Supporting Information

Cu-Promoted Reaction of β-Keto Trifluoromethyl Amines Enabling Stereoselective Synthesis of Trifluoromethylated Aziridines

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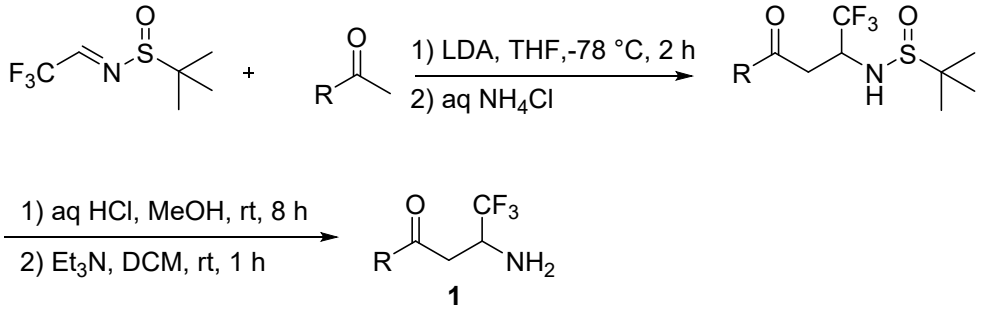
1. General information

All the commercial reagents including solvents were used directly without further purification. Amines **1a-y** were synthesized according to the literature[1]. All the experiments were monitored by thin layer chromatography (TLC) with UV light. The TLC employed 0.25 mm silica gel coated on glass plates. Purification of products was carried out by silica gel 60 F-254 TLC plates of 20 cm × 20 cm and column chromatography with silica gel 60 (300-400 mesh). Melting points were recorded without correction on RY-1G of Tianjin Xintianguang instrument company. NMR spectra were recorded on Bruker 400 MHz and 600 MHz spectrometers. High resolution mass spectra (HRMS) were measured on Agilent 6210 ESI/TOF MS instrument. The X-ray data were collected at 100 K on a Rigaku Oxford Diffraction Supernova Dual Source, Cu at Zero equipped with an AtlasS2 CCD using Cu Kα radiation.

Reference:

(1) Mei, H.; Xiong, Y.; Han, J.; Pan, Y. *Org. Biomol. Chem.* **2011**, *9*, 1402-1406.

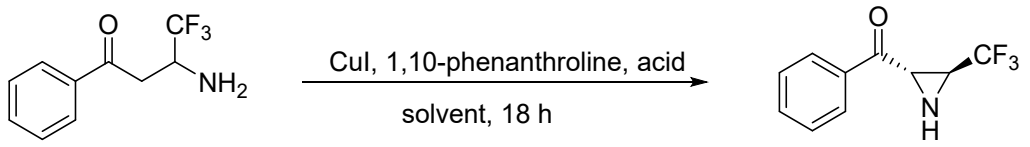
2. General procedure for the preparation of amines 1a-u[1]



Into a vial was taken ketone (8.5 mmol, 1.7 equiv) and anhydrous THF (20.0 mL). The reaction vial was cooled to −78 °C and LDA (2 M in THF, 4.68 mL) was added dropwise with stirring. After 40 min at −78 °C, sulfinylimine (5.0 mmol) dissolved in anhydrous THF (5.0 mL) was added dropwise.

Stirring was continued at −78 °C for 2 h, then the reaction was quenched with saturated NH_4Cl (10.0 mL), followed by H_2O (10.0 mL) and the mixture was brought to room temperature. The organic layer was taken and the aqueous layer was extracted with EtOAc (3 × 15 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was removed to give the crude Mannich adduct, which was purified by the silica gel column (petroleum ether:EtOAc = 4 : 1). Mannich adduct (1.0 mmol) and MeOH (10 mL) were placed in a round-bottom flask and aq HCl (36%, 2 mL) was added. The reaction was stirred at room temperature for 8 h. Volatiles were removed under reduced pressure. The residue was dissolved in CH_2Cl_2 (10 mL) and Et_3N (30.0 mmol) was added. The mixture was stirred at room temperature for 1 h, then H_2O (10 mL) was added. The organic layer was taken, washed with H_2O (3 × 10 mL), dried with anhydrous Na_2SO_4, filtered and the solvent was removed to give the crude product **1**, which was purified by by the silica gel column (petroleum ether:EtOAc = 4 : 1).

3. Table S1. Optimization of reaction conditions[a]



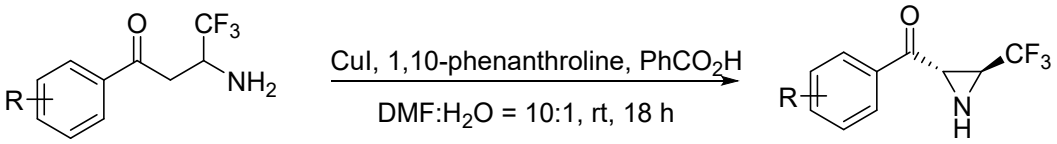
1a **2a**

entry	CuI (equiv)	phen (equiv)	acid (equiv)	solvent	T (°C)	yield (%)[b]
1	0.5	0.5	1	DMF: H_2O = 10: 1	rt	65
2	0	1	1	DMF: H_2O = 10: 1	rt	nr
3	1	1	1	DMF: H_2O = 10: 1	rt	79
4	2	2	1	DMF: H_2O = 10: 1	rt	72
5	1	1	0	DMF: H_2O = 10: 1	rt	53
6	1	1	0.5	DMF: H_2O = 10: 1	rt	72
7	1	1	2	DMF: H_2O = 10: 1	rt	79
8	1	1	1	DMF	rt	57
9	1	1	1	DCM	rt	trace
10	1	1	1	THF	rt	trace
11	1	1	1	DCM: H_2O = 10: 1	rt	trace
12	1	1	1	THF: H_2O = 10: 1	rt	36
13	1	1	1	DMF: H_2O = 10: 1	60	54
14	1	1	1	DMF: H_2O = 10: 1	0	37
15	1	1	1	DMF: H_2O = 10: 1	rt	58[c]
16	1	1	CH_3CO_2H	DMF: H_2O = 10: 1	rt	77[d]

17	1	1	H_2SO_4	DMF: H_2O = 10: 1	rt	13[e]

[a] Reaction conditions: β-amino ketone **1a** (0.1 mmol), CuI, 1,10-phenanthroline, acid and solvent (2.2 mL) were dissolved in a vial, and stirred for 18 h. [b] Isolated yield based on amine **1a**. [c] Under nitrogen atmosphere. [d] CH_3CO_2H (0.1 mmol) was used. [e] H_2SO_4 (0.1 mmol) was used.

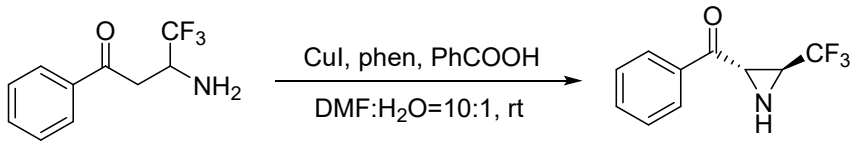
4. General procedure for synthesis of aziridine



1 **2**

β-Keto amine **1** (0.2 mmol), CuI (0.2 mmol), 1,10-phenanthroline (0.2 mmol), $PhCO_2H$ (0.2 mmol) and DMF/H_2O (4.4 mL, DMF : H_2O = 10:1) were taken into a vail. The mixture was stirred at room temperature. After 18 h, the reaction was quenched with H_2O (20 mL). Then organic layer was taken and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was removed in vacuum. The product **2** was purified by TLC plate of 20 cm × 20 cm using petroleum ether/ethyl acetate (8:1, v/v) as eluent.

5. Large scale synthesis



1a **2a**

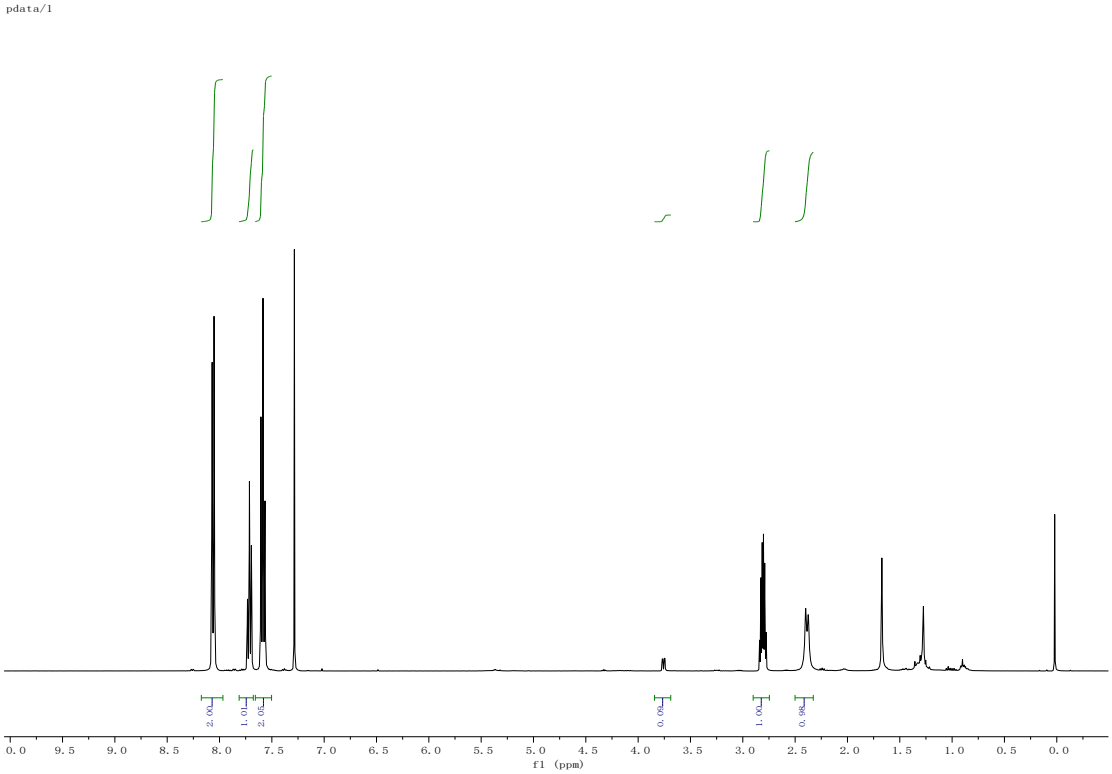
76% yield

Amine **1a** (5 mmol), CuI (5 mmol), phen (5 mmol), $PhCO_2H$ (5 mmol) and DMF/H_2O (22 mL, DMF:H_2O = 10:1) were taken into a flask. The mixture was stirred at room temperature. After 18 h, the reaction was quenched with H_2O (30 mL). Then organic layer was taken and the aqueous

layer was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was removed in vacuum. The product **2a** was purified by column chromatography using petroleum ether/ethyl acetate (8:1, v/v) as eluent (0.817 g, 76% yield).

6. Reaction conducted in DMF/D_2O

β-Keto amine **1a** (0.1 mmol), CuI (0.1 mmol), 1,10-phenanthroline (0.1 mmol), $PhCO_2H$ (0.1 mmol) and DMF/D_2O (2.2 mL, DMF:D_2O = 10:1) were taken into a vail. The mixture was stirred at room temperature. After 18 h, the reaction was quenched with H_2O (20 mL). Then organic layer was taken and the aqueous layer was extracted with EtOAc (3 × 10 mL). The combined organic layers were dried with anhydrous Na_2SO_4, filtered and the solvent was removed in vacuum. The product **2a** was purified by TLC plate of 20 cm × 20 cm using petroleum ether/ethyl acetate (8:1, v/v) as eluent.



^{1}H NMR of **D-2a** (400 MHz, $CDCl_3$)

7. X-ray crystallography of 2a

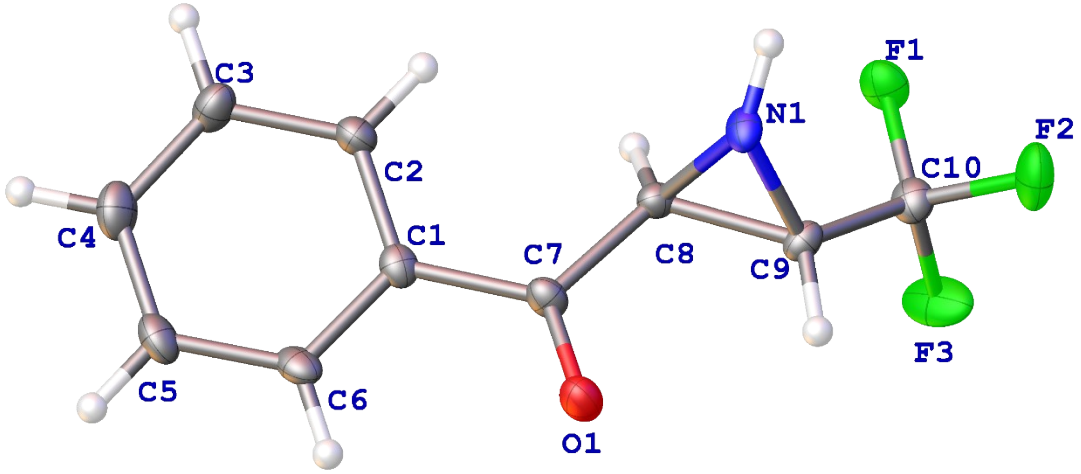
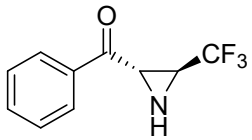


Figure S2. ORTEP diagram showing of **2a**

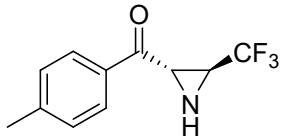
(CCDC number is 2245954, the ellipsoids are drawn at a 30% probability level)

Suitable crystals of compound **2a** were obtained by slowly evaporating a mixture of petroleum ether and ethyl acetate solution at ambient temperature.

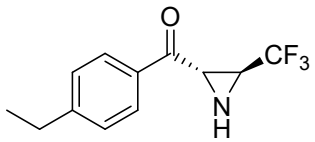
8. Characterization data of 2



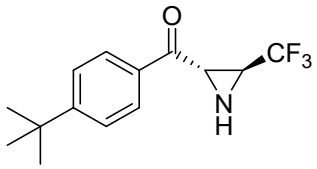
Compound **2a**: 34.0 mg, 79% yield, white solid, mp 80-82 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.06-8.04 (m, 2H), 7.72-7.68 (m, 1H), 7.59-7.55 (m, 2H), 3.75 (d, *J* = 8.00 Hz, 1H), 2.81-2.78 (m, 1H), 2.41-2.37 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.1, 135.1, 134.6, 129.1, 128.5, 127.1 (q, *J* = 271.5 Hz), 39.1 (q, *J* = 40.3 Hz), 34.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{10}H_9F_3NO^+$ 216.0631, found 216.0625.



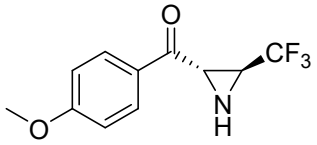
Compound **2b**: 36.9 mg, 81% yield, white solid, mp 74-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.97 (d, *J* = 8.24 Hz, 2H), 7.38 (d, *J* = 8.00 Hz, 2H), 3.74-3.72 (m, 1H), 2.80-2.75 (m, 1H), 2.49 (s, 3H), 2.39-2.35 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 145.9, 132.6, 129.8, 128.6, 124.4 (d, *J* = 271.7 Hz), 38.6 (d, *J* = 40.2 Hz), 34.5, 21.9. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO^+$ 230.0787, found 230.0785.



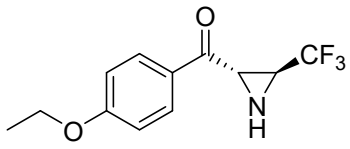
Compound **2c**: 42.5 mg, 87% yield, white solid, mp 47-49 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00 (d, *J* = 8.04 Hz, 2H), 7.40 (d, *J* = 7.92 Hz, 2H), 3.74 (d, *J* = 7.92 Hz, 1H), 2.80-2.74 (m, 3H), 2.40-2.36 (m, 1H), 1.32-1.28 (m, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 152.0, 132.8, 128.7, 128.6, 124.4 (d, *J* = 271.9 Hz), 38.9 (q, *J* = 40.3 Hz), 34.5, 29.1, 15.1. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{13}F_3NO^+$ 244.0944, found 244.0942.



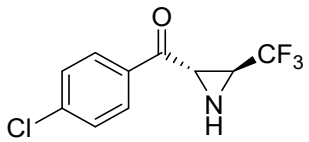
Compound **2d**: 41.7 mg, 77% yield, white solid, mp 68-71 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 8.40 Hz, 2H), 7.60 (d, *J* = 8.44 Hz, 2H), 3.76-3.73 (m, 1H), 2.80-2.74 (m, 1H), 2.41-2.36 (m, 1H), 1.39 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.5, 158.8, 132.5, 128.5, 127.1 (q, *J* = 271.8 Hz), 126.1, 38.9 (q, *J* = 40.2 Hz), 35.4, 34.5, 31.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{17}F_3NO^+$ 272.1257, found 272.1256.



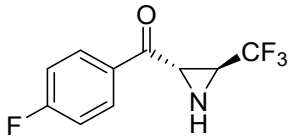
Compound **2e**: 44.7 mg, 91% yield, white solid, mp 64-66 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.05 (d, *J* = 8.40 Hz, 2H), 7.04 (d, *J* = 8.44 Hz, 2H), 3.92 (s, 3H), 3.70 (d, *J* = 7.88 Hz, 1H), 2.76 (s, 1H), 2.36 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.1, 164.8, 130.9, 128.1, 127.2 (t, *J* = 271.8 Hz), 114.3, 55.6, 38.8 (q, *J* = 40.3 Hz), 34.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_{10}F_3N_2O^+$ 246.0736, found 246.0737.



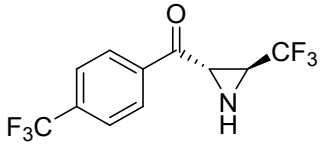
Compound **2f**: 46.9 mg, 90% yield, white solid, mp 103-106 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.04-8.00 (m, 2H), 7.02-6.99 (m, 2H), 4.17-4.12 (m, 2H), 3.70-3.67 (m, 1H), 2.78-2.74 (m, 1H), 2.37-2.33 (m, 1H), 1.49 (t, *J* = 7.00 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.0, 164.2, 130.9, 127.9, 124.5 (d, *J* = 271.6 Hz), 114.7, 64.0, 38.7 (q, *J* = 40.3 Hz), 34.2, 14.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{13}F_3NO_2^+$ 260.0893, found 260.0892.



Compound **2g**: 31.9 mg, 64% yield, white solid, mp 65-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01-7.97 (m, 2H), 7.56-7.53 (m, 2H), 3.70-3.68 (m, 1H), 2.84-2.78 (m, 1H), 2.41 (t, *J* = 8.52 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.0, 141.4, 133.4, 129.8, 129.5, 127.0 (q, *J* = 271.7 Hz), 39.2 (q, *J* = 40.5 Hz), 34.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{10}H_8ClF_3NO^+$ 250.0241, found 250.0240.

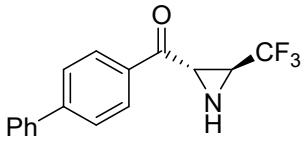


Compound **2h**: 33.8 mg, 72% yield, white solid, mp 73-76 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.11-8.07 (m, 2H), 7.27-7.23 (m, 2H), 3.71-3.69 (m, 1H), 2.83-2.78 (m, 1H), 2.41 (t, *J* = 8.56 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 192.5, 168.0 (d, *J* = 256.3 Hz), 131.6 (d, *J* = 3.1 Hz), 131.3 (d, *J* = 9.8 Hz), 127.0 (q, *J* = 271.4 Hz), 116.5 (d, *J* =22.1 Hz), 39.1 (q, *J* = 40.4 Hz), 34.5. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F), -101.8 (s, 1F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_8F_3N_2^+$ 234.0537, found 234.0530.

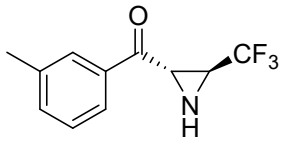


Compound **2i**: 37.4 mg, 66% yield, white solid, mp 48-52 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.17 (d, *J* = 8.12 Hz, 2H), 7.85 (d, *J* = 8.20 Hz, 2H), 3.75-3.73 (m, 1H), 2.90-2.82 (m, 1H), 2.45-2.41 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.6, 137.6, 136.0 (d, *J* = 33.0 Hz), 128.8, 127.4 (q, *J* = 271.2 Hz), 126.9 (q, *J* = 271.8 Hz), 126.2 (q, *J* = 3.6 Hz), 39.5 (q, *J* = 40.6 Hz), 34.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -63.4 (s, 3F), -71.6 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_8F_6NO^+$

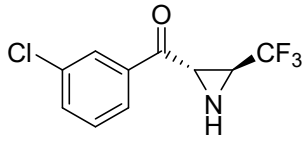
284.0505, found 284.0503.



Compound **2j**: 45.3 mg, 78% yield, white solid, mp 97-99 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.15-8.13 (m, 2H), 7.81-7.79 (m, 2H), 7.69-7.66 (m, 2H), 7.55-7.51 (m, 2H), 7.49-7.44 (m, 1H), 3.81-3.78 (m, 1H), 2.86-2.81 (m, 1H), 2.44 (t, *J* = 8.72 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.6, 147.4, 139.4, 133.7, 129.1, 128.7, 127.7, 127.3, 124.4, 121.7, 39.1 (q, *J* = 40.2 Hz), 34.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{16}H_{13}F_3NO^+$ 292.0944, found 292.0934.

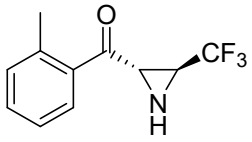


Compound **2k**: 36.5 mg, 80% yield, white solid, mp 65-68 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.86-7.84 (m, 2H), 7.52-7.43 (m, 2H), 3.74-3.72 (m, 1H), 2.82-2.75 (m, 1H), 2.47 (s, 3H), 2.40 (t, *J* = 8.48 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.2, 139.1, 135.5, 135.1, 129.0, 128.9, 125.8, 124.4 (d, *J* = 271.4 Hz), 39.1 (q, *J* = 40.2 Hz), 34.6, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO^+$ 230.0787, found 230.0785.

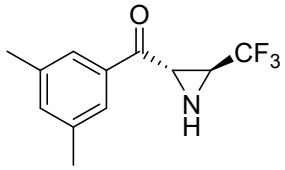


Compound **2l**: 30.9 mg, 62% yield, white solid, mp 81-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.01 (t, *J* = 1.8 Hz, 1H), 7.95-7.92 (m, 1H), 7.69-7.66 (m, 1H), 7.55 (t, *J* = 7.92 Hz, 1H), 3.71-3.68 (m, 1H), 2.86-2.79 (m, 1H), 2.41 (t, *J* = 8.6 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.2, 136.5, 135.6, 134.6, 130.5, 128.5, 126.9 (d, *J* = 271.7 Hz), 126.6, 39.4 (q, *J* = 40.5 Hz), 34.6. ^{19}F NMR

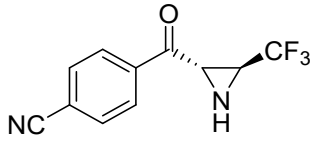
(376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{10}H_8ClF_3NO^+$ 250.0241, found250.0241.



Compound **2m**: 32.5 mg, 71% yield, white solid, mp 56-59 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.86 (d, *J* = 7.72 Hz, 1H), 7.54 (t, *J* = 7.52 Hz, 1H), 7.41-7.34 (m, 2H), 3.59 ((d, *J* = 8.08 Hz, 1H)), 2.81-2.77 (m, 1H), 2.57 (s, 3H), 2.41 (t, *J* = 8.16 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 196.6, 139.5, 134.9, 133.1, 132.4, 129.6, 126.2, 124.4 (d, *J* = 271.6 Hz), 39.2 (q, *J* = 40.2 Hz), 36.7, 21.3. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_{11}F_3NO^+$ 230.0787, found 230.0786.

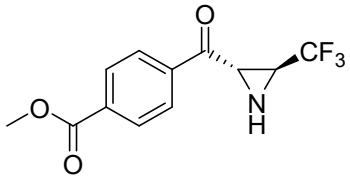


Compound **2n**: 38.3 mg, 79% yield, white solid, mp 45-47 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 7.65 (s, 2H), 7.33 (s, 1H), 3.73 (d, *J* = 8.00 Hz, 1H), 2. 77 (s, 1H), 2.43 (s, 6H), 2.38 (t, *J* = 8.64 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 194.4, 138.9, 136.3, 135.2, 126.2, 124.4 (d, *J* = 271.6 Hz), 39.0 (q, *J* = 40.3 Hz), 34.6, 21.2. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{13}F_3NO^+$ 244.0944, found 244.0942.

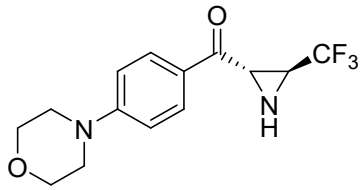


Compound **2o**: 22.6 mg, 47% yield, white solid, mp 110-113 °C. ^1H NMR (400 MHz, $CDCl_3$): δ = 8.16 (d, *J* = 7.96 Hz, 2H), 7.90 (d, *J* = 8.00 Hz, 2H), 3.73 (d, *J* = 7.96 Hz, 1H), 2.86 (s, 1H), 2.45 (t, *J* = 8.48 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.3, 137.9, 132.9, 128.9, 124.1 (d, *J* = 271.8

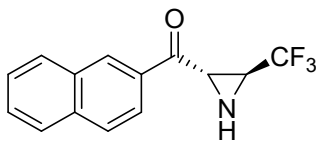
Hz), 117.9, 117.5, 39.7 (q, J = 40.4 Hz), 34.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{11}H_8F_3N_2O^+$ 241.0583, found 241.0575.



Compound **2p**: 36.4 mg, 67% yield, white solid, mp 88-90 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.23 (d, J = 8.36 Hz, 2H), 8.11 (d, J = 8.48 Hz, 2H), 3.99 (s, 3H), 3.76-3.74 (m, 1H), 2.88-2.81 (m, 1H), 2.43 (t, J = 8.72 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.9, 165.8, 138.1, 135.3, 130.2, 128.4, 124.2 (d, J = 271.7 Hz), 52.7, 39.4 (q, J = 40.5 Hz), 34.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{11}F_3NO_3^+$ 274.0686, found 274.0679.

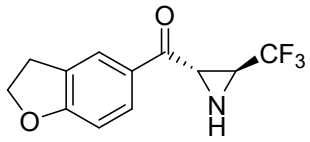


Compound **2q**: 55.8 mg, 93% yield, white solid, mp 138-141 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.00-7.96 (m, 2H), 6.95-6.91 (m, 2H), 3.90-3.87 (m, 4H), 3.69-3.66 (m, 1H), 3.41-3.38 (m, 4H), 2.78-2.71 (m, 1H), 2.36 (t, J = 8.72 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.2, 155.1, 130.8, 127.3 (t, J = 271.4 Hz), 125.4, 113.2, 66.4, 47.1, 38.6 (q, J = 40.3 Hz), 34.0. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{16}F_3N_2O_2^+$ 301.1158, found 301.1156.

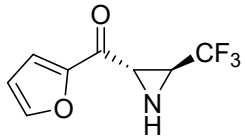


Compound **2r**: 38.9 mg, 73% yield, white solid, mp 80-83 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ =

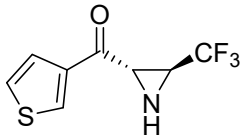
8.58 (s, 1H), 8.07-8.03 (m, 2H), 7.98-7.92 (m, 2H), 7.71-7.61 (m, 2H), 3.91-3.89 (m, 1H), 2.91-2.84 (m, 1H), 2.48 (t, J = 8.20 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 193.9, 136.2, 132.5, 132.4, 130.9, 129.9, 129.4, 129.1, 127.9, 127.3, 124.5 (d, J = 271.8 Hz), 123.4, 39.2 (q, J = 40.3 Hz), 34.6. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.3 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{14}H_{11}F_3NO^+$ 266.0787, found 266.0777.



Compound **2s**: 47.1 mg, 92% yield, white solid, mp 81-84 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.91 (s, 2H), 6.91 (d, J = 8.56 Hz, 1H), 4.74 (t, J = 8.68 Hz, 2H), 3.67 (d, J = 7.96 Hz, 1H), 3.33 (t, J = 8.72 Hz, 2H), 2.74 (s, 1H), 2.37 (t, J = 8.48 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 191.8, 165.8, 130.8, 128.5, 128.4, 127.2 (q, J = 271.6 Hz), 125.8, 109.7, 72.5, 38.7 (q, J = 40.2 Hz), 34.2, 28.8. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.4 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_{12}H_{11}F_3NO_2^+$ 258.0736, found 258.0735.



Compound **2t**: 27.7 mg, 67% yield, white solid, mp 87-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 7.77 (s, 1H), 7.45 (s, 1H), 6.69 (s, 1H), 3.68 (d, J = 7.92 Hz, 1H), 2.86 (s, 1H), 2.23 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 182.4, 151.5, 148.3, 124.2 (d, J = 271.7 Hz), 119.7, 113.1, 38.9 (q, J = 40.4 Hz), 34.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.6 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_8H_7F_3NO_2^+$ 206.0423, found 206.0422.



Compound **2u**: 30.6 mg, 69% yield, white solid, mp 85-89 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ = 8.31 (s, 1H), 7.65-7.64 (m, 1H), 7.45 (s, 1H), 3.60 (d, *J* = 7.92 Hz, 1H), 2.82 (s, 1H), 2.30 (s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ = 187.9, 140.2, 134.2, 127.5, 126.6, 124.3 (d, *J* = 271.7 Hz), 38.9 (q, *J* = 40.4 Hz), 35.4. ^{19}F NMR (376 MHz, $CDCl_3$): δ = -71.5 (s, 3F). HRMS (ESI) m/z: $[M+H]^+$ calcd for $C_8H_7F_3NOS^+$ 222.0195, found 222.0194.

9. Computational details

DFT calculations were carried out with the Gaussian 16 software package. Geometry optimization calculations were performed with the B3LYP functional including the Empirical Dispersion D3. The optimized geometries were confirmed to be minima (no imaginary frequencies) by frequency calculations.

trans-**2a**

Zero-point correction=	0.166416 (Hartree/Particle)
Thermal correction to Energy=	0.178886
Thermal correction to Enthalpy=	0.179830
Thermal correction to Gibbs Free Energy=	0.125642
Sum of electronic and zero-point Energies=	-815.421269
Sum of electronic and thermal Energies=	-815.408799
Sum of electronic and thermal Enthalpies=	-815.407855
Sum of electronic and thermal Free Energies=	-815.462043

6	-1.951700000	3.893729000	3.250105000
6	-1.579046000	5.124187000	2.715315000
6	-1.173337000	5.220739000	1.386034000
6	-1.144463000	4.075567000	0.575990000
6	-1.536163000	2.842105000	1.121164000
6	-1.929947000	2.750791000	2.448501000
1	-2.262190000	3.823640000	4.286687000
1	-1.607413000	6.015271000	3.331997000
1	-0.905977000	6.180846000	0.967314000
1	-1.522938000	1.968785000	0.481318000
1	-2.222627000	1.791915000	2.860725000
6	-0.737625000	4.074450000	-0.864353000
6	0.070899000	5.187485000	-1.494253000
6	1.249532000	5.802869000	-0.816130000
1	1.477858000	5.543659000	0.212473000
6	2.479678000	6.095658000	-1.627654000
9	3.209486000	7.079694000	-1.061794000
9	2.166831000	6.501398000	-2.882297000
9	3.270085000	5.012417000	-1.730212000
7	0.038413000	6.584121000	-1.014753000
8	-0.982612000	3.123930000	-1.584023000
1	0.166231000	5.028145000	-2.563466000
1	0.140000000	7.211751000	-1.809084000

cis-**2a**

Zero-point correction=	0.166079 (Hartree/Particle)
Thermal correction to Energy=	0.178587
Thermal correction to Enthalpy=	0.179531
Thermal correction to Gibbs Free Energy=	0.124967
Sum of electronic and zero-point Energies=	-815.416885
Sum of electronic and thermal Energies=	-815.404378
Sum of electronic and thermal Enthalpies=	-815.403433
Sum of electronic and thermal Free Energies=	-815.457997

6	-3.920802000	3.582601000	-2.103602000
6	-3.415217000	4.712983000	-1.466232000
6	-2.061845000	4.796793000	-1.150099000
6	-1.200068000	3.738489000	-1.470997000
6	-1.718619000	2.604196000	-2.116952000
6	-3.067638000	2.526681000	-2.430440000
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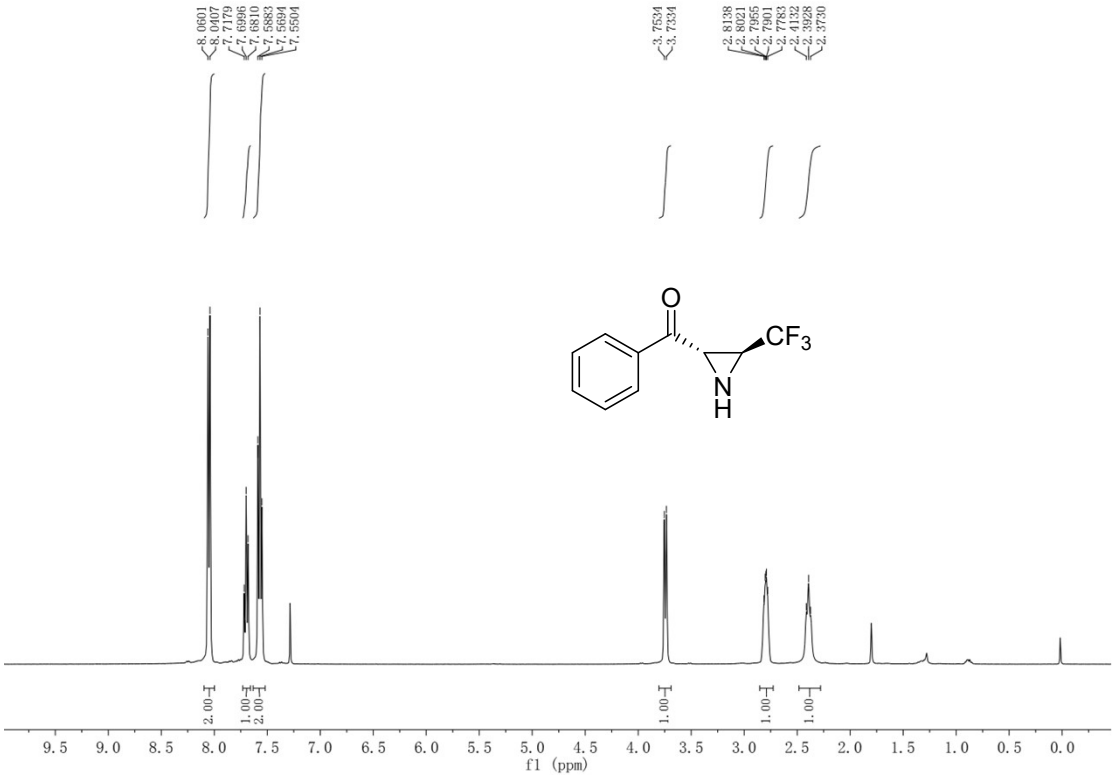
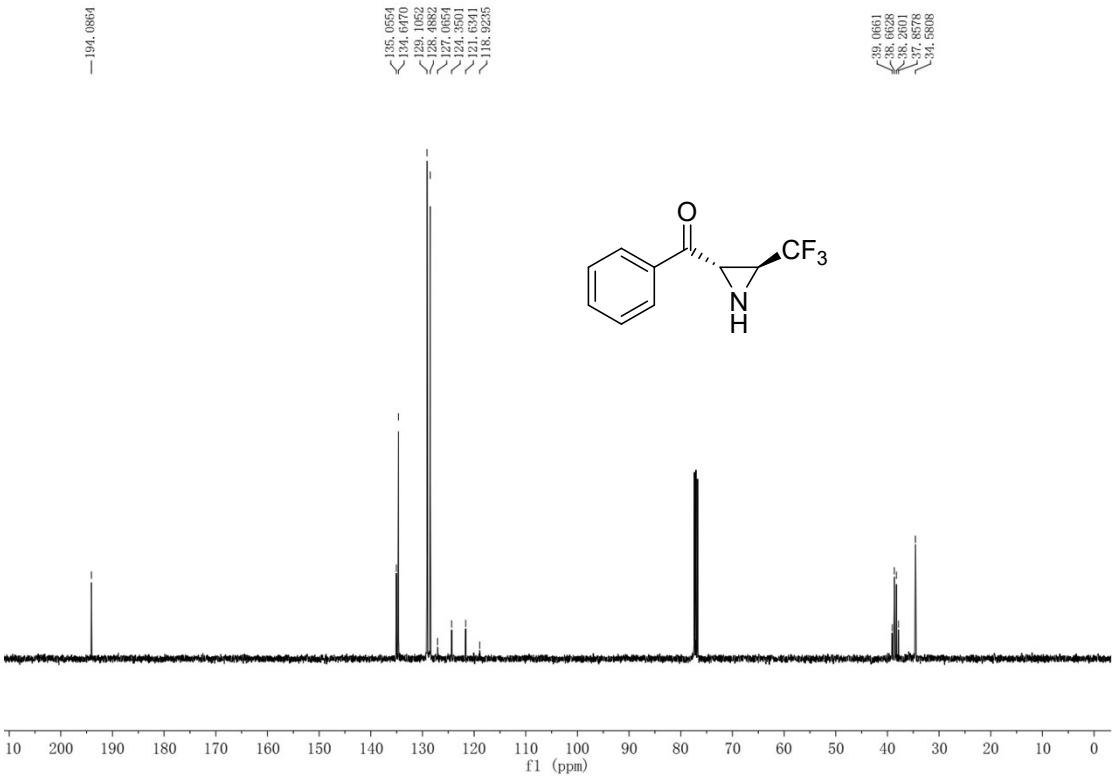
1	-4.074932000	5.536836000	-1.218783000
1	-1.665589000	5.683831000	-0.679602000
1	-1.040984000	1.795755000	-2.360783000
1	-3.457650000	1.646586000	-2.928869000
6	0.256637000	3.721612000	-1.154038000
6	0.970076000	4.814085000	-0.364063000
6	1.642194000	5.990467000	-0.988275000
1	2.620864000	6.270531000	-0.609929000
6	1.499761000	6.348136000	-2.443107000
9	1.592617000	7.685333000	-2.613269000
9	0.328682000	5.951171000	-2.968573000
9	2.490732000	5.780944000	-3.161258000
7	0.460730000	6.174031000	-0.157345000
1	0.703838000	6.531235000	0.761323000
8	0.965513000	2.781140000	-1.458983000
1	1.549963000	4.356337000	0.433981000

10. ^{1}H, ^{13}C, ^{19}F and ^{31}P NMR spectra

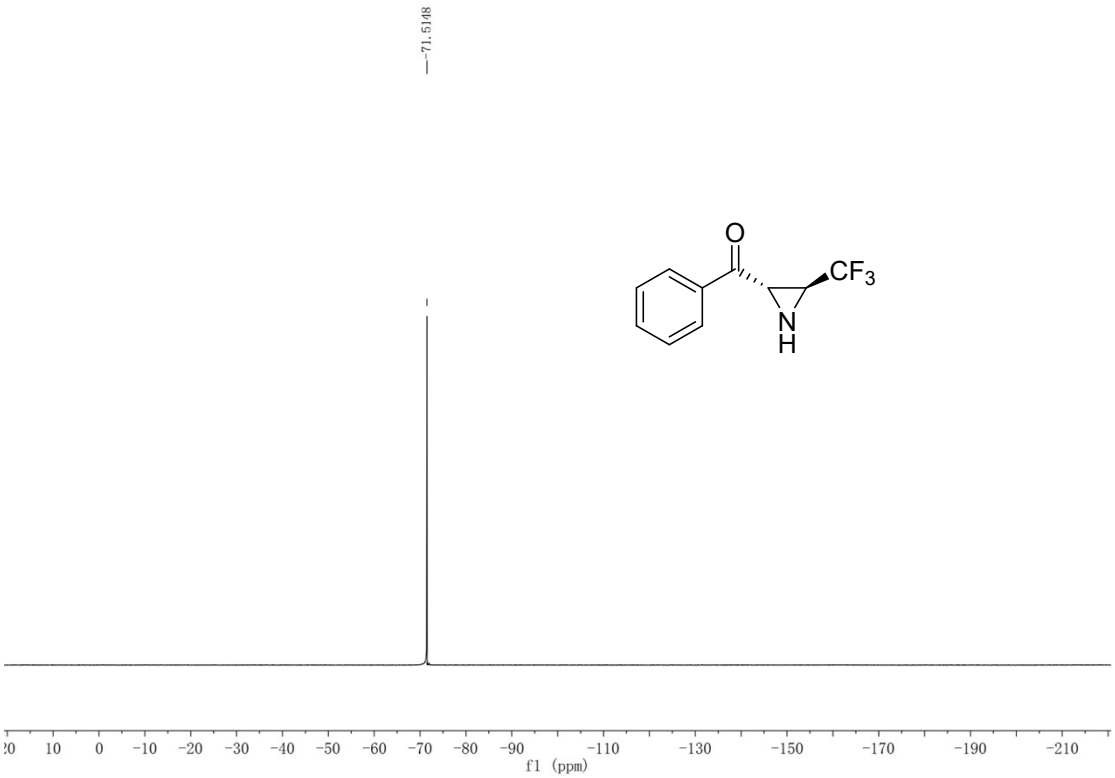
^{1}H NMR (400 MHz, $CDCl_3$) of **2a**:



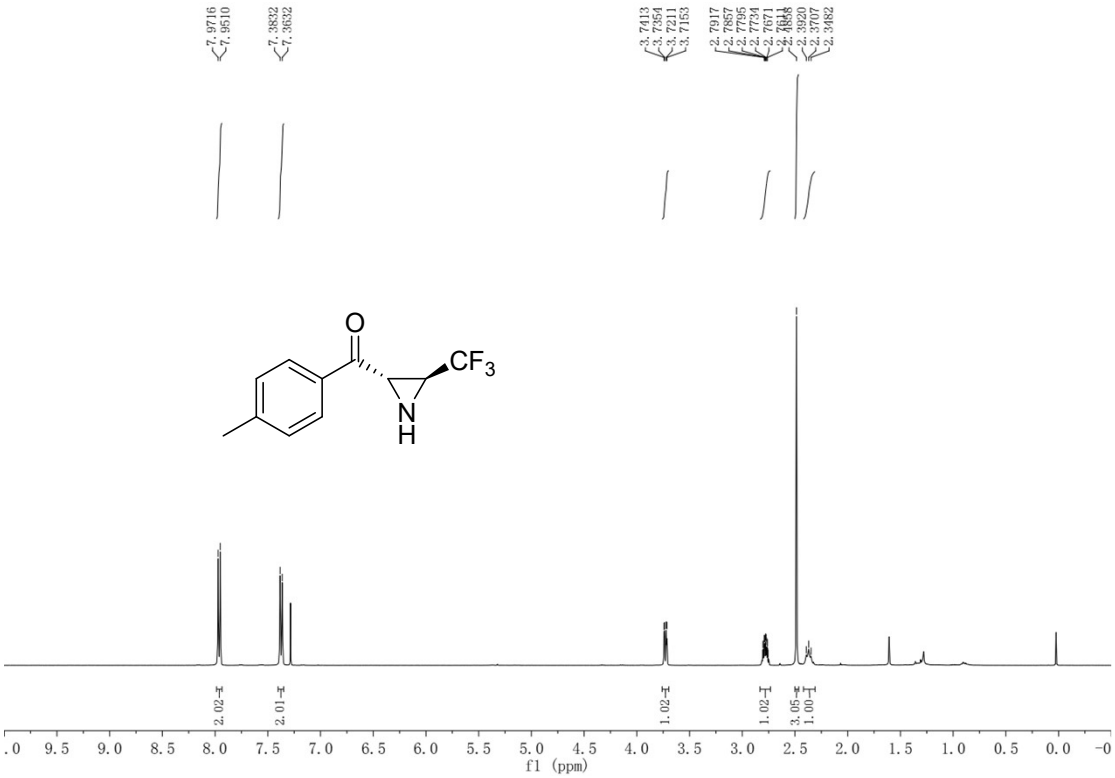
^{13}C NMR (100 MHz, $CDCl_3$) of **2a**:



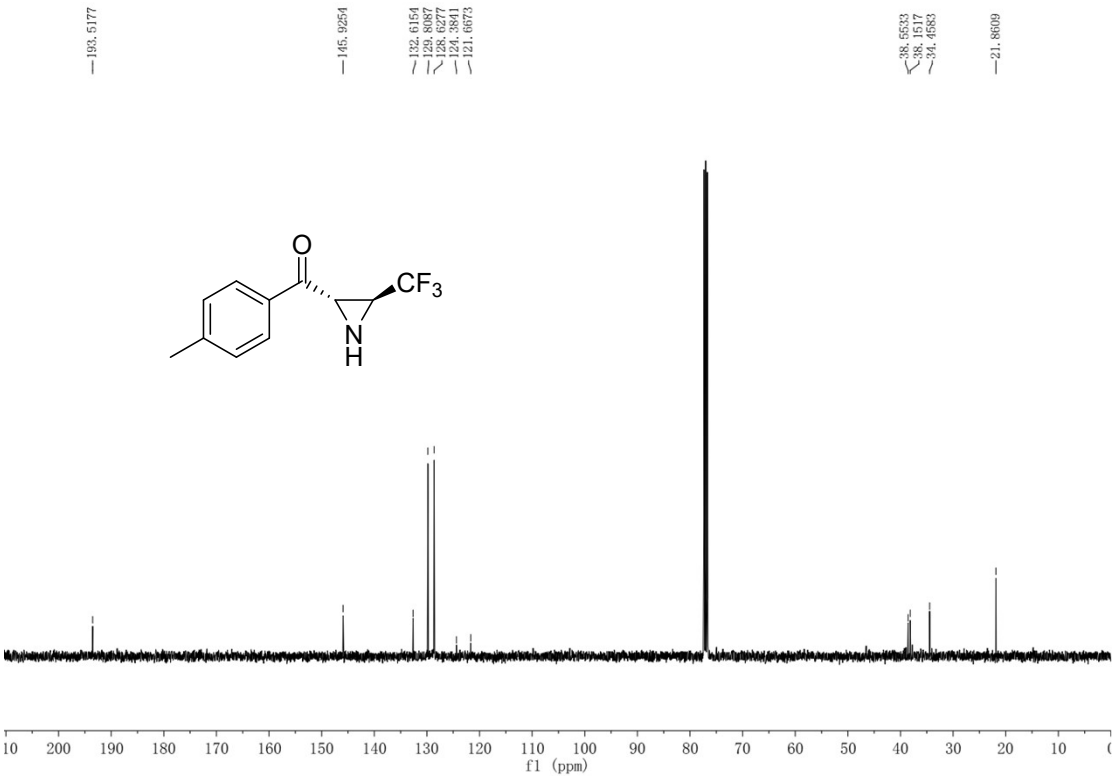
^{19}F NMR (376 MHz, $CDCl_3$) of **2a**:



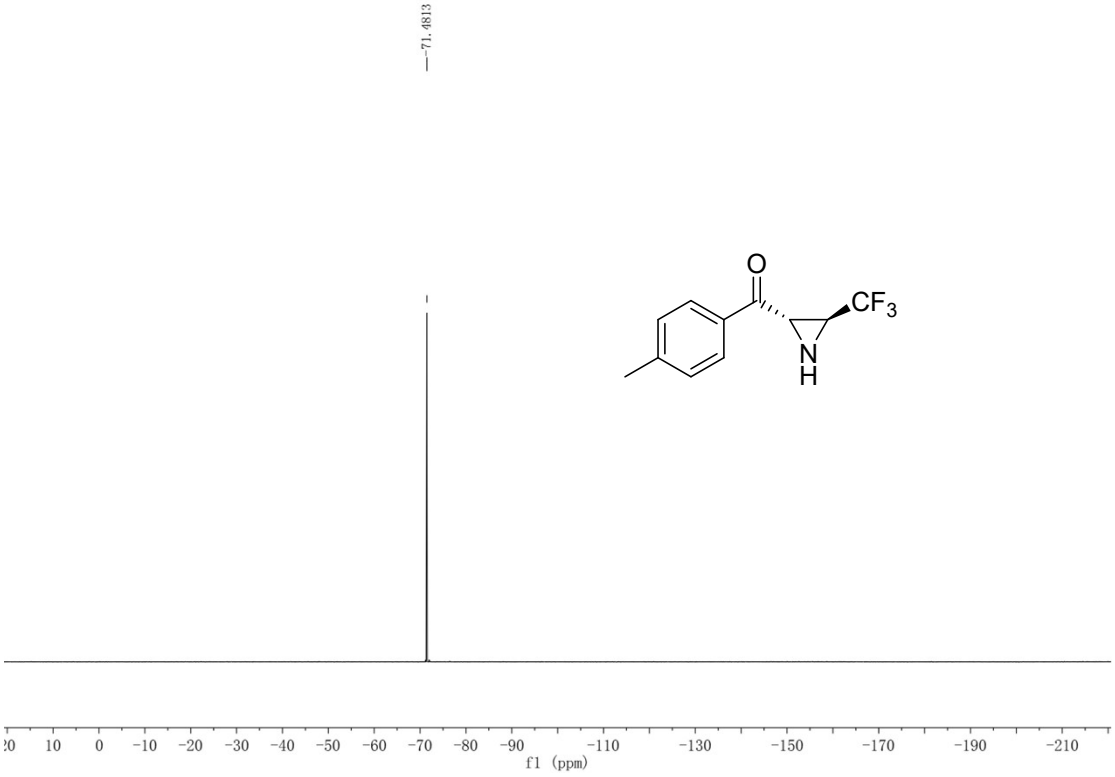
^{1}H NMR (400 MHz, $CDCl_3$) of **2b**:



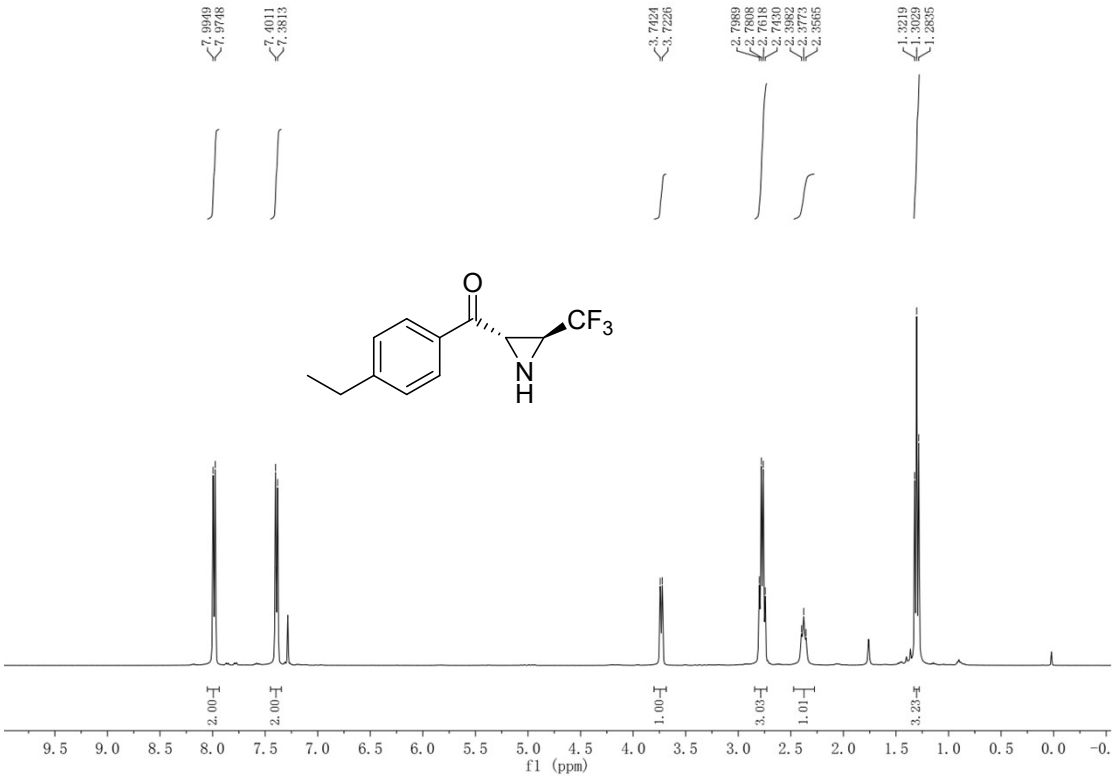
^{13}C NMR (100 MHz, $CDCl_3$) of **2b**:



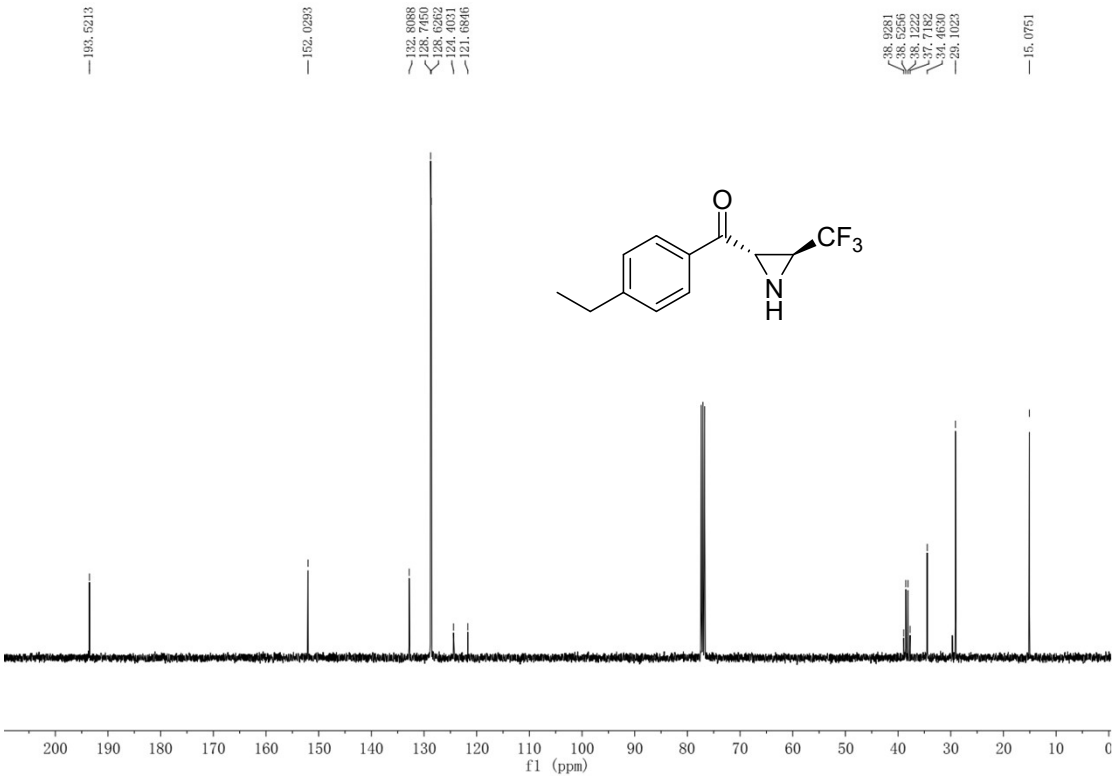
^{19}F NMR (376 MHz, $CDCl_3$) of **2b**:



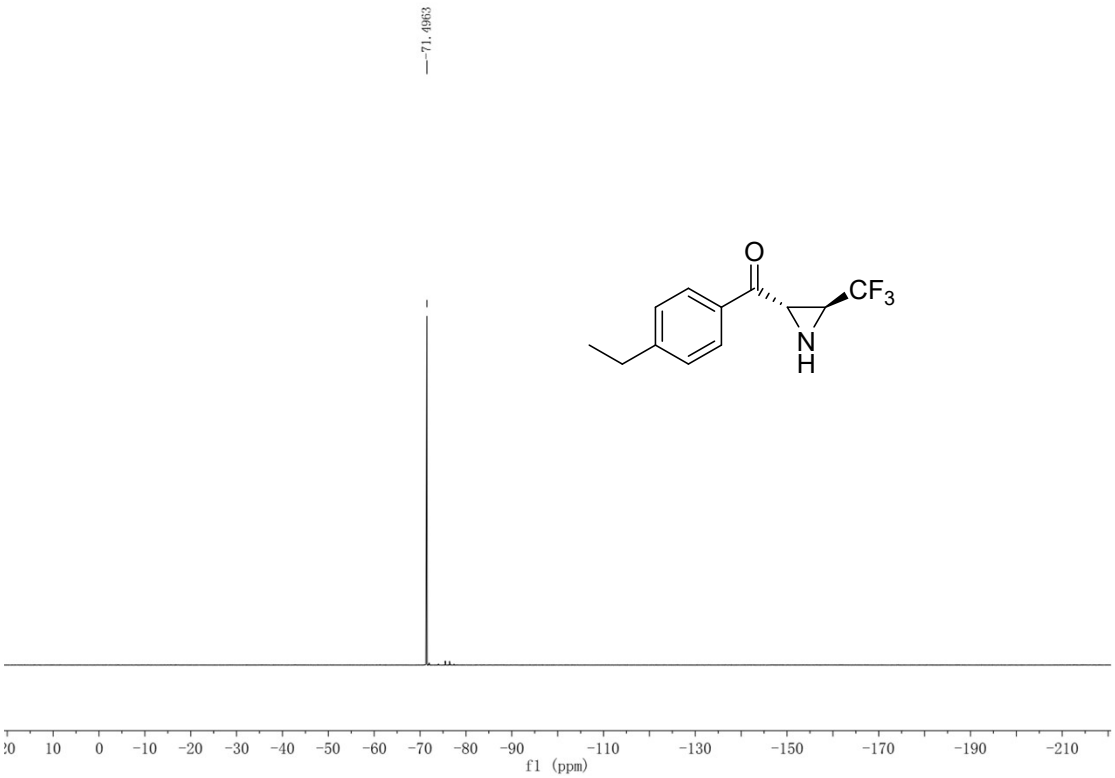
^{1}H NMR (400 MHz, $CDCl_3$) of **2c**:



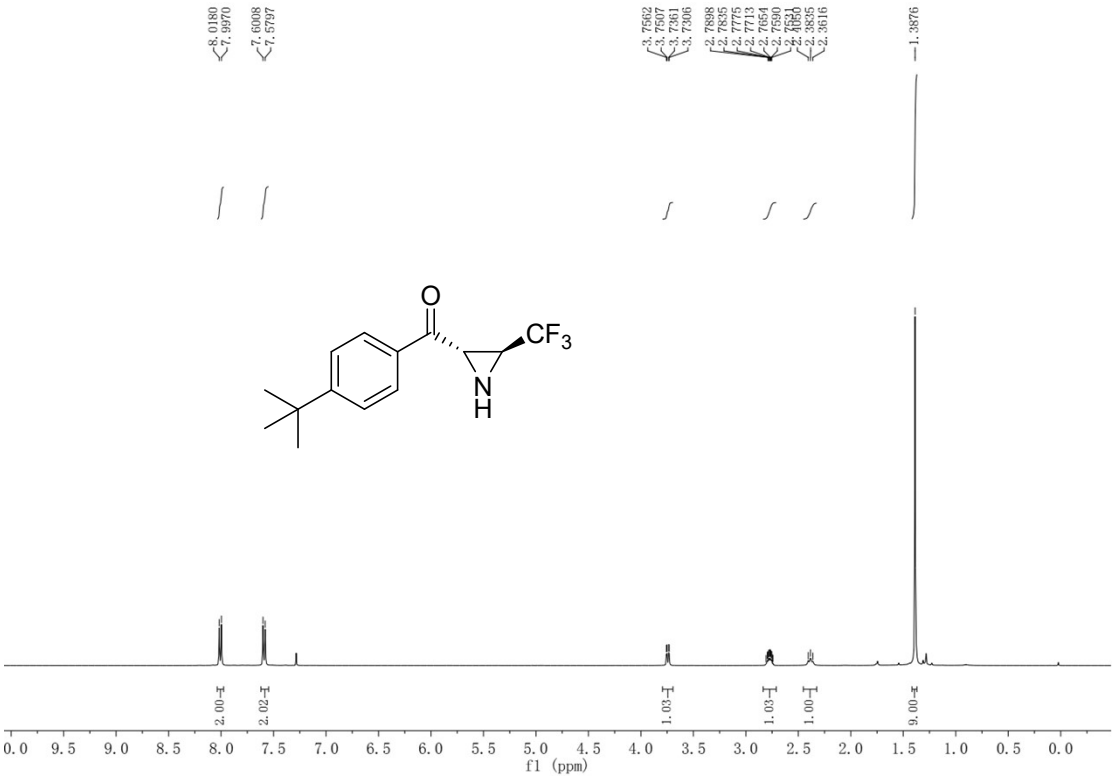
^{13}C NMR (100 MHz, $CDCl_3$) of **2c**:



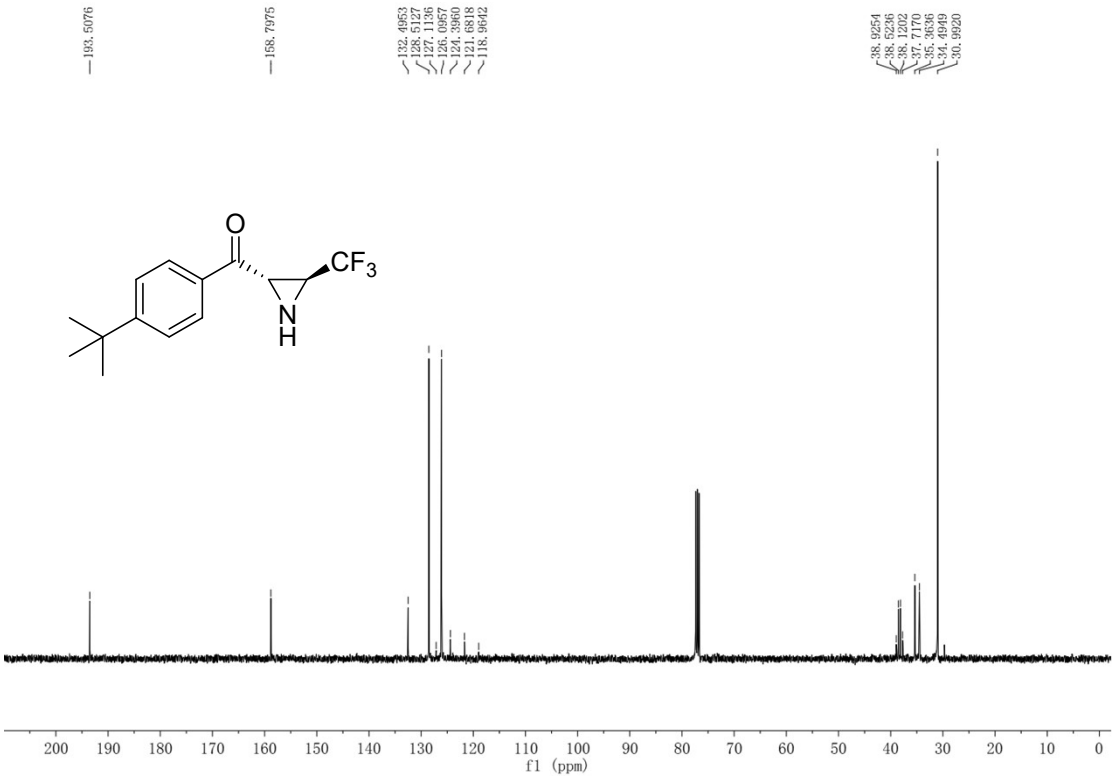
^{19}F NMR (376 MHz, $CDCl_3$) of **2c**:



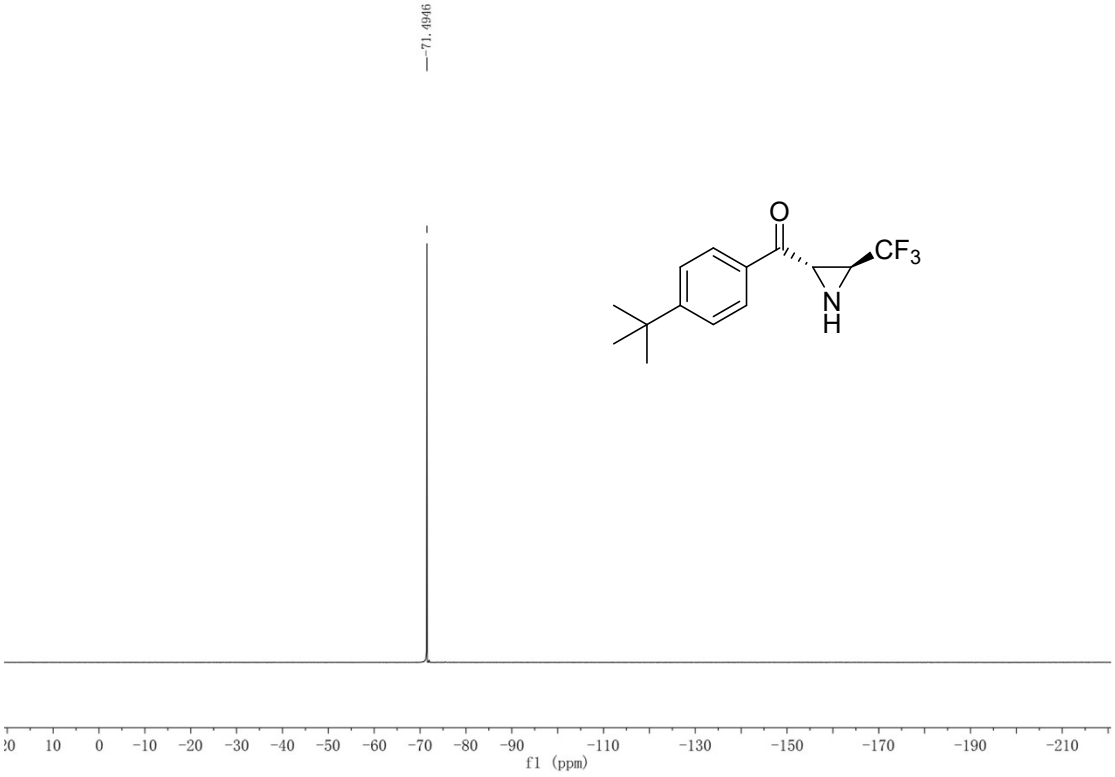
^{1}H NMR (400 MHz, $CDCl_3$) of **2d**:



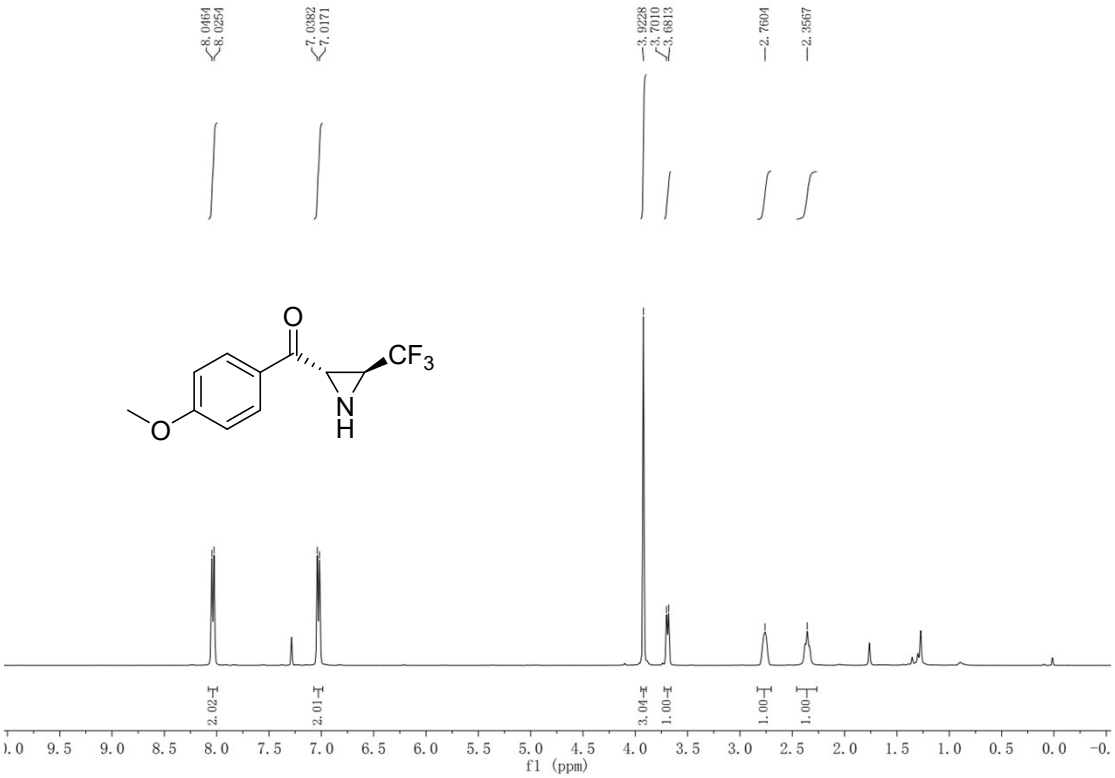
^{13}C NMR (100 MHz, $CDCl_3$) of **2d**:



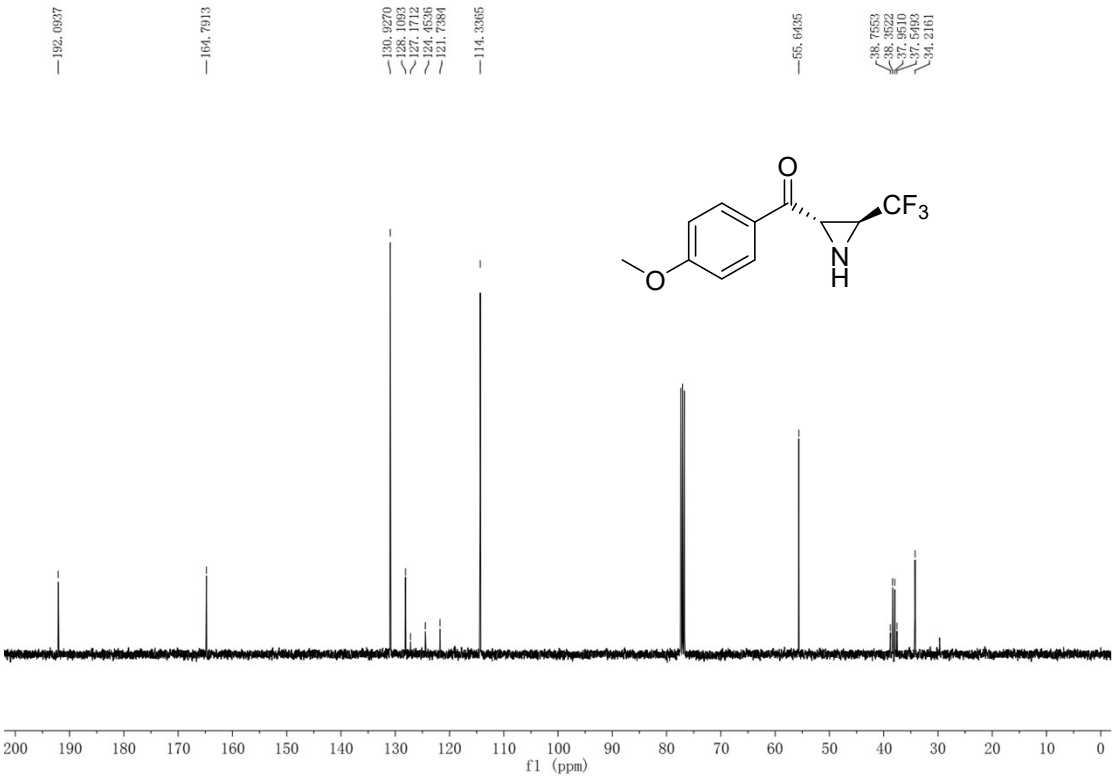
^{19}F NMR (376 MHz, $CDCl_3$) of **2d**:



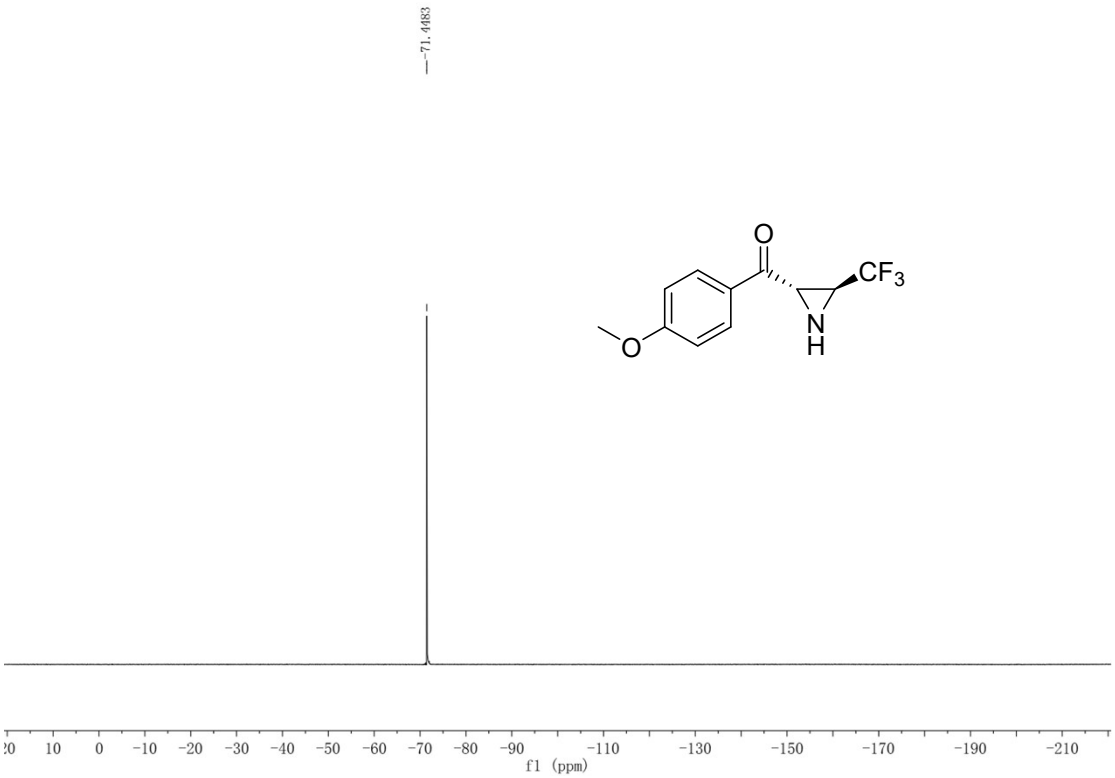
^{1}H NMR (400 MHz, $CDCl_3$) of **2e**:



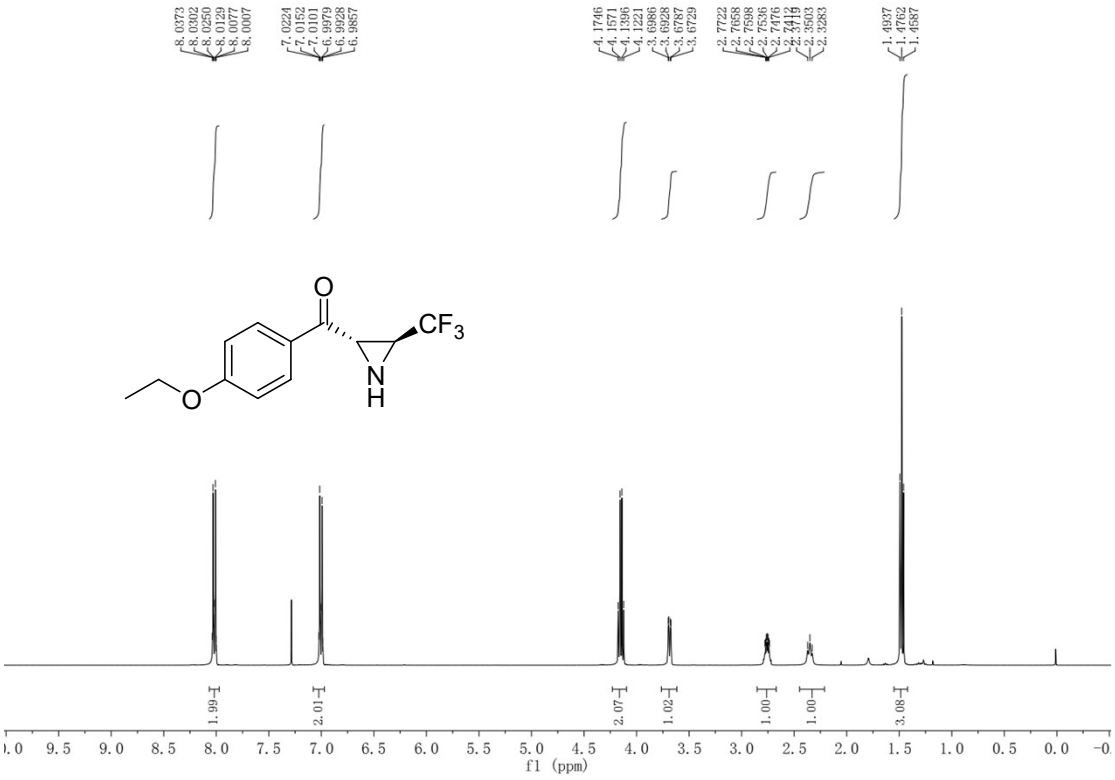
^{13}C NMR (100 MHz, $CDCl_3$) of **2e**:



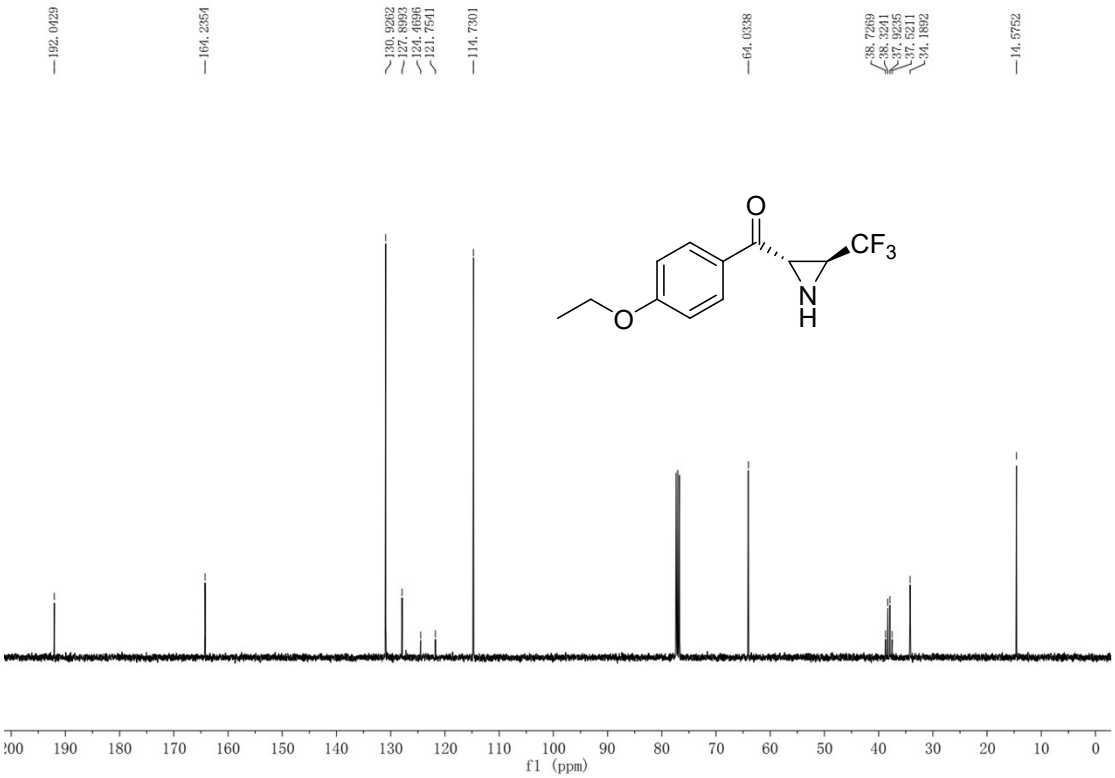
^{19}F NMR (376 MHz, $CDCl_3$) of **2e**:



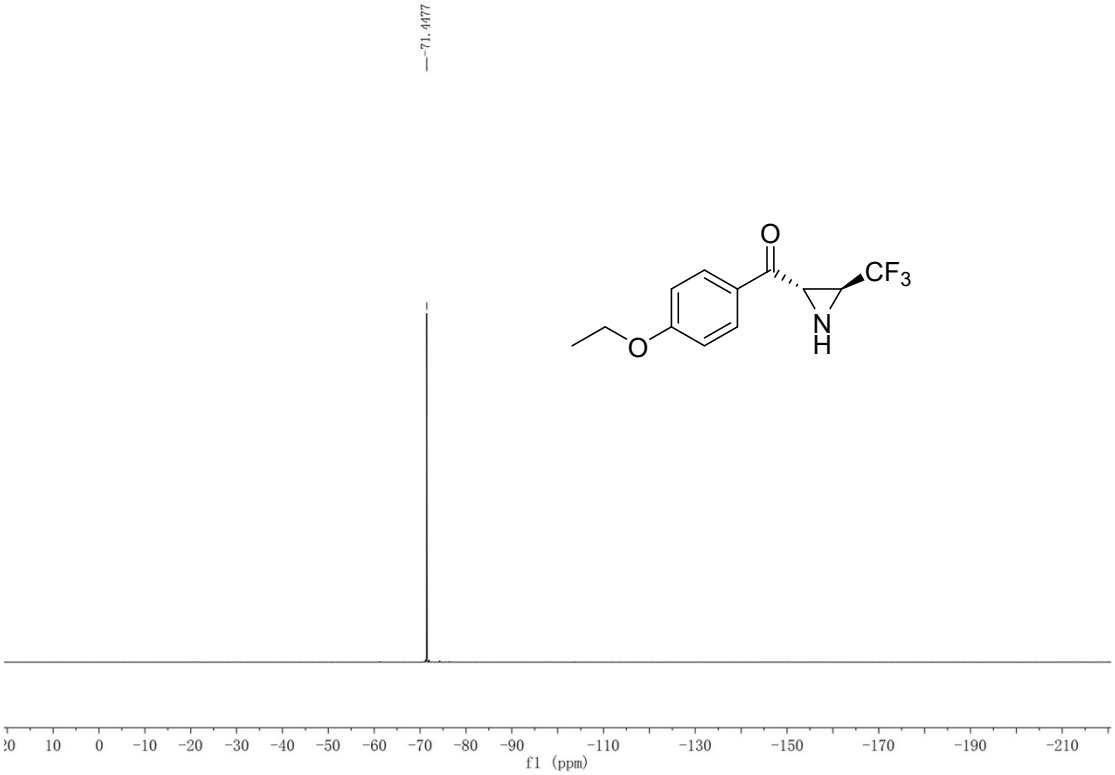
^{1}H NMR (400 MHz, $CDCl_3$) of **2f**:



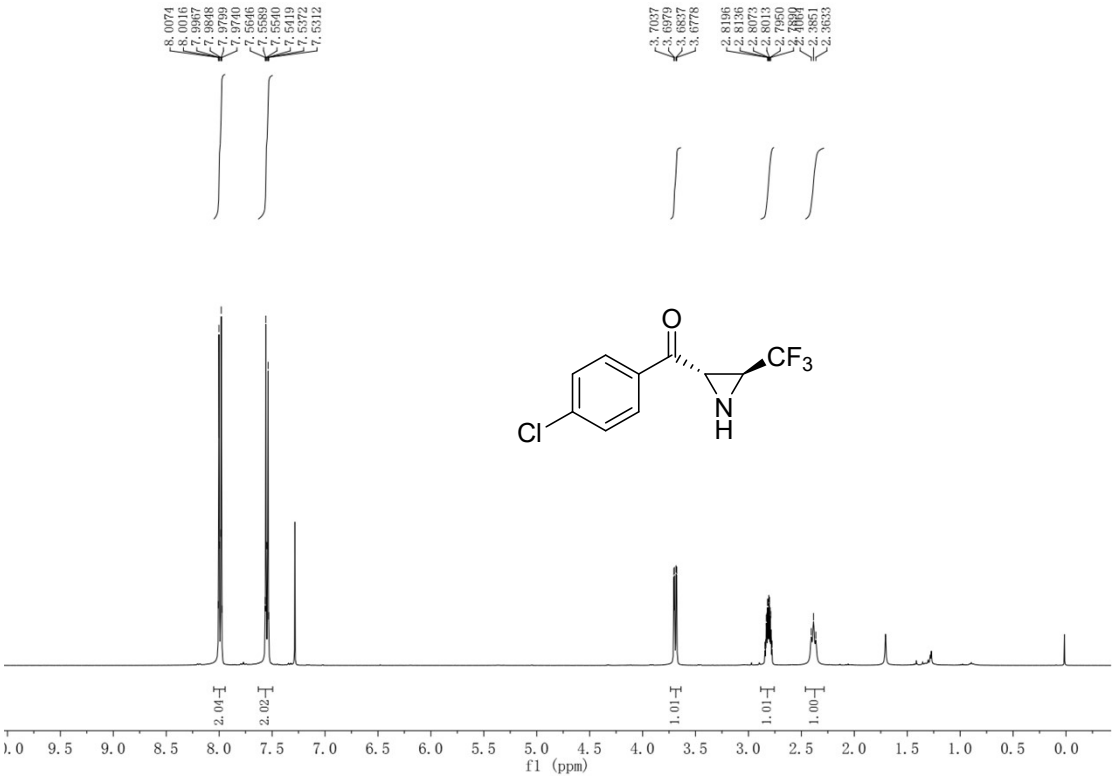
^{13}C NMR (100 MHz, $CDCl_3$) of **2f**:



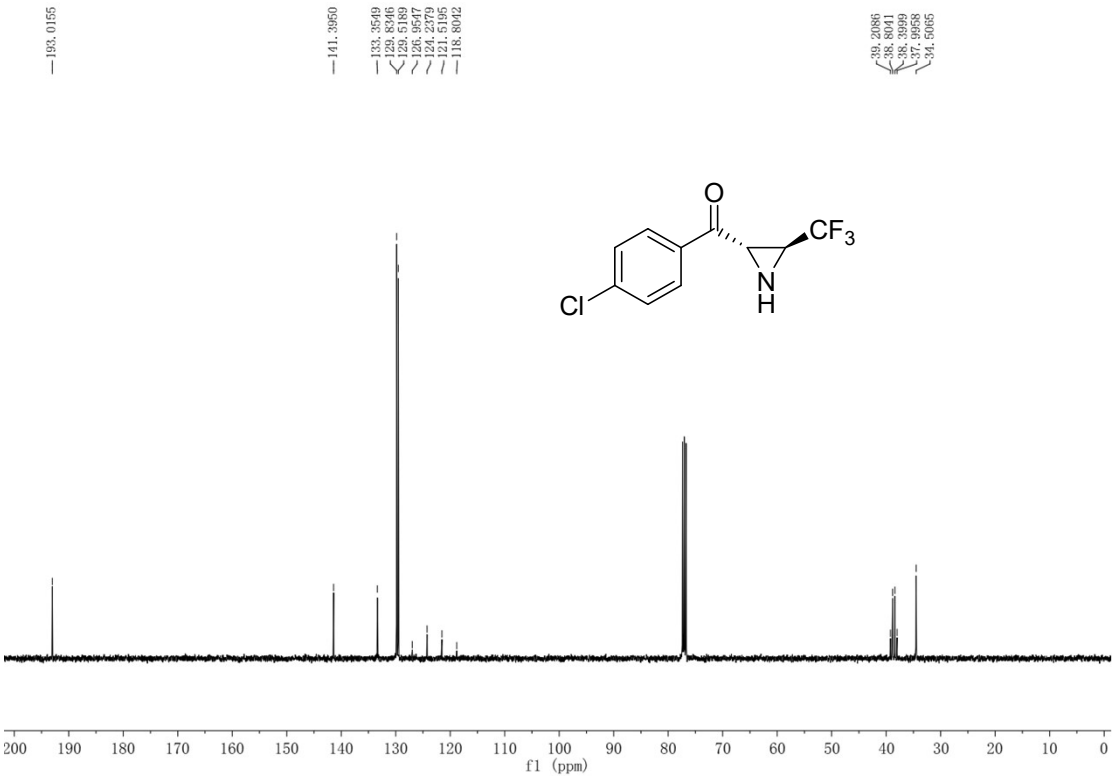
^{19}F NMR (376 MHz, $CDCl_3$) of **2f**:



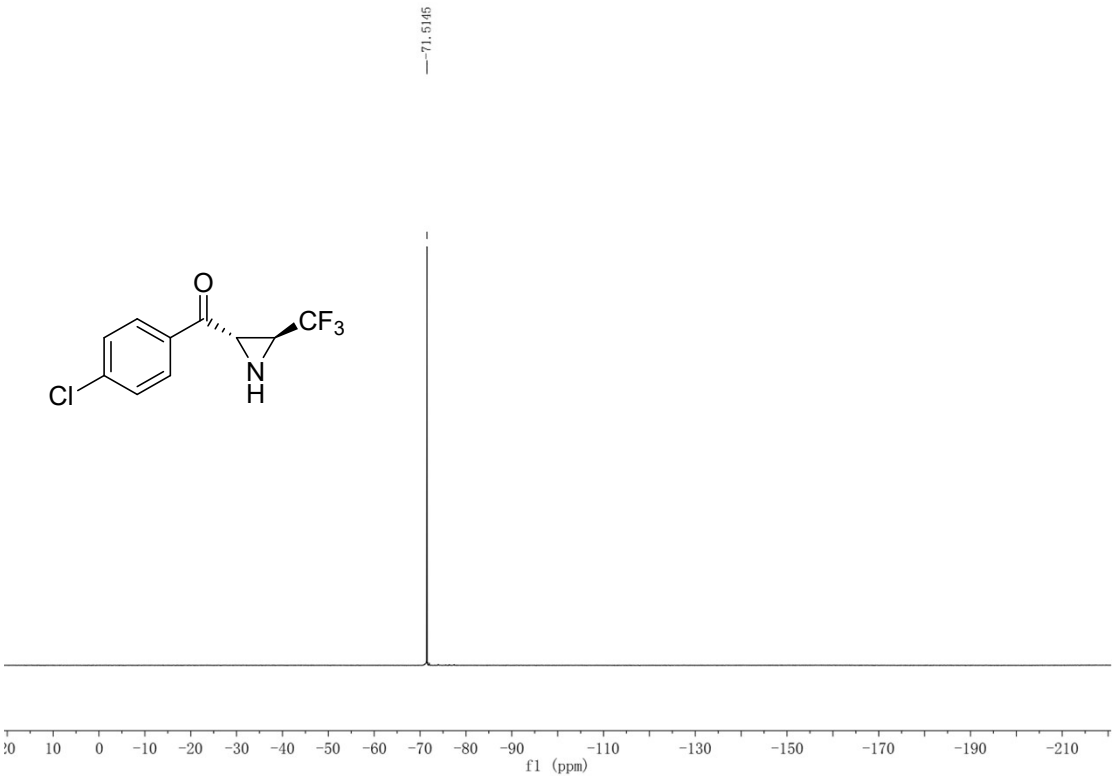
^{1}H NMR (400 MHz, $CDCl_3$) of **2g**:



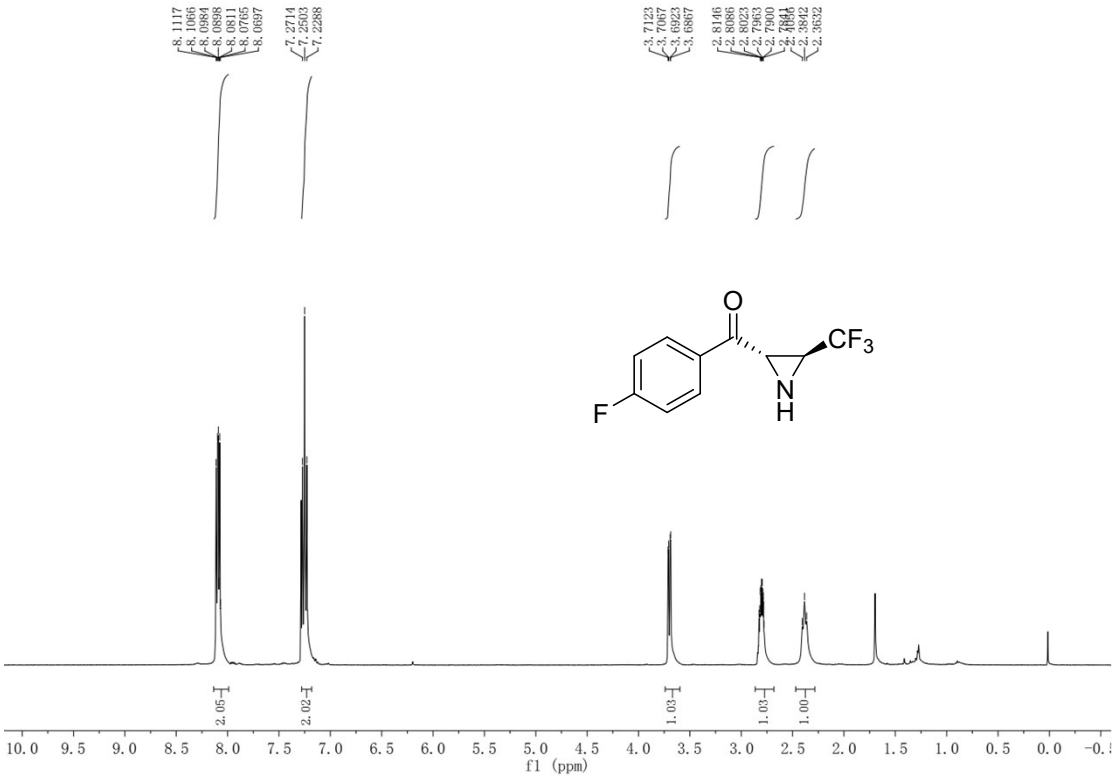
^{13}C NMR (100 MHz, $CDCl_3$) of **2g**:



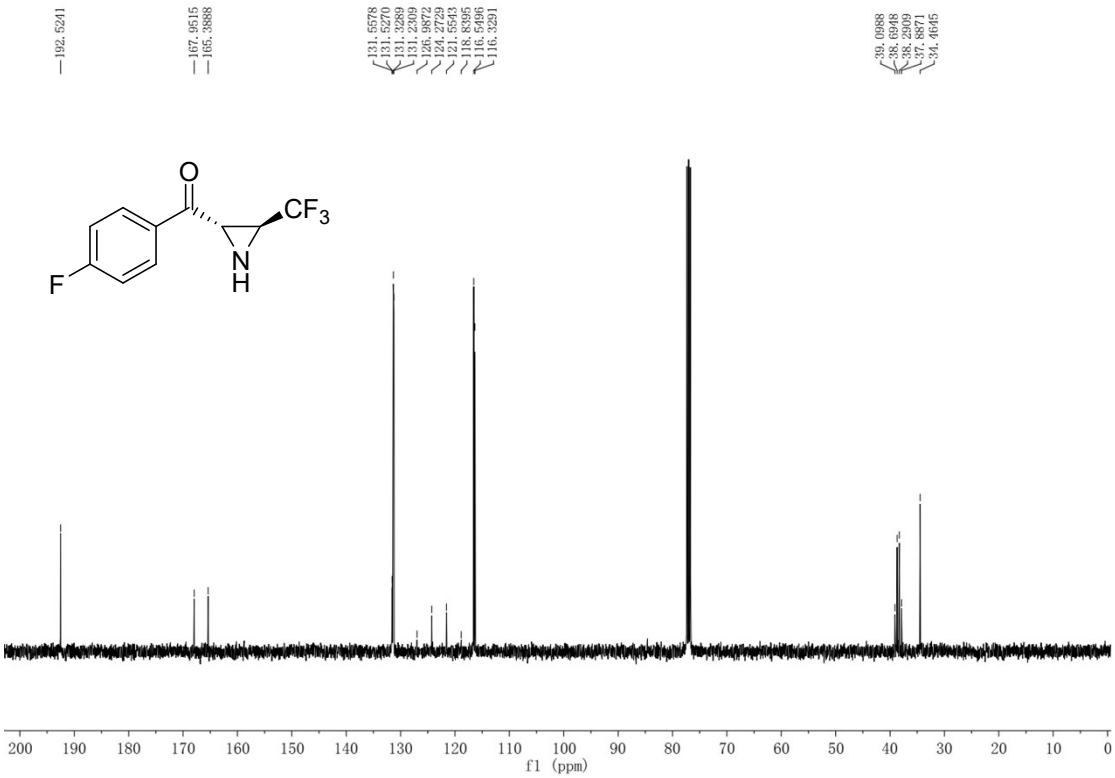
^{19}F NMR (376 MHz, $CDCl_3$) of **2g**:



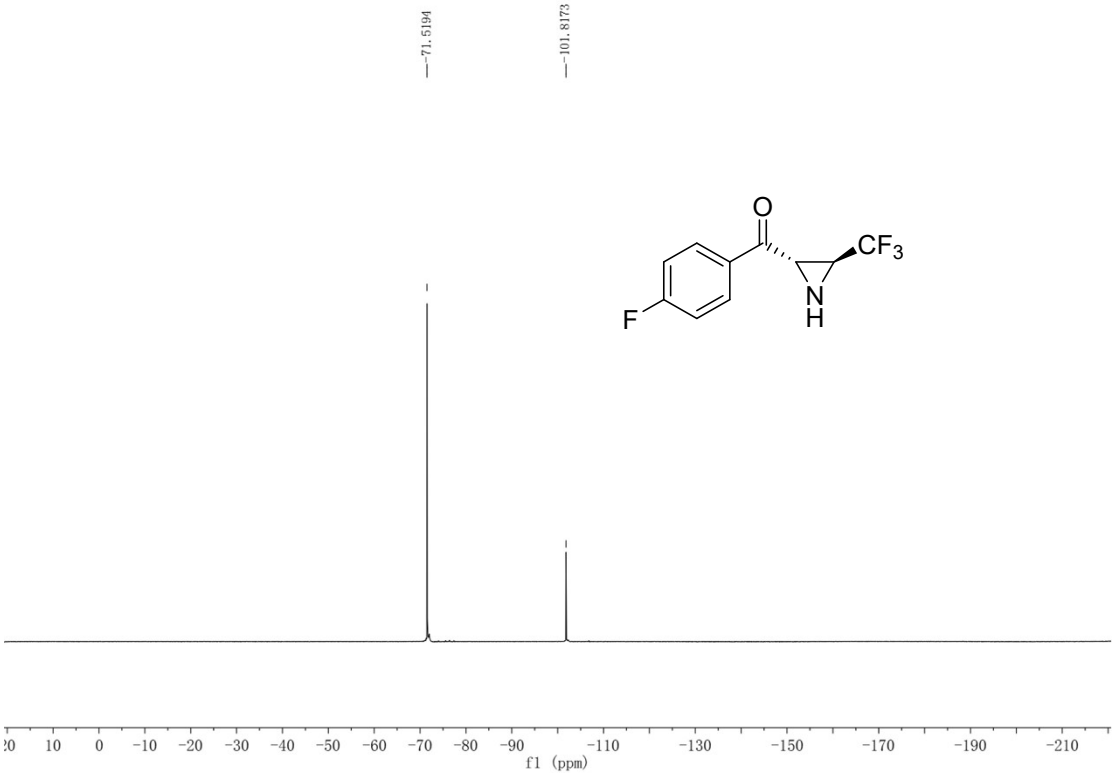
^{1}H NMR (400 MHz, $CDCl_3$) of **2h**:



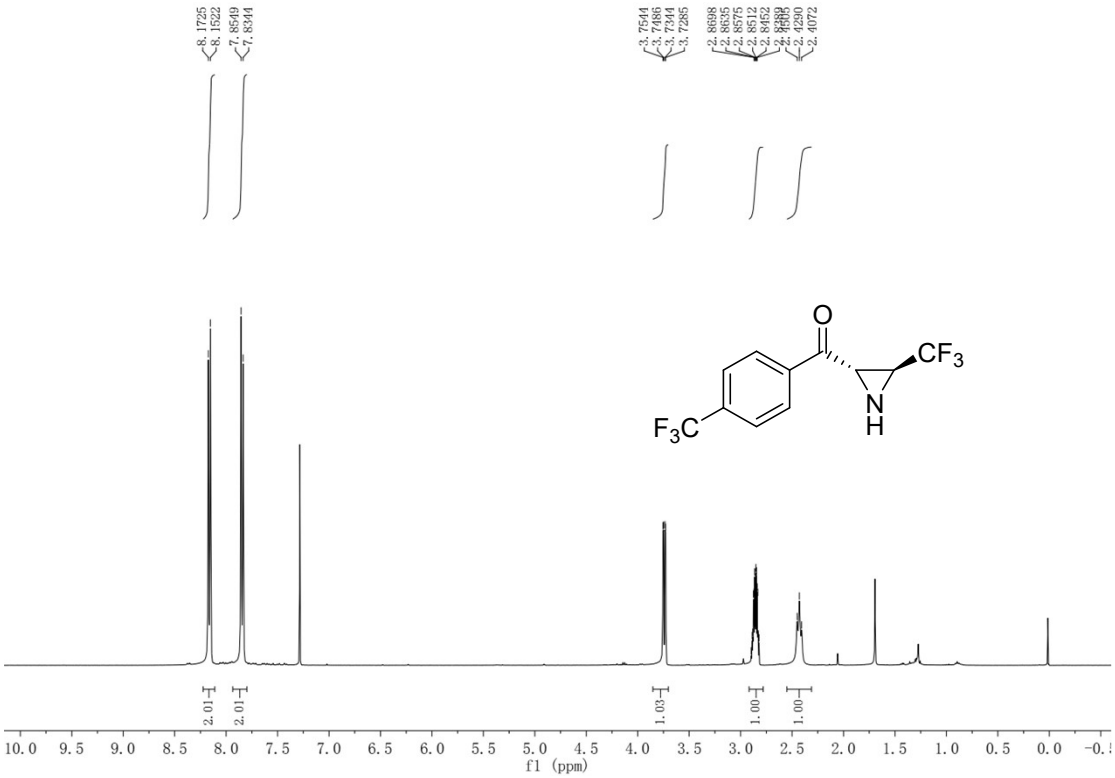
^{13}C NMR (100 MHz, $CDCl_3$) of **2h**:



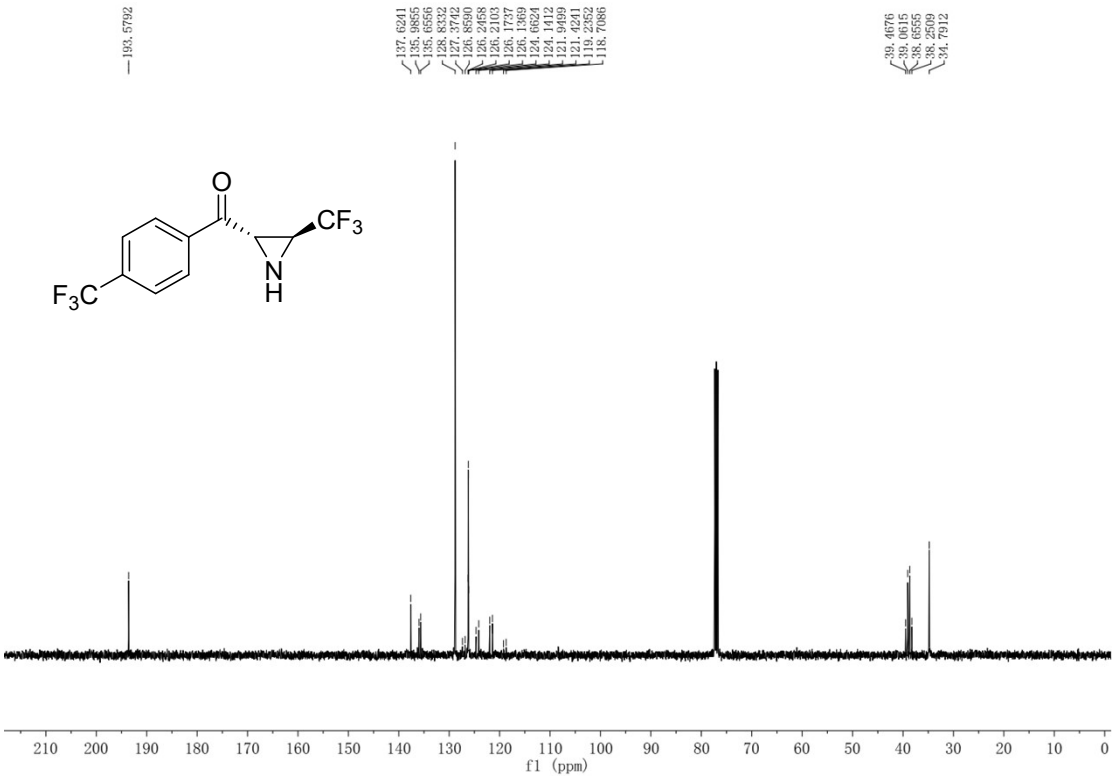
^{19}F NMR (376 MHz, $CDCl_3$) of **2h**:



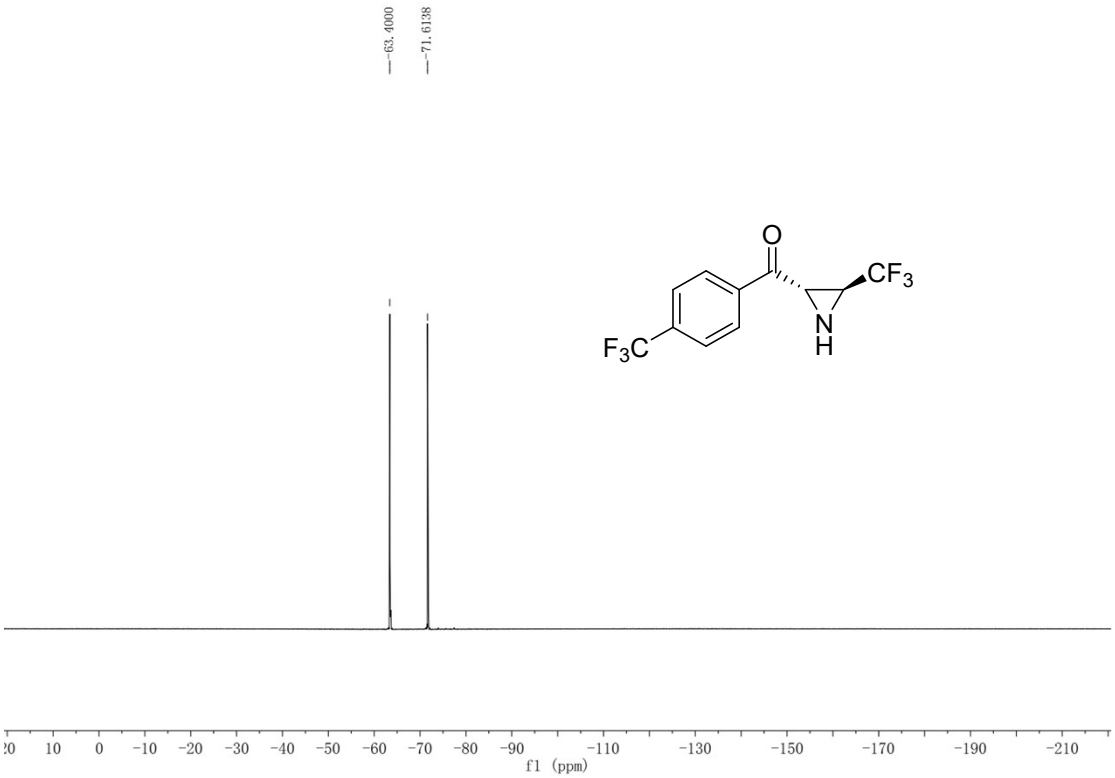
^{1}H NMR (400 MHz, $CDCl_3$) of **2i**:



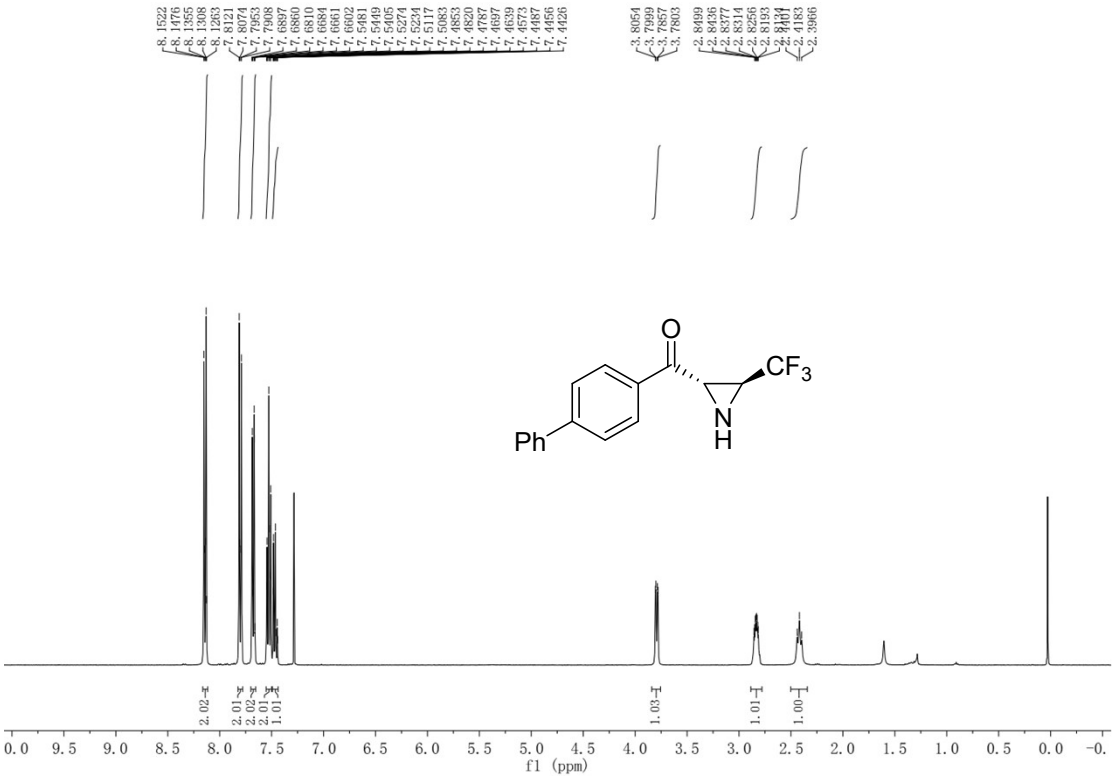
^{13}C NMR (100 MHz, $CDCl_3$) of **2i**:



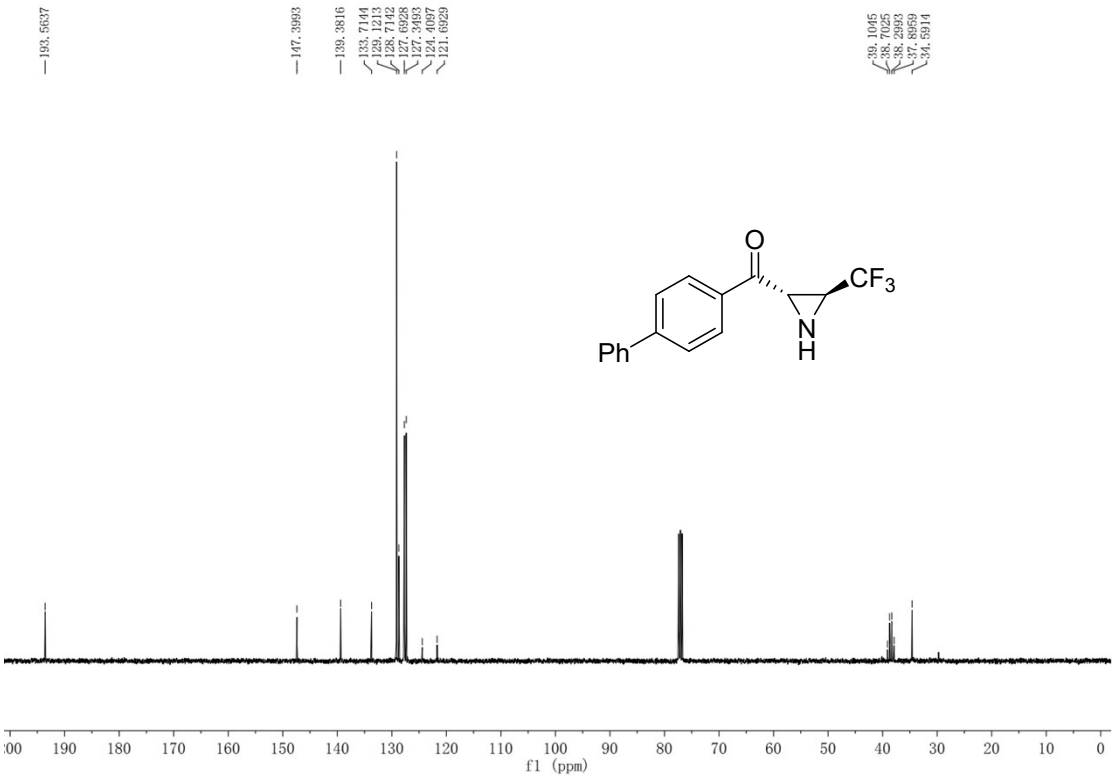
^{19}F NMR (376 MHz, $CDCl_3$) of **2i**:



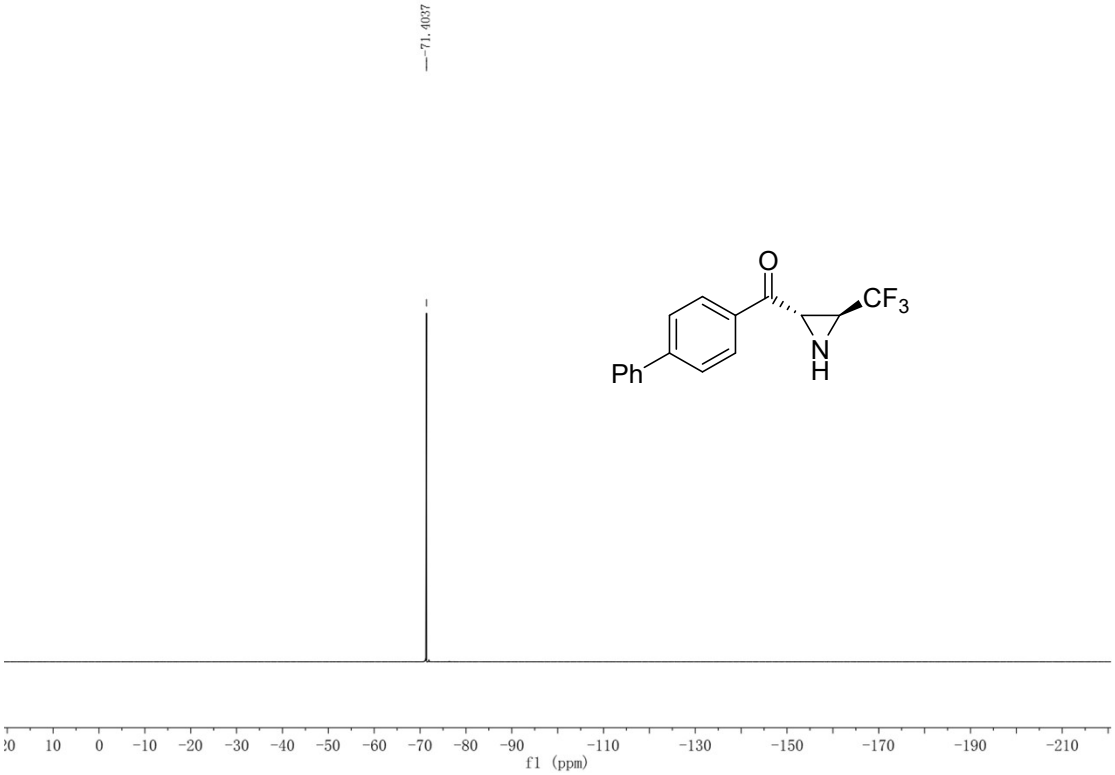
^{1}H NMR (400 MHz, $CDCl_3$) of **2j**:



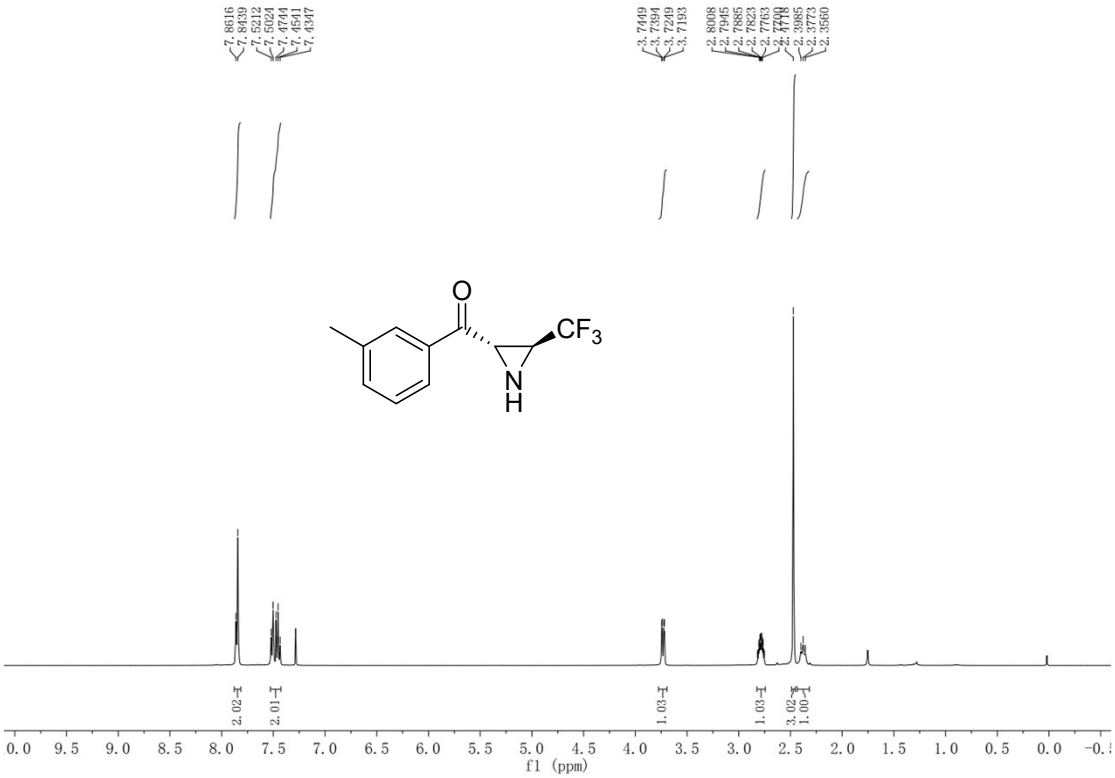
^{13}C NMR (100 MHz, $CDCl_3$) of **2j**:



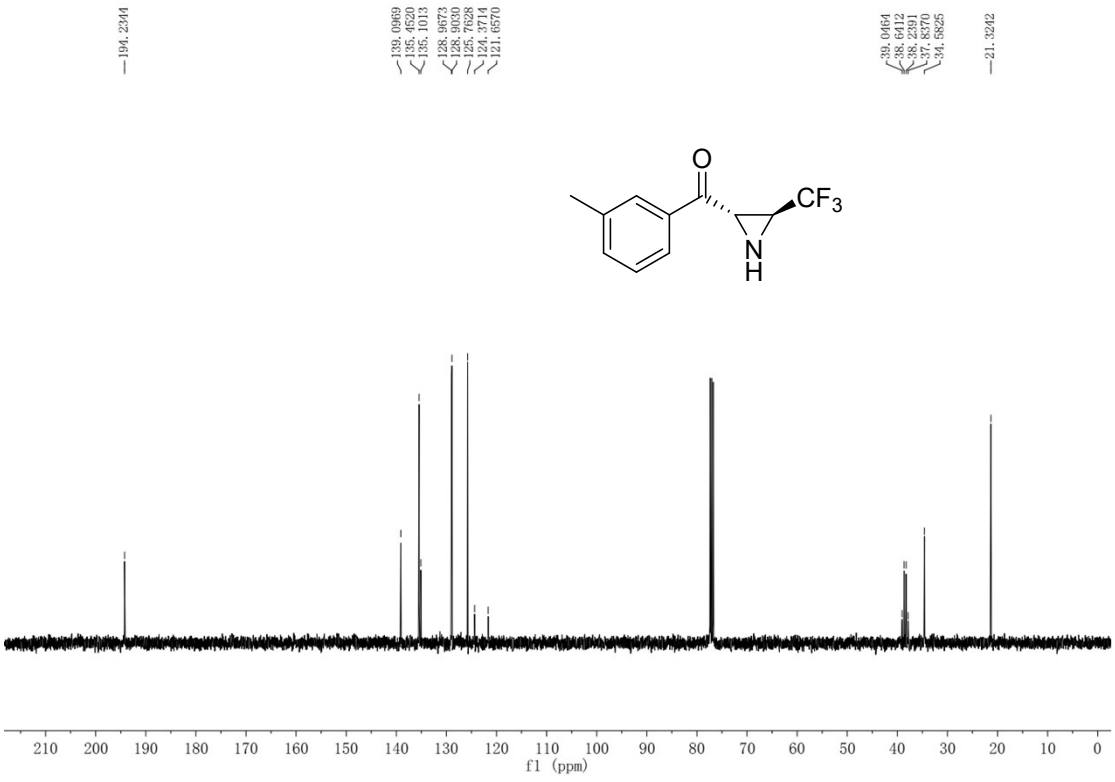
^{19}F NMR (376 MHz, $CDCl_3$) of **2j**:



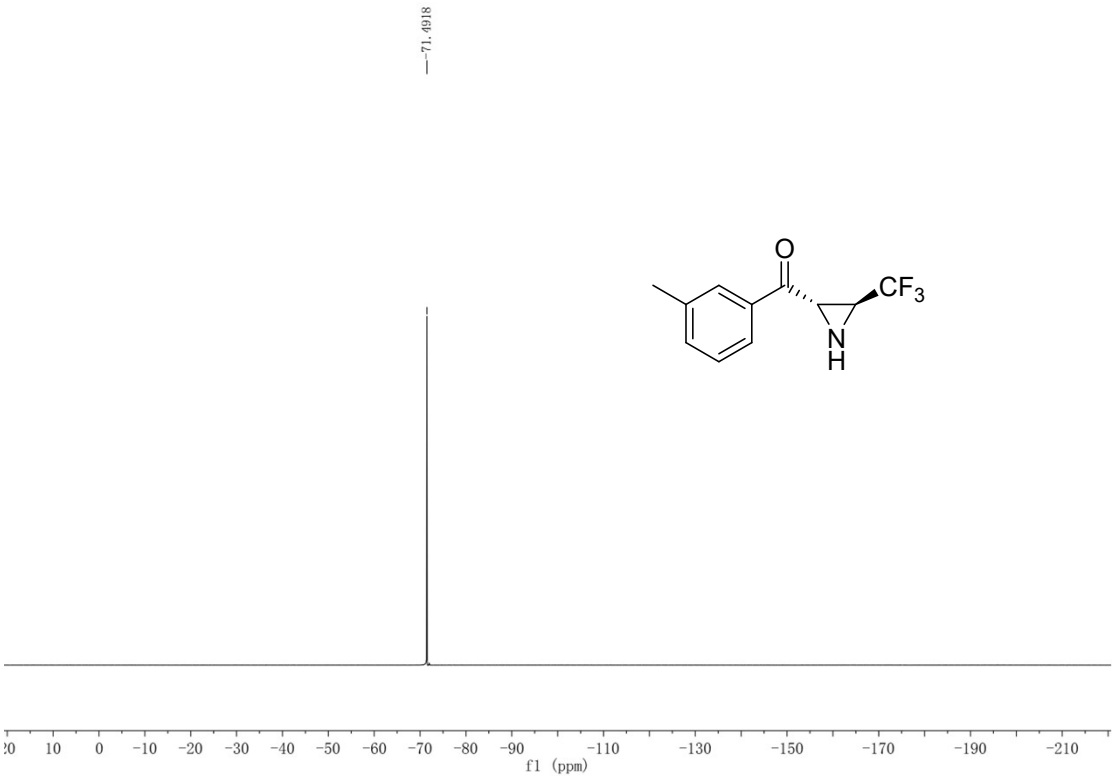
^{1}H NMR (400 MHz, $CDCl_3$) of **2k**:



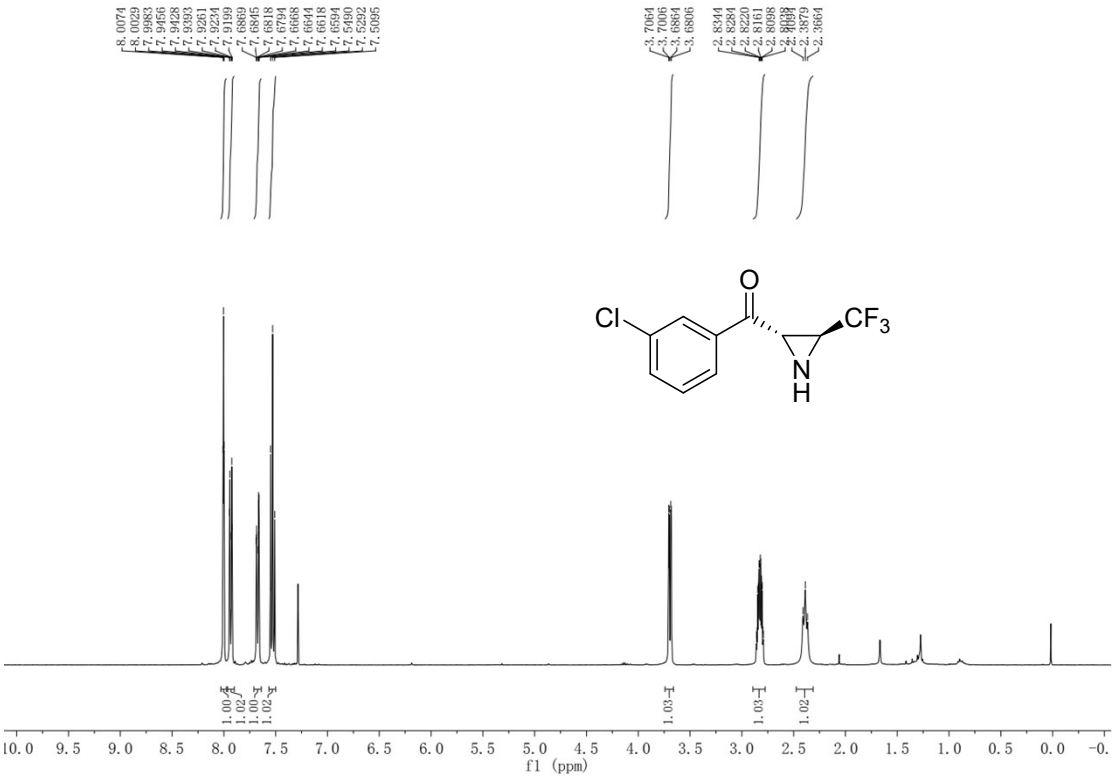
^{13}C NMR (100 MHz, $CDCl_3$) of **2k**:



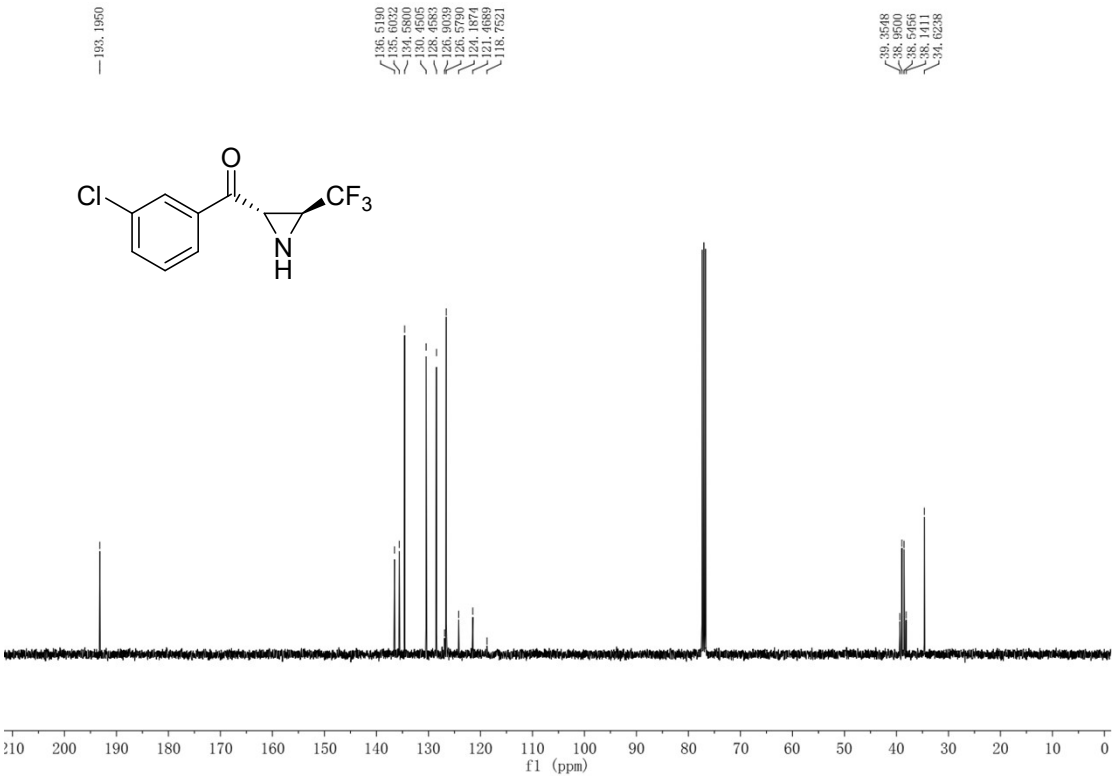
^{19}F NMR (376 MHz, $CDCl_3$) of **2k**:



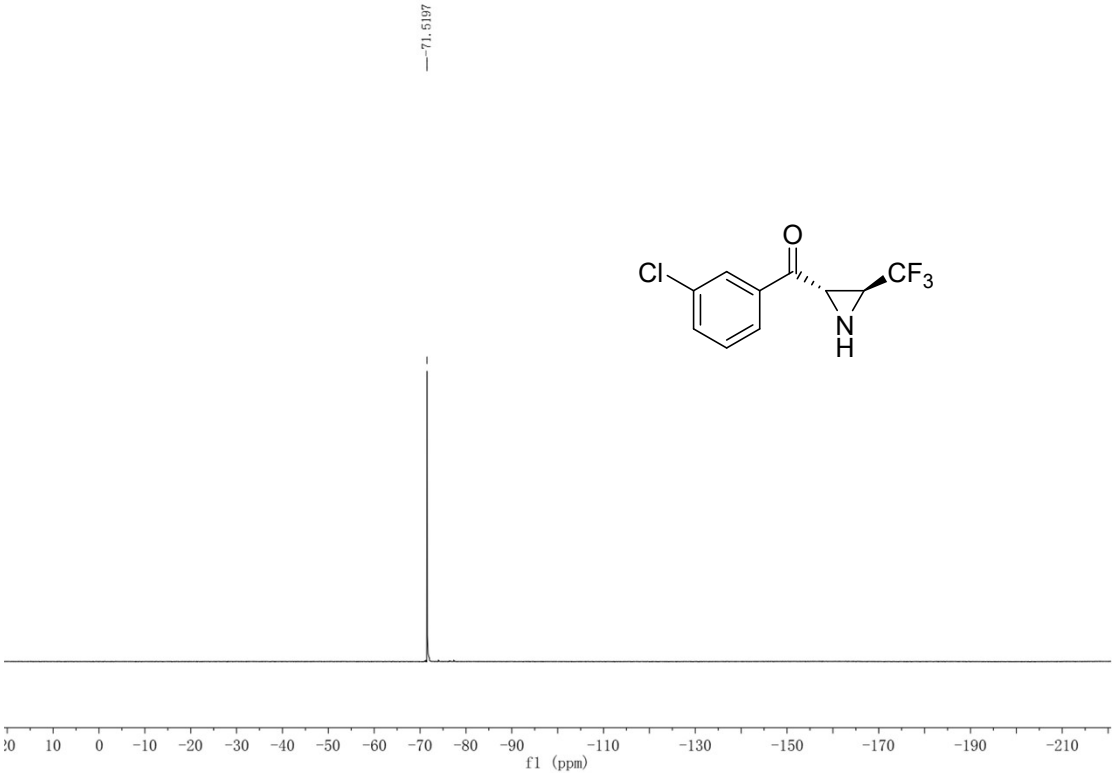
^{1}H NMR (400 MHz, $CDCl_3$) of **2l**:



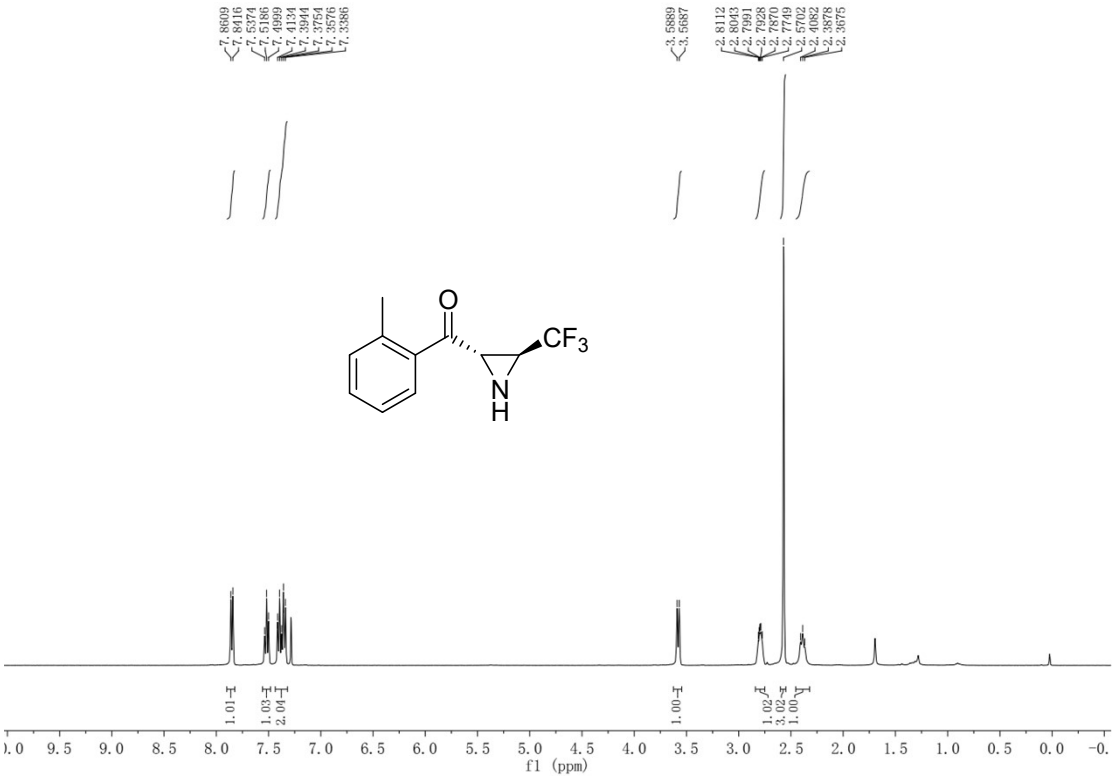
^{13}C NMR (100 MHz, $CDCl_3$) of **2l**:



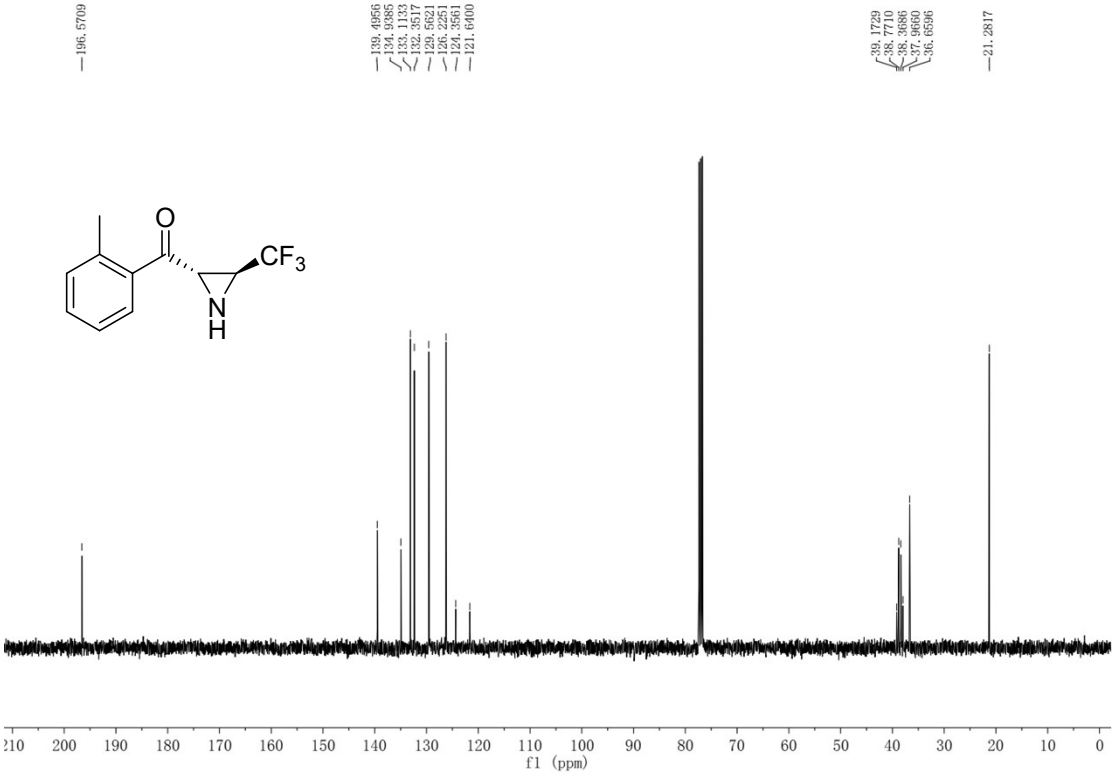
^{19}F NMR (376 MHz, $CDCl_3$) of **2l**:



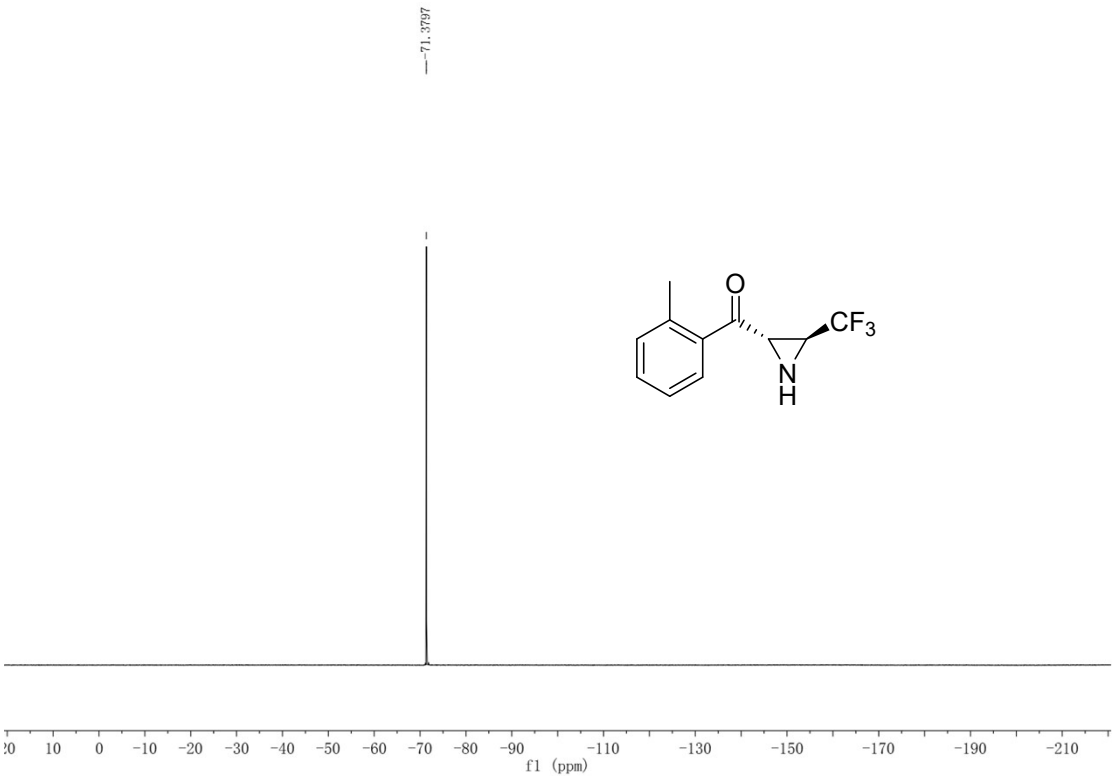
^{1}H NMR (400 MHz, $CDCl_3$) of **2m**:



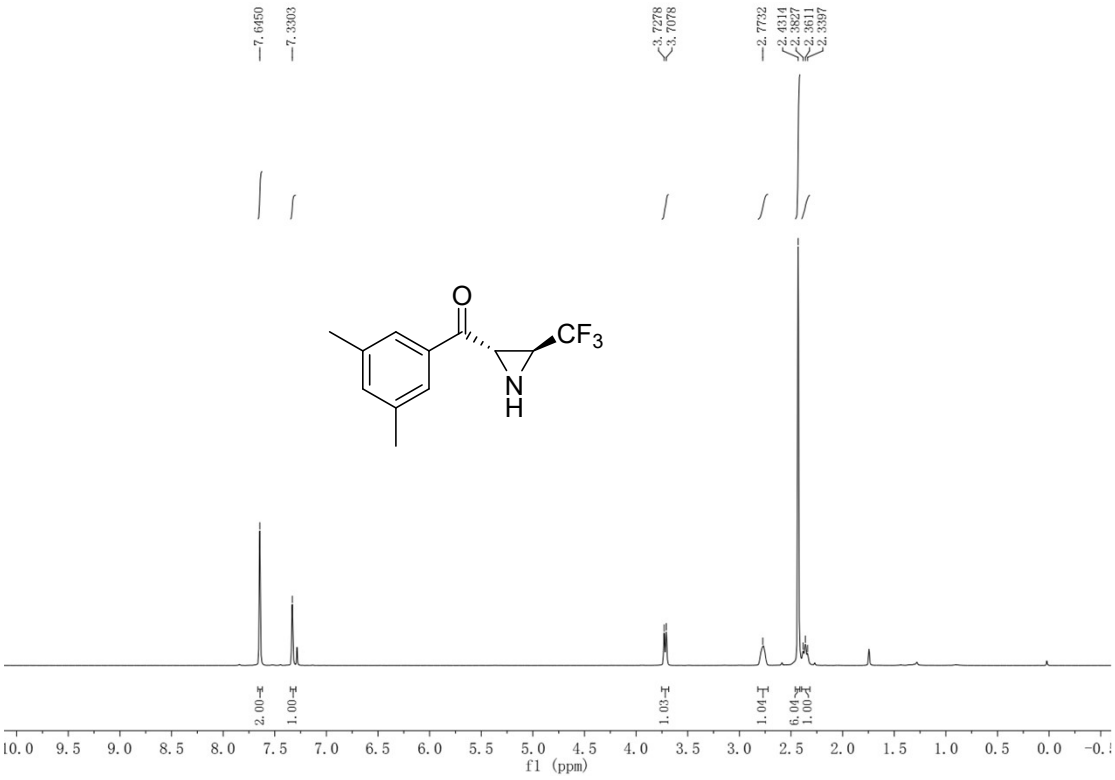
^{13}C NMR (100 MHz, $CDCl_3$) of **2m**:



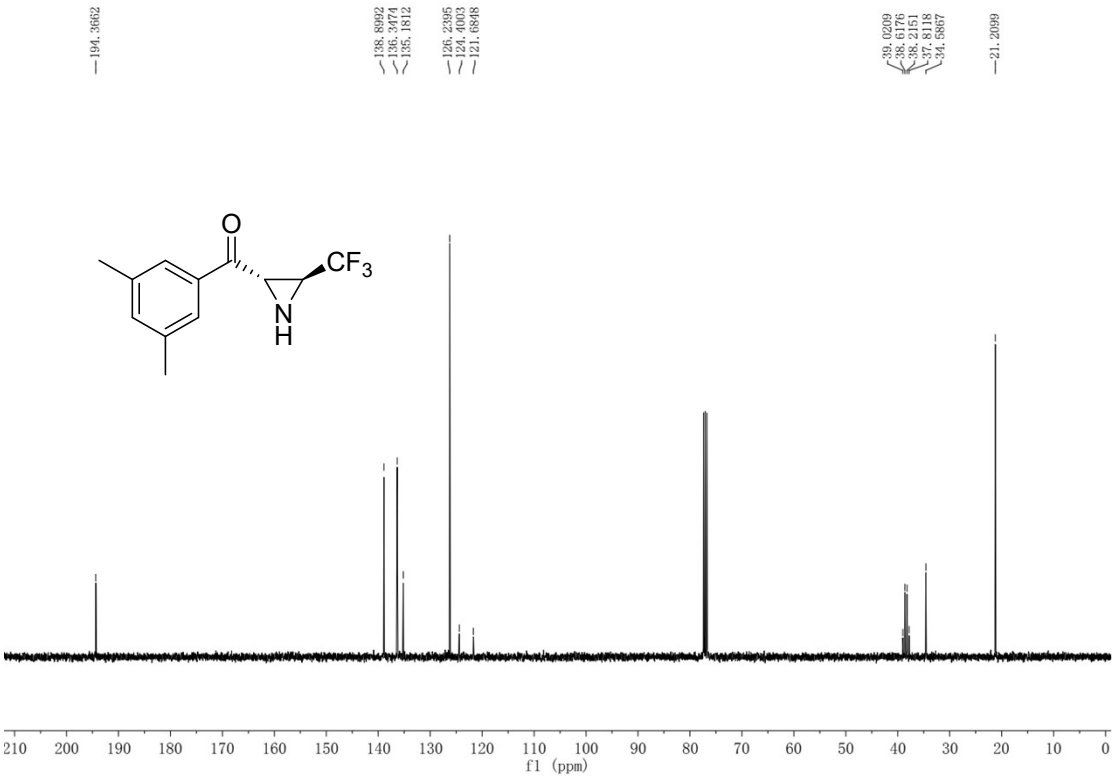
^{19}F NMR (376 MHz, $CDCl_3$) of **2m**:



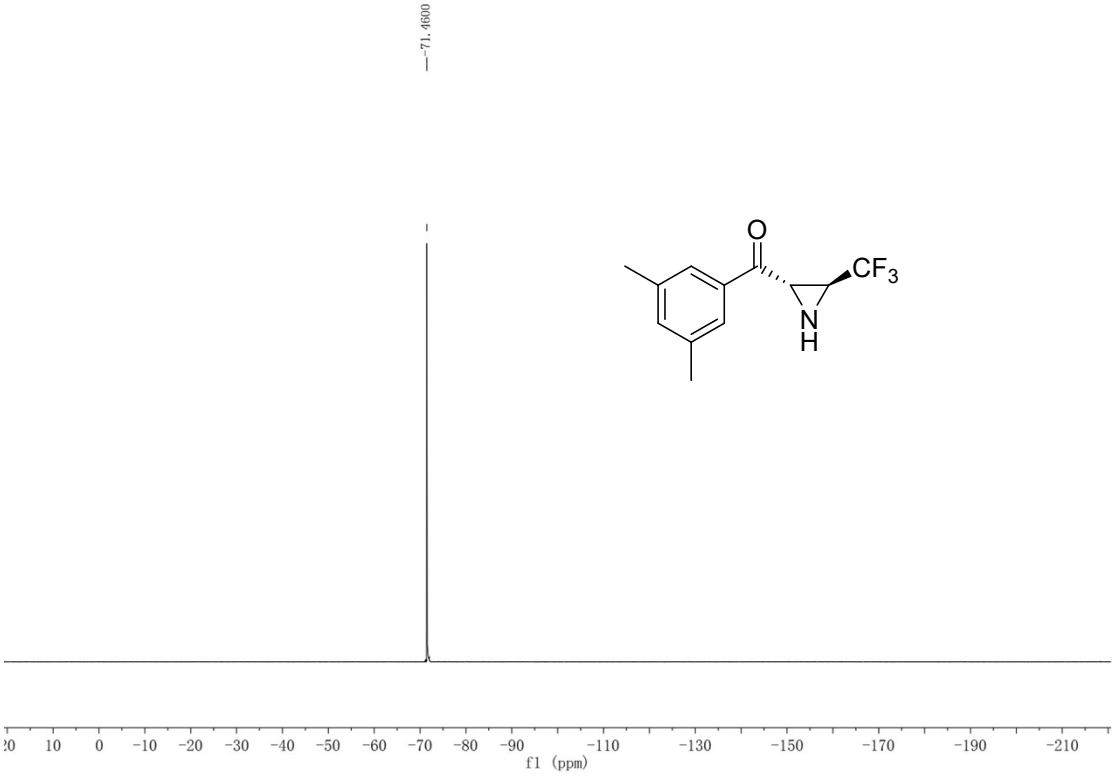
^{1}H NMR (400 MHz, $CDCl_3$) of **2n**:



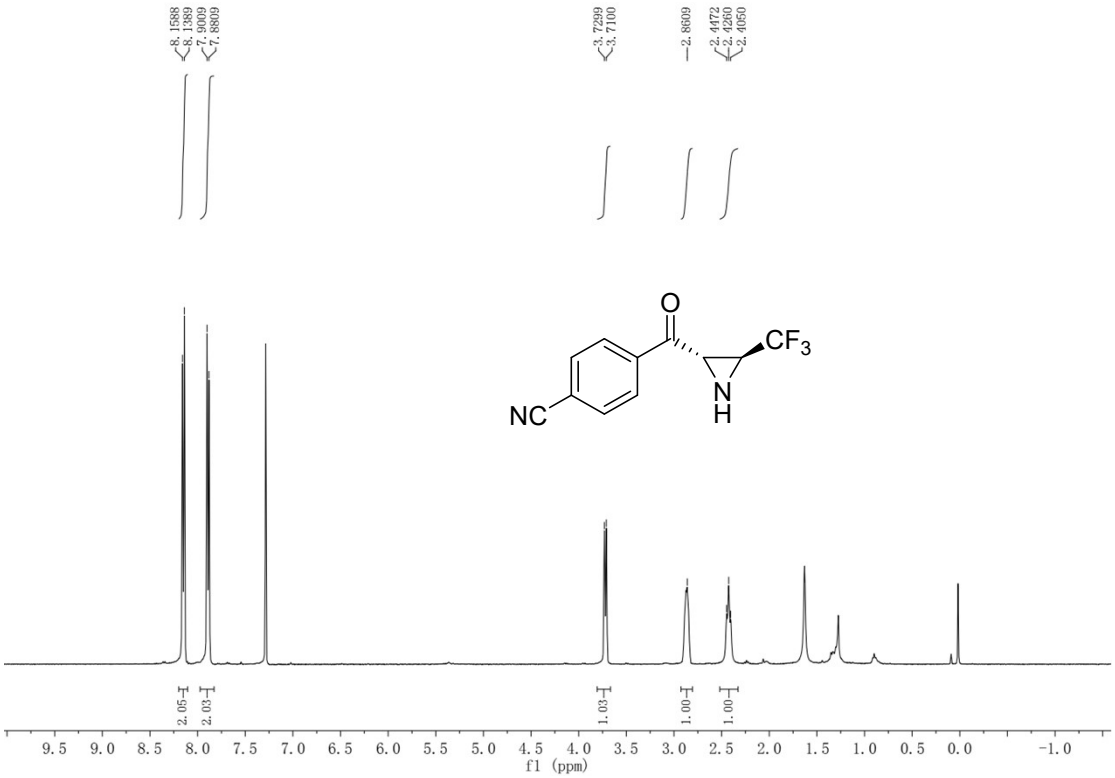
^{13}C NMR (100 MHz, $CDCl_3$) of **2n**:



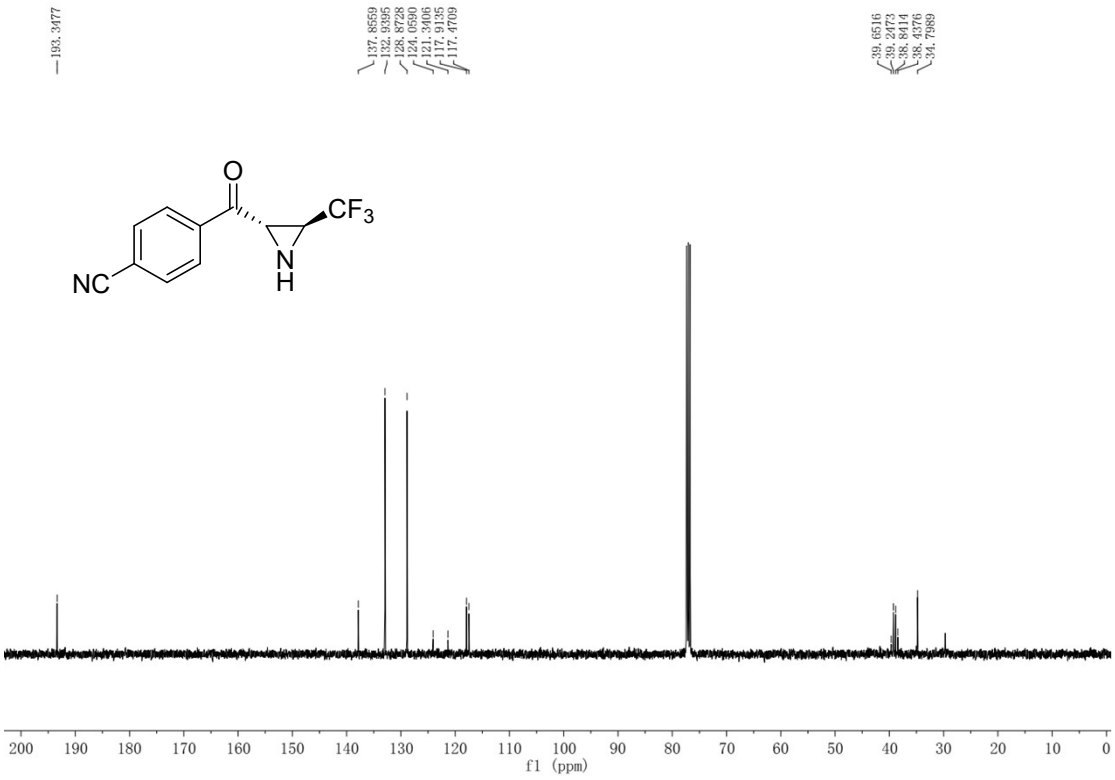
^{19}F NMR (376 MHz, $CDCl_3$) of **2n**:



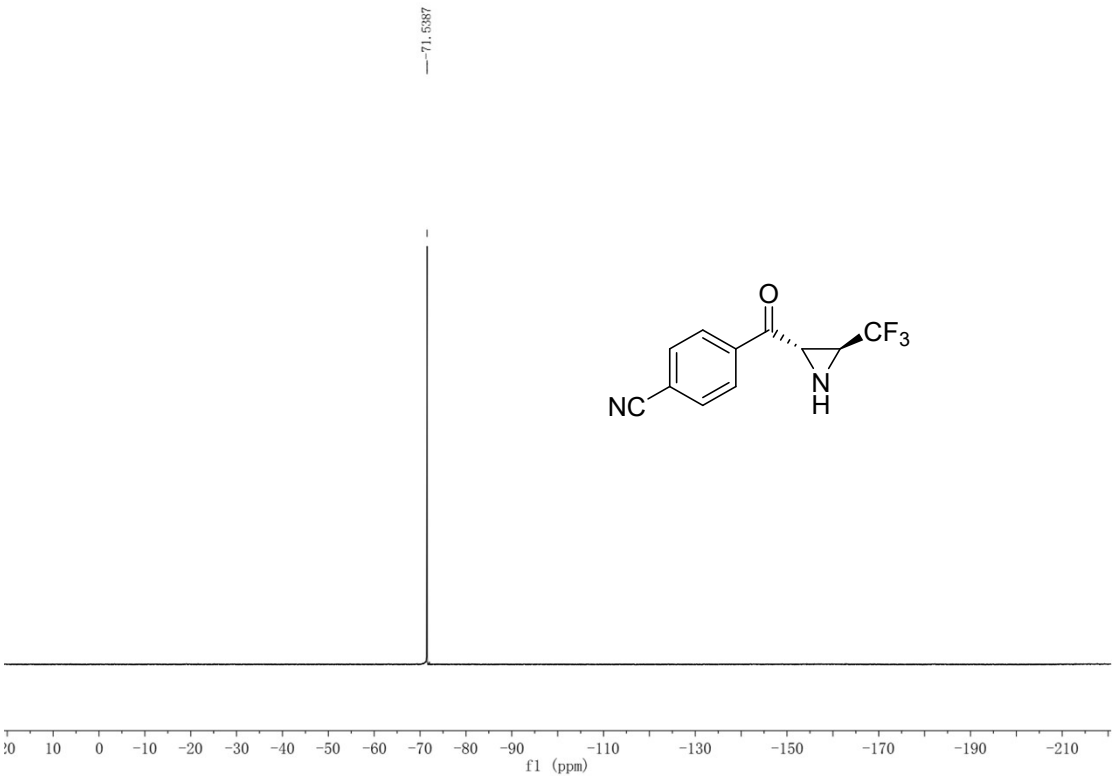
^{1}H NMR (400 MHz, $CDCl_3$) of **2o**:



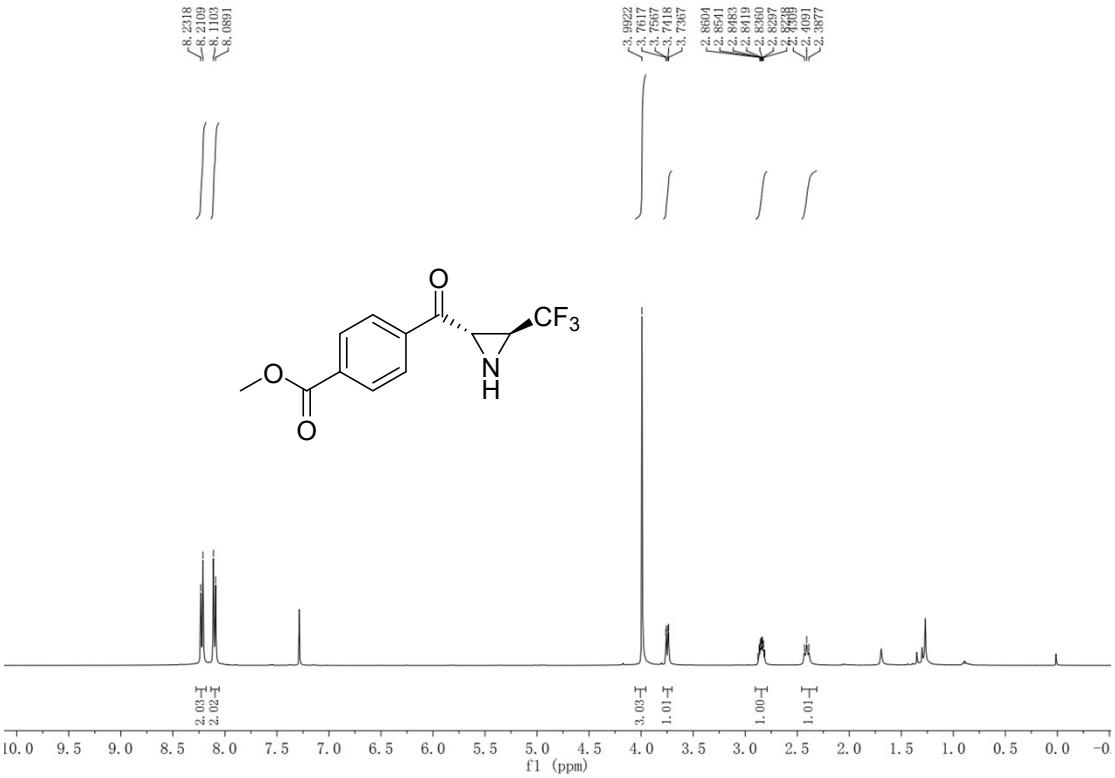
^{13}C NMR (100 MHz, $CDCl_3$) of **2o**:



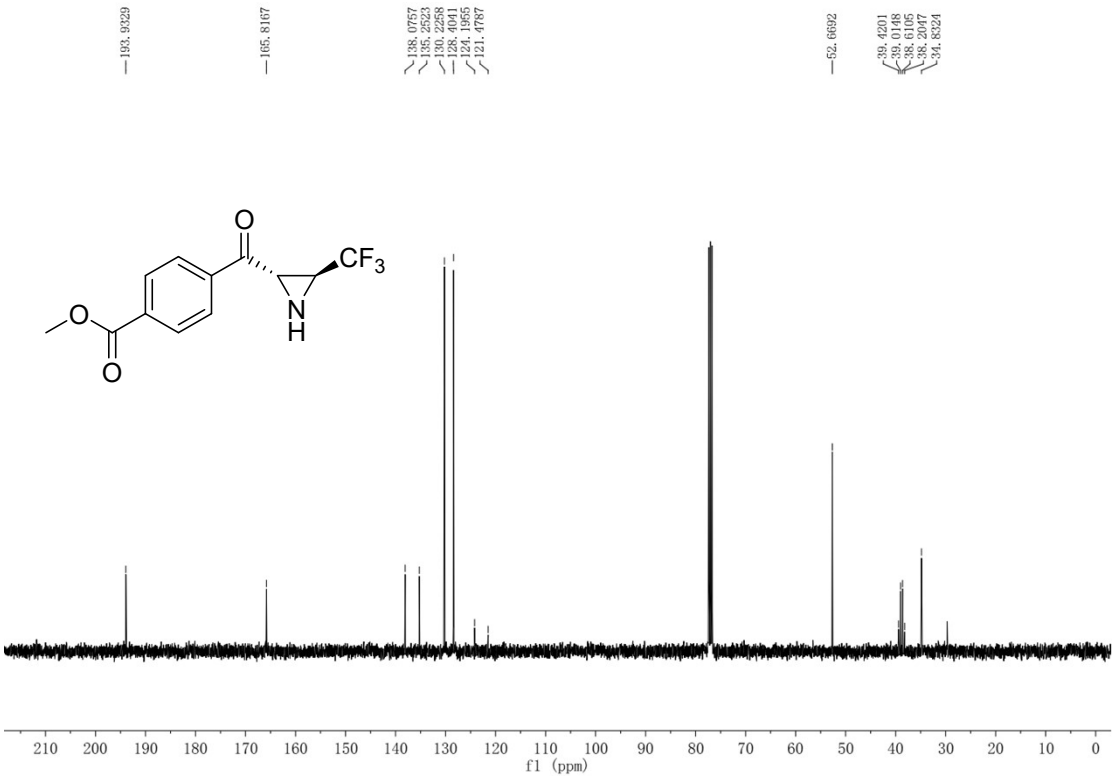
^{19}F NMR (376 MHz, $CDCl_3$) of **2o**:



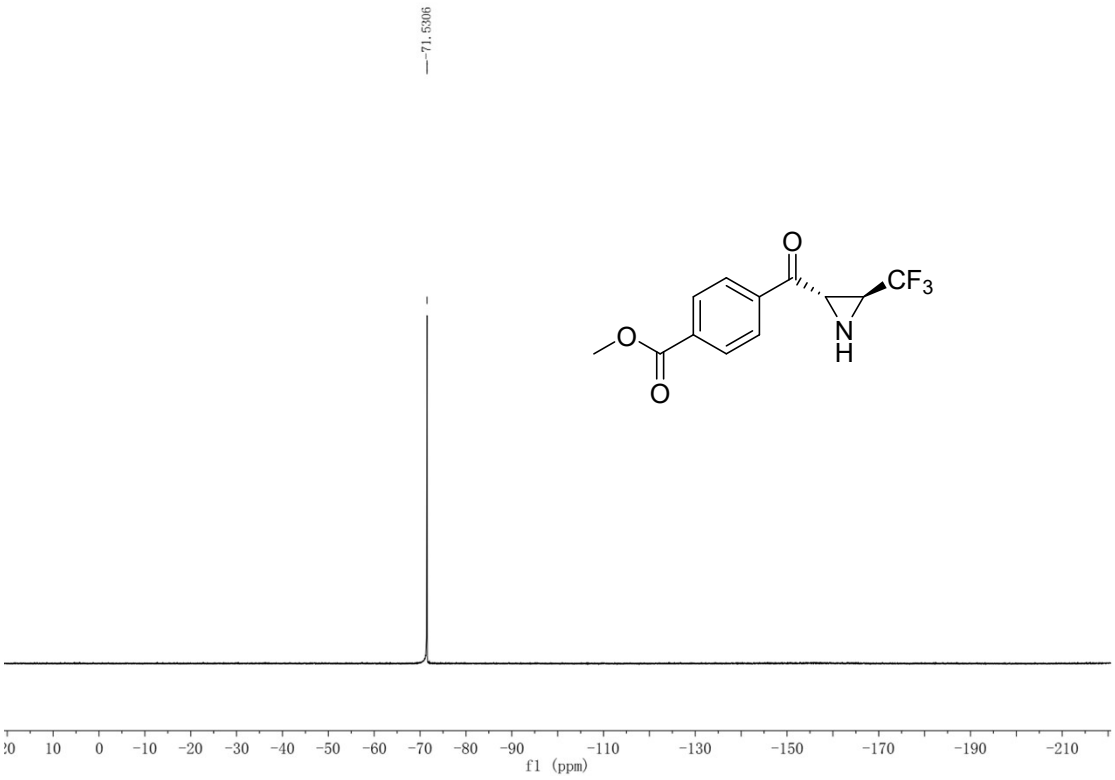
^{1}H NMR (400 MHz, $CDCl_3$) of **2p**:



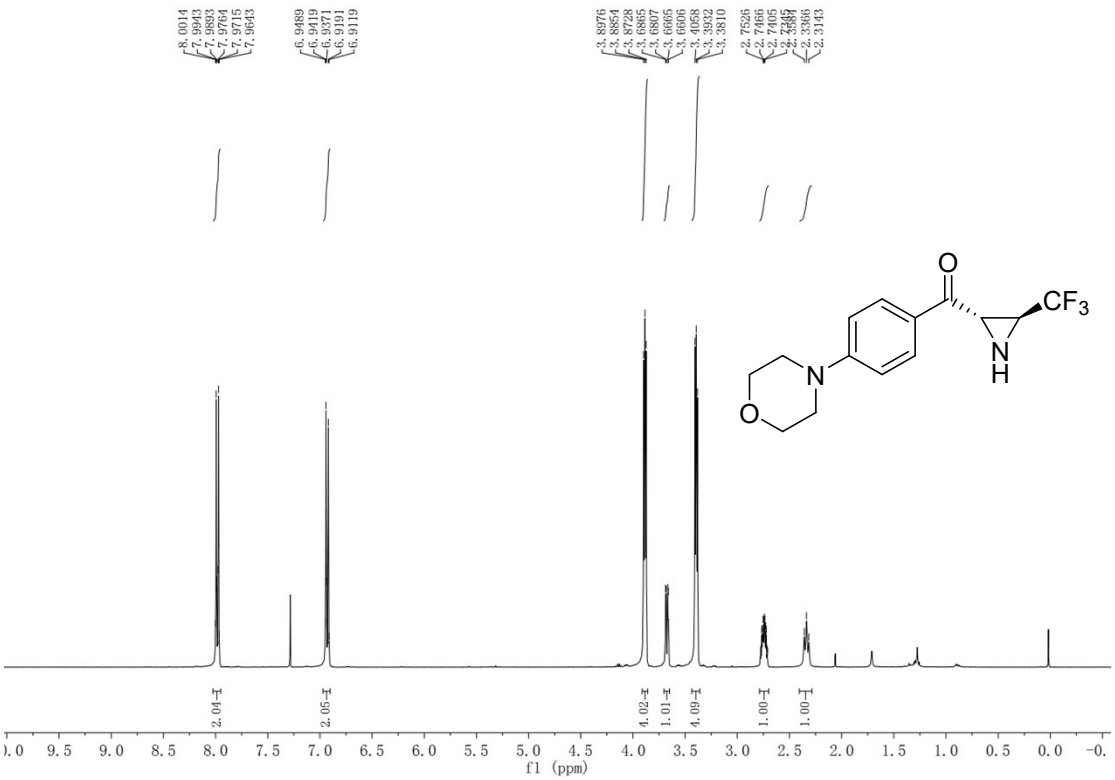
^{13}C NMR (100 MHz, $CDCl_3$) of **2p**:



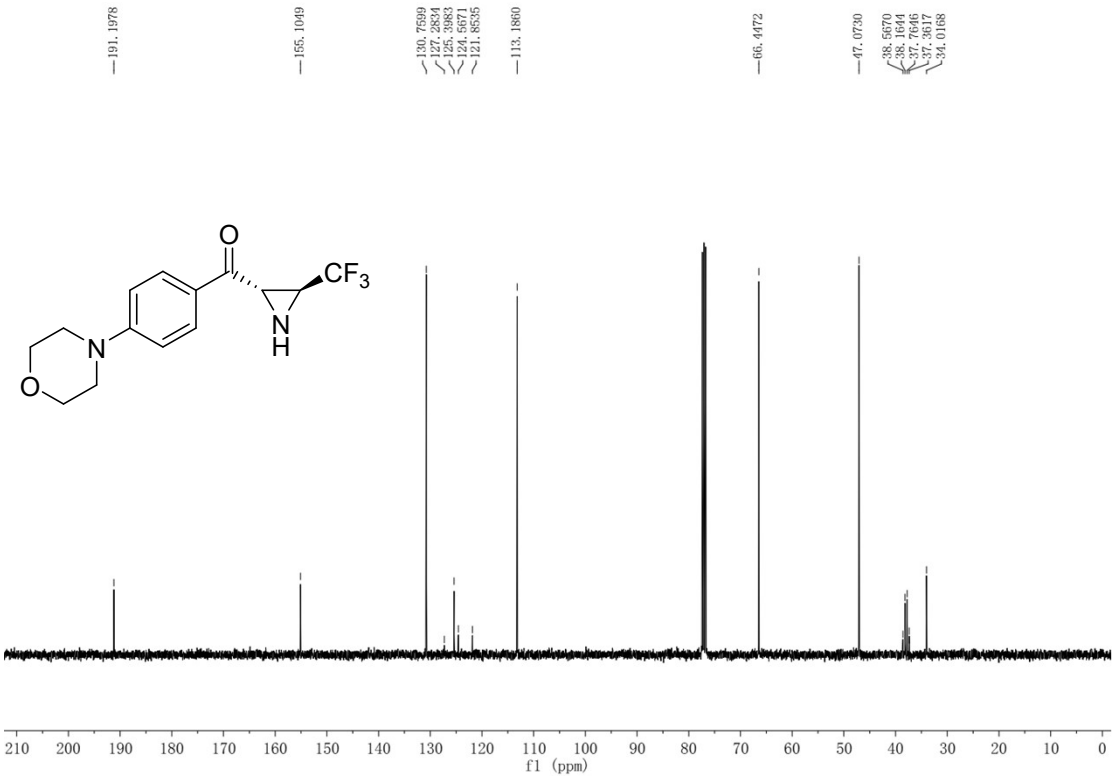
^{19}F NMR (376 MHz, $CDCl_3$) of **2p**:



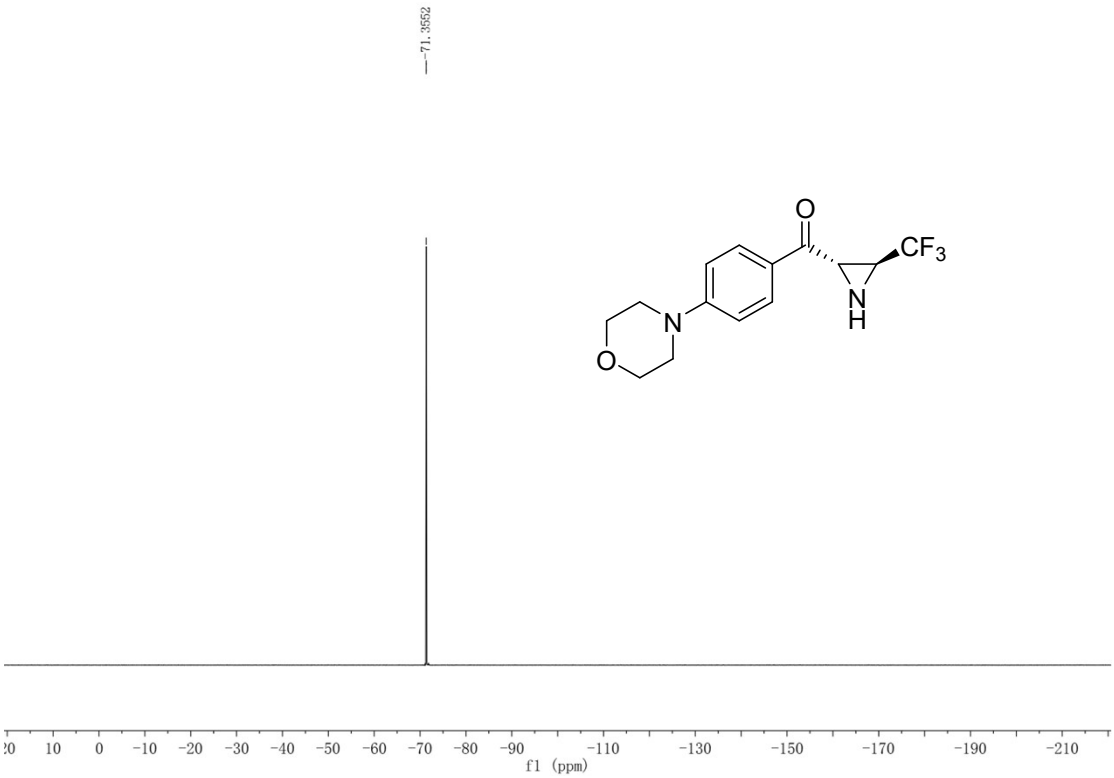
^{1}H NMR (400 MHz, $CDCl_3$) of **2q**:



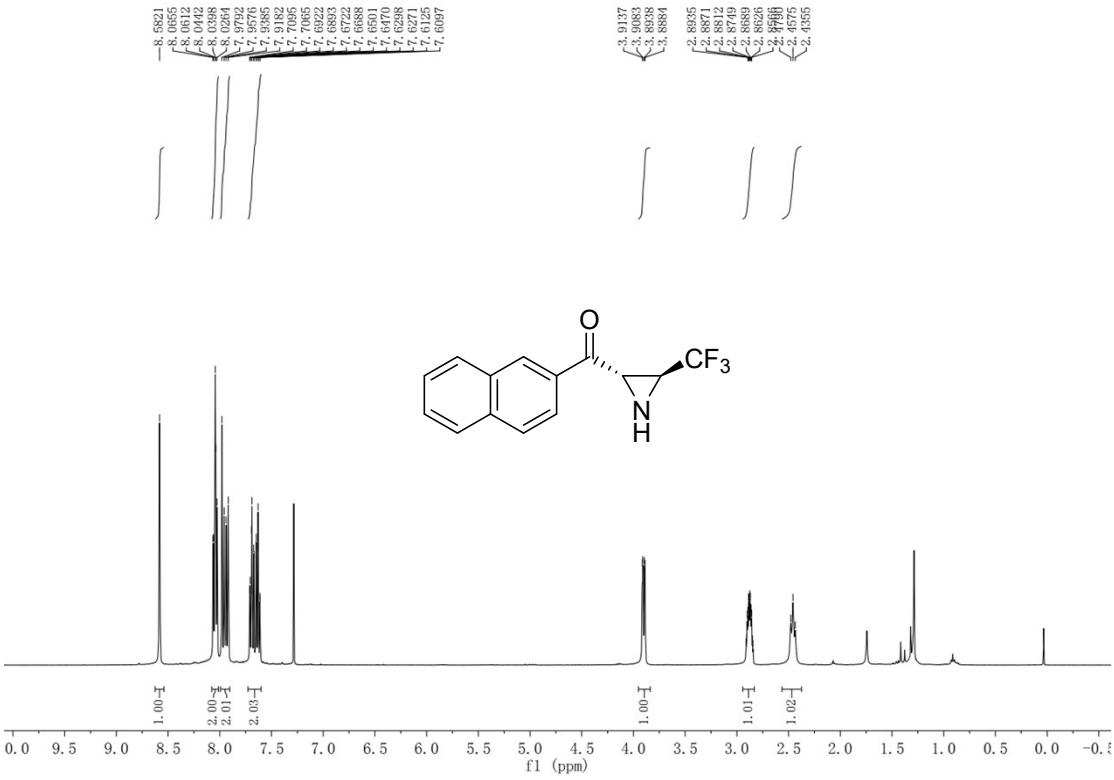
^{13}C NMR (100 MHz, $CDCl_3$) of **2q**:



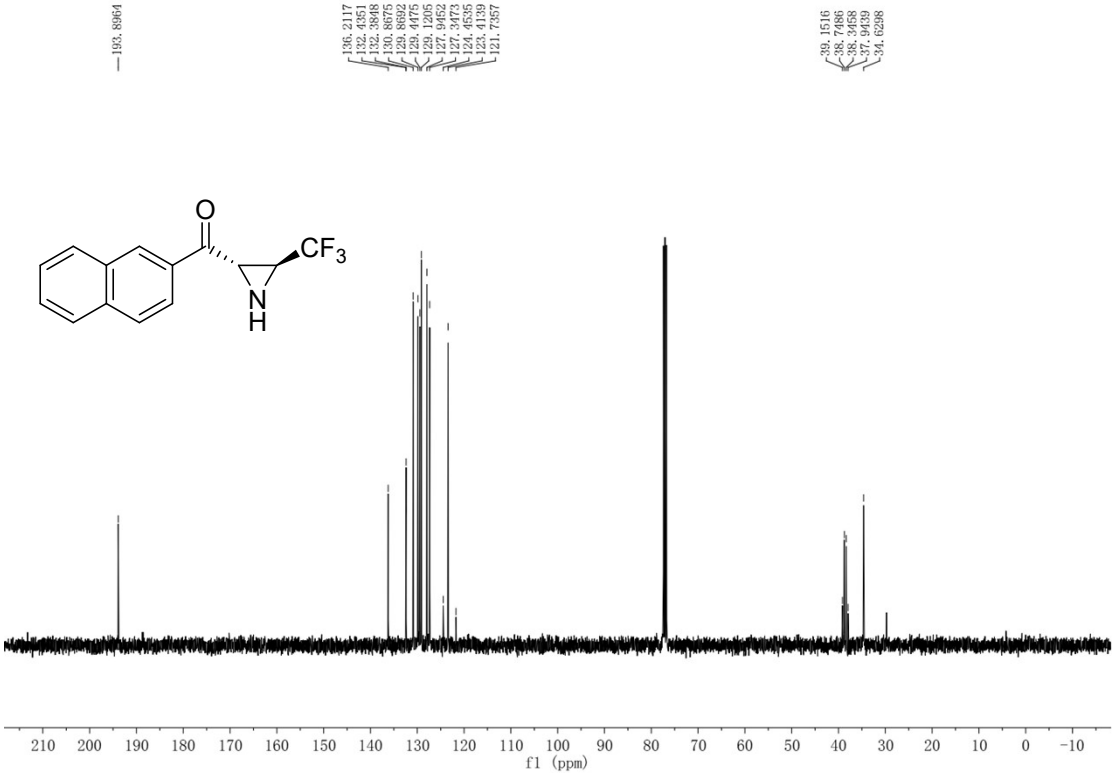
^{19}F NMR (376 MHz, $CDCl_3$) of **2q**:



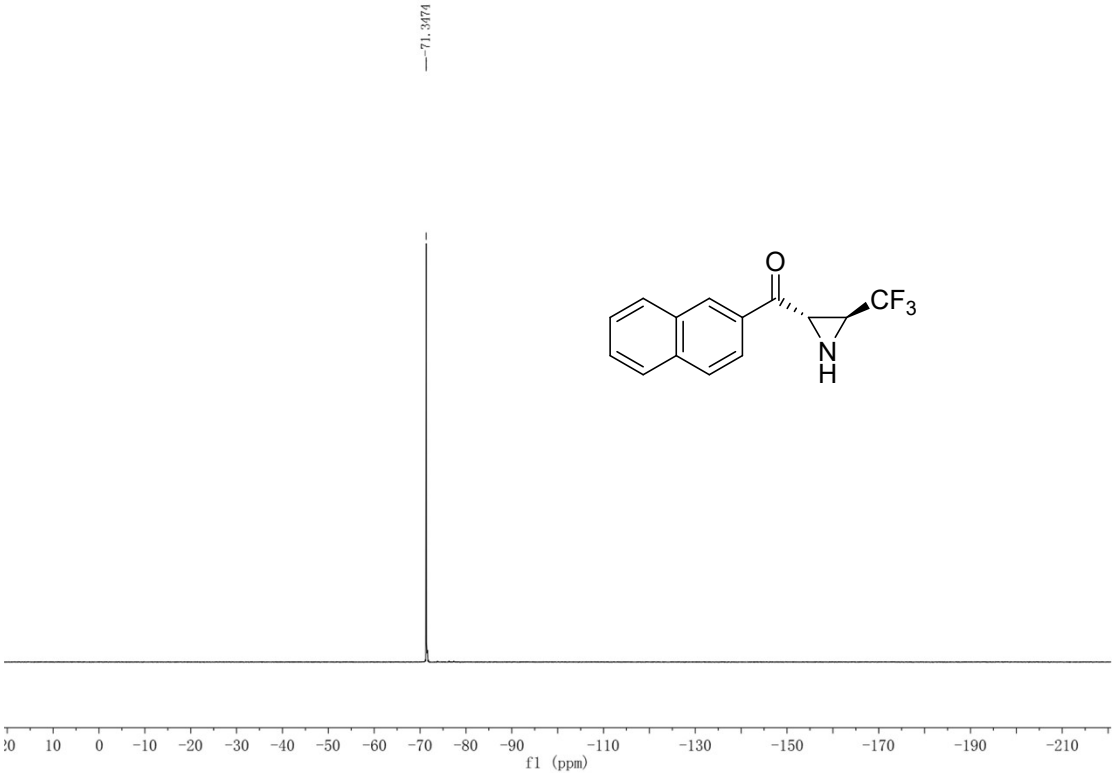
^{1}H NMR (400 MHz, $CDCl_3$) of **2r**:



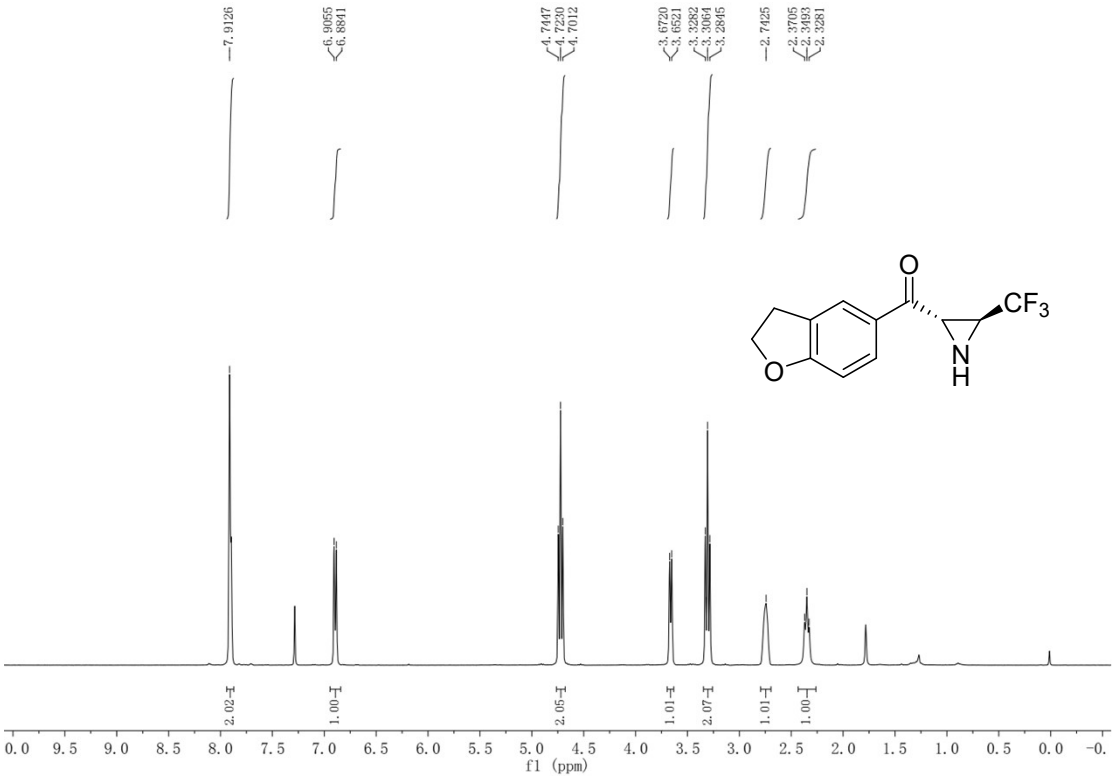
^{13}C NMR (100 MHz, $CDCl_3$) of **2r**:



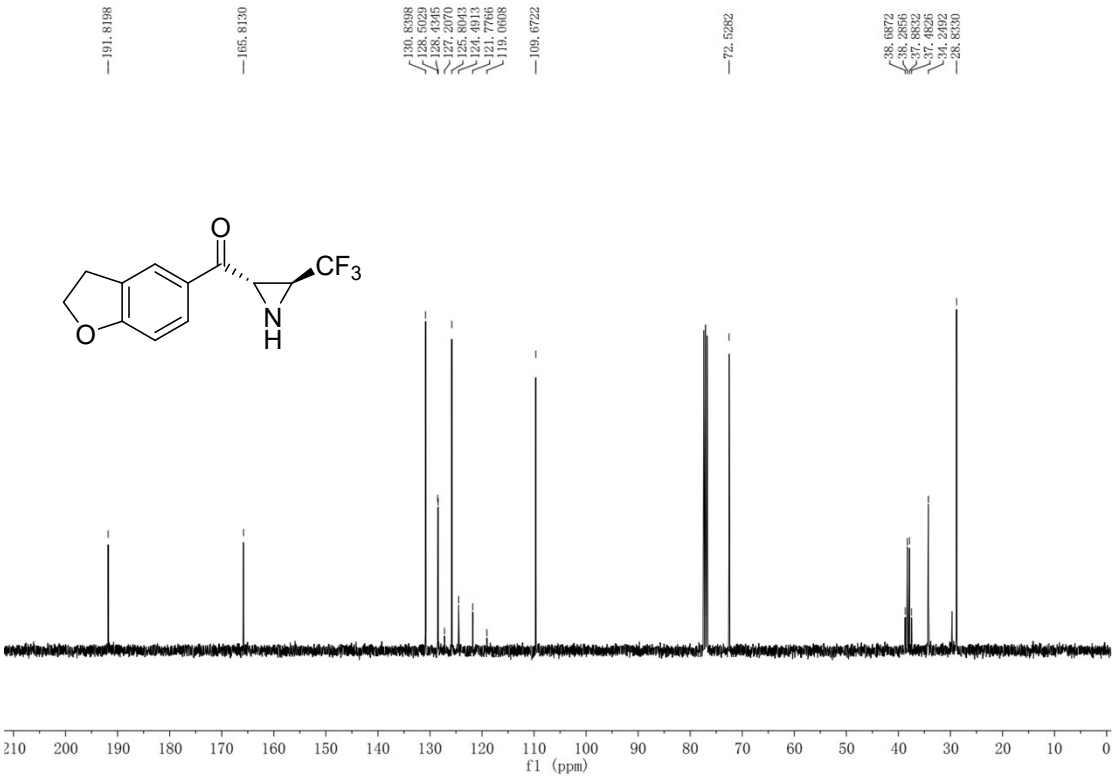
^{19}F NMR (376 MHz, $CDCl_3$) of **2r**:



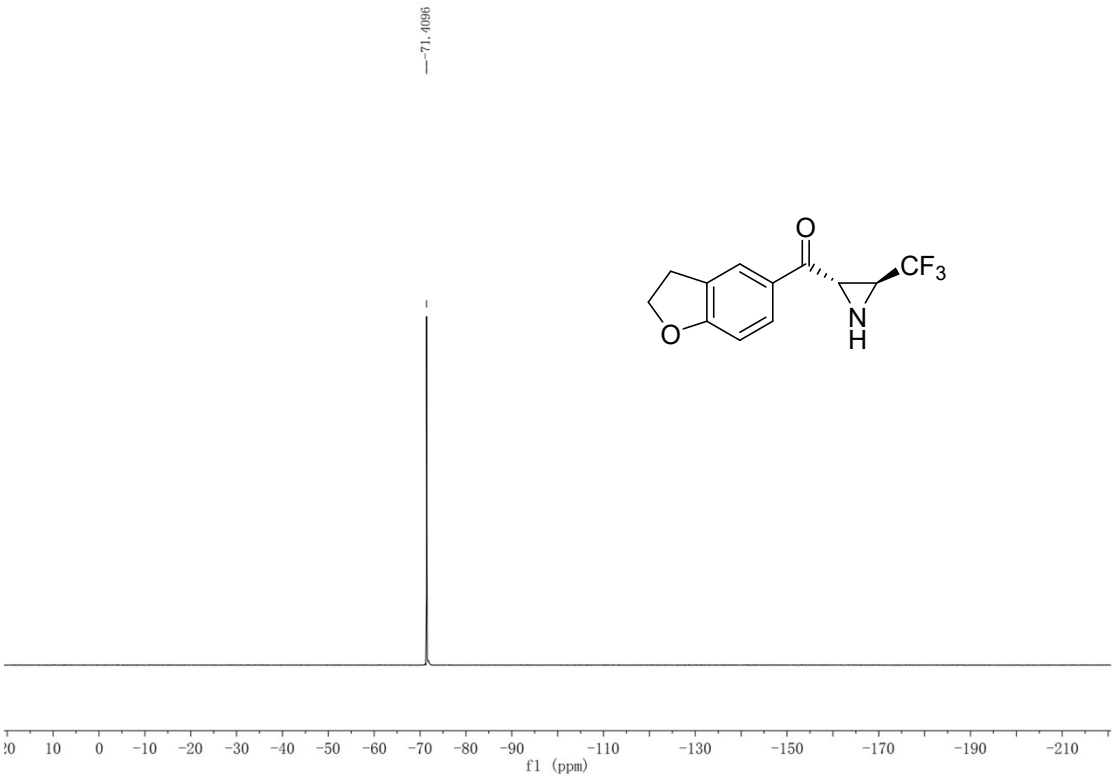
^{1}H NMR (400 MHz, $CDCl_3$) of **2s**:



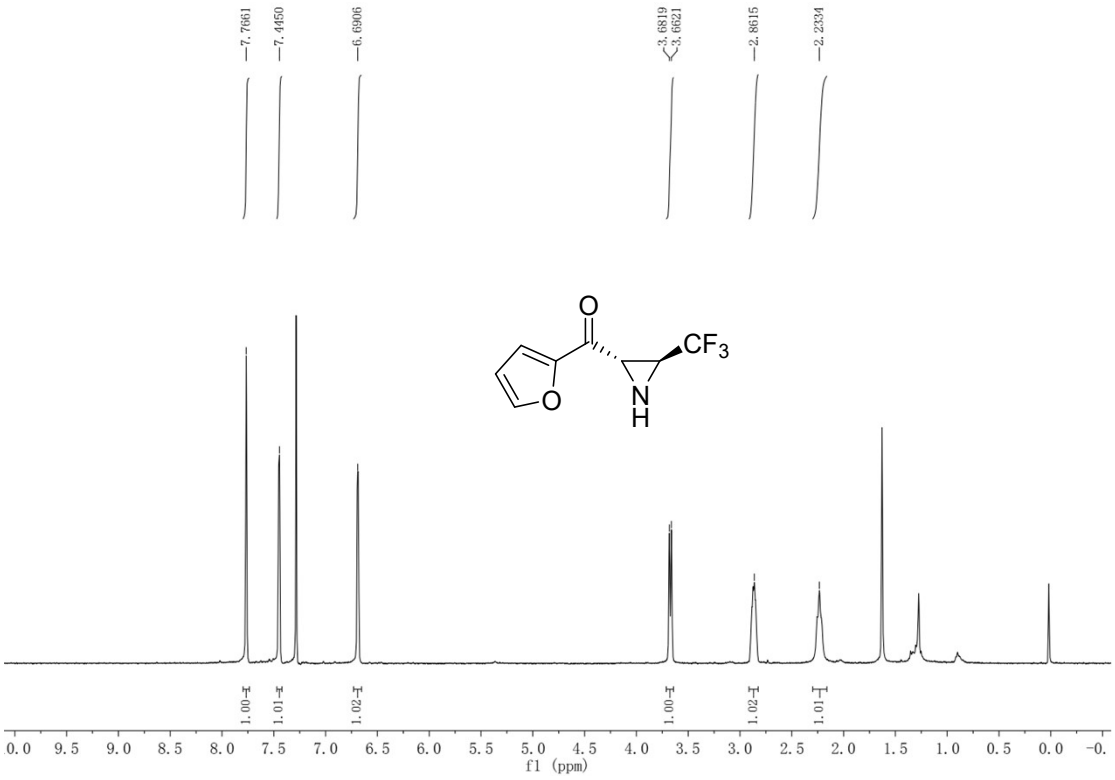
^{13}C NMR (100 MHz, $CDCl_3$) of **2s**:



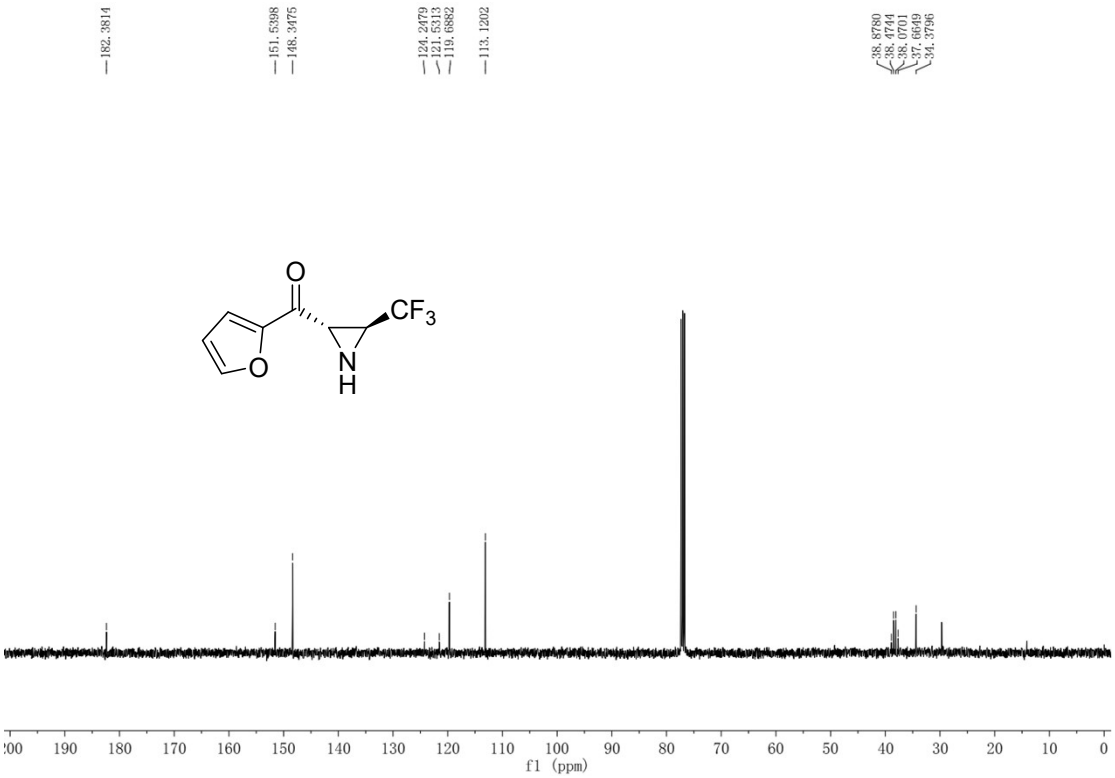
^{19}F NMR (376 MHz, $CDCl_3$) of **2s**:



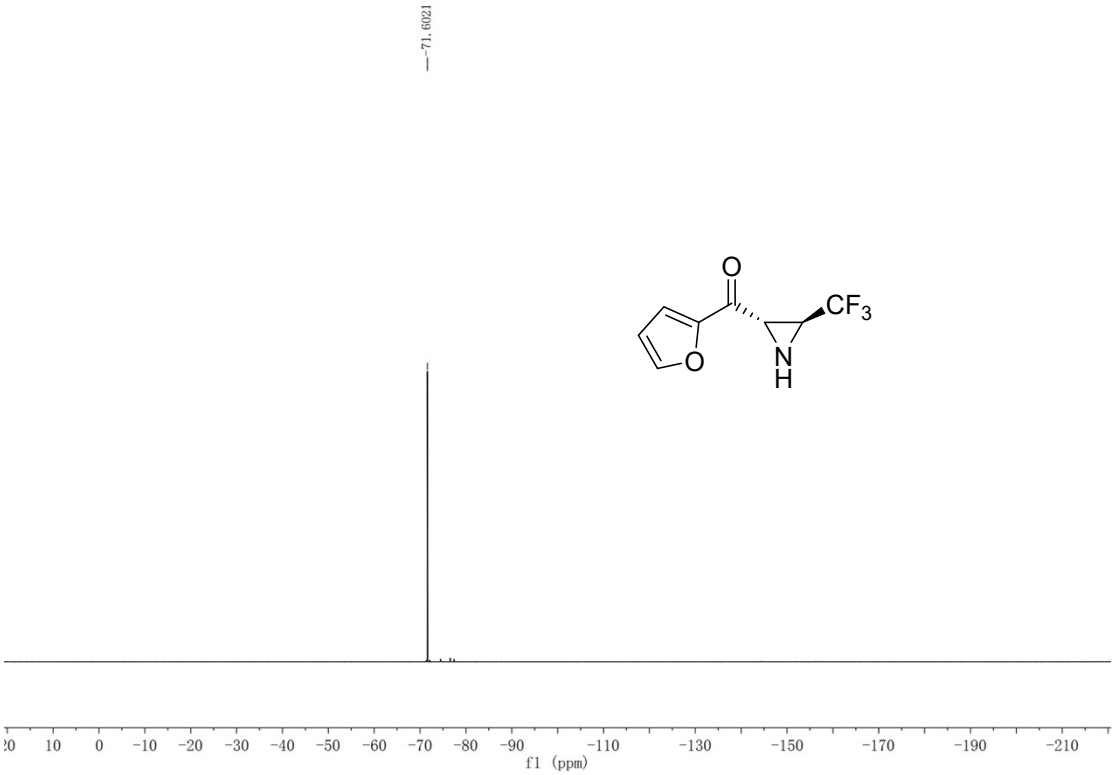
^{1}H NMR (400 MHz, $CDCl_3$) of **2t**:



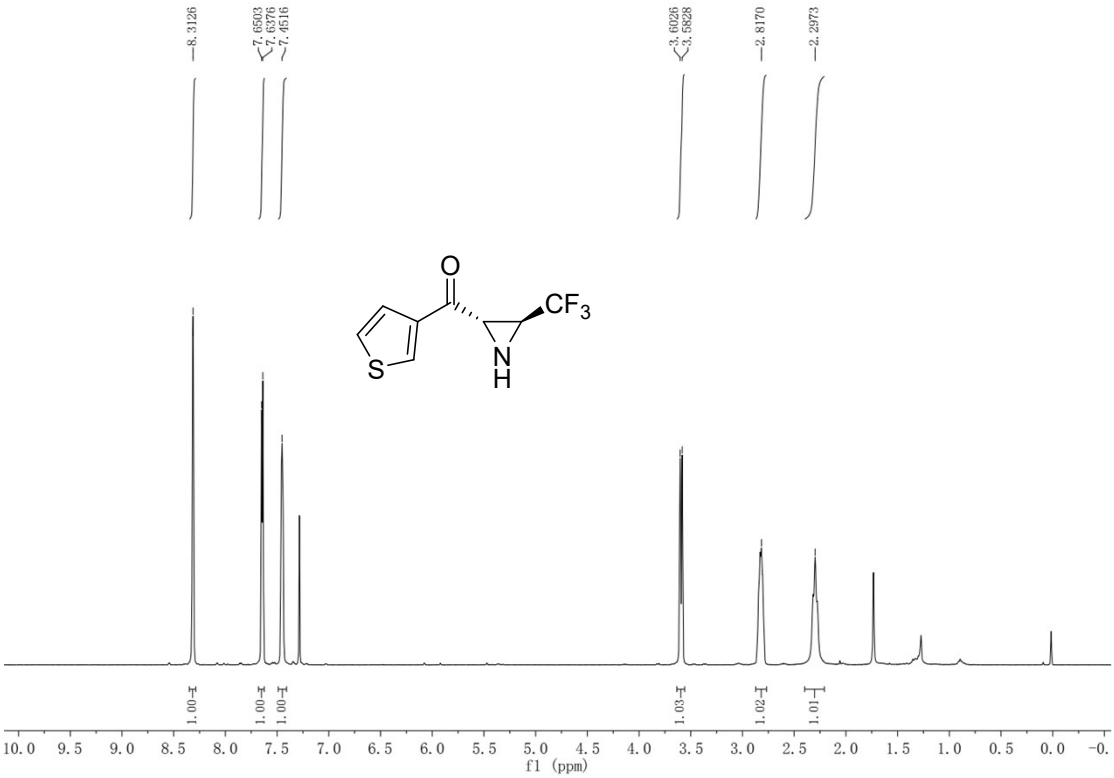
^{13}C NMR (100 MHz, $CDCl_3$) of **2t**:



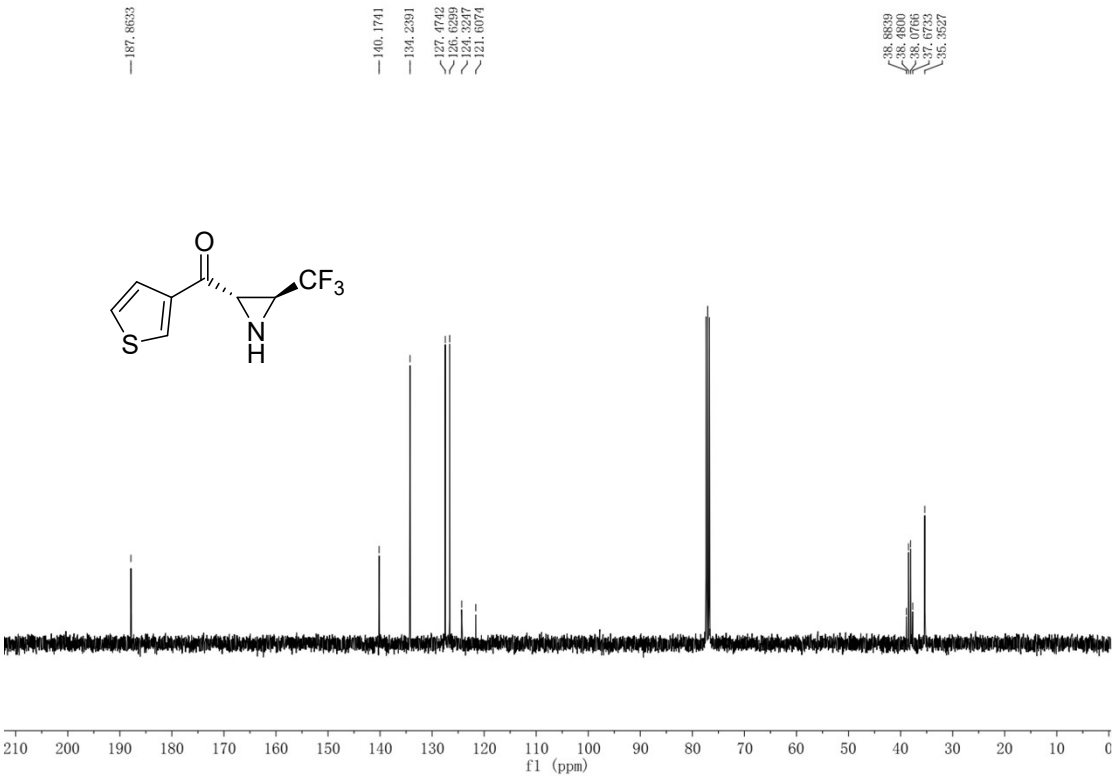
^{19}F NMR (376 MHz, $CDCl_3$) of **2t**:



^{1}H NMR (400 MHz, $CDCl_3$) of **2u**:



^{13}C NMR (100 MHz, $CDCl_3$) of **2u**:



^{19}F NMR (376 MHz, $CDCl_3$) of **2u**: