JOC Article

Facile Preparation of β-Fluoro Amines by the Reaction of Aziridines with Potassium Fluoride Dihydrate in the Presence of Bu_4NHSO_4

Ren-Hua Fan,[†] Yong-Gui Zhou,[‡,§] Wan-Xuan Zhang,[‡] Xue-Long Hou,*[,†,‡] and Li-Xin Dai[‡]

State Key Laboratory of Organometallic Chemistry and Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, 354 Fenglin Road, Shanghai 200032, China

xlhou@mail.sioc.ac.cn

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Potassium fluoride combined with tetrabutylammonium bisulfate is an efficient reagent to convert a variety of aziridines derived from cyclic and acyclic alkenes to β-fluoro amine derivatives in high yield.

Introduction

Organic compounds with low fluorine content have received much interest because of their physiological properties.[1] Among them, β-fluoro amines exhibit biological activity on the central nervous system.[2] Although many procedures have been developed to introduce fluorine atom into organic molecules,[3] reports on the preparation of such β-fluoro amines is rare because of the reactivity of most fluorinating reagents toward the amino group.[4] Since functionalized aziridines are now easily accessible,[5] the ring-opening reaction of them with fluoride should be the most convenient route to β-fluoro amines.[6] Indeed, some reports appeared using hydrogen fluoride, hydrogen fluoride−pyridine (Olah's reagent),[7] and diethylaminosulfur trifluoride (DAST).[8] However, all of these reagents have suffered from the fact that they are highly toxic and corrosive to glass, so some special care was needed. In addition, the acidity of Olah's reagent would cause the rearrangement of some aziridines.[9] On the other hand, alkali metal fluorides, as well as their modifications, such as KF/18-crown-6,[10] polymer-supported fluoride,[11] "spray-dried" KF,[12] calcium fluoride supported on alkali metal fluoride,[13] and $Bu_4NH_2F_3$,[14] have also been applied as fluorination reagents, but none of them was reported to be used in the ring-opening reaction of aziridines. In the course of our studies on the synthesis and transformations of aziridines,[15b,16] β-fluoro amine derivative was detected from the reaction of aziridines with allyltrimethylsilane in the presence of tetrabutylammonium fluoride (TBAF). Further studies showed that potassium fluoride dihydrate ($KF·2H_2O$) combined with tetrabutylammonium bisulfate[17] is a more efficient reagent for the ring-opening reaction of aziri-

* Corresponding author.
[†] Shanghai-Hong Kong Joint Laboratory in Chemical Synthesis, Shanghai Institute of Organic Chemistry.
[‡] State Key Laboratory of Organometallic Chemistry, Shanghai Institute of Organic Chemistry.
[§] Permanent address: Dalian Institute of Chemical Physics, Chinese Academy of Sciences, 457 Zhongshan Road, Dalian, Liaoning 116230, P. R. China.

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SCHEME 1

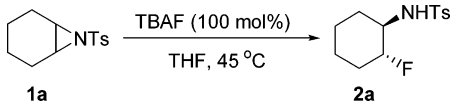
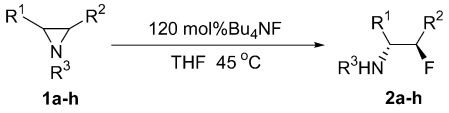


TABLE 1. Ring Opening of Aziridine with TBAF[a]



Entry	Substrate		Product		Yield (%)[b]
1	NTs	**1a**	NHTs, F	**2a**	99
2	NBs	**1b**	NHBs, F	**2b**	97
3	NCOPh	**1c**	NHCOPh, F	**2c**	79
4	NTs	**1d**	NHTs, F	**2d**	94
5	NTs	**1e**	NHTs, F	**2e**	87
6	NPh	**1g**	-		No reaction
7	NCH_2Ph	**1h**	-		No reaction

[a] All reactions were conducted in THF at 45 °C under Ar. [b] Isolated yield.

dines to give rise to β-fluoro amine derivatives. In this paper, we present an efficient method for the synthesis of β-fluoro amines under mild conditions from the ring-opening reactions of aziridines with $KF{\cdot}2H_2O$ in the presence of Bu_4NHSO_4.

Results and Discussion

In our previous work,[15] Bu_4NF (TBAF) was found as a good trigger for the reactions of imines or aziridines with trimethylsilyl compounds. However, when we tried the reaction of aziridine **1a** with allyltrimethylsilane in the presence of 10 mol % Bu_4NF in THF, no expected allylation product was obtained; instead, an unexpected β-fluoro amine **2a** was isolated in 9% yield. When the amount of Bu_4NF was increased to 120 mol %, 99% yield of **2a** was provided (Scheme 1).

To show the capacity of TBAF and the scope of the reaction, many different types of aziridines were examined, and the results are shown in Table 1. It can be seen that the reactions proceeded with activated aziridines **1a**−**f** to give rise to the corresponding β-fluoro amines in high yields, but no reaction occurred when the non-activated aziridines **1g** and **1h** were the starting material.

Our previous studies on the mechanism of the reactions of aziridines with trimethylsilyl compounds triggered by TBAF showed that tetrabutylammonium cation (Bu_4N^+) played an important role in the reactions.[15b] Thus, several tetrabutylammonium salts (Bu_4NX, X = Cl, Br, and I) were added into the reaction of aziridine **1a** with KF, but the X^- attacked products were obtained. These results suggested that the selection of counterion of quaternary ammonium salt with less nucleophilicity is important in order to avoid the formation of undesired products. Thus, Bu_4NHSO_4 (TBAHS) and Bu_4NNO_3 were chosen.[18]

In the presence of 100 mol % of Bu_4NHSO_4, the reaction of aziridine **1a** with $KF{\cdot}2H_2O$ in THF provided product **2a** in 64% yield. The optimization of the reaction conditions showed that CH_3CN is the best solvent, in which the yield increased to 96%, but no product was detected if anhydrous KF and Bu_4NHSO_4 in CH_3CN were used as reagent. With the decrease of the amount of Bu_4NHSO_4 to 10 mol %, the yield of product was also dropped to 8%. However, when 1 equiv of Bu_4NNO_3 was used, only 23% yield was obtained under the same reaction conditions. No reaction occurred in the presence of 1 equiv of $NaHSO_4$, but the reaction proceeded slowly to provide product **2a** in 56% yield if 1 equiv of Bu_4NNO_3 was added into the above reaction mixture.

Table 2 illustrates that the ring-opening reactions of activated and nonactivated aziridines derived from a variety of kind of cyclic alkenes with $KF{\cdot}2H_2O$ in the presence of Bu_4NHSO_4 to provide the corresponding β-fluoro amines in moderate to high yields. The substituent on nitrogen atom of aziridines can be Ts, Bz, Bs, Ph, and Bn. In the case of aziridine **1f** (entry 6, Table 2), only one product was obtained. To the reaction of *N*-benzoylaziridine **1c**, no corresponding rearrangement product oxazolidones, which would be formed using Olah's reagent**,** were detected (entry 3, Table 2).[9]

It is unexpected that the reactions of aziridines derived from acyclic alkenes **1i** and **1j** were very complex under the same conditions (entries 9 and 10, Table 2), and no corresponding β-fluoro amines could be separated from the mixtures. Some isolated compounds showed the presence of the skeleton of aziridine and fluorine atom, but their ^1H NMR spectra were too complex to determine their structure. The reaction also failed to provide β-fluoro amine using some other fluoride sources, for example, Bu_4NF, CsF, LiF, and NaF, in different solvents, such as DMF, DMSO, EtOAc, and *t*-BuOH.

It is interesting, however, that the addition of water as cosolvent made the fluorination reaction of aziridine **1i** proceed smoothly. Whereas the reactions were very complex in pure CH_3CN, this reaction occurred at 50 °C with the addition of 33% (v/v) water to the mixture, and β-fluoro amines **2i** and **3i** were formed in 36% yield with the hydrolysis product as byproduct in 60% yield. Further experiments showed that the amount of water was vital

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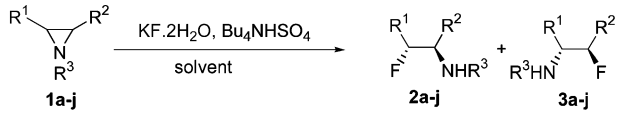
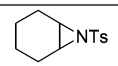
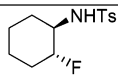
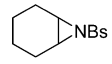
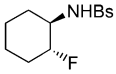
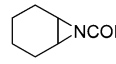
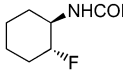
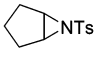
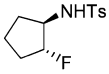
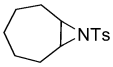
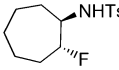
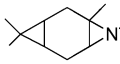
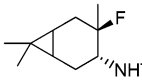
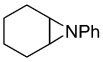
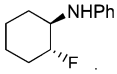
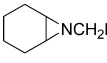
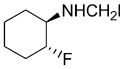
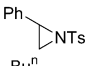
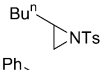
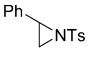
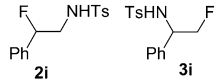
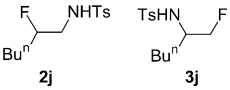
TABLE 2. Ring Opening of Aziridines with KF·2H$_2$O in the Presence of Bu$_4$NHSO$_4$



Entry	Substrate		Condition [b]	Product		Yield (%)[c]
1		**1a**	**A**		**2a**	96
2		**1b**	**A**		**2b**	95
3		**1c**	**A**		**2c**	91
4		**1d**	**A**		**2d**	85
5		**1e**	**A**		**2e**	85
6		**1f**	**A**		**2f**	76[e]
7		**1g**	**A**		**2g**	61
8		**1h**	**A**		**2h**	75
9		**1i**	**A**	-		Complex
10		**1j**	**A**	-		Complex
11		**1i**	**B**	 **2i** **3i**		78 (82:18)[d]
12		**1j**	**B**	 **2j** **3j**		74 (14:86)[d]

[a] Ts = *p*-CH$_3$C$_6$H$_4$SO$_2$, Bs = C$_6$H$_5$SO$_2$, Bz = C$_6$H$_5$CO; [b] Condition A = 100 mol % Bu$_4$NHSO$_4$, 200 mol % KF·2H$_2$O, CH$_3$CN, 45 °C. Condition B = 200 mol % Bu$_4$NHSO$_4$, 400 mol % KF·2H$_2$O, CH$_3$CN/H$_2$O (v/v) = 3:1, 30 °C. [c] Isolated yield. [d] Ratios of the two regioisomers was determined by 300 MHz ^{1}H NMR. [e] No other regioisomer was detected.

to the reaction. When the ratio of H$_2$O to CH$_3$CN decreased to 1:6, the reaction was as complex as that in CH$_3$CN. When the ratio increased to 1:2, only hydrolysis product was obtained. The reaction proceeded more slowly at 35 °C, but β-fluoro amines became the major products in 45% yield after 7 days. With the use of 2 equiv of Bu$_4$NHSO$_4$ and 4 equiv of KF·2H$_2$O, the yield of β-fluoro amines increased to 65% at 35 °C after 7 days. Under a lower temperature (30 °C) and a longer reaction time (10 days), 78% yields of β-fluoro amines were obtained.

Under the optimized conditions (condition **B**) in Table 2, the reactions of aziridines **1i** and **1j** derived from the acyclic terminal alkenes proceeded smoothly to afford the corresponding β-fluoro amines in good yields with minimal byproducts. The phenyl-substituted aziridine **1i** led to the formation of two regioisomers, incorporating the fluoride at the phenyl-substituted carbon as the major product, which reflected the expected competition of opening pathways for this type of aziridine.[19] However, for the alkyl-substituted aziridine **1j**, two products **2j** and **3j** were formed in a ratio of 14:86, resulting from fluoride attack at the less substituted carbon atom of the aziridine.

The ^{19}F NMR gave the signal at −148 ppm for KF·2H$_2$O/TBAHSO$_4$ in CH$_3$CN/H$_2$O (v/v = 3:1) and −156 ppm for KF·2H$_2$O/TBAHSO$_4$ in CH$_3$CN, whereas KF·2H$_2$O in CH$_3$CN/H$_2$O (v/v = 3:1) gave the signal at −120 ppm. These data are close to that for Bu$_4$NHF$_2$, Bu$_4$NH$_2$F$_3$, and Bu$_4$NF, which gave the signal at −145, −160, and −120 ppm, respctively.[20] Landini reported the synthesis of Bu$_4$NF, Bu$_4$NHF$_2$, and Bu$_4$NH$_2$F$_3$ using Bu$_4$NHSO$_4$ and KF and a stoichiometric amount of KHF$_2$ or excess KH$_2$F$_3$, respectively,[20] and the ring-opening reaction of epoxides with Bu$_4$NH$_2$F$_3$.[14] However, only 30% and 42% yield of ring opening product **2a** as well as 68% and 55% recovery of starting material **1a** were provided when the reaction proceeded in CH$_3$CN at 45 °C using Bu$_4$NHF$_2$ and Bu$_4$NH$_2$F$_3$ as reagent, respectively. Also, only a trace of fluorinated product was detected if aziridine **1e** reacted with Bu$_4$NHF$_2$ or Bu$_4$NH$_2$F$_3$ under the same conditions. Even the reaction of aziridine **1j** with Bu$_4$NHF$_2$ in CH$_3$CN/H$_2$O with a ratio of 3:1 as solvent gave only 12% yield of **2j** and **3j** as well as 4% yield of hydrolysis product and 78% recovery of **1j**; if Bu$_4$NH$_2$F$_3$ was used under the same conditions, a trace of products was detected. Thus, the role of HSO_4^- and water is not clear at moment.

In conclusion, a facile and convenient approach to formation of the β-fluoro amines via ring-opening reactions of aziridines using KF·2H$_2$O in the presence of Bu$_4$NHSO$_4$ under neutral conditions was devised. It is a mild, economic, and environmentally benign process. Further investigations of the reaction mechanism as well as the reactions using other kinds of substrates are in progress.

Experimental Section

General Experimental Conditions. The commercially available reagents were used as received without further purification.[21] Melting points are uncorrected. ^{1}H NMR and ^{19}F NMR spectra were recorded on 300 and 282 MHz spectrometers, and the chemical shifts were referenced to tetramethylsilane, CF$_3$COOH, and CFCl$_3$ in CDCl$_3$. IR spectra were measured in cm^{-1}.

General Procedure for Ring-Opening Reactions of Aziridines 1 with Bu$_4$NF. To a stirred solution of aziridine **1** (0.5 mmol) in THF (2.0 mL) was added Bu$_4$NF (1 M in THF, 0.6 mL, 0.6 mmol), and the resulting mixture was stirred at 45 °C until complete consumption of the substrate (monitored by TLC). The solvent was removed in a vacuum, and the crude product was purified by flash column chromatography to provide the corresponding product.

General Procedure for Ring-Opening Reactions of Aziridines 1 with KF·2H$_2$O in the Presence of Bu$_4$NHSO$_4$. Procedure A. To a stirred solution of aziridine **1** (0.5 mmol) and KF·2H$_2$O (94 mg, 1 mmol) in CH$_3$CN (2.0 mL) was added Bu$_4$NHSO$_4$ (170 mg, 0.5 mmol), and the resulting mixture was stirred at 45 °C until complete consumption of the substrate

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(20) Landini, D.; Molinari, H.; Penso, M.; Rampoldi, A. *Synthesis* **1988**, 953.

(21) Bu$_4$NF in THF solution was purchased from Aldrich, Bu$_4$NHSO$_4$ (>98%) was purchased from TCI, and KF·2H$_2$O (>99%) was purchased from The Third Factory, Shanghai Chemical Reagent Co. Ltd., China.

(monitored by TLC). The solvent was removed in a vacuum, and the crude product was purified by flash column chromatography to provide the corresponding product.

Procedure B. To a stirred solution of aziridine **1** (0.5 mmol) and KF·2H_2O in the mixture of organic solvent with water was added Bu_4NHSO_4, and the resulting mixture was stirred at the corresponding temperature until complete consumption of substrate (monitored by TLC). The mixture was extracted CH_2Cl_2 (2 × 5 mL), and then the solvent was removed in a vacuum and the crude product was purified by flash column chromatography to provide the corresponding product.

***N*-(2-Fluorocyclohexyl)-4-methylbenzenesulfonamide (2a):** 96% yield; solid; mp 95−97 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.05−1.25 (m, 4H), 1.26−1.44 (m, 1H), 1.45−1.62 (m, 1H), 1.87−2.08 (m, 2H), 2.38 (s, 3H), 3.02−3.21 (m, 1H), 4.06 and 4.23 (double multiplet, $^2J_{H-F}$ = 50.1 Hz, 1H), 5.03 (d, J = 6.1 Hz, 1H), 7.22 (d, J = 8.6 Hz, 2H). 7.71 (d, J = 7.9 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −178.8 (double multiplet, $^2J_{H-F} \cong$ 50.2 Hz); IR (film) $\tilde{\nu}$ = 3304, 2951, 1598, 1496 cm^{-1}; EI-MS m/z 271 (M^+, 37), 210 (100), 155 (67). Anal. Calcd for $C_{13}H_{17}FNO_2S$: C, 57.54; H, 6.69; N, 5.16. Found: C, 57.49; H, 6.73; N, 4.96.

***N*-(2-Fluorocyclohexyl)benzenesulfonamide (2b):** 95% yield; solid; mp 105−107 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.13−1.29 (m, 4H), 1.32−1.52 (m, 1H), 1.71−1.76 (m, 1H), 2.04−2.15 (m, 2H), 3.20−3.28 (m, 1H), 4.21 (dddd, $^2J_{H-F}$ = 50.1 Hz, $^3J_{H-H}$ = 9.9, 9.0, 4.5 Hz, 1H), 4.90 (d, J = 5.7 Hz, 1H), 7.51−7.60 (m, 3H), 7.90−7.93 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −178.5 (d, $^2J_{H-F}$ = 49.1 Hz); IR (film) $\tilde{\nu}$ = 3262, 2943, 1459, 1329 cm^{-1}; EI-MS m/z 257 (M^+, 36). Anal. Calcd for $C_{12}H_{15}FNO_2S$: C, 56.01; H, 6.27; N, 5.44. Found: C, 56.07; H, 6.44; N, 5.31.

***N*-(2-Fluorocyclohexyl)benzamide (2c):** 91% yield; solid; mp 154−156 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.20−1.50 (m, 2H), 1.52−1.91 (m, 4H), 2.13−2.34 (m, 2H), 4.09−4.16 (m, 1H), 4.40 (ddt, $^2J_{H-F}$ = 50.1 Hz, $^3J_{H-H}$ = 4.8, 9.6 Hz, 1H), 6.16 (br, 1H), 7.41−7.75 (m, 3H), 7.76−7.79 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −179.0 (double multiplet, $^2J_{H-F} \cong$ 52.1 Hz); IR (film) $\tilde{\nu}$ = 3309, 3032, 1632, 1537 cm^{-1}; EI-MS m/z 221 (M^+, 0.26), 201 (40), 105 (100). Anal. Calcd for $C_{13}H_{16}FNO$: C, 70.56; H, 7.29; N, 6.33. Found: C, 70.47; H, 7.27; N, 6.16.

***N*-(2-Fluorocyclopentyl)-4-methylbenzenesulfonamide (2d):** 85% yield; solid; mp 75−77 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.35−1.42 (m, 1H), 1.61−2.09 (m, 5H), 2.41 (s, 3H), 3.56−3.68 (m, 1H), 4.71 (d, J = 6.1 Hz, 1H), 4.78 and 4.96 (double multiplet, $^2J_{H-F}$ = 51.9 Hz, 1H), 7.32 (d, J = 7.5 Hz, 2H), 7.78 (d, J = 7.6 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −175.9 (double multiplet, $^2J_{H-F} \cong$ 56.6 Hz); IR (film) $\tilde{\nu}$ = 3265, 3029, 1597, 1326 cm^{-1}; EI-MS m/z 257 (M^+, 21), 210 (52), 155 (51), 91 (100). Anal. Calcd for $C_{12}H_{15}FNO_2S$: C, 56.01; H, 6.27; N, 5.44. Found: C, 56.11; H, 6.24; N, 5.35.

***N*-(2-Fluorocycloheptyl)-4-methylbenzenesulfonamide (2e):** 85% yield; solid; mp 64−66 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.35−1.71 (m, 7H), 1.73−1.98 (m, 3H), 2.42 (s, 3H), 3.31−3.38 (m, 1H), 4.32 (ddt, $^2J_{H-F}$ = 47.8 Hz, $^3J_{H-H}$ = 3.9, 7.3 Hz, 1H), 4.95 (d, J = 6.1 Hz, 1H), 7.29 (d, J = 8.1 Hz, 2H), 7.76 (d, J = 8.5 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −169.9 (double multiplet, $^2J_{H-F} \cong$ 47.9 Hz); IR (film) $\tilde{\nu}$ = 3265, 3066, 2937, 1898 cm^{-1}; EI-MS m/z 285 (M^+, 20), 210 (100), 155 (78). Anal. Calcd for $C_{14}H_{19}FNO_2S$: C, 58.92; H, 7.06; N, 4.91. Found: C, 59.20; H, 6.98; N, 4.82.

***N*-(4-Fluoro-4,7,7-trimethylbicyclo[4.1.0]hept-3-yl)-4-methylbenzenesulfonamide (2f):** 76% yield; solid; mp 130−132 °C; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 0.63−0.76 (m, 3H), 0.90 (s, 3H), 0.99 (s, 3H), 1.02−1.22 (m, 1H), 1.28 (d, $^3J_{F-H}$ = 7.5 Hz, 3H), 1.86−1.91 (m, 1H), 2.07−2.22 (m, 1H), 3.42−3.57 (m, 1H), 4.52 (d, J = 9.0 Hz, 1H), 7.32 (d, J = 8.1 Hz, 2H), 7.79 (d, J = 8.4 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −128.1 (m); IR (film) $\tilde{\nu}$ = 3260, 3017, 1598, 1463 cm^{-1}; EI-MS m/z 326 (MH^+, 2.3), 306 (32), 91 (100). Anal. Calcd for $C_{17}H_{24}FNO_2S$: C, 62.74; H, 7.43; N, 4.30. Found: C, 62.96; H, 7.41; N, 4.15.

(2-Fluorocyclohexyl)phenylamine (2g): 61% yield; liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.21−1.56 (m, 3H), 1.60−1.73 (m, 2H), 1.81−1.86 (m, 1H), 2.10−2.25 (m, 2H), 3.35−3.48 (m, 1H), 3.64−3.75 (m, 1H), 4.37 (dddd, $^2J_{H-F}$ = 50.1 Hz, J_{H-H} = 9.9, 9.0, 4.5 Hz, 1H), 6.67−6.74 (m, 3H), 7.15−7.28 (m, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −178.4 (double multiplet, $^2J_{H-F} \cong$ 52.1 Hz); IR (film) $\tilde{\nu}$ = 3421, 1603, 1511 cm^{-1}; EI-MS m/z 193 (M^+, 57), 132 (100). Anal. Calcd for $C_{14}H_{19}FNO_2S$: C, 74.58; H, 8.74; N, 7.25. Found: C, 74.88; H, 8.98; N, 7.03.

Benzyl(2-fluorocyclohexyl)amine (2h): 75% yield; liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 1.05−1.42 (m, 3H), 1.44−1.55 (m, 1H), 1.63−1.70 (m, 1H), 1.72−1.78 (m, 1H), 2.00−2.12 (m, 2H), 2.62−2,74 (m, 1H), 3.77 (d, J = 13.2 Hz, 1H), 3.90 (d, J = 12.9 Hz, 1H), 4.34 (dddd, $^2J_{H-F}$ = 50.4 Hz, J_{H-H} = 11.1, 9.0, 4.8 Hz, 1H), 7.21−7.34 (m, 5H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −179.0 (double multiplet, $^2J_{H-F} \cong$ 51.0 Hz); IR (film) $\tilde{\nu}$ = 3331, 1604, 1496 cm^{-1}; EI-MS m/z 207 (M^+, 25), 146 (55), 91 (100). Anal. Calcd for $C_{14}H_{19}FNO_2S$: C, 75.33; H, 8.95; N, 6.88. Found: C, 75.12; H, 9.19; N, 7.12.

***N*-(2-Fluoro-2-phenylethyl)-4-methylbenzenesulfonamide (2i) and *N*-(2-Fluoro-1-phenylethyl)-4-methylbenzenesulfonamide (3i):** 78% yield (**2i**/**3i** = 82:18); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ 2.35 (s, 3H, **3i**), 2.38 (s, 3H, **2i**), 3.21−3.51 (m, 2H, **2i**), 4.41−4.45 (m, 1H, **3i**), 4.55−4.63 (m, 2H, **3i**), 4.82−4.87 (m, 1H, **2i**), 5.17 (d, J = 6.0 Hz, 1H, **3i**), 5.48 (ddd, $^2J_{F-H}$ = 48.3 Hz, J_{H-H} = 8.4, 3.6 Hz, 1H, **2i**), 7.11−7.40 (m, 7H), 7.58−7.61 (m, 2H, **3i**), 7.70−7.80 (m, 2H, **2i**); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −183.2 (double multiplet, $^2J_{H-F} \cong$ 48.5 Hz, **2i**), −223.5 (m, **3i**); IR (film) $\tilde{\nu}$ = 3303, 1599, 1328 cm^{-1}; EI-MS m/z 294 (MH^+, 1), 293 (M^+, 1), 260 (38), 155 (100). Anal. Calcd for $C_{19}H_{23}NSO_3$: C, 61.41; H, 5.50; N, 4.77. Found: C, 61.23; H, 5.46; N, 4.51.

***N*-(1-Fluoromethylpentyl)-4-methylbenzenesulfonamide (2j) and *N*-(2-Fluorohexyl)-4-methylbenzenesulfonamide (3j)**: 74% yield (**2j**/**3j** = 14:86); liquid; ^{1}H NMR (300 MHz, $CDCl_3$, 25 °C, TMS) δ = 0.80 (t, J = 6.9 Hz, 3H, **3j**), 0.89 (t, J = 7.2 Hz, 3H, **2j**), 1.14−1.32 (m, 6H), 2.44 (s, 3H), 2.98−3.35 (m, 2H, **2j**), 3.41−3.50 (m, 1H, **3j**), 4.28 (ddd, $^2J_{F-H}$ = 46.8 Hz, J_{H-H} = 9.6, 3.6 Hz, 2H, **3j**), 4.50−4.85 (m, 1H, **2j**), 4.71 (d, J = 8.5 Hz, 1H, **3j**), 4.75−4.79 (m, 1H, **2j**), 7.32 (d, J = 8.0 Hz, 2H), 7.78 (d, J = 8.0 Hz, 2H); ^{19}F NMR (282 MHz, $CDCl_3$, 25 °C, CF_3COOH) δ −186.3 (m, **2j**), −230.5 (m, **3j**); IR (film) $\tilde{\nu}$ = 3279, 1599, 1496 cm^{-1}; EI-MS m/z 273 (M^+, 1), 240 (73), 91 (100). Anal. Calcd for $C_{19}H_{23}NSO_3$: C, 57.12; H, 7.37; N, 5.12. Found: C, 57.33; H, 7.53; N, 4.88.

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