74.1, 66.1, 65.9, 64.7, 64.6, 64.3, 54.5 (q, *J*=31.2 Hz), 54.4 (q, *J*=30.4 Hz), 21.6, 21.51, 21.49; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.9 (d, *J*=6.8 Hz, 3F), −74.8 (d, *J*=6.8 Hz, 3F); GC–MS *m*/*z* 320 (1), 252 (9), 180 (54), 155 (100), 139 (27), 112 (24), 92 (23), 91 (92), 65 (20), 53 (27); Anal. Calcd for $C_{14}H_{16}F_3NO_3S$: C, 50.14; H, 4.81; N, 4.18. Found: C, 50.21; H, 4.78; N, 4.20%.

4.6. *N*-(1,1,1-Trifluoro-3-(4-hydroxybut-2-ynyloxy)propan-2-yl)toluenesulfonamide (4e)

Colorless oil; yield 46%; IR (neat) 3491, 3278, 2926, 1599, 1447, 1335, 1162, 1019, 815, 665 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, *J*=8.0 Hz, 2H), 7.31 (d, *J*=8.0 Hz, 2H), 5.54 (d, *J*=9.2 Hz, 1H), 4.32 (d, *J*=5.6 Hz, 2H), 4.26–4.07 (m, 2H), 4.26–3.99 (m, 1H), 3.87–3.82 (m, 1H), 3.73–3.69 (m, 1H), 2.43 (s, 3H), 2.38–2.31 (m, 1H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 144.0, 137.2, 129.6, 127.1, 123.8 (q, *J*=282.6 Hz), 86.3, 80.2, 66.0, 59.1, 54.4 (q, *J*=31.2 Hz), 50.8, 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.6 (d, *J*=8.2 Hz); GC–MS *m*/*z* 285 (1), 266 (12), 196 (12), 178 (36), 155 (73), 139 (52), 112 (31), 91 (100), 69 (17), 65 (22); Anal. Calcd for $C_{14}H_{16}F_3NO_4S$: C, 47.86; H, 4.59; N, 3.99. Found: C, 47.73; H, 4.68; N, 3.93%.

4.7. *N*-(1,1,1-Trifluoro-3-(4-(3,3,3-trifluoro-2-(toluenesulfonylamino)-propyloxy)-but-2-ynyloxy)propan-2-yl)toluenesulfonamide (4ee)

Mixture of diastereomers; white solid; yield 52%; mp: 86.1–88.7 °C; IR (KBr) 3270, 2926, 2254, 1927, 1599, 1444, 1277, 1128, 1020, 944, 815, 664 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.79–7.74 (m, 8H), 7.32–7.29 (m, 8H), 5.68 (d, *J*=9.6 Hz, 2H), 5.52 (d, *J*=9.6 Hz, 2H), 4.27–4.10 (m, 8H), 4.10–4.00 (m, 4H), 3.84–3.81 (m, 4H), 3.76–3.70 (m, 4H), 2.43 (s, 12H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.90, 143.86, 129.6, 123.9 (q, *J*=281.9 Hz), 82.42, 82.40, 66.11, 66.06, 58.8, 54.4 (q, *J*=31.1 Hz), 54.3 (q, *J*=31.1 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.7-(-74.5) (m, 6F); GC–MS *m*/*z* 461 (2), 429 (2), 333 (5), 281 (7), 266 (39), 207 (15), 178 (69), 155 (80), 139 (31), 91 (100); Anal. Calcd for $C_{24}H_{26}F_6N_2O_6S_2$: C, 46.75; H, 4.25; N, 4.54. Found: C, 46.93; H, 4.18; N, 4.46%.

4.8. *N*-(1,1,1-Trifluoro-3-(propen-3-yloxy)propan-2-yl)toluenesulfonamide (4f)

White solid; yield 74%; mp: 106.3–107.5 °C; IR (KBr) 3315, 3269, 1598, 1376, 1339, 1244, 1180, 1164, 1143, 1087, 933, 820, 661 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, *J*=8.1 Hz, 2H), 7.31 (d, *J*=8.1 Hz, 2H), 5.85–5.72 (m, 1H), 5.29 (d, *J*=9.1 Hz, 1H), 5.26–5.18 (m, 2H), 4.07–3.95 (m, 1H), 3.93 (d, *J*=5.7 Hz, 2H), 3.67 (dd, *J*=10.3, 2.7 Hz, 1H), 3.48 (ddd, *J*=10.3, 3.1, 1.2 Hz, 1H), 2.44 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.8, 137.5, 133.4, 129.6, 126.9, 123.9 (q, *J*=282.6 Hz), 117.9, 72.3, 65.8, 54.5 (q, *J*=31.2 Hz), 21.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.8 (d, *J*=6.8 Hz); GC–MS *m*/*z* 323 (1, M^+), 284 (1), 266 (33), 207 (5), 168 (35), 155 (100), 132 (18), 112 (32), 91 (99), 71 (13), 65 (21), 63 (4); Anal. Calcd for $C_{13}H_{16}F_3NO_3S$: C, 48.29; H, 4.99; N, 4.33. Found: C, 48.54; H, 4.95; N, 4.38%.

4.9. (*E*)-*N*-(1,1,1-Trifluoro-3-(1-phenylpropen-3-yloxy)propan-2-yl)toluenesulfonamide (4g)

White solid; yield 50%; mp: 128.8–129.1 °C; IR (KBr) 3268, 2970, 2919, 2878, 1599, 1477, 1333, 1288, 1233, 1173, 1036, 968, 812, 754, 694 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, *J*=8.3 Hz, 2H), 7.39–7.25 (m, 7H), 6.54 (d, *J*=15.9 Hz, 1H), 6.14 (dt, *J*=15.9, 6.2 Hz, 1H), 5.43 (d, *J*=9.4 Hz, 1H), 4.06–4.01 (m, 2H), 4.01–3.99 (m. 1H), 3.70 (dd, *J*=10.3, 2.9 Hz, 1H), 3.50 (ddd, *J*=10.3, 2.9, 1.4 Hz, 1H), 2.38 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.9, 137.4, 136.2, 133.6, 129.7, 128.6, 128.0, 127.0, 126.6, 124.4, 123.9 (q, *J*=282.6 Hz), 72.2, 65.9, 54.4 (q, *J*=31.2 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.8 (d, *J*=6.8 Hz); GC–MS *m*/*z* 244 (56), 155 (26), 140 (41), 134 (10), 133 (100), 117 (54), 115 (39), 112 (33), 91 (65), 65 (10); Anal. Calcd for $C_{19}H_{20}F_3NO_3S$: C, 57.13; H, 5.05; N, 3.51. Found: C, 57.14; H, 5.05; N, 3.47%.

4.10. *N*-(1,1,1-Trifluoro-3-(benzyloxy)propan-2-yl)toluenesulfonamide (4h)

White solid; yield 82%; mp: 85.0–85.5 °C; IR (KBr) 3248, 3036, 2950, 2862, 1600, 1333, 1290, 1240, 1180, 1091, 946, 814, 564 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.73 (d, *J*=7.8 Hz, 2H), 7.38–7.30 (m, 3H), 7.28–7.22 (m, 4H), 5.31 (d, *J*=8.4 Hz, 1H), 4.02 (s, 2H), 4.08–3.98 (m, 1H), 3.68 (dd, *J*=10.4, 2.7 Hz, 1H), 3.51–3.45 (m, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.9, 137.4, 136.8, 129.6, 128.5, 128.1, 127.7, 127.0, 124.0 (q, *J*=282.6 Hz), 73.6, 66.1, 54.5 (q, *J*=32.0 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.7 (d, *J*=8.1 Hz); GC–MS *m*/*z* 281 (1), 266 (1), 252 (3), 218 (29), 186 (1), 155 (33), 112 (53), 92 (12), 91 (100), 65 (12); Anal. Calcd for $C_{17}H_{18}F_3NO_3S$: C, 54.68; H, 4.86; N, 3.75. Found: C, 54.73; H, 4.89; N, 3.77%.

4.11. *N*-(1,1,1-Trifluoro-3-(4-methoxybenzyloxy)propan-2-yl)toluenesulfonamide (4i)

White solid; yield 74%; mp: 76.0–76.5 °C; IR (KBr) 3263, 2962, 2914, 2876, 1613, 1513, 1332, 1258, 1175, 1093, 1032, 997, 948, 813, 676, 549 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.72 (d, *J*=7.9 Hz, 2H), 7.26 (d, *J*=7.9 Hz, 2H), 7.16 (d, *J*=8.4 Hz, 2H), 6.88 (d, *J*=8.4 Hz, 2H), 5.30 (d, *J*=9.4 Hz, 1H), 4.39 (s, 2H), 4.03–3.97 (m, 1H), 3.82 (s, 3H), 3.64 (dd, *J*=10.2, 2.9 Hz, 1H), 3.47–3.41 (m, 1H), 2.42 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 159.5, 143.8, 137.4, 129.6, 129.3, 128.8, 127.0, 123.9 (q, *J*=282.6 Hz), 113.9, 73.1, 65.6, 55.2, 54.4 (q, *J*=31.2 Hz), 21.4; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −74.7 (d, *J*=8.1 Hz); GC–MS *m*/*z* 403 (3, M^+), 266 (1), 249 (4), 248 (33), 155 (6), 137 (100), 95 (121), 112 (13), 91 (31), 65 (8); Anal. Calcd for $C_{18}H_{20}F_3NO_4S$: C, 53.59; H, 5.00; N, 3.47. Found: C, 53.36; H, 5.05; N, 3.47%.

4.12. *N*-(1,1,1-Trifluoro-3-(3-methoxyphenyloxy)propan-2-yl)toluenesulfonamide (4j)

White solid; yield 88%; mp: 98.5–100.0 °C; IR (KBr) 3305, 2972, 1618, 1586, 1495, 1341, 1276, 1189, 1156, 972, 858, 818, 758, 676, 571, 545 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, *J*=8.0 Hz, 2H), 7.25 (d, *J*=8.0 Hz, 1H), 7.14 (t, *J*=8.2 Hz, 2H), 6.50 (ddd, *J*=8.2, 2.4, 0.8 Hz, 1H), 6.33 (ddd, *J*=8.2, 2.4, 0.8 Hz, 1H), 6.29 (t, *J*=2.4 Hz, 1H), 5.54 (d, *J*=9.8 Hz, 1H), 4.22 (m, 1H), 4.11 (dd, *J*=10.4, 3.5 Hz, 1H), 4.00–3.97 (m, 1H), 3.76 (s, 3H), 2.40 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 160.8, 158.7, 144.0, 137.3, 130.0, 129.7, 128.0, 124.1 (q, *J*=282.6 Hz), 107.6, 106.4, 101.2, 64.5, 55.3, 54.3 (q, *J*=31.2 Hz), 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.4 (d, *J*=6.8 Hz); GC–MS *m*/*z* 389 (77, M^+), 266 (76), 155 (37), 139 (21), 125 (17), 124 (100), 107 (21), 92 (19), 91 (73), 77 (19); HRMS (FAB, *m*/*z*) Calcd for $C_{17}H_{18}F_3NO_4S$: 389.0909; Found: 389.0923.

4.13. *N*-(1,1,1-Trifluoro-3-(toluenesulfonylamino)propan-2-yl) toluenesulfonamide (5a)

White solid; yield 91%; mp: 152.7–153.7 °C; IR (KBr) 3298, 1598, 1327, 1295, 1251, 1161, 955, 925, 813, 665, 548 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.76 (d, J=8.2 Hz, 2H), 7.70 (d, J=8.2 Hz, 2H), 7.33 (d, J=8.2 Hz, 4H), 5.42 (d, J=9.1 Hz, 1H), 4.88 (t, J=6.4 Hz, 1H), 4.00–3.93 (m, 1H), 3.30–3.20 (m, 1H), 3.20–3.10 (m, 1H), 2.45 (s, 6H); ^{13}C NMR (DMSO-d_6+$CDCl_3$, 101 MHz) δ 141.72, 141.67, 137.2, 135.4, 128.2, 128.1, 125.5, 125.4, 53.4 (q, J=29.6 Hz), 39.9, 20.12, 20.10, CF_3 is obscure; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.1 (d, J=6.9 Hz); GC–MS m/z 302 (1), 282 (1), 257 (5), 242 (1), 166 (81), 155 (57), 139 (16), 112 (21), 91 (100), 69 (46); HRMS (FAB, m/z) Calcd for $C_{17}H_{20}F_3N_2O_4S_2$: 437.0817 (MH^+); Found: 437.0814.

4.14. *N*-(1,1,1-Trifluoro-3-(*N*-phthalimidyl)propan-2-yl)toluenesulfonamide (5b)

White solid; yield 89%; mp: 257.0–257.8 °C; IR (KBr) 3263, 1780, 1720, 1597, 1380, 1351, 1171, 1031, 952, 717, 667, 580, 551 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.80–7.72 (m, 4H), 7.55 (d, J=8.2 Hz, 2H), 6.95 (d, J=8.0 Hz, 2H), 5.27 (d, J=9.2 Hz, 1H), 4.37–4.22 (m, 1H), 3.96–3.85 (m, 2H), 2.13 (s, 3H); ^{13}C NMR (DMSO-d_6, 151 MHz) δ 167.9, 143.3, 138.7, 135.1, 131.5, 123.0, 129.9, 126.0, 124.6 (q, J=283.9 Hz), 53.3 (q, J=29.9 Hz), 36.7, 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −76.4 (d, J=6.8 Hz); GC–MS m/z 257 (57), 239 (3), 219 (1), 160 (100), 155 (7), 133 (6), 104 (6), 91 (19), 77 (8), 65 (6); Anal. Calcd for $C_{18}H_{15}F_3N_2O_4S$: C, 52.43; H, 3.67; N, 6.79. Found: C, 52.31; H, 3.67; N, 6.81%.

4.15. *N*-(1,1,1-Trifluoro-3-(2-pyrrolidonyl)propan-2-yl)toluenesulfonamide (5c)

White solid; yield 87%; mp: 244.0–244.2 °C; IR (KBr) 3087, 2899, 1930, 1651, 1549, 1428, 1345, 1264, 1179, 1130, 959, 821, 665, 570 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.74 (d, J=8.0 Hz, 2H), 7.30 (d, J=8.0 Hz, 2H), 5.78 (d, J=7.6 Hz, 1H), 4.28–4.16 (m, 1H), 3.91 (dd, J=14.2, 10.7 Hz, 1H), 3.51 (dd, J=8.4, 14.3 Hz, 1H), 3.37 (dd, J=8.6, 14.3 Hz, 1H), 3.19 (dd, J=14.2, 3.3 Hz, 1H), 2.42 (s, 3H), 2.39–2.30 (m, 2H), 2.09–1.90 (m, 2H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 175.3, 142.3, 137.9, 128.7, 125.7, 123.3 (q, J=282.6 Hz), 52.3 (q, J=29.6 Hz), 47.2, 40.5, 29.5, 20.5, 16.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −76.1 (d, J=6.8 Hz); GC–MS m/z 350 (1, M^+), 253 (1), 195 (22), 179 (2), 155 (2), 99 (9), 98 (100), 91 (14), 70 (11), 65 (5); Anal. Calcd for $C_{14}H_{17}F_3N_2O_3S$: C, 47.99; H, 4.89; N, 8.00. Found: C, 48.09; H, 4.92; N, 8.09%.

4.16. *N*-(1,1,1-Trifluoro-3-(*N*-indolyl)propan-2-yl)toluenesulfonamide (5d)

White solid; yield 98%; mp: 152.5–153.5 °C; IR (KBr) 3254, 1596, 1466, 1342, 1270, 1249, 1191, 1159, 1129, 948, 725, 569 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.54 (d, J=8.1 Hz, 1H), 7.42 (dd, J=8.2 Hz, 2H), 7.23–7.17 (m, 2H), 7.13–7.04 (m, 1H), 7.06 (d, J=8.2 Hz, 2H), 6.92 (d, J=3.1 Hz, 1H), 6.39 (dd, J=3.1, 0.8 Hz, 1H), 4.89 (d, J=9.4 Hz, 1H), 4.50 (dd, J=14.3, 3.7 Hz, 1H), 4.38–4.26 (m, 2H), 2.35 (s, 3H); ^{13}C NMR (DMSO-d_6, 151 MHz) δ 143.8, 136.3, 135.9, 129.5, 128.8, 128.1, 126.4, 123.0 (q, J=282.6 Hz), 122.3, 121.1, 120.0, 108.7, 102.9, 54.9 (q, J=30.4 Hz), 45.2, 21.5; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.4 (d, J=6.8 Hz); GC–MS m/z 382 (26, M^+), 383 (6), 131 (11), 130 (100), 103 (5), 91 (5), 77 (5); Anal. Calcd for $C_{18}H_{17}F_3N_2O_2S$: C, 56.54; H, 4.48; N, 7.33. Found: C, 56.74; H, 4.57; N, 7.40%.

4.17. *N*-(1,1,1-Trifluoro-3-(dodecanylsulfanyl)propan-2-yl)toluenesulfonamide (6a)

White solid; yield 80%; mp: 63.5–64.5 °C; IR (KBr) 3300, 2924, 2854, 1600, 1453, 1338, 1272, 1175, 1159, 1120, 918, 814, 683 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.75 (d, J=8.0 Hz, 2H), 7.29 (d, J=8.0 Hz, 2H), 5.17 (d, J=8.8 Hz, 1H), 4.10–4.07 (m, 1H), 2.76 (d, J=5.9 Hz, 2H), 2.41 (t, J=14.7 Hz, 2H), 2.41 (s, 3H), 1.52–1.46 (m, 2H), 1.31–1.29 (m, 18H), 0.68 (t, J=6.6 Hz, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.9, 137.5, 129.6, 127.1, 124.2 (q, J=282.6 Hz), 53.9 (q, J=30.4 Hz), 31.9, 31.4, 29.1, 29.2, 29.3, 29.5, 29.5, 29.60, 29.61, 28.7, 22.7, 21.5, 1.41; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.7 (d, J=6.8 Hz); GC–MS m/z 467 (3, M^+), 312 (64), 215 (100), 199 (70), 172 (16), 155 (51), 91 (68); HRMS (FAB, m/z) Calcd for $C_{22}H_{37}F_3NO_2S_2$: 468.2218 (MH^+); Found: 468.2181.

4.18. *N*-(1,1,1-Trifluoro-3-(toluylsulfanyl)propan-2-yl)toluenesulfonamide (6b)

White solid; yield 94%; mp: 94.0–94.5 °C; IR (KBr) 3217, 2926, 1906, 1599, 1493, 1378, 1338, 1274, 1158, 1114, 920, 810, 677, 559 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (d, J=8.5 Hz, 2H), 7.25–7.20 (m, 4H), 7.10 (d, J=7.8 Hz, 2H), 5.50 (d, J=9.0 Hz, 1H), 4.11–4.01 (m, 1H), 3.14 (dd, J=4.3, 14.3 Hz, 1H), 3.08–2.98 (m, 1H), 2.40 (s, 3H), 2.33 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 143.8, 137.8, 137.5, 131.5, 130.1, 130.0, 129.5, 127.0, 124.1 (q, J=282.6 Hz), 54.3 (q, J=31.1 Hz), 34.8, 21.5, 21.0; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −75.8 (d, J=6.8 Hz); GC–MS m/z 389 (50, M^+), 266 (2), 218 (36), 203 (1), 155 (7), 149 (4), 137 (100), 123 (8), 91 (35), 65 (10); Anal. Calcd for $C_{17}H_{18}F_3NO_2S_2$: C, 52.43; H, 4.66; N, 3.60. Found: C, 52.49; H, 4.69; N, 3.64%.

4.19. Dimethyl 2-(3,3,3-trifluoro-2-(toluenesulfonylamino) propyl) malonate (7a)

White solid; yield 65%; mp: 92.0–93.3 °C; IR (KBr) 3283, 2959, 1747, 1599, 1439, 1346, 1269, 1164, 1135, 967, 895, 816, 665 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.71 (d, J=8.2 Hz, 2H), 7.28 (d, J=8.2 Hz, 2H), 5.21 (d, J=9.5 Hz, 1H), 4.16–4.03 (m, 1H), 3.80 (s, 3H), 3.78 (s, 3H), 3.71 (dd, J=8.8, 5.3 Hz, 1H), 2.42 (s, 3H), 2.11–2.01 (m, 2H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 169.4, 168.7, 143.7, 137.3, 129.5, 126.8, 124.3 (q, J=281.8 Hz), 53.7 (q, J=32.0 Hz), 52.9, 52.8, 47.1, 27.8, 21.3; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −77.1 (d, J=6.8 Hz); GC–MS m/z 366 (2), 301 (12), 242 (75), 210 (48), 178 (32), 155 (52), 150 (12), 132 (10), 91 (100), 65 (19), 55 (10); Anal. Calcd for $C_{15}H_{18}F_3NO_6S$: C, 45.34; H, 4.57; N, 3.52. Found: C, 45.23; H, 4.43; N, 3.72%.

4.20. Ethyl 2-(3,3,3-trifluoro-2-(toluenesulfonylamino)propyl)cyanoacetate (7b)

Mixture of diastereomers; colorless oil; yield 81%; IR (neat) 3272, 2987, 2257, 1748, 1599, 1443, 1343, 1266, 1163, 1138, 1094, 816, 665 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.77 (d, J=8.4 Hz, 2H), 7.72 (d, J=8.4 Hz, 2H), 7.35–7.29 (m, 4H), 5.40 (d, J=10.0 Hz, 1H), 5.34 (d, J=10.0 Hz, 1H), 4.40–4.28 (m, J=4H), 4.25–4.10 (m, 1H), 4.10–4.00 (m, 1H), 3.95–3.85 (m, 2H), 2.56–2.48 (m, 1H), 2.44 (s, 6H), 2.39–2.21 (m, 2H), 2.10–2.00 (m, 1H), 1.40–1.31 (m, 6H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 165.2, 165.0, 144.4, 144.3, 136.53, 136.49, 129.83, 129.77, 127.14, 127.06, 124.0 (q, J=281.8 Hz), 123.9 (q, J=282.6 Hz), 63.7, 63.6, 53.4 (q, J=31.9 Hz), 53.2 (q, J=31.9 Hz), 33.6, 31.9, 29.53, 29.52, 21.5, 13.8; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −76.9 (d, J=6.9 Hz, 3F), −76.8 (d, J=6.9 Hz, 3F); GC–MS m/z 378 (12, M^+), 333 (3), 306 (8), 268 (3), 242 (6), 223 (24), 177 (4), 155 (51), 91 (100), 65 (16); Anal. Calcd for $C_{15}H_{17}F_3N_2O_4S$: C, 47.62; H, 4.53; N, 7.40. Found: C, 47.30; H, 4.57; N, 7.16%.

4.21. 4,4,4-Trifluoro-3-(toluenesulfonylamino)-1,1-bis(phenylsulfonyl)butane (7c)

White solid; yield 68%; mp: 178.5–180.0 °C; IR (KBr) 3313, 2926, 1586, 1449, 1332, 1163, 1091, 946, 741, 663, 576 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 8.01 (d, J=8.4 Hz, 2H), 7.92 (d, J=8.3 Hz, 2H), 7.75–7.68 (m, 4H), 7.56 (t, J=7.7 Hz, 4H), 7.31 (d, J=8.2 Hz, 2H), 5.14 (d, J=7.5 Hz, 1H), 5.01 (d, J=10.2 Hz, 1H), 4.23–4.10 (m, 1H), 2.71 (dd, J=7.6, 2.3 Hz, 1H), 2.48–2.40 (m, 1H), 2.43 (s, 3H); ^{13}C NMR ($CDCl_3$, 101 MHz) δ 144.5, 137.5, 136.8, 136.2, 134.9, 134.7, 129.8, 129.6, 129.5, 129.4, 129.2, 127.3, 123.8 (q, J=282.6 Hz), 77.0, 54.3 (q, J=31.2 Hz), 25.0, 21.6; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −77.1 (d, J=7.8 Hz, 3F); GC–MS m/z 406 (10), 350 (4), 264 (100), 155 (32), 143 (32), 141 (24), 125 (72), 91 (82), 77 (61), 65 (15), 51 (11); Anal. Calcd for $C_{23}H_{22}F_3NO_6S_3$: C, 49.19; H, 3.95; N, 2.49. Found: C, 49.29; H, 3.88; N, 2.49%.

4.22. 1,4-Ditosyl-2,5-bis(trifluoromethyl)piperazine (8)

A 25 mL two-necked flask equipped with a magnetic stir bar, a stopcock, and a three-way stopcock, was charged with CsF (27.5 mg, 0.181 mmol). After heating the flask with a heat gun under reduced pressure for 10 min, the mixture allowed to cool to room temperature. To this mixture was added ^{t}BuOTMS (34.8 μL, 0.181 mmol) and DMSO (1 mL) and the mixture warmed to 60 °C for 30 min. To the mixture was added *N*-Ts-2-CF_3-aziridine **1** (32.0 mg, 0.121 mmol) and the mixture warmed to 80 °C for 24 h. The reaction was quenched by the addition of saturated aqueous ammonium chloride solution. The aqueous layer was extracted with EtOAc. An additional extraction was repeated twice. The combined organic solution was dried over Na_2SO_4, filtered, and concentrated in vacuo. The resulting dark brown solid attached on the inner wall of the flask was very carefully washed with hexane/EtOAc=3/1 several times then acetone one time to give **8** as a white solid (10.5 mg, 33%): mp: 274.2–275.8 °C; IR (KBr) 1598, 1384, 1343, 1298, 1248, 1160, 971, 817, 695, 639, 575 cm^{-1}; ^1H NMR ($CDCl_3$, 400 MHz) δ 7.66 (d, J=8.2 Hz, 4H), 7.30 (d, J=8.2 Hz, 4H), 4.59–4.49 (m, 2H), 4.23 (d, J=14.1 Hz, 2H), 3.55 (dd, J=14.1, 3.4 Hz, 2H), 2.43 (s, 6H); ^{13}C NMR (DMSO-d_6, 101 MHz) δ 144.3, 136.2, 130.0, 127.3, 124.6 (q, J=288.0 Hz), 50.1 (q, J=29.6 Hz), 21.2, NCH_2 is obscure; ^{19}F NMR ($CDCl_3$, 376 MHz) δ −70.5 (d, J=6.8 Hz); GC–MS m/z 530 (5, M^+), 461 (4), 429 (2), 375 (53), 355 (3), 306 (10), 281 (10), 207 (20), 155 (100), 91 (97), 65 (14); Anal. Calcd for $C_{20}H_{20}F_6N_2O_4S_2$: C, 45.28; H, 3.80; N, 5.28. Found: C, 45.11; H, 3.70; N, 5.20%.

4.23. Crystal data for 8

($C_{20}H_{20}F_6N_2O_4S_2$): M=530.52, T=143 (2) K, triclinic, space group P−1, a=6.084 (5) Å, b=8.217 (9) Å, c=11.308 (9) Å, V=540.0 (9) $Å^3$, Z=1, Dx=1.631 Mg m^{-3}, m=0.330 mm^{-1}, l=0.71073 Å, q_{max}=27.44°, 5442 measured reflection, 2453 independent reflections, 194 refined parameters, GOF=0.991, $R[F^2>2s(F^2)]$=0.1672, $wR(F^2)$=0.1849. The intensity data were collected on a Rigaku RAXIS-RAPID diffractometer. The structure was solved by direct methods (SIR2004[10]) and the non-hydrogen atoms were refined anisotropically by full-matrix least-squares procedures on F^2 for all reductions (SHELXL97[11]). Some hydrogen atoms were determined by difference Fourier synthesis, and others were positioned geometrically and refined as riding. CCDC-919854 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge via www.ccdc.cam.ac.uk/data_request/cif, or by emailing data_request@ccdc.cam.ac.uk, or by contacting The Cambridge Crystallographic Data Centre, 12, Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336033.

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Supplementary data

Spectral data for new compounds are available. Supplementary data related to this article can be found at http://dx.doi.org/10.1016/j.tet.2013.06.044.

References and notes

1. (a) Ojima, I. *Fluorine in Medicinal Chemistry and Chemical Biology*; Wiley-Blackwell: Chichester, UK, 2009; (b) Bégué, J. P.; Bonnet-Delpon, D. *Bioorganic and Medicinal Chemistry of Fluorine*; Wiley-Interscience: Hoboken, NJ, 2008; (c) Uneyama, K. *Organofluorine Chemistry*; Blackwell: Oxford, UK, 2006; (d) Chambers, R. D. *Fluorine in Organic Chemistry*; Blackwell: Oxford, UK, 2004; (e) Hiyama, T. *Organofluorine Compounds*; Springer: New York, NY, 2000.
2. For recent examples: (a) Yasu, Y.; Koike, T.; Akita, M. *Angew. Chem., Int. Ed.* **2012**, *51*, 9567–9571; (b) Zhang, X.-G.; Dai, H.-X.; Wasa, M.; Yu, J.-Q. *J. Am. Chem. Soc.* **2012**, *134*, 11948–11951; (c) Besset, T.; Schneider, C.; Cahard, D. *Angew. Chem., Int. Ed.* **2012**, *51*, 5048–5050; (d) Wu, X.-F.; Neumann, H.; Beller, M. *Chem.—Asian J.* **2012**, *7*, 1744–1754; (e) Morandi, B.; Carreira, E. M. *Angew. Chem., Int. Ed.* **2011**, *50*, 9085–9088; (f) Pham, P. V.; Nagib, D. A.; MacMillan, D. W. C. *Angew. Chem., Int. Ed.* **2011**, *50*, 6119–6122; (g) Kowalczyk, R.; Edmunds, A. J. F.; Hall, R. G.; Bolm, C. *Org. Lett.* **2011**, *13*, 768–771.
3. (a) Schweitzer-Chaput, B.; Keita, M.; Milcent, T.; Ongeri, S.; Crousse, B. *Tetrahedron* **2012**, *68*, 7028–7034; (b) Katagiri, T.; Katayama, Y.; Taeda, M.; Ohshima, T.; Iguchi, N.; Uneyama, K. *J. Org. Chem.* **2011**, *76*, 9305–9311; (c) Palacios, F.; Ochoa, A.; Alonso, J. *J. Org. Chem.* **2006**, *71*, 6141–6148; (d) Rinaudo, G.; Narizuka, S.; Askari, N.; Crousse, B.; Bonnet-Delpon, D. *Tetrahedron Lett.* **2006**, *47*, 2065–2068; (e) Yamauchi, Y.; Kawate, T.; Katagiri, T.; Uneyama, K. *Tetrahedron* **2003**, *59*, 9839–9847; (f) Yamauchi, Y.; Kawate, T.; Itahashi, H.; Katagiri, T.; Uneyama, K. *Tetrahedron Lett.* **2003**, *44*, 6319–6322; (g) Davoli, P.; Forni, A.; Franciosi, C.; Moretti, I.; Prati, F. *Tetrahedron: Asymmetry* **1999**, *10*, 2361–2371.
4. (a) Rao, R. K.; Karthikeyan, I.; Sekar, G. *Tetrahedron* **2012**, *68*, 9090–9094; (b) Grellepois, F.; Nonnenmacher, J.; Lachaud, F.; Portella, C. *Org. Biomol. Chem.* **2011**, *9*, 1160–1168; (c) Rao, R. K.; Naidu, A. B.; Sekar, G. *Org. Lett.* **2009**, *11*, 1923–1926; (d) Ding, C.-H.; Dai, L.-X.; Hou, X.-L. *Tetrahedron* **2005**, *61*, 9586–9593; (e) Crousse, B.; Narizuka, S.; Bonnet-Delpon, D.; Bégué, J.-P. *Synlett* **2001**, 679–681; (f) Katagiri, T.; Takahashi, M.; Fujiwara, Y.; Ihara, H.; Uneyama, K. *J. Org. Chem.* **1999**, *64*, 7323–7329; (g) Katagiri, T.; Ihara, H.; Takahashi, M.; Kashino, S.; Funuhashi, K.; Uneyama, K. *Tetrahedron: Asymmetry* **1997**, *8*, 2933–2937; (h) Quinze, K.; Mison, A. *J. Fluorine Chem.* **1989**, *44*, 233–265.
5. (a) Maeda, R.; Ishibashi, R.; Kamaishi, R.; Hirotaki, K.; Furuno, H.; Hanamoto, T. *Org. Lett.* **2011**, *13*, 6240–6243; (b) Maeda, R.; Ooyama, K.; Anno, R.; Shiosaki, M.; Azema, T.; Hanamoto, T. *Org. Lett.* **2010**, *12*, 2548–2550.
6. Wang, L.; Liu, Q.-B.; Wang, D.-S.; Li, X.; Han, X.-W.; Xiao, W.-J.; Zhou, Y.-G. *Org. Lett.* **2009**, *11*, 1119–1122.
7. Compared with the reactivity of the corresponding 2-isopropyl-N-Ts aziridine with a propargyl alcohol under basic conditions, that of 2-trifluoromethyl-N-Ts aziridine **1** is relatively high. See Ref. 6 in SD.
8. (a) Trinchera, P.; Musio, B.; Degennaro, L.; Moliterni, A.; Falcicchio, A.; Luisi, R. *Org. Biomol. Chem.* **2012**, *10*, 1962–1965; (b) Shainyan, B. A.; Moskalik, M. Y.; Starke, I.; Schilde, U. *Tetrahedron* **2010**, *66*, 8383–8386.
9. In the GC–MS spectrum of the crude reaction mixture that contained **9**, a major peak appeared at m/z=375 (M^+–Ts), M=530 ($C_{20}H_{20}F_6N_2O_4S_2$). The crude ^1H NMR spectrum showed two vinyl proton signals at 6.21 (s, 1H) and 6.14–6.12 (m, 1H), respectively. The crude ^{19}F NMR displayed two CF_3 signals at −66.2 (s, 3F) and −75.7 (d, J=6.8 Hz, 3F), respectively.
10. Burla, M. C.; Caliandro, R.; Camalli, M.; Carrozzini, B.; Cascarano, G. L.; De Caro, L.; Giacovazzo, C.; Polidori, G.; Spagna, R. *J. Appl. Crystallogr.* **2005**, *38*, 381–388.
11. Sheldrick, G. M. SHELXL-97, Program for Refinement of Crystal Structures; University of Göttingen, 1997.