Supporting Information (SI)

Green and controllable synthesis of symmetrical and unsymmetrical difluoromethylated diarylmethanes via a direct bisarylation strategy enabled by HFIP–$B(C_6F_5)_3$ adduct

Xindi Li,[a] Yiping Zhu,[a] Zhina Gong,[a] Jinshan Li,*[a,b] Jialin Xie,[a,b] Zhendong Zhao,[c] Jianwei Li[d] and Chunman Jia*[a,b,c]

[a]*Hainan Provincial Key Lab of Fine Chem, School of Chemistry and Chemical Engineering, Hainan University, Haikou 570228, China.*

[b]*One Health Institute, Hainan University, Haikou 570228, China.*

[c]*Analytical & Testing Center, Hainan University, Haikou 570228, China*

[d]*MediCity Research Laboratory, University of Turku, Tykistökatu 6, Turku, 20520, Finland*

*E-mail: lijinshan@hainanu.edu.cn

*E-mail: jiachunman@hainanu.edu.cn

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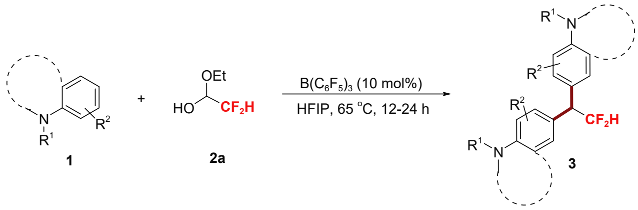
1. General information

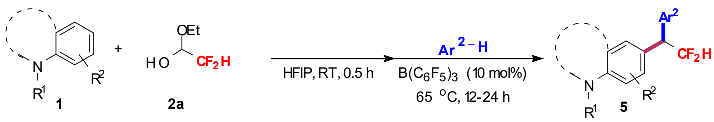
Unless otherwise indicated, all reactions were carried out in air. All reagents and solvents were obtained commercially and used as received without further purification. Analytical thin layer chromatography was performed on 0.20 mm Qingdao Haiyang silica gel plates. Silica gel (200-300 mesh) (from Qingdao Haiyang Chem. Company, Ltd.) was used for flash chromatography. ^{1}H, ^{13}C and ^{19}F were recorded on Bruker AV 400 MHz instrument at 400 MHz (^{1}H NMR), 100 MHz (^{13}C NMR), as well as 376 MHz (^{19}F NMR). Chemical shifts were reported in ppm down field from internal Me_4Si and external CCl_3F, respectively. $CDCl_3$ (7.26 ppm for ^{1}H NMR, 77.0 ppm for ^{13}C NMR) was used as a reference. Data for ^{1}H were reported as follows: chemical shift (ppm), multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, dd = doublet of doublets, m = multiplet, br = broad singlet), coupling constants (Hz), and integration. Data for ^{13}C NMR were reported as ppm. High-resolution mass spectra analyses were performed on a Waters SYNAPT G2-Si Q-TOF mass spectrometer. Melting points were determined using a X-4 digital micro melting point apparatus. Thin-layer chromatography (TLC) was performed, and visualization of the compounds was accomplished with UV light (254 nm). Flash column chromatography was performed on silica gel (200−300 mesh).

2. General procedure for synthesis of symmetrical difluoromethylated diarylmethanes and analogues (3a-3t)



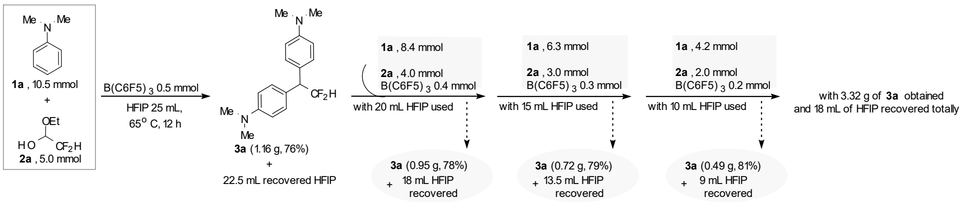
To a 25 mL Schlenk tube was added aniline **1** (1.05 mmol, 2.1 equiv.) and **2a** (0.5 mmol, 63.1 mg, 1.0 equiv.) and $B(C_6F_5)_3$ (0.05 mmol, 25.6 mg, 0.1 equiv.), then 2.5 mL HFIP was added. The resulting mixture was stirred at 65 °C in an oil bath until the completion of the reaction (monitored by TLC, approximately 12–24 hours). Then the mixture was concentrated under reduced pressure. The residue was purified by column chromatography to afford the desired products **3**, using the indicated eluent.

3. General procedure for synthesis of unsymmetrical difluoromethylated diarylmethanes (5a-5o)



To a 25 mL Schlenk tube was added aniline **1** (0.5 mmol, 1.0 equiv.) and **2a** (0.5 mmol, 63.1 mg, 1.0 equiv.) and HFIP (2.5 mL). The resulting mixture was stirred at room temperature until the completion of the reaction (monitored by TLC, approximately 0.5–1.0 hour). Then another arene (indole or aniline 0.55 mmol, 1.1 equiv.) and $B(C_6F_5)_3$ (0.05 mmol, 25.6 mg, 0.1 equiv.) were added. The resulting mixture was stirred at 65 °C in an oil bath until the completion of the reaction (monitored by TLC, approximately 12–24 hours). Then the mixture was concentrated under reduced pressure. The residue was purified by column chromatography to afford the desired products **5**, using the indicated eluent.

4. Recyclability and reusability of the HFIP solvent in the gram-scale experiment and transformation of difluoromethylated diarylmethane



Initial reaction

To a 100 mL Schlenk tube added *N*,*N*-dimethylaniline **1a** (1.27 g, 10.5 mmol, 2.1 equiv.) and difluoroacetaldehyde ethyl hemiacetal **2a** (0.63 g, 5.0 mmol, 1.0 equiv.) and $B(C_6F_5)_3$ (0.5 mmol, 0.26 g, 0.1 equiv.) in 25 mL of HFIP. The resulting mixture was stirred at 65 °C in an oil bath. After completion of the reaction (monitored by TLC) the HFIP solvent was recovered by distillation directly from the reaction pot (60–70 ˚C, 22.5 mL, 90%). The residue was purified by column chromatography on silica gel to give **3a** (1.16 g, 76%) as white solid.

2 nd reaction, using recovered HFIP solvent

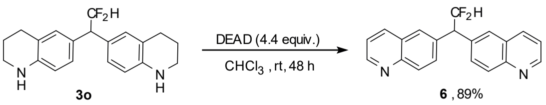
To a solution of *N*,*N*-dimethylaniline **1a** (1.02 g, 8.4 mmol, 2.1 equiv.) and difluoroacetaldehyde ethyl hemiacetal **2a** (0.51 g, 4.0 mmol, 1.0 equiv.) and $B(C_6F_5)_3$ (0.4 mmol, 0.20 g, 0.1 equiv.) in 20 mL of recovered HFIP. The resulting mixture was stirred at 65 °C in an oil bath. After completion of the reaction (monitored by TLC) the HFIP solvent was recovered by distillation directly from the reaction pot (60–70 ˚C, 18.0 mL, 90%). The residue was purified by column chromatography on silica gel to give **3a** (0.95 g, 78%) as white solid.

3 rd reaction, using 2-times recovered HFIP solvent

To a solution of *N*,*N*-dimethylaniline **1a** (0.76 g, 6.3 mmol, 2.1 equiv.) and difluoroacetaldehyde ethyl hemiacetal **2a** (0.38 g, 3.0 mmol, 1.0 equiv.) and $B(C_6F_5)_3$ (0.3 mmol, 0.15 g, 0.1 equiv.) in 15 mL of recovered HFIP. The resulting mixture was stirred at 65 °C in an oil bath. After completion of the reaction (monitored by TLC) the HFIP solvent was recovered by distillation directly from the reaction pot (60–70 ˚C, 13.5 mL, 90%). The residue was purified by column chromatography on silica gel to give **3a** (0.72 g, 79%) as white solid.

4 th reaction, using 3-times recovered HFIP solvent

To a solution of *N*,*N*-dimethylaniline **1a** (0.51 g, 4.2 mmol, 2.1 equiv.) and difluoroacetaldehyde ethyl hemiacetal **2a** (0.26 g, 2.0 mmol, 1.0 equiv.) and $B(C_6F_5)_3$ (0.2 mmol, 0.10 g, 0.1 equiv.) in 10 mL of recovered HFIP. The resulting mixture was stirred at 65 °C in an oil bath. After completion of the reaction (monitored by TLC) the HFIP solvent was recovered by distillation directly from the reaction pot (60–70 ˚C, 9.0 mL, 90%). The residue was purified by column chromatography on silica gel to give **3a** (0.49 g, 81%) as white solid.



To a solution of **3o** (65.7 mg, 0.2 mmol) in $CHCl_3$ (0.4 mL) was added DEAD (153.2 mg, 0.88 mmol, 4.4 equiv.). The reaction mixture was stirred at room temperature for 48 h. The solvent was removed by rotary evaporation. The crude product was purified by flash column chromatography using petroleum ether/ethyl acetate (5/1, v/v) to give 57.2 mg of **6** (89% yield).

5. Mechanistic investigation by NMR experiments

5.1. ^{1}H NMR study

^{1}H NMR of individual species (HFIP, **1a** and **2a**), three binary mixtures (HFIP : $B(C_6F_5)_3$ and HFIP : **1a** and HFIP : **2a**), two ternary mixture (HFIP : $B(C_6F_5)_3$: **1a** and HFIP : $B(C_6F_5)_3$: **2a**) and one quaternary mixture (HFIP : $B(C_6F_5)_3$: **1a** : **2a**) were recorded at a 0.06 mmol scale of aniline **1a**, 0.06 mmol scale of difluoroacetaldehyde ethyl hemiacetal **2a**, 0.012 mmol (20 mol%) scale of $B(C_6F_5)_3$, 0.06 mmol scale of HFIP and 0.6 mL $CDCl_3$.

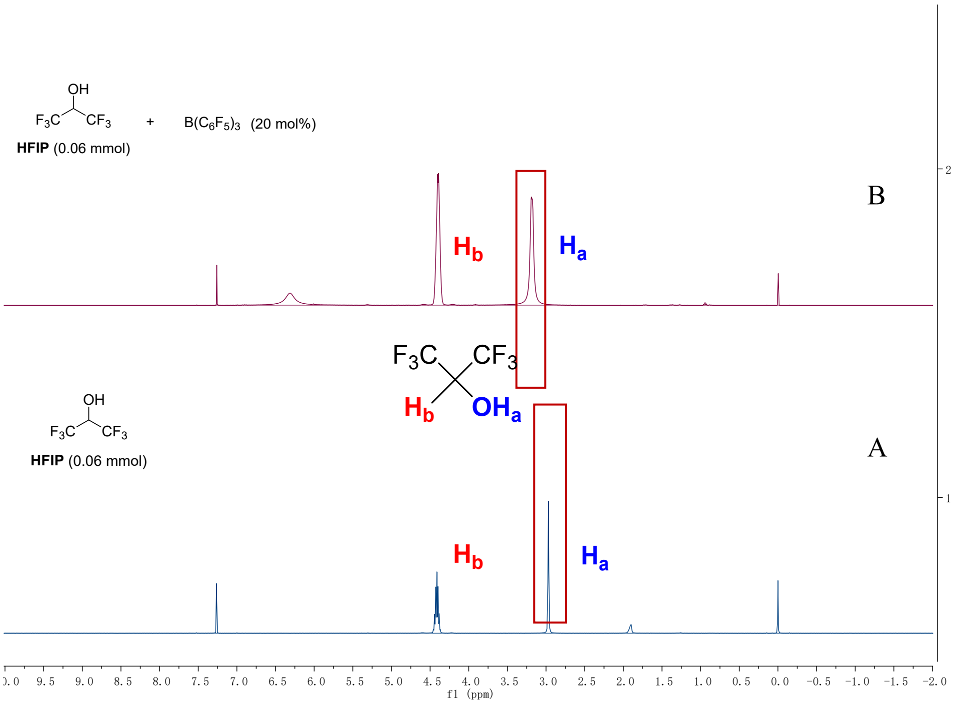


Figure S1 ^{1}H NMR of the individual specie (A) and the two binary mixture (B).

Signal	Species	
	HFIP	Binary mixture (HFIP : $B(C_6F_5)_3$)
OHa (HFIP)	2.99, d, J = 8.1 Hz	3.18, d, J = 5.1 Hz (+0.19)

Table S1. Significant changes for the binary mixture with respect to individual specie.

The most significant changes found in ^{1}H NMR for the HFIP : $B(C_6F_5)_3$) binary mixture (Figure S1B) compared to the individual specie (Figure S1A) are the downfield shift (deshieled) of the OH (HFIP), from a frequency of 2.99 ppm to 3.18 ppm ($\Delta\delta$ = 0.19). These data suggest a strong interaction between $B(C_6F_5)_3$ and HFIP in solution presumably through coordination of the hydroxyl oxygen atom of HFIP to the boron atom in $B(C_6F_5)_3$ (Table S1). The broad peak (6.0–6.5 ppm) should be the OH signal of $[(C_6F_5)_3B(OH_2)]$ adduct, which was formed with the residual water in deuterium reagent according to the reference (*Organometallics*, 2001, **20**, 4927–4938).

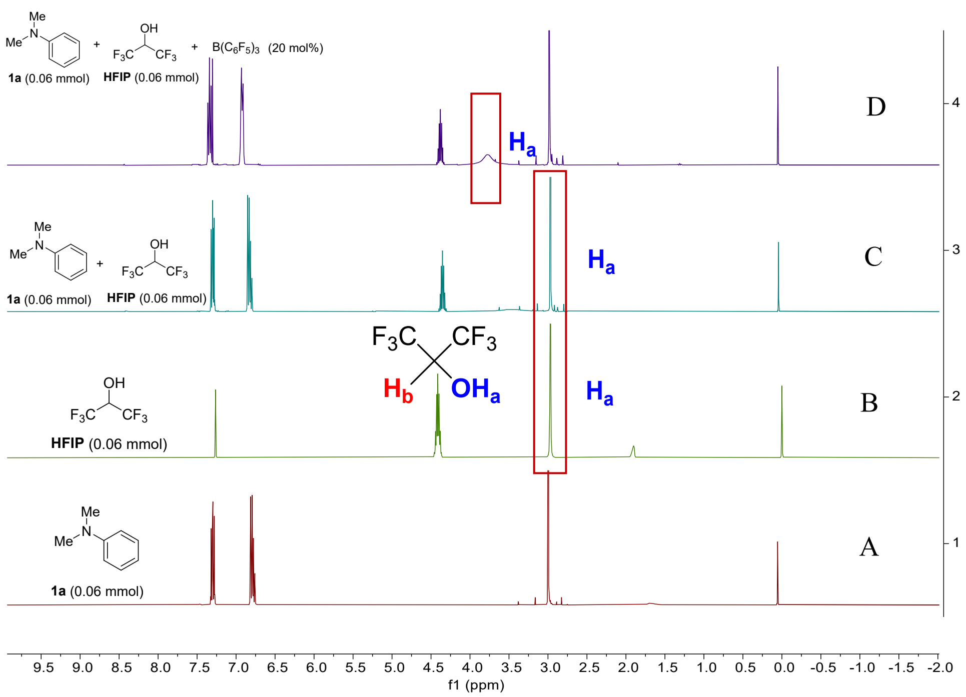


Figure S2 [1]H NMR of the individual species (A–B), the two binary mixture (C) and the ternary mixture (D).

Signal	**Species**		
	HFIP	**Binary mixture (1a : HFIP)**	**Ternary mixture (1a : HFIP : $B(C_6F_5)_3$)**
OHa (HFIP)	2.99, d, $J = 8.1$ Hz	No significant change	3.74, br s (+0.75)

Table S2. Significant changes for the ternary mixture with respect to individual species and the binary mixture.

The most significant changes found in [1]H NMR for the **1a** : HFIP : $B(C_6F_5)_3$) ternary mixture (Figure S2D) compared to the individual specie (Figure S2B) and **1a** : HFIP binary mixture (Figure S2C) are the downfield shift (deshieled) of the OH (HFIP), from a frequency of 2.99 ppm to 3.74 ppm ($\Delta\delta = 0.75$), supporting a stronger interaction between HFIP–$B(C_6F_5)_3$ adduct and **1a** in solution *vs* Figure S1 (Table S2).

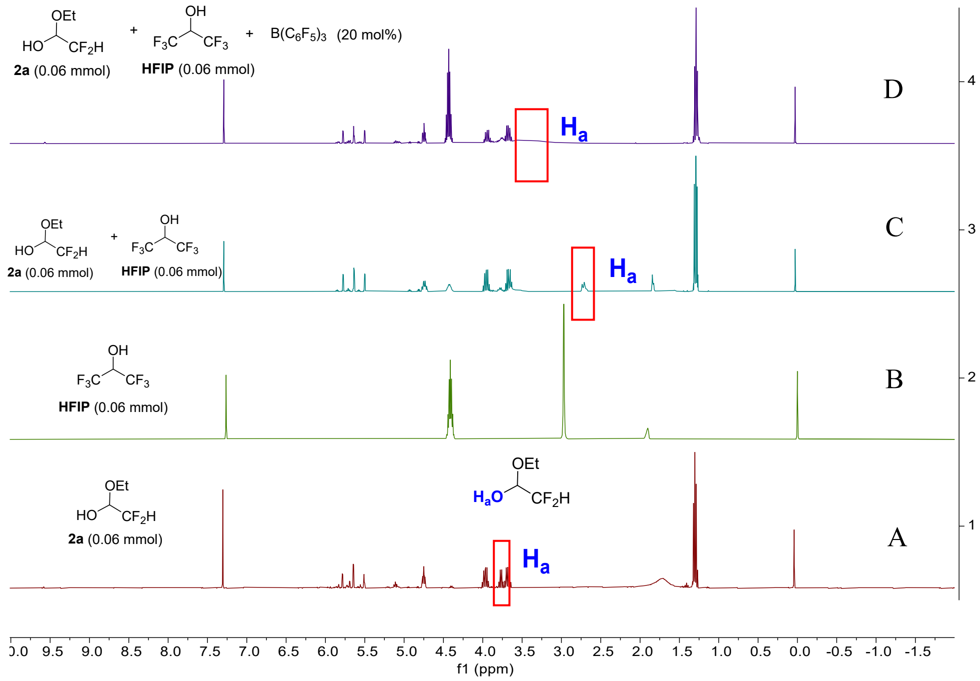


Figure S3 ^{1}H NMR of the individual species (A–B), the two binary mixture (C) and the ternary mixture (D).

Signal	Species		
	HFIP	**Binary mixture (HFIP : B($C_6F_5)_3$)**	**Ternary mixture (2a : HFIP : B($C_6F_5)_3$)**
OHa (2a)	3.77, q, J = 7.0 Hz	2.72, d, J = 10.4 Hz (-1.05)	3.41, br s (-0.36)

Table S3. Significant changes for the ternary mixture with respect to individual species and the binary mixture.

The most significant changes found in ^{1}H NMR for the **2a** : HFIP : B($C_6F_5)_3$) ternary mixture (Figure S3D) and **2a** : HFIP binary mixture (Figure S3C) compared to the individual specie (Figure S3A) are the upfield shift of the OH (**2a**), from a frequency of 3.77 ppm to 2.72 ppm ($\Delta\delta$ = 1.05) and 3.74 ppm ($\Delta\delta$ = 0.36), respectively. These data support strong interactions between HFIP and **2a** as well as HFIP–B($C_6F_5)_3$ adduct and **2a** (Table S3).

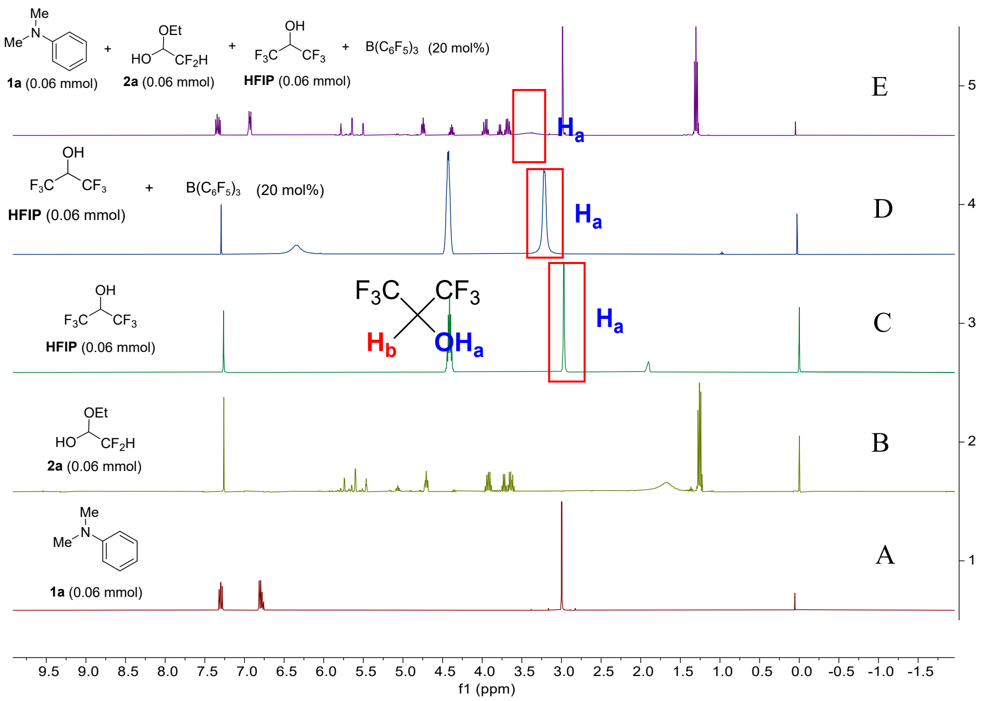


Figure S4 ^{1}H NMR of the individual species (A–C), the two binary mixture (D) and the quaternary mixture (E).

Signal	**Species**		
	HFIP	**Binary mixture (1a : HFIP)**	**Quaternary mixture (1a : 2a : HFIP : B(C_6F_5)$_3$)**
OHa (HFIP)	2.99, d, *J* = 8.1 Hz	3.18, d, *J* = 5.1 Hz (+0.19)	3.49, br s (+0.50) for binary mixture (+0.31)

Table S4. Significant changes for the quaternary mixture with respect to individual species and the two binary mixture.

The most significant changes found in ^{1}H NMR for the **1a** : **2a** : HFIP : B(C_6F_5)$_3$) quaternary mixture (Figure S4E) compared to the individual specie (Figure S4C) and HFIP : B(C_6F_5)$_3$) binary mixture (Figure S4D) are the downfield shift (deshieled) of the OH (HFIP), from a frequency of 2.99 ppm to 3.49 ppm (Δδ = 0.50) and 3.18 ppm to 3.49 ppm (Δδ = 0.31), further supporting strong interactions between HFIP–B(C_6F_5)$_3$ adduct and the two reactants (Table S4).

5.2. ^{19}F NMR study

^{19}F NMR of individual species (HFIP, $B(C_6F_5)_3$) and binary mixture (HFIP : $B(C_6F_5)_3$) were recorded at a 0.06 mmol scale of HFIP, 0.012 mmol (20 mol%) scale of $B(C_6F_5)_3$ and 0.6 mL $CDCl_3$.

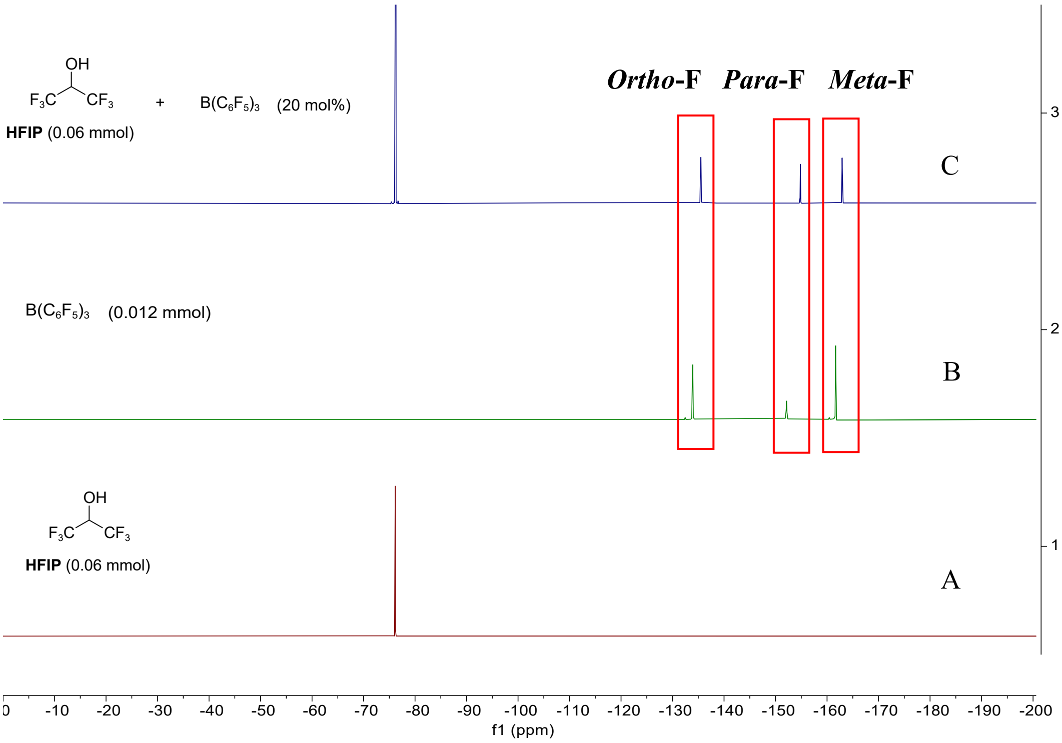


Figure S5 ^{19}F NMR of the individual species (A, B) and the two binary mixture (C).

Signal	**Species**		
	HFIP	**$B(C_6F_5)_3$**	**Binary mixture (HFIP : $B(C_6F_5)_3$)**
CF_3 of (HFIP)	-76.15, d, J = 5.9 Hz	–	-76.19, d, J = 5.8 Hz
***Ortho*-F of ($B(C_6F_5)_3$)**	–	-133.90, d, J = 18.5 Hz	-135.49, dd, J = 22.8, 7.3 Hz (-1.75)
***Meta*-F of ($B(C_6F_5)_3$)**	–	-161.67, td, J = 23.0, 8.6 Hz	-162.93 (td, J = 23.0, 8.6 Hz) (-1.26)
***Para*-F of ($B(C_6F_5)_3$)**	–	-152.14, s	-154.82, t, J = 20.0 Hz (-2.68)

Table S5. Significant changes for the binary mixture with respect to individual species.

The most significant changes found in ^{19}F NMR for the binary mixture (Figure S5C) compared to the individual species (Figure S5A–B) are the upfield shift of the *ortho*-F, *meta*-F and *para*-F of $B(C_6F_5)_3$ about 1.75 ppm, 1.26 ppm and 2.68 ppm, respectively (Table S5). These results also suggest a strong interaction between $B(C_6F_5)_3$ and HFIP in solution presumably through coordination of the hydroxyl oxygen atom of HFIP to the boron atom in $B(C_6F_5)_3$ as the observations in FigureS1.

5.3. ^{1}H NMR titration studies with 4 and HFIP with gradual addition of $B(C_6F_5)_3$

To evaluate the interaction between the catalyst and substrate in the reaction profile, the mixture of **4** and HFIP was titrated with $B(C_6F_5)_3$ (0 mol%, 20.0 mol%, 50.0 mol%, and 100.0 mol%) and the process was monitored by ^{1}H NMR (Figure S6). A gradual downfield shift of the –OH proton of HFIP was noticed with the sequential addition of $B(C_6F_5)_3$. The initial broad –OH peak at 2.99 ppm for pure HFIP in $CDCl_3$ solvent shifted to around 3.41 ppm with the addition of 20.0 mol% of $B(C_6F_5)_3$. Furthermore, with the sequential addition of more $B(C_6F_5)_3$ the –OH peak shifted further downfield to 4.07 ppm (with 1.0 equiv. of $B(C_6F_5)_3$). The signal for the C–H proton of HFIP was almost unchanged even with the addition of 1.0 equiv. of $B(C_6F_5)_3$. This further indicates that the –OH protons of HFIP interact with the $B(C_6F_5)_3$. Furthermore, the gradual downfield shift of the aromatic H of **4** was noticed with the sequential addition of $B(C_6F_5)_3$, which also supporting potential interactions between **4** and HFIP–$B(C_6F_5)_3$ adduct.

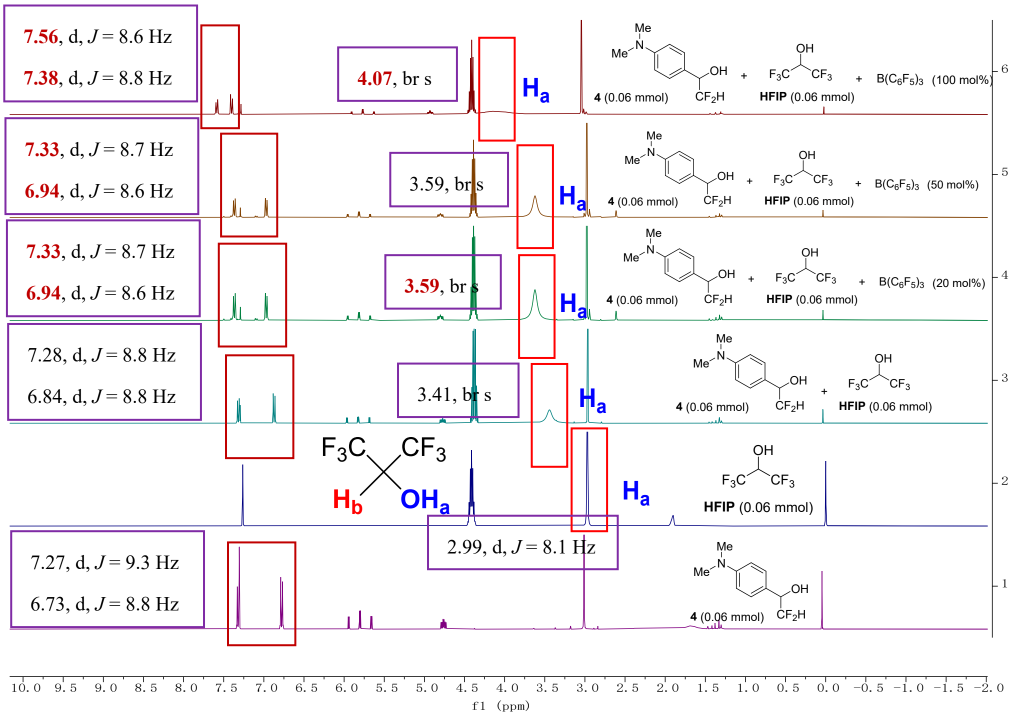


Figure S6 ^{1}H NMR titration studies with **4** and HFIP with gradual addition of $B(C_6F_5)_3$

In 4th NMR tube having stock solution of **4** and HFIP (0.06 mmol each) 20 mol% $B(C_6F_5)_3$ (6.1 mg), 0.6 mL of $CDCl_3$ was added and NMR 4 was recorded immediately.

In 5th NMR tube having stock solution of **4** and HFIP (0.06 mmol each) 50 mol% $B(C_6F_5)_3$ (15.3 mg), 0.6 mL of $CDCl_3$ was added and NMR 5 was recorded immediately.

In 6th NMR tube having stock solution of **4** and HFIP (0.06 mmol each) 100 mol% $B(C_6F_5)_3$ (30.7 mg), 0.6 mL of $CDCl_3$ was added and NMR 6 was recorded immediately.

2.99, d, J = 8.1 Hz

5.4. The HFIP–$B(C_6F_5)_3$ adduct capture experiment

$B(C_6F_5)_3$ (0.1 mmol) was dissolved in HFIP (1.0 mL). The solution was determined by the HRMS. The peak of $[B(C_6F_5)_3][HFIP]$ was detected [HRMS (ESI) Calcd for $[C_{21}HBF_{21}O]^-$: 678.9790, Found: 678.9794].

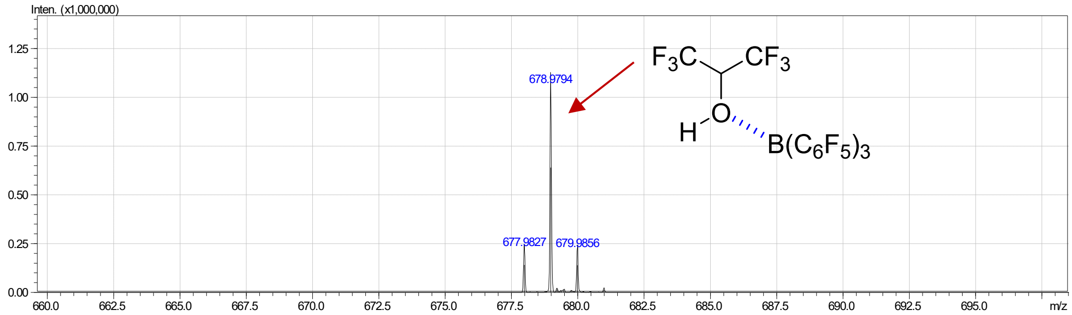


Figure S7

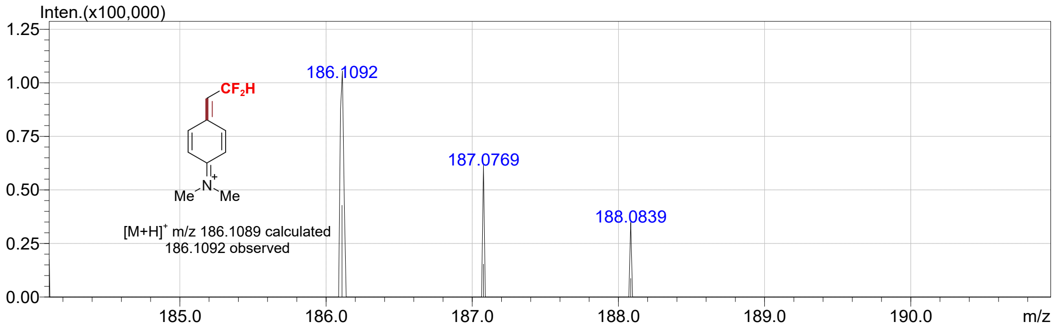
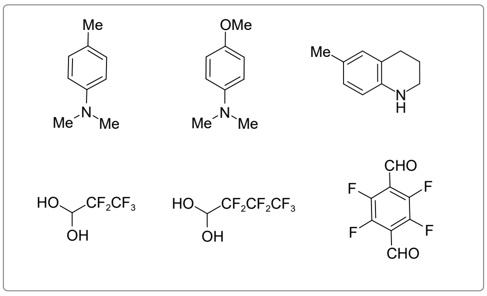


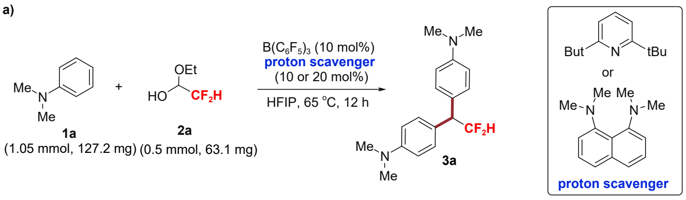
Figure S8

6. Unsuccessful substrates



7. Control experiments

a)



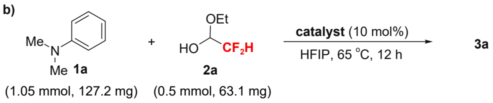
For the addition of 10 mol% 2,6-di-tert-butylpyridine, 35% yield of **3a** (53.4 mg) along with 19% yield of **4** (19.2 mg) were obtained and 9% of **1a** (11.5 mg) recovered.

For the addition of 20 mol% 2,6-di-tert-butylpyridine, 31% yield of **3a** (47.3 mg) along with 24% yield of **4** (24.3 mg) were obtained and 13% of **1a** (16.5 mg) recovered.

For the addition of 10 mol% *N,N,N',N'*-tetramethyl-1,8-naphthalenediamine, 39% yield of **3a** (59.5 mg) along with 14% yield of **4** (14.1 mg) were obtained and 11% of **1a** (13.9 mg) recovered.

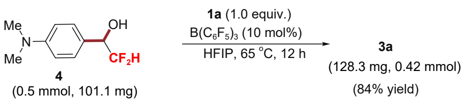
For the addition of 20 mol% *N,N,N',N'*-tetramethyl-1,8-naphthalenediamine, 32% yield of **3a** (48.8 mg) along with 17% yield of **4** (17.2 mg) were obtained and 15% of **1a** (19.1 mg) recovered.

b)



catalyst	**3a** yield
$[PhNMe_2H][B(C_6F_5)_4]$	19.9 mg, 13% yield (with 28.3 mg of **4** obtained simultaneously, 28% yield)
$[Ph_3C][B(C_6F_5)_4]$	24.3 mg, 16% yield (with 34.4 mg of **4** obtained simultaneously, 34% yield)

c)

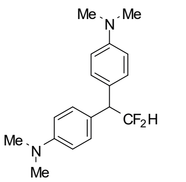


a) To a 25 mL Schlenk tube was added aniline **1a** (1.05 mmol, 127.2 mg, 2.1 equiv.), **2a** (0.5 mmol, 63.1 mg, 1.0 equiv.), $B(C_6F_5)_3$ (0.05 mmol, 25.6 mg, 0.1 equiv.) and 2,6-di-tert-butylpyridine or *N*,*N*,*N'*,*N'*-tetramethyl-1,8-naphthalenediamine (10 or 20 mol %) as a proton scavenger, then 2.5 mL HFIP was added. The resulting mixture was stirred at 65 °C in an oil bath for 12 hours according to the optimized reaction conditions. Then the mixture was concentrated under reduced pressure. The residue was purified by column chromatography to afford the corresponding products as shown in the figure above.

b) To a 25 mL Schlenk tube was added aniline **1a** (1.05 mmol, 127.2 mg, 2.1 equiv.), **2a** (0.5 mmol, 63.1 mg, 1.0 equiv.), $[PhNMe_2H][B(C_6F_5)_4]$ (0.05 mmol, 40.1 mg, 0.1 equiv.) or $[Ph_3C][B(C_6F_5)_4]$ (0.05 mmol, 46.1 mg, 0.1 equiv.), then 2.5 mL HFIP was added. The resulting mixture was stirred at 65 °C in an oil bath for 12 hours according to the optimized reaction conditions. Then the mixture was concentrated under reduced pressure. The residue was purified by column chromatography to afford the corresponding products as shown in the figure above.

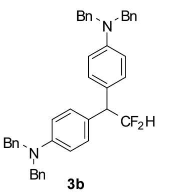
c) To a 25 mL Schlenk tube was added **4** (0.5 mmol, 101.1 mg), aniline **1a** (0.5 mmol, 60.5 mg, 1.0 equiv.), $B(C_6F_5)_3$ (0.05 mmol, 25.6 mg, 0.1 equiv.), then 2.5 mL HFIP was added. The resulting mixture was stirred at 65 °C in an oil bath for 12 hours according to the optimized reaction conditions. Then the mixture was concentrated under reduced pressure. The residue was purified by column chromatography to afford the desired product **3a** (white solid, 128.3 mg, 0.42 mmol, 84% yield).

8. Characterization data of the products



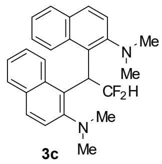
3a

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*,*N*-dimethylaniline) (3a): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **3a** (white solid, 124.8 mg, 0.41 mmol, 81% yield). M.p.: 72–74 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (d, J = 8.7 Hz, 4H), 6.69 (d, J = 8.8 Hz, 4H), 6.22 (td, J = 56.4, 4.5 Hz, 1H), 4.23 (td, J = 16.2, 4.4 Hz, 1H), 2.93 (s, 12H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.92 (dd, J = 56.5, 16.9 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 129.6, 125.5 (t, $^3J_{C-F}$ = 3.6 Hz), 117.5 (t, $^1J_{C-F}$ = 243.9 Hz), 112.6, 53.2 (t, $^2J_{C-F}$ = 20.4 Hz), 40.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}F_2N_2$: 305.1824, Found: 305.1823.



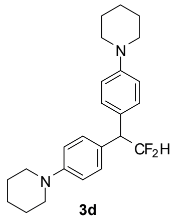
3b

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*,*N*-dibenzylaniline) (3b): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **3b** (white solid, 222.1 mg, 0.37 mmol, 73% yield). M.p.: 112–113 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (t, J = 7.3 Hz, 8H), 7.24 (t, J = 8.6 Hz, 12H), 7.07 (d, J = 8.6 Hz, 4H), 6.66 (d, J = 8.6 Hz, 4H), 6.15 (td, J = 56.4, 4.3 Hz, 1H), 4.62 (s, 8H), 4.13 (td, J = 16.3, 4.2 Hz, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.77 (dd, J = 56.5, 16.5 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.2, 138.5 , 129.7, 128.6, 126.9, 126.6, 125.5 (t, $^{1}J_{C-F}$ = 3.5 Hz), 117.5 (t, $^{1}J_{C-F}$ = 244.2 Hz), 112.23, 54.2, 53.3 (t, $^{2}J_{C-F}$ = 20.4 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{42}H_{39}F_2N_2$: 609.3076, Found: 609.3080.



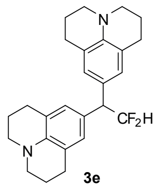
3c

1,1'-(2,2-difluoroethane-1,1-diyl)bis(*N*,*N*-dimethylnaphthalen-2-amine) (3c): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **3c** (white solid, 139.6 mg, 0.35 mmol, 69% yield). M.p.: 50–52 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.32 – 8.28 (m, 2H), 8.08 – 8.03 (m, 2H), 7.50 – 7.41 (m, 6H), 7.01 (d, J = 7.9 Hz, 2H), 6.56 (td, J = 55.7, 4.2 Hz, 1H), 5.90 (td, J = 14.5, 4.1 Hz, 1H), 2.87 (s, 12H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.77 (dd, J = 56.2, 14.3 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.6, 133.0, 129.3, 127.8 (t, $^{3}J_{C-F}$ = 3.2 Hz), 126.5, 126.4, 125.0, 124.9, 123.6, 117.9 (t, $^{1}J_{C-F}$ = 245.0 Hz), 113.3, 45.2, 44.7 (t, $^{2}J_{C-F}$ = 20.6 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{27}F_2N_2$: 405.2137, Found: 405.2139.



3d

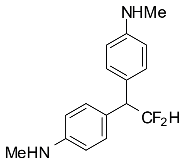
1,1'-((2,2-difluoroethane-1,1-diyl)bis(4,1-phenylene))dipiperidine (3d): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3d** (white solid, 151.9 mg, 0.39 mmol, 79% yield). M.p.: 79–81 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.16 (t, J = 8.6 Hz, 4H), 6.89 (d, J = 8.8 Hz, 4H), 6.21 (td, J = 56.3, 5.1 Hz, 1H), 4.38 – 4.06 (m, 1H), 3.13 (s, 8H), 1.69 (s, 8H), 1.56 (s, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.95 (ddd, J = 56.3, 15.8, 8.3 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.2, 129.5, 127.8 (t, $^{3}J_{C-F}$ = 3.6 Hz), 117.3 (t, $^{1}J_{C-F}$ = 244.1 Hz), 116.2, 53.3 (t, $^{2}J_{C-F}$ = 20.5 Hz), 50.3 , 25.8 , 24.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{24}H_{31}F_2N_2$: 385.2450, Found: 385.2449.



3e

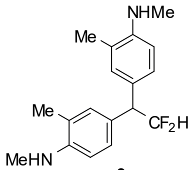
9,9'-(2,2-difluoroethane-1,1-diyl)bis(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline) (3e): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3e** (white solid, 175.7 mg, 0.43 mmol, 86% yield). M.p.: 90–92 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.72 (s, 4H), 6.17 (td, J = 56.6, 4.5 Hz, 1H), 3.98 (td, J = 16.3, 4.4 Hz, 1H), 3.19 – 3.03 (m, 8H), 2.74 (t, J = 6.5 Hz, 8H), 1.96 (p, J = 6.0 Hz, 8H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.52 (dd, J = 56.5, 16.7 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.0, 127.3, 124.9 (t, $^{3}J_{C-F}$ = 3.4 Hz), 121.4, 117.7 (t, $^{1}J_{C-F}$ = 243.7 Hz), 53.6 (t, $^{2}J_{C-F}$ = 20.3

Hz), 49.9, 27.6, 22.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{26}H_{31}F_2N_2$: 409.2450, Found: 409.2456.



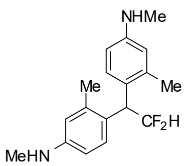
3f

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*-methylaniline) (3f): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **3f** (pale yellow oil, 114.7 mg, 0.41 mmol, 83% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (d, J = 8.5 Hz, 4H), 6.58 (d, J = 8.6 Hz, 4H), 6.21 (td, J = 56.4, 4.4 Hz, 1H), 4.21 (td, J = 16.2, 4.3 Hz, 1H), 3.46 (s, 2H), 2.82 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.93 (dd, J = 56.2, 16.0 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.3, 129.7, 126.3 (t, $^3J_{C-F}$ = 3.7 Hz), 117.5 (t, $^1J_{C-F}$ = 243.9 Hz), 112.4, 53.4 (t, $^2J_{C-F}$ = 20.4 Hz), 30.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{19}F_2N_2$: 277.1511, Found: 277.1510.



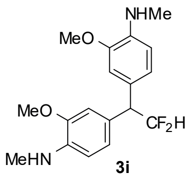
3g

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*,2-dimethylaniline) (3g): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **3g** (yellow solid, 132.4 mg, 0.44 mmol, 87% yield). M.p.: 70–72 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.13 (dd, J = 8.2, 2.0 Hz, 2H), 7.01 (d, J = 1.4 Hz, 2H), 6.60 (d, J = 8.3 Hz, 2H), 6.25 (td, J = 56.4, 4.6 Hz, 1H), 4.20 (td, J = 16.2, 4.5 Hz, 1H), 3.57 (s, 2H), 2.90 (s, 6H), 2.13 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.74 (dd, J = 56.4, 15.7 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.2, 130.6, 127.4, 126.0 (t, $^3J_{C-F}$ = 3.7 Hz), 122.0, 117.6 (t, $^1J_{C-F}$ = 243.8 Hz), 109.1, 53.5 (t, $^2J_{C-F}$ = 20.4 Hz), 30.7, 17.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}F_2N_2$: 305.1824, Found: 305.1821.



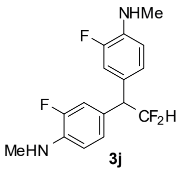
3h

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*,3-dimethylaniline) (3h): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **3h** (yellow solid, 112.6 mg, 0.37 mmol, 74% yield). M.p.: 89–91 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.08 (d, J = 8.9 Hz, 2H), 6.44 (d, J = 5.8 Hz, 4H), 6.21 (dd, J = 56.2, 4.6 Hz, 1H), 4.56 (td, J = 14.9, 4.5 Hz, 1H), 3.44 (s, 2H), 2.81 (s, 6H), 2.26 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.97 (dd, J = 56.3, 14.5 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 148.0, 137.8, 128.9, 124.9 (t, $^3J_{C-F}$ = 3.5 Hz), 118.3 (t, $^1J_{C-F}$ = 243.4 Hz), 114.7, 109.8, 45.4 (t, $^2J_{C-F}$ = 20.5 Hz), 30.7, 20.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}F_2N_2$: 305.1824, Found: 305.1822.



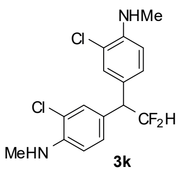
3i

4,4'-(2,2-difluoroethane-1,1-diyl)bis(2-methoxy-*N*-methylaniline) (3i): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (15/1 to 10/1, v/v) as eluent to give compound **3i** (white solid, 159.8 mg, 0.48 mmol, 95% yield). M.p.: 94–96 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.86 (dd, J = 8.0, 1.6 Hz, 2H), 6.70 (d, J = 1.5 Hz, 2H), 6.56 (d, J = 8.1 Hz, 2H), 6.24 (td, J = 56.4, 4.3 Hz, 1H), 4.23 (td, J = 16.2, 4.3 Hz, 1H), 4.22 (s, 2H), 3.81 (s, 6H), 2.86 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.55 (dd, J = 56.5, 16.6 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.8, 138.4, 125.5 (t, $^{3}J_{C-F}$ = 3.5 Hz), 121.5, 117.5 (t, $^{1}J_{C-F}$ = 244.1 Hz), 110.3, 109.0, 55.4, 54.0 (t, $^{2}J_{C-F}$ = 20.3 Hz), 30.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{23}F_2N_2O_2$: 337.1723, Found: 337.1719.



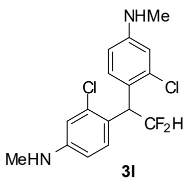
3j

4,4'-(2,2-difluoroethane-1,1-diyl)bis(2-fluoro-*N*-methylaniline) (3j): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **3j** (yellow solid, 99.7 mg, 0.32 mmol, 64% yield). M.p.: 44–46 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.14 (t, J = 8.5 Hz, 2H), 6.51 – 6.10 (m, 5H), 4.81 (td, J = 15.5, 4.8 Hz, 1H), 3.80 (s, 2H), 2.79 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.33 (d, J = 9.1 Hz, 2F), -118.40 (dd, J = 56.4, 15.8 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.8 (d, $^{1}J_{C-F}$ = 244.1 Hz), 150.2 (d, $^{3}J_{C-F}$ = 11.5 Hz), 130.3 (d, $^{3}J_{C-F}$ = 6.2 Hz), 116.5 (t, $^{1}J_{C-F}$ = 243.9 Hz), 111.9 (dt, $^{3}J_{C-F}$ = 15.3, 3.6 Hz), 108.5, 99.0 (d, $^{2}J_{C-F}$ = 26.9 Hz), 40.4 (t, $^{2}J_{C-F}$ = 22.4 Hz), 30.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}F_4N_2$: 313.1323, Found: 313.1320.



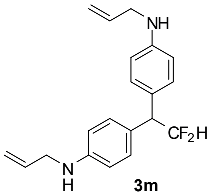
3k

4,4'-(2,2-difluoroethane-1,1-diyl)bis(2-chloro-*N*-methylaniline) (3k): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **3k** (yellow solid, 120.8 mg, 0.35 mmol, 70% yield). M.p.: 59–61 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.17 (d, J = 2.0 Hz, 2H), 7.09 (dd, J = 8.4, 2.0 Hz, 2H), 6.61 (d, J = 8.4 Hz, 2H), 6.17 (td, J = 56.1, 4.1 Hz, 1H), 4.35 (s, 2H), 4.15 (td, J = 16.2, 4.0 Hz, 1H), 2.89 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.15 (dd, J = 55.9, 14.9 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.2, 129.4, 128.4, 125.7 (t, $^{3}J_{C-F}$ = 3.5 Hz), 119.1, 116.8 (t, $^{1}J_{C-F}$ = 244.6 Hz), 110.6, 52.8 (t, $^{2}J_{C-F}$ = 20.8 Hz), 30.4; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}F_2Cl_2N_2$: 345.0732, Found: 345.0731.



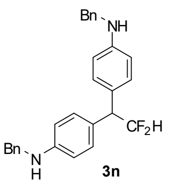
3l

4,4'-(2,2-difluoroethane-1,1-diyl)bis(3-chloro-*N*-methylaniline) (3l): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **3l** (white solid, 129.4 mg, 0.38 mmol, 75% yield). M.p.: 77–79 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.5 Hz, 2H), 6.63 (s, 2H), 6.47 (d, *J* = 8.6 Hz, 2H), 6.24 (td, *J* = 55.7, 3.3 Hz, 1H), 5.25 (td, *J* = 16.7, 3.1 Hz, 1H), 3.74 (s, 2H), 2.78 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -119.08 (dd, *J* = 54.9, 16.7 Hz); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.2, 135.5, 130.3, 122.1 (t, $^{3}J_{C-F}$ = 2.8 Hz), 116.8 (t, $^{1}J_{C-F}$ = 245.3 Hz), 112.6, 111.1, 45.8 (t, $^{2}J_{C-F}$ = 20.9 Hz), 30.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{16}H_{17}F_2Cl_2N_2$: 345.0732, Found: 345.0730.



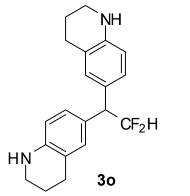
3m

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*-allylaniline) (3m): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3m** (pale yellow oil, 90.3 mg, 0.28 mmol, 55% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.12 (d, *J* = 8.4 Hz, 4H), 6.60 (d, *J* = 8.6 Hz, 4H), 6.21 (td, *J* = 56.4, 4.4 Hz, 1H), 5.96 (ddd, *J* = 22.5, 10.5, 5.4 Hz, 2H), 5.30 (dd, *J* = 17.2, 1.5 Hz, 2H), 5.18 (dd, *J* = 10.3, 1.4 Hz, 2H), 4.20 (td, *J* = 16.2, 4.3 Hz, 1H), 3.77 (d, *J* = 5.4 Hz, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.89 (dd, *J* = 56.4, 16.7 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.1, 135.4, 129.7, 126.4 (t, $^{3}J_{C-F}$ = 3.6 Hz), 117.4 (t, $^{1}J_{C-F}$ = 244.0 Hz), 116.2 , 112.9 , 53.3 (t, $^{2}J_{C-F}$ = 20.3 Hz), 46.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{23}F_2N_2$: 329.1824, Found: 329.1824.



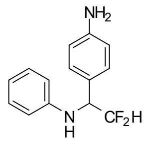
3n

4,4'-(2,2-difluoroethane-1,1-diyl)bis(*N*-benzylaniline) (3n): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3n** (yellow solid, 113.6 mg, 0.26 mmol, 53% yield). M.p.: 117–119 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.42 – 7.34 (m, 8H), 7.33 – 7.27 (m, 2H), 7.12 (d, *J* = 8.5 Hz, 4H), 6.61 (d, *J* = 8.6 Hz, 4H), 6.21 (td, *J* = 56.3, 4.4 Hz, 1H), 4.32 (s, 4H), 4.20 (td, *J* = 16.2, 4.3 Hz, 1H), 4.05 (s, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.86 (dd, *J* = 56.5, 16.9 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.2, 139.3, 129.8, 128.6, 127.5, 127.2, 126.5 (t, $^{3}J_{C-F}$ = 3.5 Hz), 117.4 (t, $^{1}J_{C-F}$ = 244.1 Hz), 112.8, 53.4 (t, $^{2}J_{C-F}$ = 20.3 Hz), 48.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{28}H_{27}F_2N_2$: 429.2137, Found: 429.2132.



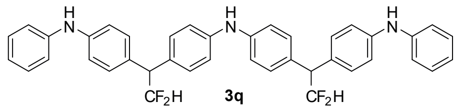
3o

6,6'-(2,2-difluoroethane-1,1-diyl)bis(1,2,3,4-tetrahydroquinoline) (3o): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3o** (yellow oil, 116.4 mg, 0.36 mmol, 71% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.01 – 6.79 (m, 4H), 6.44 (d, *J* = 8.1 Hz, 2H), 6.20 (td, *J* = 56.5, 4.6 Hz, 1H), 4.24 – 3.97 (m, 1H), 3.64 (s, 2H), 3.35 – 3.13 (m, 4H), 2.76 (t, *J* = 6.4 Hz, 4H), 1.94 (ddd, *J* = 15.3, 7.6, 4.4 Hz, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.67 (dd, *J* = 56.5, 16.8 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.7 , 130.0 , 127.1 , 126.0 (t, $^3J_{C-F}$ = 3.6 Hz), 121.4 , 117.6 (t, $^1J_{C-F}$ = 243.9 Hz), 114.1 , 53.6 (t, $^2J_{C-F}$ = 20.4 Hz), 41.9 , 26.9 , 22.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{23}F_2N_2$: 329.1824, Found: 329.1820.



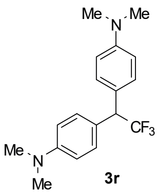
3p

***N*-(1-(4-aminophenyl)-2,2-difluoroethyl)aniline (3p):** The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **3p** (yellow oil, 45.9 mg, 0.19 mmol, 37% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.3 Hz, 2H), 7.14 (t, *J* = 7.9 Hz, 2H), 6.73 (t, *J* = 7.3 Hz, 1H), 6.68 (d, *J* = 8.4 Hz, 2H), 6.62 (d, *J* = 7.8 Hz, 2H), 5.94 (td, *J* = 56.0, 3.0 Hz, 1H), 4.59 (td, *J* = 13.2, 2.8 Hz, 1H), 4.28 (s, 1H), 3.61 (s, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -124.94 (ddd, *J* = 277.4, 56.1, 13.2 Hz, 1F), -127.21 (ddd, *J* = 277.4, 56.0, 13.2 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 146.6, 146.2, 129.2, 128.7, 125.0 (dd, $^3J_{C-F}$ = 3.4, 1.2 Hz), 118.5, 116.0 (t, $^1J_{C-F}$ = 246.9 Hz), 115.3, 113.9, 59.7 (t, $^2J_{C-F}$ = 21.8 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{14}H_{15}F_2N_2$: 249.1198, Found: 249.1196.



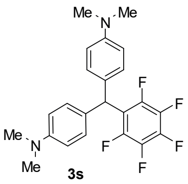
3q

bis(4-(2,2-difluoro-1-(4-(phenylamino)phenyl)ethyl)phenyl)amine (3q): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3q** (white solid, 72.6 mg, 0.12 mmol, 46% yield). M.p.: 142–144 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.35 – 7.29 (m, 6H), 7.24 (d, *J* = 8.4 Hz, 8H), 7.14 – 7.06 (m, 12H), 6.99 (t, *J* = 7.3 Hz, 2H), 6.30 (td, *J* = 56.1, 4.2 Hz, 2H), 4.33 (dt, *J* = 15.8, 8.0 Hz, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -118.02 (dd, *J* = 56.1, 16.1 Hz, 4F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.7, 142.4, 142.1, 129.9, 129.6, 129.3, 121.3, 118.1, 117.8, 117.6, 117.1 (t, $^1J_{C-F}$ = 244.3 Hz), 53.7 (t, $^2J_{C-F}$ = 20.5 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{40}H_{34}F_4N_3$: 632.2684, Found: 632.2689.



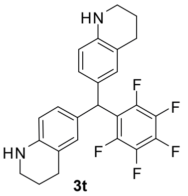
3r

4,4'-(2,2,2-trifluoroethane-1,1-diyl)bis(*N*,*N*-dimethylaniline) (3r): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **3r** (white solid, 111.2 mg, 0.34 mmol, 69% yield). M.p.: 115–117 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.22 (d, *J* = 8.6 Hz, 4H), 6.68 (d, *J* = 8.8 Hz, 4H), 4.49 (q, *J* = 10.2 Hz, 1H), 2.93 (s, 12H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -66.43 (d, *J* = 10.2 Hz, 3F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.8, 129.7, 126.8 (d, $^{1}J_{C-F}$ = 280.2 Hz), 123.8, 112.4, 53.8 (q, $^{2}J_{C-F}$ = 27.1 Hz), 40.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{22}F_3N_2$: 323.1730, Found: 323.1726.



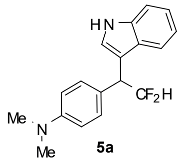
3s

4,4'-((perfluorophenyl)methylene)bis(*N*,*N*-dimethylaniline) (3s): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1, v/v) as eluent to give compound **3s** (pale green solid, 185.3 mg, 0.44 mmol, 88% yield). M.p.: 120–122 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.06 (d, *J* = 8.6 Hz, 4H), 6.67 (d, *J* = 8.8 Hz, 4H), 5.71 (s, 1H), 2.93 (s, 12H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –140.09 (dd, *J* = 23.8, 8.7 Hz, 2F), –157.48 (t, *J* = 21.4 Hz, 1F), –162.33 (td, *J* = 23.5, 8.9 Hz, 2F); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 149.4, 146.5 – 146.1 (m), 144.0 – 143.5 (m), 141.1 – 140.8 (m), 139.0 – 138.3 (m), 136.7 – 136.1 (m), 129.2, 128.3, 119.0 – 118.4 (m), 112.4, 44.1, 40.5; **HRMS** (ESI) m/z: $[M + Na]^+$ Calcd for $C_{23}H_{21}F_5N_2Na$ 443.1517; Found 443.1523.

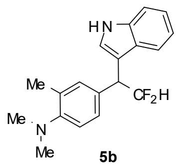


3t

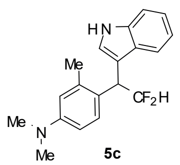
6,6'-((perfluorophenyl)methylene)bis(1,2,3,4-tetrahydroquinoline) (3t): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (10/1, v/v) as eluent to give compound **3t (**white solid, 188.9 mg, 0.42 mmol, 85% yield). M.p.: 93–95 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 6.76 (d, J = 9.5 Hz, 4H), 6.56 – 6.28 (m, 2H), 5.57 (s, 1H), 3.80 (s, 2H), 3.38 – 3.14 (m, 4H), 2.69 (t, J = 6.4 Hz, 4H), 2.02 – 1.77 (m, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ –139.98 (dd, J = 24.3, 7.2 Hz, 2F), –157.72 (t, J = 21.6 Hz, 1F), –162.43 (td, J = 23.4, 8.8 Hz, 2F); **^{13}C{^{1}H} NMR** (100 MHz, $CDCl_3$) δ 146.4 – 146.2 (m), 143.9 – 143.7 (m), 143.5, 136.6 – 136.3 (m), 136.7 – 136.2 (m), 129.6, 128.8, 126.9, 121.3, 119.1 – 118.7 (m), 114.0, 44.4, 41.9, 27.0, 22.1; **HRMS** (ESI) m/z: $[M - H]^-$ Calcd for $C_{25}H_{20}F_5N_2$ 443.1541; Found 443.1537.


5a

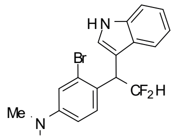
4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*,*N*-dimethylaniline (5a): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5a** (white solid, 129.6 mg, 0.43 mmol, 85% yield). M.p.: 124–126 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.41 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.2 Hz, 1H), 7.23 (d, *J* = 8.6 Hz, 3H), 7.18 (t, *J* = 7.3 Hz, 1H), 7.05 (t, *J* = 7.5 Hz, 1H), 6.70 (d, *J* = 7.8 Hz, 2H), 6.25 (td, *J* = 56.5, 3.7 Hz, 1H), 4.62 (td, *J* = 16.4, 3.5 Hz, 1H), 2.92 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.61 (ddd, *J* = 274.3, 56.5, 16.4 Hz, 1F), -118.69 (ddd, *J* = 274.2, 56.5, 17.0 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 136.1, 129.9, 127.0, 122.4, 122.3, 119.7, 119.3, 117.4 (t, $^1J_{C-F}$ = 244.7 Hz), 112.7 (t, $^3J_{C-F}$ = 8.8 Hz), 112.2, 111.0, 46.2 (t, $^2J_{C-F}$ = 21.2 Hz), 40.7; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{19}F_2N_2$: 301.1511, Found: 301.1510.


5b

4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*,*N*,2-trimethylaniline (5b): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5b** (white solid, 114.7 mg, 0.36 mmol, 73% yield). M.p.: 129–131 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (s, 1H), 7.47 (d, *J* = 8.0 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.25 – 7.13 (m, 4H), 7.09 (t, *J* = 7.5 Hz, 1H), 6.98 (d, *J* = 8.1 Hz, 1H), 6.28 (td, *J* = 56.5, 3.7 Hz, 1H), 4.64 (td, *J* = 16.6, 3.6 Hz, 1H), 2.69 (s, 6H), 2.31 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.38 (ddd, *J* = 274.3, 56.4, 15.2 Hz, 1F), -118.48 (ddd, *J* = 274.4, 56.5, 17.1 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.8, 136.0, 131.9, 130.5 (t, $^3J_{C-F}$ = 2.8 Hz), 127.1, 127.0, 122.6, 122.3, 119.7, 119.1, 118.3, 117.3 (t, $^1J_{C-F}$ = 244.9 Hz), 111.9 (t, $^3J_{C-F}$ = 3.9 Hz), 111.1, 46.4 (t, $^2J_{C-F}$ = 21.0 Hz), 44.1; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}F_2N_2$: 315.1668, Found: 315.1667.

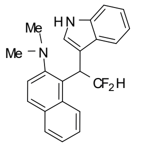

5c

4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*,*N*,3-trimethylaniline (5c): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5c** (white solid, 97.5 mg, 0.31 mmol, 62% yield). M.p.: 137–139 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.08 (s, 1H), 7.62 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.27 (d, *J* = 1.6 Hz, 1H), 7.23 (s, 1H), 7.22 – 7.16 (m, 2H), 7.13 – 7.06 (m, 2H), 6.28 (td, *J* = 56.7, 3.8 Hz, 1H), 5.63 (ddd, *J* = 18.7, 15.8, 3.7 Hz, 1H), 2.69 (s, 6H), 2.28 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.80 (ddd, *J* = 271.8, 56.6, 15.5 Hz, 1F), -118.61 (ddd, *J* = 273.6, 57.0, 18.4 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.7, 135.9, 133.7, 133.0 (t, $^3J_{C-F}$ = 3.0 Hz), 130.1, 128.8, 127.5, 122.9, 122.2, 120.9, 119.6, 119.4, 118.0 (t, $^1J_{C-F}$ = 245.1 Hz), 112.4 (t, $^3J_{C-F}$ = 3.7 Hz), 111.0, 46.0, 39.5 (t, $^{2}J_{C-F}$ = 21.2 Hz), 21.1; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}F_2N_2$: 315.1668, Found: 315.1666.



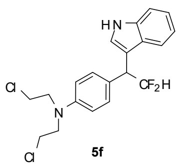
5d

3-bromo-4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*,*N*-dimethylaniline (5d): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5d** (white solid, 142.7 mg, 0.38 mmol, 75% yield). M.p.: 156–158 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.43 (d, *J* = 7.9 Hz, 1H), 7.36 (d, *J* = 8.1 Hz, 1H), 7.31 (s, 1H), 7.18 (t, *J* = 7.5 Hz, 1H), 7.11 (d, *J* = 8.7 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 1.9 Hz, 1H), 6.54 (d, *J* = 8.7 Hz, 1H), 6.26 (td, *J* = 56.2, 2.5 Hz, 2H), 5.28 (dd, *J* = 24.5, 8.9 Hz, 1H), 2.91 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.93 (ddd, *J* = 274.4, 56.3, 14.6 Hz, 1F), -120.92 (ddd, *J* = 277.1, 56.4, 17.6 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.5, 135.9, 130.9, 127.1, 125.9, 122.9 (dd, $^{3}J_{C-F}$ = 4.3, 1.9 Hz), 122.5, 122.3, 119.8, 119.3, 117.0 (t, $^{1}J_{C-F}$ = 245.5 Hz), 115.8, 111.8, 111.6 (dd, $^{3}J_{C-F}$ = 3.9, 1.6 Hz), 111.0, 44.7 (t, $^{2}J_{C-F}$ = 21.2 Hz), 40.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}BrF_2N_2$: 379.0616, Found: 379.0621.



5e

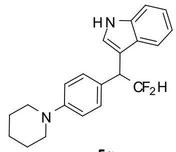
1-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*,*N*-dimethylnaphthalen-2-amine (5e): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5e** (white solid, 105.1 mg, 0.30 mmol, 60% yield). M.p.: 112–113 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.38 – 8.32 (m, 1H), 8.17 – 8.12 (m, 1H), 8.04 (s, 1H), 7.54 – 7.49 (m, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.19 (t, *J* = 7.5 Hz, 1H), 7.12 (s, 1H), 7.05 (dd, *J* = 17.9, 7.8 Hz, 2H), 6.46 (td, *J* = 56.2, 3.3 Hz, 1H), 5.58 – 5.47 (m, 1H), 2.89 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.66 (ddd, *J* = 274.4, 56.5, 13.9 Hz, 1F), -118.55 (ddd, *J* = 274.4, 56.3, 17.0 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.5, 136.1, 133.0, 129.2, 127.3 (dd, $^{3}J_{C-F}$ = 4.0, 3.1 Hz), 127.0, 126.3, 125.0, 124.9, 123.6, 123.4, 122.3, 119.7, 119.2, 117.6 (t, $^{1}J_{C-F}$ = 245.0 Hz), 113.5, 112.2 (t, $^{3}J_{C-F}$ = 3.5 Hz), 111.1, 45.2, 41.7 (t, $^{2}J_{C-F}$ = 21.4 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{21}F_2N_2$: 351.1668, Found: 351.1667.



5f

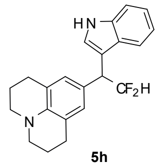
***N*,*N*-bis(2-chloroethyl)-4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)aniline (5f):** The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 15/1, v/v) as eluent to give compound **5f** (white solid, 99.3 mg, 0.25 mmol, 50% yield). M.p.: 136–138 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.00 (s, 1H), 7.39 (d, *J* = 8.0 Hz, 1H), 7.30 (d, *J* = 8.1 Hz, 1H), 7.19 (dd, *J* = 13.2, 7.6 Hz, 4H), 7.04 (t, *J* = 7.5 Hz, 1H), 6.56 (d, *J* = 8.4 Hz, 2H), 6.22 (td, *J* = 56.5, 3.3

Hz, 1H), 4.66 – 4.52 (m, 1H), 3.62 (t, J = 7.0 Hz, 4H), 3.53 (t, J = 6.7 Hz, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -116.99 (ddd, J = 274.4, 56.4, 14.6 Hz, 1F), -119.09 (ddd, J = 275.5, 56.5, 18.3 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 145.3, 136.0, 130.5, 126.8, 125.4 (t, $^3J_{C-F}$ = 2.7 Hz), 122.4, 122.3, 119.7, 119.1, 117.2 (t, $^1J_{C-F}$ = 244.8 Hz), 111.8 (dd, $^3J_{C-F}$ = 5.2, 2.8 Hz), 111.2, 53.3, 46.0 (t, $^2J_{C-F}$ = 21.1 Hz), 40.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{21}Cl_2F_2N_2$: 397.1045, Found: 397.1050.



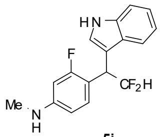
5g

3-(2,2-difluoro-1-(4-(piperidin-1-yl)phenyl)ethyl)-1*H*-indole (5g): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (25/1 to 15/1, v/v) as eluent to give compound **5g** (white solid, 107.3 mg, 0.31 mmol, 63% yield). M.p.: 111–113 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.09 (s, 1H), 7.39 (d, J = 8.0 Hz, 1H), 7.31 (d, J = 8.1 Hz, 1H), 7.22 (d, J = 8.8 Hz, 2H), 7.19 – 7.12 (m, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.87 (d, J = 8.7 Hz, 2H), 6.23 (td, J = 56.5, 3.7 Hz, 1H), 4.60 (td, J = 16.4, 3.6 Hz, 1H), 3.13 – 3.09 (m, 4H), 1.68 (dt, J = 11.2, 5.8 Hz, 4H), 1.54 (dt, J = 11.2, 5.8 Hz, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.53 (ddd, J = 274.2, 56.4, 15.1 Hz, 1F), -118.61 (ddd, J = 275.1, 56.5, 17.1 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 151.3 , 136.0 , 129.8 , 127.0 , 122.5 , 122.3 , 119.6 , 119.2 , 116.2 , 117.4 (t, $^1J_{C-F}$ = 244.8 Hz), 112.0 (t, $^3J_{C-F}$ = 3.9 Hz), 111.1 , 50.4 , 46.3 (t, $^2J_{C-F}$ = 21.0 Hz), 25.8 , 24.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{23}F_2N_2$: 341.1824, Found: 341.1819.



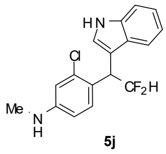
5h

9-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinoline (5h): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **5h** (white solid, 96.8 mg, 0.28 mmol, 55% yield). M.p.: 119–120 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.17 (s, 1H), 7.49 (d, J = 7.9 Hz, 1H), 7.36 (d, J = 8.1 Hz, 1H), 7.23 (s, 1H), 7.17 (t, J = 7.9 Hz, 1H), 7.07 (t, J = 7.1 Hz, 1H), 6.76 (s, 2H), 6.21 (td, J = 56.7, 3.7 Hz, 1H), 4.49 (td, J = 16.6, 3.6 Hz, 1H), 3.20 – 3.00 (m, 4H), 2.77 – 2.63 (m, 4H), 2.00 – 1.87 (m, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.79 (dd, J = 16.5, 7.4 Hz, 1F), -117.94 (dd, J = 16.6, 7.6 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 142.2, 136.0, 127.5, 127.2, 123.5 (t, $^3J_{C-F}$ = 3.2 Hz), 122.5, 122.2, 121.4, 119.6, 119.3, 117.6 (t, $^1J_{C-F}$ = 244.1 Hz), 112.4 (t, $^3J_{C-F}$ = 3.9 Hz), 111.0, 49.9, 46.3 (t, $^2J_{C-F}$ = 21.0 Hz), 27.7, 22.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{23}F_2N_2$: 353.1824, Found: 353.1820.



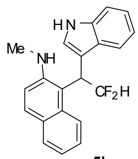
5i

4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-3-fluoro-*N*-methylaniline (5i): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5i** (yellow oil, 130.8 mg, 0.43 mmol, 86% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.48 (d, J = 7.9 Hz, 1H), 7.35 (d, J = 8.1 Hz, 1H), 7.20 (t, J = 7.2 Hz, 1H), 7.12 – 7.00 (m, 2H), 6.47 – 6.10 (m, 3H), 5.00 (td, J = 16.2, 3.6 Hz, 1H), 3.79 (brs, 1H), 2.78 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.34 – -117.47 (m, 1F), -118.35 (dd, J = 56.5, 16.6 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 161.9 (d, $^{1}J_{C-F}$ = 243.3 Hz), 150.3 (d, $^{3}J_{C-F}$ = 11.3 Hz), 135.9, 132.0 (d, $^{3}J_{C-F}$ = 10.1 Hz), 131.0 (d, $^{3}J_{C-F}$ = 5.9 Hz), 128.6 (d, $^{3}J_{C-F}$ = 12.0 Hz), 126.9, 122.6, 122.3, 119.7, 118.9, 116.9 (td, $^{1}J_{C-F}$ = 244.8, 1.3 Hz), 111.5 (t, $^{3}J_{C-F}$ = 3.4 Hz), 111.3 (t, $^{3}J_{C-F}$ = 3.2 Hz), 111.1, 108.7 (d, $^{3}J_{C-F}$ = 2.5 Hz), 98.8, 98.5, 39.0 (t, $^{2}J_{C-F}$ = 22.8 Hz), 30.5; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}F_3N_2$: 305.1261, Found: 305.1261.



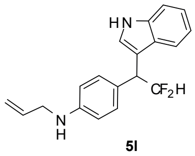
5j

3-chloro-4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*-methylaniline (5j): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5j** (yellow solid, 136.3 mg, 0.42 mmol, 85% yield). M.p.: 97–99 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.01 (s, 1H), 7.37 (d, J = 8.0 Hz, 1H), 7.29 (d, J = 8.1 Hz, 1H), 7.23 (d, J = 1.7 Hz, 1H), 7.20 – 7.11 (m, 3H), 7.04 (t, J = 7.5 Hz, 1H), 6.55 (d, J = 8.4 Hz, 1H), 6.19 (td, J = 56.4, 3.5 Hz, 1H), 4.63 – 4.49 (m, 1H), 4.28 (s, 1H), 2.81 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.10 (ddd, J = 274.6, 56.4, 14.4 Hz, 1F), -119.34 (ddd, J = 275.2, 56.5, 18.7 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 144.3, 136.0, 129.6, 128.7, 126.8, 125.1 (t, $^{3}J_{C-F}$ = 2.8 Hz), 122.4, 122.3, 119.7, 119.0, 118.9, 117.0 (t, $^{1}J_{C-F}$ = 244.8 Hz), 111.4 (dd, $^{3}J_{C-F}$ = 5.2, 2.6 Hz), 111.2, 110.4, 45.9 (t, $^{2}J_{C-F}$ = 21.2 Hz), 30.3; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{17}H_{16}ClF_2N_2$: 321.0965, Found: 321.0964.



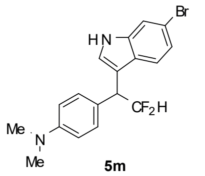
5k

1-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)-*N*-methylnaphthalen-2-amine (5k): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5k** (white solid, 99.2 mg, 0.29 mmol, 59% yield). M.p.: 87–89 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.13 (d, J = 8.1 Hz, 1H), 8.06 (s, 1H), 7.87 (d, J = 8.0 Hz, 1H), 7.46 (dq, J = 22.5, 7.8, 7.3 Hz, 4H), 7.34 (d, J = 8.1 Hz, 1H), 7.17 (dd, J = 15.2, 7.1 Hz, 2H), 7.03 (t, J = 7.5 Hz, 1H), 6.60 (d, J = 8.0 Hz, 1H), 6.58 – 6.28 (m, 1H), 5.53 – 5.38 (m, 1H), 3.00 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.66 (ddd, J = 274.1, 56.3, 12.7 Hz, 1F), -118.57 (ddd, J = 274.1, 56.4, 17.0 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 143.7, 136.1, 132.5, 127.1 (d, $^{3}J_{C-F}$ = 2.5 Hz), 126.3, 124.6, 124.0, 123.8, 123.5, 122.2, 120.6, 119.7, 119.3, 117.7 (t, $^{1}J_{C-F}$ = 245.0 Hz), 112.5 (t, $^{3}J_{C-F}$ = 3.4 Hz), 111.1, 104.0, 41.6 (t, $^{2}J_{C-F}$ = 21.3 Hz), 31.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{21}H_{19}F_2N_2$: 337.1511, Found: 337.1518.



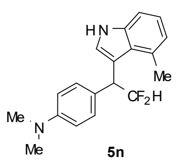
5l

***N*-allyl-4-(2,2-difluoro-1-(1*H*-indol-3-yl)ethyl)aniline (5l):** The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5l** (white solid, 106.2 mg, 0.34 mmol, 68% yield). M.p.: 91–93 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.05 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.34 (d, *J* = 8.1 Hz, 1H), 7.19 (d, *J* = 7.9 Hz, 4H), 7.08 (t, *J* = 7.5 Hz, 1H), 6.59 (d, *J* = 8.5 Hz, 2H), 6.26 (td, *J* = 56.5, 3.7 Hz, 1H), 5.96 (ddt, *J* = 15.7, 10.6, 5.4 Hz, 1H), 5.30 (d, *J* = 17.2 Hz, 1H), 5.18 (d, *J* = 10.3 Hz, 1H), 4.62 (td, *J* = 16.5, 3.5 Hz, 1H), 3.76 (d, *J* = 5.4 Hz, 2H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.49 (ddd, *J* = 274.1, 56.5, 16.4 Hz, 1F), -118.62 (ddd, *J* = 274.1, 56.5, 17.0 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 147.3, 136.0, 135.43, 130.0, 127.0, 125.4 (t, $^{3}J_{C-F}$ = 3.2 Hz), 122.5, 122.2, 119.6, 119.2, 117.4 (t, $^{1}J_{C-F}$ = 244.7 Hz), 116.3, 112.9, 112.1 (t, $^{3}J_{C-F}$ = 3.9 Hz), 111.1, 46.5, 46.3 (t, $^{2}J_{C-F}$ = 21.1 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{19}F_2N_2$: 313.1511, Found: 313.1509.



5m

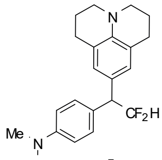
4-(1-(6-bromo-1*H*-indol-3-yl)-2,2-difluoroethyl)-*N*,*N*-dimethylaniline (5m): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5m** (white solid, 142.6 mg, 0.37 mmol, 75% yield). M.p.: 142–143 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.44 (d, *J* = 8.0 Hz, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 7.31 (s, 1H), 7.18 (t, *J* = 7.6 Hz, 1H), 7.12 (d, *J* = 8.7 Hz, 1H), 7.06 (t, *J* = 7.5 Hz, 1H), 6.94 (d, *J* = 2.0 Hz, 1H), 6.54 (dd, *J* = 8.7, 2.0 Hz, 1H), 6.26 (td, *J* = 56.2, 2.6 Hz, 2H), 5.33 – 5.22 (m, 1H), 2.91 (s, 6H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.91 (ddd, *J* = 275.2, 56.3, 15.5 Hz, 1F), -120.90 (ddd, *J* = 274.7, 56.0, 18.0 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.5, 135.9, 130.9, 127.1, 125.9, 122.9 (d, $^{3}J_{C-F}$ = 4.4 Hz), 122.5, 122.3, 119.8, 119.3, 117.0 (t, $^{1}J_{C-F}$ = 245.5 Hz), 115.8, 111.8, 111.6 (dd, $^{3}J_{C-F}$ = 4.2, 1.8 Hz), 111.0, 44.7 (t, $^{2}J_{C-F}$ = 21.2 Hz), 40.2; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{18}H_{18}BrF_2N_2$: 379.0616, Found: 379.0611.



5n

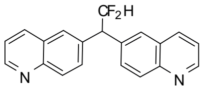
4-(2,2-difluoro-1-(4-methyl-1*H*-indol-3-yl)ethyl)-*N*,*N*-dimethylaniline (5n): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (20/1 to 15/1, v/v) as eluent to give compound **5n** (white solid, 72.6 mg, 0.23 mmol, 46% yield). M.p.: 120–122 °C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (s, 1H), 7.28 (s, 1H), 7.19 (t, *J* = 9.2 Hz, 3H), 7.12 – 7.05 (m, 1H), 6.81 (d, *J* = 7.1 Hz, 1H), 6.71 (d, *J* = 8.8 Hz, 2H), 6.27 (td, *J* = 56.6, 3.2 Hz, 1H), 4.98 (ddd, *J* = 19.7, 14.5, 3.0 Hz, 1H), 2.94 (s, 6H), 2.54 (s, 3H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -115.25 (ddd, *J* = 274.0, 56.5, 14.2 Hz, 1F), -120.03 (ddd, *J* = 273.7, 56.7, 20.0 Hz, 1F);

^{13}C NMR (100 MHz, $CDCl_3$) δ 149.9, 136.4, 130.8, 130.4, 125.6, 124.9, 122.4, 122.3, 121.6, 117.6 (t, $^{1}J_{C-F}$ = 244.7 Hz), 112.5, 109.2, 46.9 (t, $^{2}J_{C-F}$ = 20.6 Hz), 40.6, 20.6; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{19}H_{21}F_2N_2$: 315.1668, Found: 315.1665.



5o

4-(2,2-difluoro-1-(2,3,6,7-tetrahydro-1*H*,5*H*-pyrido[3,2,1-*ij*]quinolin-9-yl)ethyl)-*N*,*N*-dimethylaniline (5o): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (30/1 to 20/1, v/v) as eluent to give compound **5o** (yellow oil, 119.4 mg, 0.34 mmol, 67% yield). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.19 (d, *J* = 8.7 Hz, 2H), 6.71 (dd, *J* = 6.6, 2.1 Hz, 4H), 6.20 (td, *J* = 56.5, 4.6 Hz, 1H), 4.11 (td, *J* = 16.2, 4.5 Hz, 1H), 3.14 – 3.09 (m, 4H), 2.94 (s, 6H), 2.73 (t, *J* = 6.5 Hz, 4H), 2.02 – 1.86 (m, 4H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ ^{19}F NMR (377 MHz, $CDCl_3$) δ -117.15 (ddd, *J* = 73.2, 56.5, 16.2 Hz, 1F), -118.22 (ddd, *J* = 72.1, 56.5, 16.2 Hz, 1F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 149.6, 142.0, 129.6, 127.3, 125.7 (t, $^{3}J_{C-F}$ = 3.5 Hz), 124.6 (t, $^{3}J_{C-F}$ = 3.7 Hz), 121.5, 117.6 (t, $^{1}J_{C-F}$ = 243.9 Hz), 112.6, 53.4 (t, $^{2}J_{C-F}$ = 20.3 Hz), 49.9, 40.6, 27.7, 22.0; **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{22}H_{27}F_2N_2$: 357.2137, Found: 357.2131.

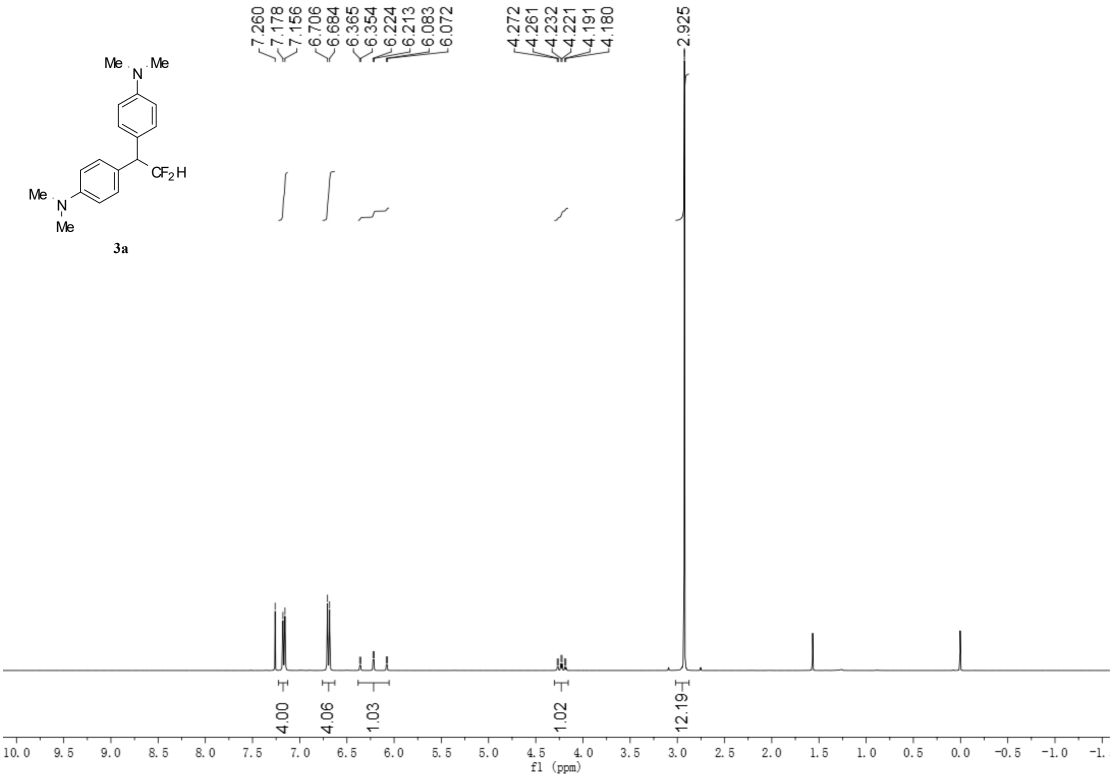


6

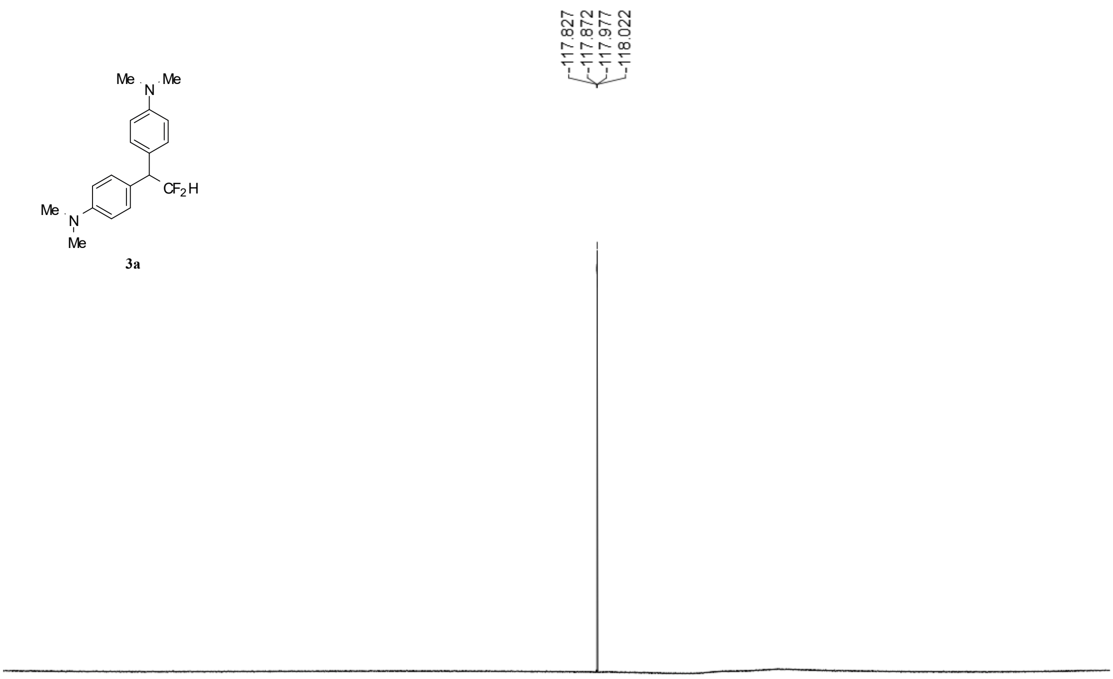
6,6'-(2,2-difluoroethane-1,1-diyl)diquinoline (6): The crude products were purified by column chromatography with petroleum ether/ethyl acetate (5/1, v/v) as eluent to give compound **6** (white solid, 57.2 mg, 0.18 mmol, 89% yield). M.p.: 67–69 ^{o}C; **^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.90 (dd, *J* = 4.2, 1.7 Hz, 2H), 8.13 (dd, *J* = 8.3, 0.8 Hz, 2H), 8.08 (d, *J* = 8.8 Hz, 2H), 7.81 (d, *J* = 1.6 Hz, 2H), 7.64 (dd, *J* = 8.8, 2.0 Hz, 2H), 7.40 (dd, *J* = 8.3, 4.2 Hz, 2H), 6.52 (td, *J* = 55.4, 4.0 Hz, 1H), 4.81 (td, *J* = 15.8, 3.9 Hz, 1H); **^{19}F NMR** (376 MHz, $CDCl_3$) δ -117.97 (dd, *J* = 55.5, 15.8 Hz, 2F); **^{13}C NMR** (100 MHz, $CDCl_3$) δ 150.7, 147.4, 136.3, 134.9 (t, $^{3}J_{C-F}$ = 3.2 Hz), 130.8, 130.0, 128.2, 127.9, 121.6, 116.5 (t, $^{1}J_{C-F}$ = 245.0 Hz), 54.7 (t, $^{2}J_{C-F}$ = 21.0 Hz); **HRMS** (ESI) m/z: $[M+H]^+$ Calcd for $C_{20}H_{15}F_2N_2$: 321.1198, Found: 321.1191.

9. NMR spectra of the related compounds

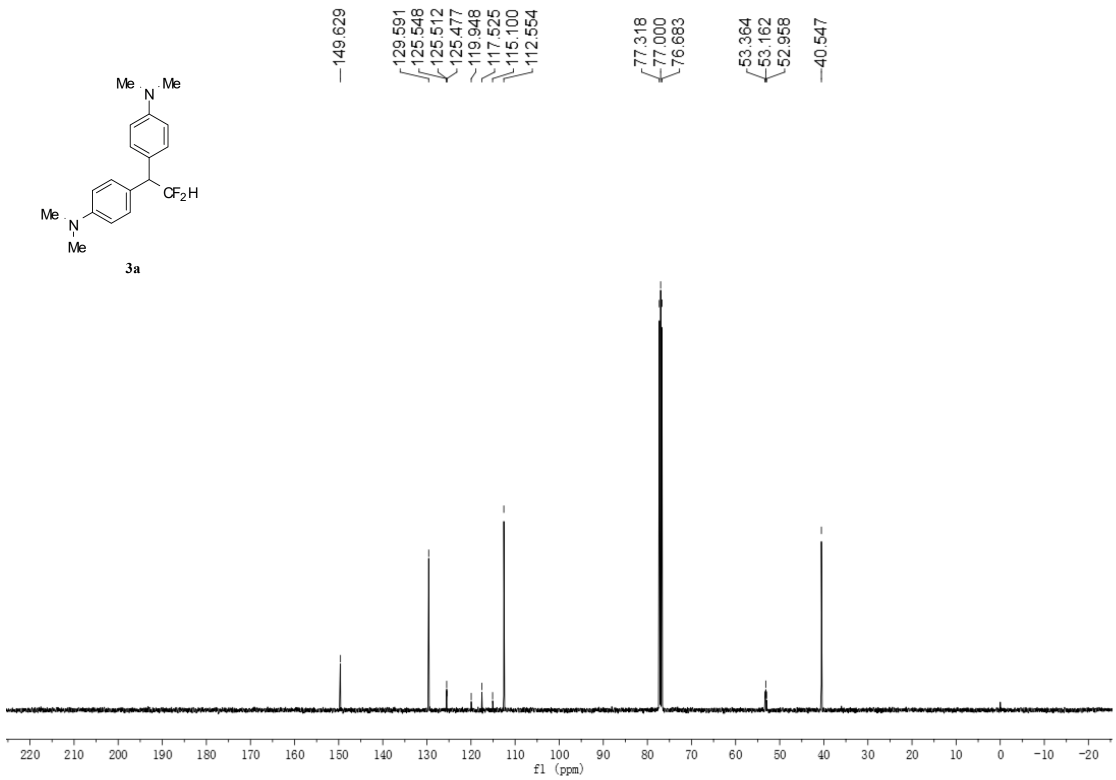
^{1}H NMR (400 MHz, $CDCl_3$) of **3a**



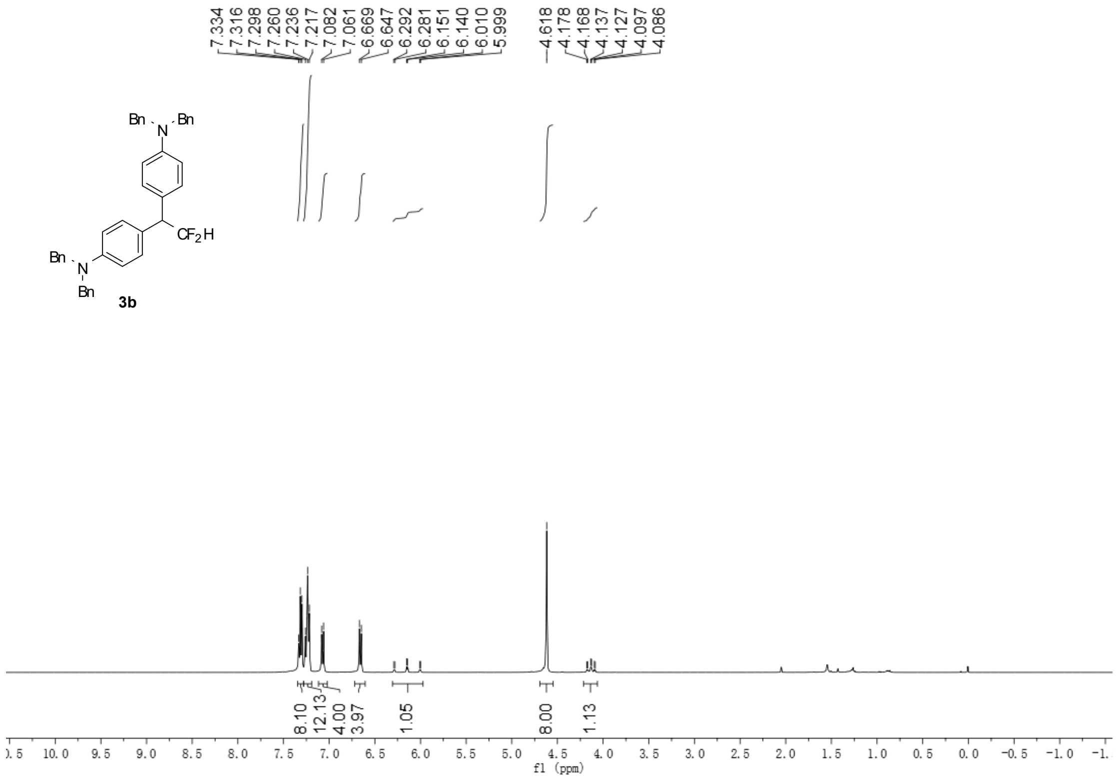
^{19}F NMR (376 MHz, $CDCl_3$) of **3a**



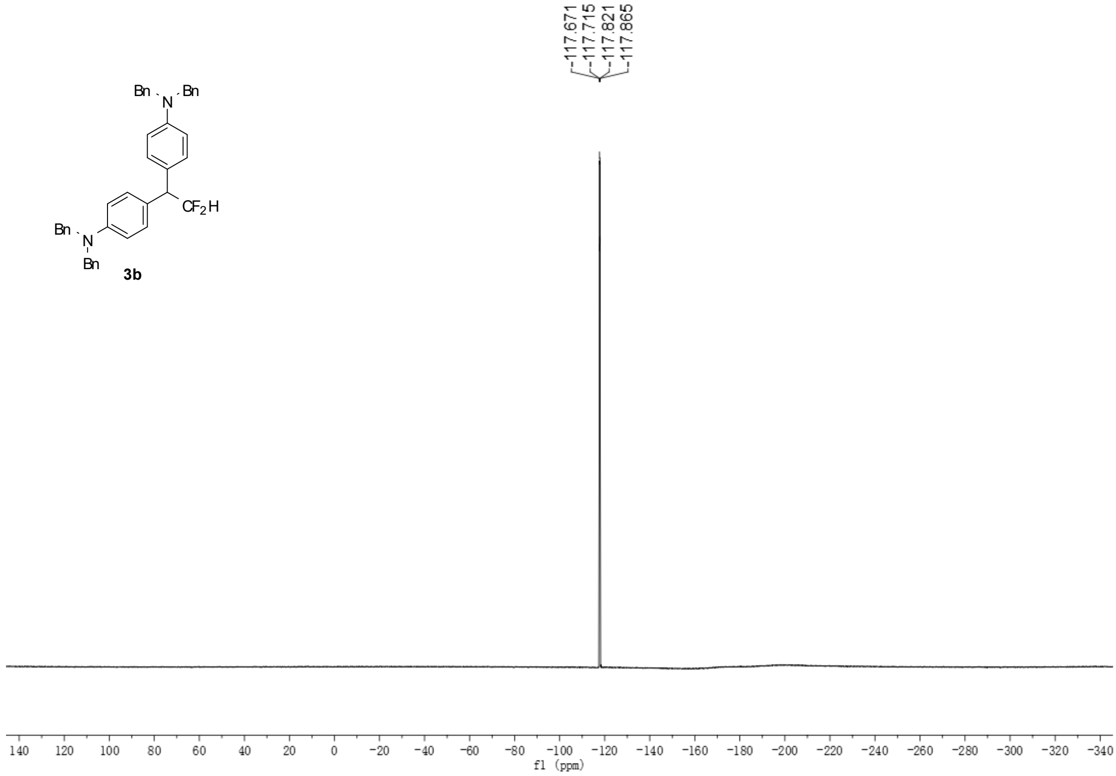
^{13}C NMR (100 MHz, CDCl$_3$) of **3a**



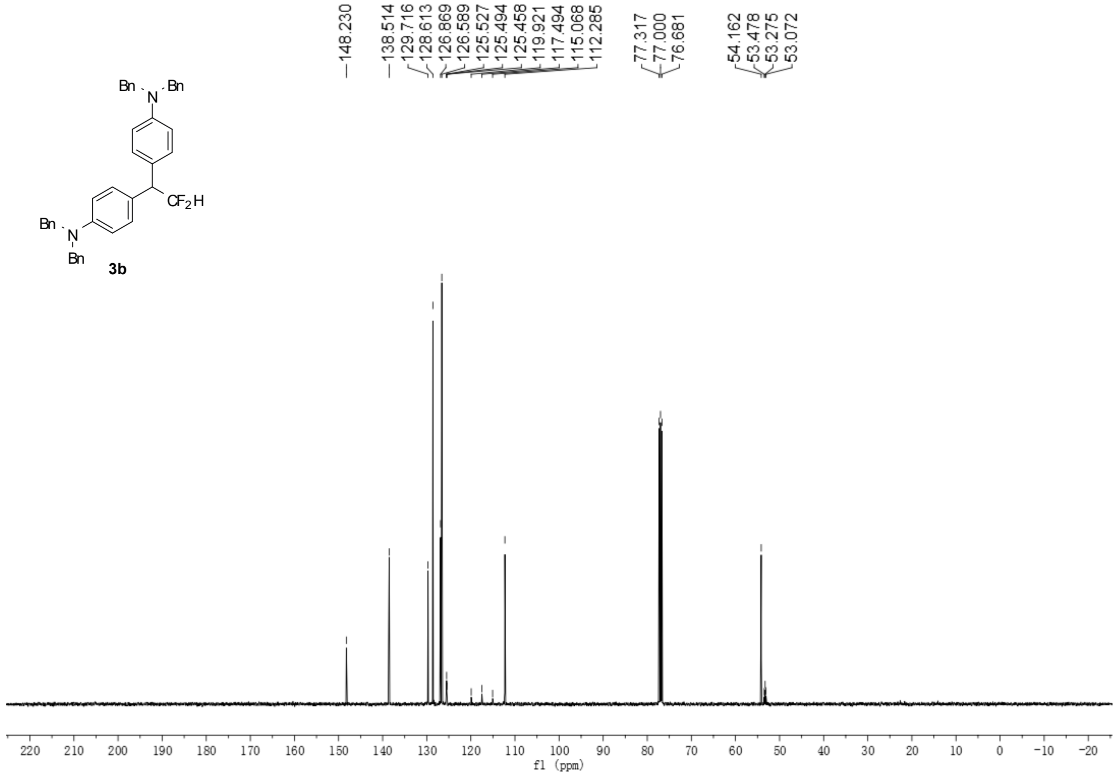
^{1}H NMR (400 MHz, CDCl$_3$) of **3b**



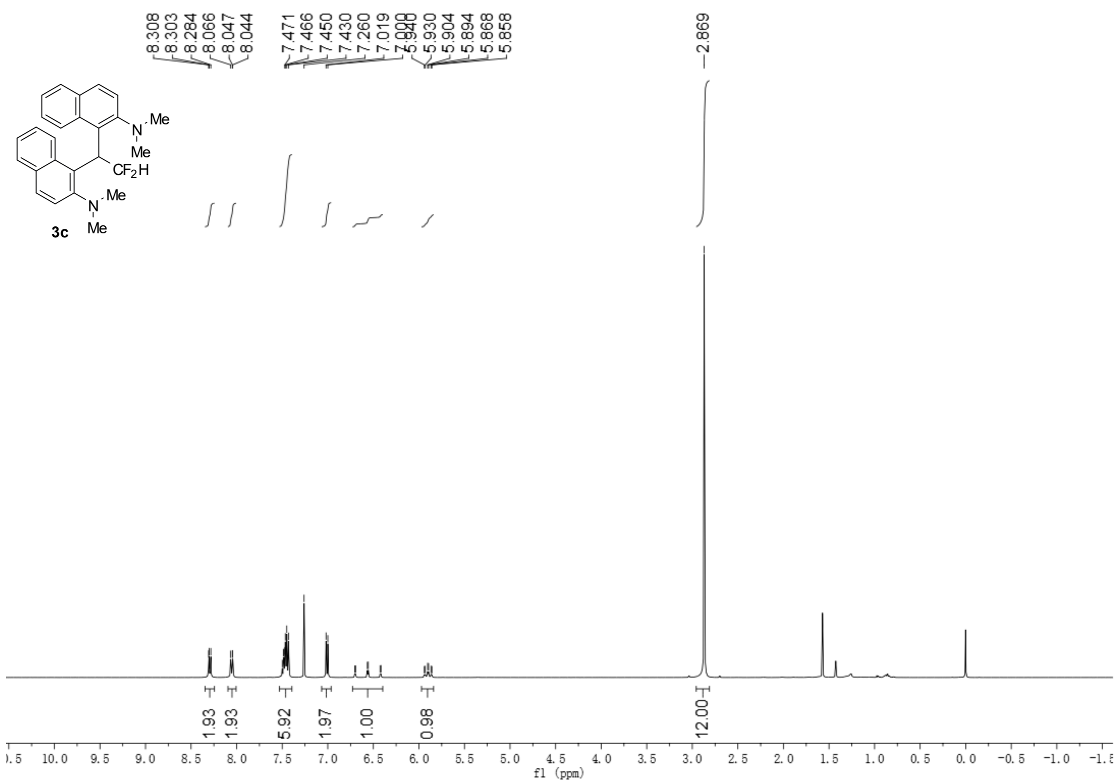
^{19}F NMR (376 MHz, $CDCl_3$) of **3b**



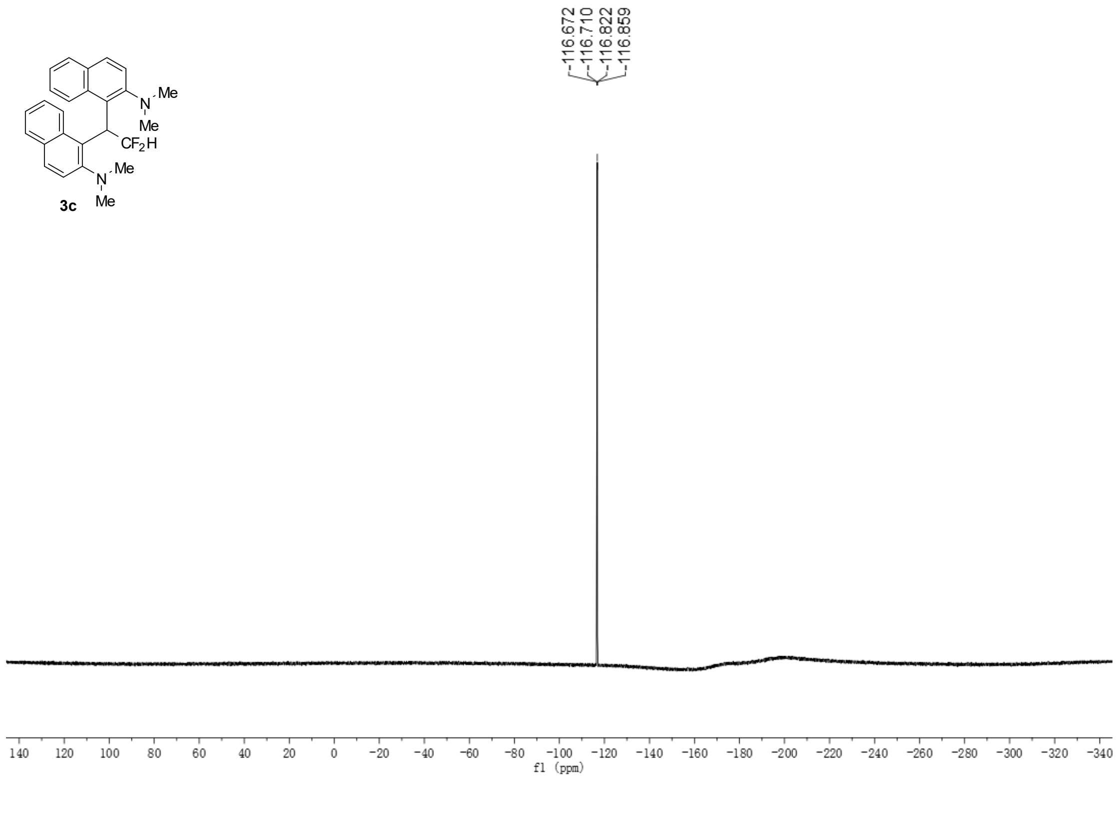
^{13}C NMR (100 MHz, $CDCl_3$) of **3b**



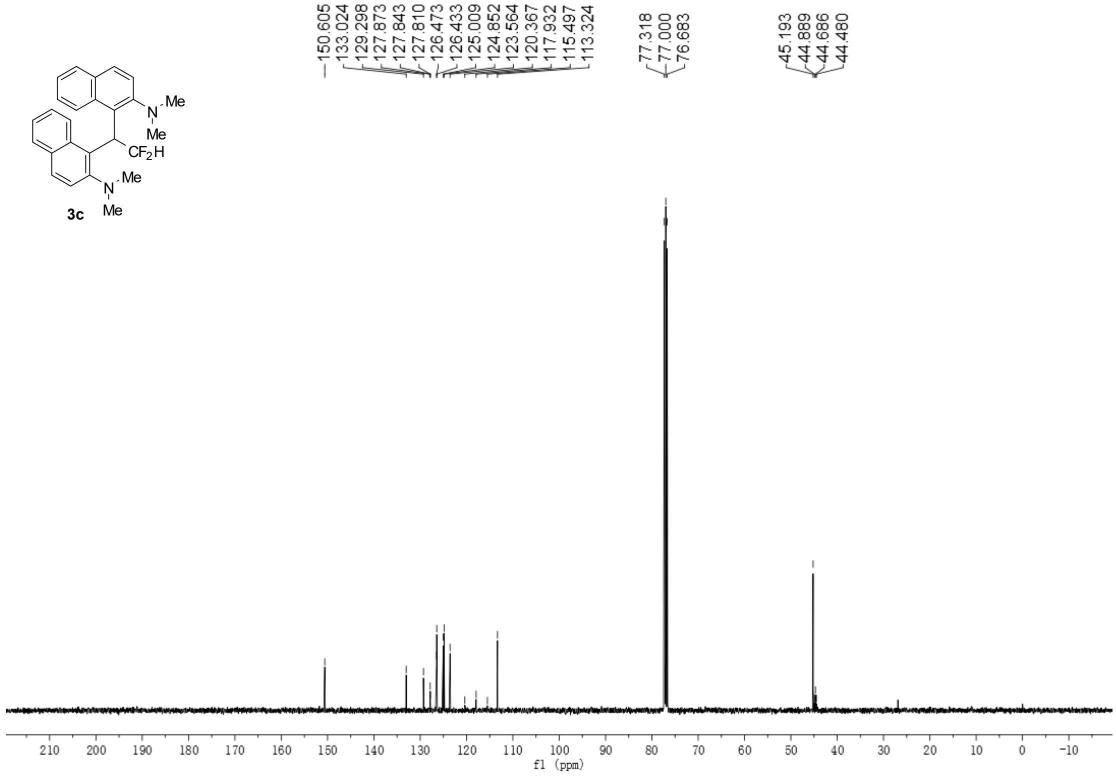
[1]H NMR (400 MHz, $CDCl_3$) of **3c**



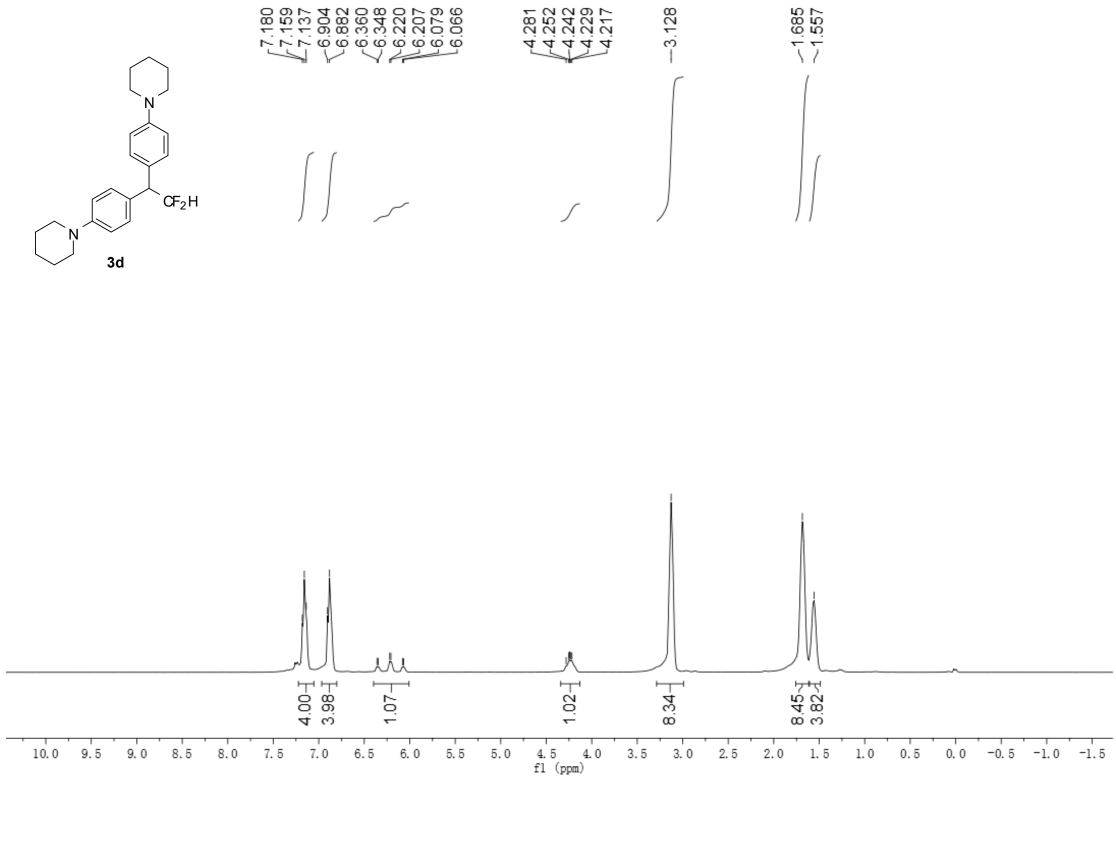
[19]F NMR (376 MHz, $(CD_3)_2CO$) of **3c**



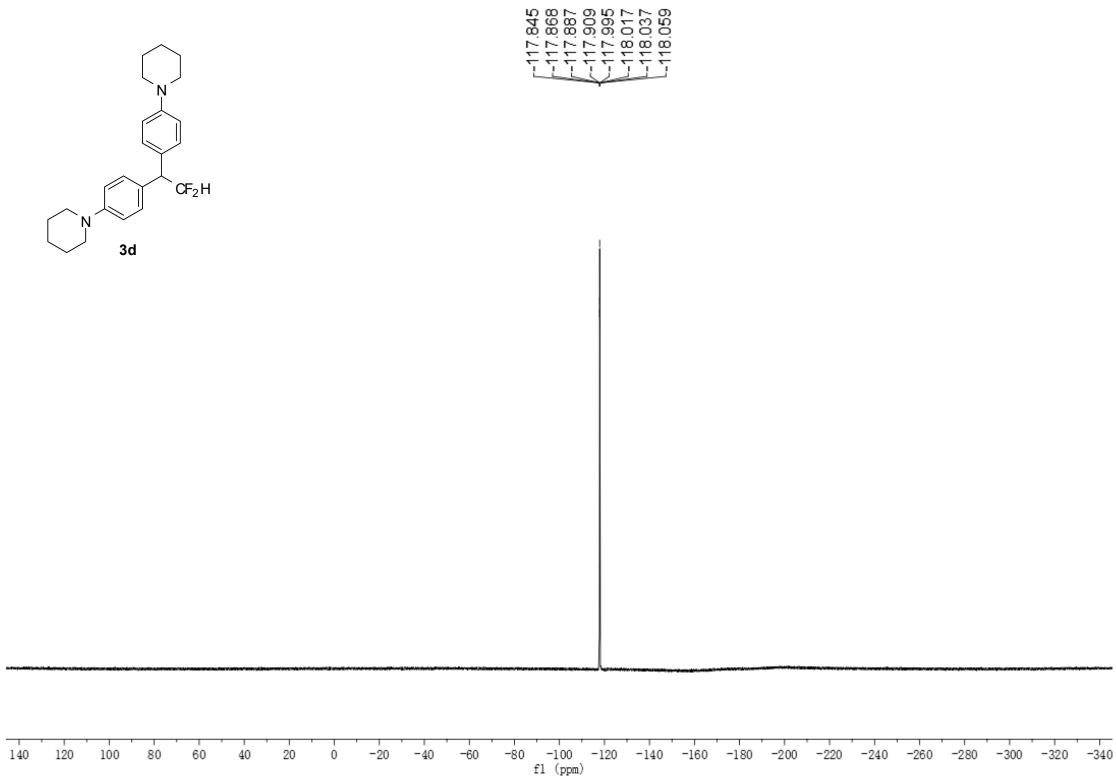
^{13}C NMR (100 MHz, $(CD_3)_2CO$) of **3c**



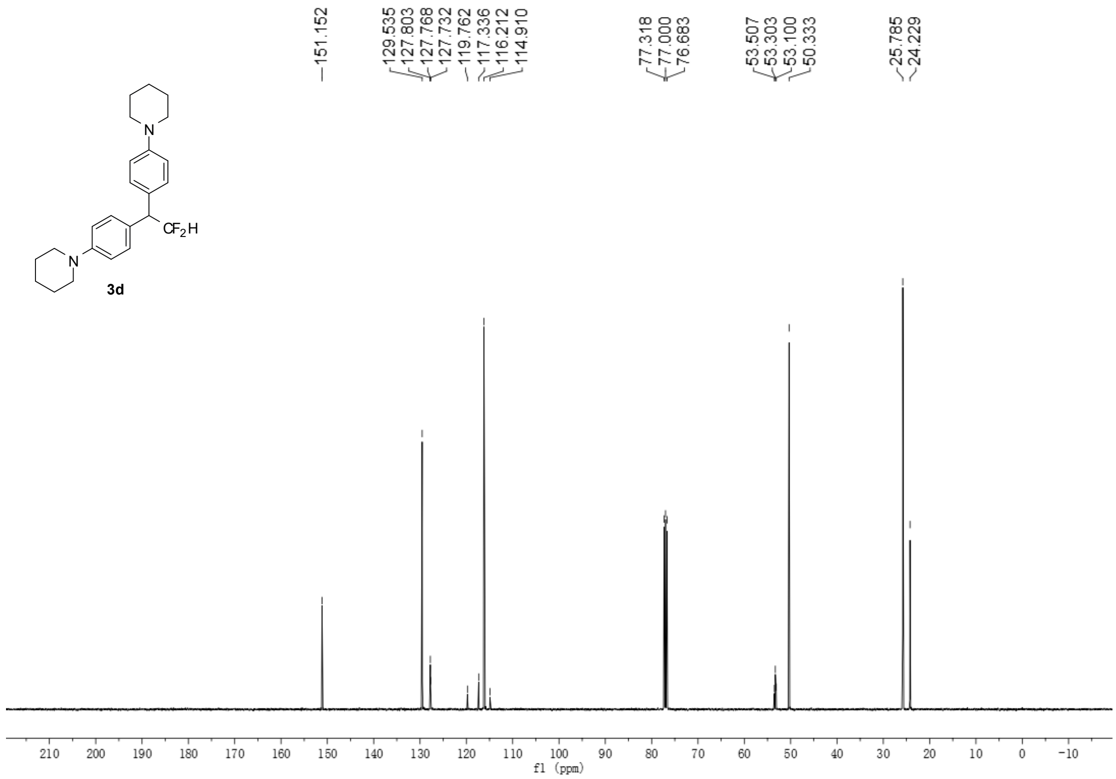
^{1}H NMR (400 MHz, $CDCl_3$) of **3d**



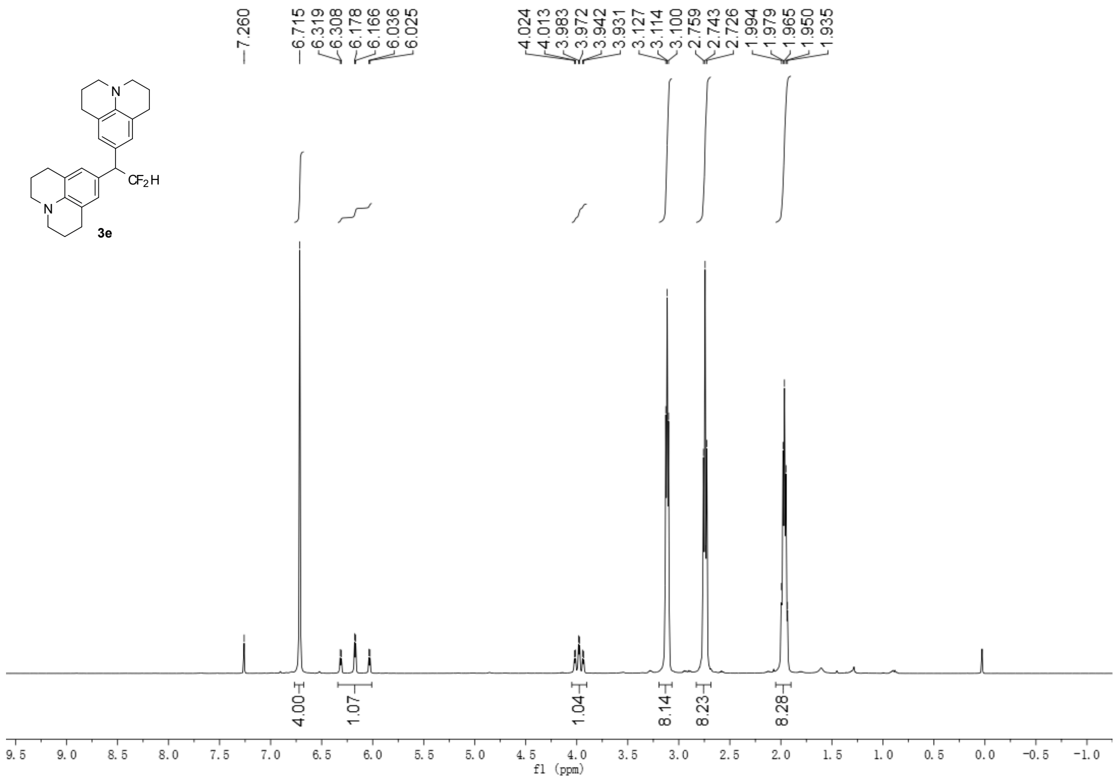
^{19}F NMR (376 MHz, $(CD_3)_2CO$) of **3d**



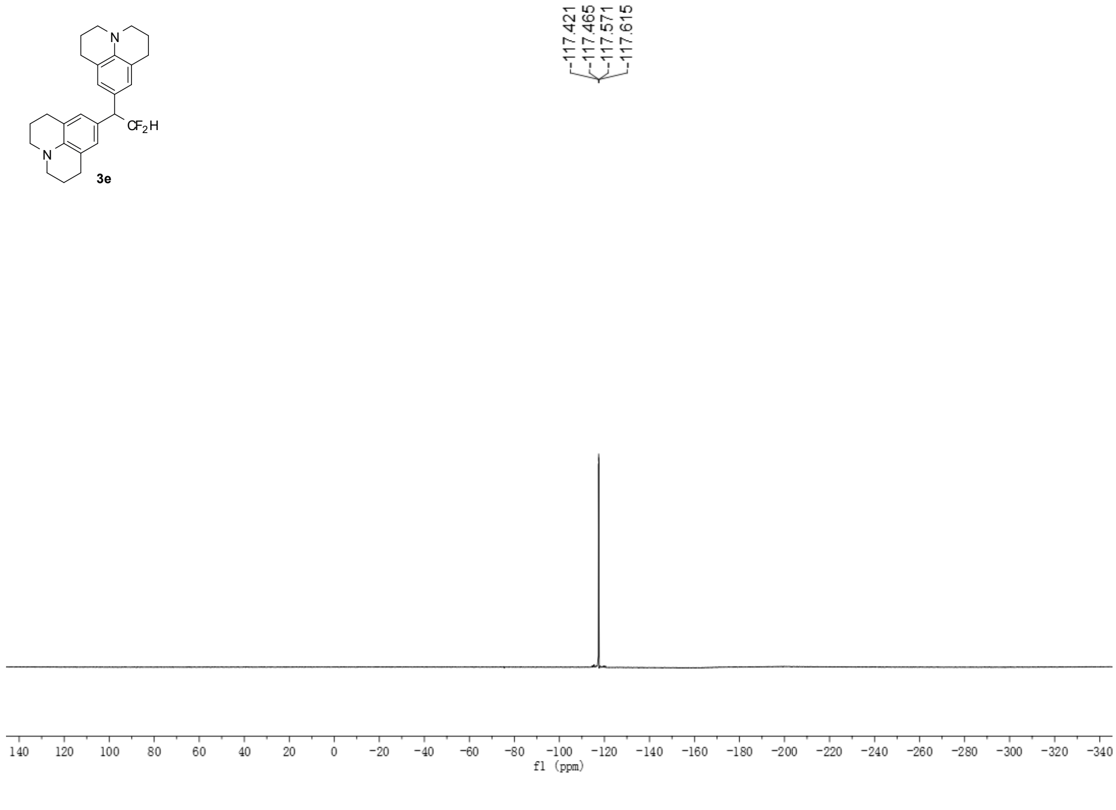
^{13}C NMR (100 MHz, $(CD_3)_2CO$) of **3d**



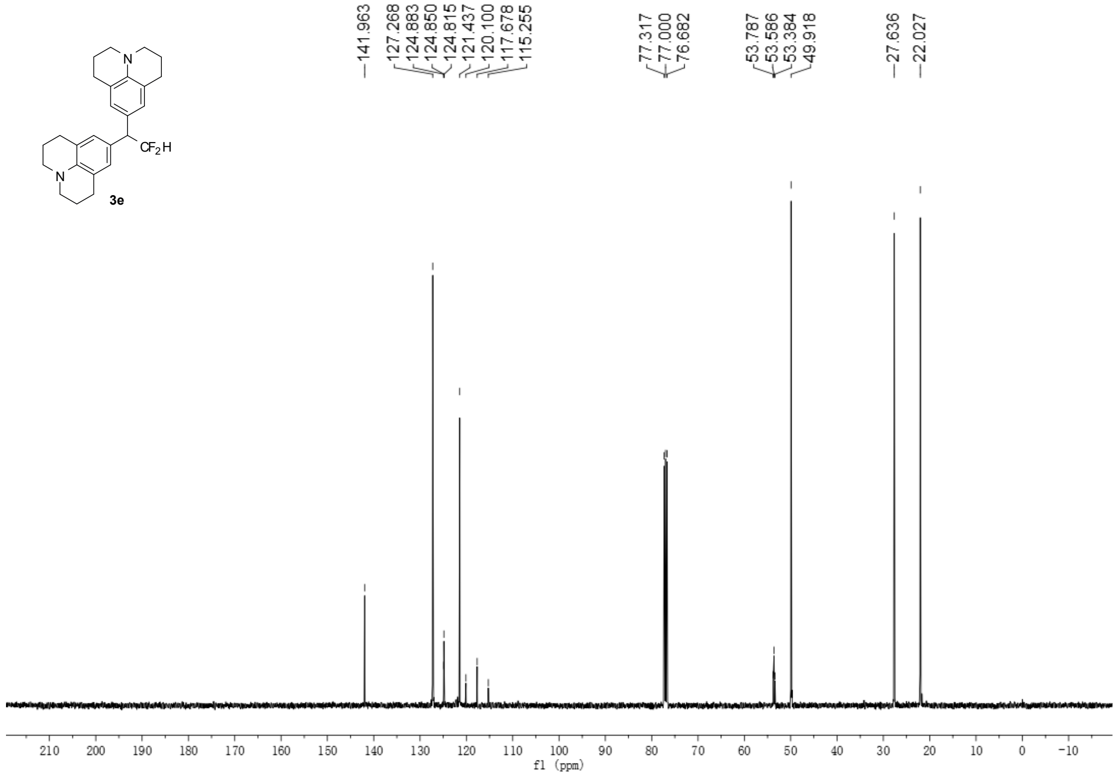
[1]H NMR (400 MHz, $CDCl_3$) of **3e**



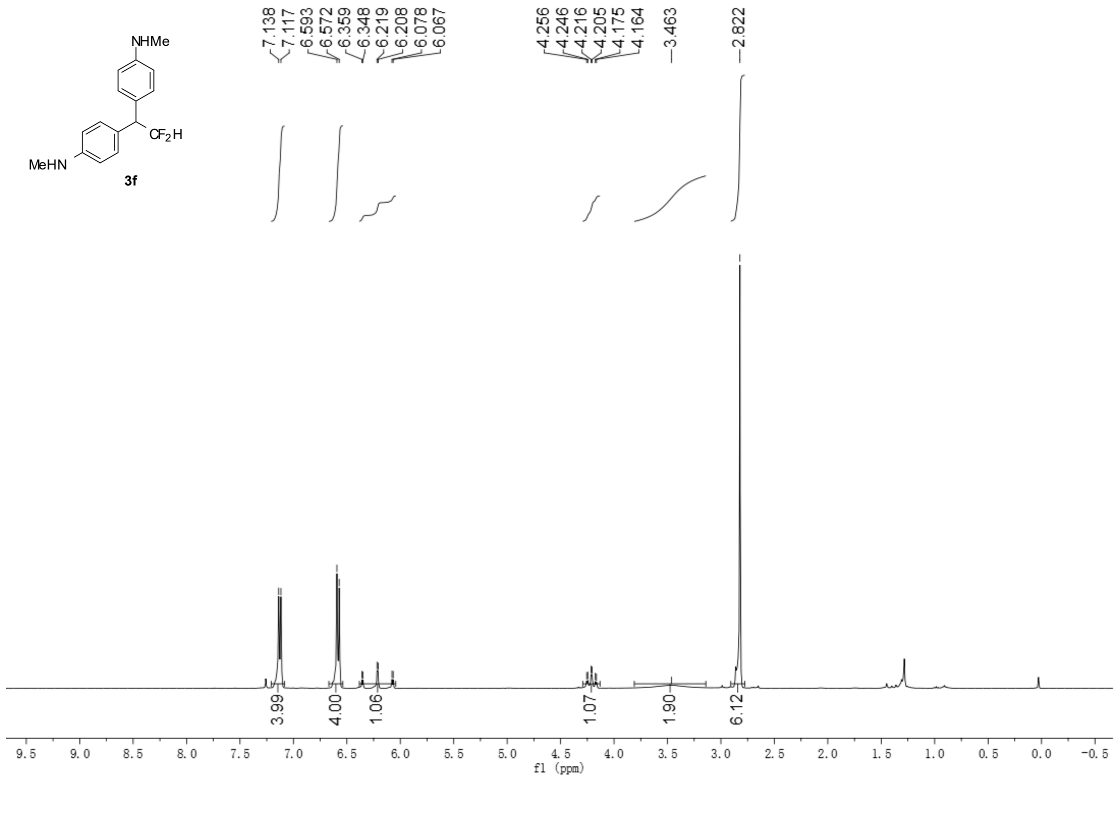
[19]F NMR (376 MHz, $CDCl_3$) of **3e**



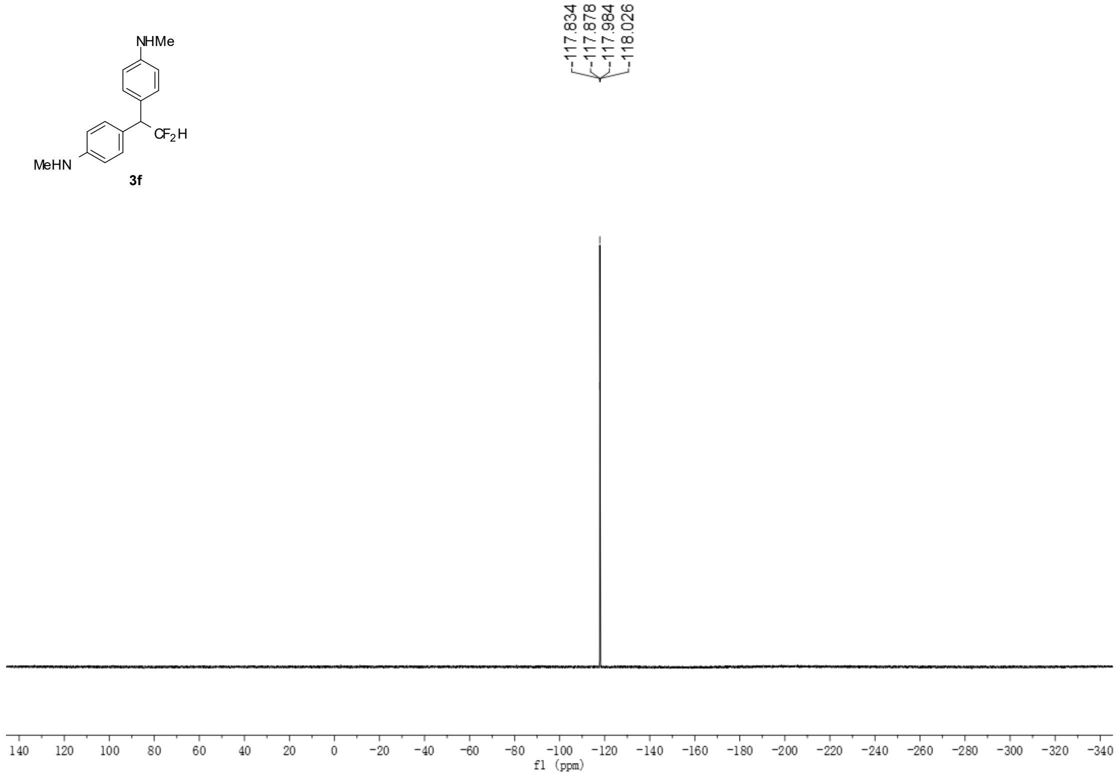
^{13}C NMR (100 MHz, $CDCl_3$) of **3e**



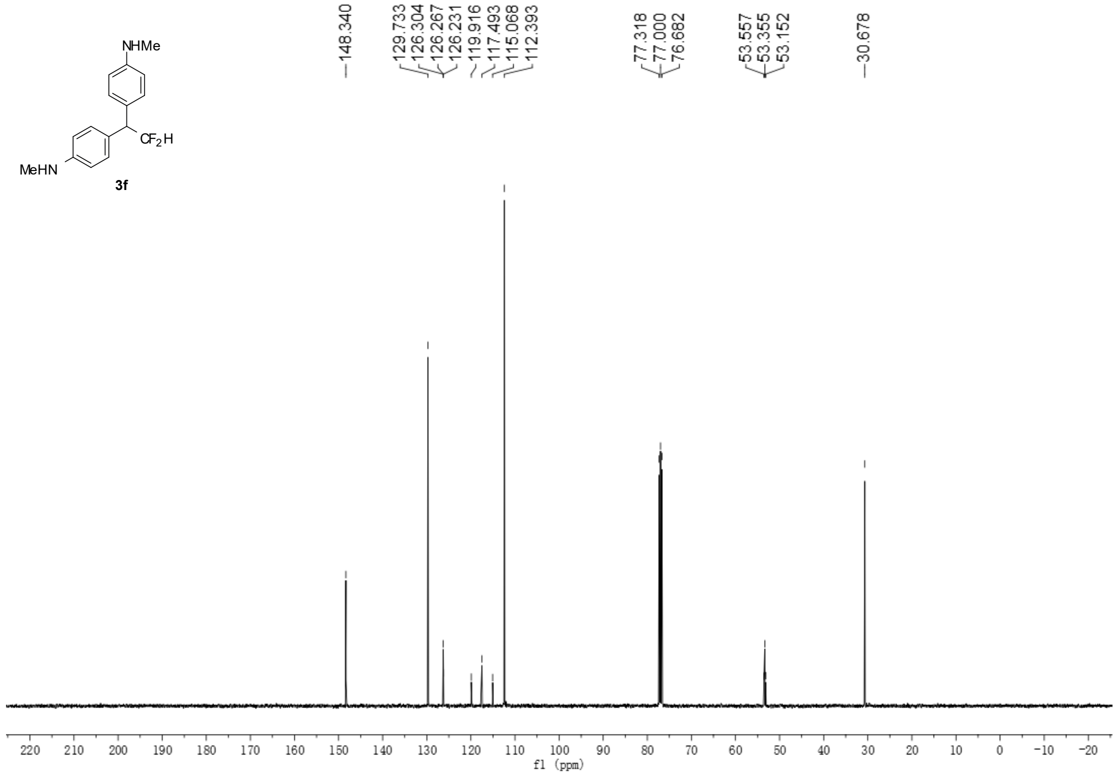
^{1}H NMR (400 MHz, $CDCl_3$) of **3f**



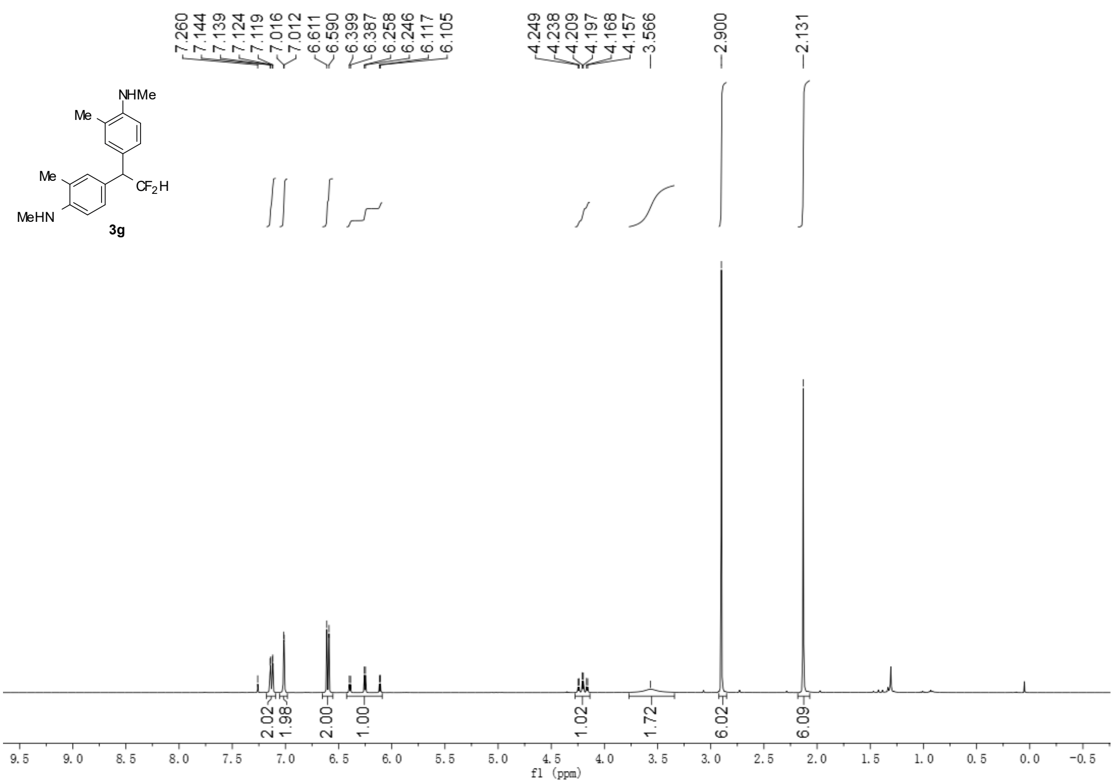
^{19}F NMR (376 MHz, $CDCl_3$) of **3f**



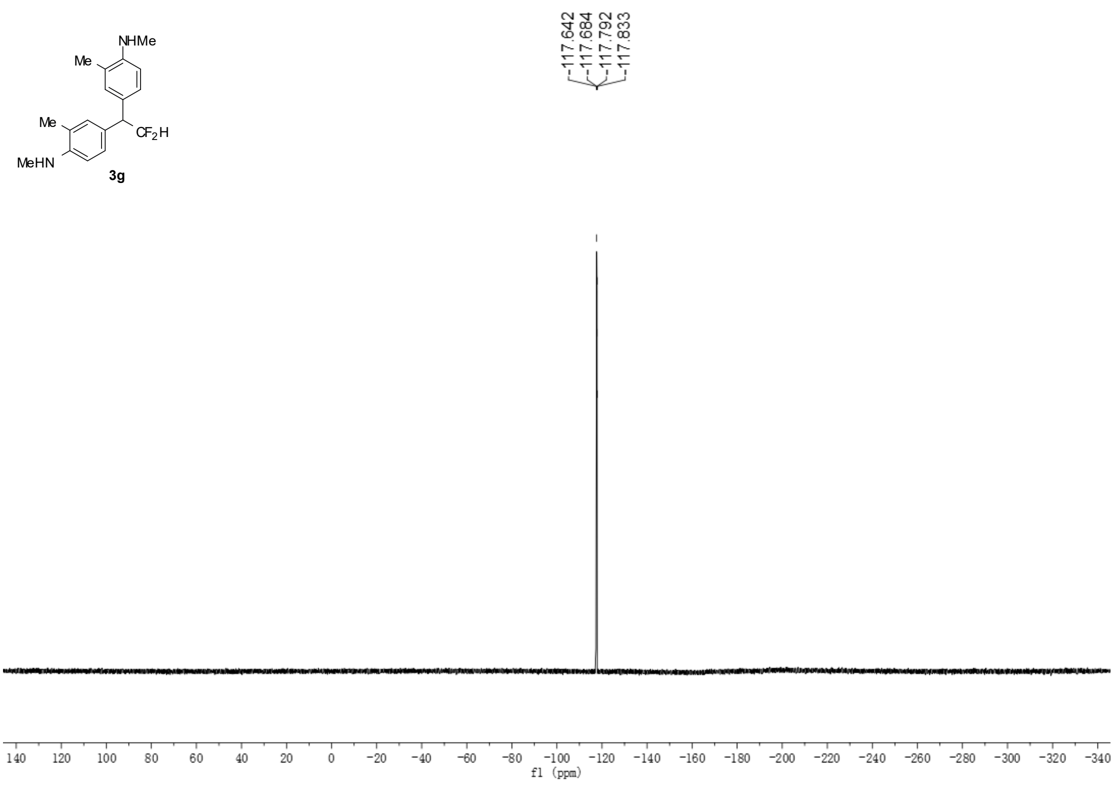
^{13}C NMR (100 MHz, $CDCl_3$) of **3f**



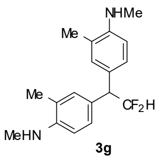
^{1}H NMR (400 MHz, $CDCl_3$) of **3g**



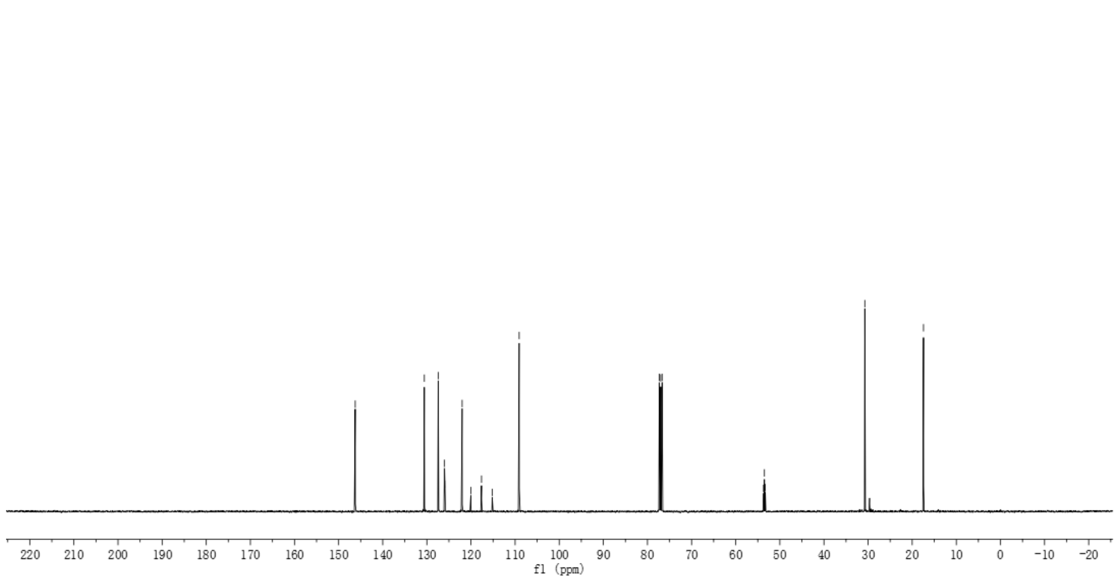
^{19}F NMR (376 MHz, $CDCl_3$) of **3g**



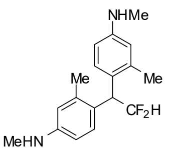
^{13}C NMR (100 MHz, $CDCl_3$) of **3g**



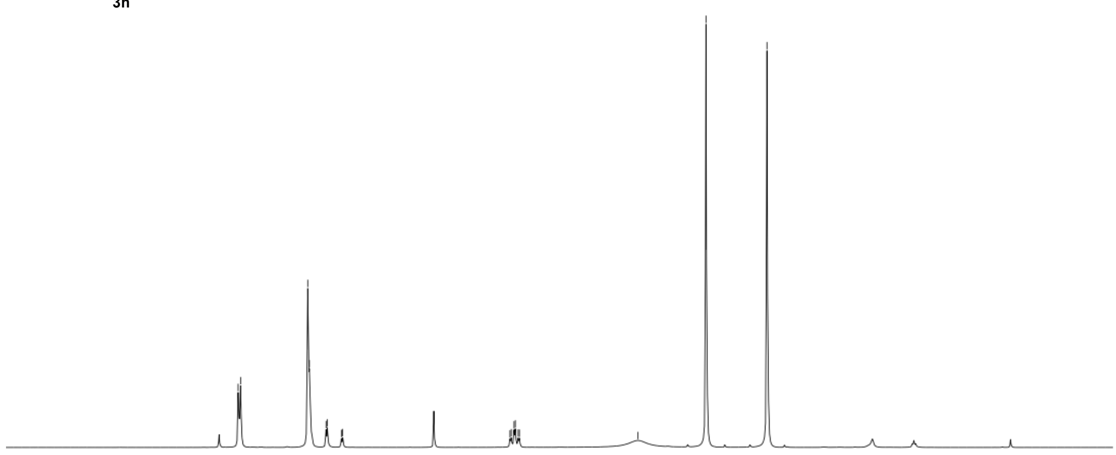
3g



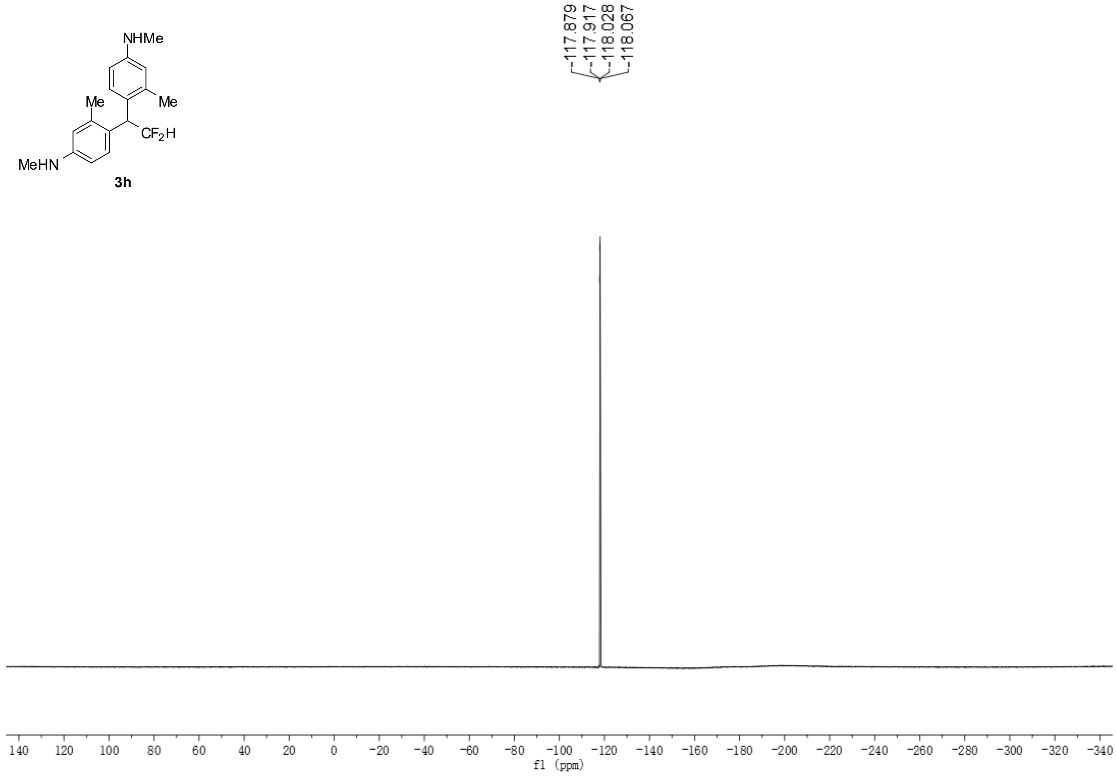
^{1}H NMR (400 MHz, $CDCl_3$) of **3h**



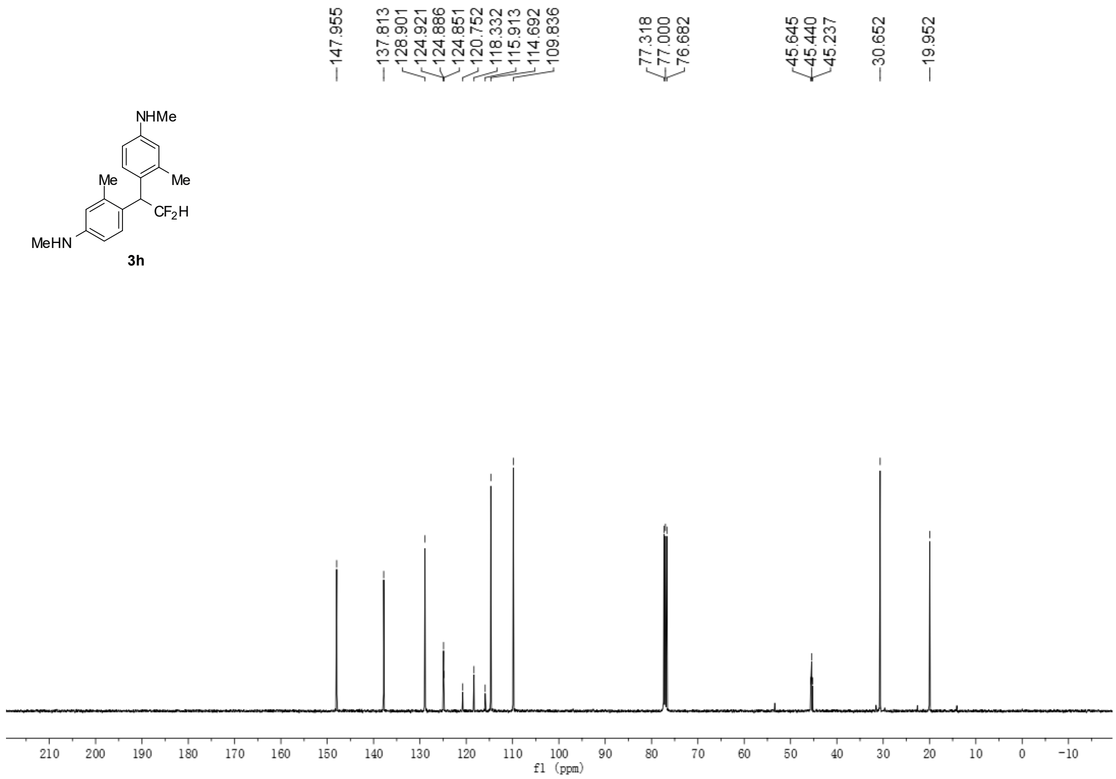
3h



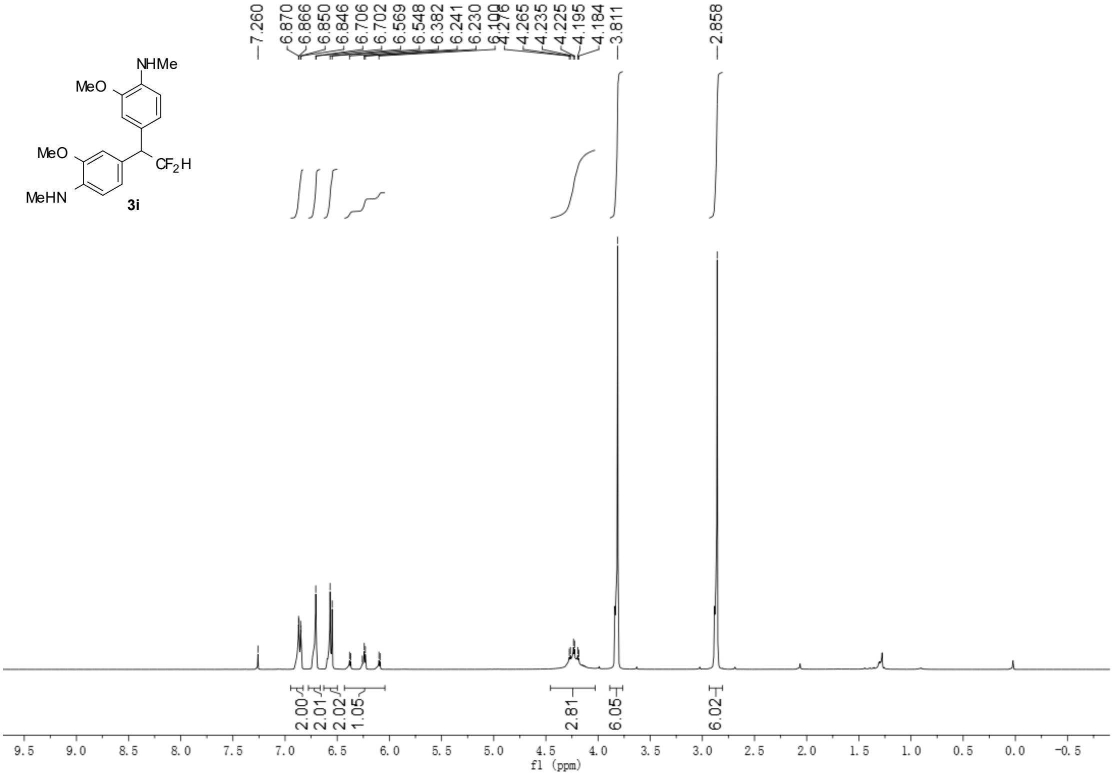
^{19}F NMR (376 MHz, $CDCl_3$) of **3h**



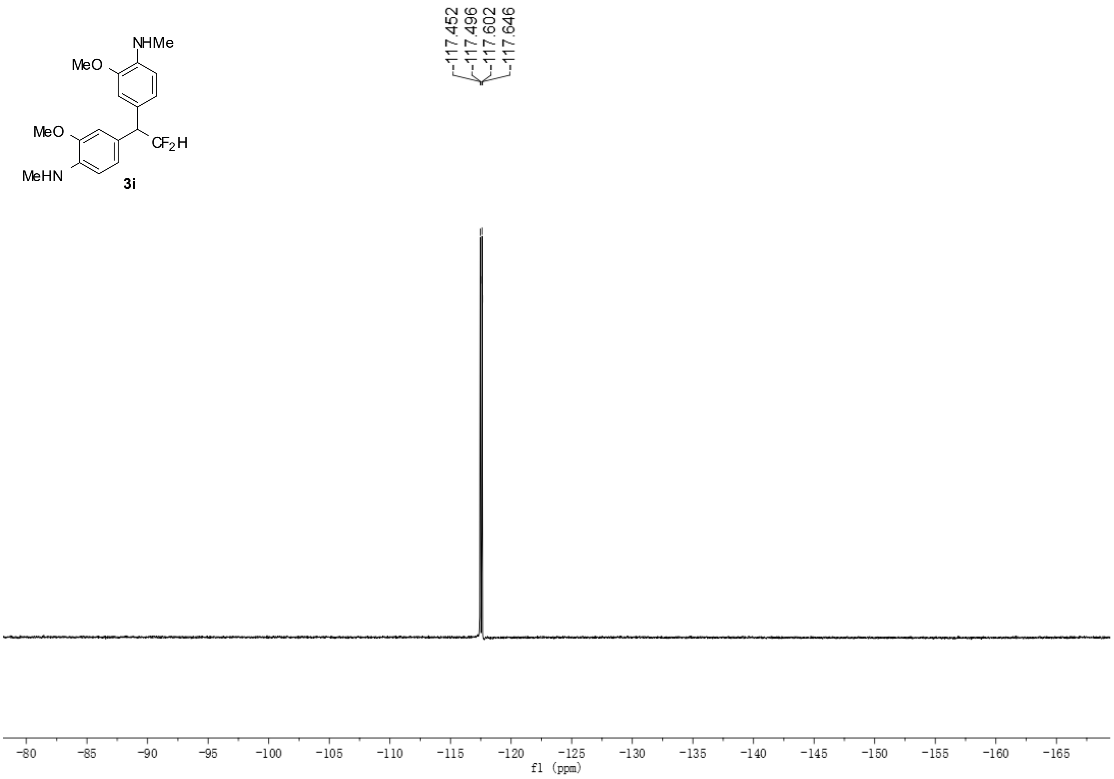
^{13}C NMR (100 MHz, $CDCl_3$) of **3h**



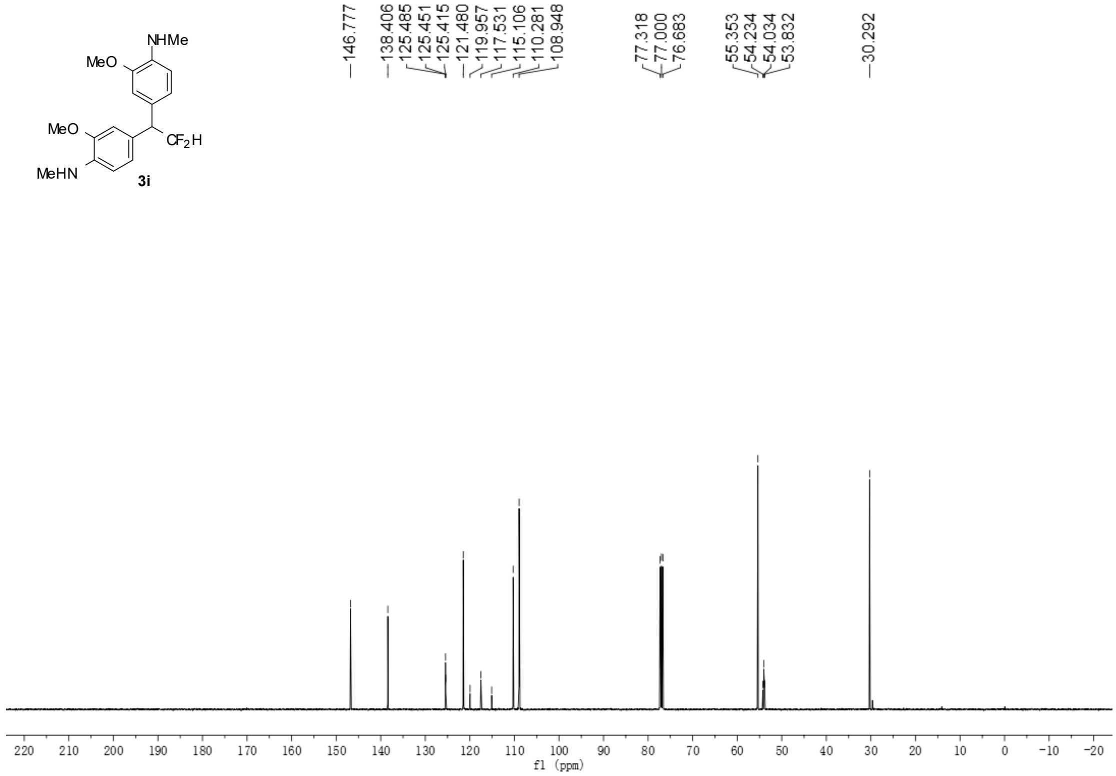
^{1}H NMR (400 MHz, $CDCl_3$) of **3i**



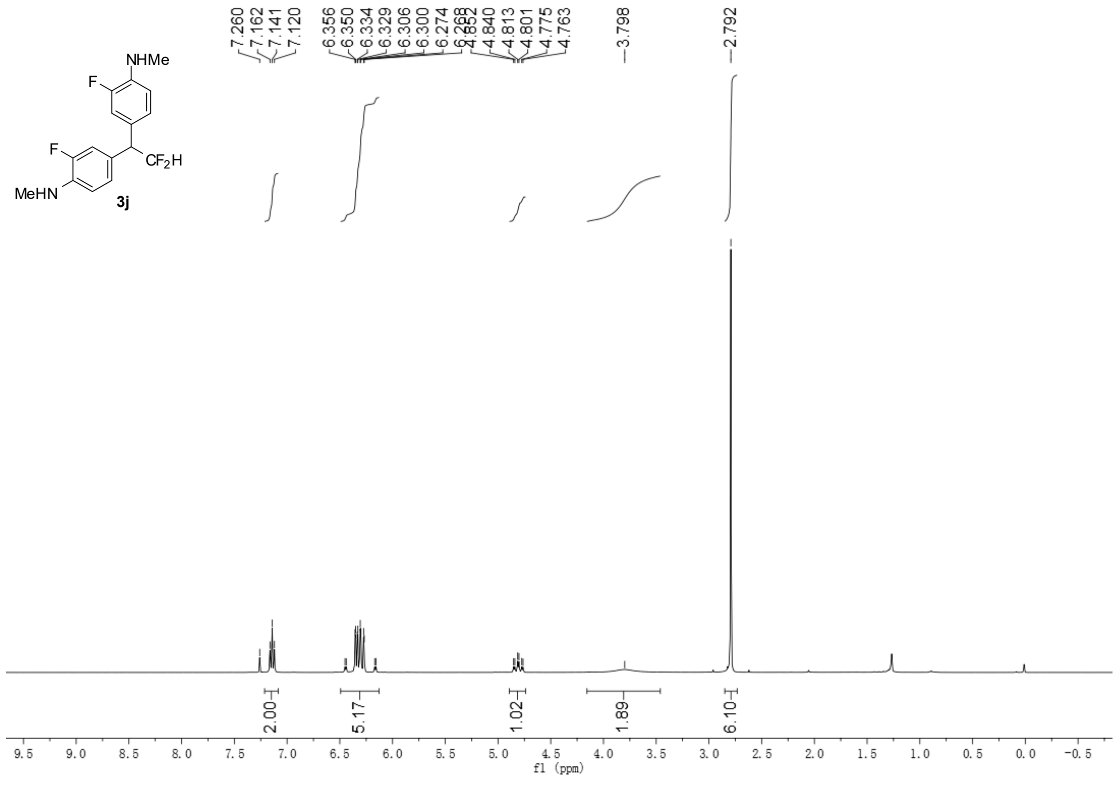
^{19}F NMR (376 MHz, $CDCl_3$) of **3i**



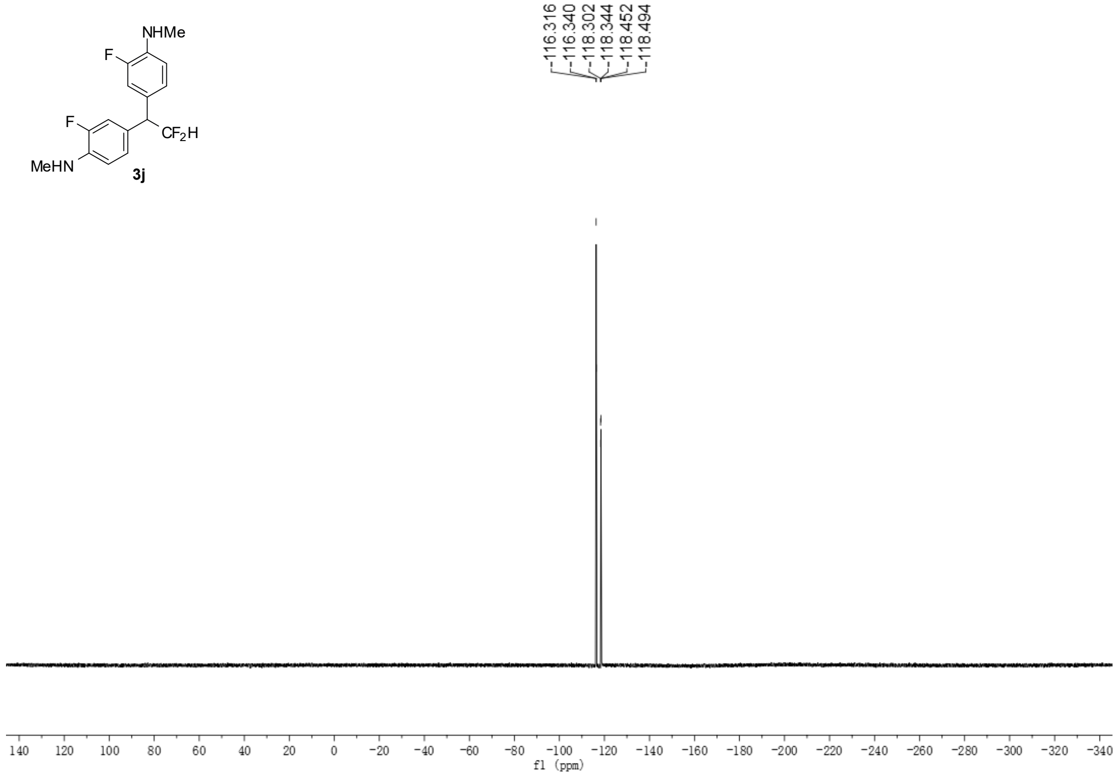
^{13}C NMR (100 MHz, $CDCl_3$) of **3i**



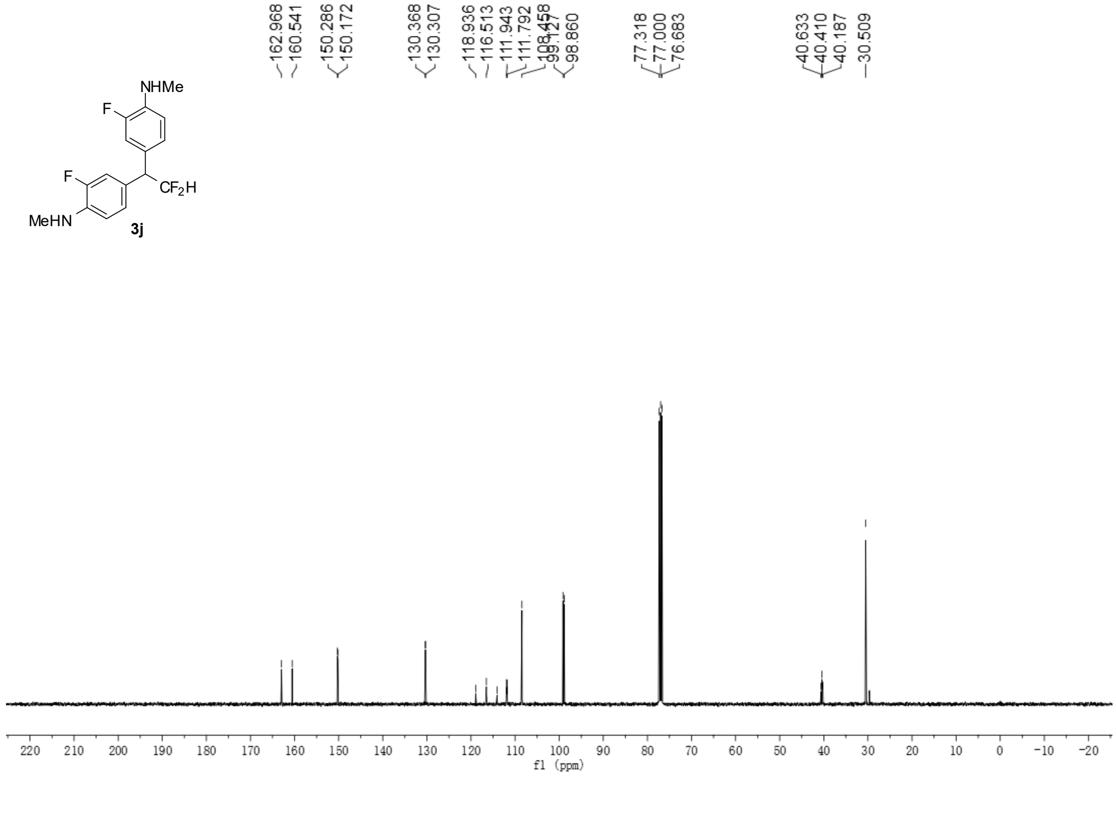
^{1}H NMR (400 MHz, $CDCl_3$) of **3j**



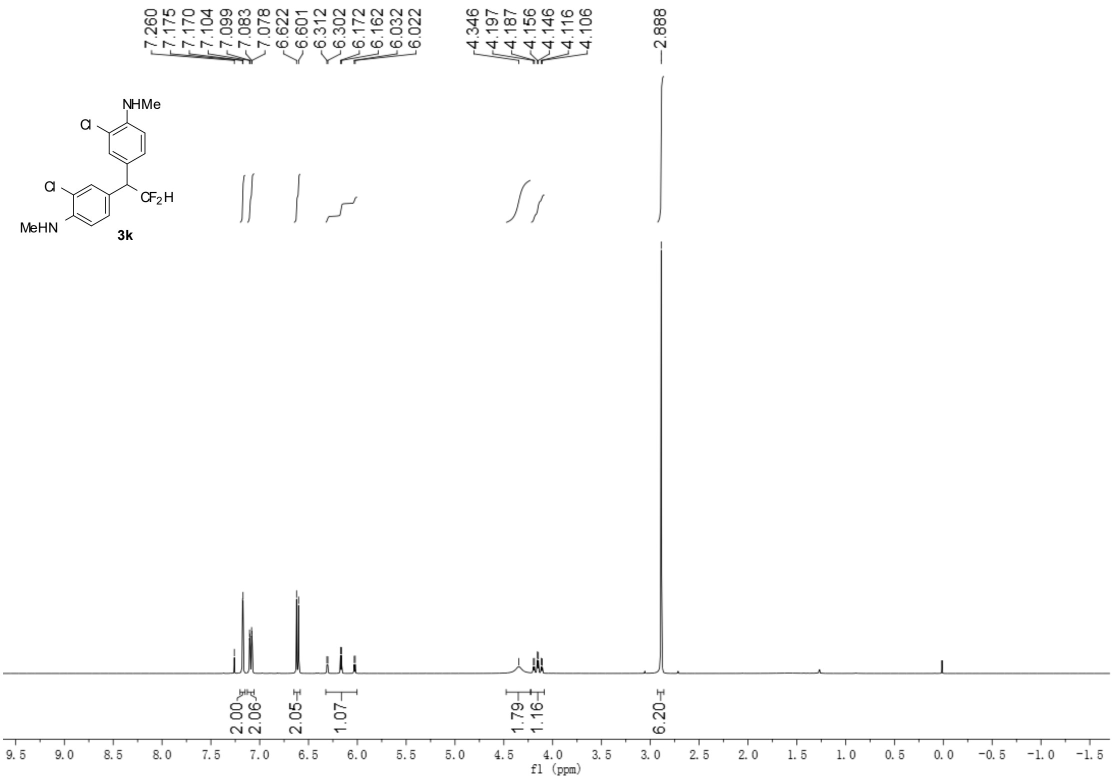
^{19}F NMR (376 MHz, $CDCl_3$) of **3j**



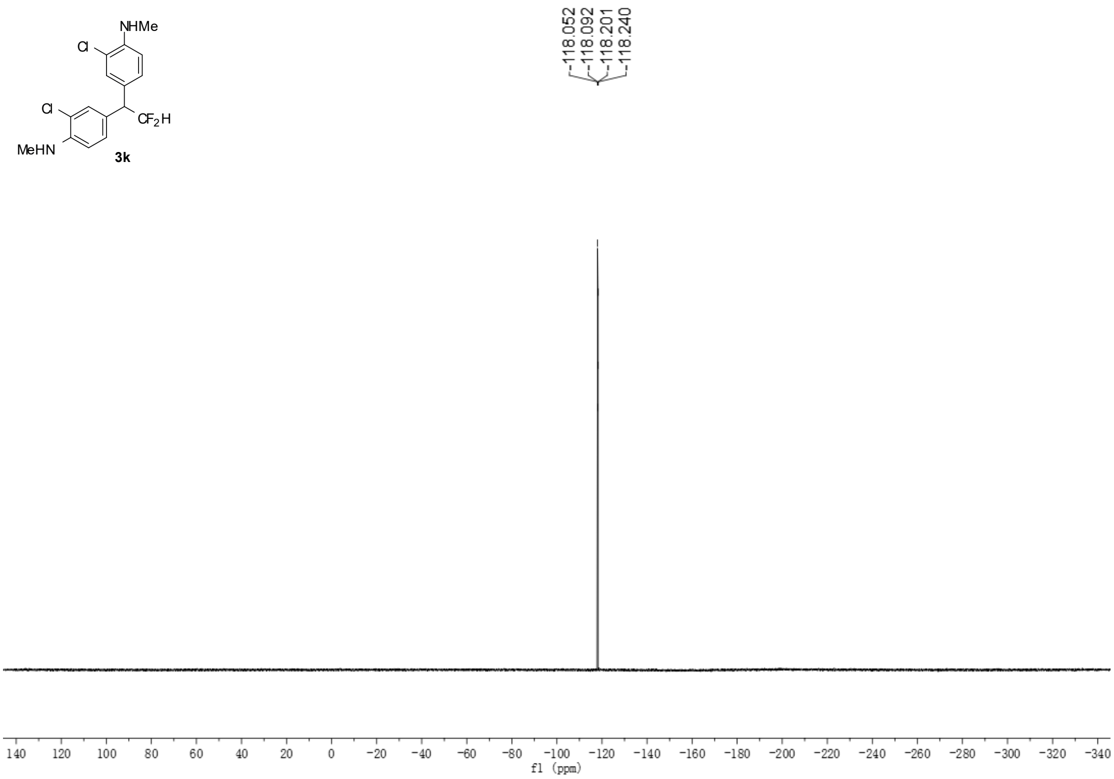
^{13}C NMR (100 MHz, $CDCl_3$) of 3**j**



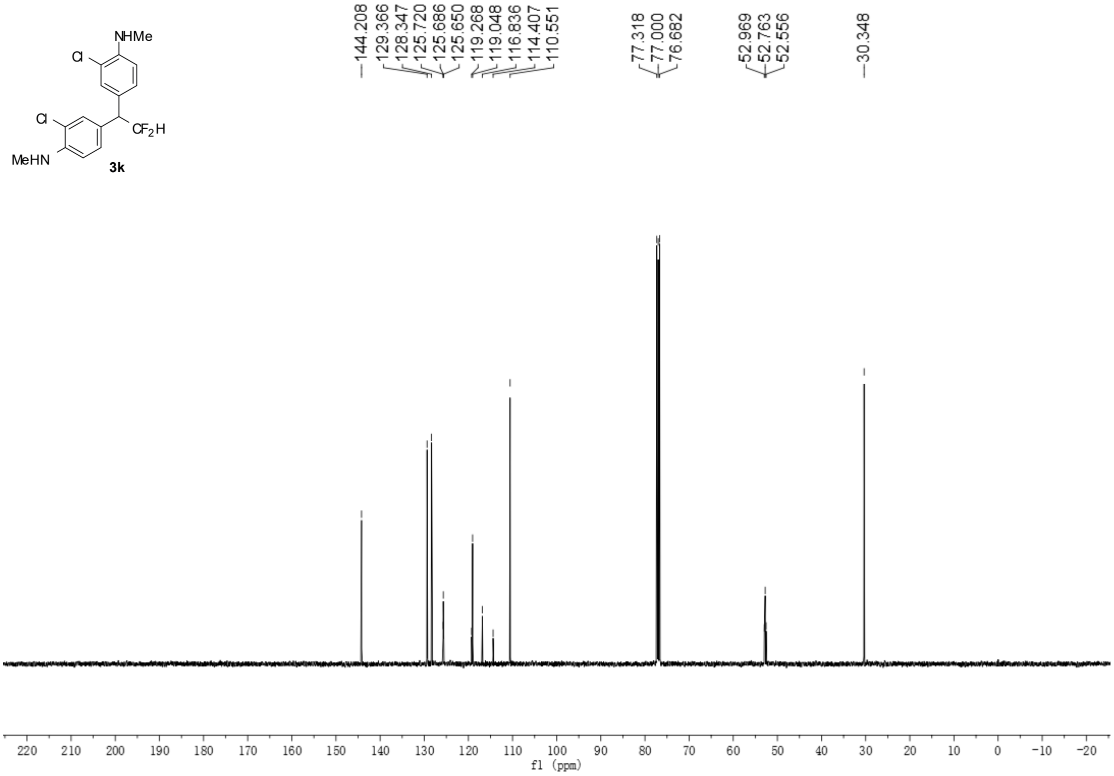
[1]H NMR (400 MHz, $CDCl_3$) of **3k**



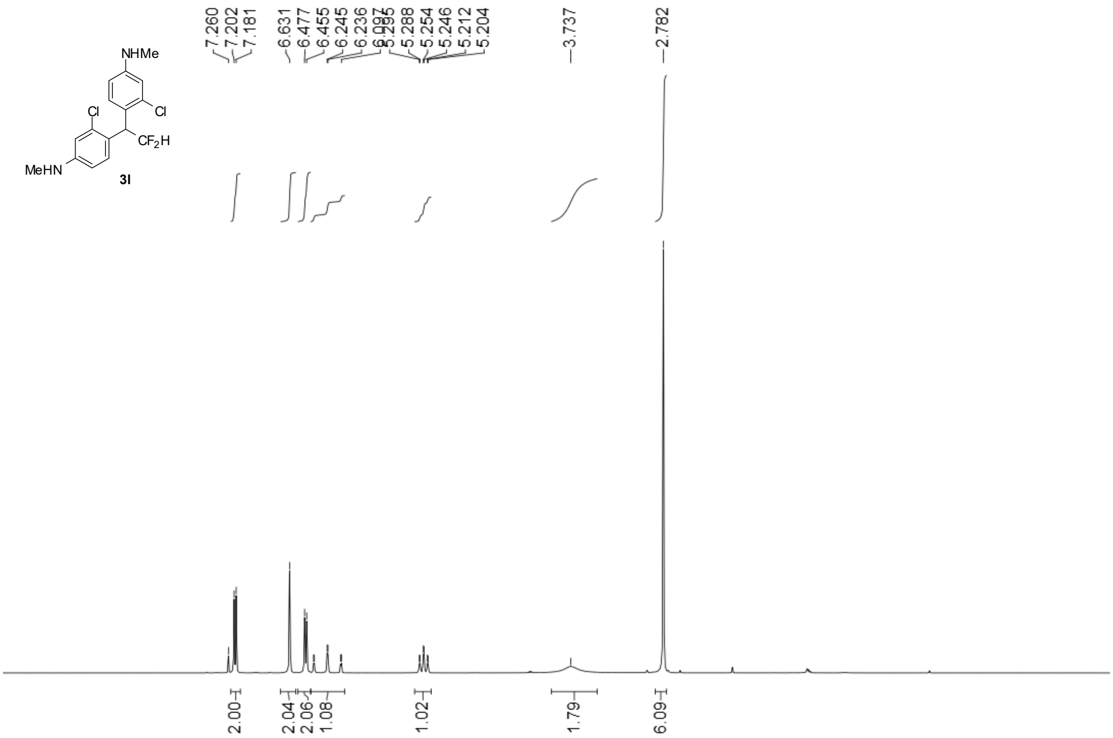
[19]F NMR (376 MHz, $CDCl_3$) of **3k**



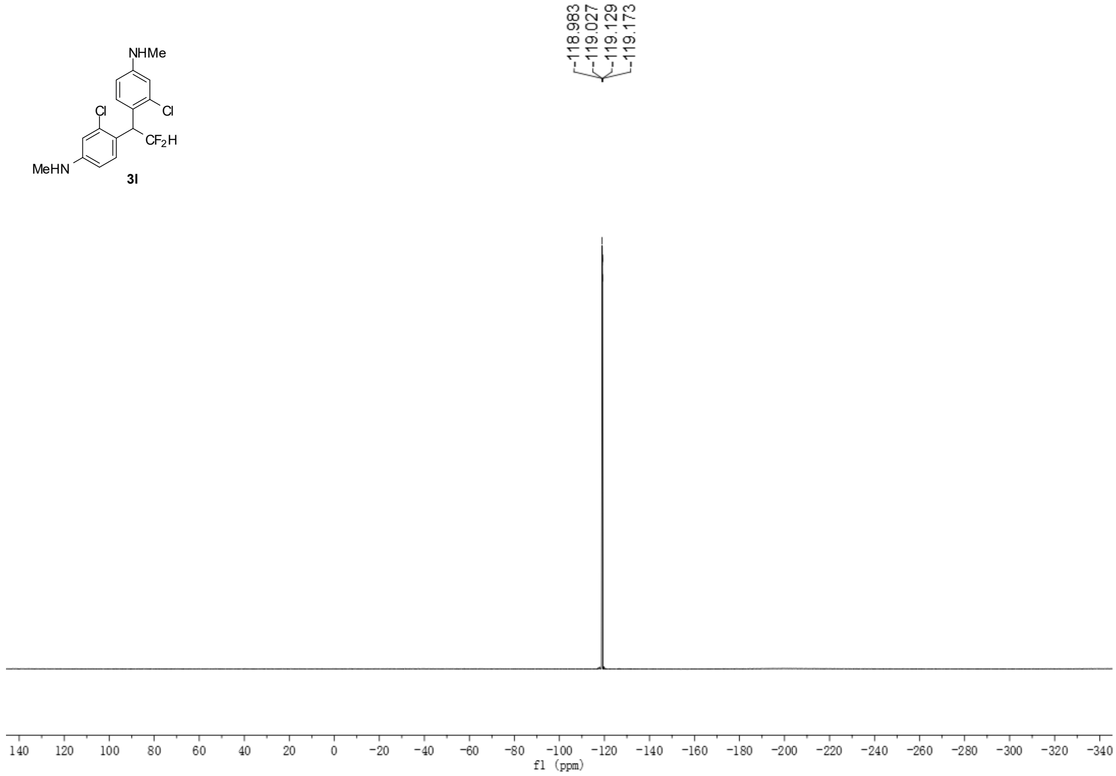
^{13}C NMR (100 MHz, $CDCl_3$) of **3k**



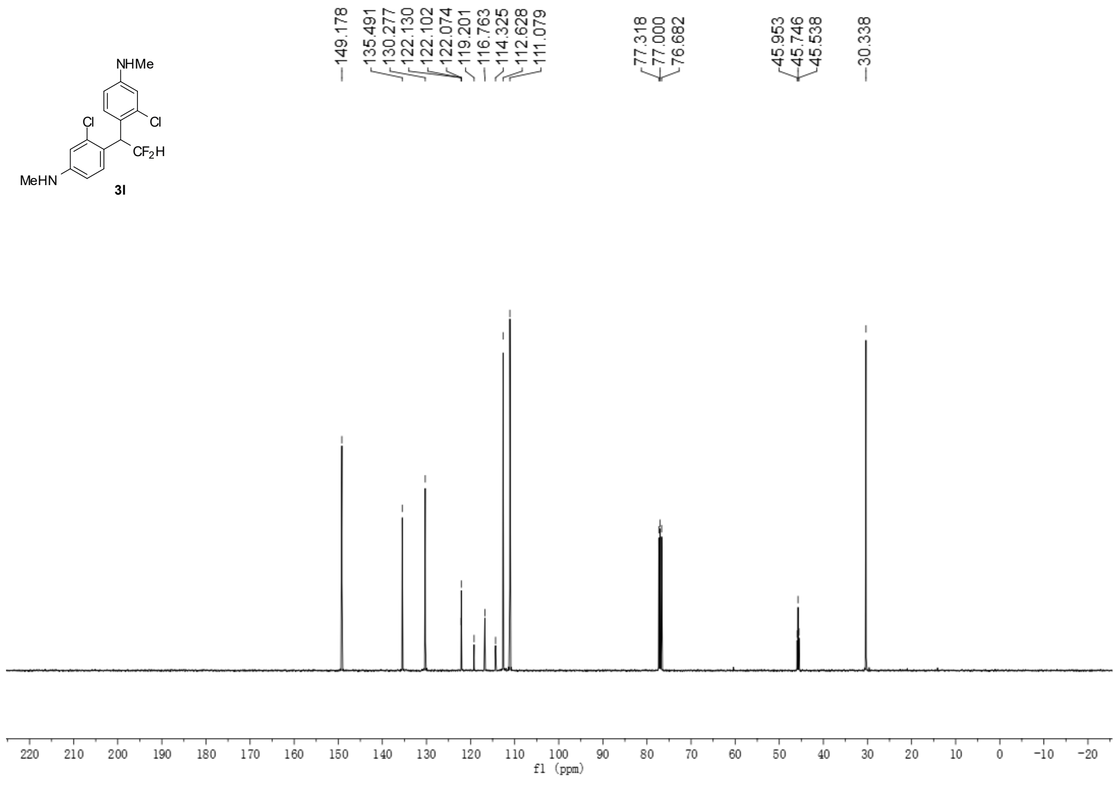
^{1}H NMR (400 MHz, $CDCl_3$) of **3l**



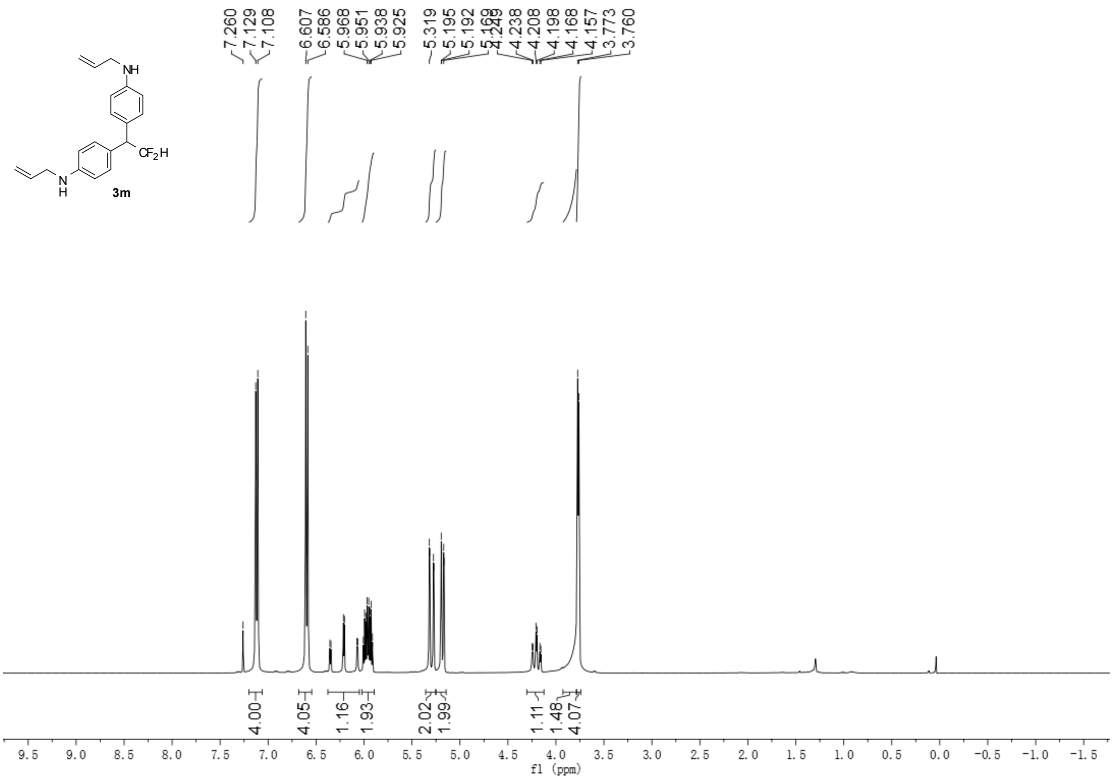
^{19}F NMR (376 MHz, $CDCl_3$) of **3l**



^{13}C NMR (100 MHz, $CDCl_3$) of **3l**

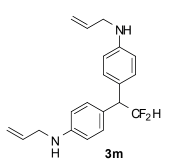


^{1}H NMR (400 MHz, $CDCl_3$) of **3m**

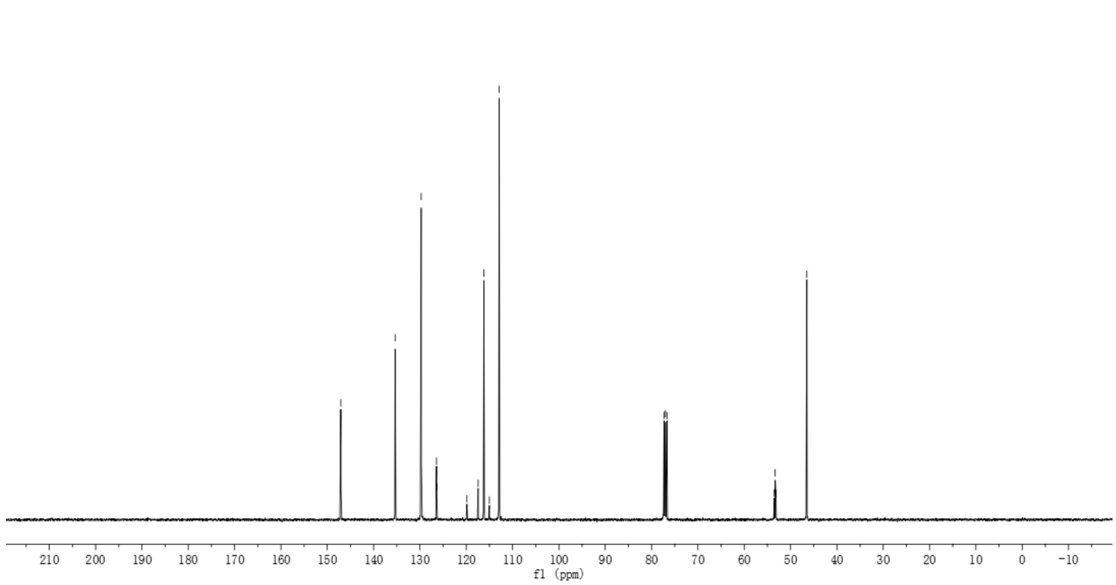


^{19}F NMR (376 MHz, $CDCl_3$) of **3m**

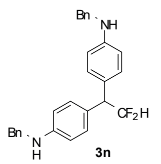
^{13}C NMR (100 MHz, $CDCl_3$) of **3m**



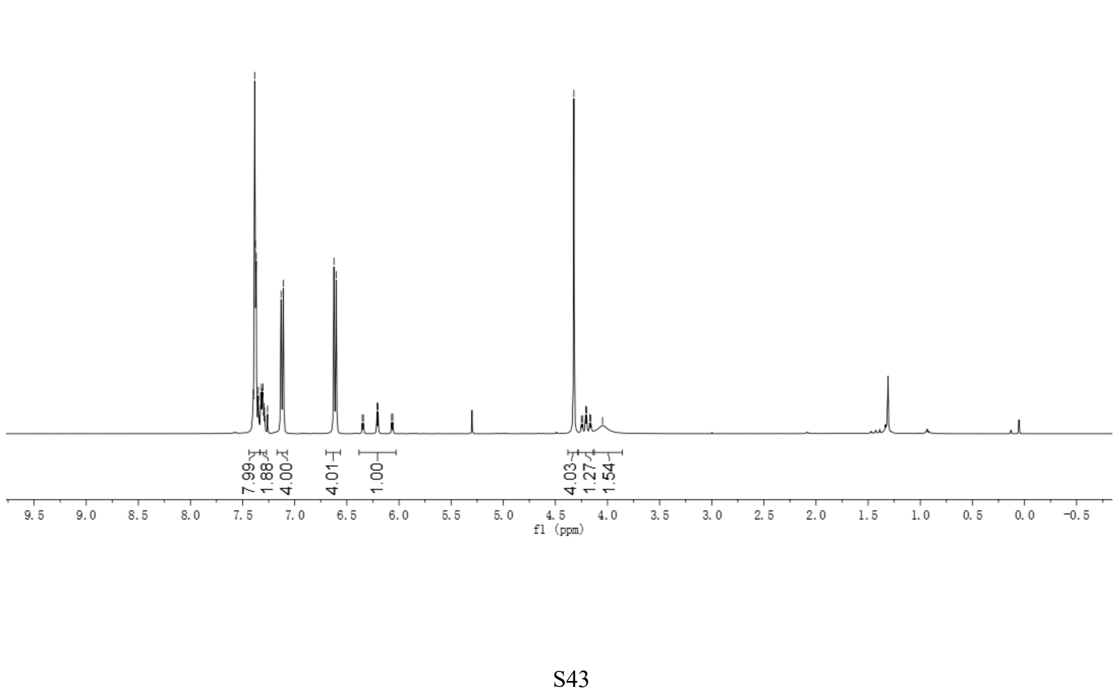
3m



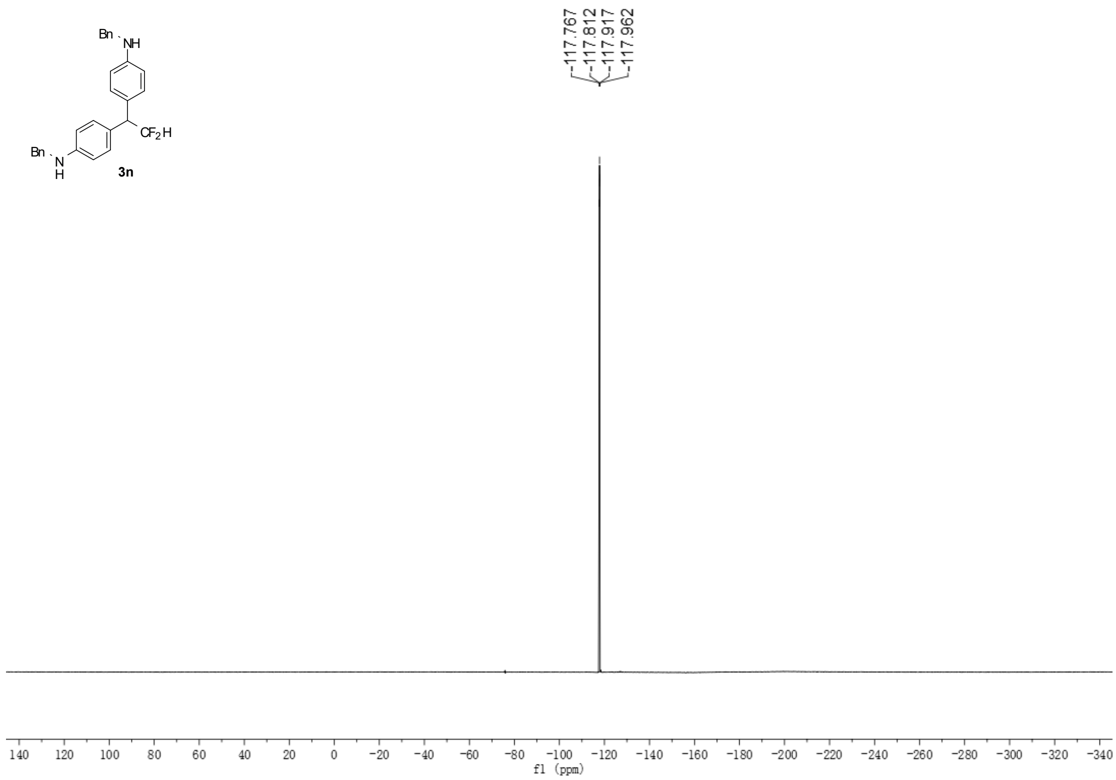
^{1}H NMR (400 MHz, $CDCl_3$) of **3n**



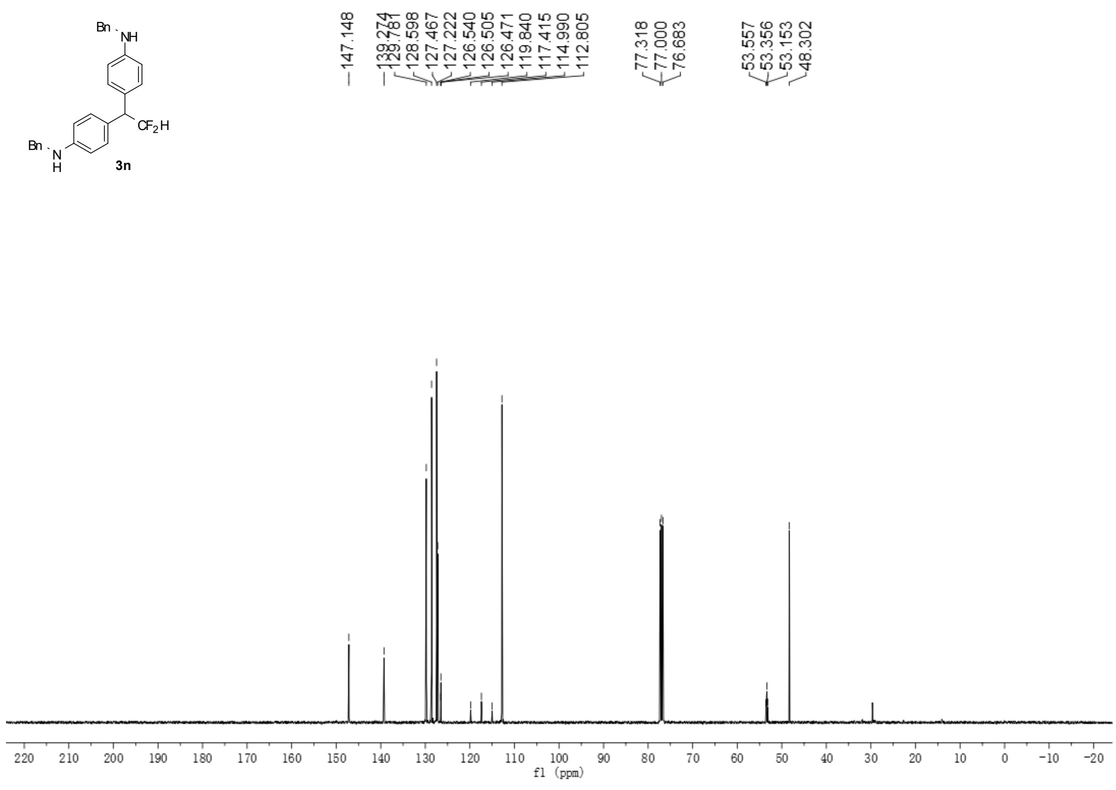
3n



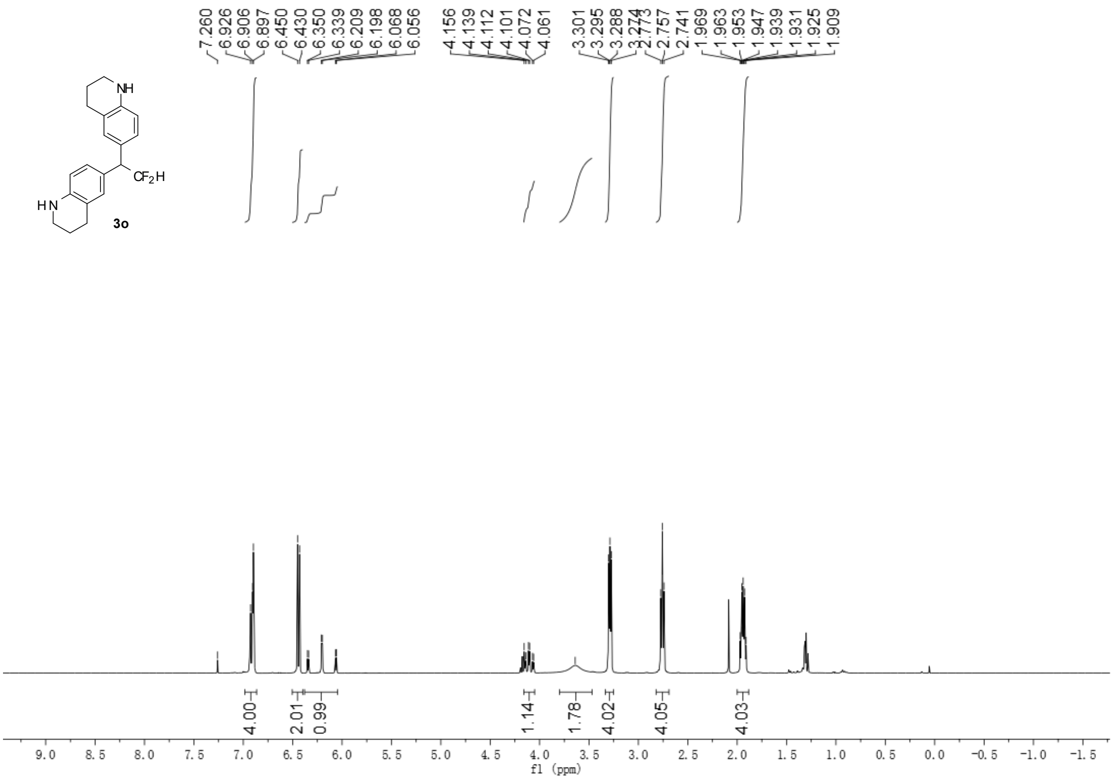
^{19}F NMR (376 MHz, $CDCl_3$) of **3n**



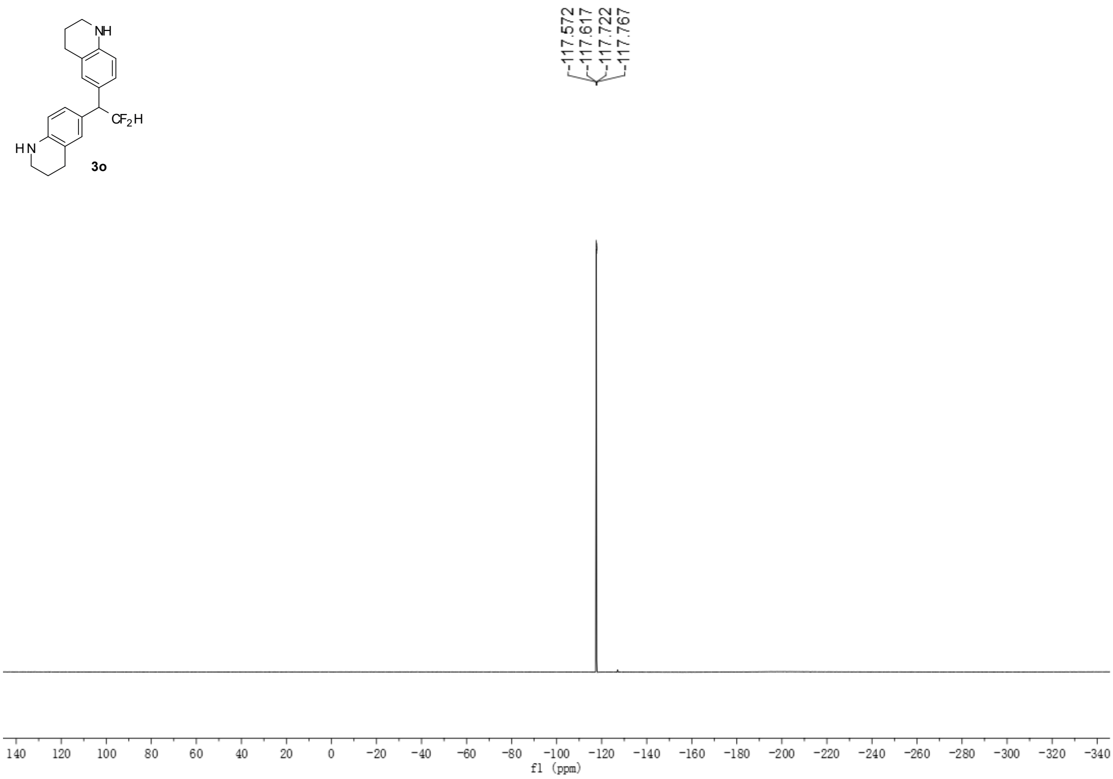
^{13}C NMR (100 MHz, $CDCl_3$) of **3n**



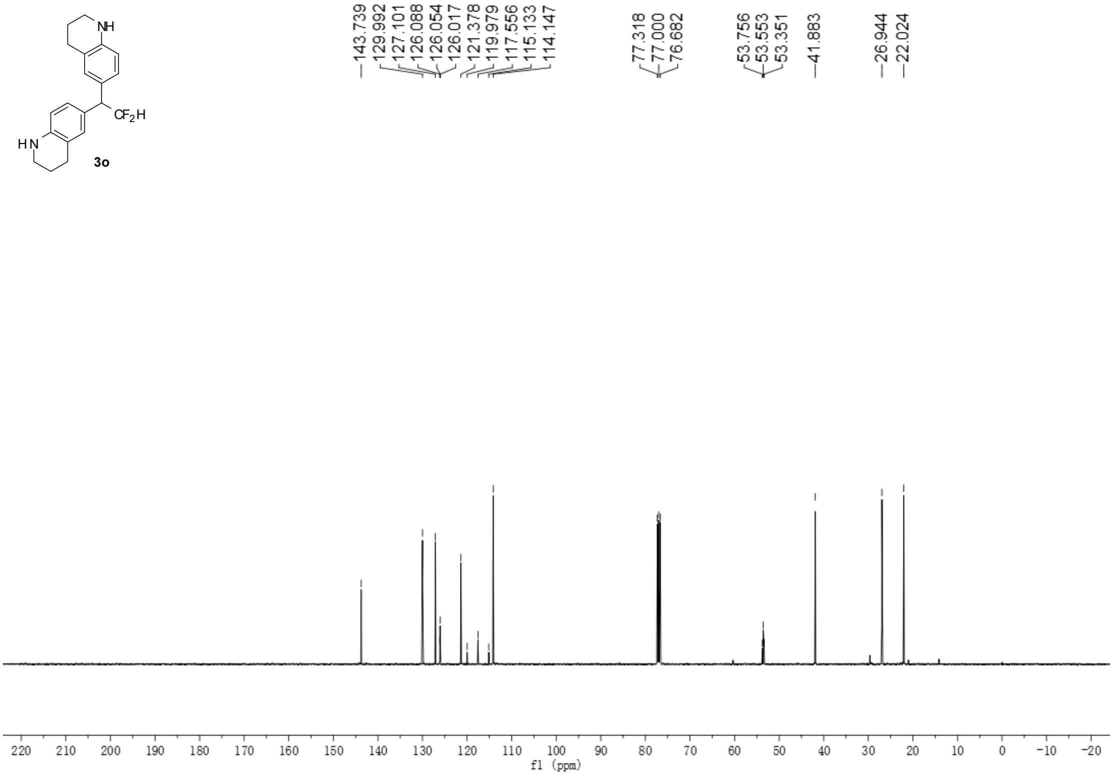
[1]H NMR (400 MHz, $CDCl_3$) of **3o**



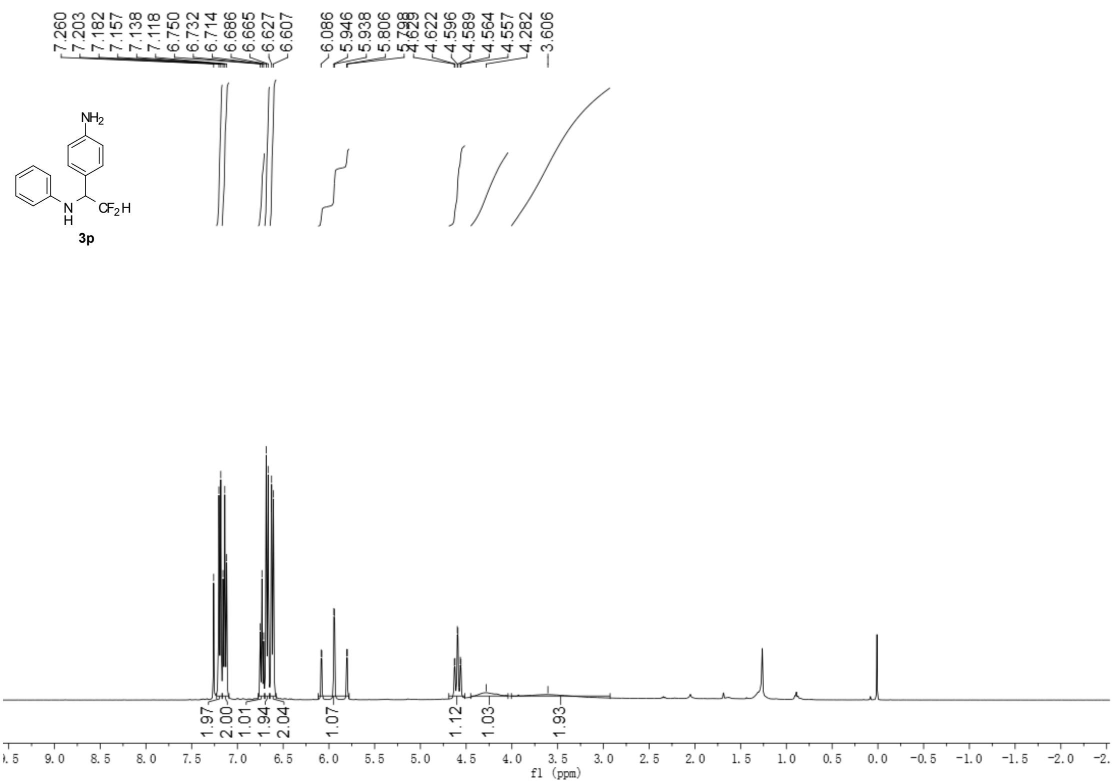
[19]F NMR (376 MHz, $CDCl_3$) of **3o**



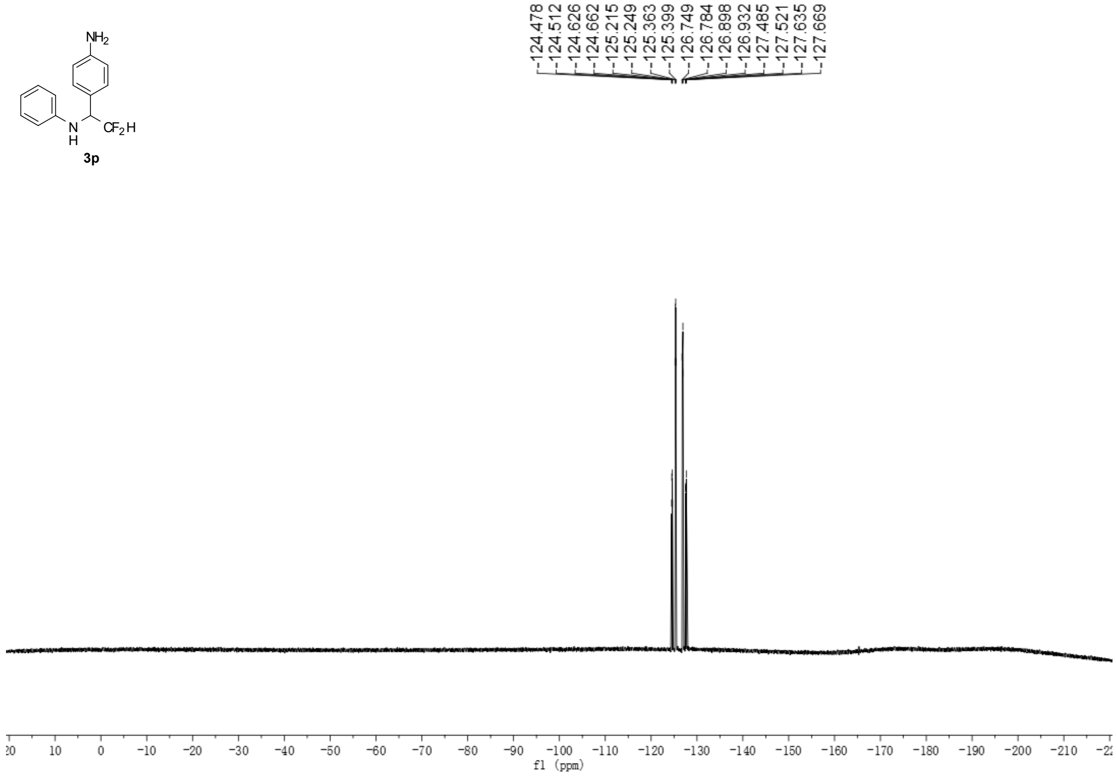
^{13}C NMR (100 MHz, $CDCl_3$) of **3o**



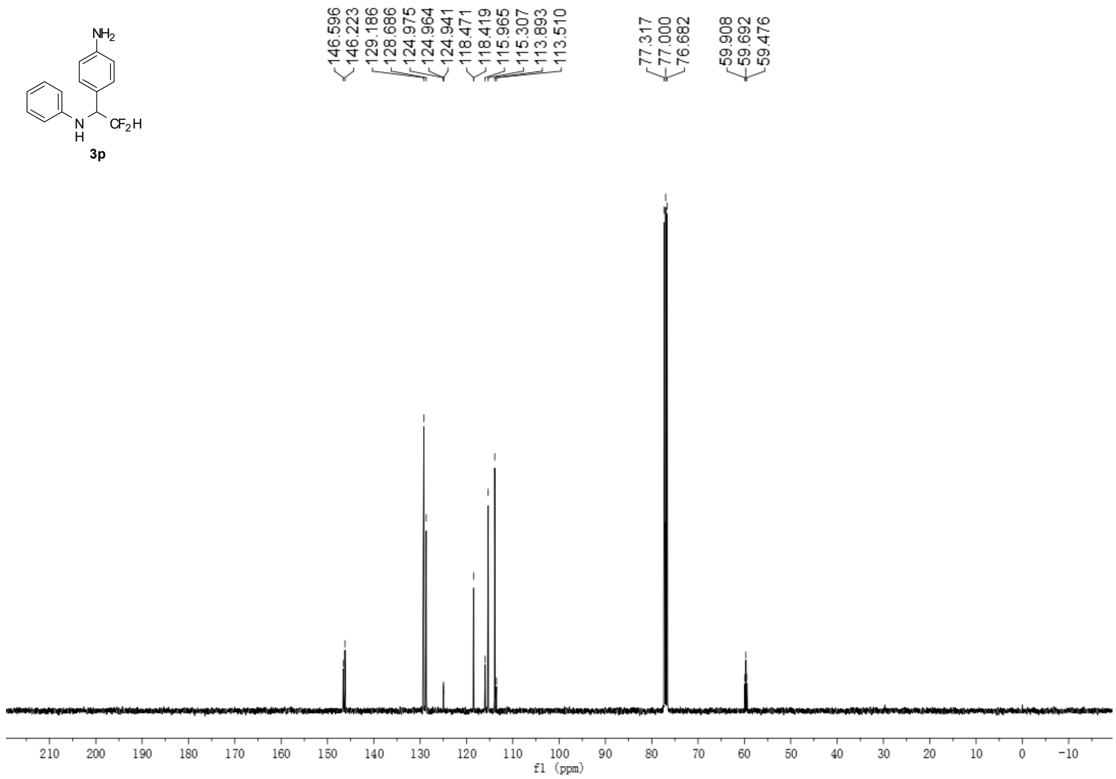
^{1}H NMR (400 MHz, $CDCl_3$) of **3p**



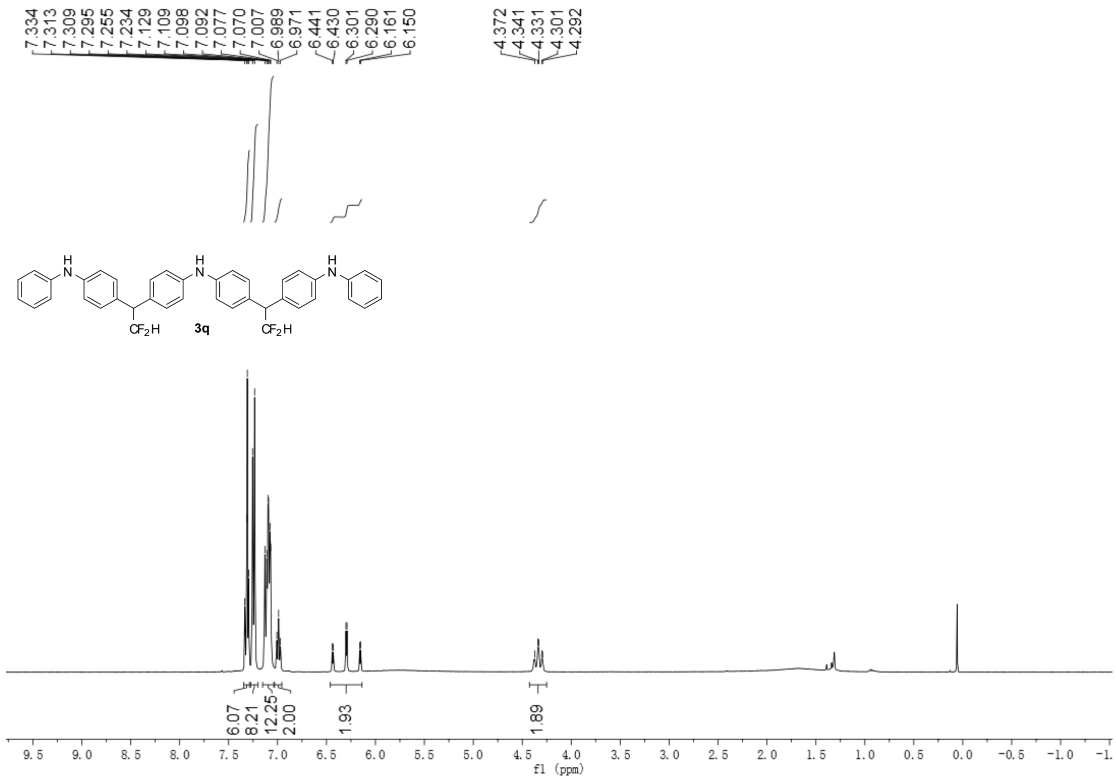
^{19}F NMR (376 MHz, $CDCl_3$) of **3p**



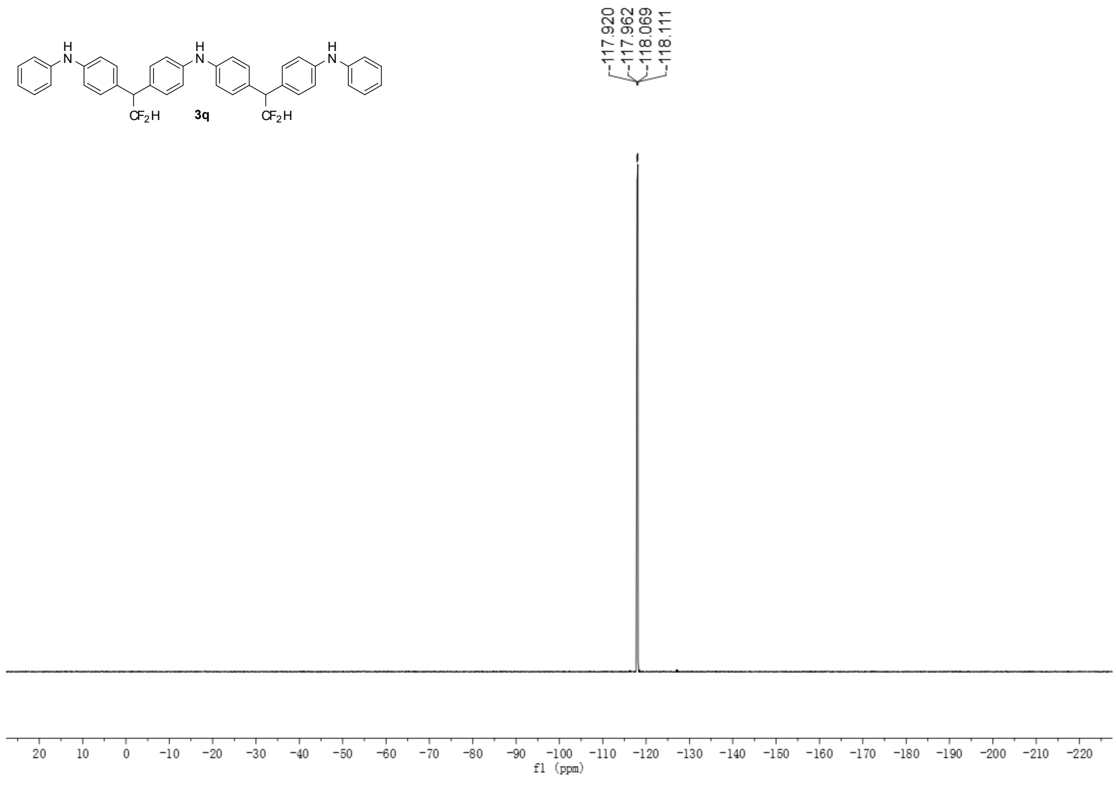
^{13}C NMR (100 MHz, $CDCl_3$) of **3p**



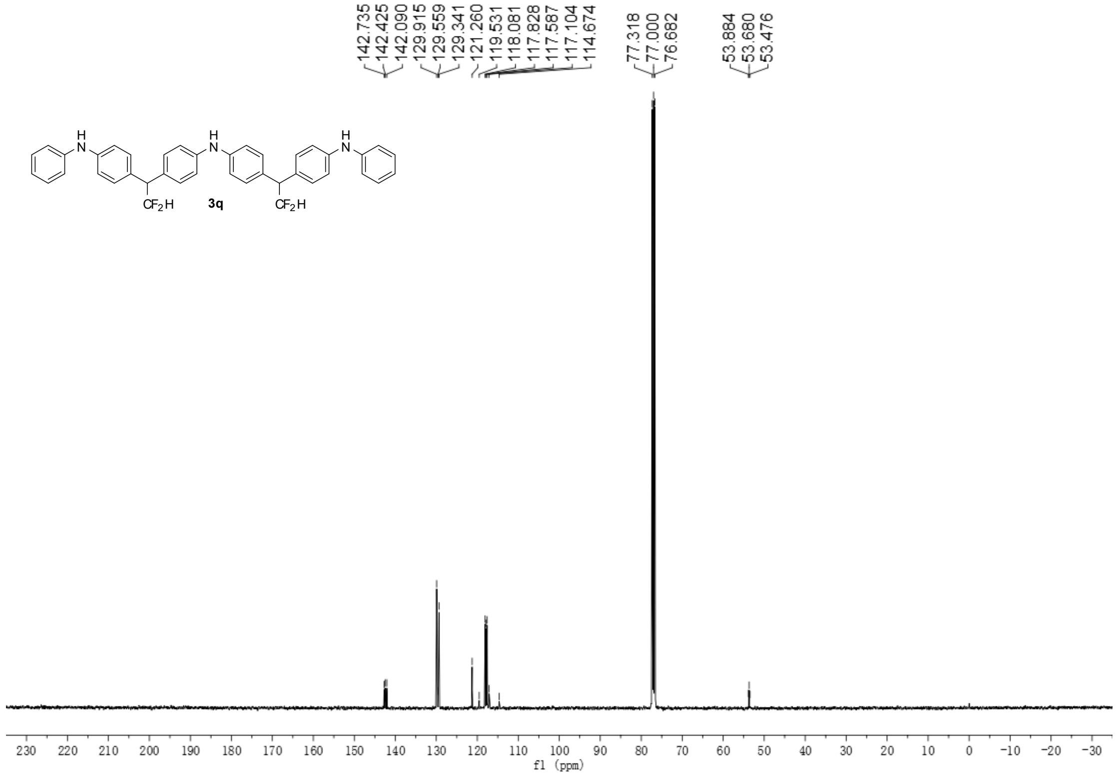
^{1}H NMR (400 MHz, $CDCl_3$) of **3q**



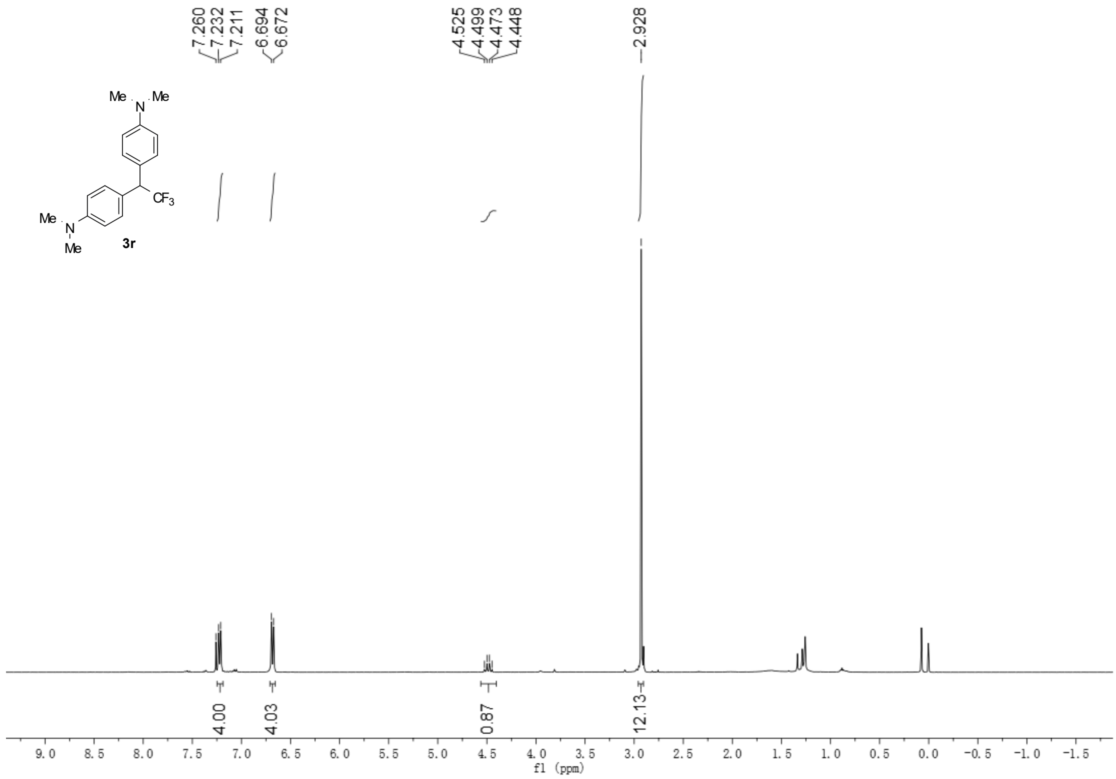
^{19}F NMR (376 MHz, $CDCl_3$) of **3q**



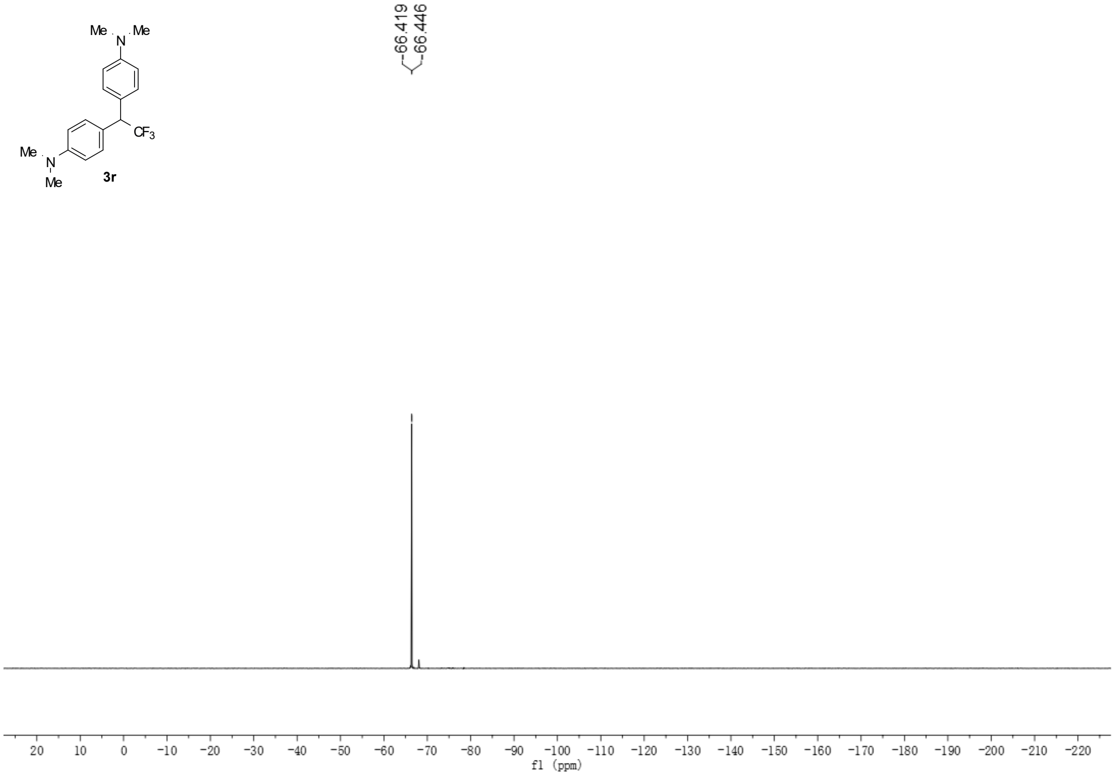
^{13}C NMR (100 MHz, $CDCl_3$) of **3q**



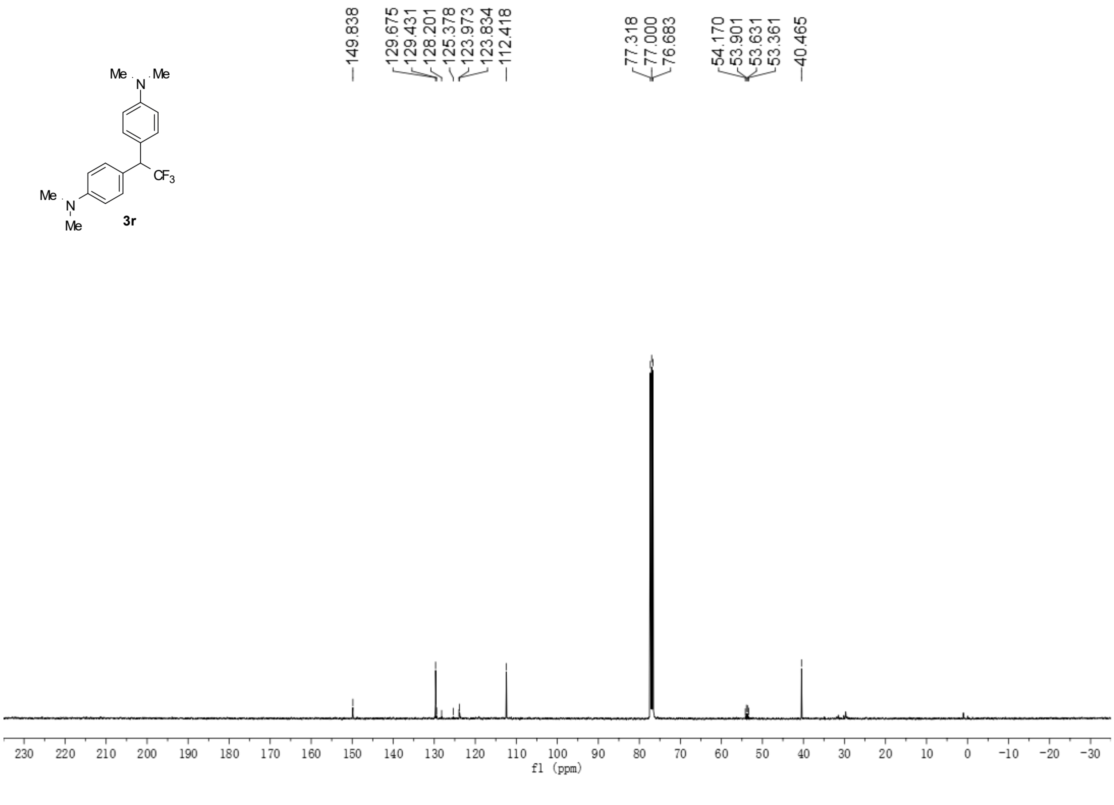
^{1}H NMR (400 MHz, $CDCl_3$) of **3r**



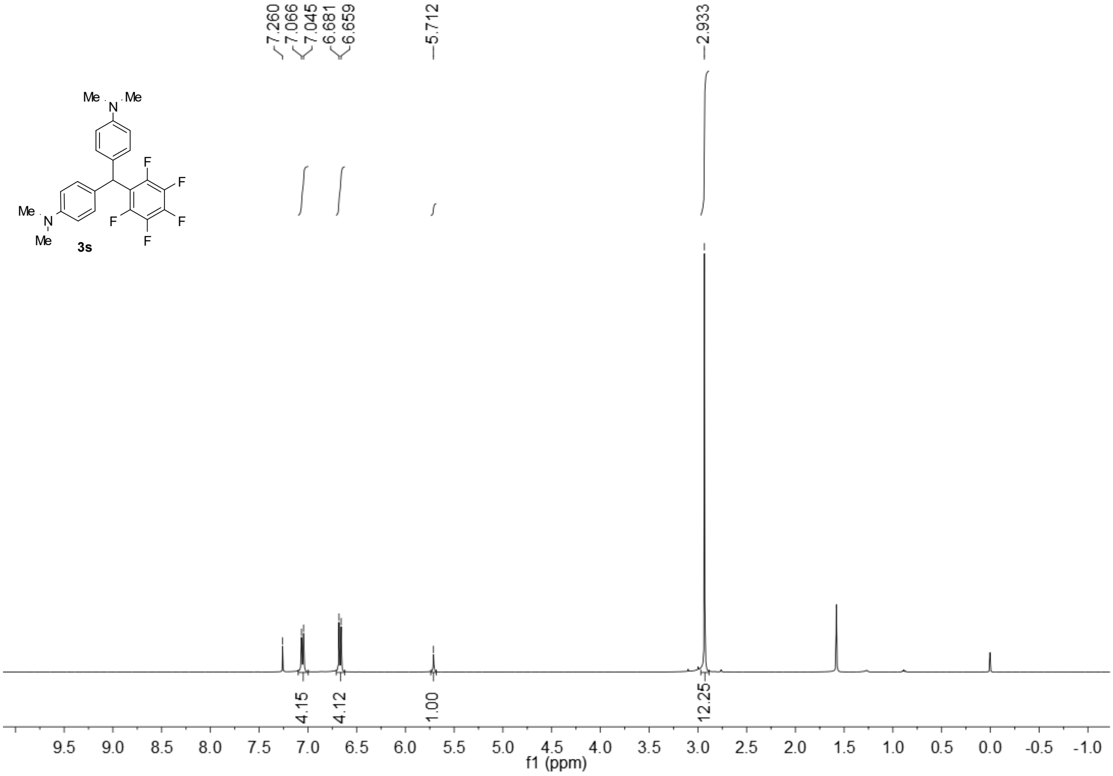
^{19}F NMR (376 MHz, $CDCl_3$) of **3r**



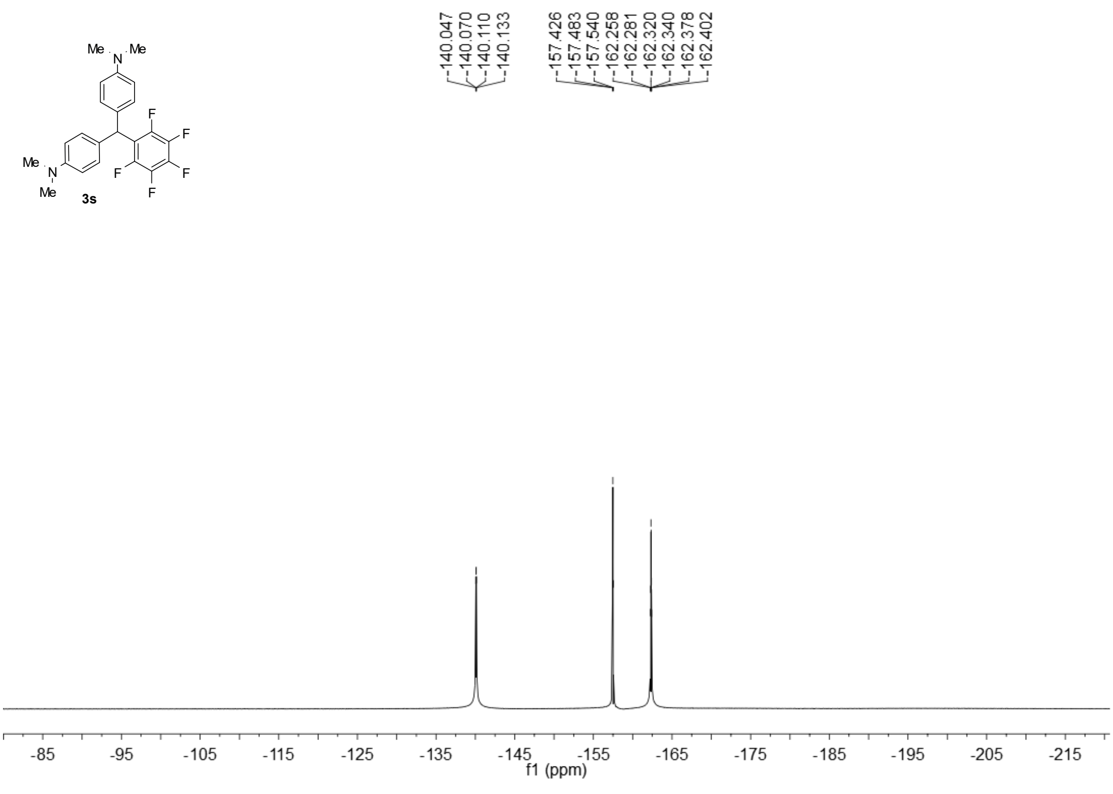
^{13}C NMR (100 MHz, $CDCl_3$) of **3r**



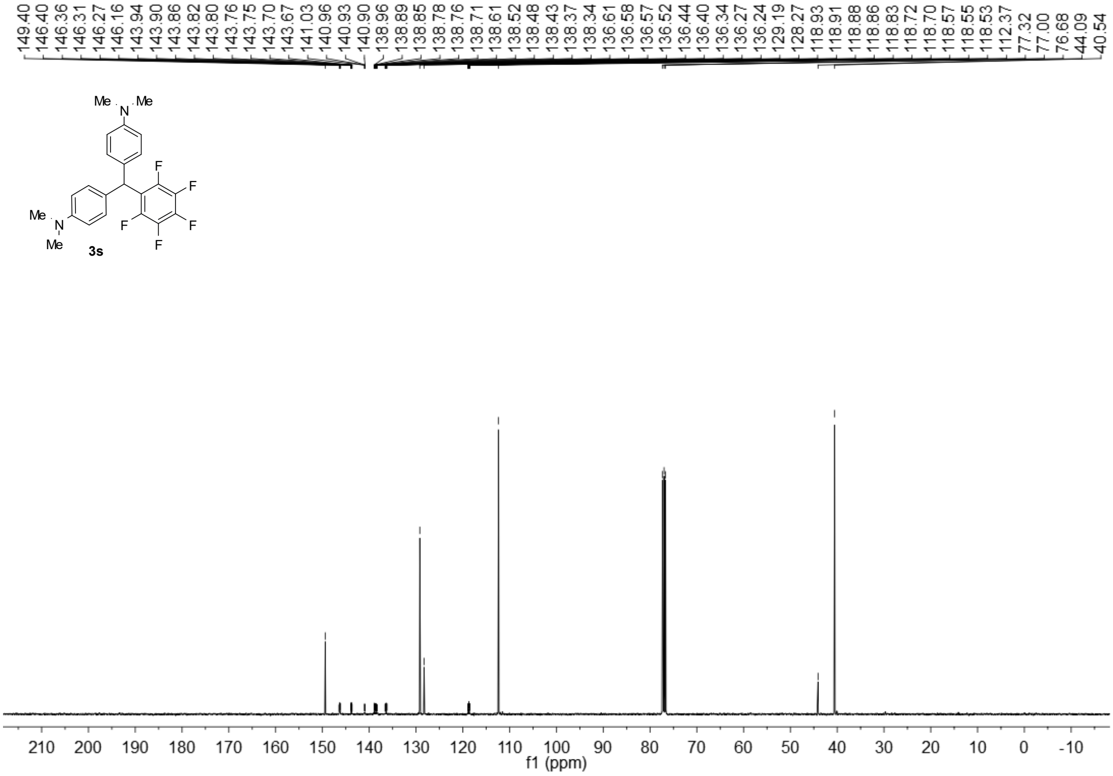
^{1}H NMR (400 MHz, $CDCl_3$) of **3s**



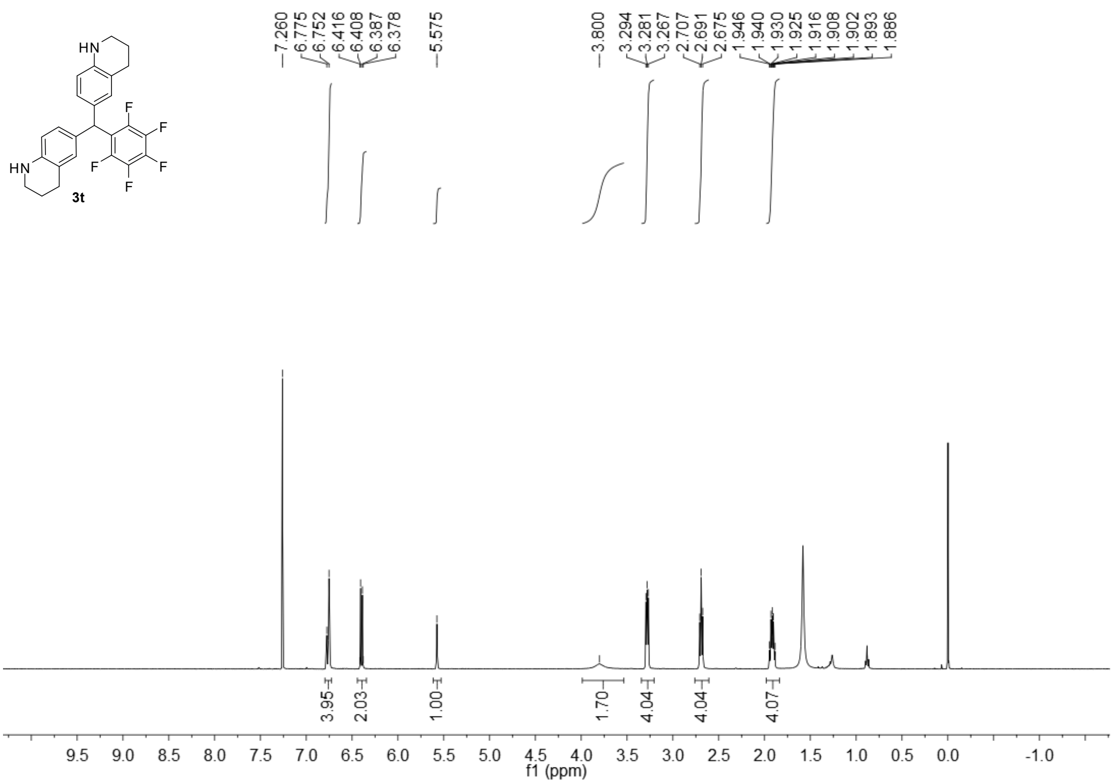
^{19}F NMR (376 MHz, $CDCl_3$) of **3s**



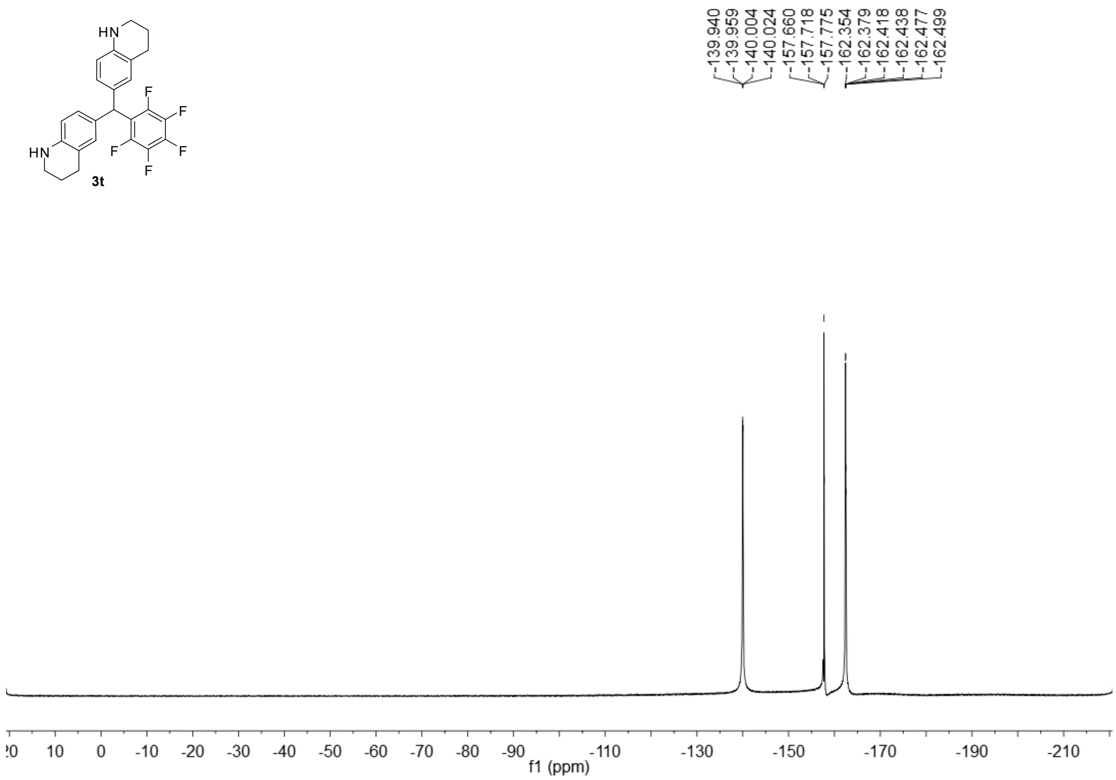
^{13}C NMR (100 MHz, $CDCl_3$) of **3s**



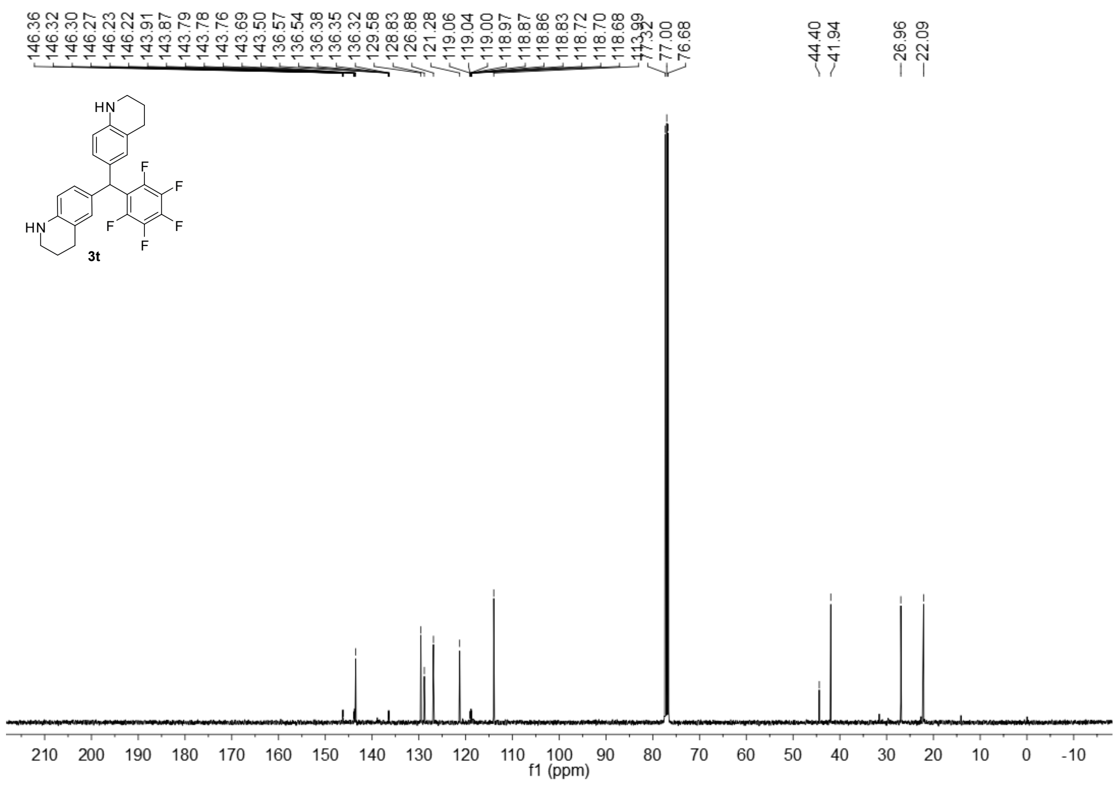
^1H NMR (400 MHz, $CDCl_3$) of **3t**



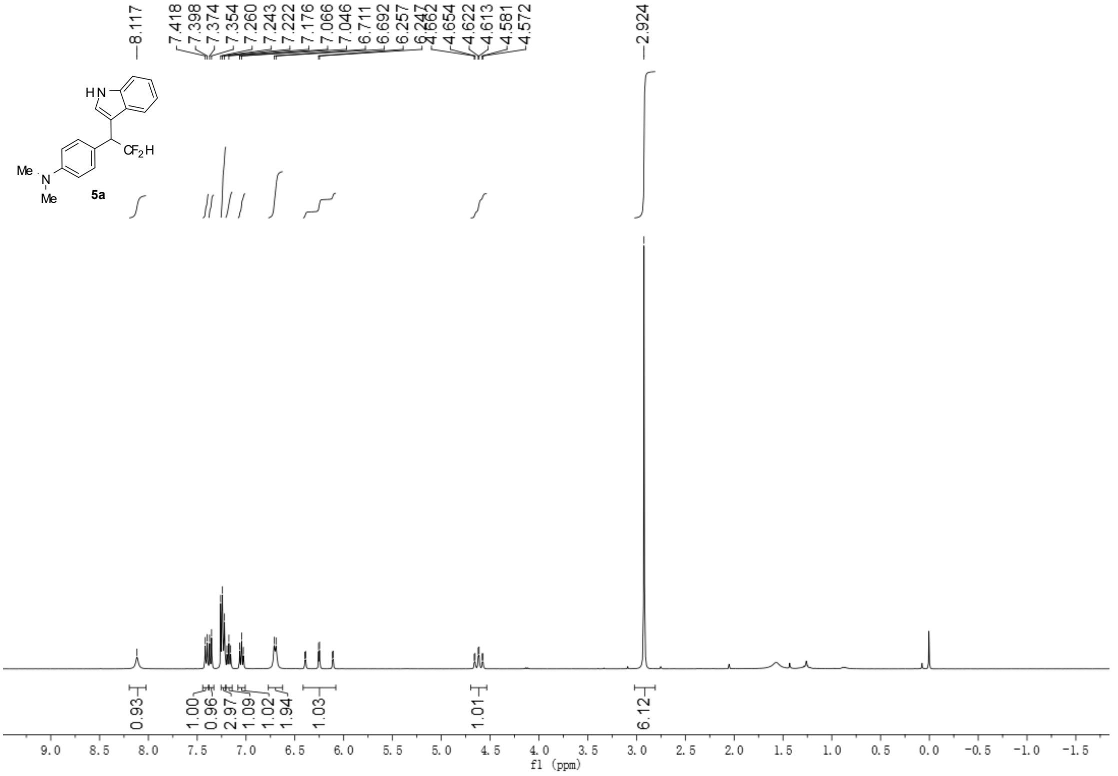
^{19}F NMR (376 MHz, $CDCl_3$) of **3t**



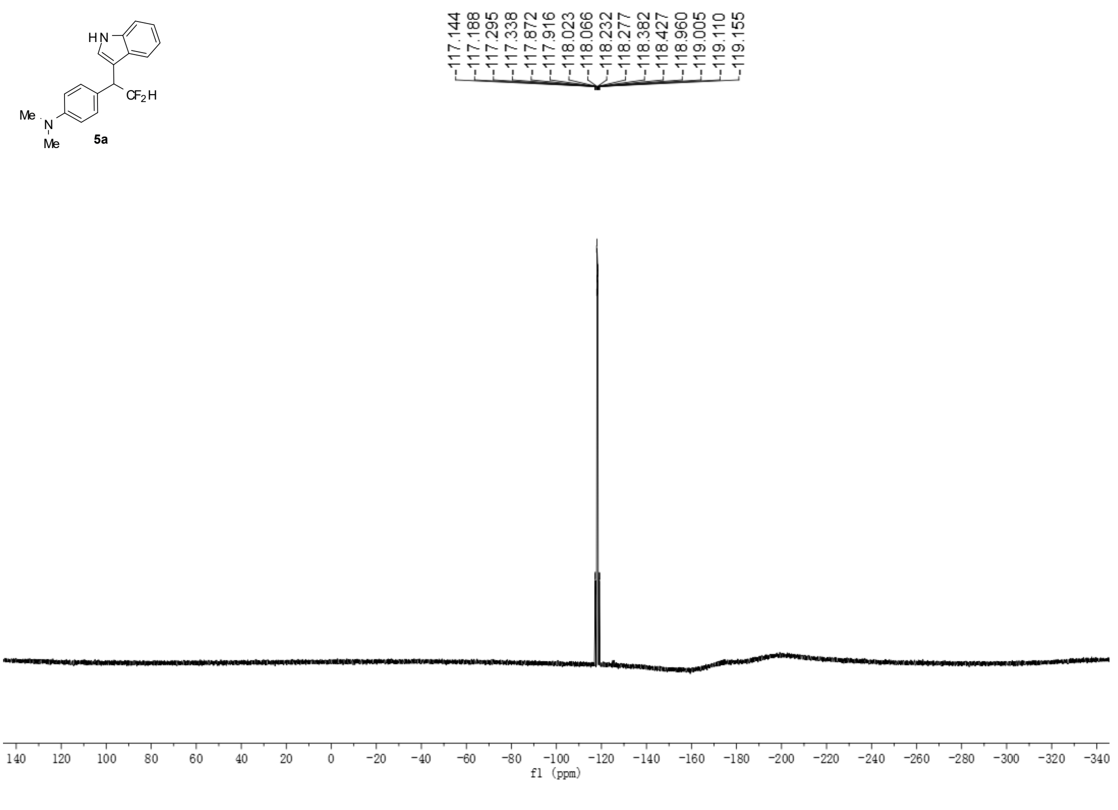
^{13}C NMR (100 MHz, $CDCl_3$) of **3t**



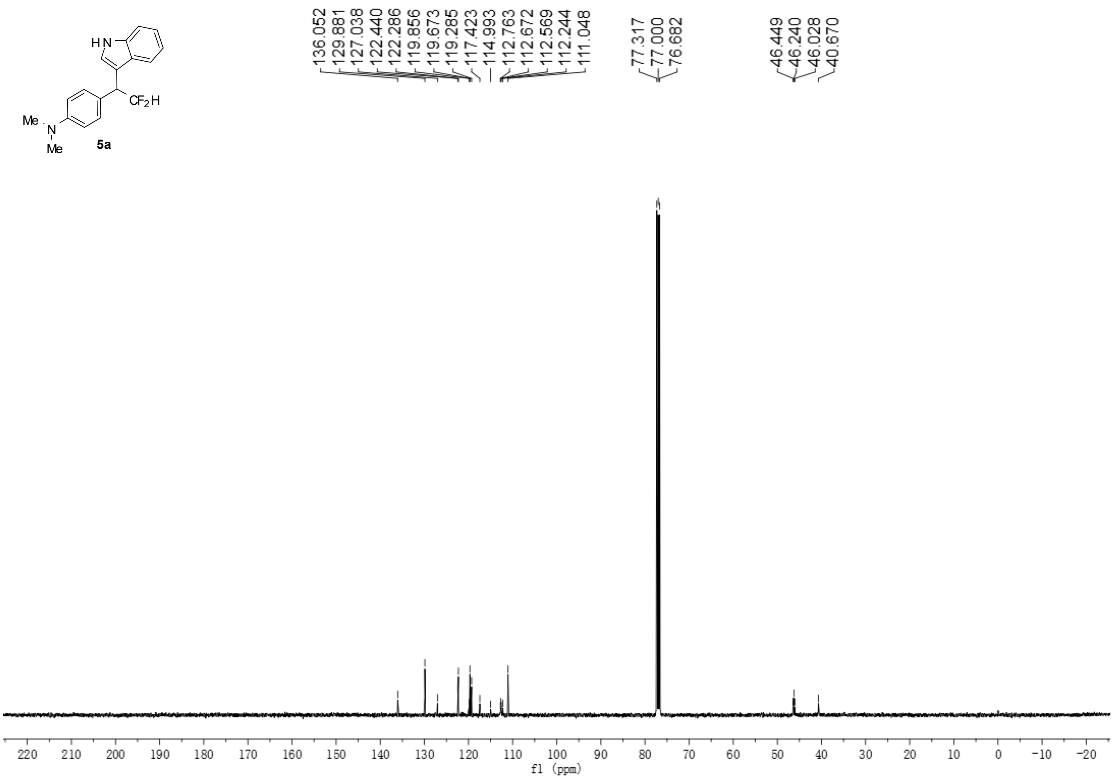
^{1}H NMR (400 MHz, $CDCl_3$) of **5a**



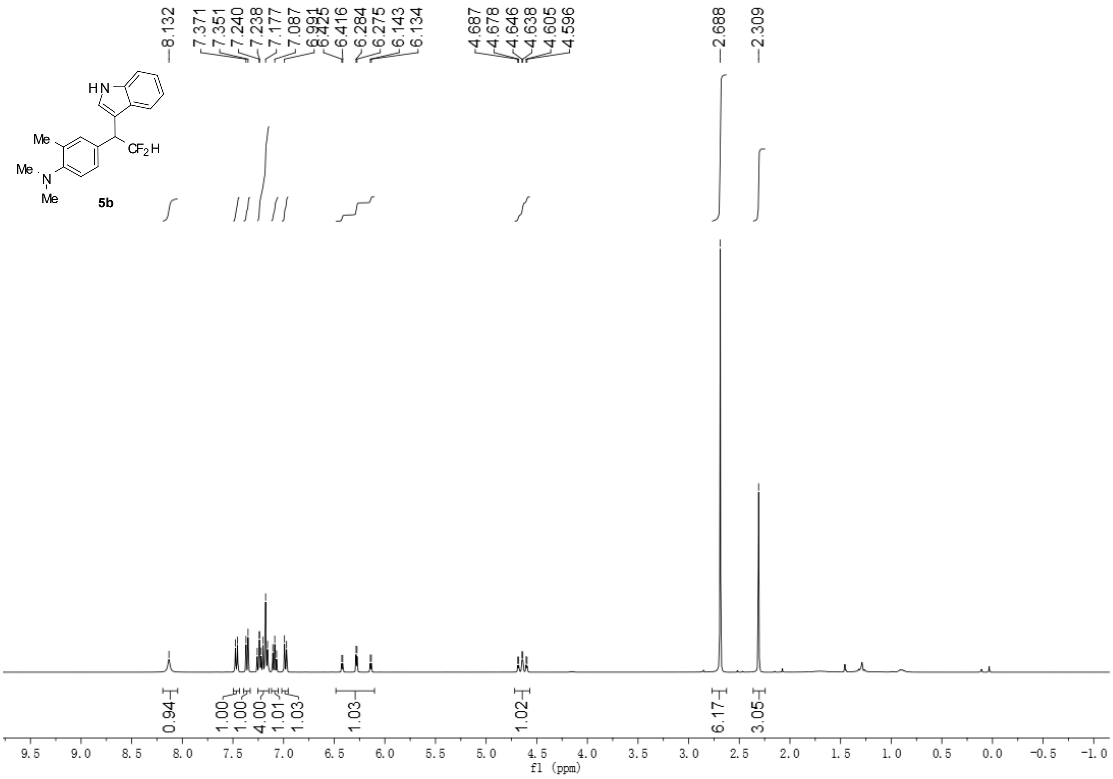
^{19}F NMR (376 MHz, $CDCl_3$) of **5a**



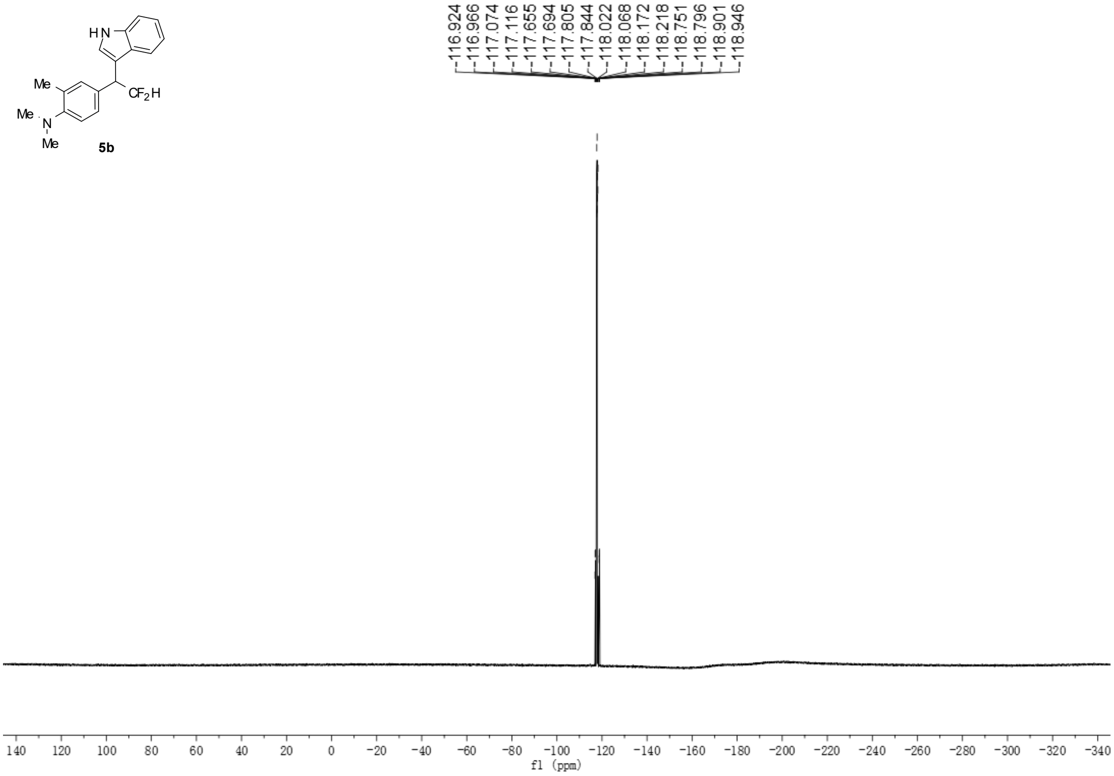
^{13}C NMR (100 MHz, $CDCl_3$) of **5a**



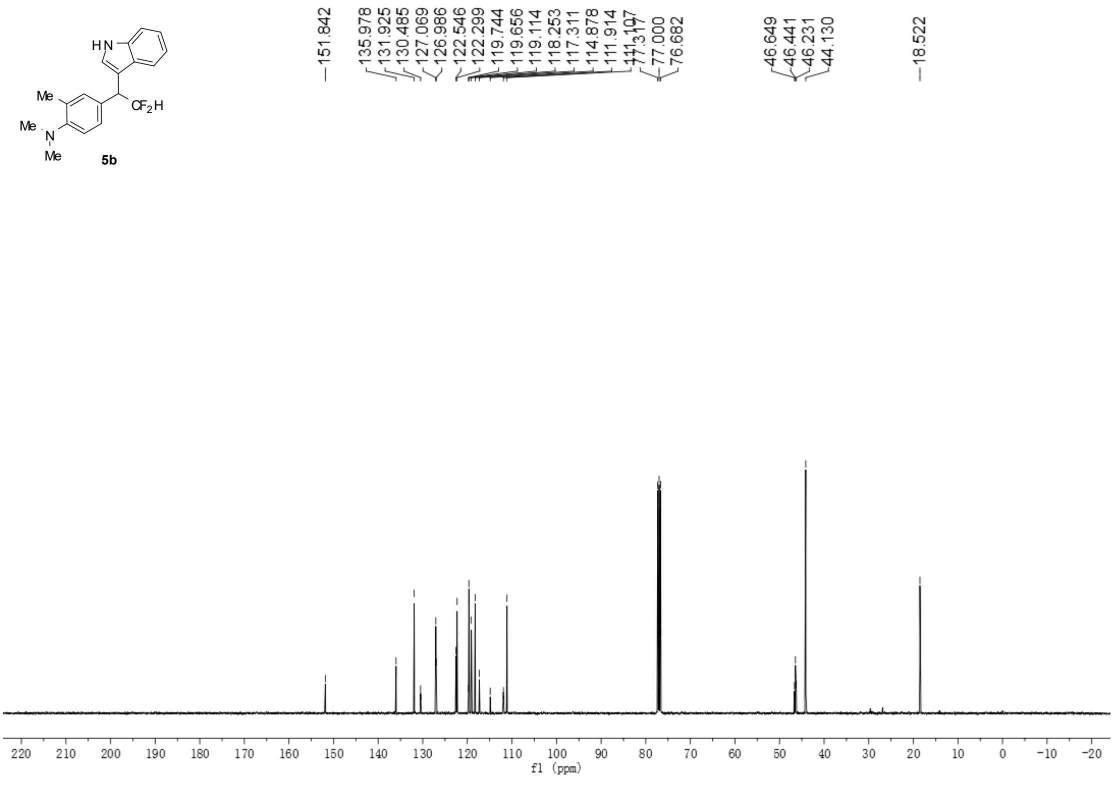
^{1}H NMR (400 MHz, $CDCl_3$) of **5b**



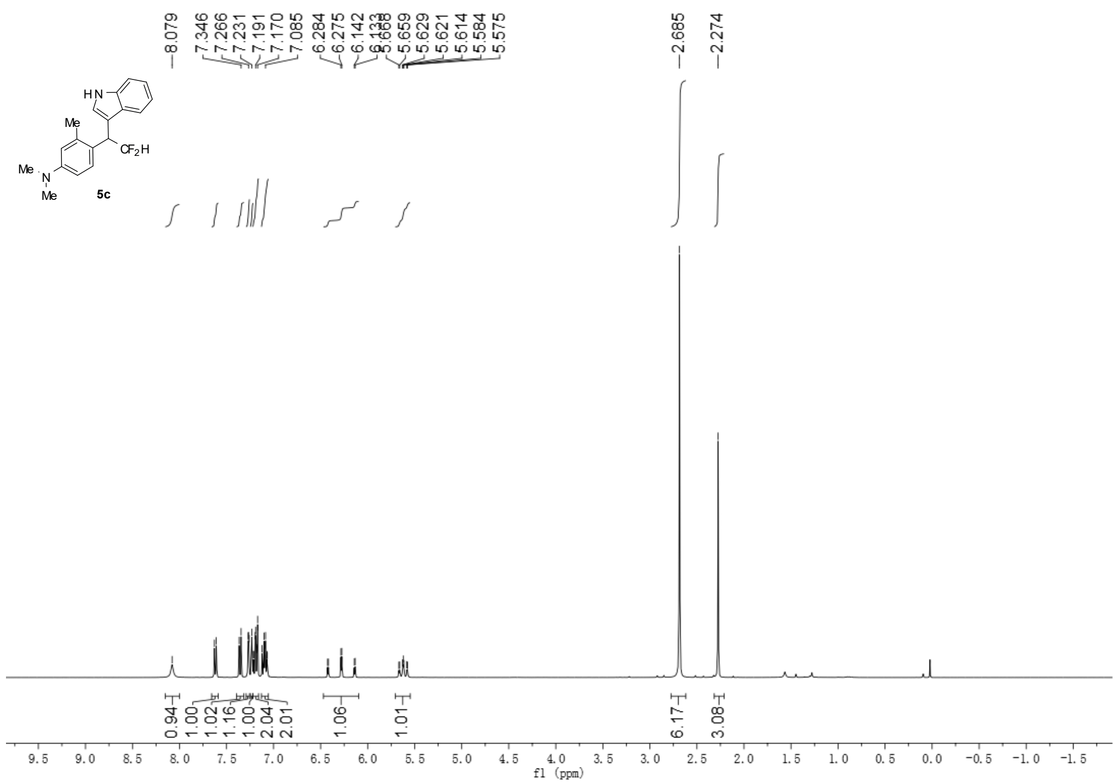
^{19}F NMR (376 MHz, $(CD_3)_2CO$) of **5b**



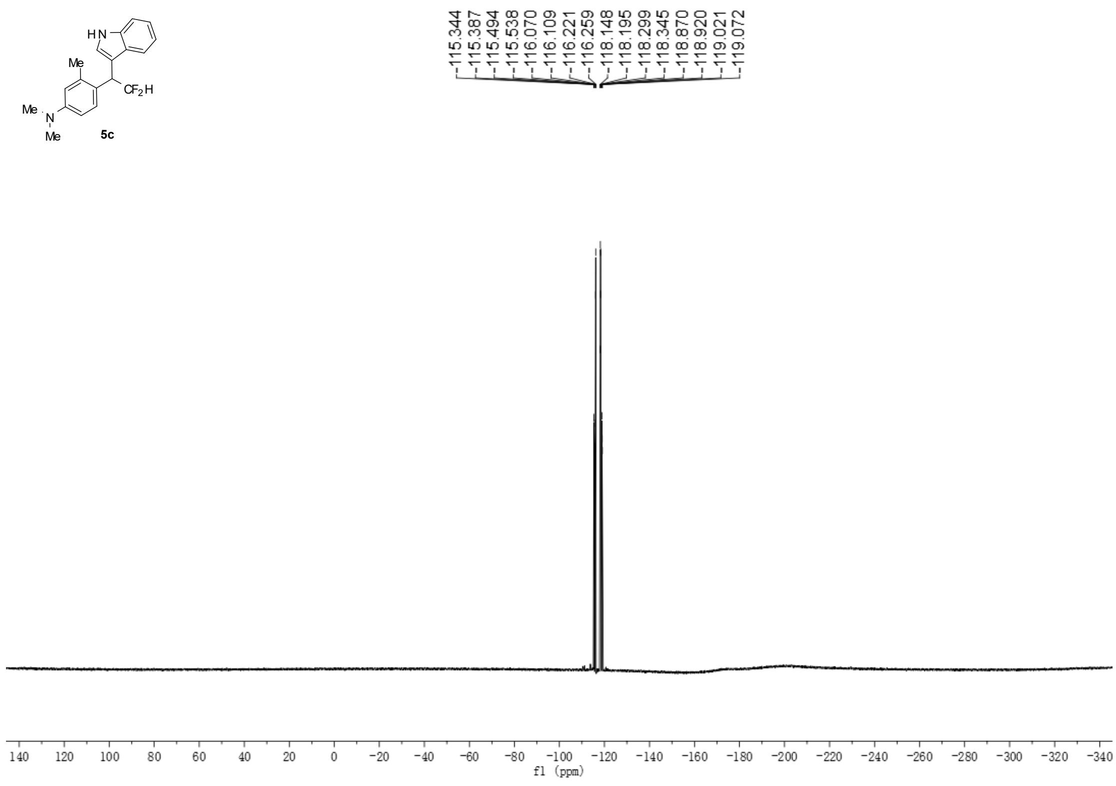
^{13}C NMR (100 MHz, $(CD_3)_2CO$) of **5b**



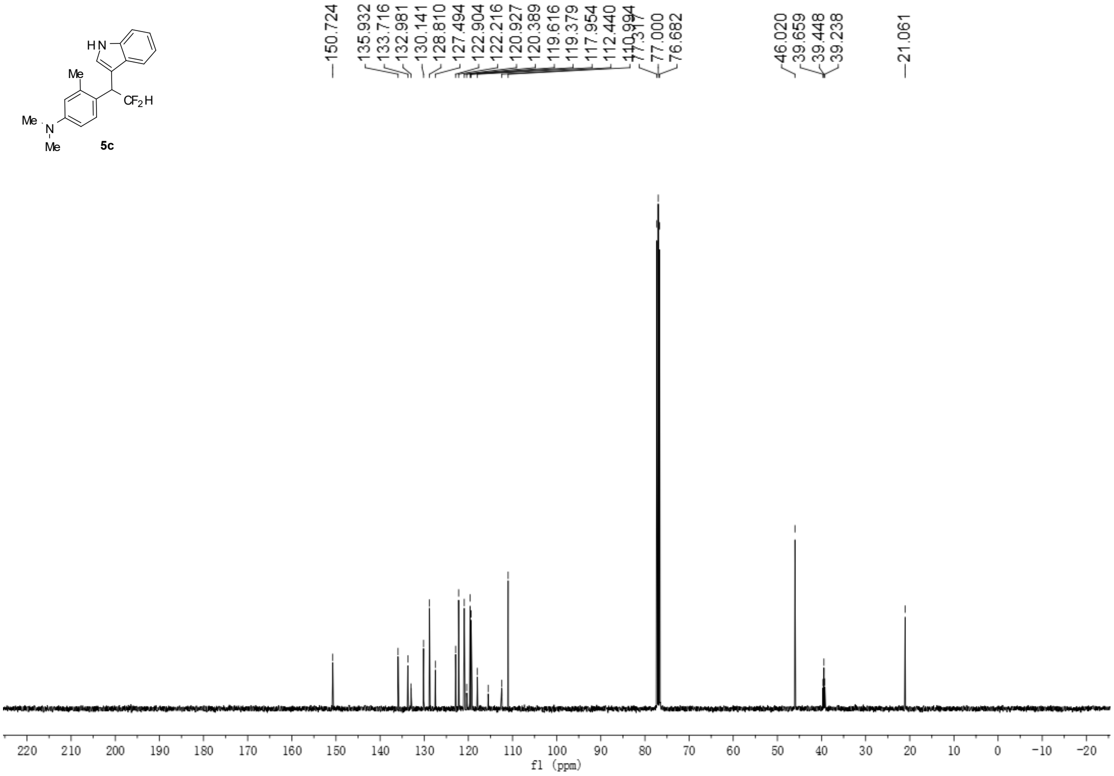
^{1}H NMR (400 MHz, $CDCl_3$) of **5c**



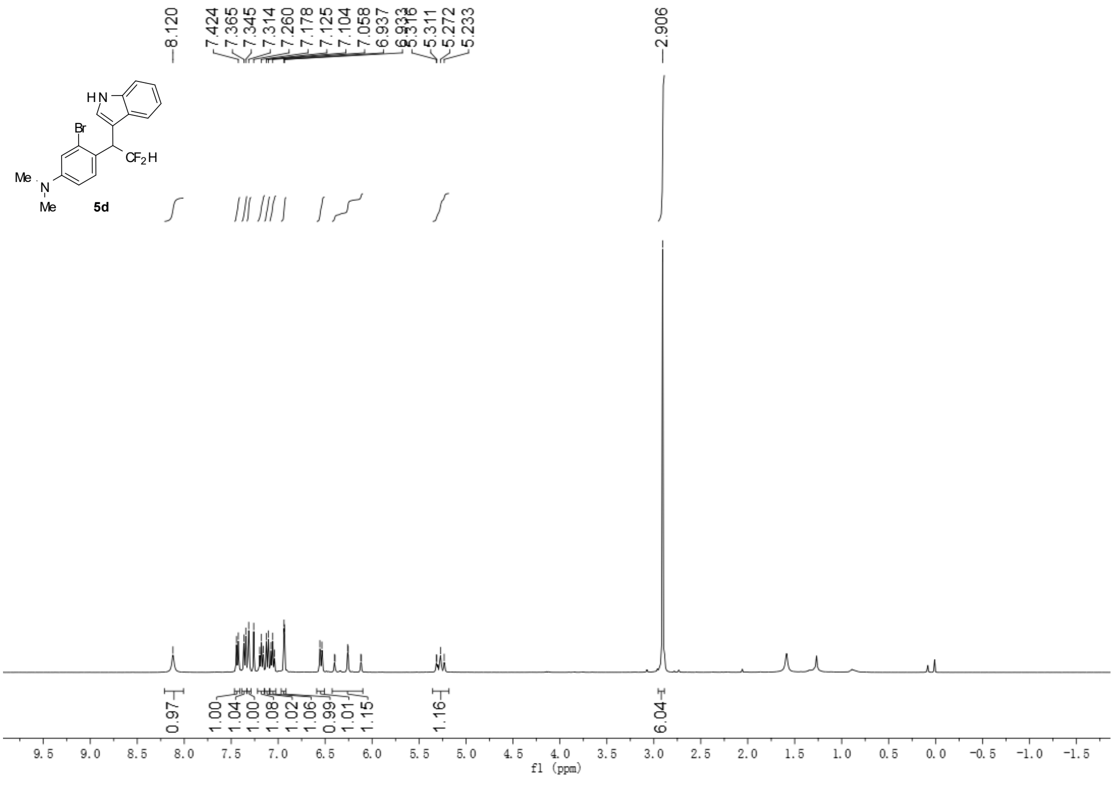
^{19}F NMR (376 MHz, $CDCl_3$) of **5c**



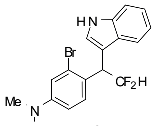
^{13}C NMR (100 MHz, $CDCl_3$) of **5c**



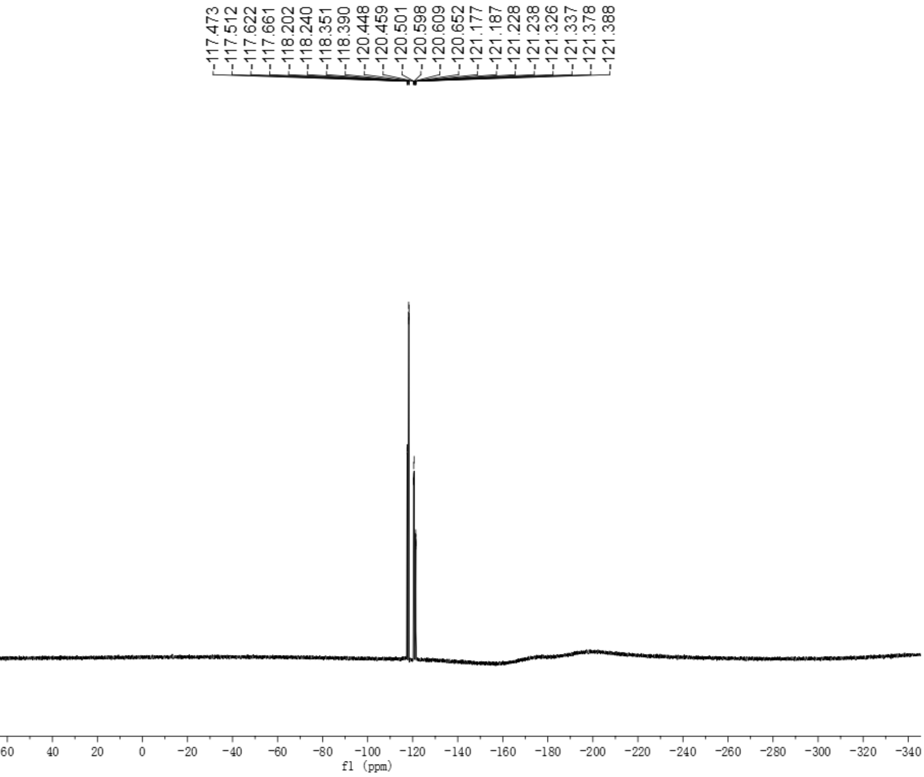
^{1}H NMR (400 MHz, $CDCl_3$) of **5d**



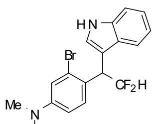
^{19}F NMR (376 MHz, $CDCl_3$) of **5d**



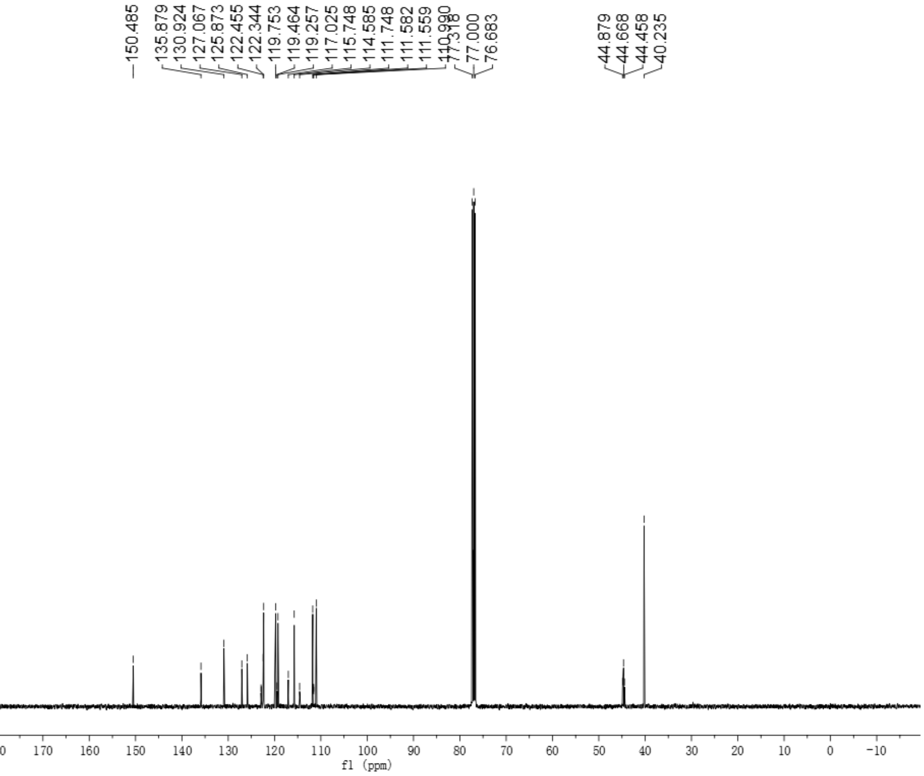
5d



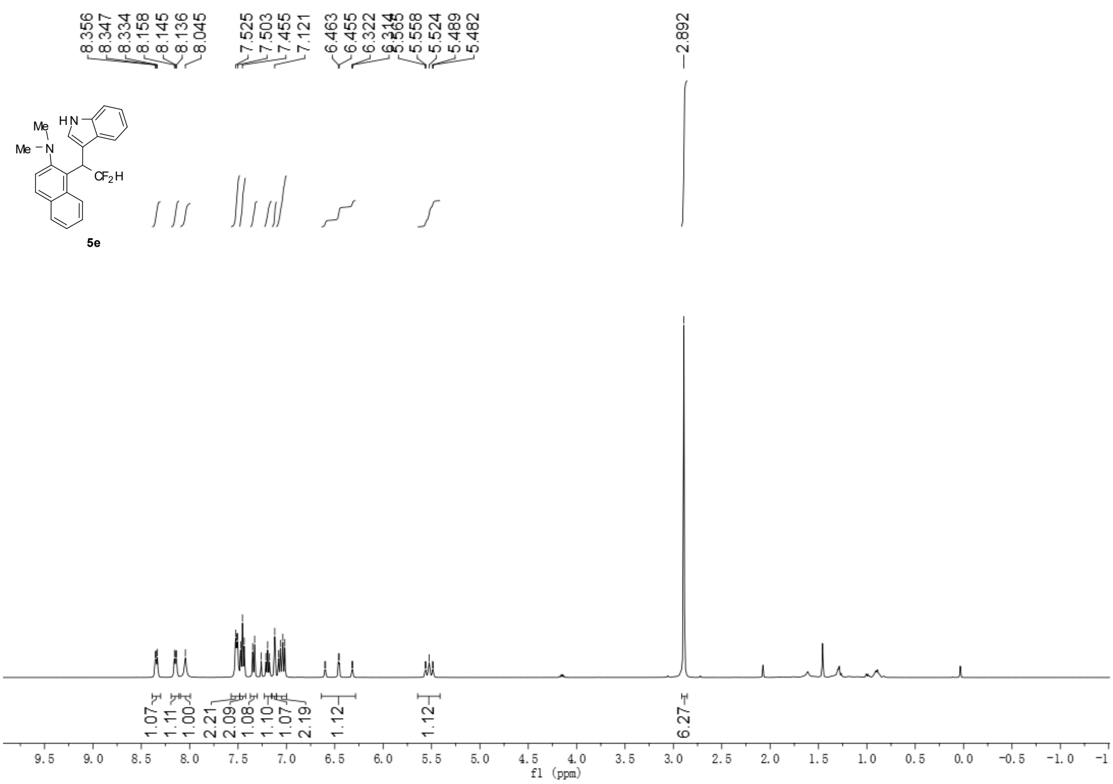
^{13}C NMR (100 MHz, $CDCl_3$) of **5d**



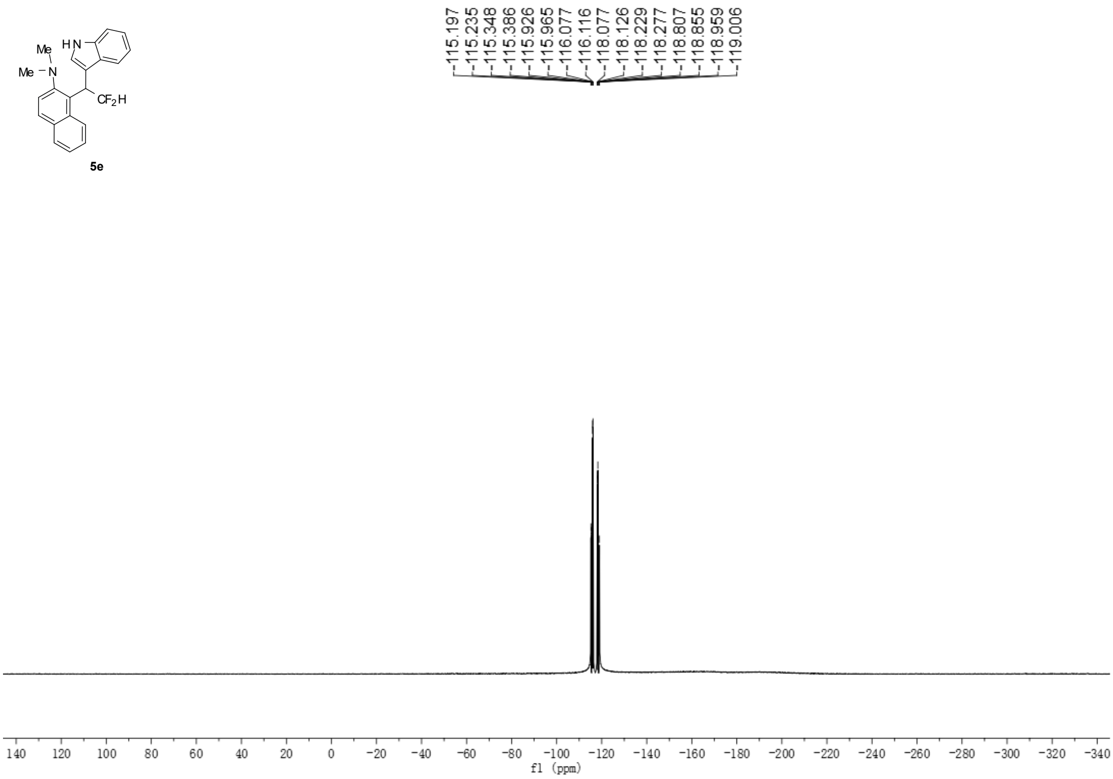
5d



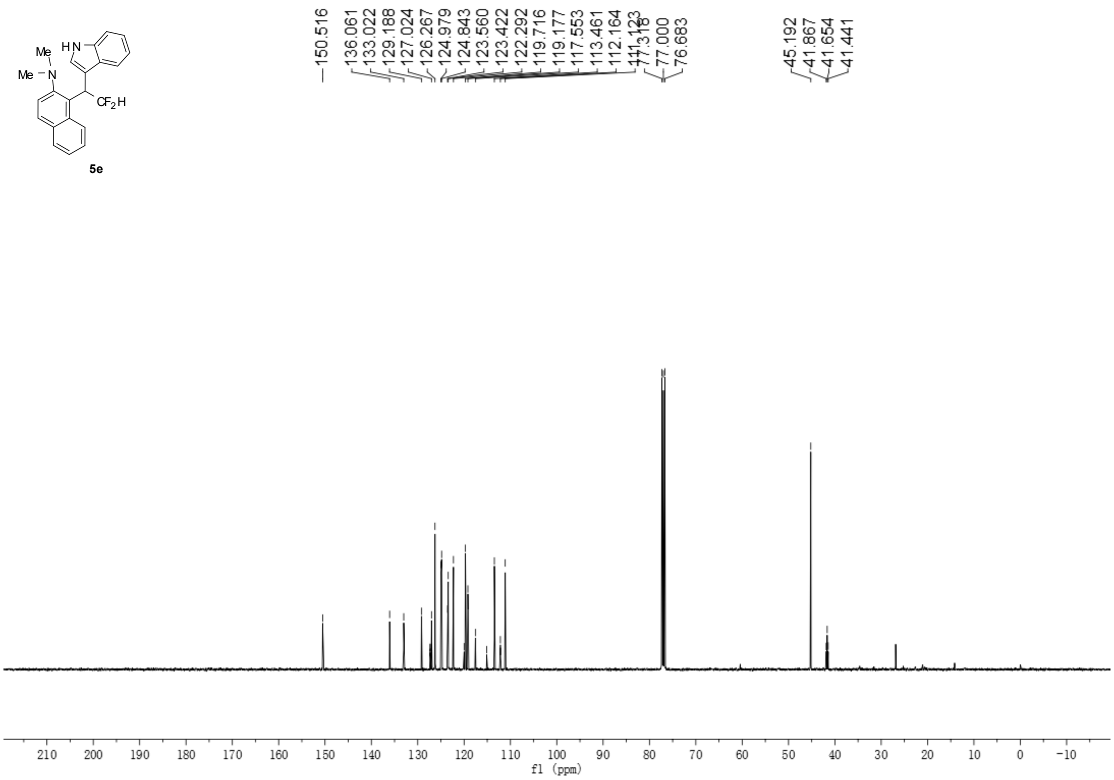
^{1}H NMR (400 MHz, $CDCl_3$) of **5e**



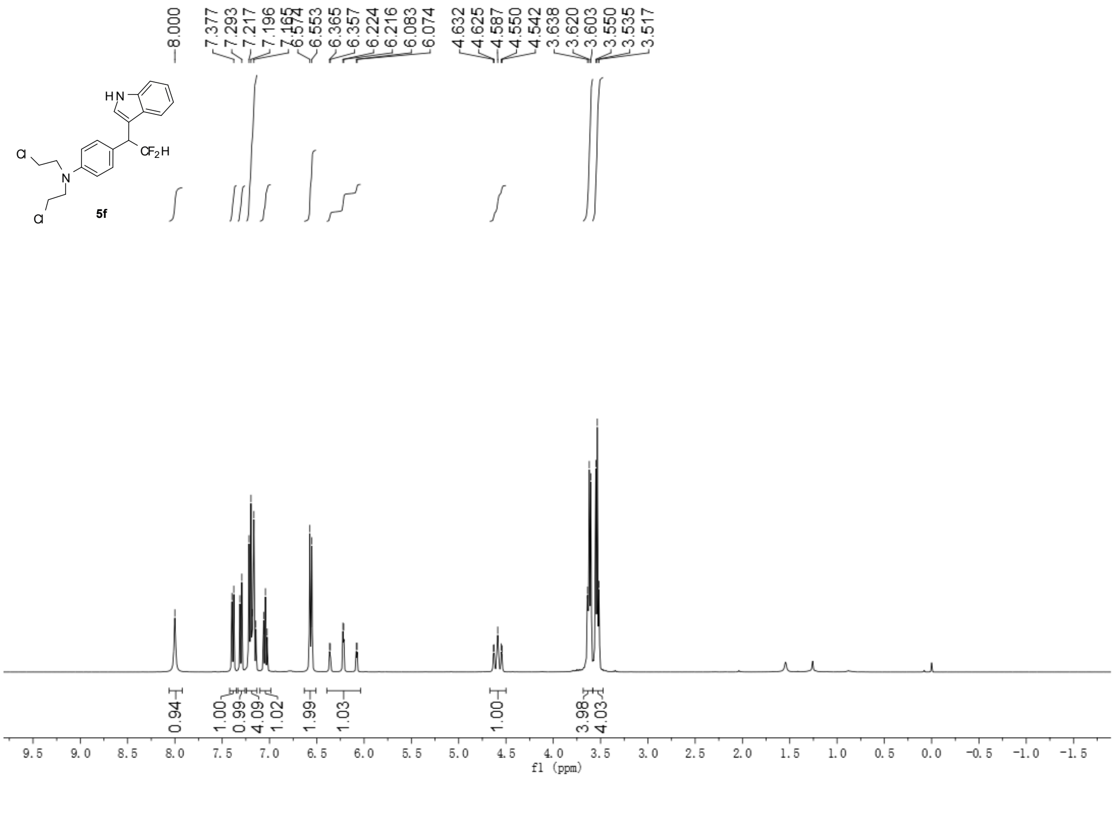
^{19}F NMR (376 MHz, $CDCl_3$) of **5e**



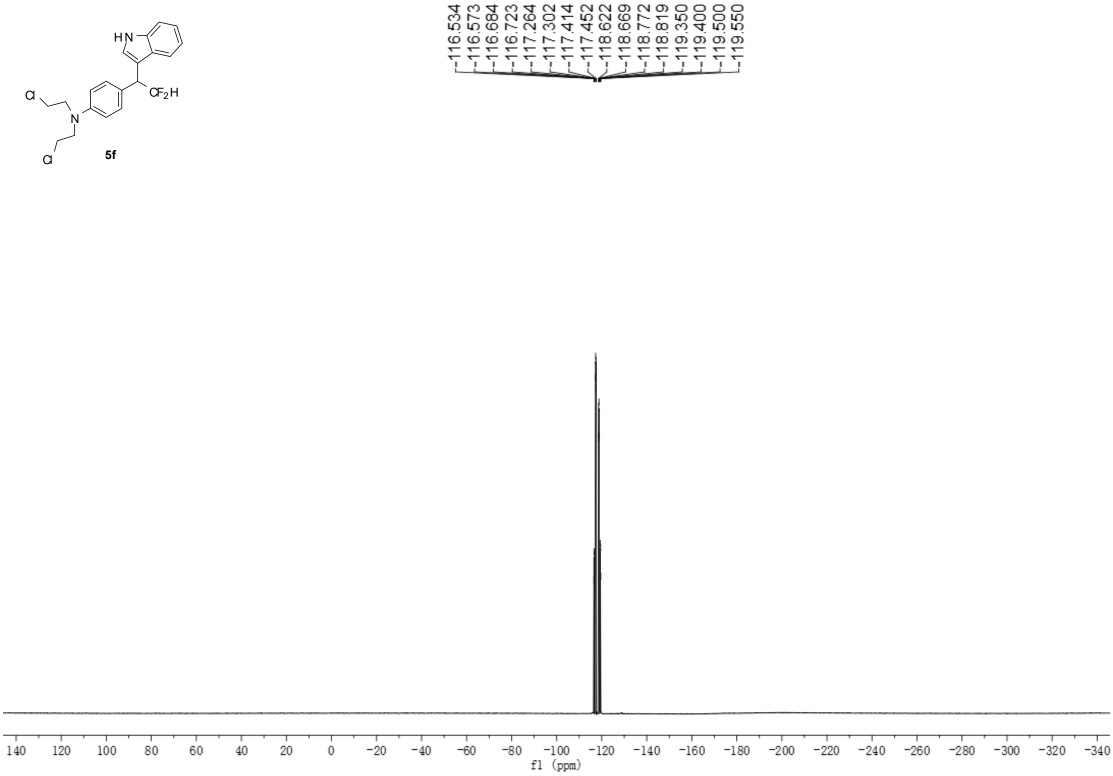
^{13}C NMR (100 MHz, $CDCl_3$) of **5e**



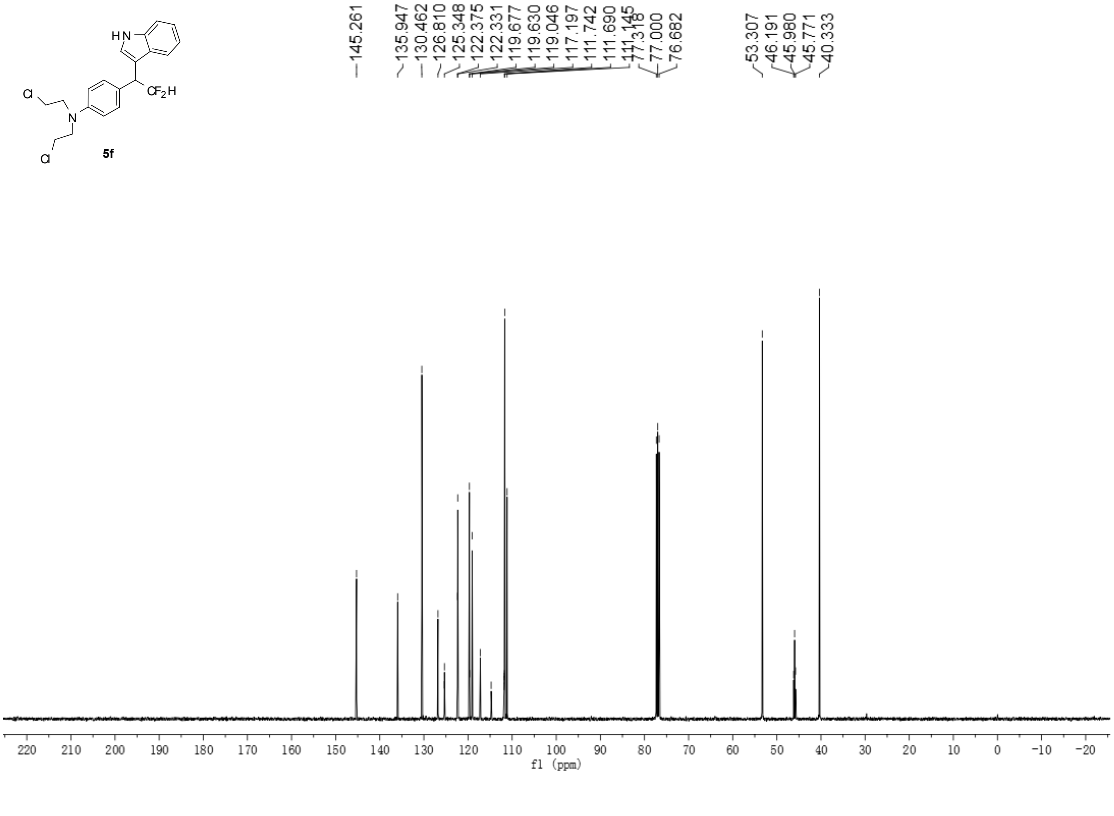
^{1}H NMR (400 MHz, $CDCl_3$) of **5f**



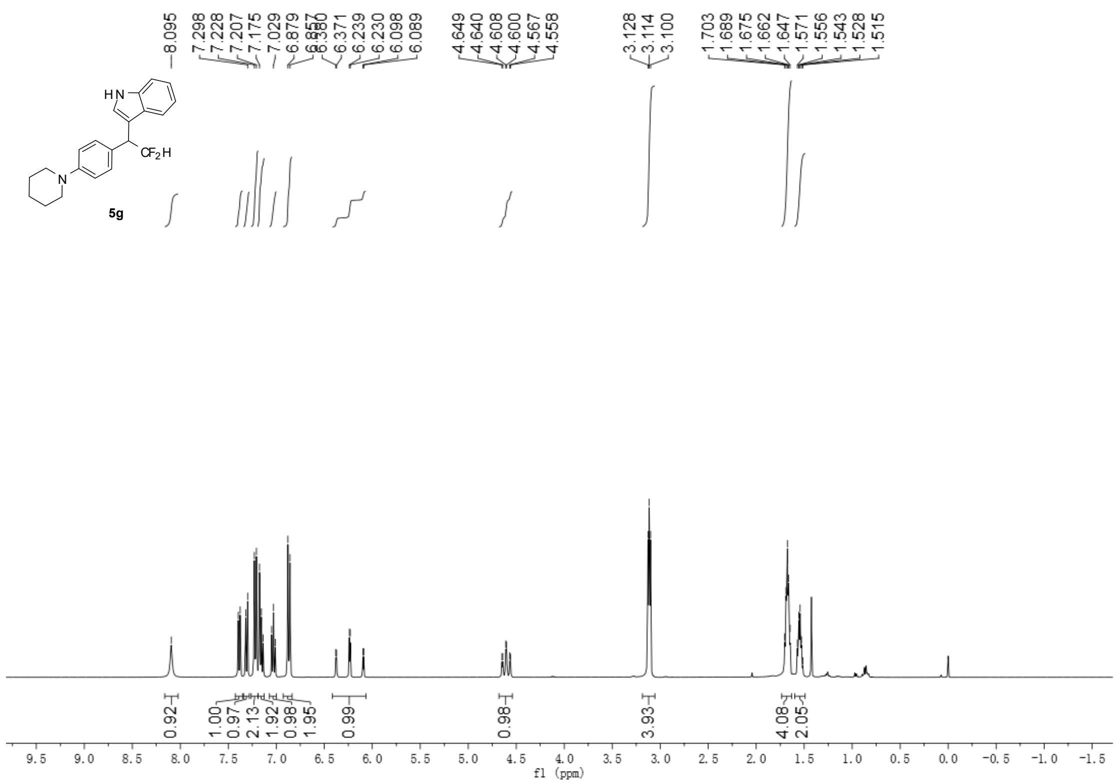
^{19}F NMR (376 MHz, $CDCl_3$) of **5f**



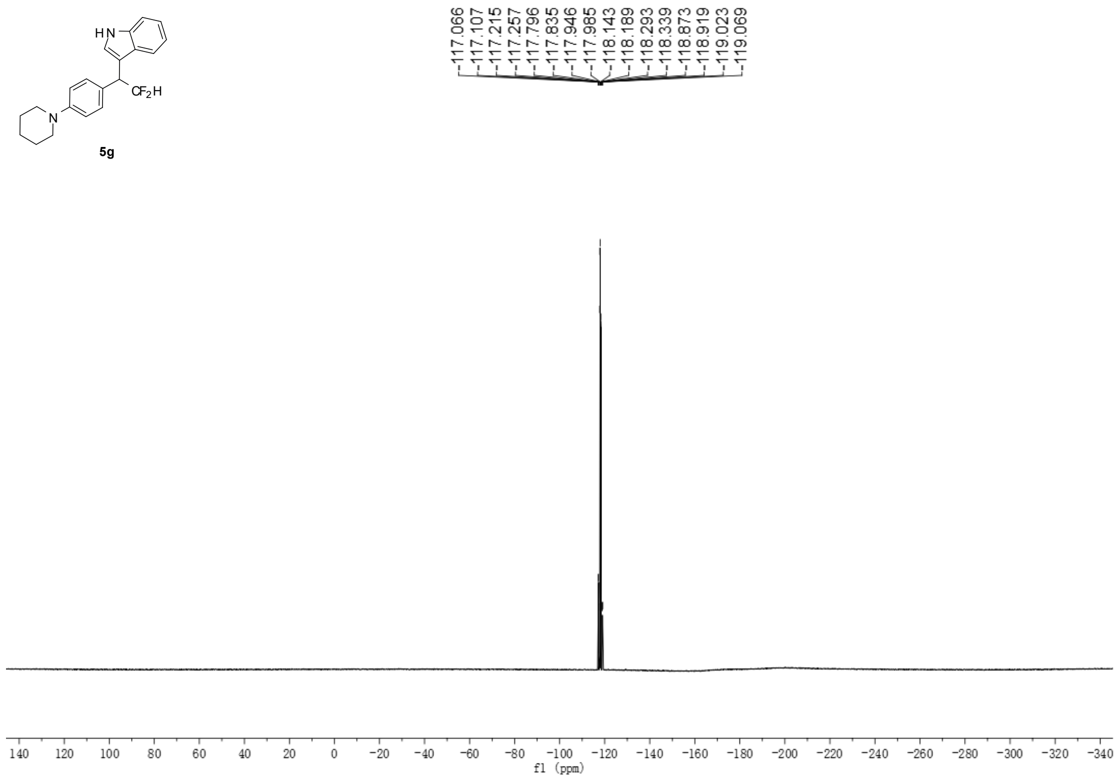
^{13}C NMR (100 MHz, $CDCl_3$) of **5f**



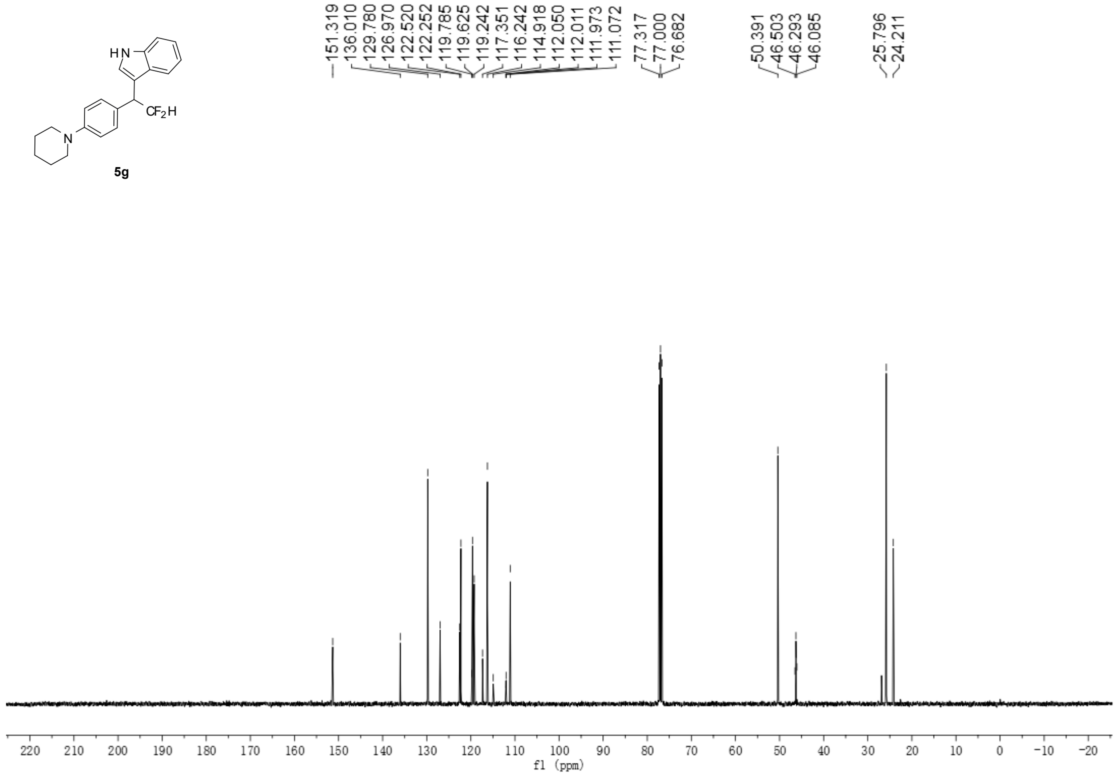
^{1}H NMR (400 MHz, $CDCl_3$) of **5g**



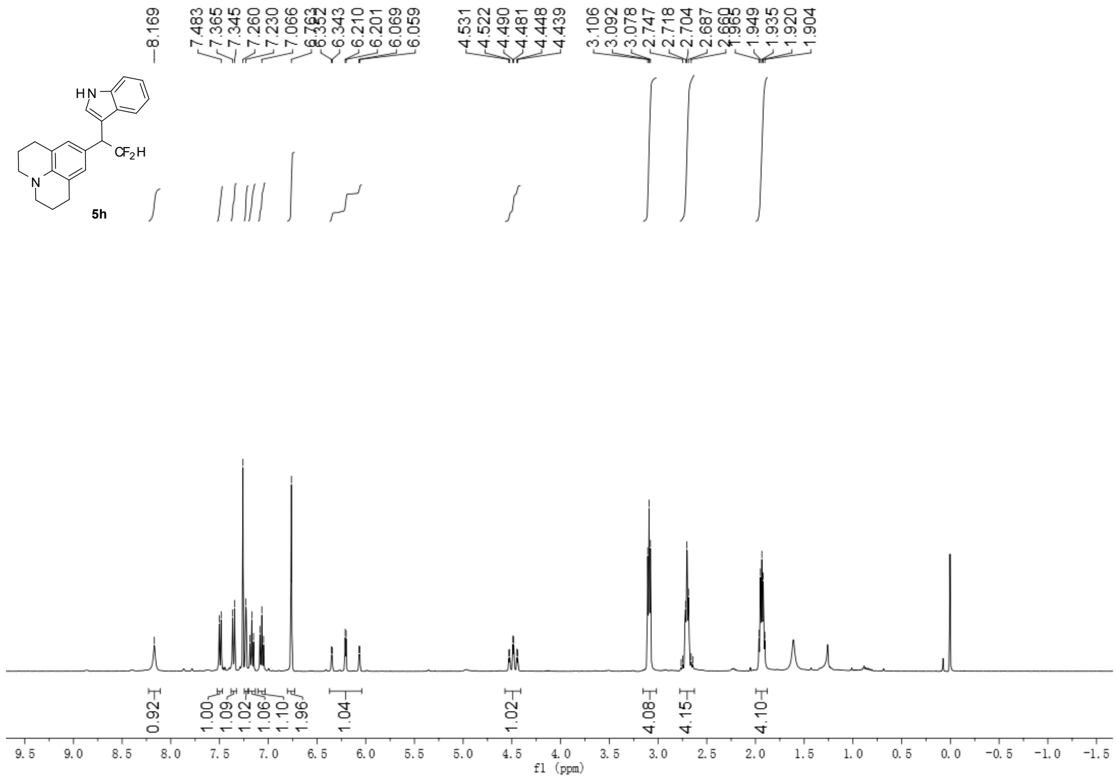
^{19}F NMR (376 MHz, $CDCl_3$) of **5g**



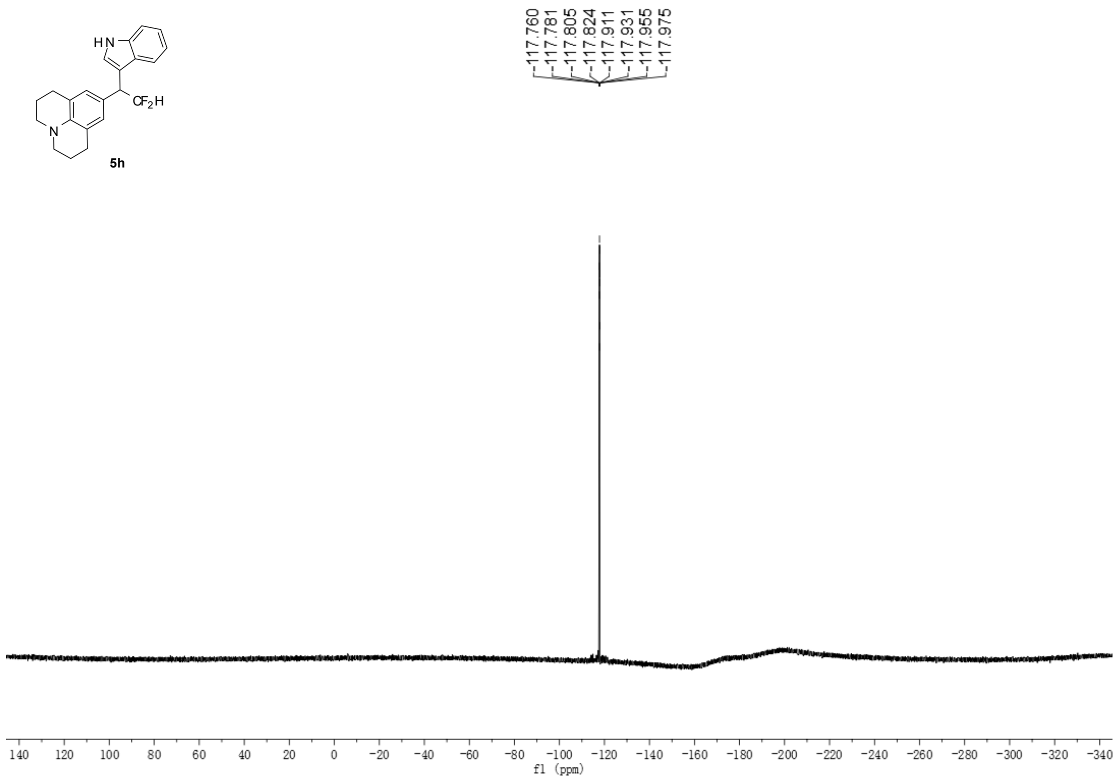
^{13}C NMR (100 MHz, $CDCl_3$) of **5g**



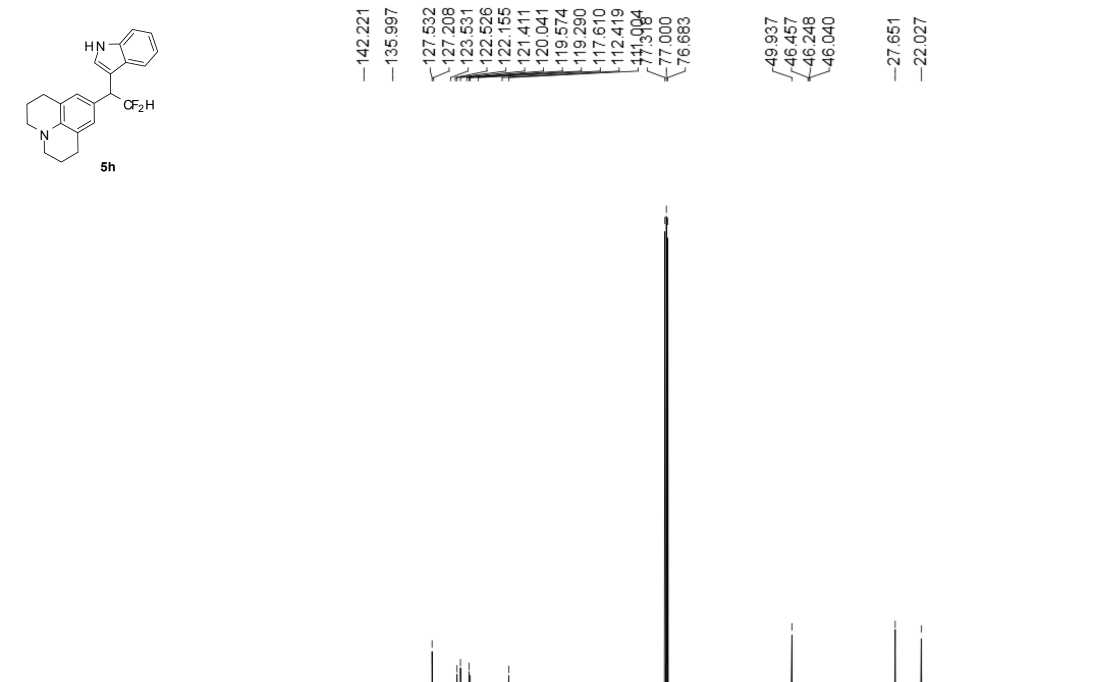
^{1}H NMR (400 MHz, $CDCl_3$) of **5h**



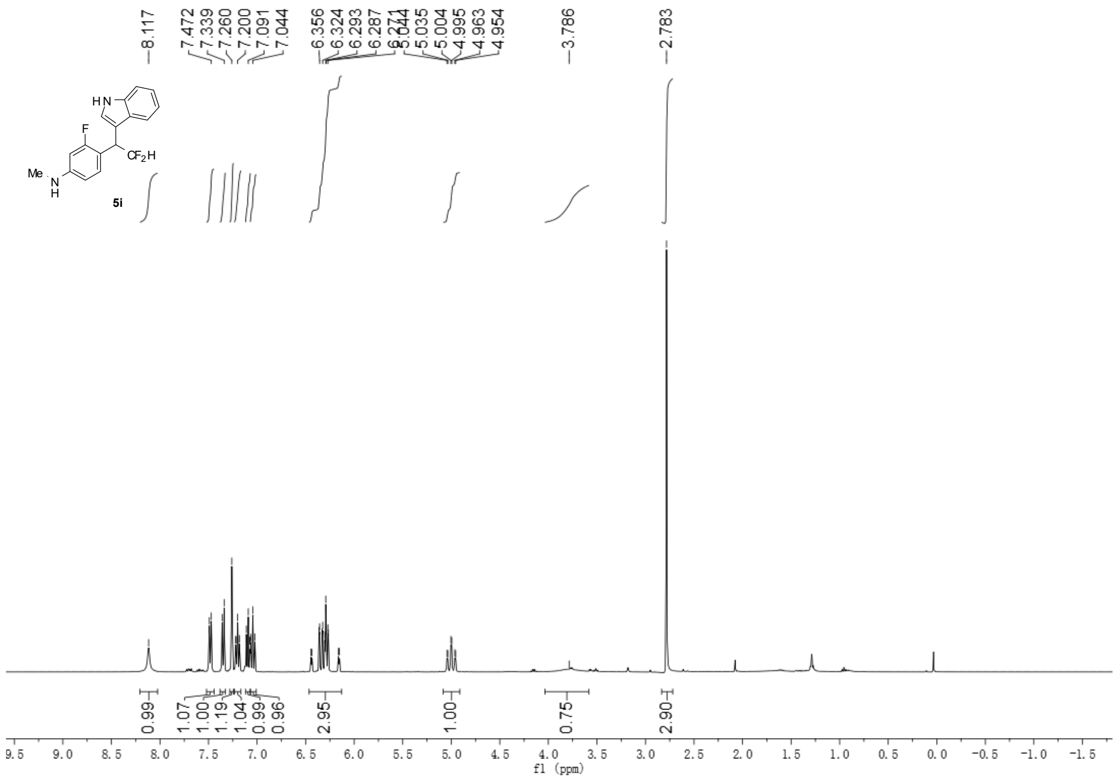
^{19}F NMR (376 MHz, $CDCl_3$) of **5h**



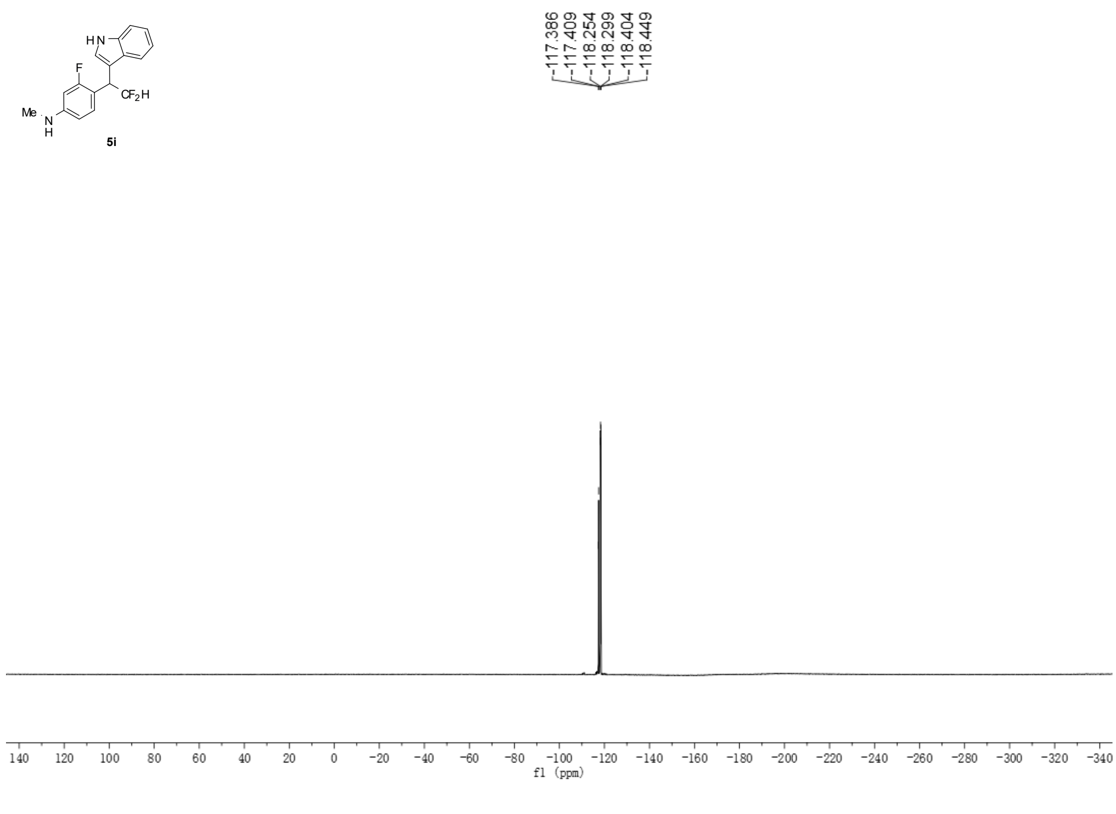
^{13}C NMR (100 MHz, $CDCl_3$) of **5h**



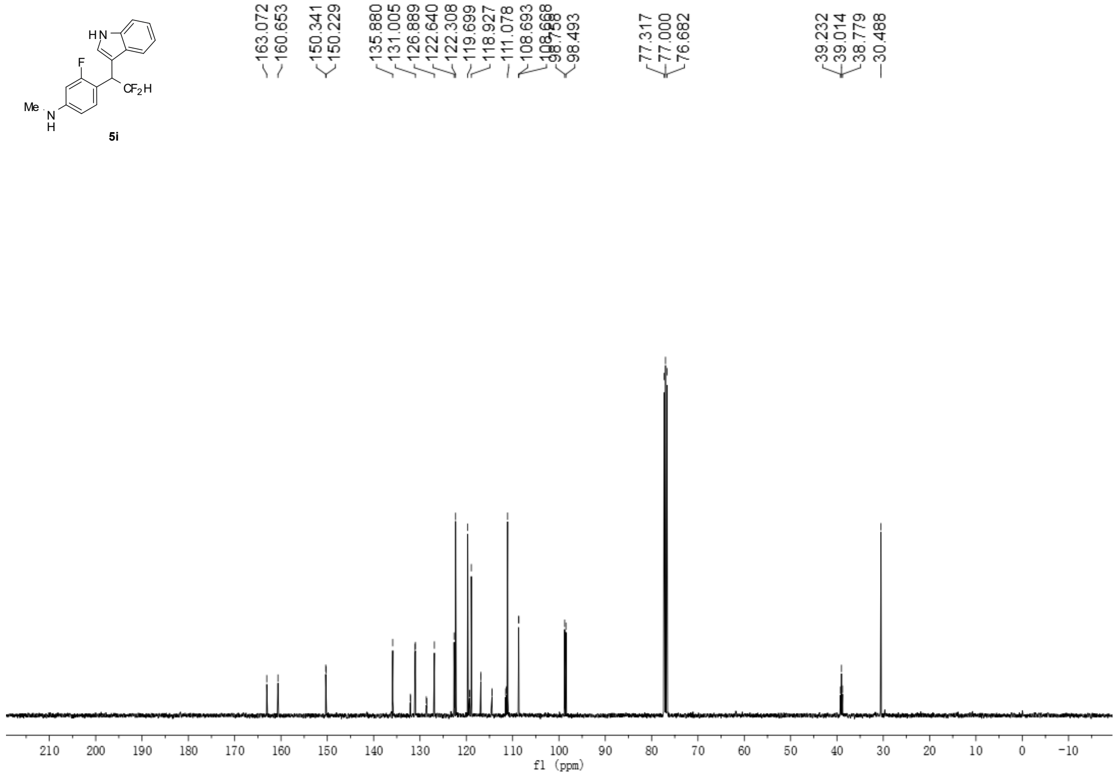
^1H NMR (400 MHz, $CDCl_3$) of **5i**



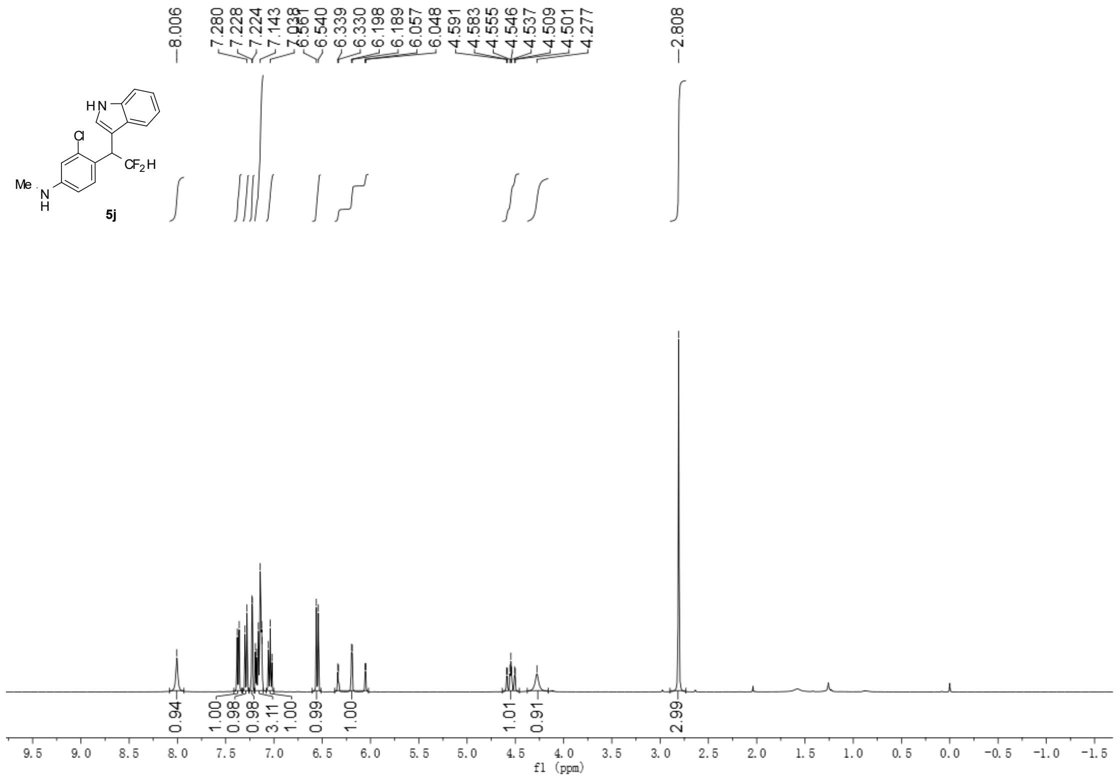
^{19}F NMR (376 MHz, $CDCl_3$) of **5i**



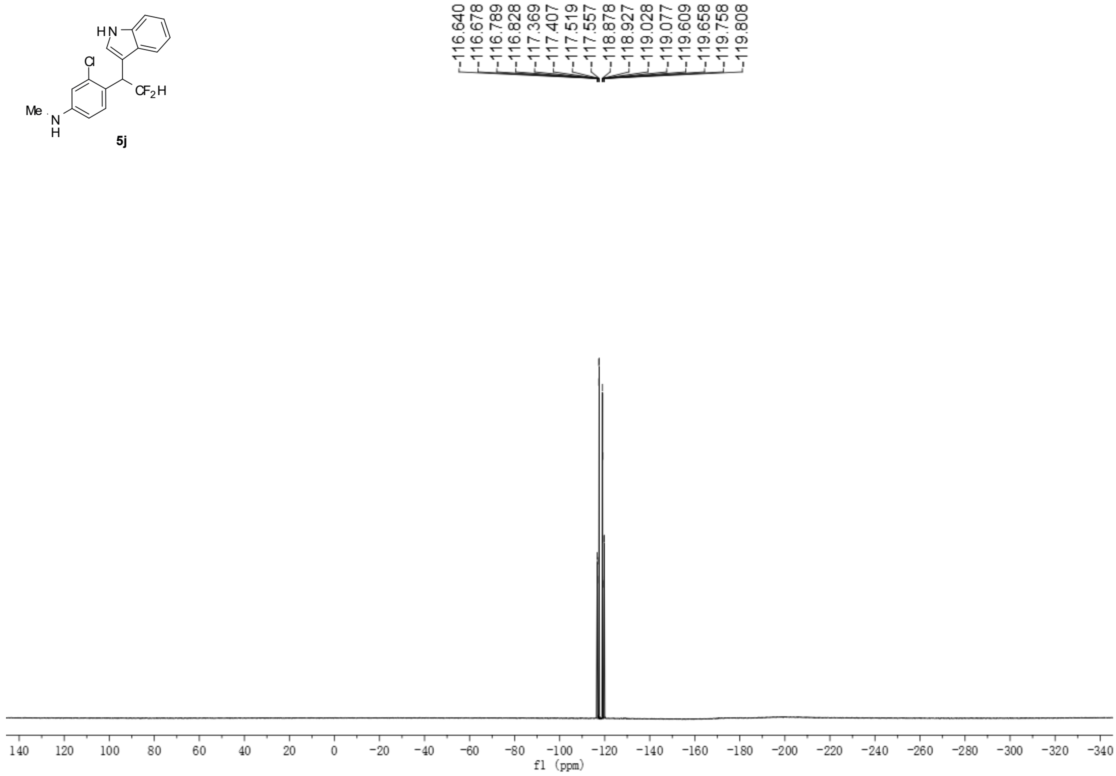
^{13}C NMR (100 MHz, $CDCl_3$) of **4i**



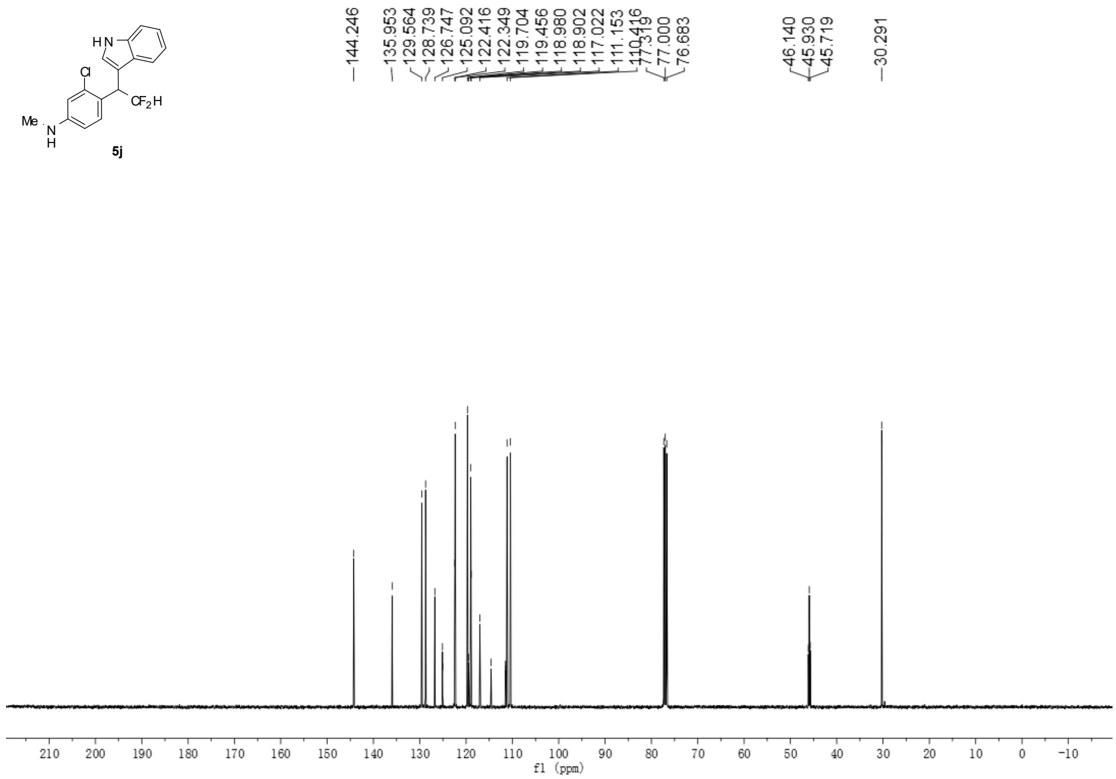
^{1}H NMR (400 MHz, $CDCl_3$) of **5j**



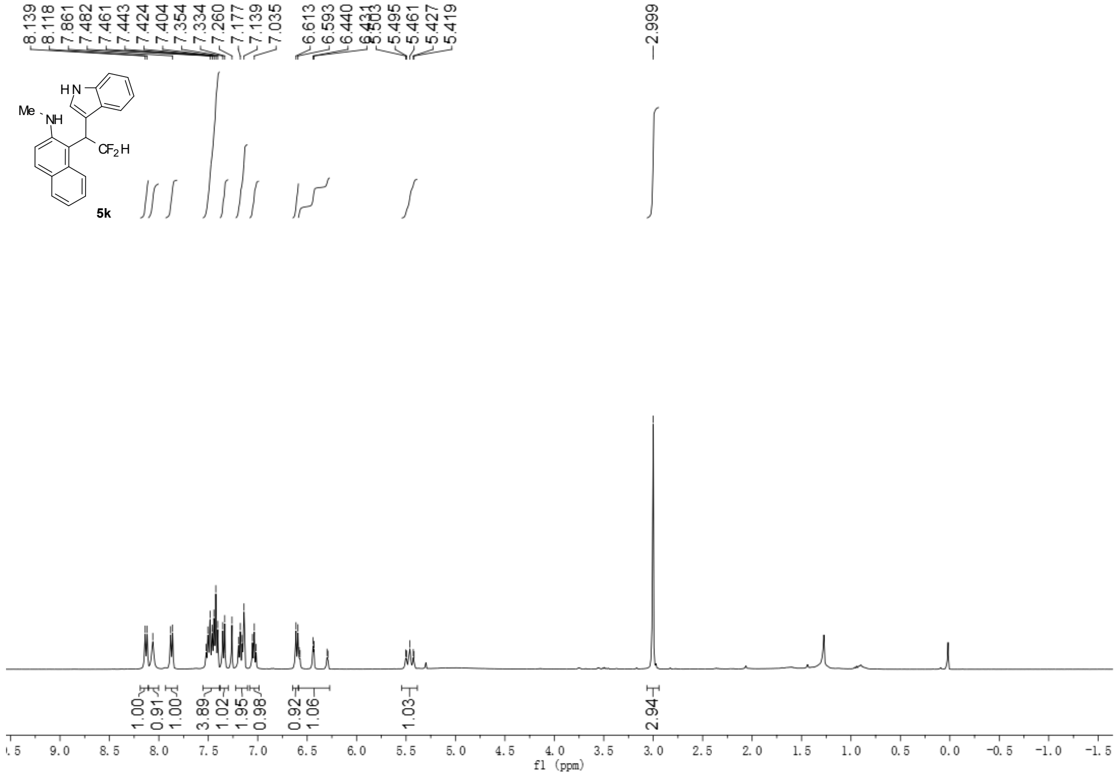
^{19}F NMR (376 MHz, $CDCl_3$) of **5j**



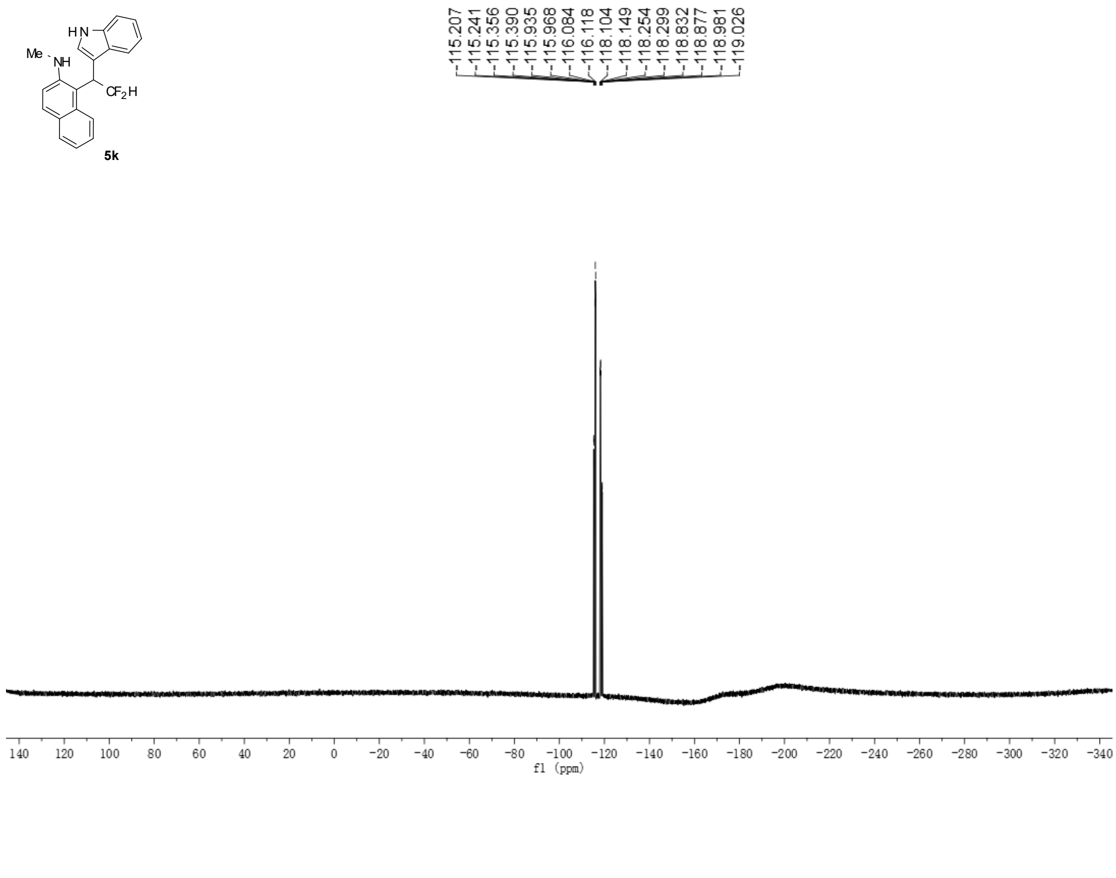
^{13}C NMR (100 MHz, $CDCl_3$) of **5j**



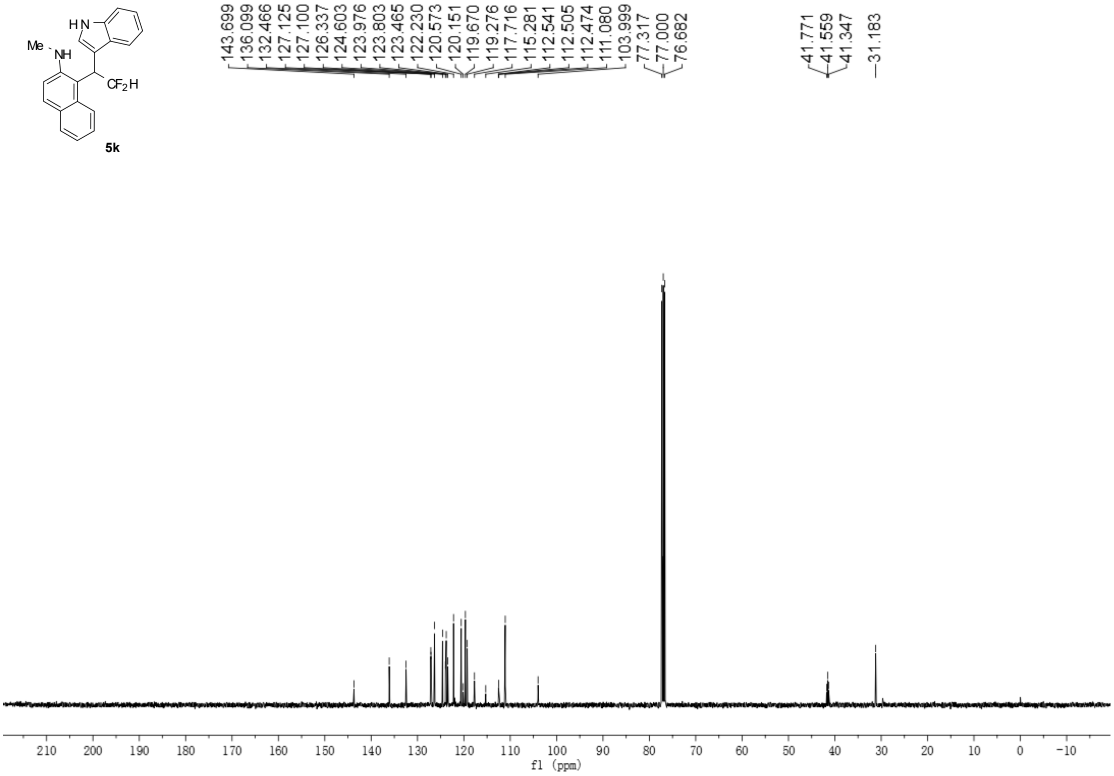
^{1}H NMR (400 MHz, $CDCl_3$) of **5k**



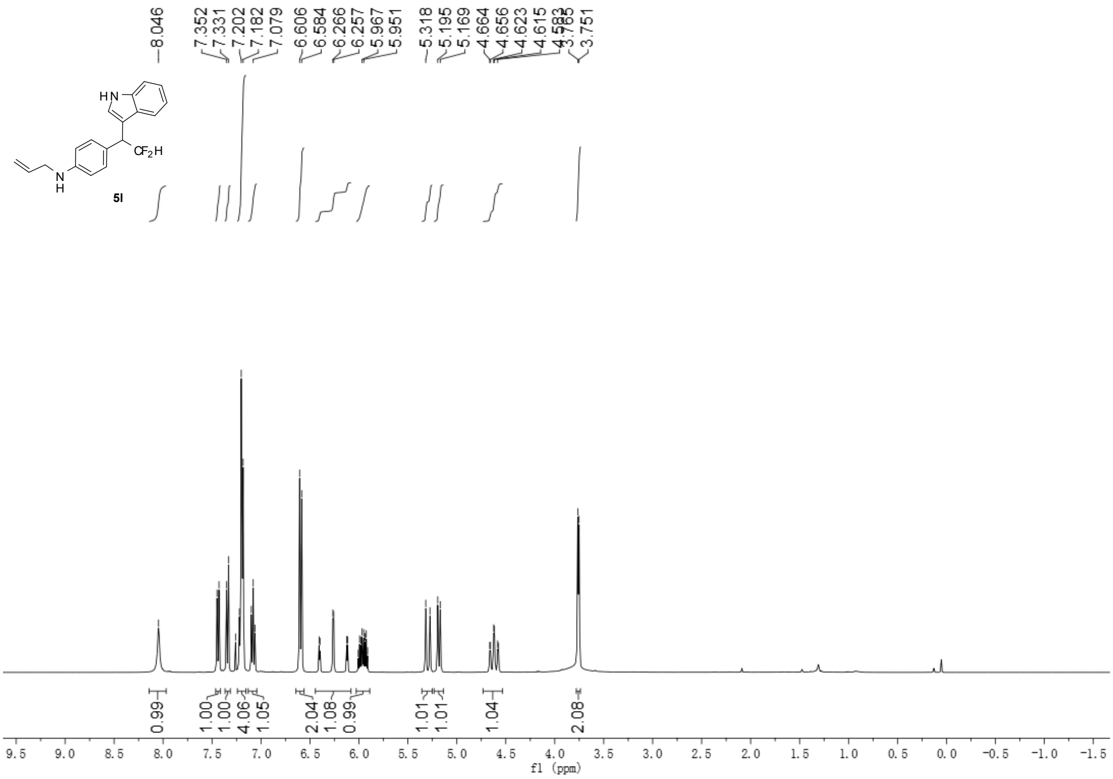
^{19}F NMR (376 MHz, $CDCl_3$) of **5k**



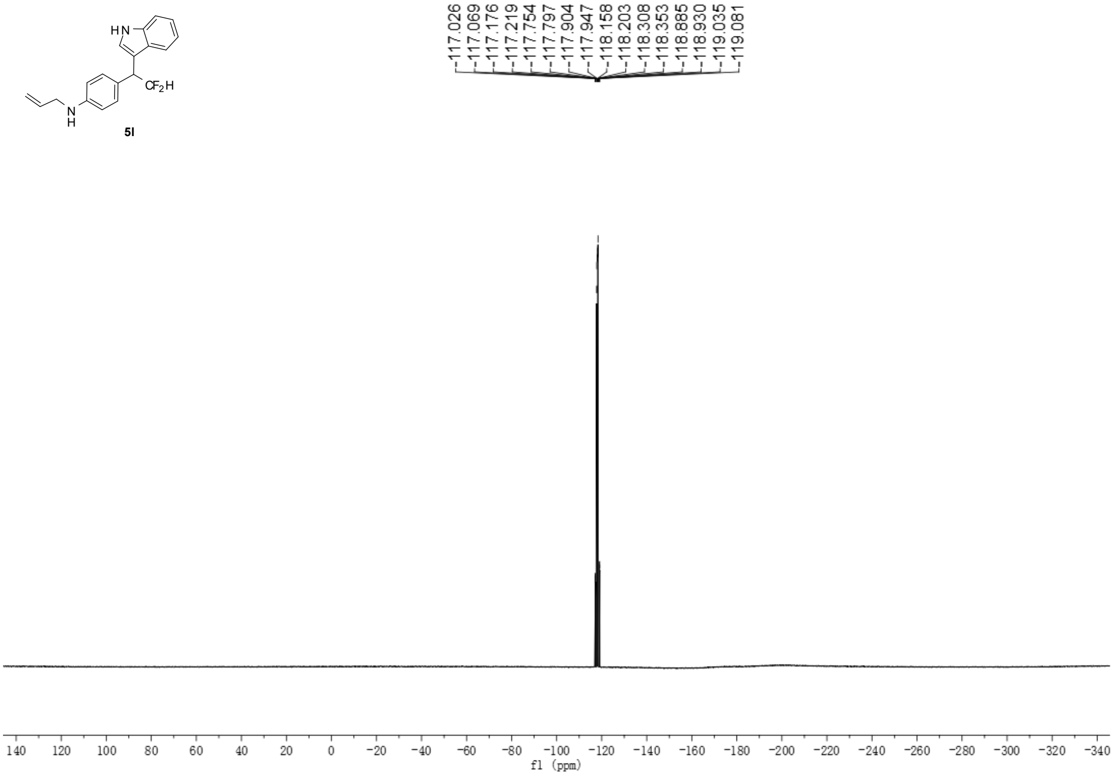
^{13}C NMR (100 MHz, $CDCl_3$) of **5k**



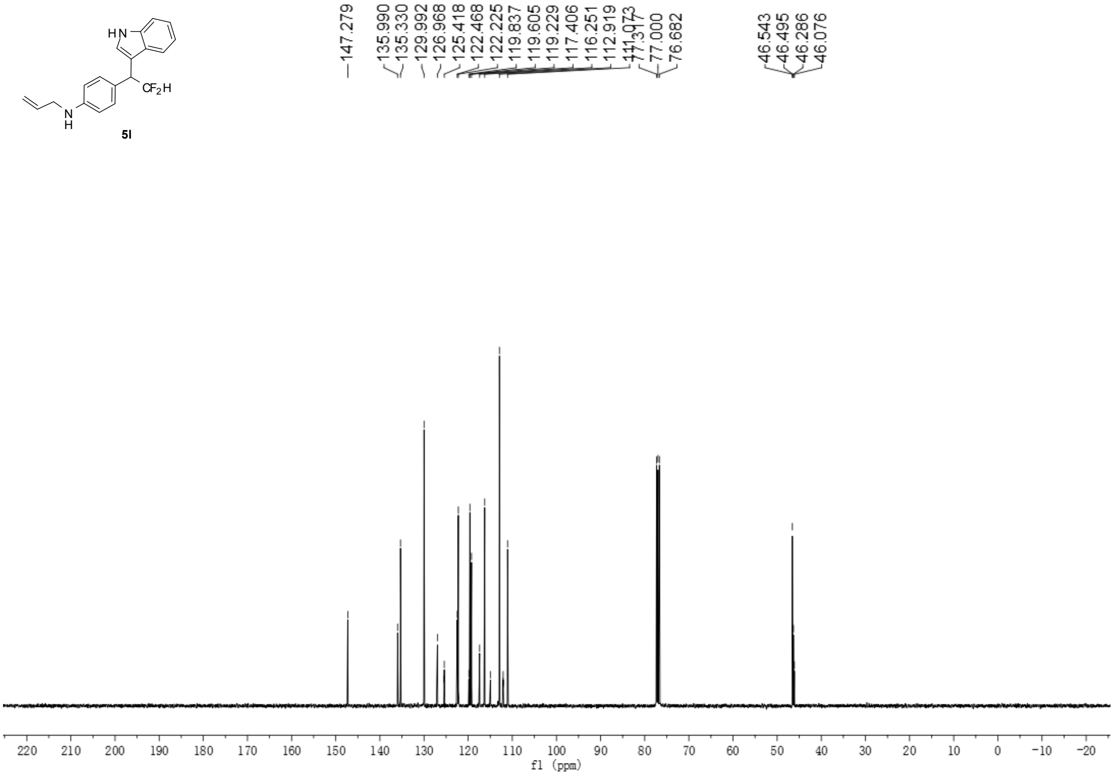
^{1}H NMR (400 MHz, $CDCl_3$) of **5l**



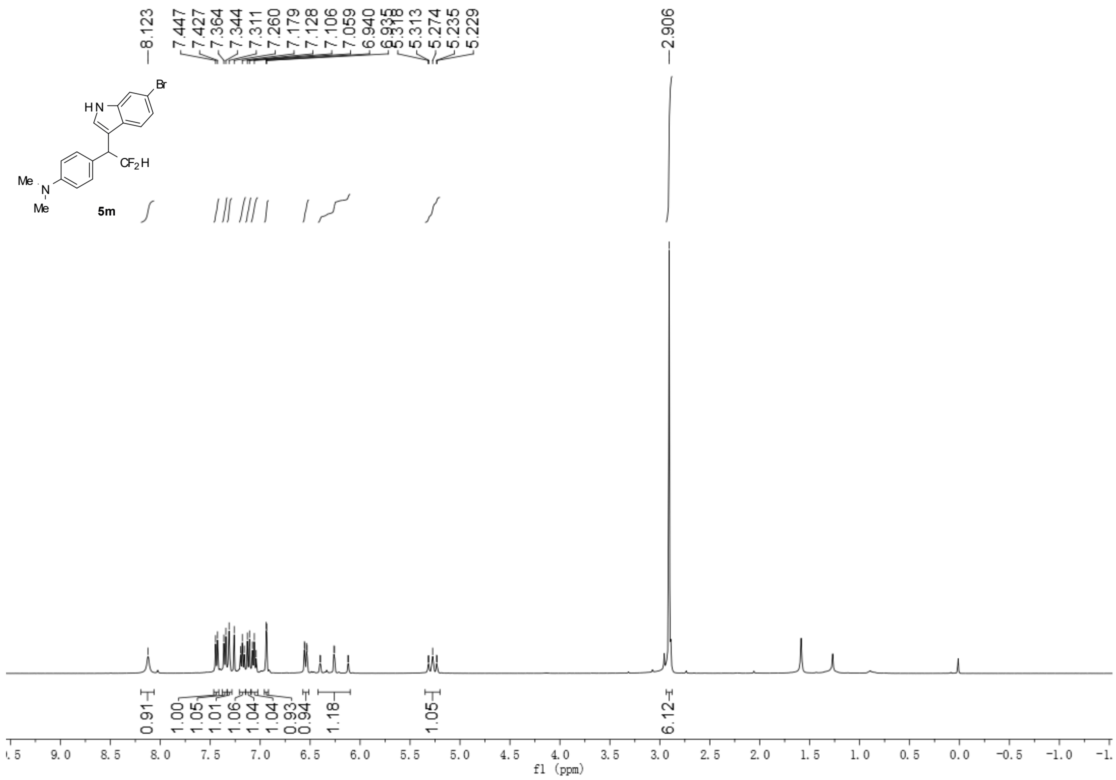
^{19}F NMR (376 MHz, $CDCl_3$) of **5l**



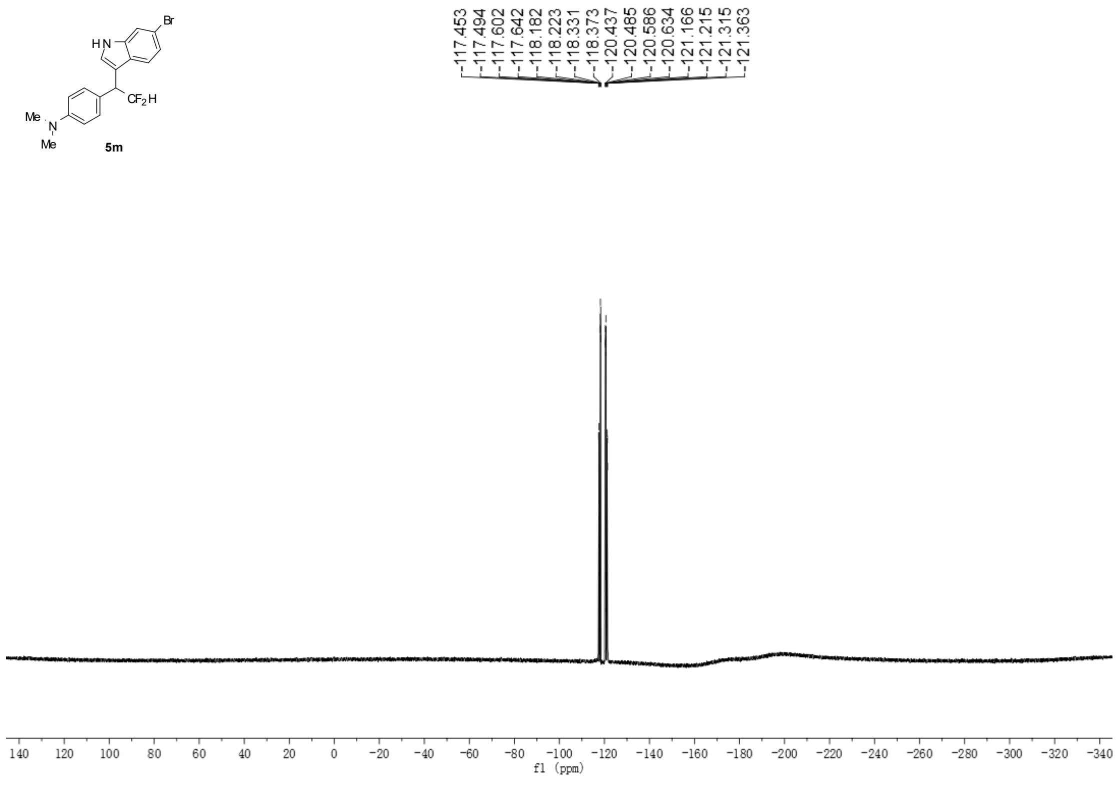
^{13}C NMR (100 MHz, $CDCl_3$) of **5l**



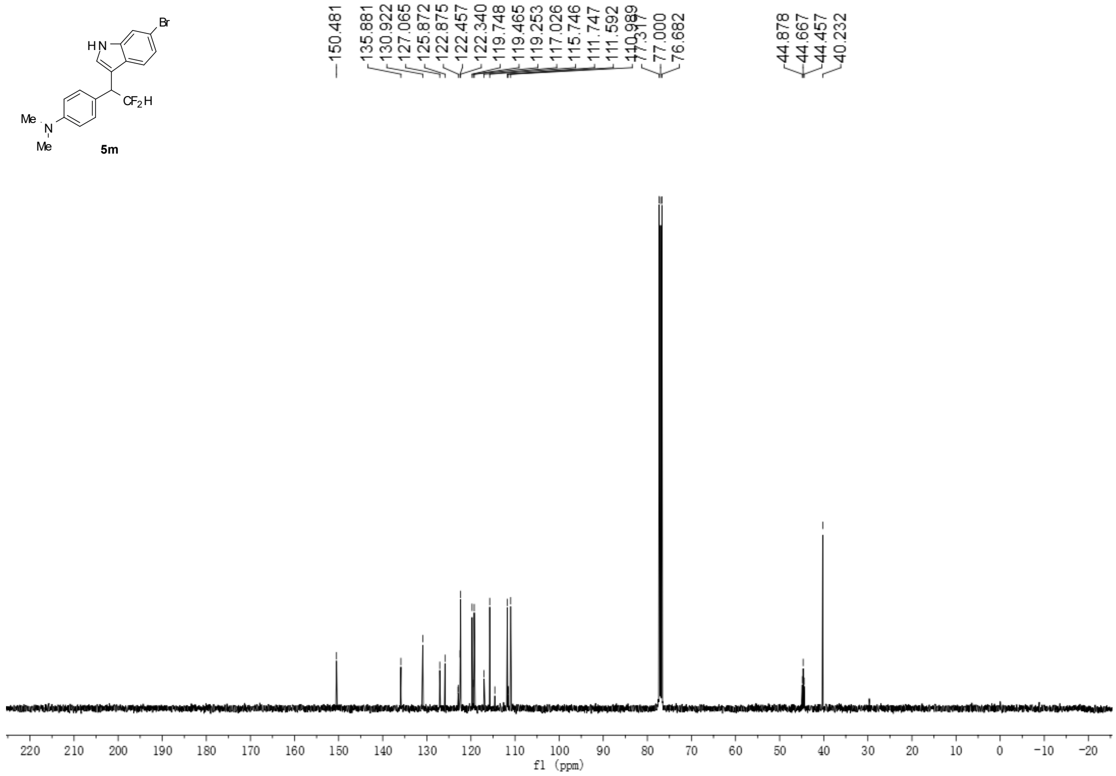
^{1}H NMR (400 MHz, $CDCl_3$) of **5m**



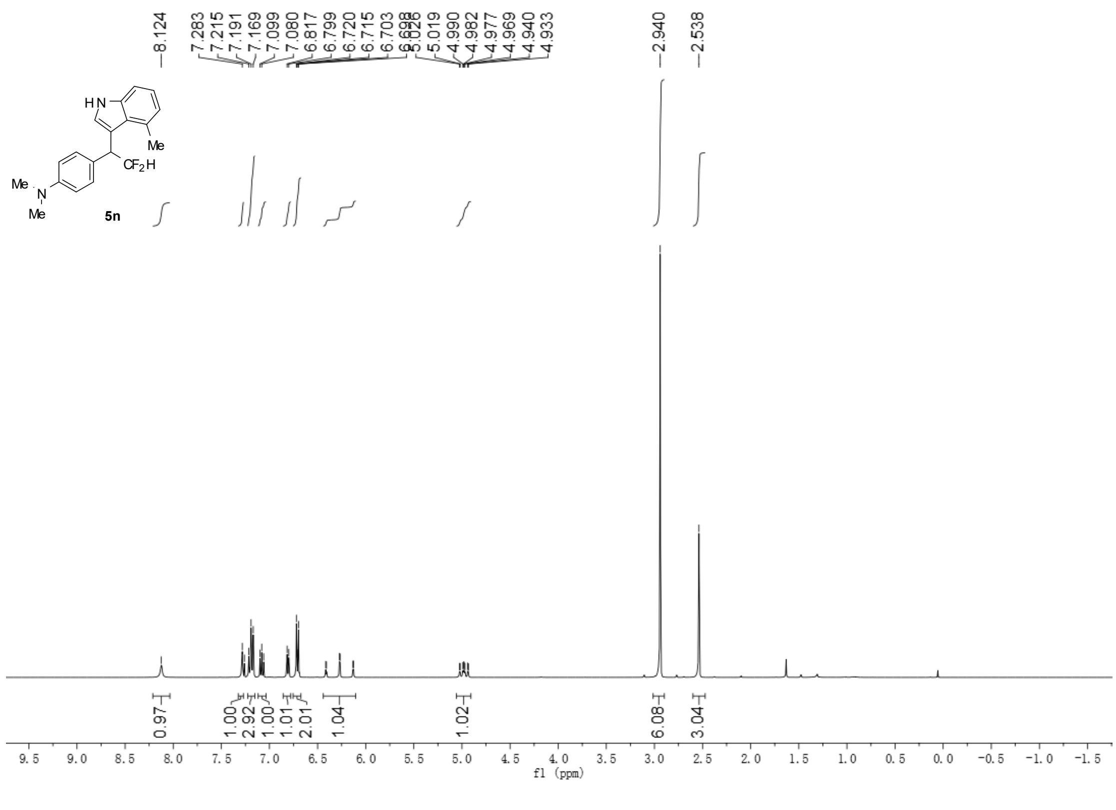
^{19}F NMR (376 MHz, $CDCl_3$) of **5m**



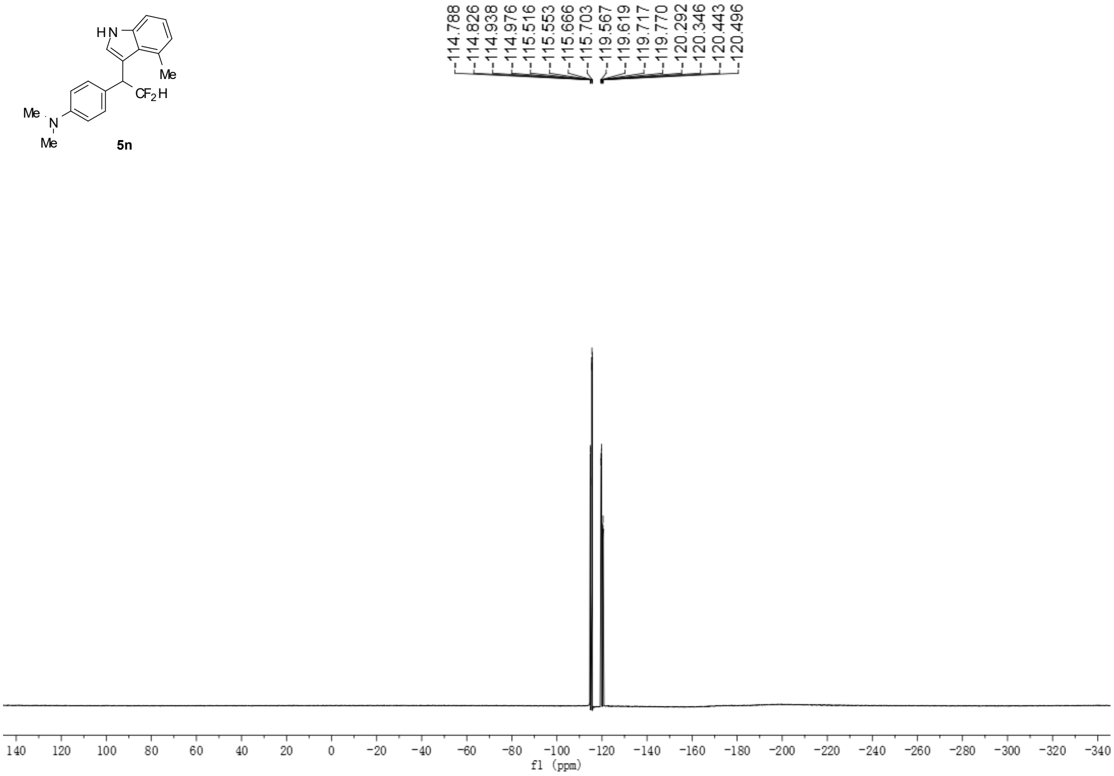
[13]C NMR (100 MHz, $CDCl_3$) of **5m**



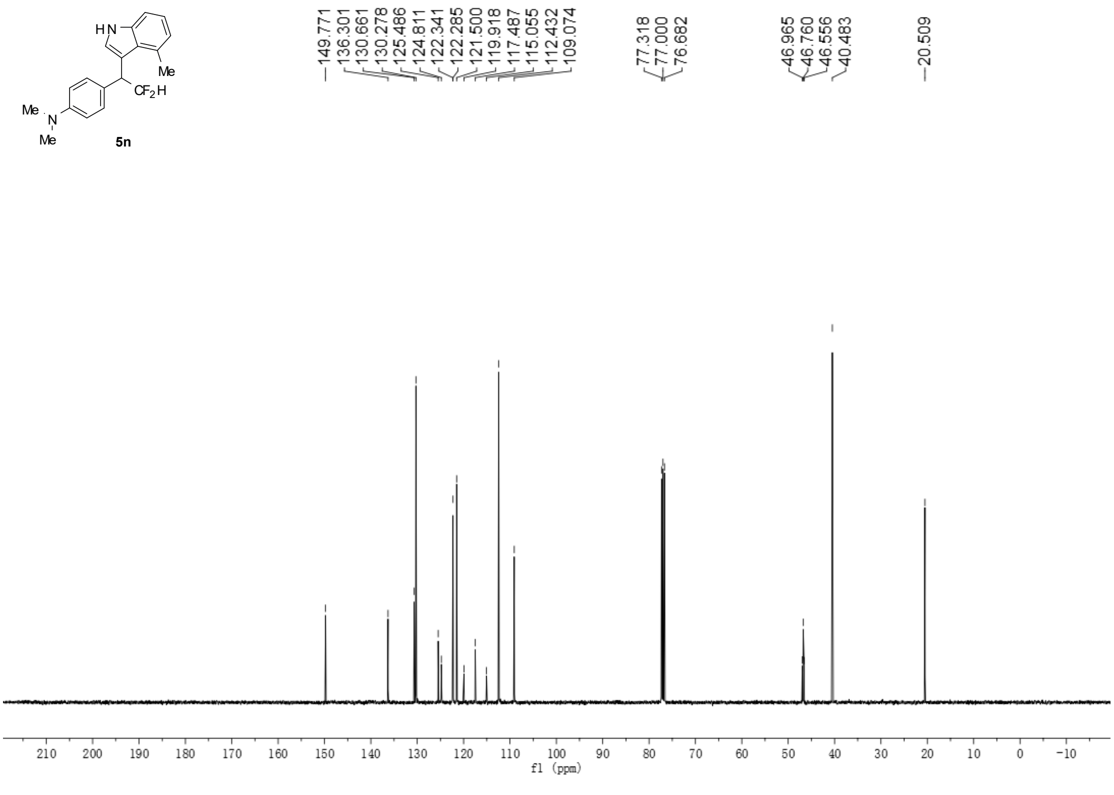
[1]H NMR (400 MHz, $CDCl_3$) of **5n**



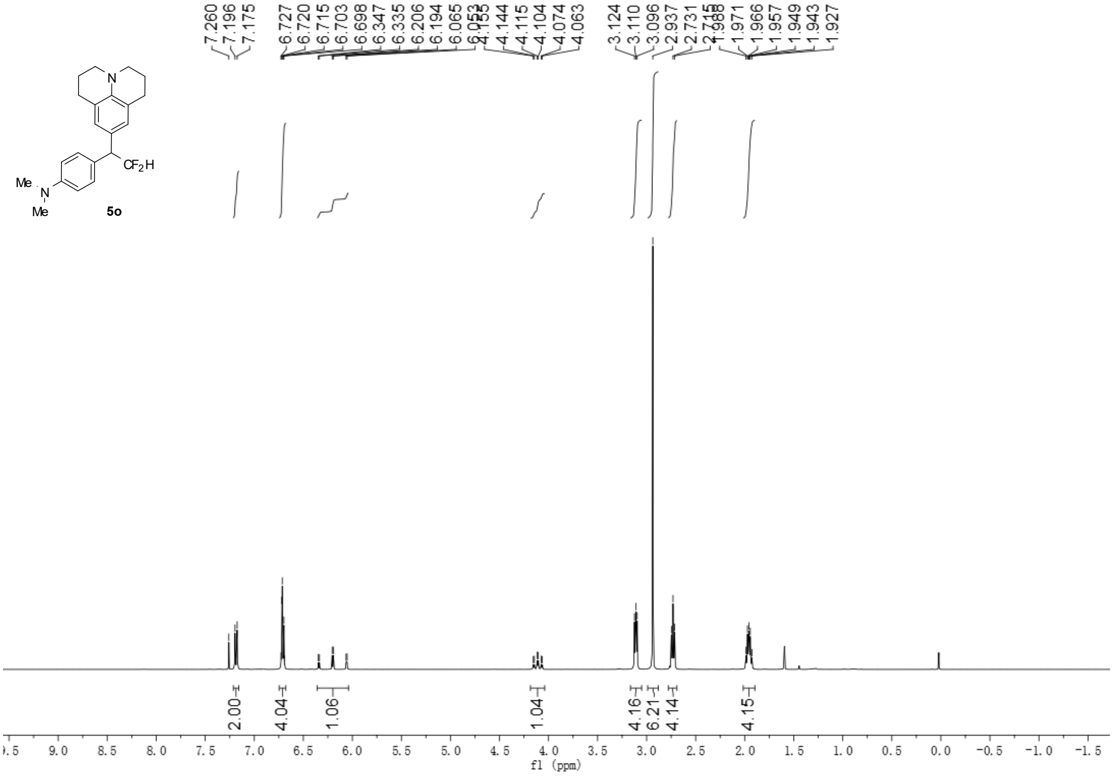
^{19}F NMR (376 MHz, $CDCl_3$) of **5n**



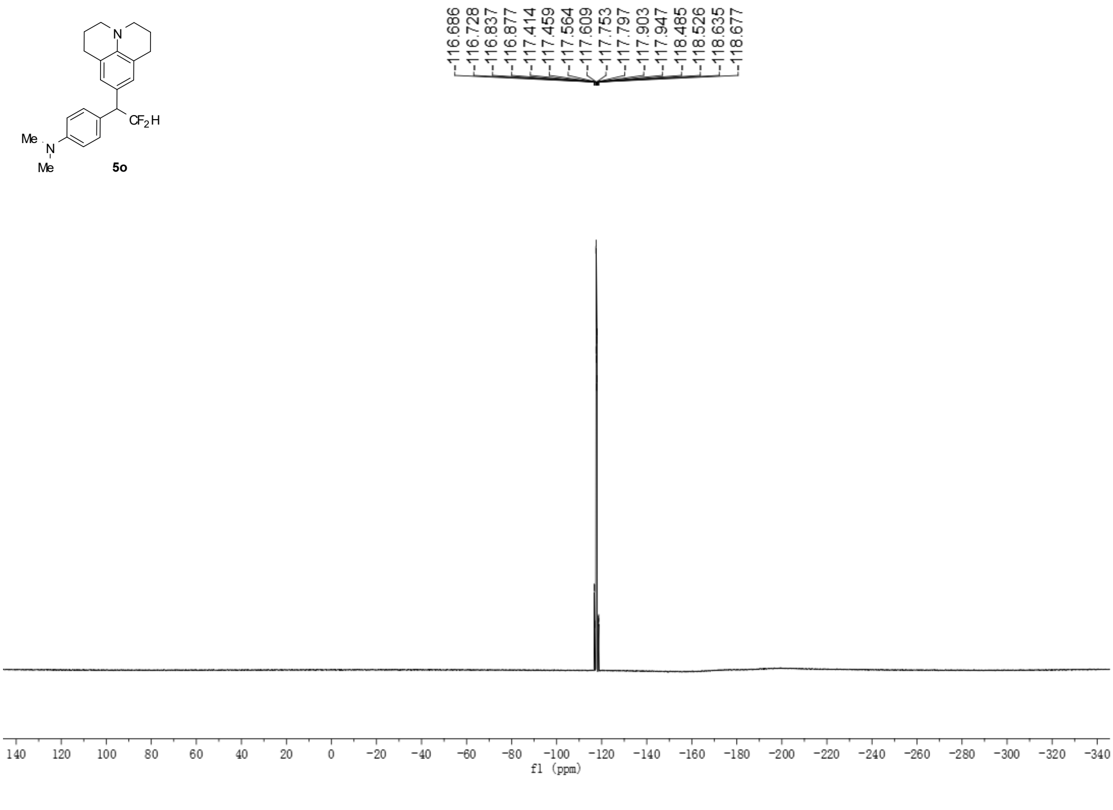
^{13}C NMR (100 MHz, $CDCl_3$) of **5n**



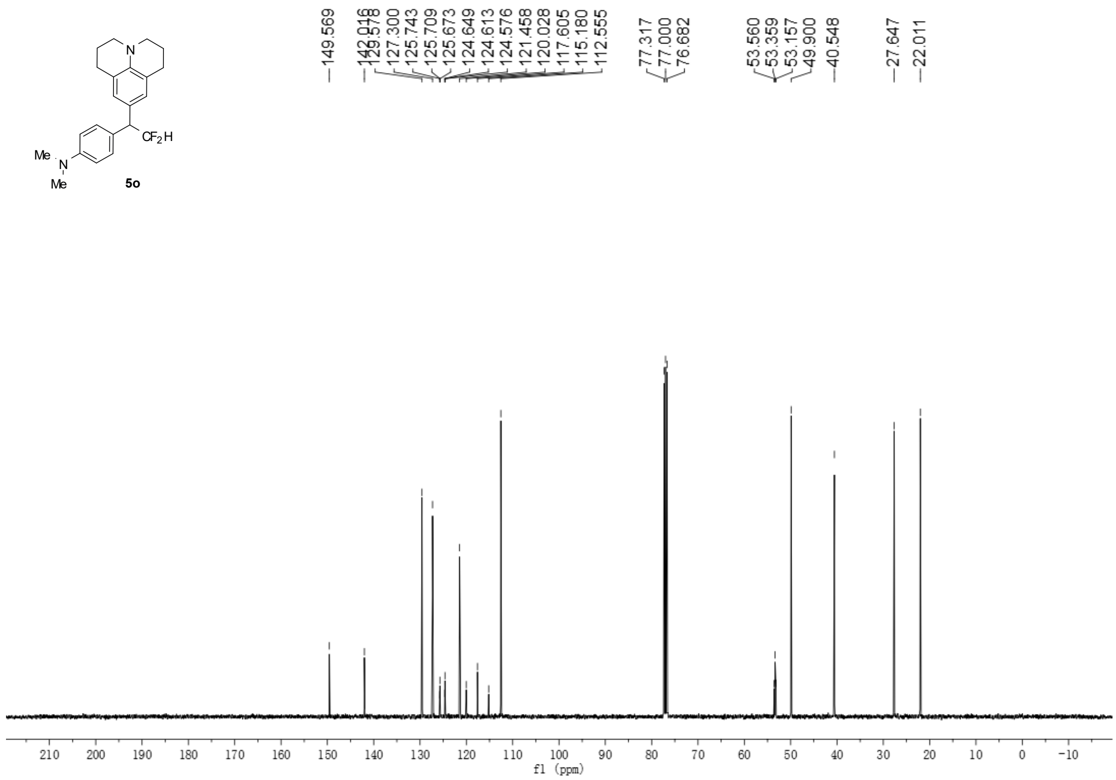
[1]H NMR (400 MHz, $CDCl_3$) of **5o**



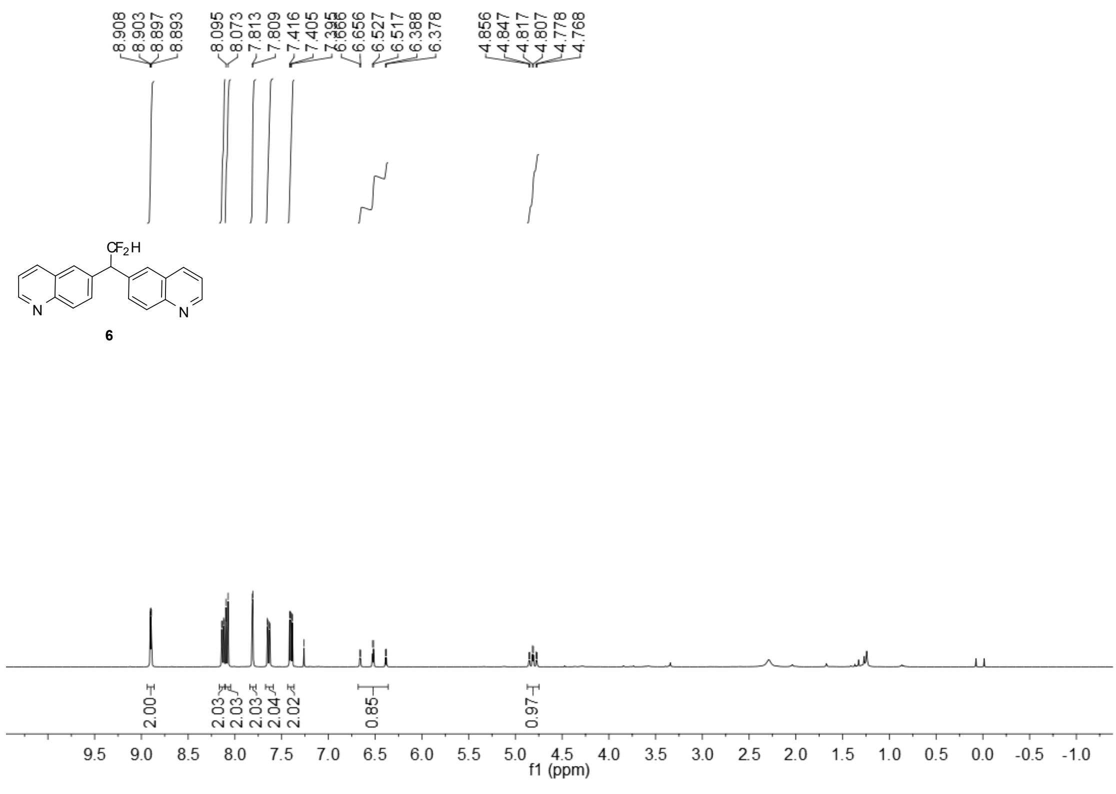
[19]F NMR (376 MHz, $CDCl_3$) of **5o**



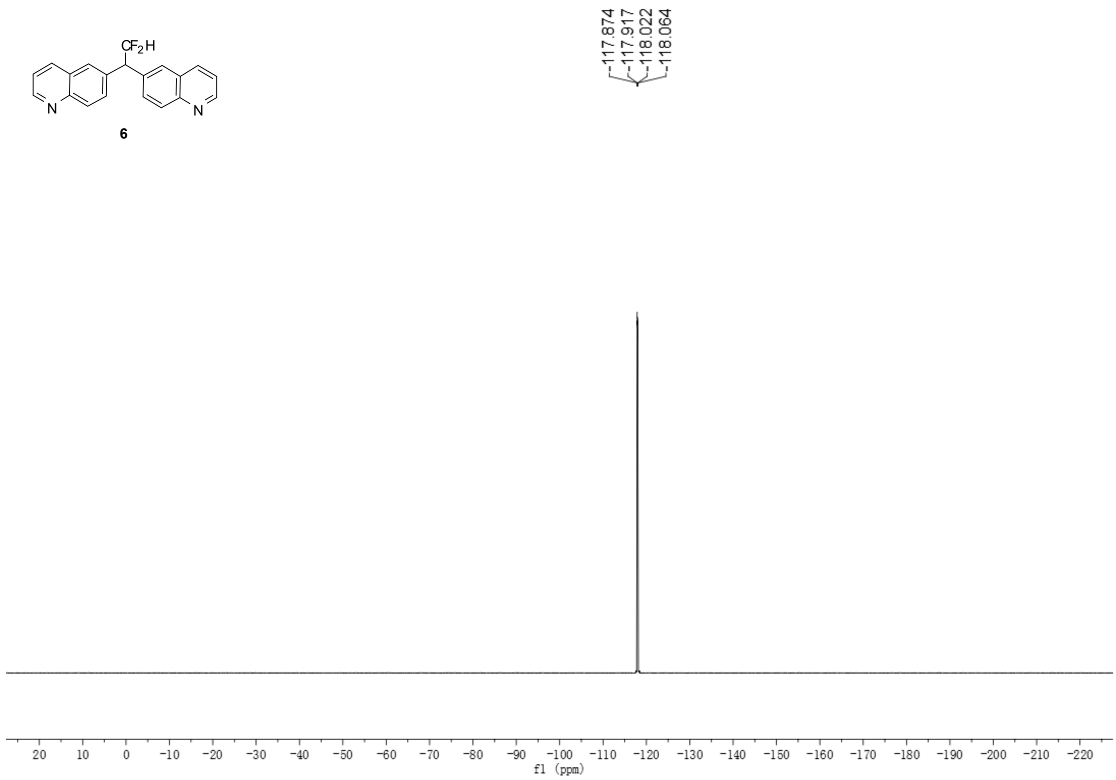
^{13}C NMR (100 MHz, $CDCl_3$) of **5o**



^{1}H NMR (400 MHz, $CDCl_3$) of **6**



^{19}F NMR (376 MHz, $CDCl_3$) of **6**



^{13}C NMR (100 MHz, $CDCl_3$) of **6**