Supporting information

Electrochemically catalyzed fluoroalkylation/cyclization of unactivated alkenes: synthesis of polycyclic benzimidazoles containing CF_3 group

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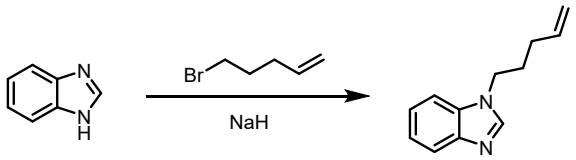
1. General information

All reagents were obtained from commercial sources and used without further purification unless otherwise indicated. The starting materials were purchased from Aladdin (https://www.aladdin-e.com/). Silica gel for column chromatography was purchased from Qingdao Haiyang Chemical Co., Ltd. Reactions were stirred using Teflon-coated magnetic stir bars. Thin-layer chromatography (TLC) was used to monitor the reaction.Melting points were determined using a Büchi B-540 capillary melting point apparatus. ^{1}H NMR (400/600 MHz), ^{13}C NMR (101/151 MHz) and ^{19}F NMR (376/565 MHz) spectra were recorded with $CDCl_3$. Chemical shifts are reported downfield from TMS (=0) for ^{1}H NMR. For $^{13}C\{^{1}H\}$ NMR, chemical shifts are reported in the scale relative to $CDCl_3$ (= 77.0). High resolution mass spectrometry (HRMS) analysis was performed on an Agilent 1290–6540 UHPLC Q-Tof HR-MS System (ESI) spectrometer. Cyclic voltammetry experiments were carried out in an equipment of CHI761E. CV curves were recorded using a three-electrode scheme. The working electrode was a glassy carbon electrode, A platinum electrode served as counter electrode. Ag/AgCl (KCl sat'd) was used as the reference electrode. The working electrode was polished before recording each CV curve.

2. General Procedure for the preparation of substrates

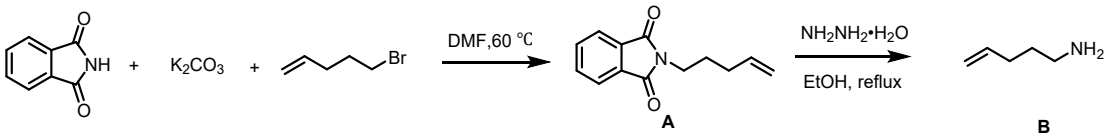
General procedure for the synthesis of N-substituted benzoimidazole[1]



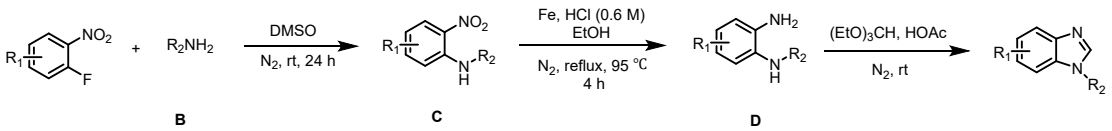
To a 25 mL Schlenk tube equipped with a magnetic stirring bar were added benzimidazole (354 mg, 3 mmol) and anhydrous tetrahydrofuran (5 mL) under nitrogen atmosphere at room temperature. After cooling to 0 ºC, NaH (180 mg, 4.5 mmol) was added and stirring was continued for 15 min at room temperature. Subsequently, bromo alkene (3.6 mmol) was added and stirring was further continued for 0.5 h at 80 ºC to confirm completion of the reaction by TLC analysis. Water was added to quench the

reaction and the organic layer was separated. The aqueous layer was extracted with chloroform twice. The combined organic layers were dried over anhydrous magnesium sulfate for several hours and concentrated under reduced pressure to leave a crude solid. Flash column chromatography on silica gel using ethyl acetate as an eluent afforded the corresponding N-substituted benzimidazole.

General procedure for the synthesis of Single substitution N-substituted benzoimidazole[2,3]



A solution of 5-bromopent-1-ene (16.7 g, 112.08 mmol), potassium carbonate (15.4 g, 111.59 mmol) and phthalimide (15.0 g, 102.04 mmol) in DMF (60 mL) were stirred overnight at 60 ℃ for 8h. The solution was diluted with water (100 mL), and extracted with diethyl ether (80 mL × 3). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo to give **A** as a crude product, which was used for the next step without further purification. A mixture of **A** and hydrazine monohydrate (4.2 mL, 85 mmol) was refluxed in ethanol (200 mL) for 8 h. Concentrated HCl (30 mL) was added dropwise at 0 °C . The mixture was filtered and the filtrate was concentrated in vacuo. The residue was diluted by water (80 mL) and washed by ethyl acetate (40 mL × 2). The aqueous layer was separated and basified with 3 M NaOH to pH 10 at 0°C. The solution was extracted with ethyl ether (50 mL × 3). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo (below 20 °C) to give **B** as a yellow oil, which was used for the next step without further purification.



Step 1. To an oven dried round flask equipped with a magnetic stir bar was added 1-fluoro-4-methyl-2-nitro benzene or its derivatives (3 mmol, 1 equiv.) in DMSO (5 mL).

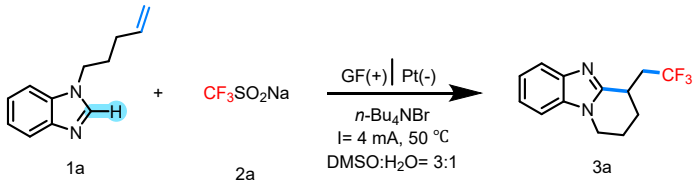
Subsequently, amine (3.6 mmol, 1.2 equiv.) was added to this solution. After stirring for 24 hours at room temperature, the solution was poured into water (100 mL) and the resulting mixture was extracted with EtOAc (3 × 50 mL). The combined organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product **C**. The crude product C was used in the next step without further purification.

Step 2. Aquous HCl (0.6 M, 6.5 mL) was added to a suspension of **C** and iron powder (1.68 g, 30 mmol, 10 equiv.) in ethanol (25 mL). The resulting mixture was stirred for 3 hours at 95 ℃. Upon completion, the reaction was cooled to room temperature and filtered through a pad of celite. The filtrate was diluted with EtOAc (100 mL) and washed with saturated $NaHCO_3$ solution (25 mL) and saturated NaCl solution (25 mL). The organic layers were dried over Na_2SO_4 and concentrated under reduced pressure to obtain crude product **D**. The crude product **D** was used in the next step without further purification.

Step 3. To a flame-dried 200 mL round bottom flask equipped with a stir bar was added **D** in HOAc (10 mL). Then $(EtO)_3CH$ (444.6 mg, 3 mmol) was added and the resulting solution was stirred at room temperature until the reaction was complete (monitored by thin layer chromatography). The solution was diluted with EtOAc, washed with saturated $NaHCO_3$ (2 × 50 mL) and extracted with ethyl acetate (2 × 30 mL). The organic layers were combined, dried over anhydrous Na_2SO_4, filtered and concentrated in vacuo. The crude products were purified by column chromatography on silica gel eluting with n-pentane/EtOAc to give the desired product.

3. Optimization of reaction condition

Table S1 Other variations of reaction conditions [a]

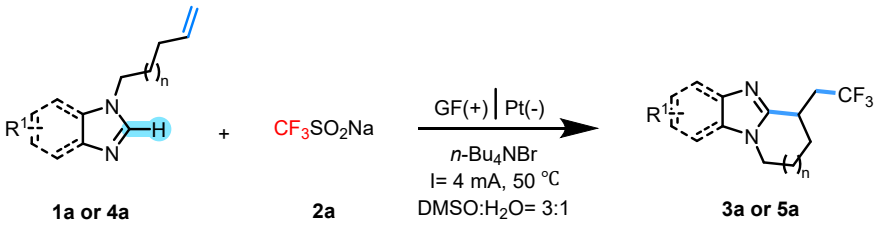


Entry	variation from titled conditions	Yield (%) [b]
1	none	58

2	CH_3CN:HFIP= 5:1	N.R
3	CH_3CN:H_2O= 1:1	46
4	DMF:H_2O= 3:1	40
5	1,4-dioxane= 3:1	23
6	*n*-Bu_4NPF_6 instead of *n*-Bu_4NBr	52
7	*n*-Bu_4NI instead of *n*-Bu_4NBr	N.R
8	KI instead of *n*-Bu_4NBr	N.R
9	1.5 equiv. of CF_3SO_2Na	21
10	3.5 equiv. of CF3SO2Na	63
11	rt instead of 50℃	trace
12 [c]	CH_3COOH as additive	33
13 [d]	PhCOCOOH as additive	48
14 [e]	DMAP as additive	34
15 [f]	KOAc as additive	40
16	Without *n*-Bu_4NBr	25

[a] Reaction Condition: **1a** (0.3 mmol), **2a** (0.6 mmol), solvent (6 mL), with 1 equiv. *n*-Bu_4NBr as electrolyte, 4 mA constant current, undivided cell, GF anode (1.5 cm×1.0 cm×0.6 cm) and Pt cathode (1.5 cm× 1.0 cm×0.6 cm), 50 ℃, 10 h. [b] Isolated yield. [c] CH_3COOH (1 equiv.). [d] PhCOCOOH (1 equiv.). [e] DMAP (1 equiv.). [f] KOAc (1 equiv.).

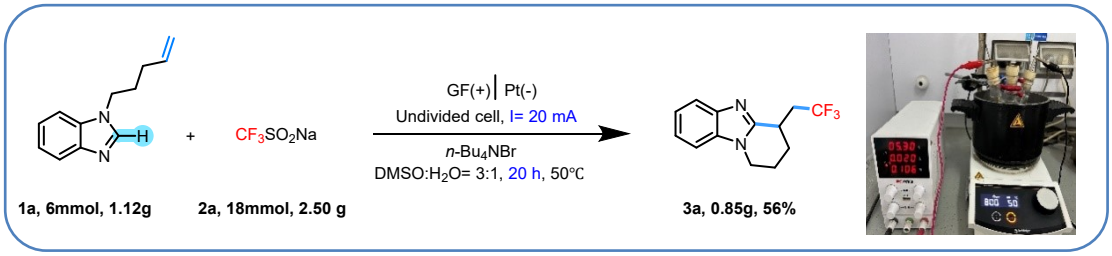
4. General procedure of the synthesis of the products



A schlenk tube was charged with **1a** or **4a** (0.2 mmol, 1.0 equiv.), sodium trifluoromethanesulfinate **2a** (94 mg, 0.6 mmol, 3 equiv.), and *n*-Bu_4NBr (64.4 mg, 0.2 mmol, 1.0 equiv.). The tube was equipped with a graphite felt anode (1.5 cm x 1 cm x 0.5 cm) and a Pt (1.5 cm x 1 cm) cathode. DMSO (3 mL) and H_2O (1 mL) were added. The constant current (4 mA) electrolysis was carried out at 50 °C (oil bath temperature) for 10 h. After complete consumption of the starting material, the reaction mixture was cooled to ambient temperature, extracted with H_2O (30 mL) and ethyl acetate (3 x 20

mL). The combined organic solution was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product.

5. Procedure for gram-scale experiment

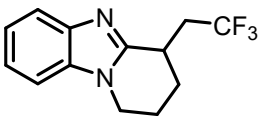


Conditions: Undivided cell, graphite felt anode (2 cm* 3 cm), Ni foam cathode (2 cm* 3 cm), **1a** (6 mmol), **2a** (18 mmol), *n*-Bu_4NBr (6 mmol), DMSO (30 mL), H_2O (10 mL), 20h, 50 ℃, j = 3.3 mA/cm^2, constant current: 20 mA, isolated yield.

To a pore cylindrical glass instrument, **1a** (1.12g, 6mmol), sodium trifluoromethanesulfinate **2a** (2.50 g, 16 mmol) and *n*-Bu_4NBr (1.93g, 6mmol) was added. The glass instrument was equipped with a graphite felt anode and a Pt cathode. DMSO (30 mL) and H_2O (10 mL) were added. The resulting reaction mixture was stirred at 50℃ under the constant current of 20 mA for 20 hours. After complete consumption of the starting material, the reaction mixture was cooled to ambient temperature, extracted with H_2O (150 mL) and ethyl acetate (100 mL) three times. The combined organic solution was washed with brine, dried over Na_2SO_4 and concentrated under reduced pressure. The residue was purified by flash column chromatography using a mixture of petroleum ether and ethyl acetate as eluent to give the desired product **3a** (0.85 g, 56% yield).

6. Analytical data of the synthesized derivatives

4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3a)

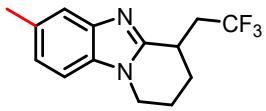


Yellow oil; 70% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 (dd, J = 8.0, 4.6 Hz, 1H), 7.36 – 7.25 (m, 3H), 4.29 – 4.19 (m, 1H), 3.98 (td, J = 11.6, 5.0 Hz,

1H), 3.59 – 3.36 (m, 2H), 2.54 – 2.42 (m, 1H), 2.44 – 2.25 (m, 2H), 2.18 – 2.02 (m, 1H), 1.75 (q, J = 13.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.1, 142.2, 134.7, 126.8(q, J_{C-F}= 277.8 Hz) 122.5, 122.3, 119.1, 109.1, 42.4, 37.1 (q, J_{C-F}= 28.3 Hz), 31.4 (q, J_{C-F}= 2.9 Hz), 26.7, 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{13}F_3N_2$ $[M+H]^+$ 255.1104, found 255.1094.

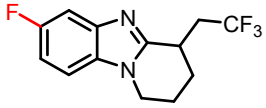
(R)-7-methyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3b)



White solid; 60% yield; m.p.= 129.9-132.6 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.50 (s, 1H), 7.18 (d, J = 8.2 Hz, 1H), 7.08 (dd, J = 8.2, 1.4 Hz, 1 H), 4.25 – 4.14 (m, 1H), 3.94 (td, J = 11.6, 5.0 Hz, 1H), 3.54 – 3.38 (m, 2H), 2.47 (s, 4H), 2.38 – 2.22 (m, 2H), 2.13 – 2.02 (m, 1H), 1.79 – 1.65 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.0, 142.6, 132.8, 132.2, 126.9 (q, J_{C-F}= 278.8 Hz), 123.7, 118.9, 108.5, 42.3, 37.1 (q, J_{C-F}= 28.1 Hz), 31.4 (q, J_{C-F}= 2.9 Hz), 26.6 , 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{14}H_{16}F_3N_2$ $[M+H]^+$ 269.1260, found 269.1258.

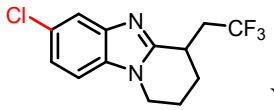
(R)-7-fluoro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3c)



Yellow solid; 68% yield; m.p.= 108.5-110.3 ℃. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.37 (dd, J = 9.4, 2.4 Hz, 1H), 7.20 (dd, J = 8.7, 4.5 Hz, 1H), 7.00 (td, J = 9.1, 2.4 Hz, 1H), 4.23 – 4.17 (m, 1H), 3.96 (td, J = 11.5, 5.0 Hz, 1H), 3.49 – 3.36 (m, 2H), 2.46 (dd, J = 11.0, 5.4 Hz, 1H), 2.37 – 2.24 (m, 2H), 2.13 – 2.05 (m, 1H), 1.78 – 1.68 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 159.5 (d, J_{C-F}= 237.2 Hz), 153.6, 142.7 (d, J_{C-F}= 12.6 Hz), 131.3, 126.7 (q, J_{C-F}= 277.1 Hz), 110.5 (d, J_{C-F}= 26.0 Hz), 109.3 (d, J_{C-F}= 10.3 Hz), 105.0 (d, J_{C-F}= 24.3 Hz), 42.5, 37.0 (q, J_{C-F}= 28.3 Hz), 31.4 (q, J_{C-F}= 2.9 Hz), 26.4 , 21.5. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -63.5(s, 3F), -120.6(s, 1F).

HRMS-ESI (m/z): calcd for $C_{13}H_{13}F_4N_2$ $[M+H]^+$ 273.1009, found 273.1004.

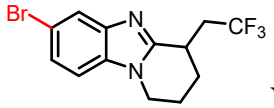
(R)-7-chloro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3d)



Yellow solid; 72% yield; m.p.= 113.4-115.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.68 (s, 1H), 7.20 (s, 2H), 4.26 – 4.15 (m, 1H), 3.96 (td, *J* = 11.6, 4.9 Hz, 1H), 3.51 – 3.34 (m, 2H), 2.52 – 2.42 (m, 1H), 2.32 (ddd, *J* = 19.8, 9.6, 3.7 Hz, 2H), 2.16 – 2.04 (m, 1H), 1.73 (q, *J* = 13.1, 12.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.4, 143.1, 133.4 128.0, 126.7 (q, $J_{C\text{-}F}$= 277.8 Hz), 122.7, 118.9, 109.8, 42.5, 37.0 (q, $J_{C\text{-}F}$= 28.4 Hz), 31.43 (q, $J_{C\text{-}F}$= 2.5 Hz), 26.43, 21.50. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}ClF_3N_2$ $[M+H]^+$ 288.0641, found 288.0845.

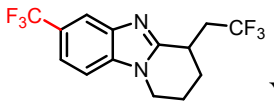
(R)-7-bromo-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3e)



Yellow solid; 65% yield; m.p.= 100.1-102.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.83 (s, 1H), 7.34 (d, *J* = 8.6 Hz, 1H), 7.15 (d, *J* = 8.5 Hz, 1H), 4.24 – 4.15 (m, 1H), 3.95 (td, *J* = 11.6, 5.0 Hz, 1H), 3.48 – 3.35 (m, 2H), 2.51 – 2.43 (m, 1H), 2.38 – 2.26 (m, 2H), 2.16 – 2.03 (m, 1H), 1.73 (q, *J* = 11.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.3, 143.7, 133.7, 126.6 (q, $J_{C\text{-}F}$= 278.8 Hz), 125.3, 120.0, 115.4, 110.2, 42.5, 37.0 (q, $J_{C\text{-}F}$= 28.5 Hz), 31.4 (q, $J_{C\text{-}F}$= 2.5 Hz), 26.4, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}BrF_3N_2$ $[M+H]^+$ 333.0209, found 333.0205.

(R)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3f)

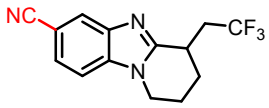


Yellow solid; 59% yield; m.p.= 113.4-115.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.51 (d, *J* = 8.5 Hz, 1H), 7.38 (d, *J* = 8.4 Hz, 1H), 4.33 –

4.21 (m, 1H), 4.01 (td, J = 11.6, 5.0 Hz, 1H), 3.54 – 3.37 (m, 2H), 2.57 – 2.44 (m, 1H), 2.46 – 2.27 (m, 2H), 2.20 – 2.05 (m, 1H), 1.82 – 1.71 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.3, 141.8, 136.7, 127.7 (q, J_{C-F}= 276.3 Hz), 125.7 (d, J = 6.3 Hz), 125.1 (q, J = 32.3 Hz), 119.3 (q, J = 3.6 Hz), 116.8 (q, J = 4.2 Hz), 109.5, 42.9, 37.0 (q, J_{C-F}= 28.5 Hz), 31.6 (d, J_{C-F}= 2.1 Hz), 26.5, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -60.7 (s, 3F), -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{14}H_{12}F_6N_2$ $[M+H]^+$ 322.0905, found 322.0909.

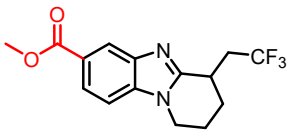
(R)-4-(2,2,2-trifluoroethyl)-7-(trifluoromethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3g)



Brown solid; 43% yield; m.p.= 154.5-155.8 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.99 (s, 1H), 7.50 (d, J = 8.3 Hz, 1H), 7.38 (d, J = 8.3 Hz, 1H), 4.33 – 4.25 (m, 1H), 4.03 (td, J = 11.6, 5.0 Hz, 1H), 3.51 – 3.39 (m, 2H), 2.55 – 2.47 (m, 1H), 2.43 – 2.31 (m, 2H), 2.19 – 2.08 (m, 1H), 1.78 (q, J = 13.3 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.0, 142.0, 137.5, 126.6 (q, J_{C-F}= 277.8 Hz), 125.8, 124.1, 119.8, 110.1, 105.6, 42.7, 36.9 (q, J_{C-F}= 28.6 Hz), 31.6 (q, J_{C-F}= 2.9 Hz), 26.4, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{14}H_{12}F_3N_3$ $[M+H]^+$ 280.1056, found 280.1050.

(R)-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine-7-carbonitrile (3h)

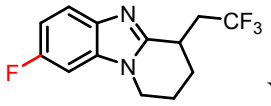


Yellow oil; 34% yield. **^{1}H NMR** (400 MHz, DMSO-d_6) δ 8.20 (d, J = 1.5 Hz, 1H), 7.89 (dd, J = 8.4, 1.6 Hz, 1H), 7.61 (d, J = 8.5 Hz, 1H), 4.38 – 4.28 (m, 1H), 4.00 (td, J = 11.6, 4.7 Hz, 1H), 3.87 (s, 3H), 3.36 – 3.22 (m, 2H), 2.76 – 2.62 (m, 1H), 2.31 – 2.16 (m, 2H), 2.12 – 2.02 (m, 1H), 1.86 – 1.76 (m, 1H).**^{13}C NMR** (101 MHz, DMSO-d_6) δ 166.8, 154.8, 141.3, 138.0, 127.3 (q, J_{C-F}= 278.8 Hz), 123.5, 123.0, 119.8, 110.1, 52.0, 42.4, 36.0 (q, J_{C-F}= 27.2 Hz), 30.7 (d, J_{C-F}= 3.3 Hz), 25.8, 20.7. **^{19}F**

NMR (376 MHz, DMSO-d_6) δ -62.0 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{15}H_{16}F_3N_2O_2$ $[M+H]^+$ 313.1158, found 313.1156.

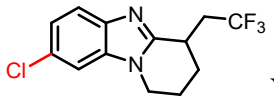
(R)-8-fluoro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3j)



Yellow solid; 63% yield; m.p.= 103.5-105.2 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.65 – 7.59 (m, 1H), 7.04 – 6.94 (m, 2H), 4.20 – 4.12 (m, 1H), 3.97 – 3.88 (m, 1H), 3.49 – 3.34 (m, 2H), 2.52 – 2.42 (m, 1H), 2.40 – 2.26 (m, 2H), 2.14 – 2.04 (m, 1H), 1.79 – 1.68 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.4 (d, J = 239.5 Hz), 152.9 (d, J = 2.9 Hz), 138.6, 134.8 (d, J = 13.0 Hz), 127.0 (q, $J_{C\text{-}F}$= 277.2 Hz), 119.8 (d, J = 10.0 Hz), 110.7 (d, J = 24.9 Hz), 95.90 (d, J = 27.4 Hz), 42.5, 37.0 (q, $J_{C\text{-}F}$= 28.3 Hz), 31.49 (q, $J_{C\text{-}F}$= 2.9 Hz), 26.6, 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5(s, 3F), -119.2(s, 1F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}F_4N_2$ $[M+H]^+$272.0937, found 272.0943.

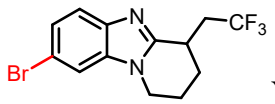
(R)-8-chloro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3k)



Yellow solid; 78% yield; m.p.= 98.2-101.6 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.61 (d, J = 8.6 Hz, 1H), 7.29 (s, 1H), 7.22 (d, J = 8.6 Hz, 1H), 4.22 – 4.13 (m, 1H), 3.94 (td, J = 11.6, 4.5 Hz, 1H), 3.52 – 3.34 (m, 2H), 2.51 – 2.43 (m, 1H), 2.40 – 2.26 (m,2H), 2.15 – 2.04 (m, 1H), 1.74 (q, J = 13.4, 12.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.1, 141.0, 135.4, 128.1 (d, J = 3.2 Hz), 126.7 (q, $J_{C\text{-}F}$= 276.3 Hz), 123.1 (d, J = 3.2 Hz), 120.0, 109.3, 42.5, 37.0 (q, $J_{C\text{-}F}$= 28.4 Hz), 31.50 (d, $J_{C\text{-}F}$= 2.9 Hz), 26.5, 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{13}ClF_3N_2$ $[M+H]^+$289.0714, found 289.0722.

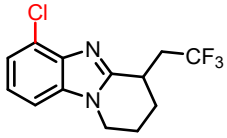
(R)-8-bromo-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3l)



Yellow solid; 59% yield; m.p.= 101.3-103.4 °C. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.56 (d, *J* = 8.5 Hz, 1H), 7.44 (d, *J* = 1.8 Hz, 1H), 7.36 (dd, *J* = 8.5, 1.8 Hz, 1H), 4.27 – 4.09 (m, 1H), 3.93 (td, *J* = 11.5, 5.0 Hz, 1H), 3.51 – 3.32 (m, 2H), 2.51 – 2.43 (m, 1H), 2.40 – 2.25 (m, 2H), 2.14 – 2.02 (m, 1H), 1.73 (q, *J* = 13.3, 12.0 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.0, 141.4, 135.9, 126.7 (q, $J_{C\text{-}F}$= 276.3 Hz), 125.7 (d, *J* = 2.0 Hz), 120.4, 115.5, 112.3, 42.5, 37.0 (q, $J_{C\text{-}F}$= 28.3 Hz), 31.5 (q, $J_{C\text{-}F}$= 2.9 Hz), 26.5, 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}BrF_3N_2$ $[M+H]^+$332.0136, found 332.0132.

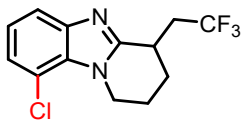
(R)-6-chloro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3m)



Yellow oil; 57% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.30 – 7.12 (m, 3H), 4.26 – 4.15 (m, 1H), 3.97 (td, *J* = 11.4, 5.0 Hz, 1H), 3.62 – 3.40 (m,2H), 2.52 – 2.40 (m, 1H), 2.39 – 2.25 (m, 2H), 2.16 – 2.02 (m, 1H), 1.82 – 1.67 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.9, 139.7, 135.8, 128.8, 126.7 (q, $J_{C\text{-}F}$= 277.8 Hz), 122.8, 122.4, 107.8, 42.7, 37.0 (q, $J_{C\text{-}F}$= 28.3 Hz), 31.4 (q, $J_{C\text{-}F}$= 2.9 Hz), 26.3, 21.3. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.2 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{13}ClF_3N_2$ $[M+H]^+$289.0714, found 289.0712.

(R)-9-chloro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3n)

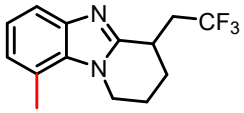


Yellow solid; 64% yield; m.p.= 149.1-150.8 °C. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.58 (dd, *J* = 7.8, 1.2 Hz, 1H), 7.19 – 7.09 (m, 2H), 4.88 (ddd, *J* = 12.5, 5.9, 2.8 Hz, 1H), 4.32 (td, J = 11.9, 5.0 Hz, 1H), 3.50 – 3.35 (m, 2H), 2.42 (d, *J* = 14.7 Hz, 1H), 2.39 – 2.23 (m, 2H), 2.05 (td, *J* = 17.0, 11.8 Hz, 0H), 1.70 (tdd, *J* = 13.2, 10.8, 2.7 Hz, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.3, 144.4, 131.2, 126.7 (q, $J_{C\text{-}F}$= 276.3

Hz), 123.7, 122.9, 118.0, 116.2, 45.5, 37.3 (q, J_{C-F}= 28.3 Hz), 31.9 (q, J_{C-F}= 2.9 Hz), 26.0, 22.1. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{13}ClF_3N_2$ $[M+H]^+$289.0714, found 289.0710.

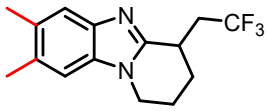
(R)-9-methyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3o)



White solid; 74% yield; m.p.= 127.3-129.6 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.54 (d, *J* = 8.1 Hz, 1H), 7.11 (t, *J* = 7.7 Hz, 1H), 6.95 (d, *J* = 7.9 Hz, 1H), 4.70 – 4.60 (m, 1H), 4.29 (td, *J* = 11.5, 5.0 Hz, 1H), 3.56 – 3.35 (m, 2H), 2.70(s, 3H), 2.42 – 2.24 (m, 3H), 2.13 – 2.00 (m, 1H), 1.76 – 1.61 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.0, 142.5, 133.6, 126.79 (q, J_{C-F}= 277.8 Hz), 124.8, 122.3, 121.3, 117.1, 45.4, 37.3 (q, J_{C-F}= 28.1 Hz), 31.7 (q, J_{C-F}= 2.7 Hz), 26.1, 22.3, 18.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{14}H_{16}F_3N_2$ $[M+H]^+$269.1260, found 269.1253.

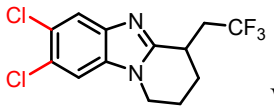
(R)-7,8-dimethyl-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3p)



White solid; 60% yield; m.p.= 168.3-170.7 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (s, 1H), 7.06 (s, 1H), 4.23 – 4.10 (m, 1H), 3.90 (td, *J* = 11.6, 4.7 Hz, 1H), 3.56 – 3.29 (m, 2H), 2.47 – 2.40 (m, 1H), 2.37 (d, *J* = 6.5 Hz, 6H), 2.31 – 2.21 (m, 2H), 2.11 – 2.00 (m, 1H), 1.69 (q, *J* = 12.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.2, 140.9, 133.3, 131.3 (d, *J* = 17.2 Hz), 126.8 (q, J_{C-F}= 278.8 Hz), 119.2, 109.3, 42.3, 37.1 (q, J_{C-F}= 28.1 Hz), 31.5 – 31.21 (m), 26.7, 21.6, 20.4 (d, *J* = 14.9 Hz). **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{15}H_{18}F_3N_2$ $[M+H]^+$283.1417, found 283.1424.

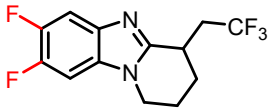
(R)-7,8-dichloro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3q)



White solid; 64% yield; m.p.= 130.9-133.4 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.76 (s, 1H), 7.38 (s, 1H), 4.22 – 4.11 (m, 1H), 3.94 (td, J = 11.6, 4.8 Hz, 1H), 3.52 – 3.31 (m, 2H), 2.53 – 2.43 (m, 1H), 2.41 – 2.27 (m, 2H), 2.18 – 2.03 (m, 1H), 1.74 (q, J = 12.7, 12.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 154.3, 141.7, 134.0, 126.4 (d, J = 10.6 Hz), 126.6 (q, J_{C-F}= 278.8 Hz), 120.3, 110.4, 42.6, 36.9 (q, J_{C-F}= 28.5 Hz), 31.5 (d, J_{C-F}= 3.0 Hz), 26.3, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}Cl_2F_3N_2$ $[M+H]^+$323.0324, found 323.0330.

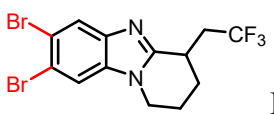
(R)-7,8-difluoro-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3r)



Yellow solid; 56% yield; m.p.= 150.1-152.0 ℃. **^{1}H NMR** δ 7.46 (dd, J = 10.5, 7.2 Hz, 1H), 7.06 (dd, J = 9.6, 6.8 Hz, 1H), 4.18 – 4.11 (m, 1H), 3.93 (td, J = 11.5, 5.0 Hz, 1H), 3.47 – 3.34 (m,2H), 2.50 – 2.44 (m, 1H), 2.39 – 2.29 (m, 2H), 2.16 – 2.04 (m, 1H), 1.79 – 1.69 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 153.7 (d, J_{C-F}= 3.0 Hz), 148.7 (dd, J_{C-F}= 15.2, 4.8 Hz), 147.1 (dd, J_{C-F}= 15.2, 2.7 Hz), 137.5 (d, J_{C-F}= 10.5 Hz), 130.0 (d, J_{C-F}= 10.7 Hz), 126.7 (q, J_{C-F}= 277.1 Hz), 106.6 (d, J_{C-F}= 19.9 Hz), 97.1 (d, J_{C-F}= 22.6 Hz), 42.6, 37.0 (q, J_{C-F}= 28.5 Hz), 31.5 (q, J_{C-F}= 2.8 Hz), 26.4, 21.5. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -63.5 (s, 3F), -142.24 (d, J = 20.4 Hz, 1F), -143.51 (d, J = 20.5 Hz, 1F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}F_5N_2$ $[M+H]^+$291.0915, found 291.0909.

(R)-7,8-dibromo-4-(2,2,2-trifluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (3s)

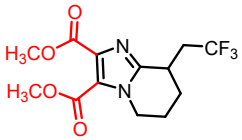


Brown solid; 62% yield; m.p.= 122.7-125.3 ℃. **^{1}H NMR** (600 MHz, $CDCl_3$) δ 7.95 (s, 1H), 7.57 (s, 1H), 4.16 (ddd, J = 11.9, 5.9, 2.6 Hz, 1H), 4.00 – 3.85 (m, 1H), 3.52 – 3.30 (m, 2H), 2.51 – 2.44 (m, 1H), 2.38 – 2.27 (m, 2H), 2.14 –

2.05 (m, 1H), 1.80 – 1.69 (m, 1H). **^{13}C NMR** (151 MHz, $CDCl_3$) δ 154.2, 142.7, 135.0, 126.6 (q, J_{C-F}= 278.8 Hz), 123.6, 117.6 (d, J = 15.4 Hz), 113.7, 42.6, 36.9 (q, J_{C-F}= 28.5 Hz), 31.5 (q, J_{C-F}= 2.6 Hz), 26.3, 21.5. **^{19}F NMR** (565 MHz, $CDCl_3$) δ -63.5 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{12}Br_2F_3N_2$ $[M+H]^+$410.9314, found 410.9315.

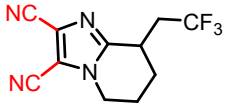
Dimethyl (R)-8-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine-2,3-dicarboxylate (4a)



Yellow liquid; 46% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.44 – 4.33 (m, 1H), 4.11 – 3.99 (m, 1H), 3.92 (d, J = 5.9 Hz, 6H), 3.42 – 3.21 (m, 2H), 2.42 – 2.32 (m, 1H), 2.30 – 2.14 (m, 2H), 2.05 – 1.91 (m, 1H), 1.74 – 1.63 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 163.1, 160.4, 148.4, 136.0, 126.5 (q, J_{C-F}= 278.8 Hz), 124.4, 52.4 (d, J = 6.1 Hz), 45.5, 37.1 (q, J_{C-F}= 28.3 Hz), 31.0 (q, J_{C-F}= 2.8 Hz), 25.6, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{13}H_{16}F_3N_2O_2$ $[M+H]^+$321.1057, found 321.1051.

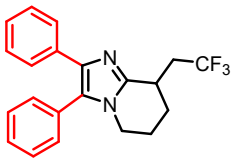
(R)-8-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine-2,3-dicarbonitrile (4b)



Yellow liquid; 56% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 4.32 – 4.21 (m, 1H), 4.04 (td, J = 12.1, 4.9 Hz, 1H), 3.32 – 3.16 (m, 2H), 2.52 – 2.40 (m, 1H), 2.38 – 2.25 (m, 2H), 2.16 – 2.00 (m, 1H), 1.80 – 1.65 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.16 , 126.11 (q, J_{C-F}= 278.8 Hz), 121.68 , 111.64 (d, J = 2.3 Hz), 107.84, 45.28, 36.47 (q, J_{C-F}= 29.0 Hz), 31.12 (q, J_{C-F}= 2.9 Hz), 25.62, 21.05. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{11}H_{10}F_3N_4$ $[M+H]^+$255.0852, found 255.0850.

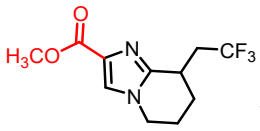
(R)-2,3-diphenyl-8-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine (4c)



Yellow liquid; 62% yield; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.51 – 7.37 (m, 5H), 7.36 – 7.29 (m, 2H), 7.19 (t, *J* = 7.4 Hz, 2H), 7.13 (dd, *J* = 8.4, 6.1 Hz, 1H), 3.74 (ddd, *J* = 9.0, 7.2, 3.3 Hz, 1H), 3.65 (td, *J* = 12.6, 11.7, 4.7 Hz, 1H), 3.57 – 3.45 (m, 1H), 3.42 – 3.29 (m, 1H), 2.44 – 2.25 (m, 2H), 2.14 – 2.02 (m, 1H), 1.99 – 1.85 (m, 1H), 1.69 (q, *J* = 10.2 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.0, 136.7 134.2, 130.6, 128.9, 128.5, 128.1, 127.9, 126.9, (q, $J_{C\text{-}F}$= 277.8 Hz), 126.8, 126.4, 43.8, 37.5 (q, $J_{C\text{-}F}$= 27.8 Hz), 30.9 (d, $J_{C\text{-}F}$= 2.9 Hz), 26.6, 21.9. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.2 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{21}H_{20}F_3N_2$ $[M+H]^+$357.1573, found 357.1569.

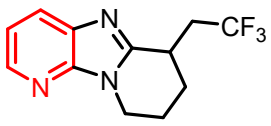
methyl (R)-8-(2,2,2-trifluoroethyl)-5,6,7,8-tetrahydroimidazo[1,2-a]pyridine-2-carboxylate (4d)



Yellow liquid; 40% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.69 (s, 1H), 4.56 (ddd, *J* = 13.9, 5.7, 3.1 Hz, 1H), 4.12 – 4.00 (m,1H), 3.84 (s, 3H), 3.37 – 3.18 (m, 2H), 2.37 – 2.13 (m, 3H), 2.03 – 1.88 (m, 1H), 1.65 (q, *J* = 10.1 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 160.7, 150.3, 136.3, 126.6 (q, $J_{C\text{-}F}$= 278.8 Hz), 122.4, 51.3, 45.1, 37.1 (q, $J_{C\text{-}}$= 28.2 Hz), 31.1 (q, $J_{C\text{-}F}$= 2.8 Hz), 25.8, 21.7. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.6 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{11}H_{13}F_3N_2O_2$ $[M+H]^+$263.1002, found 263.1006.

(R)-6-(2,2,2-trifluoroethyl)-6,7,8,9-tetrahydroimidazo[1,2-a:5,4-b']dipyridine (4e)

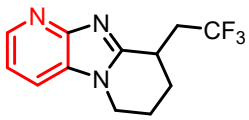


Yellow solid; 51% yield; m.p.= 124.6-125.9 °C. **^{1}H NMR** (400

MHz, $CDCl_3$) δ 8.35 (dd, *J* = 4.8, 1.4 Hz, 1H), 7.98 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.23 (dd, *J* = 8.0, 4.8 Hz, 1H), 4.54 – 4.44 (m, 1H), 4.10 – 3.98 (m, 1H), 3.53 – 3.37 (m, 2H), 2.51 (dt, *J* = 8.1, 4.0 Hz, 1H), 2.43 – 2.28 (m, 2H), 2.17 – 2.00 (m, 1H), 1.85 – 1.70 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.6, 147.7, 143.5, 134.6, 126.7 (q, J_{C-F}= 277.8 Hz), 126.6, 118.6, 41.5, 36.9 (q, J_{C-F}= 28.5 Hz), 31.7 (q, J_{C-F}= 2.7 Hz), 26.6, 21.5. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{12}H_{13}F_3N_3$ $[M+H]^+$256.1056, found 256.1047.

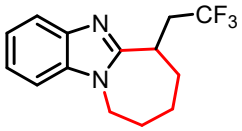
(R)-9-(2,2,2-trifluoroethyl)-6,7,8,9-tetrahydroimidazo[1,2-a:4,5-b']dipyridine (4f)



White solid; 58% yield; m.p.= 128.7-130.8 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.48 (dd, *J* = 4.9, 1.5 Hz, 1H), 7.58 (dd, *J* = 8.0, 1.5 Hz, 1H), 7.15 (dd, *J* = 8.0, 4.8 Hz, 1H), 4.27 – 4.17 (m, 1H), 3.98 (td, *J* = 11.6, 5.0 Hz, 1H), 3.60 – 3.48 (m, 1H), 3.48 – 3.35 (m, 1H), 2.54 – 2.42 (m, 1H), 2.42 – 2.26 (m, 2H), 2.20 – 2.05 (m, 1H), 1.82 – 1.67 (m, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.2, 154.7, 144.7, 126.9, 126.7 (q, J_{C-F}= 277.8 Hz), 117.3, 117.0, 42.3, 36.8 (q, J_{C-F}= 28.3 Hz), 31.5 (q, J_{C-F}= 2.9 Hz), 26.3, 21.4. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.4 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{12}H_{13}F_3N_3$ $[M+H]^+$256.1056, found 256.1049.

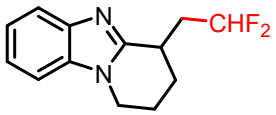
(R)-6-(2,2,2-trifluoroethyl)-7,8,9,10-tetrahydro-6H-benzo[4,5]imidazo[1,2-a]azep -ine (4g)



White solid; 45% yield; m.p.= 115.1-116.8 ℃. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.80 – 7.67 (m, 1H), 7.35 – 7.21 (m, 2H), 4.47 – 4.36 (m, 1H), 4.05 – 3.93 (m, 1H), 3.51 – 3.32 (m, 2H), 2.66 – 2.52 (m, 1H), 2.27 – 2.02 (m, 3H), 1.94 – 1.79 (m, 1H), 1.64 – 1.46 (m, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.4, 141.6, 135.6, 127.1 (q, J_{C-F}= 276.8 Hz), 122.4, 121.9, 119.4, 108.8, 44.0, 36.1 (q, J_{C-F}= 28.2 Hz), 34.2 (q, J_{C-F}= 2.6 Hz), 31.7, 29.3, 28.1. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -63.9 (s, 3F).

HRMS-ESI (m/z): calcd for $C_{14}H_{16}F_3N_2$ $[M+H]^+$269.1260, found 269.1263.

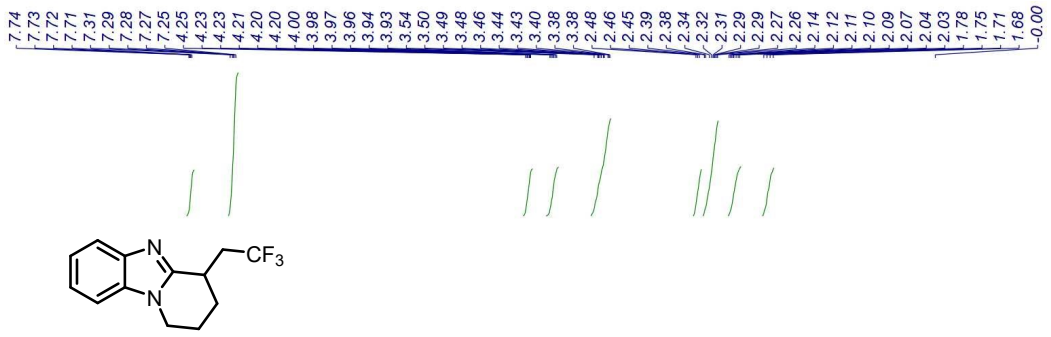
(R)-4-(2,2-difluoroethyl)-1,2,3,4-tetrahydrobenzo[4,5]imidazo[1,2-a]pyridine (4j)



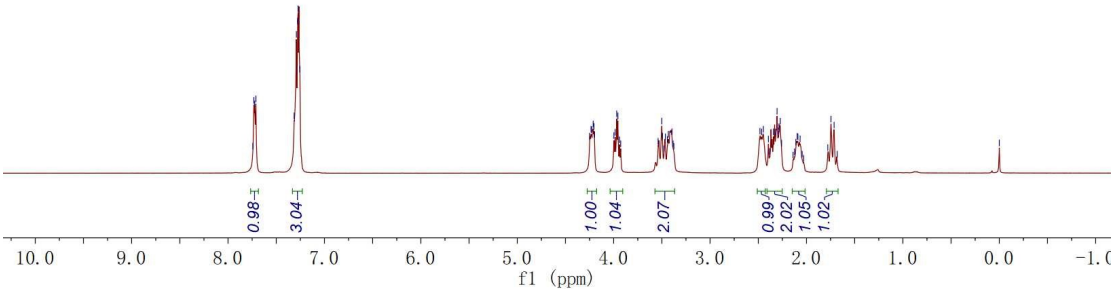
Yellow liquid; 65% yield. **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.74 – 7.67 (m, 1H), 7.31 – 7.19 (m, 3H), 6.39 (tdd, *J* = 56.8, 5.5, 3.8 Hz, 1H), 4.20 – 4.10 (m, 1H), 3.97 – 3.91 (m, 1H), 3.26 (dt, *J* = 12.2, 5.4 Hz, 1H), 2.84 – 2.63 (m, 1H), 2.33 – 1.98 (m, 4H), 1.72 (q, *J* = 10.4 Hz, 1H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.2, 142.5, 134.5, 122.1 (d, *J* = 14.3 Hz), 119.0, 116.7 (t, $J_{C\text{-}F}$= 239.4 Hz), 109.0, 42.3, 38.0 (t, $J_{C\text{-}F}$= 21.4 Hz), 31.2 (dd, *J* = 6.6, 4.8 Hz), 27.4, 21.6. **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.6 (q, 2F).

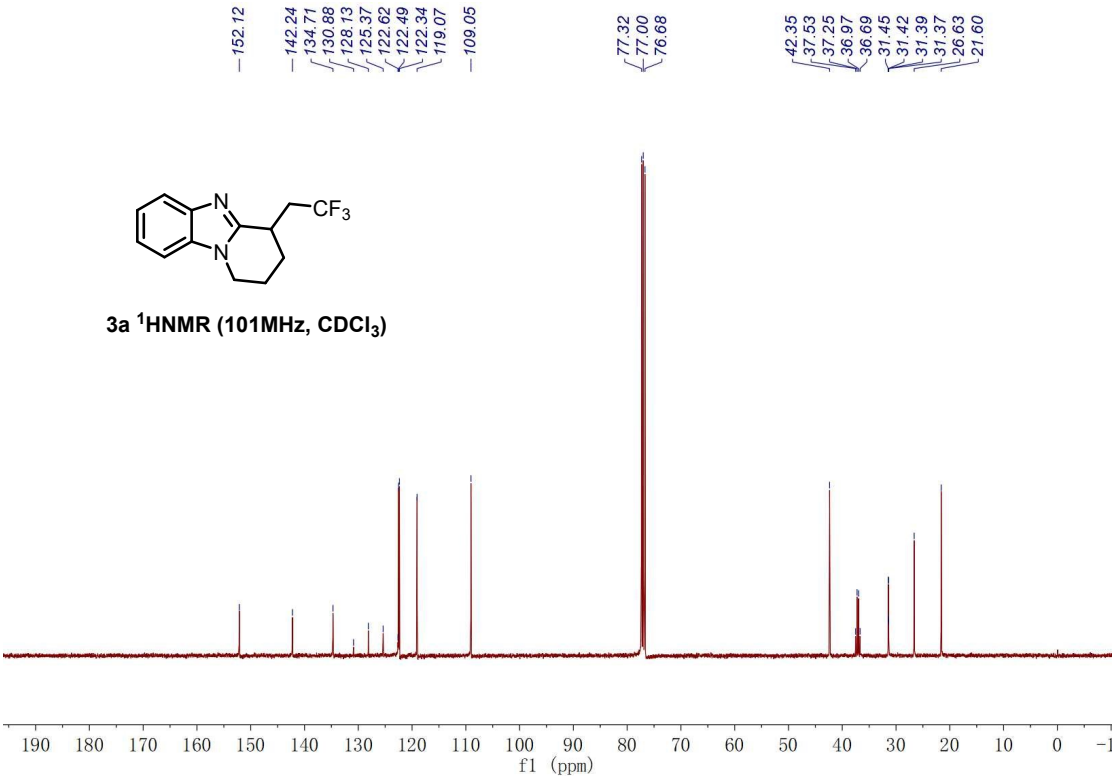
HRMS-ESI (m/z): calcd for $C_{13}H_{15}F_2N_2$ $[M+H]^+$237.1198, found 237.1198.

7. ^{1}H NMR, ^{13}C NMR and ^{19}F NMR of compounds

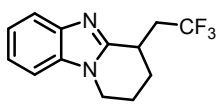


3a ^{1}HNMR (400MHz, $CDCl_3$)

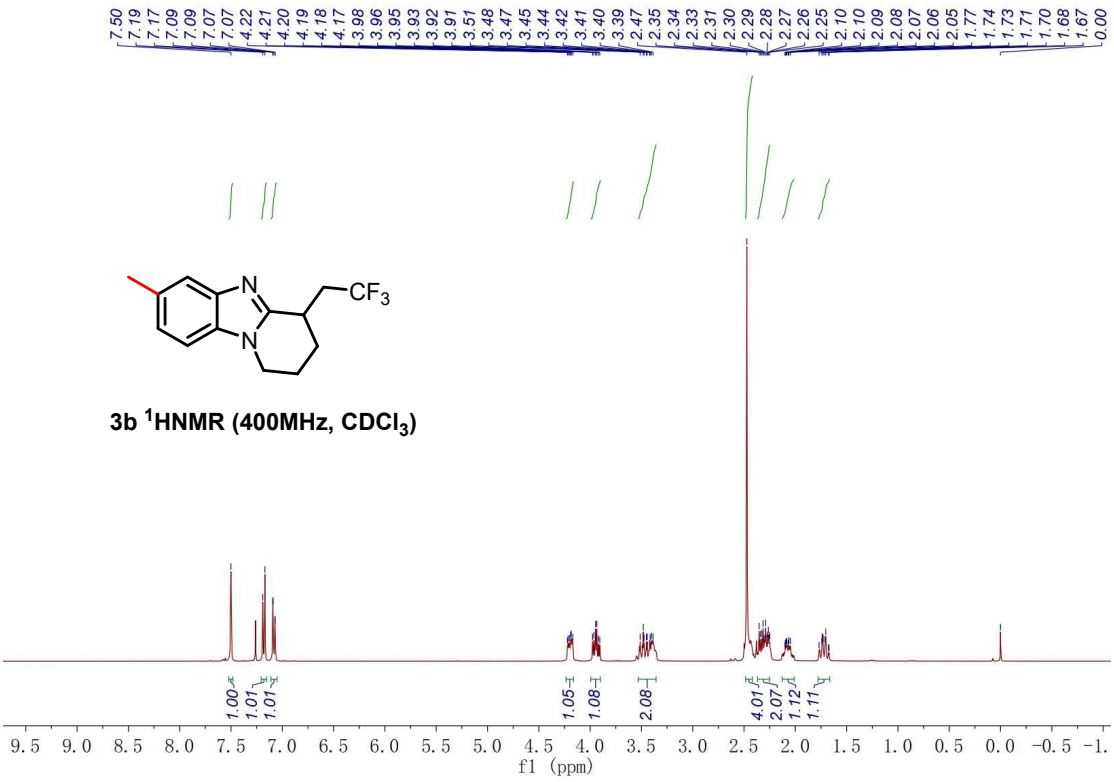




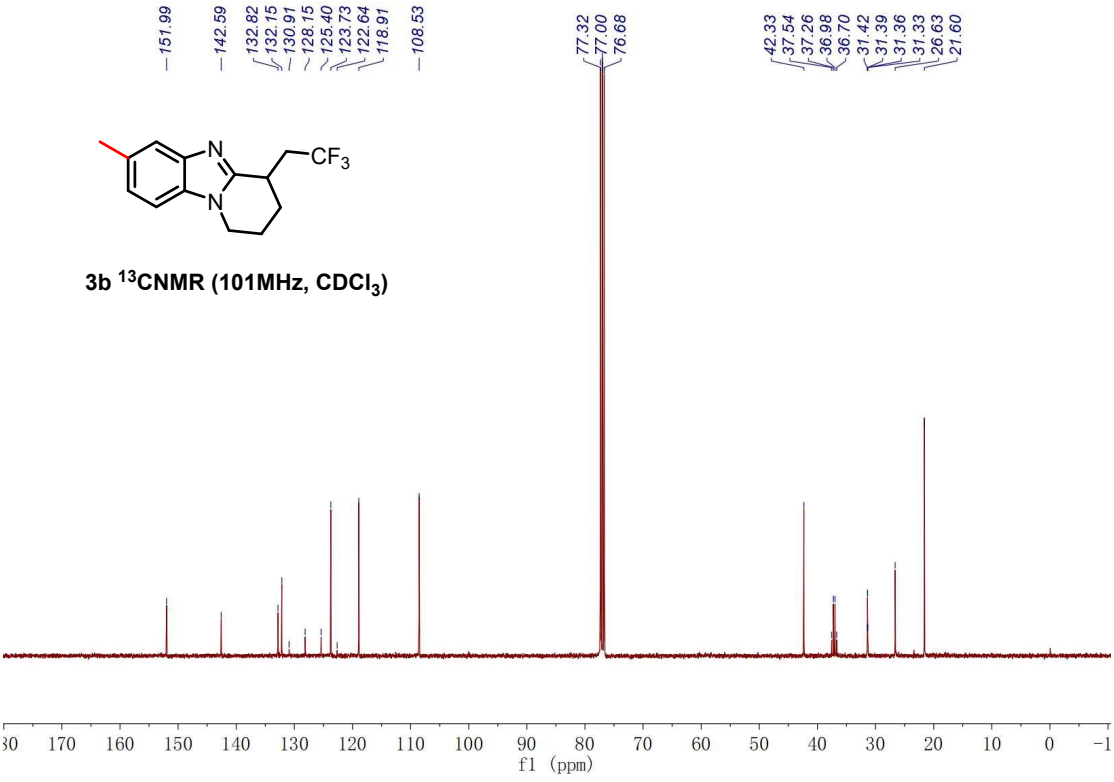
3a ^{1}HNMR (101MHz, $CDCl_3$)



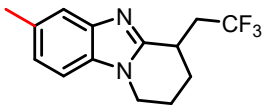
3a ^{19}FNMR (376MHz, $CDCl_3$)



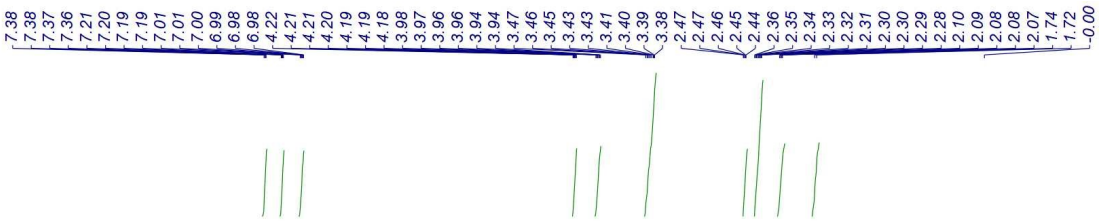
3b ^{1}HNMR (400MHz, $CDCl_3$)

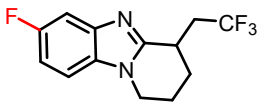


3b ^{13}CNMR (101MHz, $CDCl_3$)

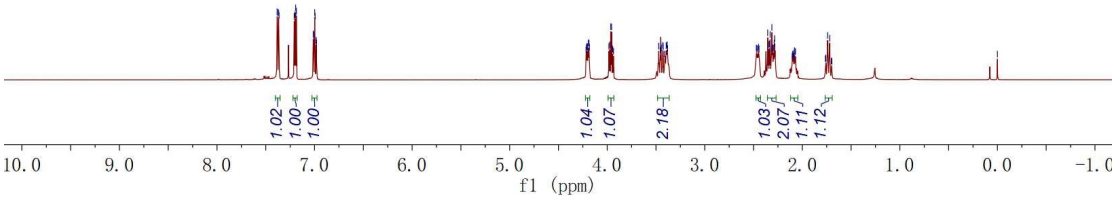


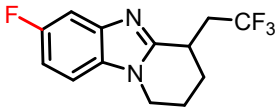
3b ^{19}FNMR (376MHz, $CDCl_3$)



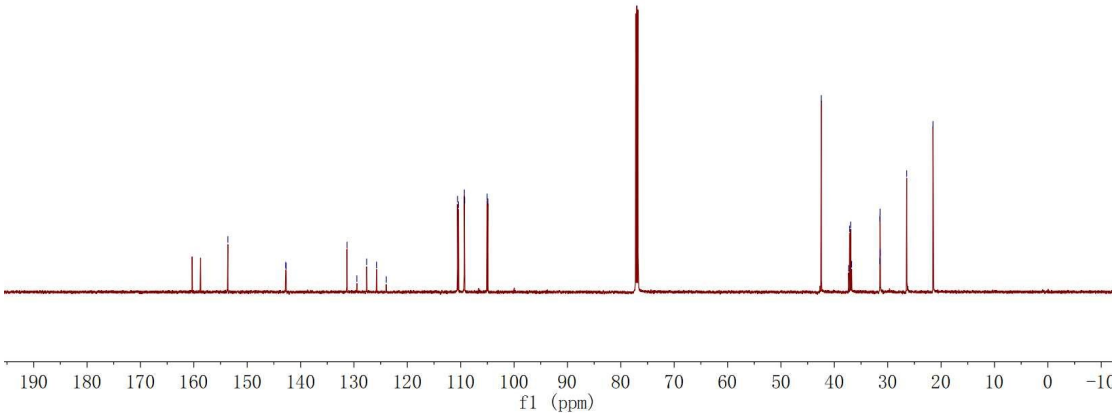


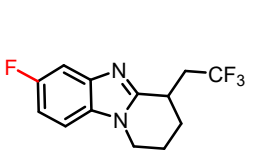
3c ^{1}HNMR (600MHz, $CDCl_3$)



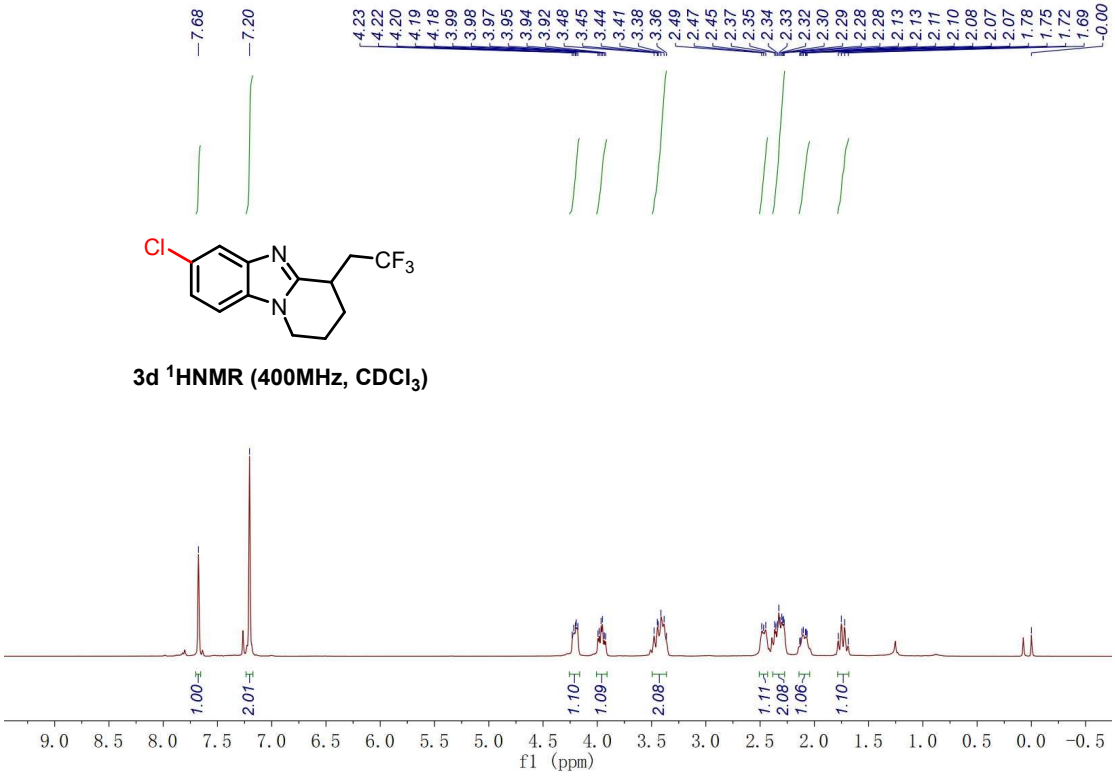


3c ^{13}CNMR (151MHz, $CDCl_3$)

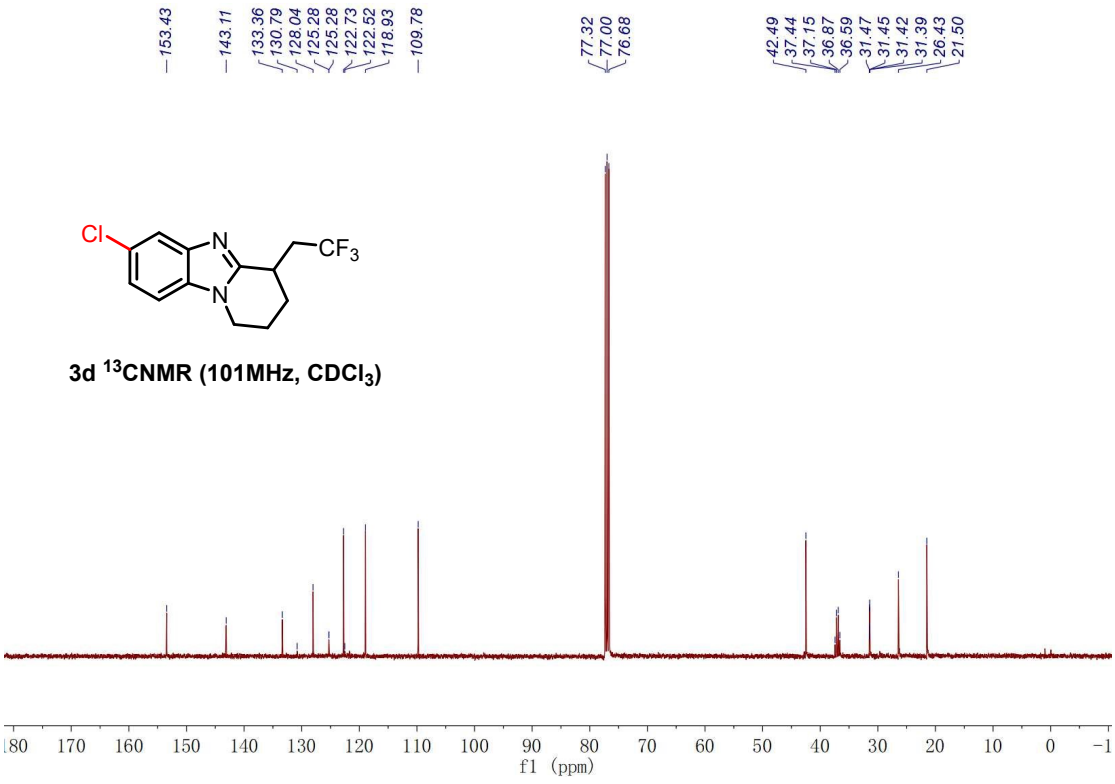




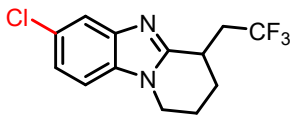
3c ^{19}FNMR (565MHz, $CDCl_3$)



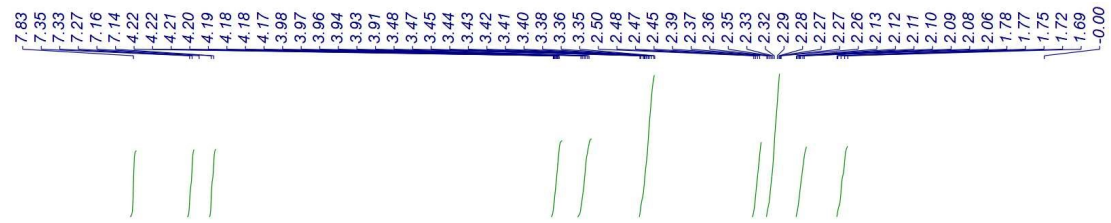
3d ^{1}HNMR (400MHz, $CDCl_3$)

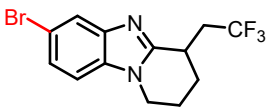


3d ^{13}CNMR (101MHz, $CDCl_3$)

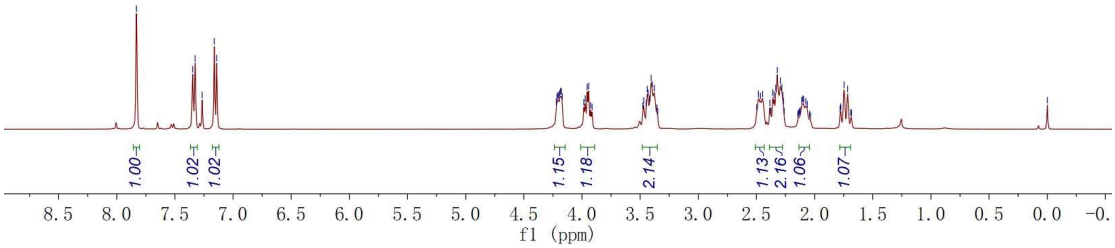


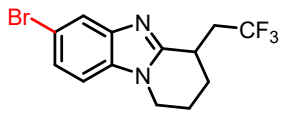
3d ^{19}FNMR (376MHz, $CDCl_3$)



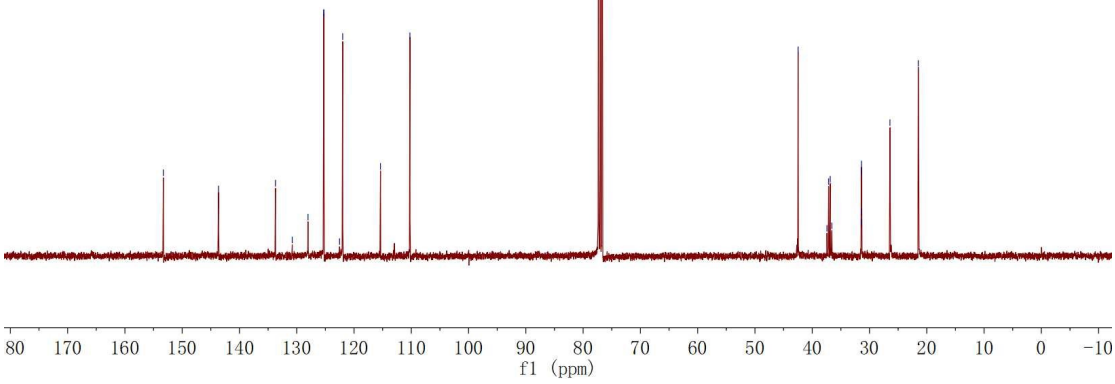


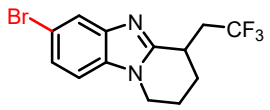
3e ^{1}HNMR (400MHz, $CDCl_3$)



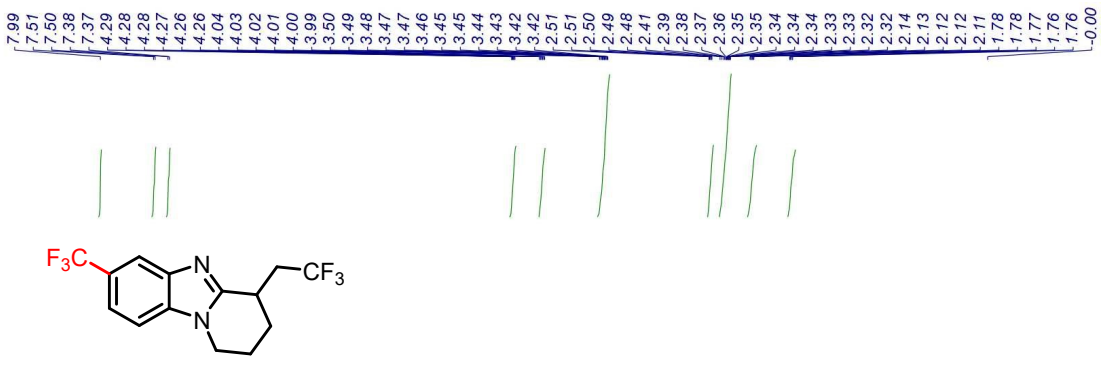


3e ^{13}CNMR (101MHz, $CDCl_3$)

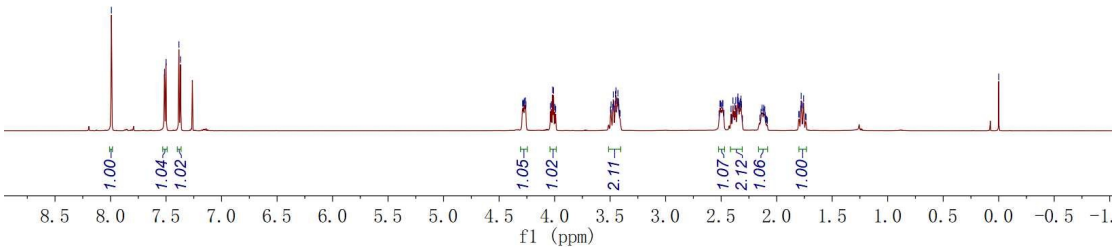


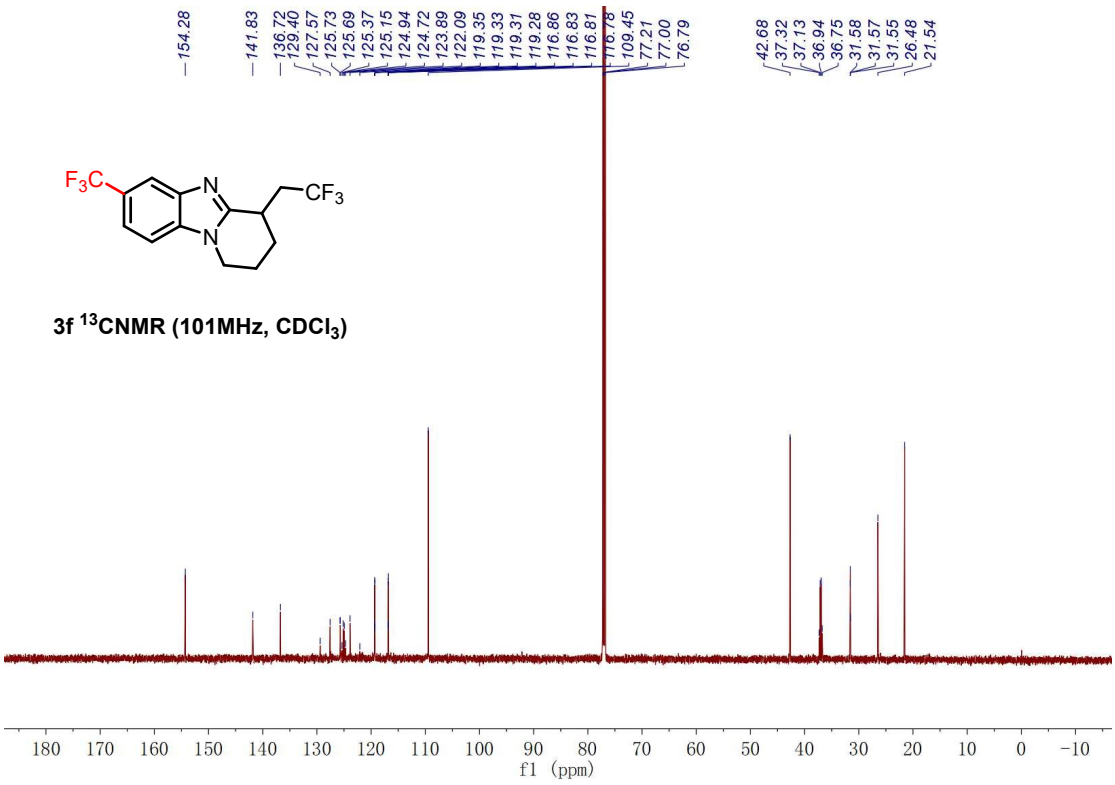


3e ^{19}FNMR (376MHz, $CDCl_3$)

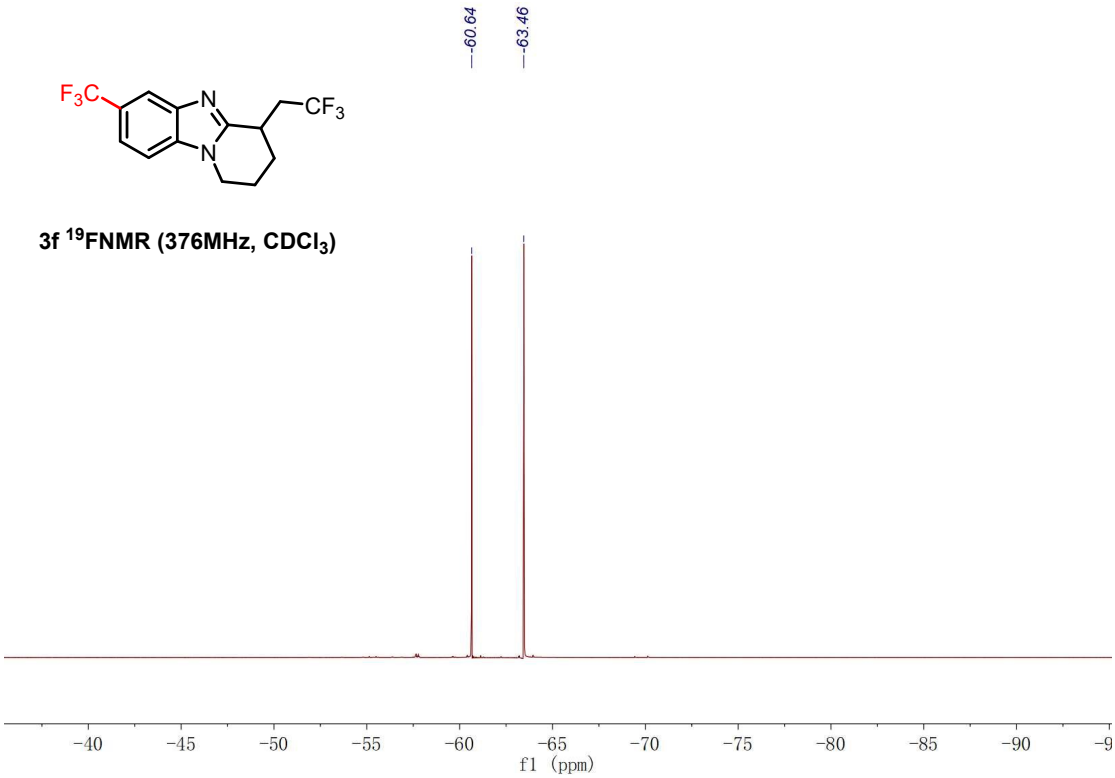


3f ^{1}HNMR (400MHz, $CDCl_3$)

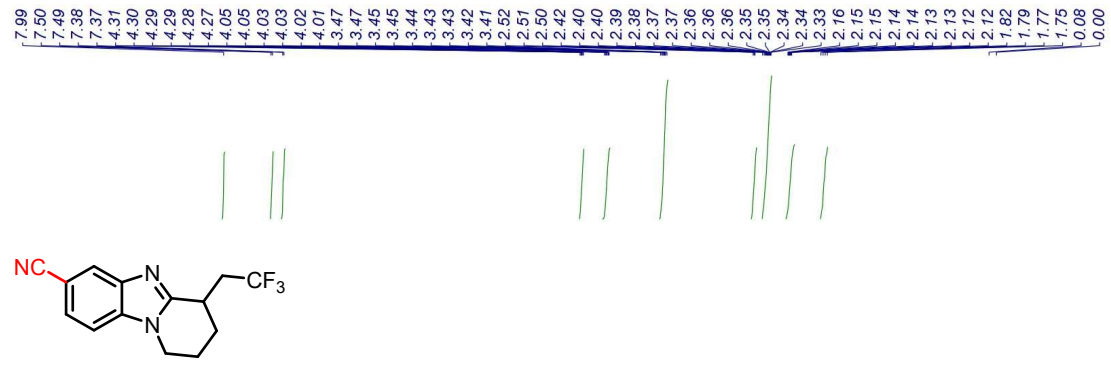




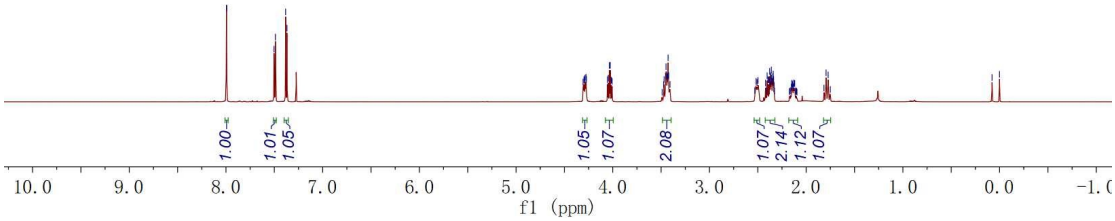
3f ^{13}CNMR (101MHz, $CDCl_3$)

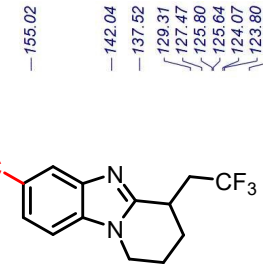


3f ^{19}FNMR (376MHz, $CDCl_3$)

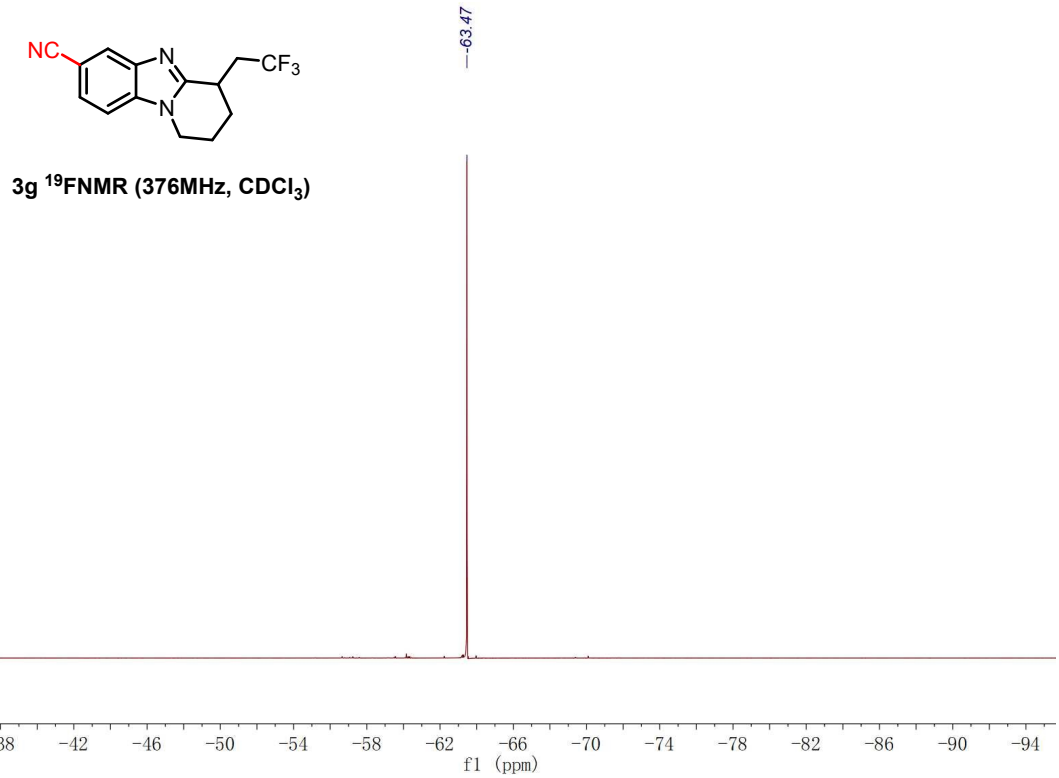


3g ^{1}HNMR (400MHz, $CDCl_3$)

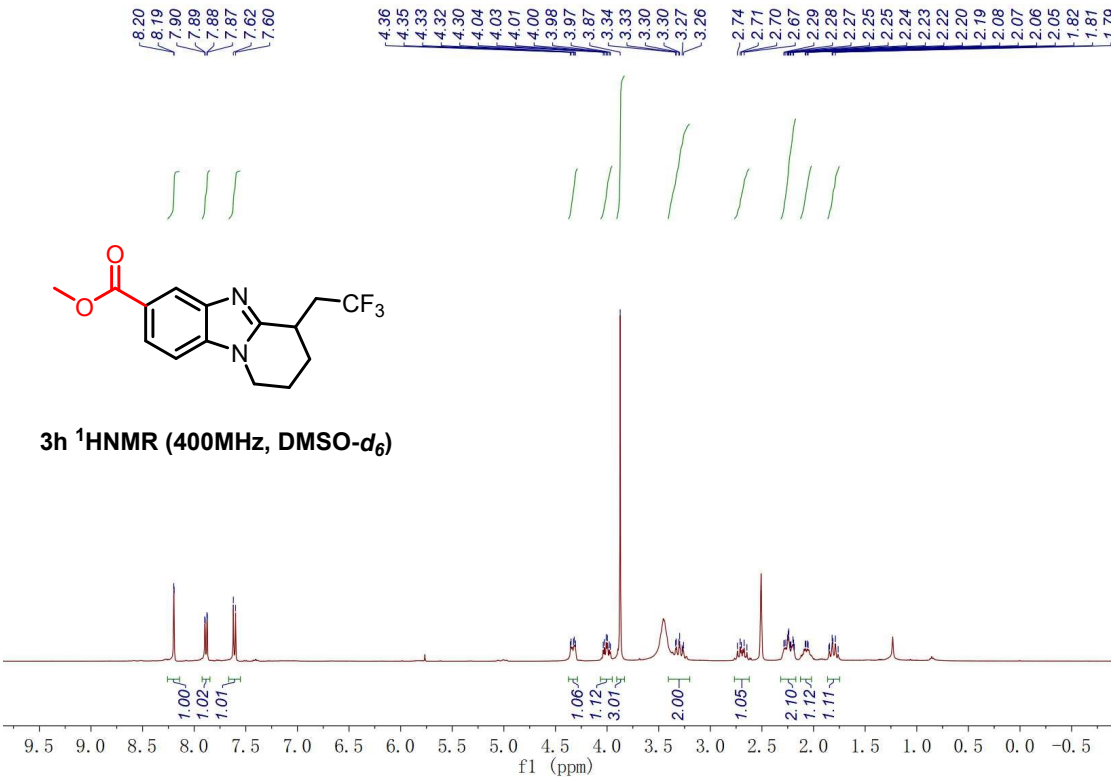




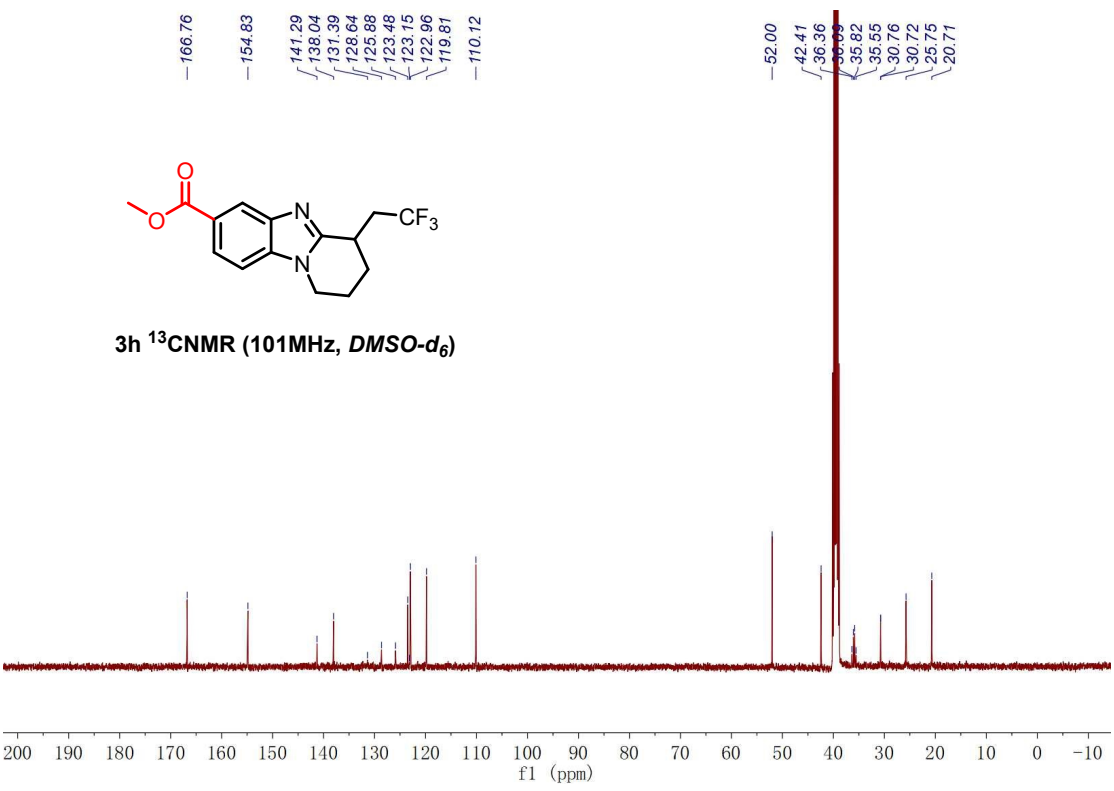
3g ^{13}CNMR (101MHz, $CDCl_3$)



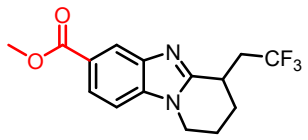
3g ^{19}FNMR (376MHz, $CDCl_3$)



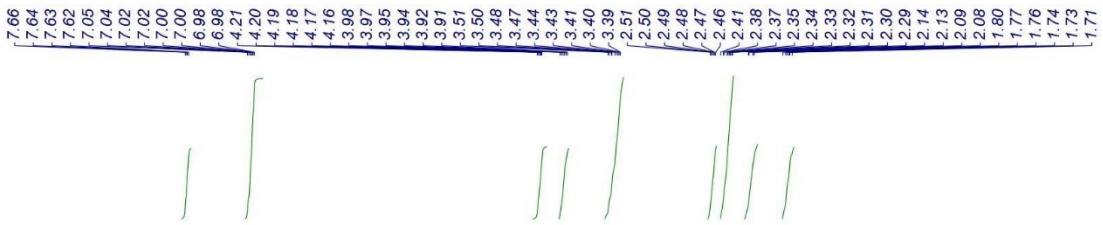
3h ^{1}HNMR (400MHz, DMSO-d_6)

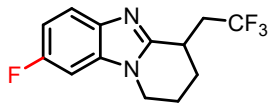


3h ^{13}CNMR (101MHz, *DMSO-d_6*)

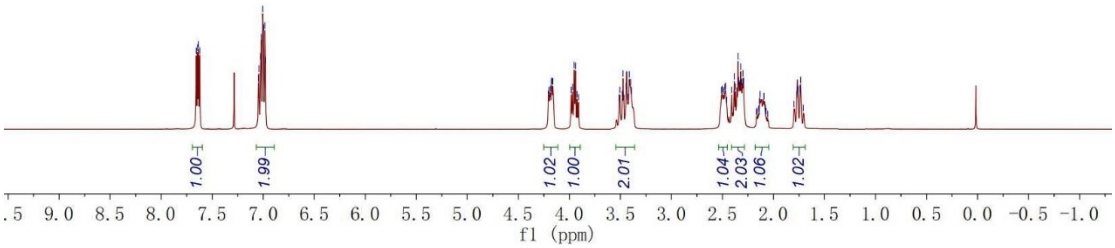


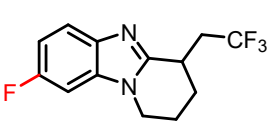
3h ^{19}FNMR (376MHz, DMSO-d_6)



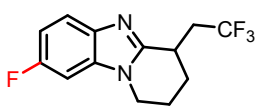


3j ^{1}HNMR (400MHz, $CDCl_3$)

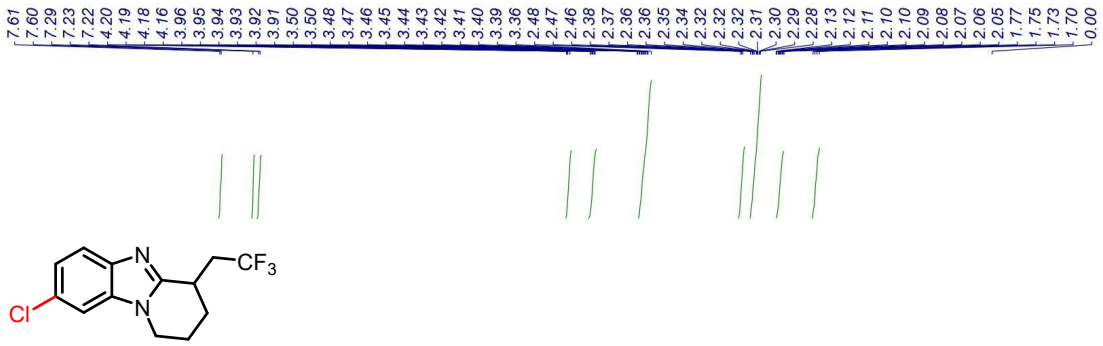




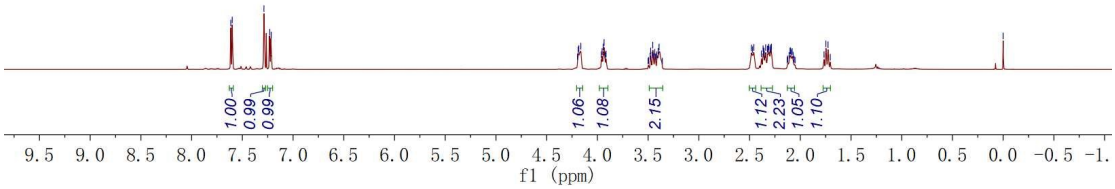
3j ^{13}CNMR (101MHz, $CDCl_3$)

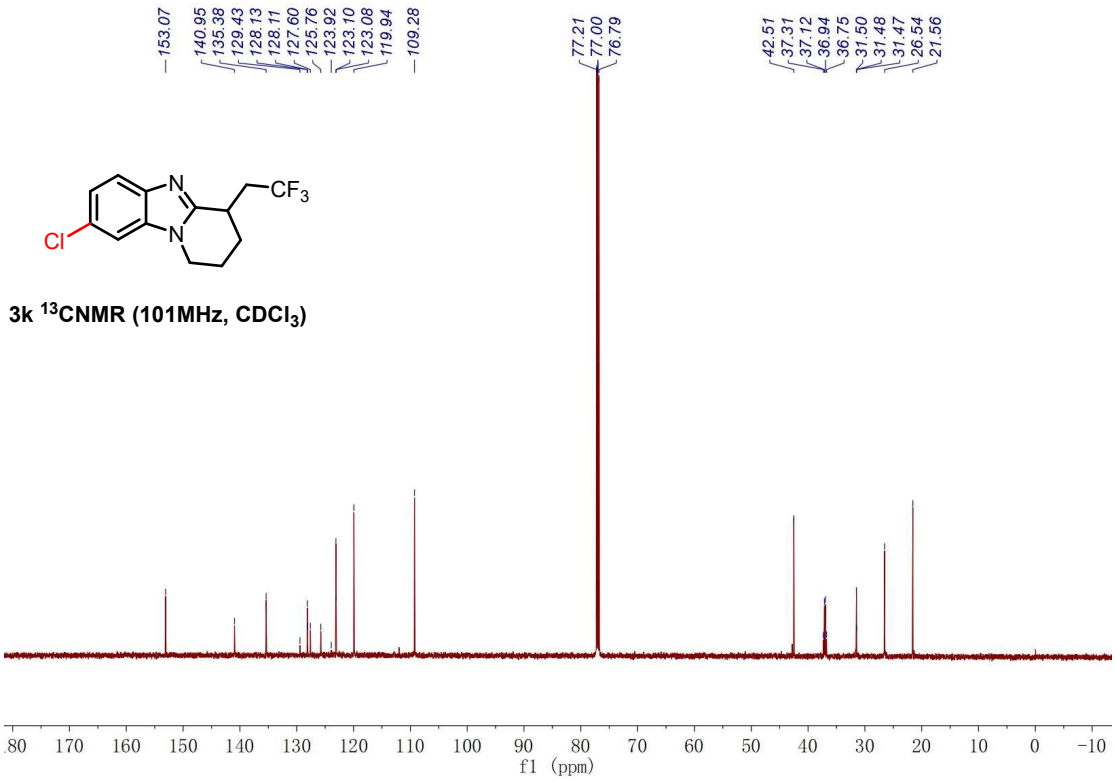


3j ^{19}FNMR (376MHz, $CDCl_3$)

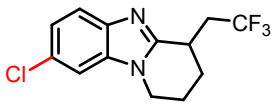


3k ^{1}HNMR (400MHz, $CDCl_3$)

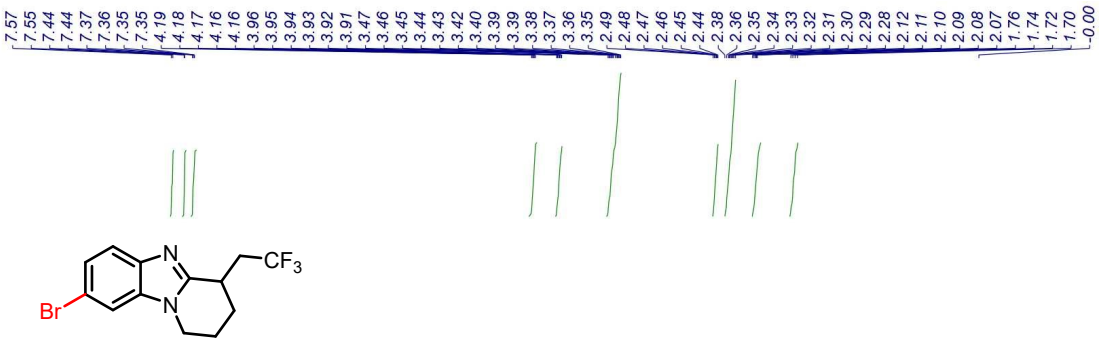




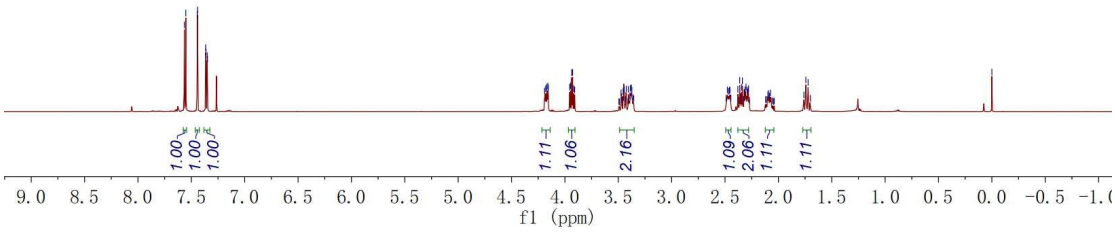
3k ^{13}CNMR (101MHz, $CDCl_3$)

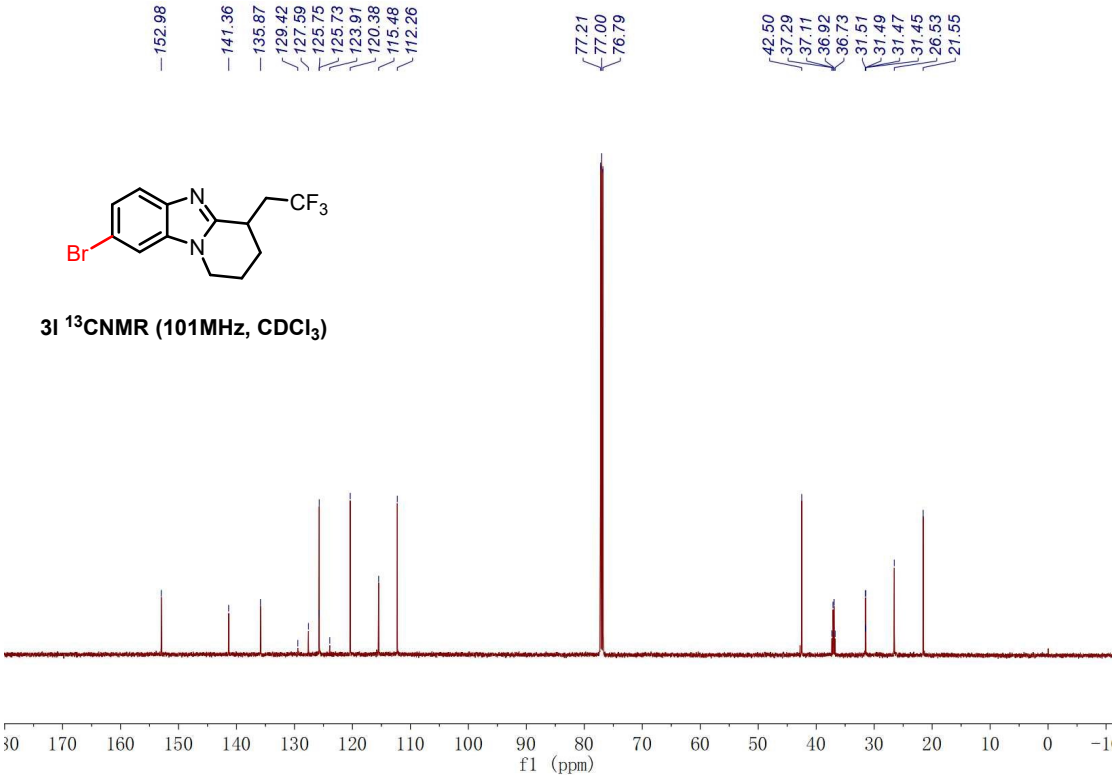


3k ^{19}FNMR (376MHz, $CDCl_3$)

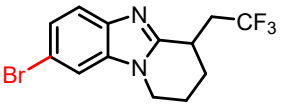


3l ^{1}HNMR (400MHz, $CDCl_3$)

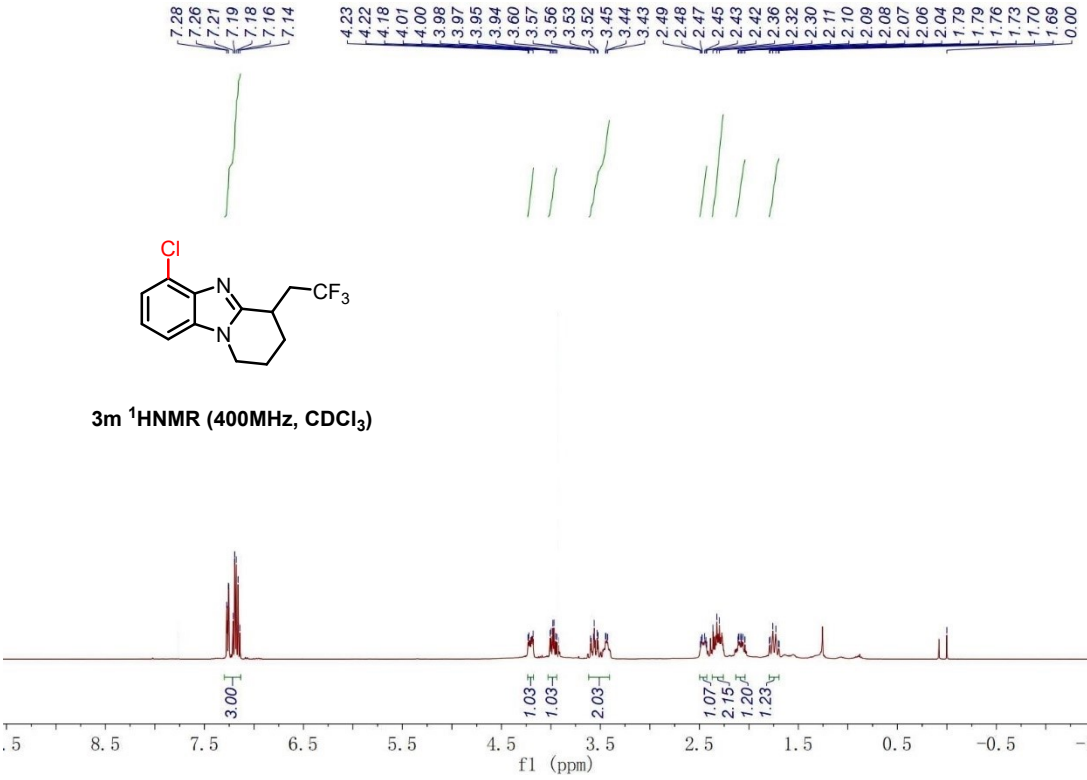




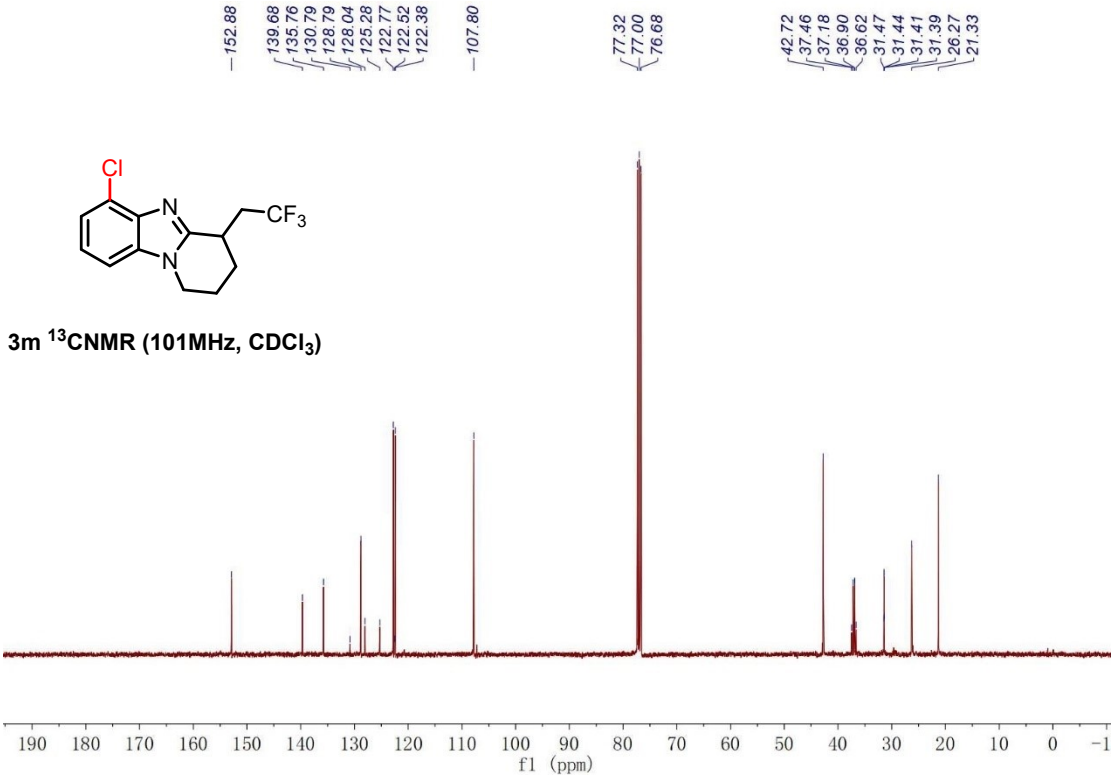
3l ^{13}CNMR (101MHz, $CDCl_3$)



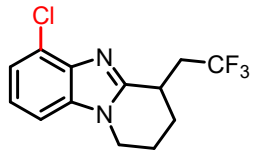
3l ^{19}FNMR (376MHz, $CDCl_3$)



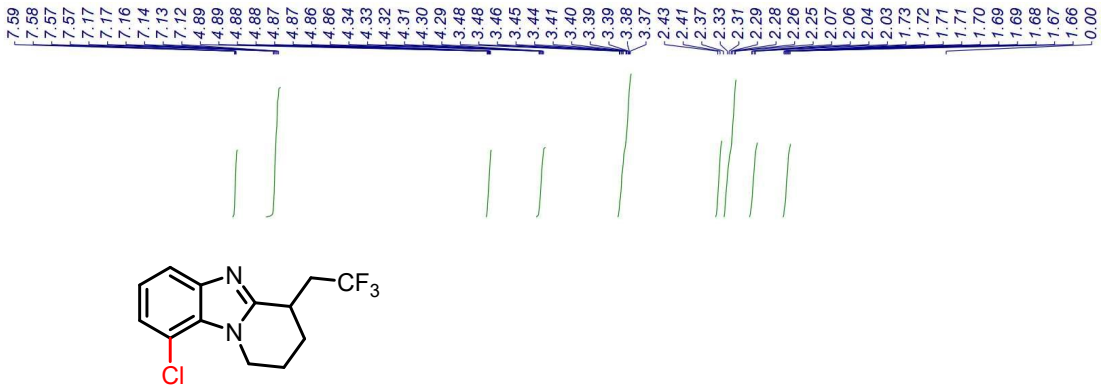
3m ^{1}HNMR (400MHz, $CDCl_3$)



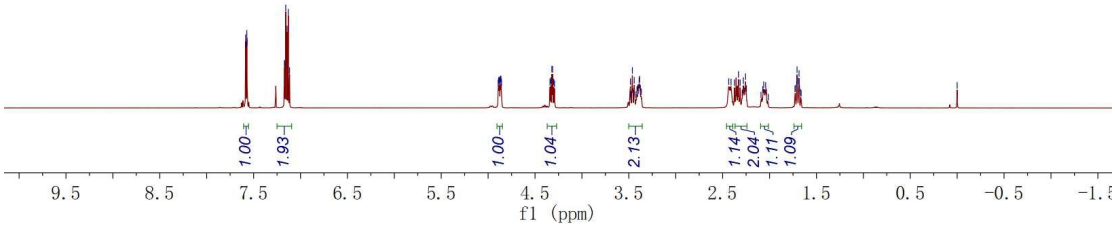
3m ^{13}CNMR (101MHz, $CDCl_3$)

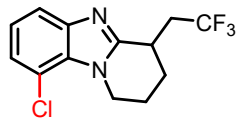


3m ^{19}FNMR (376MHz, $CDCl_3$)

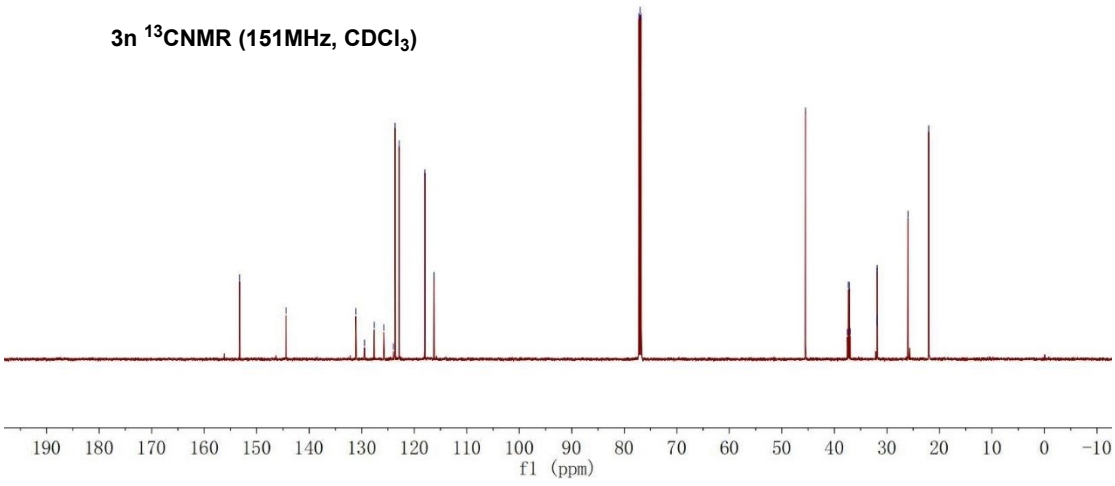


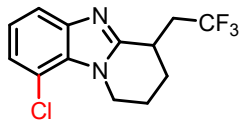
3n ^{1}HNMR (600MHz, $CDCl_3$)



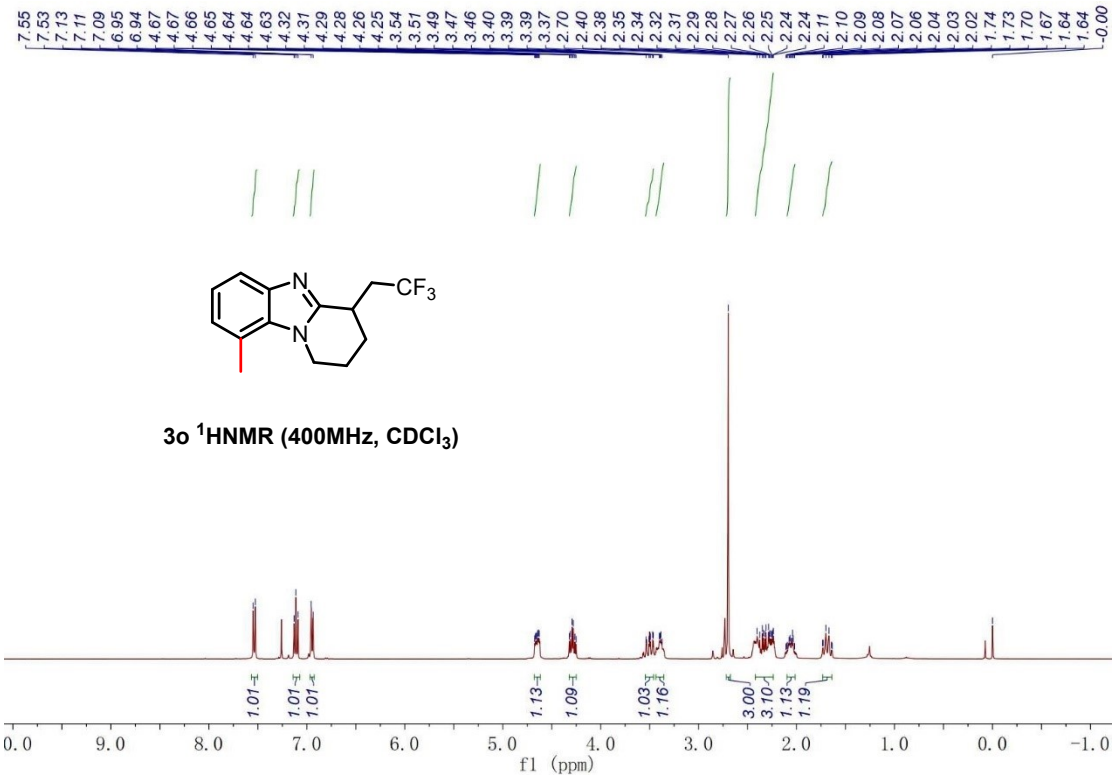


3n ^{13}CNMR (151MHz, $CDCl_3$)

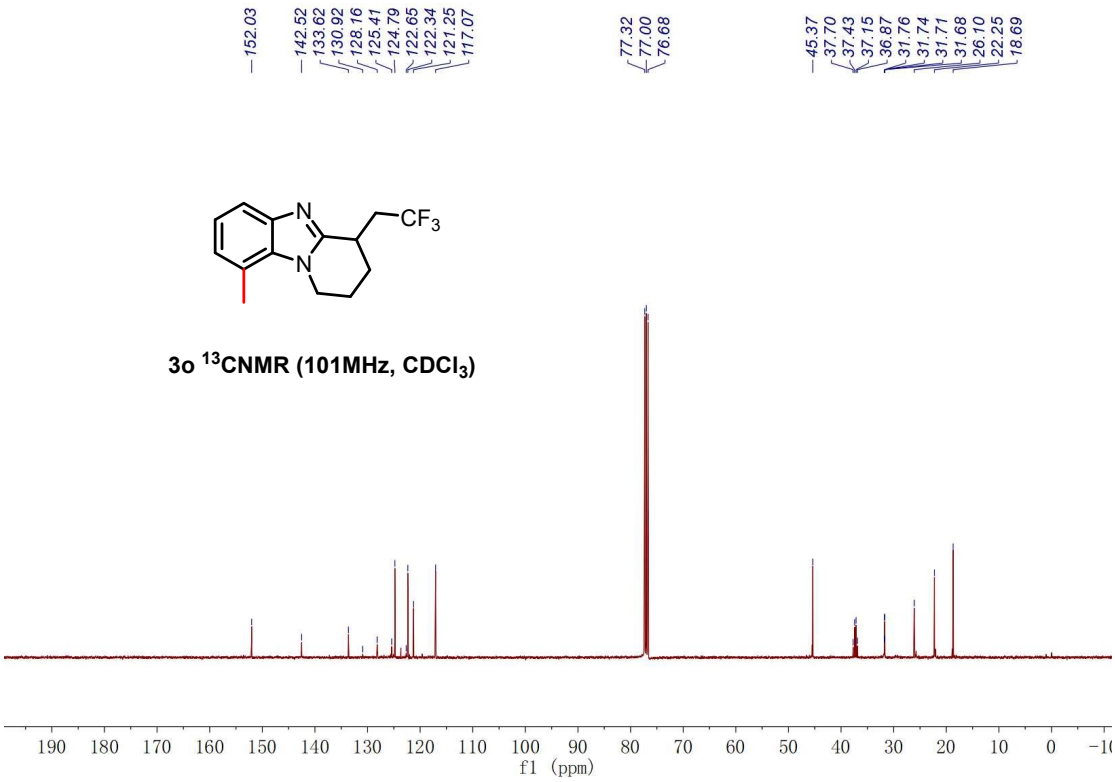




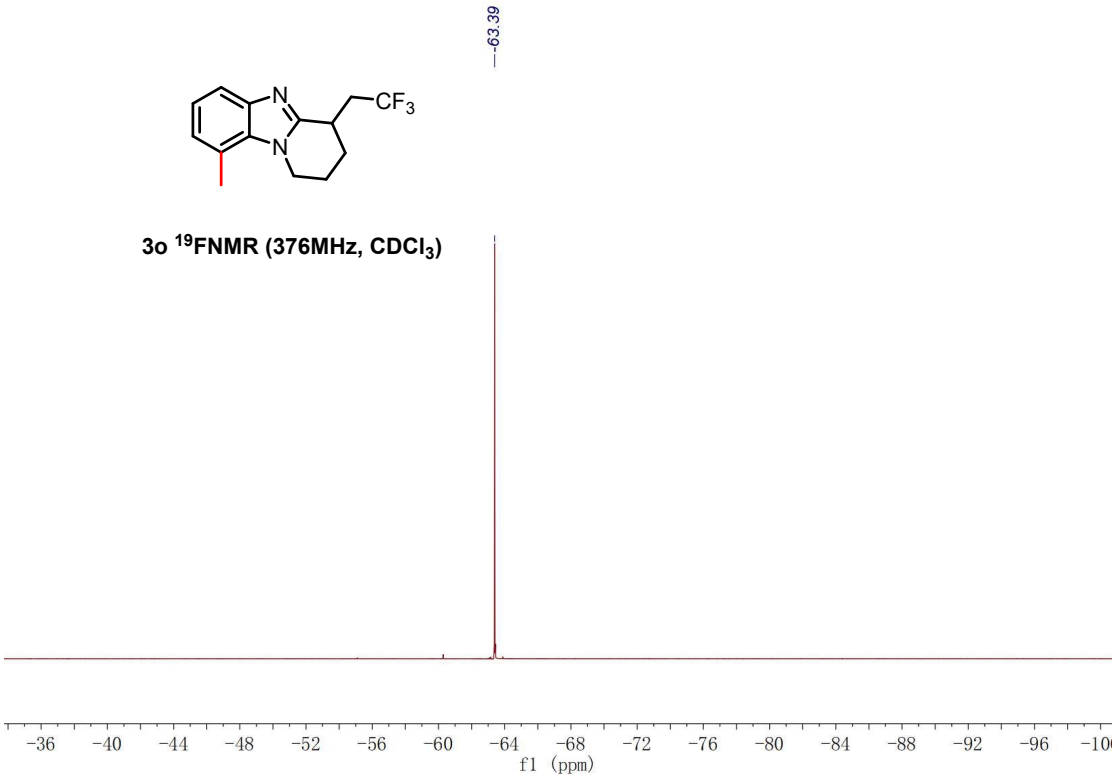
3n ^{19}FNMR (565MHz, $CDCl_3$)



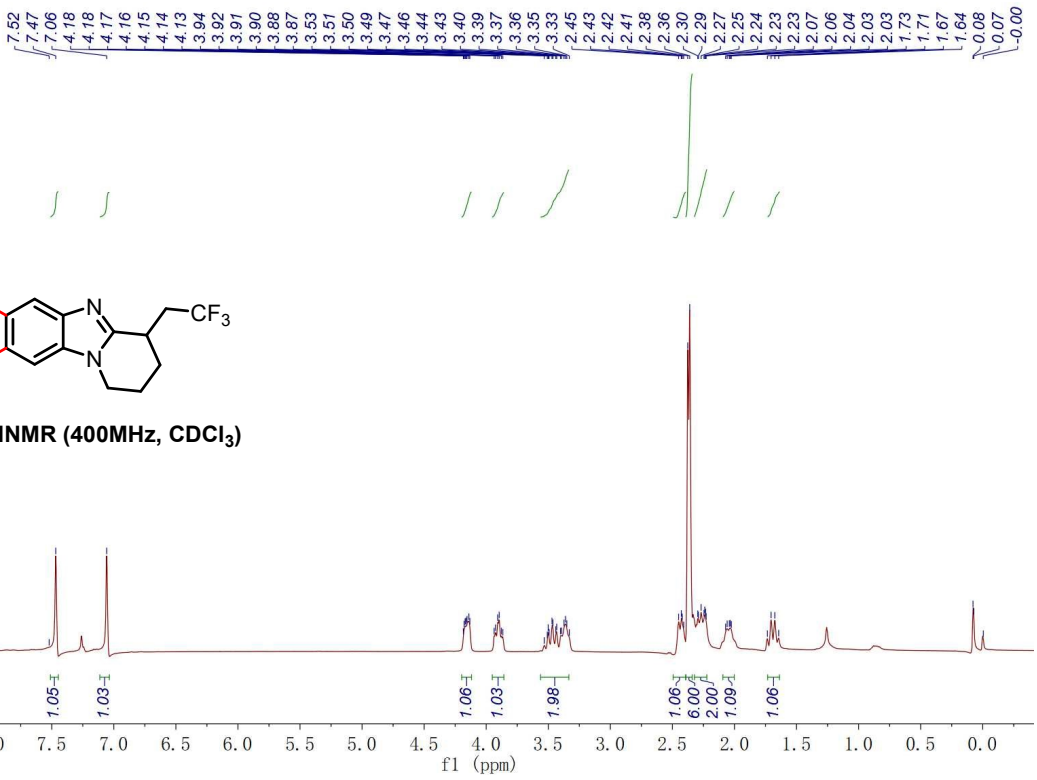
3o ^{1}HNMR (400MHz, $CDCl_3$)



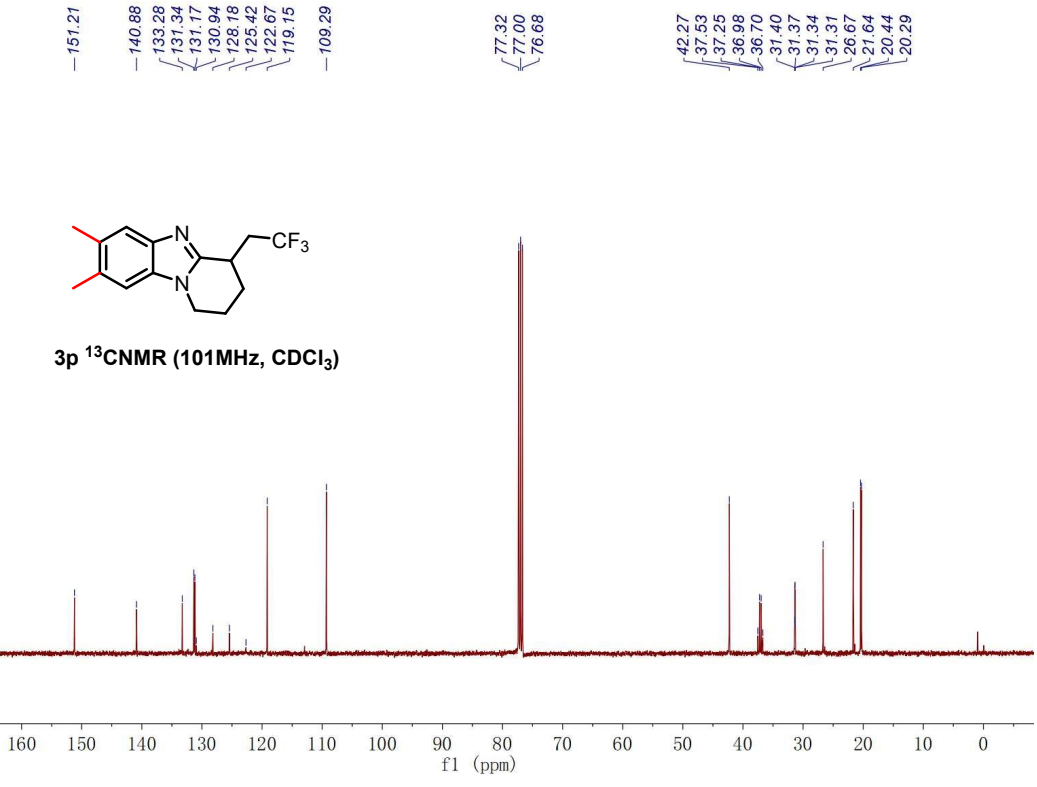
3o ^{13}CNMR (101MHz, $CDCl_3$)



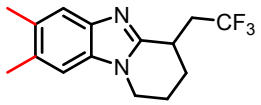
3o ^{19}FNMR (376MHz, $CDCl_3$)



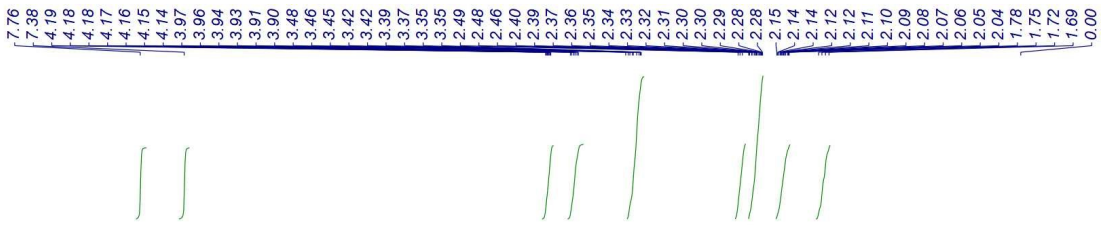
3p ^{1}HNMR (400MHz, $CDCl_3$)

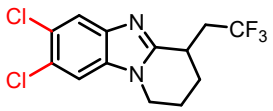


3p ^{13}CNMR (101MHz, $CDCl_3$)

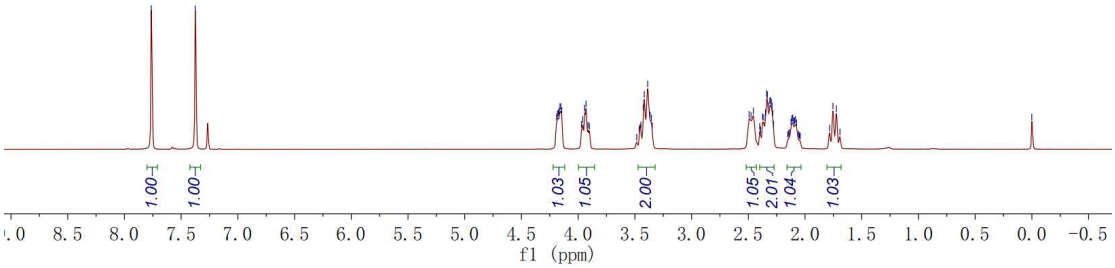


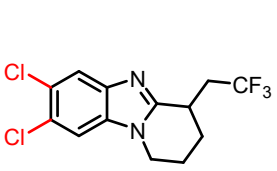
3p ^{19}FNMR (376MHz, $CDCl_3$)



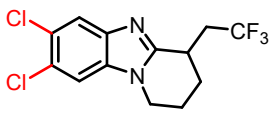


3q ^{1}HNMR (400MHz, $CDCl_3$)

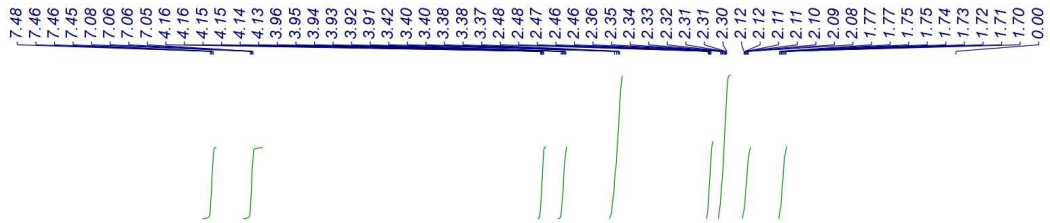


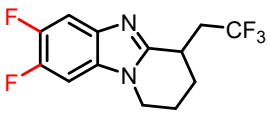


3q ^{13}CNMR (101MHz, $CDCl_3$)

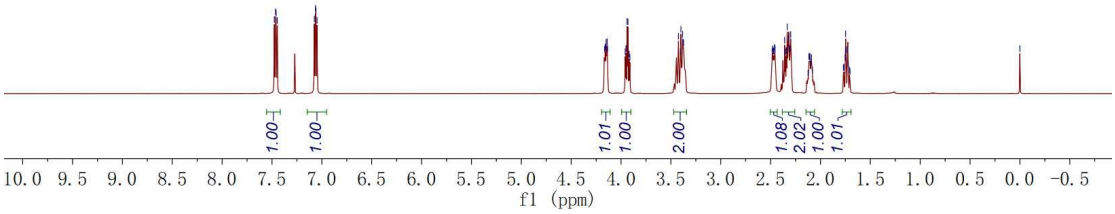


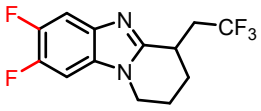
3q ^{19}FNMR (376MHz, $CDCl_3$)



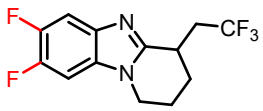


3r ^{1}HNMR (600MHz, $CDCl_3$)

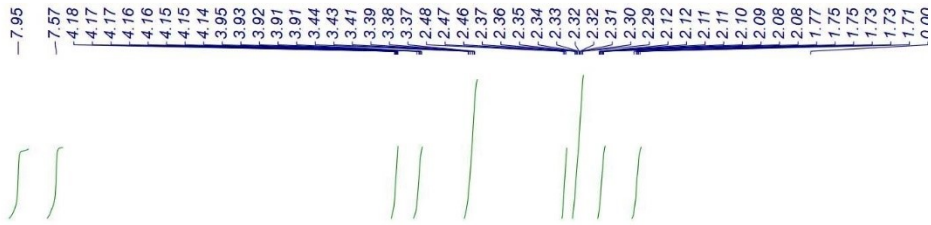


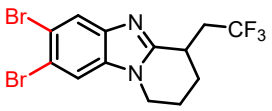


3r ^{13}CNMR (151MHz, $CDCl_3$)

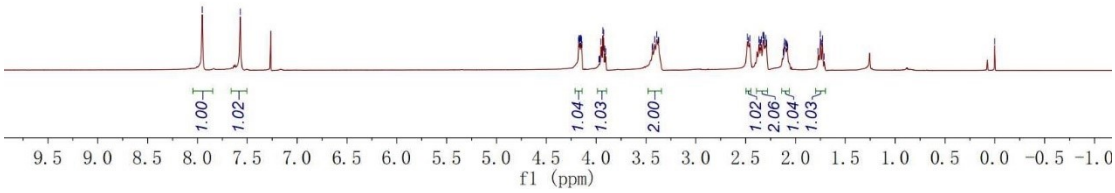


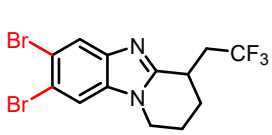
3r ^{19}FNMR (565MHz, $CDCl_3$)



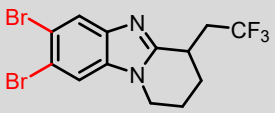


3s ^{1}HNMR (600MHz, $CDCl_3$)

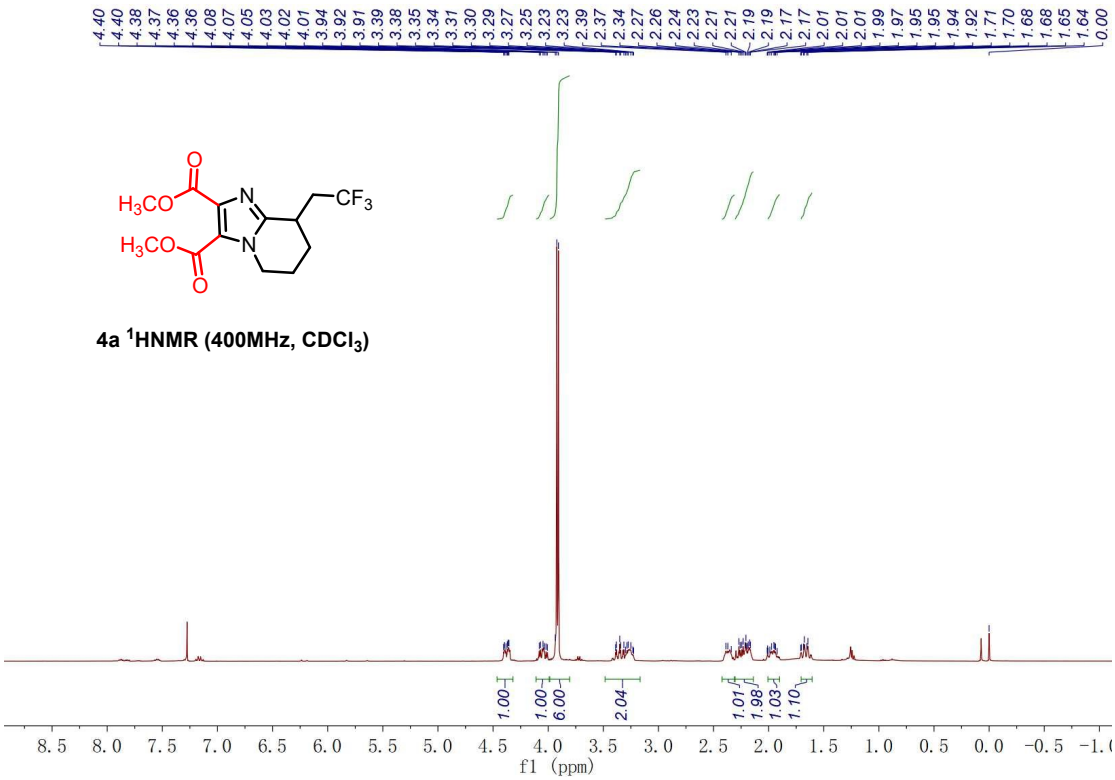




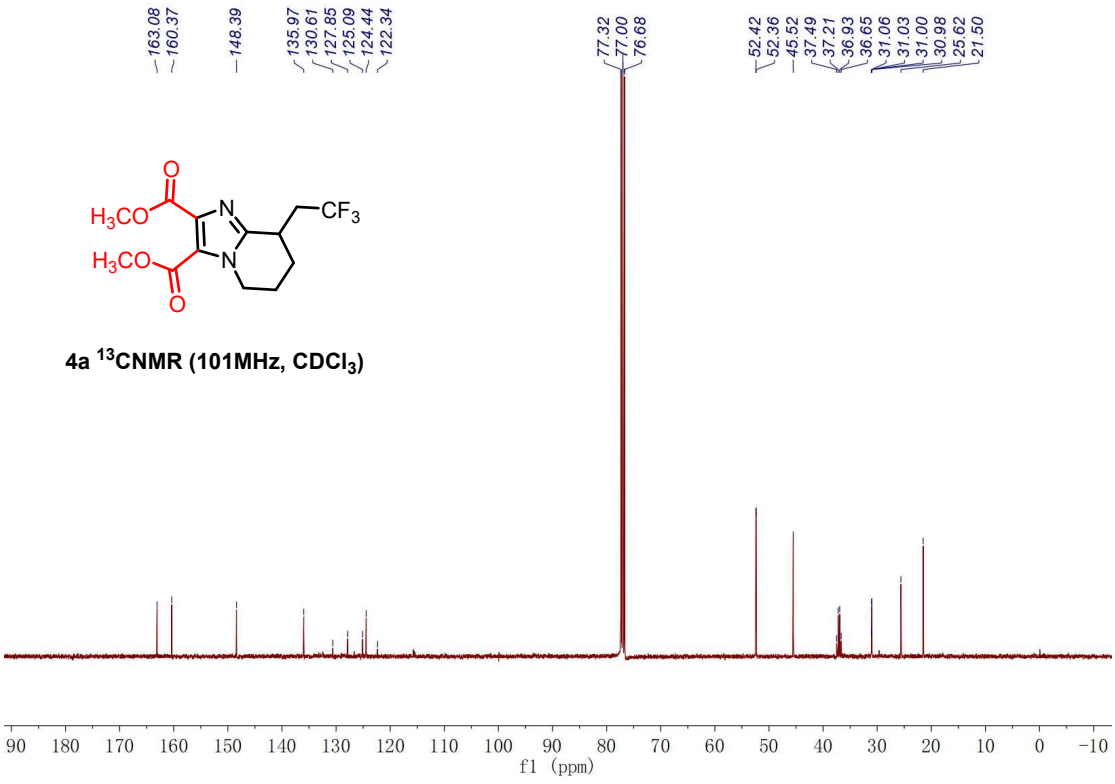
3s ^{13}CNMR (151MHz, $CDCl_3$)



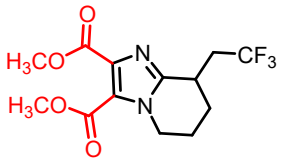
3s ^{19}FNMR (565MHz, $CDCl_3$)



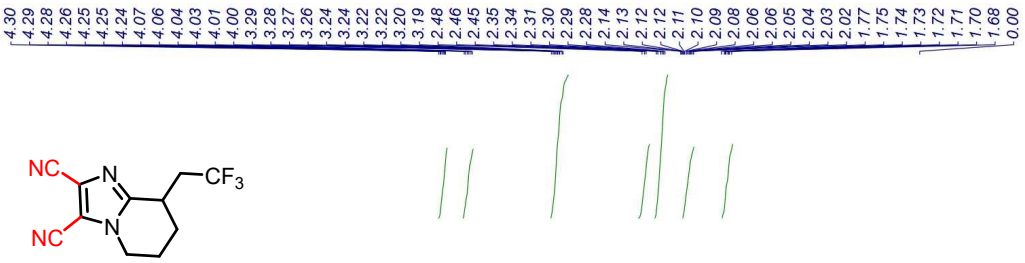
4a ^{1}HNMR (400MHz, $CDCl_3$)



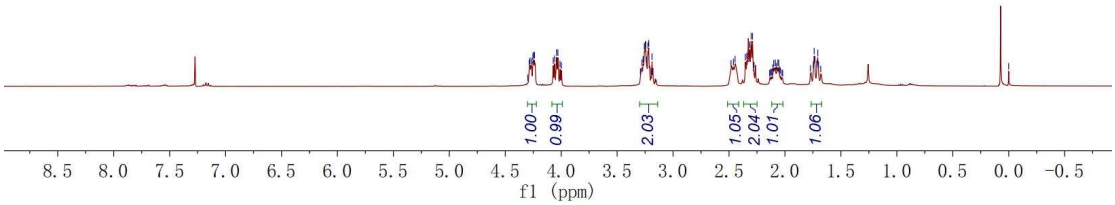
4a ^{13}CNMR (101MHz, $CDCl_3$)

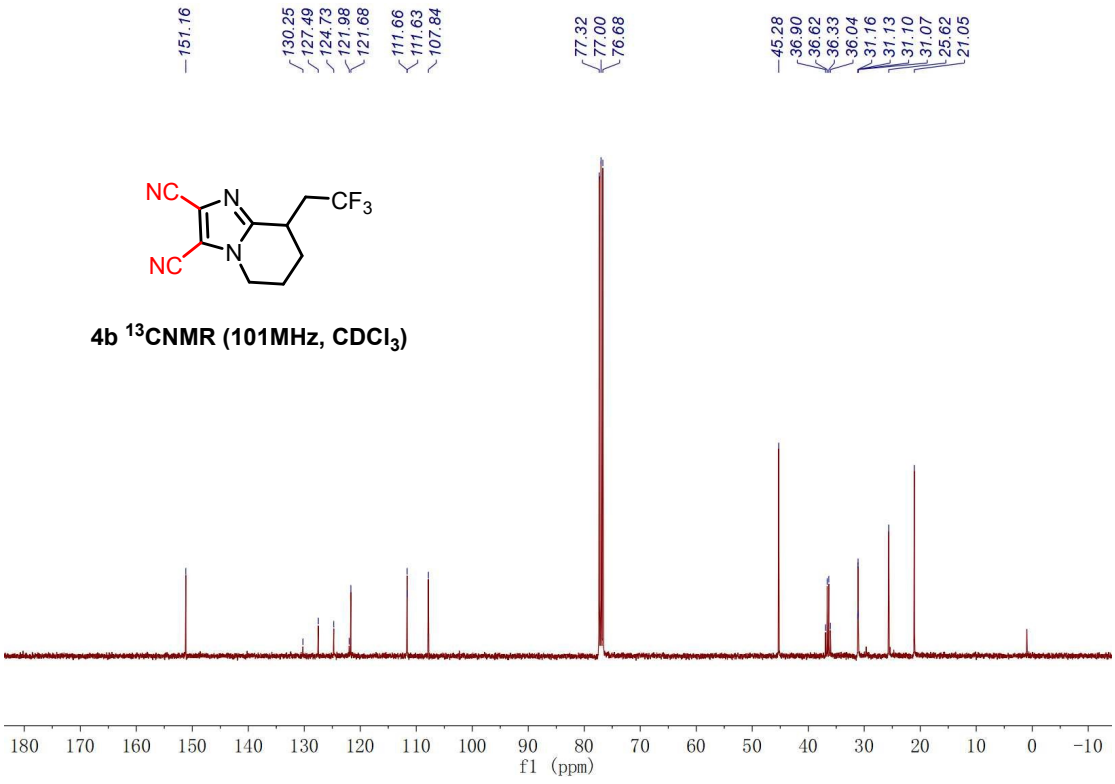


4a ^{19}FNMR (376MHz, $CDCl_3$)

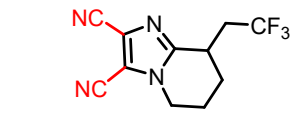


4b ^{1}HNMR (400MHz, $CDCl_3$)

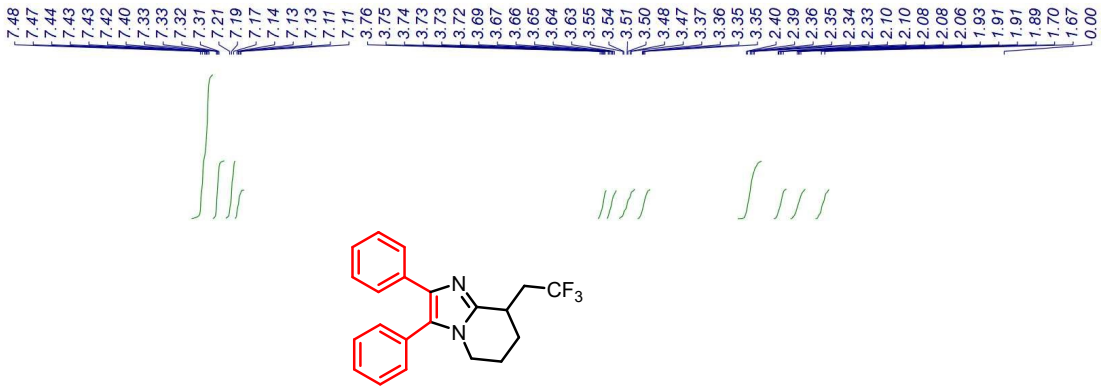




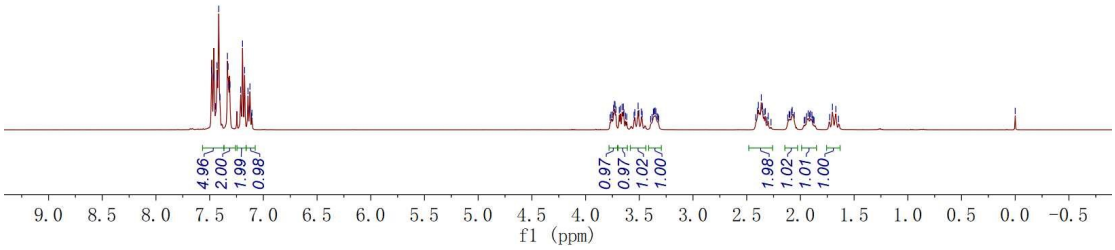
4b ^{13}CNMR (101MHz, $CDCl_3$)



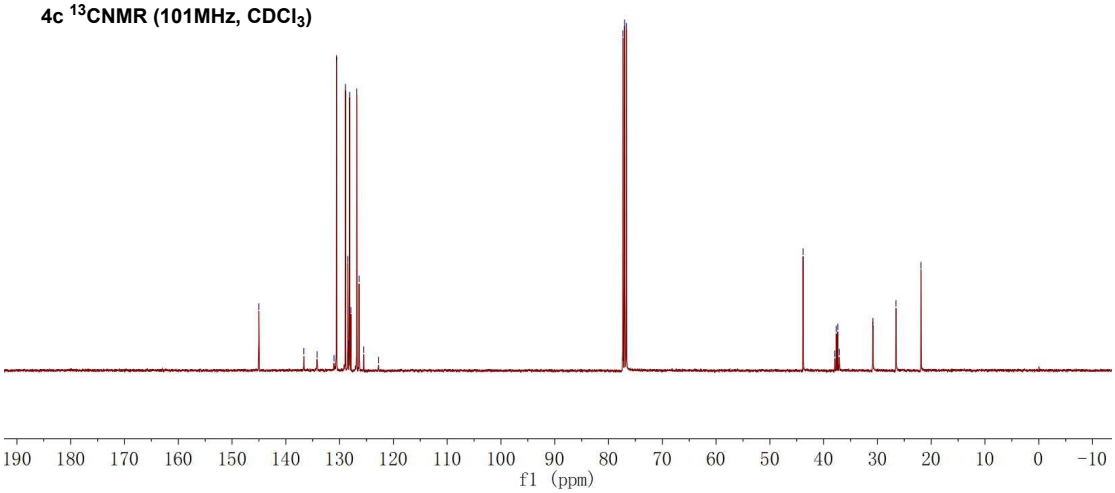
4b ^{19}FNMR (376MHz, $CDCl_3$)

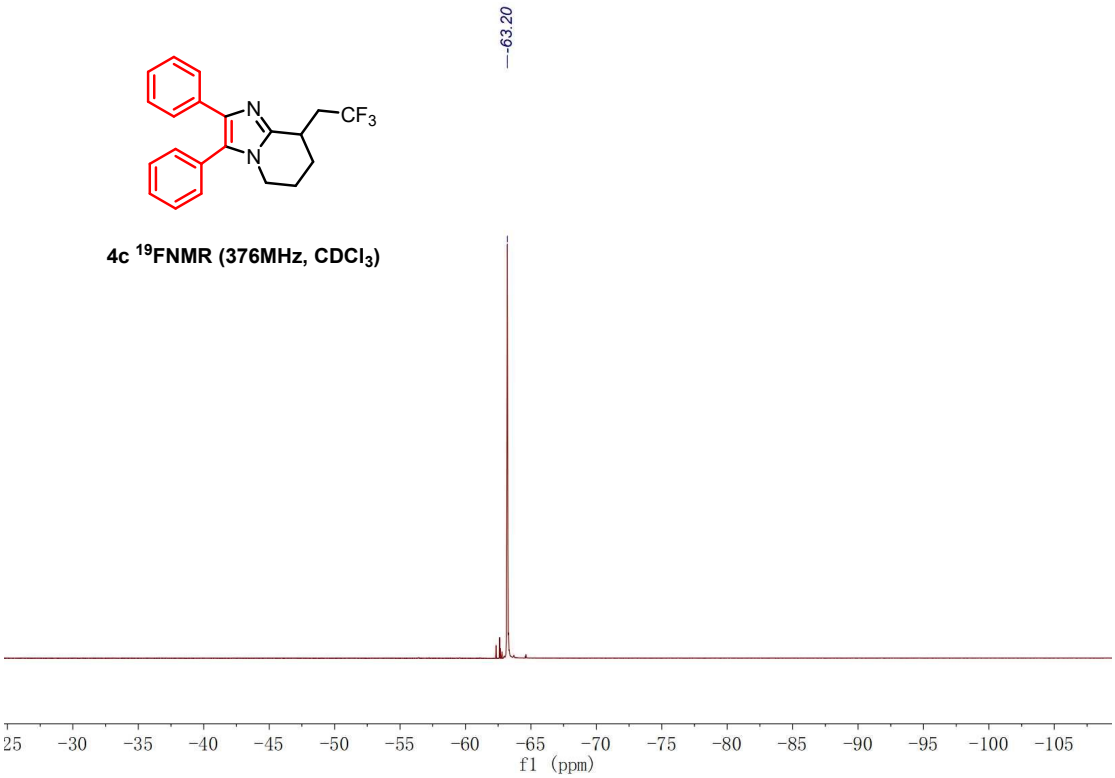


4c ^{1}HNMR (400MHz, $CDCl_3$)

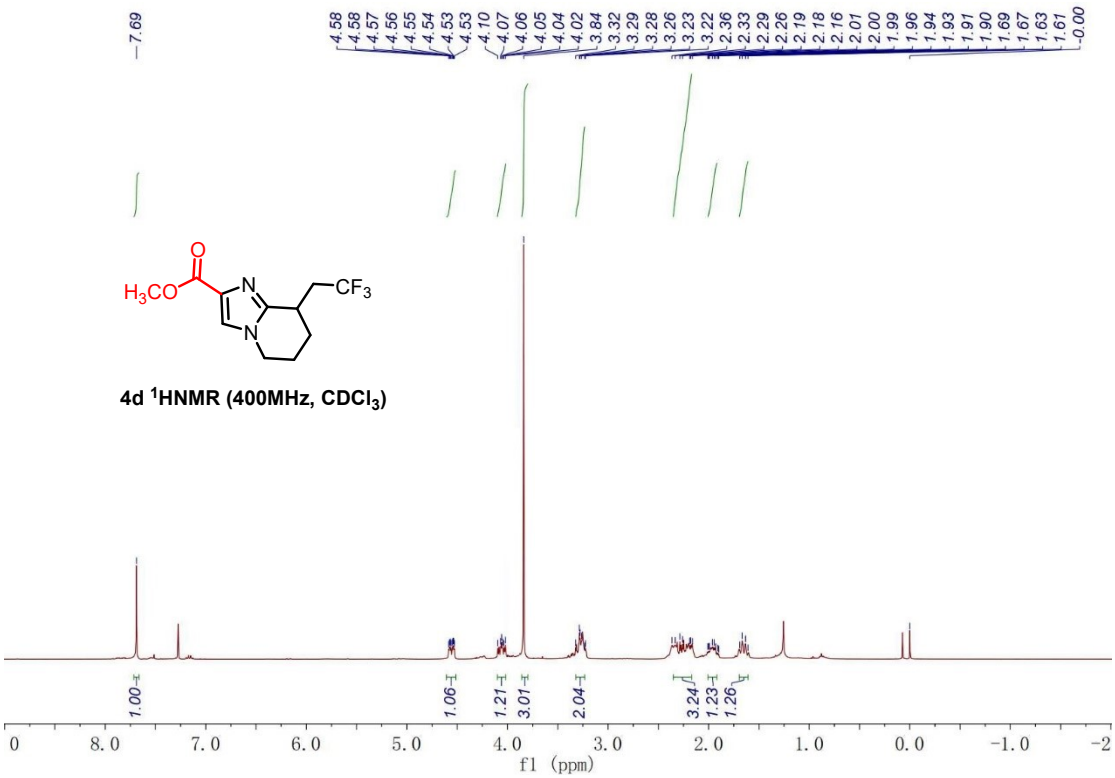


4c ^{13}CNMR (101MHz, $CDCl_3$)

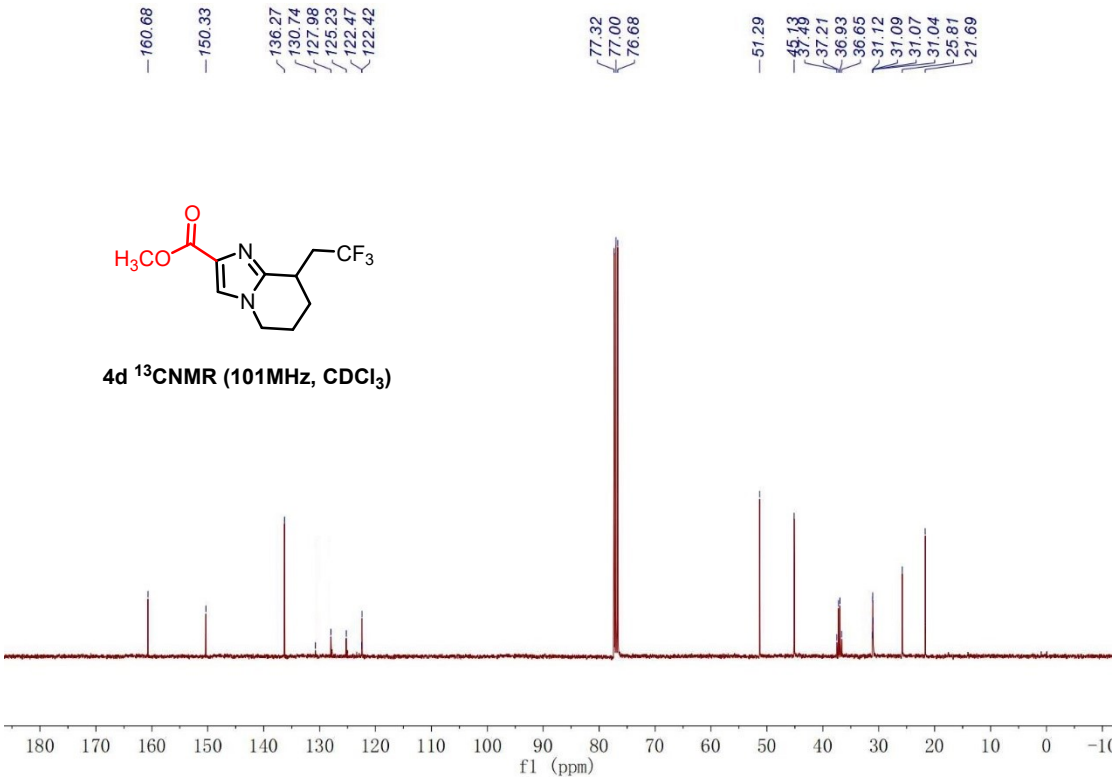




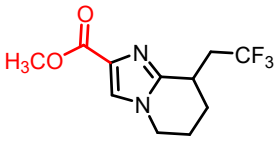
4c ^{19}FNMR (376MHz, $CDCl_3$)



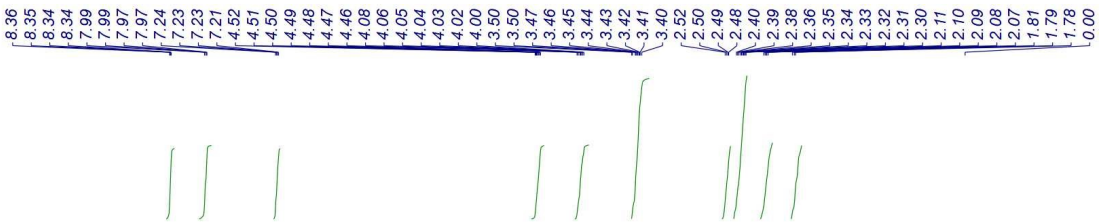
4d ^{1}HNMR (400MHz, $CDCl_3$)

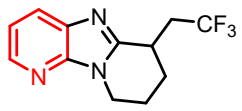


4d ^{13}CNMR (101MHz, $CDCl_3$)

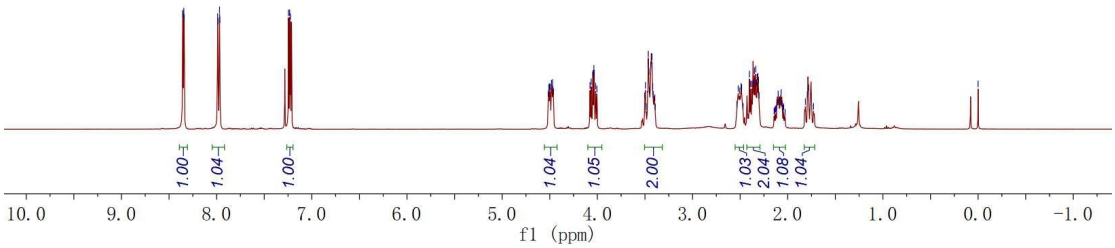


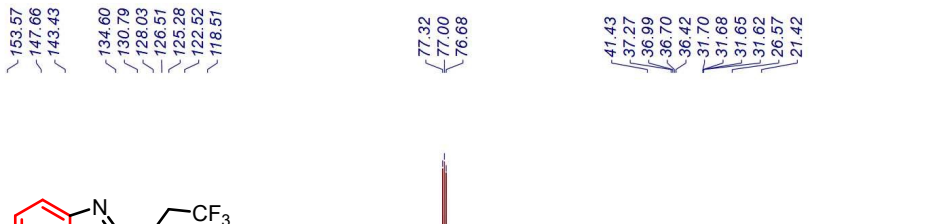
4d ^{19}FNMR (376MHz, $CDCl_3$)

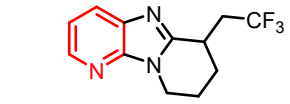




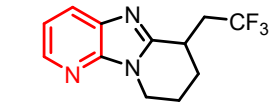
4e ^{1}HNMR (400MHz, $CDCl_3$)



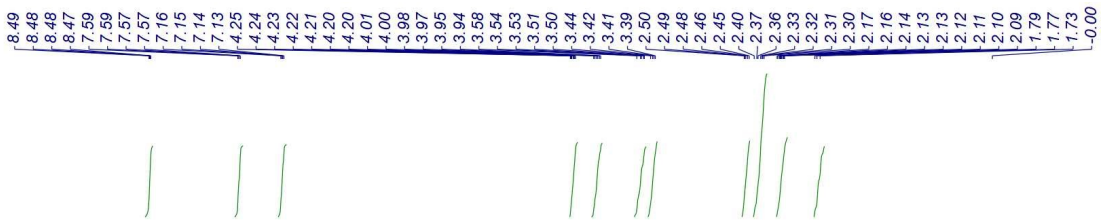


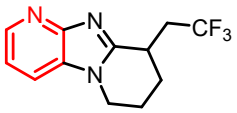


4e ^{13}CNMR (101MHz, $CDCl_3$)

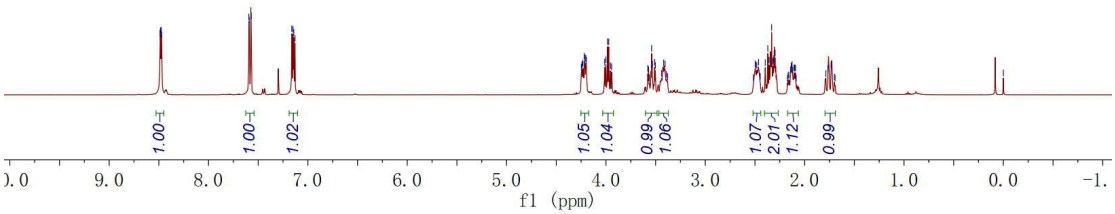


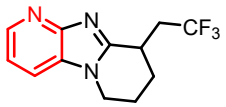
4e ^{19}FNMR (376MHz, $CDCl_3$)



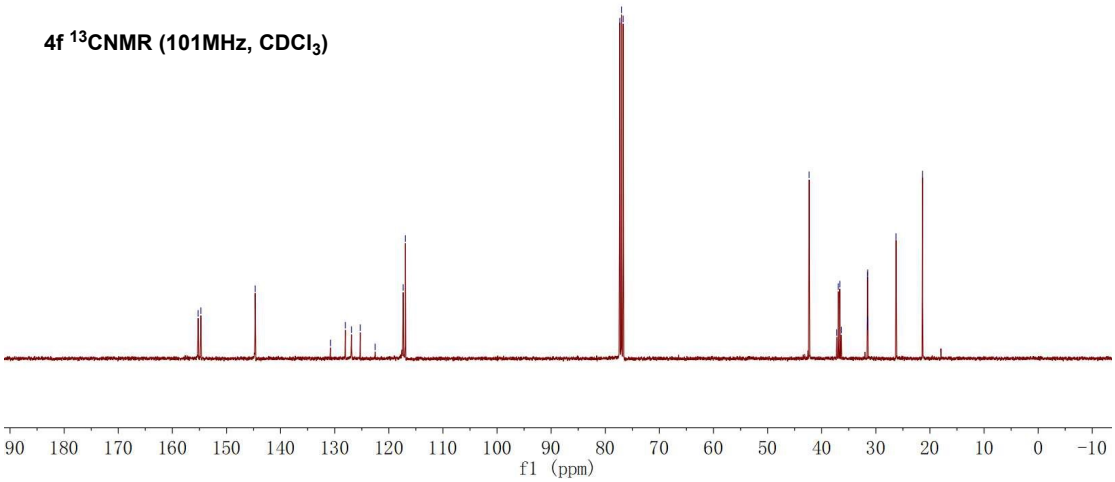


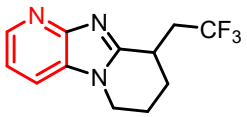
4f ^{1}HNMR (400MHz, $CDCl_3$)



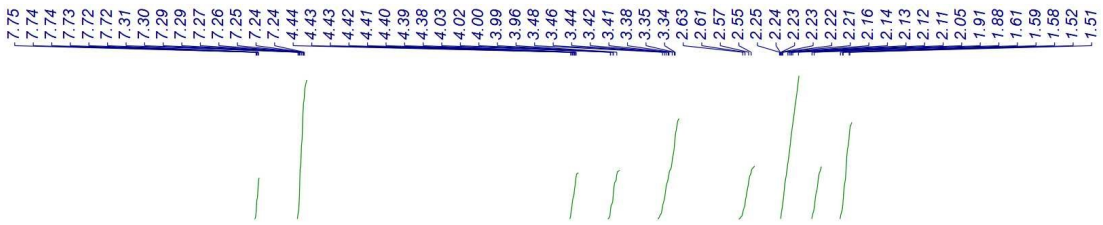


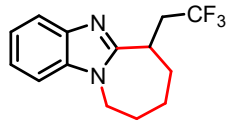
4f ^{13}CNMR (101MHz, $CDCl_3$)



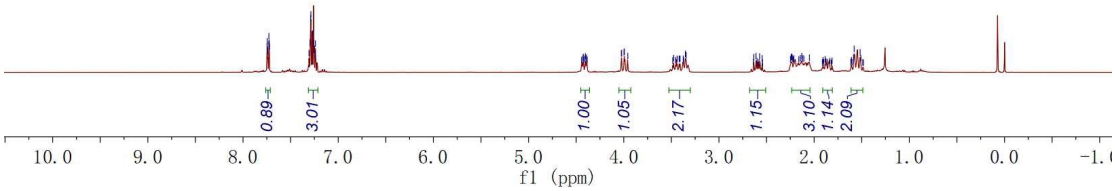


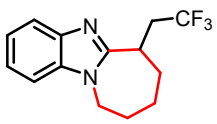
4f ^{19}FNMR (376MHz, $CDCl_3$)



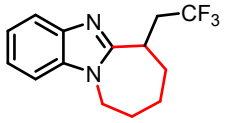


4g ^{1}HNMR (400MHz, $CDCl_3$)

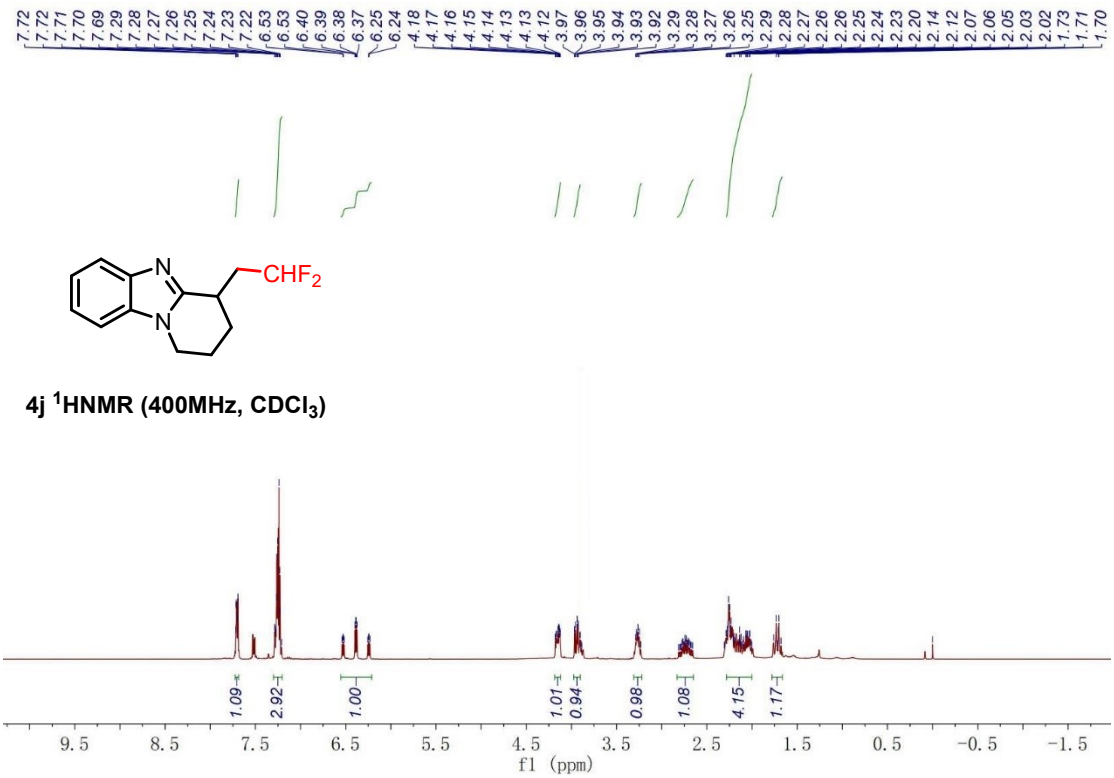




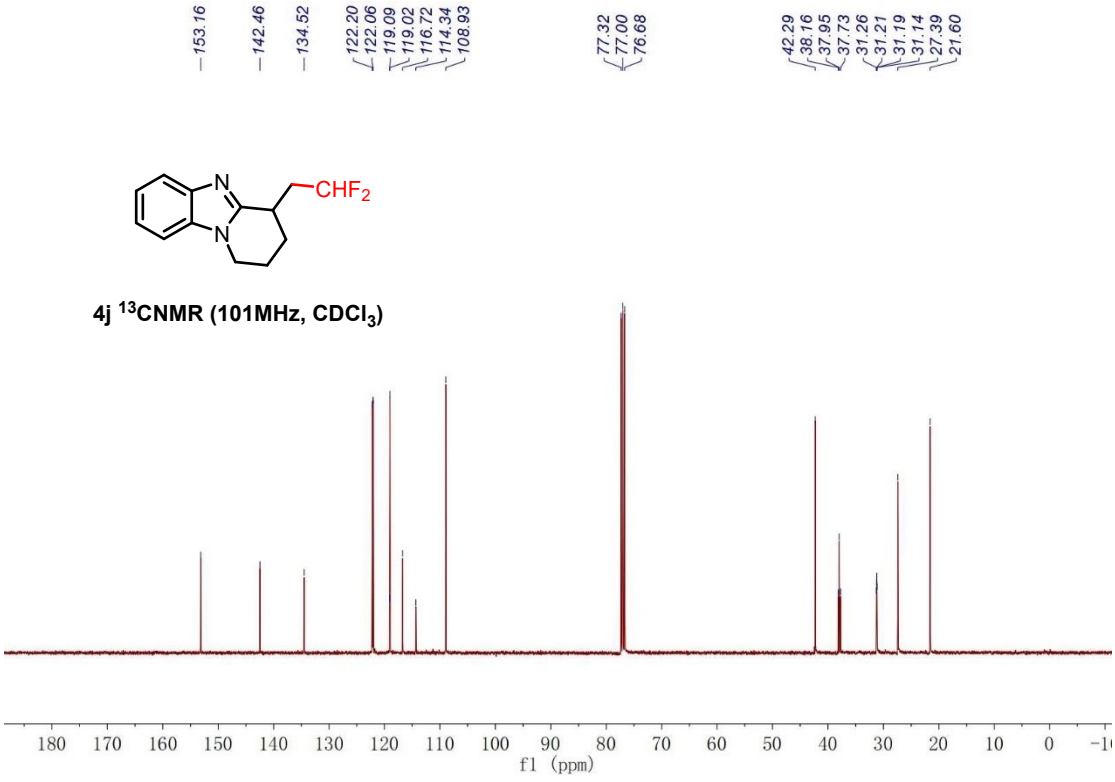
4g ^{13}CNMR (101MHz, $CDCl_3$)



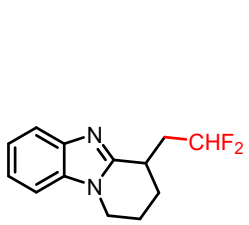
4g ^{19}FNMR (376MHz, $CDCl_3$)



4j ^{1}HNMR (400MHz, $CDCl_3$)



4j ^{13}CNMR (101MHz, $CDCl_3$)



4j ^{19}FNMR (376MHz, $CDCl_3$)

8. Reference

1. N. Shotaro, S.Takashi, S. Atsushi, K. Tohru, Y. Tsuyoshi, M. Atsunori, Axially Chiral Macrocyclic *E*-Alkene Bearing Bisazole Component Formed by Sequential C–H Homocoupling and Ring-Closing Metathesis**,** *Org. Lett.,* 2012, **14**, 2476-2479.

2. N.-L. Sheng, Y Chen, X.-D. Luo, Y. Li, Sustainable Cascades to Difluoroalkylated Polycyclic Imidazoles, *Eur. J. Org. Chem*., 2021,4485–448.

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