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Stereoselective fluorination of methylenecyclopropanes with *N*-F reagents: A modular entry to γ-fluorohomoallylic sulfonimides and γ-fluorohomoallylic amides

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ABSTRACT

A convenient and efficient method for fluorination of methylenecyclopropanes is reported. This is exemplified in the stereoselective preparation of *N*-[(*E*)-3-fluorobut-3-en-1-yl]-benzenesulfonimides by the reaction of methylenecyclopropanes with *N*-fluorobenzenesulfonimide in good to excellent yields. Moreover, γ-fluorohomoallylic amides are synthesized using Selectfluor in R_3CN at 60 °C.

1. Introduction

The presence of a fluorine atom to enhance biological and therapeutic activities of organic compounds has led to wide spread interest in selective introduction of fluorine atom and fluoroalkyl groups into organic molecules [1,2]. Recently, the selective introduction of a fluoro group into olefin-containing compounds such as pheromones [3–6] and retinoids [7–10] has been proved to be attractive due to the potential biological properties. Of paramount importance in the synthesis of olefin-containing molecules is the regio- and stereocontrol of the olefinic bond [11]. In this regard, there exists an increasing demand for the efficient introduction of fluorine atom into olefin-containing compounds. Among the many methods used for the introduction of fluorine, electrophilic fluorination using *N*-F reagents has grown in popularity and applications to the selective fluorination of activated aromatics, alkenes, and enolates in recent years [12–17]. Despite increased use of these regents, no example on the reaction of electrophilic fluorinating agents with methylenecyclopropanes has been disclosed thus far.

Methylenecyclopropanes (MCPs), which are highly strained but readily accessible molecules, have served as useful building blocks in organic synthesis. They can undergo a variety of ring-opening reactions because the relief of ring strain provides a potent thermodynamic driving force for this process [18–22]. In the past several years, a number of methods for construction of complex and interesting organic molecules from MCPs have been developed. Transition metal-catalyzed reactions of MCPs using transition metal catalysts such as palladium complexes [23–25] or Lewis acids such as metal triflates [26,27] have been most extensively investigated to achieve numerous transformations. During our study on the chemistry of MCPs [28–31], we imagined that the fluorine chemistry of MCPs, which has not been well established, may be a nice way to introduce fluorine atoms into organic molecules. In this paper, we wish to describe our results on the reaction between MCPs and *N*-F reagents under mild conditions to give the corresponding fluorinated derivatives in moderate yields (Scheme 1).

2. Results and discussion

Firstly, we conducted the reaction of methylenecyclopropane **1a** with 1.0 equiv. of *N*-fluorobenzenesulfonimide (NFSI) in CH_2Cl_2 at room temperature. The reaction proceeded smoothly to give the ring-opened product **2a** in 65% yield along with **3a** in 20% yield (Table 1, entry 1). With this encouraging result, a systematic study was undertaken to screen various solvents and reaction temperatures for the fluorination process. The results are summarized in Table 1. As can be seen from Table 1, under similar conditions, the yields of **2a** and **3a** were similar with the use of 1.3 or 1.5 equiv. of

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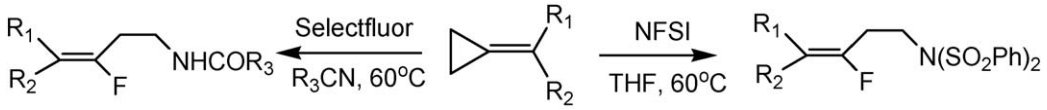
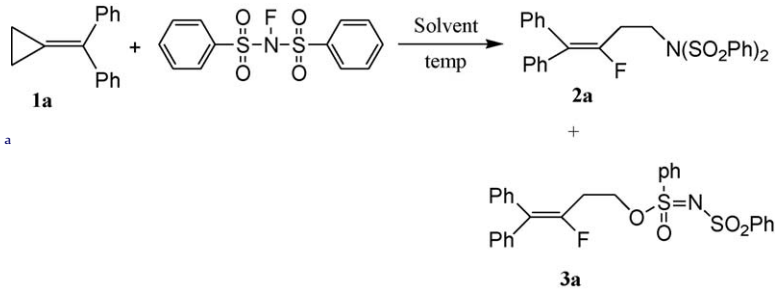


Scheme 1.

Table 1
Reaction of MCPs **1a** with NFSI under various conditions.



[a]

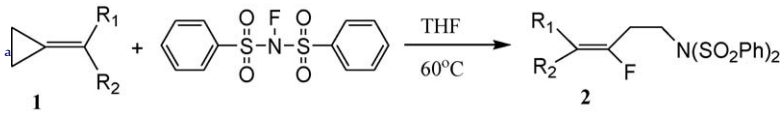
Entry	**1a**/NFSI	Solvent	Temp (°C)	Time (h)	Yield (%)[b]	
					2a	**3a**
1	1/1	CH_2Cl_2	rt	36	65	20
2	1/1.3	CH_2Cl_2	rt	36	69	14
3	1/1.5	CH_2Cl_2	rt	36	68	11
4	1/1	DCE	60	12	72	15
5	1/1	THF	60	12	80	–
6	1/1	toluene	60	20	45	34
7	1/1	Et_2O	rt	36	48	32
8	1/1	THF	rt	36	69	–
9[c]	1/1	CH_3CN	60	30	44	16

[a] Reaction conditions: **1a** (0.5 mmol), NFSI (*x* mmol), solvent (5.0 mL) and the reactions were carried out at various temperatures.
[b] Isolated yield.
[c] In this case, compound **4a** (see Table 3) was also obtained in 30% yield.

NFSI. When the reaction was carried out at 60 °C in dichloroethane (DCE), **2a** and **3a** were obtained in 72% and 15% yield, respectively. Significantly, we found that in THF for 12 h, the ring-opened product **2a** was obtained in 80% yield as a sole product without the isolation of compound **3a** (Table 1, entry 5). On using other solvent such as Et_2O or toluene, the desired product **2a** could be isolated in slightly lower yield. Using acetonitrile as the solvent, the unexpected product **4a** was obtained in 30% yield along with the production of **2a** and **3a** in 44% and 16% yield, respectively (Table 1, entry 9). Therefore, as the optimized conditions we chose the reaction of 1.0 equiv. **1a** with 1.0 equiv. NFSI in THF at 60 °C (Table 1, entry 5).

With the optimized conditions in hand, we next carried out this ring-opening reaction of a variety of methylenecyclopropanes **1**

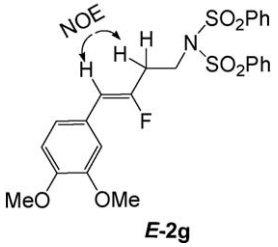
Table 2
Fluorination of methylenecyclopropanes with NFSI.



[a]

Entry	R_1	R_2	Time (h)	Yield (%)[b]
1	C_6H_5	C_6H_5	12	**2a**, 80
2	4-MeC_6H_4	4-MeC_6H_4	12	**2b**, 84
3	4-$MeOC_6H_4$	4-$MeOC_6H_4$	9	**2c**, 90
4	4-ClC_6H_4	4-ClC_6H_4	30	**2d**, 65
5	4-FC_6H_4	4-FC_6H_4	36	**2e**, 48
6	4-MeC_6H_4	H	12	**2f**, 77(4:1)[c]
7	3,4-$(MeO)_2C_6H_3$	H	12	**2g**, 93(>98:2)[c]
8	4-FC_6H_4	C_6H_5	36	**2h**, 66(1:1)[d]
9	4-ClC_6H_4	C_6H_5	36	**2i**, 70(13:7)[d]
10	-$(CH_2)_5$-	H	24	**2j**, complex
11	C_4H_9	C_4H_9	24	**2k**, complex
12	C_4H_9	H	24	**2l**, NR

[a] Reaction conditions: **1** (0.5 mmol), NFSI (0.5 mmol), solvent (5.0 mL), at 60 °C.
[b] Isolated yield.
[c] The ratio was determined by ^1H NMR spectroscopic data.
[d] The ratio was determined by ^{19}F NMR spectroscopic data.

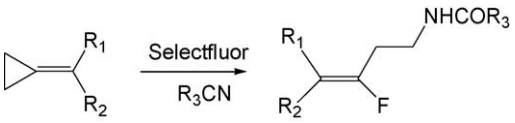


Scheme 2. Configurations of *E*-**2g**.

with NFSI. The results are summarized in Table 2. As indicated, the substituents on the benzene ring of MCPs **1** significantly affect the reaction. For MCPs **1** having an electron-donating group on the benzene ring led to **2** in higher yields within shorter reaction time than those with electron-withdrawing group. Unsymmetric MCPs having a hydrogen group and an aromatic group (Table 2, entries 6 and 7) were converted to the corresponding ring-opened products **2** in good yields under mild conditions giving rise to *E*-**2f** or *E*-**2g** as the major products. Although the unsymmetrical MCP **1 h** having phenyl and 4-fluorophenyl provided 1:1 mixture *E*- and *Z*-isomer **2h**, the reaction of 4-chlorophenyl derivative **1i** proceeded in a highly stereoselective manner to give *E*-isomer **2i** as a major product (Table 2, entries 8 and 9). Configuration of the product *E*-**2g** was established by the NOESY spectrum studies (Scheme 2). In the cases of aliphatic MCP **1j** and **1k**, complicated reaction products were formed without the isolation of the expected products **2j** and **2k** (Table 2, entries 10 and 11). Using unsymmetrical aliphatic MCP **1l** as the substrate, no reaction occurred (Table 2, entry 12).

It was interesting to observe that the reaction of methylenecyclopropane **1a** with 1.0 equiv. of Selectfluor (F-TEDA-BF_4) in acetonitrile afforded the amide derivative **4a** in 67% yield (see Scheme 1 and Table 3, entry 1). Then a series of methylenecyclopropanes were tested. The results in Table 3 show that the reactions proceeded smoothly to give the corresponding products **4**. We found the electronic nature of the substituents on the benzene rings is significant on the reaction outcomes. With the substrates **1b** and **1c** having electron-donating substituents on the benzene ring, the corresponding products **4b** and **4c** were obtained in 89 and 91% yields, respectively (Table 3, entries 2 and 3). However, in the cases of methylenecyclopropanes **1d** having chlorine as an electron-inductive substituent on the benzene ring, **4d** was formed in lower yield (Table 3, entry 4).

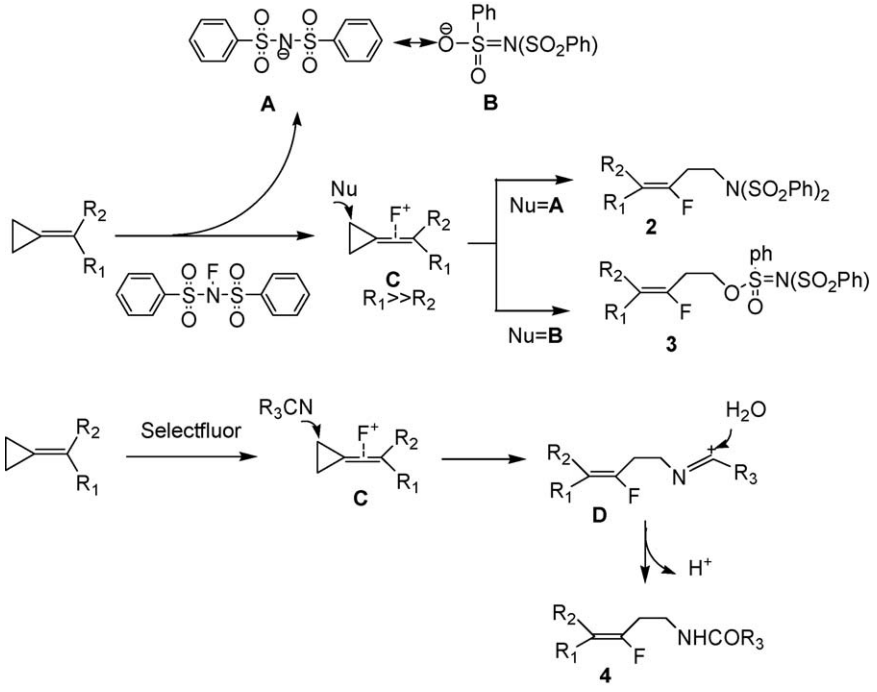
Table 3
Fluorination of Methylenecyclopropanes with Selectfluor.[a]



Entry	R_1	R_2	R_3	Time (h)	Yields (%)[b]
1	C_6H_5	C_6H_5	CH_3	24	**4a**, 67
2	4-MeC_6H_4	4-MeC_6H_4	CH_3	24	**4b**, 89
3	4-$MeOC_6H_4$	4-$MeOC_6H_4$	CH_3	24	**4c**, 91
4	4-ClC_6H_4	4-ClC_6H_4	CH_3	24	**4d**, 65
5	C_6H_5	C_6H_5	$C_6H_5CH_2$	36	**4e**, 70
6	C_6H_5	C_6H_5	*n*-Pr	30	**4f**, 63

[a] Reaction conditions: **1** (0.5 mmol), Selectfluor (0.5 mmol), solvent (3.0 mL), at 60 °C.
[b] Isolated yield.

A plausible mechanism for the reaction of MCPs **1** with *N*-F reagents is outlined in Scheme 3. Initially, the interaction between NFSI and MCPs leads to the intermediate **C** and the anionic intermediate **A** under the standard reaction conditions, in which the anionic intermediate **A** can be transformed to another anionic intermediate **B** [32,33]. In the intermediate **C**, if R_1 is sterically bulkier than R_2, subsequently, the intermediate **C** is attacked by the corresponding anion from the sterically smaller group R_2 side to give ring-opened products **2**. Similarly, reaction of MCPs with Selectfluor gives intermediate **C**. Then the ring-opening of the cyclopropyl group would give intermediate **D** which would produce the final products **4** after hydrolysis.



Scheme 3. Proposed mechanism for the reaction of MCPs with *N*-F reagents.

3. Conclusion

In conclusion, we have disclosed the reactions of methylenecyclopropanes with *N*-F reagents to give the corresponding fluorinated derivatives **2** and **4** in moderate to excellent yields. Further studies, including the reaction mechanism and synthetic application of this methodology, are in progress.

4. Experimental

4.1. General

Chemicals used were obtained from commercial suppliers and used without further purifications. ^{1}H NMR spectra and ^{13}C NMR spectra were measured in $CDCl_3$ and recorded on Bruker Avance-400 spectrometer (400 MHz for ^{1}H NMR, 100 MHz for ^{13}C NMR) with TMS as an internal standard. IR spectra were run on a Bruker vector 22 spectrometer. EIMS were determined with a HP5989B mass spectrometer. Elemental analyses were performed on an EA-1110 instrument.

4.2. Typical procedure for fluorination of methylenecyclopropane 1 with N-fluorobenzenesulfonimide

N-Fluorobenzenesulfonimide (0.5 mmol) was added to a stirred solution of the methylenecyclopropane **1** (0.5 mmol) in THF (5 mL). The mixture was stirred at 60 °C until the reaction completed. The solvent was removed under reduced pressure and the residue was purified by SiO_2 gel column chromatography to give the corresponding products **2**.

Compound **2a**: white solid, mp 100–101 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.71 (t, J = 6.8 Hz, 2H), 3.97 (t, J = 6.8 Hz, 2H), 7.20–7.27 (m, 7H), 7.36–7.41 (m, 7H), 7.60 (t, J = 7.6 Hz, 2H), 7.96 (d, J = 7.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7 (d, J = 27.2 Hz), 46.2, 122.8 (d, J_{C-F} = 13.6 Hz), 127.2, 127.6, 128.0, 128.2, 128.5, 129.1, 129.4, 129.6, 130.0, 130.1, 134.0, 136.7, 138.0, 138.1, 139.5, 153.7 (d, J_{C-F} = 260.2 Hz); MS (EI) m/z 521 (M^+). Anal. Calcd for $C_{28}H_{24}FNO_4S_2$: (%) C, 64.47; H, 4.64; N, 2.69. Found: C, 64.41; H, 4.83; N, 2.58.

Compound **2b**: oil, ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 3H), 2.40 (s, 3H), 2.68 (t, J = 7.2 Hz, 2H), 3.99 (t, J = 7.2 Hz, 2H), 7.05–7.16 (m, 6H), 7.20 (d, J = 9.2 Hz, 2H), 7.44 (t, J = 8.0 Hz, 4H), 7.60 (d, J = 8 Hz, 2H), 7.90 (d, J = 9.2 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 21.2, 31.7 (d, J_{C-F} = 27.2 Hz), 46.5, 122.4 (d, J_{C-F} = 13.6 Hz), 128.0, 128.6, 129.1, 129.2, 129.4, 129.9, 133.7, 134.0, 135.1, 135.3, 136.8, 137.2, 139.5, 153.3 (d, J_{C-F} = 259.1 Hz); MS (EI) m/z 549 (M^+). Anal. Calcd for $C_{30}H_{28}FNO_4S_2$: (%) C, 65.55; H, 5.13; N, 2.55. Found: C, 65.48; H, 5.38; N, 2.62.

Compound **2c**: oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ2.69 (t, J = 7.2 Hz, 2H), 3.78 (s, 3H), 3.84 (s, 3H), 4.02 (t, J = 7.2 Hz, 2H), 6.80 (d, J = 8.0 Hz, 2H), 6.96 (d, J = 8.8 Hz, 2H), 7.12 (d, J = 8.4 Hz, 2H), 7.22 (d, J = 8.4 Hz, 2H), 7.50 (t, J = 7.6 Hz, 4H), 7.61 (t, J = 7.6 Hz, 2H), 7.94 (d, J = 8.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7 (d, J_{C-F} = 27.9 Hz), 46.4, 55.0, 55.1, 113.2, 113.6, 114.0, 121.8(d, J_{C-F} = 13.4 Hz), 127.9, 128.4, 129.0, 129.3, 130.3, 130.4, 130.6, 130.7, 131.1, 133.7, 133.8, 139.5, 152.7 (d, J_{C-F} = 257.8 Hz), 158.5, 158.9; MS (EI) m/z 581 (M^+). Anal. Calcd for $C_{30}H_{28}FNO_6S_2$: (%) C, 61.95; H, 4.85; N, 2.41. Found: C, 61.78; H, 5.10; N, 2.32.

Compound **2d**: white solid, mp 108–109 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.65 (t, J = 7.6 Hz, 2H), 3.95 (t, J = 7.6 Hz, 2H), 7.08 (d, J = 8.0 Hz, 2H), 7.13 (d, J = 8.4 Hz, 2H), 7.22–7.30 (m, 3H), 7.35 (d, J = 8.0 Hz, 2H), 7.44–7.52 (m, 4H), 7.64 (t, J = 8.0 Hz, 2H), 7.92 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.8 (d, J_{C-F} = 27.0 Hz), 46.4, 122.6(d, J_{C-F} = 14.2 Hz), 127.2, 127.5, 128.0, 128.1, 128.6, 129.0, 129.4, 129.5, 130.1, 130.2, 133.9, 136.8, 138.1, 138.2, 139.6, 153.7 (d, J_{C-F} = 259.4 Hz); MS (EI) m/z 589 (M^+). Anal. Calcd for $C_{28}H_{22}Cl_2FNO_4S_2$: (%) C, 56.95; H, 3.76; N, 2.37. Found: C, 56.80; H, 3.98; N, 2.45.

Compound **2e**: white solid, mp 112–114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.67 (t, J = 8.4 Hz, 2H), 3.94 (t, J = 8.4 Hz, 2H), 6.87 (d, J = 8.0 Hz, 2H), 7.02 (d, J = 8.4 Hz, 2H), 7.17–7.26 (m, 3H), 7.32 (d, J = 8.0 Hz, 2H), 7.45–7.51 (m, 4H), 7.60 (t, J = 8.0 Hz, 2H), 7.94 (d, J = 8.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.7 (d, J_{C-F} = 27.8 Hz), 46.3, 122.2(d, J_{C-F} = 15.4 Hz), 126.1, 127.3, 128.6, 128.9, 129.0, 129.5, 130.5, 131.3, 132.0, 133.6, 135.4, 138.0, 138.2, 139.0, 148.6, 154.6(d, J_{C-F} = 261.2 Hz); MS (EI) m/z 557 (M^+). Anal. Calcd for $C_{28}H_{22}F_3NO_4S_2$: (%) C, 60.31; H, 3.98; N, 2.51. Found: C, 60.45; H, 4.20; N, 2.42.

Compound **2f**: oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.31 (s, 0.6H), 2.34 (s, 2.4H), 2.61–2.72 (m, 2H), 3.91–3.98 (m, 2H), 5.43 (, d, J = 38.0 Hz, 0.8H), 6.25 (d, J = 22.8 Hz, 0.2H), 6.80 (d, J = 8.0 Hz, 0.5H), 6.95 (s, 1H), 7.11–7.18 (m, 2H), 7.31 (d, J = 8.0 Hz, 2H), 7.49–7.56 (m, 5H), 7.61–7.68 (m, 3H), 7.98–8.05 (m, 5.5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.1, 21.3, 34.1 (d, J_{C-F} = 27.2 Hz), 46.3, 108.2, 108.4, 127.2, 127.3, 128.1, 128.2, 128.31, 128.34, 128.4, 128.5, 128.9, 129.1, 129.2, 129.3, 129.6, 130.0, 130.10, 130.14, 131.9, 133.9, 134.0, 134.1, 134.8, 137.0, 139.0, 139.5, 139.7, 155.6 (d, J_{C-F} = 265.0 Hz); MS (EI) m/z 459 (M^+). Anal. Calcd for $C_{23}H_{22}FNO_4S_2$: (%) C, 60.11; H, 4.83; N, 3.05. Found: C, 60.23; H, 4.58; N, 3.20.

Compound **2g**: oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.73 (t, J = 8.0 Hz, 2H), 3.76 (s, 3H), 3.81 (s, 3H), 3.96 (t, J = 8.0 Hz, 2H), 5.81 (d, J = 40.0 Hz, 1H), 7.53 (t, J = 8.4 Hz, 5H), 7.63–7.66 (m, 4H), 8.05 (d, J = 8.0 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 34.3 (d, J_{C-F} = 27.5 Hz), 46.1, 55.4, 55.6, 98.1, 101.6, 104.8, 114.9, 127.6, 128.1, 129.0, 130.3, 130.4, 133.9, 139.6, 155.6 (d, J_{C-F} = 256.5 Hz), 157.1, 159.8; MS (EI) m/z 505 (M^+). Anal. Calcd for $C_{24}H_{24}FNO_6S_2$: (%) C, 57.02; H, 4.78; N, 2.77. Found: C, 57.26; H, 4.50; N, 2.91.

Compound **2h**: oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.61–2.74 (m, 2H), 3.96–3.99 (m, 2H), 6.93 (t, J = 8.8 Hz, 1H), 7.01–7.28 (m, 6H), 7.33–7.49 (m, 6H), 7.54–7.63 (m, 2H), 7.92 (, t, J = 9.6 Hz, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.5, 31.7 (d, J_{C-F} = 26.8 Hz), 46.1, 46.2, 114.8 (d, J_{C-F} = 20.8 Hz), 115.6 (d, J_{C-F} = 20.8 Hz), 121.80, 121.83, 121.93, 121.98, 127.0, 127.3, 127.8, 128.01, 128.06, 128.7, 129.1, 129.3, 129.4, 129.9, 130.0, 131.13, 131.18, 131.20, 131.26, 131.6, 131.72, 131.77, 132.7, 133.90, 133.93, 136.5, 137.7, 137.8, 139.50, 139.51, 153.6 (d, J_{C-F} = 268.0 Hz), 153.7 (d, J_{C-F} = 259.6 Hz), 161.7 (d, J_{C-F} = 246.9 Hz), 162.2 (d, J_{C-F} = 246.1 Hz); MS (EI) m/z 539 (M^+). Anal. Calcd for $C_{28}H_{23}F_2NO_4S_2$: (%) C, 62.32; H, 4.30; N, 2.60. Found: C, 62.25; H, 4.53; N, 2.71.

Compound **2i**: oil. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.61–2.72 (m, 2H), 3.95–3.99 (m, 2H), 7.12 (d, J = 8.8 Hz, 1H), 7.15–7.36 (m, 6H), 7.35–7.45 (m, 2H), 7.44–7.53 (m, 4H), 7.54–7.64 (m, 2H), 7.88–7.91 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 31.98 (d, J_{C-F} = 25.8 Hz), 46.3, 121.7 (d, J_{C-F} = 14.4 Hz), 127.3, 127.7, 127.8, 127.9, 128.6, 128.7, 128.9, 129.1, 129.3, 129.6, 130.4, 130.6, 131.2, 131.4, 132.8, 133.6, 133.7, 134.8, 136.1, 136.2, 136.3, 137.4, 139.3, 153.0 (d, J_{C-F} = 256.7 Hz), 153.8 (d, J_{C-F} = 248.2 Hz); MS (EI) m/z 555 (M^+). Anal. Calcd for $C_{28}H_{23}ClFNO_4S_2$: (%) C, 60.48; H, 4.17; N, 2.52. Found: C, 60.45; H, 4.32; N, 2.61.

Compound **3a**: white solid, mp 102–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.70 (dt, J = 20.0, 5.6 Hz, 2H), 4.41–4.50 (m, 2H), 7.07–7.10 (m, 2H), 7.20–7.32 (m, 8H), 7.40–7.53 (m, 5H), 7.61–7.65 (m, 1H), 7.90–7.97 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.3 (d, J_{C-F} = 27.8 Hz), 67.7, 126.7, 127.3, 127.7, 127.8, 128.6, 128.7, 129.2, 129.4, 130.0, 130.1, 132.5, 134.6, 135.5, 136.6, 142.6, 153.5 (d, J_{C-F} = 260.8 Hz); MS (EI) m/z 521 (M^+). Anal. Calcd for $C_{28}H_{24}FNO_4S_2$: (%) C, 64.47; H, 4.64; N, 2.69. Found: C, 64.36; H, 4.35; N, 2.78.

4.3. Typical procedure for fluorination of methylenecyclopropane 1 with F-TEDA-BF_4

1-Chloromethyl-4-fluoro-1,4-diazoniabicyclo[2.2.2]octane bis (tetrafluoroborate) (0.5 mmol) was added to a stirred solution of

methylenecyclopropane **1** (0.5 mmol) in R_3CN(3 mL). The mixture was stirred at 60 °C until the reaction completed. The solvent was removed under reduced pressure and the residue was purified by SiO_2 gel column chromatography to give the corresponding products **4**.

Compound **4a**: solid, mp 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.96 (s, 3H), 2.56 (dt, J = 30.0, 8.8 Hz, 2H), 3.58 (dt, J = 8.8, 8.8 Hz, 2H), 5.60 (br s, 1H), 7.16–7.39 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.3, 30.6 (d, J_{C-F} = 26.0 Hz), 37.0, 122.5 (d, J_{C-F} = 12.0 Hz), 127.1, 127.6, 128.0, 128.6, 129.4, 129.5,130.0, 130.1, 137.0, 138.2, 138.3, 155.4 (d, J_{C-F} = 260 Hz), 169.9; MS (EI) m/z 283 (M^+). Anal. Calcd for $C_{18}H_{18}FNO$: (%) C, 76.30; H, 6.40; N, 4.94. Found: C, 76.45; H, 6.21; N, 4.88.

Compound **4b**: solid, mp 137–138 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.96 (s, 3H), 2.31 (s, 3H), 2.33 (s, 3H), 2.54 (dt, J = 29.4, 8.0 Hz, 2H), 3.55 (dt, J = 8.0, 8.0 Hz, 2H), 5.56 (br s, 1H), 7.10–7.14 (m, 8H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 21.2, 21.3, 23.3, 30.5 (d, J_{C-F} = 25.6 Hz), 36.9, 123.0 (d, J_{C-F} = 12.6 Hz), 128.5, 128.6, 128.9, 129.1, 129.5, 130.3,131.2, 131.4, 137.1, 137.5, 143.9, 154.8(d, J_{C-F} = 260 Hz), 170.0; MS (EI) m/z 311 (M^+). Anal. Calcd for $C_{20}H_{22}FNO$: (%) C, 77.14; H, 7.12; N, 4.50. Found: C, 77.27; H, 7.51; N, 4.62.

Compound **4c**: solid, mp 105–106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.95 (s, 3H), 2.55 (dt, J = 30.2.4, 8.8 Hz, 2H), 3.56 (dt, J = 8.8, 8.8 Hz, 2H), 3.81 (s, 3H), 3.83 (s, 3H), 5.54 (br s, 1H), 6.82–6.89 (m, 4H) 7.02–7.16 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 30.6 (d, J_{C-F} = 26.0 Hz), 37.2, 55.2, 55.3, 113.6, 113.8, 124.5 (d, J_{C-F} = 12.2 Hz), 130.8, 131.2, 134.2, 136.9, 155.0(d, J_{C-F} = 258.0 Hz), 159.4, 160.2, 170.2; MS (EI) m/z 343 (M^+). Anal. Calcd for $C_{20}H_{22}FNO_3$: (%) C, 69.95; H, 6.46; N, 4.08. Found: C, 69.78; H, 6.20; N, 4.12.

Compound **4d**: solid, mp 95–97 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 1.94 (s, 3H), 2.53 (dt, J = 30.4, 8.4 Hz, 2H), 3.56 (dt, J = 8.4, 8.4 Hz, 2H), 5.57 (br s, 1H), 7.15 (t, J = 8.2 Hz, 4H), 7.31–7.26 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 23.1, 30.3 (d, J_{C-F} = 26.0 Hz), 36.8, 122.0 (d, J_{C-F} = 12.6 Hz), 128.5, 128.7, 130.1, 130.2, 133.4, 133.5, 137.9, 138.6, 155.1(d, J_{C-F} = 262.2 Hz), 169.6; MS (EI) m/z 351 (M^+). Anal. Calcd for $C_{18}H_{16}Cl_2FNO$: (%) C, 61.38; H, 4.58; N, 3.98. Found: C, 61.44; H, 4.29; N, 3.87.

Compound **4e**: solid, mp 115–116 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 2.51 (dt, J = 29.4, 7.6 Hz, 2H), 3.53 (s, 2H), 3.59 (dt, J = 7.6, 7.6 Hz, 2H), 5.41(br s, 1H), 7.01–7.33 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 30.3 (d, J_{C-F} = 27.0 Hz), 37.4, 43.88, 122.7 (d, J_{C-F} = 12.5 Hz), 127.1, 127.2, 127.4, 127.5, 128.0, 128.6, 129.0,129.3, 129.5,129.6, 131.2, 131.9, 136.3, 138.0, 138.7, 156.0 (d, J_{C-F} = 258.2 Hz), 170.3; MS (EI) m/z 359 (M^+). Anal. Calcd for $C_{24}H_{22}FNO$: (%) C, 80.20; H, 6.17; N, 3.90. Found: C, 80.29; H, 6.43; N, 4.04.

Compound **4f**: solid, mp 101–103 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 0.90 (t, J = 7.2 Hz, 3H), 1.58–1.63(m, 2H), 2.08 (t, J = 7.2 Hz, 2H), 2.57 (dt, J = 30.3, 8.4 Hz, 2H), 3.60 (dt, J = 8.4, 8.4 Hz, 2H), 5.63 (br s, 1H), 7.13–7.35 (m, 10H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 13.8, 19.2, 23.3, 30.1 (d, J_{C-F} = 26.4 Hz), 37.2, 39.3, 122.7 (d, J_{C-F} = 12.0 Hz), 127.2, 127.5, 128.2, 128.6, 129.3, 129.5,130.0, 130.3, 137.4, 138.2, 138.3, 155.1 (d, J_{C-F} = 258.2 Hz), 170.1; MS (EI) m/z 311 (M^+). Anal. Calcd for $C_{20}H_{22}FNO$: (%) C, 77.14; H, 7.12; N, 4.50. Found: C, 77.26; H, 7.35; N, 4.58.

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