Supporting Information

Silver-Catalyzed C–H Aryloxydifluoromethylation and Arylthiodifluoromethylation of Heteroarenes

Xiao-Lei Zhu,† Yangen Huang,† Xiu-Hua Xu,‡ and Feng-Ling Qing*,†,‡

† College of Chemistry, Chemical Engineering and Biotechnology, Donghua University, 2999 North Renmin Lu, Shanghai 201620, China

‡Key Laboratory of Organofluorine Chemistry, Center for Excellence in Molecular Synthesis, Shanghai Institute of Organic Chemistry, University of Chinese Academy of Science, Chinese Academy of Science, 345 Lingling Lu, Shanghai 200032, China

E-mail: flq@mail.sioc.ac.cn

Contents

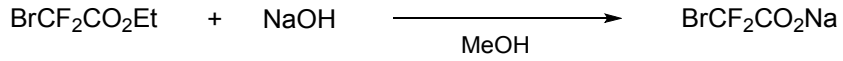
1. General Information

^{1}H NMR (TMS as the internal standard) were recorded on a Bruker AM 400 or 600 spectrometer, ^{13}C NMR and ^{19}F NMR ($CFCl_3$ as outside standard and low field is positive) spectra were recorded on a Bruker AM 400 or 600 spectrometer. For the determination of ^{19}F NMR yield, $PhCF_3$ was used as an internal standard and the relaxation delay (d1) was set to 5 s. Chemical shifts (δ) were reported in per million (ppm), and coupling constants (*J*) were in Hertz (Hz). The following abbreviations were used to explain the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet. High resolution mass spectra (HRMS) were obtained on a GC-TOF mass spectrometer.

Materials: Unless otherwise noted, all reagents were obtained commercially and used without further purification. Substrates were purchased from commercial sources or prepared according to literature procedures. Reactions were performed using glassware that was flame-dried under vacuum.

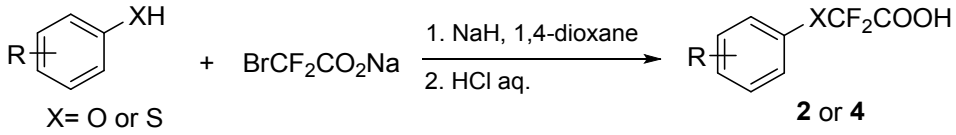
2. Preparation of $ArOCF_2CO_2H$ and $ArSCF_2CO_2H$

Preparation of $BrCF_2COONa$.



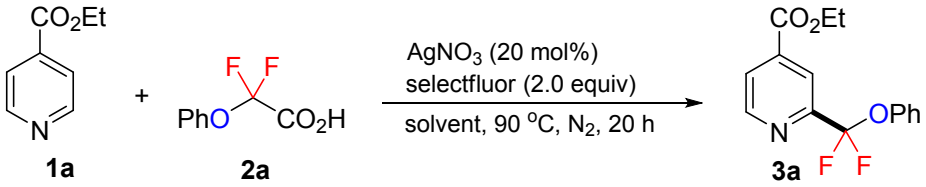
To a 500 mL oven-dried round-bottom flask equipped with a stir bar were added sodium hydroxide (8.0 g, 200 mmol) and MeOH (180 mL). Then, $BrCF_2CO_2Et$ (41.0 g, 202 mmol) was added to the resulting solution at 0 ºC. Upon addition, the mixture was warmed to room temperature and stirred for 24 h. The solvent was evaporated under vacuum and the residue was further dried under reduced pressure to give $BrCF_2CO_2Na$ as a white solid (39.1 g, 99%).

General Procedures for the Synthesis of Aryloxydifluoroacetic acid ($ArOCF_2CO_2H$) and Arylthiodifluoroacetic acid ($ArSCF_2CO_2H$).



$ArOCF_2CO_2H$ and $ArSCF_2CO_2H$ were prepared following the reported procedures (Zhou, M.; Ni, C.; He, Z.; Hu, J. *Org. Lett.* **2016**, *18*, 3754). To a 50 mL oven-dried Schlenk tube equipped with a stir bar was added phenol (3.0 mmol, 1.0 equiv) or thiophenol (3.0 mmol, 1.0 equiv) under N_2 atmosphere. 1,4-Dioxane (10.0 mL) was added to dissolve the phenol or thiophenol. Then, NaH (60% purity) (132.0 mg, 3.3 mmol, 1.1 equiv) and 1,4-dioxane (2.0 mL) were added under N_2 atmosphere. The solution was stirred at room temperature for 30 min. Then $BrCF_2COONa$ (647.1 mg, 3.3 mmol, 1.1 equiv) and 1,4-dioxane (3.0 mL) were added. After the mixture was heated at 60-100 ºC in an oil bath for hours (monitor by TLC), then the mixture was cooled down to room temperature and acidified with 3M HCl (aq) to pH = 1. The mixture was extracted with ethyl acetate for three times. The combined organic phase was washed by saturated brines and dried over $MgSO_4$. After the solution was filtered and the solvent was evaporated under vacuum, the crude product was purified by flash column chromatography using petroleum ether and ethyl acetate as eluent to give the product **2** or **4**.

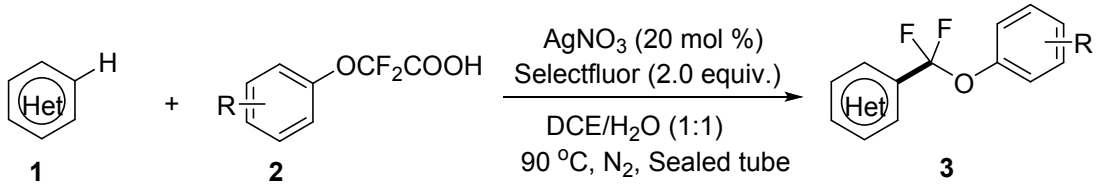
3. Screening of the Solvents[a]



entry	solvent	yield (%)[b]
1	DCE	0
2	H_2O	50
3	MeCN	0
4	DMSO	0
5	DCE/H_2O (1:1)	78
6	toluene/H_2O (1:1)	60
7	MeCN/H_2O (1:1)	6
8	MeOH/H_2O (1:1)	0
9	DMSO/H_2O (1:1)	0
10	DCE/H_2O (2:1)	73
11	DCE/H_2O (1:2)	59

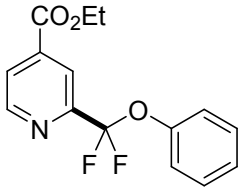
[a]Reaction conditions: **1a** (0.2 mmol), **2a** (0.6 mmol), $AgNO_3$ (0.04 mmol), selectfluor (0.4 mmol), solvent (2.0 mL), N_2, 90 °C, 20 h. [b]Yields were determined by ^{19}F NMR spectroscopy using trifluoromethoxybenzene as an internal standard.

4. General Procedures for Aryloxydifluoromethylation of Heteroarenes



To a sealed tube equipped with a stir bar were added **1** (0.6 mmol, 1.0 equiv), $AgNO_3$ (20.4 mg, 0.12 mmol, 20 mol%), and selectfluor (425.1 mg, 1.2 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then aryloxydifluoroacetic acid **2** (1.8 mmol, 3.0 equiv) in DCE/H_2O (3.0/3.0 mL) were added. The tube was sealed and the mixture was heated at 90 °C in an oil bath for 20 h. After the reaction was complete, saturated $NaHCO_3$ solution was added. The resulting mixture was extracted with ethyl acetate for three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by silica gel flash column chromatography to give the product **3**.

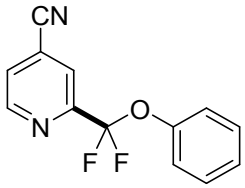
Ethyl 2-(difluoro(phenoxy)methyl)isonicotinate (3a)



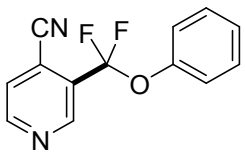
3a

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3a** (105.5 mg, 60%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.78 (d, *J* = 4.9 Hz, 1H), 8.24 (s, 1H), 7.90 (dd, *J* = 4.9, 1.3 Hz, 1H), 7.28-7.20 (m, 4H), 7.14-7.06 (m, 1H), 4.33 (q, *J* = 7.1 Hz, 2H), 1.30 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -70.26 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 163.1, 151.1 (t, *J* = 34.3 Hz), 149.5, 149.1, 138.2, 128.4, 124.9, 123.9, 121.1, 119.2 (t, *J* = 2.8 Hz), 118.6 (t, *J* = 264.6 Hz), 114.4, 61.2, 13.1; **IR** (thin film) *v* 1728, 1592, 1491, 1326, 1249, 1150, 1055, 897, 762, 689 cm^{-1}; **MS** (ESI): *m*/*z* 294 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{14}F_2NO_3$ 294.0936; Found 294.0934.

2-(Difluoro(phenoxy)methyl)isonicotinonitrile (3b), 3-(Difluoro(phenoxy)methyl)isonicotinonitrile (3b′)



3b



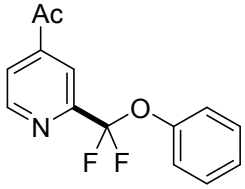
3b'

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 8:1) to afford **3b** (69.3 mg, 47%) and **3b′** (35.4 mg, 24%) as yellowish liquids.

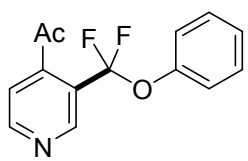
3b: **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.96 (d, *J* = 4.9 Hz, 1H), 8.05 (s, 1H), 7.71 (d, *J* = 4.8 Hz, 1H), 7.42-7.38 (m, 2H), 7.32-7.27 (m, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -70.49 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 152.7 (t, *J* = 35.1 Hz), 150.8, 149.8, 129.6, 127.3, 126.3, 122.8 (t, *J* = 2.9 Hz), 122.0, 118.9 (t, *J* = 265.1 Hz), 115.7; **IR** (thin film) *v* 1592, 1491, 1415, 1321, 1199, 1153, 1056, 854, 739, 688 cm^{-1}; **MS** (ESI): *m*/*z* 247 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{13}H_9F_2N_2O$ 247.0677; Found 247.0673.

3b′: **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.22 (s, 1H), 8.99 (d, *J* = 4.8 Hz, 1H), 7.75 (d, *J* = 4.8 Hz, 1H), 7.45-7.39 (m, 3H), 7.35-7.23 (m, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -65.94 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 152.8, 149.6, 147.9 (t, *J* = 5.3 Hz), 129.7, 127.0, 126.6, 122.2, 119.8 (t, *J* = 265.0 Hz), 119.1, 114.1; **IR** (thin film) *v* 1589, 1490, 1278, 1190, 1138, 1060, 837, 739, 687 cm^{-1}; **MS** (ESI): *m*/*z* 247 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{13}H_9F_2N_2O$ 247.0677; Found 247.0672.

1-(2-(Difluoro(phenoxy)methyl)pyridin-4-yl)ethan-1-one (3c), 1-(3-(Difluoro(phenoxy)methyl)pyridin-4-yl)ethan-1-one (3c′)



3c



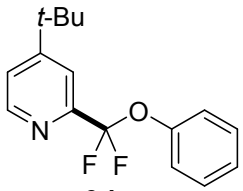
3c'

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to afford **3c** (88.4 mg, 56%) as a yellowish solid and **3c′** (28.4 mg, 18%) as a yellowish liquid.

3c: m.p. 57-59 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.84 (d, *J* = 4.9 Hz, 1H), 8.13 (s, 1H), 7.80 (d, *J* = 4.9 Hz, 1H), 7.31-7.27 (m, 2H), 7.23 (d, *J* = 8.0 Hz, 2H), 7.18-7.15 (m, 1H), 2.59 (s, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -70.26 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 195.2, 151.6 (t, *J* = 34.3 Hz), 149.9, 149.1, 143.1, 128.5, 125.0, 122.3, 121.1, 118.6 (t, *J* = 264.7 Hz), 117.5 (t, *J* = 2.8 Hz), 25.7; **IR** (thin film) *v* 1696, 1588, 1489, 1323, 1239, 1165, 1053, 855, 748, 688 cm^{-1}; **MS** (ESI): *m*/*z* 264 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{14}H_{12}F_2NO_2$ 264.0831; Found 264.0825.

3c′: **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.00 (s, 1H), 8.78 (s, 1H), 7.34-7.30 (m, 2H), 7.22-7.18 (m, 4H), 2.53 (s, 3H). **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -61.73 (s, 2F). **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 199.9, 151.6, 148.6, 1 47.1 (t, *J* = 5.0 Hz), 146.9, 128.6, 125.3, 120.9, 119.9 (t, *J* = 264.7 Hz), 118.7, 29.9. **IR** (thin film) *v* 1712, 1591, 1491, 1325, 1283, 1190, 1049, 1026, 732, 688 cm^{-1}; **MS** (ESI): *m*/*z* 264 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{14}H_{12}F_2NO_2$ 264.0831; Found 264.0825.

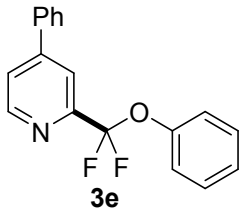
4-(*Tert*-butyl)-2-(difluoro(phenoxy)methyl)pyridine (3d)



3d

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3d** (69.9 mg, 42%) as a yellowish solid. m.p. 54-56 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.65 (d, *J* = 5.2 Hz, 1H), 7.77 (s, 1H), 7.41 (dd, *J* = 5.2, 1.8 Hz, 1H), 7.38-7.32 (m, 4H), 7.24-7.20 (m, 1H), 1.33 (s, 9H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -70.30 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 161.8, 151.1 (t, *J* = 33.1 Hz), 150.4, 149.6, 129.4, 125.8, 122.6, 122.3, 120.2 (t, *J* = 264.5 Hz), 117.8 (t, *J* = 2.9 Hz), 35.0, 30.4; **IR** (thin film) *v* 1777, 1592, 1491, 1324, 1259, 1161, 1051, 869, 733, 688 cm^{-1}; **MS** (ESI): *m*/*z* 278 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{16}H_{18}F_2NO$ 278.1351; Found 278.1345.

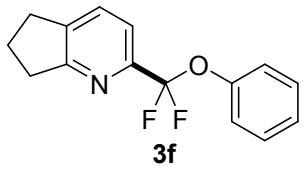
2-(Difluoro(phenoxy)methyl)-4-phenylpyridine (3e)



3e

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3e** (67.7 mg, 38%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.79 (d, *J* = 5.1 Hz, 1H), 8.01 (s, 1H), 7.69-7.64 (m, 3H), 7.54-7.46 (m, 3H), 7.40-7.34 (m, 4H), 7.27-7.22 (m, 1H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -70.31 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 151.9 (t, *J* = 33.5 Hz), 150.3, 150.2, 150.0, 137.3, 129.7, 129.5, 129.3, 127.2, 125.9, 123.5, 122.2, 120.1 (t, *J* = 264.6 Hz), 118.9 (t, *J* = 2.8 Hz); **IR** (thin film) *v* 1602, 1490, 1413, 1330, 1256, 1147, 1048, 849, 760, 688 cm^{-1}; **MS** (ESI): *m*/*z* 298 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{18}H_{14}F_2NO$ 298.1038; Found 298.1035.

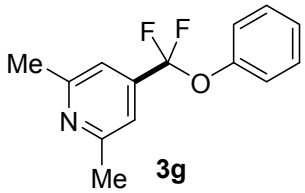
2-(Difluoro(phenoxy)methyl)-6,7-dihydro-5*H*-cyclopenta[*b*]pyridine (3f)



3f

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 8:1) to afford **3f** (84.6 mg, 54%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.39 (d, *J* = 5.1 Hz, 1H), 7.30-7.26 (m, 3H), 7.17-7.13 (m, 3H), 3.12 (t, *J* = 7.5 Hz, 2H), 2.99 (t, *J* = 7.8 Hz, 2H), 2.11-2.04 (m, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -67.86 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 167.8, 150.1, 148.2, 137.4 (t, *J* = 33.2 Hz), 134.2, 129.5, 125.9, 121.8, 121.3 (t, *J* = 264.3 Hz), 117.0 (t, *J* = 4.4 Hz), 34.1, 30.0, 22.7; **IR** (thin film) *v* 1593, 1491, 1393, 1305, 1203, 1139, 1204, 1140, 1044, 831, 732, 689 cm^{-1}; **MS** (ESI): *m*/*z* 262 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{14}F_2NO$ 262.1038; Found 262.1036.

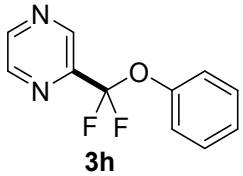
3-(Difluoro(phenoxy)methyl)-2,6-dimethylpyridine (3g)



3g

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3g** (76.2 mg, 51%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 7.30-7.26 (m, 2H), 7.21 (s, 2H), 7.18-7.13 (m, 3H), 2.51 (s, 6H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -67.32 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 157.8, 149.0, 141.3 (t, *J* = 32.9 Hz), 128.5, 124.9, 120.9, 120.0 (t, *J* = 263.6 Hz), 118.6, 115.5 (t, *J* = 3.5 Hz), 114.6, 23.4; **IR** (thin film) *v* 1588, 1491, 1387, 1346, 1234, 1142, 1049, 865, 728, 689 cm^{-1}; **MS** (ESI): *m*/*z* 250 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{14}H_{14}F_2NO$ 250.1038; Found 250.1036.

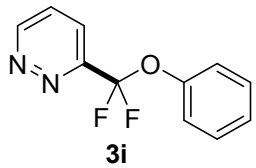
2-(Difluoro(phenoxy)methyl)pyrazine (3h)



3h

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3h** (60.0 mg, 45%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.02 (s, 1H), 8.71 (s, 1H), 8.66 (s, 1H), 7.34-7.31 (m, 2H), 7.26-7.18 (m, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -69.91 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 148.8, 145.8, 145.8 (t, *J* = 34.2 Hz), 143.1, 141.4 (t, *J* = 3.2 Hz), 128.5, 125.2, 121.0, 118.3 (t, *J* = 264.6 Hz); **IR** (thin film) *v* 1591, 1491, 1326, 1190, 1058, 1017, 859, 754, 723, 689 cm^{-1}; **MS** (ESI): *m*/*z* 223 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{11}H_9F_2N_2O$ 223.0677; Found 223.0676.

3-(Difluoro(phenoxy)methyl)pyridazine (3i)

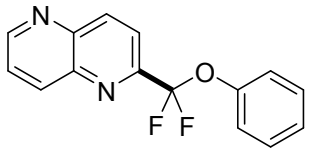


3i

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to afford **3i** (53.3 mg, 40%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.46 (s, 1H), 9.33 (d, *J* = 5.2 Hz, 1H), 7.70 (d, *J* = 3.9 Hz, 1H), 7.33-7.29 (m, 2H), 7.21-7.17 (m, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -66.98 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 150.6, 148.4, 146.6 (t, *J* = 2.9 Hz), 131.3 (t, *J* = 35.1 Hz), 128.7, 125.5, 121.5 (t, *J* = 3.5 Hz), 120.8, 119.0 (t, *J* = 263.8 Hz); **IR** (thin film) *v* 1592, 1491, 1363, 1322, 1152, 1046, 865, 748, 706, 688 cm^{-1};

MS (ESI): *m/z* 223 $[M+H]^+$; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{11}H_9F_2N_2O$ 223.0677; Found 223.0676.

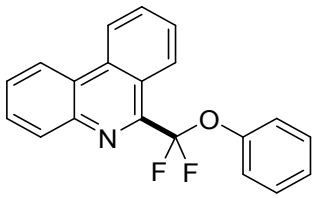
2-(Difluoro(phenoxy)methyl)-1,5-naphthyridine (3j)



3j

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to afford **3j** (106.1 mg, 65%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.15 (dd, *J* = 4.0, 1.3 Hz, 1H), 9.06 (d, *J* = 4.3 Hz, 1H), 8.45 (dd, *J* = 8.5, 1.3 Hz, 1H), 8.01 (d, *J* = 4.4 Hz, 1H), 7.68 (dd, *J* = 8.5, 4.1 Hz, 1H), 7.39-7.32 (m, 4H), 7.21-7.18 (m, 1H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -64.46 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 151.7, 150.7, 150.4, 144.6, 139.9, 138.4 (t, *J* = 31.5 Hz), 137.6, 129.5, 125.9, 124.8, 122.1, 121.7 (t, *J* = 5.1 Hz), 121.0 (t, *J* = 265.0 Hz); **IR** (thin film) *v* 1593, 1492, 1319, 1270, 1200, 1135, 974, 869, 736, 648 cm^{-1}; **MS** (ESI): *m/z* 273 $[M+H]^+$; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{15}H_{11}F_2N_2O$ 273.0834; Found 273.0832.

6-(Difluoro(phenoxy)methyl)phenanthridine (3k)

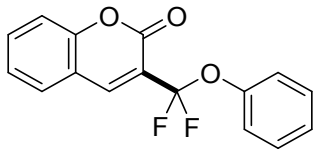


3k

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 15:1) to afford **3k** (61.8 mg, 32%) as a white solid. m.p. 78-80 ^oC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.55 (d, *J* = 8.3 Hz, 1H), 8.50 (d, *J* = 8.3 Hz, 1H), 8.42 (d, *J* = 8.0 Hz, 1H), 8.20 (d, *J* = 8.1 Hz, 1H), 7.73-7.71 (m, 1H), 7.67-7.58 (m, 3H), 7.33-7.24 (m, 4H), 7.13-7.09 (m, 1H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -67.21 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 149.4, 148.2 (t, *J* = 31.5 Hz), 140.8, 132.9, 129.9, 128.5, 128.0, 127.6, 126.6, 125.8 (t, *J* = 2.9 Hz), 124.7, 123.9, 121.3, 121.2, 120.9, 120.6, 119.3 (t, *J* = 265.1 Hz); **IR** (thin film) *v* 1589, 1490, 1374, 1255, 1063, 865, 789, 724, 687 cm^{-1}; **MS** (ESI): *m/z* 322 $[M+H]^+$; **HRMS** (ESI) *m/z*: $[M+H]^+$ Calcd. for $C_{20}H_{14}F_2NO$ 322.1038; Found 322.1034. These assignments

matched with those previously reported (Xiao, P.; Ni, C.; Miao, W.; Zhou, M.; Hu, J.; Chen, D.; Hu, J. *J. Org. Chem.* **2019**, *84*, 8345).

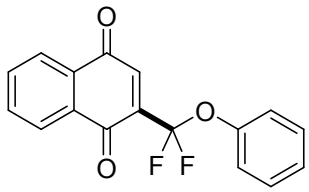
3-(Difluoro(phenoxy)methyl)-2*H*-chromen-2-one (3l)



3l

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 8:1) to afford **3l** (60.5 mg, 35%) as a white solid. m.p. 100-102 ^{o}C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ ppm 8.25 (s, 1H), 7.67-7.62 (m, 2H), 7.41-7.34 (m, 6H), 7.28-7.26 (m, 1H); **^{19}F NMR** (565 MHz, $CDCl_3$) δ ppm -69.13 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 156.5, 154.6, 150.0, 142.7 (t, *J* = 5.0 Hz), 133.7, 129.5, 129.3, 126.1, 125.0, 122.2, 120.5 (t, *J* = 33.2 Hz), 119.5 (t, *J* = 264.6 Hz), 117.3, 116.9; **IR** (thin film) *v* 1728, 1636, 1568, 1489, 1249, 1042, 962, 745, 689 cm^{-1}; **MS** (ESI): *m*/*z* 289 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{16}H_{11}F_2O_3$ 289.0671; Found 289.0669.

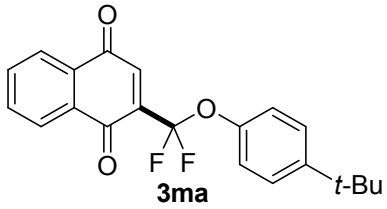
2-(Difluoro(phenoxy)methyl)naphthalene-1,4-dione (3m)



3m

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3m** (135 mg, 75%) as a bright yellow solid. m.p. 88-90 ^{o}C; **^{1}H NMR** (400 MHz, DMSO-*d*6) δ ppm 8.09 (d, *J* = 6.5 Hz, 1H), 8.04 (d, *J* = 8.2 Hz, 1H), 7.99-7.89 (m, 2H), 7.50-7.46 (m, 3H), 7.35-7.32 (m, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -68.47 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.3, 180.3, 149.7, 139.2 (t, *J* = 30.3 Hz), 136.5 (t, *J* = 4.9 Hz), 134.7, 134.3, 132.1, 131.6, 129.6, 127.0, 126.4, 126.2, 122.2, 119.0 (t, *J* = 265.9 Hz); **IR** (thin film) *v* 1664, 1590, 1366, 1149, 1062, 929, 781, 683 cm^{-1}; **MS** (ESI): *m*/*z* 323 $[M+Na]^+$; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd. for $C_{17}H_{10}F_2NaO_3$ 323.0490; Found 323.0483.

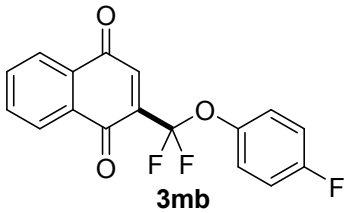
2-((4-(*Tert*-butyl)phenoxy)difluoromethyl)naphthalene-1,4-dione (3ma)



3ma

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3ma** (119.6 mg, 56%) as a yellow solid. m.p. 84-86 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.18 (d, *J* = 6.9 Hz, 1H), 8.10 (d, *J* = 6.8 Hz, 1H), 7.83-7.80 (m, 2H), 7.40-7.38 (m, 3H), 7.22 (d, *J* = 8.5 Hz, 2H), 1.32 (s, 9H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -68.47 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.4, 180.3, 149.1, 147.3, 139.4 (t, *J* = 30.9 Hz), 136.5 (t, *J* = 4.9 Hz), 134.6, 134.2, 132.1, 131.6, 127.0, 126.4, 126.3, 121.6, 119.0 (t, *J* = 265.7 Hz), 34.5, 31.4; **IR** (thin film) *v* 1671, 1594, 1508, 1364, 1245, 1152, 1065, 923, 779, 717 cm^{-1}; **MS** (ESI): *m*/*z* 379 $[M+Na]^+$; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd. for $C_{21}H_{18}F_2NaO_3$ 379.1116; Found 379.1109.

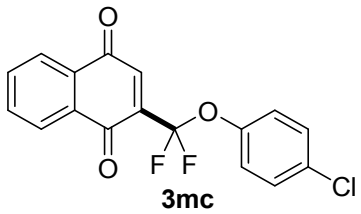
2-(Difluoro(4-fluorophenoxy)methyl)naphthalene-1,4-dione (3mb)



3mb

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3mb** (152.6 mg, 80%) as a bright yellow solid. m.p. 109-111 ^{o}C; **^{1}H NMR** (400 MHz, CD_3CN) δ ppm 8.15 (d, *J* = 6.9 Hz, 1H), 8.08 (d, *J* = 7.8 Hz, 1H), 7.95-7.85 (m, 2H), 7.43 (s, 1H), 7.36 (dd, *J* = 8.6, 4.5 Hz, 2H), 7.22-7.18 (m, 2H); **^{19}F NMR** (377 MHz, CD_3CN) δ ppm -69.10 (s, 2F), -117.54– -117.75 (m, 1F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.2, 180.2, 160.6 (d, *J* = 246.4 Hz), 145.4, 139.1 (t, *J* = 31.3 Hz), 136.6 (t, *J* = 5.0 Hz), 134.6, 134.3, 132.1, 131.6, 127.0, 126.4, 123.9 (d, *J* = 8.0 Hz), 118.9 (t, *J* = 266.7 Hz), 116.2 (d, *J* = 23.5 Hz); **IR** (thin film) *v* 1666, 1591, 1501, 1369, 1142, 1048, 922, 777, 716 cm^{-1}; **MS** (ESI): *m*/*z* 341 $[M+Na]^+$; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd. for $C_{17}H_9F_3NaO_3$ 341.0396; Found 341.0391.

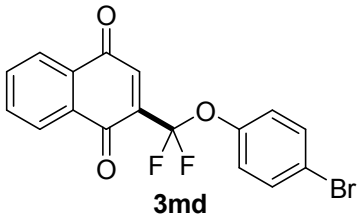
2-((4-Chlorophenoxy)difluoromethyl)naphthalene-1,4-dione (3mc)



3mc

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3mc** (156.3 mg, 78%) as a bright yellow solid. m.p. 98-100 ^{o}C; **^{1}H NMR** (400 MHz, CD_3CN) δ ppm 8.14 (d, *J* = 6.6 Hz, 1H), 8.08 (d, *J* = 6.8 Hz, 1H), 7.93-7.87 (m, 2H), 7.3-7.40 (m, 3H), 7.33 (d, *J* = 8.4 Hz, 2H); **^{19}F NMR** (377 MHz, CD_3CN) δ ppm -68.95 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.2, 180.2, 148.1, 139.0 (t, *J* = 30.3 Hz), 136.6 (t, *J* = 5.1 Hz), 134.7, 134.3, 132.0, 131.8, 131.6, 129.6, 127.0, 126.4, 123.6, 119.0 (t, *J* = 266.6 Hz); **IR** (thin film) *v* 1670, 1597, 1489, 1370, 1248, 1072, 918, 778, 714 cm^{-1}; **MS** (EI): *m*/*z* 334 M^+; **HRMS** (EI) *m*/*z*: M^+ Calcd. for $C_{17}H_9ClF_2O_3$ 334.0203; Found 334.0204.

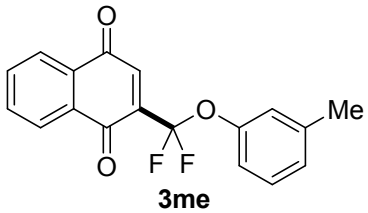
2-((4-Bromophenoxy)difluoromethyl)naphthalene-1,4-dione (3md)



3md

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3md** (161 mg, 71%) as a yellow solid. m.p. 102-104 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.18 (d, *J* = 7.0 Hz, 1H), 8.11 (d, *J* = 7.1 Hz, 1H), 7.85-7.81 (m, 2H), 7.50 (d, *J* = 8.5 Hz, 2H), 7.37 (s, 1H), 7.20 (d, *J* = 8.4 Hz, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -68.92 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.2, 180.2, 148.7, 138.9 (t, *J* = 30.3 Hz), 136.6 (t, *J* = 5.0 Hz), 134.7, 134.4, 132.7, 132.0, 131.5, 127.0, 126.4, 124.0, 119.5, 118.9 (t, *J* = 266.8 Hz); **IR** (thin film) *v* 1671, 1587, 1488, 1371, 1143, 1050, 919, 775, 669 cm^{-1}; **MS** (EI): *m*/*z* 378 M^+; **HRMS** (EI) *m*/*z*: M^+ Calcd. for $C_{17}H_9BrF_2O_3$ 377.9698; Found 377.9694.

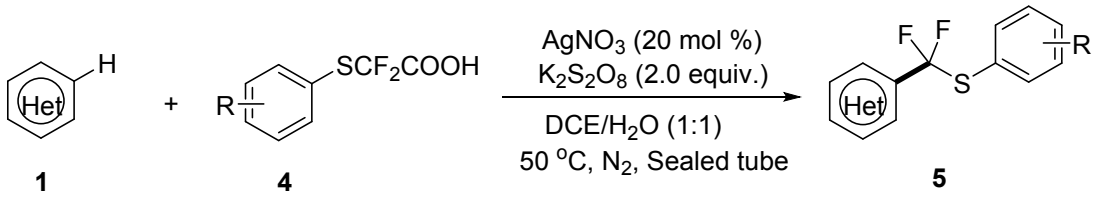
2-(Difluoro(*m*-tolyloxy)methyl)naphthalene-1,4-dione (3me)



3me

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **3me** (135.6 mg, 72%) as a yellow solid. m.p. 87-89 ^{o}C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ ppm 8.15 (d, *J* = 6.1 Hz, 1H), 8.07 (d, *J* = 6.0 Hz, 1H), 7.81-7.76 (m, 2H), 7.36 (s, 1H), 7.27-7.24 (m, 1H), 7.13-7.11 (m, 1H), 7.06 (d, *J* = 7.6 Hz, 2H), 2.37 (s, 3H); **^{19}F NMR** (565 MHz, $CDCl_3$) δ ppm -68.36 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 184.1, 180.2, 149.6, 139.8, 139.2 (t, *J* = 30.8 Hz), 136.5 (t, *J* = 4.9 Hz), 134.6, 134.3, 132.0, 131.5, 129.3, 127.0, 126.9, 126.3, 122.8, 119.1, 118.9 (t, *J* = 265.6 Hz), 21.3; **IR** (thin film) *v* 1671, 1593, 1488, 1364, 1246, 1146, 1055, 919, 779, 686 cm^{-1}; **MS** (ESI): *m*/*z* 337 $[M+Na]^+$; **HRMS** (ESI) *m*/*z*: $[M+Na]^+$ Calcd. for $C_{18}H_{12}F_2NaO_3$ 337.0647; Found 337.0641.

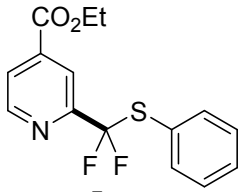
5. General Procedures for Arylthiodifluoromethylation of Heteroarenes



1 **4** **5**

To a sealed tube equipped with a stir bar were added **1** (0.6 mmol, 1.0 equiv), $AgNO_3$ (20.4 mg, 0.12 mmol, 20 mol %), and $K_2S_2O_8$ (324.4 mg, 1.2 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then arylthiodifluoroacetic acid **4** (1.8 mmol, 3.0 equiv) in DCE/H_2O (3.0/3.0 mL) were added. The tube was sealed and the mixture was heated at 50 °C in an oil bath for 20 h. After the reaction was complete, saturated $NaHCO_3$ solution was added. The resulting mixture was extracted with ethyl acetate for three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by silica gel flash column chromatography to give the product **5**.

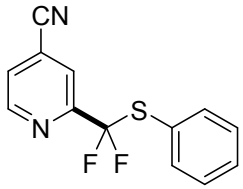
Ethyl 2-(difluoro(phenylthio)methyl)isonicotinate (5a)



5a

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5a** (142.8 mg, 77%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.85 (d, *J* = 4.9 Hz, 1H), 8.13 (s, 1H), 7.96 (dd, *J* = 4.9, 1.0 Hz, 1H), 7.68-7.65 (m, 2H), 7.46-7.42 (m, 1H), 7.40-7.36 (m, 2H), 4.43 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.79 (s, 2F); **^{13}C NMR** (151 MHz, $CDCl_3$) δ ppm 164.1, 154.4 (t, *J* = 28.2 Hz), 150.3, 139.1, 136.8, 130.2, 129.1, 126.3, 126.2 (t, *J* = 278.8 Hz), 124.7, 119.6 (t, *J* = 3.2 Hz), 62.2, 14.2; **IR** (thin film) *v* 1727, 1566, 1368, 1307, 1224, 1016, 961, 867, 749 cm^{-1}; **MS** (ESI): *m*/*z* 310 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{14}F_2NO_2S$ 310.0708; Found 310.0706.

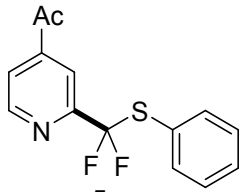
2-(Difluoro(phenylthio)methyl)isonicotinonitrile (5b)



5b

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 8:1) to afford **5b** (102.2 mg, 65%) as a white solid. m.p. 80-82 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.89 (d, *J* = 4.9 Hz, 1H), 7.75 (s, 1H), 7.64-7.61 (m, 3H), 7.49-7.45 (m, 1H), 7.41-7.37 (m, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -75.64 (s); **^{13}C NMR** (151 MHz, $CDCl_3$) δ ppm 154.9 (t, *J* = 28.9 Hz), 150.6, 136.8, 130.5, 129.3, 127.0, 125.7, 125.6 (t, *J* = 279.3 Hz), 122.0, 121.7, 115.6; **IR** (thin film) *v* 1599, 1473, 1289, 1048, 969, 860, 804, 710, 640 cm^{-1}; **MS** (ESI): *m*/*z* 263 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{13}H_9F_2N_2S$ 263.0449; Found 263.0448.

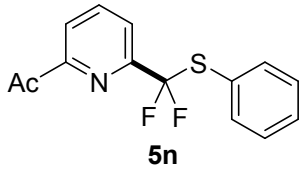
1-(2-(Difluoro(phenylthio)methyl)pyridin-4-yl)ethan-1-one (5c)



5c

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to afford **5c** (95.4 mg, 57%) as a yellow liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.89 (d, *J* = 5.0 Hz, 1H), 7.97 (s, 1H), 7.83 (d, *J* = 4.9 Hz, 1H), 7.65 (d, *J* = 7.2 Hz, 2H), 7.47-7.43 (m, 1H), 7.40-7.37 (m, 2H), 2.62 (s, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.95 (s, 2F); **^{13}C NMR** (151 MHz, $CDCl_3$) δ ppm 196.1, 154.8 (t, *J* = 28.2 Hz), 150.8, 144.0, 136.8, 130.2, 129.1, 126.3, 126.2 (t, *J* = 278.8 Hz), 122.9, 118.0 (t, *J* = 3.2 Hz), 26.7; **IR** (thin film) *v* 1698, 1560, 1360, 1295, 1213, 1054, 947, 847, 690 cm^{-1}; **MS** (ESI): *m*/*z* 280 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{14}H_{12}F_2NOS$ 280.0602; Found 280.0600.

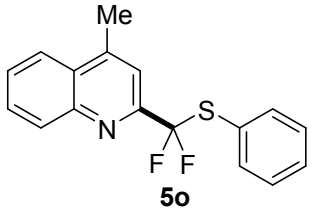
1-(6-(Difluoro(phenylthio)methyl)pyridin-2-yl)ethan-1-one (5n)



5n

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 5:1) to afford **5n** (100.4 mg, 60%) as a yellow liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.63 (d, *J* = 5.0 Hz, 1H), 8.05 (s, 1H), 7.47-7.43 (m, 3H), 7.36-7.32 (m, 1H), 7.28-7.24 (m, 2H), 2.63 (s, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -75.05 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 198.9, 154.1, 149.5, 145.1 (t, *J* = 27.2 Hz), 136.6, 130.5, 129.3, 126.1 (t, *J* = 280.1 Hz), 126.0, 122.7 (t, *J* = 4.2 Hz), 117.8 (t, *J* = 4.4 Hz), 25.8; **IR** (thin film) *v* 1700, 1353, 1213, 1052, 906, 845, 749, 659, 589 cm^{-1}; **MS** (ESI): *m*/*z* 280 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{14}H_{12}F_2NOS$ 280.0602; Found 280.0600.

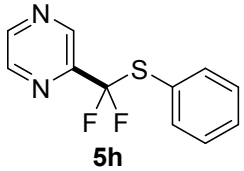
2-(Difluoro(phenylthio)methyl)-4-methylquinoline (5o)



5o

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5o** (81.3 mg, 45%) as a white solid. m.p. 79-81 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.37 (d, *J* = 8.3 Hz, 1H), 7.99 (d, *J* = 8.4 Hz, 1H), 7.66-7.62 (m, 1H), 7.52-7.47 (m, 3H), 7.34-7.23 (m, 4H), 2.60 (s, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -71.27 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 157.1, 147.7, 138.4 (t, *J* = 24.1 Hz), 135.5, 129.3, 128.7, 128.4, 128.1, 128.0, 125.5 (t, *J* = 280.1 Hz), 125.4, 124.1 (t, *J* = 3.0 Hz), 120.7, 117.8 (t, *J* = 6.7 Hz) 24.3; **IR** (thin film) *v* 1603, 1510, 1440, 1329, 1236, 1134, 1024, 964, 750, 642 cm^{-1}; **MS** (ESI): *m*/*z* 302 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{17}H_{14}F_2NS$ 302.0810; Found 302.0807.

2-(Difluoro(phenylthio)methyl)pyrazine (5h)

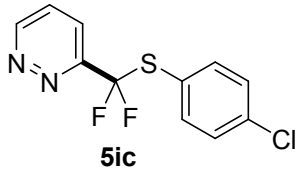


5h

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 8:1) to afford **5h** (42.8 mg, 30%) as a yellow solid. m.p. 62-64 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.74 (s, 1H), 8.62-8.59 (m, 2H), 7.55 (d, *J* = 7.3 Hz, 2H), 7.39-7.36 (m, 1H), 7.32-7.29 (m, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm

-75.90 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 147.9 (t, *J* = 28.5 Hz), 145.4, 142.8, 140.8 (t, *J* = 3.8 Hz), 135.8, 129.4, 128.2, 124.8 (t, *J* = 279.5 Hz), 124.7; **IR** (thin film) *v* 1475, 1407, 1283, 1078, 1018, 927, 849, 747, 688 cm^{-1}; **MS** (ESI): *m*/*z* 239 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{11}H_9F_2N_2S$ 239.0449; Found 239.0447.

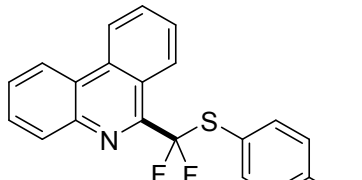
3-(((4-Chlorophenyl)thio)difluoromethyl)pyridazine (5ic)



5ic

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 4:1) to afford **5ic** (138.7 mg, 85%) as a white solid. m.p. 102-104 ^oC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 9.33 (d, *J* = 5.4 Hz, 2H), 7.52-7.48 (m, 3H), 7.39-7.36 (m, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -76.25 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 151.2, 147.1 (t, *J* = 3.8 Hz), 137.9, 137.7, 134.4 (t, *J* = 27.9 Hz), 129.8, 125.0 (t, *J* = 280.6 Hz), 123.6, 121.9 (t, *J* = 4.4 Hz); **IR** (thin film) *v* 1568, 1472, 1386, 1265, 1046, 926, 824, 718 cm^{-1}; **MS** (ESI): *m*/*z* 273 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{11}H_8ClF_2N_2S$ 273.0059; Found 273.0057.

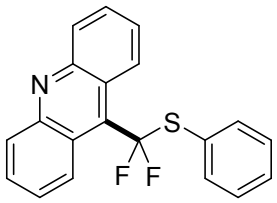
6-(((4-Chlorophenyl)thio)difluoromethyl)phenanthridine (5kc)



5kc

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 15:1) to afford **5kc** (140.2 mg, 63%) as a white solid. m.p. 124-126 ^oC; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.61 (d, *J* = 8.3 Hz, 1H), 8.53-8.50 (m, 2H), 8.25 (d, *J* = 7.5 Hz, 1H), 7.85-7.81 (m, 1H), 7.77-7.65 (m, 5H), 7.40 (d, *J* = 8.3 Hz, 2H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -65.59 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 150.8 (t, *J* = 28.3 Hz), 141.6, 138.4, 136.6, 134.0, 131.2, 130.8, 129.7 (t, *J* = 280.1 Hz), 129.3, 129.2, 128.9, 127.7, 126.8 (t, *J* = 5.4 Hz), 126.0, 125.0, 122.5, 122.1, 121.8; **IR** (thin film) *v* 1571, 1474, 1363, 1133, 1048, 874, 824, 778, 724 cm^{-1}; **MS** (ESI): *m*/*z* 372 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{20}H_{13}ClF_2NS$ 372.0420; Found 372.0416.

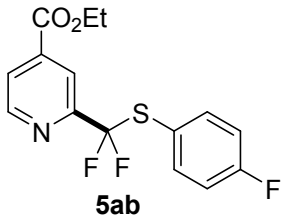
9-(Difluoro(phenylthio)methyl)acridine (5p)



5p

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 6:1) to afford **5p** (117.3 mg, 58%) as a yellow solid. m.p. 169-171 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.53 (d, *J* = 8.2 Hz, 2H), 8.16 (d, *J* = 8.3 Hz, 2H), 7.70-7.64 (m, 4H), 7.51-7.48 (m, 2H), 7.37-7.31 (m, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -59.30 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 149.0, 136.8, 135.7 (t, *J* = 23.4 Hz), 130.5, 130.4, 129.7, 129.3, 129.1 (t, *J* = 283.2 Hz), 127.0, 126.4, 125.6 (t, *J* = 8.4 Hz), 122.8; **IR** (thin film) *v* 1521, 1439, 1344, 1128, 1037, 981, 864, 749, 687 cm^{-1}; **MS** (ESI): *m*/*z* 338 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{20}H_{14}F_2NS$ 338.0810; Found 338.0808.

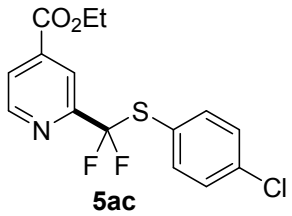
Ethyl 2-(difluoro((4-fluorophenyl)thio)methyl)isonicotinate (5ab)



5ab

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5ab** (153 mg, 78%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.86 (d, *J* = 4.9 Hz, 1H), 8.13 (s, 1H), 7.98 (d, *J* = 4.9 Hz, 1H), 7.67-7.63 (m, 2H), 7.11-7.07 (m, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -75.06 (s, 2F), -109.92–-110.00 (m, 1F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 164.2 (d, *J* = 251.5 Hz), 164.1, 154.2 (t, *J* = 28.2 Hz), 150.4, 139.2, 139.0 (d, *J* = 8.8 Hz), 126.0 (t, *J* = 279.8 Hz), 124.8, 121.5, 119.6 (t, *J* = 3.3 Hz), 116.4 (d, *J* = 22.1 Hz), 62.3, 14.2; **IR** (thin film) *v* 1727, 1589, 1490, 1307, 1223, 1060, 960, 833, 718 cm^{-1}; **MS** (ESI): *m*/*z* 328 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{13}F_3NO_2S$ 328.0614; Found 328.0611.

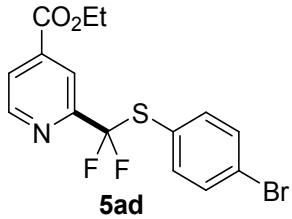
Ethyl 2-(((4-chlorophenyl)thio)difluoromethyl)isonicotinate (5ac)



5ac

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5ac** (154.4 mg, 75%) as a white solid. m.p. 44-46 °C; **^{1}H NMR** (600 MHz, $CDCl_3$) δ ppm 8.86 (d, *J* = 4.9 Hz, 1H), 8.14 (s, 1H), 7.98 (d, *J* = 4.9 Hz, 1H), 7.60 (d, *J* = 8.4 Hz, 2H), 7.37 (d, *J* = 8.4 Hz, 2H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.48 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 164.1, 154.1 (t, *J* = 28.1 Hz), 150.4, 139.2, 138.0, 136.9, 129.4, 126.0 (t, *J* = 280.1 Hz), 124.9, 124.8, 119.6 (t, *J* = 3.3 Hz), 62.3, 14.2; **IR** (thin film) *v* 1724, 1567, 1477, 1368, 1302, 1225, 1093, 996, 824, 760 cm^{-1}; **MS** (ESI): *m*/*z* 344 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{13}ClF_2NO_2S$ 344.0318; Found 324.0317.

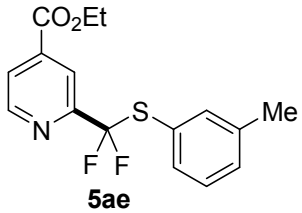
Ethyl 2-(((4-bromophenyl)thio)difluoromethyl)isonicotinate (5ad)



5ad

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5ad** (150.9 mg, 65%) as a white solid. m.p. 58-60 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.85 (d, *J* = 4.9 Hz, 1H), 8.14 (s, 1H), 7.98 (d, *J* = 4.9 Hz, 1H), 7.59-7.52 (m, 4H), 4.45 (q, *J* = 7.1 Hz, 2H), 1.43 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.37 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 164.1, 154.1 (t, *J* = 28.0 Hz), 150.4, 139.3, 138.2, 132.4, 126.0 (t, *J* = 280.2 Hz), 125.4, 125.2, 124.9, 119.6 (t, *J* = 3.3 Hz), 62.3, 14.2; **IR** (thin film) *v* 1724, 1561, 1474, 1369, 1303, 1262, 1065, 819, 760, 718 cm^{-1}; **MS** (ESI): *m*/*z* 388 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{13}BrF_2NO_2S$ 387.9813; Found 387.9809.

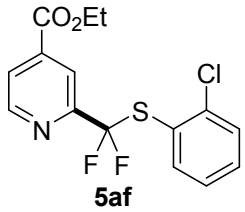
Ethyl 2-(difluoro(m-tolylthio)methyl)isonicotinate (5ae)



5ae

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5ae** (139.5 mg, 72%) as a yellowish liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.76 (d, *J* = 4.9 Hz, 1H), 8.04 (s, 1H), 7.87 (d, *J* = 4.9 Hz, 1H), 7.39-7.36 (m, 2H), 7.20-7.14 (m, 2H), 4.34 (q, *J* = 7.1 Hz, 2H), 2.27 (s, 3H), 1.32 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.87 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 164.2, 154.5 (t, *J* = 28.2 Hz), 150.3, 139.1, 139.0, 137.3, 133.7, 131.0, 128.9, 126.2 (t, *J* = 279.7 Hz), 126.0, 124.6, 119.6 (t, *J* = 3.3 Hz), 62.2, 21.2, 14.2; **IR** (thin film) *v* 1728, 1565, 1475, 1368, 1289, 1224, 1060, 960, 866, 762 cm^{-1}; **MS** (ESI): *m*/*z* 324 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{16}H_{16}F_2NO_2S$ 324.0864; Found 324.0863.

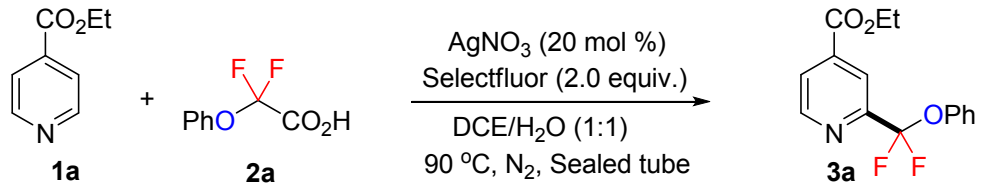
Ethyl 2-(((2-chlorophenyl)thio)difluoromethyl)isonicotinate (5af)



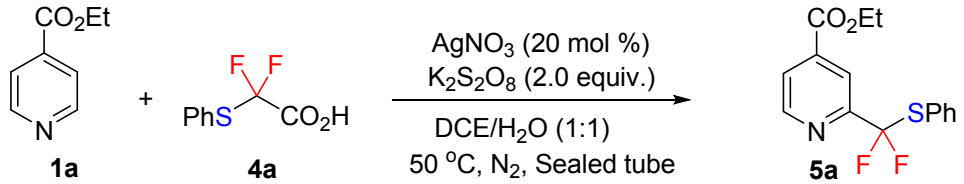
5af

The product mixture was purified by silica gel column chromatography (hexane/EtOAc = 10:1) to afford **5af** (127.6 mg, 62%) as a yellow liquid. **^{1}H NMR** (400 MHz, $CDCl_3$) δ ppm 8.85 (d, *J* = 4.9 Hz, 1H), 8.15 (s, 1H), 7.98 (d, *J* = 4.9 Hz, 1H), 7.84 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.49 (dd, *J* = 8.0, 1.4 Hz, 1H), 7.40-7.36 (m, 1H), 7.33-7.28 (m, 1H), 4.44 (q, *J* = 7.1 Hz, 2H), 1.42 (t, *J* = 7.1 Hz, 3H); **^{19}F NMR** (377 MHz, $CDCl_3$) δ ppm -74.14 (s, 2F); **^{13}C NMR** (101 MHz, $CDCl_3$) δ ppm 164.1, 154.1 (t, *J* = 27.9 Hz), 150.3, 140.2, 139.2, 139.1, 131.6, 130.3, 127.3, 126.2 (t, *J* = 281.4 Hz), 126.0, 124.8, 119.5 (t, *J* = 3.4 Hz), 62.3, 14.2; **IR** (thin film) *v* 1727, 1565, 1452, 1289, 1224, 1063, 959, 815, 754 cm^{-1}; **MS** (ESI): *m*/*z* 344 $[M+H]^+$; **HRMS** (ESI) *m*/*z*: $[M+H]^+$ Calcd. for $C_{15}H_{13}ClF_2NO_2S$ 344.0318; Found 324.0315.

6. Scale-up Experiments



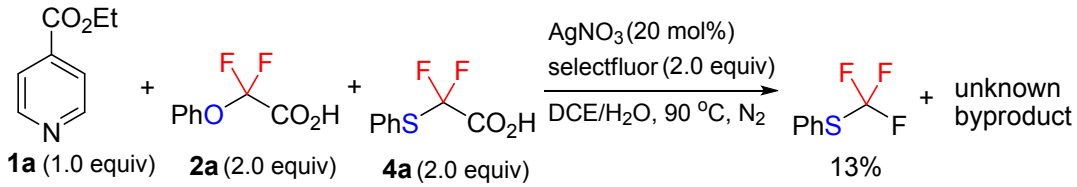
To a sealed tube equipped with a stir bar were added **1a** (181.2 mg, 1.2 mmol, 1.0 equiv), $AgNO_3$ (40.8 mg, 0.24 mmol, 20 mol %), and selectfluor (850.2 mg, 2.4 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenoxydifluoroacetic acid **2a** (677.2 mg, 3.6 mmol, 3.0 equiv) in DCE/H_2O (6.0/6.0 mL) were added. The tube was sealed and the mixture was heated at 90 °C in an oil bath for 20 h. After the reaction was complete, saturated $NaHCO_3$ solution was added. The resulting mixture was extracted with ethyl acetate for three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by silica gel flash column chromatography (hexane/EtOAc = 10:1) to give **3a** (204.8 mg, 58%) as a yellowish liquid.



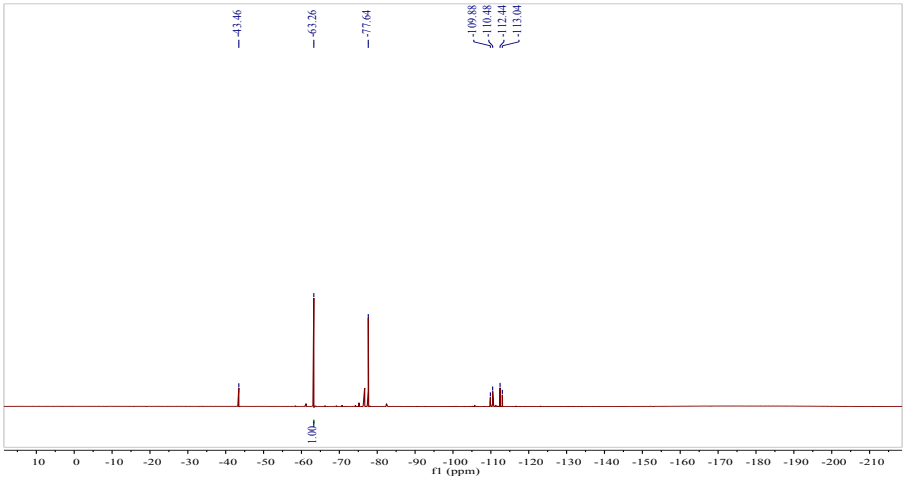
To a sealed tube equipped with a stir bar were added **1a** (181.2 mg, 1.2 mmol, 1.0 equiv), $AgNO_3$ (40.8 mg, 0.24 mmol, 20 mol %), and $K_2S_2O_8$ (648.7 mg, 2.4 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenylthiodifluoroacetic acid **4a** (735.1 mg, 3.6 mmol, 3.0 equiv) in DCE/H_2O (6.0/6.0 mL) were added. The tube was sealed and the mixture was heated at 50 °C in an oil bath for 20 h. After the reaction was complete, saturated $NaHCO_3$ solution was added. The resulting mixture was extracted with ethyl acetate for three times. The combined organic layer was washed with brine, dried over anhydrous Na_2SO_4, and concentrated under reduced pressure. The resulting residue was purified by silica gel flash column chromatography (hexane/EtOAc = 10:1) to give **5a** (273.9 mg, 74%) as a yellowish liquid.

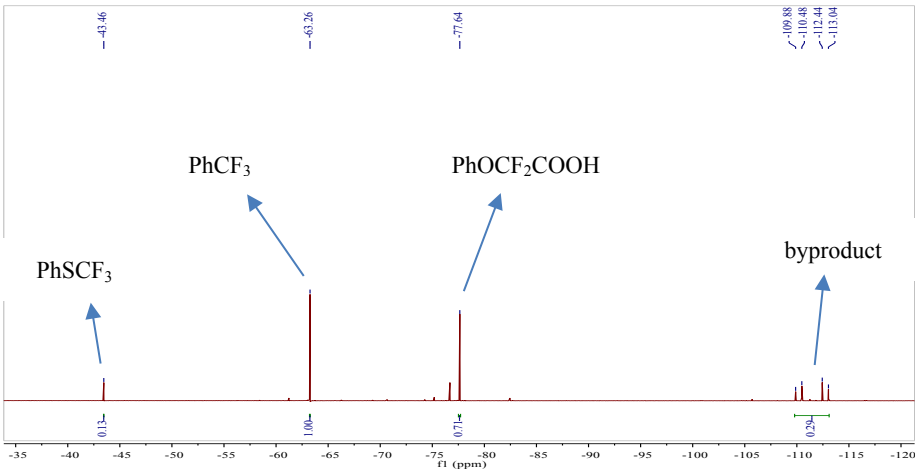
7. Competition Experiments

Under $AgNO_3$/selectfluor reaction system

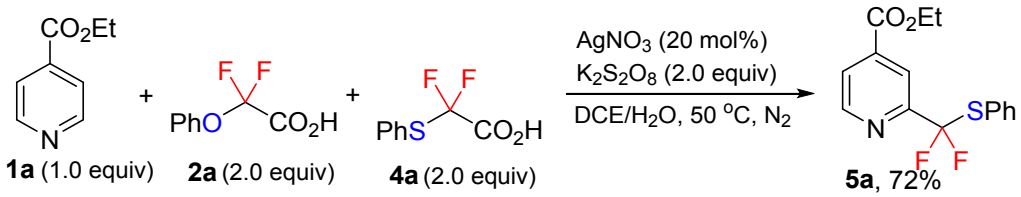


To a sealed tube equipped with a stir bar were added **1a** (90.7 mg, 0.6 mmol, 1.0 equiv), $AgNO_3$ (20.4 mg, 0.12 mmol, 20 mol%), and selectfluor (425.1 mg, 1.2 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenoxydifluoroacetic acid **2a** (225.7 mg, 1.2 mmol, 2.0 equiv) and phenylthiodifluoroacetic acid **4a** (245.0 mg, 1.2 mmol, 2.0 equiv) in DCE/H_2O (3.0/3.0 mL) were added. The tube was sealed and the mixture was heated at 90 °C in an oil bath for 20 h. The internal standard $PhCF_3$ (73.7 μL, 0.6 mmol, 1.0 equiv) was added, and the solution was then analyzed by ^{19}F NMR spectroscopy. The ^{19}F NMR spectroscopy indicated the formation of $PhSCF_3$ (13%) and an unknown byproduct.

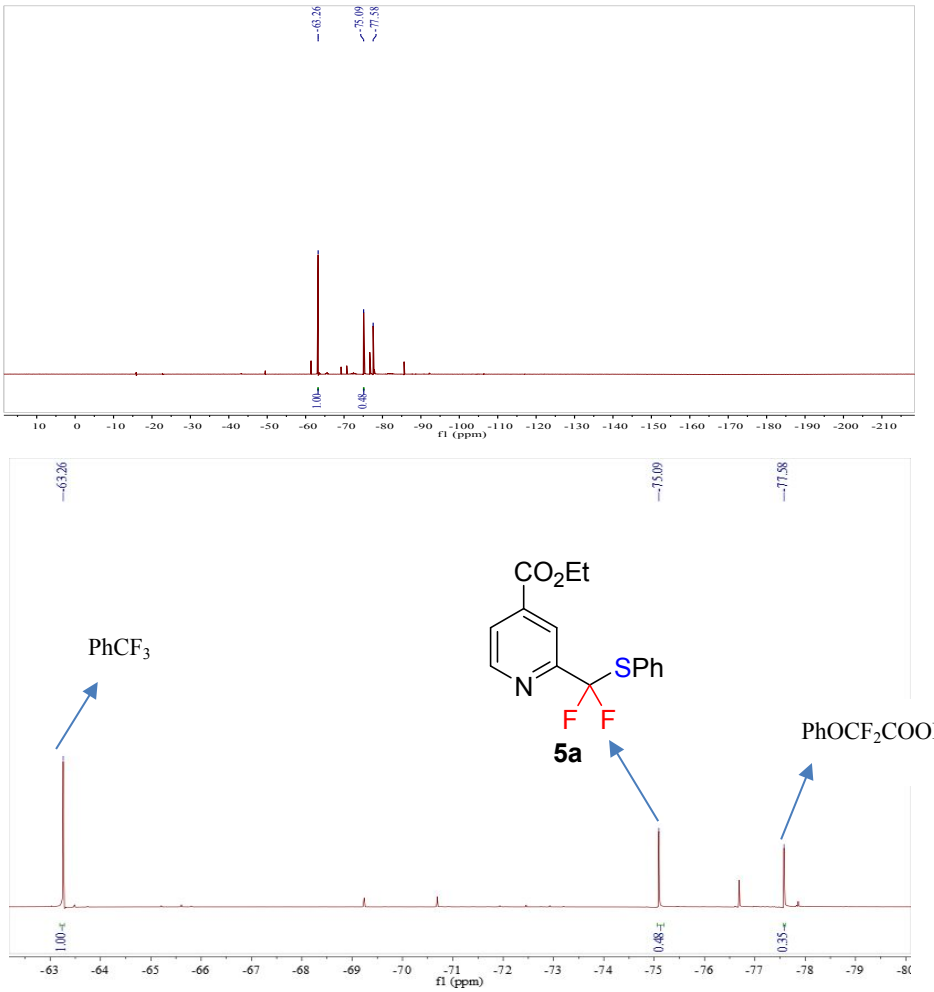




Under $AgNO_3/K_2S_2O_8$ reaction system

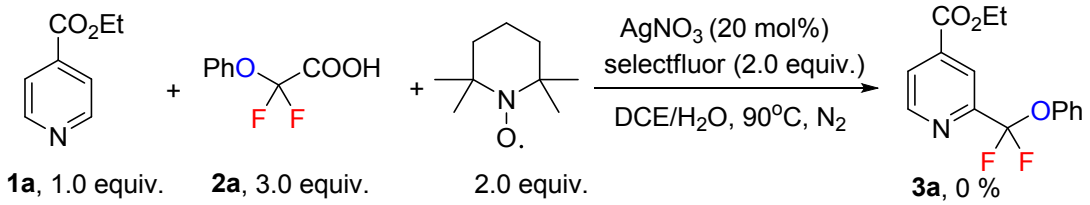


To a sealed tube equipped with a stir bar were added **1a** (90.7 mg, 0.6 mmol, 1.0 equiv), $AgNO_3$ (20.4 mg, 0.12 mmol, 20 mol %), and $K_2S_2O_8$ (324.4 mg, 1.2 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenoxydifluoroacetic acid **2a** (225.7 mg, 1.2 mmol, 2.0 equiv) and phenylthiodifluoroacetic acid **4a** (245.0 mg, 1.2 mmol, 2.0 equiv) in DCE/H_2O (3.0/3.0 mL) were added. The tube was sealed and the mixture was heated at 50 °C in an oil bath for 20 h. The internal standard $PhCF_3$ (73.7 μL, 0.6 mmol, 1.0 equiv) was added, and the solution was then analyzed by ^{19}F NMR spectroscopy. The ^{19}F NMR spectroscopy indicated the formation of **5a** (72%).



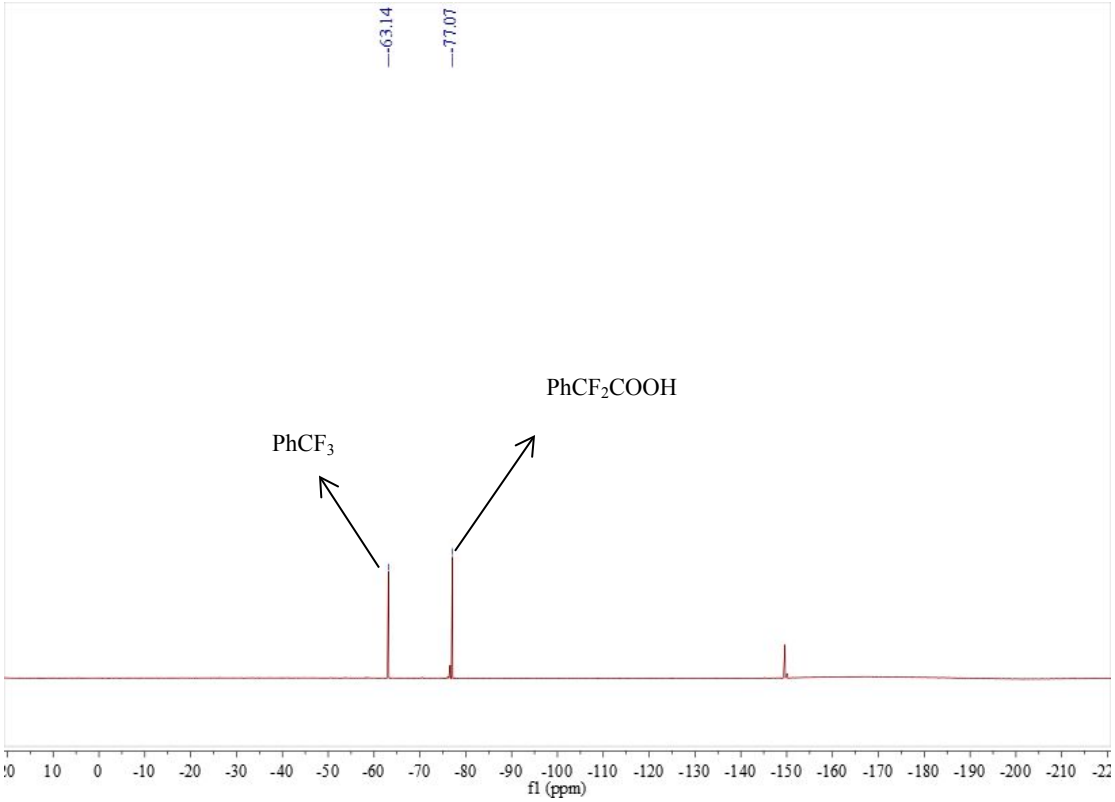
8. Radical Inhibition Experiments

Aryloxydifluoromethylation in the presence of TEMPO

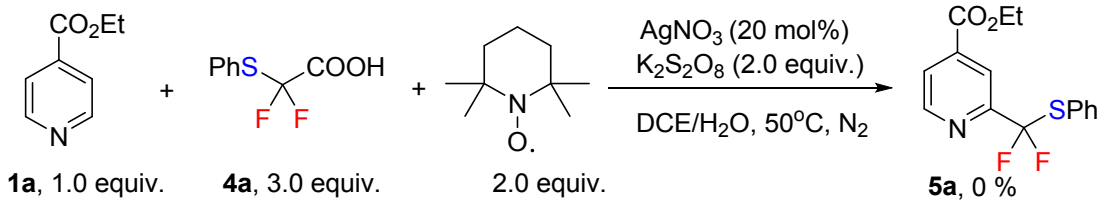


1a, 1.0 equiv. **2a**, 3.0 equiv. 2.0 equiv. **3a**, 0 %

To a sealed tube equipped with a stir bar were added **1a** (30.2 mg, 0.2 mmol, 1.0 equiv), TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv), $AgNO_3$ (6.8 mg, 0.04 mmol, 20 mol%), and selectfluor (141.7 mg, 0.4 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenoxydifluoroacetic acid **2a** (112.8 mg, 0.6 mmol, 3.0 equiv) in DCE/H_2O (1.0/1.0 mL) were added. The tube was sealed and the mixture was heated at 90 °C in an oil bath for 20 h. The internal standard $PhCF_3$ (24.6 μL, 0.2 mmol, 1.0 equiv) was added, and the solution was then analyzed by ^{19}F NMR spectroscopy. The ^{19}F NMR spectroscopy indicated that the desired product **3a** was completely inhibited in the presence of 2.0 equiv. of TEMPO.

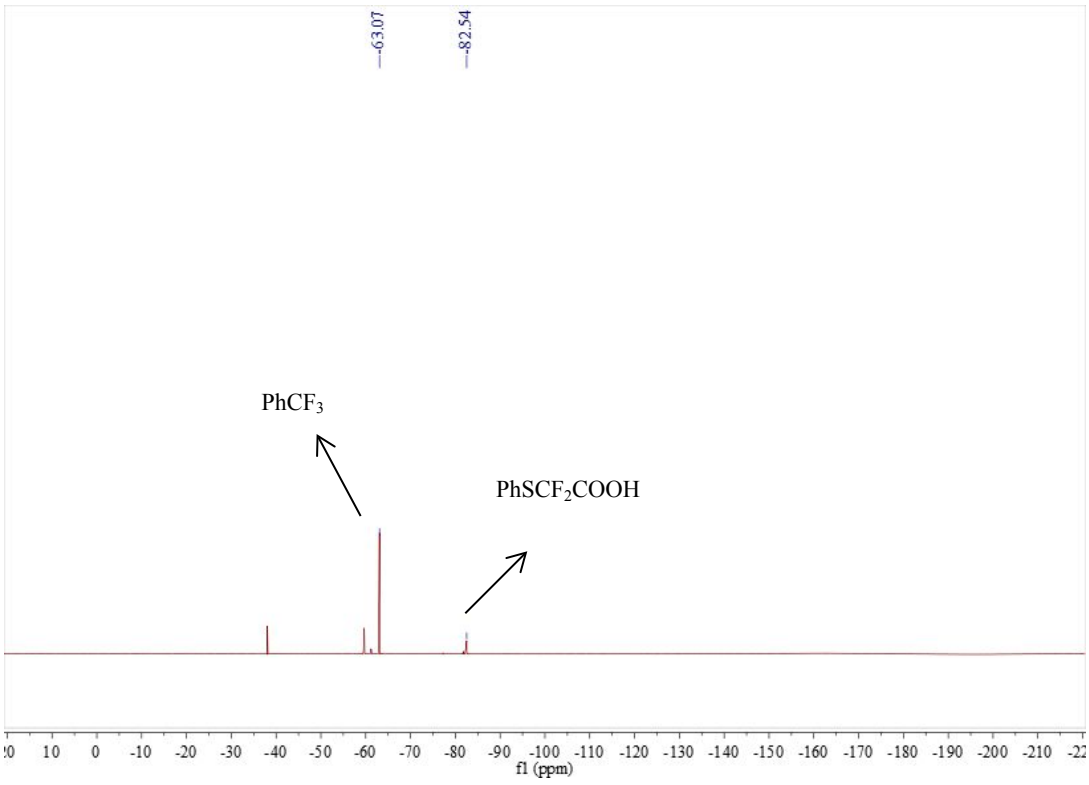


Arylthiodifluoromethylation in the presence of TEMPO



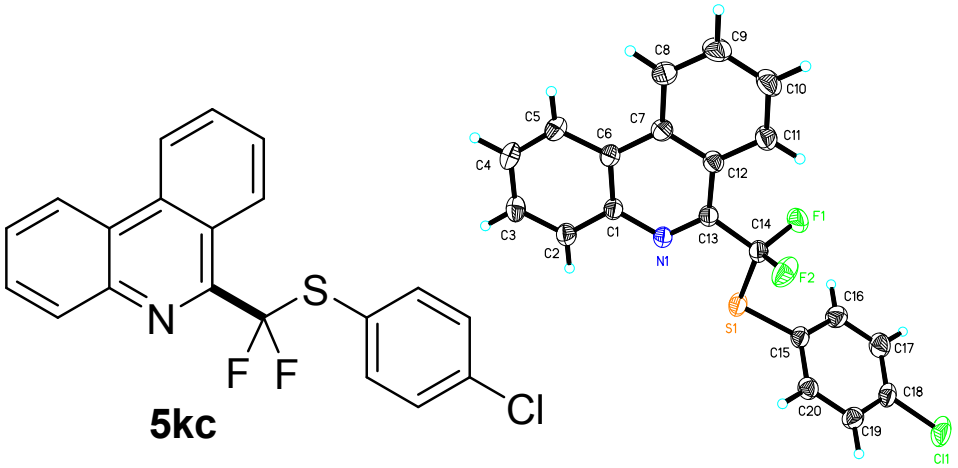
1a, 1.0 equiv. **4a**, 3.0 equiv. 2.0 equiv. **5a**, 0 %

To a sealed tube equipped with a stir bar were added **1a** (30.2 mg, 0.2 mmol, 1.0 equiv), TEMPO (62.5 mg, 0.4 mmol, 2.0 equiv), $AgNO_3$ (6.8 mg, 0.04 mmol, 20 mol%), and $K_2S_2O_8$ (108.1 mg, 0.4 mmol, 2.0 equiv). The tube was evacuated and backfilled with pure N_2 for three times. Then phenoxydifluoroacetic acid **4a** (122.4 mg, 0.6 mmol, 3.0 equiv) in DCE/H_2O (1.0/1.0 mL) were added. The tube was sealed and the mixture was heated at 50 °C in an oil bath for 20 h. The internal standard $PhCF_3$ (24.6 μL, 0.2 mmol, 1.0 equiv) was added, and the solution was then analyzed by ^{19}F NMR spectroscopy. The ^{19}F NMR spectroscopy indicated that the desired product **5a** was completely inhibited in the presence of 2.0 equiv. of TEMPO.



9. ORTEP Drawing of the X-Ray Crystallographic Structure of Product 5kc

The crystals were obtained from a solution of dichloromethane and hexane upon slow volatilization. The X-ray intensity data were measured at 293(2) K, on a Rigaku AFC7R diffractometer.



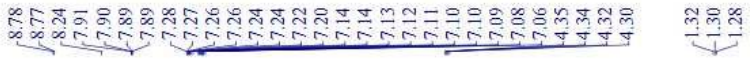
The crystal structure has been deposited at the Cambridge Crystallographic Date Center and allocated the deposition number CCDC 2001370. The thermal ellipsoids are shown at the 30% probability level. This data can be obtained free of charge from the Cambridge Crystallographic Date Center via www.ccdc.cam.ac.uk/data_request/cif

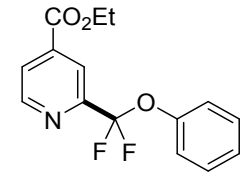
Crystal data and structure refinement for 5kc

Identification code	**5kc**	
Empirical formula	C20 H12 Cl F2 N S	
Formula weight	371.82	
Temperature	293(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.2778(12) Å	α= 71.910(4)°.
	b = 9.4259(13) Å	β= 80.287(4)°.
	c = 11.5784(17) Å	γ = 85.508(4)°.
Volume	846.1(2) $Å^3$	
Z	2	
Density (calculated)	1.459 Mg/m^3	
Absorption coefficient	0.371 mm^{-1}	
F(000)	380	
Crystal size	0.200 x 0.160 x 0.130 mm^3	
Theta range for data collection	2.884 to 25.998°.	
Index ranges	-10<=h<=10, -11<=k<=11, -14<=l<=14	
Reflections collected	20622	
Independent reflections	3286 [R(int) = 0.0320]	
Completeness to theta = 25.242°	98.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7456 and 0.6652	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	3286 / 0 / 227	
Goodness-of-fit on F^2	1.048	
Final R indices [I>2sigma(I)]	R1 = 0.0350, wR2 = 0.0870	
R indices (all data)	R1 = 0.0402, wR2 = 0.0907	
Extinction coefficient	0.025(8)	
Largest diff. peak and hole	0.233 and -0.253 $e.Å^{-3}$	

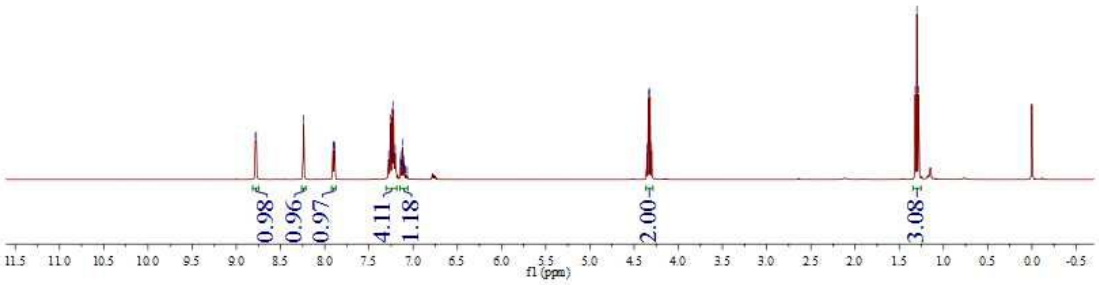
10.Copies of ^{1}H, ^{19}F, and ^{13}C NMR Spectra for the Products

^{1}H NMR (400 MHz, $CDCl_3$)

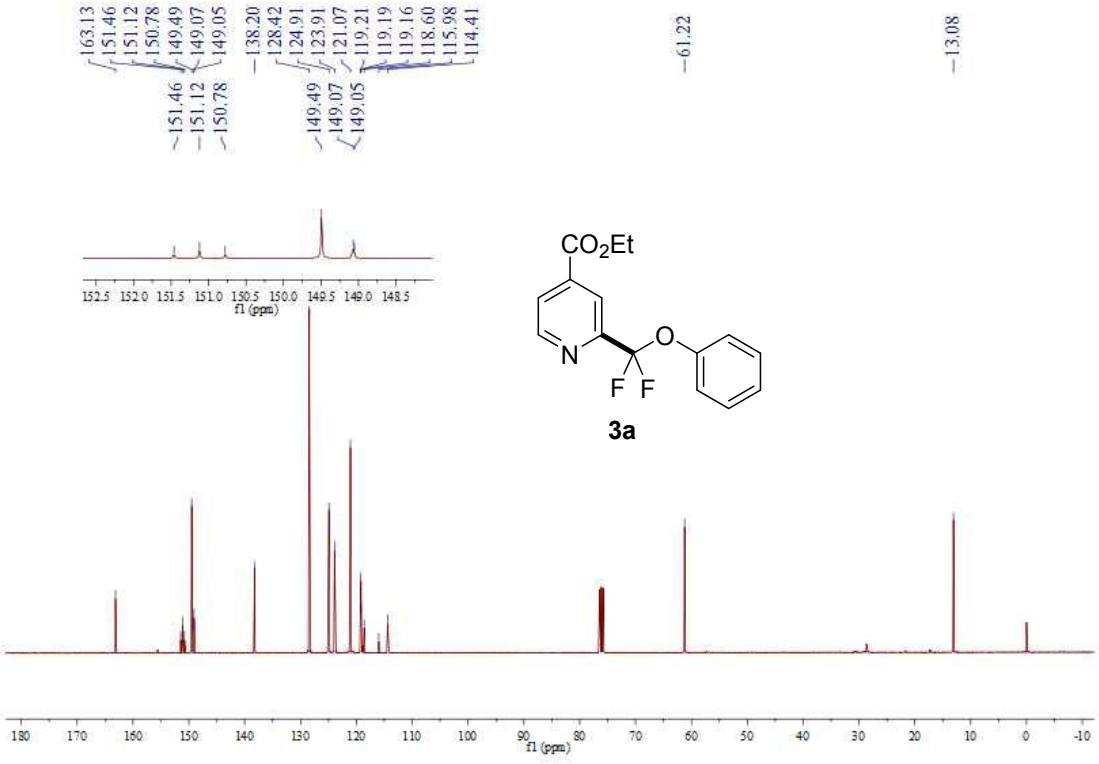




3a

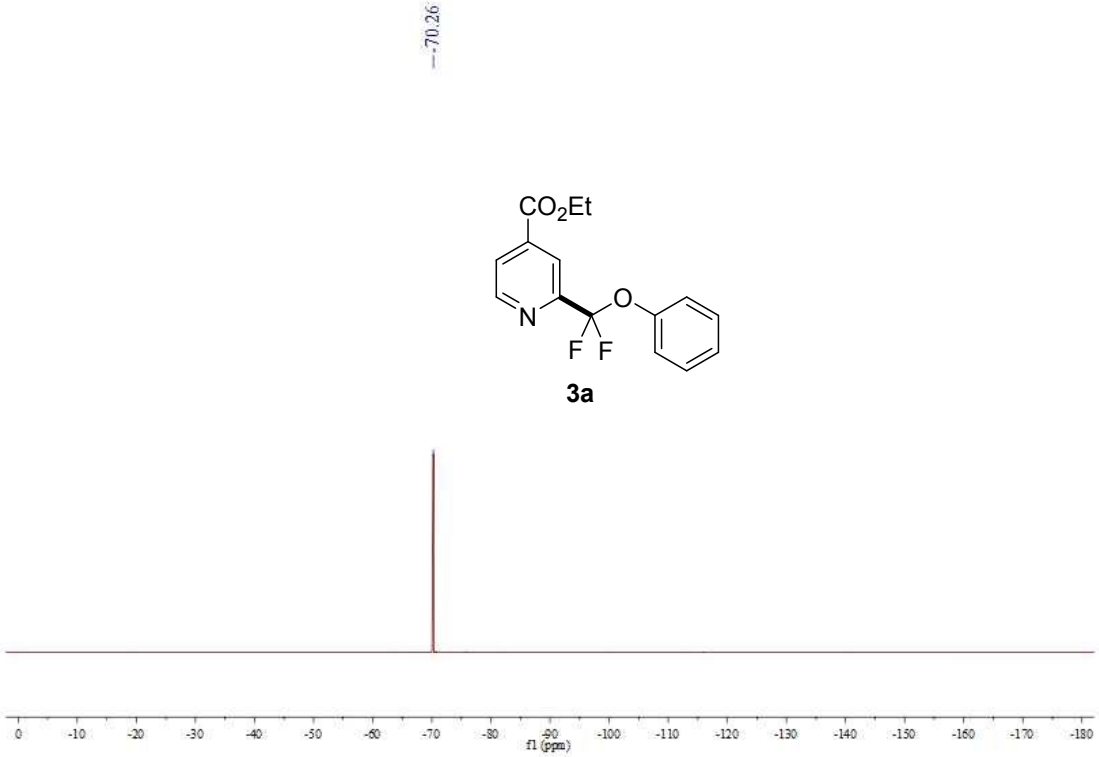


^{13}C NMR (101 MHz, $CDCl_3$)

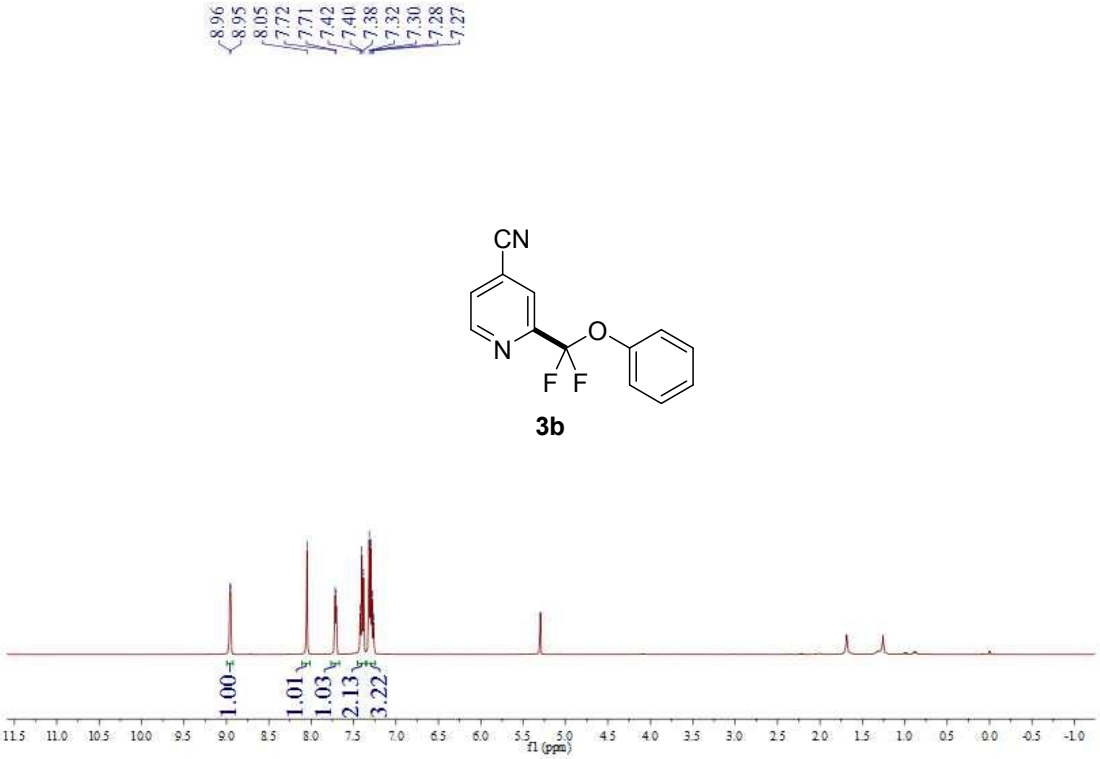


3a

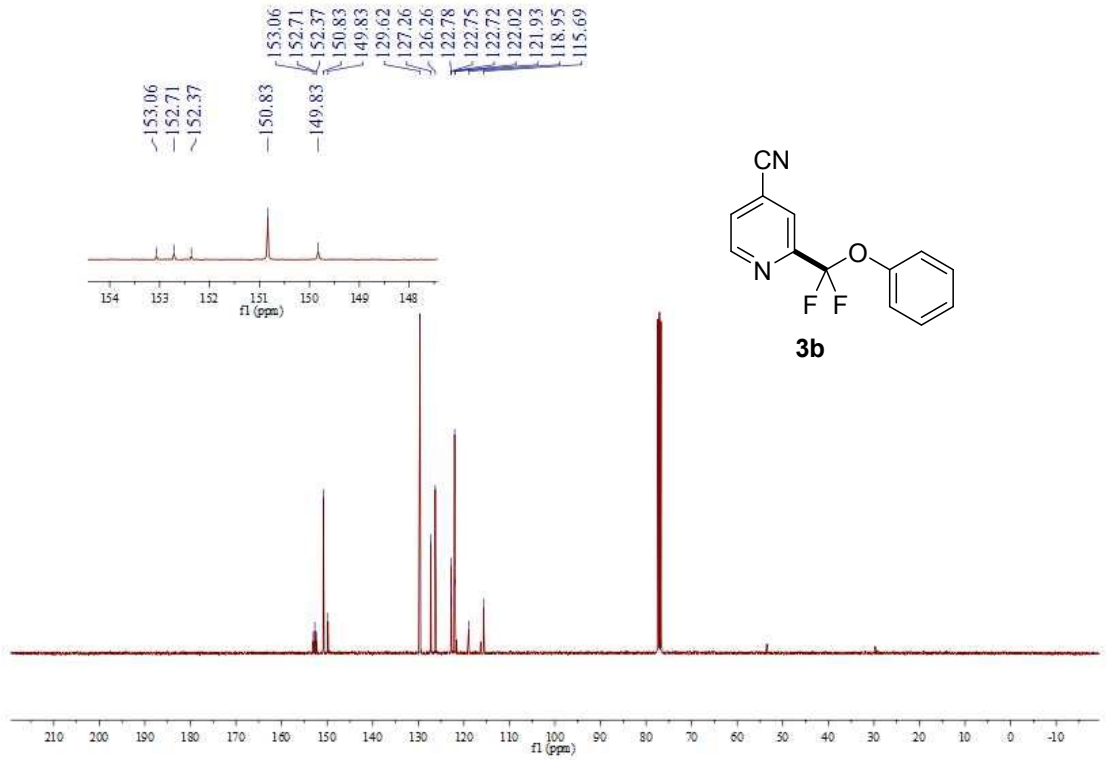
^{19}F NMR (377 MHz, $CDCl_3$)



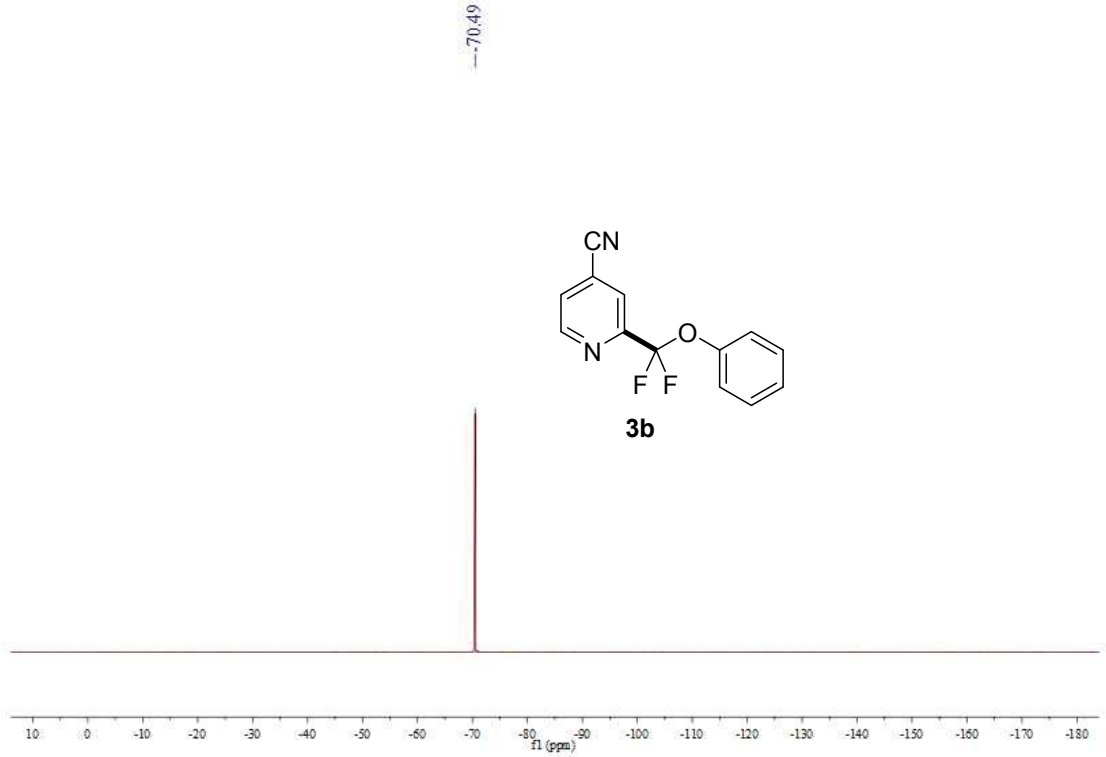
^{1}H NMR (400 MHz, $CDCl_3$)



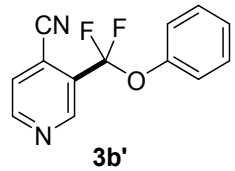
^{13}C NMR (101 MHz, $CDCl_3$)



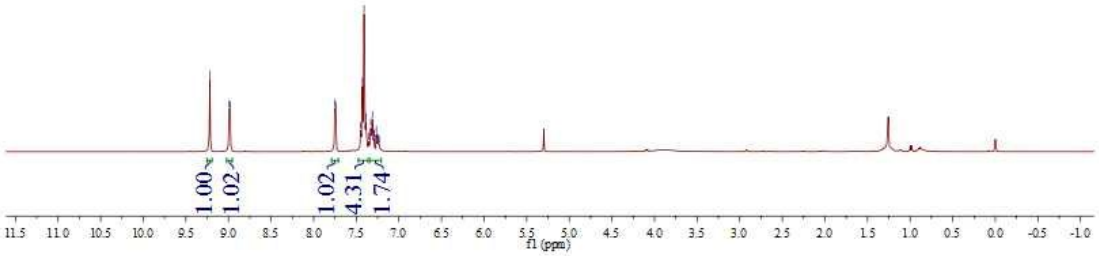
^{19}F NMR (377 MHz, $CDCl_3$)



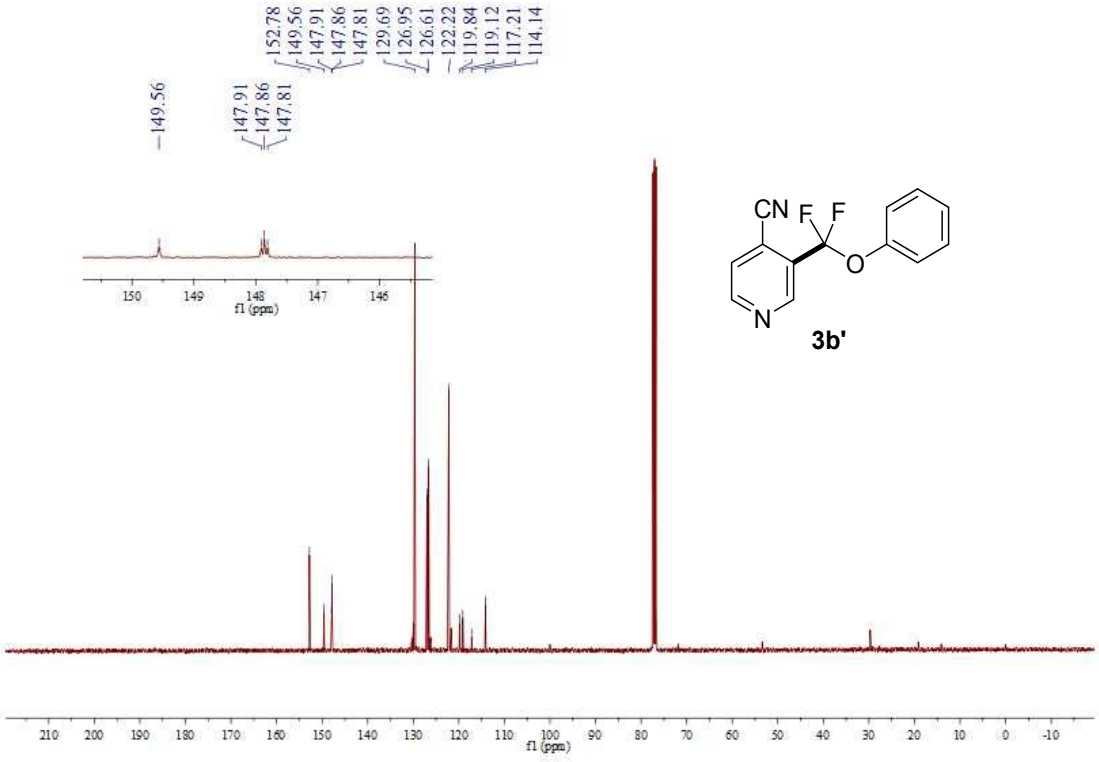
^{1}H NMR (400 MHz, $CDCl_3$)



3b'

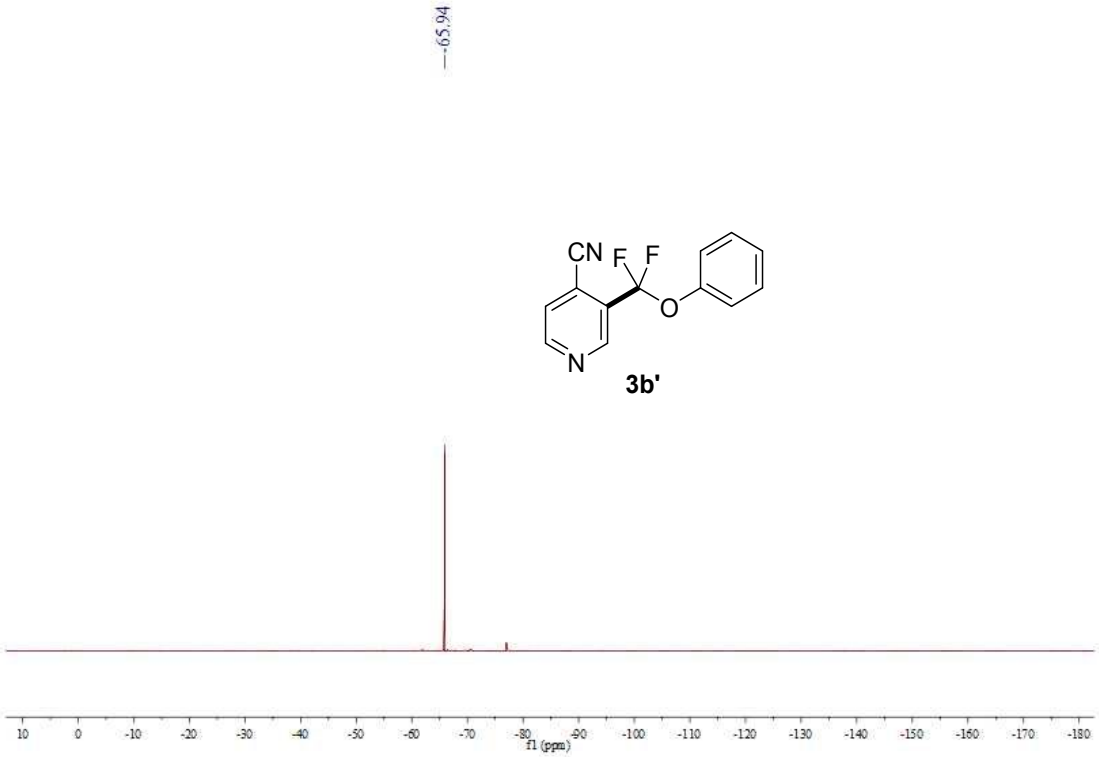


^{13}C NMR (101 MHz, $CDCl_3$)

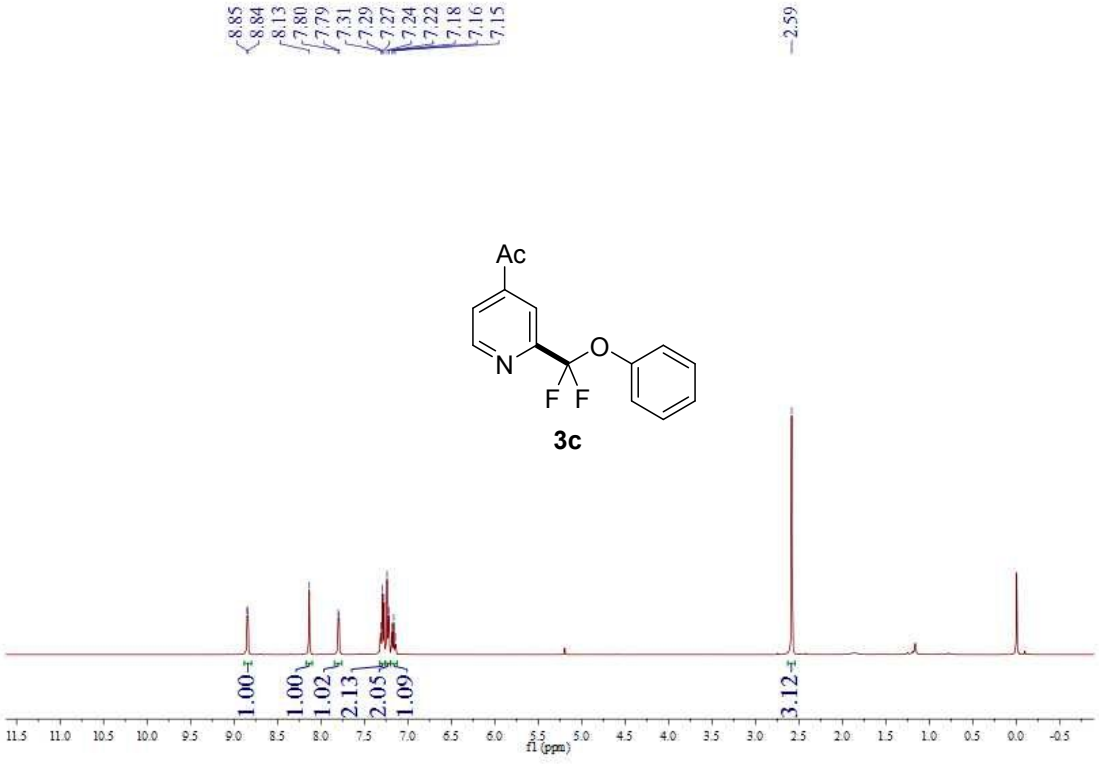


3b'

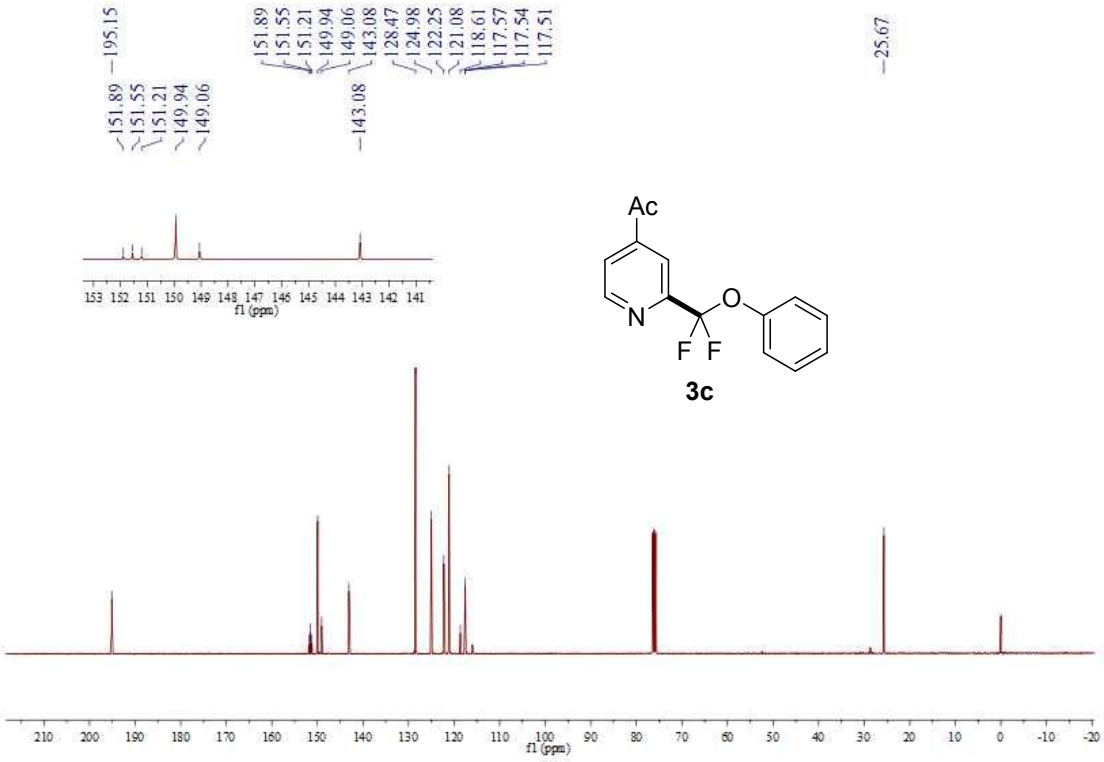
^{19}F NMR (377 MHz, $CDCl_3$)



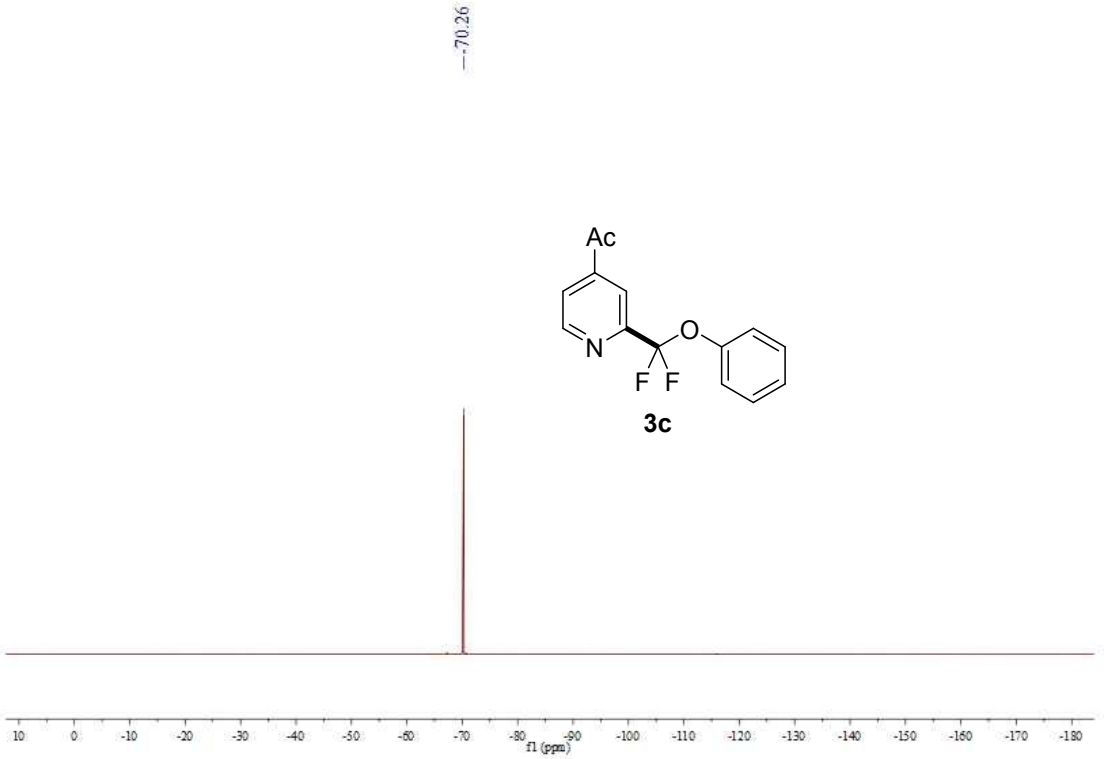
^{1}H NMR (400 MHz, $CDCl_3$)



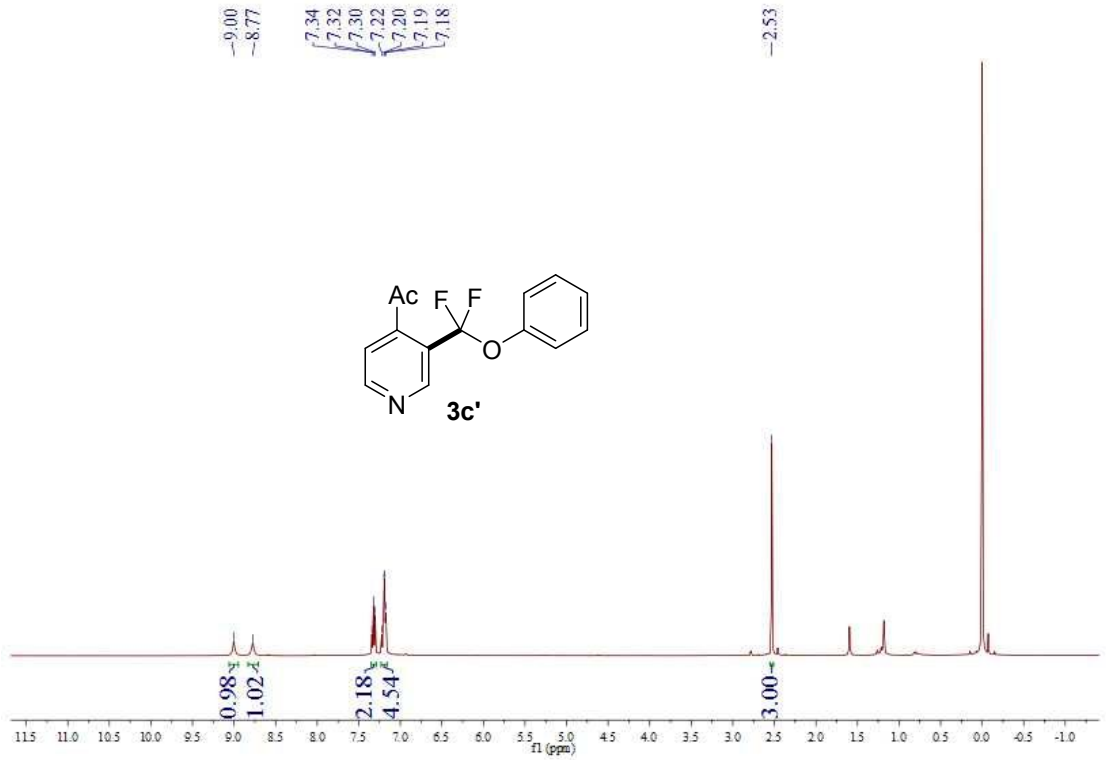
^{13}C NMR (101 MHz, $CDCl_3$)



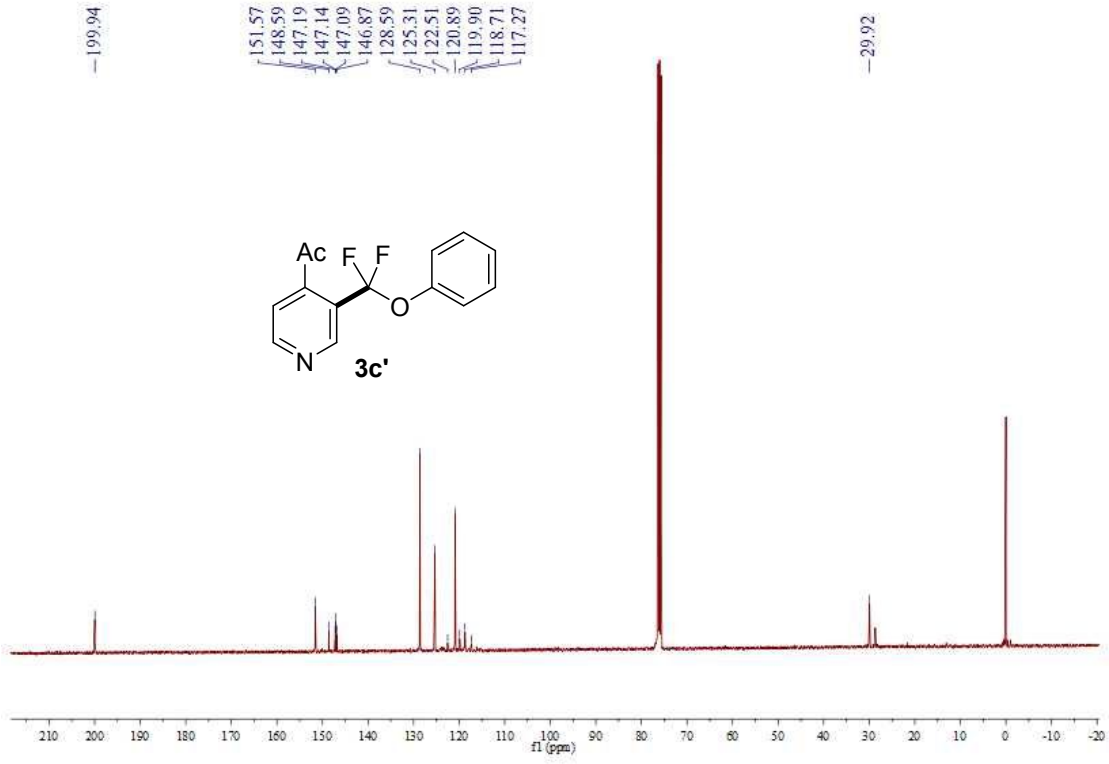
^{19}F NMR (377 MHz, $CDCl_3$)



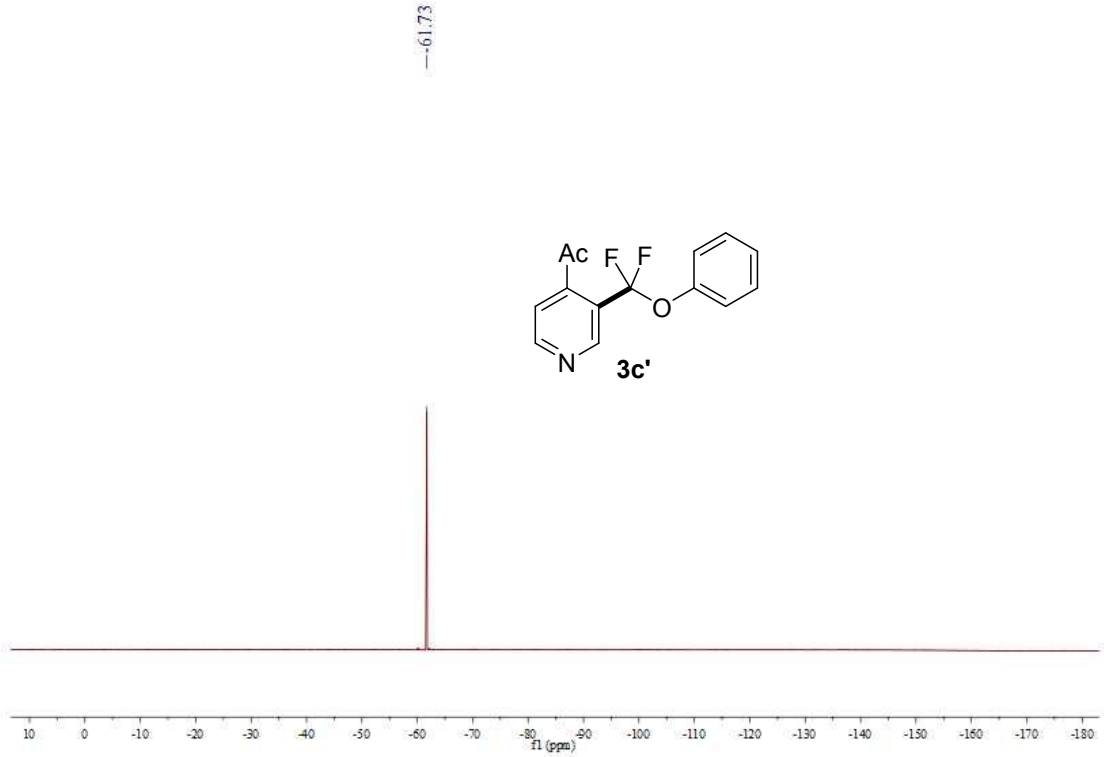
^{1}H NMR (400 MHz, $CDCl_3$)



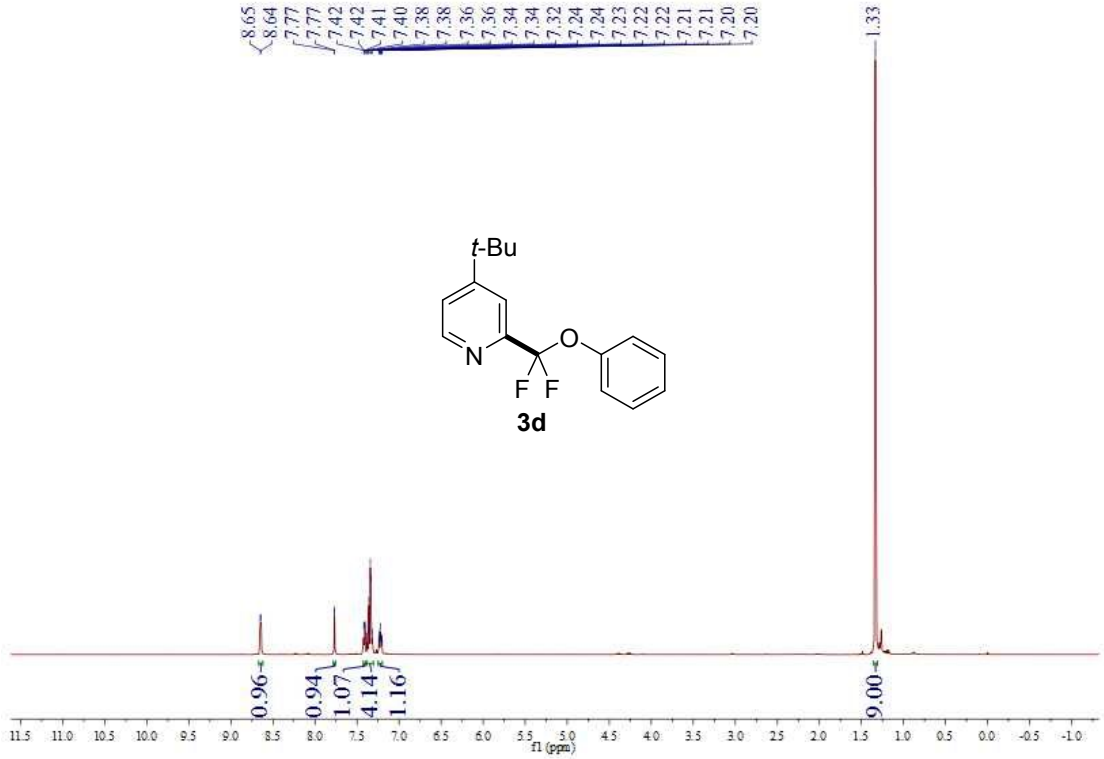
^{13}C NMR (101 MHz, $CDCl_3$)



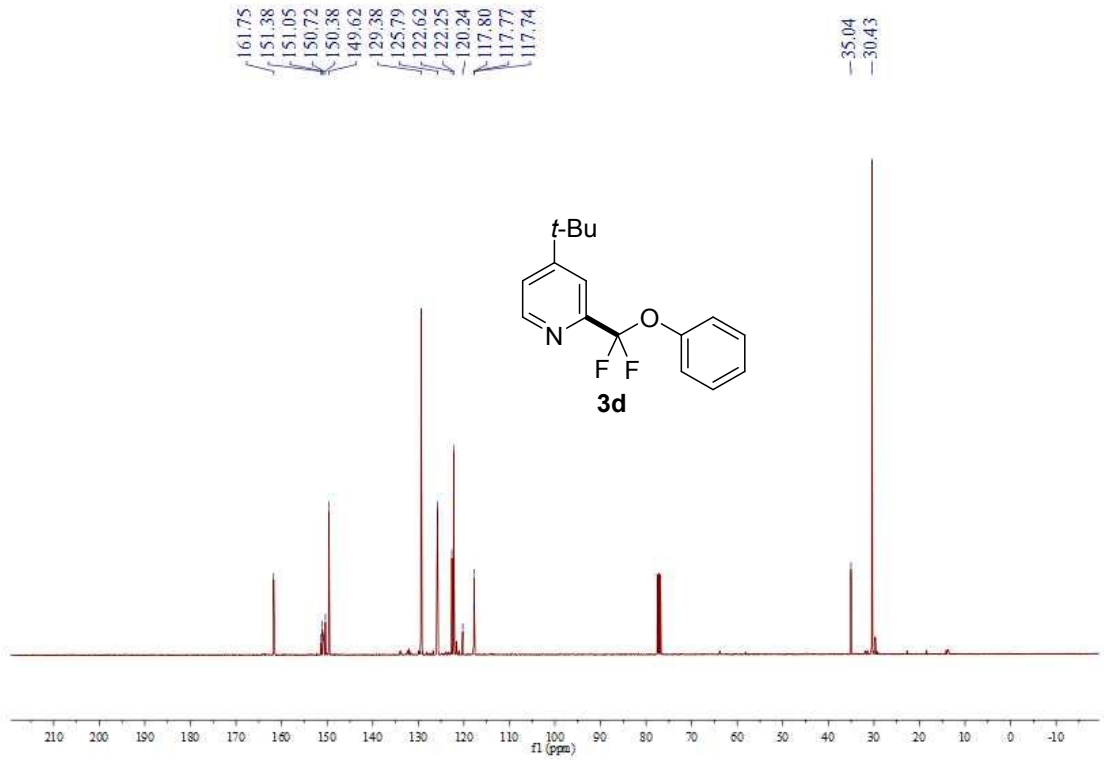
^{19}F NMR (377 MHz, $CDCl_3$)



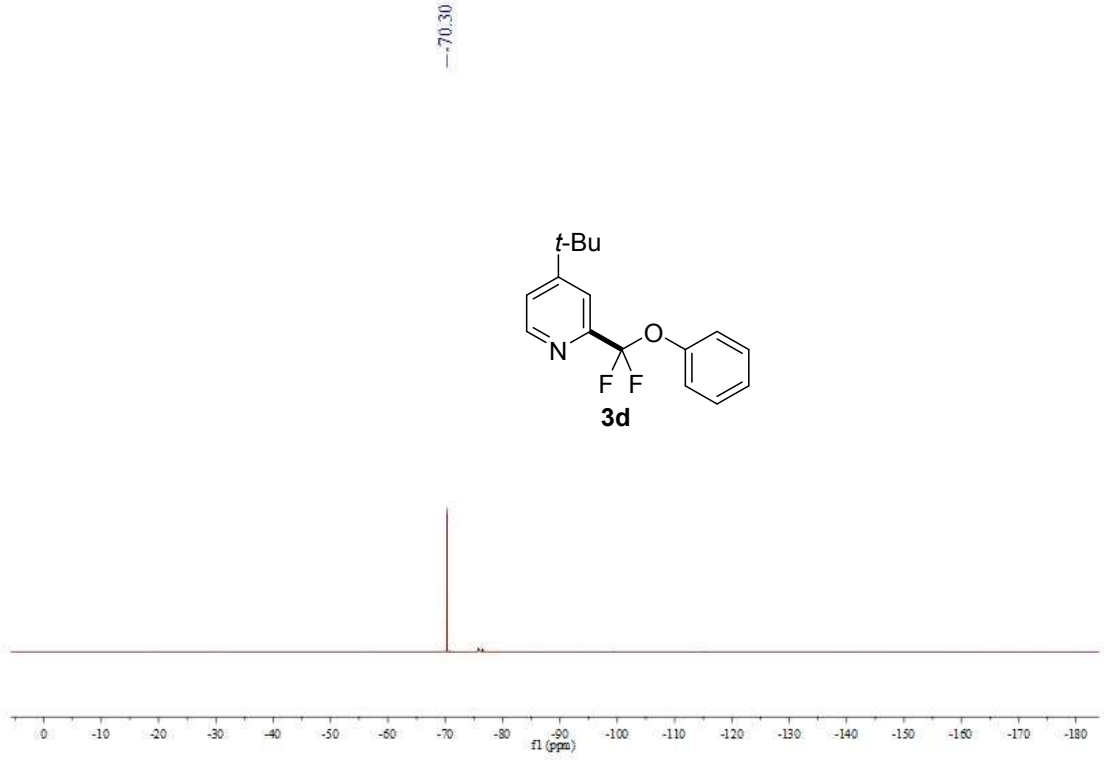
^{1}H NMR (400 MHz, $CDCl_3$)



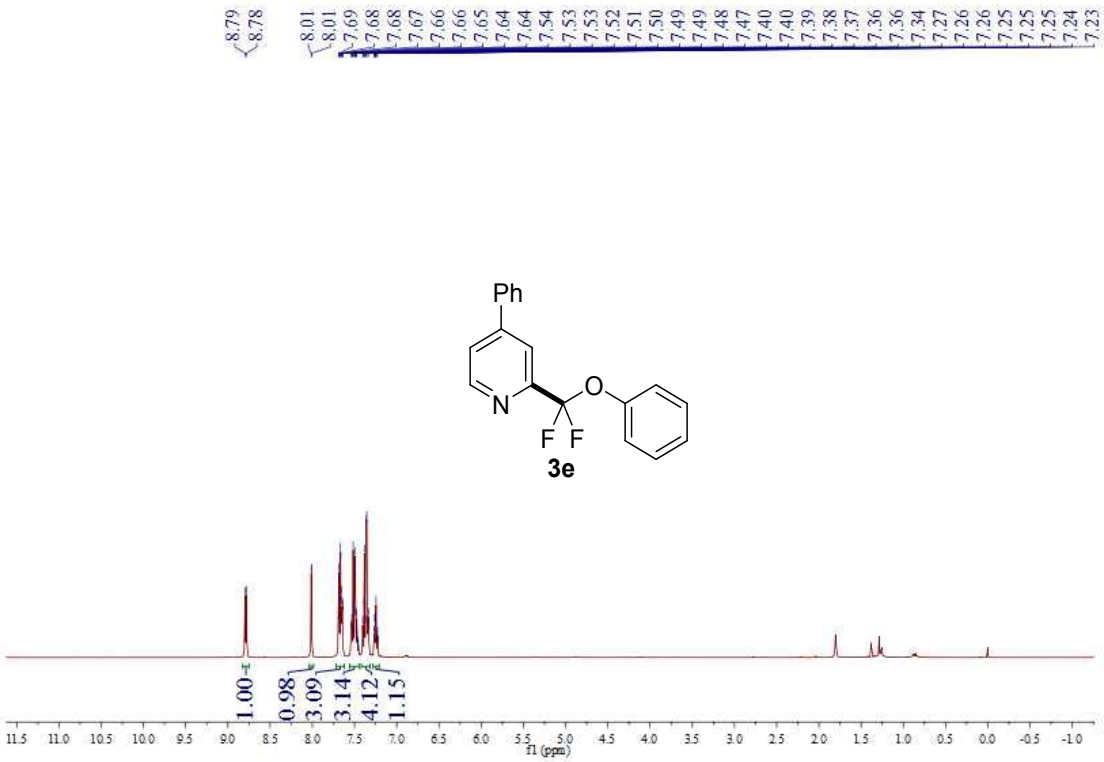
^{13}C NMR (101 MHz, $CDCl_3$)



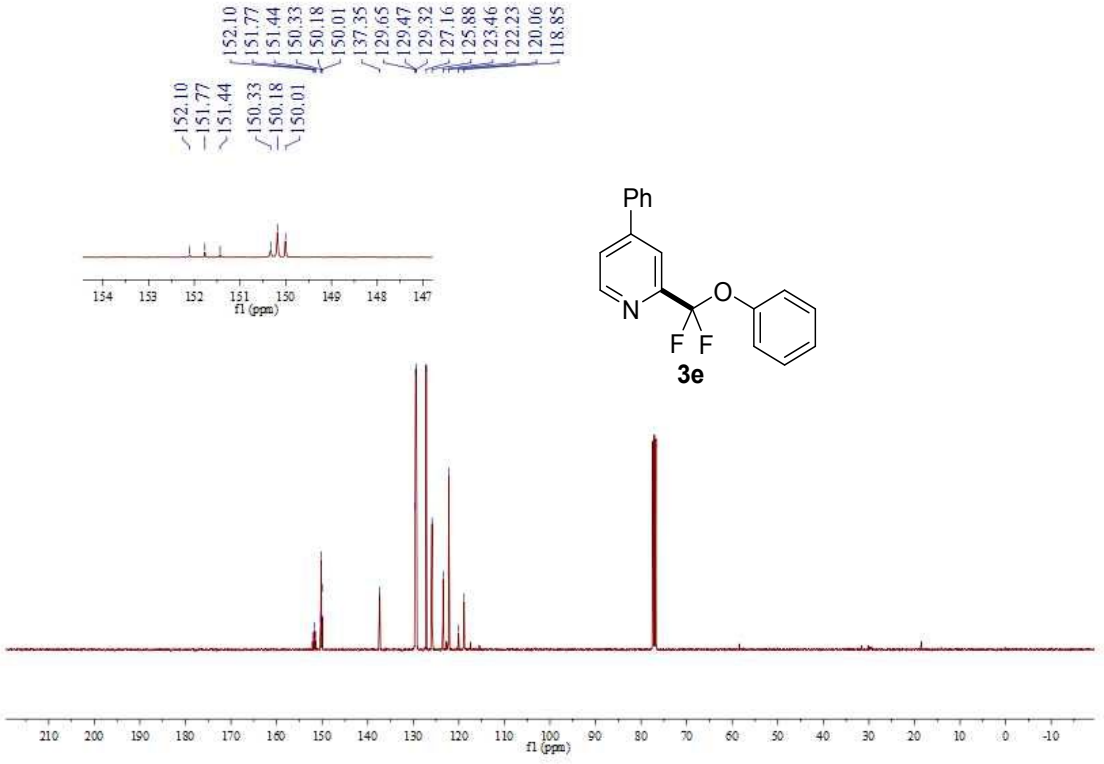
^{19}F NMR (377 MHz, $CDCl_3$)



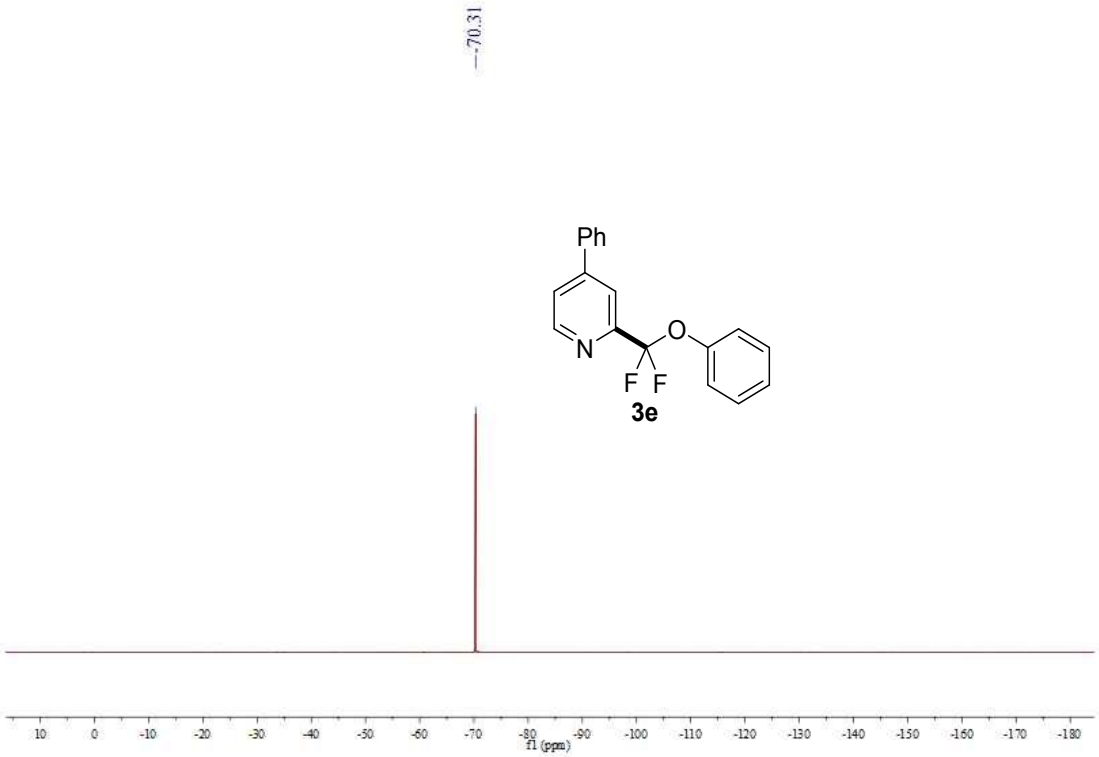
^{1}H NMR (400 MHz, $CDCl_3$)



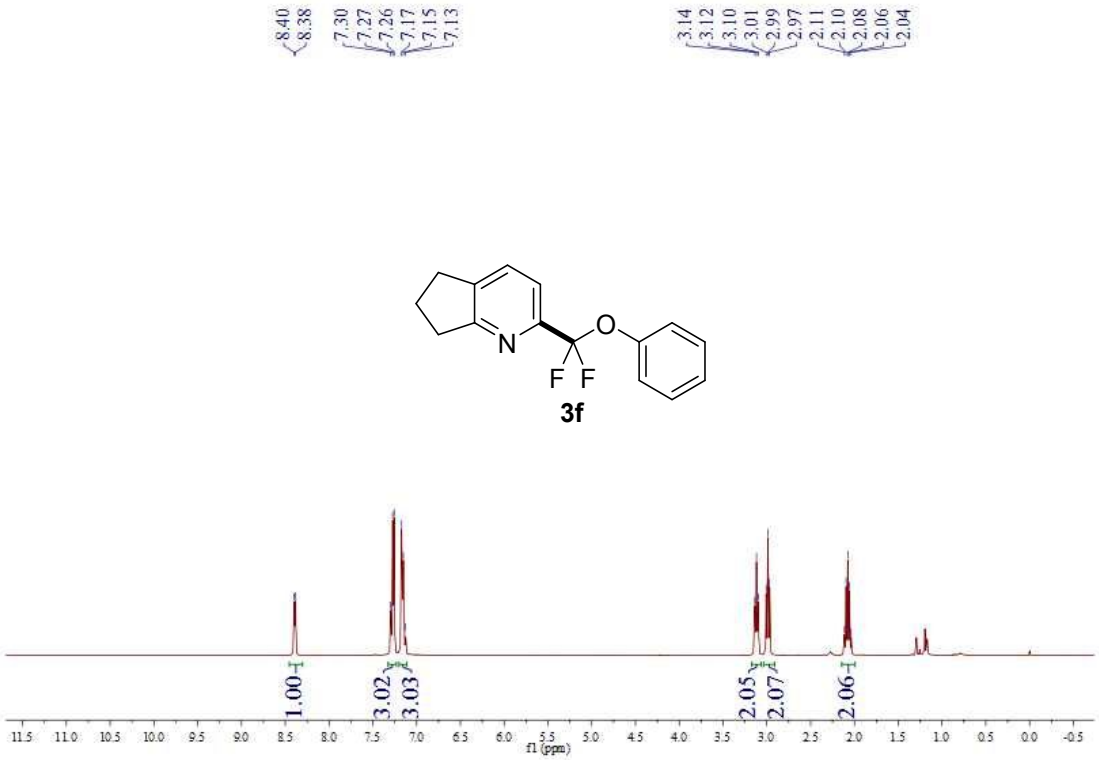
^{13}C NMR (101 MHz, $CDCl_3$)



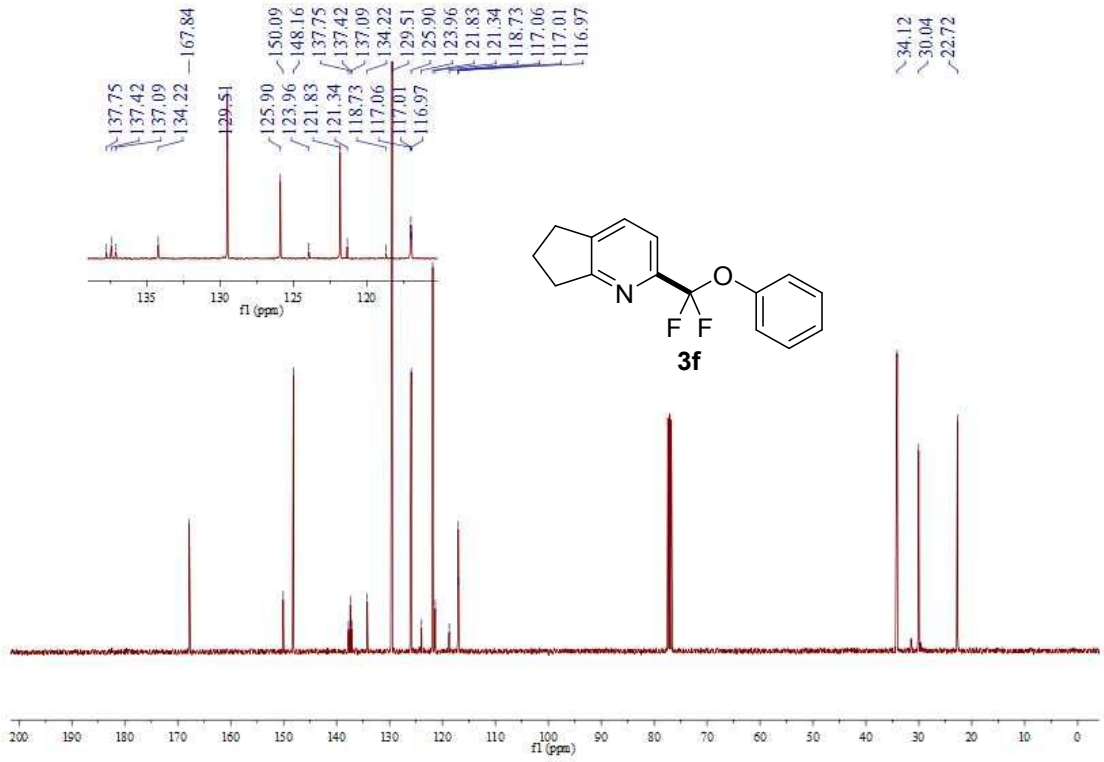
^{19}F NMR (377 MHz, $CDCl_3$)



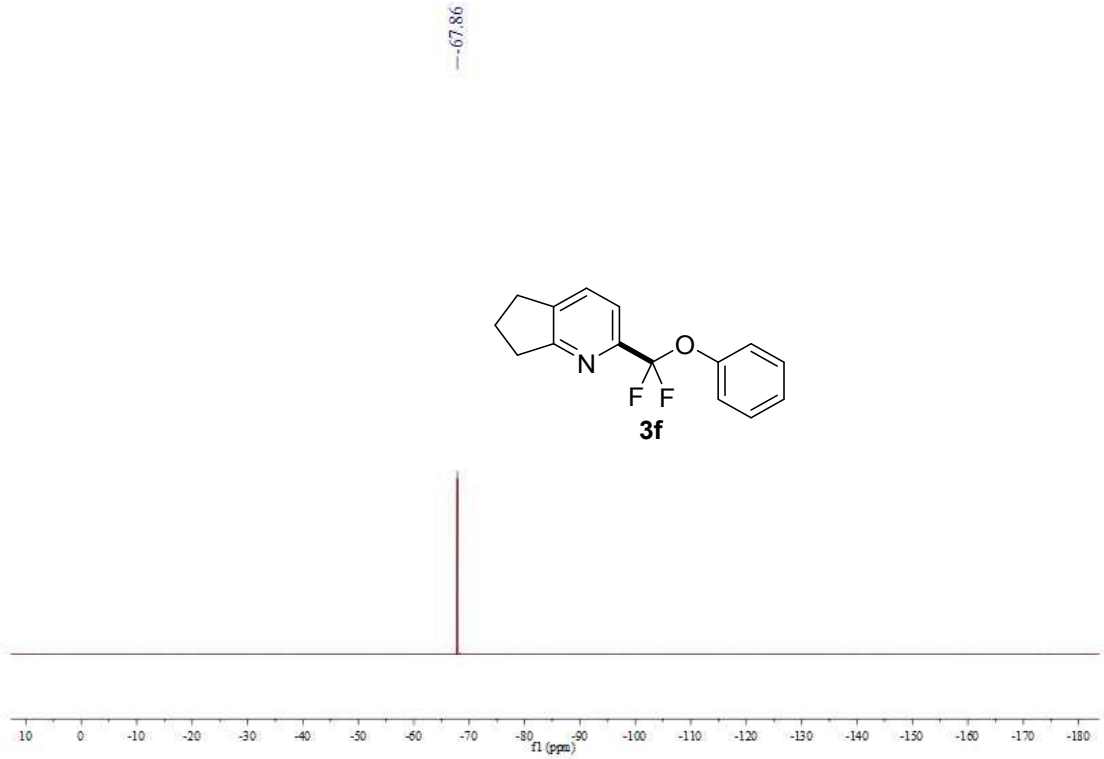
^{1}H NMR (400 MHz, $CDCl_3$)



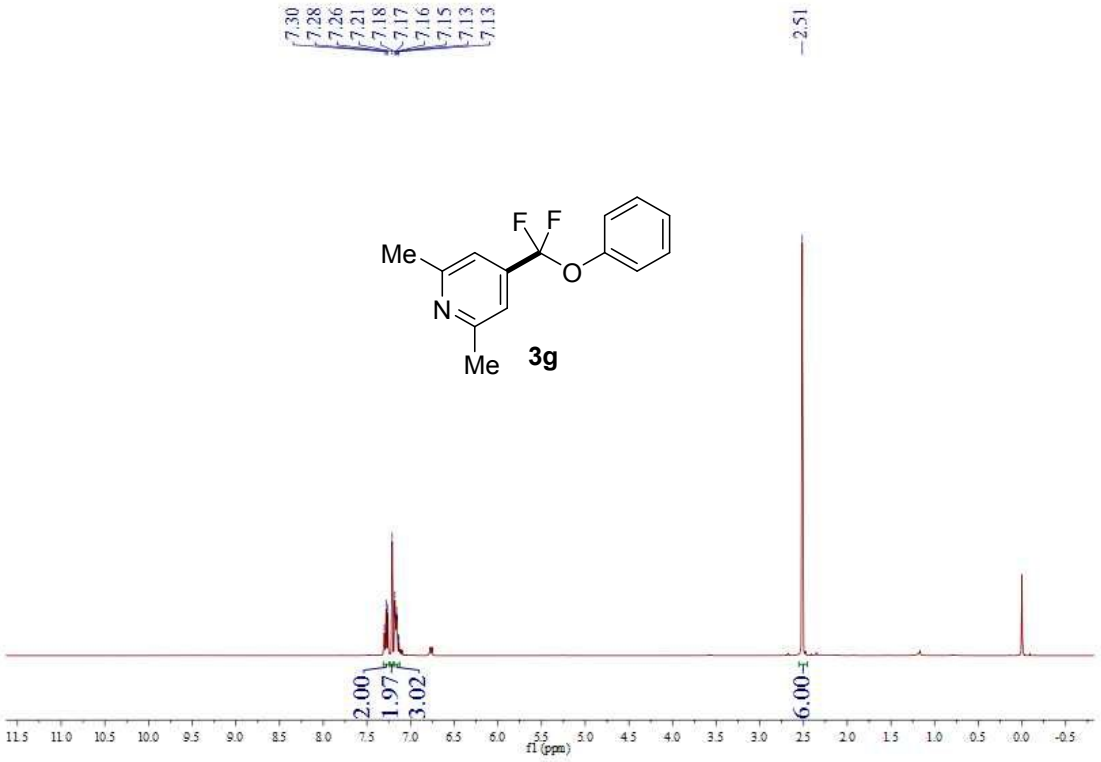
^{13}C NMR (101 MHz, $CDCl_3$)



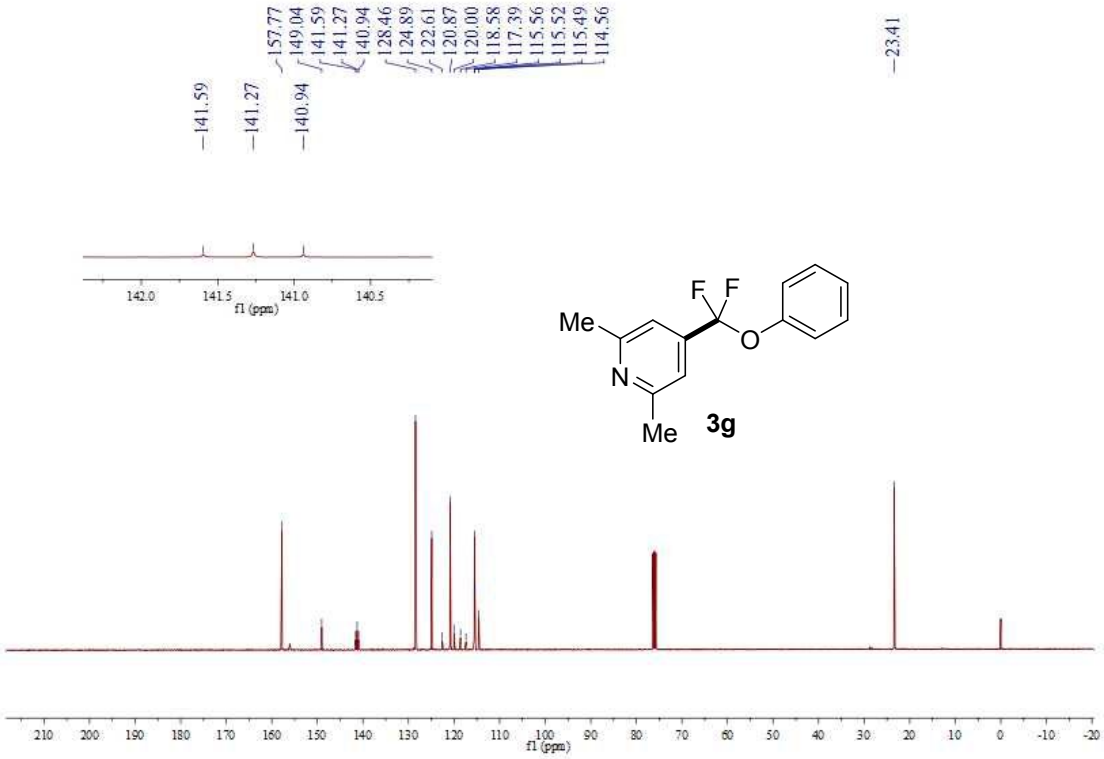
^{19}F NMR (377 MHz, $CDCl_3$)



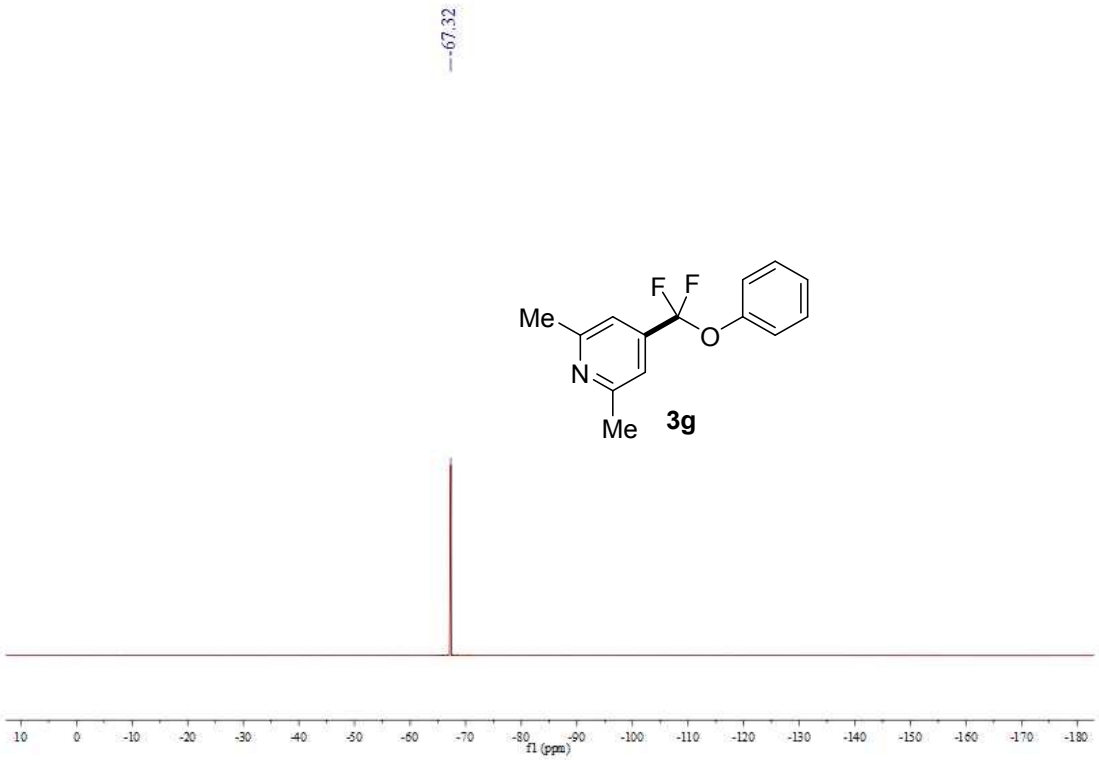
^{1}H NMR (400 MHz, $CDCl_3$)



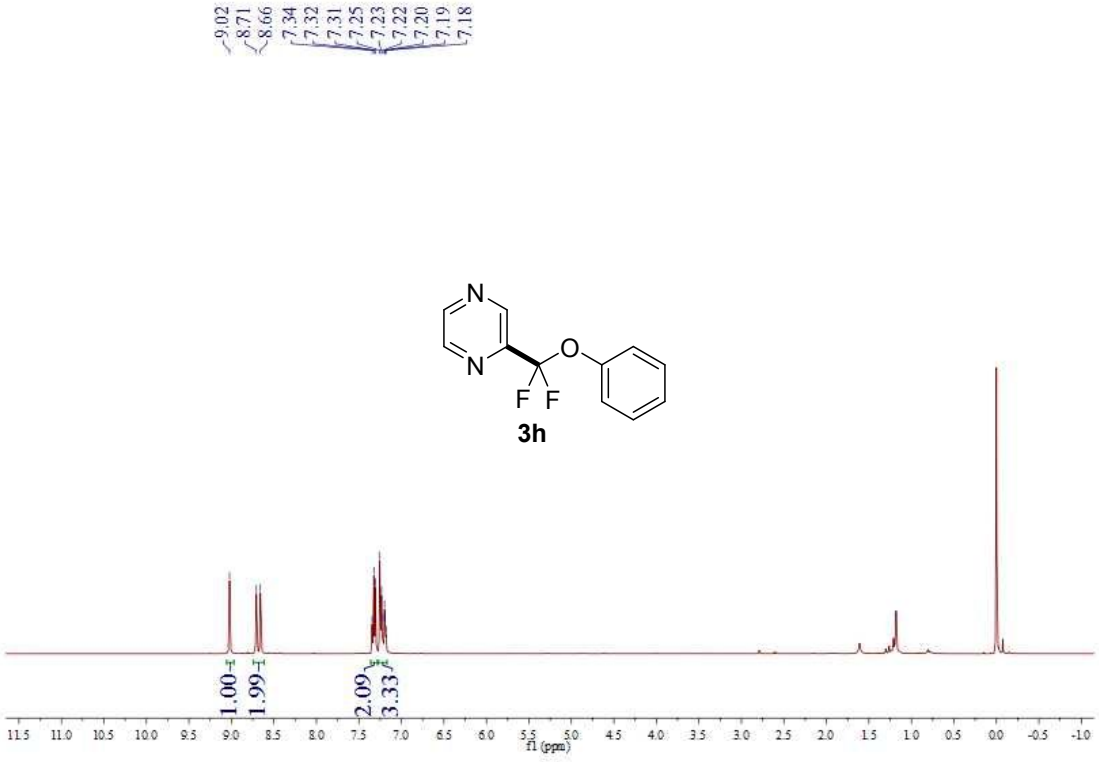
^{13}C NMR (101 MHz, $CDCl_3$)



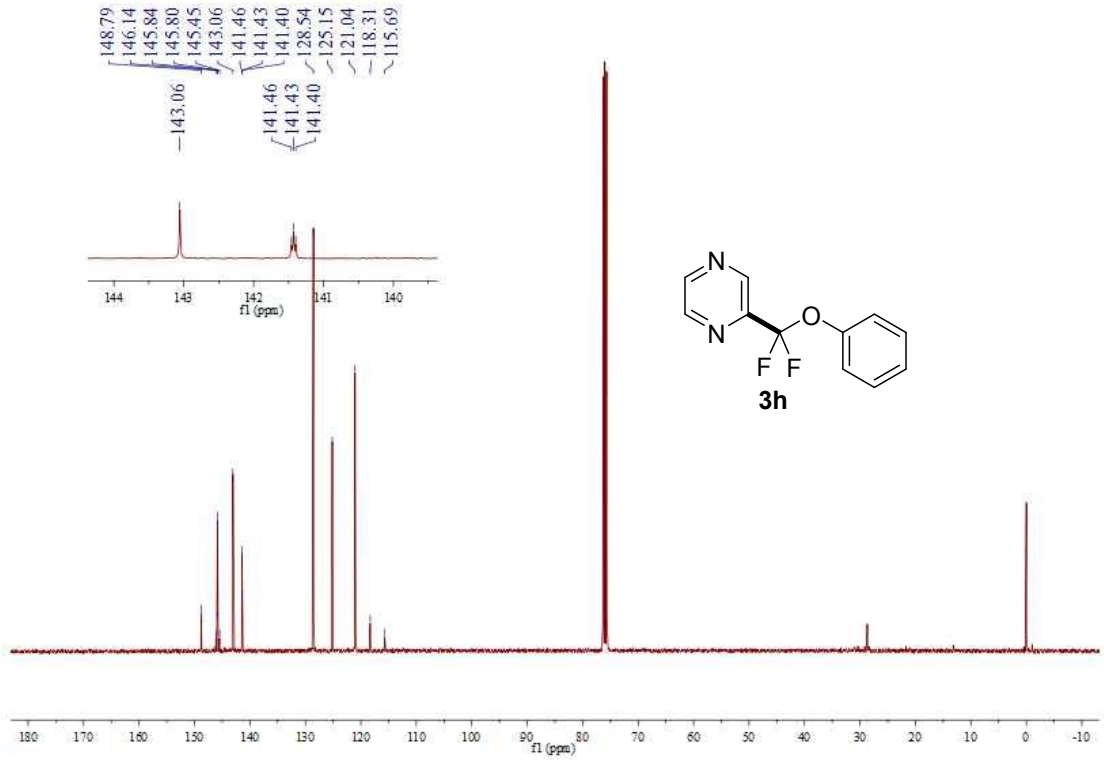
^{19}F NMR (377 MHz, $CDCl_3$)



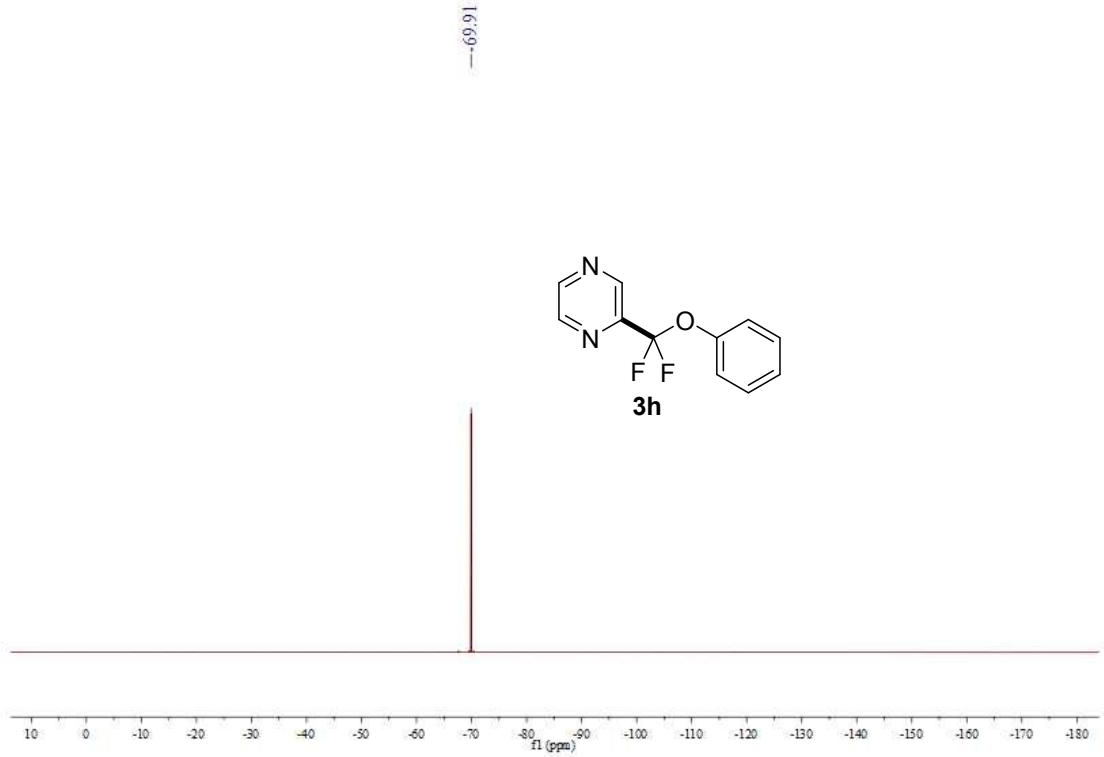
^{1}H NMR (400 MHz, $CDCl_3$)



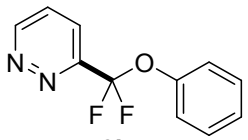
^{13}C NMR (101 MHz, $CDCl_3$)



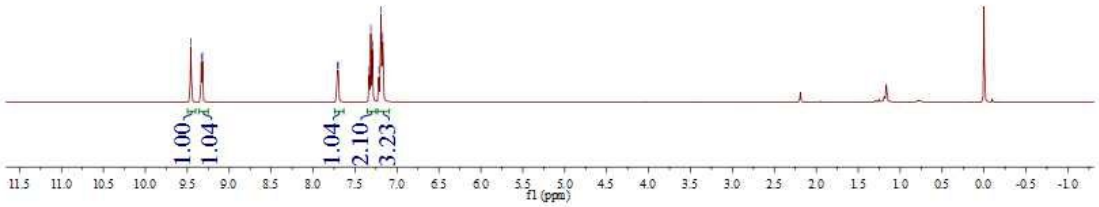
^{19}F NMR (377 MHz, $CDCl_3$)



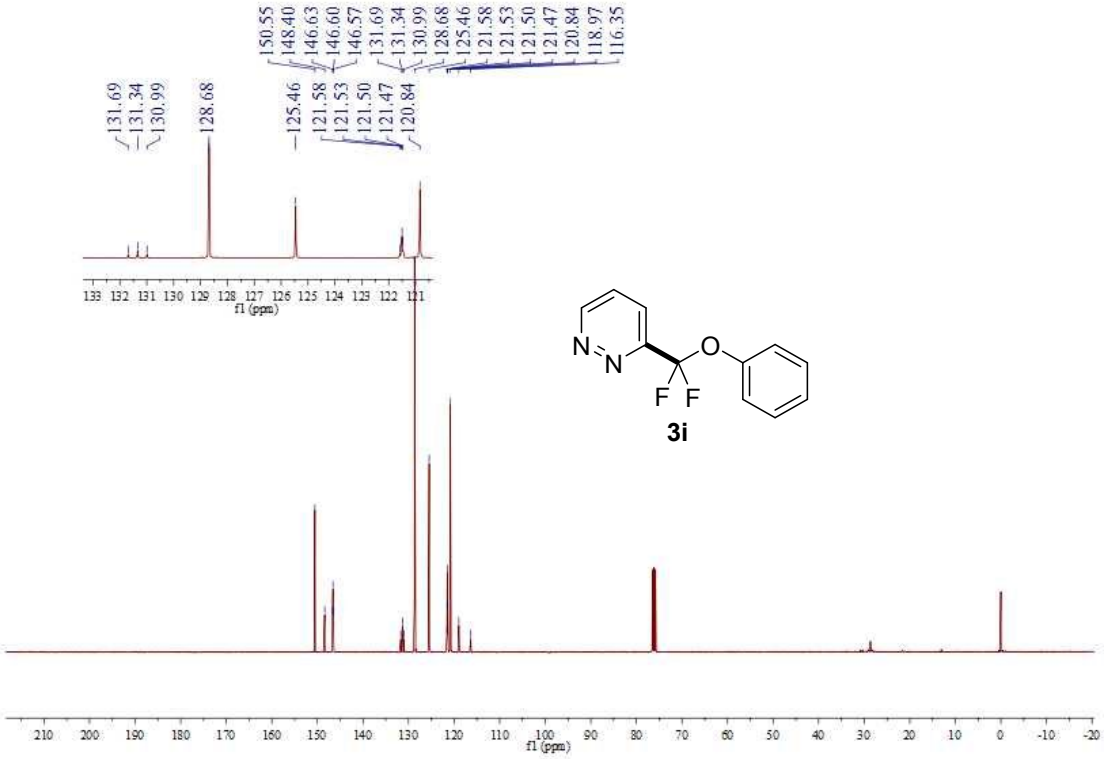
^{1}H NMR (400 MHz, $CDCl_3$)



3i

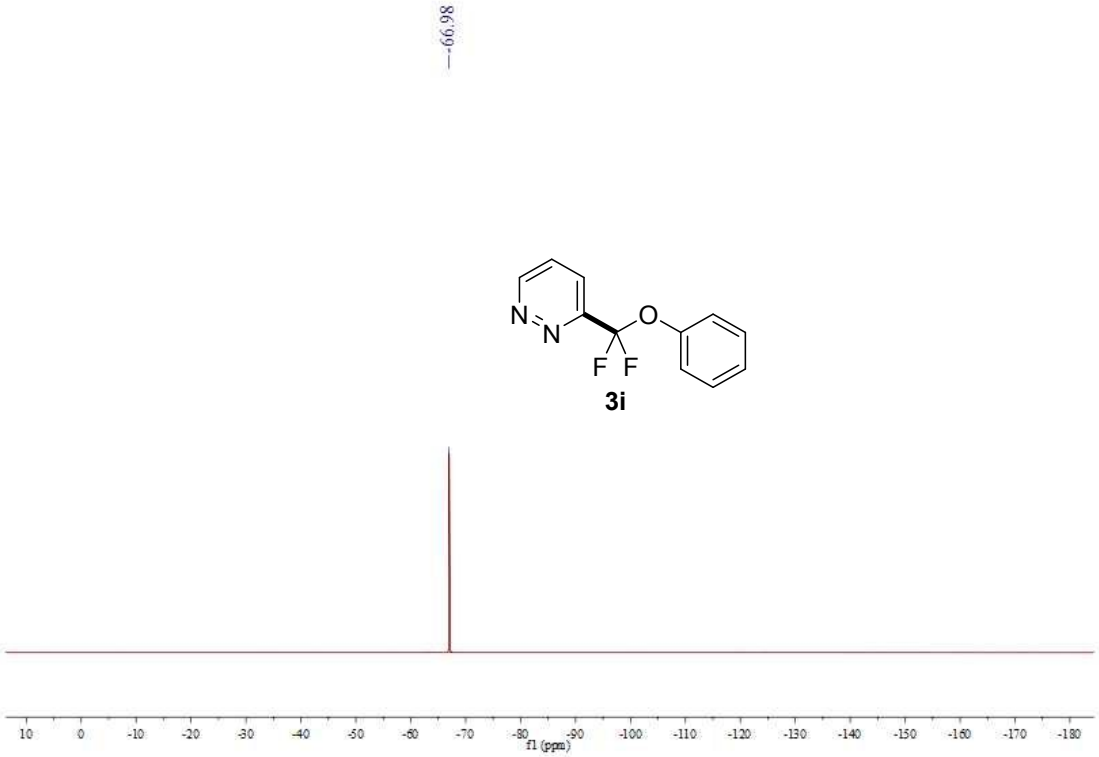


^{13}C NMR (101 MHz, $CDCl_3$)

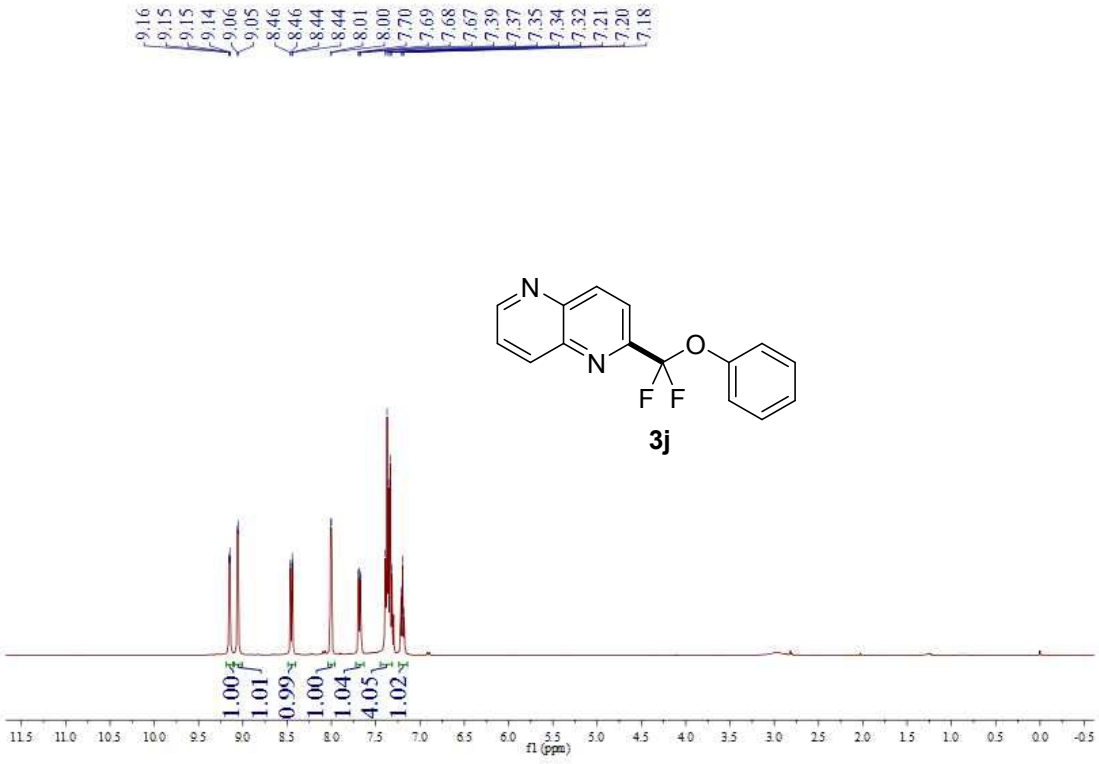


3i

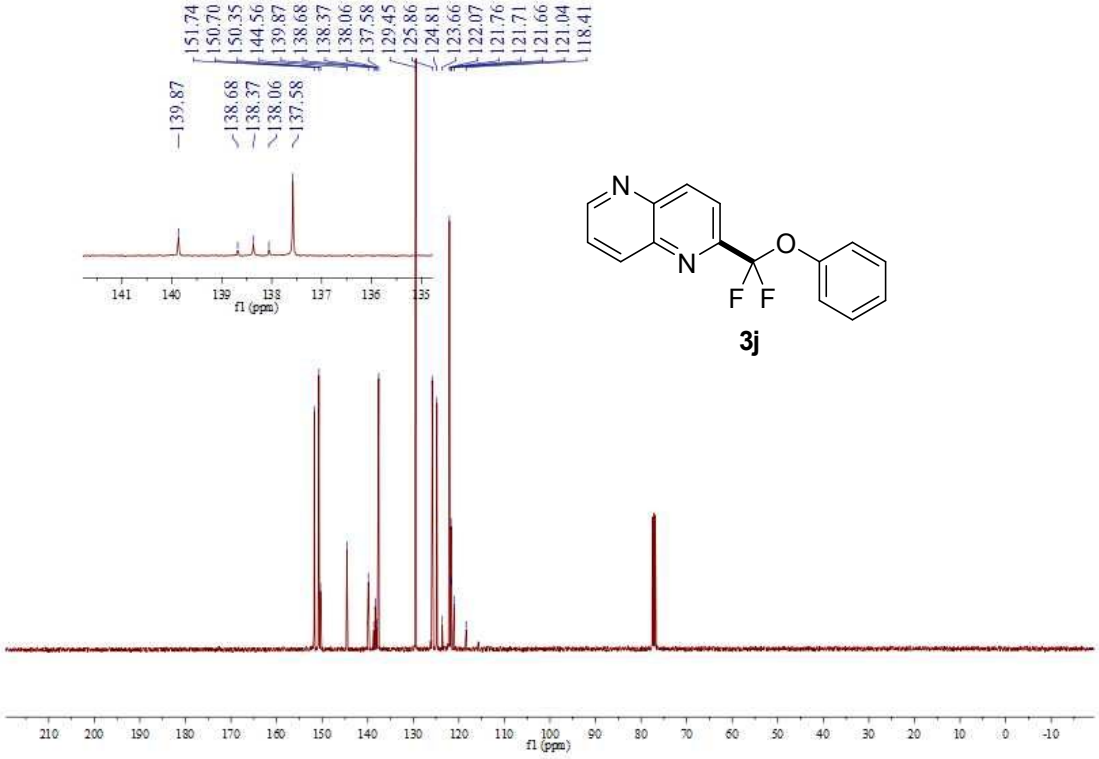
^{19}F NMR (377 MHz, $CDCl_3$)



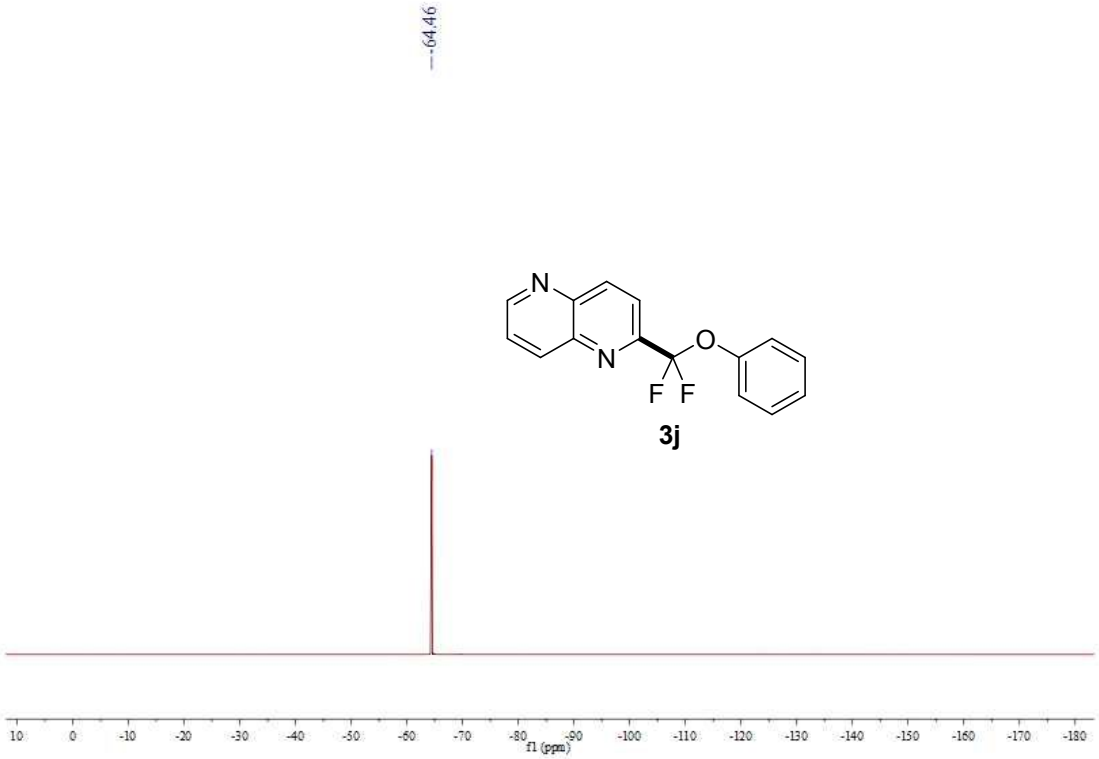
^{1}H NMR (400 MHz, $CDCl_3$)



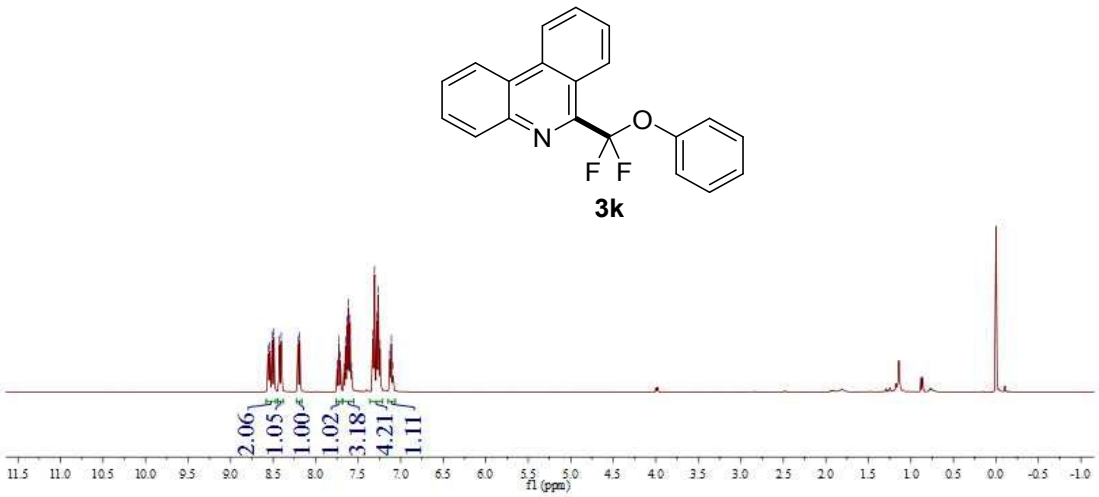
^{13}C NMR (101 MHz, $CDCl_3$)



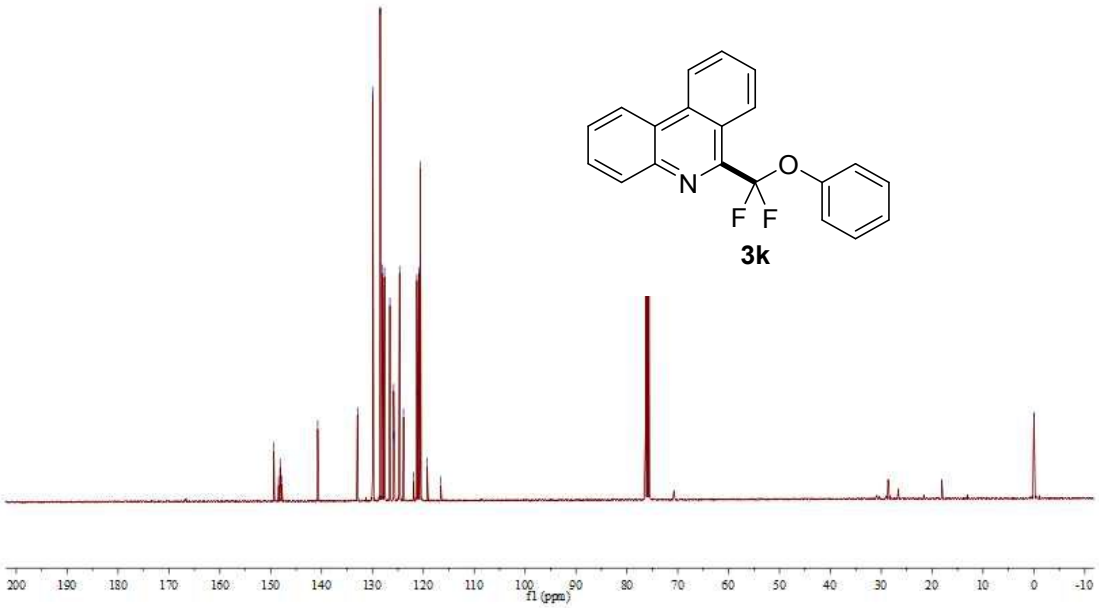
^{19}F NMR (377 MHz, $CDCl_3$)



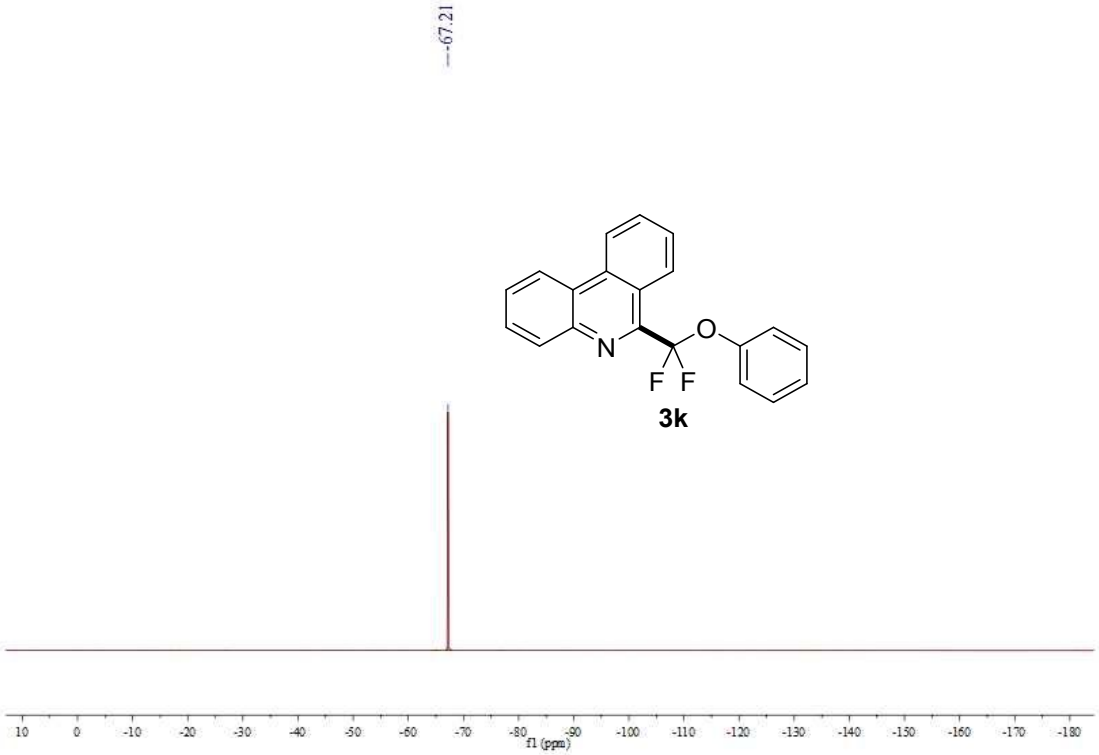
[1]H NMR (400 MHz, $CDCl_3$)



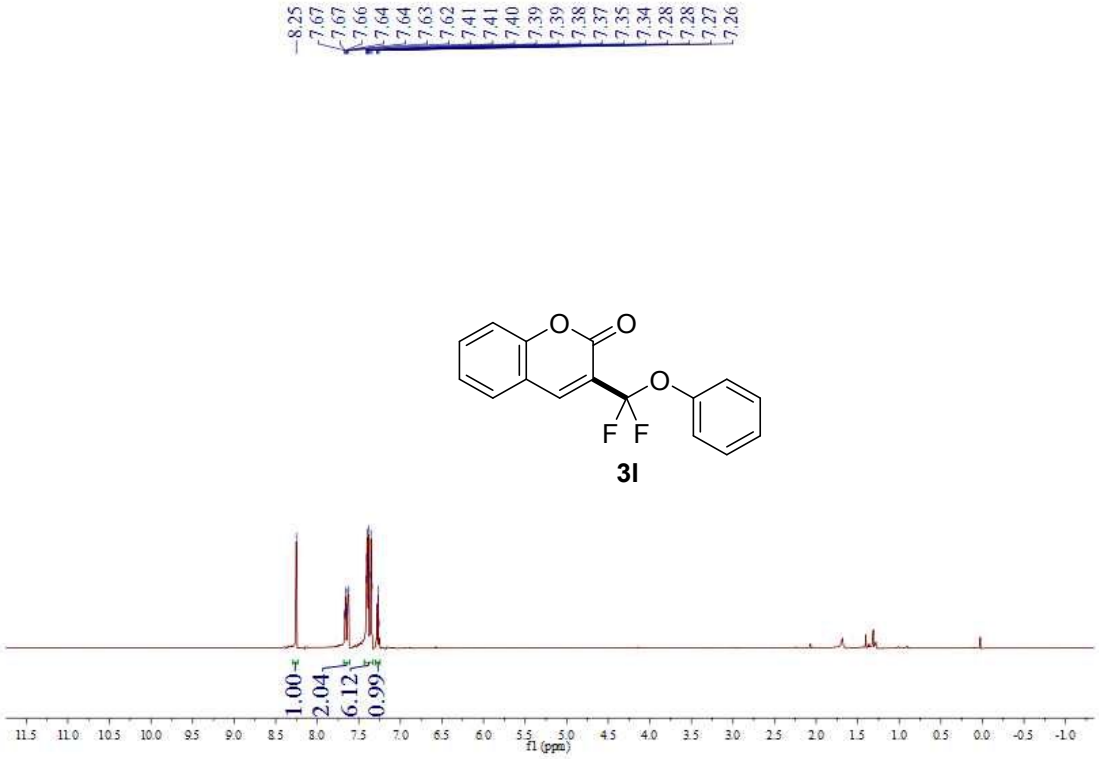
[13]C NMR (101 MHz, $CDCl_3$)



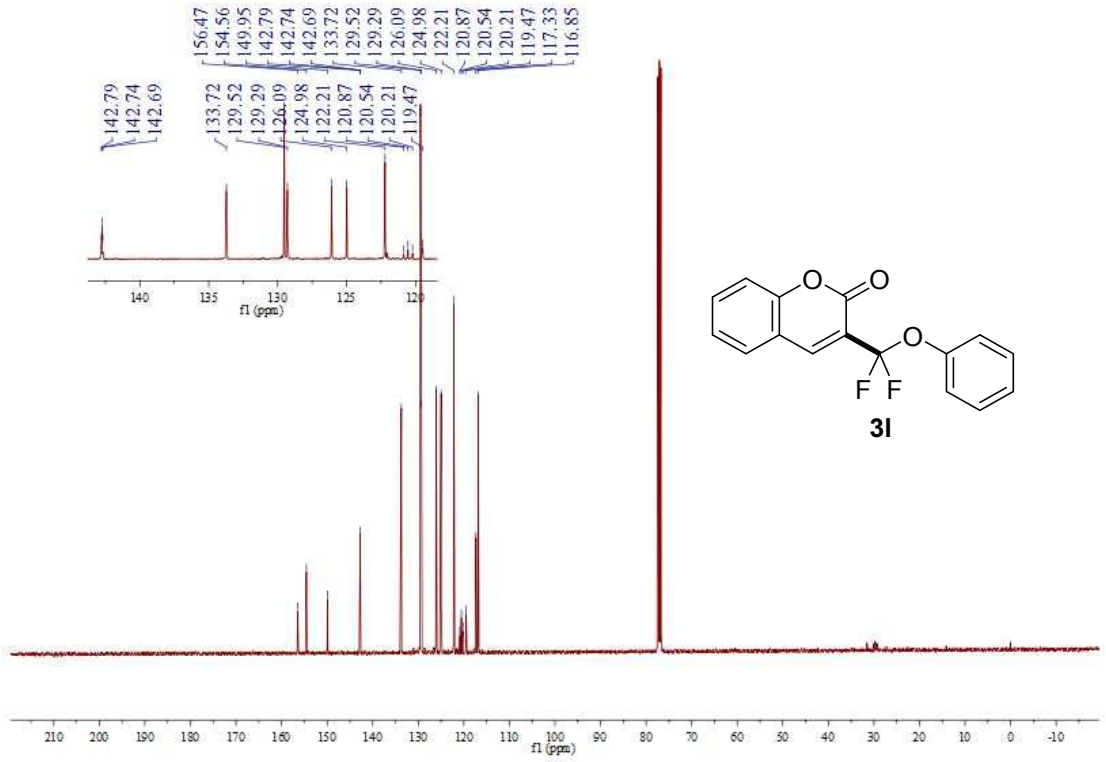
^{19}F NMR (377 MHz, $CDCl_3$)



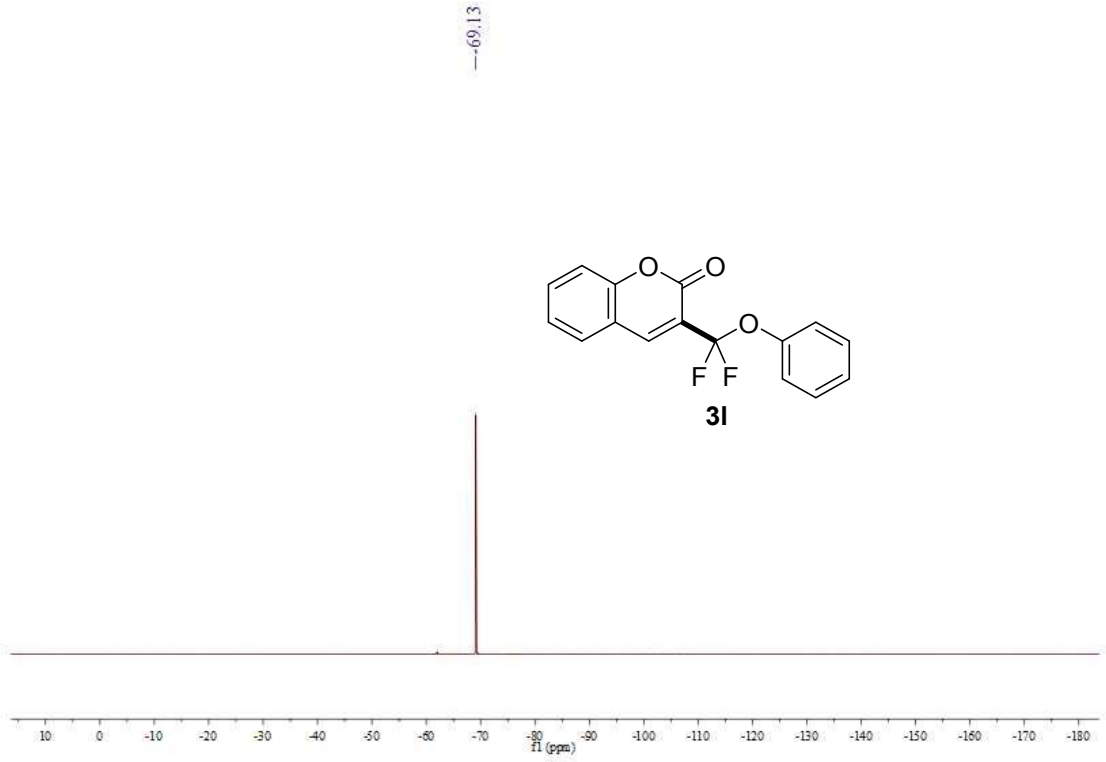
^{1}H NMR (600 MHz, $CDCl_3$)



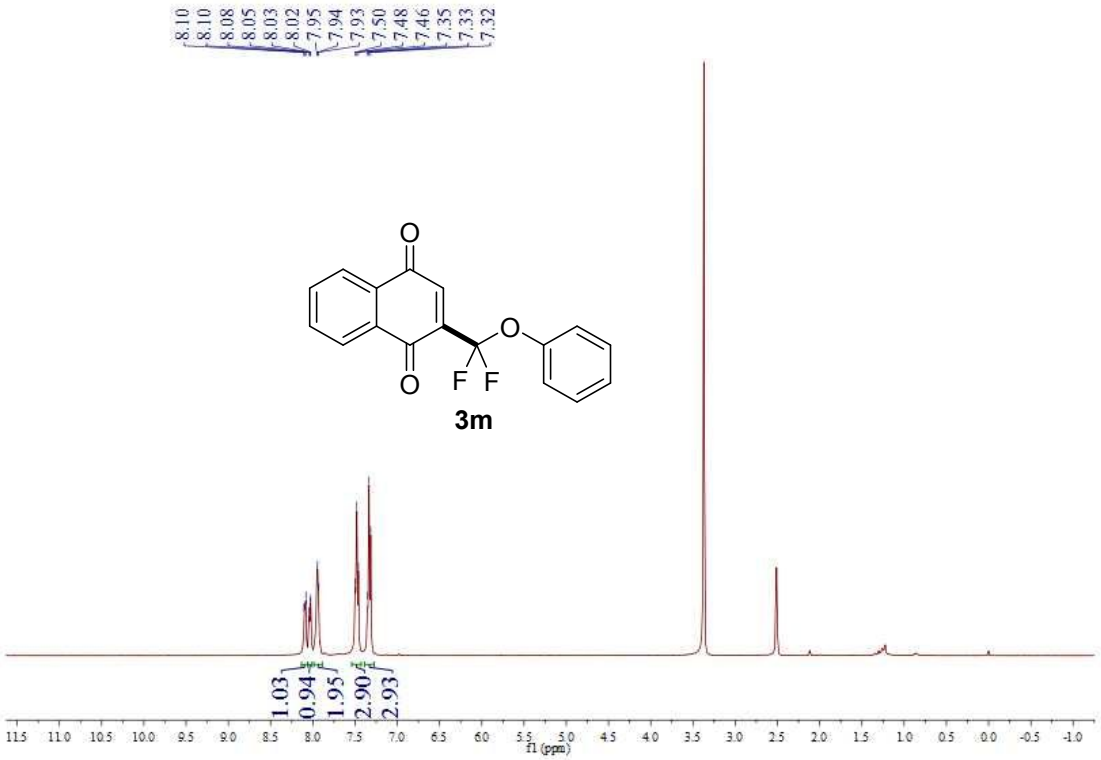
^{13}C NMR (101 MHz, $CDCl_3$)



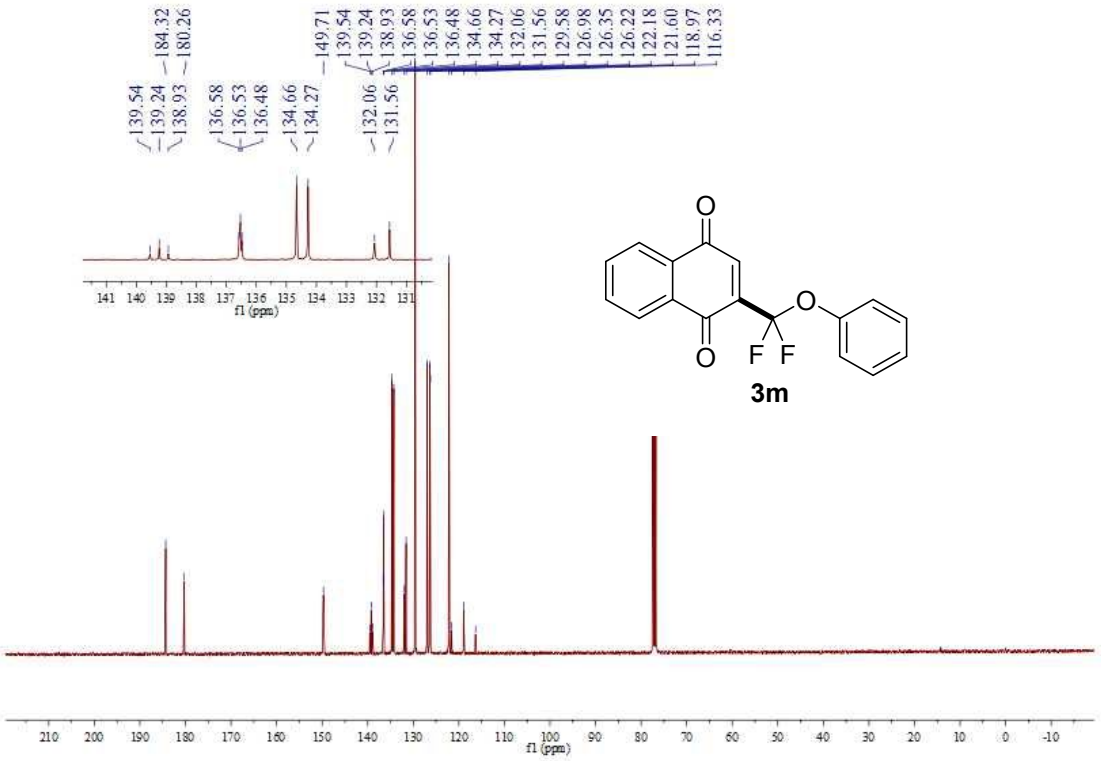
^{19}F NMR (565 MHz, $CDCl_3$)



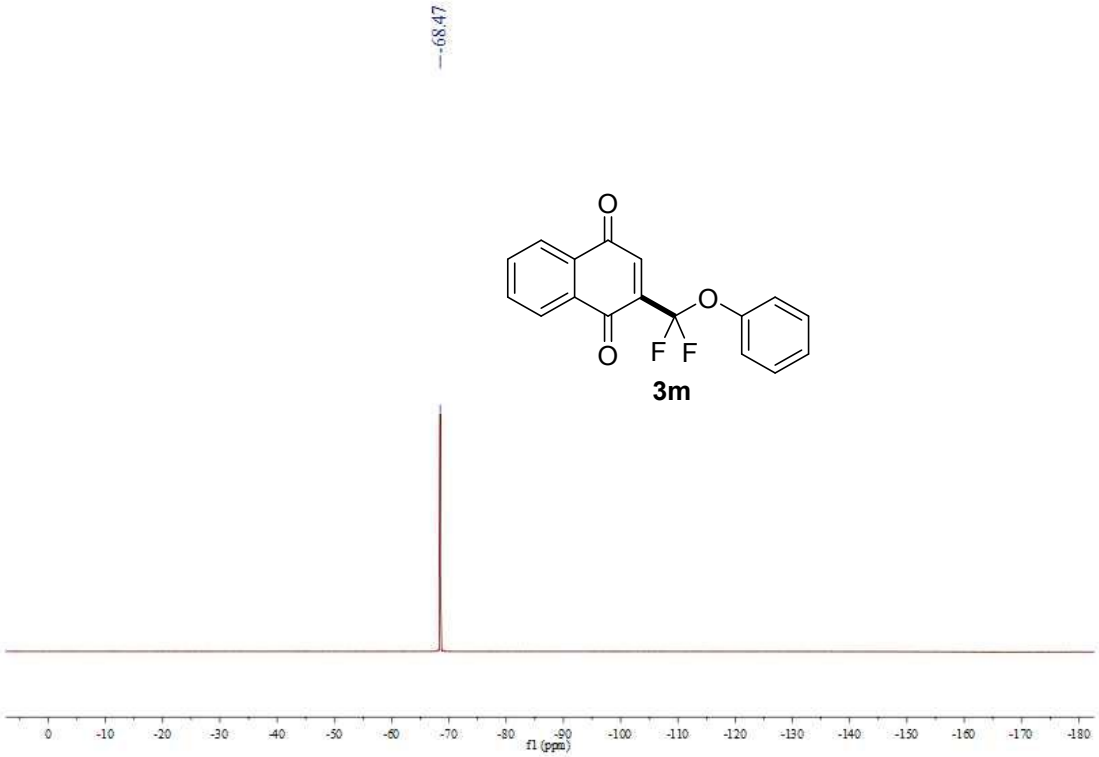
[1]H NMR (400 MHz, DMSO-d6)



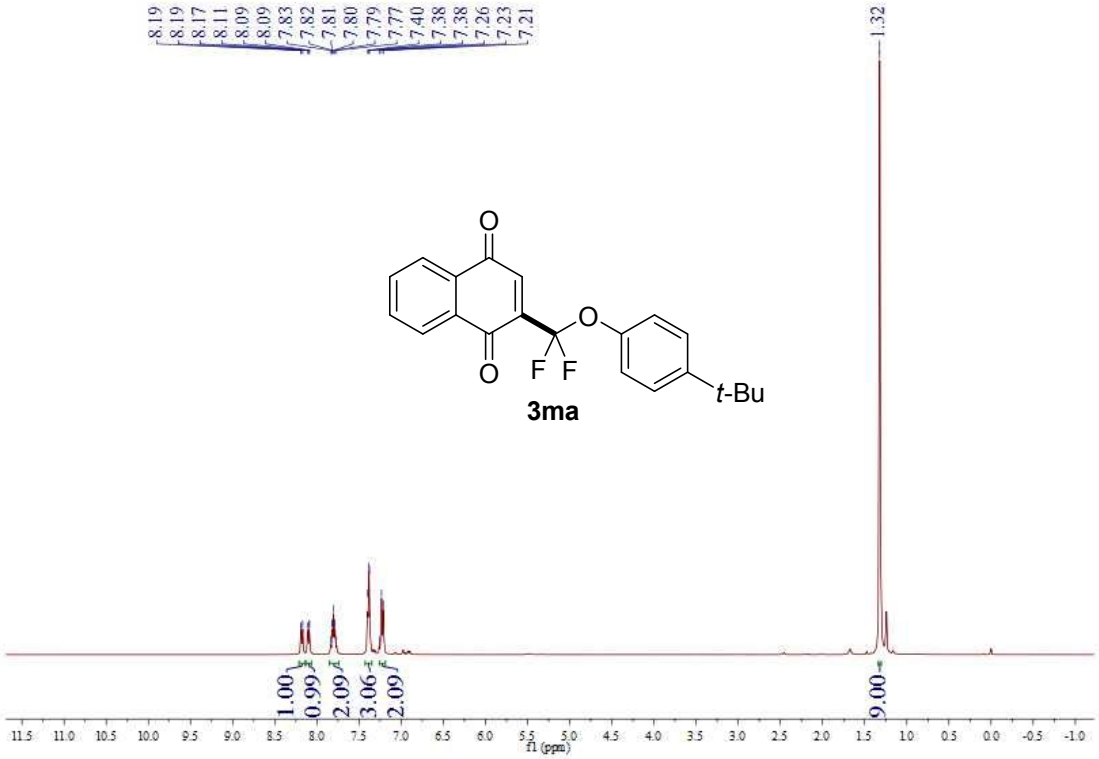
[13]C NMR (101 MHz, $CDCl_3$)



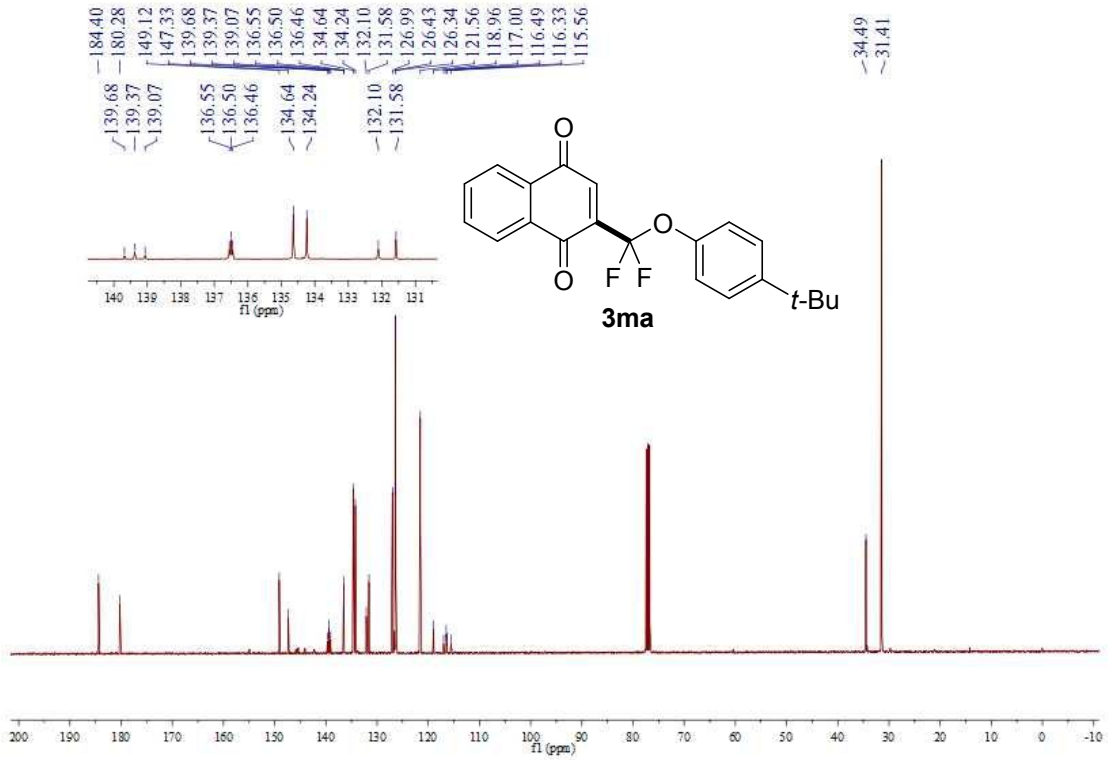
^{19}F NMR (377 MHz, $CDCl_3$)



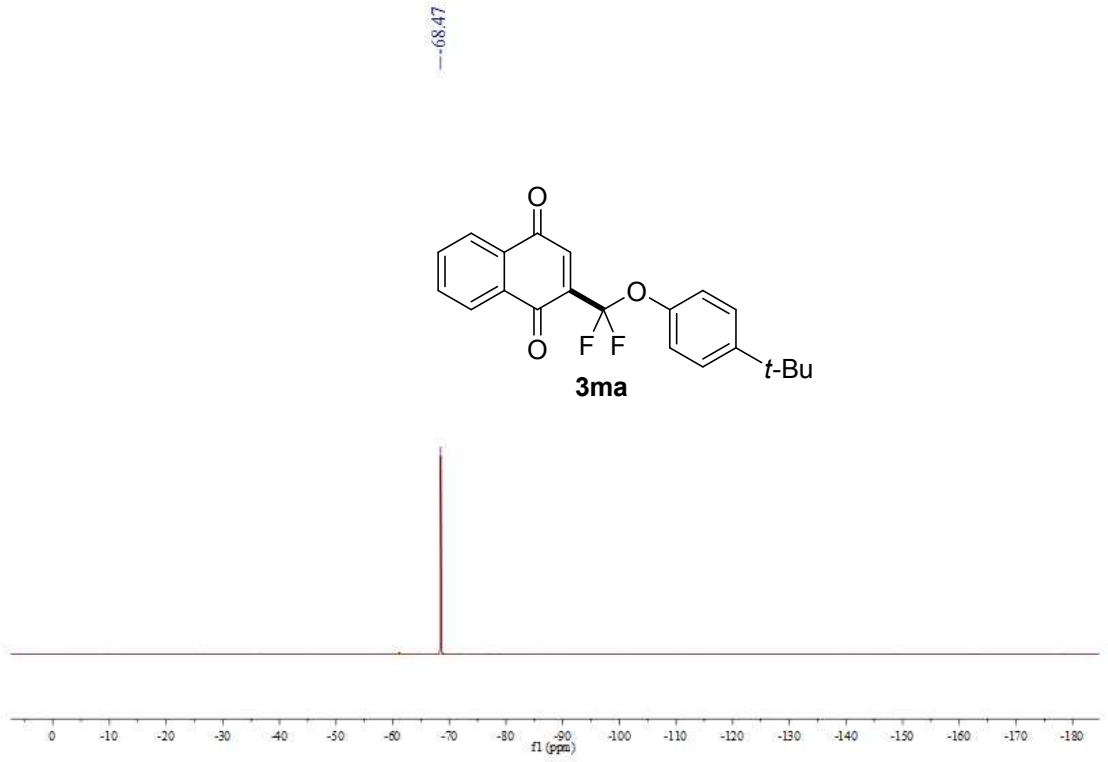
^{1}H NMR (400 MHz, $CDCl_3$)



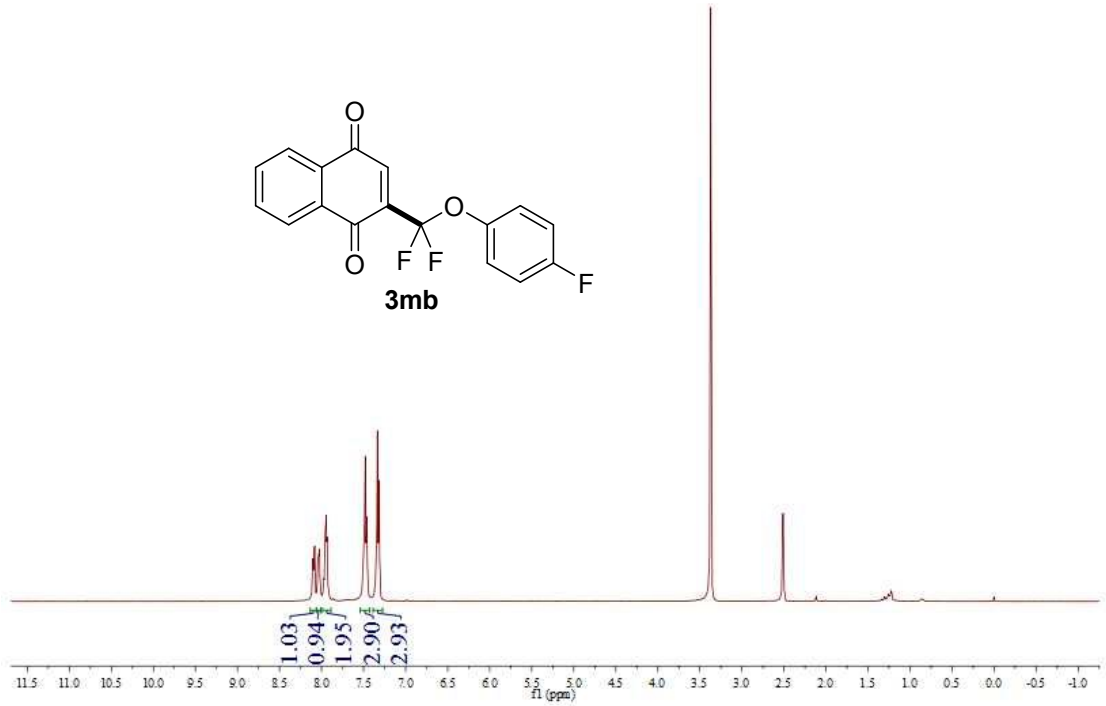
^{13}C NMR (101 MHz, $CDCl_3$)



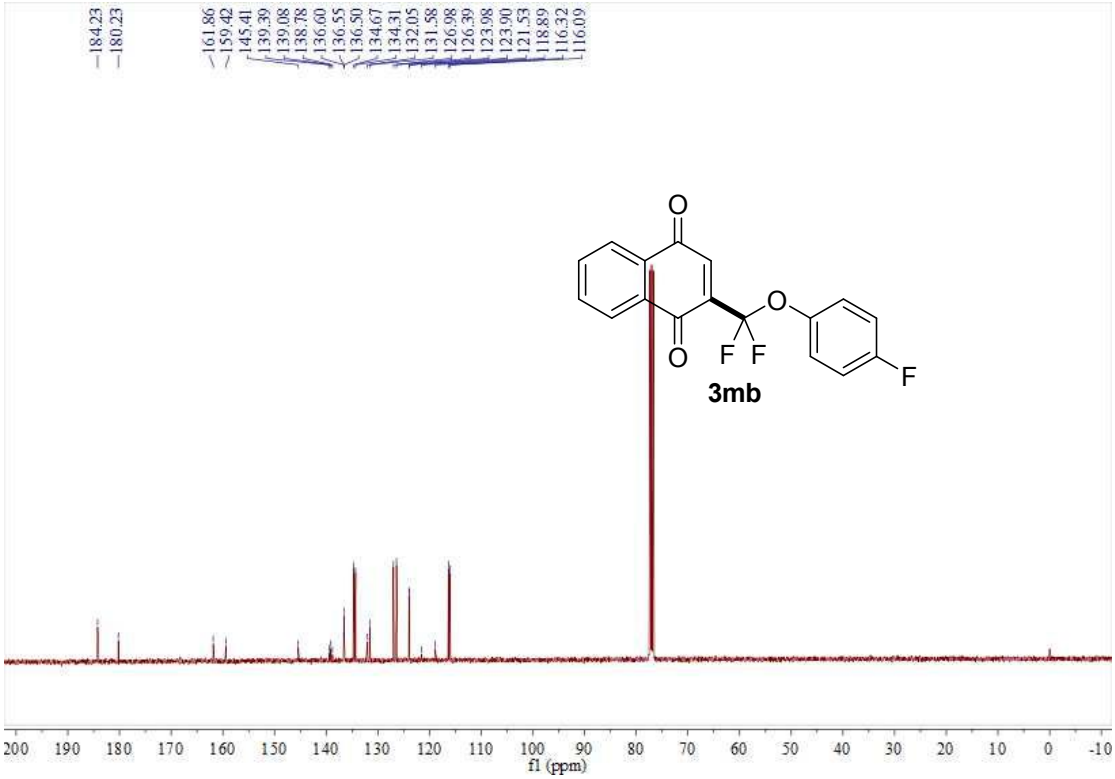
^{19}F NMR (377 MHz, $CDCl_3$)



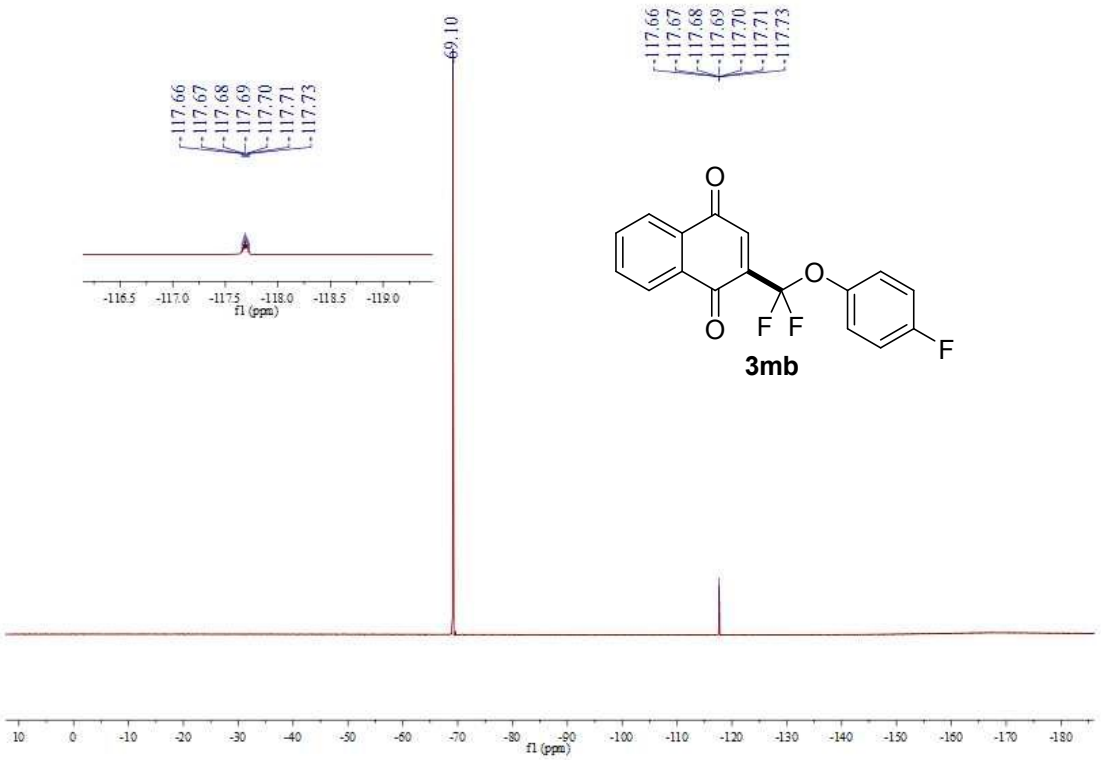
[1]H NMR (400 MHz, CD_3CN)



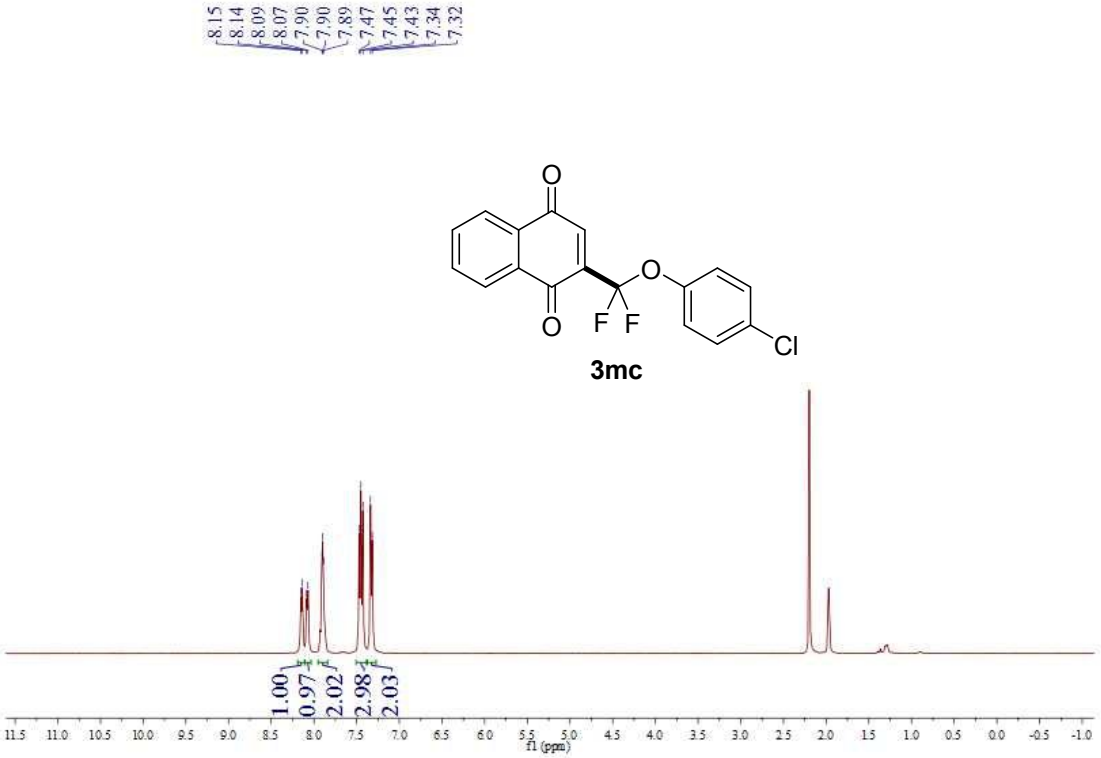
[13]C NMR (101 MHz, $CDCl_3$)



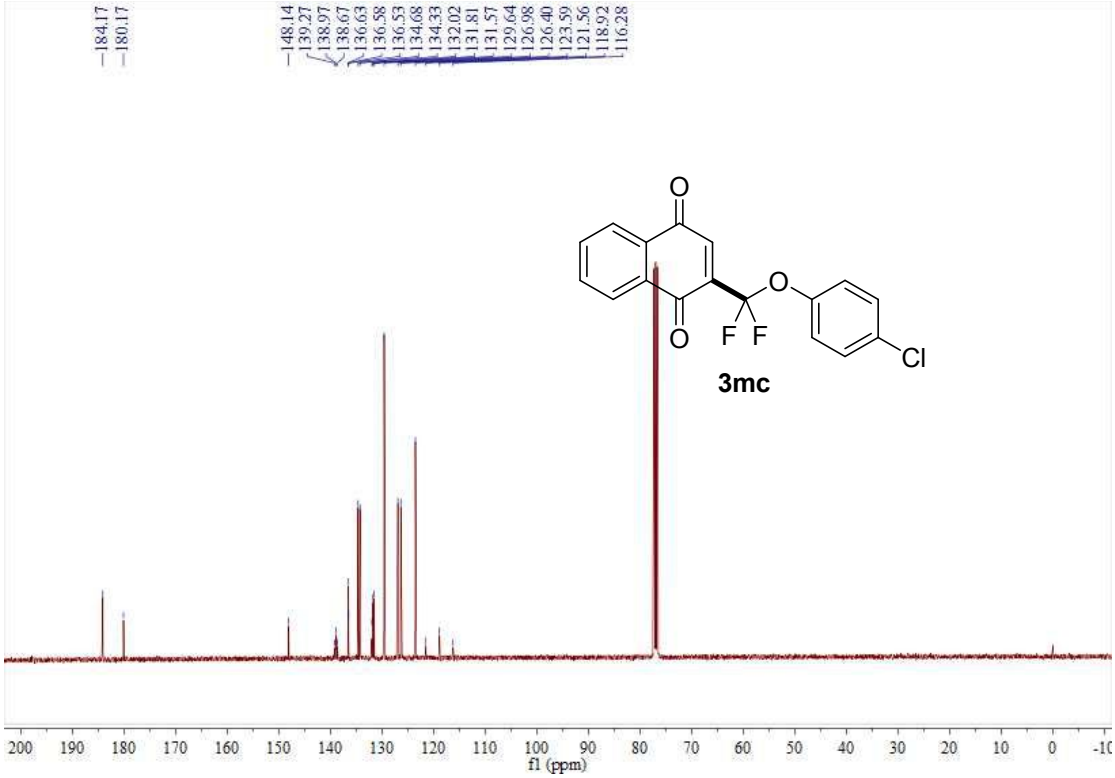
[19]F NMR (377 MHz, CD_3CN)



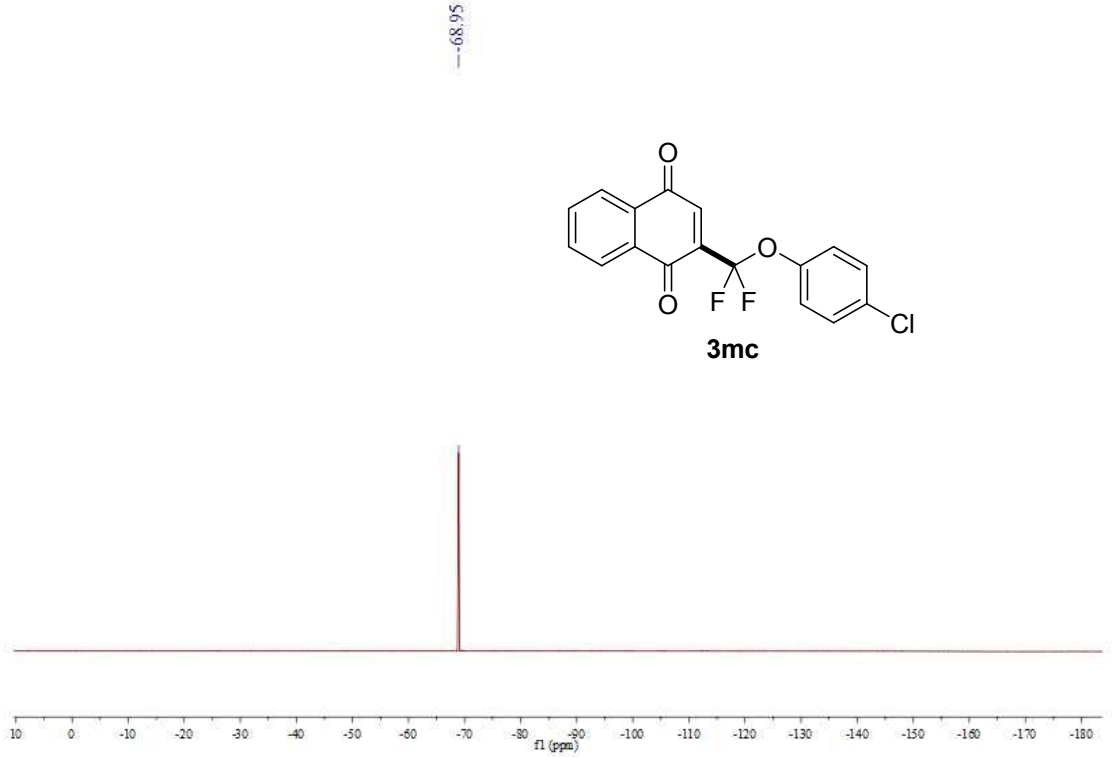
[1]H NMR (400 MHz, CD_3CN)



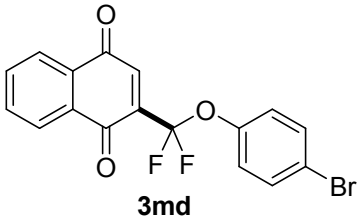
^{13}C NMR (101 MHz, $CDCl_3$)



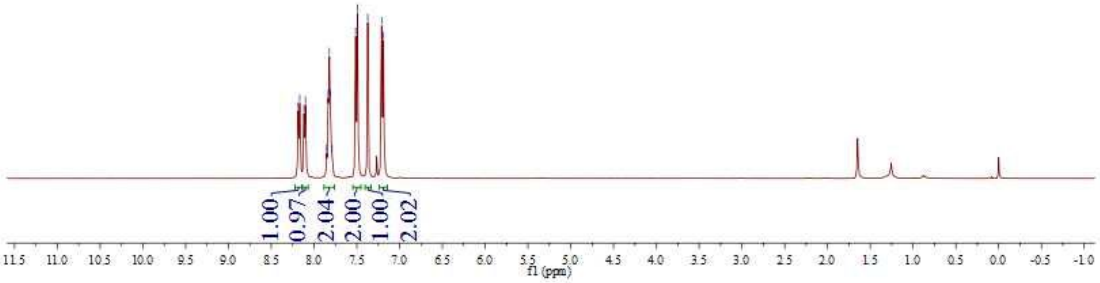
^{19}F NMR (377 MHz, CD_3CN)



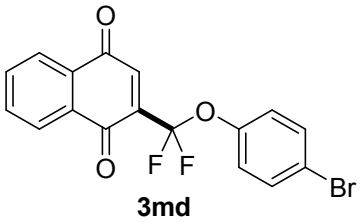
^{1}H NMR (400 MHz, $CDCl_3$)



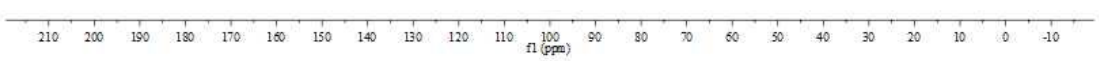
3md



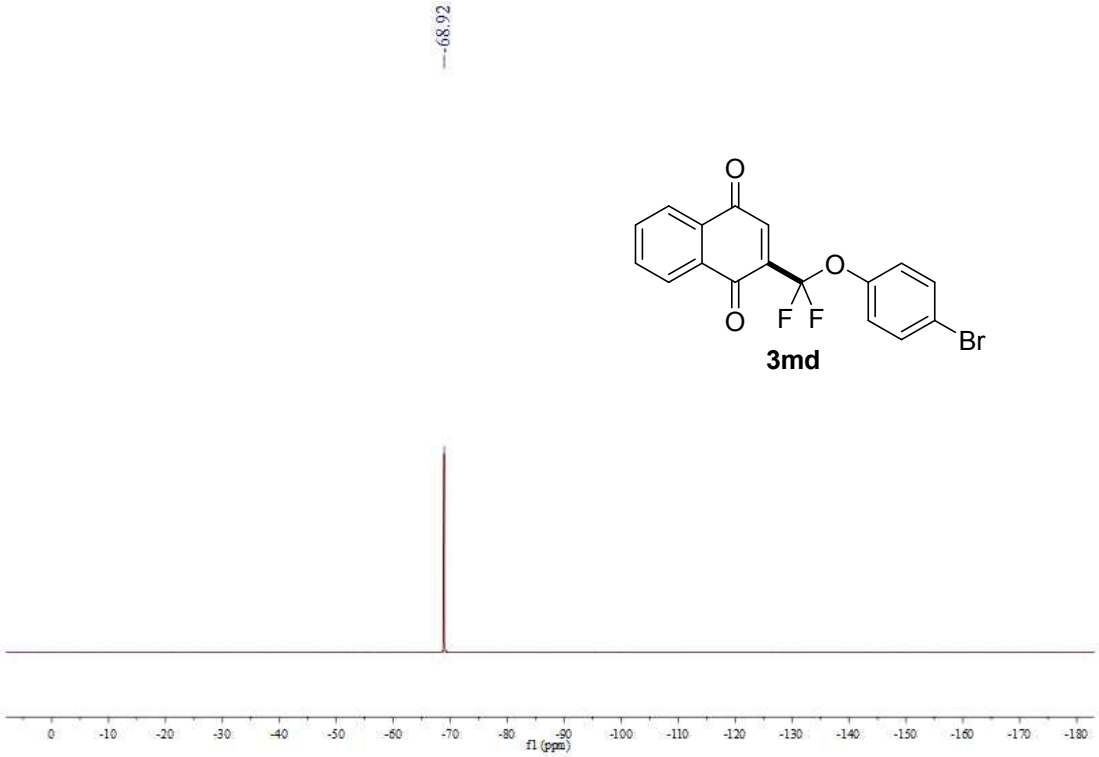
^{13}C NMR (101 MHz, $CDCl_3$)



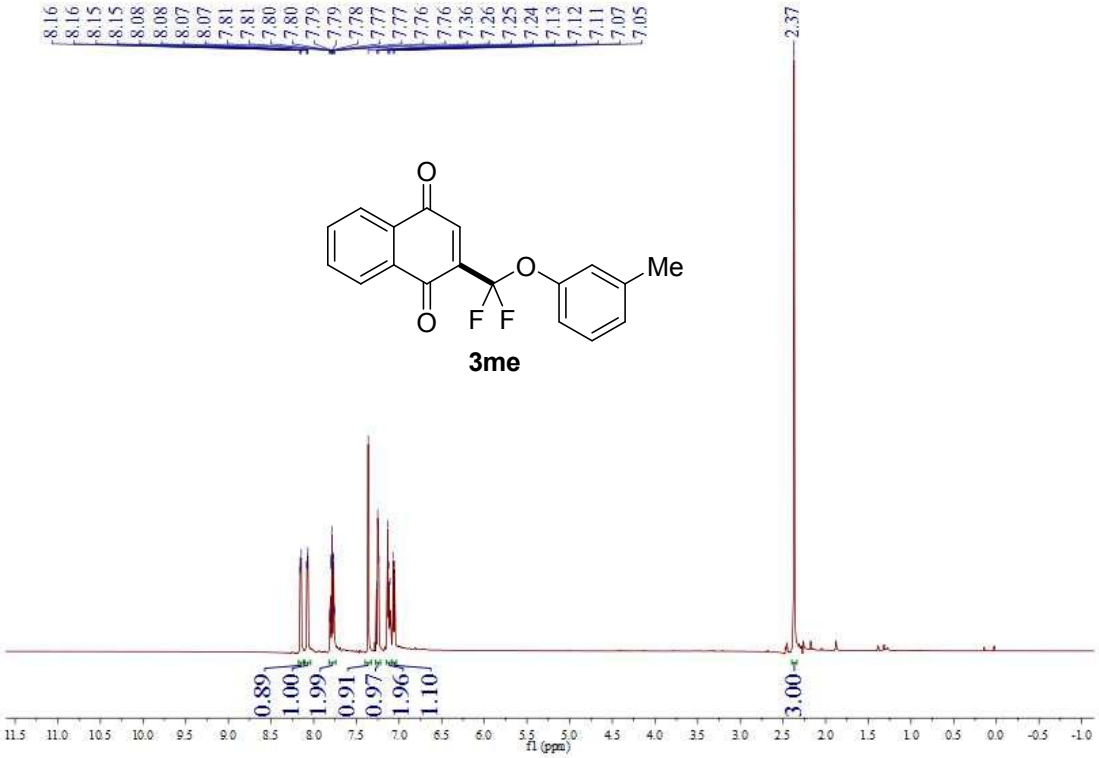
3md



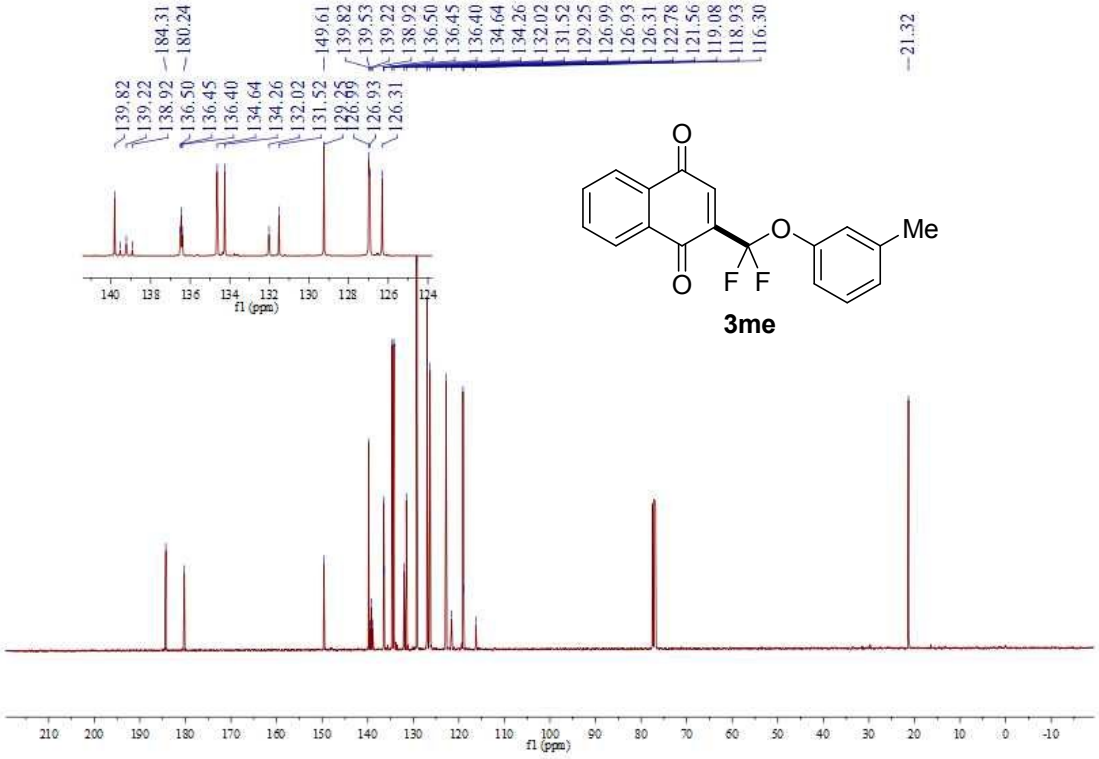
^{19}F NMR (377 MHz, $CDCl_3$)



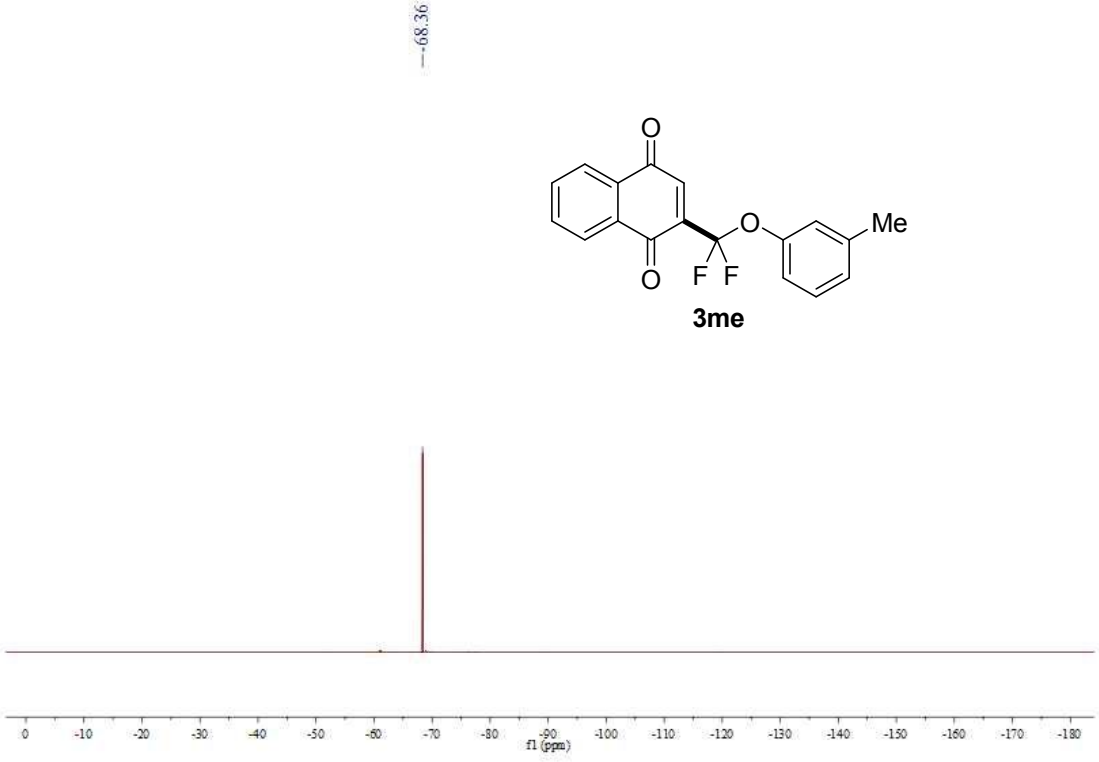
^{1}H NMR (600 MHz, $CDCl_3$)



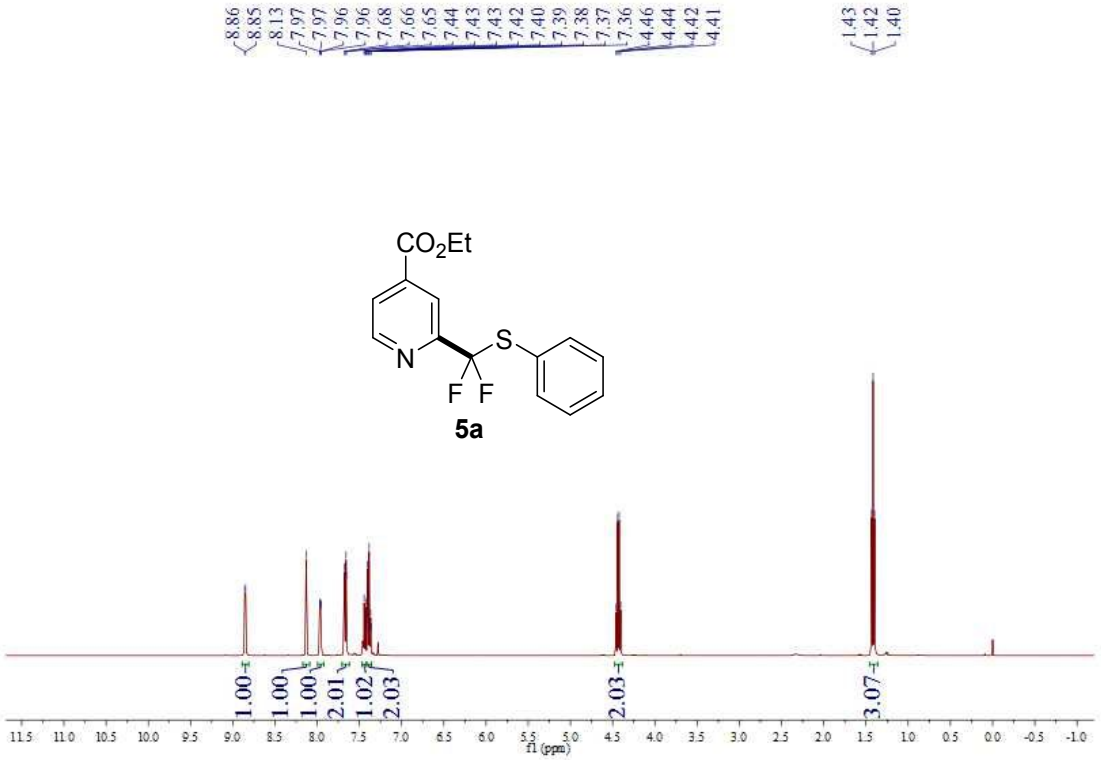
^{13}C NMR (101 MHz, $CDCl_3$)



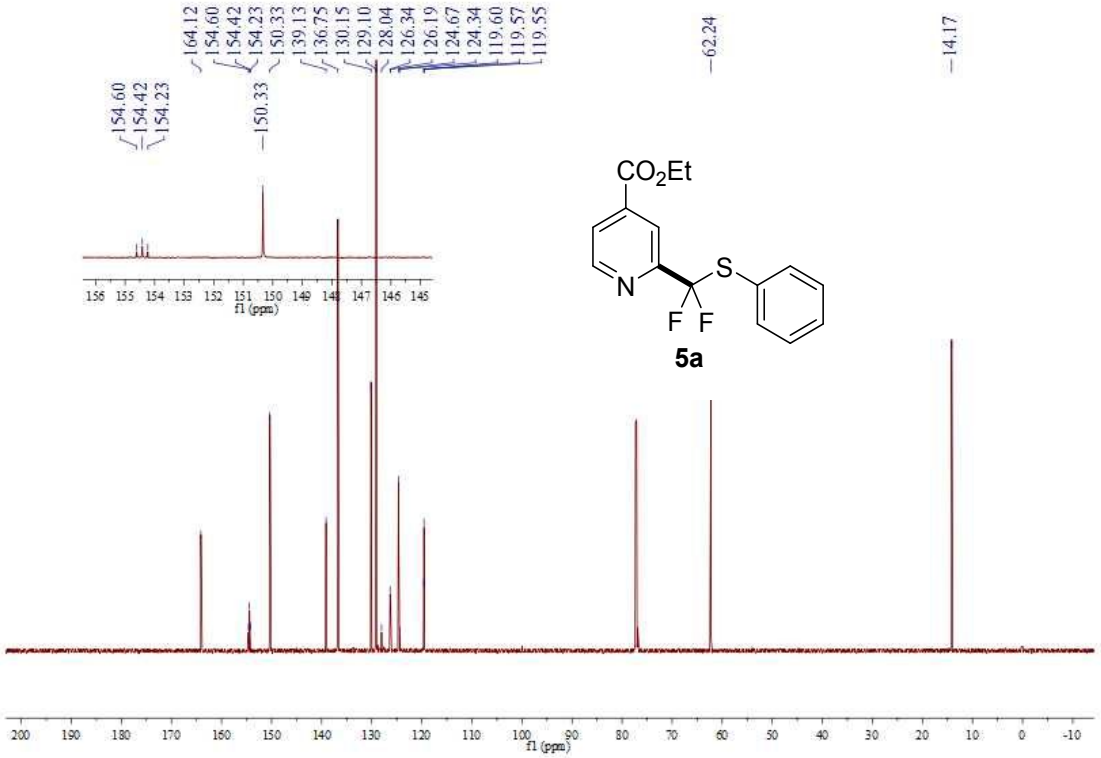
^{19}F NMR (565 MHz, $CDCl_3$)



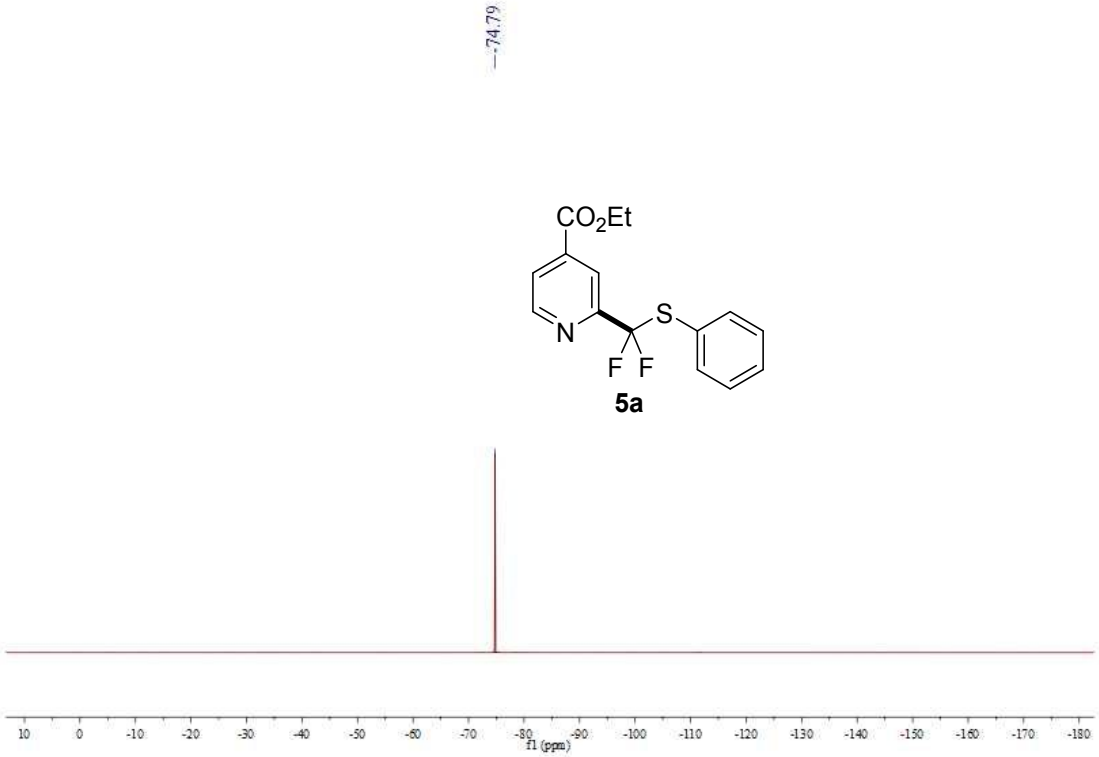
^{1}H NMR (400 MHz, $CDCl_3$)



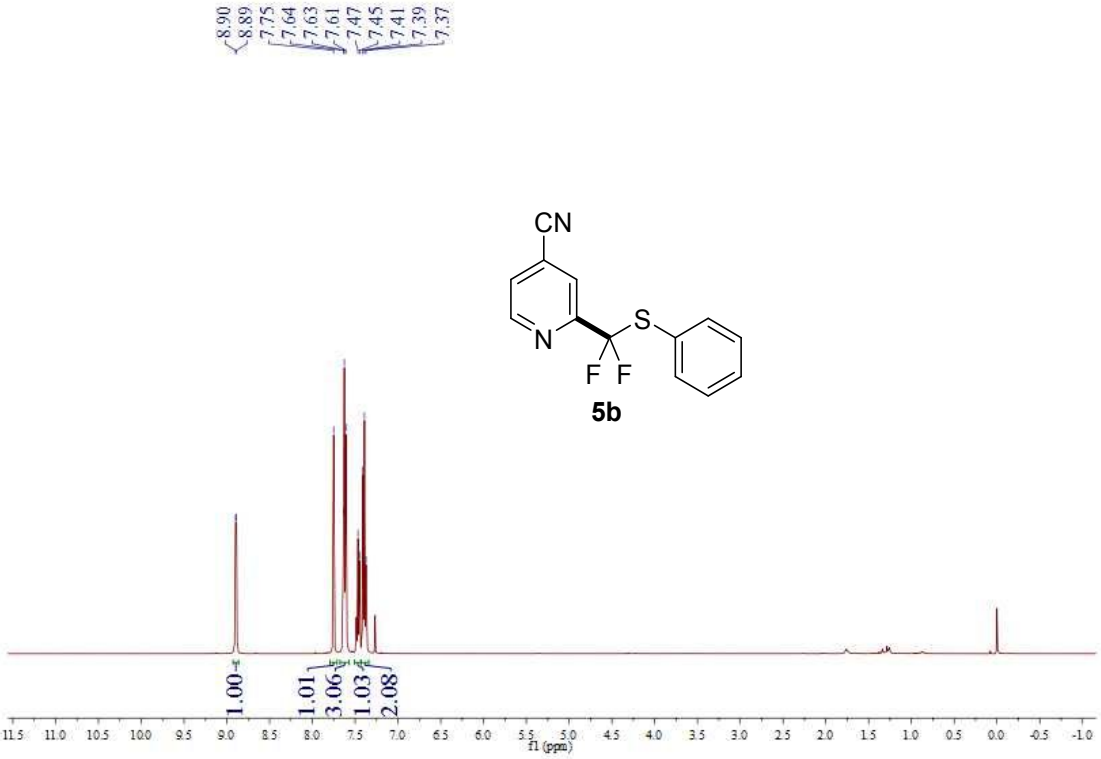
^{13}C NMR (151 MHz, $CDCl_3$)



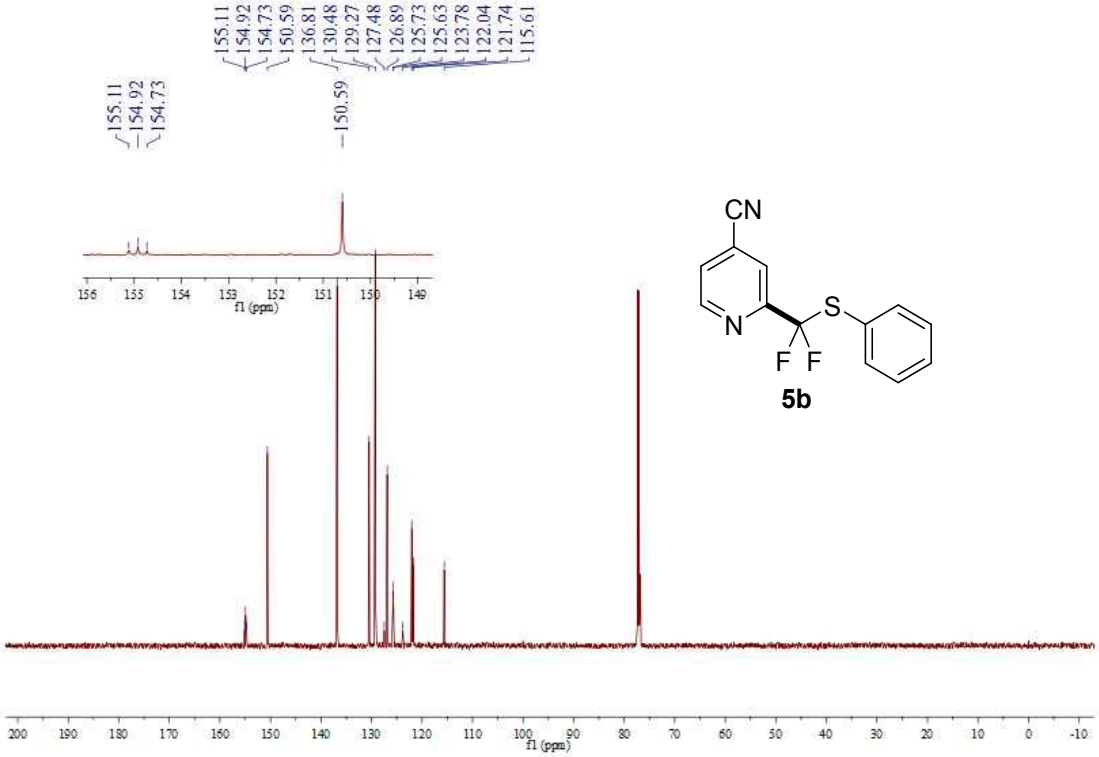
^{19}F NMR (377 MHz, $CDCl_3$)



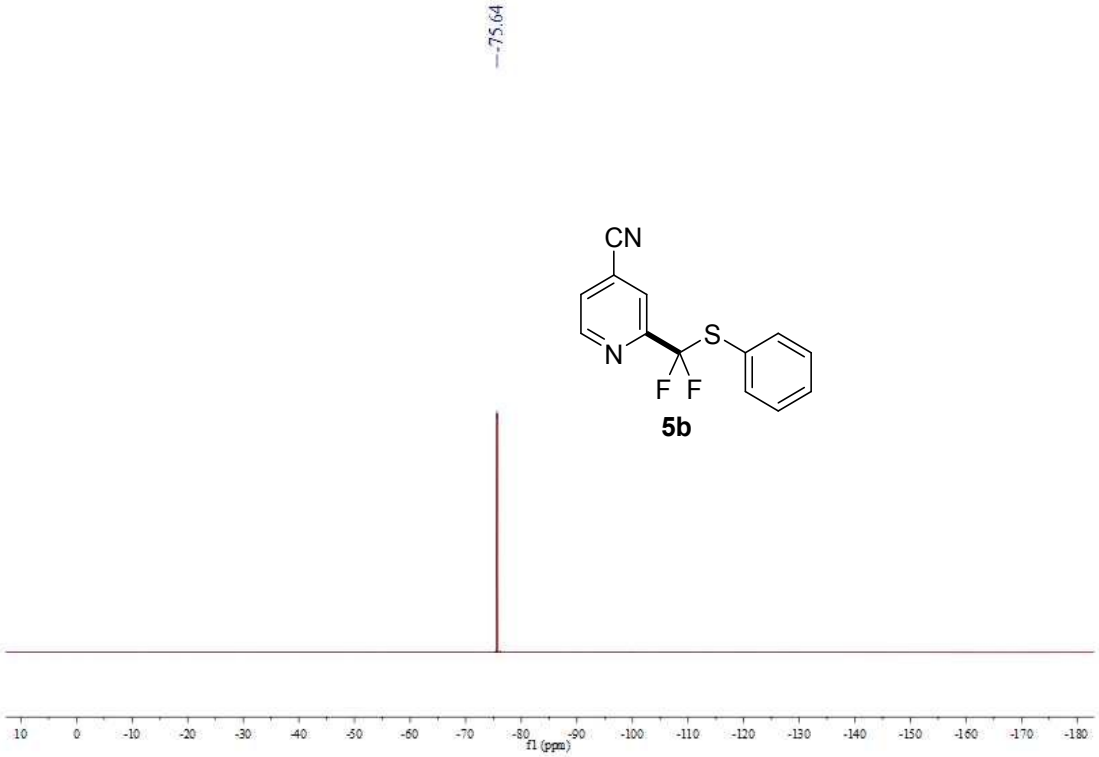
^{1}H NMR (400 MHz, $CDCl_3$)



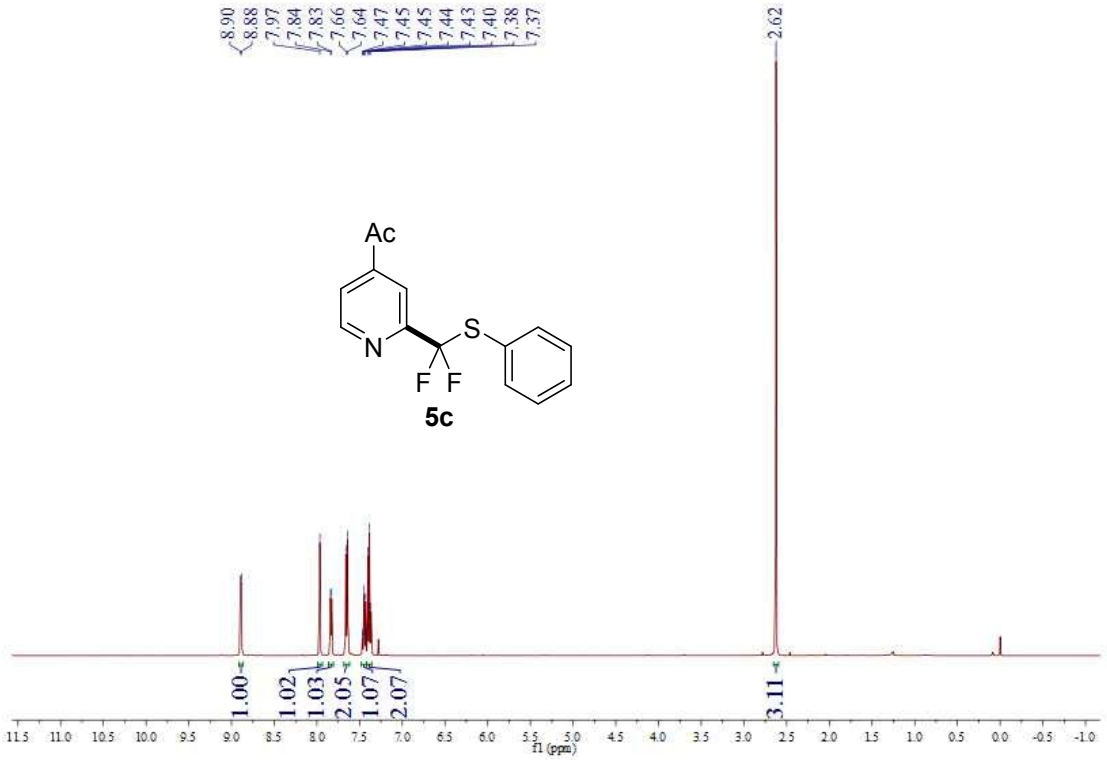
^{13}C NMR (151 MHz, $CDCl_3$)



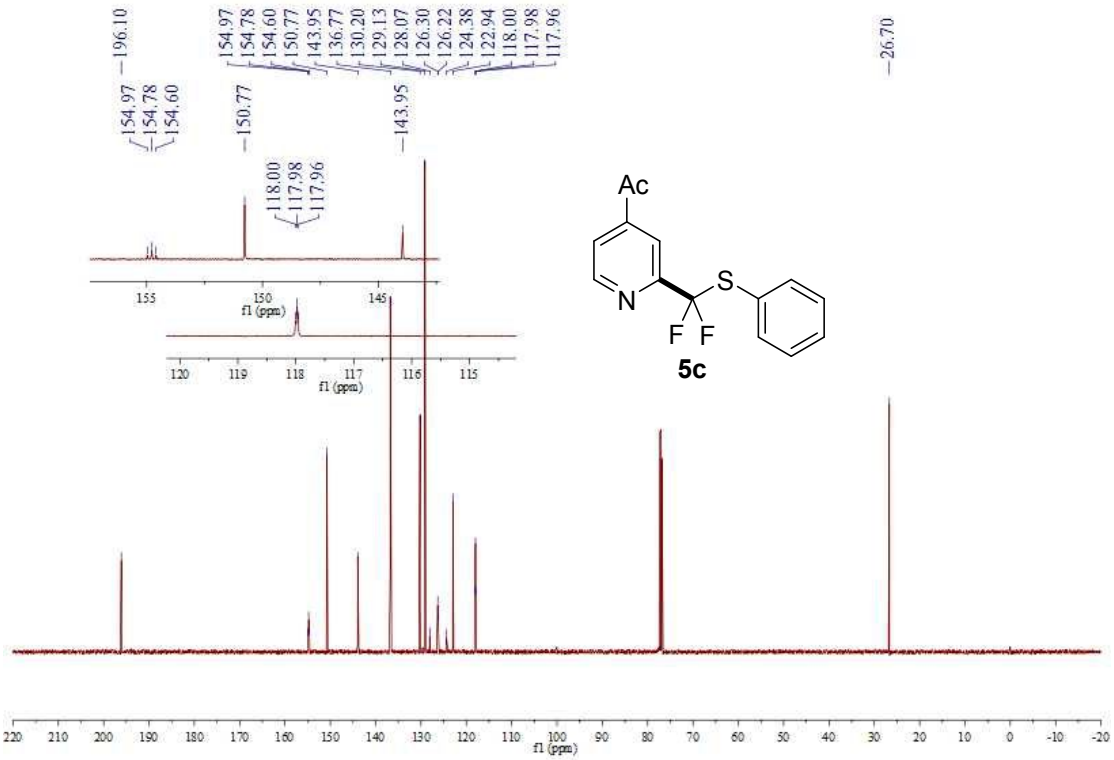
^{19}F NMR (377 MHz, $CDCl_3$)



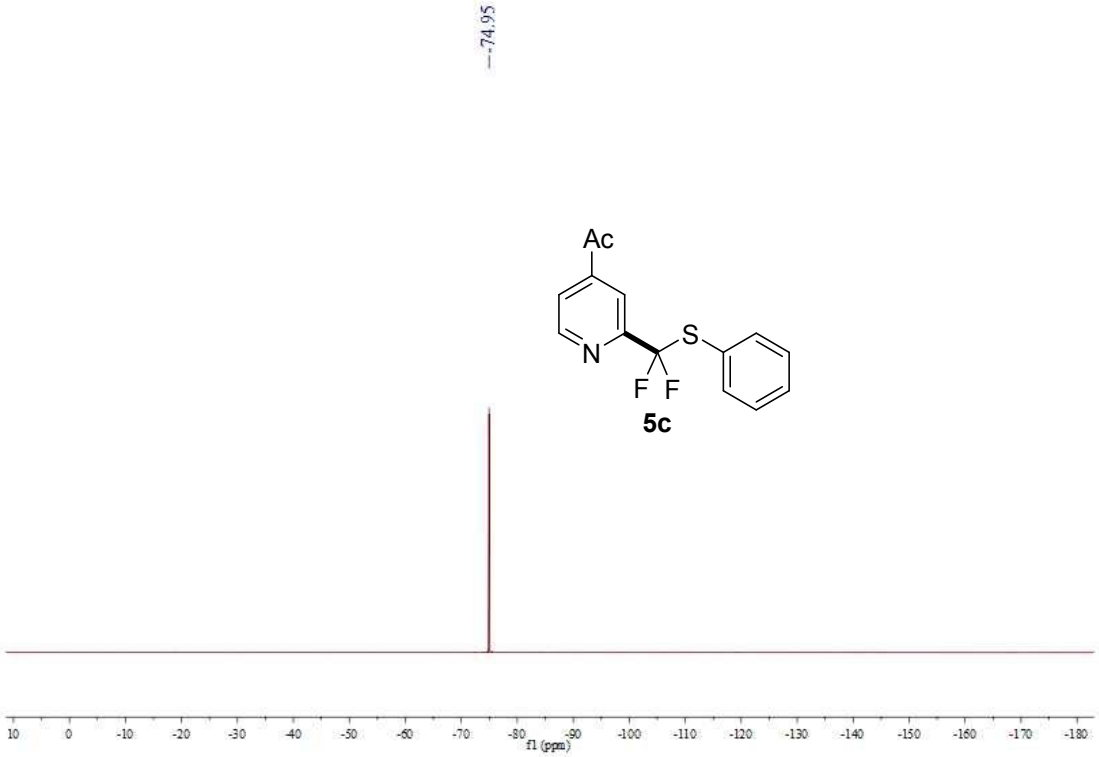
^{1}H NMR (400 MHz, $CDCl_3$)



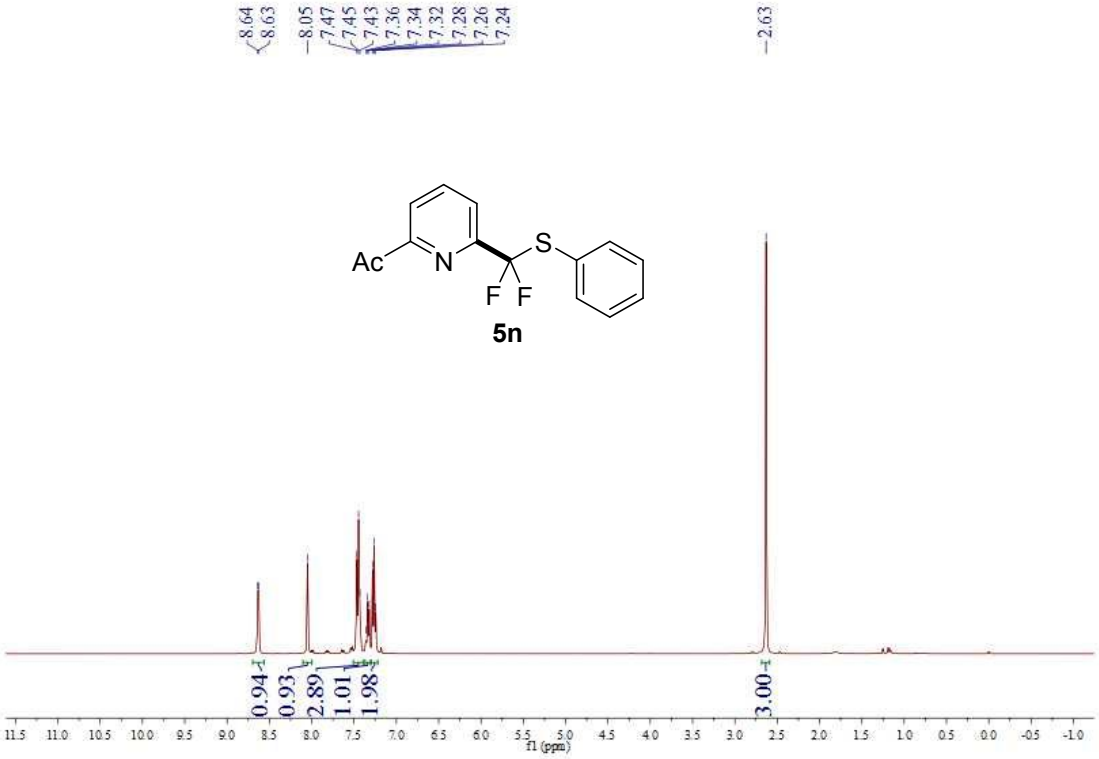
^{13}C NMR (151 MHz, $CDCl_3$)



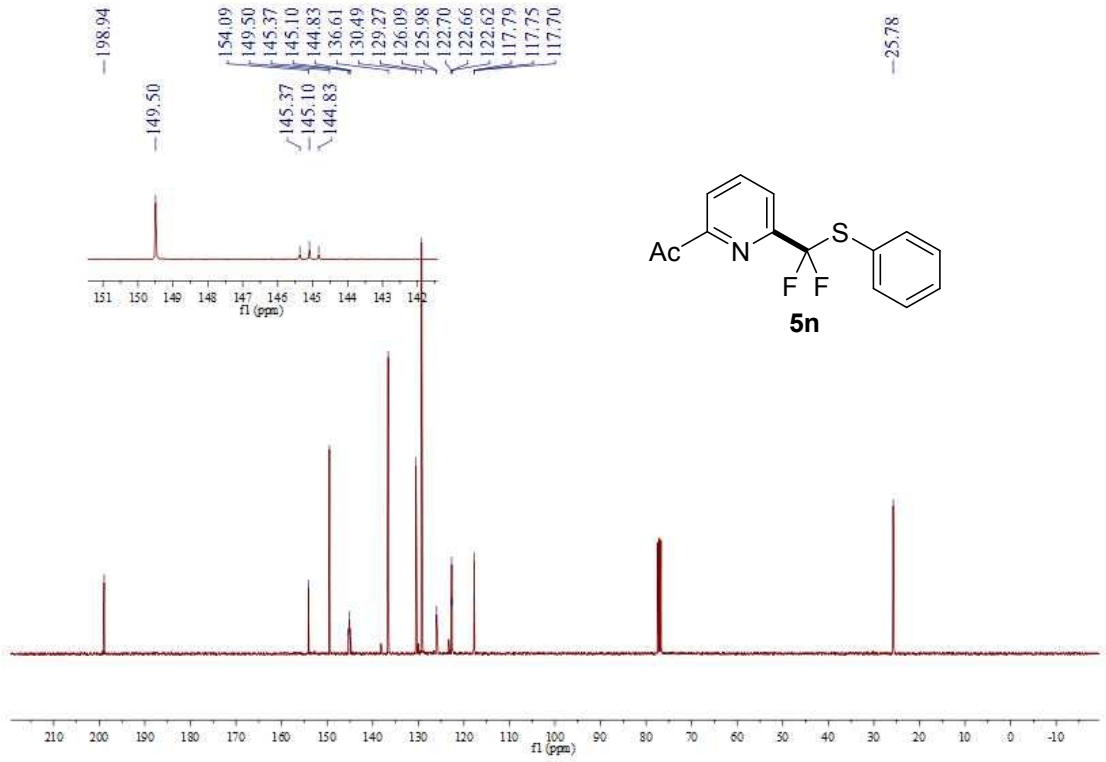
^{19}F NMR (377 MHz, $CDCl_3$)



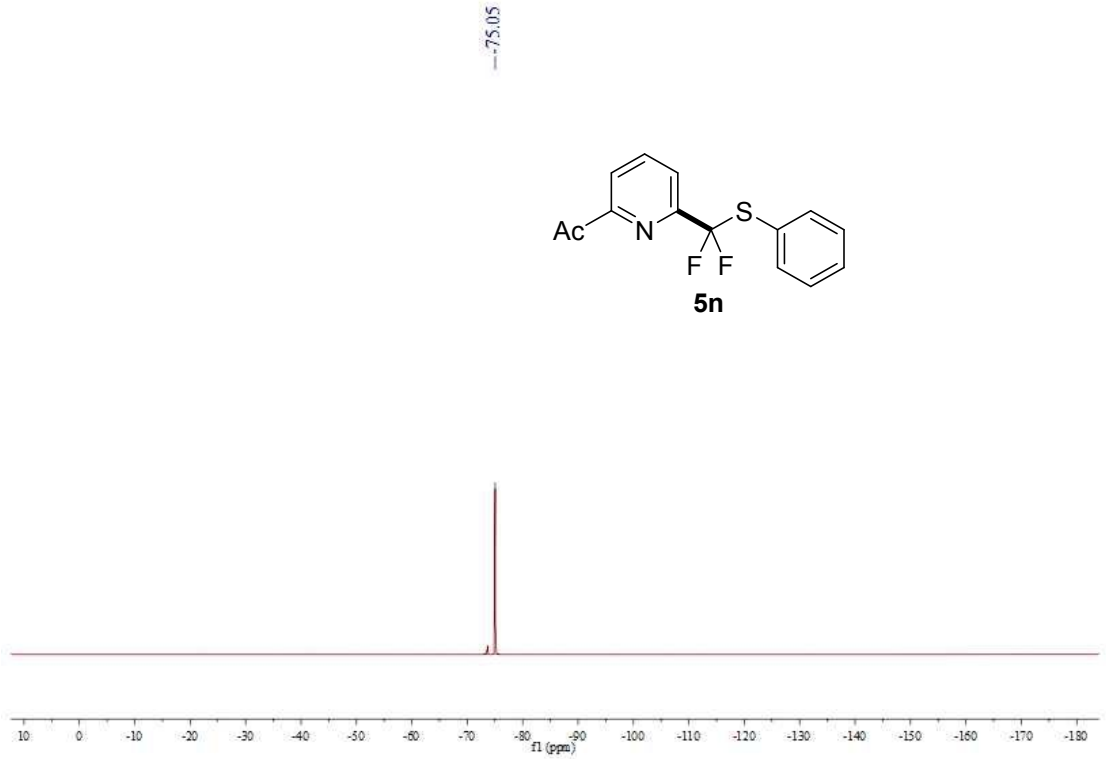
^{1}H NMR (400 MHz, $CDCl_3$)



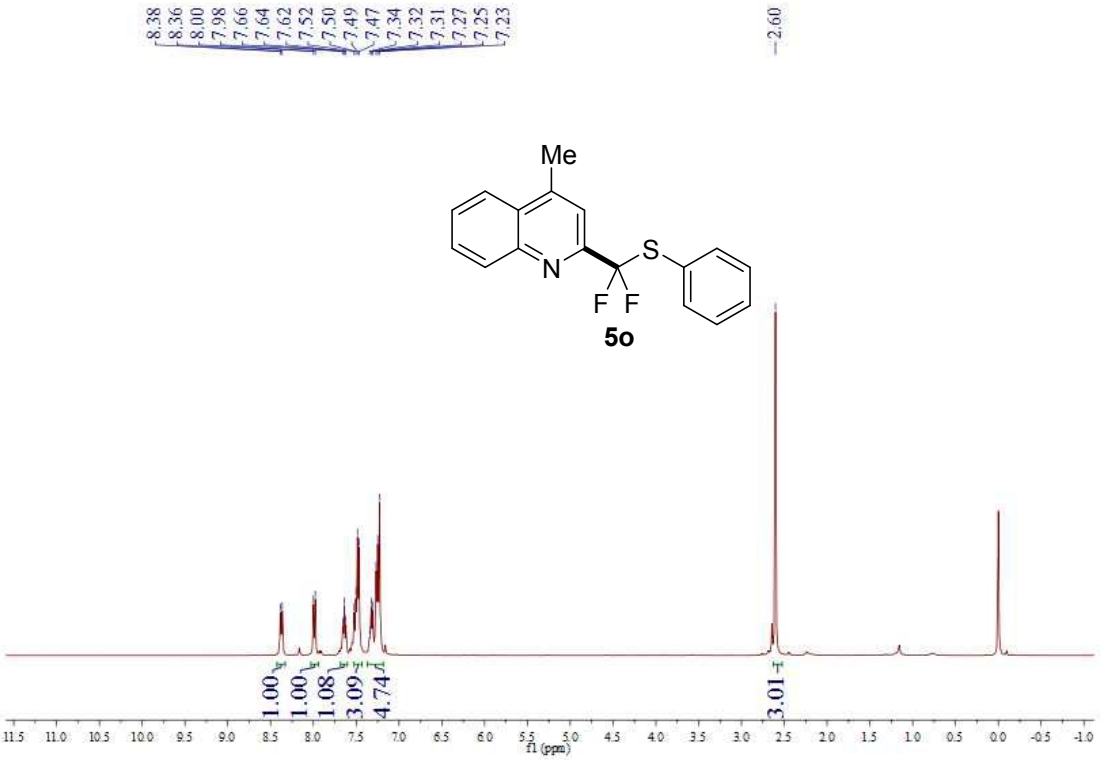
^{13}C NMR (101 MHz, $CDCl_3$)



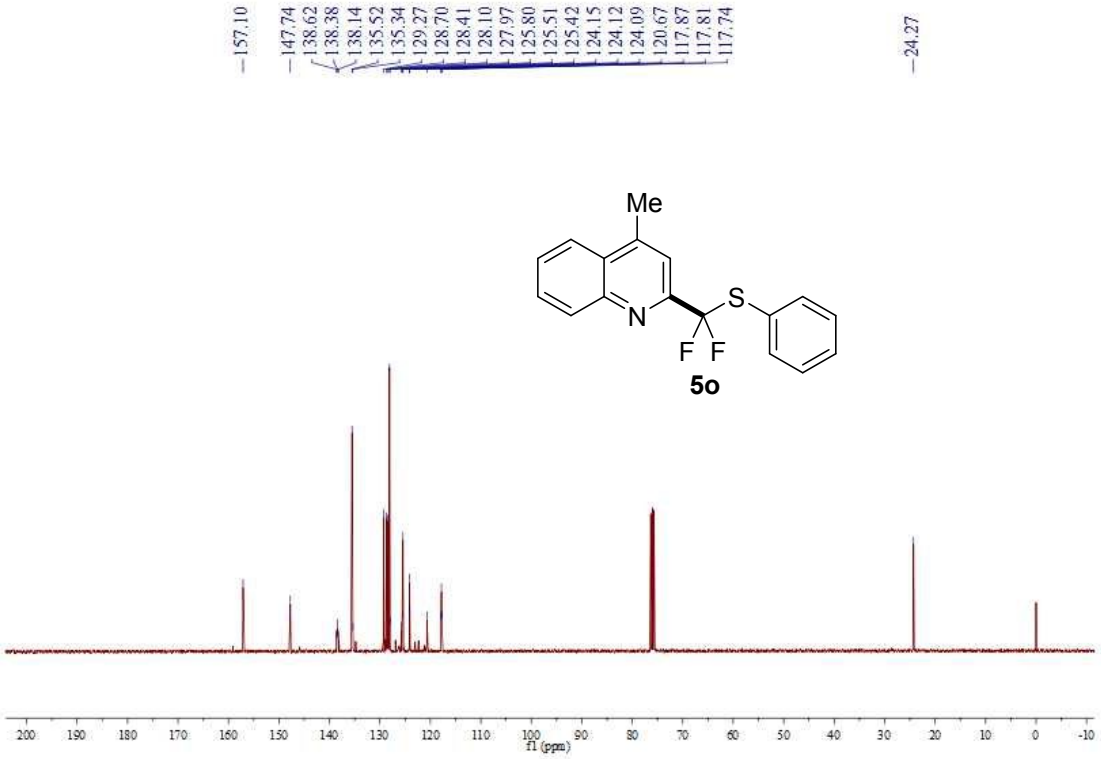
^{19}F NMR (377 MHz, $CDCl_3$)



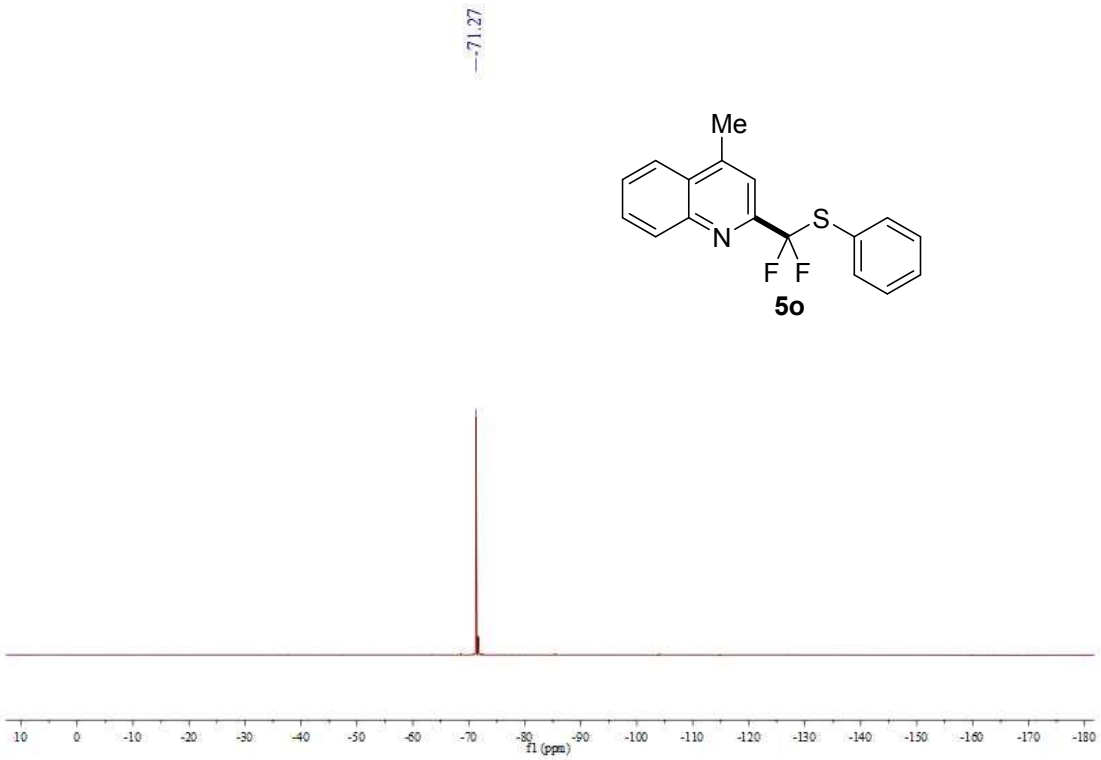
^{1}H NMR (400 MHz, $CDCl_3$)



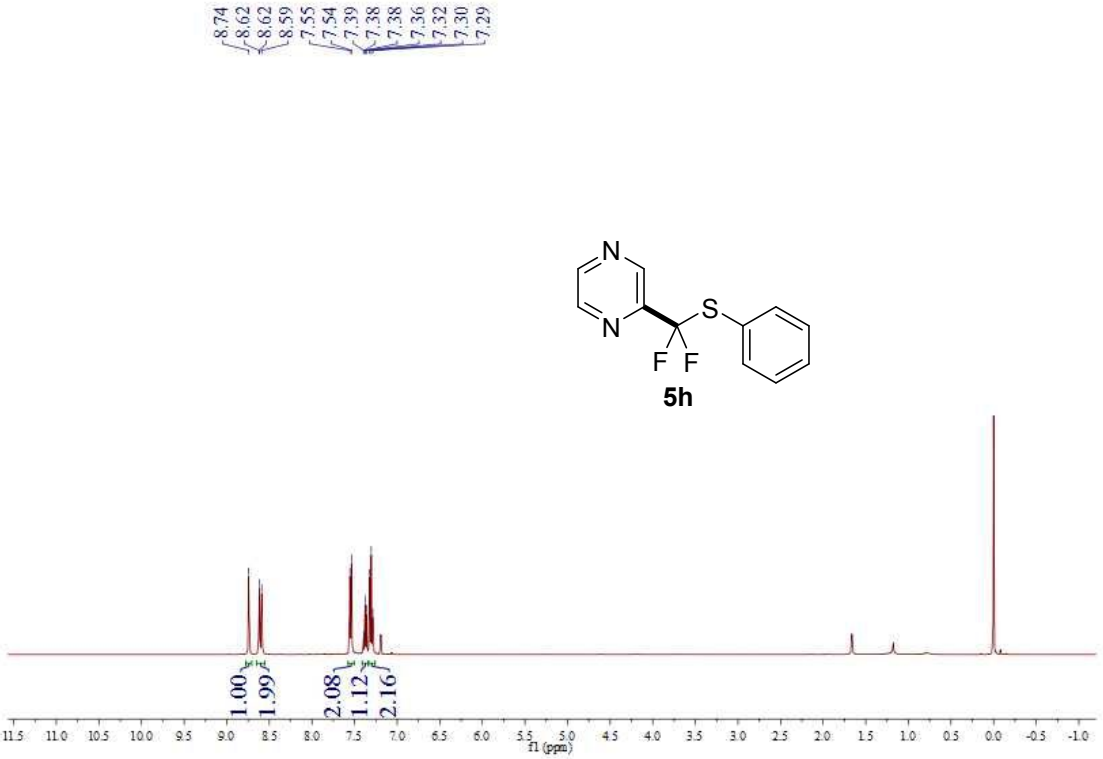
^{13}C NMR (101 MHz, $CDCl_3$)



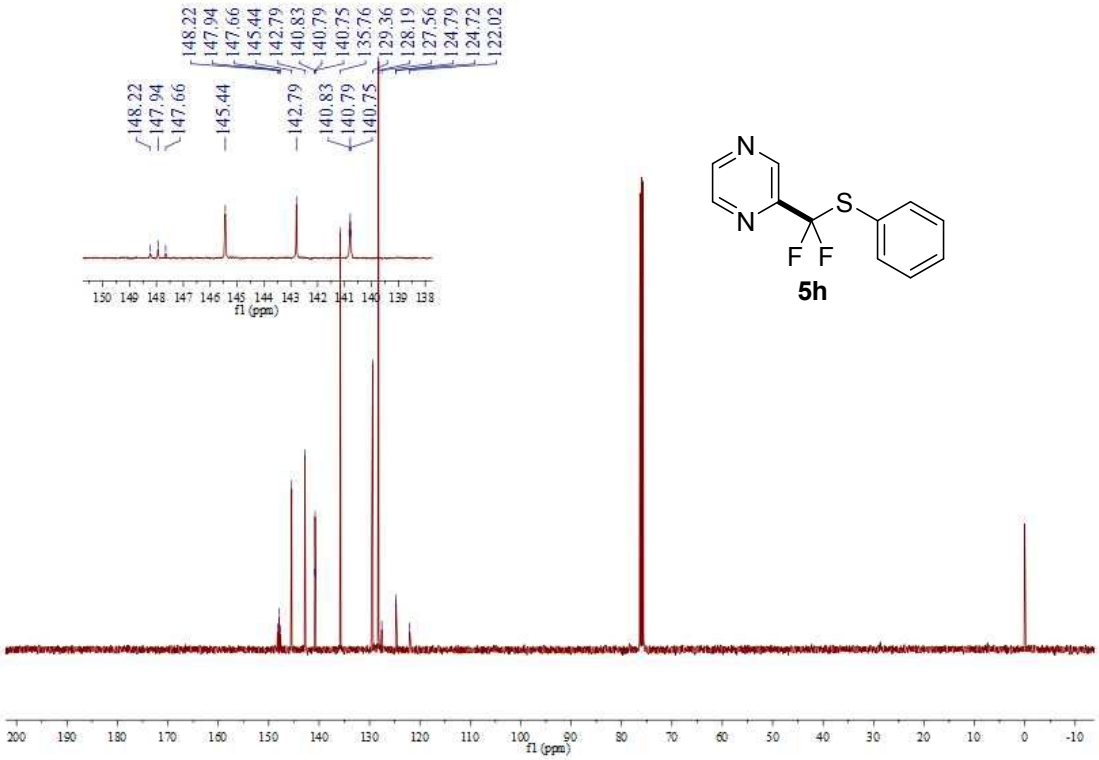
^{19}F NMR (377 MHz, $CDCl_3$)



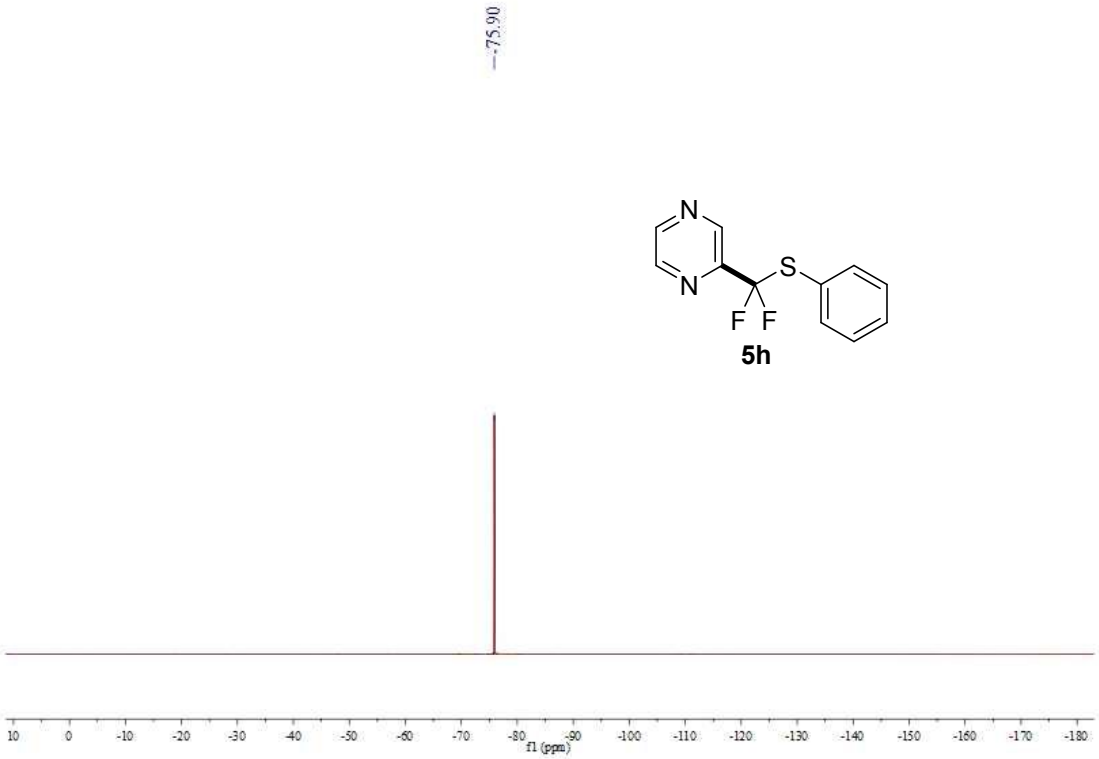
^{1}H NMR (400 MHz, $CDCl_3$)



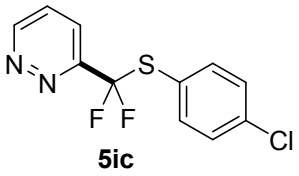
^{13}C NMR (101 MHz, $CDCl_3$)



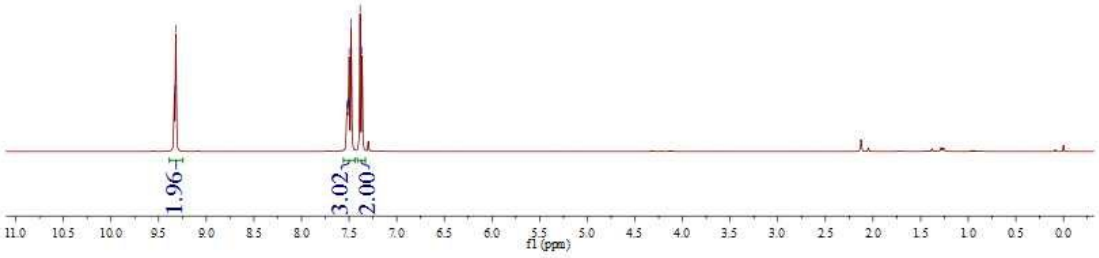
^{19}F NMR (377 MHz, $CDCl_3$)



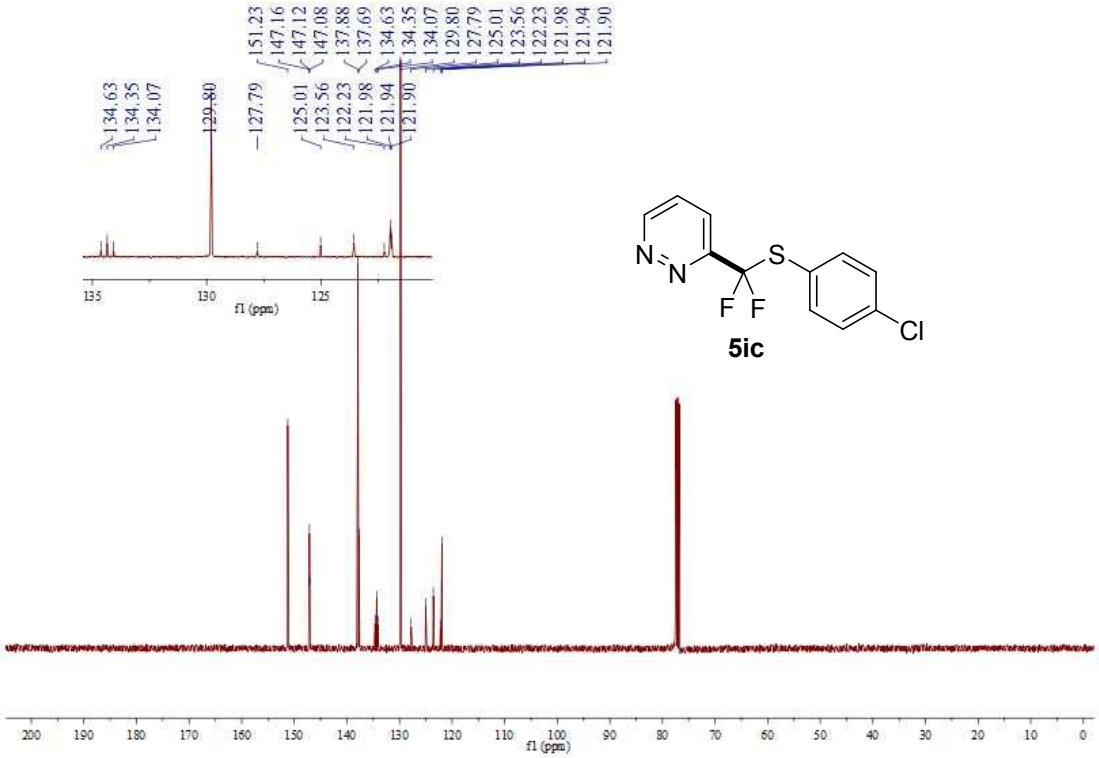
^{1}H NMR (400 MHz, $CDCl_3$)



5ic

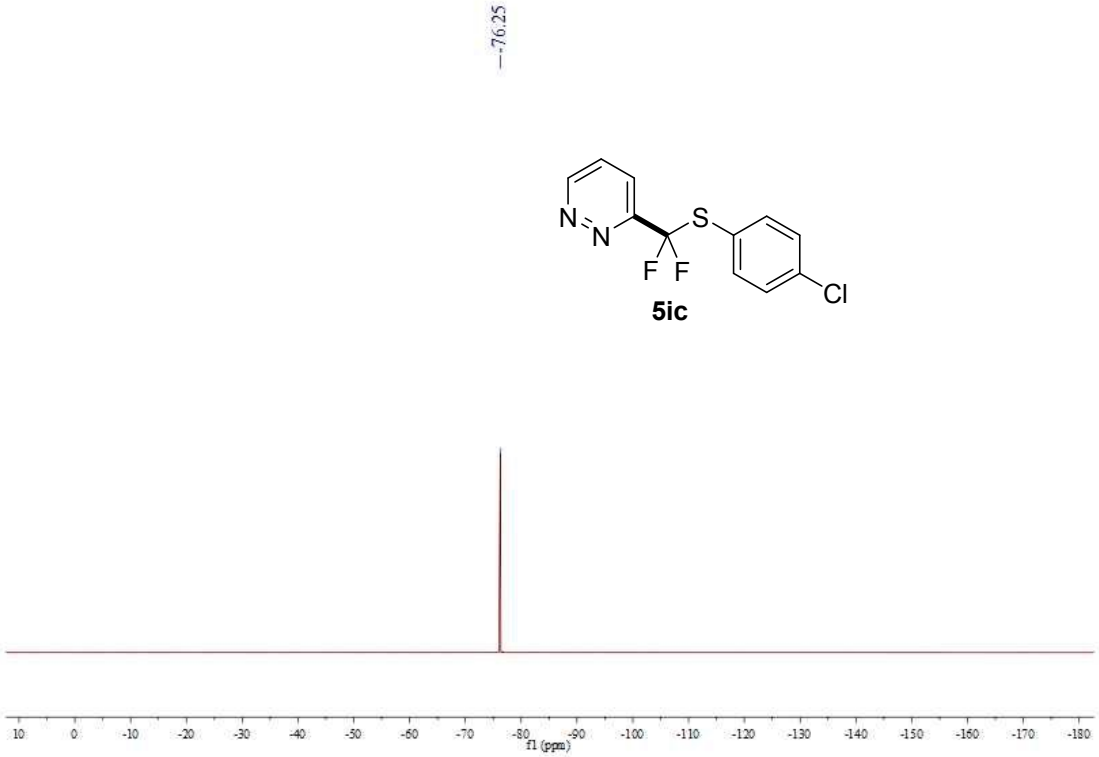


^{13}C NMR (101 MHz, $CDCl_3$)

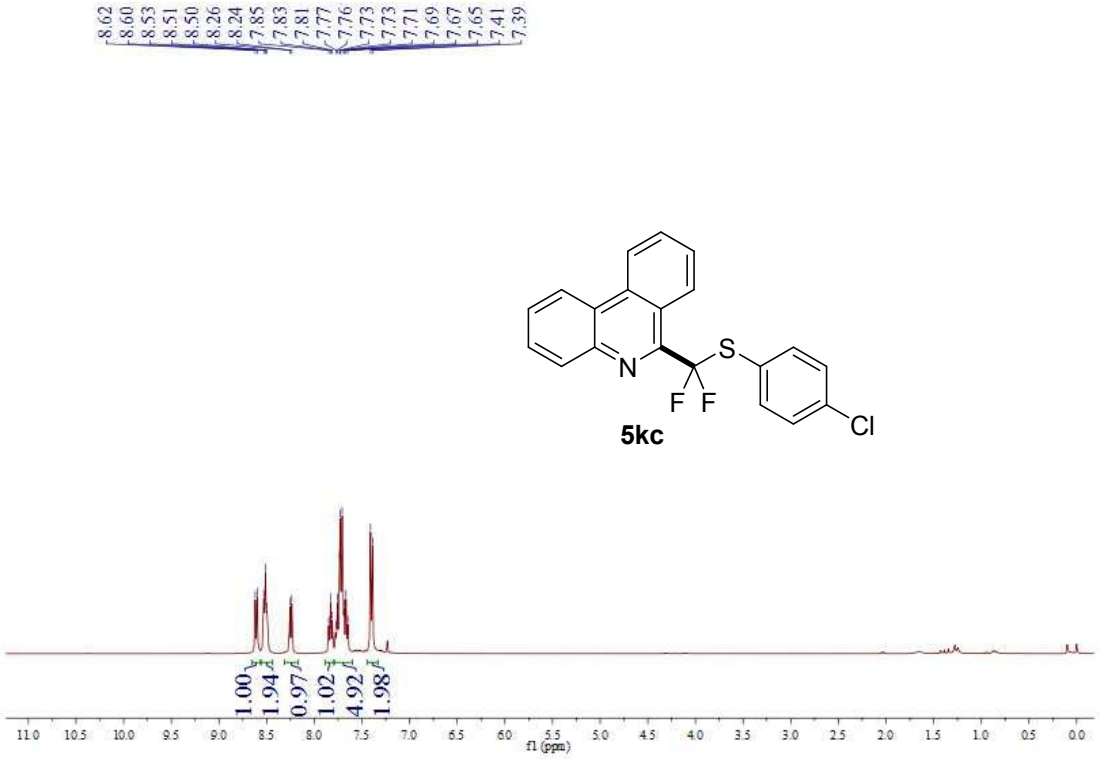


5ic

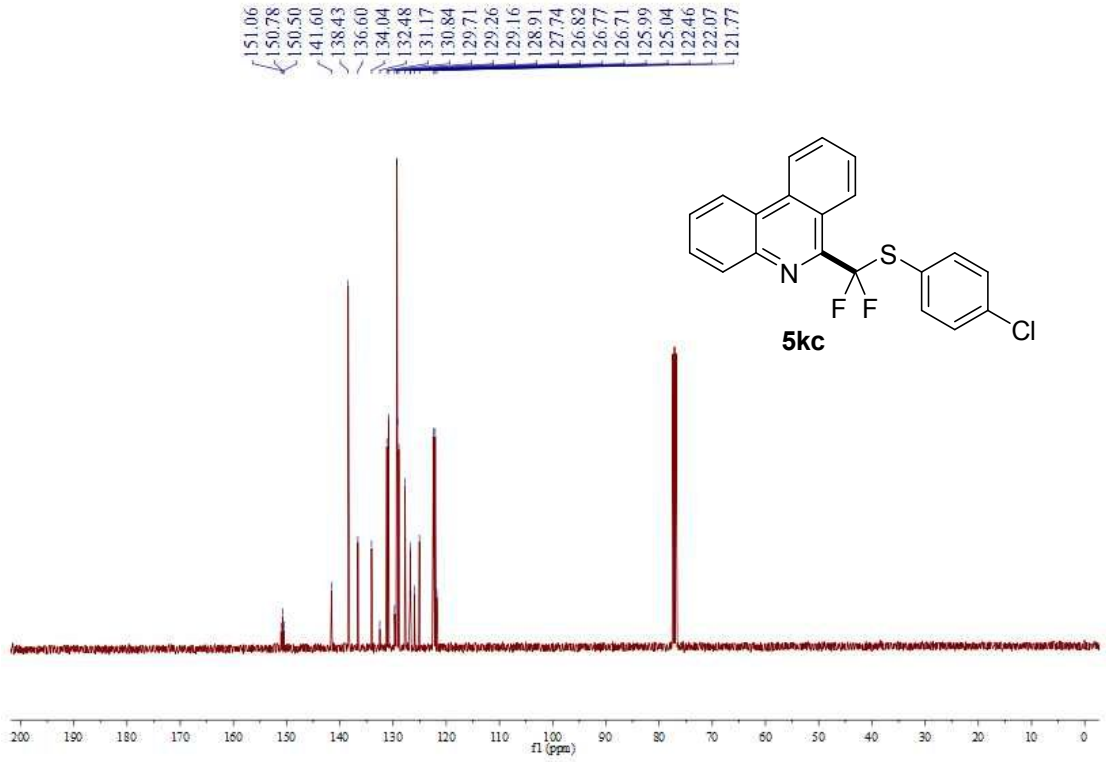
^{19}F NMR (377 MHz, $CDCl_3$)



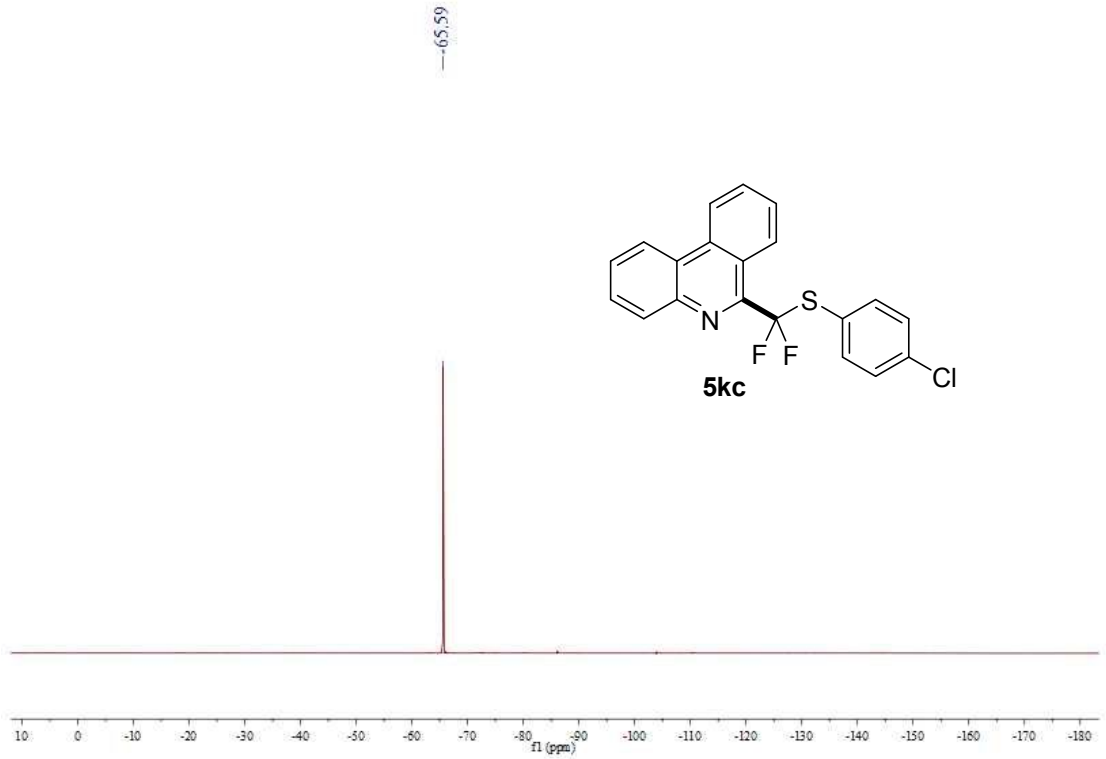
^{1}H NMR (400 MHz, $CDCl_3$)



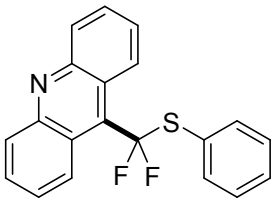
^{13}C NMR (101 MHz, $CDCl_3$)



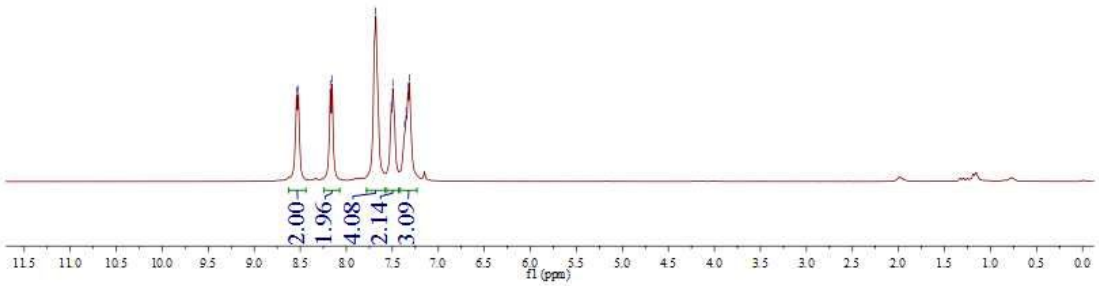
^{19}F NMR (377 MHz, $CDCl_3$)



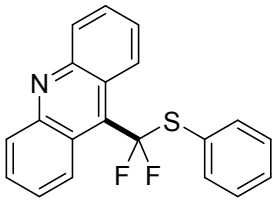
^{1}H NMR (400 MHz, $CDCl_3$)



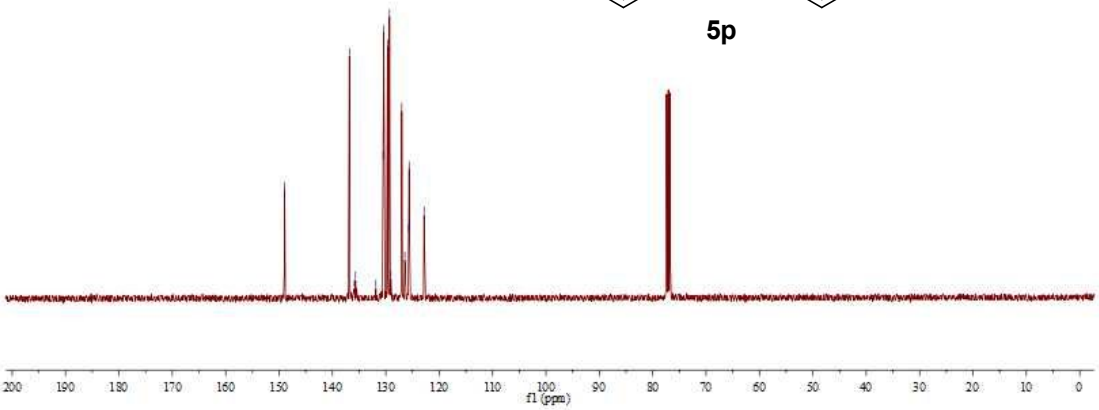
5p



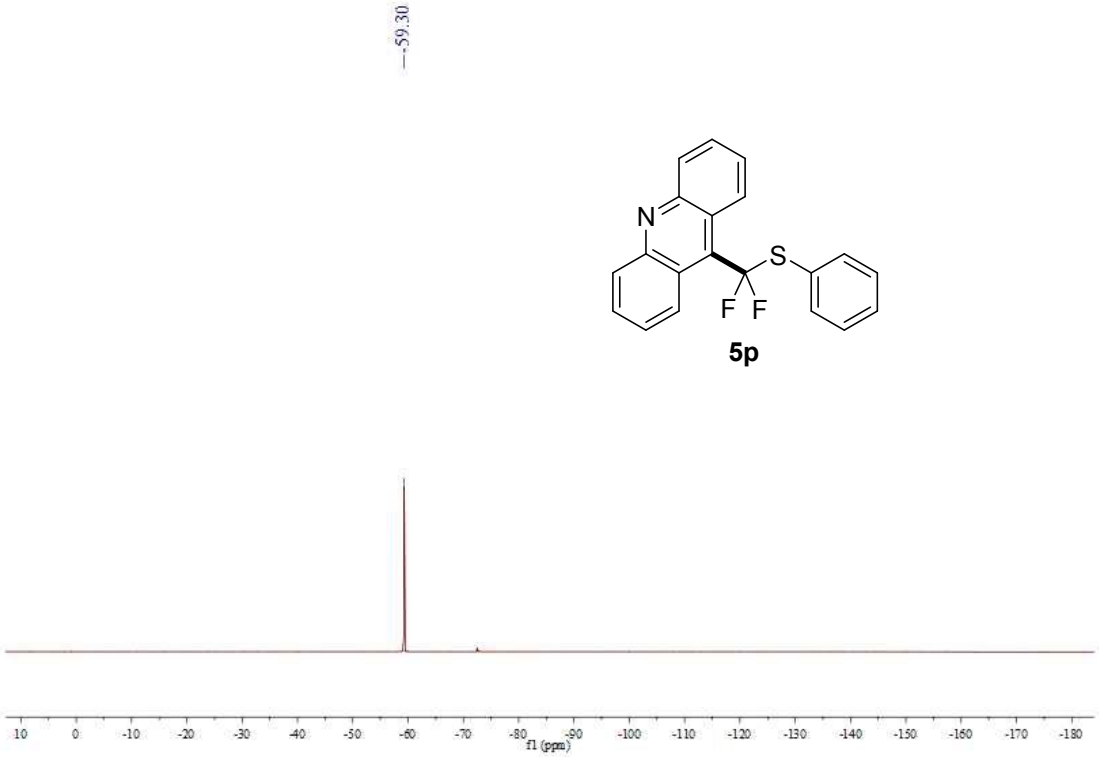
^{13}C NMR (101 MHz, $CDCl_3$)



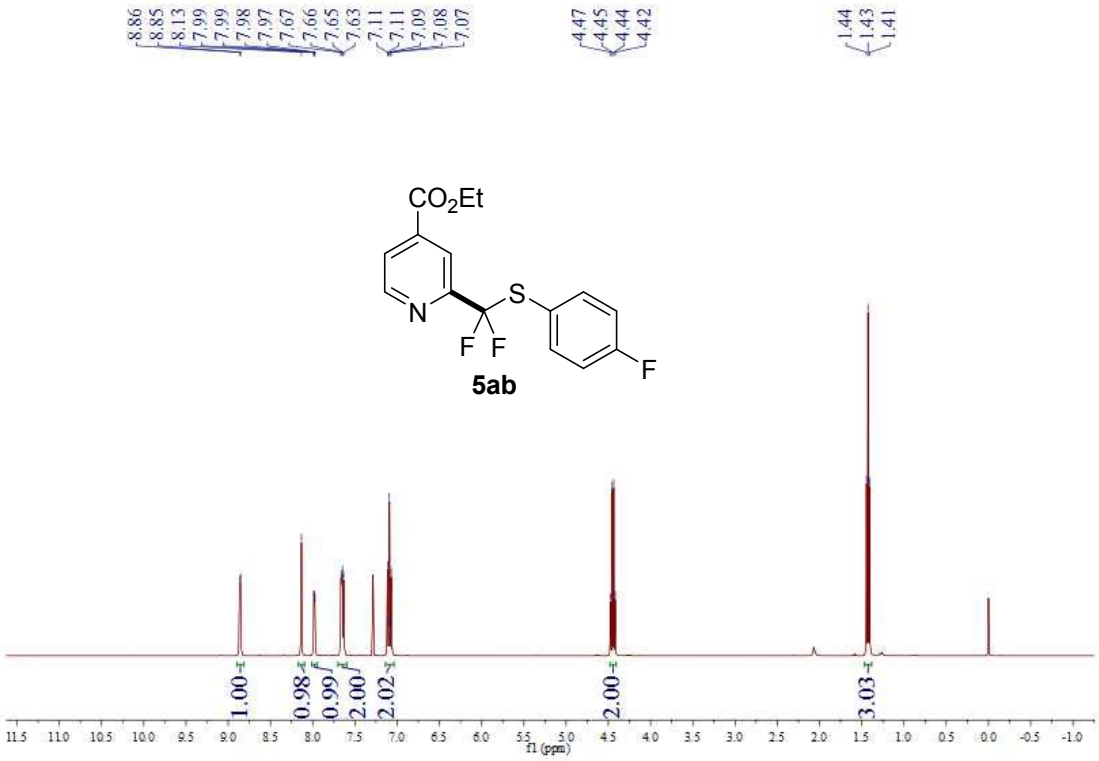
5p



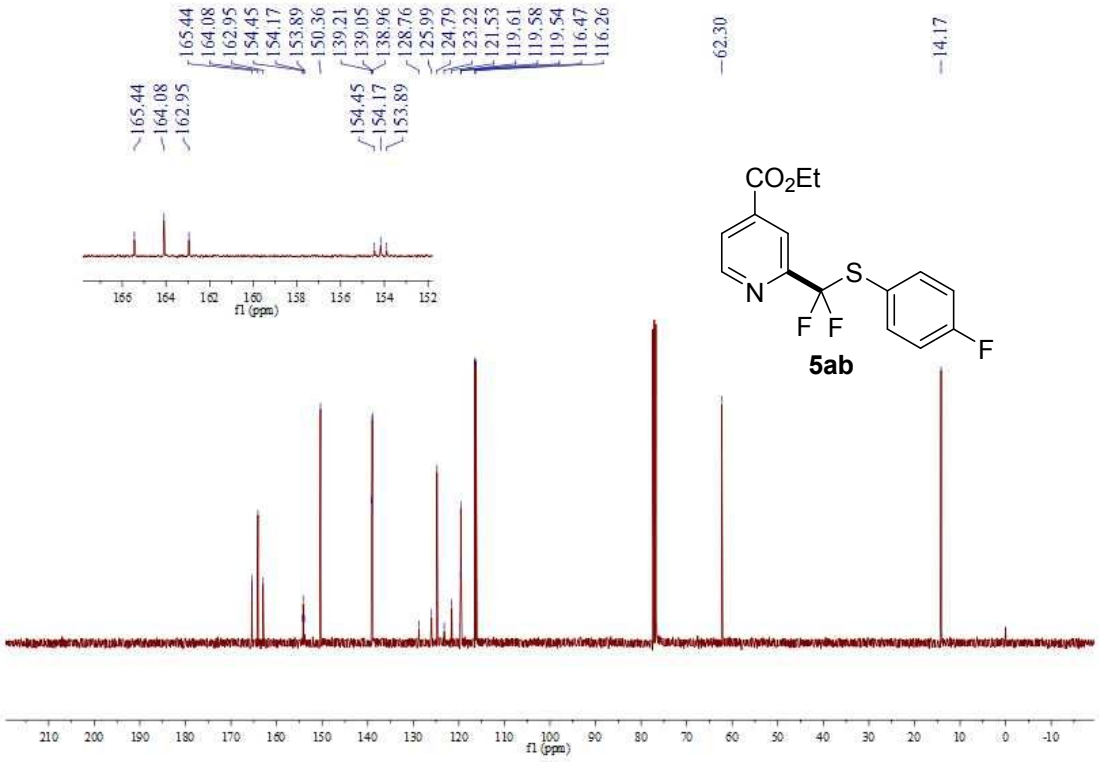
^{19}F NMR (377 MHz, $CDCl_3$)



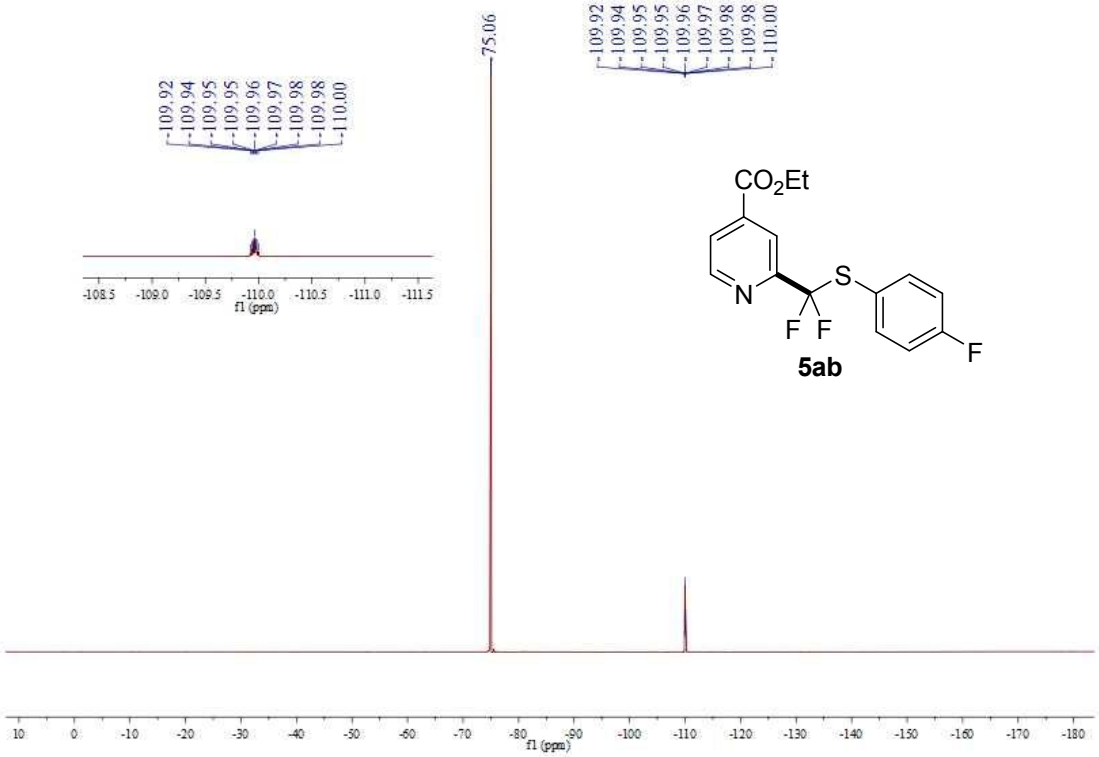
^{1}H NMR (400 MHz, $CDCl_3$)



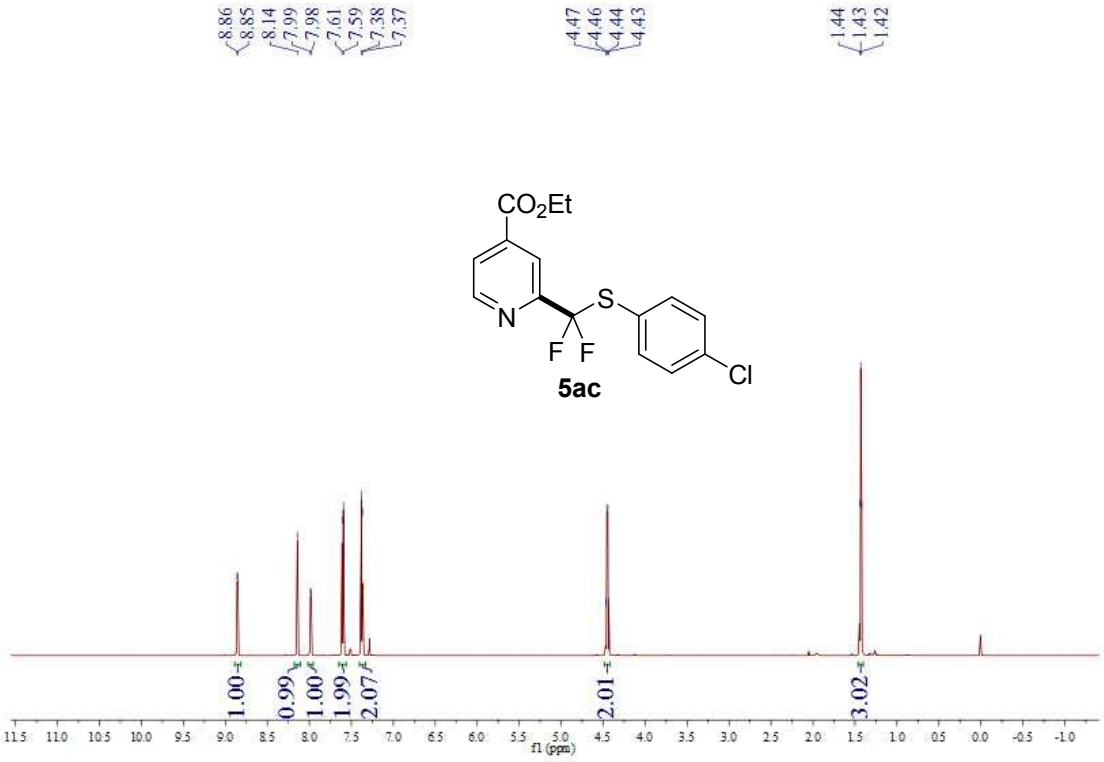
^{13}C NMR (101 MHz, $CDCl_3$)



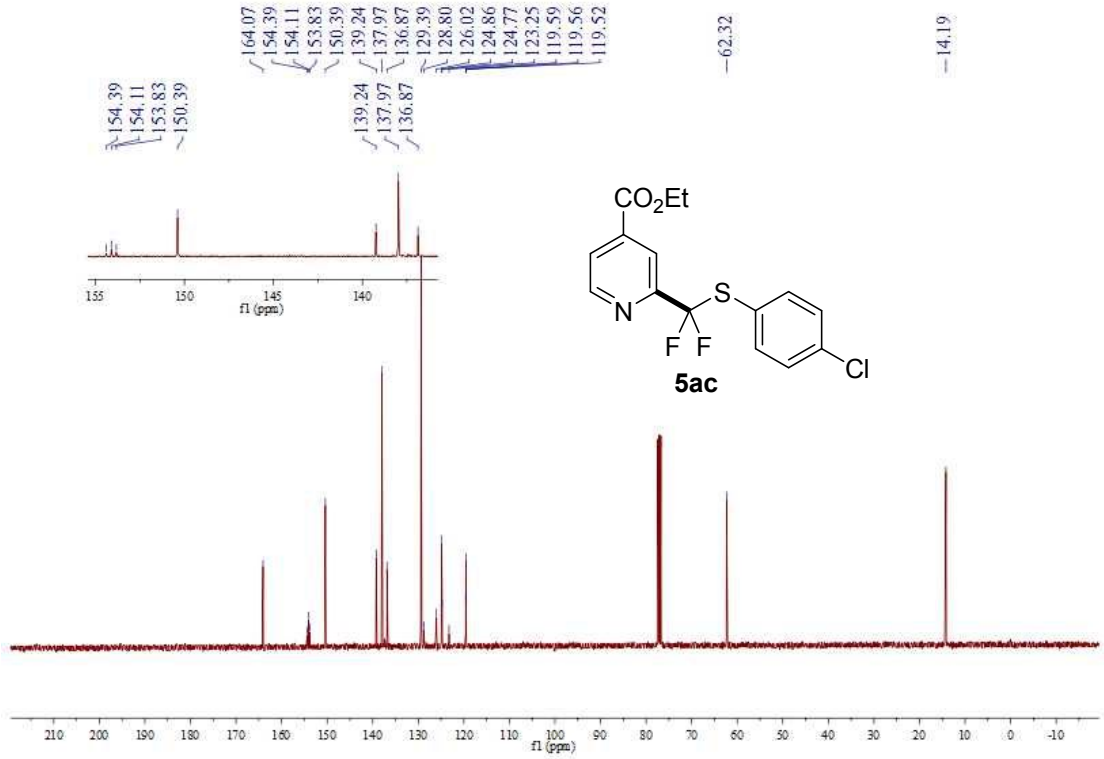
^{19}F NMR (377 MHz, $CDCl_3$)



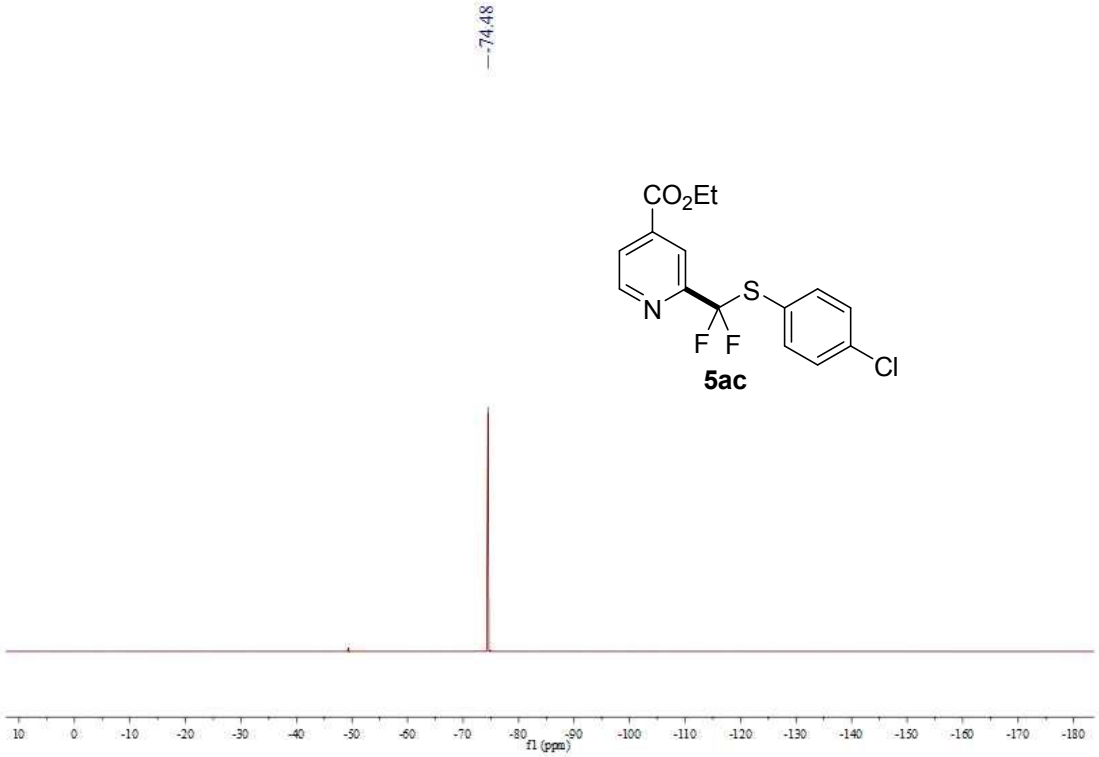
^{1}H NMR (400 MHz, $CDCl_3$)



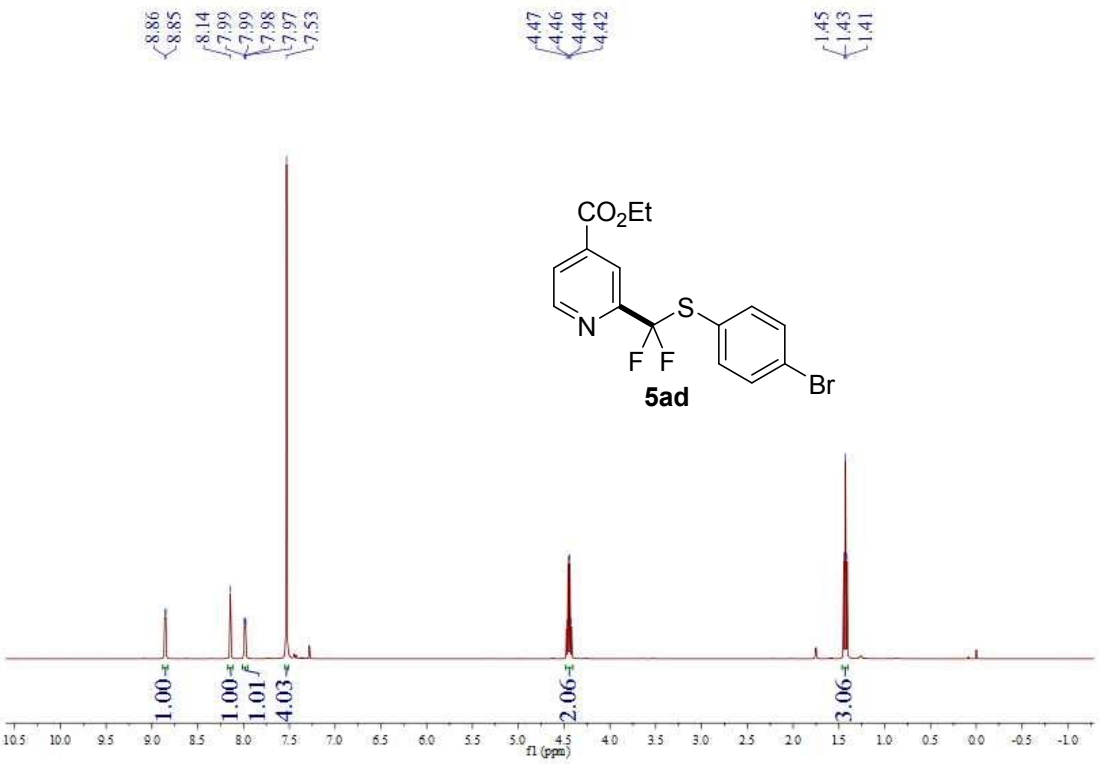
^{13}C NMR (101 MHz, $CDCl_3$)



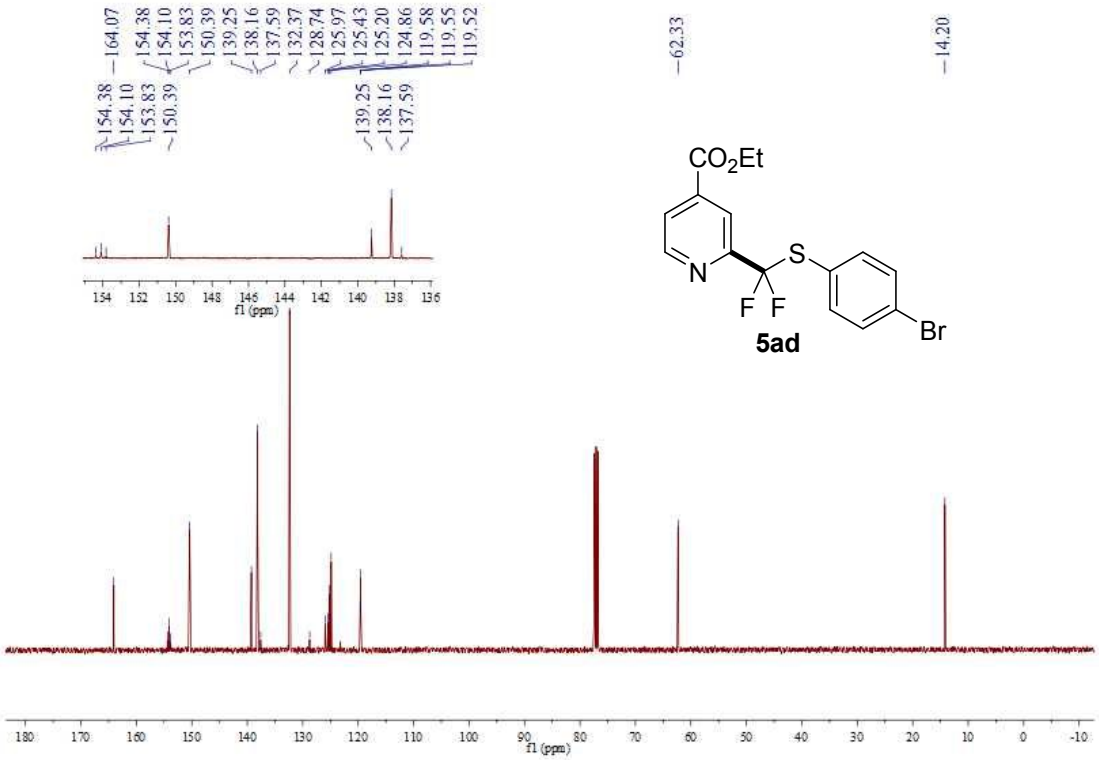
^{19}F NMR (377 MHz, $CDCl_3$)



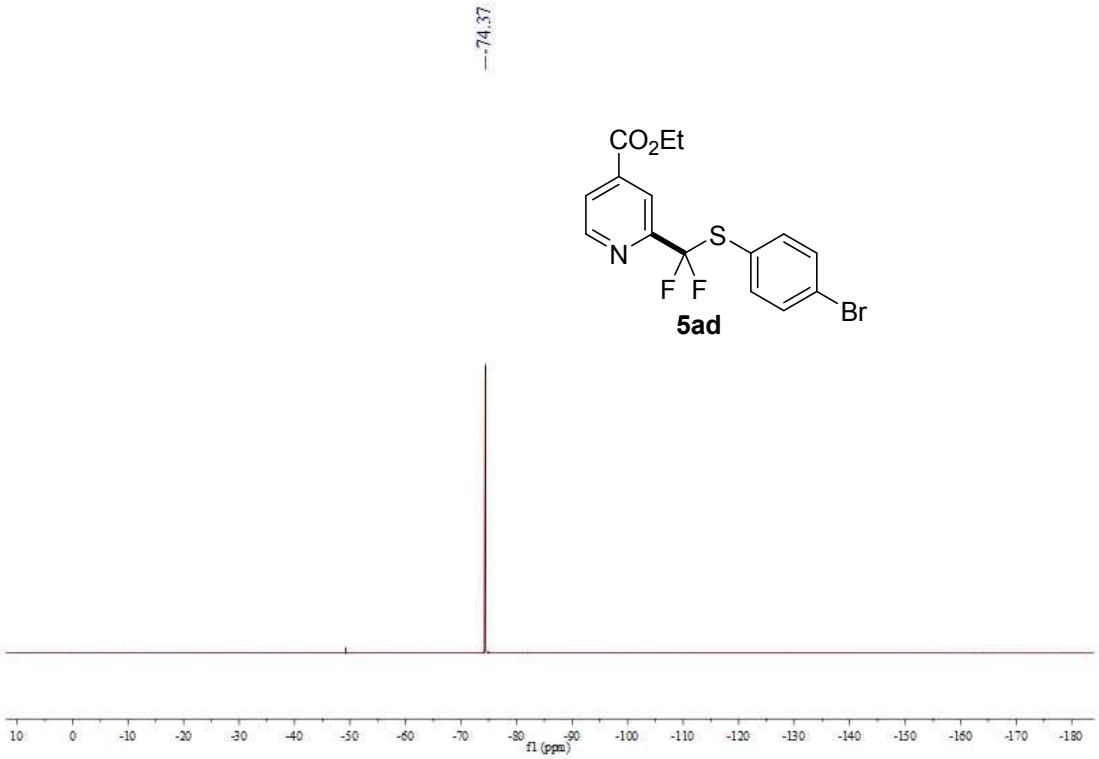
^{1}H NMR (400 MHz, $CDCl_3$)



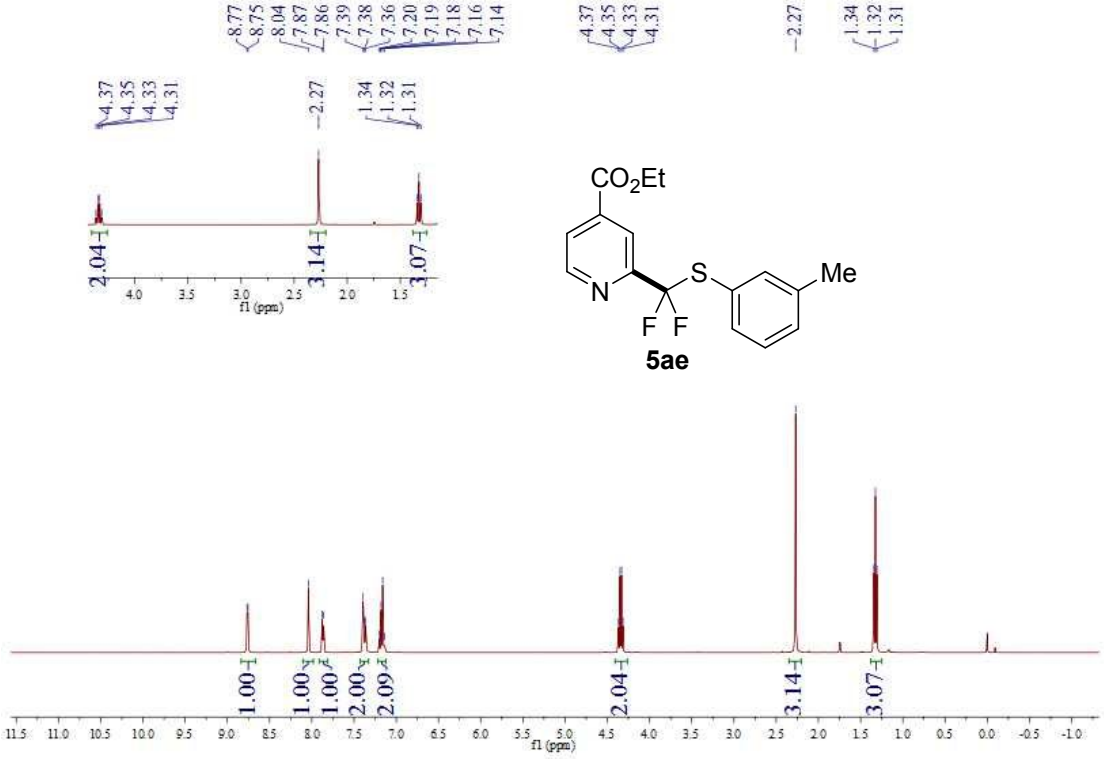
^{13}C NMR (101 MHz, $CDCl_3$)



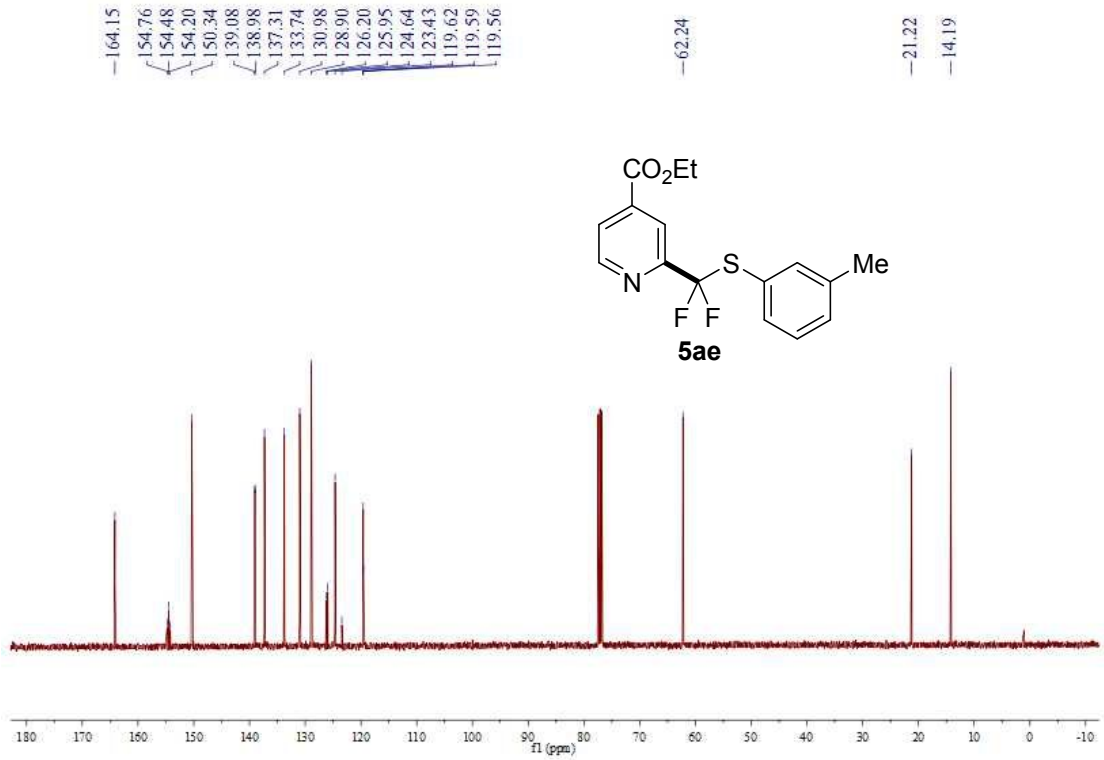
^{19}F NMR (377 MHz, $CDCl_3$)



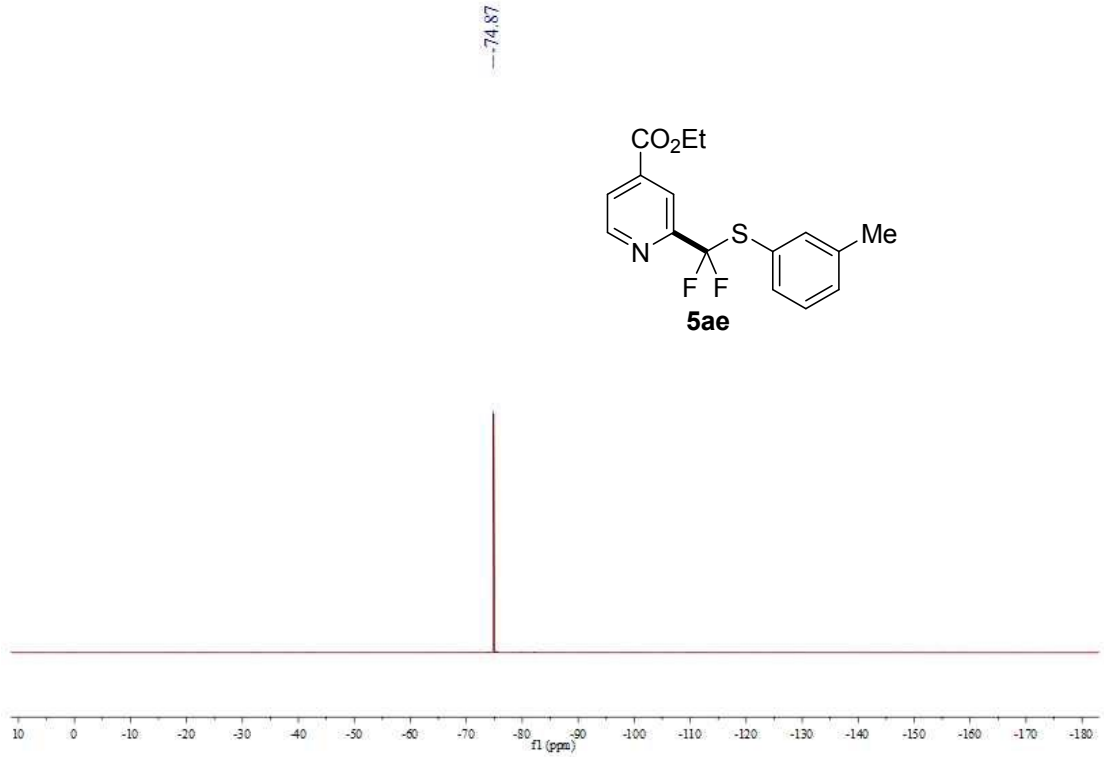
[1]H NMR (400 MHz, $CDCl_3$)



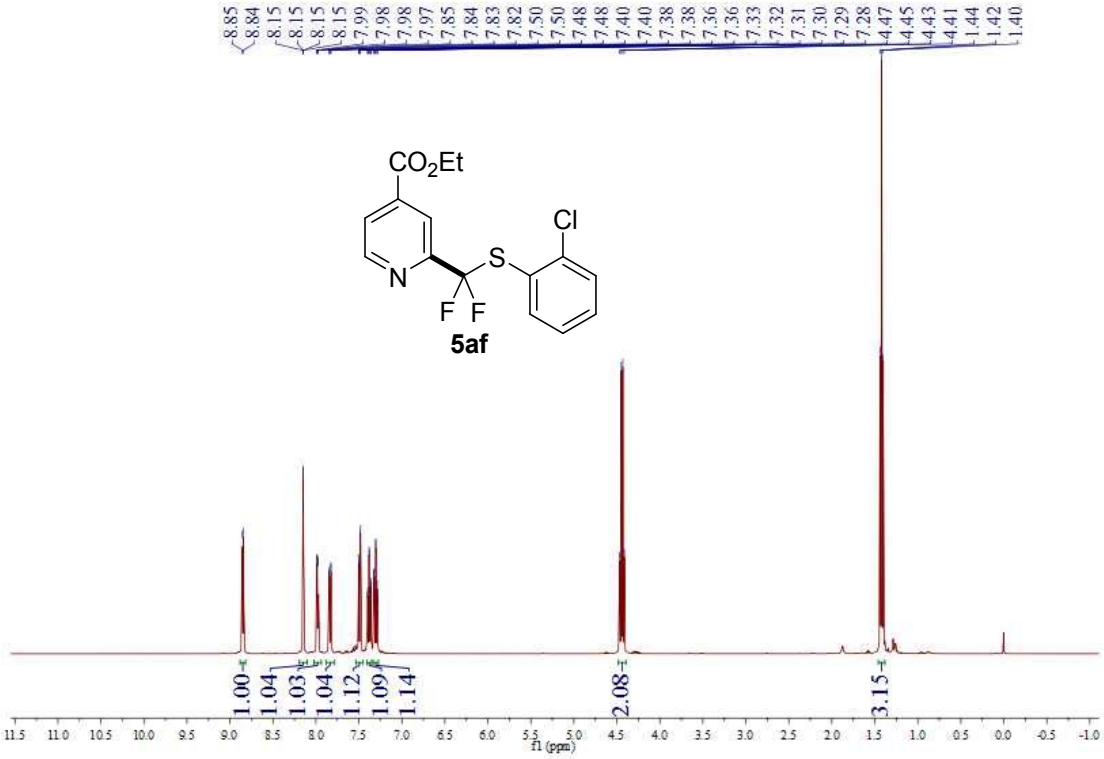
[13]C NMR (101 MHz, $CDCl_3$)



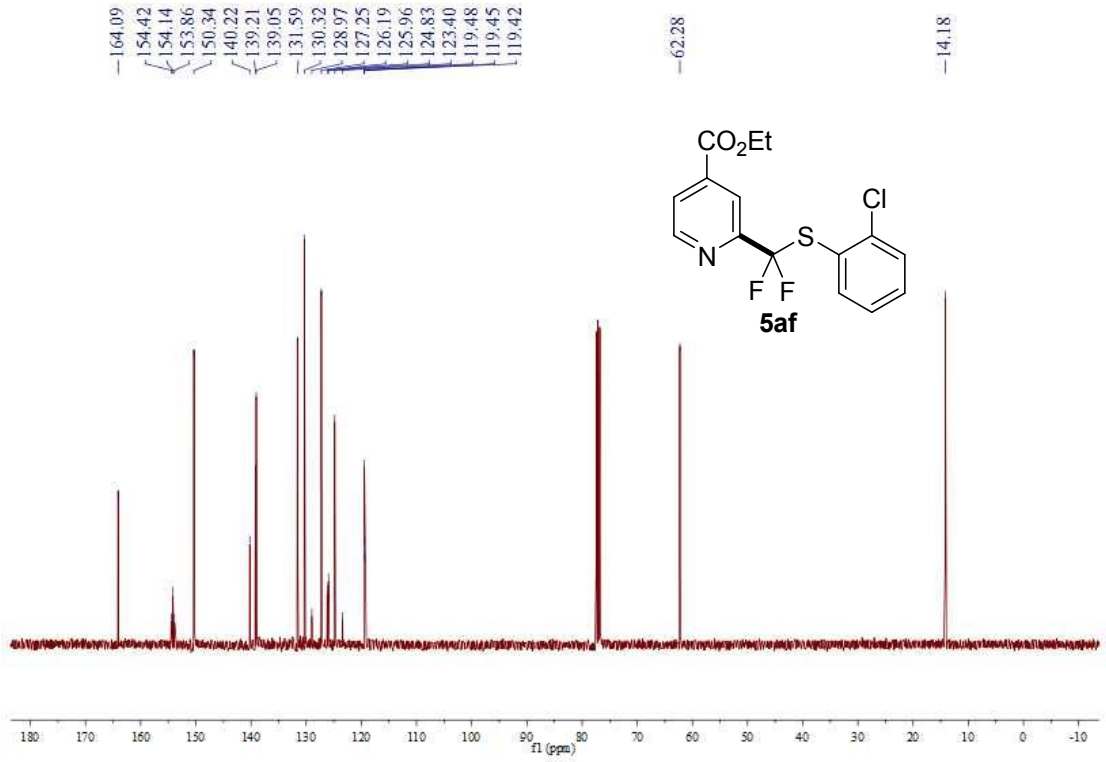
^{19}F NMR (377 MHz, $CDCl_3$)



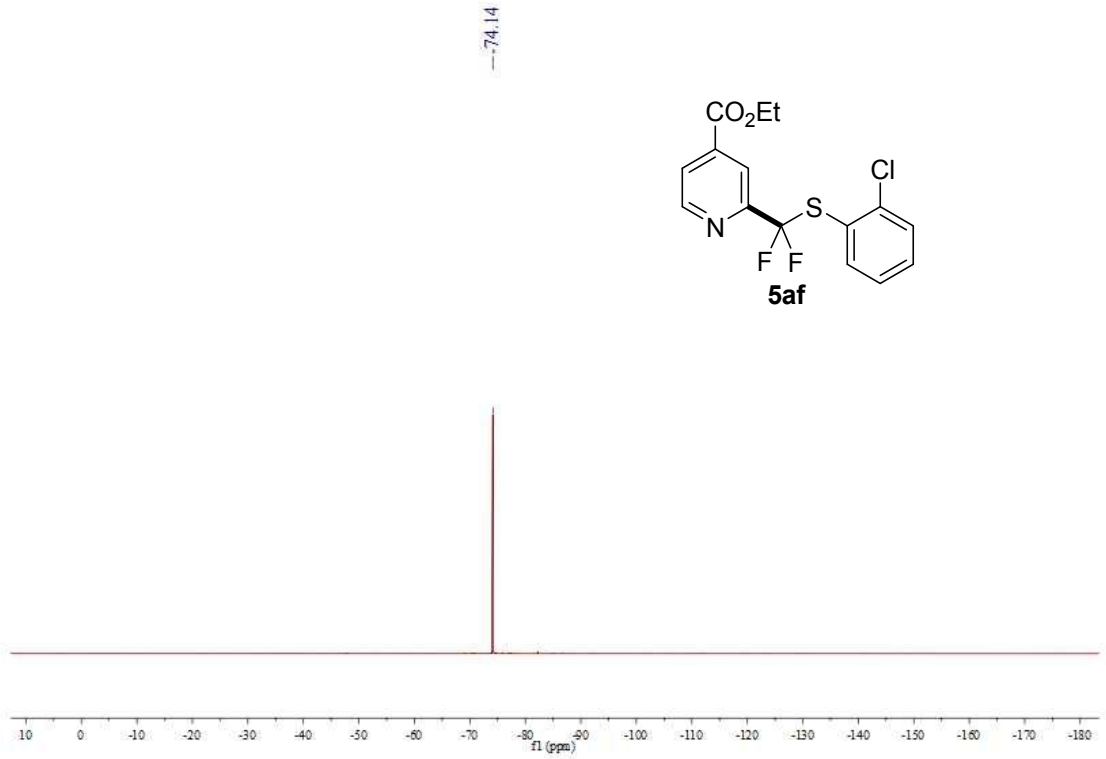
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (101 MHz, $CDCl_3$)



^{19}F NMR (377 MHz, $CDCl_3$)



11.Copies of HRMS Analysis Reports for the Products

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

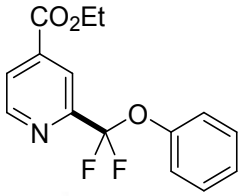
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191543

Sample Serial Number: ZXL-12

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3a

Elemental composition search on mass 294.09

m/z= 289.09-299.09

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
294.0934	294.0934	0.00	12.0	$C_{16}H_{14}N_4S$
	294.0934	-0.19	5.0	$C_{10}H_{13}O_3N_4F_3$
	294.0935	-0.31	-5.0	$C_4H_{21}O_4N_4ClF_2S$
	294.0932	0.67	3.0	$C_{12}H_{19}O_5FS$
	294.0936	-0.87	8.5	$C_{15}H_{14}O_3NF_2$
	294.0937	-0.99	-1.5	$C_9H_{22}O_4NClFS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

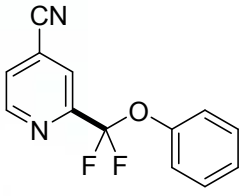
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190789

Sample Serial Number: ZXL-7

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3b

Elemental composition search on mass 247.07

m/z= 242.07-252.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
247.0673	247.0677	-1.76	9.5	$C_{13}H_9ON_2F_2$
	247.0666	2.86	13.5	$C_{16}H_8N_2F$
	247.0664	3.67	10.0	$C_{11}H_7N_5F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

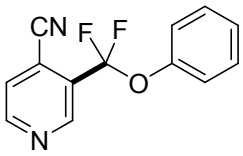
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190788

Sample Serial Number: ZXL-8

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3b'

Elemental composition search on mass 247.07

m/z= 242.07-252.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
247.0672	247.0677	-2.29	9.5	$C_{13}H_9ON_2F_2$
	247.0666	2.34	13.5	$C_{16}H_8N_2F$
	247.0664	3.14	10.0	$C_{11}H_7N_5F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

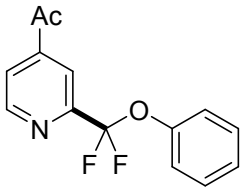
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190787

Sample Serial Number: ZXL-9

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3c

Elemental composition search on mass 264.08

m/z= 259.08-269.08

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
264.0825	264.0831	-2.28	8.5	$C_{14}H_{12}O_2NF_2$
	264.0817	2.81	9.0	$C_{12}H_{13}ON_4F_2$
	264.0813	4.45	4.0	$C_6H_{12}O_6N_6$

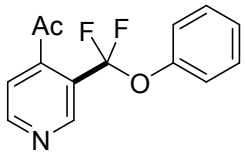
National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190786

Sample Serial Number: ZXL-10

Operator: Songw Date: 2019/05/29



3c'

Operation Mode: ESI Positive Ion Mode

Elemental composition search on mass 264.08

m/z= 259.08-269.08

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
264.0825	264.0831	-2.16	8.5	$C_{14}H_{12}O_2NF_2$
	264.0817	2.92	9.0	$C_{12}H_{10}ON_4F_2$
	264.0813	4.57	4.0	$C_6H_{12}O_6N_6$

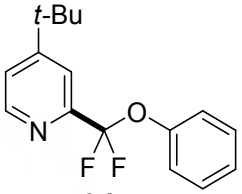
National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190785

Sample Serial Number: ZXL-11

Operator: Songw Date: 2019/05/29



3d

Operation Mode: ESI Positive Ion Mode

Elemental composition search on mass 278.13

m/z= 273.13-283.13

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
278.1345	278.1351	-1.97	7.5	$C_{16}H_{18}ONF_2$
	278.1340	2.14	11.5	$C_{19}H_{17}NF$
	278.1338	2.86	8.0	$C_{14}H_{16}N_4F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

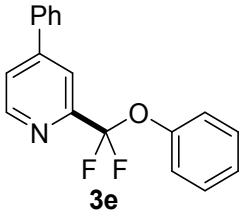
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191542

Sample Serial Number: ZXL-13

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3e

Elemental composition search on mass 298.10

m/z= 293.10-303.10

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
298.1035	298.1036	-0.36	8.0	$C_{13}H_{13}ON_4F_3$
	298.1036	-0.48	-2.0	$C_7H_{21}O_2N_4ClF_2S$
	298.1033	0.49	6.0	$C_{15}H_{19}O_3FS$
	298.1038	-1.03	11.5	$C_{18}H_{14}ONF_2$
	298.1038	-1.15	1.5	$C_{12}H_{22}O_2NClFS$
	298.1031	1.16	2.5	$C_{10}H_{18}O_3N_3F_2S$
	298.1038	-1.20	2.0	$C_9H_{19}O_5N_4Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution ESI- MS REPORT

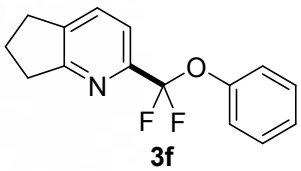
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E201006

Sample Serial Number: ZXC-32

Operator: Songw Date: 2020/06/19

Operation Mode: ESI Positive Ion Mode



3f

Elemental composition search on mass 262.10

m/z= 257.10-267.10

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
262.1036	262.1038	-0.83	8.5	$C_{15}H_{14}ONF_2$
	262.1027	3.53	12.5	$C_{18}H_{13}NF$
	262.1025	4.29	9.0	$C_{13}H_{12}N_4F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

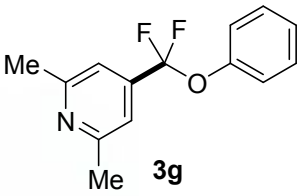
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191541

Sample Serial Number: ZXL-14

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3g

Elemental composition search on mass 250.10

m/z= 245.10-255.10

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
250.1036	250.1036	-0.05	-6.0	$C_3H_{21}O_2N_4ClF_2S$
	250.1036	0.09	4.0	$C_9H_{13}ON_4F_3$
	250.1038	-0.71	7.5	$C_{14}H_{14}ONF_2$
	250.1038	-0.85	-2.5	$C_8H_{22}O_2NClFS$
	250.1038	-0.92	-2.0	$C_5H_{19}O_5N_4Cl$
	250.1033	1.10	2.0	$C_{11}H_{19}O_3FS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

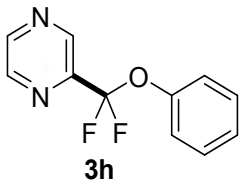
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191540

Sample Serial Number: ZXL-15

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3h

Elemental composition search on mass 223.07

m/z= 218.07-228.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
223.0676	223.0676	0.04	-6.0	$H_{16}O_2N_5ClF_2S$
	223.0675	0.20	4.0	$C_6H_8ON_5F_3$
	223.0677	-0.70	7.5	$C_{11}H_9ON_2F_2$
	223.0678	-0.86	-2.5	$C_5H_{17}O_2N_2ClFS$
	223.0678	-0.93	-2.0	$C_2H_{14}O_5N_5Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

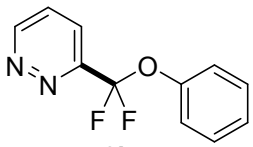
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191539

Sample Serial Number: ZXL-16

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3i

Elemental composition search on mass 223.07

m/z= 218.07-228.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
223.0676	223.0676	-0.05	-6.0	$H_{16}O_2N_5ClF_2S$
	223.0675	0.11	4.0	$C_6H_8ON_5F_3$
	223.0677	-0.79	7.5	$C_{11}H_9ON_2F_2$
	223.0678	-0.95	-2.5	$C_5H_{17}O_2N_2ClFS$
	223.0678	-1.02	-2.0	$C_2H_{14}O_5N_5Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

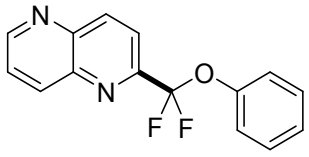
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191536

Sample Serial Number: ZXL-19

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3j

Elemental composition search on mass 273.08

m/z= 268.08-278.08

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
273.0832	273.0832	0.01	7.0	$C_{10}H_{10}ON_5F_3$
	273.0832	-0.11	-3.0	$C_4H_{18}O_2N_5ClF_2S$
	273.0834	-0.72	10.5	$C_{15}H_{11}ON_2F_2$
	273.0834	-0.85	0.5	$C_9H_{19}O_2N_2ClFS$
	273.0834	-0.91	1.0	$C_6H_{16}O_5N_5Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

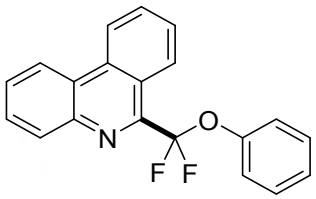
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191538

Sample Serial Number: ZXL-17

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3k

Elemental composition search on mass 322.10

m/z= 317.10-327.10

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
322.1034	322.1033	0.30	8.0	$C_{17}H_{19}O_3FS$
	322.1036	-0.49	10.0	$C_{15}H_{13}ON_4F_3$
	322.1036	-0.60	0.0	$C_9H_{21}O_2N_4ClF_2S$
	322.1031	0.92	4.5	$C_{12}H_{18}O_3N_3F_2S$
	322.1038	-1.11	13.5	$C_{20}H_{14}ONF_2$
	322.1038	-1.22	3.5	$C_{16}H_{22}O_2NClFS$
	322.1038	-1.27	4.0	$C_{11}H_{19}O_5N_4Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

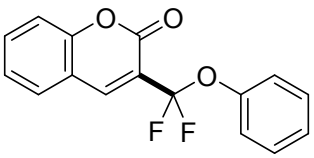
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191537

Sample Serial Number: ZXL-18

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



3l

Elemental composition search on mass 289.07

m/z= 284.07-294.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
289.0669	289.0669	-0.01	-3.0	$C_5H_{13}O_4N_3ClF_2S$
	289.0669	0.11	7.0	$C_{11}H_{10}O_3N_3F_3$
	289.0668	0.31	14.0	$C_{17}H_{11}N_3S$
	289.0671	-0.58	10.5	$C_{16}H_{11}O_3F_2$
	289.0671	-0.70	0.5	$C_{10}H_{19}O_4ClFS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

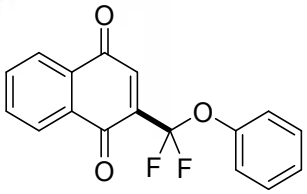
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190792

Sample Serial Number: ZXL-1

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3m

Elemental composition search on mass 323.05

m/z= 318.05-328.05

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
323.0483	323.0477	1.86	12.0	$C_{15}H_8O_2N_3F_2Na$
	323.0490	-2.30	11.5	$C_{17}H_{10}O_3F_2Na$
	323.0474	2.71	10.5	$C_{14}H_9O_5N_2F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

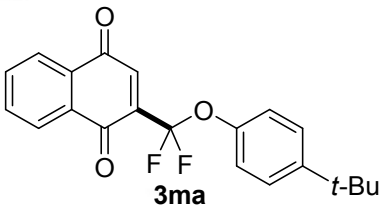
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190790

Sample Serial Number: ZXL-5

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3ma

Elemental composition search on mass 379.11

m/z= 374.11-384.11

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
379.1109	379.1103	1.72	12.0	$C_{19}H_{14}O_2N_3F_2Na$
	379.1116	-1.83	11.5	$C_{21}H_{18}O_3F_2Na$
	379.1100	2.44	10.5	$C_{18}H_{17}O_5N_2F_2$
	379.1127	-4.63	15.0	$C_{21}H_{15}O_2N_3F_2$
	379.1091	4.73	16.0	$C_{22}H_{15}ON_3FNa$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

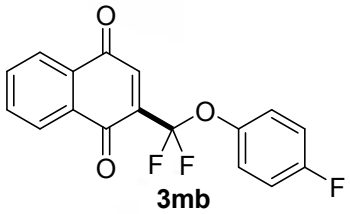
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190792

Sample Serial Number: ZXL-2

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3mb

Elemental composition search on mass 341.04

m/z= 336.04-346.04

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
341.0391	341.0396	-1.58	11.5	$C_{17}H_9O_3F_3Na$
	341.0383	2.35	12.0	$C_{15}H_7O_2N_3F_3Na$
	341.0380	3.04	10.5	$C_{14}H_{10}O_7N_2Na$
	341.0380	3.16	10.5	$C_{14}H_8O_5N_2F_3$
	341.0404	-4.01	13.5	$C_{16}H_9O_7N_2$
	341.0407	-4.70	15.0	$C_{17}H_6O_2N_3F_3$
	341.0407	-4.81	15.0	$C_{17}H_8O_4N_3Na$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution EI-MS REPORT

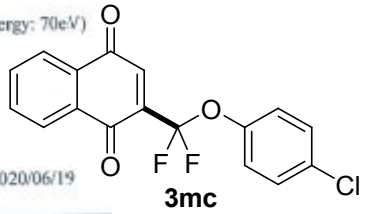
Instrument: Waters Premier GC-TOF MS

Operation Mode: EI Positive Ion Mode (Electron Energy: 70eV)

Card Serial Number: GCT-P-T20-06-1274

Sample Serial Number: 2013067-ZXL-33

Operator: Li Date: 2020/06/19



3mc

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
334.0204	334.0203	0.36	12.0	$C_{17}H_9O_3ClF_2$
	334.0207	-0.83	16.0	$C_{18}H_7O_2N_2FS$
	334.0208	-1.11	-1.0	$C_6H_{14}O_6N_2ClF_3S$
	334.0196	2.31	3.0	$C_9H_{13}O_5N_2ClF_2S$
	334.0196	2.42	13.0	$C_{15}H_5O_4N_2F_3$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution EI-MS REPORT

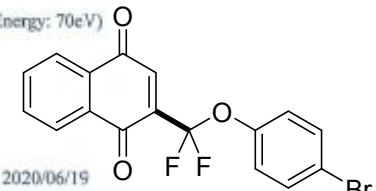
Instrument: Waters Premier GC-TOF MS

Operation Mode: EI Positive Ion Mode (Electron Energy: 70eV)

Card Serial Number: GCT-P-T20-06-1275

Sample Serial Number: 2013067-ZXL-34

Operator: Li Date: 2020/06/19



3md

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
377.9694	377.9694	0.02	23.0	$C_{22}ONF_2S$
	377.9691	0.76	3.0	$C_9H_{13}O_5N_2BrF_2S$
	377.9691	0.77	11.5	$C_{17}H_{11}ONBrClF$
	377.9698	-0.96	12.0	$C_{17}H_9O_3BrF_2$
	377.9698	-1.06	2.0	$C_{11}H_{17}O_4BrClFS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS ESI REPORT

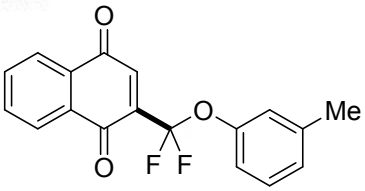
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E190791

Sample Serial Number: ZXL-6

Operator: Songw Date: 2019/05/29

Operation Mode: ESI Positive Ion Mode



3me

Elemental composition search on mass 337.06

m/z= 332.06-342.06

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
337.0641	337.0647	-1.73	11.5	$C_{18}H_{12}O_3F_2Na$
	337.0633	2.26	12.0	$C_{16}H_{10}O_2N_3F_2Na$
	337.0631	3.07	10.5	$C_{15}H_{11}O_5N_2F_2$
	337.0657	-4.88	15.0	$C_{18}H_9O_2N_3F_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

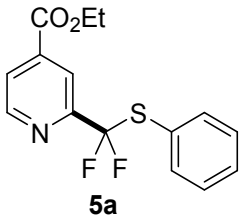
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191535

Sample Serial Number: ZXL-20

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5a

Elemental composition search on mass 310.07

m/z= 305.07-315.07

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
310.0706	310.0706	0.12	5.0	$C_{10}H_{13}O_2N_4F_3S$
	310.0708	-0.52	8.5	$C_{15}H_{14}O_2NF_2S$
	310.0708	-0.58	9.0	$C_{12}H_{11}O_5N_4F$
	310.0710	-1.22	12.5	$C_{17}H_{12}O_5N$
	310.0711	-1.45	0.5	$C_7H_{16}ON_5ClF_3S$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

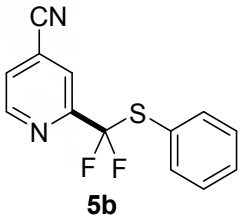
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191529

Sample Serial Number: ZXL-26

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5b

Elemental composition search on mass 263.04

m/z= 258.04-268.04

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
263.0448	263.0449	-0.35	9.5	$C_{13}H_9N_2F_2S$
	263.0449	-0.41	10.0	$C_{10}H_6O_3N_5F$
	263.0450	-0.55	0.0	$C_4H_{14}O_4N_5ClS$
	263.0451	-1.17	13.5	$C_{15}H_7O_3N_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

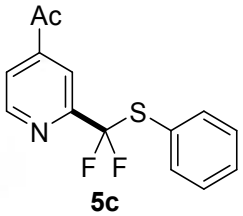
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191528

Sample Serial Number: ZXL-27

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5c

Elemental composition search on mass 280.06

m/z= 275.06-285.06

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
280.0600	280.0602	-0.74	8.5	$C_{14}H_{12}ONF_2S$
	280.0602	-0.80	9.0	$C_{11}H_9O_4N_4F$
	280.0603	-0.93	-1.0	$C_5H_{17}O_5N_4ClS$
	280.0604	-1.52	12.5	$C_{16}H_{10}O_4N$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution ESI- MS REPORT

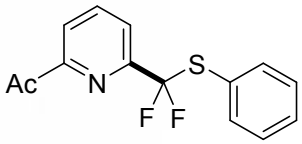
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E201007

Sample Serial Number: ZXC-35

Operator: Songw Date: 2020/06/19

Operation Mode: ESI Positive Ion Mode



5n

Elemental composition search on mass 280.06

m/z= 275.06-285.06

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
280.0600	280.0602	-0.88	8.5	$C_{14}H_{12}ONF_2S$
	280.0604	-1.66	12.5	$C_{16}H_{10}O_4N$
	280.0591	3.20	12.5	$C_{17}H_{11}NFS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

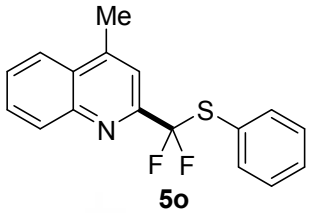
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191527

Sample Serial Number: ZXL-28

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5o

Elemental composition search on mass 302.08

m/z= 297.08-307.08

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
302.0807	302.0805	0.60	5.5	$C_{11}H_{16}O_5N_3S$
	302.0810	-0.84	10.5	$C_{17}H_{14}NF_2S$
	302.0810	-0.89	11.0	$C_{14}H_{11}O_3N_4F$
	302.0810	-1.01	1.0	$C_8H_{19}O_4N_4ClS$
	302.0803	1.28	10.5	$C_{14}H_{13}ON_5Cl$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

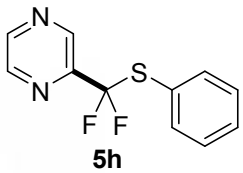
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191526

Sample Serial Number: ZXL-29

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5h

Elemental composition search on mass 239.04

m/z= 234.04-244.04

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
239.0447	239.0449	-0.89	7.5	$C_{11}H_9N_2F_2S$
	239.0445	0.93	2.5	$C_5H_{11}O_5N_4S$
	239.0449	-0.96	8.0	$C_8H_6O_3N_5F$
	239.0450	-1.10	-2.0	$C_2H_{14}O_4N_5ClS$
	239.0451	-1.79	11.5	$C_{13}H_7O_3N_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

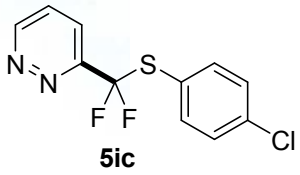
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191524

Sample Serial Number: ZXL-31

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5ic

Elemental composition search on mass 273.01

m/z= 268.01-278.01

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
273.0057	273.0057	0.15	16.0	$C_{16}H_9O_4N$
	273.0055	0.75	2.5	$C_5H_{10}O_5N_4ClS$
	273.0059	-0.84	7.5	$C_{11}H_8N_2ClF_2S$
	273.0055	0.88	12.5	$C_{11}H_2O_4N_4F$
	273.0059	-0.90	8.0	$C_8H_5O_3N_5ClF$
	273.0054	0.94	12.0	$C_{14}H_5ONF_2S$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

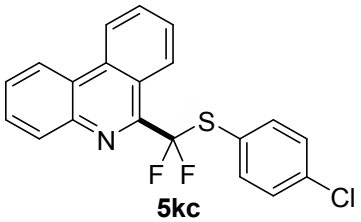
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191525

Sample Serial Number: ZXL-30

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5kc

Elemental composition search on mass 372.04

m/z= 367.04-377.04

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
372.0416	372.0415	0.15	8.5	$C_{14}H_{15}O_5N_3ClS$
	372.0415	0.24	18.5	$C_{20}H_7O_4N_3F$
	372.0415	0.29	18.0	$C_{23}H_{10}OF_2S$
	372.0417	-0.30	22.0	$C_{25}H_8O_4$
	372.0420	-1.02	13.5	$C_{20}H_{13}NClF_2S$
	372.0420	-1.07	14.0	$C_{17}H_{10}O_3N_4ClF$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution ESI- MS REPORT

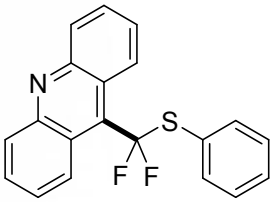
Instrument: Thermo Scientific Q Exactive HF Orbitrap-FTMS

Card Serial Number: E201008

Sample Serial Number: ZXC-36

Operator: Songw Date: 2020/06/19

Operation Mode: ESI Positive Ion Mode



5p

Elemental composition search on mass 338.08

m/z= 333.08-343.08

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
338.0808	338.0810	-0.42	13.5	$C_{20}H_{14}NF_2S$
	338.0812	-1.06	17.5	$C_{22}H_{12}O_3N$
	338.0823	-4.44	13.5	$C_{19}H_{13}O_4NF$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

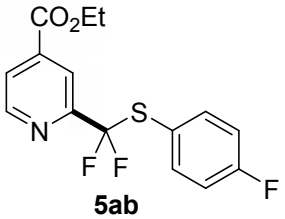
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191534

Sample Serial Number: ZXL-21

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5ab

Elemental composition search on mass 328.06

m/z= 323.06-333.06

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
328.0611	328.0609	0.67	12.0	$C_{17}H_{13}O_3N_2Cl$
	328.0614	-0.67	8.5	$C_{15}H_{13}O_2NF_3S$
	328.0614	-0.72	9.0	$C_{12}H_{10}O_5N_4F_2$
	328.0607	1.28	8.5	$C_{12}H_{12}O_3N_5ClF$
	328.0607	1.33	8.0	$C_{15}H_{15}N_2ClF_2S$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

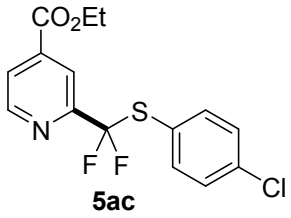
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191533

Sample Serial Number: ZXL-22

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5ac

Elemental composition search on mass 344.03

m/z= 339.03-349.03

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
344.0317	344.0318	-0.32	8.5	$C_{15}H_{13}O_2NClF_2S$
	344.0318	-0.37	9.0	$C_{12}H_{10}O_5N_4ClF$
	344.0320	-0.95	12.5	$C_{17}H_{11}O_5NCl$
	344.0313	1.10	13.0	$C_{18}H_{10}O_3F_2S$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

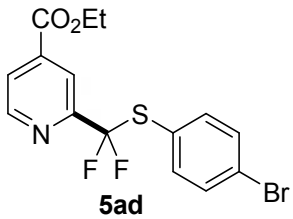
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191532

Sample Serial Number: ZXL-23

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5ad

Elemental composition search on mass 387.98

m/z= 382.98-392.98

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
387.9809	387.9807	0.39	19.5	$C_{21}H_4O_4NClF$
	387.9807	0.60	8.5	$C_{12}H_{12}O_3N_5BrCl$
	387.9811	-0.64	23.5	$C_{22}H_2O_3N_3S$
	387.9806	0.65	8.0	$C_{15}H_{15}N_2BrClFS$
	387.9805	0.90	16.0	$C_{16}H_3O_4N_4ClF_2$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

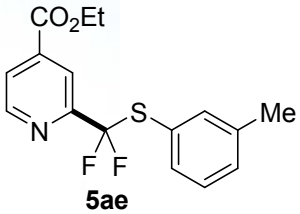
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191531

Sample Serial Number: ZXL-24

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5ae

Elemental composition search on mass 324.09

m/z= 319.09-329.09

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
324.0863	324.0864	-0.35	8.5	$C_{16}H_{16}O_2NF_2S$
	324.0864	-0.40	9.0	$C_{13}H_{13}O_5N_4F$
	324.0866	-1.02	12.5	$C_{18}H_{14}O_5N$
	324.0858	1.62	8.5	$C_{13}H_{15}O_3N_5Cl$
	324.0858	1.68	8.0	$C_{16}H_{18}N_2ClFS$

National Center for Organic Mass Spectrometry in Shanghai
Shanghai Institute of Organic Chemistry
Chinese Academic of Sciences
High Resolution MS DATA REPORT

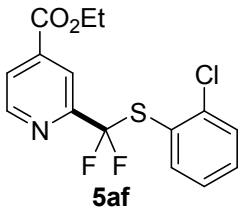
Instrument: Thermo Fisher Scientific LTQ FT Ultra

Card Serial Number : D191530

Sample Serial Number: ZXL-25

Operator : DONG Date: 2019/05/27

Operation Mode: DART POSITIVE



5af

Elemental composition search on mass 344.03

m/z= 339.03-349.03

m/z	Theo. Mass	Delta (ppm)	RDB equiv.	Composition
344.0315	344.0313	0.46	13.0	$C_{18}H_{10}O_3F_2S$
	344.0318	-0.96	8.5	$C_{15}H_{13}O_2NClF_2S$
	344.0318	-1.01	9.0	$C_{12}H_{10}O_5N_4ClF$
	344.0320	-1.59	12.5	$C_{17}H_{11}O_5NCl$