A dual-radical process for tri/di-fluoromethylarylation of alkenes enabled by indirect electroreduction

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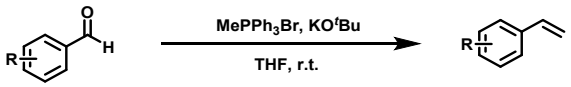
General experimental information

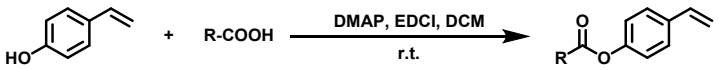
All reactions were carried out in dried sealed Schlenk tubes with magnetic stirring under a nitrogen atmosphere. The instrument for electrolysis is DC POWER SUPPLY (DP3005B)(made in China). Unless otherwise noted, all chemicals and solvents used in the experiments were obtained from commercial sources and used directly without further treatment. All products were isolated by short chromatography on a silica gel (300-400 mesh) column using hexane and ethyl acetate. ^{1}H, ^{13}C and ^{19}F NMR spectra were recorded on a Bruker Advance 400 spectrometer at ambient temperature with $CDCl_3$ or DMSO-d_6 as solvent and tetramethylsilane (TMS) as the internal standard. The frequencies for ^{1}H, ^{13}C and ^{19}F NMR test are 400 MHz, 100 MHz and 376 MHz respectively. Analyti rmed on Merk precoated TLC (silica gel 60 F254) p

Figure S1. The experimental setup for electrolysis

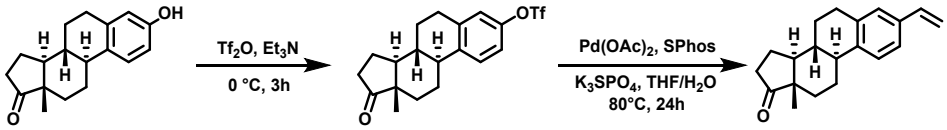
General procedures for preparing alkenes



1am, 1an, 1ao, 1aq[1] An oven-dried round bottom flask equipped with a stir bar, $MePPh_3Br$ (5.71 g, 16 mmol, 1.6 equiv.), potassium tert-butoxide (1.79 g, 16 mmol, 1.6 equiv.) were placed in the flask. And then the flask was flushed with nitrogen before dry THF (20 mL) was added. After stirring for 30 mins, aldehydes (2.08 g, 10 mmol, 1.0 equiv.) were added. The reaction was allowed to stir at room temperature overnight before being diluted with hexane (30 mL) and filtered through celite. The crude was purified with hexane and obtained as a white solid (1.50 g, 73%).

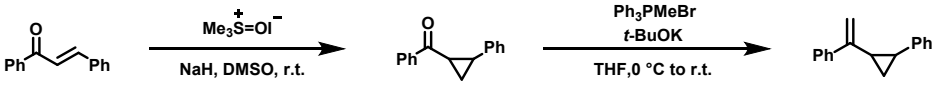


1aw, 1ax, 1ay[2] Carboxylic acid compound (1.0 mmol), a hydroxyl compound (1.02 mmol), 1-(3-dimethylaminopropyl)-3-ethylcarbodiimide hydrochloride (287.6 mg, 1.5 mmol), and DMAP (2.5 mg, 0.02 mmol) were dissolved in CH_2Cl_2 (20.0 mL) was stirred at room temperature for 2.5 h. The reaction mixture was added to H_2O and extracted with CH_2Cl_2. The organic layers were washed with brine, dried over $MgSO_4$, filtered, concentrated in vacuo, and flash chromatographed to afford the product.



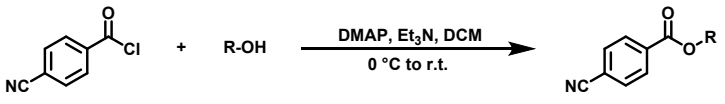
1az[1] An oven dried Schlenk flask equipped with a magnetic stir bar, (+)-Estrone (2.70 g, 10.0 mmol, 1.0 equiv.), triethylamine (2.8 mL, 20.0 mmol, 2.0 equiv.) were dissolved in dry dichloromethane (30 mL) were added via syringe under argon. The mixture was cooled to 0 °C and triflic anhydride (1.9 mL, 11.0 mmol, 1.1 equiv.) was added dropwise via syringe. The reaction mixture was stirred for 2 h at 0 °C before it was poured into an aqueous saturated solution of $NaHCO_3$. The biphasic mixture was extracted with dichloromethane (3 x 15 mL). The combined organic phases were dried over $MgSO_4$ and the solvent was removed *in vacuo*. The crude material was purified by column chromatography (cyclohexane: ethyl acetate = 4:1) to afford 3-(trifluoromethanesulfonyl)estrone as a white solid. A Schlenk flask was charged with 3-(trifluoromethanesulfonyl)estrone (1.94 g, 5.0 mmol, 1.0 equiv.), SPhos (240 mg, 0.56 mmol, 0.1 equiv.), K_3PO_4 (3.19 g, 15.0 mmol, 3.0 equiv.), 4,4,5,5-tetramethyl-2-vinyl-1,3,2-dioxaborolane (1.7 mL, 10.0 mmol, 2.0 equiv.), 1,4-dioxane (30

mL) and water (5 mL). The reaction vessel was sealed with a septum, evacuated and refilled with argon (cycle 3 times). $Pd(OAc)_2$ (56 mg, 0.24 mmol, 5 mol%) was added under a flow of argon and the reaction mixture was heated to 80 °C and stirred for 24 h. The reaction mixture was allowed to cool to ambient temperature and was subsequently diluted with ethyl acetate (3 x 10 mL). The mixture was filtered through a plug of silica. The organic phase was washed with brine (20 mL), dried over $MgSO_4$ and the solvent was removed *in vacuo*. The residue was purified by column chromatography (cyclohexane: ethyl acetate = 15:1) and the product (1.24 g, 4.6 mmol, 94%) was obtained as a white solid.



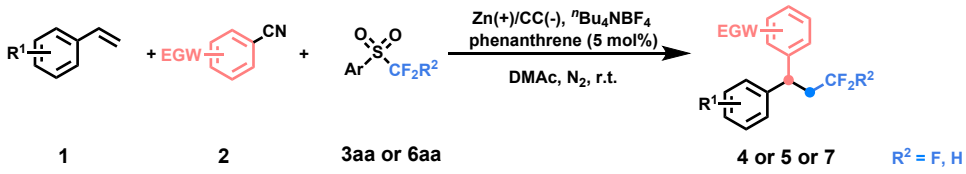
6[1] An oven-dried two-necked round flask equipped with a magnetic stir bar, sodium hydride (0.40 g, 60% in mineral oil, 10 mmol, 1.0 equiv.) was placed in flask. Then dry DMSO and trimethylsulfoxonium iodide (2.64 g, 12 mmol, 1.2 equiv.) were added to the flask at room temperature under an N_2 atmosphere. After hydrogen evolution ceased, the reaction mixture was stirred for an additional 15 mins, during which time the solution became clear. Chalcone (2.08 g, 10 mmol, 1.0 equiv.) was then added in one portion to the clear solution. The reaction solution was stirred at room temperature for 5 h. After completion of the reaction (TLC), the reaction was quenched with ice-cold water and the mixture was diluted with ethyl acetate. The combined organic layer was washed with brine, dried over Na_2SO_4. The product was purified by flash silica gel column chromatography using (petroleum ether/ethyl acetate) as eluent to afford the cyclopropyl ketone product. Then, to an oven dried flask, methyl triphenylphosphonium bromide (4.28 g, 12.0 mmol, 1.2 equiv.) and THF (30 mL) were added. The suspension was cooled to 0 ℃, *t*-BuOK (1.34 g, 12.0 mmol, 1.2 equiv.) was added and the resulting yellow suspension was stirred at 0 ℃ for 1 hour. To this suspension, the solution of the corresponding ketone (2.22 g, 10.0 mmol, 1.0 equiv.) in THF (10 mL) was added slowly and the resulting mixture was warmed gradually to room temperature and stirred at room temperature for 18 hours. The reaction mixture was concentrated under reduced pressure and filtered over celite. The filtrate was concentrated under reduced pressure and purified by column chromatography to afford the desired product.

General procedures for preparing cyanoarenes



2bd, 2be[3] In an oven dried Schlenk flask equipped with a magnetic stir bar, the 4-cyanobenzoyl chloride (827.9 mg, 5.0 mmol, 1.0 equiv.) and 4-Dimethylaminopyridine (122.2 mg, 1.0 mmol, 0.1 equiv.) were dissolved in anhydrous CH_2Cl_2 (10 mL) under nitrogen atmosphere and the resulting mixture was cooled to 0 °C (ice-water bath). Then, the ROH (6.0 mmol, 1.2 equiv.) dissolved in CH_2Cl_2 (5 mL) was added dropwise followed by the slow addition of triethylamine (607.1 mg, 6.0 mmol, 1.2 equiv.). After completion of the addition, the ice bath was removed and the reaction was stirred for 5 hours. The solution was transferred into a separatory funnel and sequentially washed with H_2O, 1 M NaOH and saturated brine solution. The organic phase was dried over Na_2SO_4, concentrated under reduced pressure. The crude product was purified by chromatography (petroleum ether/ethyl acetate = 10:1) to give the compound as a white solid.

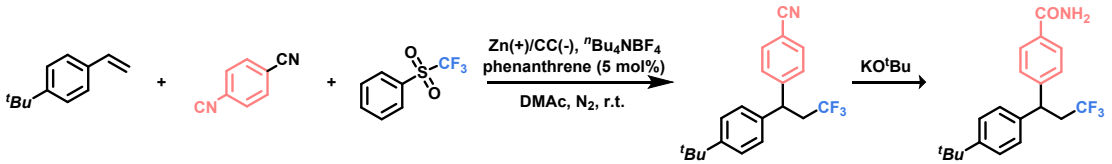
General procedure for the synthesis of 4 or 5 or 7



1 **2** **3aa or 6aa** **4 or 5 or 7** R^2 = F, H

Prepare a 1 × 2.5 cm carbon cloth and a 1 × 2.5 cm zinc sheet to fabricate the electrode. A mixture of alkenes (1.5 mmol, 5.0 equiv.), cyanoarenes (0.3 mmol, 1.0 equiv.), fluoroalkyl sulfones (0.6 mmol, 2.0 equiv.), phenanthrene (5 mol%), ^{n}Bu$_4$NBF$_4$ (0.15 mmol, 0.5 equiv.) in 5 mL dry DMAc was added to an Schlenk tubes (50 mL). The solution was electrolyzed at ambient temperature under a constant current (8 mA) in an N_2-protected environment for 7 h. After the completion of the reaction, the solvent was removed. The residue was subjected to silica gel column chromatography to obtain pure products by using mixed petroleum ether and ethyl acetate (PE: EA = 50: 1) as an eluent.

Scale-up experiment and further derivatization.

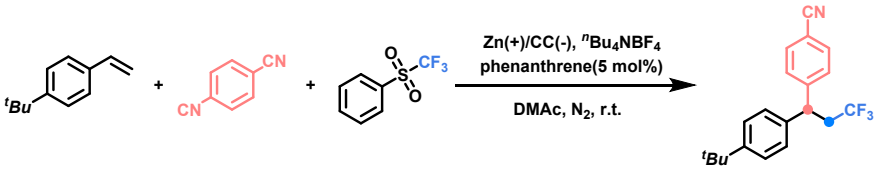


1aa, 30 mmol **2aa**, 6 mmol **3aa**, 9 mmol **4aa**, 1.59g, 79% **8**, 77%

Prepare a 2 × 5 cm carbon cloth and a 2 × 5 cm zinc sheet to fabricate the electrode. A mixture of **1aa** (30mmol, 5.0 equiv.), **2aa** (6 mmol, 1.0 equiv.), **3aa** (12 mmol, 2.0 equiv.), phenanthrene (5 mol%), ^{n}Bu$_4$NBF$_4$ (2.1 mmol, 0.35 equiv.) in 100 mL dry DMAc was added to a two-neck flask (250 mL) with a magnetic stir bar. The solution was electrolyzed under nitrogen atmosphere at room temperature, applying a constant current of 24 mA for 22 hours. After the completion of the reaction,

the solvent was removed. The residue was subjected to silica gel column chromatography to obtain pure products by using mixed petroleum ether and ethyl acetate (PE: EA = 50: 1) as an eluent. Then a two-neck flask with a magnetic stir bar was charged with **4aa** (4 mmol, 1.0 equiv.) and KO^{t}Bu (12 mmol, 3.0 equiv.), and dry tert-butyl alcohol (25 mL) was added. The reaction mixture was stirred at 30 ℃ for 12 h under nitrogen atmosphere, and the progress of the reaction was monitored by TLC. Upon completion, the crude residue was purified by flash column chromatography (PE: EA).

Optimized reaction conditions[a]:



1aa 2aa 3aa 4aa

Entry	electrode	electricity	solvent	3aa	Electrolyte	additives	Yield[b](%)
1	C(+)/C(-)	8 mA	MeCN (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	N.D.
2	C(+)/C(-)	8 mA	DMSO (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	N.D.
3	C(+)/C(-)	8 mA	DMF (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	N.D.
4	C(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	N.D.
5	C(+)/C(-)	8 mA	DMAc (5 mL)	CF_3SO_2Na	^{n}Bu$_4$NBF$_4$	None	N.D.
6	C(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	N.D.
7	C(+)/Ni(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	13
8	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	21
9	Fe(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	13
10	Mg(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	12
11	Al(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	13
12	Zn(+)/C(-)	6 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	16
13	Zn(+)/C(-)	10 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	20
14	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	^{n}Bu$_4$NBF$_4$	None	27
15	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	TBAB	None	19
16	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	TBAI	None	16
17	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	TBACl	None	15
18	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	$LiClO_4$	None	trace

19	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	$^{n}Bu_4NOAc$	None	13
20	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	Et_4NClO_4	None	15
21	Zn(+)/C(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	None	43
22	Zn(+)/C(-)	8 mA	DMAc (5 mL)	CF_3I	$^{n}Bu_4NBF_4$	None	26
23	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	None	56
24	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	Togni's reagent II	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	53
25	Zn(+)/C(-)	8 mA	DMAc (5 mL)	Togni's reagent II	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	43
27	Zn(+)/C(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	73
27	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	88
28	Zn(+)/CC(-)	8 mA	DMAc (6 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	85
29	Zn(+)/CC(-)	10 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	86
30	Zn(+)/CC(-)	6 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	63
31	Zn(+)/CC(-)	8 mA	DMAc (3 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	80
32	Zn(+)/CC(-)	8 mA	DMAc (7 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	85
31	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% dimethylterephthalate	59
32	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% 9,10-dicyanoanthracen	53
33	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% anthraquinone	55
34	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% anthracene	72
35	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	1 mol% phenanthrene	72
36	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	10 mol% phenanthrene	89
37	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	10 mol% phenanthrene	78
38	C(+)/Ni(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	10 mol% phenanthrene	35
39	Zn(+)/CC(-)	0 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	10 mol% phenanthrene	N.D.
40[c]	Zn(+)/CC(-)	8 mA	DMAc (5 mL)	$PhSO_2CF_3$	$^{n}Bu_4NBF_4$	5 mol% phenanthrene	trace

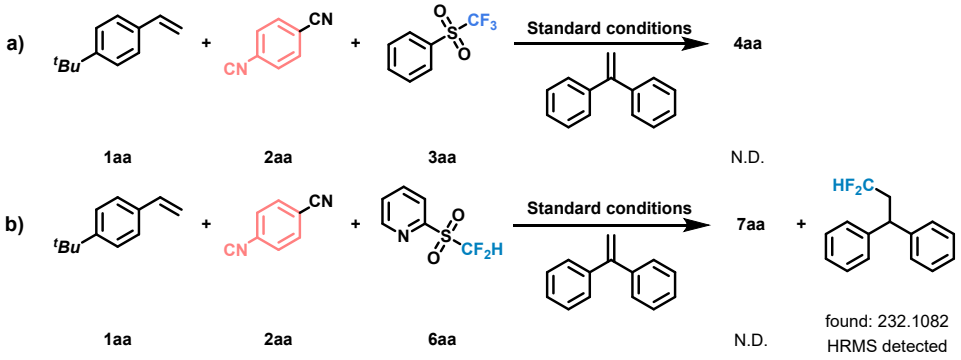
[a)] Reaction conditions: **1aa** (1.5 mmol), **2aa** (0.3 mmol), **3aa** (0.6 mmol), electrolyte (0.15 mmol), solvent, additives, N_2, constant current, 25 °C, undivided cell, 7 h, 6.9 F/mol of starting material **2aa**. [b)] The isolated yield is based on **2aa**. [c)] Under atmosphere.

Mechanistic stduies

To gain insight into the reaction mechanism, a series of experiments were conducted.

(a) Radical trapping experiments

First, products **4aa** and **7aa** were not obtained when the reaction was carried out in the presence of 1,1-diphenylethylene. Additionally, the difluoromethyl radical was captured and detected by HRMS; however, neither the aryl radical nor the trifluoromethyl radical was observed.



Scheme S1. Radical trapping experiments.

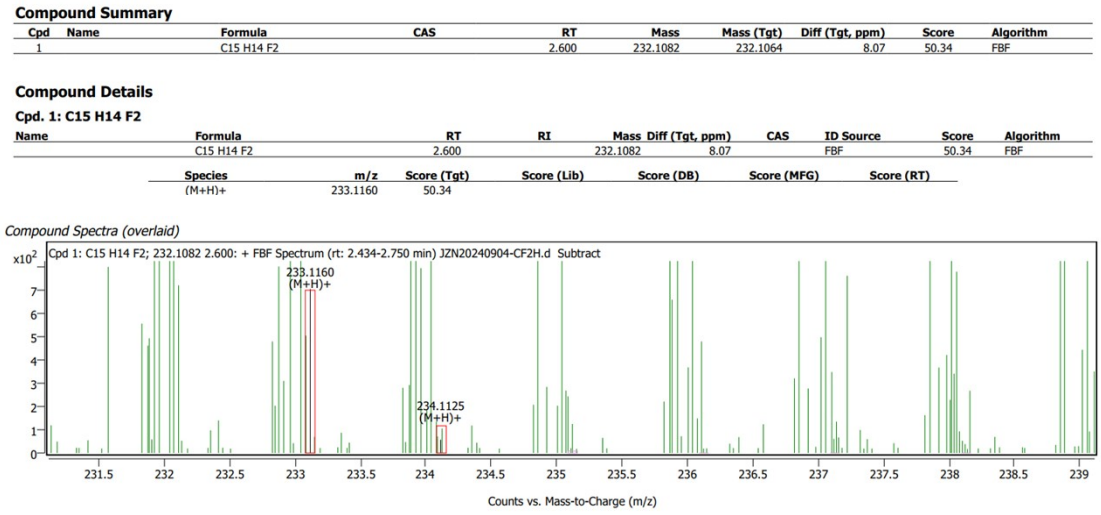
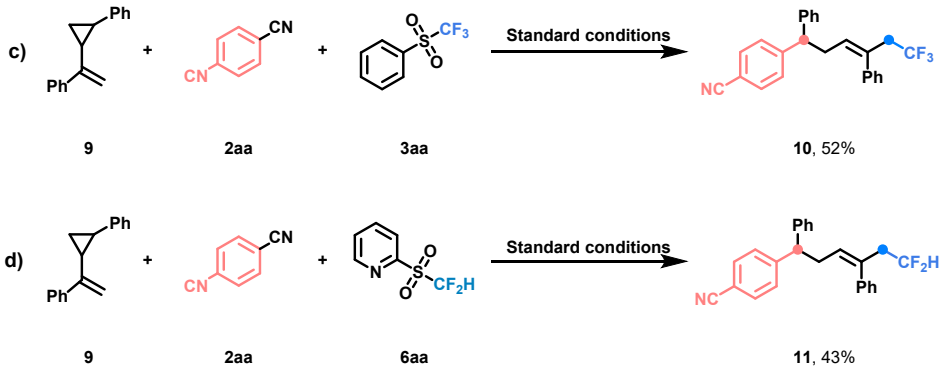


Figure S2. HRMS for radical trapping experiments

(b) Radical clock experiments

The radical clock experiments formed products **10** and **11**, which underwent a ring-opening process with 56 % and 43% yields, respectively.



Scheme S2. Radical clock experiments.

(c) Cyclic voltammetry (CV) experiments

The cyclic voltammetry (CV) experiments were conducted in a Schlenk tube containing the electrolyte (0.06 M $^{n}Bu_4NBF_4$ in DMAc, 2.5 mL) under a nitrogen atmosphere at room temperature. A three-electrode system was used, consisting of a glassy carbon working electrode (polished with 0.05 μm Al_2O_3 powder before measurements), a platinum wire counter electrode, and an Ag/Ag^+ reference electrode (stored in silver nitrate solution and activated before measurements). The relevant parameters were controlled by an electrochemical workstation CHI600E.

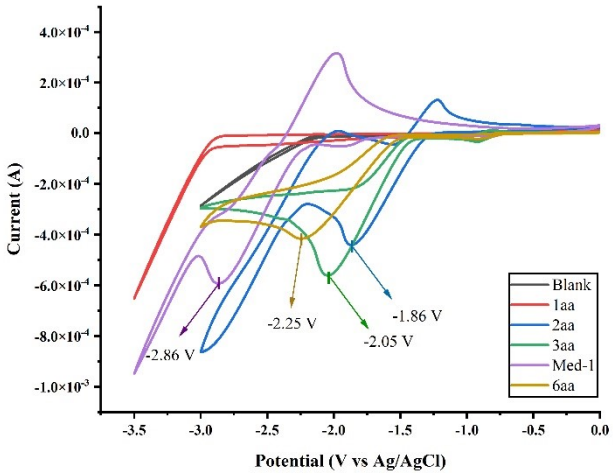


Figure S3. Cyclic voltammograms of reaction substrates. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **1aa** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **2aa** (0.06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); green line: **3aa** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); purple line: **Med-1** (0.06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). brown line: **6aa** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^+ as the counter and reference electrodes.

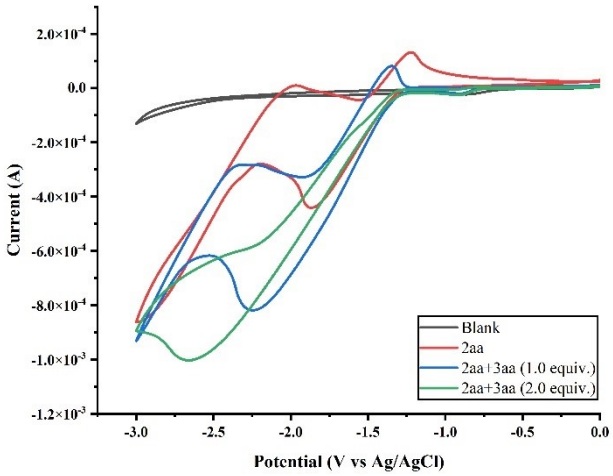


Figure S4. Cyclic voltammograms of **2aa and 3aa**. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **2aa** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **2aa** (0. 06 M), **3aa** (0.06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); green line: **2aa** (0. 06 M), **3aa** (0.12 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^{+} as the counter and reference electrodes.

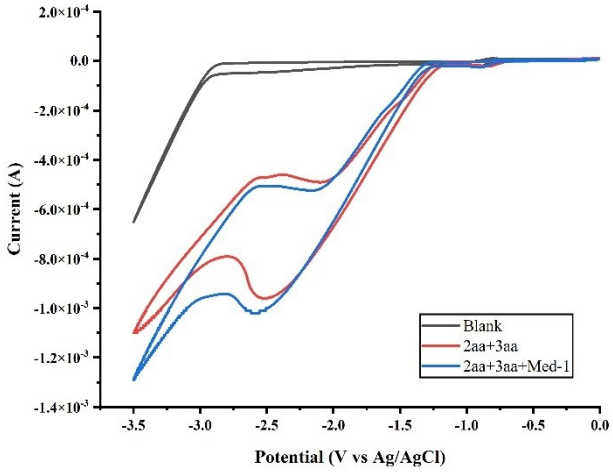


Figure S5. Cyclic voltammograms of **2aa and 3aa and Med-1**. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **2aa** (0. 06 M), **3aa** (0.12 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **2aa** (0. 06 M), **3aa** (0.12 M), **Med-1** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^{+} as the counter and reference electrodes.

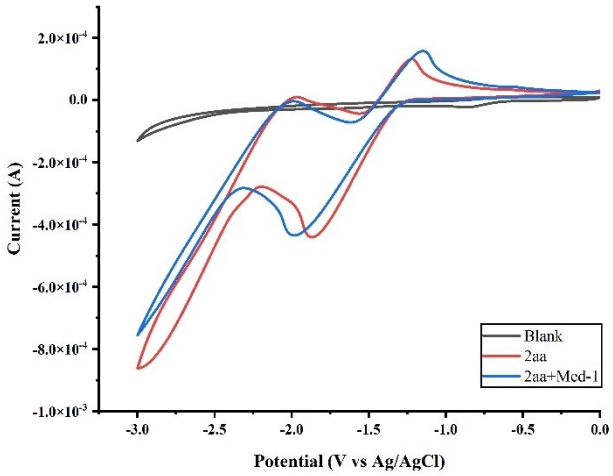


Figure S6. Cyclic voltammograms of **2aa** and **Med-1**. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **2aa** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **2aa** (0. 06 M), **Med-1** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^{+} as the counter and reference electrodes.

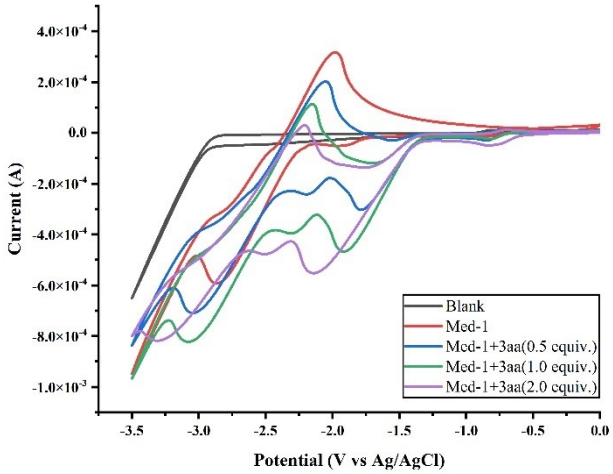


Figure S7. Cyclic voltammograms of **Med-1** and **3aa**. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **Med-1** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **Med-1** (0. 06 M), **3aa** (0.03 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); green line: **Med-1** (0. 06 M), **3aa** (0.06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); purple line: **Med-1** (0. 06 M), **3aa** (0.12 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^{+} as the counter and reference electrodes.

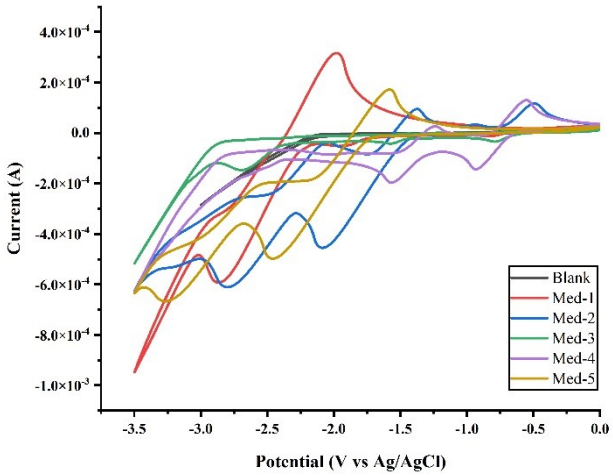
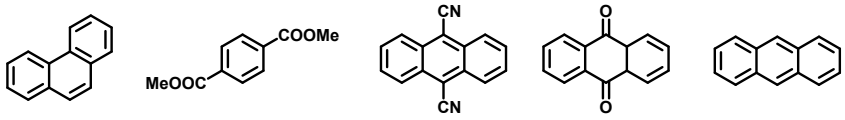
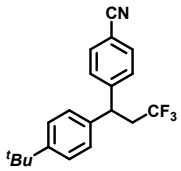


Figure S8. Cyclic voltammograms of mediators. Test conditions: CV of 0.06 M $^{n}Bu_4NBF_4$ solution in DMAc (2.5 mL) at room temperature under a nitrogen atmosphere: **black line**: 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); red line: **Med-1** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); blue line: **Med-2** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); green line: **Med-3** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); purple line: **Med-4** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc); brown line: **Med-5** (0. 06 M), 2.5 mL $^{n}Bu_4NBF_4$ (0.06 M) solution (in DMAc). The voltammogram was obtained at a scan rate of 100 mV s^{-1} with glass carbon as the working electrode and a Pt wire and Ag/ Ag^{+} as the counter and reference electrodes.



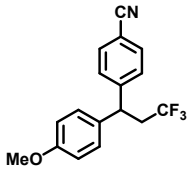
Med-1 **Med-2** **Med-3** **Med-4** **Med-5**

Characterization of the products



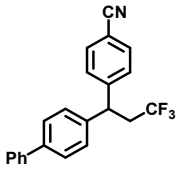
4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzonitrile (4aa).

Yellow oil in 88 % yield (88 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.57 (m, 2H), 7.40 – 7.35 (m, 2H), 7.36 – 7.31 (m, 2H), 7.15 – 7.10 (m, 2H), 4.35 (t, J = 7.4 Hz, 1H), 2.90 (m, 2H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.38, 148.17, 138.25, 132.57, 128.46, 126.91, 126.61 (q, $J_{C\text{-}F}$ = 276.0 Hz), 125.97, 118.68, 110.81, 44.713 (q, $J_{C\text{-}F}$ = 2.6), 39.24 (q, $J_{C\text{-}F}$ = 27.7), 34.47, 31.27. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.69. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{20}F_3N$: 331.3822; found: 331.3826.



4-(3,3,3-trifluoro-1-(4-methoxyphenyl)propyl)benzonitrile (4ab).

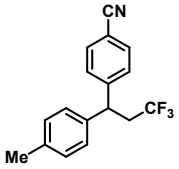
Yellow oil in 78 % yield (72 mg). 1H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.37 – 7.33 (m, 2H), 7.14 – 7.09 (m, 2H), 6.87 – 6.83 (m, 2H), 4.33 (t, J = 7.4 Hz, 1H), 3.78 (s, 3H), 2.87 (qd, J = 10.2, 7.4 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.79, 148.38, 133.32, 132.57, 128.38, 128.31, 126.11 (q, $J_{C\text{-}F}$ = 276.0 Hz), 118.64, 114.42, 110.80, 55.28, 44.35 (q, $J_{C\text{-}F}$ = 2.7 Hz), 39.30 (q, $J_{C\text{-}F}$ = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.60. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3NO$: 305.1027; found: 305.1031.



4-(1-([1,1'-biphenyl]-4-yl)-3,3,3-trifluoropropyl)benzonitrile (4ac).

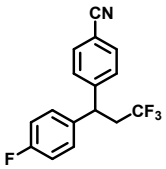
Yellow oil in 72 % yield (76 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 2H), 7.58 – 7.53 (m, 4H), 7.43 (m, 4H), 7.38 – 7.33 (m, 1H), 7.30 – 7.26 (m, 2H), 4.43 (t, J = 7.4 Hz, 1H), 2.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.89, 140.43, 140.28, 140.23, 132.67, 128.85, 128.44,

127.77, 127.76, 127.54, 127.03, 126.10 (q, J_{C-F} = 276.1 Hz), 118.60, 111.03, 44.85 (q, J_{C-F} = 2.7 Hz), 39.18 (q, J_{C-F} = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.58. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{16}F_3N$: 351.1235; found: 351.1239.



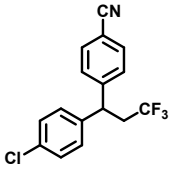
4-(3,3,3-trifluoro-1-(p-tolyl)propyl)benzonitrile (4ad).

Yellow oil in 85 % yield (74 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.38 – 7.33 (m, 2H), 7.11 (q, *J* = 8.2 Hz, 4H), 4.34 (t, *J* = 7.4 Hz, 1H), 2.89 (m, 2H), 2.31 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.26, 138.30, 137.19, 132.58, 129.74, 128.35, 127.19,127.12 (q, J_{C-F} = 276.0 Hz), 118.63, 110.84, 44.77 (q, J_{C-F} = 27 Hz), 39.20 (q, J_{C-F} = 27 Hz), 20.98. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.66. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3N$: 289.1078; found: 289.1075.



4-(3,3,3-trifluoro-1-(4-fluorophenyl)propyl)benzonitrile (4ae).

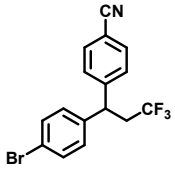
Yellow oil in 80 % yield (70 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.38 – 7.32 (m, 2H), 7.22 – 7.15 (m, 2H), 7.06 – 6.98 (m, 2H), 4.38 (t, J = 7.4 Hz, 1H), 2.93 – 2.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.43 (d, J_{C-F} = 245.3 Hz), 147.70, 137.00 (d, J_{C-F} = 3.3 Hz), 132.68, 128.97 (d, J_{C-F} = 8.1 Hz), 128.30, 125.97 (q, J_{C-F} = 275.9 Hz), 118.50, 115.99 (d, J_{C-F} = 21.3 Hz), 111.12, 44.40 (q, J_{C-F} = 2.7 Hz), 39.25 (q, J_{C-F} = 27.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.62, -114.77. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{11}F_4N$: 343.0796; found: 343.0795.



4-(1-(4-chlorophenyl)-3,3,3-trifluoropropyl)benzonitrile (4af).

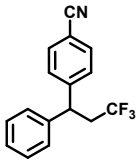
Yellow oil in 71 % yield (66 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 2H), 7.37 – 7.26 (m, 4H), 7.18 – 7.11 (m, 2H), 4.36 (t, *J* = 7.4 Hz, 1H), 2.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.39, 139.66, 133.41, 132.72, 129.26, 128.75, 128.31, 125.92 (q, J_{C-F} = 275.9 Hz), 118.48,

111.21, 44.53 (q, J_{C-F} = 2.9 Hz), 39.05 (q, J_{C-F} = 27.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.60. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{11}ClF_3N$: 309.0532; found: 309.0530.



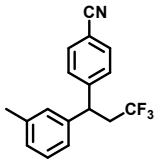
4-(1-(4-bromophenyl)-3,3,3-trifluoropropyl)benzonitrile (4ag).

Yellow oil in 57 % yield (61 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.59 (m, 2H), 7.48 – 7.43 (m, 2H), 7.36 – 7.31 (m, 2H), 7.11 – 7.07 (m, 2H), 4.34 (t, J = 7.4 Hz, 1H), 2.88 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.29, 140.17, 132.73, 132.22, 129.10, 128.31, 125.91 (q, J_{C-F} = 275.9 Hz), 118.46, 111.23, 44.60 (q, J_{C-F} = 2.9 Hz), 38.99 (q, J_{C-F} = 72.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.59. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{11}BrF_3N$: 353.0027; found: 353.0029.



4-(3,3,3-trifluoro-1-phenylpropyl)benzonitrile (4ah).

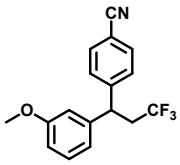
Yellow oil in 53 % yield (52 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.40 – 7.35 (m, 2H), 7.33 (dd, J = 8.1, 6.6 Hz, 2H), 7.28 – 7.24 (m, 1H), 7.24 – 7.19 (m, 2H), 4.38 (t, J = 7.4 Hz, 1H), 2.91 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.95, 141.26, 132.61, 129.09, 128.41, 127.47, 127.35, 126.09 (q, J_{C-F} = 276.3 Hz), 118.61, 110.93, 45.14 (q, J_{C-F} = 2.8 Hz), 39.14 (q, J_{C-F} = 27.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.65. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{12}F_3N$: 275.0922; found: 275.0920.



4-(3,3,3-trifluoro-1-(m-tolyl)propyl)benzonitrile (4ai).

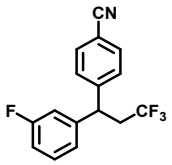
Yellow oil in 81 % yield (71 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.55 (m, 2H), 7.41 – 7.33 (m, 2H), 7.22 (t, J = 7.9 Hz, 1H), 7.09 – 7.04 (m, 1H), 7.03 – 6.98 (m, 2H), 4.34 (t, J = 7.4 Hz, 1H), 2.97 – 2.84 (m, 2H), 2.33 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.10, 141.25, 138.82, 132.59, 128.95, 128.41, 128.21, 128.14, 126.13 (q, J_{C-F} = 276.0 Hz), 124.27, 118.67, 110.85, 45.1 (q, J_{C-F} = 2.1 Hz), 39.130 (q, J_{C-F} = 27.8 Hz), 21.47. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.67. HRMS (ESI) m/z:

$[M+H]^+$ Calculated for $C_{17}H_{14}F_3N$: 289.1078; found: 289.1076.



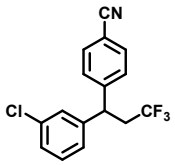
4-(3,3,3-trifluoro-1-(3-methoxyphenyl)propyl)benzonitrile (4aj).

Yellow oil in 74 % yield (68 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.58 (m, 2H), 7.40 – 7.35 (m, 2H), 7.25 (t, J = 8.0 Hz, 1H), 6.79 (m, 2H), 6.73 (t, J = 2.2 Hz, 1H), 4.34 (t, J = 7.4 Hz, 1H), 3.78 (s, 3H), 2.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 159.99, 147.82, 142.84, 132.60, 130.13, 128.39, 126.08 (q, $J_{C\text{-}F}$ = 276.0 Hz), 119.57, 118.63, 113.90, 112.02, 110.94, 55.25, 45.090 (q, $J_{C\text{-}F}$ = 2.7 Hz), 39.06 (q, $J_{C\text{-}F}$ = 27.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.67. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3NO$: 305.1027; found: 305.1025.



4-(3,3,3-trifluoro-1-(3-fluorophenyl)propyl)benzonitrile (4ak).

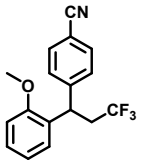
Yellow oil in 65 % yield (57 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.36 (d, J = 8.3 Hz, 2H), 7.30 (m, 1H), 7.01 (m, 1H), 6.98 – 6.93 (m, 1H), 6.91 (m, 1H), 4.37 (t, J = 7.4 Hz, 1H), 2.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ163.01 (d, $J_{C\text{-}F}$= 246.0 Hz), 147.18, 143.64 (d, $J_{C\text{-}F}$= 3.5 Hz), 132.73, 130.67 (d, $J_{C\text{-}F}$ = 4.2 Hz), 128.36, 125.91 (q, $J_{C\text{-}F}$ = 275.9 Hz), 123.09 (d, $J_{C\text{-}F}$ = 3.0 Hz), 118.48, 114.60, 114.39 (d, $J_{C\text{-}F}$ = 0.7 Hz), 111.26, 44.82 (q, $J_{C\text{-}F}$ = 2.4 Hz), 39.00 (q, $J_{C\text{-}F}$ = 27.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.65, -111.68. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{16}H_{11}F_4N$: 293.0828; found: 293.0820.



4-(1-(3-chlorophenyl)-3,3,3-trifluoropropyl)benzonitrile (4al).

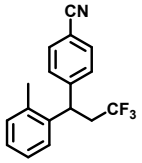
Yellow oil in 50 % yield (46 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.60 (m, 2H), 7.38 – 7.33 (m, 2H), 7.30 – 7.22 (m, 2H), 7.19 (t, J = 1.9 Hz, 1H), 7.10 (m, 1H), 4.35 (t, J = 7.4 Hz, 1H), 2.89 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.07, 143.17, 134.92, 132.76, 130.37, 128.36, 127.74, 127.60,125.89 (q, $J_{C\text{-}F}$ = 276.0 Hz), 125.61, 118.47, 111.29, 44.803 (q, $J_{C\text{-}F}$ = 2.7 Hz), 38.957 (q, $J_{C\text{-}F}$ = 27.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.62. HRMS (ESI) m/z: $[M+H]^+$ Calculated for

$C_{16}H_{11}ClF_3N$: 309.0532; found: 309.0529.



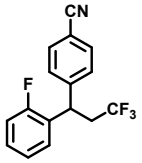
4-(3,3,3-trifluoro-1-(2-methoxyphenyl)propyl)benzonitrile (4am).

Yellow oil in 73 % yield (67 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.59 – 7.54 (m, 2H), 7.39 (d, J = 8.1 Hz, 2H), 7.27 – 7.22 (m, 1H), 7.15 (dd, J = 7.6, 1.7 Hz, 1H), 6.94 (m, 1H), 6.86 (d, J = 8.2 Hz, 1H), 4.74 (t, J = 7.4 Hz, 1H), 3.79 (s, 3H), 2.90 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 156.49, 147.83, 132.19, 129.69, 128.75, 128.66, 127.60, 125.37 (q, $J_{C\text{-}F}$ = 275.9 Hz), 120.84, 118.87, 111.12, 110.43, 55.39, 38.99 (q, $J_{C\text{-}F}$ = 2.9 Hz), 37.93 (q, $J_{C\text{-}F}$ = 2.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.91. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3NO$: 305.1027; found: 305.1030.



4-(3,3,3-trifluoro-1-(o-tolyl)propyl)benzonitrile (4an).

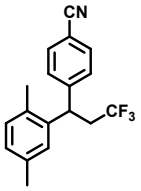
Yellow oil in 73 % yield (63 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.56 (m, 2H), 7.36 – 7.33 (m, 2H), 7.25 – 7.20 (m, 2H), 7.19 – 7.15 (m, 2H), 4.60 (t, J = 7.2 Hz, 1H), 2.88 (m, 2H), 2.30 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.48, 139.34, 135.80, 132.46, 131.23, 128.85, 127.40, 126.62, 126.19, 126.18 (q, $J_{C\text{-}F}$ = 275.9 Hz), 118.63, 110.80, 40.66 (q, $J_{C\text{-}F}$ = 2.7 Hz) 39.48 (q, $J_{C\text{-}F}$ = 27.6 Hz), 19.74. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.71. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3N$: 289.1078; found: 289.1073.



4-(3,3,3-trifluoro-1-(2-fluorophenyl)propyl)benzonitrile (4ao).

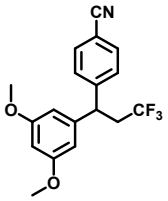
Yellow oil in 50 % yield (44 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.63 – 7.58 (m, 2H), 7.43 – 7.38 (m, 2H), 7.29 – 7.25 (m, 1H), 7.23 (dd, *J* = 7.2, 1.9 Hz, 1H), 7.14 (m, 1H), 7.04 (m, 1H), 4.64 (t, *J* = 7.4 Hz, 1H), 2.95 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.27 (d, $J_{C\text{-}F}$= 245.7 Hz), 146.65, 132.59, 129.368 (d, $J_{C\text{-}F}$ = 8.5 Hz), 128.45, 128.40, 128.38 (d, $J_{C\text{-}F}$ = 13.7 Hz), 126.01 (q, $J_{C\text{-}F}$ = 276.0 Hz), 124.69 (d, $J_{C\text{-}F}$ = 3.5 Hz), 118.56, 116.212 (d, $J_{C\text{-}F}$ = 11.1 Hz), 111.12, 35.06 (q, $J_{C\text{-}F}$ = 5.4 Hz), 37.971 (q, $J_{C\text{-}F}$ = 26.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -64.04, -116.51. HRMS (ESI)

m/z: $[M+H]^+$ Calculated for $C_{16}H_{11}F_4N$: 293.0828; found: 293.0821.



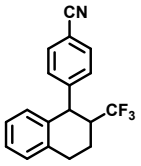
4-(1-(2,5-dimethylphenyl)-3,3,3-trifluoropropyl)benzonitrile (4ap).

Yellow oil in 78 % yield (71 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 – 7.57 (m, 2H), 7.37 – 7.33 (m, 2H), 7.05 (d, J = 7.9 Hz, 1H), 6.99 (d, J = 6.8 Hz, 2H), 4.56 (dd, J = 8.3, 6.2 Hz, 1H), 2.98 – 2.77 (m, 2H), 2.33 (s, 3H), 2.25 (s, 3H) ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.60, 139.23, 136.08, 132.58, 132.44, 131.09, 128.84, 128.07, 126.89, 126.25 (q, $J_{C\text{-}F}$ = 276.0 Hz), 118.69, 110.72, 40.60 (q, $J_{C\text{-}F}$ = 2.8 Hz), 39.47 (q, $J_{C\text{-}F}$ = 27.5 Hz), 21.23, 19.27. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.71. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}F_3N$: 303.1235; found: 303.1229.



4-(1-(3,5-dimethoxyphenyl)-3,3,3-trifluoropropyl)benzonitrile (4aq).

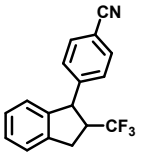
Yellow oil in 55 % yield (55 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.57 (m, 2H), 7.41 – 7.35 (m, 2H), 6.34 (s, 3H), 4.28 (t, *J* = 7.4 Hz, 1H), 3.76 (s, 6H), 2.87 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.20, 147.67, 143.58, 132.58, 128.36, 126.06 (q, $J_{C\text{-}F}$ = 275.9 Hz), 118.63, 110.96, 105.87, 98.43, 55.35, 45.23 (q, $J_{C\text{-}F}$ = 2.5 Hz), 39.00 (q, $J_{C\text{-}F}$ = 27.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.69. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{16}F_3NO_2$: 335.1133; found: 335.1126.



4-(2-(trifluoromethyl)-1,2,3,4-tetrahydronaphthalen-1-yl)benzonitrile (4ar).

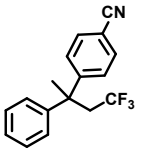
Yellow oil in 49 % yield (44 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.56 (m, 2H), 7.24 – 7.20 (m, 2H), 7.19 – 7.13 (m, 2H), 7.06 (m, 1H), 6.70 (d, *J* = 7.8 Hz, 1H), 4.35 (d, *J* = 8.0 Hz, 1H), 3.00 – 2.94 (m, 2H), 2.77 – 2.63 (m, 1H), 2.22 (m, 1H), 1.91 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.97, 136.05, 135.98, 132.45, 130.23, 129.77, 128.84, 127.48 (q, $J_{C\text{-}F}$ = 278.8 Hz), 126.81, 126.70, 118.75, 110.70, 46.74 (q, $J_{C\text{-}F}$ = 25.1 Hz), 44.88 (q, $J_{C\text{-}F}$ = 2.1 Hz), 27.69, 21.41 (q, $J_{C\text{-}F}$ = 2.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -69.63. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{18}H_{14}F_3N$:

301.1078; found: 301.1073.



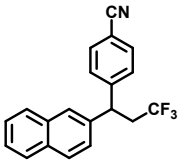
4-(2-(trifluoromethyl)-2,3-dihydro-1H-inden-1-yl)benzonitrile (4as).

Yellow oil in 47 % yield (40 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.61 (m, 2H), 7.34 – 7.27 (m, 4H), 7.26 (s, 1H), 7.19 (t, J = 7.4 Hz, 1H), 6.82 (d, J = 7.6 Hz, 1H), 4.61 (d, J = 8.0 Hz, 1H), 3.40 – 3.20 (m, 2H), 3.14 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.71, 143.08, 140.40, 132.63, 129.27, 128.06, 127.66, 127.53 (q, $J_{C\text{-}F}$= 276.5 Hz), 125.01, 124.60, 118.70, 111.21, 52.28 (q, $J_{C\text{-}F}$ = 26.6 Hz, 51.94 (q, $J_{C\text{-}F}$ = 2.6 Hz), 33.36 (q, $J_{C\text{-}F}$ = 2.6 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -70.07. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{12}F_3N$: 287.0922; found: 287.0917.



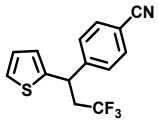
4-(4,4,4-trifluoro-2-phenylbutan-2-yl)benzonitrile (4at).

Yellow oil in 40 % yield (35 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.31 (dd, J = 8.2, 6.5 Hz, 4H), 7.26 – 7.22 (m, 1H), 7.15 – 7.10 (m, 2H), 3.03 (q, J = 10.7 Hz, 2H), 1.85 (d, J = 1.6 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 152.85, 146.58, 132.08, 128.59, 127.95, 126.93, 126.64, 126,19 (q, $J_{C\text{-}F}$ = 277.3 Hz), 118.69, 110.45, 44.32 (q, $J_{C\text{-}F}$ = 26.4 Hz), 44.25 (q, $J_{C\text{-}F}$ = 1.6 Hz), 27.34 (q, $J_{C\text{-}F}$ = 1.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -58.31. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{14}F_3N$: 289.1078; found: 289.1083.



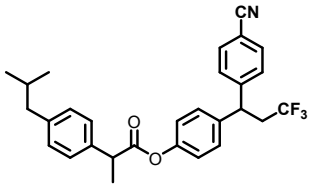
4-(3,3,3-trifluoro-1-(naphthalen-2-yl)propyl)benzonitrile (4au).

Yellow oil in 75 % yield (73 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.81 (m, 3H), 7.69 (d, J = 1.9 Hz, 1H), 7.63 – 7.58 (m, 2H), 7.54 – 7.45 (m, 2H), 7.44 – 7.40 (m, 2H), 7.29 – 7.26 (m, 1H), 4.55 (t, J = 7.4 Hz, 1H), 3.02 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.81, 138.57, 133.41, 132.62, 132.50, 129.01, 128.56, 127.80, 127.70, 126.66, 126.146 (q, $J_{C\text{-}F}$= 276.0 Hz), 126.32, 125.81, 125.52, 118.58, 111.02, 45.187 (q, $J_{C\text{-}F}$ = 2.9 Hz), 39.04 (q, $J_{C\text{-}F}$ = 27.8 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.50. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{14}F_3N$: 325.1078; found: 325.1085.



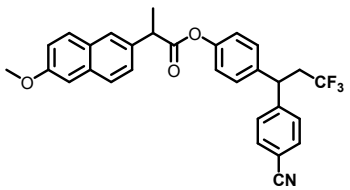
4-(3,3,3-trifluoro-1-(thiophen-2-yl)propyl)benzonitrile (4av).

Yellow oil in 52 % yield (44 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.66 – 7.60 (m, 2H), 7.43 – 7.38 (m, 2H), 7.22 (dd, J = 5.1, 1.2 Hz, 1H), 6.95 (dd, J = 5.1, 3.6 Hz, 1H), 6.87 (dt, J = 3.6, 1.1 Hz, 1H), 4.62 (dd, J = 8.9, 5.9 Hz, 1H), 3.06 – 2.82 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 147.34, 144.80, 132.71, 128.37, 125.68 (q, $J_{C\text{-}F}$ = 276.5 Hz), 125.06, 124.71, 118.54, 111.41, 40.63 (q, $J_{C\text{-}F}$ = 27.9 Hz), 40.88 (q, $J_{C\text{-}F}$ = 2.9 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.72. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{14}H_{10}F_3NS$: 281.0486; found: 281.0493.



4-(1-(4-cyanophenyl)-3,3,3-trifluoropropyl)phenyl 2-(4-isobutylphenyl)propanoate (4aw).

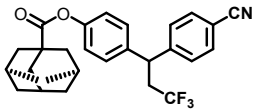
Yellow oil in 61 % yield (88 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.57 (m, 2H), 7.37 – 7.33 (m, 2H), 7.31 – 7.27 (m, 2H), 7.21 – 7.13 (m, 4H), 7.02 – 6.97 (m, 2H), 4.38 (t, J = 7.4 Hz, 1H), 3.94 (q, J = 7.1 Hz, 1H), 2.89 (m, 2H), 2.49 (d, J = 7.2 Hz, 2H), 1.88 (m, 1H), 1.61 (d, J = 7.1 Hz, 4H), 0.93 (d, J = 6.6 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.16, 150.03, 147.58, 140.94, 138.60, 137.05, 132.64, 129.55, 128.38, 128.28, 127.19, 125.97 (q, $J_{C\text{-}F}$ = 276.5 Hz), 122.04, 118.54, 111.04, 45.24, 45.04,44.54 (q, $J_{C\text{-}F}$ = 2.8 Hz), 39.18 (q, $J_{C\text{-}F}$ = 27.8 Hz), 30.21, 22.40, 18.45. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.62. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{29}H_{28}F_3NO_2$: 479.2072; found: 479.2065.



4-(1-(4-cyanophenyl)-3,3,3-trifluoropropyl)phenyl 2-(6-methoxynaphthalen-2-yl)propanoate (4ax).

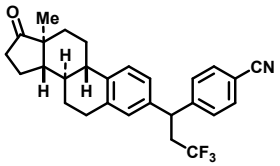
Yellow oil in 56 % yield (85 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.77 – 7.70 (m, 3H), 7.60 – 7.55 (m, 2H), 7.47 (dd, J = 8.6, 1.8 Hz, 1H), 7.34 – 7.29 (m, 2H), 7.19 – 7.12 (m, 4H), 6.97 – 6.92 (m, 2H), 4.34 (t, J = 7.4 Hz, 1H), 4.08 (q, J = 7.1 Hz, 1H), 3.92 (s, 3H), 2.93 – 2.79 (m, 2H), 1.67 (d, J

= 7.1 Hz, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.10, 157.81, 150.00, 147.54, 138.64, 134.94, 133.85, 132.63, 129.32, 128.98, 128.37, 128.29, 127.42, 126.16, 126.06, 125.96 (q, J_{C-F} = 275.8 Hz), 122.02, 119.19, 118.54, 111.03, 105.61, 55.35, 45.56, 44.53 (q, J_{C-F} = 3.0 Hz), 39.17 (q, J_{C-F} = 27.7 Hz), 18.45. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.62. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{30}H_{24}F_3NO_3$: 503.1708; found: 503.1700.



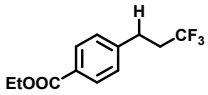
4-(1-(4-cyanophenyl)-3,3,3-trifluoropropyl)phenyl (3r,5r,7r)-adamantane-1-carboxylate (4ay).

Yellow oil in 56 % yield (84 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, *J* = 8.1 Hz, 2H), 7.37 – 7.33 (m, 2H), 7.22 – 7.17 (m, 2H), 7.05 – 6.98 (m, 2H), 4.38 (t, *J* = 7.4 Hz, 1H), 2.89 (m, 2H), 2.07 (p, *J* = 2.9 Hz, 3H), 2.02 (d, *J* = 2.9 Hz, 6H), 1.82 – 1.71 (m, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.09, 150.27, 147.65, 138.38, 132.64, 128.41, 128.29, 122.20, 126.00 (q, J_{C-F} = 276.1 Hz), 111.03, 44.56 (q, J_{C-F} = 2.7 Hz), 41.04, 39.22 (q, J_{C-F} = 27.7 Hz), 38.72, 36.41, 27.87. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.61. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{27}H_{26}F_3NO_2$: 453.1916; found: 453.1923.



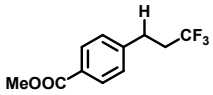
4-(3,3,3-trifluoro-1-((8R,9S,13S,14S)-13-methyl-17-oxo-7,8,9,11,12,13,14,15,16,17-decahydro-6H-cyclopenta[a]phenanthren-3-yl)propyl)benzonitrile (4az).

Yellow oil in 51 % yield (69 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.59 (m, 2H), 7.40 (d, *J* = 8.2 Hz, 2H), 7.26 (d, *J* = 8.1 Hz, 1H), 7.01 (dd, *J* = 8.1, 2.1 Hz, 1H), 6.94 (d, *J* = 1.9 Hz, 1H), 4.33 (t, *J* = 7.4 Hz, 1H), 2.97 – 2.85 (m, 4H), 2.52 (dd, *J* = 18.8, 8.6 Hz, 1H), 2.41 (m, 1H), 2.28 (m, 1H), 2.21 – 2.13 (m, 1H), 2.10 (dd, *J* = 10.5, 5.3 Hz, 1H), 2.03 (m, 1H), 1.97 (m, 1H), 1.70 – 1.52 (m, 4H), 1.51 – 1.40 (m, 2H), 0.92 (d, *J* = 1.0 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 220.80, 148.17, 139.03, 138.78, 137.29, 132.60, 128.40, 127.90, 126.07, 126.13 (q, J_{C-F} = 275.9 Hz), 124.52, 118.67, 110.81, 50.47, 47.96, 44.77 (q, J_{C-F} = 2.1 Hz), 44.23, 39.17 (q, J_{C-F} = 26.9 Hz), 38.00, 35.84, 31.55, 29.43, 26.39, 25.61, 21.57, 13.83. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.67. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{28}H_{28}F_3NO$: 451.2123; found: 451.2129.



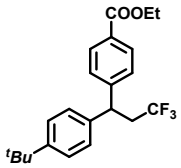
ethyl 4-(3,3,3-trifluoropropyl)benzoate (4ba)

Yellow oil in 73% yield (54 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.02 – 7.97 (m, 2H), 7.27 (d, J = 8.4 Hz, 2H), 4.37 (q, J = 7.1 Hz, 2H), 2.96 – 2.89 (m, 2H), 2.47 – 2.34 (m, 2H), 1.39 (t, J = 7.1 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.39, 144.11, 130.02, 129.07, 128.24, 126.54 (q, $J_{C\text{-}F}$ = 275.1 Hz), 60.97, 35.21 (q, $J_{C\text{-}F}$ = 28.4 Hz), 28.22 (q, $J_{C\text{-}F}$ = 28 Hz), 14.32. ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.60. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{12}H_{13}F_3O_2$: 246.0868; found: 246.0865.



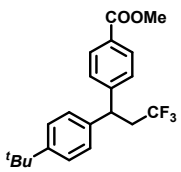
methyl 4-(3,3,3-trifluoropropyl)benzoate (4bb)

Yellow oil in 63% yield (43.9 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.01 – 7.96 (m, 2H), 7.29 – 7.25 (m, 2H), 3.91 (s, 3H), 2.96 – 2.90 (m, 2H), 2.48 – 2.34 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.87, 144.24, 130.06, 128.72, 128.30, 126,52 (q, $J_{C\text{-}F}$ = 275.1 Hz), 52.11, 35.19 (q, $J_{C\text{-}F}$ = 28.4), 28.23 (q, $J_{C\text{-}F}$ = 3.3). ^{19}F NMR (376 MHz, $CDCl_3$) δ -66.61. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{11}H_{11}F_3O_2$: 232.2022; found: 232.2026.



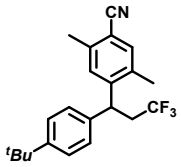
ethyl 4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzoate (5aa).

Yellow oil in 49 % yield (56 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.98 (d, J = 8.4 Hz, 2H), 7.36 – 7.29 (m, 4H), 7.17 – 7.12 (m, 2H), 4.35 (q, J = 7.1 Hz, 3H), 3.02 – 2.82 (m, 2H), 1.37 (t, J = 7.1 Hz, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.33, 149.98, 147.88, 138.98, 130.01, 129.09, 127.60, 126.96, 126.31 (q, $J_{C\text{-}F}$ = 275.9 Hz), 125.78, 60.93, 44.63 (q, $J_{C\text{-}F}$ = 2.6 Hz), 39.38 (q, $J_{C\text{-}F}$ = 27.5 Hz), 34.42, 31.29, 14.34. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.71. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{26}F_3O_2$: 378.1807; found: 378.1813.



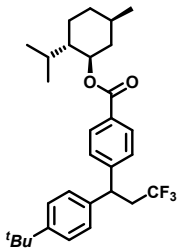
methyl 4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzoate (5ab).

Yellow oil in 53 % yield (58 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.95 (m, 2H), 7.36 – 7.29 (m, 4H), 7.18 – 7.12 (m, 2H), 4.35 (t, J = 7.4 Hz, 1H), 3.89 (s, 3H), 2.91 (m, 2H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 166.82, 150.00, 148.00, 138.93,130.26 (q, $J_{C\text{-}F}$ = 274.0 Hz), 130.06, 128.74, 126.97, 125.79, 52.10, 44.64 (q, $J_{C\text{-}F}$ = 2.9 Hz), 39.39 (q, $J_{C\text{-}F}$ = 27.5 Hz), 34.43, 31.29. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.72. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{21}H_{23}F_3O_2$: 364.1650; found: 364.1653.



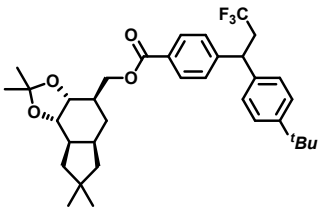
4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)-2,5-dimethylbenzonitrile (5ac).

Yellow oil in 67 % yield (72 mg). 1H NMR (400 MHz, $CDCl_3$) δ 7.37 (s, 1H), 7.33 – 7.29 (m, 2H), 7.19 (s, 1H), 7.12 – 7.08 (m, 2H), 4.53 (t, J = 7.2 Hz, 1H), 2.86 (m, 2H), 2.51 (s, 3H), 2.33 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.12, 146.09, 139.60, 137.88, 134.46, 134.28, 128.46, 127.22, 126.26 (q, $J_{C\text{-}F}$ = 276.0 Hz), 125.82, 118.15, 110.93, 39.89 (q, $J_{C\text{-}F}$ = 2.5 Hz), 39.40 (q, $J_{C\text{-}F}$ = 27.4 Hz), 34.44, 31.27, 20.29, 19.17. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.89. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{22}H_{24}F_3N$: 359.1861; found: 359.1863.



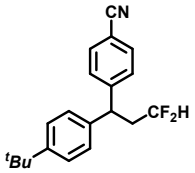
(1R,2S,5R)-2-isopropyl-5-methylcyclohexyl 4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzoate (5ad).

Yellow oil in 53 % yield (78 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 – 7.96 (m, 2H), 7.36 – 7.29 (m, 4H), 7.18 – 7.12 (m, 2H), 4.90 (m, 1H), 4.35 (t, J = 7.4 Hz, 1H), 3.02 – 2.82 (m, 2H), 2.09 (m, 1H), 1.93 (m, 1H), 1.77 – 1.68 (m, 2H), 1.58 – 1.49 (m, 2H), 1.28 (s, 9H), 1.08 (m, 2H), 0.91 (t, J = 6.4 Hz, 7H), 0.77 (d, J = 6.9 Hz, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.79, 149.97, 147.79, 139.04, 130.04, 129.44, 127.56, 126.94, 126.32 (q, $J_{C\text{-}F}$ = 275.9 Hz), 125.79, 74.79, 47.27, 44.64 (q, $J_{C\text{-}F}$ = 2.7 Hz), 40.96, 39.35 (q, $J_{C\text{-}F}$ = 28.2 Hz), 34.32, 31.44, 31.29, 26.45, 23.58, 22.05, 20.79, 16.44. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.71. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{30}H_{39}F_3O$: 488.2902; found: 488.2895.



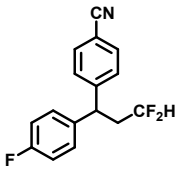
((3aS,5R,5aR,8aR,8bS)-2,2,7,7-tetramethyltetrahydro-5H-bis([1,3]dioxolo)[4,5-b:4',5'-d]pyran-5-yl)methyl 4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzoate (5ae).

Yellow oil in 43 % yield (76 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.04 – 7.99 (m, 2H), 7.36 – 7.30 (m, 4H), 7.17 – 7.12 (m, 2H), 4.67 – 4.61 (m, 2H), 4.44 (t, *J* = 2.4 Hz, 1H), 4.38 – 4.33 (m, 1H), 4.33 – 4.29 (m, 1H), 4.25 (dd, *J* = 7.9, 1.7 Hz, 1H), 3.95 (dd, *J* = 13.0, 1.9 Hz, 1H), 3.79 (dd, *J* = 12.9, 0.7 Hz, 1H), 2.90 (m, 2H), 1.54 (s, 3H), 1.44 (s, 3H), 1.38 (s, 3H), 1.33 (s, 3H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.69, 150.03, 148.20, 138.85, 130.24, 128.48, 127.71, 126.98, 126.28 (q, $J_{C\text{-}F}$ = 276.1 Hz), 125.79, 109.18, 108.83, 101.67, 70.79, 70.55, 70.10, 65.41, 61.35, 44.64 (q, $J_{C\text{-}F}$ = 2.6 Hz), 39.40 (q, $J_{C\text{-}F}$ = 27.6 Hz), 34.43, 31.28, 26.53, 25.85, 25.57, 24.02. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.71. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{35}H_{45}F_3O_4$: 586.3270 ; found: 586.3261.



4-(1-(4-(tert-butyl)phenyl)-3,3-difluoropropyl)benzonitrile (7aa).

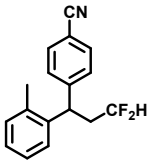
Yellow oil in 78 % yield (73 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.39 – 7.32 (m, 4H), 7.15 – 7.11 (m, 2H), 5.59 (dd, *J* = 5.4, 4.4 Hz, 1H), 4.21 (t, *J* = 8.1 Hz, 1H), 2.70 – 2.45 (m, 2H), 1.29 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 150.39, 148.69, 138.11, 132.61, 128.45, 127.20, 126.04, 118.70, 116.10 (t, $J_{C\text{-}F}$ = 237.9 Hz), 113.72, 110.72, 44.92 (t, $J_{C\text{-}F}$ = 6.0 Hz), 39.40 (t, $J_{C\text{-}F}$ = 21.5 Hz), 34.49, 31.29. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.05, -116.06, -116.81, -116.81, -117.10, -117.10, -117.85, -117.86. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{21}F_2N$: 313.1642; found: 313.1639.



4-(3,3-difluoro-1-(4-fluorophenyl)propyl)benzonitrile (7ab).

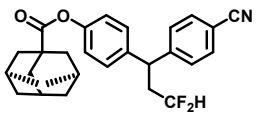
Yellow oil in 73 % yield (60 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.64 – 7.58 (m, 2H), 7.36 – 7.31

(m, 2H), 7.21 – 7.14 (m, 2H), 7.07 – 6.98 (m, 2H), 5.59 (t, J = 4.9 Hz, 1H), 4.25 (t, J = 8.0 Hz, 1H), 2.64 – 2.49 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.92 (d, $J_{C\text{-}F}$ = 245.2 Hz), 148.17, 137.07 (d, $J_{C\text{-}F}$ = 3.3 Hz), 132.72, 129.15 (d, $J_{C\text{-}F}$ = 7.9 Hz), 128.34, 118.54, 116.07 (d, $J_{C\text{-}F}$ = 21.2 Hz), 115.85 (t, $J_{C\text{-}F}$ = 238.2 Hz), 111.01, 44.56 (t, $J_{C\text{-}F}$ = 5.8 Hz), 39.40 (t, $J_{C\text{-}F}$ = 21.7 Hz). ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.77, -116.07, -116.83, -116.99, -117.75. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{21}F_2N$: 275.0922; found:275.0926.



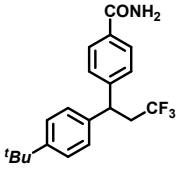
4-(3,3-difluoro-1-(3-methoxyphenyl)propyl)benzonitrile (7ac).

Yellow oil in 69 % yield (59 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.61 – 7.57 (m, 2H), 7.33 – 7.30 (m, 2H), 7.26 – 7.23 (m, 2H), 7.18 (dd, J = 4.4, 2.9 Hz, 2H), 5.61 (m, 1H), 4.47 (t, J = 8.0 Hz, 1H), 2.67 – 2.46 (m, 2H), 2.26 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 148.18, 139.06, 136.28, 132.57, 131.28, 128.72, 127.39, 126.68, 126.29, 118.65, 116.05 (t, $J_{C\text{-}F}$ = 238.0 Hz), 110.70, 40.94 (t, $J_{C\text{-}F}$ = 5.9 Hz), 39.66 (t, $J_{C\text{-}F}$ = 21.5 Hz), 19.76. ^{19}F NMR (376 MHz, $CDCl_3$) δ -115.77, -116.53, -116.73, -117.49. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{17}H_{15}F_3NO$: 287.1122; found: 287.1126.



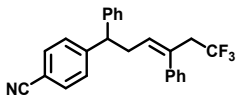
4-(1-(4-cyanophenyl)-3,3-difluoropropyl)phenyl (3r,5r,7r)-adamantane-1-carboxylate (7ad).

Yellow oil in 43 % yield (51 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 8.1 Hz, 2H), 7.34 (d, J = 8.1 Hz, 2H), 7.22 – 7.17 (m, 2H), 7.05 – 7.00 (m, 2H), 5.59 (m, 1H), 4.25 (t, J = 8.0 Hz, 1H), 2.64 – 2.50 (m, 2H), 2.10 – 2.05 (m, 3H), 2.03 (d, J = 2.9 Hz, 6H), 1.76 (q, J = 3.5 Hz, 6H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 176.13, 150.28, 148.15, 138.40, 132.68, 128.51, 128.42, 122.28, 118.58, 115.88 (t, $J_{C\text{-}F}$ = 238.0 Hz), 110.94, 44.73 (t, $J_{C\text{-}F}$ = 6.1 Hz), 41.05, 39.37 (t, $J_{C\text{-}F}$ = 21.6 Hz), 38.73, 36.42, 27.87. ^{19}F NMR (376 MHz, $CDCl_3$) δ -116.06, -116.82, -117.06, -117.82. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{27}H_{27}F_2NO_2$: 435.2010; found: 435.2019.



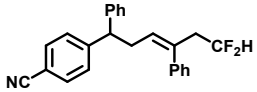
4-(1-(4-(tert-butyl)phenyl)-3,3,3-trifluoropropyl)benzamide (8)

White solid in 67 % yield (71 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 – 7.73 (m, 2H), 7.33 (dd, *J* = 8.4, 3.3 Hz, 4H), 7.18 – 7.11 (m, 2H), 6.39 (s, 2H), 4.35 (t, *J* = 7.3 Hz, 1H), 2.90 (m, 2H), 1.28 (s, 9H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 169.52, 150.03, 147.06, 138.99, 131.88, 127.89, 127.87, 126.97, 126.330 (q, $J_{C\text{-}F}$ = 2.760 Hz), 125.81, 44.54 (q, $J_{C\text{-}F}$ = 2.9 Hz), 39.38 (t, $J_{C\text{-}F}$ = 27.4 Hz), 34.43, 31.29. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.63. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{20}H_{22}F_3NO$: 349.1653; found: 349.1661.



(Z)-4-(6,6,6-trifluoro-1,4-diphenylhex-3-en-1-yl)benzonitrile (10)

Yellow oil in 56 % yield (66 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.40 – 7.37 (m, 2H), 7.34 (dd, *J* = 8.2, 6.8 Hz, 2H), 7.31 – 7.26 (m, 3H), 7.26 – 7.22 (m, 3H), 7.21 – 7.17 (m, 2H), 5.84 (t, *J* = 7.1 Hz, 1H), 4.16 (t, *J* = 7.9 Hz, 1H), 3.24 (q, *J* = 10.6 Hz, 2H), 3.00 (m, 2H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.60, 142.48, 141.64, 132.84, 132.46, 131.42 (q, $J_{C\text{-}F}$ = 2.7 Hz), 128.91, 128.77, 128.46, 127.89, 127.53, 127.10, 126.37, 125.96 (q, $J_{C\text{-}F}$ = 276.5 Hz), 118.88, 110.45, 51.08, 34.83 (q, $J_{C\text{-}F}$ = 29.2 Hz), 34.78. ^{19}F NMR (376 MHz, $CDCl_3$) δ -63.31. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{25}H_{20}F_3N$: 391.1548; found: 391.1542.

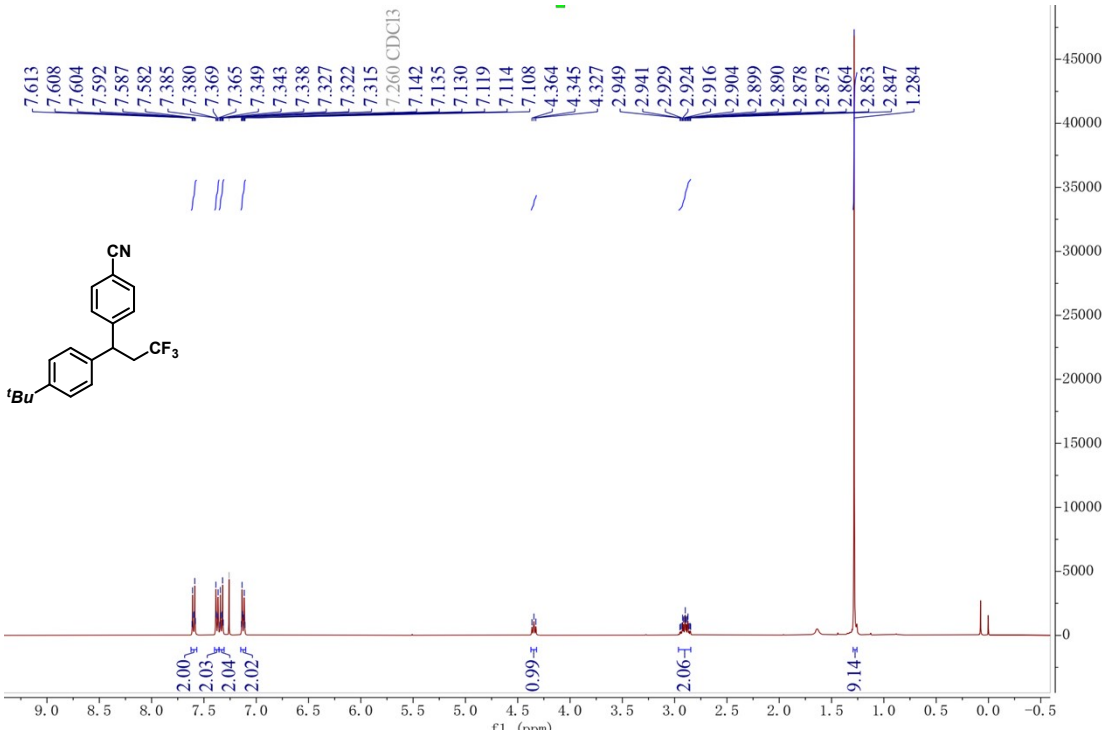


(Z)-4-(6,6-difluoro-1,4-diphenylhex-3-en-1-yl)benzonitrile (11)

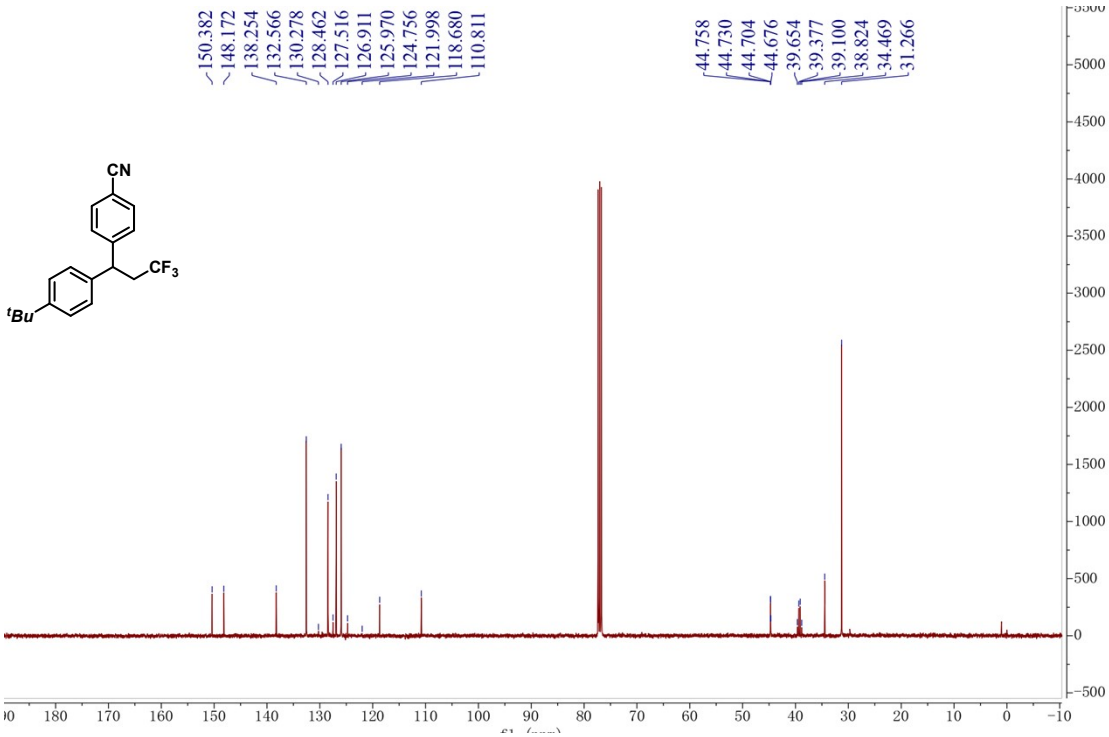
Yellow oil in 43 % yield (51 mg). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.62 – 7.58 (m, 2H), 7.39 – 7.36 (m, 2H), 7.35 – 7.29 (m, 3H), 7.29 – 7.27 (m, 2H), 7.23 (m, 3H), 7.19 – 7.16 (m, 2H), 5.74 (t, *J* = 7.1 Hz, 1H), 5.64 (t, *J* = 4.8 Hz, 1H), 4.15 (t, *J* = 7.9 Hz, 1H), 3.04 – 2.94 (m, 4H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 149.73, 142.62, 141.44, 133.23, 132.40, 130.98, 128.84, 128.82, 128.59, 127.92, 127.56, 127.01, 126.30, 118.90, 115.77 (t, $J_{C\text{-}F}$ = 240.1 Hz), 110.35, 51.24, 35.52 (t, $J_{C\text{-}F}$ = 22.6 Hz), 34.52. ^{19}F NMR (376 MHz, $CDCl_3$) δ -114.28, -114.30. HRMS (ESI) m/z: $[M+H]^+$ Calculated for $C_{25}H_{21}F_2N$: 373.1642; found: 373.1653.

^{1}H, ^{13}C and ^{19}F NMR spectra of all products

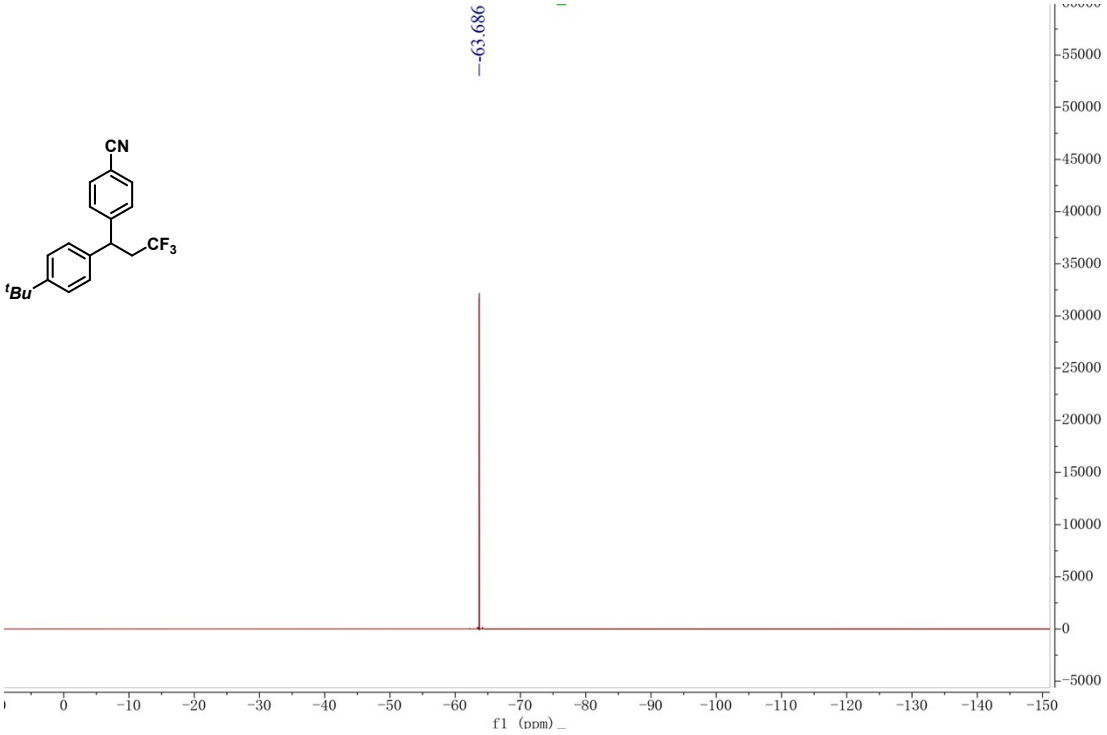
^{1}H NMR (400 MHz, $CDCl_3$) of **4aa**



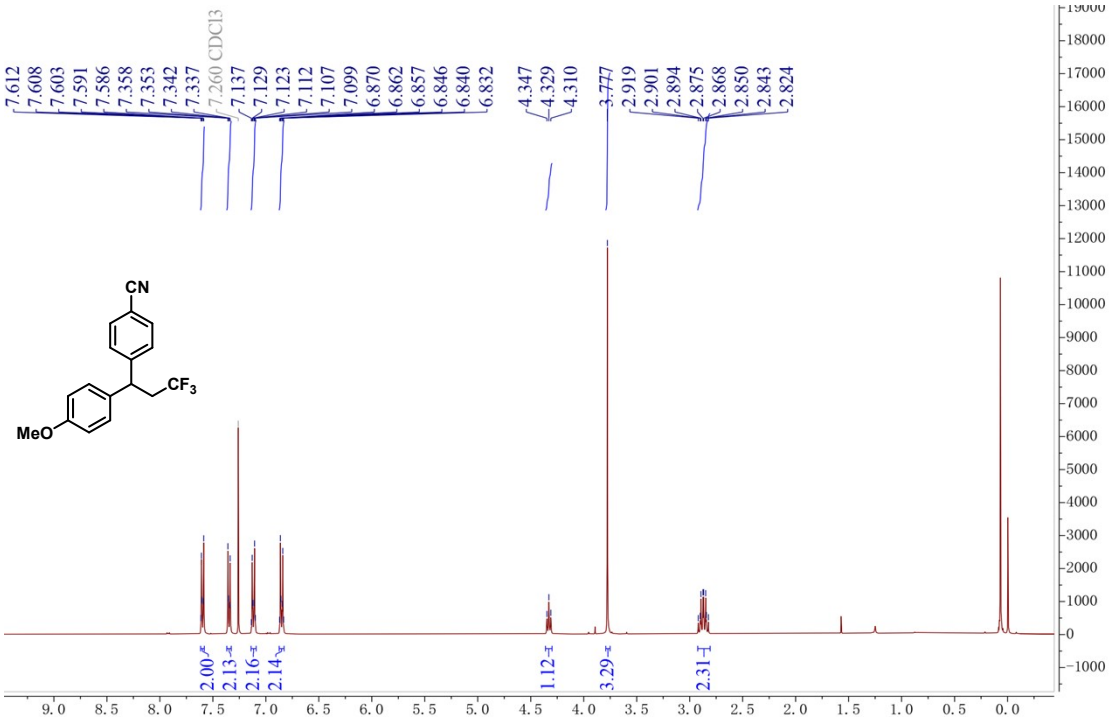
^{13}C NMR (100 MHz, $CDCl_3$) of **4aa**



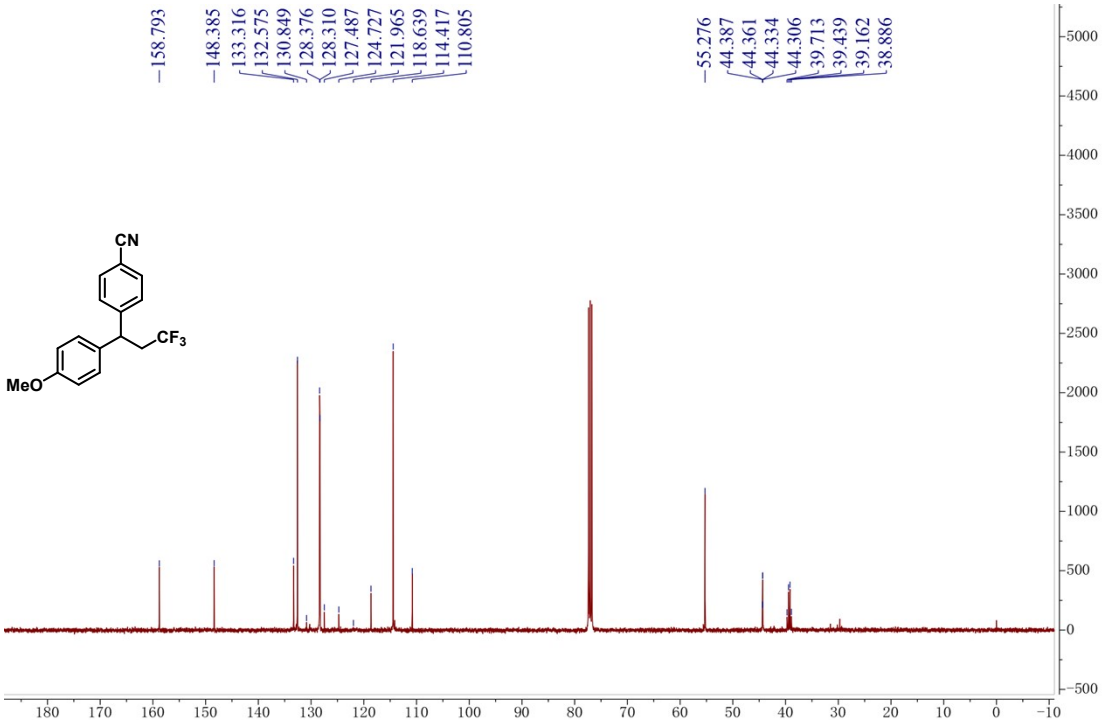
^{19}F NMR (376 MHz, $CDCl_3$) of **4aa**



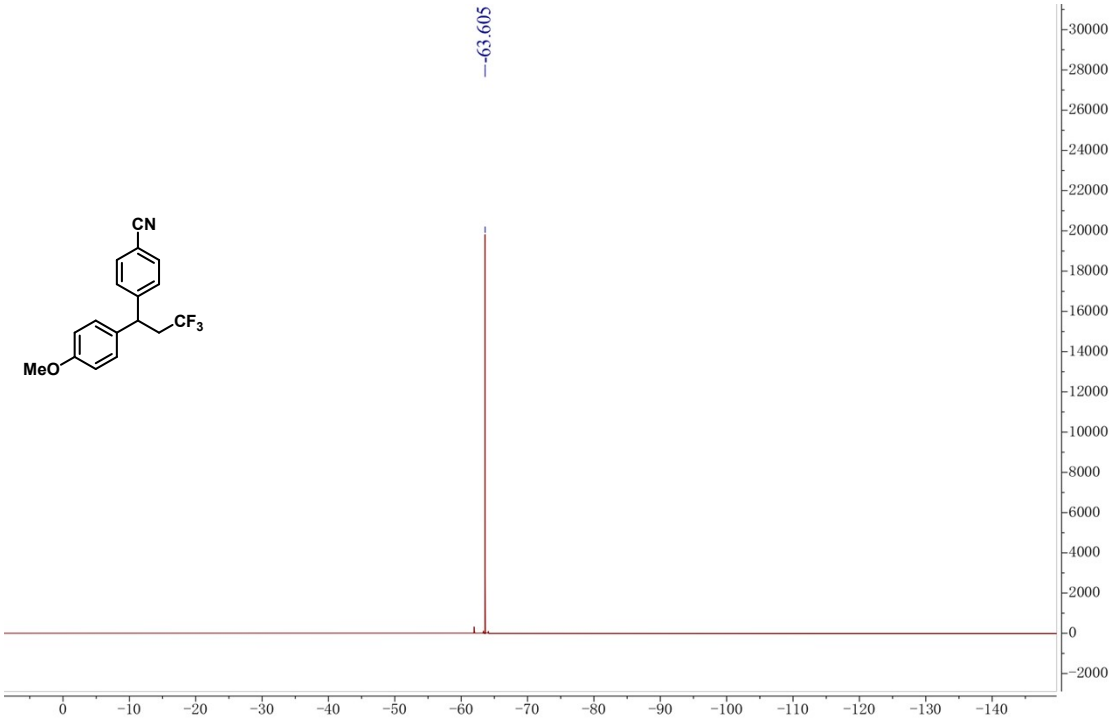
^{1}H NMR (400 MHz, $CDCl_3$) of **4ab**



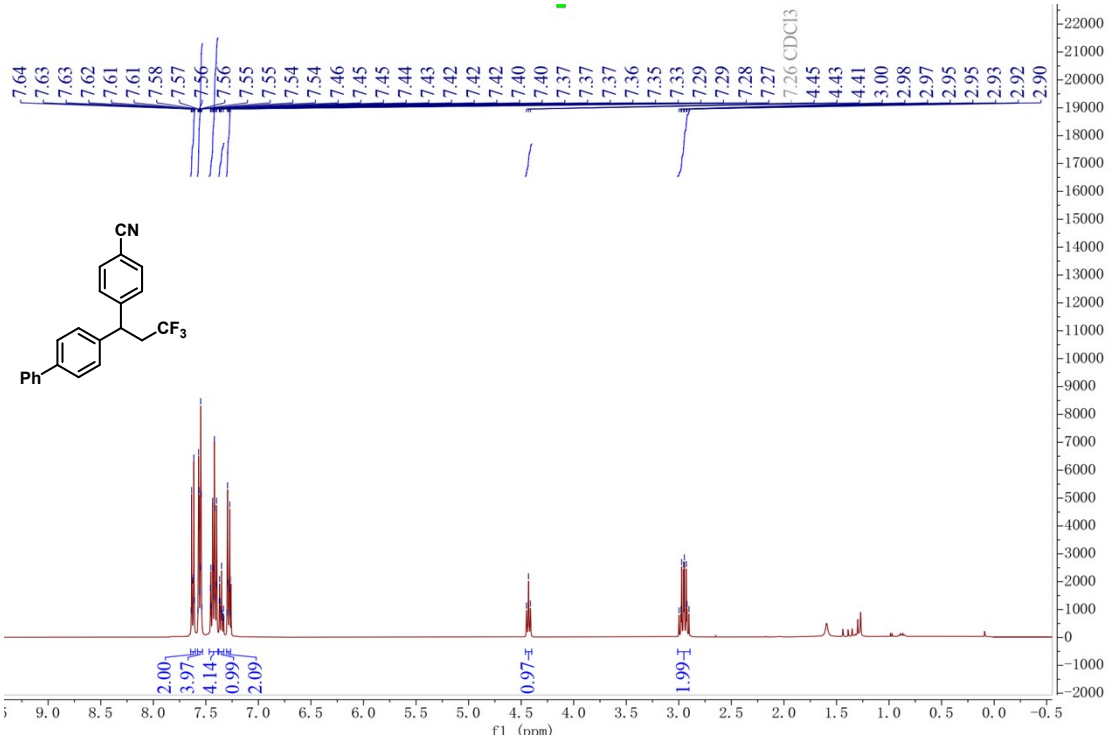
^{13}C NMR (100 MHz, $CDCl_3$) of **4ab**



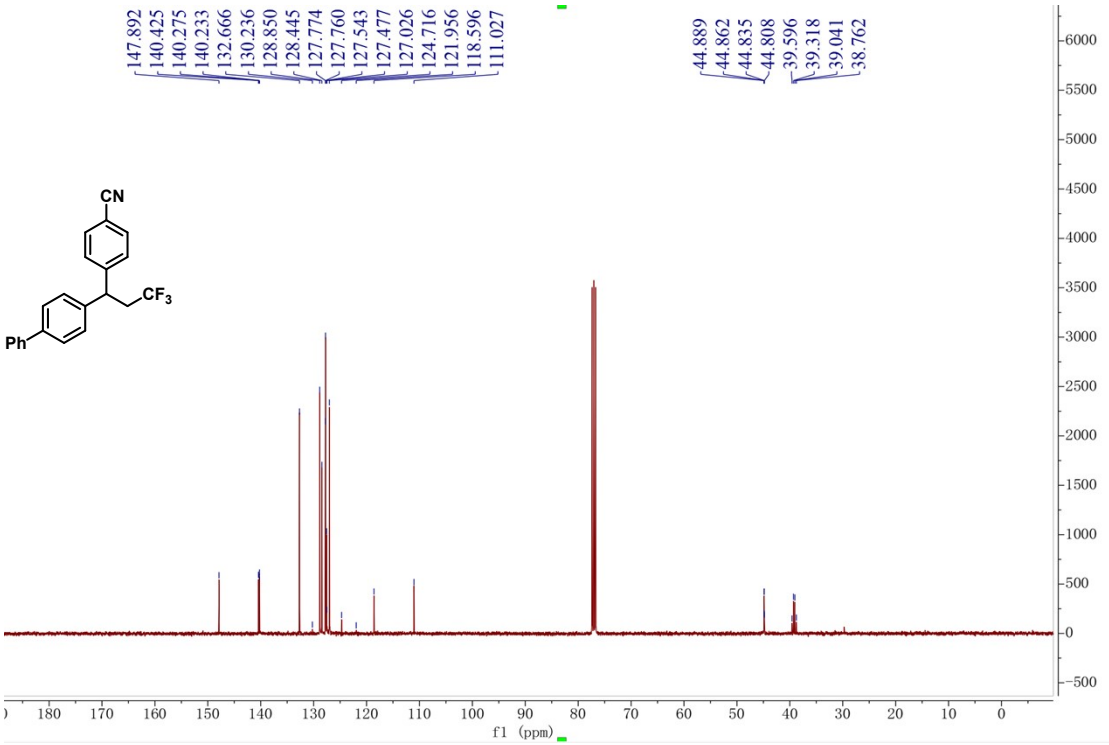
^{19}F NMR (376 MHz, $CDCl_3$) of **4ab**



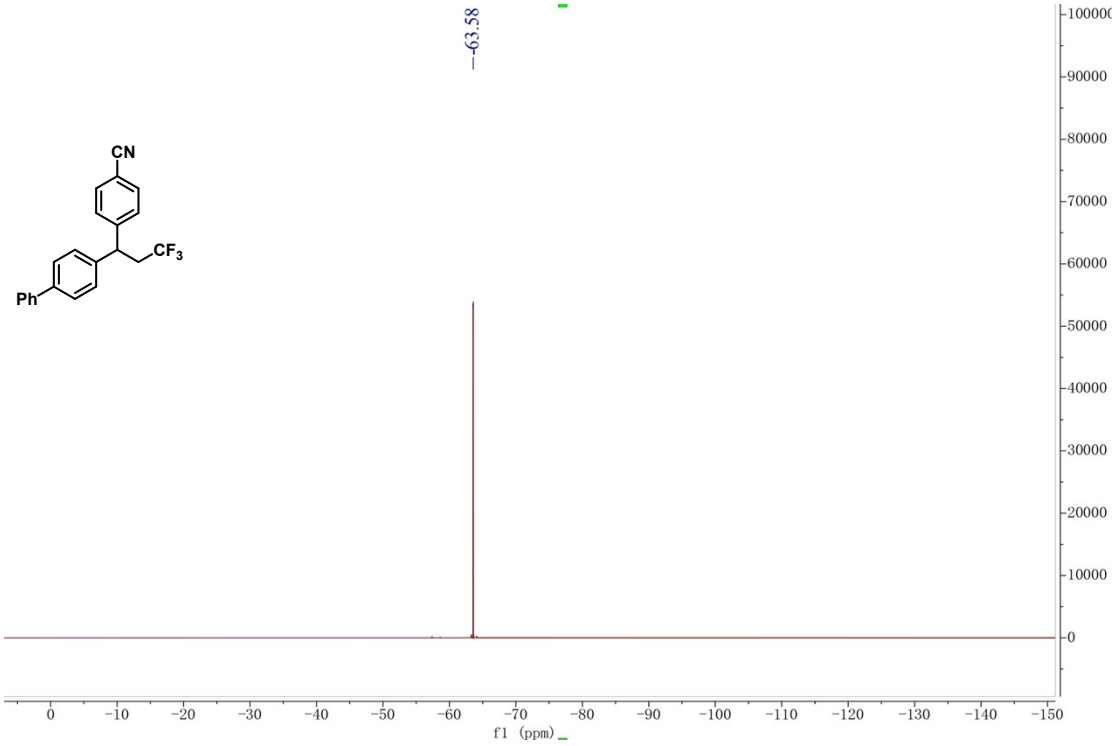
^{1}H NMR (400 MHz, $CDCl_3$) of **4ac**



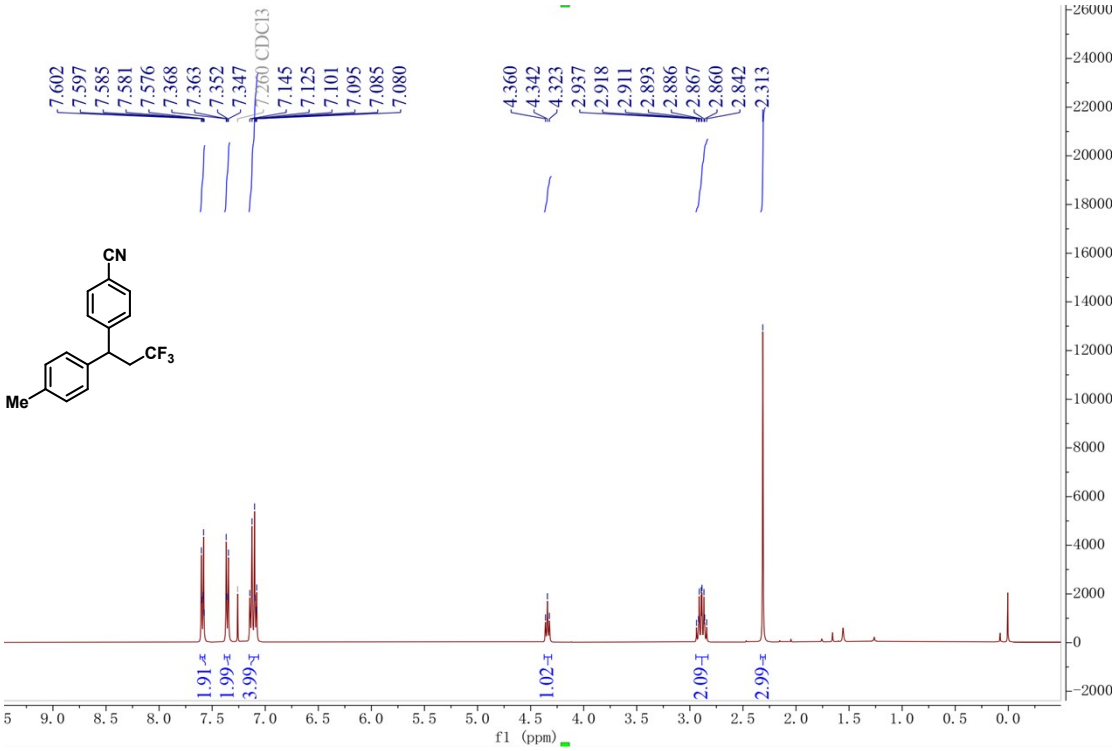
^{13}C NMR (100 MHz, $CDCl_3$) of **4ac**



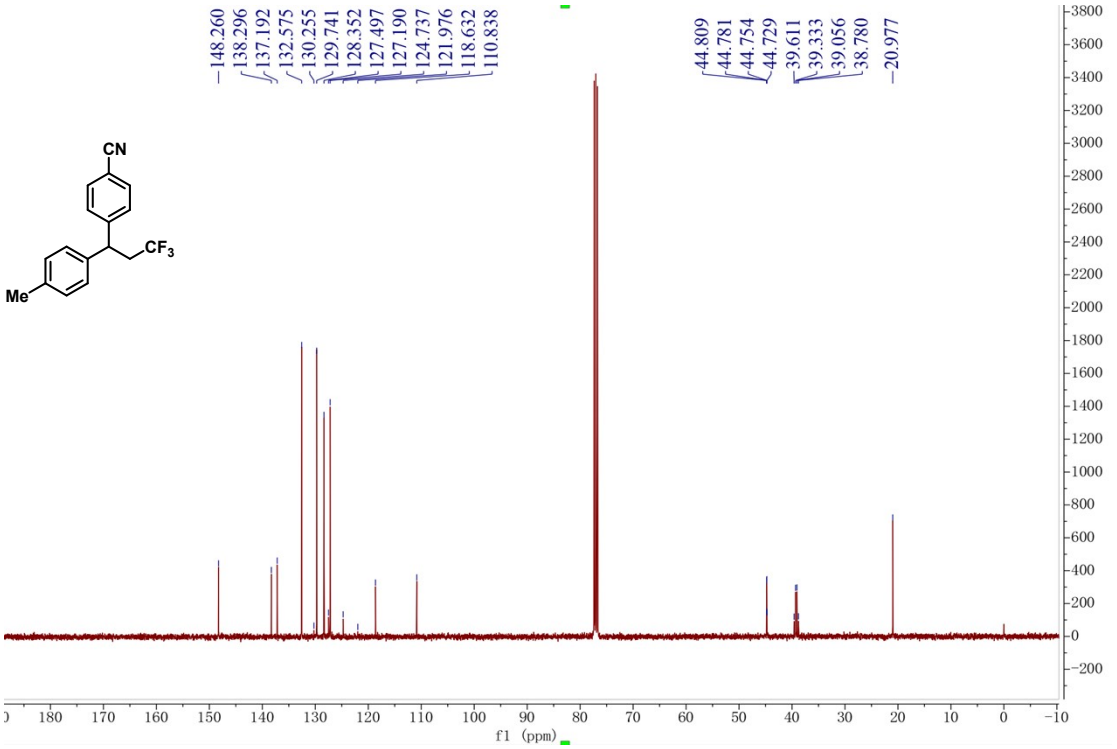
^{19}F NMR (376 MHz, $CDCl_3$) of **4ac**



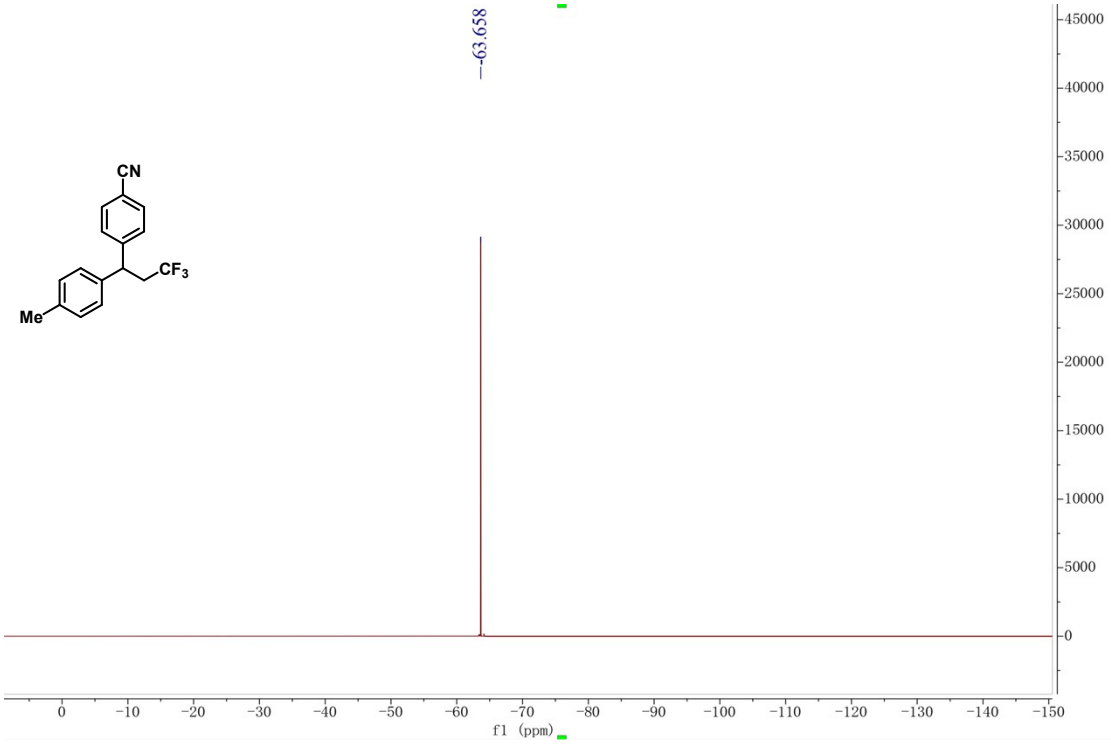
^{1}H NMR (400 MHz, $CDCl_3$) of **4ad**



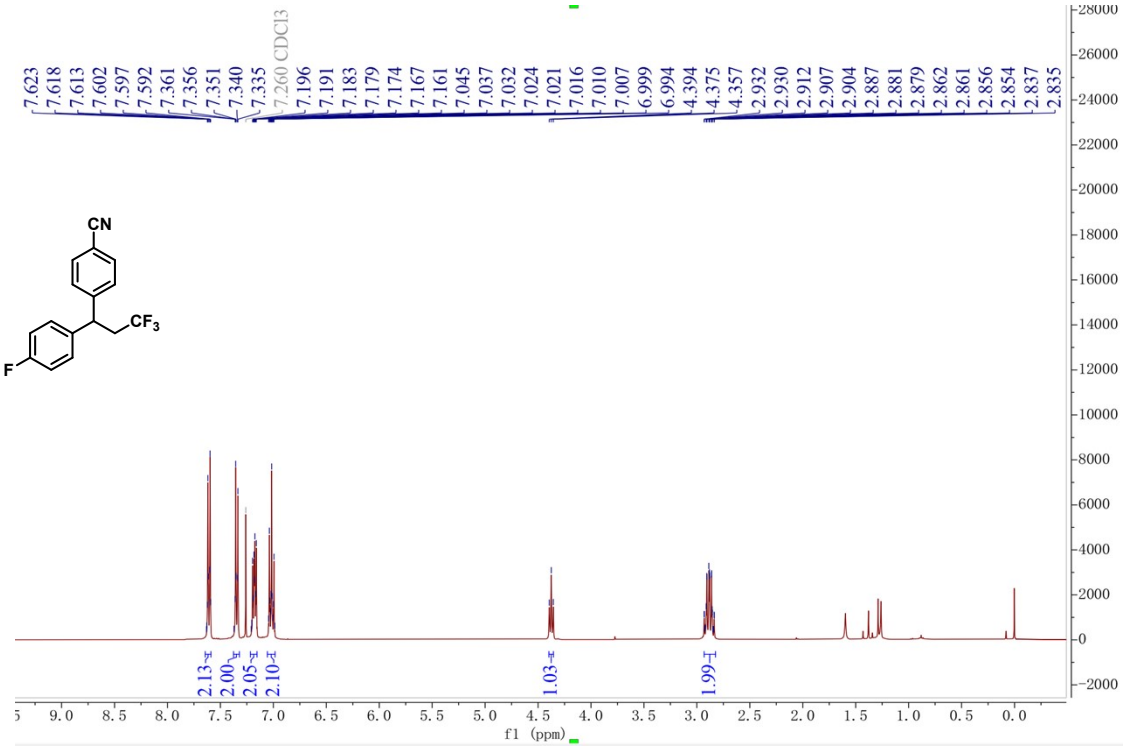
^{13}C NMR (100 MHz, $CDCl_3$) of **4ad**



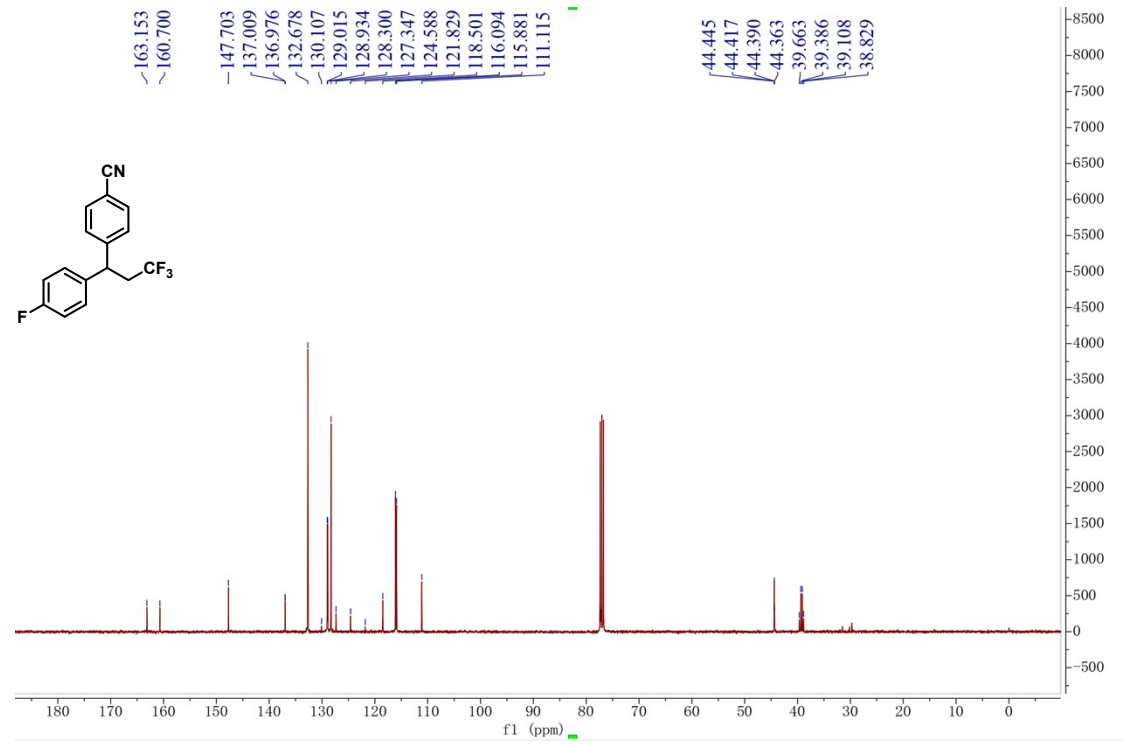
^{19}F NMR (376 MHz, $CDCl_3$) of **4ad**



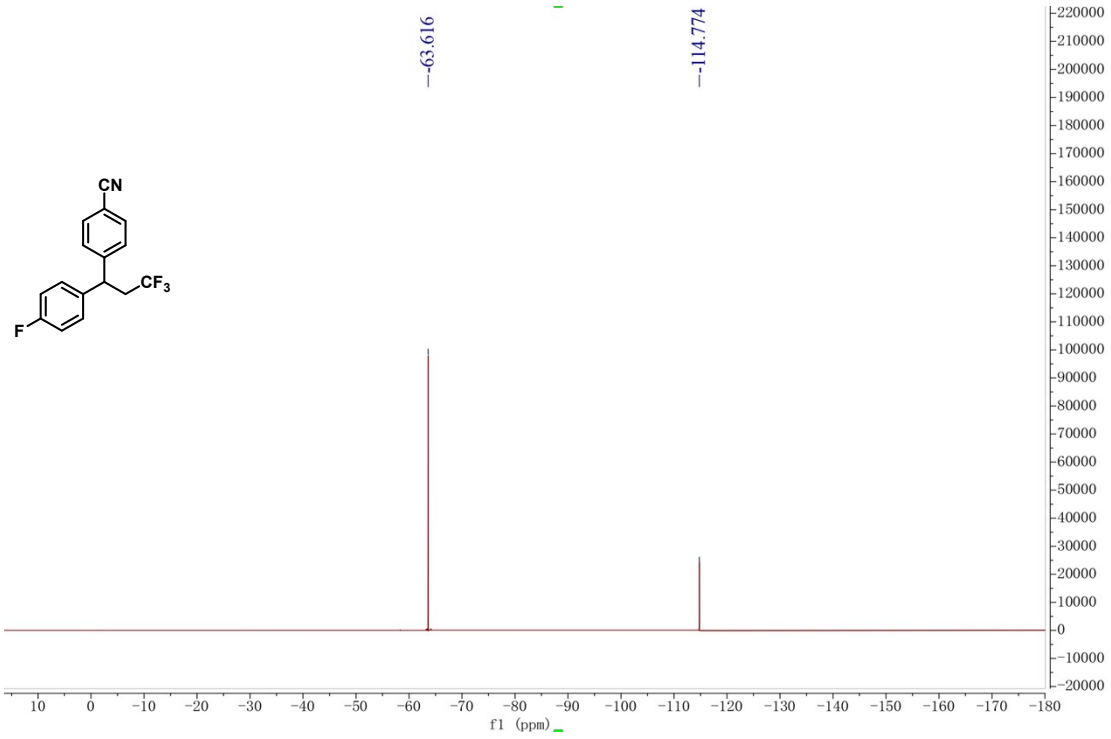
^{1}H NMR (400 MHz, $CDCl_3$) of **4ae**



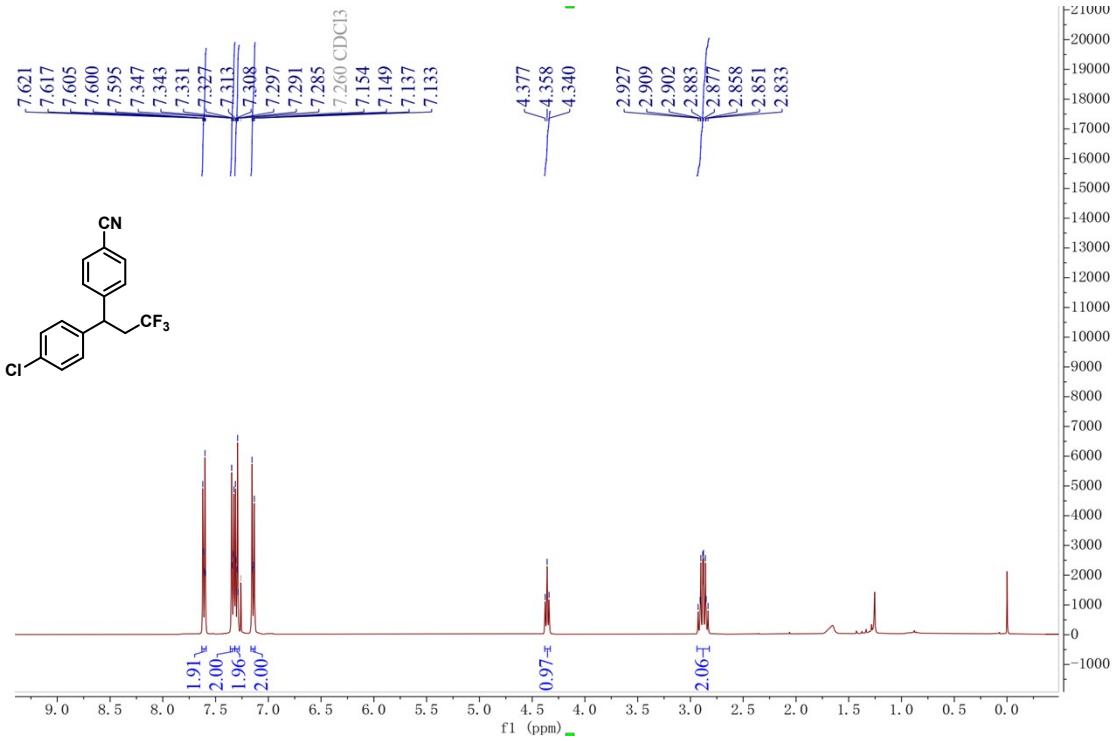
^{13}C NMR (100 MHz, $CDCl_3$) of **4ae**



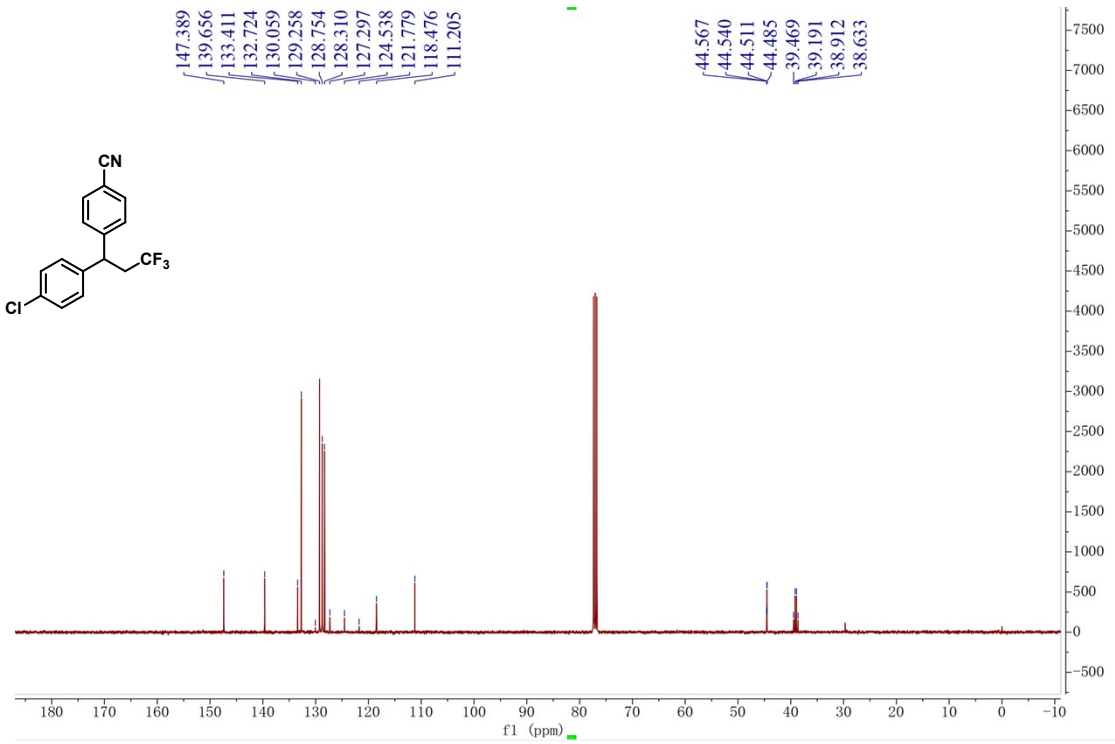
^{19}F NMR (376 MHz, $CDCl_3$) of **4ae**



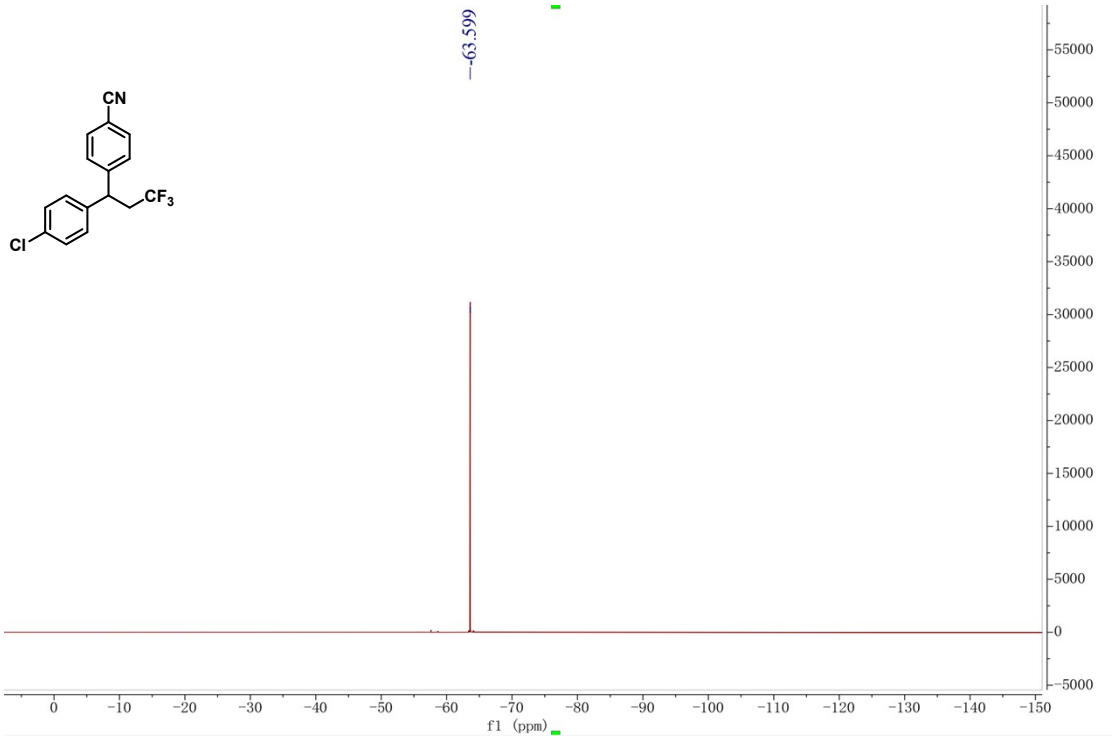
^{1}H NMR (400 MHz, $CDCl_3$) of **4af**



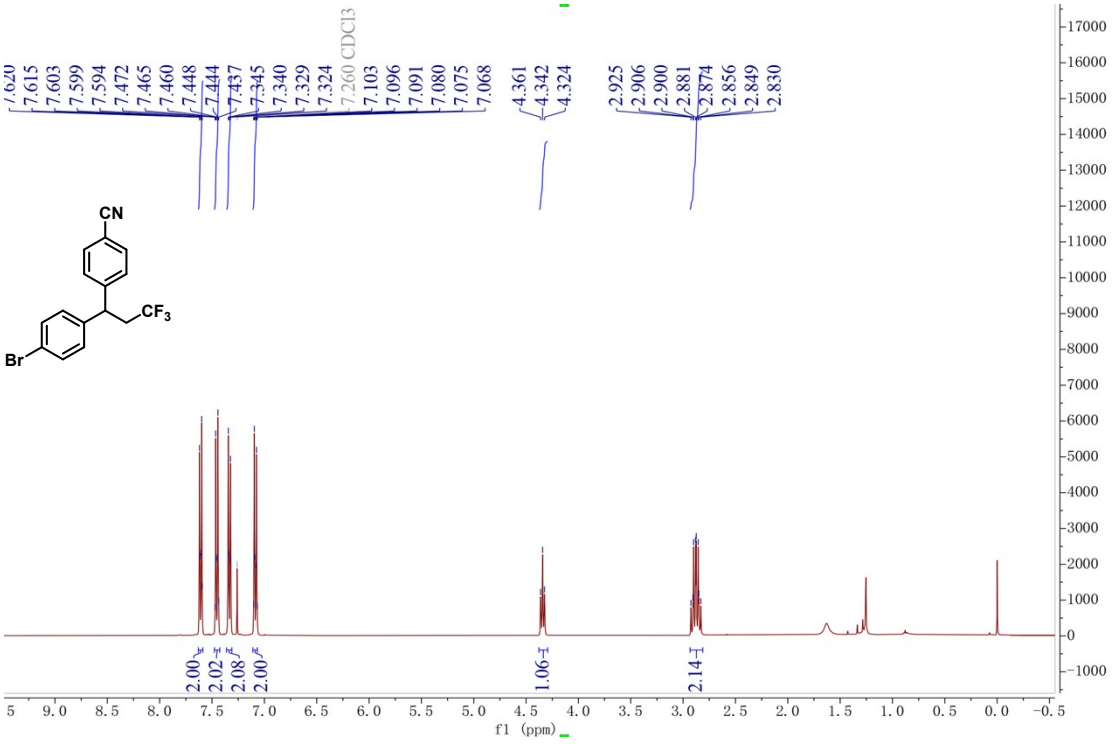
^{13}C NMR (100 MHz, $CDCl_3$) of **4af**



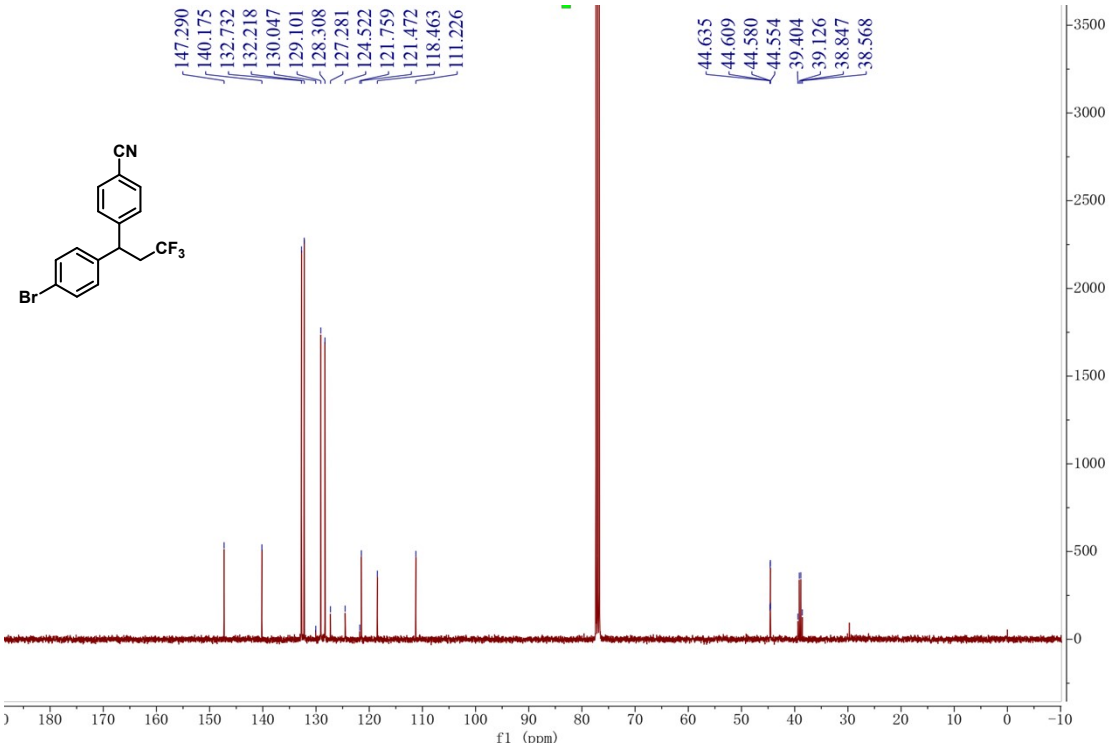
^{19}F NMR (376 MHz, $CDCl_3$) of **4af**



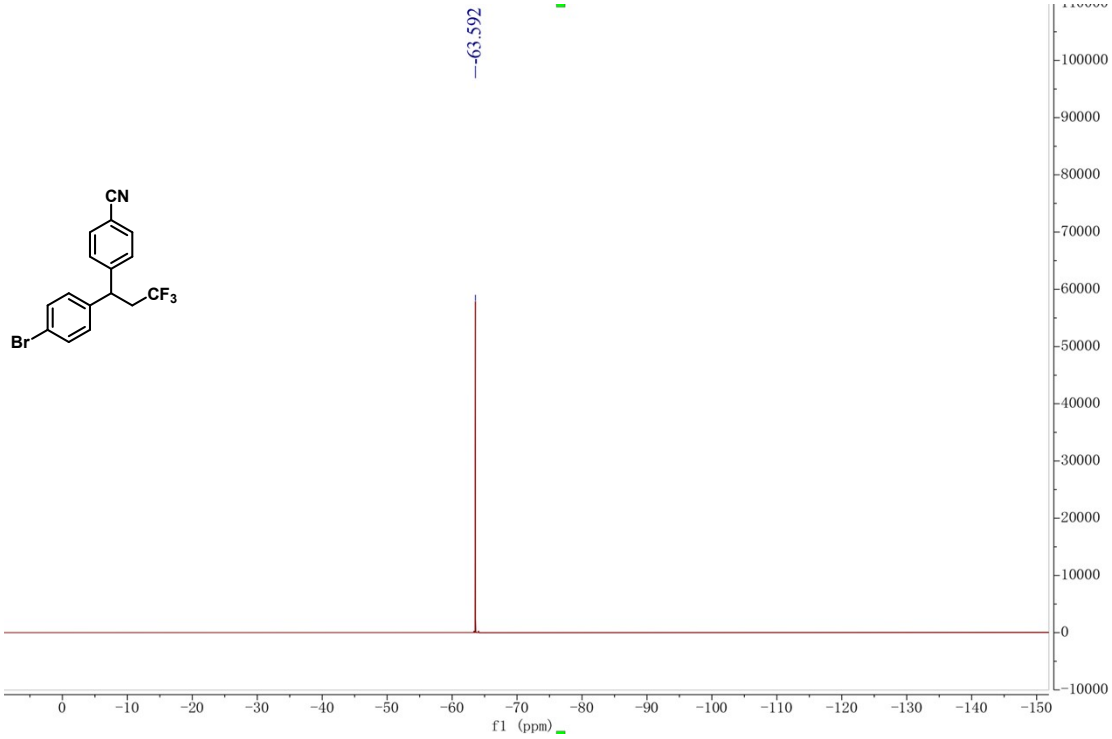
^{1}H NMR (400 MHz, $CDCl_3$) of **4ag**



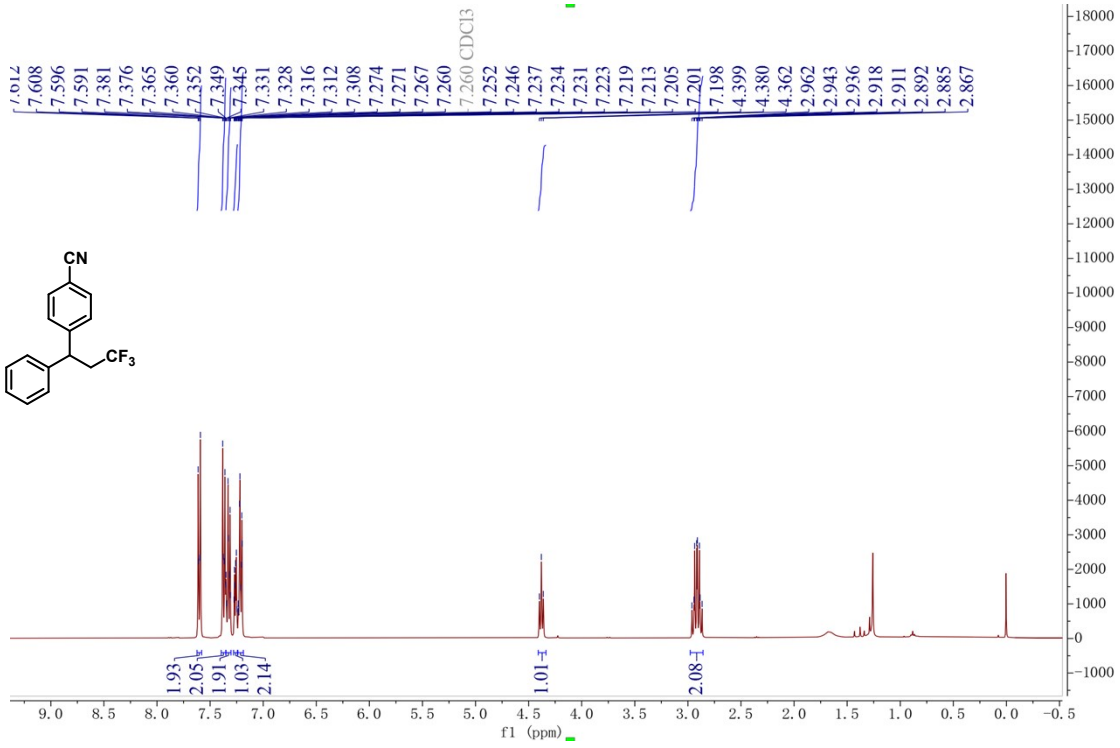
^{13}C NMR (100 MHz, $CDCl_3$) of **4ag**



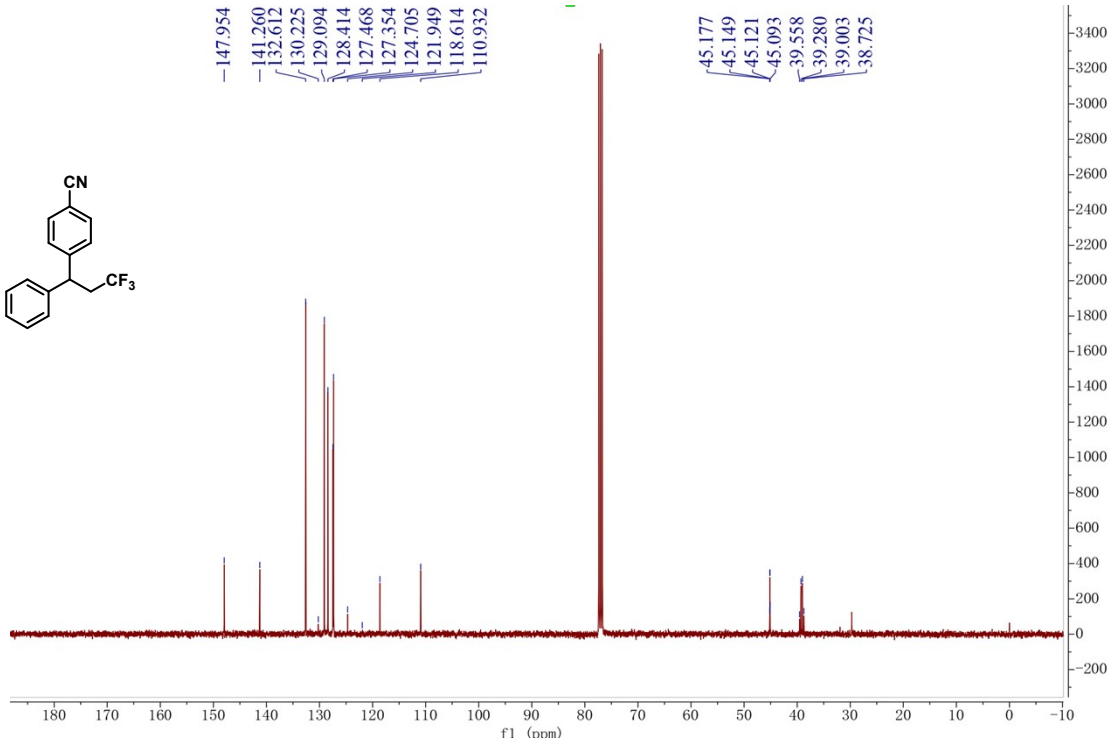
^{19}F NMR (376 MHz, $CDCl_3$) of **4ag**



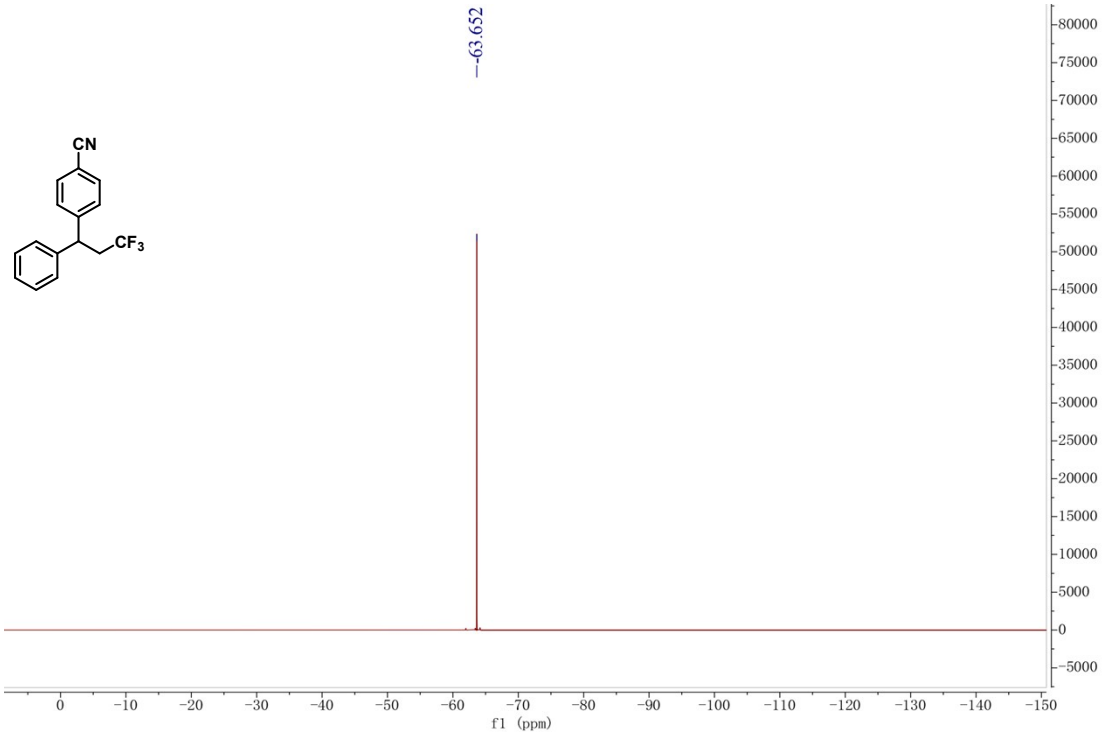
^{1}H NMR (400 MHz, $CDCl_3$) of **4ah**



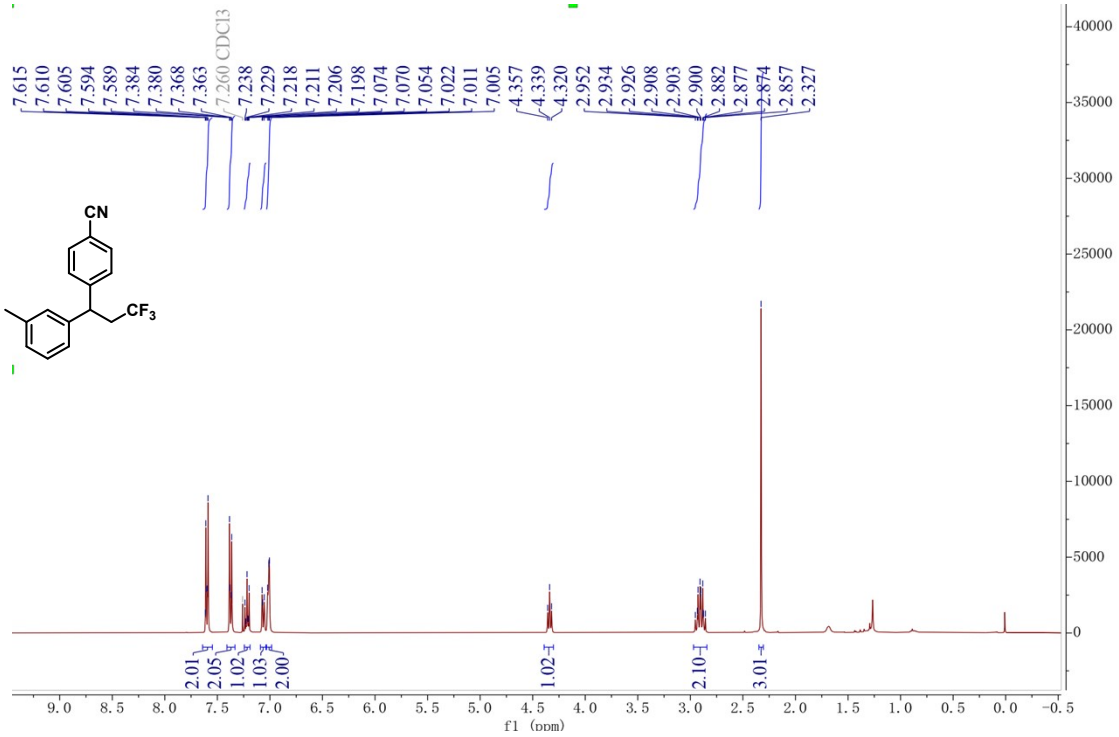
^{13}C NMR (100 MHz, $CDCl_3$) of **4ah**



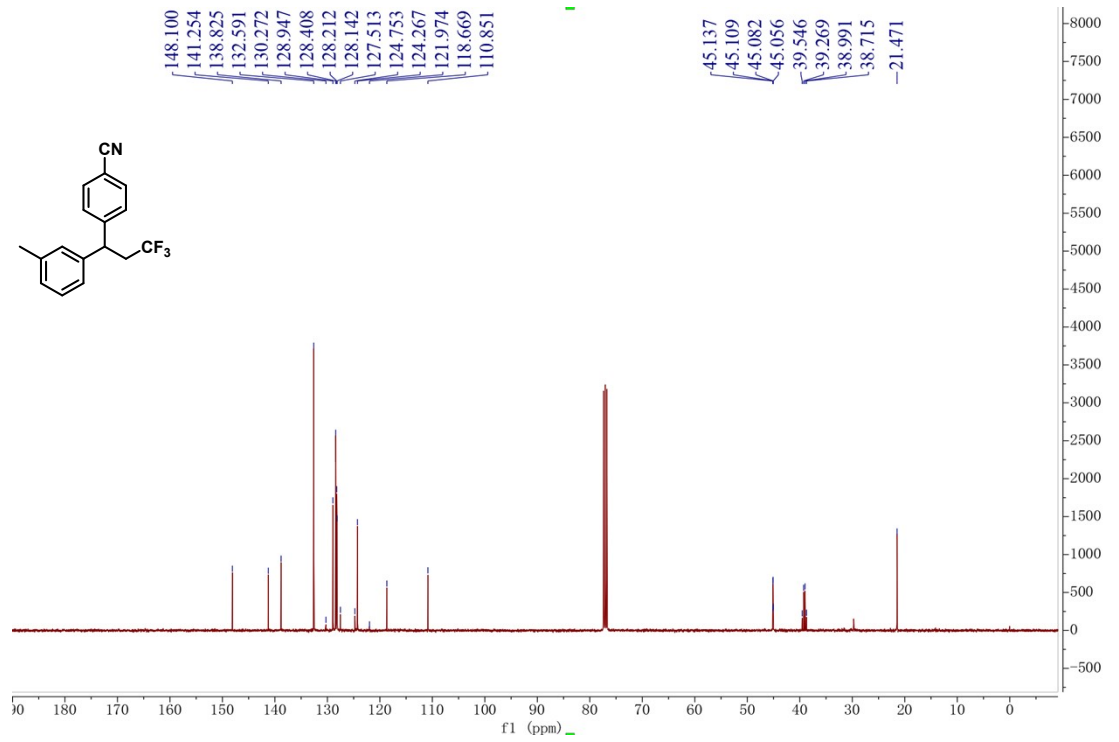
^{19}F NMR (376 MHz, $CDCl_3$) of **4ah**



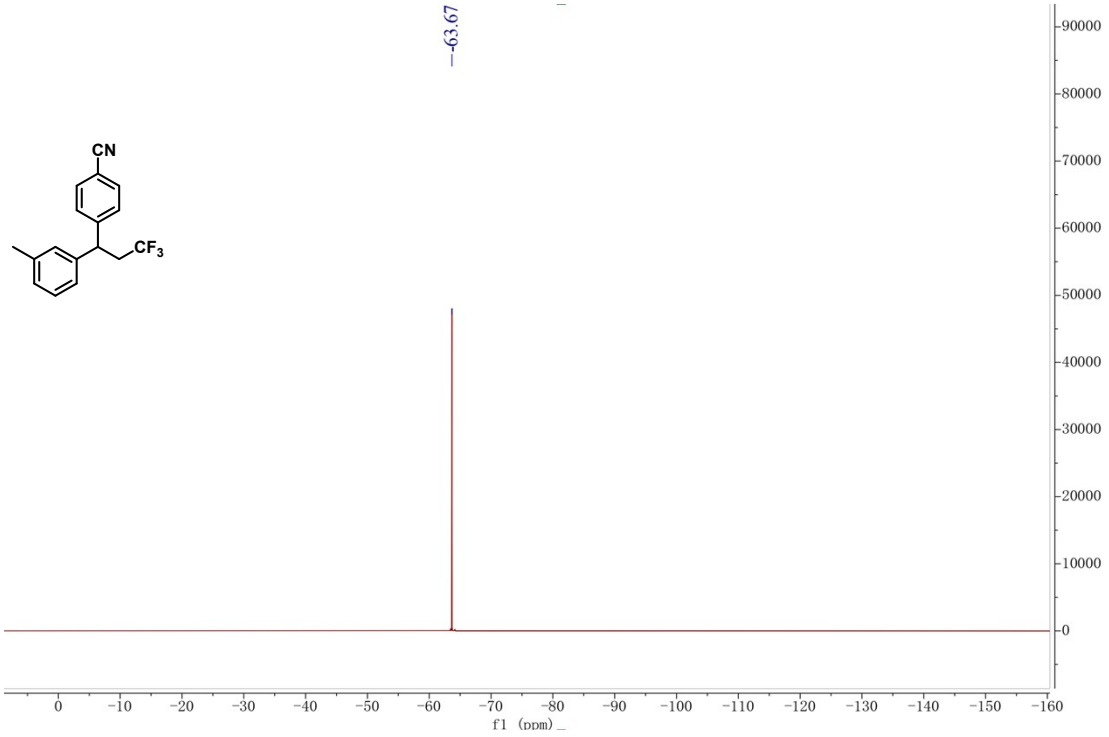
^{1}H NMR (400 MHz, $CDCl_3$) of **4ai**



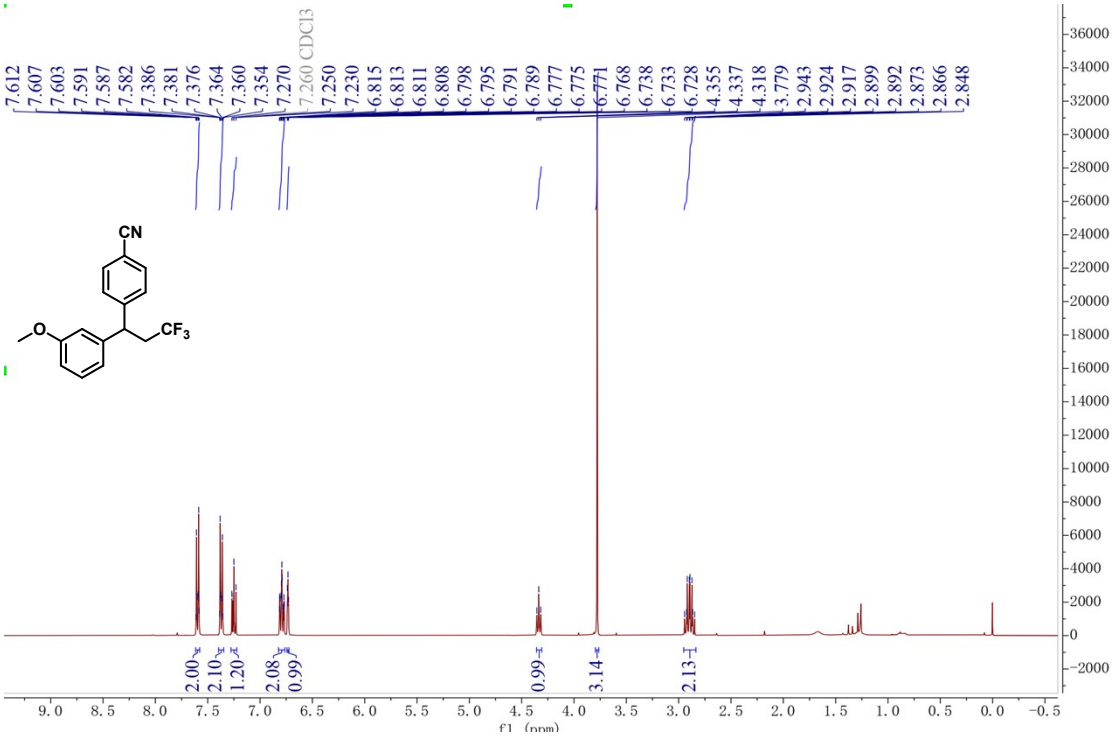
^{13}C NMR (100 MHz, $CDCl_3$) of **4ai**



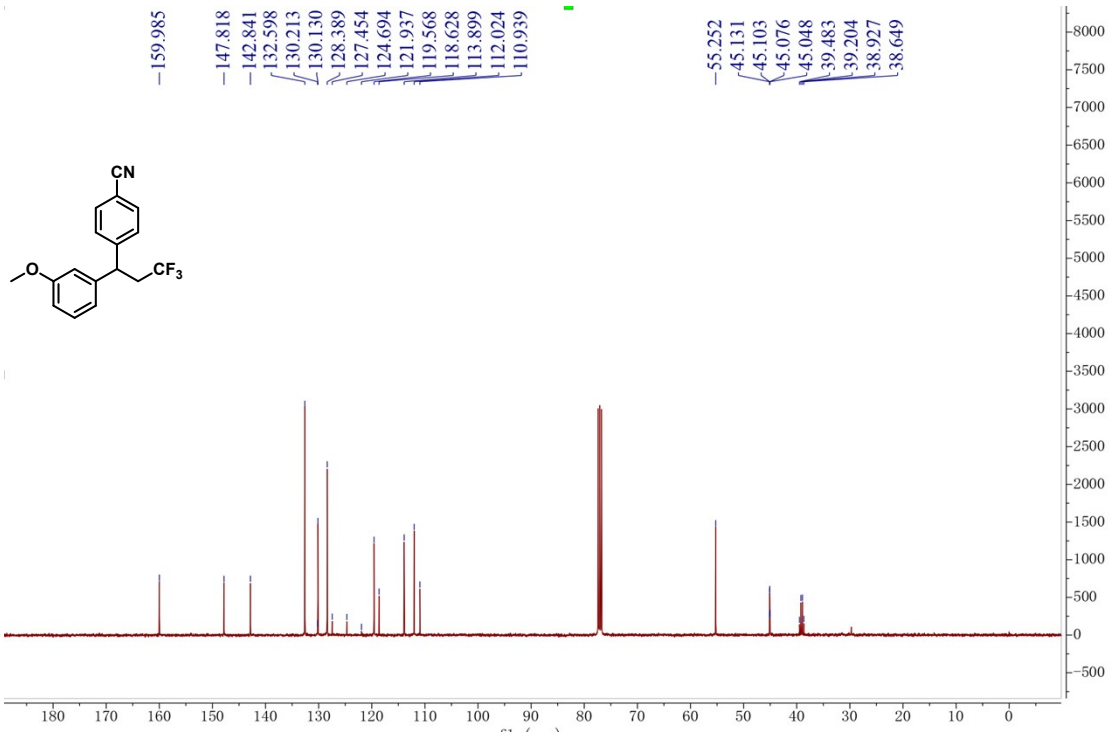
^{19}F NMR (376 MHz, $CDCl_3$) of **4ai**



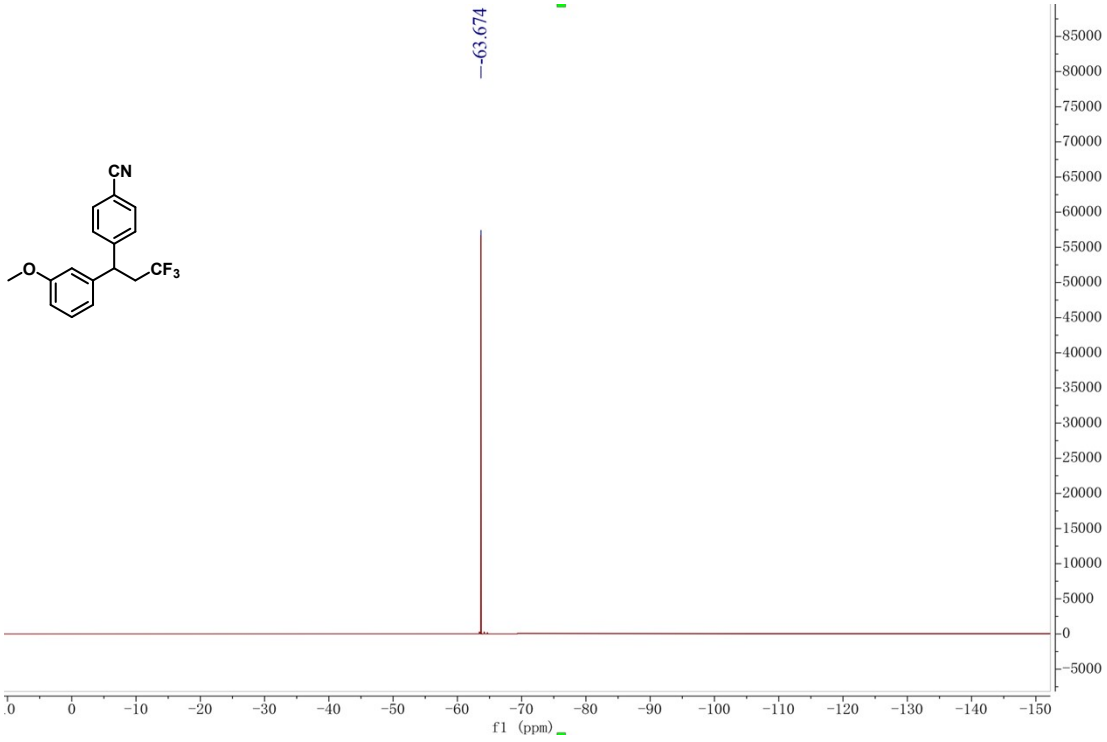
^{1}H NMR (400 MHz, $CDCl_3$) of **4aj**



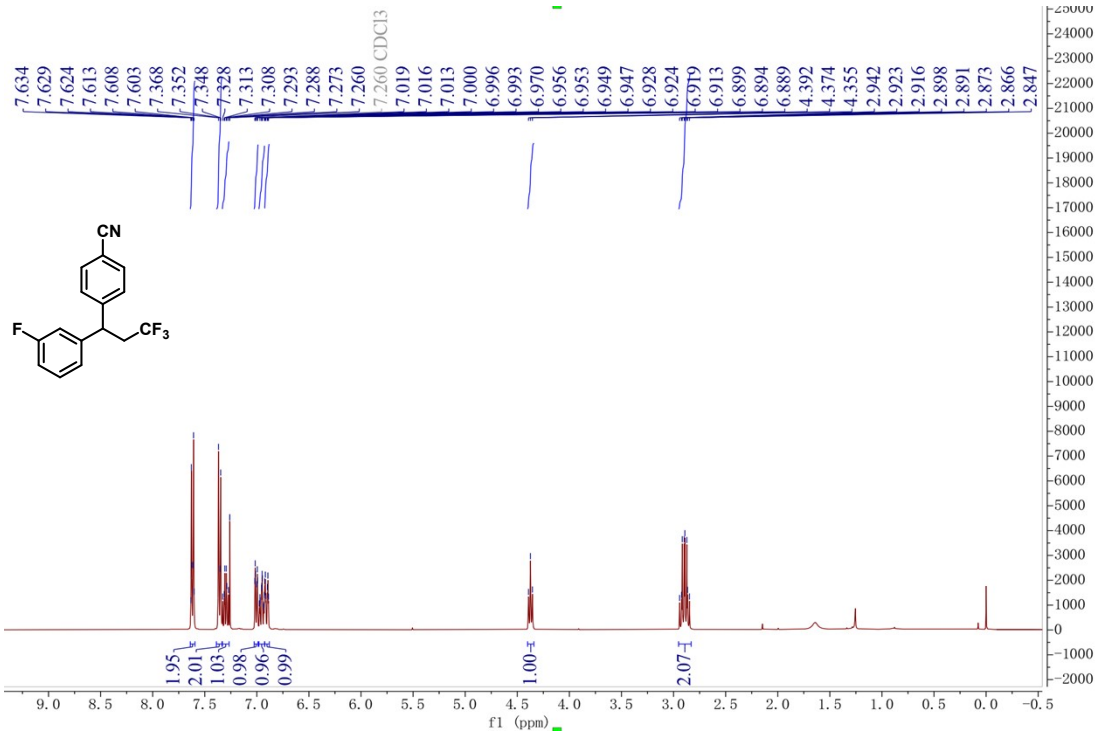
^{13}C NMR (100 MHz, $CDCl_3$) of **4aj**



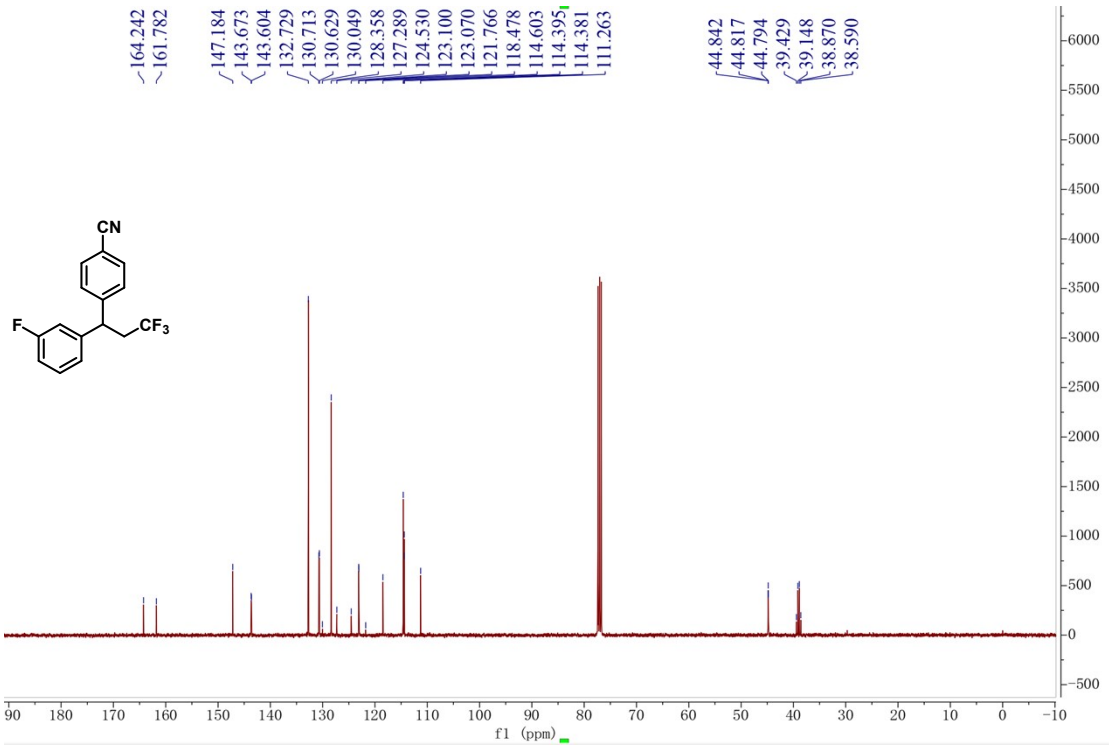
^{19}F NMR (376 MHz, $CDCl_3$) of **4aj**



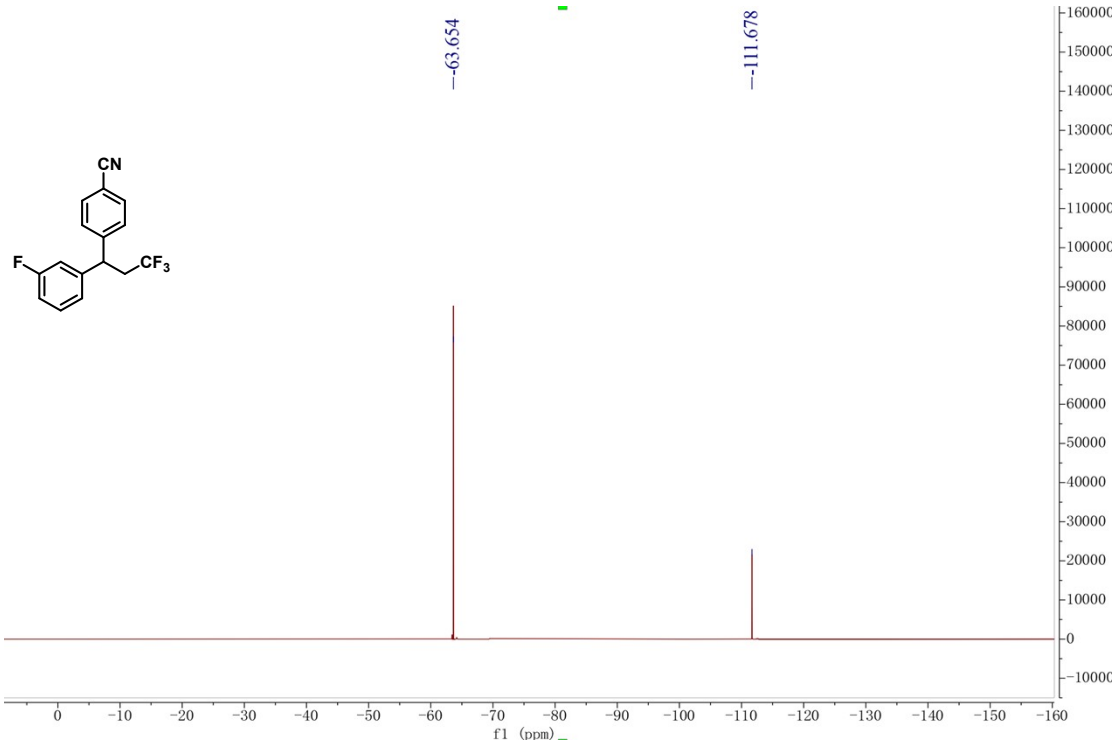
^{1}H NMR (400 MHz, $CDCl_3$) of **4ak**



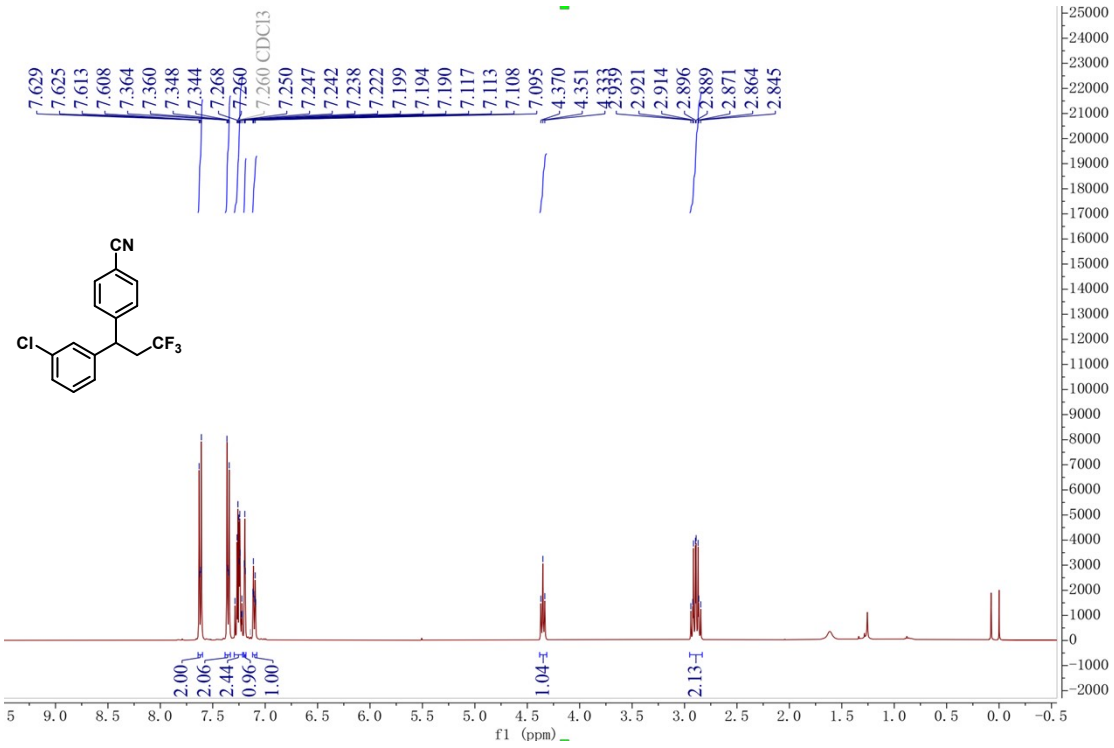
^{13}C NMR (100 MHz, $CDCl_3$) of **4ak**



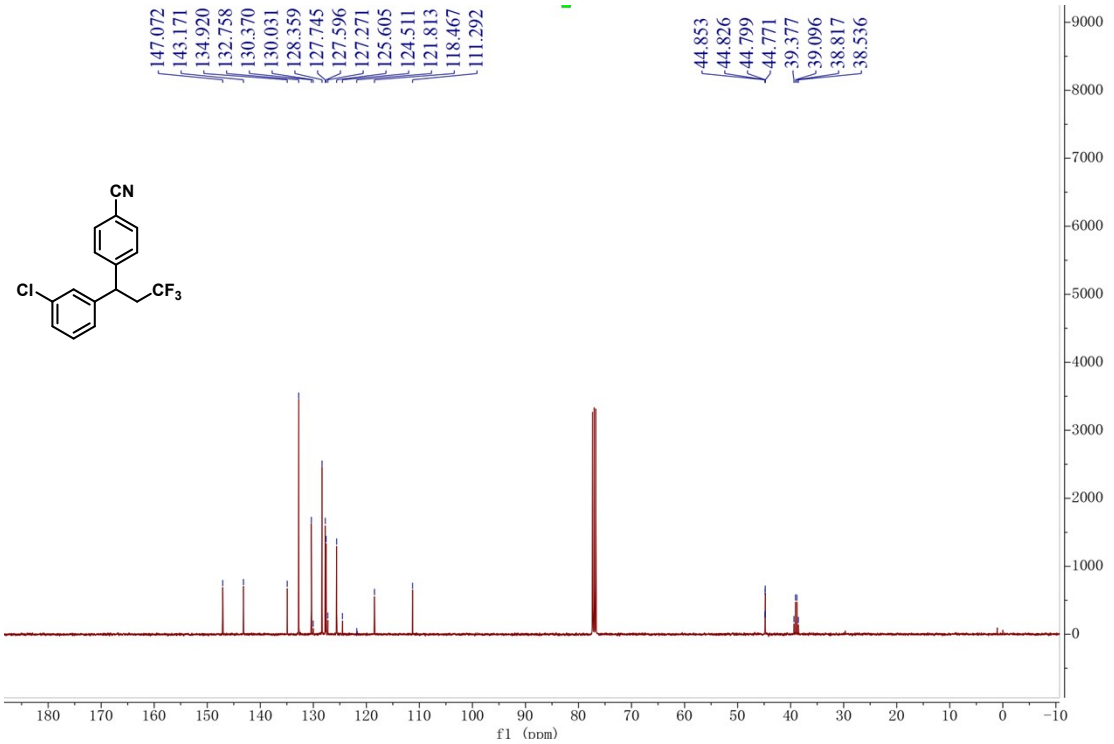
^{19}F NMR (376 MHz, $CDCl_3$) of **4ak**



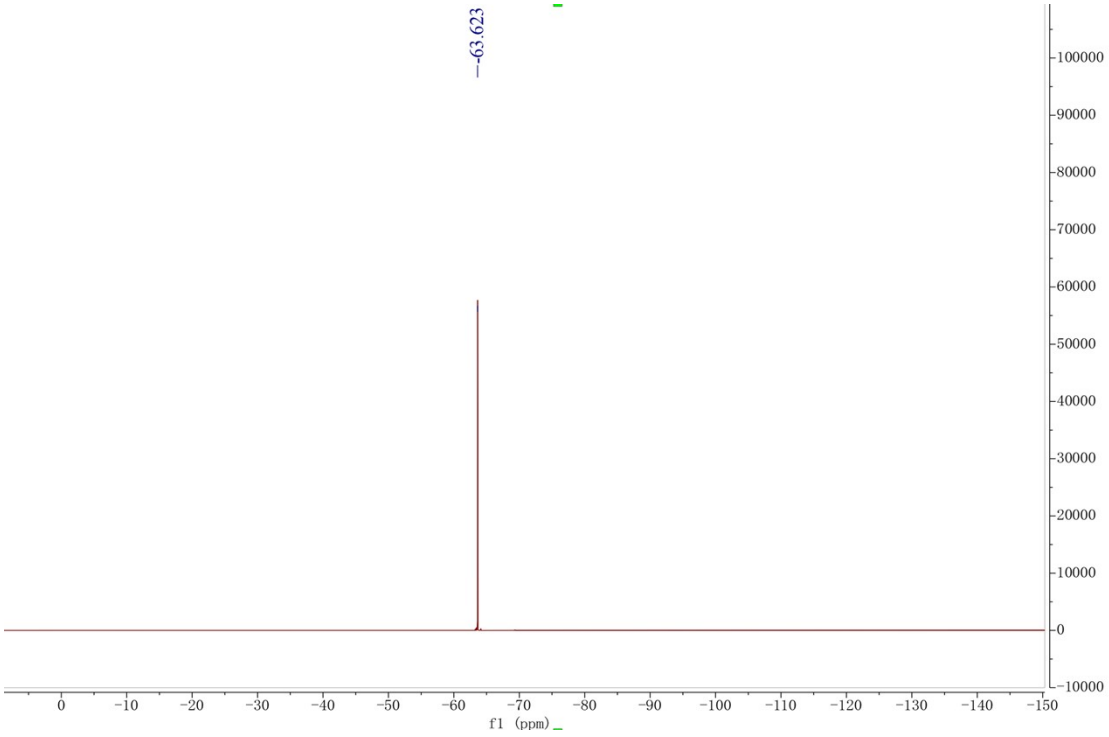
^{1}H NMR (400 MHz, $CDCl_3$) of **4al**



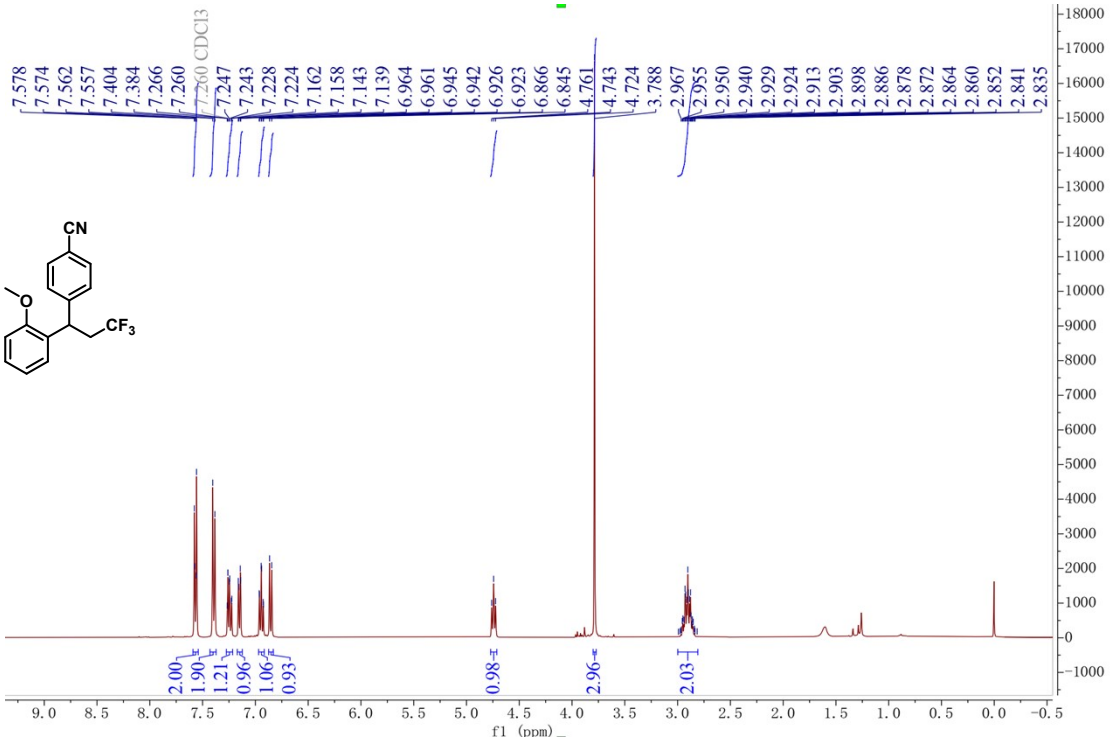
^{13}C NMR (100 MHz, $CDCl_3$) of **4al**



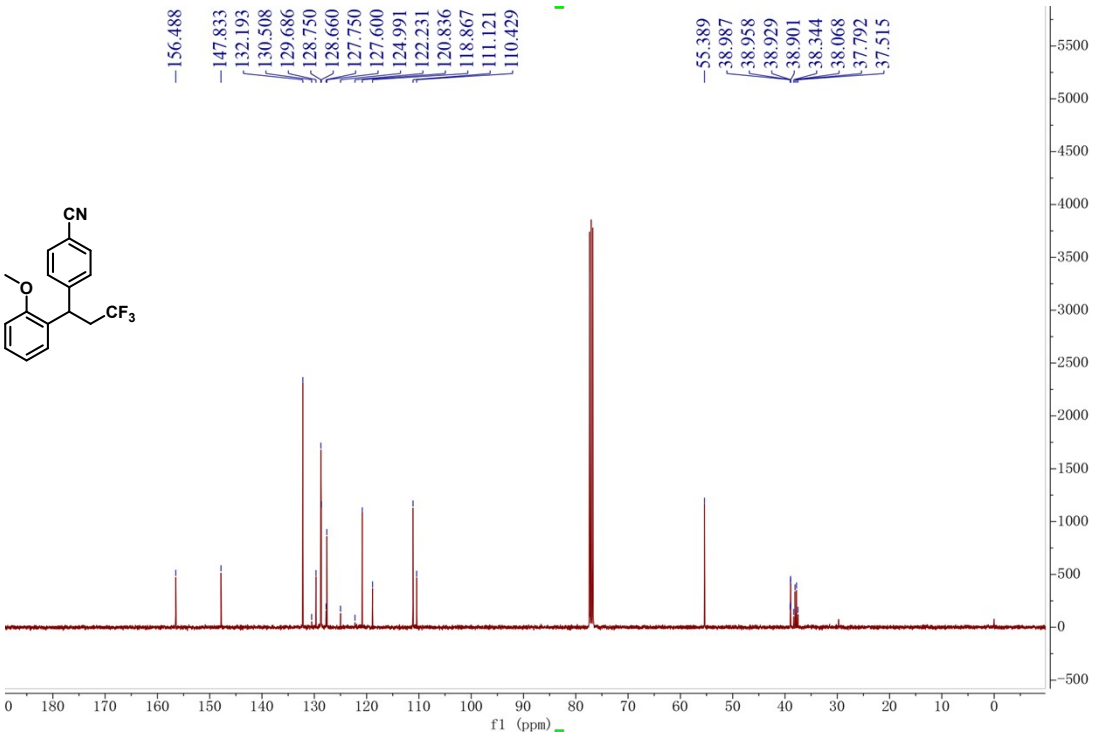
^{19}F NMR (376 MHz, $CDCl_3$) of **4al**



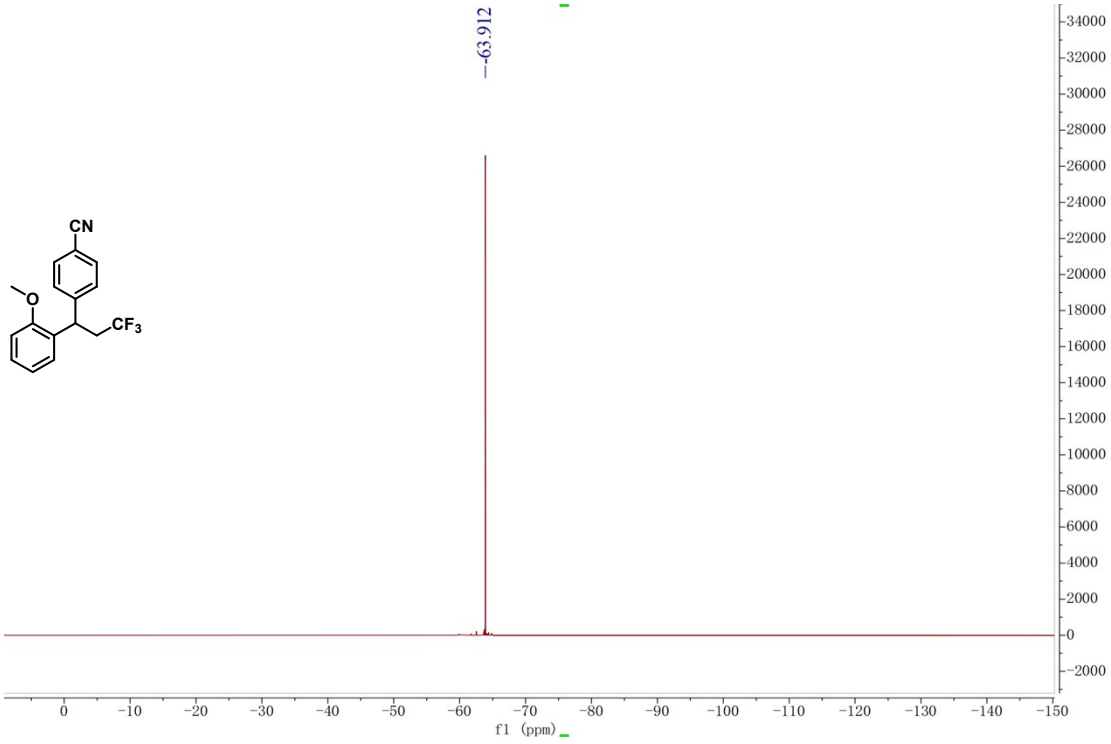
^{1}H NMR (400 MHz, $CDCl_3$) of **4am**



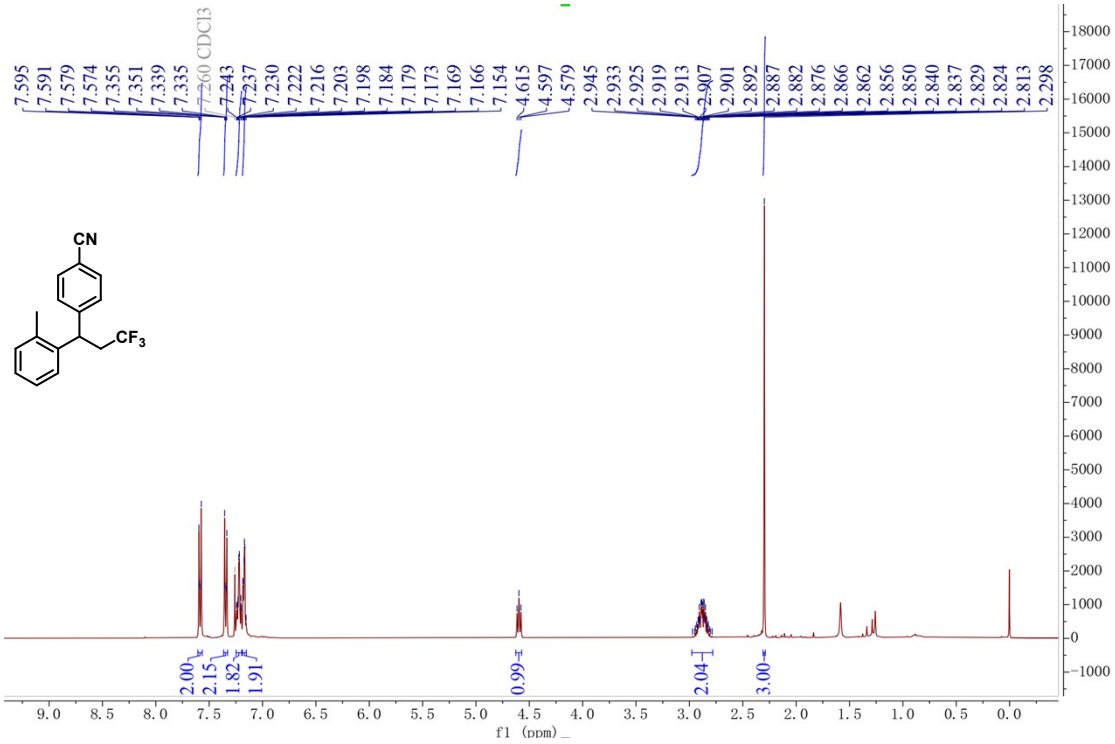
^{13}C NMR (100 MHz, $CDCl_3$) of **4am**



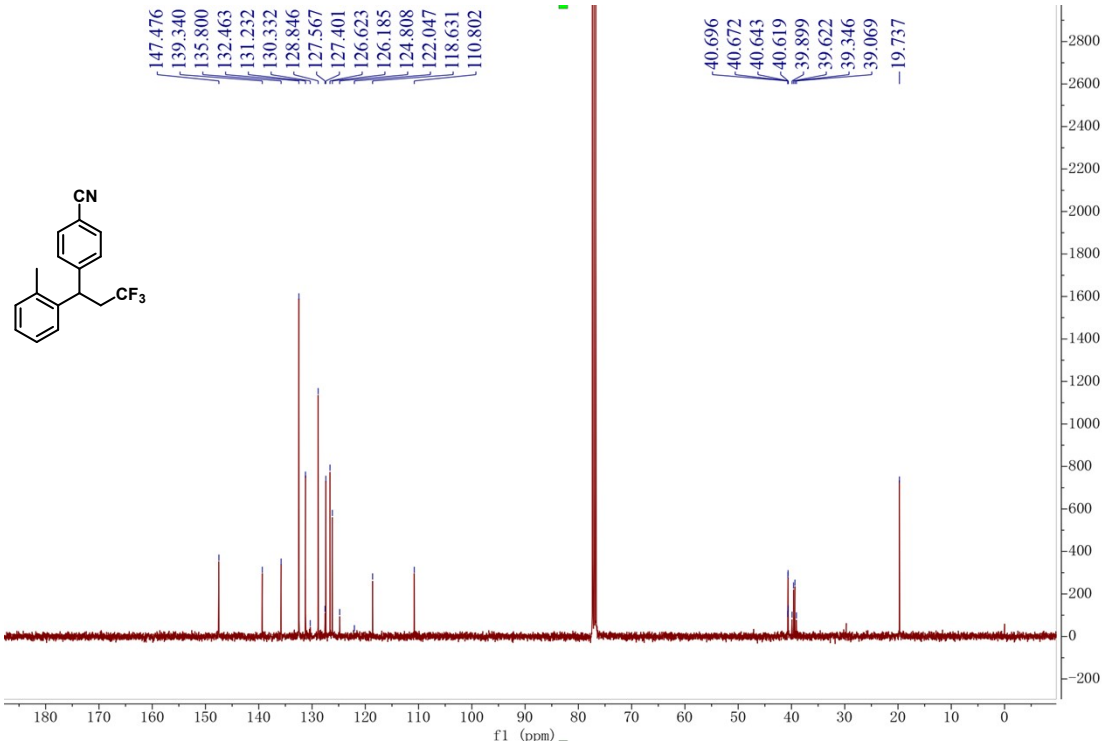
^{19}F NMR (376 MHz, $CDCl_3$) of **4am**



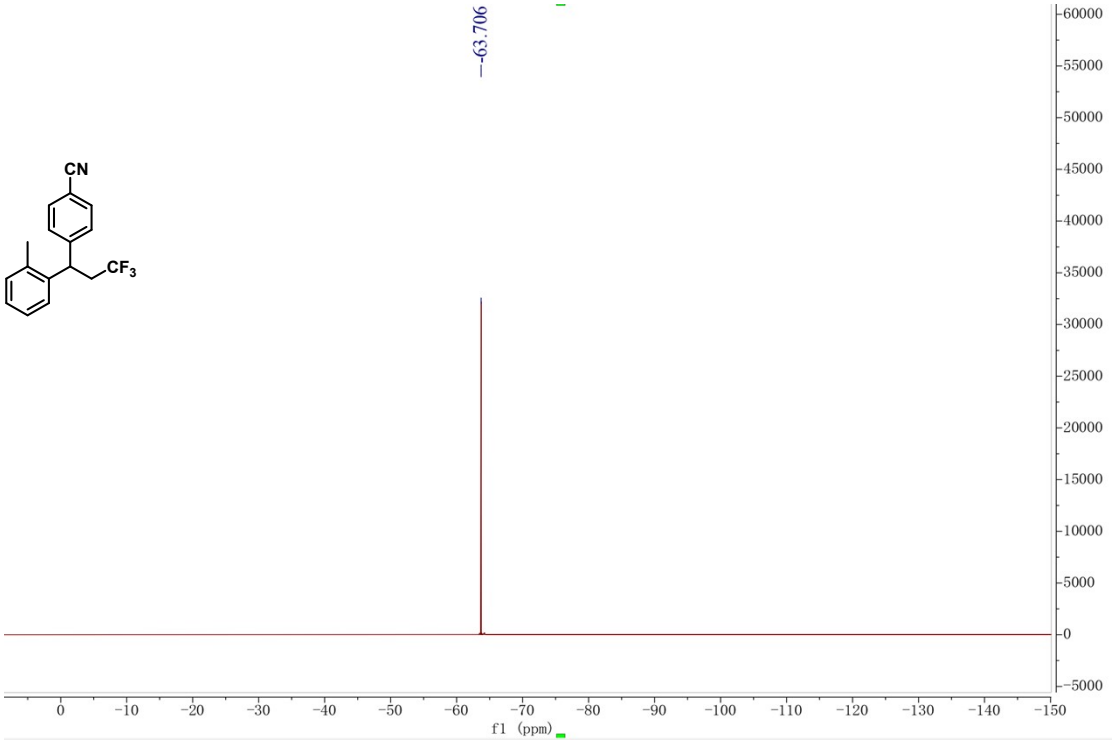
^{1}H NMR (400 MHz, $CDCl_3$) of **4an**



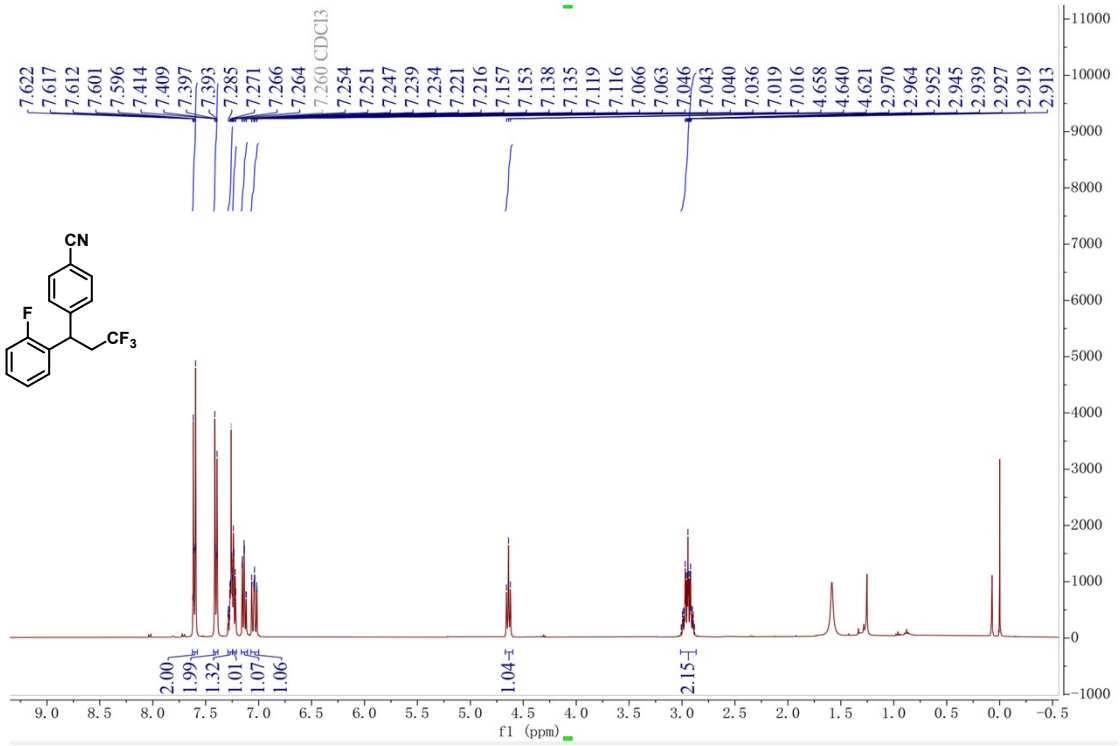
^{13}C NMR (100 MHz, $CDCl_3$) of **4an**



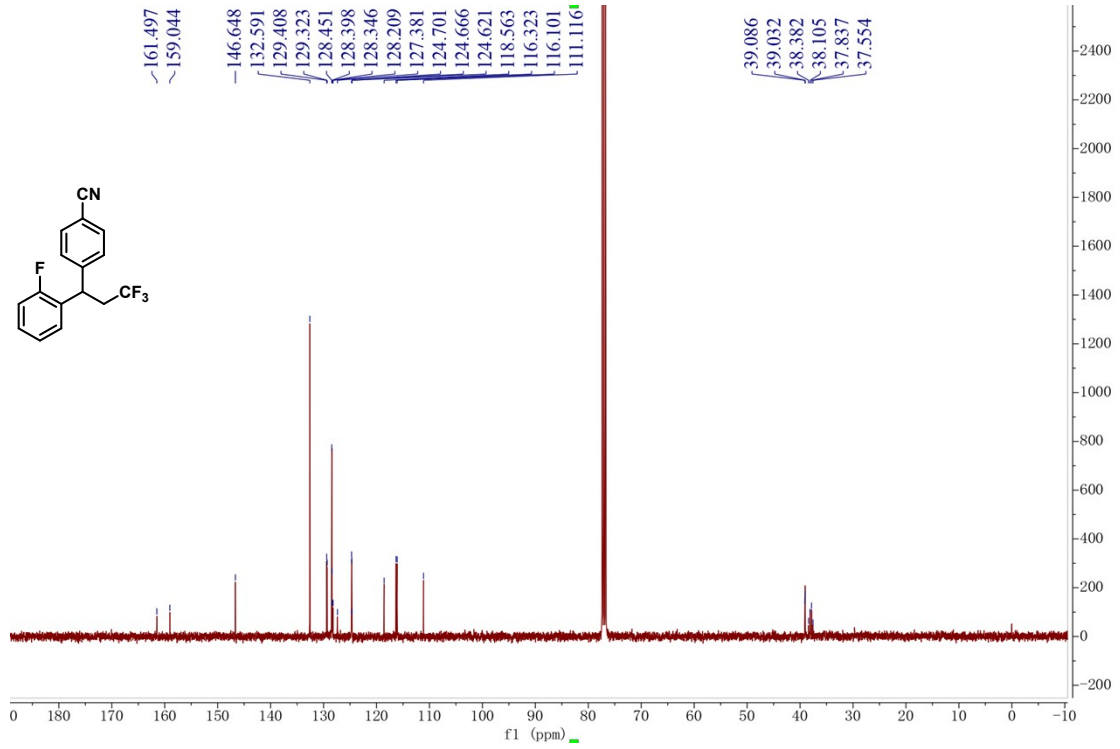
^{19}F NMR (376 MHz, $CDCl_3$) of **4an**



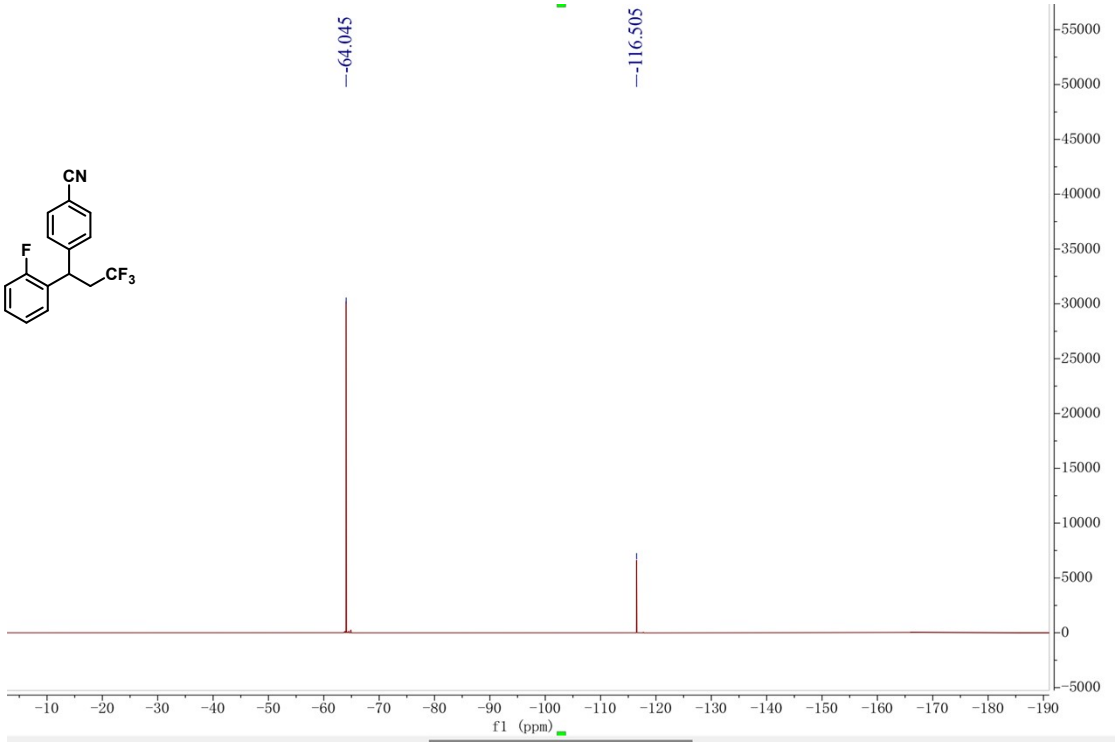
^{1}H NMR (400 MHz, $CDCl_3$) of **4ao**



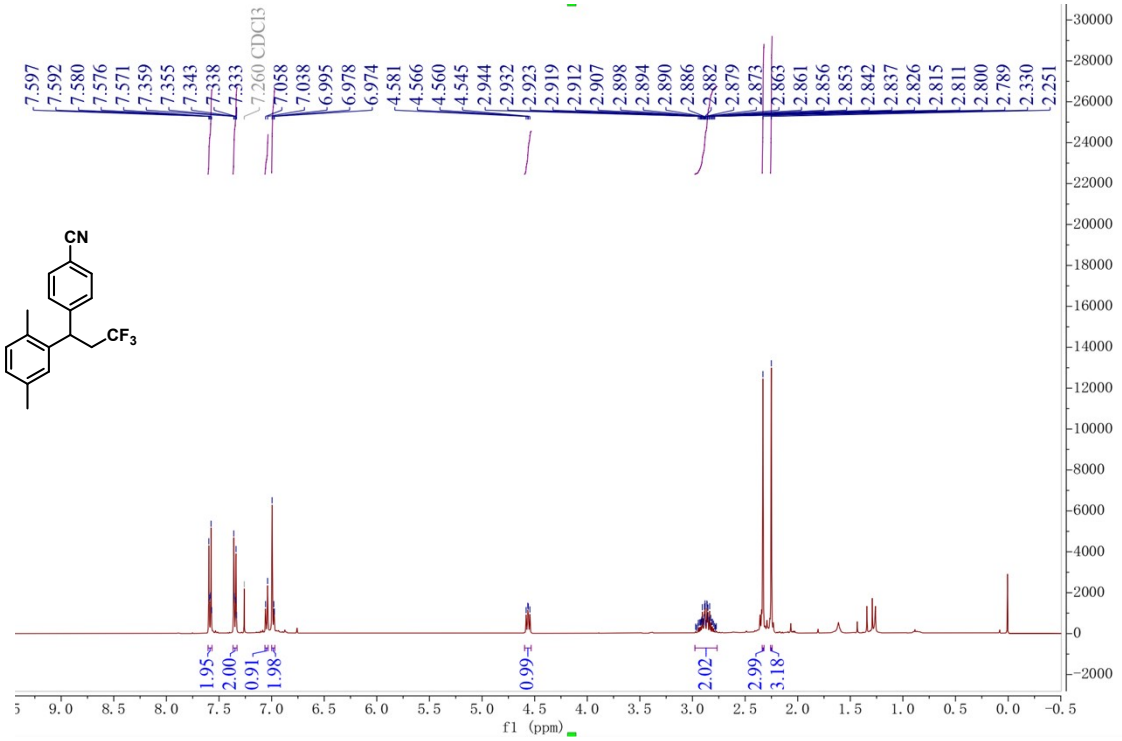
^{13}C NMR (100 MHz, $CDCl_3$) of **4ao**



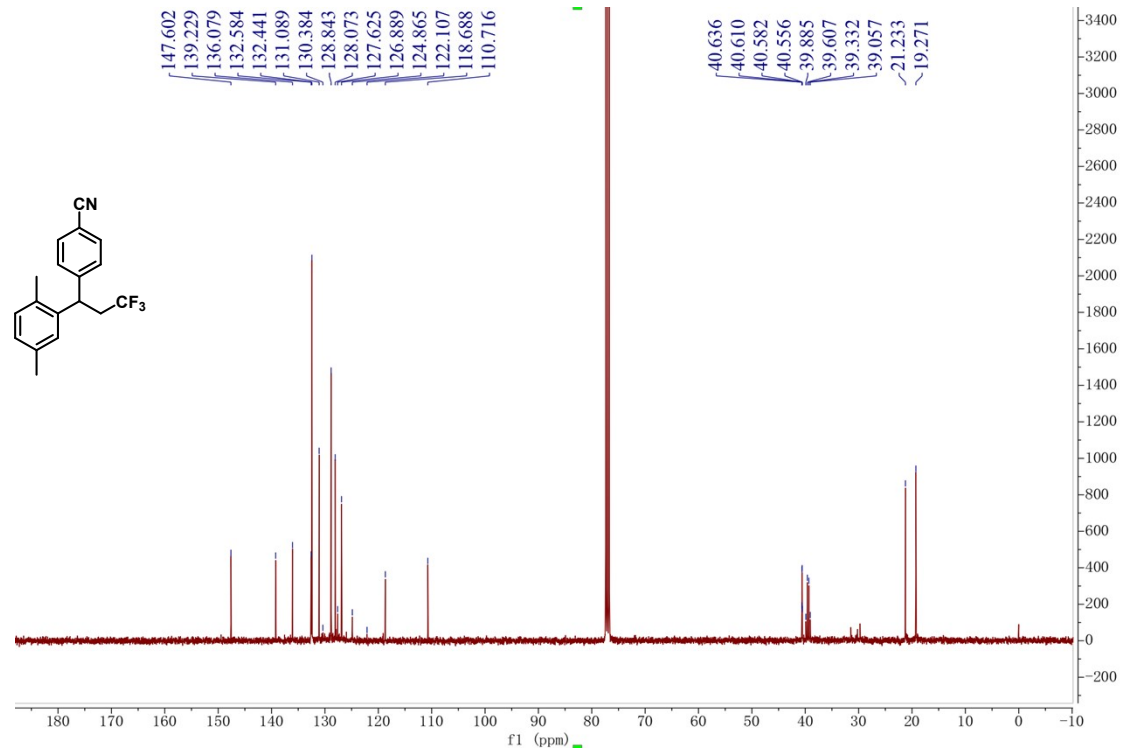
^{19}F NMR (376 MHz, $CDCl_3$) of **4ao**



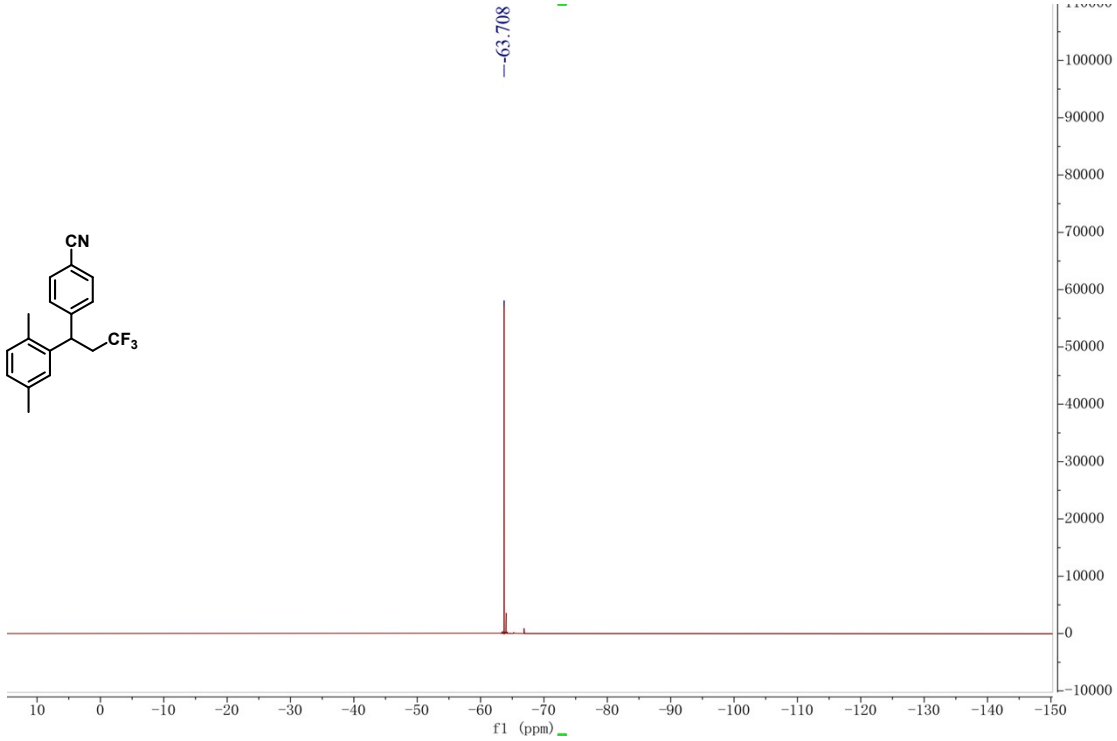
^{1}H NMR (400 MHz, $CDCl_3$) of **4ap**



^{13}C NMR (100 MHz, $CDCl_3$) of **4ap**



^{19}F NMR (376 MHz, $CDCl_3$) of **4ap**



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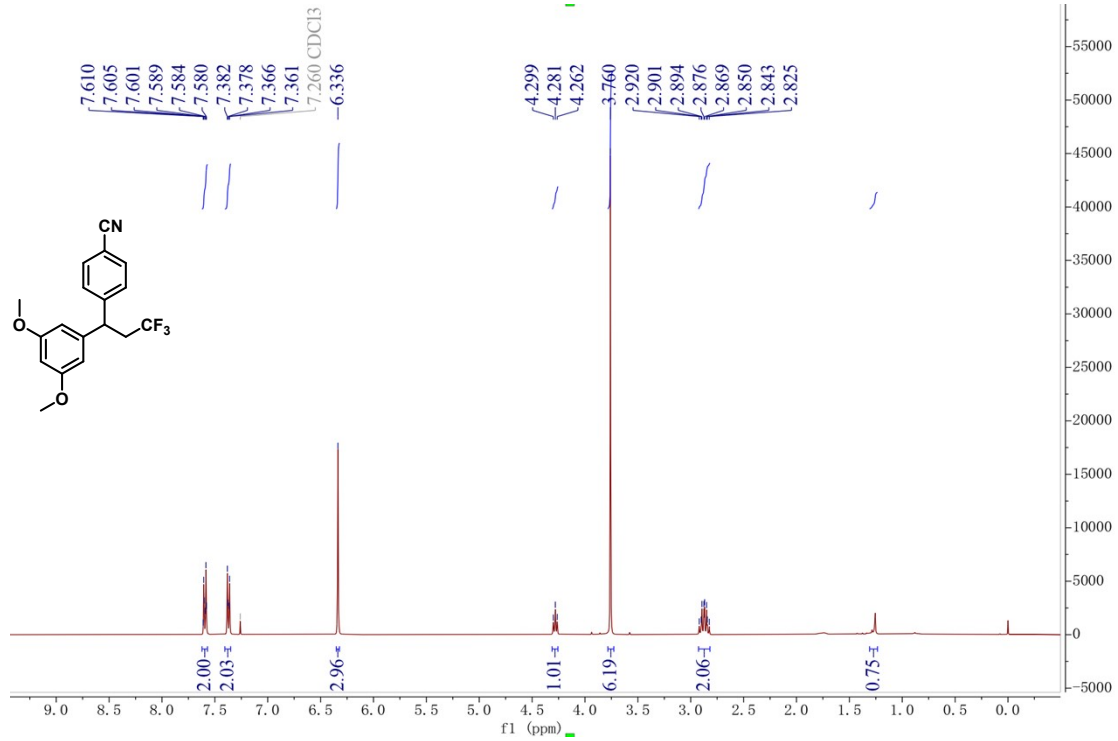
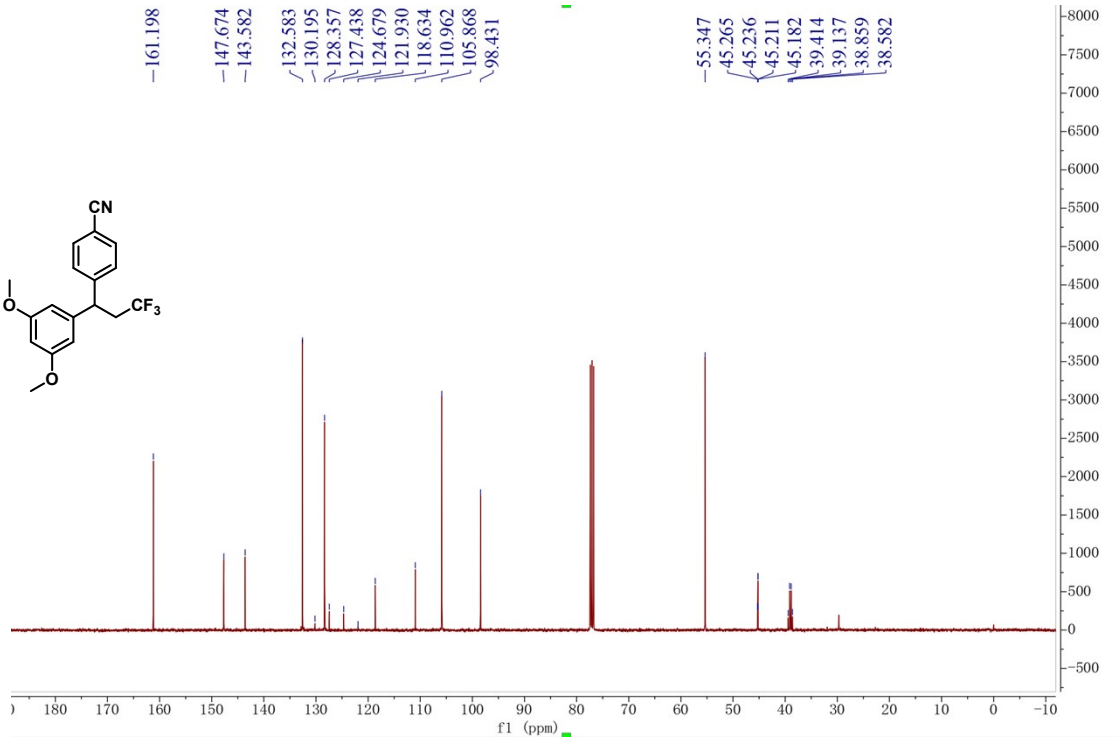
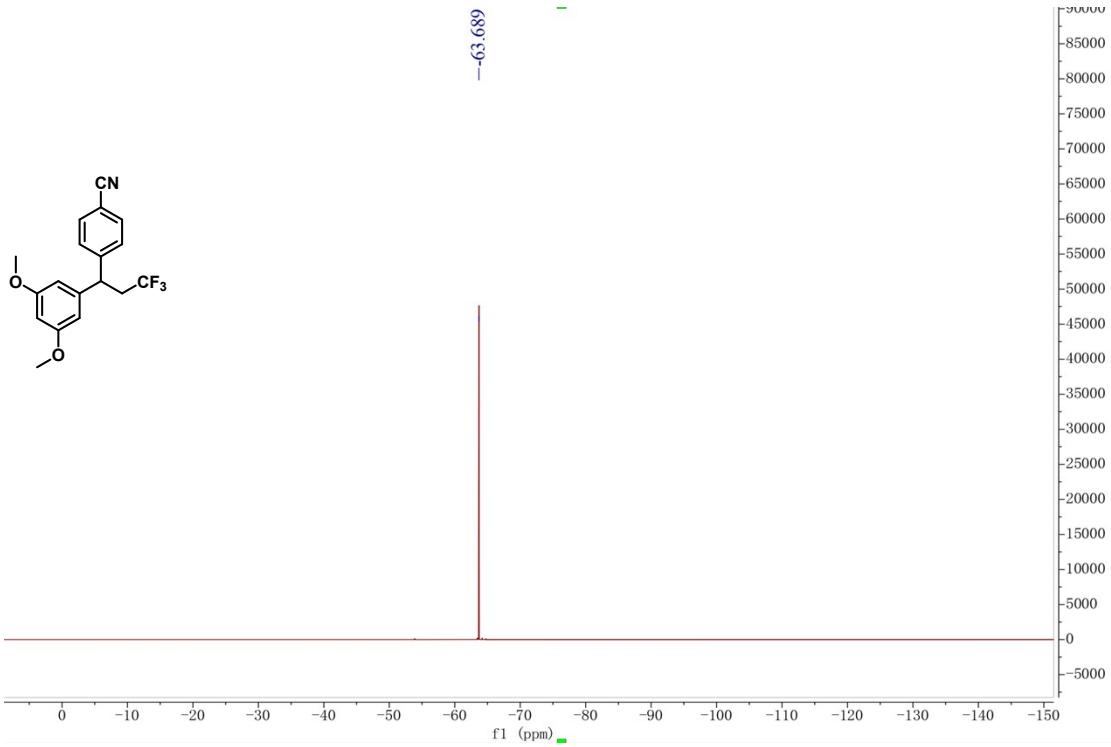


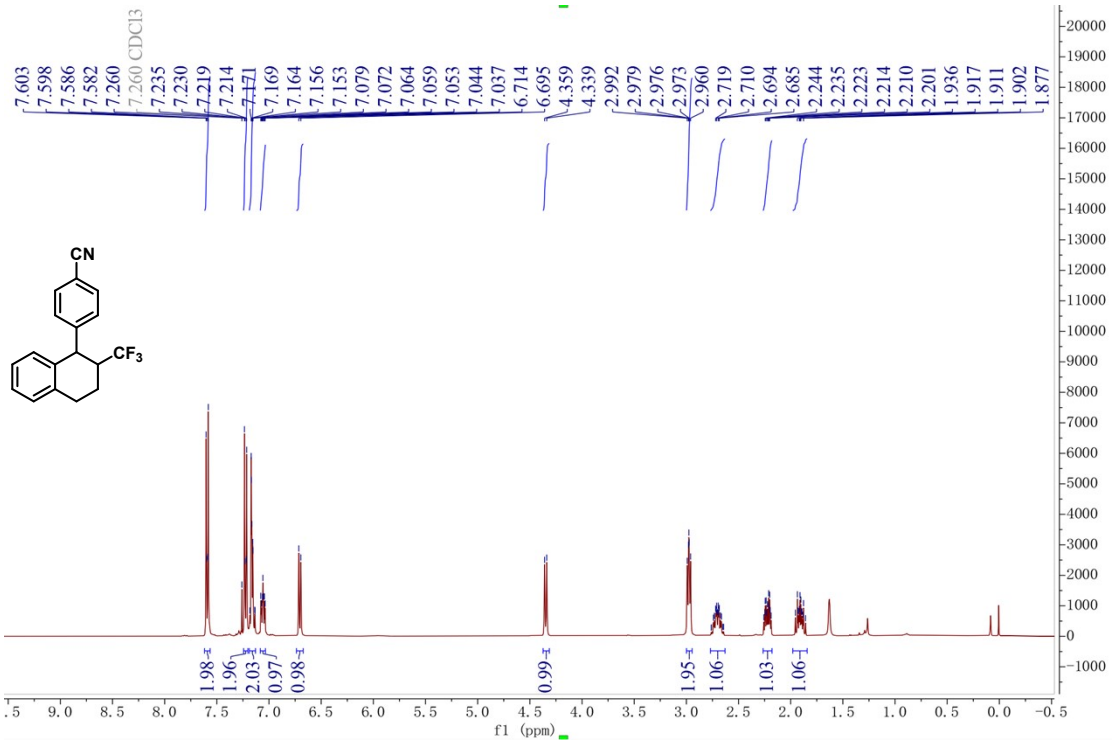
^{13}C NMR (100 MHz, $CDCl_3$) of **4aq**



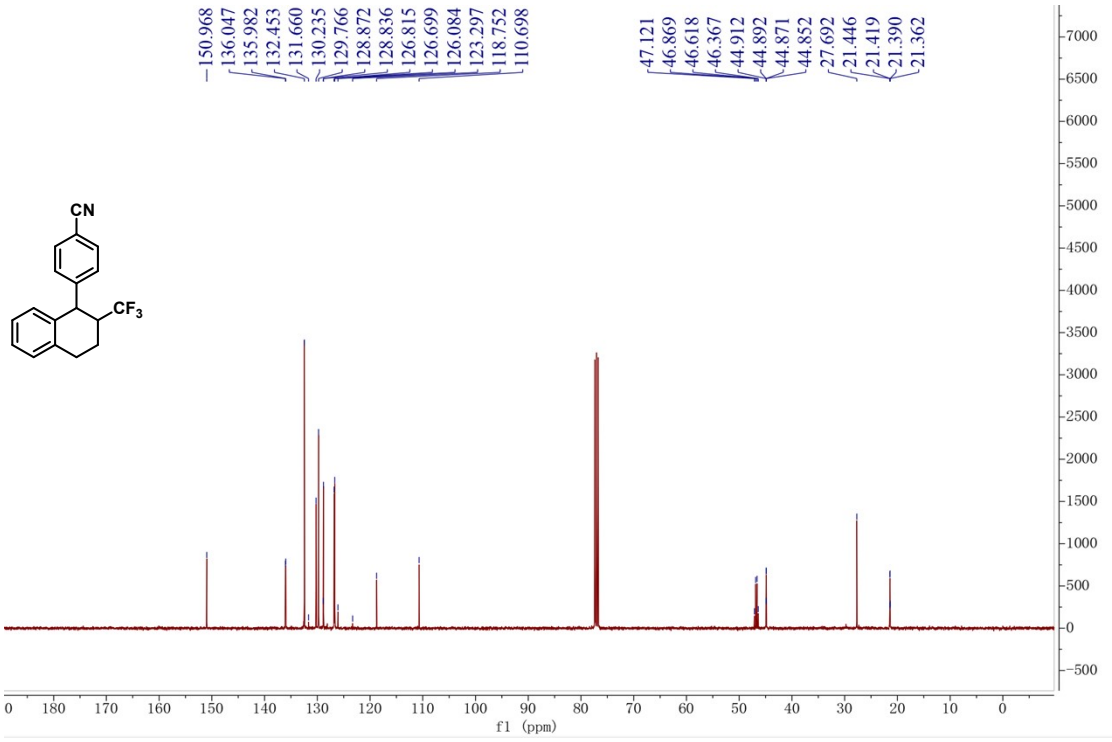
^{19}F NMR (376 MHz, $CDCl_3$) of **4aq**



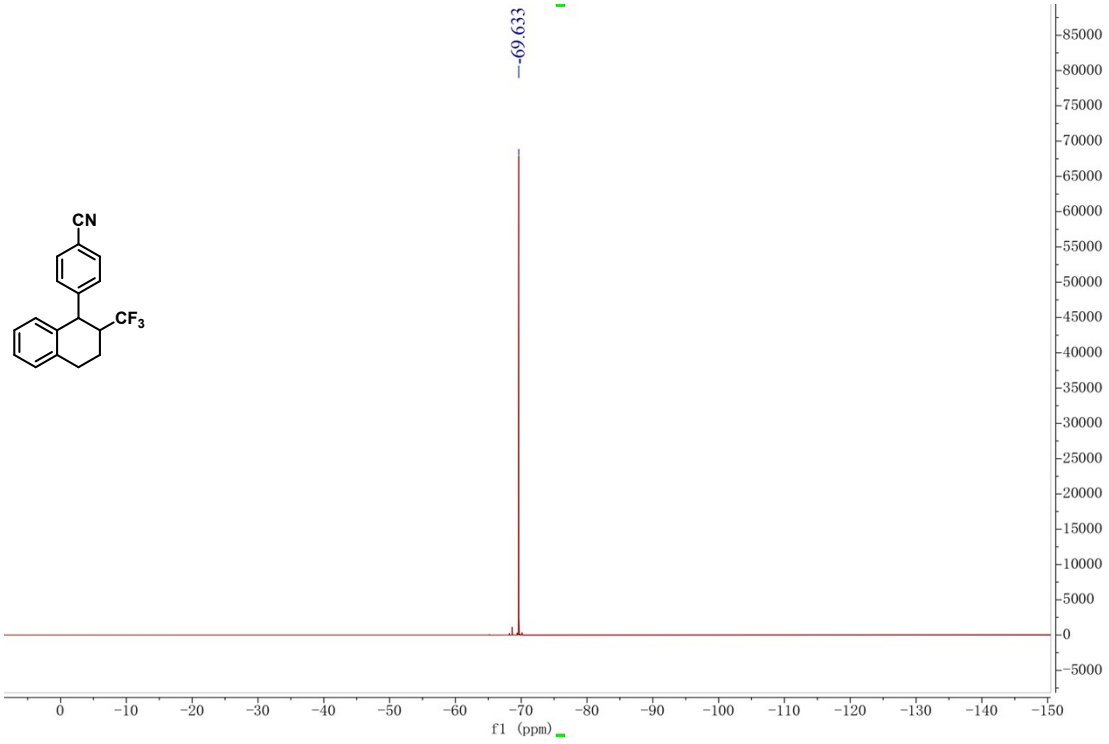
^{1}H NMR (400 MHz, $CDCl_3$) of **4ar**



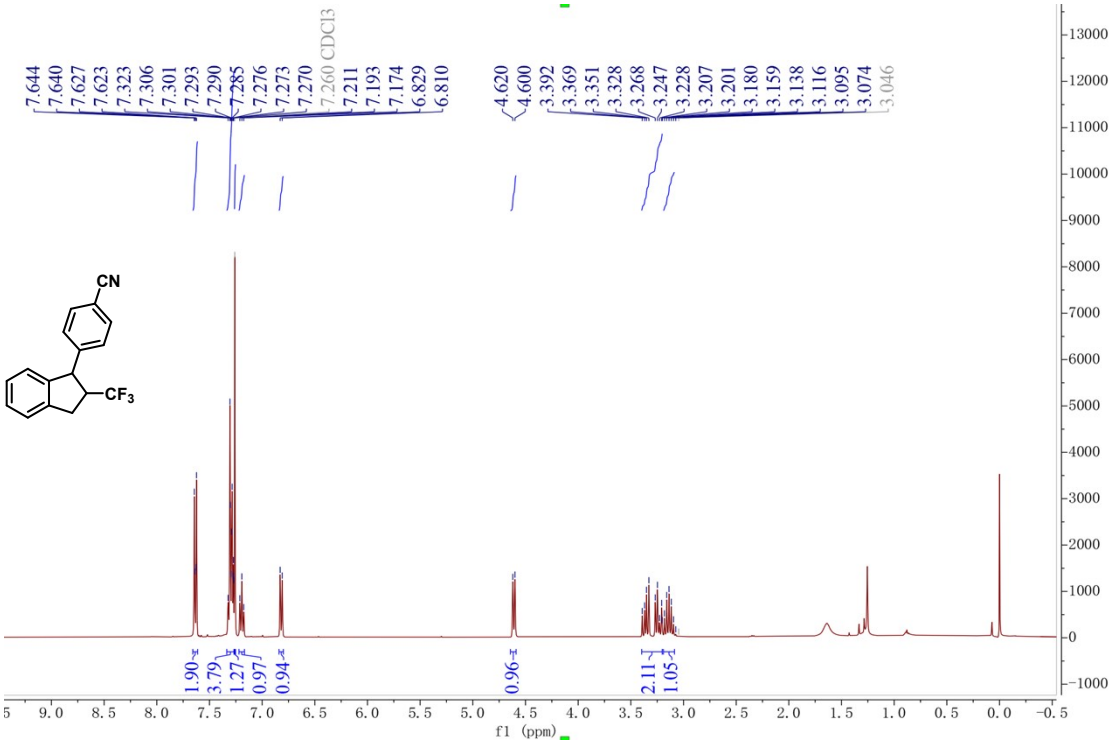
^{13}C NMR (100 MHz, $CDCl_3$) of **4ar**



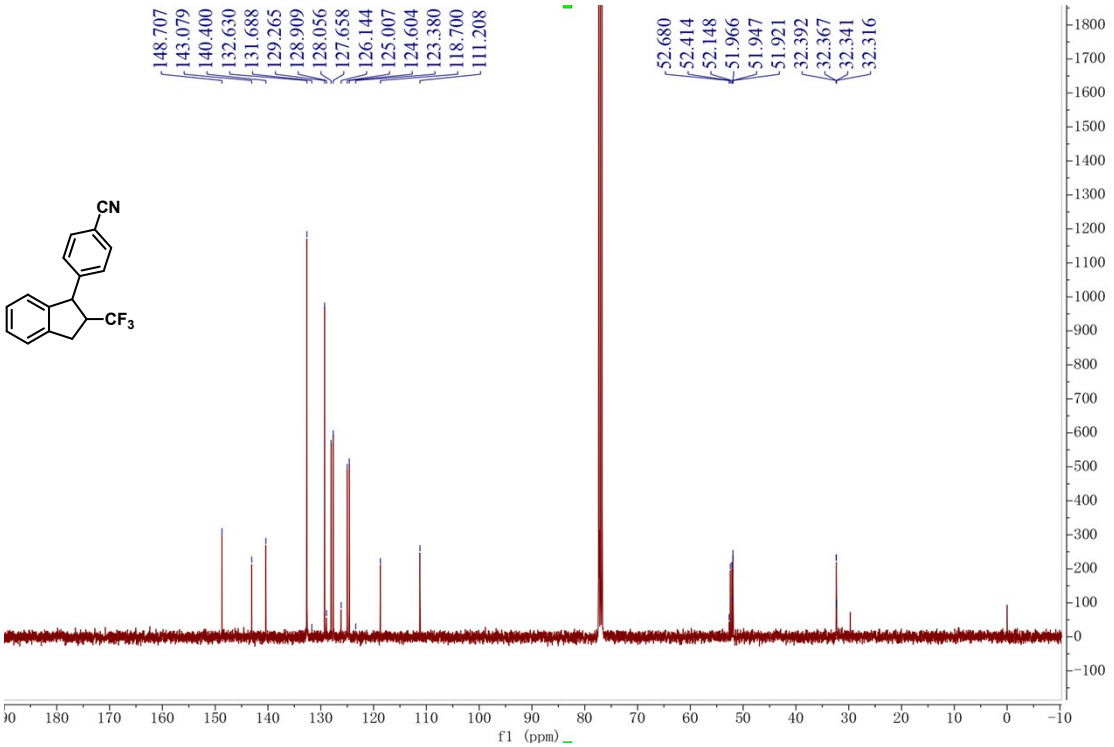
^{19}F NMR (376 MHz, $CDCl_3$) of **4ar**



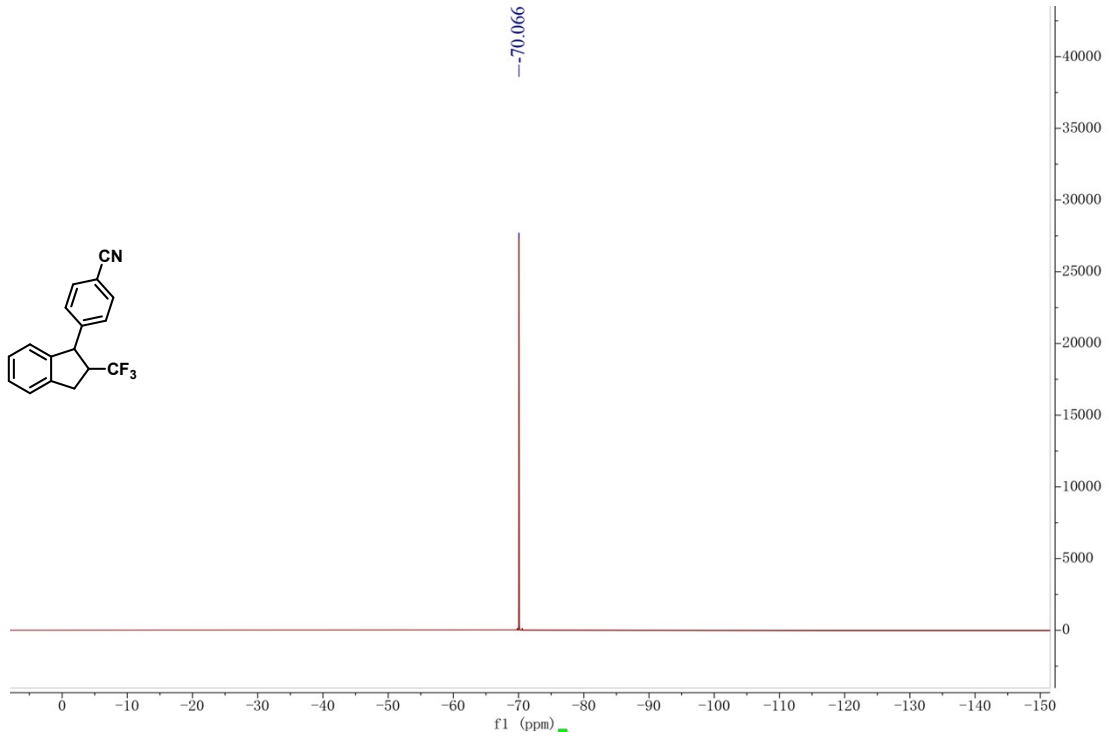
^{1}H NMR (400 MHz, $CDCl_3$) of **4as**



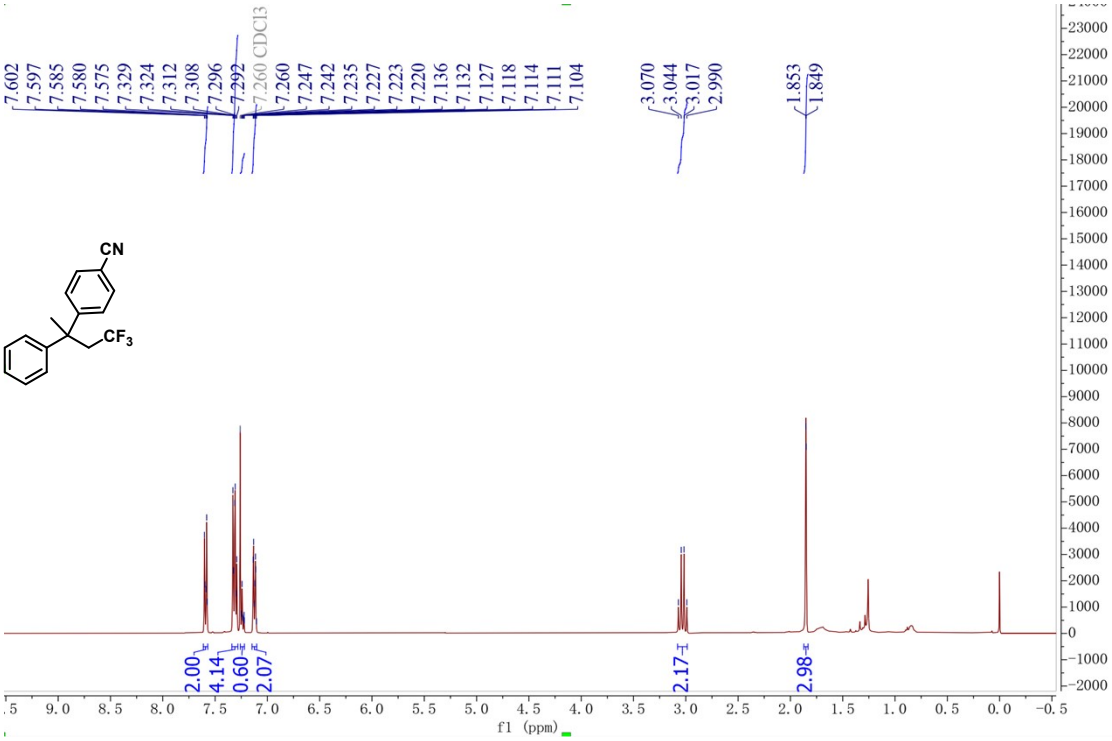
^{13}C NMR (100 MHz, $CDCl_3$) of **4as**



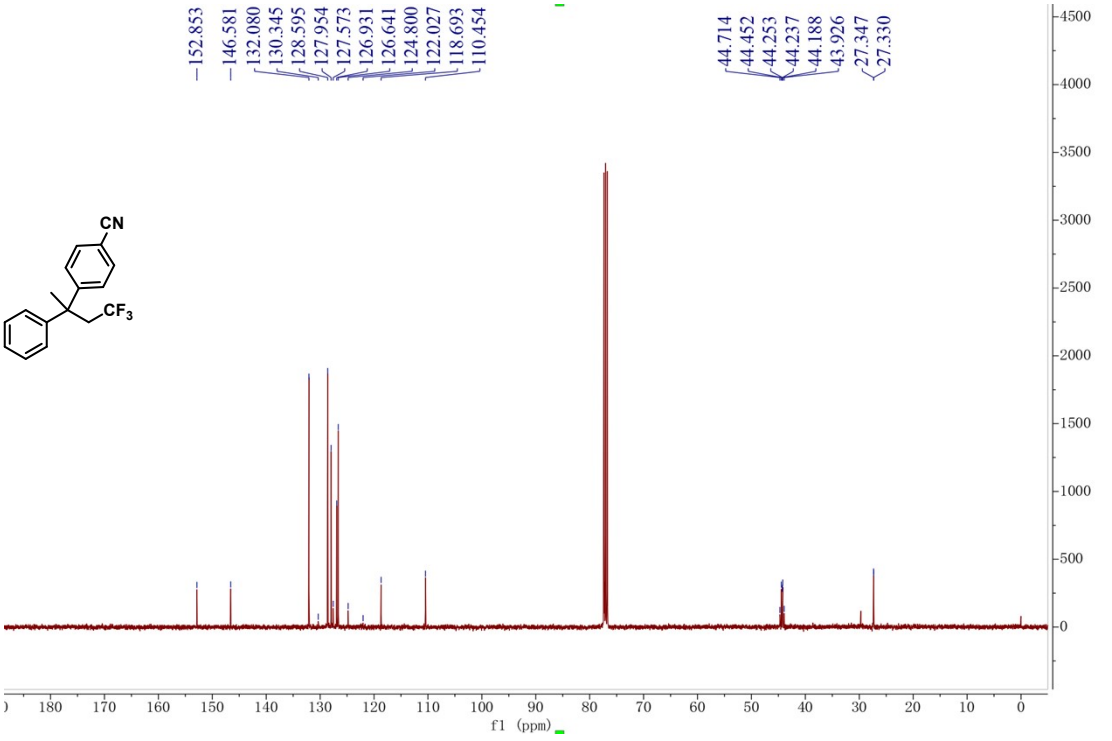
^{19}F NMR (376 MHz, $CDCl_3$) of **4as**



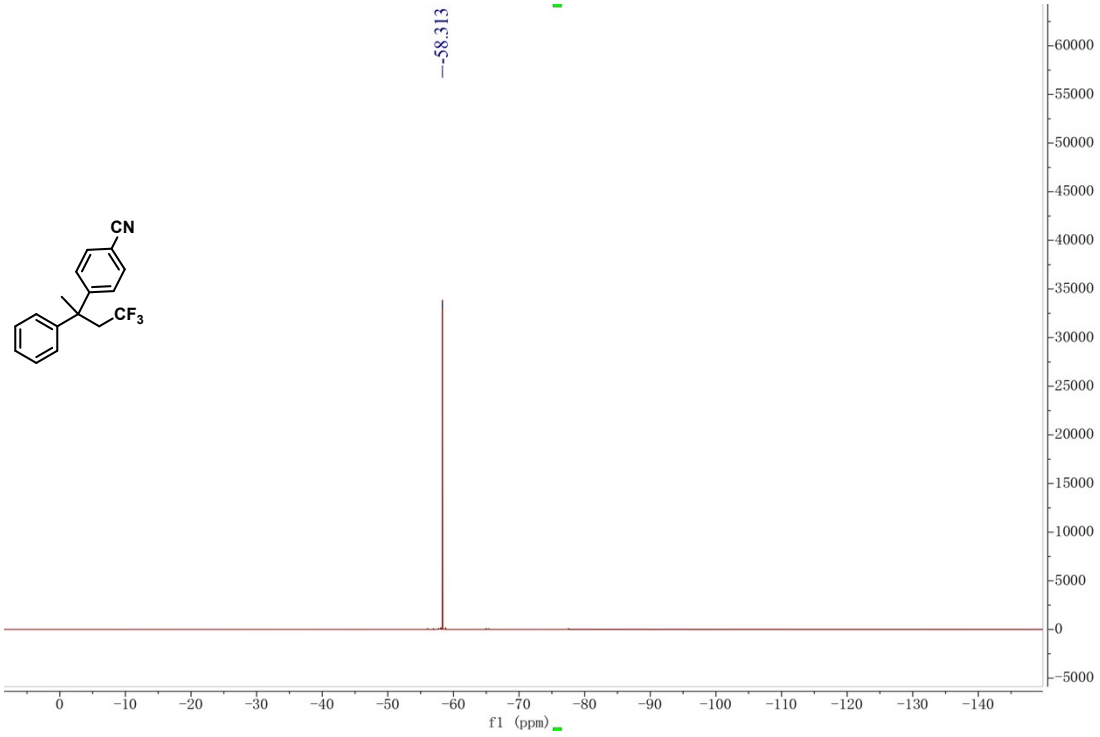
^{1}H NMR (400 MHz, $CDCl_3$) of **4at**



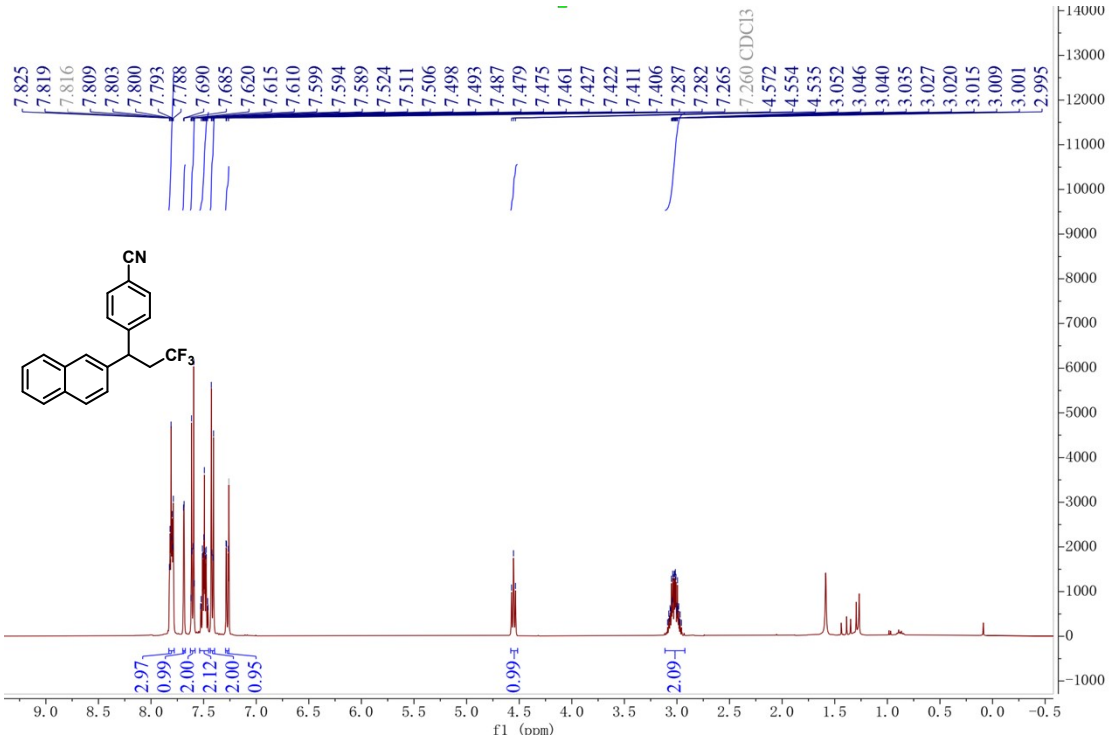
^{13}C NMR (100 MHz, $CDCl_3$) of **4at**



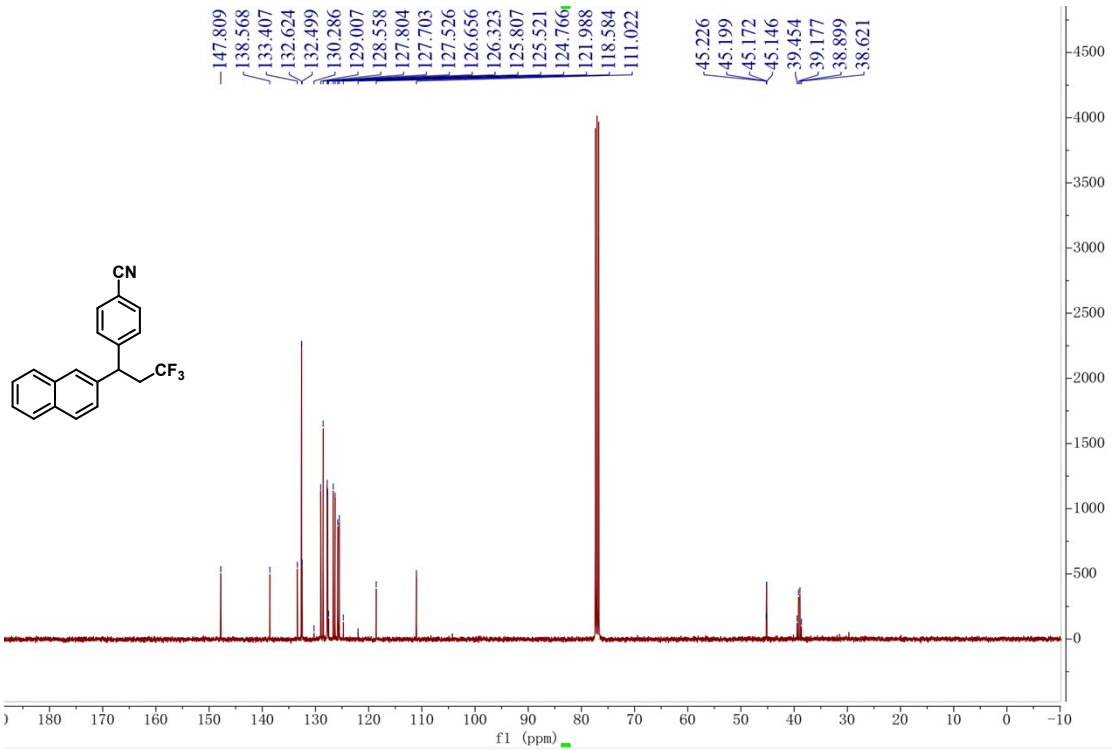
^{19}F NMR (376 MHz, $CDCl_3$) of **4at**



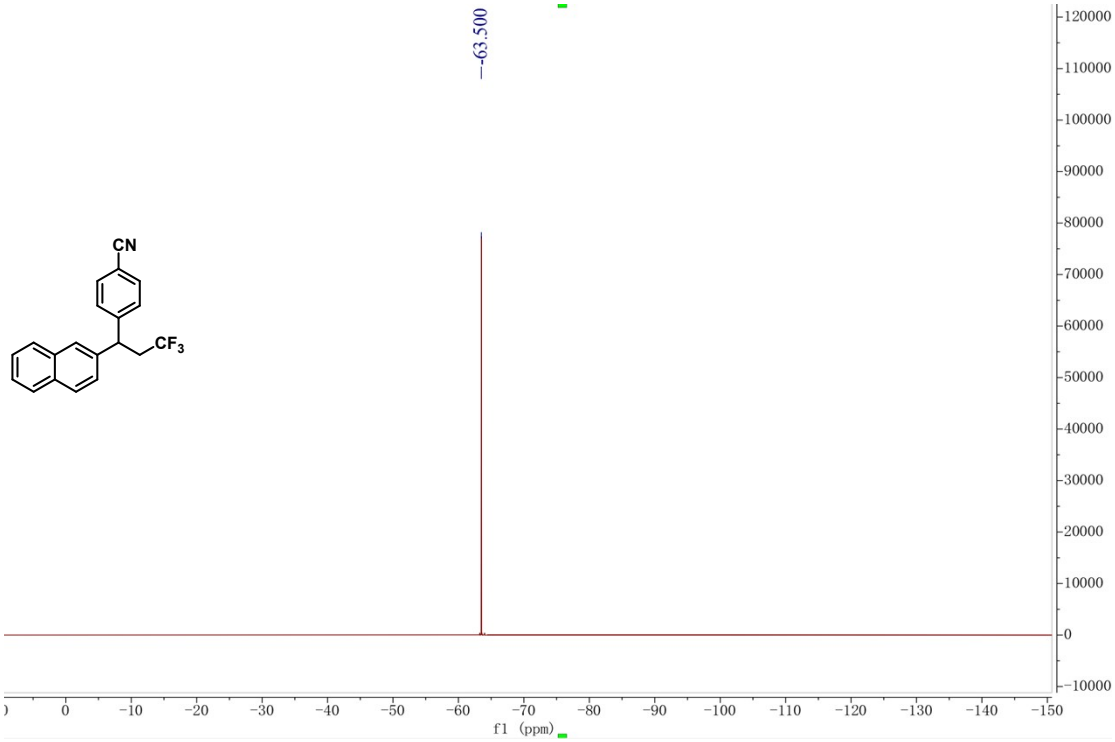
^{1}H NMR (400 MHz, $CDCl_3$) of **4au**



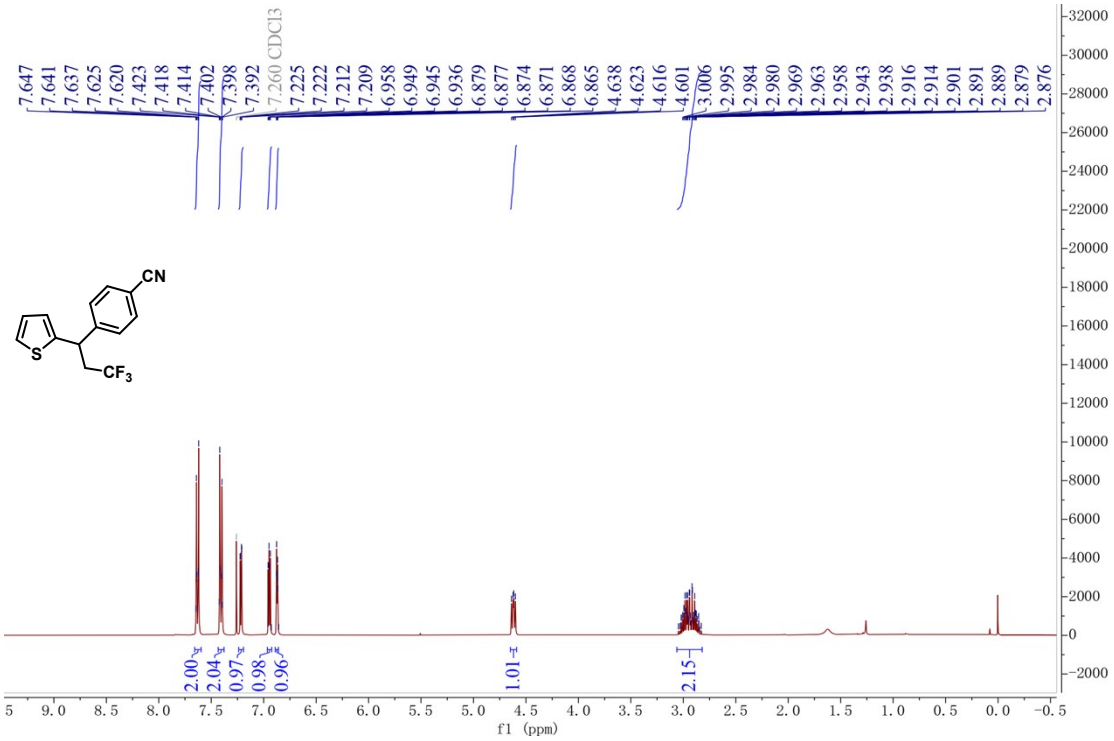
^{13}C NMR (100 MHz, $CDCl_3$) of **4au**



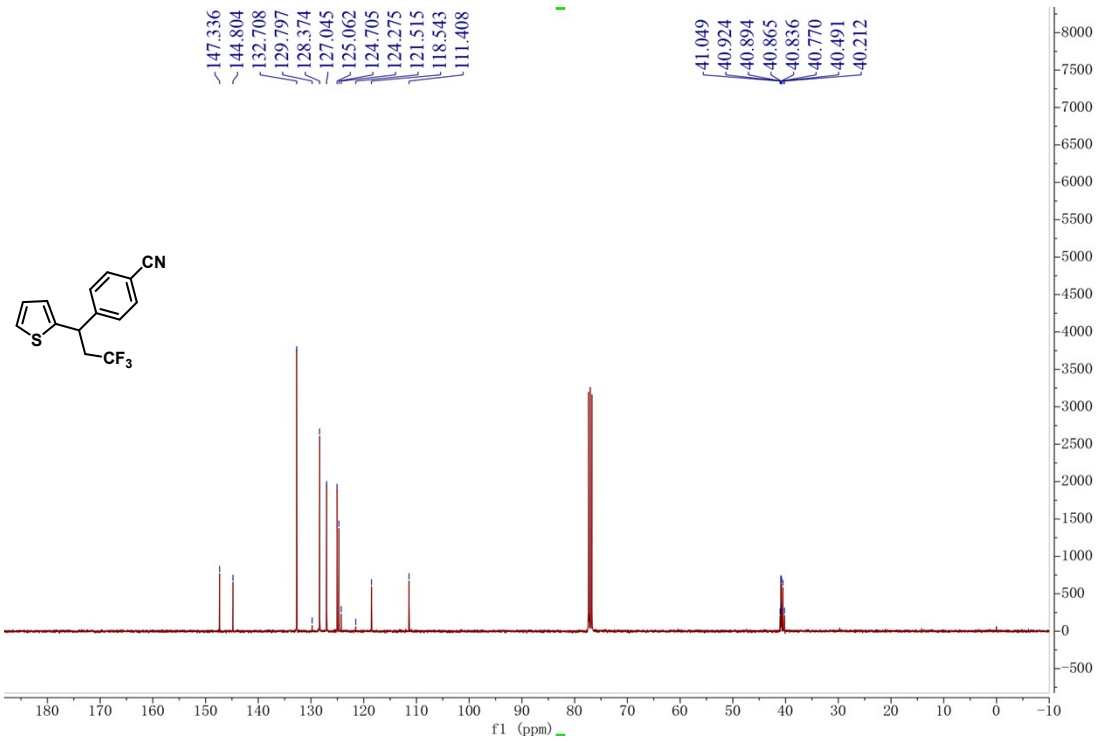
^{19}F NMR (376 MHz, $CDCl_3$) of **4au**



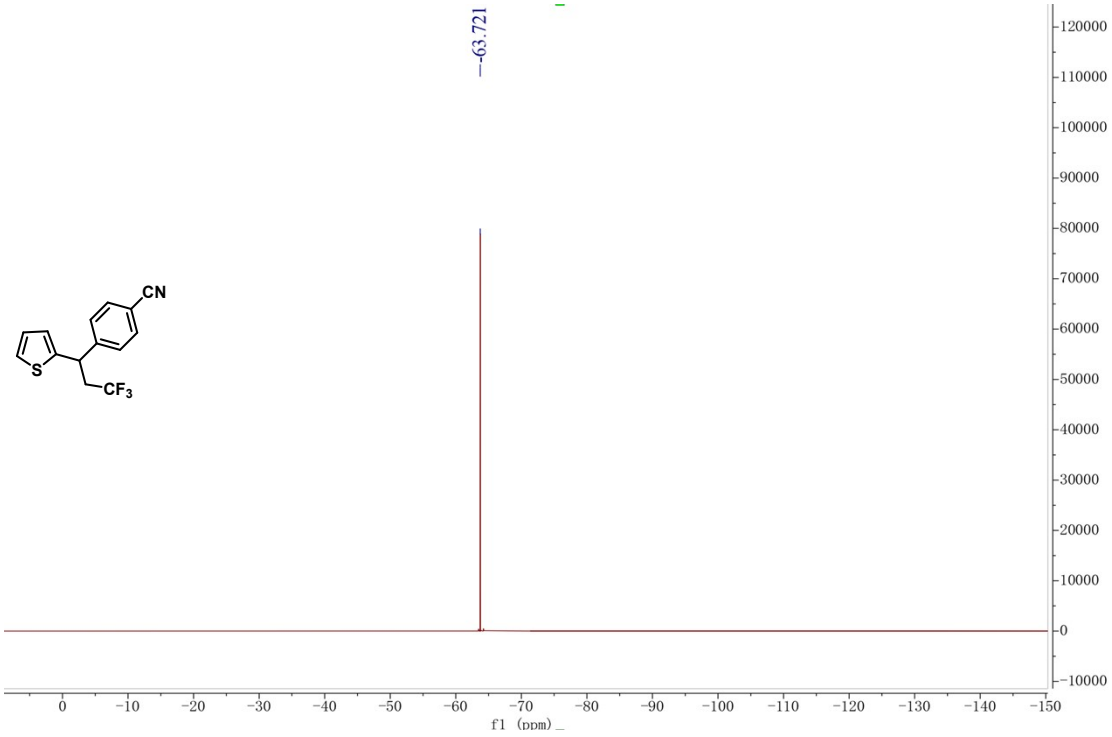
^{1}H NMR (400 MHz, $CDCl_3$) of **4av**



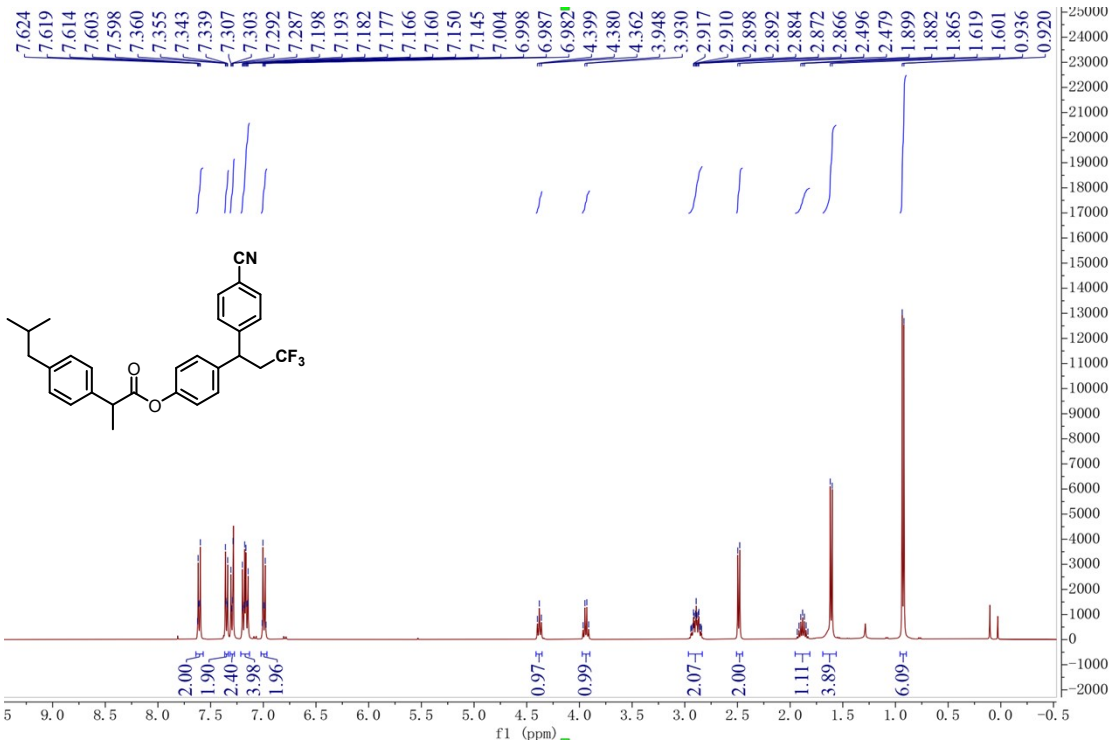
^{13}C NMR (100 MHz, $CDCl_3$) of **4au**



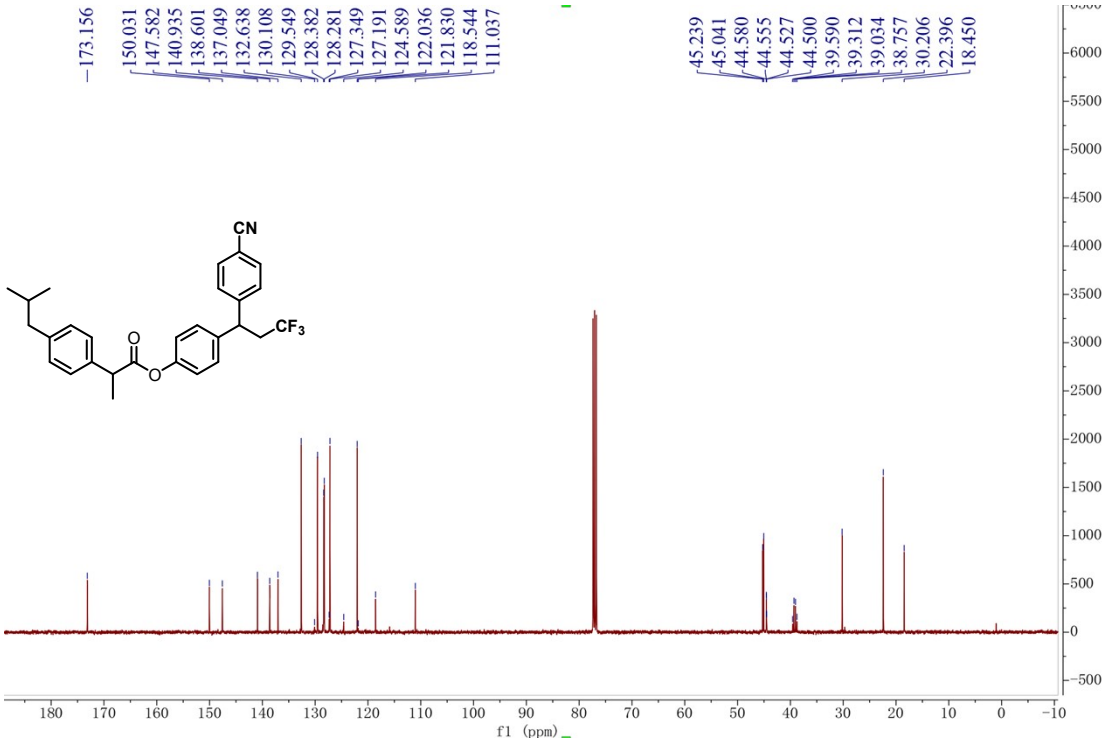
^{19}F NMR (376 MHz, $CDCl_3$) of **4au**



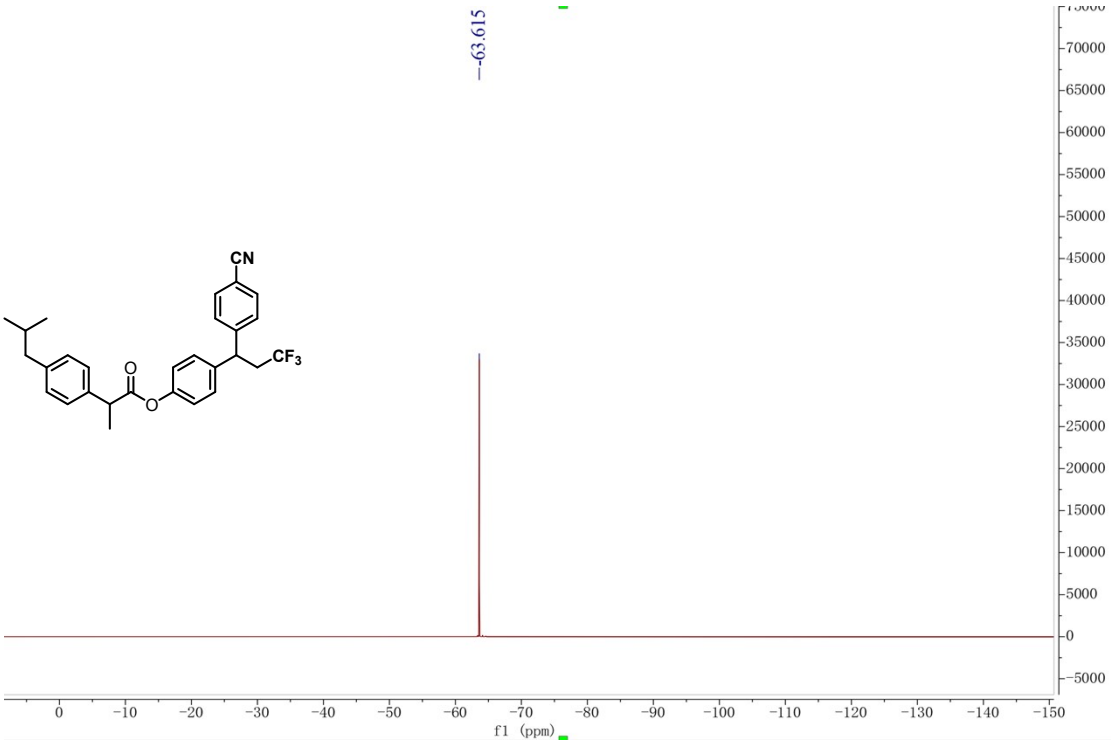
^{1}H NMR (400 MHz, $CDCl_3$) of **4aw**



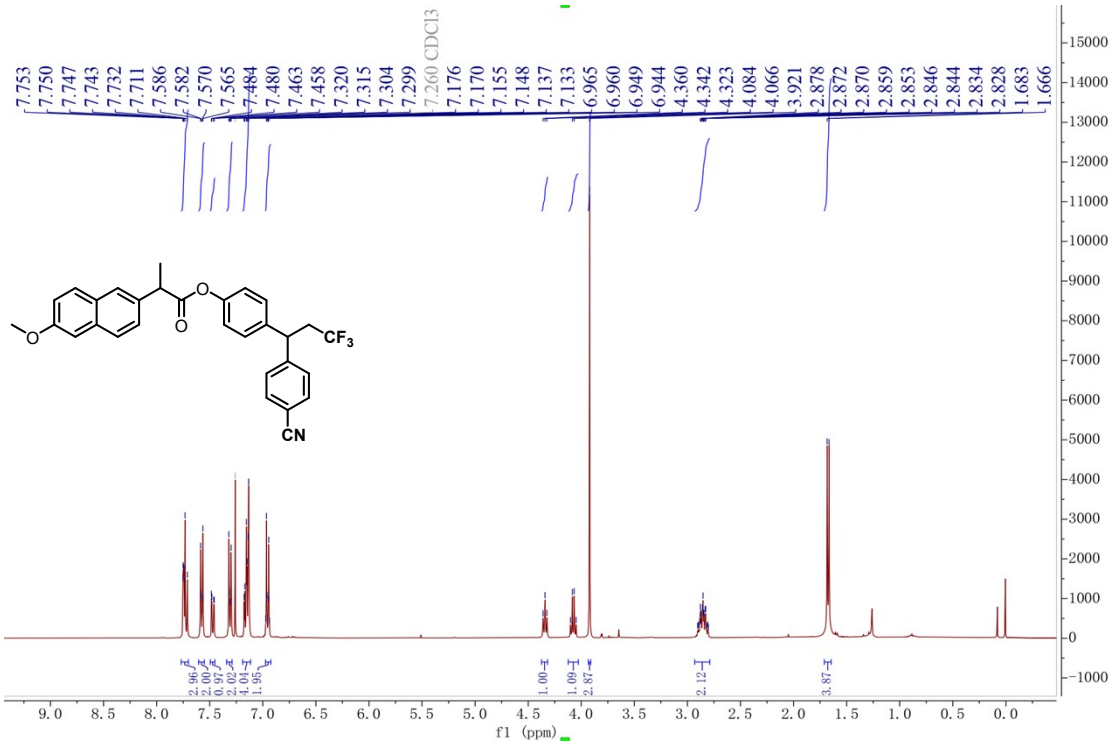
^{13}C NMR (100 MHz, $CDCl_3$) of **4aw**



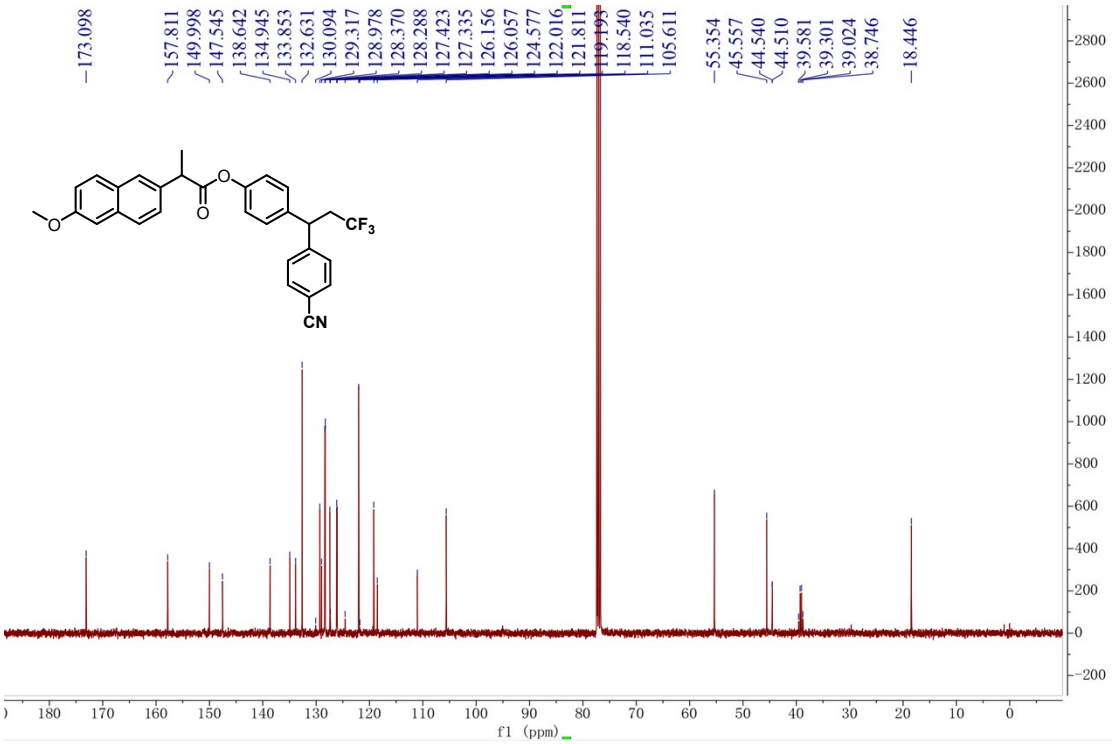
^{19}F NMR (376 MHz, $CDCl_3$) of **4aw**



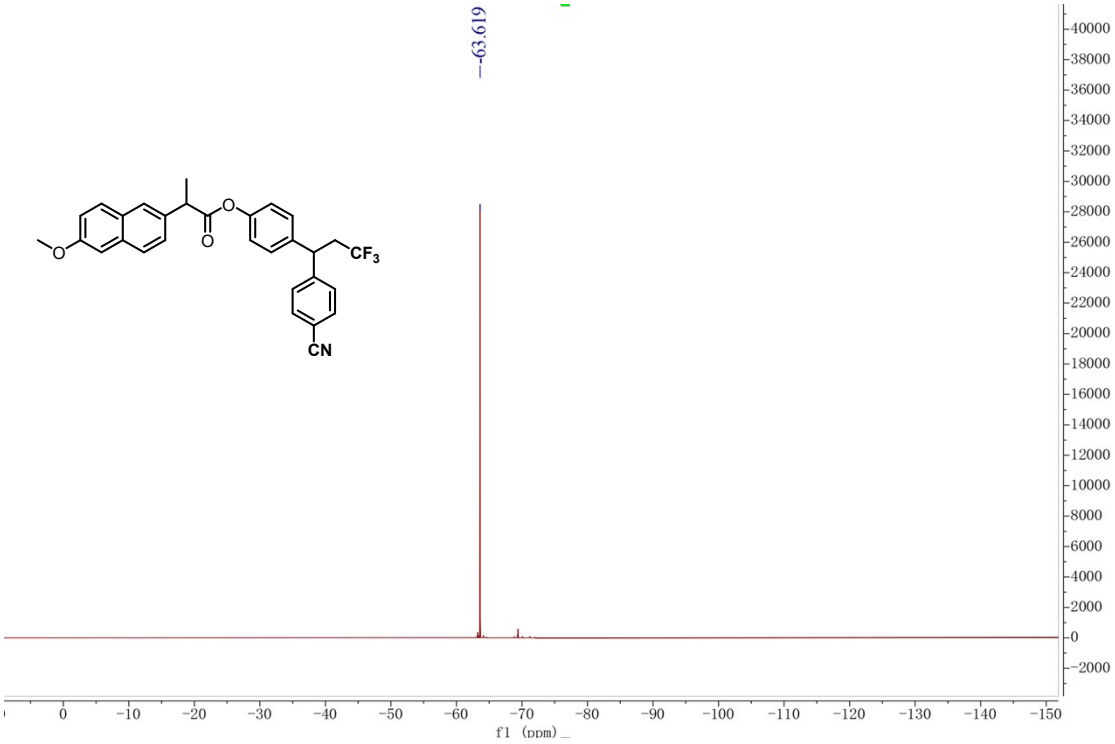
^{1}H NMR (400 MHz, $CDCl_3$) of **4ax**



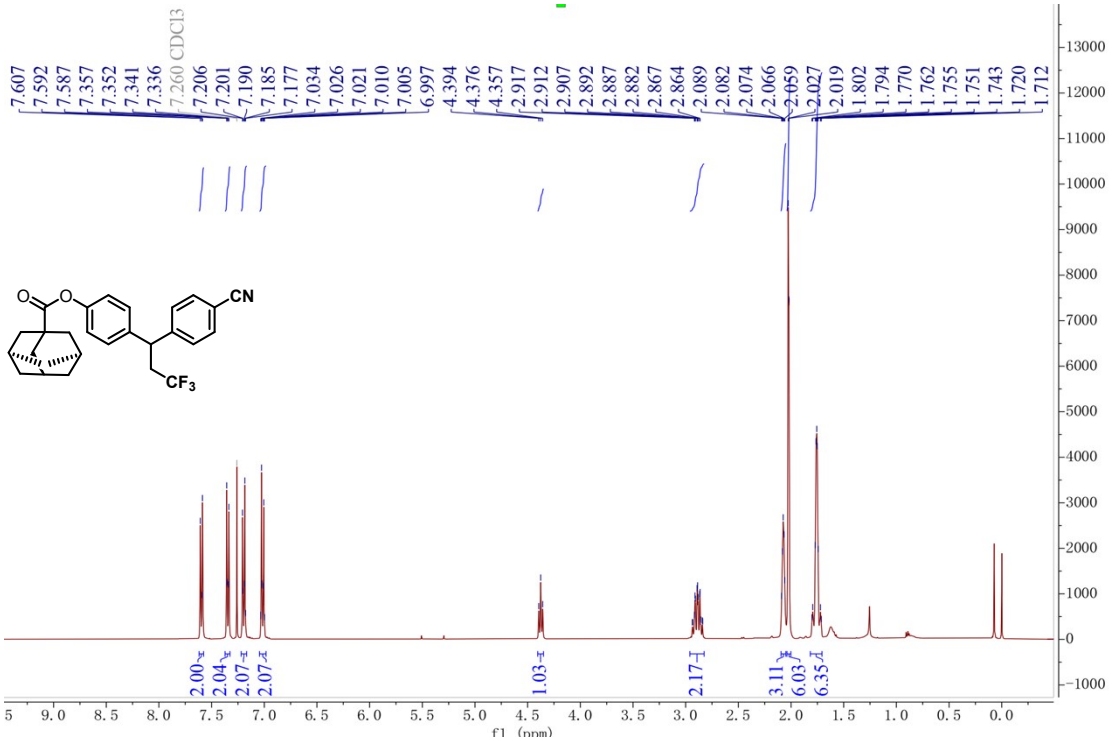
^{13}C NMR (100 MHz, $CDCl_3$) of **4ax**



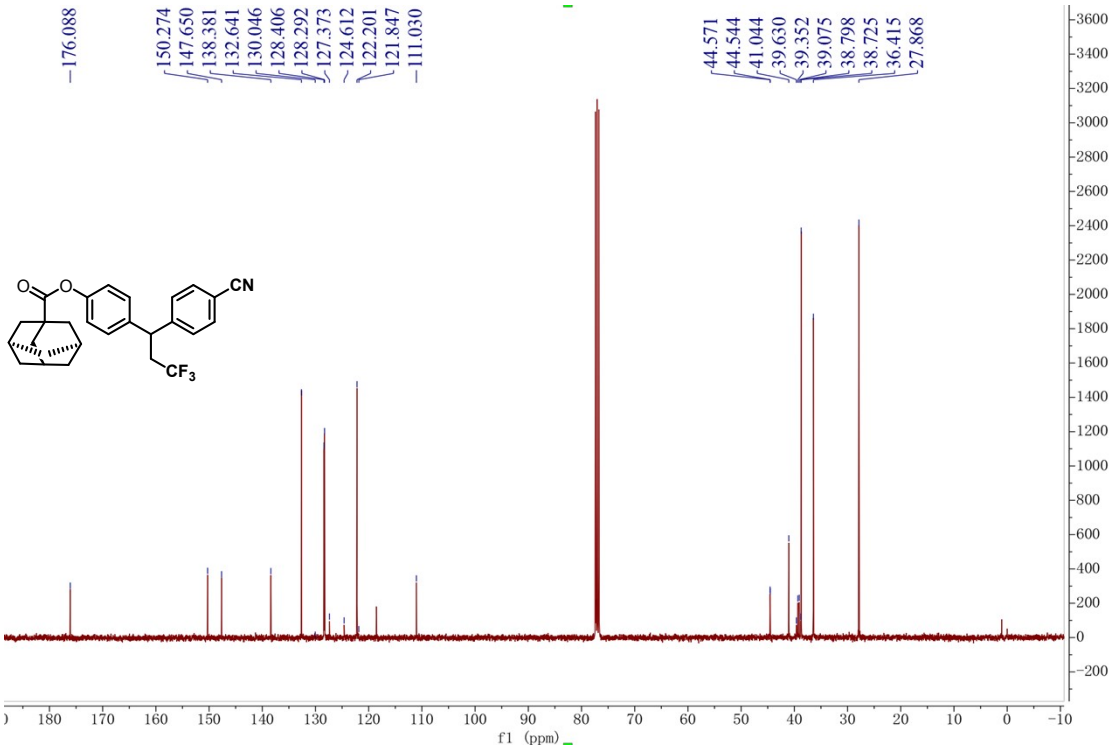
^{19}F NMR (376 MHz, $CDCl_3$) of **4ax**



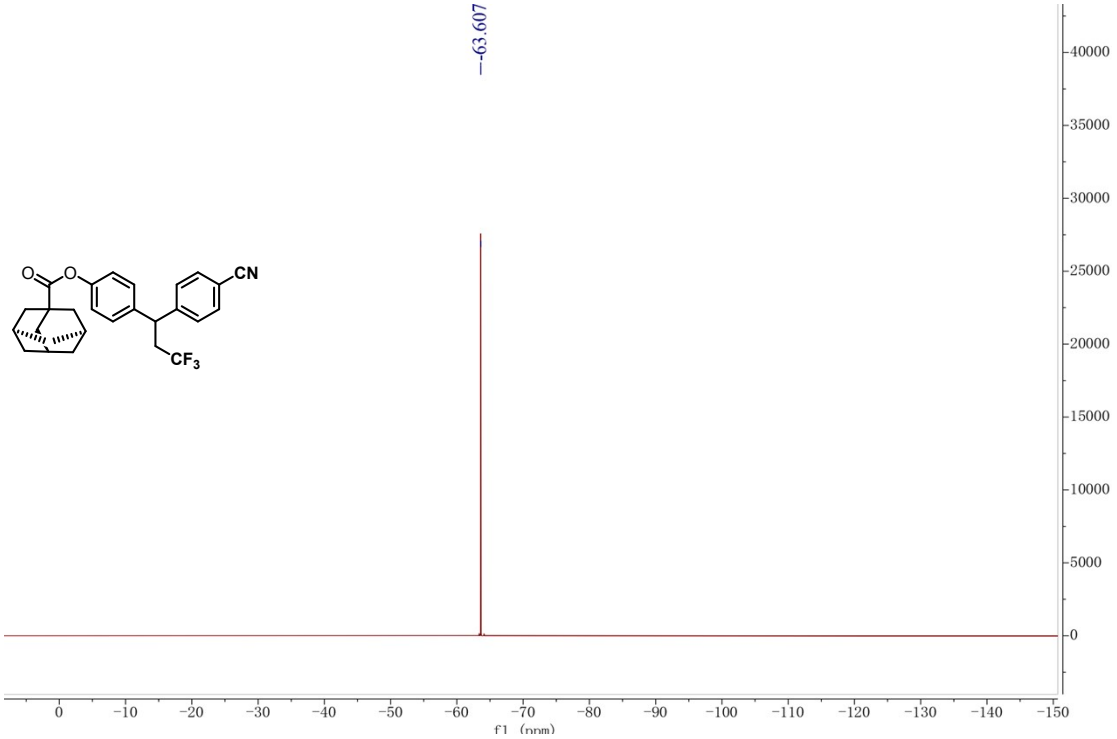
^{1}H NMR (400 MHz, $CDCl_3$) of **4ay**



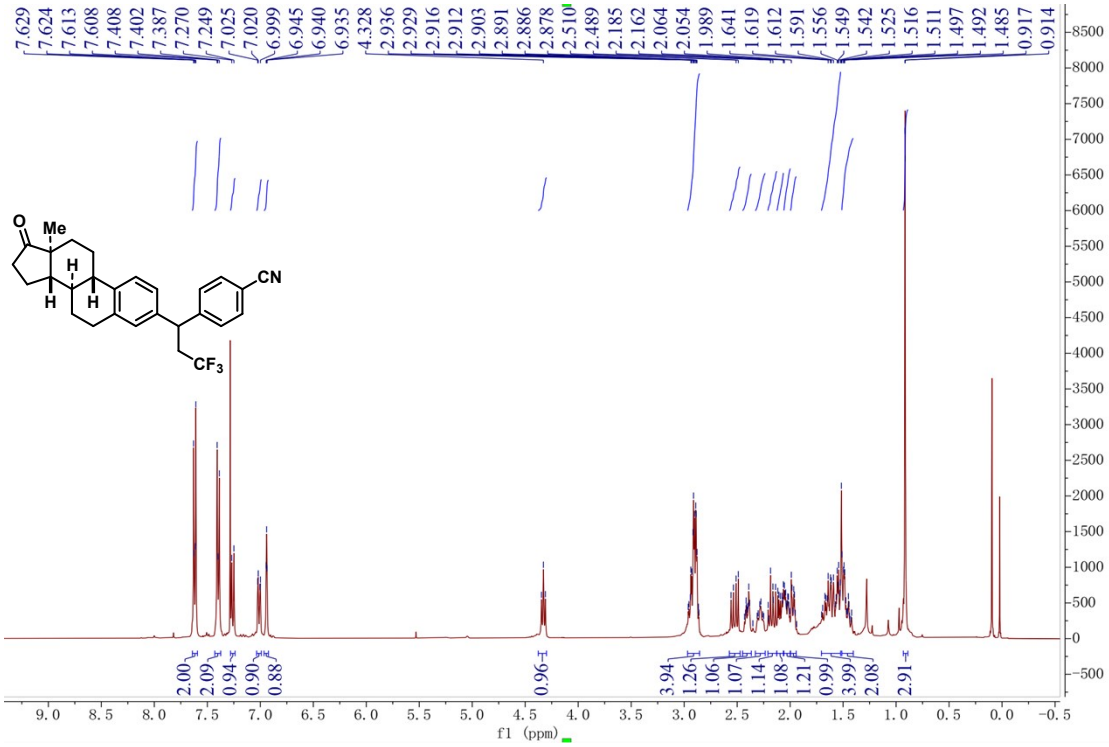
^{13}C NMR (100 MHz, $CDCl_3$) of **4ay**



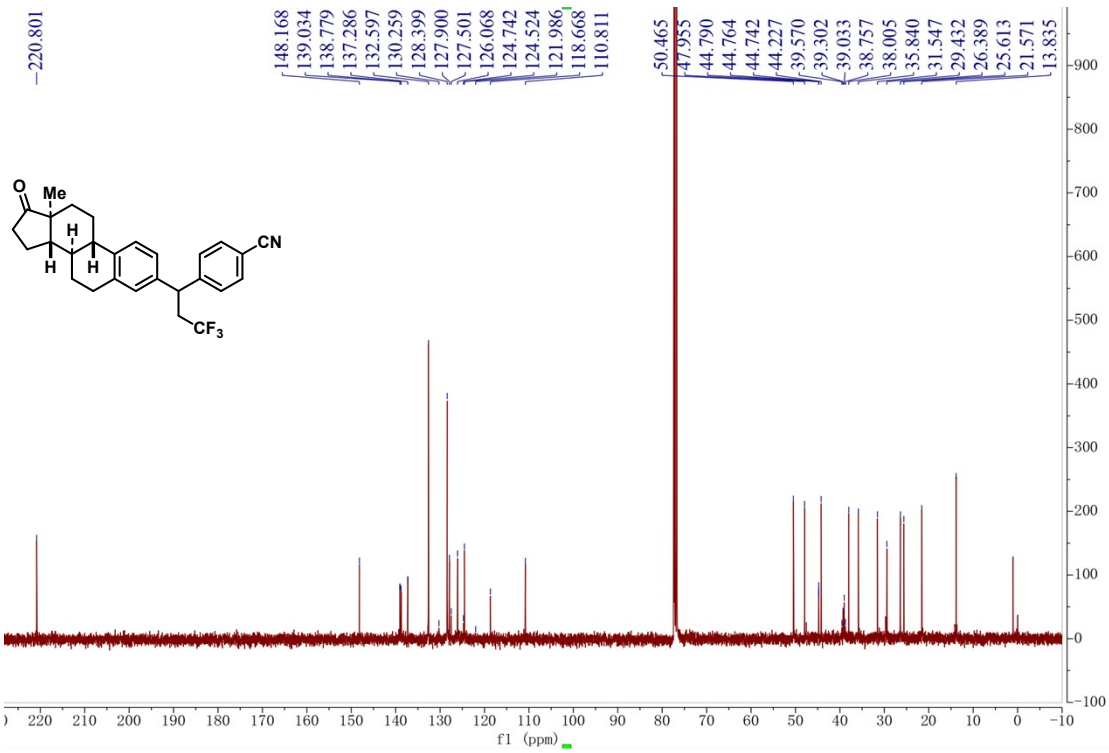
^{19}F NMR (376 MHz, $CDCl_3$) of **4ay**



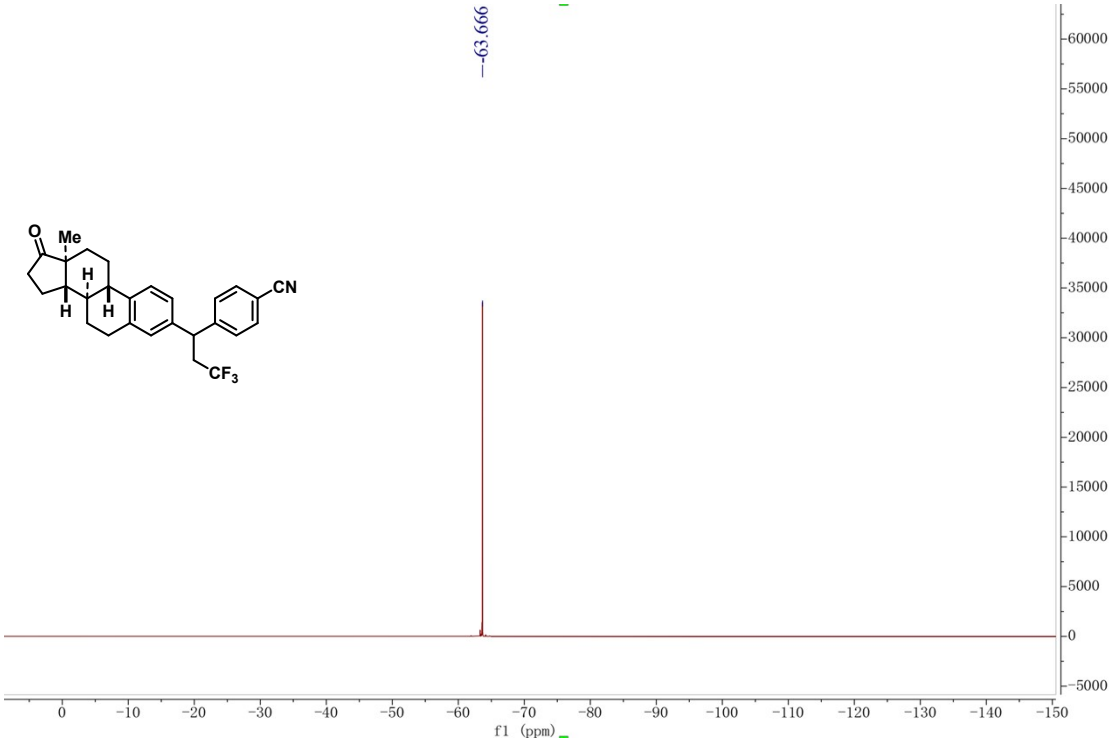
^{1}H NMR (400 MHz, $CDCl_3$) of **4az**



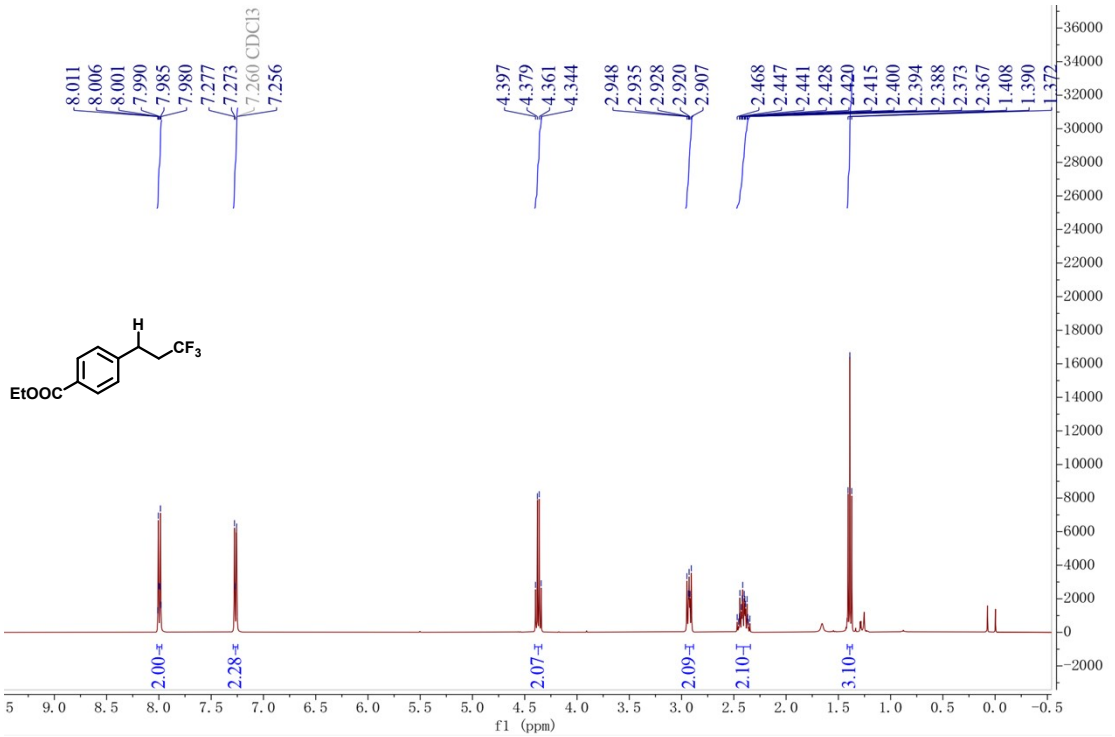
^{13}C NMR (100 MHz, $CDCl_3$) of **4az**



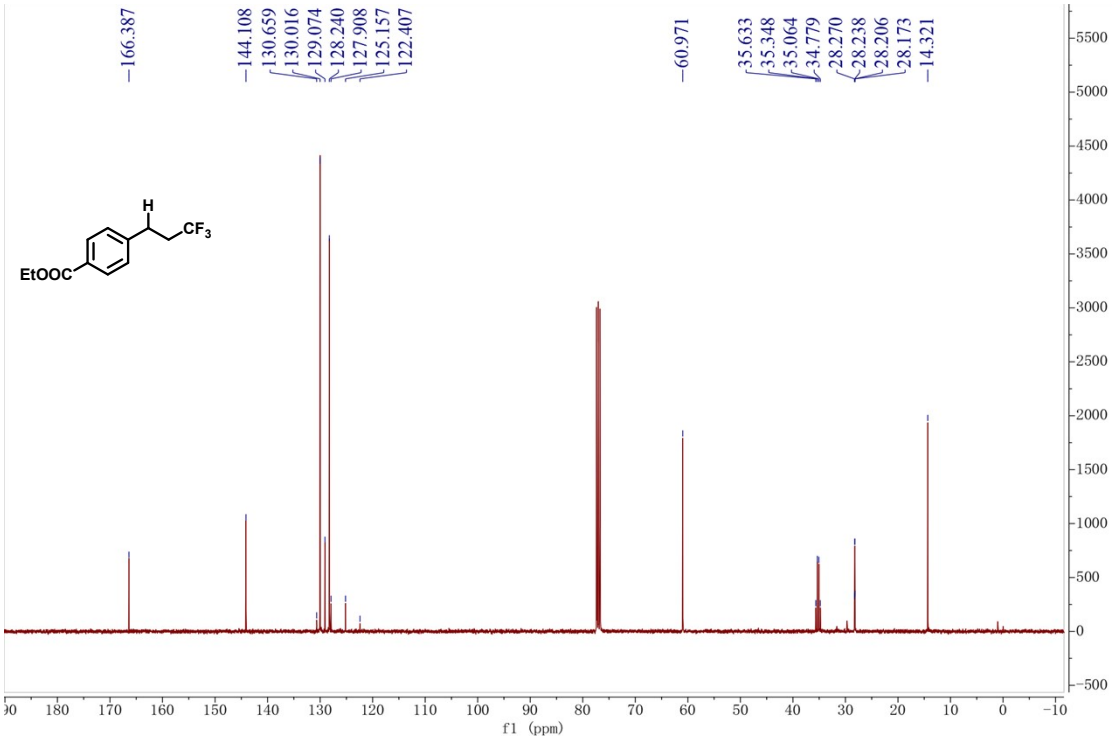
^{19}F NMR (376 MHz, $CDCl_3$) of **4az**



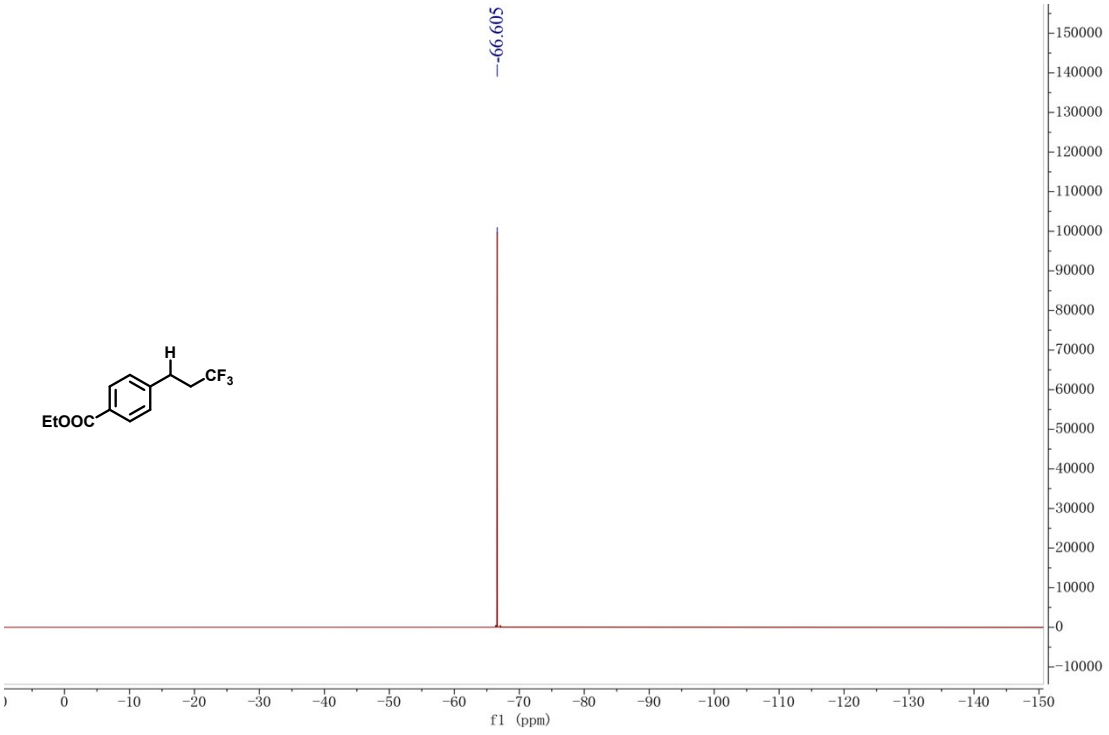
^{1}H NMR (400 MHz, $CDCl_3$) of **4ba**



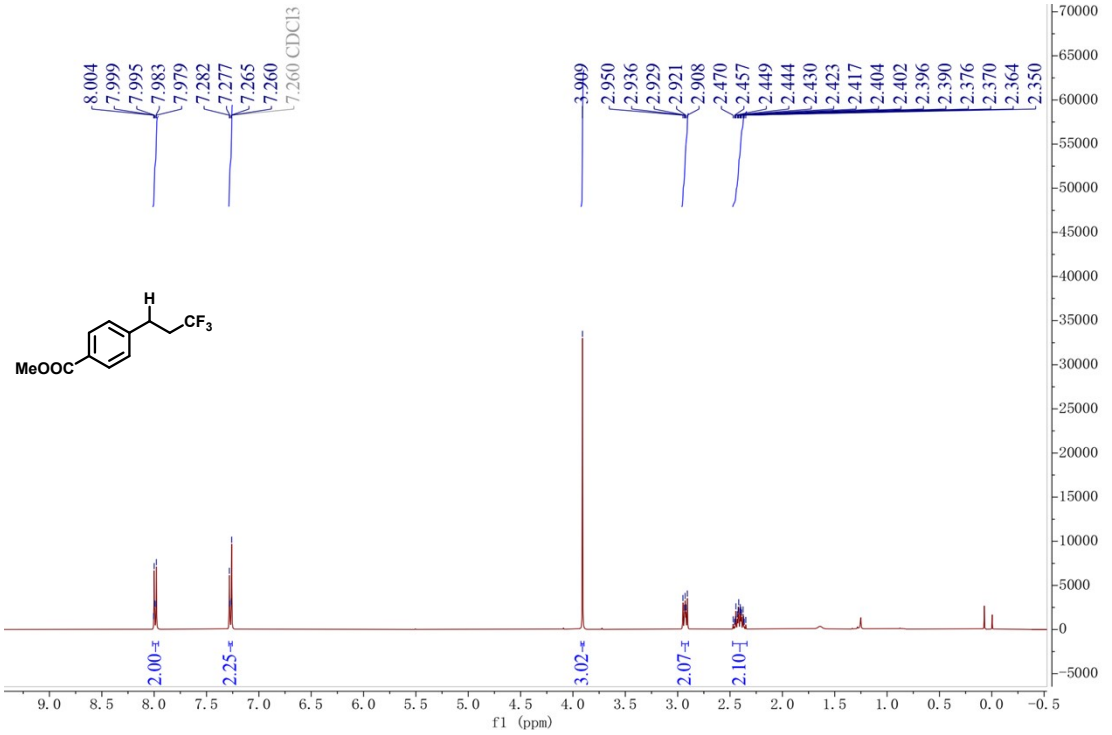
^{13}C NMR (100 MHz, $CDCl_3$) of **4ba**



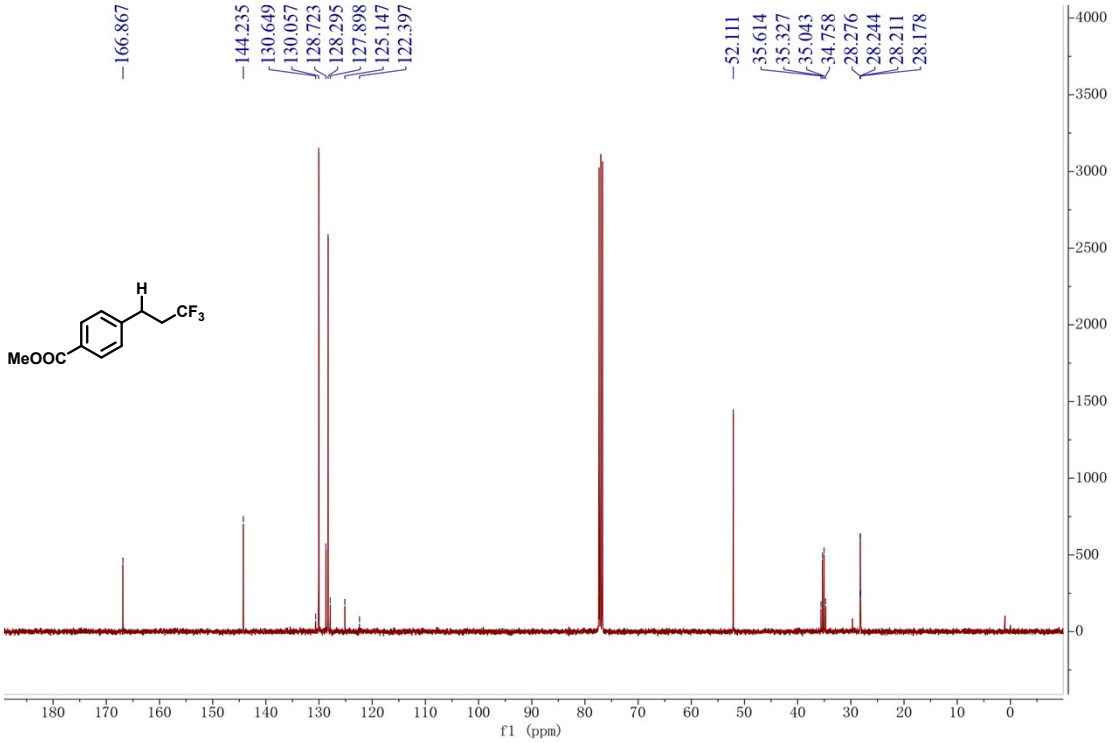
^{19}F NMR (376 MHz, $CDCl_3$) of **4ba**



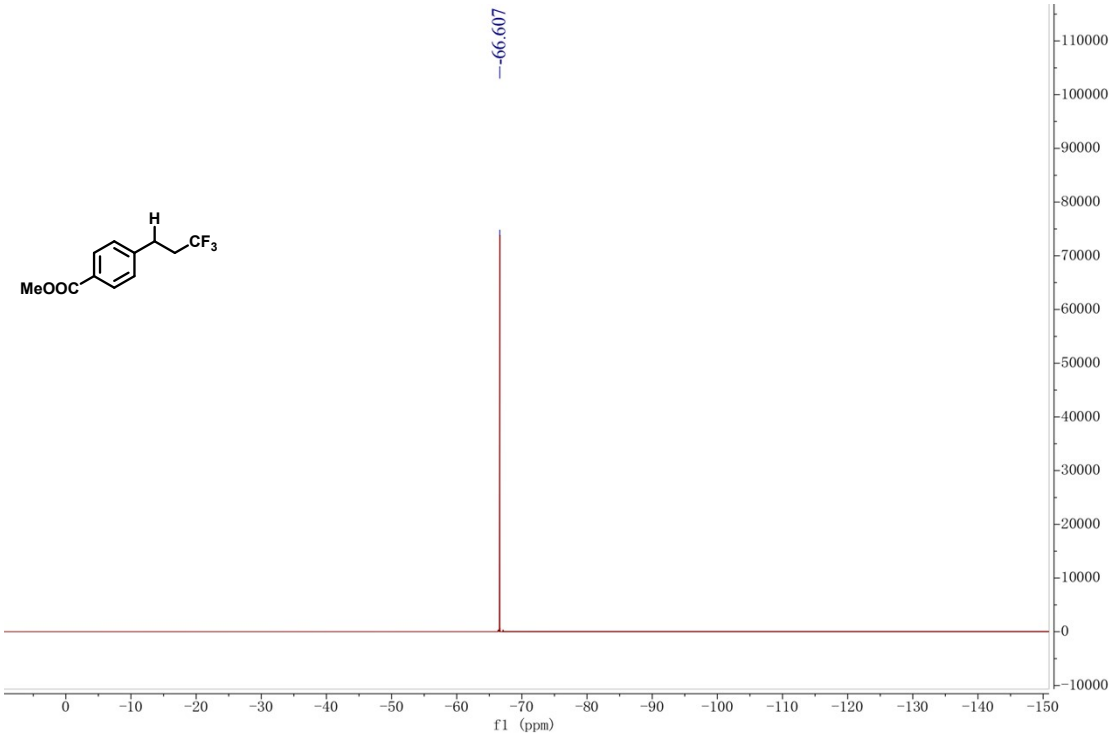
^{1}H NMR (400 MHz, $CDCl_3$) of **4bb**



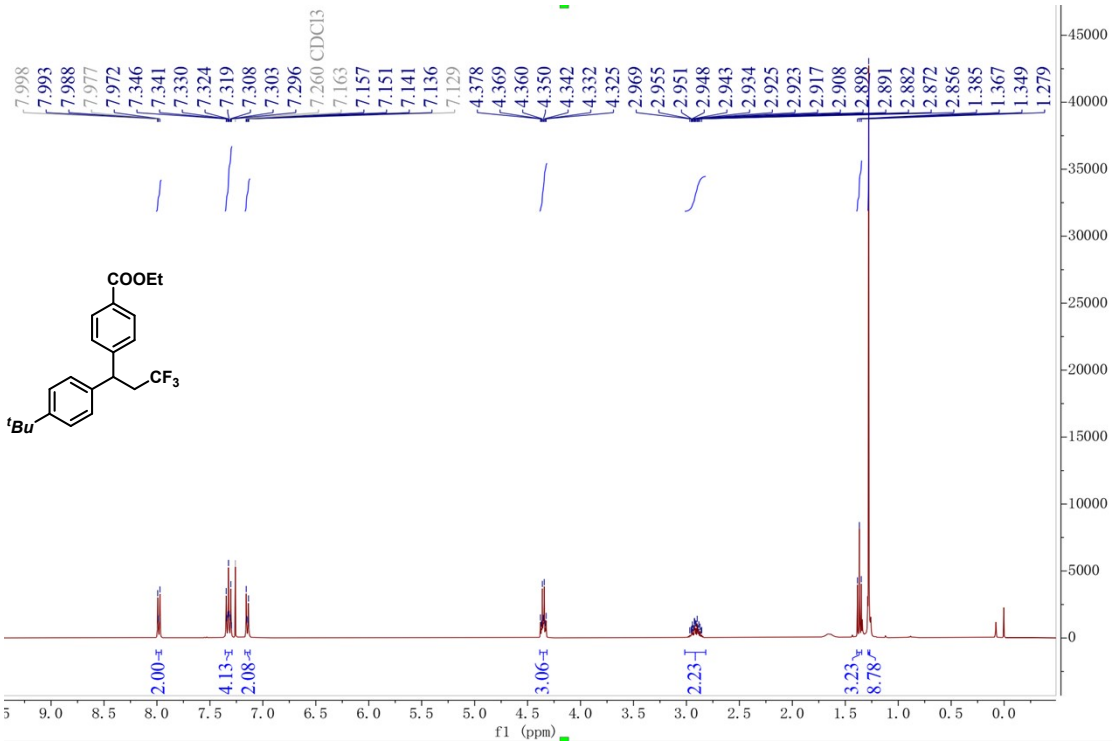
^{13}C NMR (100 MHz, $CDCl_3$) of **4bb**



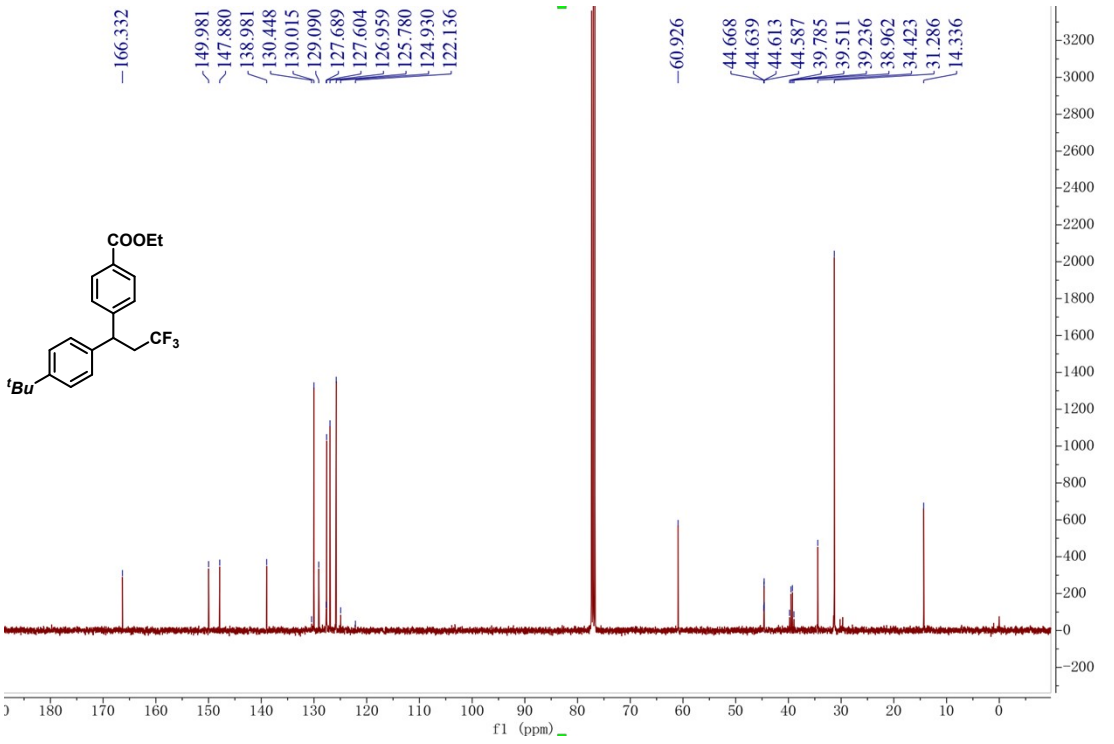
^{19}F NMR (376 MHz, $CDCl_3$) of **4bb**



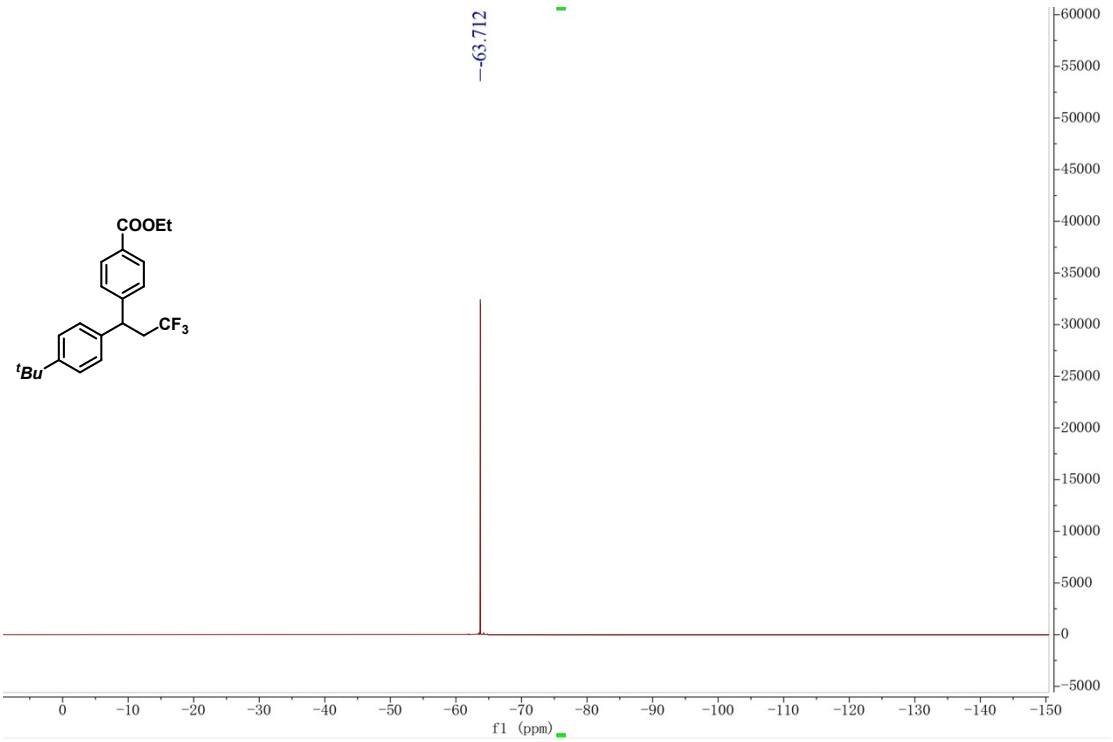
^{1}H NMR (400 MHz, $CDCl_3$) of **5aa**



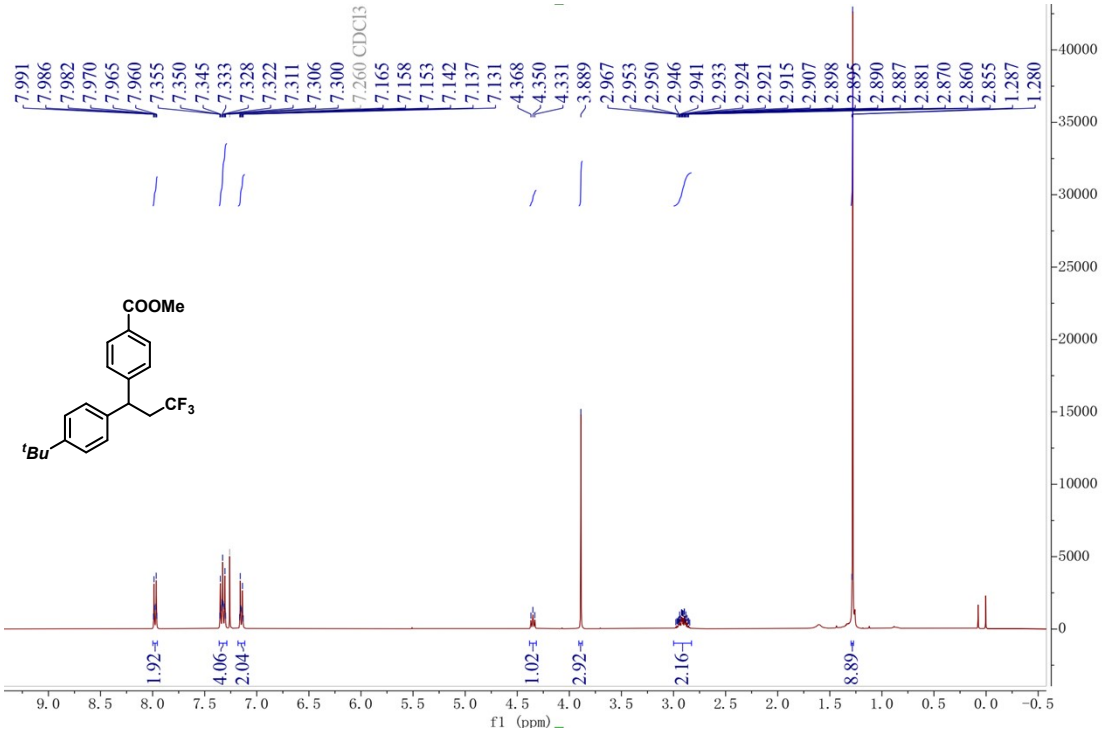
^{13}C NMR (100 MHz, $CDCl_3$) of **5aa**



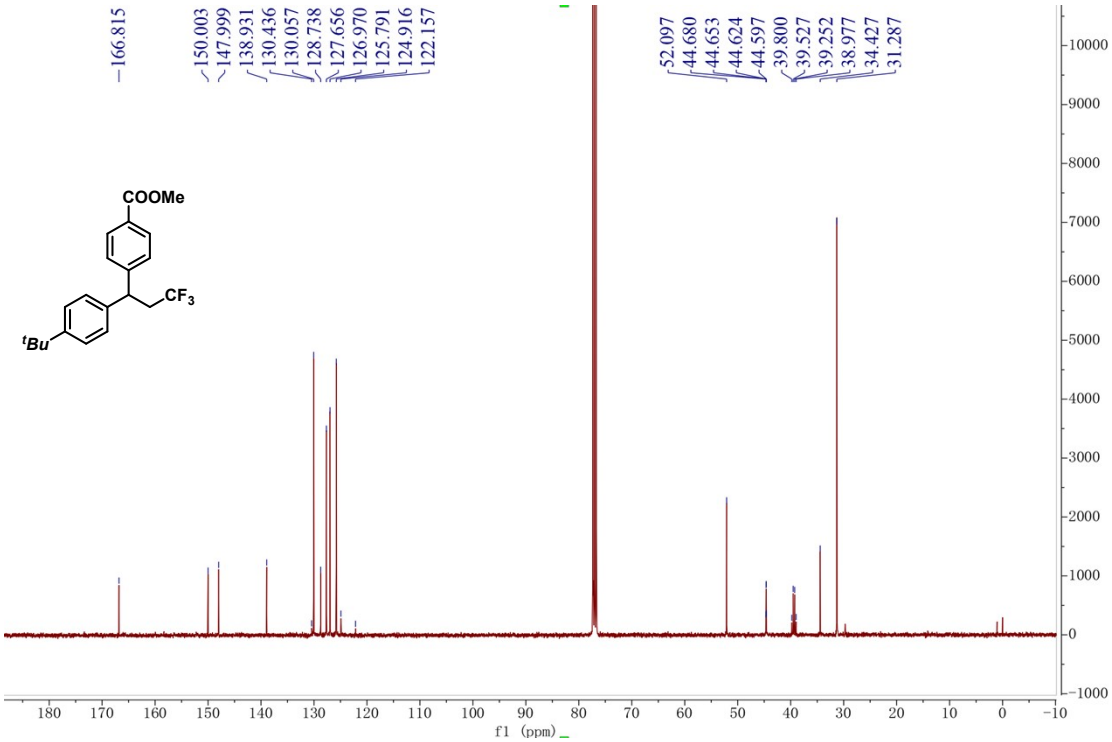
^{19}F NMR (376 MHz, $CDCl_3$) of **5aa**



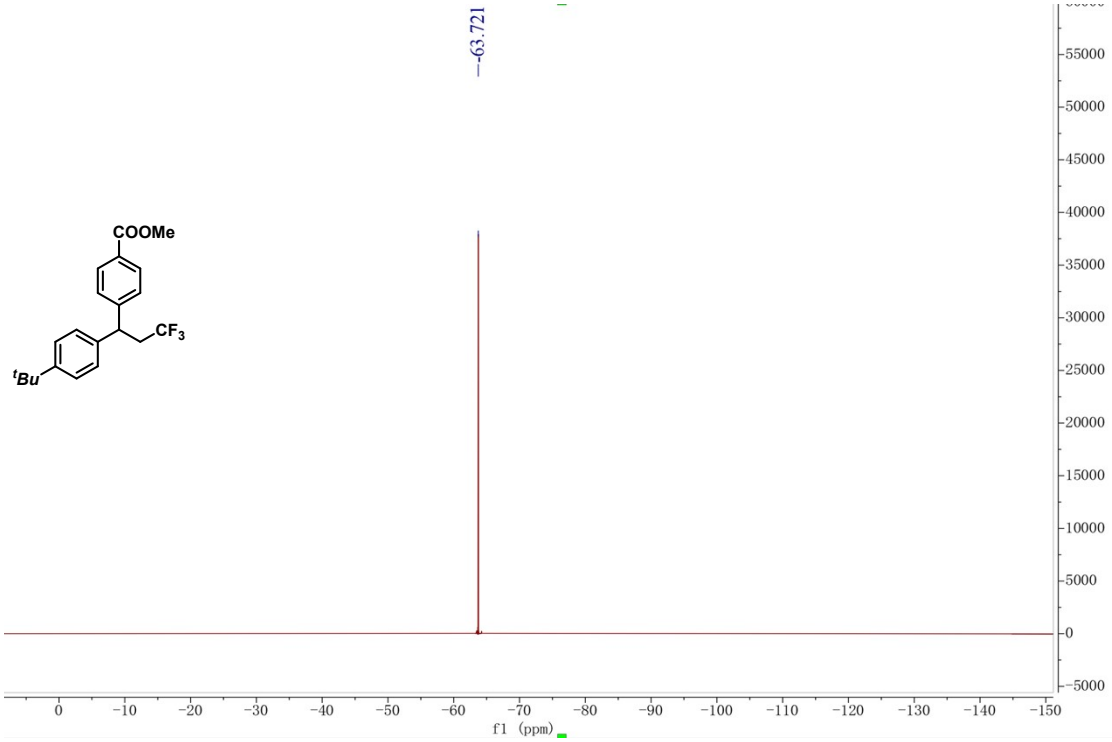
^{1}H NMR (400 MHz, $CDCl_3$) of **5ab**



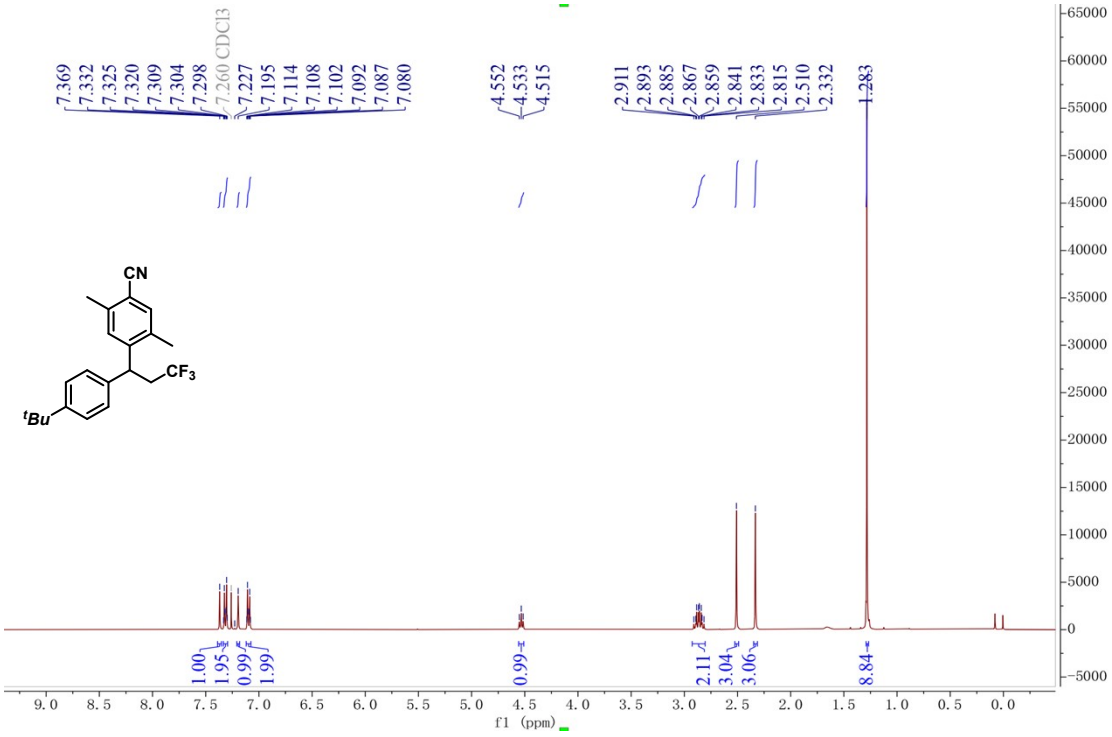
^{13}C NMR (100 MHz, $CDCl_3$) of **5ab**



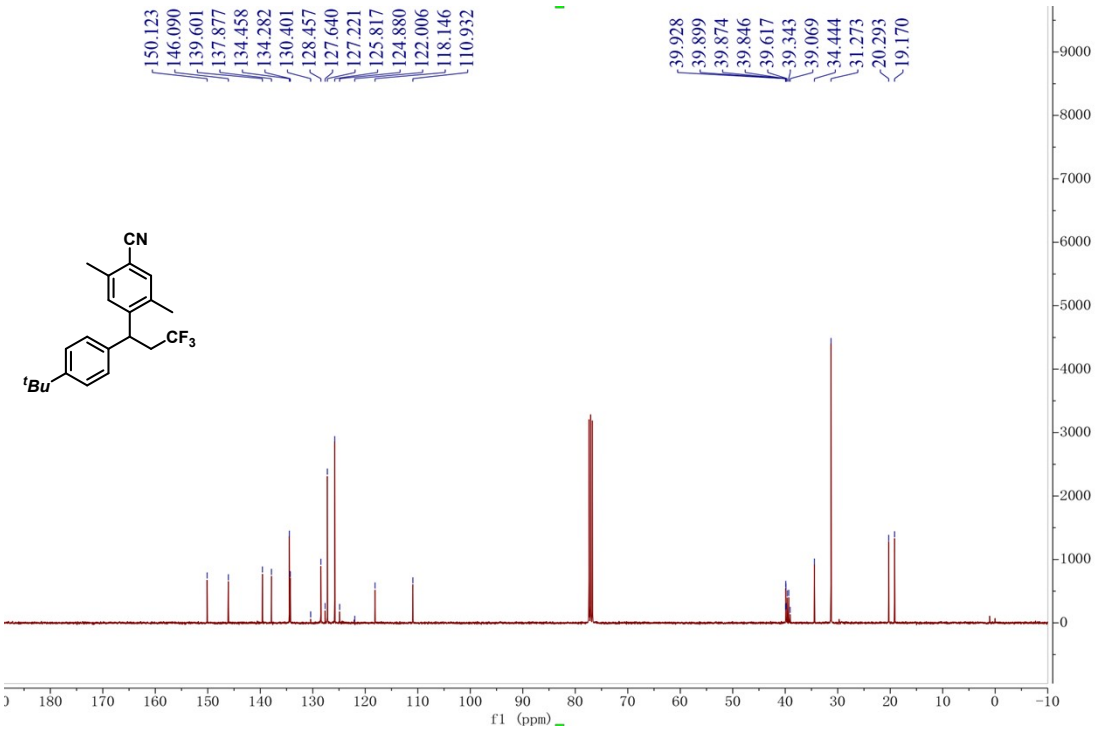
^{19}F NMR (376 MHz, $CDCl_3$) of **5ab**



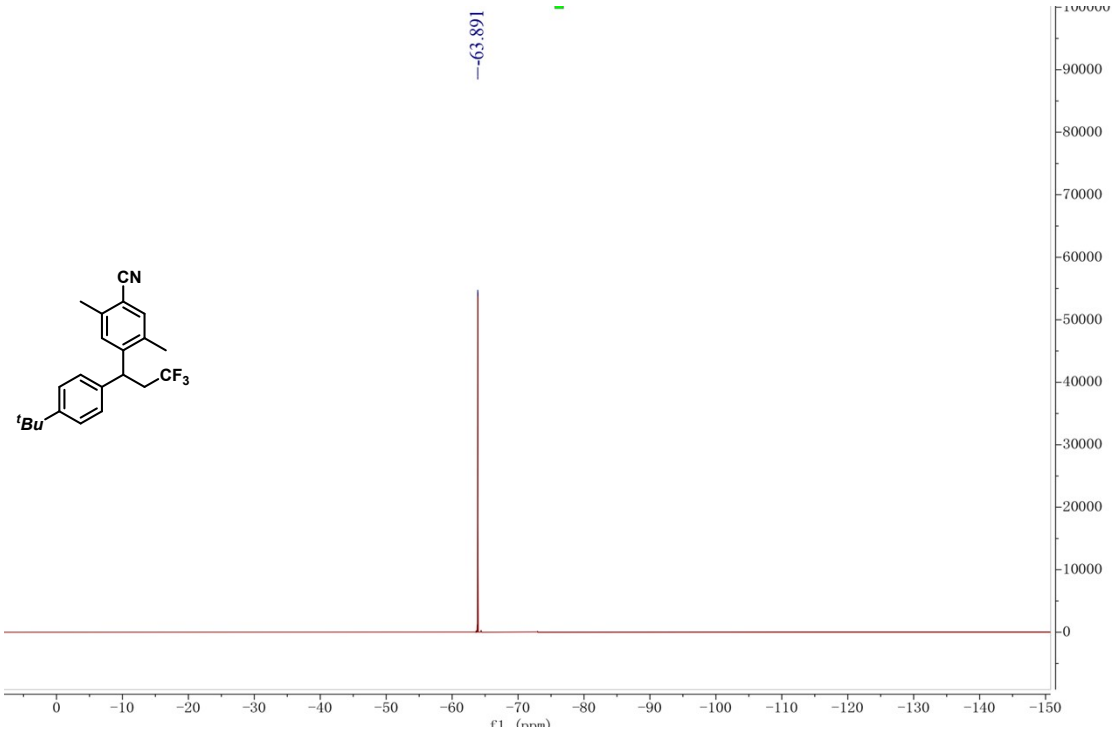
^{1}H NMR (400 MHz, $CDCl_3$) of **5ac**



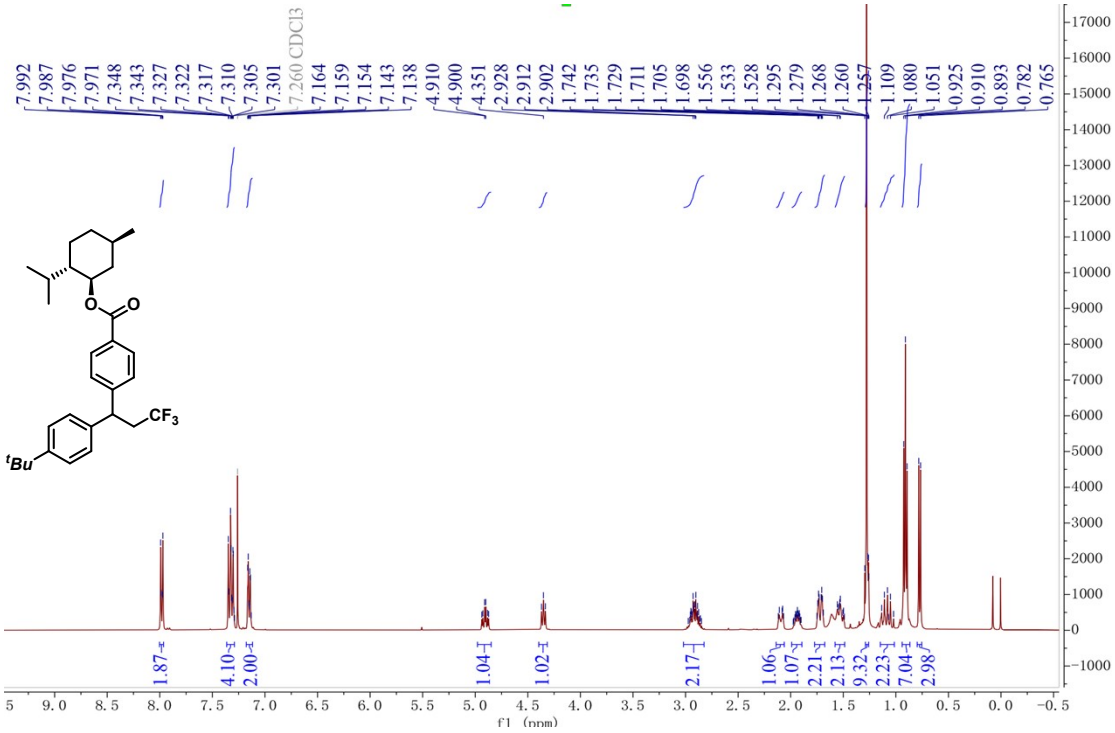
^{13}C NMR (100 MHz, $CDCl_3$) of **5ac**



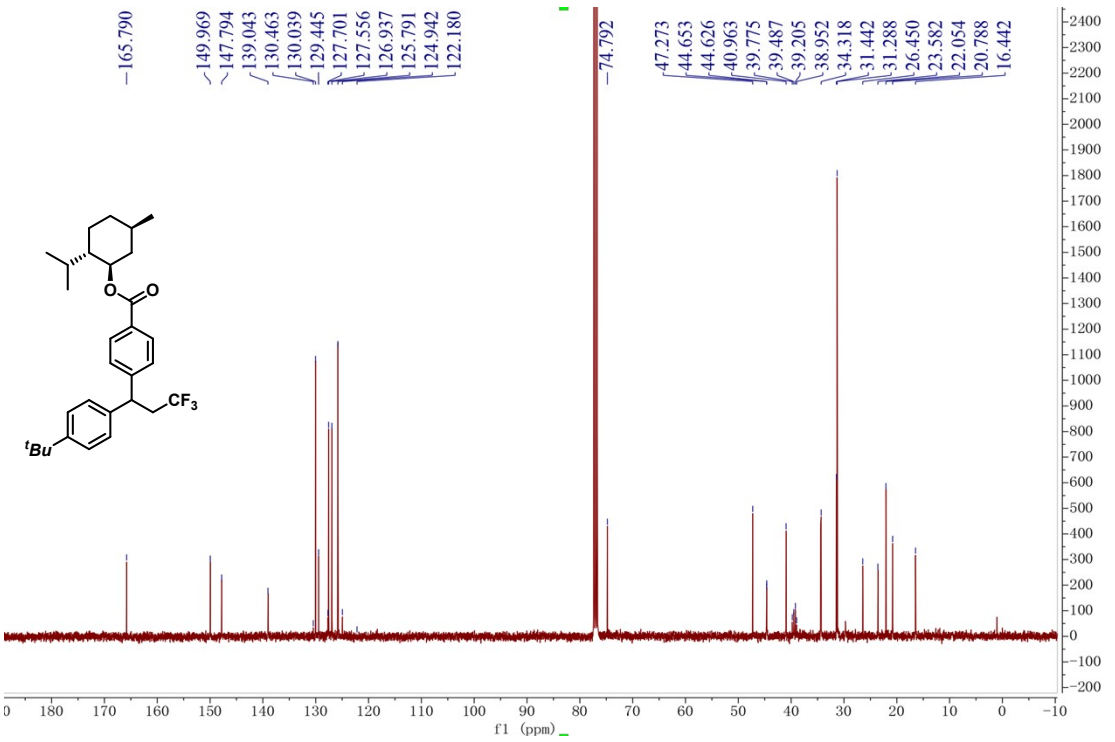
^{19}F NMR (376 MHz, $CDCl_3$) of **5ac**



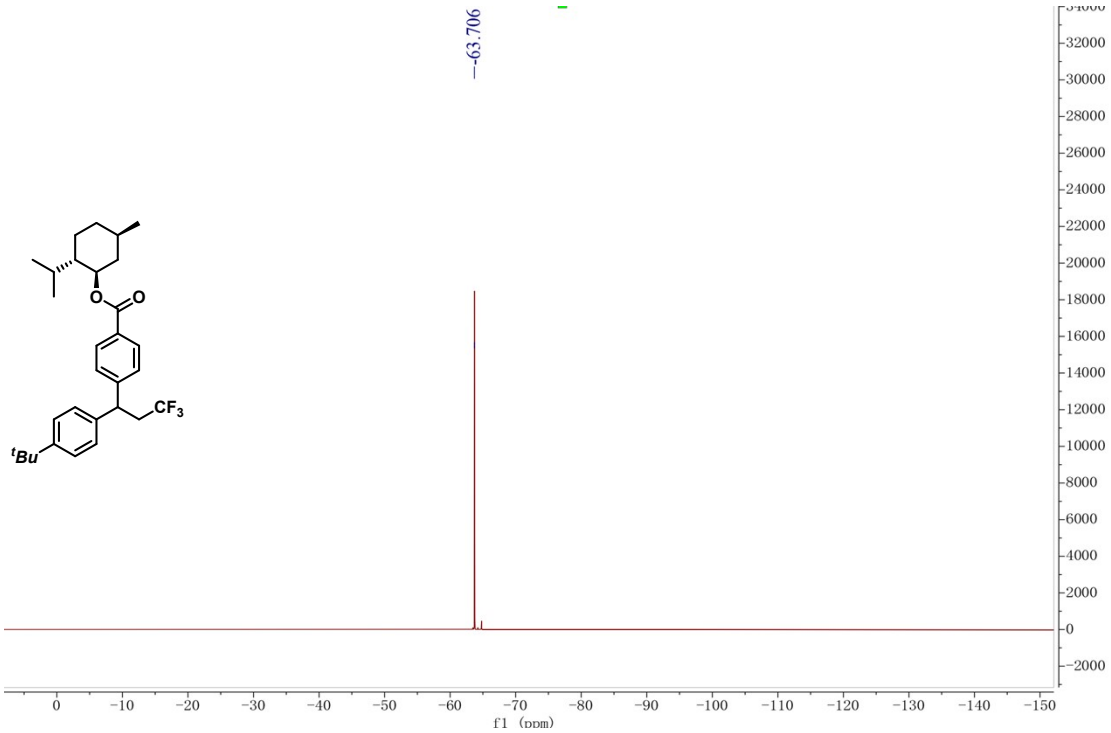
^{1}H NMR (400 MHz, $CDCl_3$) of **5ad**



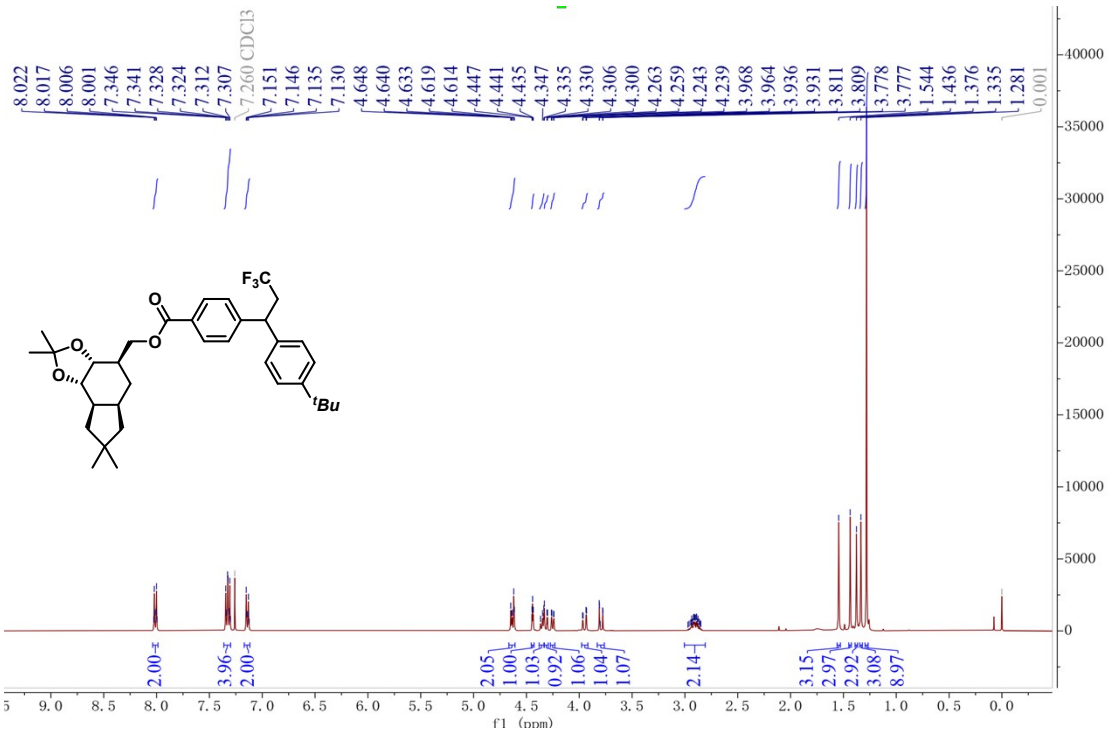
^{13}C NMR (100 MHz, $CDCl_3$) of **5ad**



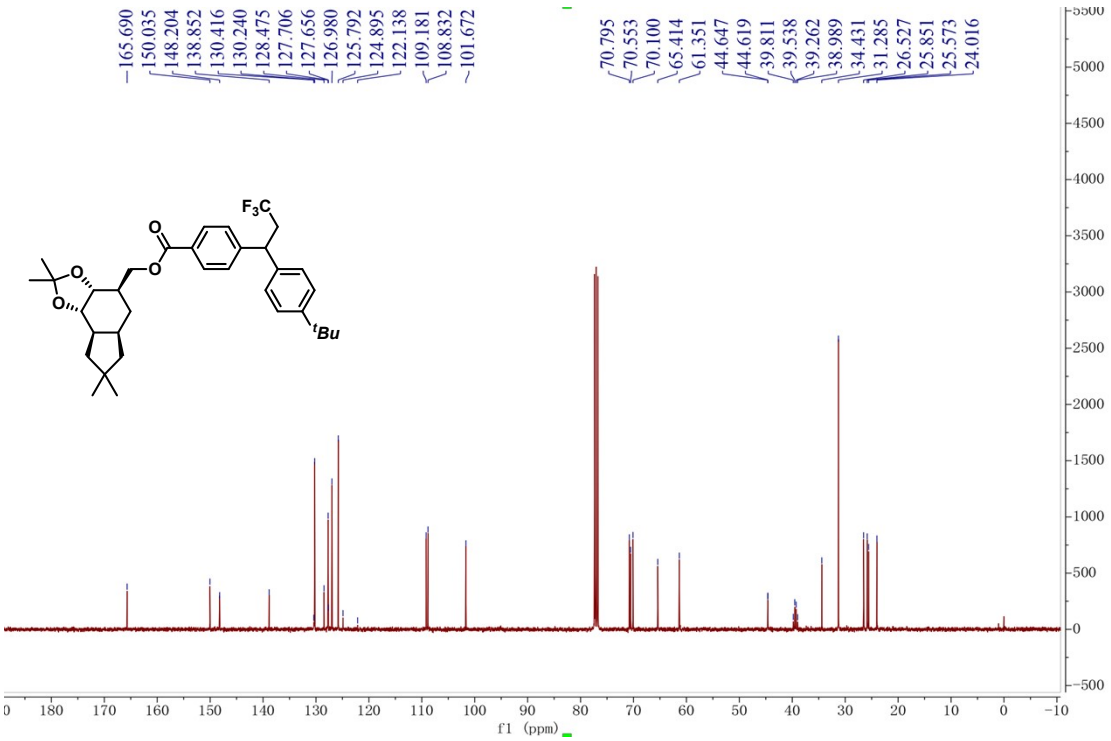
^{19}F NMR (376 MHz, $CDCl_3$) of **5ad**



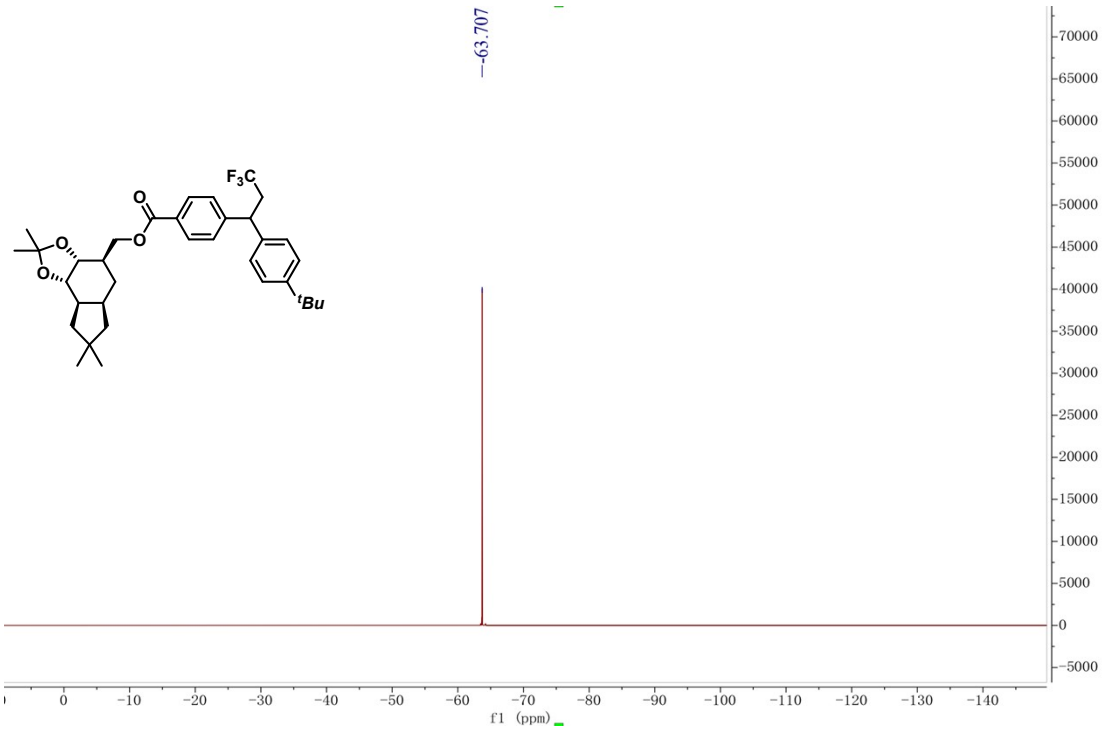
^{1}H NMR (400 MHz, $CDCl_3$) of **5ae**



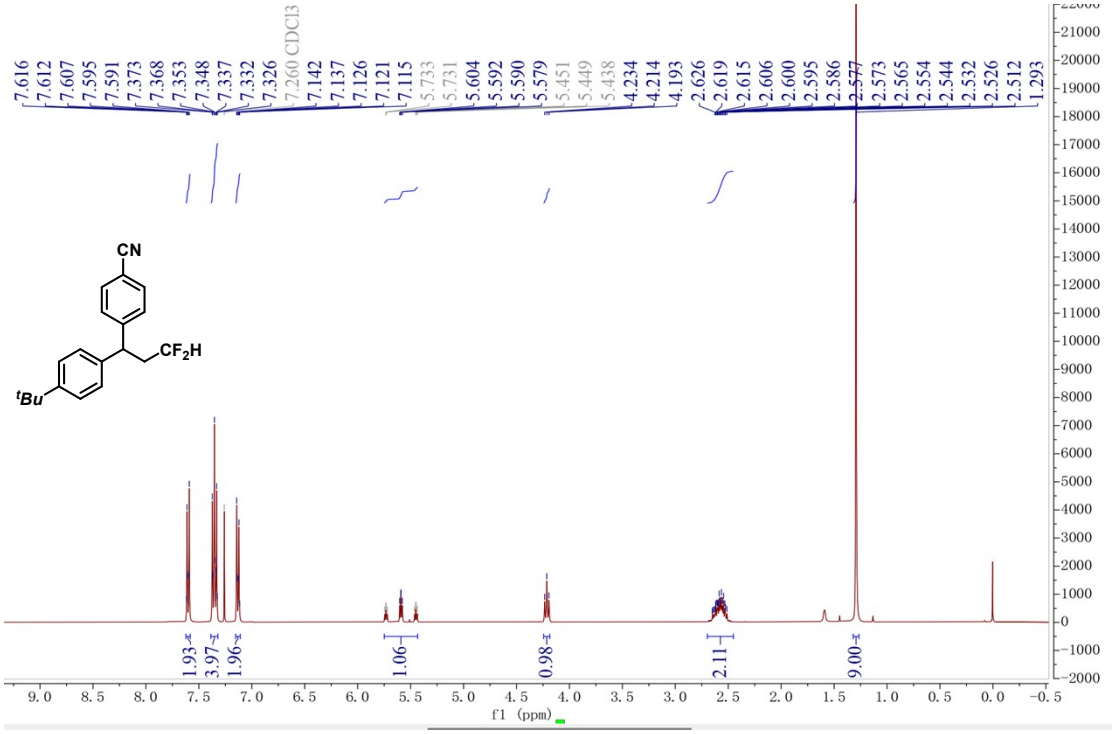
^{13}C NMR (100 MHz, $CDCl_3$) of **5ae**



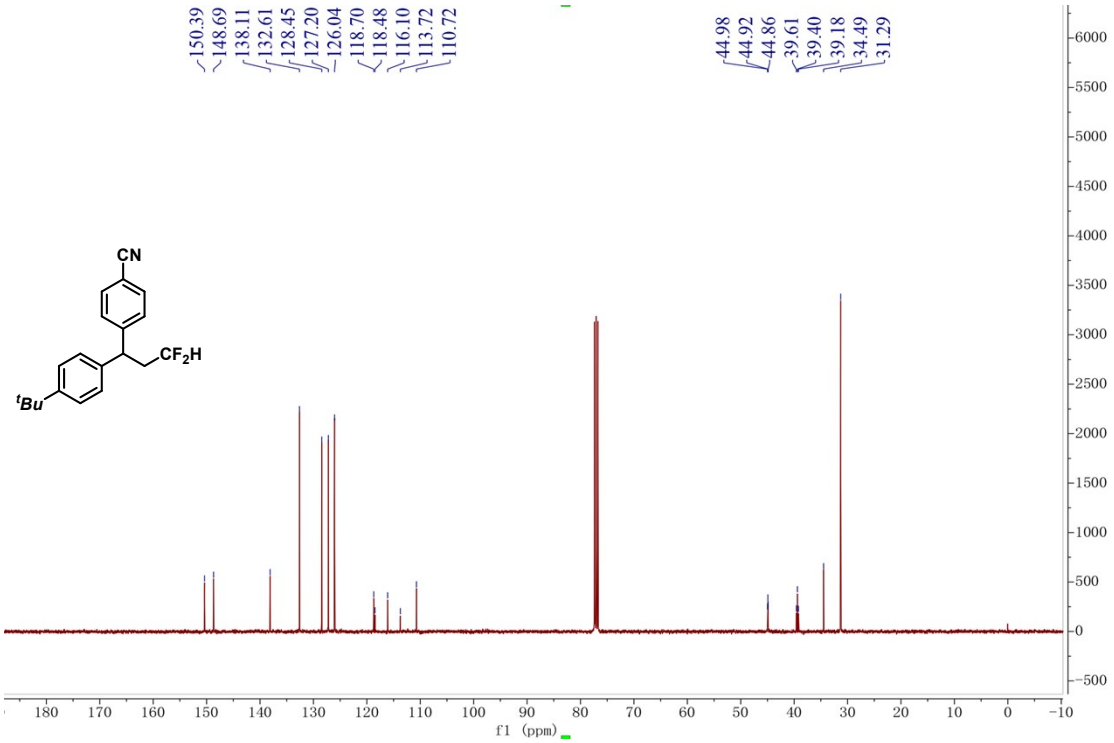
^{19}F NMR (376 MHz, $CDCl_3$) of **5ae**



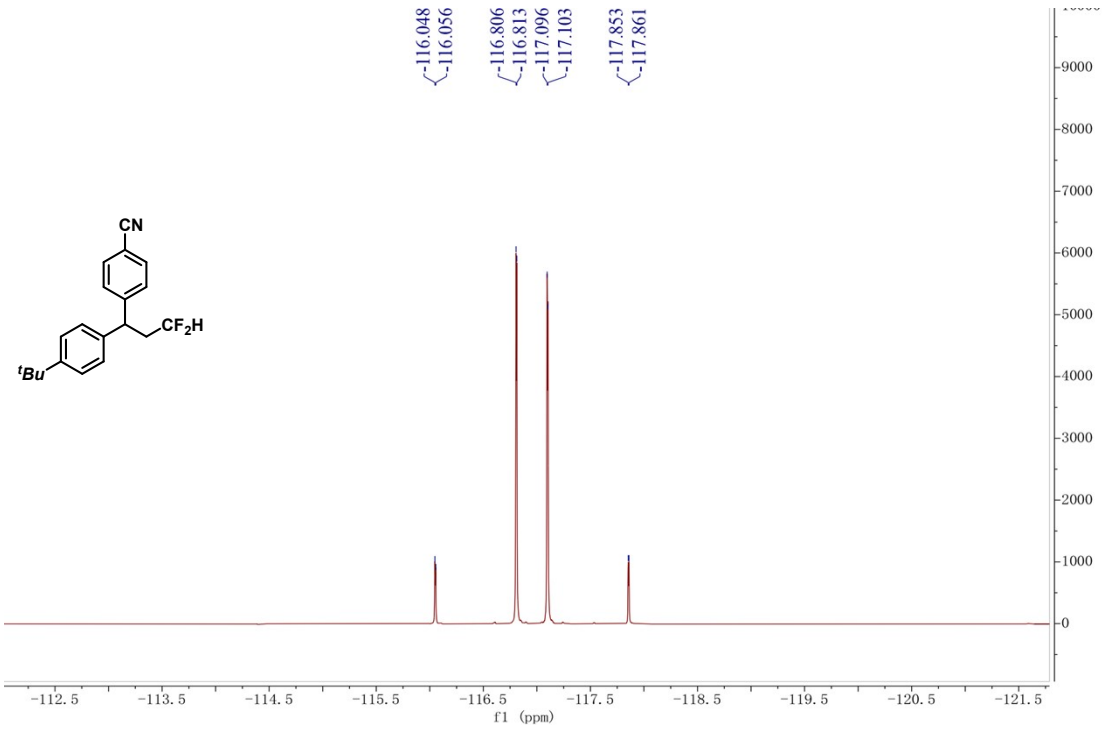
^{1}H NMR (400 MHz, $CDCl_3$) of **7aa**



^{13}C NMR (100 MHz, $CDCl_3$) of **7aa**



^{19}F NMR (376 MHz, $CDCl_3$) of **7aa**



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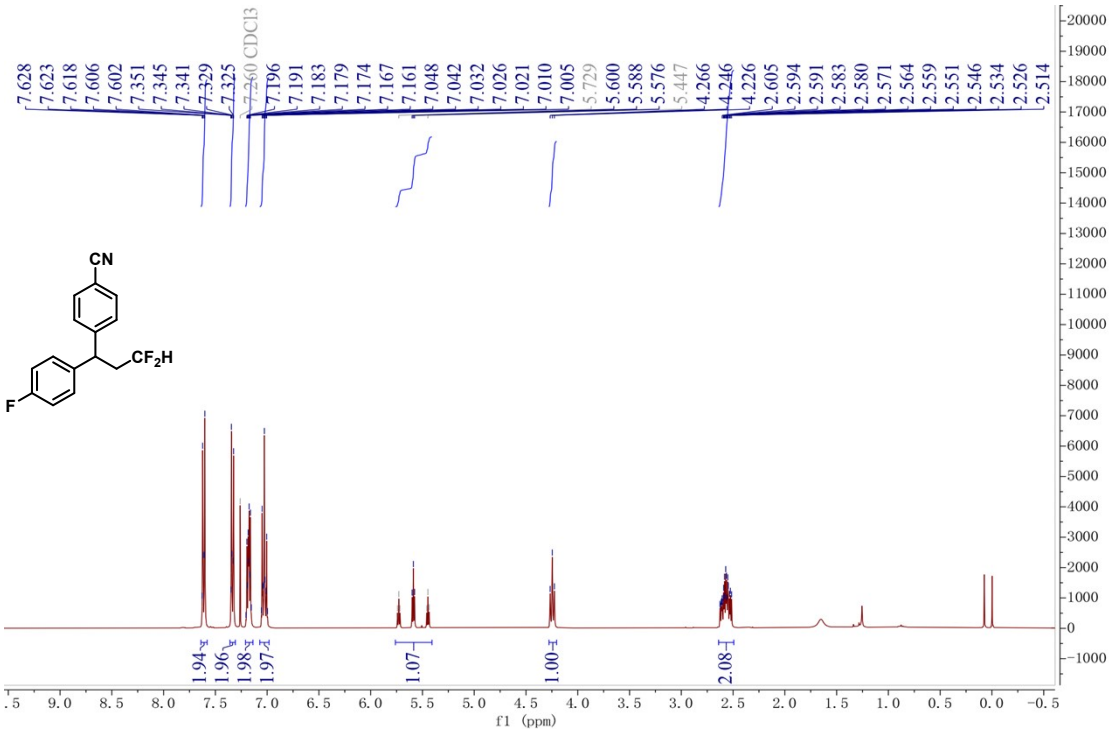
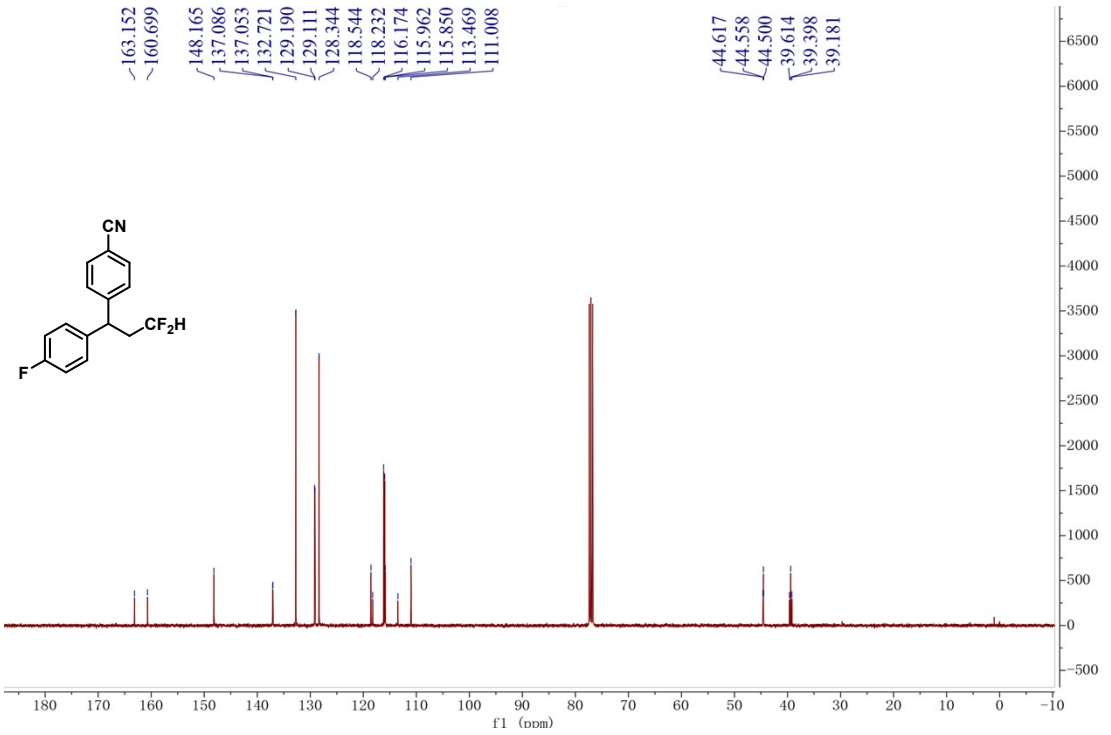


^{13}C NMR (100 MHz, $CDCl_3$) of **7ab**



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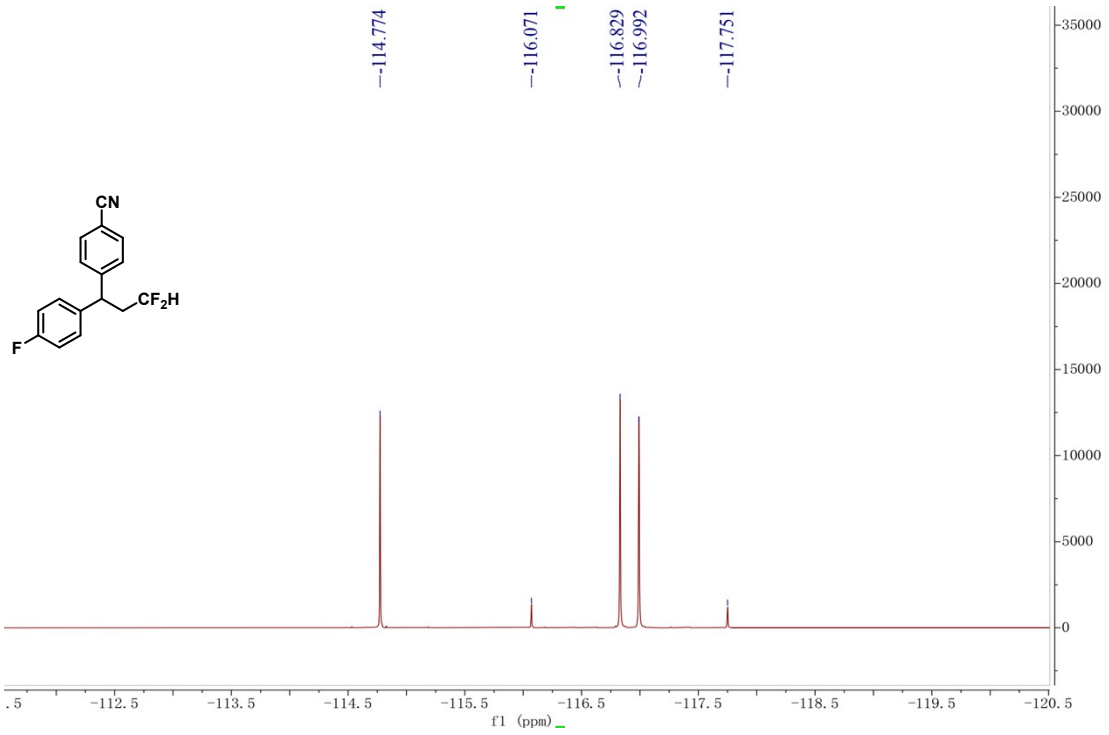
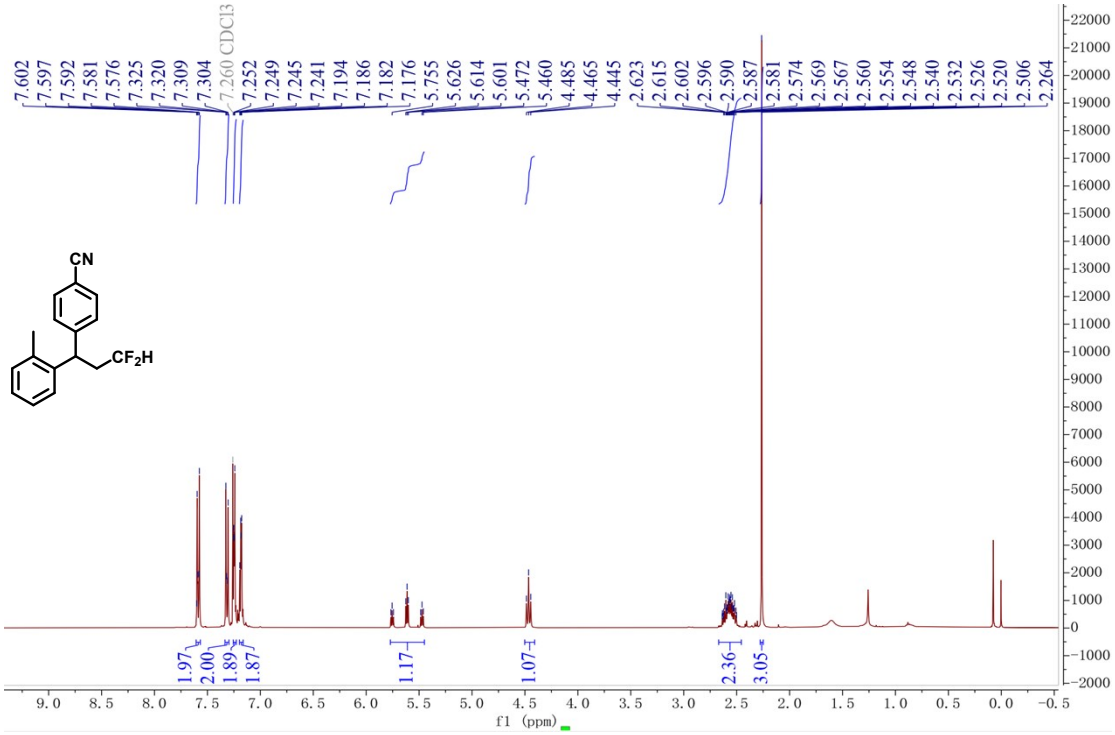
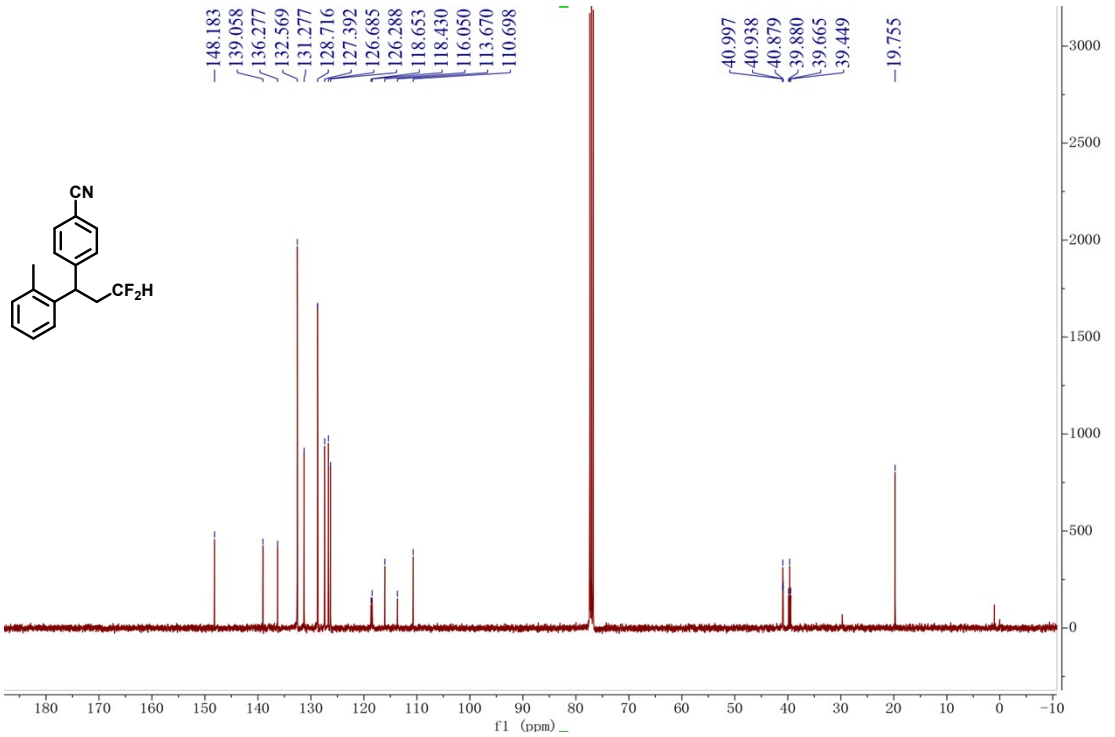


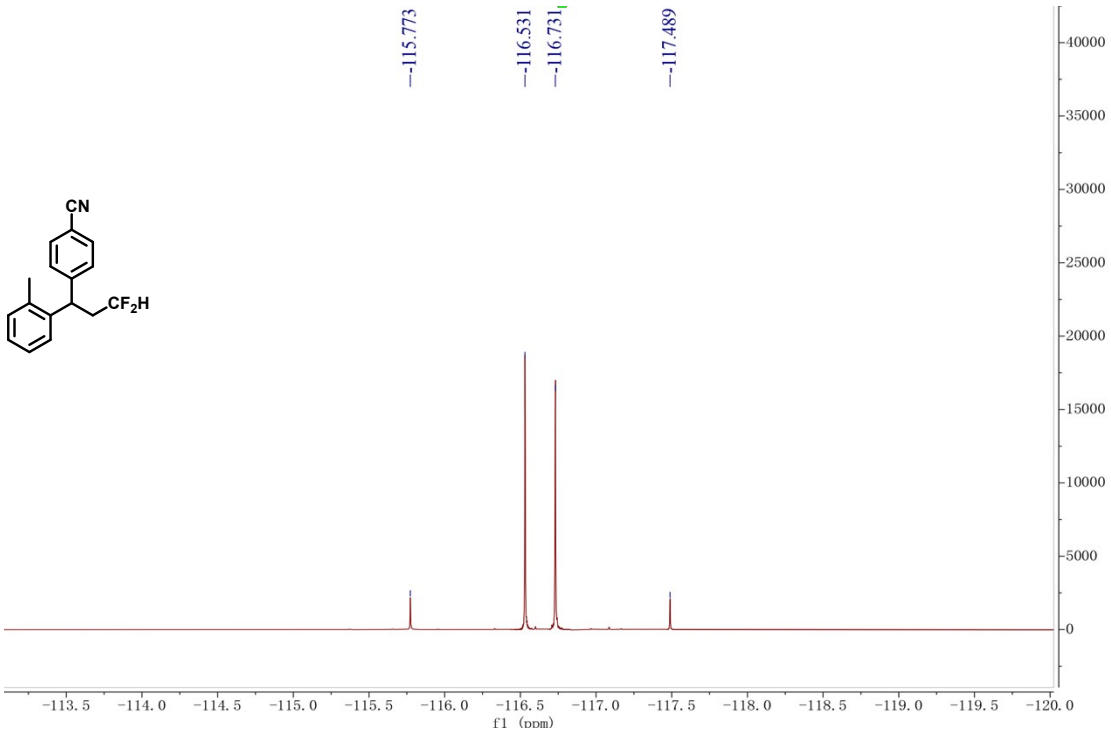
^{1}H NMR (400 MHz, $CDCl_3$) of **7ac**



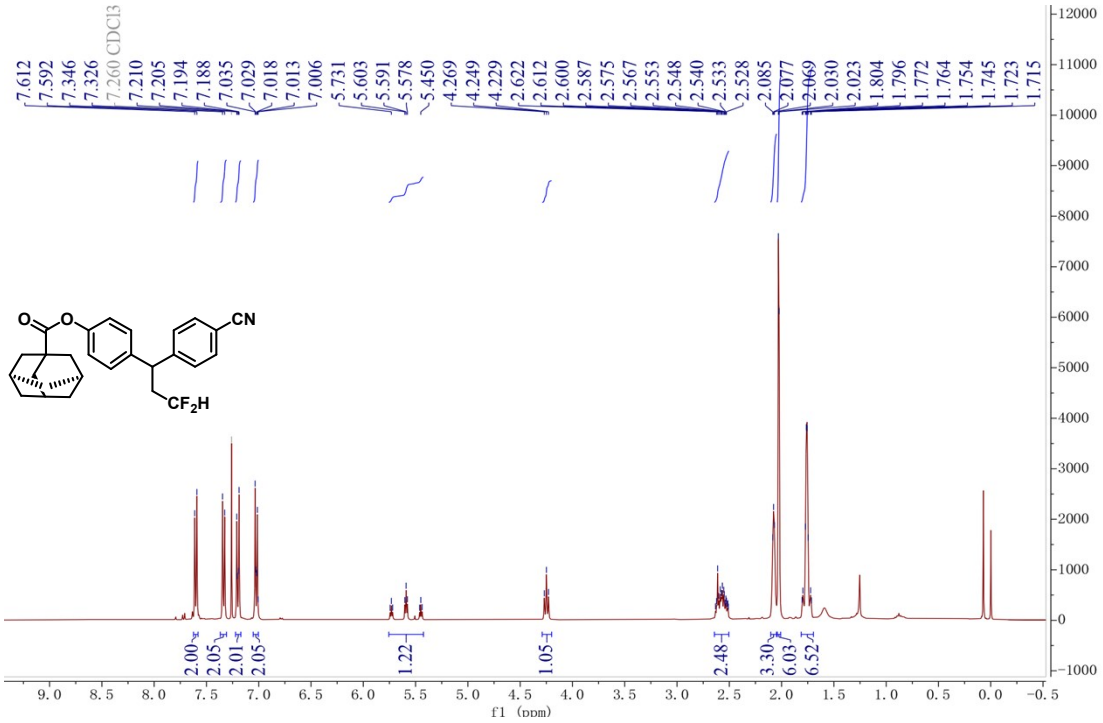
^{13}C NMR (100 MHz, $CDCl_3$) of **7ac**



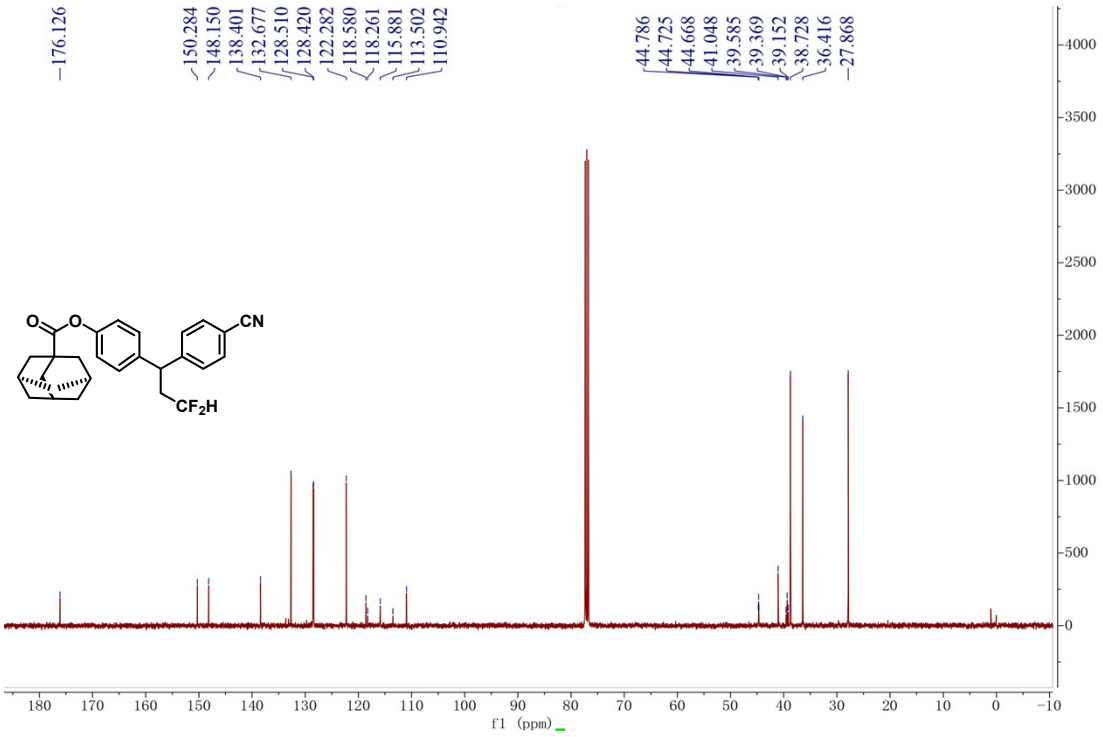
^{19}F NMR (376 MHz, $CDCl_3$) of **7ac**



^{1}H NMR (400 MHz, $CDCl_3$) of **7ad**



^{13}C NMR (100 MHz, $CDCl_3$) of **7ad**



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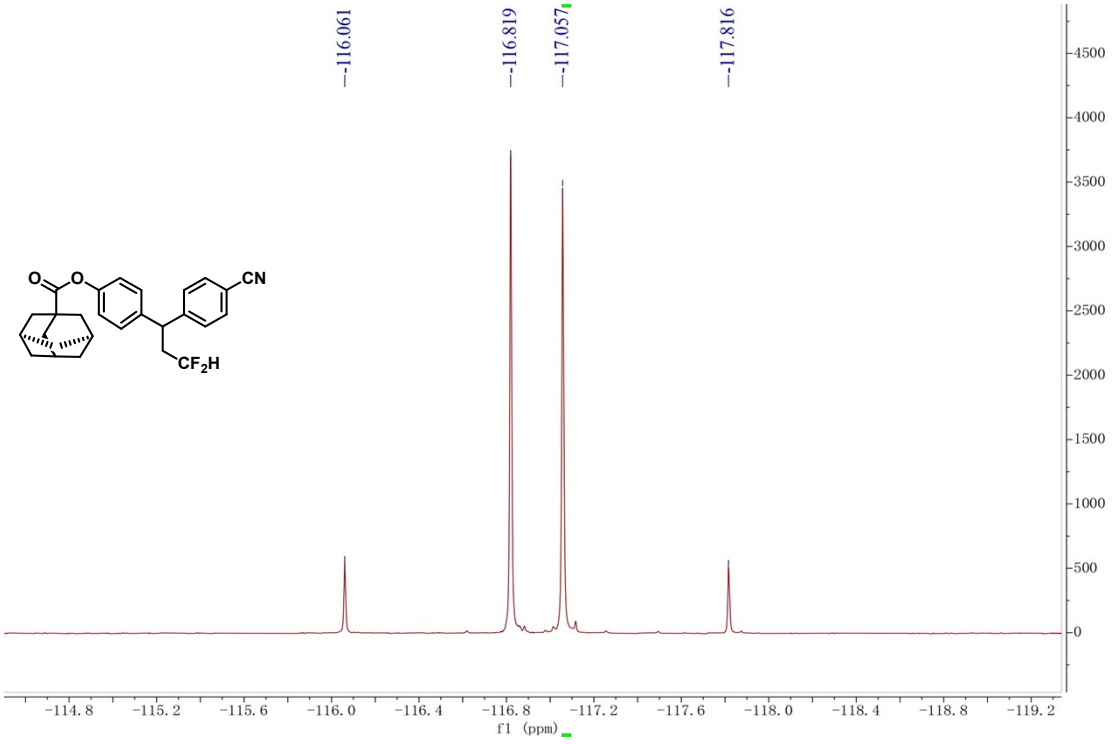
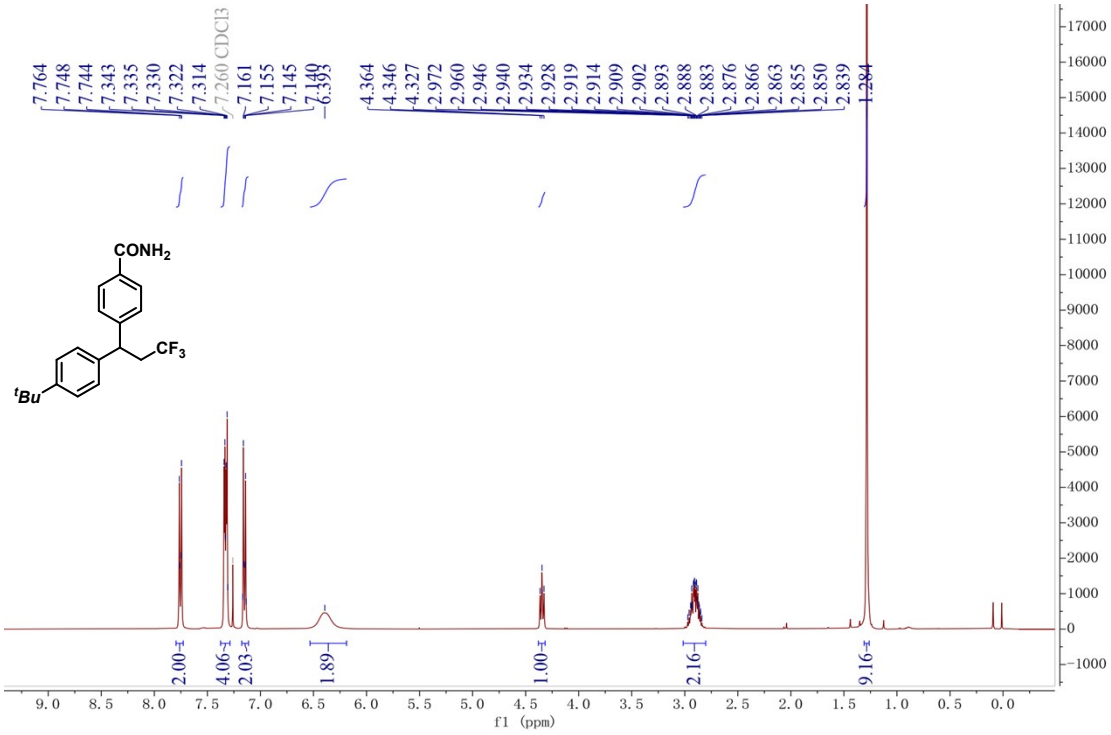
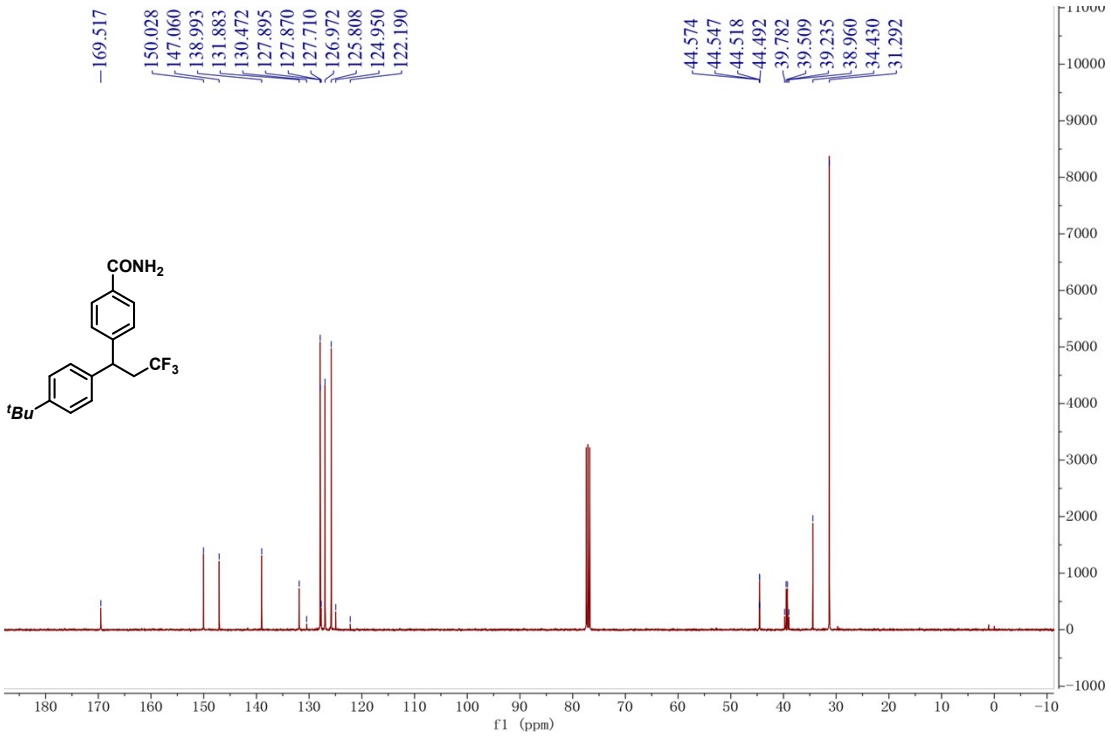


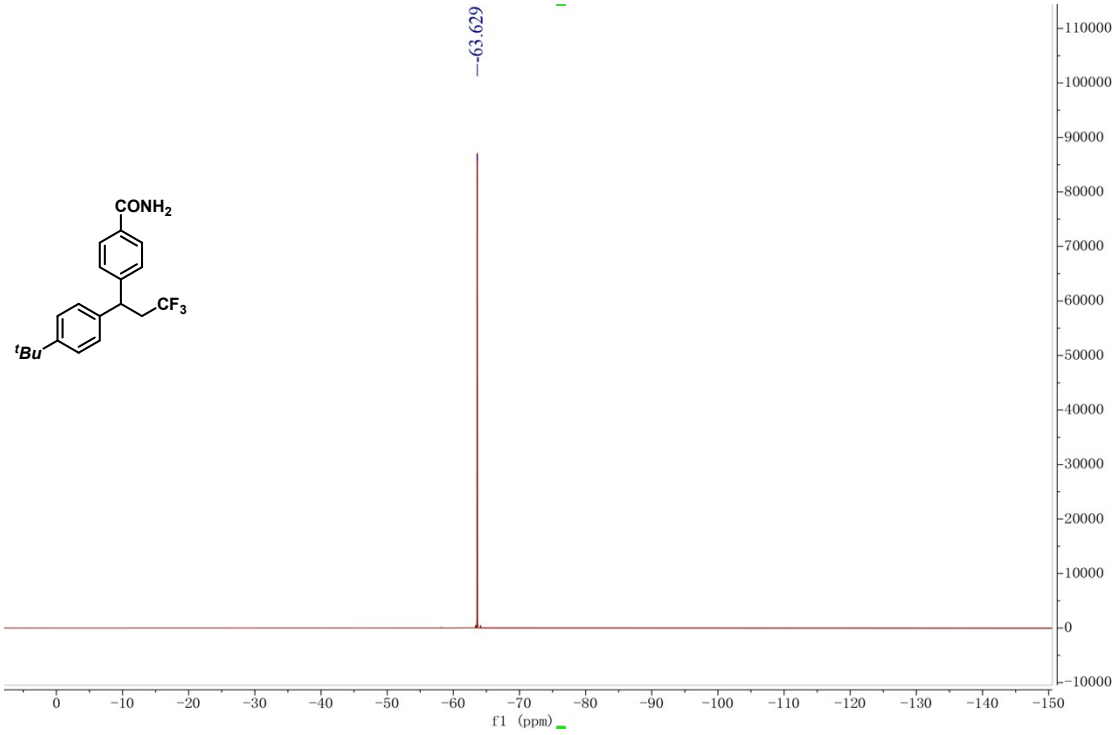
^{1}H NMR (400 MHz, $CDCl_3$) of **8**



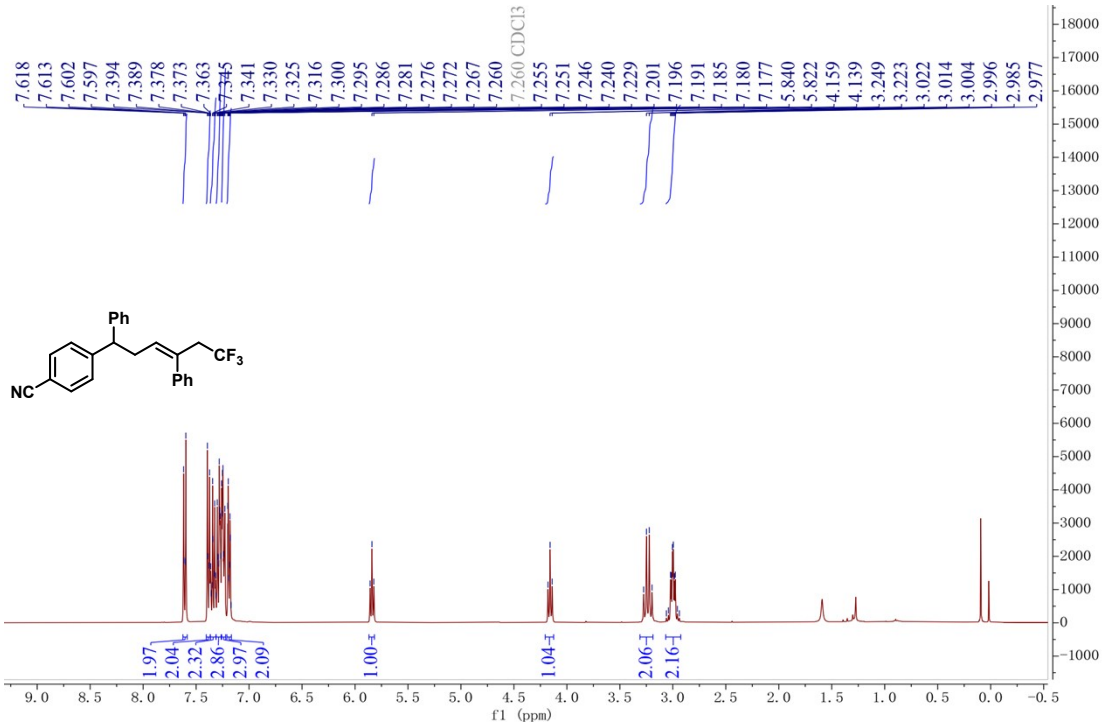
^{13}C NMR (100 MHz, $CDCl_3$) of **8**



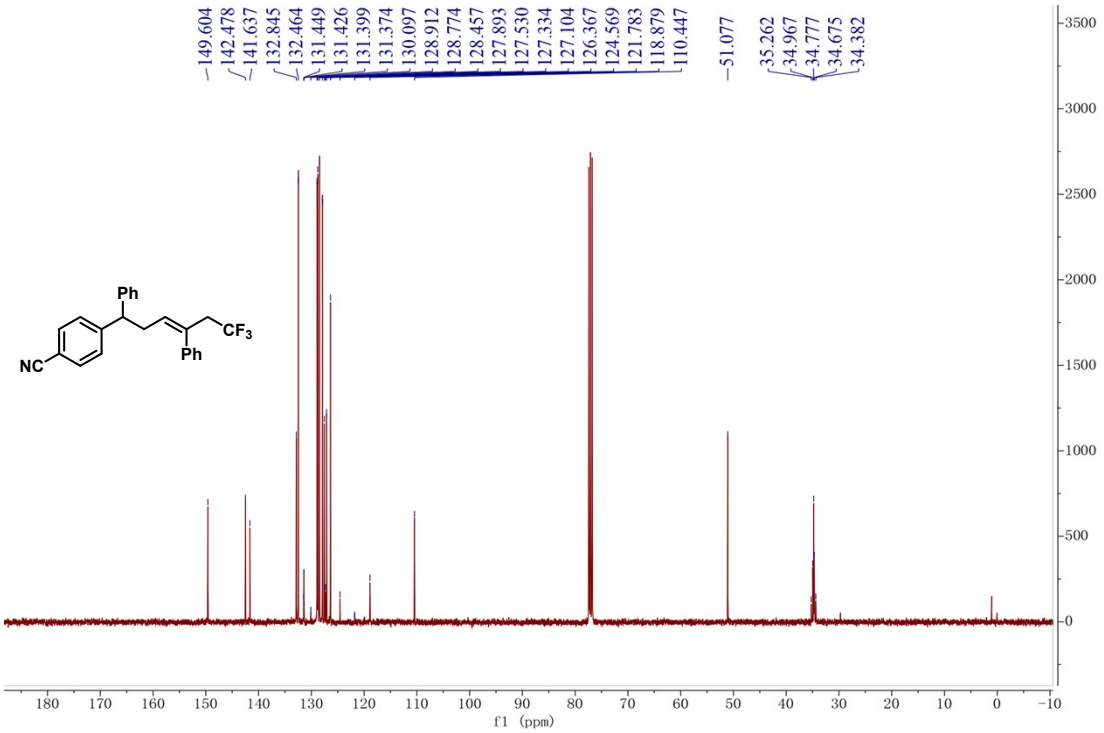
^{19}F NMR (376 MHz, $CDCl_3$) of **8**



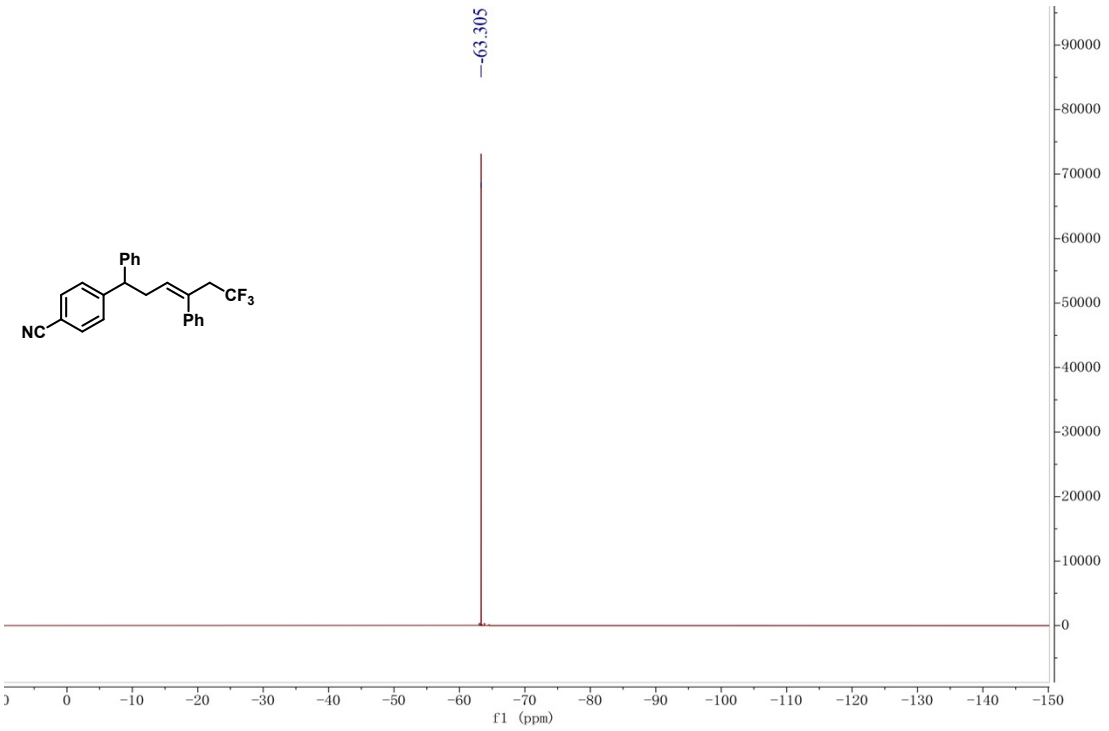
^{1}H NMR (400 MHz, $CDCl_3$) of **10**



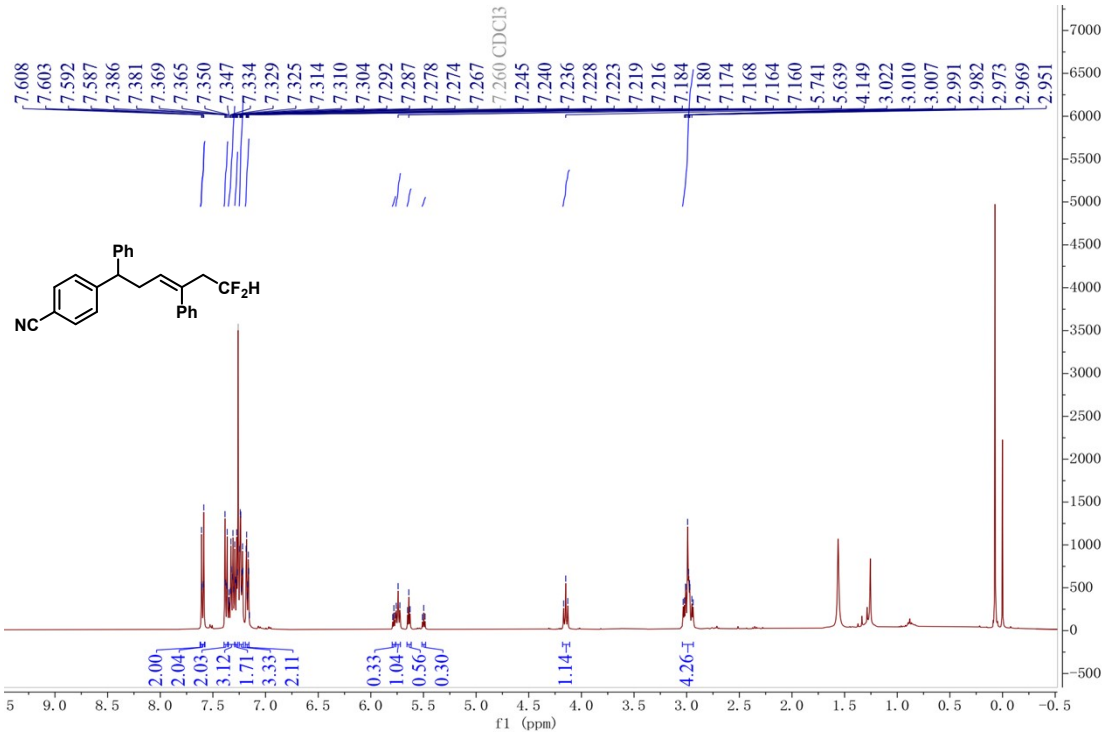
^{13}C NMR (100 MHz, $CDCl_3$) of **10**



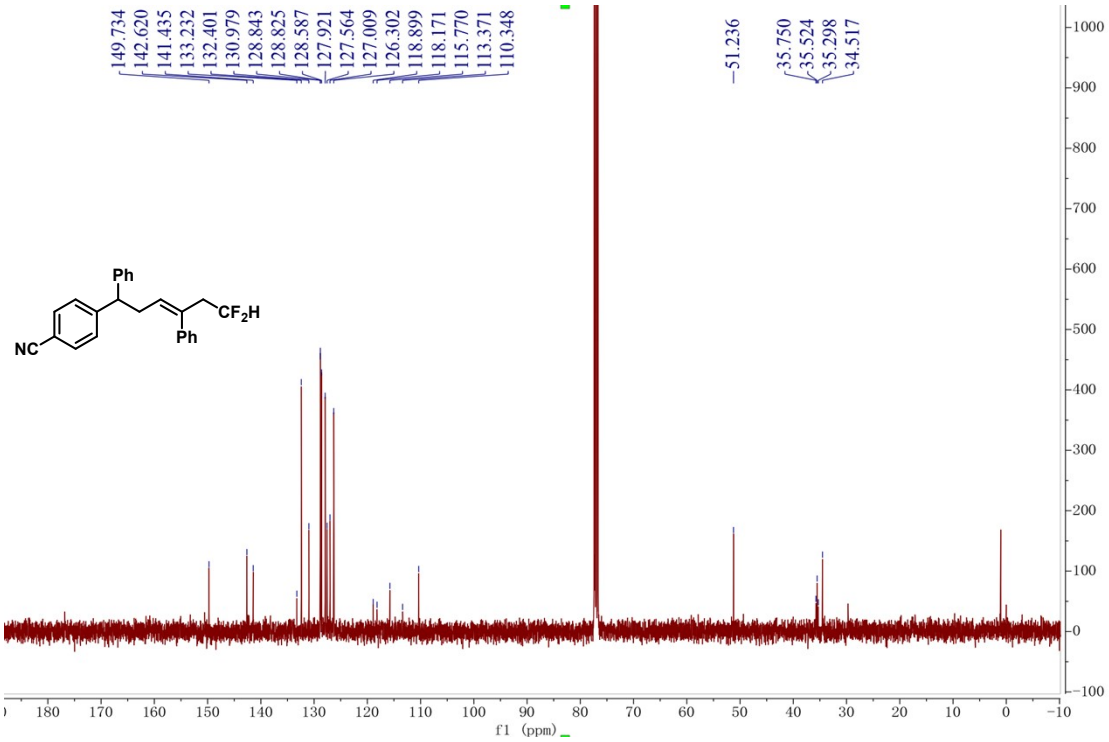
^{19}F NMR (376 MHz, $CDCl_3$) of **10**



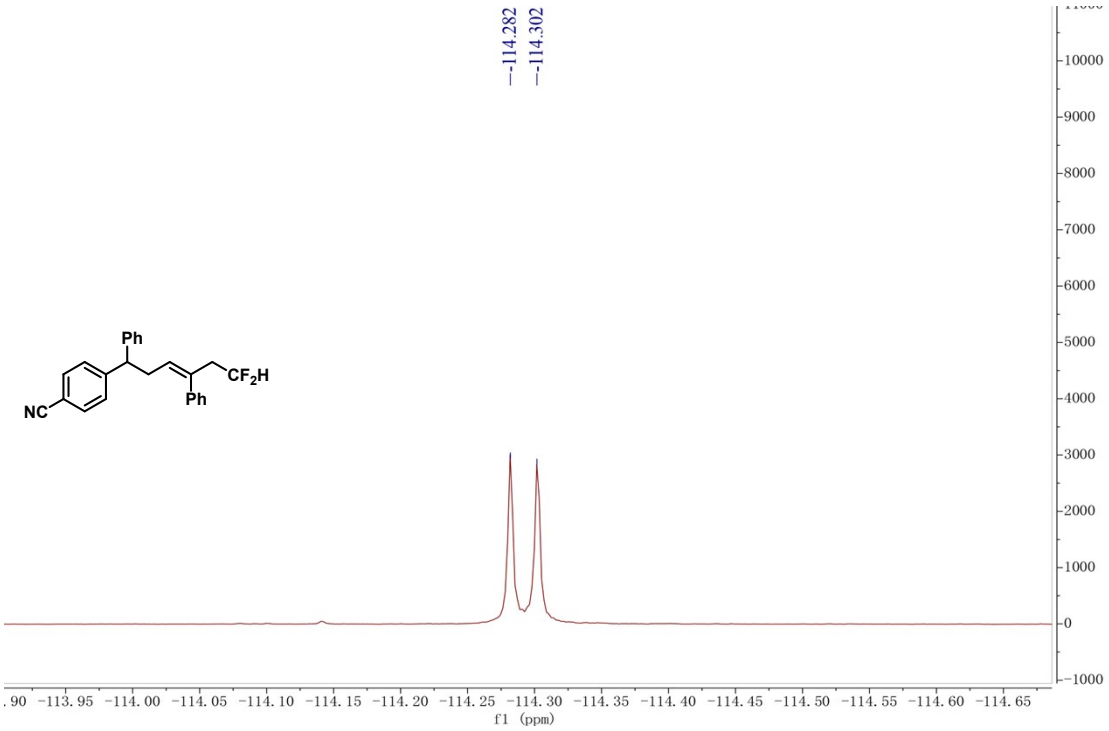
^{1}H NMR (400 MHz, $CDCl_3$) of **11**



^{13}C NMR (100 MHz, $CDCl_3$) of **11**



^{19}F NMR (376 MHz, $CDCl_3$) of **11**



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