Supporting Information

[4+2] Cycloaddition of Trifluoromethyl Ketimines with 2-Alkenyl Azaarenes through Selective C-F Bond Cleavage of CF_3

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1. General Information

Unless otherwise noted, all reagents were obtained commercially and used without further purification. Unless otherwise specified, all other reagents were purchased from Acros, Aldrich, Fisher, Adamas-beta Co. Ltd. or TCI and used without further purification. ^{1}H NMR spectra was recorded at 400 MHz, ^{13}C NMR spectra was recorded at 100 MHz. ^{19}F NMR spectra was recorded at 375 MHz. ^{1}H NMR spectra was recorded with tetramethylsilane (δ 0.00 ppm) as internal reference; ^{13}C NMR spectra was recorded with $CDCl_3$ (δ 77.00 ppm) as internal reference. Chemical shifts were reported in parts per million (ppm, δ) downfield from tetramethylsilane. Proton coupling patterns are described as singlet (s), doublet (d), triplet (t), quartet (q), multiplet (m), and broad (br). Chromatography was carried out with silica gel (200-300 mesh) using mixtures of petroleum ether (b.p. 60-80 ºC) and ethyl acetate as eluents. Mass spectrometry analysis was carried out using an electrospray spectrometer Waters Micromass Q-TOF premier Mass Spectrometer (Waters, Milford, MA, USA).

2. General Procedure for the Preparation of Substrates

2.1 Synthesis of Phenyl Trifluoromethyl Ketamine Derivatives

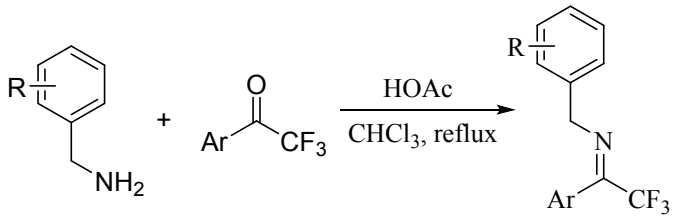


Figure S1. The synthesis of Phenyl Trifluoromethyl Ketamine Derivatives.

Benyl trifluoromethyl ketamine derivatives were synthesized according to the method reported in the literature.[1] To the mixture of benzyl amine (1.0 equiv) and acetic acid (1.0 equiv) in $CHCl_3$ (1.0 mL/mmol) was added the solution of trifluoromethyl ketone (1.0 equiv) in $CHCl_3$ (0.2 mL/mmol) in one portion. The resulting mixture was refluxed until all the ketone was consumed (indicated by TLC or by the disappearance of the insoluble solid). After cooling down to room temperature, CH_2Cl_2 (4.0 mL/mmol) was added and the mixture was washed with $NaHCO_3$ (sat., 2.0 mL/mmol). The aqueous layer was extracted with CH_2Cl_2 (4.0 mL/mmol × 2). The organic phase was combined, washed with brine, dried over Na_2SO_4 and concentrated. Then it could be used directly in the following reactions.

2.2 Synthesis of alkenes
General procedure A

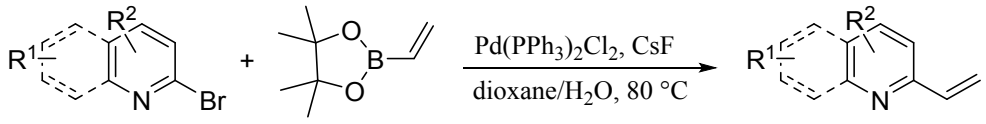
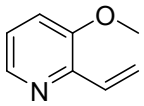


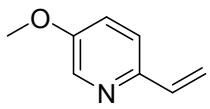
Figure S2. Synthesis of alkenylpyridines.

2b-2i were synthesized according to the method reported in the literature.[2] To a solution of bromidesubstituted azaarene (10.0 mmol, 1.0 equiv), CsF (4.6 g, 30.0 mmol) and pinacol vinylboronate (2.3 g, 15.0 mmol) in dioxane/H_2O (20 mL/10 mL) was added $Pd(PPh_3)_2Cl_2$ (0.7 g, 1.0 mmol). After stirring for 16 h at 80 °C under N_2, the

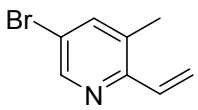
mixture was concentrated in vacuo. The crude product was further purified by column chromatography (petroleum ether/ethyl acetate = 40/1 - 10/1) on silica gel to yield the corresponding alkenylpyridines.



3-Methoxy-2-vinylpyridine (**2b**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 16/1), 572 mg (53% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.18 (t, *J* = 3.0 Hz, 1H), 7.18 (dd, *J* = 17.6, 11.2 Hz, 1H), 7.14 (d, *J* = 2.8 Hz, 2H), 6.37 (dd, *J* = 17.2, 2.0 Hz, 1H), 5.47 (dd, *J* = 10.8, 2.0 Hz, 1H), 3.84 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.9, 145.2, 141.0, 130.8, 123.1, 118.6, 117.8, 55.4 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_8H_{10}NO$ 136.0762; Found 136.0763.



5-Methoxy-2-vinylpyridine (**2c**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 16/1), 788 mg (73% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 2.8 Hz, 1H), 7.29 (d, *J* = 8.8 Hz, 1H), 7.15 (dd, *J* = 8.6, 3.0 Hz, 1H), 6.77 (dd, *J* = 17.6, 10.8 Hz, 1H), 6.03 (d, *J* = 17.6 Hz, 1H), 5.35 (d, *J* = 11.2 Hz, 1H), 3.86 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 154.9, 148.7, 137.1, 136.3, 121.5, 120.7, 115.8, 55.6 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_8H_{10}NO$ 136.0762; Found 136.0763.



5-Bromo-3-methyl-2-vinylpyridine (**3i**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 30/1), 1.0g (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.46 (d, *J* = 1.6 Hz, 1H), 7.57 (d, *J* = 1.6 Hz, 1H), 6.91 (dd, *J* = 16.8, 10.8 Hz, 1H), 6.35 (dd, *J* = 17.0, 1.8 Hz, 1H), 5.52 (dd, *J* = 10.6, 1.8 Hz, 1H), 2.33 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 152.1, 148.0, 140.2, 132.1, 132.1,

120.1, 119.0, 18.5 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for C_8H_9BrN 197.9918; Found 197.9919.

General procedure B

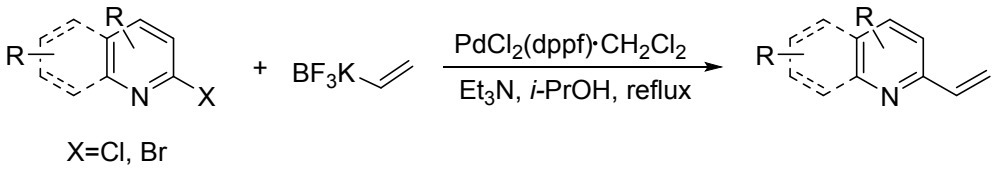
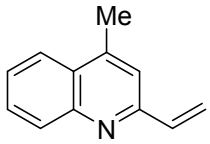


Figure S3. Synthesis of alkenylpyridines.

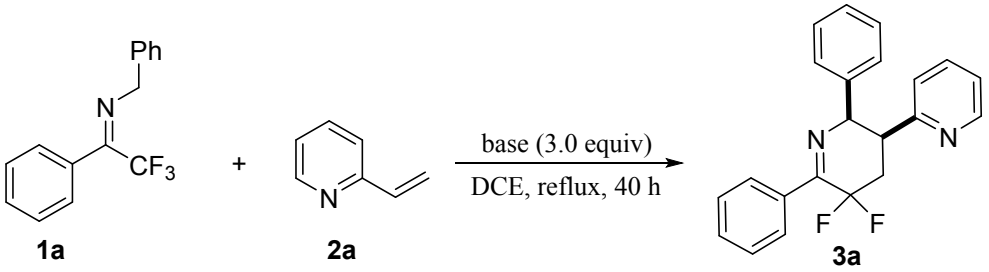
2j-2o were synthesized according to the method reported in the literature.[3] To a solution of chlorsubstituted azaarene (8.0 mmol, 1.0 equiv), potassium vinyltrifluoroborate (1.29 g, 9.6 mmol), $PdCl_2(dppf)\cdot CH_2Cl_2$ (131 mg, 0.16 mmol), and Et_3N (1.12 mL, 8.0 mmol) in *i*-PrOH (125 mL) was heated to reflux for 16 h. The mixture was cooled to room temperature and partitioned between CH_2Cl_2 (100 mL × 2) and H_2O (40 mL). The aqueous layer was separated and extracted with CH_2Cl_2 (50 mL) and the combined organic layers were washed with brine (100 mL), dried ($MgSO_4$), filtered, and concentrated in vacuo. Purification of the residue by column chromatography (petroleum ether/ethyl acetate = 40/1 - 10/1) gave the vinylpyridines



4-Methyl-2-vinylquinoline (**2n**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 865 mg (64% yield). ^1H NMR (400 MHz, $CDCl_3$): δ 8.06 (d, J = 8.4 Hz, 1H), 7.94 (d, J = 8.0 Hz, 1H), 7.68 (t, J = 7.6 Hz, 1H), 7.51 (t, J = 7.6 Hz, 1H), 7.43 (s, 1H), 7.00 (dd, J = 17.6, 10.8 Hz, 1H), 6.26 (d, J = 17.6 Hz, 1H), 5.64 (d, J = 10.8 Hz, 1H), 2.69 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 155.7, 147.8, 144.4, 138.1, 129.9, 129.3, 127.6, 126.1, 123.6, 119.6, 119.0, 18.9 ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{12}H_{12}N$ 170.0970; Found 170.0971.

3. Optimization of reaction conditions

3.1 Screening of base in reaction

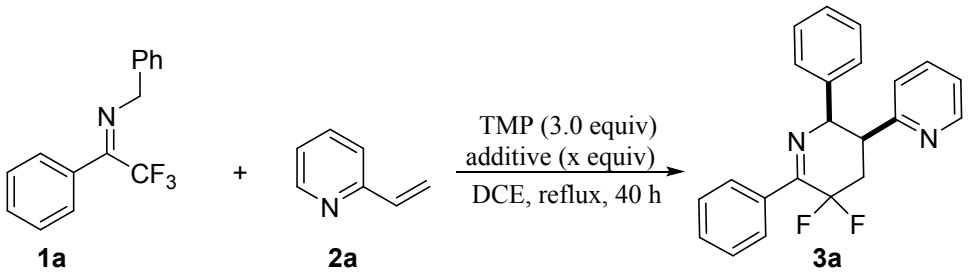


1a **2a** **3a**

entry	base	yield(%)[b]
1	TMP	45 (34)
2	PMP	38 (32)
3	Et_3N	N.R.
4	DMAP	N.R.
5	DIPEA	trace
6	DBU	N.R.
7	DABCO	N.R.
8	KHMDS	21 (32)
9	Cs_2CO_3	8 (37)
10	K_2CO_3	34 (33)
11	K_3PO_4	35 (43)
12	KO^{t}Bu	29 (24)
13	KOH	5 (63)
14	KOAc	trace
15	Na_2CO_3	36 (47)
16	$NaHCO_3$	22 (54)
17	TBAF	15 (43)

[a] Reaction conditions: unless specified otherwise, **1a** (0.6 mmol) was added to a mixture of **2a** (0.2 mmol) and base (0.6 mmol) in 1.0 mL of dry solvent. The solution was heated at reflux for 40 h. [b] Isolated yields. The yield of recovered **2a** was given in parenthesis.

3.2 Screening of additives in reaction[a]

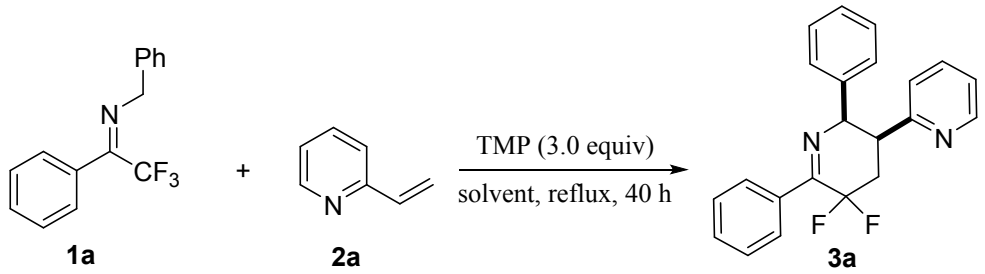


1a **2a** **3a**

entry	additive	yield(%)[b]
1[c]	$Cu(OTf)_2$	30 (33)
2[c]	$Sc(OTf)_3$	35 (32)
3[c]	$Y(OTf)_3$	34 (30)
4[c]	$InCl_3$	13 (31)
5[c]	BF_3	12 (33)
6[c]	TfOH	23 (21)
7[d]	$MeSi_3$-$MeSi_3$	21 (27)
8[d]	Me_3SiCF_3	42 (31)
9[d]	Ph_3SiH	42 (33)
10[d]	Et_3SiH	30 (28)
11[d]	Me_3SiCl	34 (27)
12[c]	$(C_6F_5)_3B$	38 (28)
13[d]	$B(OMe)_3$	35 (30)
14[d]	$B(O^tBu)_3$	42 (31)
15[d]	HBPin	20 (28)
16[d]	$PhMe_2Si$-BPin	45 (30)

[a] Reaction conditions: unless specified otherwise, **1a** (0.6 mmol) was added to a mixture of **2a** (0.3 mmol) and TMP (0.6 mmol) in 1.0 mL of dry solvent. The solution was heated at reflux for 40 h. [b] Isolated yields. The yield of recovered **2a** was given in parenthesis. [c] 0.3 equiv additive was used. [d] 3.0 equiv additive was used.

3.3 Screening of solvents in reaction[a]



1a **2a** **3a**

entry	solvent	yield(%)[b]
1	*i*-PrOH	trace
2	H_2O	N.R.
3	HFIP	23 (23)
4	THF	trace
5	acetone	trace
6	$CHCl_3$	trace
7	DMSO	N.R.
8	DMA	N.R.
9	PhCl	33 (30)
10	$PhCF_3$	40 (26)
11	*p*-xylene	32 (30)
12	hexafluorobenze	35 (27)
13	DCE: $PhCF_3$ = 1:1	32 (30)
14[c]	DCE	45 (34)

[a] Reaction conditions: unless specified otherwise, **1a** (0.6 mmol) was added to a mixture of **2a** (0.2 mmol) and TMP (0.6 mmol) in 1.0 mL of dry solvent. The solution was heated at reflux for 40 h. [b] Isolated yields. The yield of recovered **2a** was given in parenthesis. [c] The reaction was stirred under reflux conditions.

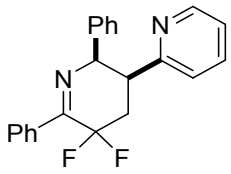
4. General Procedure for the synthesis of Products 3 and their Characterization Data.

4.1 General Procedure for the Synthesis of Products (3a as an example).

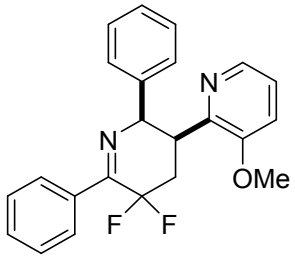
To a solution of **1a** (0.6 mmol, 157.8 mg) in 1.0 mL dry 1,2-Dichloroethane was added 2,2,6,6-tetramethylpiperidine (0.6 mmol, 84.8 mg). Then **2a** (0.2 mmol, 21 mg) was added dropwise to the solution under N_2. The mixture was moved to 85 ℃ oil bath and

refluxed for 40 h. After completion of the reaction, the solution was cooled to room temperature, H_2O (1 mL) was added. Then the mixture was extract with ethyl acetate (5 mL) for three times. After washed in brine and dried over Na_2SO_4, the combined organic phases was under reduced pressure and the residue was purified by flash chromatography (Petroleum ether/EtOAc = 13/1 to 10/1) to give the desired product **3a** as yellow oil (31 mg, 45 % yield).

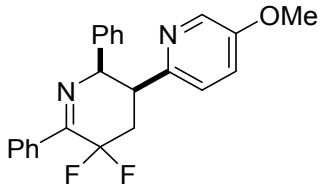
4.2 Characterization Data for Products.



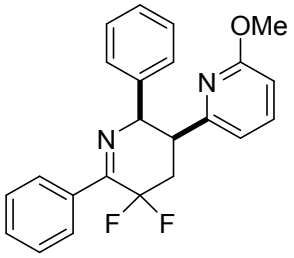
5',5'-Difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3a**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 31 mg (45% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.49 (d, *J* = 4.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 2H), 7.52 – 7.49 (m, 2H), 7.45 (t, *J* = 7.2 Hz, 2H), 7.16 – 7.12 (m, 2H), 7.09 (t, *J* = 7.2 Hz, 2H), 6.71 (d, *J* = 7.8 Hz, 1H), 6.57 (d, *J* = 7.8 Hz, 2H), 5.80 (t, *J* = 5.6 Hz, 1H), 3.99 – 3.96 (m, 1H), 2.71 – 2.60 (m, 1H), 2.55 – 2.49 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6 (dd, *J* = 29.0, 24.9 Hz), 158.7, 149.1, 136.2, 134.5 (d, *J* = 1.7 Hz), 133.8, 130.7, 128.5, 128,3, 128.3, 127.8, 127.4, 122.1, 122.0, 115.8 (dd, *J* = 248.3, 245.3 Hz), 66.6, 43.1 (d, *J* = 8.1 Hz), 30.4 (t, *J* = 23.4 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.25 (dddd, *J* = 287.6, 30.4, 20.3, 6.0 Hz, 1F), − 97.91(dd, *J* = 287.7, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{19}F_2N_2$ 349.1516; Found 349.1517.



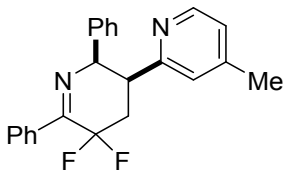
5',5'-Difluoro-3-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3b**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 45 mg (60% yield). Mp 117 - 120 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.2 Hz, 2H), 7.84 (d, *J* = 3.6 Hz, 1H), 7.49 – 7.43 (m , 3H), 7.18 – 7.05 (m, 5H), 6.56 (d, *J* = 6.8 Hz, 2H), 5.95 (t, *J* = 5.6 Hz, 1H), 4.29 – 4.24 (m, 1H), 3.95 (s, 1H), 2.87 – 2.69 (m, 1H), 2.50 – 2.42 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (dd, *J* = 29.5, 24.9 Hz), 153.8, 148.2, 140.5, 135.2 (d, *J* = 2.7 Hz), 134.0 (t, *J* = 2.6 Hz), 130.6, 128.5, 128.3, 128.0, 127.7, 127.2, 122.4, 116.4, 116.3 (dd, *J* = 248.4, 244.0 Hz), 63.6, 55.4, 37.8 (d, *J* = 8.8 Hz), 30.0 (t, *J* = 23.4 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.49 (dddd, *J* = 286.9, 32.3, 20.3, 6.0 Hz, 1F), − 98.76 (dd, *J* = 286.9, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_2N_2O$ 379.1622; Found 379.1621.



5',5'-Difluoro-4-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3c**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 38 mg (51% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01 (d, *J* = 7.2 Hz, 2H), 7.44 – 7.32 (m, 4H), 7.11 – 7.01 (m, 3H), 6.53 (d, *J* = 7.2 Hz 2H), 6.47 (d, *J* = 8.4 Hz, 1H), 6.40 (d, *J* = 7.2 Hz, 1H), 5.73 (t, *J* = 5.6 Hz, 1H), 3.78 – 3.72 (m, 1H), 3.52 (s, 3H), 2.71 – 2.54 (m, 1H), 2.43 – 2.34 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.3, 159.5 (dd, *J* = 29.3, 25.4Hz), 155.1, 137.6, 133.8 (d, *J* = 2.8 Hz), 132.8 (t, *J* = 2.8 Hz), 129.6, 127.5 (t, *J* = 2.2 Hz), 127.3, 126.7, 126.2, 115.0 (dd, *J* = 248.6, 244.5 Hz), 113.8, 107.9, 65.7, 52.0, 41.7 (d, *J* = 8.0 Hz), 29.5 (t, *J* = 23.3 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 87.75 (d, *J* = 287.6 Hz, 1F), − 97.71(d, *J* = 287.6 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_2N_2O$ 379.1622; Found 379.1620.

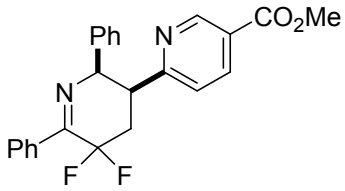


5',5'-Difluoro-6-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3d**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 35 mg (47% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.50 – 7.40 (m, 4H), 7.18 – 7.09 (m, 3H), 6.60 (d, *J* = 7.2 Hz, 2H), 6.54 (d, *J* = 8.4 Hz, 1H), 6.48 (d, *J* = 7.2 Hz, 1H), 5.73 (t, *J* = 5.6 Hz, 1H), 3.84 – 3.80 (m, 1H), 3.60 (s, 3H), 2.78 – 2.61 (m, 1H), 2.51 – 2.41 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 163.3, 160.6 (dd, *J* = 29.2, 25.0 Hz), 156.2, 138.6, 134.9 (d, *J* = 2.8 Hz), 133.9 (t, *J* = 2.8 Hz), 130.7, 128.5 (t, *J* = 2.2 Hz), 128.3, 127.7, 127.3, 116.0 (dd, *J* = 249.2, 244.1 Hz) 114.8, 108.9, 66.8, 53.0, 42.7 (d, *J* = 8.1 Hz), 30.6 (t, *J* = 23.6 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 87.76 (dddd, *J* = 287.6, 30.8, 20.6, 6.0 Hz, 1F), − 97.72 (dd, *J* = 287.8, 9.8 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_2N_2O$ 379.1622; Found 379.1623.

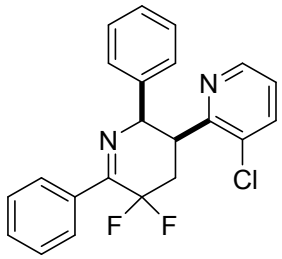


5',5'-Difluoro-5-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3e**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 34 mg (47% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.27 (d, *J* = 4.8 Hz, 1H), 8.00 (d, *J* = 7.2 Hz, 2H), 7.45 – 7.36 (m, 3H), 7.10 – 7.01 (m, 3H), 6.88 (d, *J* = 4.4 Hz, 1H), 6.49 (d, *J* = 7.2 Hz, 2H), 6.42 (s, 1H), 5.71 (t, *J* = 5.6 Hz, 1H), 3.88 – 3.83 (m, 1H), 2.64 – 2.38(m, 2H), 2.14 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.6 (dd, *J* = 29.1, 24.7 Hz), 158.5, 148.8, 147.4, 134.6 (d, *J* = 2.8 Hz), 133.8 (t, *J* = 2.8 Hz),

130.7, 128.5 (t, J = 2.2 Hz), 128.3, 127.7, 127.4, 123.1, 123.0, 115.9 (dd, J = 248.7, 244.9 Hz), 66.6, 43.0 (d, J = 7.8 Hz), 30.5 (t, J = 23.6 Hz), 21.0 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.23 (d, J = 287.6 Hz, 1F), − 97.98 (d, J = 287.3 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{21}F_2N_2O$ 363.1673; Found 363.1672.

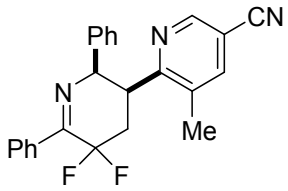


Methyl-5',5'-difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carboxylate (**3f**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 17/1), 34 mg (43% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 9.09 (d, J = 2.0 Hz, 1H), 8.11 (dd, J = 8.4, 2.4 Hz, 1H), 8.07 (d, J = 7.6 Hz, 2H), 7.51 – 7.44 (m, 4H), 7.16 (t, J = 7.6 Hz, 1H), 7.10 (t, J = 7.6 Hz, 2H), 6.80 (d, J = 8.0 Hz, 1H), 6.57 (d, J = 7.6 Hz, 2H), 5.82 (t, J = 5.6 Hz, 1H), 4.07 – 4.02 (m, 1H), 3.95 (s, 3H), 2.79 – 2.64 (m, 1H), 2.59 – 2.50 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 163.2, 160.6 (dd, J = 29.1, 24.9 Hz), 150.4, 137.3, 134.2 (d, J = 2.5 Hz), 133.6 (t, J = 2.6 Hz), 130.8, 128.5, 128.4, 128.2, 128.0, 127.7, 124.4, 121.6, 115.6 (dd, J = 248.4, 245.1 Hz), 66.3, 52.5, 43.4 (d, J = 8.1 Hz), 30.4 (t, J = 23.8 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.23 (d, J = 288.4 Hz, 1F), − 98.03 (d, J = 288.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{21}F_2N_2O_2$ 407.1571; Found 407.1572.

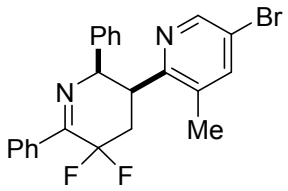


3-Chloro-5',5'-difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (**3g**,

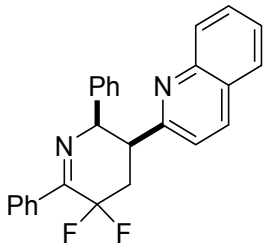
yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 39 mg (56% yield). Mp 134 - 135 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 – 8.07 (m, 3H), 7.72 (dd, *J* = 8.0, 1.2 Hz, 2H), 7.52 – 7.44 (m, 3H), 7.16 – 7.04 (m, 3H), 6.60 (d, *J* = 7.2 Hz, 2H), 6.03 (t, *J* = 5.6 Hz, 1H), 4.37 – 4.32 (m, 1H), 2.94 – 2.77 (m, 1H), 2.49 – 2.40 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (dd, *J* = 29.3, 25.1 Hz), 155.3, 147.0, 136.7, 134.9 (d, *J* = 2.8 Hz), 133.7 (t, *J* = 2.7 Hz), 131.6, 130.7, 128.5 (t, *J* = 2.1 Hz), 128.3, 127.9, 127.9, 127.5, 122.8, 116.2 (dd, *J* = 248.0, 244.2 Hz), 63.1, 39.9 (d, *J* = 8.8 Hz), 30.3 (t, *J* = 23.4 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.54 (dddd, *J* = 287.6, 32.6, 19.5, 6.0 Hz, 1F), − 99.00 (dd, *J* = 287.8, 9.0 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{22}H_{18}ClF_2N_2$ 383.1127; Found 383.1126.



5',5'-Difluoro-3-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3h**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 49mg (64% yield). Mp 113 – 114 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 1.2 Hz, 1H), 8.07 (d, *J* = 7.2 Hz, 2H), 7.75 (s, 1H), 7.53 – 7.44 (m, 3H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 2H), 6.50 (d, *J* = 7.2 Hz, 2H), 5.74 (t, *J* = 5.6 Hz, 1H), 4.15 – 4.10 (m, 1H), 3.00 – 2.82 (m, 1H), 2.62 (s, 3H), 2.46 – 2.37 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.0 (dd, *J* = 29.1, 25.1 Hz), 160.0, 148.0, 139.2, 133.2 (d, *J* = 2.7 Hz), 132.4 (t, *J* = 2.7 Hz), 131.0, 129.9, 127.5 (t, *J* = 2.0 Hz), 127.4, 127.0, 126.8, 126.8, 115.7, 114.9 (dd, *J* = 249.1, 243.3 Hz), 106.8, 62.5, 39.4 (d, *J* = 8.6 Hz), 29.6 (t, *J* = 23.6 Hz), 17.2 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.28 (d, *J* = 288.8 Hz, 1F), − 98.95 (d, *J* = 288.8 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{20}F_2N_2$ 388.1625; Found 388.1624.

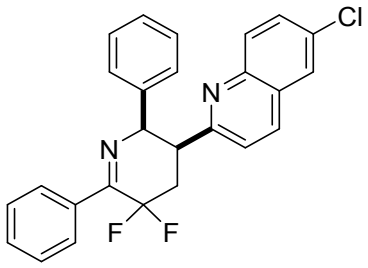


5-Bromo-5',5'-difluoro-3-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3i, yellow oil**)**, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 46 mg (53% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.01–8.00 (m, 3H), 7.56 (d, *J* = 2.0 Hz, 1H), 7.44 – 7.35 (m, 3H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.04 (t, *J* = 7.2 Hz, 1H), 6.44 (d, *J* = 7.2 Hz, 2H), 5.64 (t, *J* = 5.6 Hz, 1H), 3.95 – 3.91 (m, 1H), 2.86 – 2.68 (m, 1H), 2.46 (s, 3H), 2.36 – 2.27 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.9 (dd, *J* = 29.5, 25.1 Hz), 153.9, 146.4, 138.9, 133.5 (d, *J* = 2.8 Hz), 132.6 (t, *J* = 2.7 Hz), 132.1, 129.8, 127.4, 127.3, 127.0, 126.9, 126.5, 117.7, 115.2 (dd, *J* = 249.1, 243.4 Hz), 62.8, 38.7 (d, *J* = 8.6 Hz), 29.7 (t, *J* = 23.6 Hz), 17.2 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.22 (d, *J* = 288.0 Hz, 1F), − 98.73 (d, *J* = 288.0 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{23}H_{20}BrF_2N_2$ 441.0778; Found 441.0775.

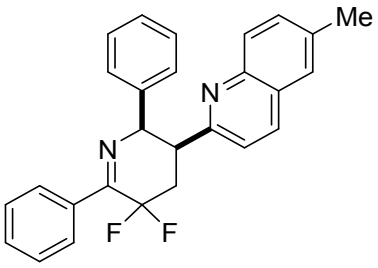


2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline (**3j**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 38 mg (48% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.10 (d, *J* = 7.6 Hz, 2H), 7.96 (dd, *J* = 14.4, 8.4 Hz, 2H), 7.76 (d, *J* = 87.8 Hz, 1H), 7.70 (t, *J* = 7.2 Hz, 1H), 7.51(dd, *J* = 13.8, 7.2 Hz, 2H), 7.47 (t, *J* = 7.2 Hz, 2H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.03 (t, *J* = 7.2 Hz, 2H), 6.78 (d, *J* = 8.4 Hz, 1H), 6.58 (d, *J* = 7.8 Hz, 2H), 5.90 (t, *J* = 5.6 Hz, 1H), 4.17 –

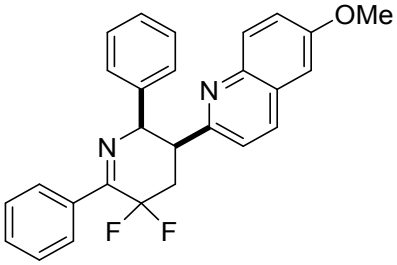
4.15 (m, 1H), 2.87 – 2.75 (m, 1H), 2.68 – 2.61 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7 (dd, *J* = 29.1, 25.7 Hz), 158.9, 147.7, 136.1, 134.6 (d, *J* = 1.7 Hz), 133.8, 130.7, 129.6, 129.2, 128.5, 128.4, 128.3, 127.8, 127.5, 127.5, 127.0, 126.3, 119.9, 115.8 (dd, *J* = 248.8, 245.0 Hz), 66.4, 44.1 (d, *J* = 8.0 Hz), 30.8 (t, *J* = 23.8 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.54 (dddd, *J* = 287.6, 31.1, 20.6, 6.8, 1F), − 97.76 (dd, *J* = 287.6, 11.3 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{21}F_2N_2$ 399.1673; Found 399.1674.



6-Chloro-2-(5,5-difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline (**3k**, brown solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 43.2 mg (50% yield). Mp 123 – 124 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (d, *J* = 7.6 Hz, 2H), 7.88 (dd, *J* = 8.8, 5.6 Hz, 2H), 7.74 (d, *J* = 2.0 Hz, 1H), 7.61 (dd, *J* = 8.8, 2.4 Hz, 1H), 7.51 – 7.44 (m, 3H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 2H), 6.84 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 7.2 Hz, 2H), 5.86 (t, *J* = 5.6 Hz, 1H), 4.15 – 4.11 (m, 1H), 2.89 – 2.72 (m, 1H), 2.68 – 2.59 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (dd, *J* = 29.5, 25.2 Hz), 159.2, 146.0, 135.2, 134.5 (d, *J* = 2.6 Hz), 133.8 (t, *J* = 2.6 Hz), 132.1, 130.8, 130.6, 128.5, 128.4, 128.3, 127.9, 127.6, 127.5, 126.2, 120.9, 115.7 (dd, *J* = 248.9, 245.0 Hz), 66.3, 44.0 (d, *J* = 8.0 Hz), 30.7 (t, *J* = 23.7 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.13 (dddd, *J* = 287.8, 30.0, 20.3, 6.0 Hz, 1F), − 98.29 (dd, *J* = 288.0, 9.7 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{20}ClF_2N_2$ 433.1283; Found 433.1284.

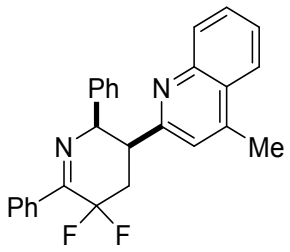


2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-6-methylquinoline (**3l**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 44 mg (54% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.6 Hz, 2H), 7.86 (dd, *J* = 10.8, 9.2 Hz, 2H), 7.53 – 7.44 (m, 5H), 7.11 (t, *J* = 7.2 Hz, 1H), 7.02 (t, *J* = 7.2 Hz, 2H), 6.71 (d, *J* = 8.4 Hz, 1H), 6.57 (d, *J* = 7.2 Hz, 2H), 5.89 (t, *J* = 5.6 Hz, 1H), 4.15 – 4.11 (m, 1H), 2.88 – 2.72 (m, 1H), 2.67 – 2.59 (m, 1H), 2.53 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.7 (dd, *J* = 29.4, 25.3 Hz), 157.9, 146.2, 136.2, 135.5, 134.6 (d, *J* = 2.8 Hz), 133.9 (t, *J* = 2.7 Hz), 132.0, 130.7, 128.8, 128.6, 128.4, 128.3, 127.8, 127.4, 127.0, 126.4, 119.9, 115.8 (dd, *J* = 248.9, 244.9 Hz), 66.4, 44.0 (d, *J* = 7.9 Hz), 30.8 (t, *J* = 23.5 Hz), 21.6 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.21 (dddd, *J* = 287.4, 30.0, 20.3, 6.0 Hz, 1F), − 97.74 (dd, *J* = 287.4, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{23}F_2N_2$ 413.1829; Found 413.1828.

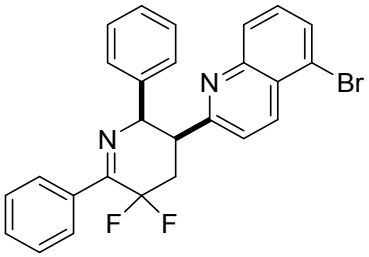


2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-6-methoxyquinoline (**3m**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 12/1), 47 mg (54 % yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.09 (d, *J* = 7.8 Hz, 2H), 7.85 (dd, *J* = 20.4, 9.6 Hz, 2H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.46 (t, *J* = 7.2 Hz, 2H), 7.35 (dd, *J* = 9.0, 2.4 Hz, 1H), 7.05 – 7.02 (m, 3H), 6.71 (d, *J* = 8.4 Hz 1H), 6.57 (d, *J* = 7.8 Hz, 2H), 5.87 (t, *J* = 5.6 Hz, 1H), 4.13 – 4.11 (m, 1H), 3.93 (s, 3H), 2.83 – 2.71 (m, 1H), 2.65 – 2.60 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6

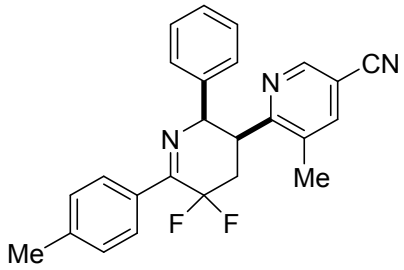
(dd, J = 28.8, 24.9 Hz), 157.6, 156.3, 143.8, 134.8, 134.7 (d, J = 2.1 Hz), 133.9, 130.7, 130.6, 128.5, 128.4, 128.3, 127.9, 127.8, 127.4, 122.3, 120.1, 115.8 (dd, J = 248.7, 245.2 Hz), 104.9, 66.5, 55.5, 43.8 (d, J = 7.9 Hz), 30.8 (t, J = 23.6 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.22 (dddd, J = 287.4, 30.0, 20.3, 6.0 Hz, 1F), − 97.68 (dd, J = 287.4, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{23}F_2N_2O$ 429.1778; Found 429.1777.



2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-4-methylquinoline (**3n**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 42 mg (51% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.02 (d, J = 7.6 Hz, 2H), 7.88 (dd, J = 17.2, 8.4 Hz, 2H), 7.61 (t, J = 7.2 Hz 1H), 7.48 – 7.37 (m, 4H), 7.04 (t, J = 7.2 Hz, 1H), 6.96 (t, J = 7.2 Hz, 2H), 6.51 (s, 1H), 6.49 (d, J = 5.6 Hz, 2H), 5.80 (t, J = 5.6 Hz, 1H), 4.05 – 4.00 (m, 1H), 2.79 – 2.62 (m, 1H), 2.59 – 2.50 (m, 1H), 2.46 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.7 (dd, J = 29.0, 25.1 Hz), 158.5, 147.4, 144.3, 134.7 (d, J = 2.7 Hz), 133.9, 130.7, 129.7, 129.3, 128.6 (t, J = 2.0 Hz), 128.4, 128.3, 127.8, 127.4, 127.0, 126.1, 123.6, 120.8, 115.8 (dd, J = 248.8, 245.1 Hz), 66.4, 44.0 (d, J = 7.9 Hz), 30.8 (t, J = 23.7 Hz), 18.7 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.20 (dddd, J = 287.4, 30.0, 20.3, 6.0 Hz, 1F), − 97.83 (dd, J = 287.4, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{27}H_{23}F_2N_2$ 413.1829; Found 413.1830.

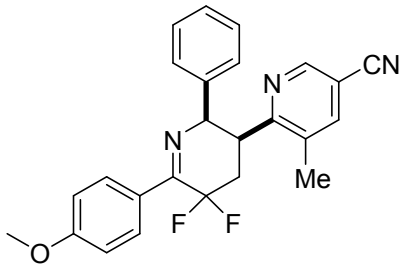


5-Bromo-2-(5,5-difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline (**3o**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 45 mg (47% yield). Mp 146 – 150 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10 (d, *J* = 7.2 Hz, 2H), 8.01 (dd, *J* = 7.6, 1.2 Hz, 1H), 7.96 (d, *J* = 8.4 Hz, 1H), 7.72 (dd, *J* = 8.0, 0.8 Hz, 1H), 7.51 – 7.44 (m, 3H), 7.35 (t, *J* = 7.6 Hz, 1H), 7.10 (t, *J* = 7.2 Hz, 1H), 7.01 (t, *J* = 7.2 Hz, 2H), 6.93 (d, *J* = 8.4 Hz, 1H), 6.60 (d, *J* = 7.2 Hz, 2H), 5.94 (t, *J* = 5.6 Hz, 1H), 4.25 – 4.20 (m, 1H), 2.99 – 2.82 (m, 1H), 2.74 – 2.65 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.6 (dd, *J* = 29.0, 25.1 Hz), 159.8, 144.5, 136.6, 134.6 (d, *J* = 2.0 Hz), 133.8, 133.2, 130.7, 128.5, 128.3, 128.0, 128.1, 127.8, 127.5, 127.3, 126.7, 125.1, 120.7, 115.8 (dd, *J* = 248.8, 244.7 Hz), 66.4, 44.0 (d, *J* = 8.0 Hz), 30.7 (t, *J* = 23.7 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.33 (dddd, *J* = 288.0, 30.0, 20.3, 5.6 Hz, 1F), − 97.67 (dd, *J* = 288.2, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{26}H_{20}BrF_2N_2$ 477.0778; Found 477.0775.

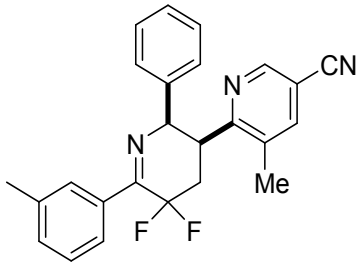


5',5'-Difluoro-3-methyl-2'-phenyl-6'-(p-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3p**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 48 mg (60% yield). Mp 160 – 163 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 2.0 Hz, 1H), 7.89 (d, *J* = 8.0 Hz, 2H), 7.66 (d, *J* = 1.6 Hz, 1H), 7.18 (d, *J* = 8.0 Hz, 2H), 7.10 (t, *J* = 7.2 Hz 1H), 7.02 (t,

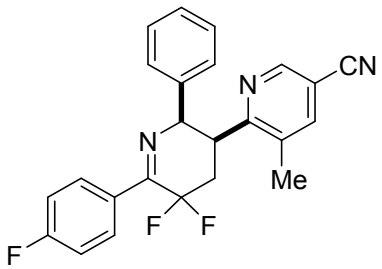
J = 7.2 Hz, 2H), 6.41 (d, *J* = 7.2 Hz, 2H), 5.64 (t, *J* = 5.6 Hz, 1H), 4.05 – 4.01 (m, 1H), 2.90 – 2.72 (m, 1H), 2.53 (s, 3H), 2.36 – 2.29 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 160.8 (dd, *J* = 29.1, 24.9 Hz), 149.1, 141.3, 140.2, 134.4 (d, *J* = 2.5 Hz), 132.1, 130.7, 129.2, 128.5, 128.0, 127.9, 127.8, 116.8, 116.4 (dd, *J* = 249.1, 244.4 Hz), 107.8, 63.5, 40.5 (d, *J* = 8.6 Hz), 30.6 (t, *J* = 23.6 Hz), 21.5 (d, *J* = 2.1 Hz), 18.3 (d, *J* = 2.1 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) : δ − 88.25 (d, *J* = 288.0 Hz, 1F), − 98.55 (d, *J* = 288.0 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3$ 402.1782; Found 402.1783.



5',5'-Difluoro-6'-(4-methoxyphenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3q**, white solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 11/1), 52 mg, (63% yield). Mp 154 – 155 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 0.8 Hz, 1H), 7.97 (d, *J* = 8.4 Hz, 2H), 7.66 (s, 1H), 7.09 (t, *J* = 7.2 Hz, 1H), 7.02, (t, *J* = 7.2 Hz, 2H), 6.88 (d, *J* = 8.8 Hz, 2H), 6.40 (d, *J* = 7.2 Hz 2H), 5.62 (t, *J* = 5.6 Hz, 1H), 4.03 – 4.00 (m, 1H), 3.78 (s, 3H), 2.90 – 2.72 (m, 1H), 2.53 (s, 3H), 2.35 – 2.27 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.5 (d, *J* = 72.7 Hz), 160.1 (dd, *J* = 28.7, 25.0 Hz), 160.0, 149.1, 140.2, 134.5 (d, *J* = 2.5 Hz), 132.1, 130.3, 129.0, 128.0 (d, *J* = 10.9 Hz), 127.7, 125.9 (t, *J* = 2.5 Hz), 116.8, 116.1 (dd, *J* = 249.2, 243.7 Hz), 113.9 (d, *J* = 29.5 Hz), 107.7, 63.4, 55.4 (dd, *J* = 10.3, 1.4 Hz), 40.5 (d, *J* = 8.6 Hz), 30.7 (t, *J* = 24.2 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.20 (d, *J* = 287.3Hz, 1F), − 98.00 (d, *J* = 287.3 Hz, 1F); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3O$ 418.1731; Found 418.1732.

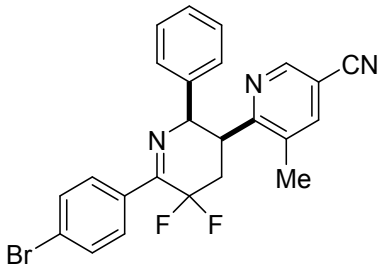


5',5'-Difluoro-3-methyl-2'-phenyl-6'-(m-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3r**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 47 mg (59% yield). Mp 149 – 151 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 1.6 Hz, 1H), 7.87 (s, 2H), 7.75 (d, *J* = 1.2 Hz, 1H), 7.37 – 7.31 (m, 2H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.11 (t, *J* = 7.2 Hz, 2H), 6.50 (d, *J* = 7.2 Hz, 2H), 5.73 (t, *J* = 5.6 Hz, 1H), 4.14 – 4.10 (m, 1H), 2.99 – 2.77 (m, 1H), 2.61 (s, 3H), 2.45 – 2.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2 (dd, *J* = 29.4, 24.7 Hz), 161.1, 149.1 , 140.2, 138.1, 134.3 (d, *J* = 2.6 Hz), 133.4 (t, *J* = 2.5 Hz), 132.1, 131.8, 128.9, 128.3, 128.1, 127.8, 127.9, 125.7 (t, *J* = 2.6 Hz), 116.7, 116.0 (dd, *J* = 249.1, 243.5 Hz), 107.8, 63.6, 40.5 (d, *J* = 8.6 Hz), 30.6 (t, *J* = 23.8 Hz), 21.5, 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.12 (dddd, *J* = 288.6, 32.0, 19.9, 5.6 Hz, 1F), − 98.88 (dd, *J* = 288.4, 9.0 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ calcd for $C_{25}H_{22}F_2N_3$ 402.1782, Found 402.1783.

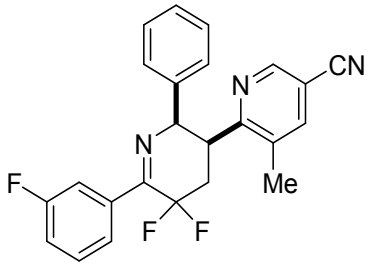


5',5'-Difluoro-6'-(4-fluorophenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3s**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 50 mg (62% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 1.8 Hz, 1H), 8.08 (dd, *J* = 8.4, 6.0 Hz, 2H), 7.75 (d, *J* = 1.2 Hz, 1H), 7.19 (t, *J* = 7.2 Hz, 1H), 7.15 – 7.10 (m, 4H), 6.48 (d, *J* = 7.2 Hz, 2H), 5.71 (t, *J* =

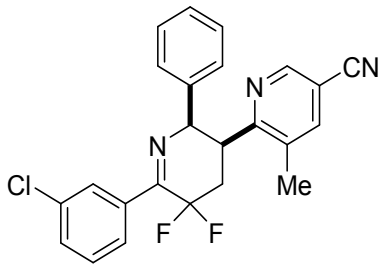
5.6 Hz, 1H), 4.12 – 4.09 (m, 1H), 2.97 – 2.85 (m, 1H), 2.61 (s, 3H), 2.44 – 2.38 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 164.5 (d, *J* = 250.1 Hz), 160.9, 159.8 (dd, *J* = 29.2, 25.3 Hz), 149.1, 140.2, 134.2 (d, *J* = 2.5 Hz), 132.1, 130.8 (d, *J* = 8.6 Hz), 129.6 (dd, *J* = 5.7, 2.9 Hz), 128.1, 127.9, 127.8, 116.7, 116.0 (dd, *J* = 249.3, 243.6 Hz), 115.5 (d, *J* = 21.5 Hz), 107.8, 63.6, 40.4 (d, *J* = 8.4 Hz), 30.6 (t, *J* = 22.9 Hz), 18.3 (d, *J* = 1.9 Hz); ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.49 (d, *J* = 288.4 Hz, 1F), − 98.65 (d, *J* = 288.4 Hz, 1F), − 109.18 (s, 1F); HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{18}F_3N_3$ 406.1531; Found 406.1532.



6'-(4-Bromophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3t**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 60 mg (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (s, 1H), 8.01 (dd, *J* = 8.0, 6 Hz, 1H), 7.87 (d, *J* = 8.4 Hz, 1H), 7.68 (s, 1H), 7.51 (d, *J* = 8.8 Hz, 1H), 7.13 – 7.02 (m, 4H), 6.41 (d, *J* = 7.6 Hz, 2H), 5.64 (t, *J* = 5.6 Hz, 1H), 4.04 – 4.01 (m, 1H), 2.92 – 2.74 (m, 1H), 2.53 (s, 3H), 2.38 – 2.29 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 160.1 (dd, *J* = 29.6, 25.1 Hz) 149.1, 140.2, 134.0 (d, *J* = 2.5 Hz), 132.3 (t, *J* = 2.6 Hz), 131.9, 131.6, 130.1, 129.6, 128.1, 127.9, 127.8, 125.8, 123.1, 116.7, 107.9, 63.7, 40.4 (d, *J* = 8.6 Hz), 30.6 (t, *J* = 23.1 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.55 (d, *J* = 288.8 Hz, 1F), − 98.89 (d, *J* = 288.8 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}BrF_2N_3$ 466.0730; Found 466.0734.

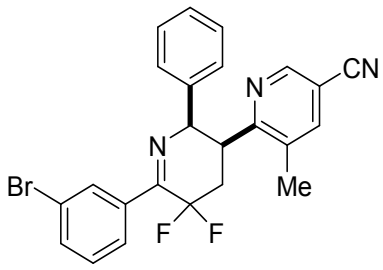


5',5'-Difluoro-6'-(3-fluorophenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3u**, brown solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 44 mg (55% yield). Mp 153 – 157 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.28 (d, *J* = 1.6 Hz, 1H), 7.86 (d, *J* = 8.0 Hz, 1H), 7.80 – 7.76 (m, 2H), 7.43 (td, *J* = 8.0 Hz, 6.0 Hz, 1H), 7.22 – 7.18 (m, 2H), 7.12 (t, *J* = 7.2 Hz, 2H), 6.49 (d, *J* = 7.2 Hz, 2H), 5.73 (t, *J* = 5.6 Hz, 1H), 4.13 – 4.08 (m, 1H), 3.00 – 2.82 (m, 1H), 2.61 (s , 3H), 2.47 – 2.38 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.7 (d, *J* = 246.6 Hz), 160.8, 160.0 (dd, *J* = 30.5, 26.4 Hz), 149.1, 140.2, 135.6 – 135.5 (m), 134.0 (d, *J* = 2.5 Hz), 132.0, 129.9 (d, *J* = 7.8 Hz), 128.1, 127.9, 127.8, 124.3, 117.9 (d, *J* = 21.2 Hz), 116.7, 115.8 (dd, *J* = 248.6, 243.9 Hz), 115.5 (d, *J* = 23.4 Hz), 107.9, 63.7, 40.4 (d, *J* = 8.6 Hz), 30.6 (t, *J* = 23.7 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.62 (dddd, *J* = 289.5, 31.9, 20.3, 6.0 Hz, 1F), − 99.06 (dd, *J* = 289.3, 9.4 Hz, 1F), − 112.56 (ddd, 14.3, 8.6, 6.0 Hz, 1F) ppm; HRMS (ESI) m/z: [M + H]$^{+}$ Calcd for $C_{24}H_{19}F_3N_3$ 406.1531; Found 406.1530.

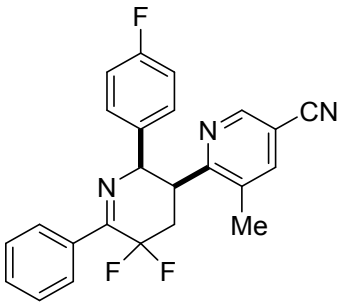


6'-(3-Chlorophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3v**, brown oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 48 mg (54% yield). ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.28 (d, *J* = 1.8 Hz, 1H), 8.06 (s, 1H), 7.96 (d, *J* = 7.8 Hz, 1H), 7.76 (d, *J* =

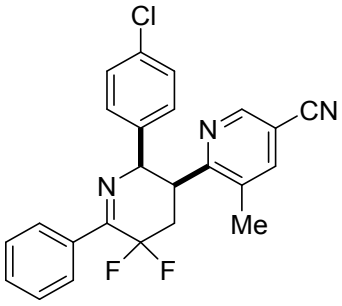
1.2 Hz, 1H), 7.49 (ddd, *J* = 8.0z, 1.8, 0.6 Hz, 1H), 7.40 (t, *J* = 7.8 Hz, 1H), 7.20 (t, *J* = 7.2 Hz, 1H), 7.13 (t, *J* = 7.8 Hz, 2H), 6.49 (d, *J* = 7.2 Hz, 2H), 5.73 (t, *J* = 5.6 Hz, 1H), 4.12 – 4.09 (m, 1H), 2.97 – 2.86 (m, 1H), 2.61 (s, 3H), 2.45 – 2.39 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 160.8, 159.9 (dd, *J* = 39.9, 25.5 Hz), 149.1, 140.2, 135.1 (t, *J* = 2.8 Hz), 134.6, 134.0 (d, *J* = 2.5 Hz), 132.0, 131.0, 129.7, 128.5, 128.1, 127.9, 127.8, 126.7 (t, *J* = 2.8 Hz), 116.7, 115.8 (dd, *J* = 249.2 Hz, 243.4 Hz), 107.9, 63.7, 40.4 (d, *J* = 8.7 Hz), 30.6 (t, *J* = 24.1 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.57 (d, *J* = 289.1 Hz, 1F), − 99.13 (d, *J* = 289.5 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}ClF_2N_3$ 422.1236; Found 422.1235.



6'-(3-Bromophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3w**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 15/1), 52 mg (56% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.20 (d, *J* = 1.2 Hz, 1H), 8.14 (s, 1H), 7.93 (d, *J* = 8.0 Hz, 1H), 7.68 (d, *J* = 0.8 Hz, 1H), 7.56 (d, *J* = 8.0 Hz, 1H), 7.26 (t, *J* = 8.0 Hz, 1H), 7.12 (t, *J* = 7.2 Hz, 1H), 7.06 (t, *J* = 7.2 Hz, 2H), 6.41 (d, *J* = 7.6 Hz, 2H), 5.65 (t, *J* = 5.6 Hz, 1H), 4.04 – 4.00 (m, 1H), 2.92 – 2.75 (m, 1H), 2.53 (s, 3H), 2.39 – 2.30 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.8, 159.8 (dd, *J* = 29.4, 25.5 Hz), 149.1, 140.2, 135.4 (t, *J* = 2.6 Hz), 134.0 (d, *J* = 2.5 Hz), 133.9, 132.1, 131.5, 129.9, 128.1, 127.9, 127.8, 127.2 (t, *J* = 2.7 Hz), 122.7, 116.7, 115.8 (dd, *J* = 248.8, 243.4 Hz) 107.9, 63.7, 40.4 (d, *J* = 8.5 Hz), 30.6 (t, *J* = 23.2 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.57 (d, *J* = 289.1 Hz, 1F), − 99.15 (d, *J* = 289.5 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}BrF_2N_3$ 466.0730; Found 466.0734.

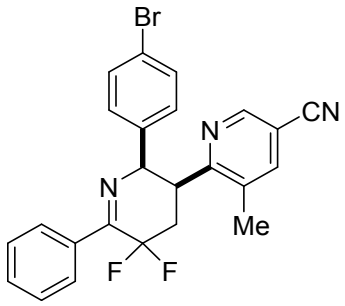


5',5'-Difluoro-2'-(4-fluorophenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3x**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 45 mg (60% yield). Mp 184 – 185 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.33 (d, *J* = 2.0 Hz, 1H), 8.06 (d, *J* = 7.2 Hz, 2H), 7.76 (d, *J* = 1.6 Hz, 1H), 7.52 (t, *J* = 7.2 Hz, 1H), 7.47 (t, *J* = 7.6 Hz, 2H), 6.82 (t, *J* = 8.8 Hz, 2H), 6.47 (dd, *J* = 8.4, 5.2 Hz, 2H), 5.71 (t, *J* = 5.6 Hz, 1H), 4.13 – 4.08 (m, 1H), 2.95 – 2.77 (m, 1H), 2.61 (s, 3H), 2.46 – 2.38 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 162.2 (d, *J* = 245.8 Hz), 161.2 (dd, *J* = 29.2, 25.0 Hz), 160.8, 149.2, 140.3, 133.3 (t, *J* = 2.3 Hz), 132.0, 131.1, 130.2 (d, *J* = 3.7 Hz), 129.4 (d, *J* = 8.2 Hz), 128.5, 128.4, 116.6, 115.8 (dd, *J* = 249.3, 245.3 Hz), 115.1 (d, *J* = 21.5 Hz), 108.0, 62.9, 40.3 (d, *J* = 8.7 Hz), 30.6 (t, *J* = 23.6 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.44 (d, *J* = 289.1 Hz, 1F), − 98.77 (d, *J* = 289.1 Hz, 1F), − 114.06 (s, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}F_3N_3$ 406.1531; Found 406.1532.

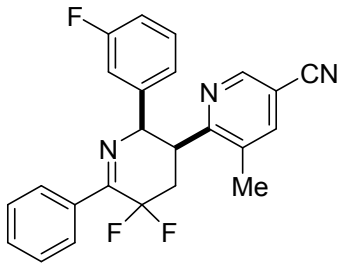


2'-(4-Chlorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3y**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 51 mg (61% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.34 (d, *J* = 1.6 Hz, 1H), 8.05 (d, *J* = 7.6 Hz, 2H), 7.76 (d, *J* = 1.2 Hz, 1H),

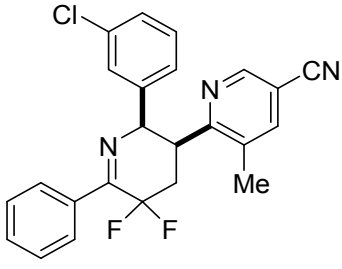
7.52 (t, J = 7.2 Hz, 1H), 7.46 (t, J = 7.2 Hz, 2H), 7.10 (d, J = 7.6 Hz, 2H), 6.43 (d, J = 8.4 Hz, 2H), 5.69 (t, J = 5.6 Hz, 1H), 4.13 – 4.09 (m, 1H), 2.93 – 2.75 (m, 1H), 2.60 (s, 3H), 2.47 – 2.38 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (dd, J = 29.1, 24.7 Hz), 160.7, 149.2, 140.4, 133.8, 133.3 (t, J = 2.5 Hz), 133.0 (d, J = 2.7 Hz), 132.06, 131.1, 129.2, 128.5, 128.5, 128.3, 116.6, 115.8 (dd, J = 249.1, 243.5 Hz), 108.0, 63.0, 40.3 (d, J = 8.5 Hz), 30.7 (t, J = 23.7 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.39, (dddd, J = 289.5, 31.5, 19.9, 5.6 Hz, 1F), − 98.67 (dd, J = 289.5, 9.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}ClF_2N_3$ 422.1236; Found 422.1235.



2'-(4-Bromophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3z**, yellow oil), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 59 mg (64% yield). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, J = 1.6 Hz, 1H), 7.97 (d, J = 7.6 Hz, 2H), 7.68 (d, J = 1.2 Hz, 1H), 7.44 (t, J = 7.2 Hz, 1H), 7.38 (t, J = 7.2 Hz, 2H), 7.17 (d, J = 8.0 Hz, 2H), 6.29 (d, J = 8.4 Hz, 2H), 5.59 (t, J = 5.6 Hz, 1H), 4.06 – 3.99 (m, 1H), 2.84 – 2.67 (m, 1H), 2.51 (s, 3H), 2.39 – 2.30 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.4 (dd, J = 29.4, 25.0 Hz), 160.7, 149.3, 140.4, 133.6 (d, J = 2.6 Hz), 133.3 (d, J = 2.6 Hz), 132.1, 131.2, 131.1, 129.5, 128.5, 122.0, 116.6, 115.8 (dd, J = 249.3, 243.8 Hz) 108.1, 63.0, 40.2 (d, J = 8.5 Hz), 30.7 (t, J = 23.8 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.36 (d, J = 289.5 Hz, 1F), − 98.62 (d, J = 289.1 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}ClF_2N_3$ 466.0730; Found 466.0729.

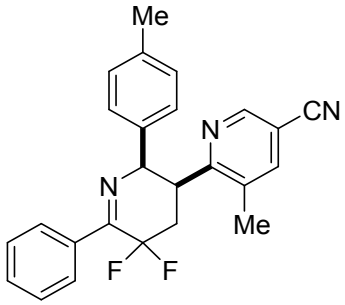


5',5'-Difluoro-2'-(3-fluorophenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3aa, brown oil**)**, purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 49 mg (61% yield). Mp 154 – 159 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.25 (d, *J* = 1.6 Hz, 1H), 7.99 (d, *J* = 7.2 Hz, 2H), 7.69 (d, *J* = 1.2 Hz, 1H), 7.45 – 7.37 (m, 3H), 7.00 (td, *J* = 8.4 Hz, 6.8 Hz, 1H), 6.84– 6.79 (m, 1H), 6.19 (d, *J* = 8.8 Hz, 2H), 5.63 (t, *J* = 5.6 Hz, 1H), 4.07 – 4.03 (m, 1H), 2.90 – 2.73 (m, 1H), 2.53 (s, 3H), 2.41– 2.32 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 162.5 (*J* = 245.4 Hz), 161.5 (dd, *J* = 29.5, 24.8 Hz), 160.7, 149.2, 140.4, 137.2 (dd, *J* = 6.6, 2.5 Hz) 133.3 (d, *J* = 2.7 Hz), 132.0, 131.1, 129.5 (d, *J* = 8.2 Hz), 128.5, 128.4, 123.6 (d, *J* = 2.9 Hz), 116.6, 115.7 (dd, *J* = 250.0, 243.8 Hz), 115.0 (d, *J* = 22.2 Hz), 114.8 (d, *J* = 20.9 Hz), 108.0, 63.1, 40.3 (d, *J* = 8.4 Hz), 30.8 (t, *J* = 24.4 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.44 (dddd, *J* = 289.5, 31.5, 19.9, 6.0 Hz, 1F), − 98.66 (dd, *J* = 289.5, 9.4 Hz, 1F), − 112.71 (td, *J* = 9.0, 5.6 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}F_3N_3$ 406.1531; Found 406.1530.

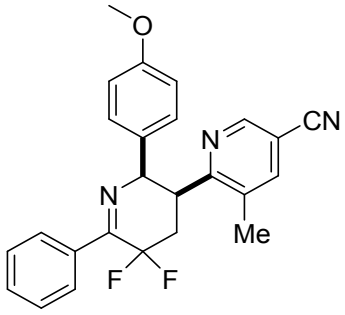


2'-(3-Chlorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3ab**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 48 mg (59% yield). Mp 159 – 162 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.19 (d, *J* = 1.6 Hz, 1H), 7.95 (d, *J* = 7.2 Hz,

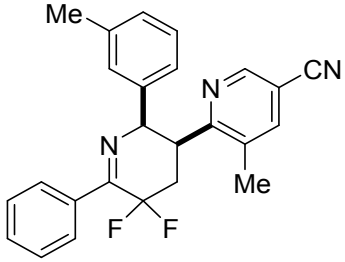
2H), 7.54 (d, *J* = 1.6 Hz 1H), 7.44 (t, *J* = 7.2 Hz, 1H),7.38 (t, *J* = 7.2 Hz, 2H), 7.18–7.05 (m, 3H), 6.85 (dd, *J* = 7.6, 1.6 Hz, 1H), 6.10 (t, *J* = 5.6 Hz, 1H), 4.14-4.08 (m, 1H), 3.01 – 2.84 (m, 1H), 2.41 (s, 3H), 2.38 – 2.28 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.7 (dd, *J* = 29.4, 24.8 Hz), 160.5, 148.6, 139.7, 133.9, 133.5, 132.8 (d, *J* = 2.2 Hz), 130.9, 130.1, 129.5, 129.1, 128.5 (t, *J* = 2.6 Hz), 128.4, 126.6, 116.9, 115.4 (dd, *J* = 249.9, 243.0 Hz), 107.8, 59.6, 39.0 (d, *J* = 7.4 Hz), 32.1 (t, *J* = 23.7 Hz), 18.6 (d, *J* = 1.1 Hz) ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.32 (d, *J* = 288.4 Hz, 1F), − 97.61 (d, *J* = 288.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{19}ClF_2N_3$ 422.1236; Found 422.1235.



5',5'-Difluoro-3-methyl-6'-phenyl-2'-(p-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3ac**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 13/1), 50 mg (67% yield). Mp 135 – 136 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.23 (d, *J* = 1.6 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.66 (d, *J* = 1.2 Hz, 1H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 6.84 (d, *J* = 8.0 Hz, 2H), 6.29 (d, *J* = 8.0 Hz, 2H), 5.63 (t, *J* = 5.6 Hz, 1H), 4.04 – 3.99 (m, 1H), 2.90 – 2.72 (m, 1H), 2.53 (s, 3H), 2.37 – 2.28 (m, 1H), 2.18 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2, 160.8 (dd, *J* = 29.5, 24.8 Hz), 149.1, 140.2, 137.6, 133.5 (t, *J* = 2.5 Hz), 132.1, 131.1 (d, *J* = 2.7 Hz), 130.9, 128.8, 128.5, 128.4, 127.8, 116.8, 116.1 (dd, *J* = 249.1, 243.6 Hz), 107.8, 63.4, 40.5 (d, *J* = 8.5 Hz), 29.7 (t, *J* = 23.7 Hz), 21.1, 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.26 (d, *J* = 288.7 Hz, 1F), − 99.03 (d, *J* = 288.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3$ 402.1782; Found 402.1783.

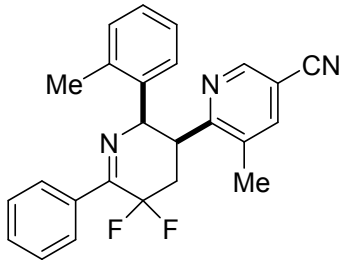


5',5'-Difluoro-2'-(4-methoxyphenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3ad**, white solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 10/1), 55 mg (66% yield). Mp 141 – 143 °C. ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.26 (d, *J* = 1.4 Hz, 1H), 7.99 (d, *J* = 7.6 Hz, 2H), 7.68 (d, *J* = 1.2 Hz, 1H), 7.44 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.2 Hz, 2H), 6.57 (d, *J* = 8.4 Hz, 2H), 6.33 (d, *J* = 8.8 Hz, 2H), 5.62 (t, *J* = 5.6 Hz, 1H), 4.04 – 3.99 (m, 1H), 3.66 (s, 3H), 2.90 – 2.72 (m, 1H), 2.54 (s, 3H), 2.37 – 2.29 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.2, 160.7 (dd, *J* = 29.4, 24.9 Hz) 159.1, 149.2, 140.2, 133.5 (t, *J* = 2.6 Hz), 132.0, 130.9, 128.9, 128.5, 128.4, 126.1 (d, *J* = 2.7 Hz), 116.8, 116.0 (dd, *J* = 248.9, 243.6 Hz), 113.5, 107.8, 63.0, 55.2, 40.5 (d, *J* = 8.7 Hz), 30.5 (t, *J* = 23.7 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.38 (d, *J* = 288.4 Hz, 1F), − 98.88 (d, *J* = 288.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3O$ 418.1731; Found 418.1732.

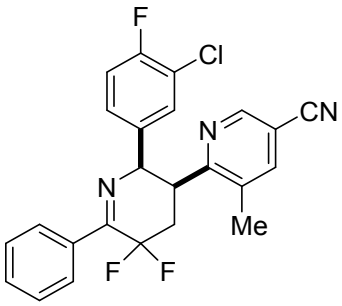


5',5'-Difluoro-3-methyl-6'-phenyl-2'-(m-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3ae**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 51 mg (64% yield). Mp 145 – 147 °C. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.30 (d, *J* = 1.6 Hz, 1H), 8.08 (d, *J* = 7.2 Hz, 2H), 7.75 (d, *J* = 1.2 Hz 1H), 7.51 (t, *J* = 7.2 Hz, 1H), 7.446 (t, *J* = 7.2 Hz, 2H), 6.98 (d, *J* = 4.8 Hz, 2H), 6.28 – 6.25 (m, 2H), 5.69 (t, *J* = 5.6 Hz, 1H), 4.13 – 4.08 (m, 1H),

3.00 – 2.81 (m, 1H), 2.61 (s, 3H), 2.45 – 2.36 (m, 1H), 2.15 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.2, 160.9 (dd, *J* = 29.5, 24.9 Hz), 149.0, 140.1, 137.6, 134.1 (d, *J* = 2.7 Hz), 133.5 (t, *J* = 2.5 Hz), 132.1, 130.9, 128.6, 128.6, 128.5, 128.4, 127.9, 125.0, 116.8, 116.0 (dd, *J* = 249.3, 243.5 Hz), 107.7, 63.5, 40.5 (d, *J* = 8.6 Hz), 30.6 (t, *J* = 23.7 Hz), 21.4, 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.29 (d, *J* = 288.4 Hz, 1F), − 99.00 (d, *J* = 288.4 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3$ 402.1782; Found 402.1783.



5',5'-Difluoro-3-methyl-6'-phenyl-2'-(o-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3af**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 42 mg (52% yield). Mp 148 – 151 °C ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.22 (d, *J* = 1.6 Hz, 1H), 7.94 (d, *J* = 7.6 Hz, 2H), 7.56 (d, *J* = 1.2 Hz, 1H), 7.42 (t, *J* = 7.2 Hz, 1H), 7.37 (t, *J* = 7.2 Hz, 2H), 7.08 – 7.06 (m, 2H), 6.89 – 6.86 (m, 1H), 6.76 – 6.73 (m, 1H), 5.85 (t, *J* = 5.6 Hz, 1H), 4.08 – 4.03 (m, 1H), 3.11 – 2.94 (m, 1H), 2.38 – 2.27 (m, 4H), 1.65 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 161.1, 161.1 (dd, *J* = 29.5, 24.7 Hz), 148.9, 139.8, 135.7, 133.8 (t, *J* = 2.4 Hz), 132.9 (d, *J* = 1.9 Hz), 132.6, 130.8, 130.7, 128.5, 128.4, 128.4, 127.7, 125.8, 116.7, 115.6 (dd, *J* = 250.2, 242.2 Hz), 107.8, 59.5, 39.6 (d, *J* = 8.1 Hz), 32.1 (t, *J* = 23.7 Hz), 18.8, 18.5 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 87.65 (d, *J* = 287.6 Hz, 1F), − 98.14 (d, *J* = 287.6 Hz, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{25}H_{22}F_2N_3$ 402.1782; Found 402.1783.



2'-(3-Chloro-4-fluorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (**3ag**, yellow solid), purified by flash column chromatography (eluent: Petroleum ether/EtOAc = 14/1), 55 mg, (63% yield). Mp 138 – 142 °C ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.37 (d, *J* = 1.6 Hz, 1H), 8.06 (d, *J* = 7.6 Hz, 2H), 7.79 (d, *J* = 1.2 Hz, 1H), 7.54 (t, *J* = 7.2 Hz, 1H), 7.48 (t, *J* = 7.2 Hz, 2H), 6.90 (t, *J* = 8.6 Hz, 1H), 6.49 (dd, *J* = 6.8, 2.4 Hz, 1H), 6.38 (ddd, *J* = 8.4, 4.4, 2.4 Hz, 1H), 5.64 (t, *J* = 5.6 Hz, 1H), 4.13 – 4.08 (m, 1H), 2.90 – 2.73 (m, 1H), 2.60 (s, 3H), 2.48 – 2.40 (m, 1H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$) δ 161.7 (dd, *J* = 29.3, 25.0 Hz), 160.5, 157.5 (d, *J* = 248.2 Hz), 149.2, 140.5, 133.1, 132.1, 131.8 (t, *J* = 3.1 Hz), 131.2, 130.1, 128.5, 127.5 (d, *J* = 7.2 Hz), 120.8 (d, *J* = 17.7 Hz), 116.4, 116.1 (d, *J* = 20.9 Hz), 115.6 (dd, *J* = 249.5, 244.0 Hz), 108.2, 62.5, 40.1 (d, *J* = 8.3 Hz), 30.7 (t, *J* = 23.9 Hz), 18.3 ppm; ^{19}F NMR (375 MHz, $CDCl_3$) δ − 88.62 (dddd, *J* = 289.5, 30.8, 19.5, 6.0 Hz, 1F), − 98.44 (dd, *J* = 289.9, 9.4 Hz, 1F), − 116.10 – − 116.16 (m, 1F) ppm; HRMS (ESI) m/z: $[M + H]^+$ Calcd for $C_{24}H_{18}ClF_3N_3$ 440.1141; Found 440.1140.

5. Mechanism Study

5.1 Calculation methods

Spin-unrestricted density functional theory (DFT) calculations were performed using the Gaussian 16 program package.[4] All structures and molecular frontier orbitals were optimized without symmetry constrains at the B3LYP/6-311G (d, P) level.[5-8] The nature of all intermediates was confirmed by performing normal-mode analysis, and transition states (TSs) were confirmed by vibrational analysis and characterized by occurrence of only one imaginary

frequency. Intrinsic reaction coordinate (IRC) calculations along the whole pathway were performed in order to further verify the TSs. To calculate the solvent effect (dichloroethane), the self-consistent reaction field method based on the SMD[9] model was utilized.

5.2 DFT calculations

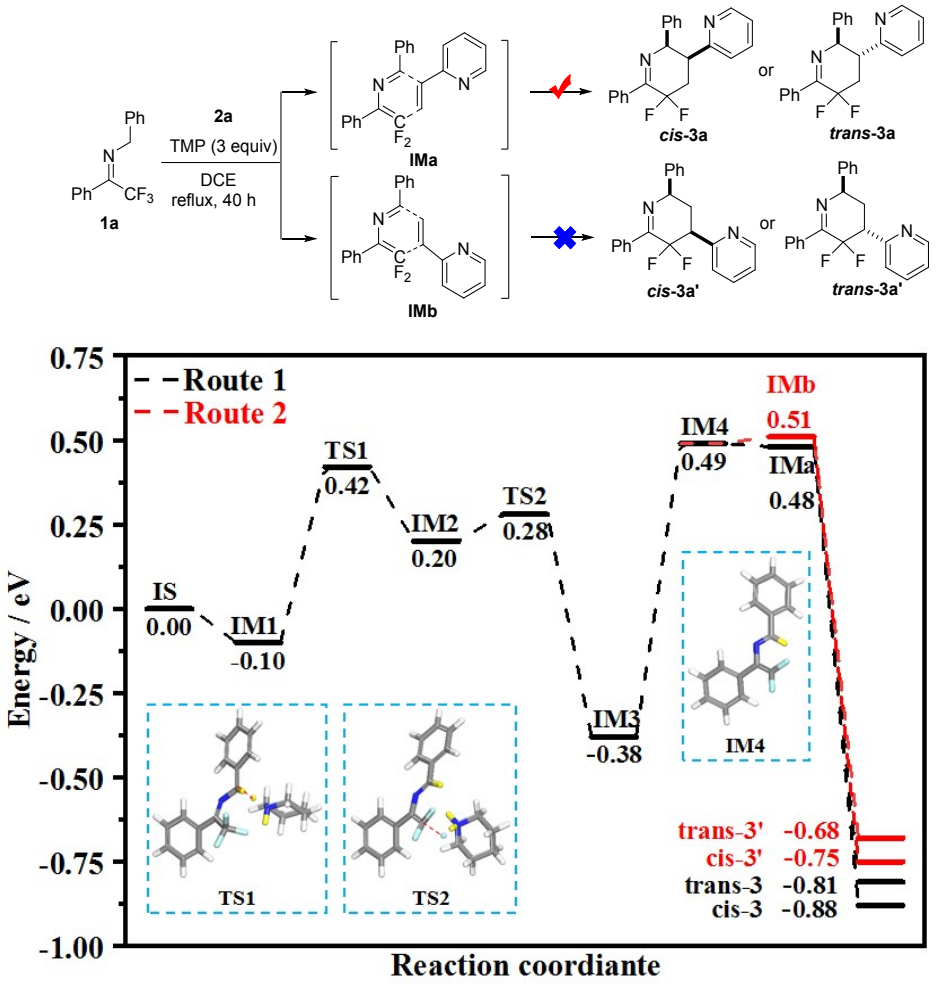


Figure S4. DFT calculations: calculated energy profiles within the process of the formation of product **3**.

Density functional theory (DFT) calculations were performed to estimate the energy profiles for the formation of product **3** together with the structures of the key transition states. We could find that (*E*)-*N*-(2,2-difluoro-1-phenylvinyl)-1-phenylmethanimine **IM4** is the key state for the formation of product **3**, and this finding is consistent with the experiment. Through calculation, we could find that **IM4** can be

obtained by removing HF through benzyl trifluoromethyl ketamine **IS1** under the action of TMP **IS3**. In addition, the activation of C-H bond is the rate-determining step of the formation of **IM4**, and the related reaction energy barrier is 0.52 eV. Next, the activation of C-F bond is relatively easy, and the reaction energy barrier of C-F bond is 0.08 eV. When **IM4** is formed, there are two routes for the addition reaction of **IM4** and 2-vinyl pyridine **IS2**, one route is the *ortho* disubstituted addition reaction (such as the black dotted path); the other route is the *meta* disubstituted addition reaction (such as the red dotted path). We could find that the co-adsorption energy of **IM4** and **IS2** in the addition reaction path to give the *ortho* disubstituted products is lower (ie, the energy of **IMa** less than **IMb** about 0.03 eV); and the *cis ortho* disubstituted product formed has the lowest energy (namely, the product of ***cis*-3a** is more stable than the other three products). This is consistent with the experimental results.

5.3 structures of the key states

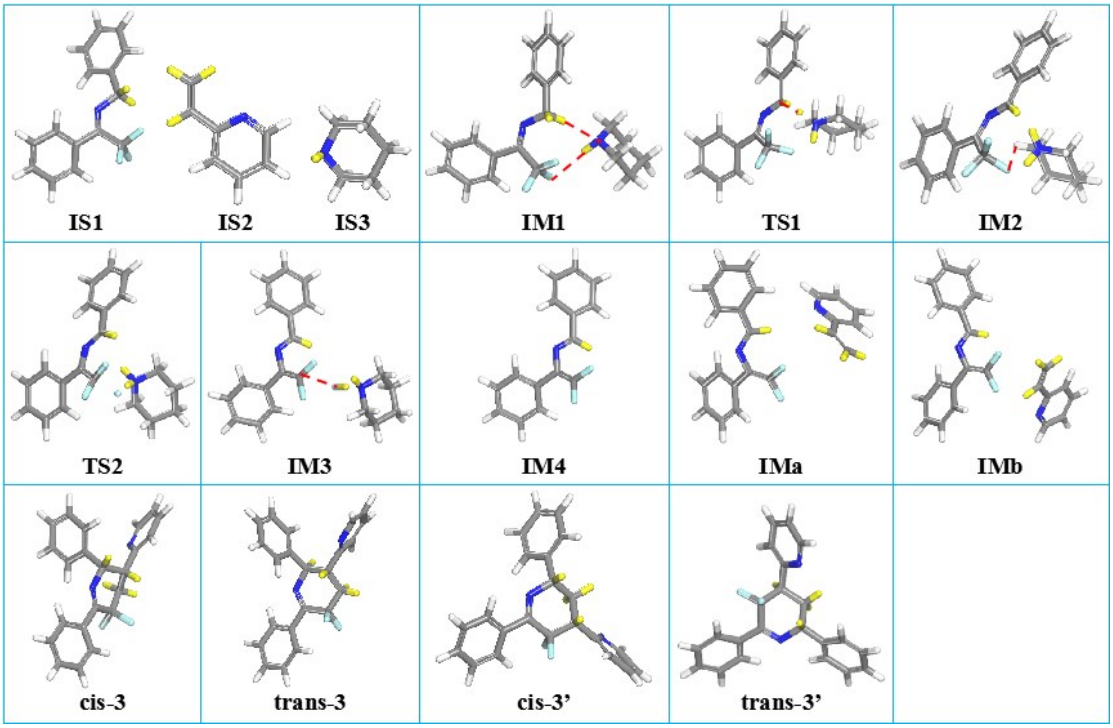


Figure S5. Calculated structures of the key states within the process of product **3** formation.

6. Determination of X-ray crystallographic structure 3q

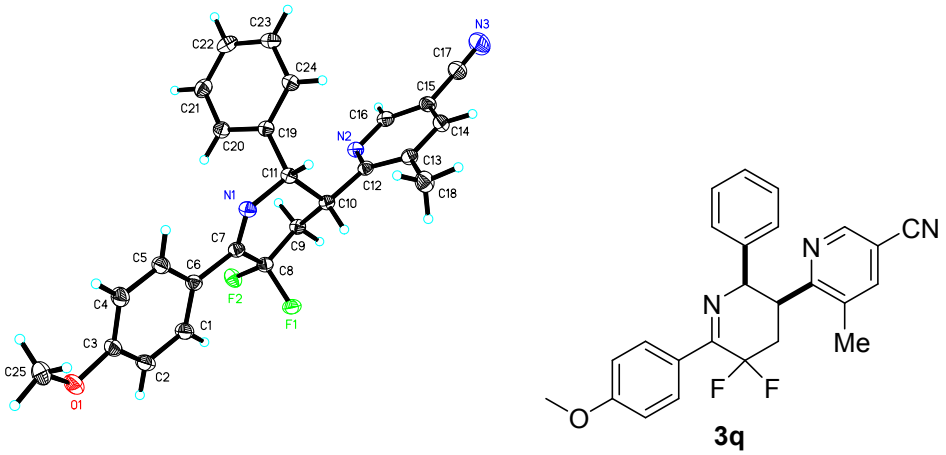


Figure S6. X-Ray crystal structure of compound **3q**

Table 1. Crystal data and structure refinement for mo_d8v19040_0m.

Identification code	mo_d8v19040_0m	
Empirical formula	C25 H21 F2 N3 O	
Formula weight	417.45	
Temperature	193(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P -1	
Unit cell dimensions	a = 8.5086(6) Å	α= 72.392(2)°.
	b = 10.5713(7) Å	β= 82.024(2)°.
	c = 12.6956(10) Å	γ = 76.981(2)°.
Volume	1057.38(13) $Å^3$	
Z	2	
Density (calculated)	1.311 Mg/m^3	
Absorption coefficient	0.094 mm^{-1}	
F(000)	436	
Crystal size	0.180 x 0.150 x 0.130 mm^3	
Theta range for data collection	2.879 to 25.999°.	
Index ranges	-10<=h<=10, -13<=k<=12, -15<=l<=15	
Reflections collected	15468	
Independent reflections	4115 [R(int) = 0.0309]	
Completeness to theta = 25.242°	98.9 %	

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.7456 and 0.6526
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4115 / 0 / 283
Goodness-of-fit on F^2	1.037
Final R indices [I>2sigma(I)]	R1 = 0.0375, wR2 = 0.0895
R indices (all data)	R1 = 0.0443, wR2 = 0.0946
Largest diff. peak and hole	0.232 and -0.164 e.$Å^{-3}$

Table 2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for mo_d8v19040_0m. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
F(1)	77(1)	6653(1)	7275(1)	41(1)
F(2)	1411(1)	7924(1)	7733(1)	41(1)
O(1)	3964(1)	2534(1)	11532(1)	48(1)
N(1)	3864(1)	5669(1)	6428(1)	31(1)
N(2)	1910(1)	9292(1)	3583(1)	31(1)
N(3)	1645(2)	10983(2)	-333(1)	80(1)
C(1)	2113(2)	5245(1)	9290(1)	39(1)
C(2)	2413(2)	4370(2)	10330(1)	42(1)
C(3)	3806(2)	3383(1)	10483(1)	37(1)
C(4)	4936(2)	3315(1)	9593(1)	40(1)
C(5)	4633(2)	4199(1)	8561(1)	37(1)
C(6)	3213(2)	5161(1)	8374(1)	32(1)
C(7)	2917(1)	5990(1)	7217(1)	29(1)
C(8)	1477(2)	7176(1)	7005(1)	31(1)
C(9)	1461(2)	8092(1)	5847(1)	30(1)
C(10)	1918(1)	7217(1)	5053(1)	28(1)
C(11)	3661(1)	6399(1)	5261(1)	28(1)
C(12)	1751(1)	7995(1)	3852(1)	28(1)
C(13)	1476(2)	7377(1)	3076(1)	34(1)
C(14)	1418(2)	8154(2)	1983(1)	40(1)
C(15)	1631(2)	9485(2)	1696(1)	39(1)
C(16)	1857(2)	10017(1)	2525(1)	35(1)
C(17)	1623(2)	10317(2)	562(1)	54(1)
C(18)	1201(2)	5946(2)	3397(1)	47(1)
C(19)	4998(1)	7217(1)	4823(1)	28(1)
C(20)	5638(2)	7770(1)	5490(1)	37(1)
C(21)	6848(2)	8515(2)	5064(1)	44(1)
C(22)	7461(2)	8686(1)	3976(1)	42(1)
C(23)	6859(2)	8119(1)	3309(1)	39(1)
C(24)	5634(2)	7394(1)	3729(1)	33(1)
C(25)	5259(2)	1393(2)	11676(1)	53(1)

Table 3. Bond lengths [Å] and angles [°] for mo_d8v19040_0m.

F(1)-C(8)	1.3819(14)
F(2)-C(8)	1.3745(14)
O(1)-C(3)	1.3668(16)
O(1)-C(25)	1.4238(19)
N(1)-C(7)	1.2751(16)
N(1)-C(11)	1.4625(15)
N(2)-C(16)	1.3311(16)
N(2)-C(12)	1.3425(16)
N(3)-C(17)	1.142(2)
C(1)-C(2)	1.3825(19)
C(1)-C(6)	1.3994(18)
C(1)-H(1)	0.9500
C(2)-C(3)	1.384(2)
C(2)-H(2)	0.9500
C(3)-C(4)	1.387(2)
C(4)-C(5)	1.3795(18)
C(4)-H(4)	0.9500
C(5)-C(6)	1.3891(18)
C(5)-H(5)	0.9500
C(6)-C(7)	1.4885(17)
C(7)-C(8)	1.5300(17)
C(8)-C(9)	1.4956(17)
C(9)-C(10)	1.5219(17)
C(9)-H(9A)	0.9900
C(9)-H(9B)	0.9900
C(10)-C(12)	1.5059(16)
C(10)-C(11)	1.5528(16)
C(10)-H(10)	1.0000
C(11)-C(19)	1.5253(17)
C(11)-H(11)	1.0000
C(12)-C(13)	1.4061(18)
C(13)-C(14)	1.3833(19)
C(13)-C(18)	1.5070(19)
C(14)-C(15)	1.390(2)
C(14)-H(14)	0.9500
C(15)-C(16)	1.386(2)

C(15)-C(17)	1.442(2)
C(16)-H(16)	0.9500
C(18)-H(18A)	0.9800
C(18)-H(18B)	0.9800
C(18)-H(18C)	0.9800
C(19)-C(20)	1.3877(18)
C(19)-C(24)	1.3917(17)
C(20)-C(21)	1.387(2)
C(20)-H(20)	0.9500
C(21)-C(22)	1.380(2)
C(21)-H(21)	0.9500
C(22)-C(23)	1.380(2)
C(22)-H(22)	0.9500
C(23)-C(24)	1.3848(19)
C(23)-H(23)	0.9500
C(24)-H(24)	0.9500
C(25)-H(25A)	0.9800
C(25)-H(25B)	0.9800
C(25)-H(25C)	0.9800

C(3)-O(1)-C(25)	117.10(12)
C(7)-N(1)-C(11)	122.86(10)
C(16)-N(2)-C(12)	118.55(11)
C(2)-C(1)-C(6)	120.91(13)
C(2)-C(1)-H(1)	119.5
C(6)-C(1)-H(1)	119.5
C(1)-C(2)-C(3)	120.49(13)
C(1)-C(2)-H(2)	119.8
C(3)-C(2)-H(2)	119.8
O(1)-C(3)-C(2)	116.16(12)
O(1)-C(3)-C(4)	124.47(13)
C(2)-C(3)-C(4)	119.37(12)
C(5)-C(4)-C(3)	119.69(13)
C(5)-C(4)-H(4)	120.2
C(3)-C(4)-H(4)	120.2
C(4)-C(5)-C(6)	122.05(12)
C(4)-C(5)-H(5)	119.0
C(6)-C(5)-H(5)	119.0

C(5)-C(6)-C(1)	117.39(12)
C(5)-C(6)-C(7)	118.53(11)
C(1)-C(6)-C(7)	124.02(11)
N(1)-C(7)-C(6)	118.47(11)
N(1)-C(7)-C(8)	122.02(11)
C(6)-C(7)-C(8)	119.49(10)
F(2)-C(8)-F(1)	104.82(9)
F(2)-C(8)-C(9)	109.26(10)
F(1)-C(8)-C(9)	109.62(10)
F(2)-C(8)-C(7)	109.65(10)
F(1)-C(8)-C(7)	107.94(10)
C(9)-C(8)-C(7)	115.04(10)
C(8)-C(9)-C(10)	108.11(10)
C(8)-C(9)-H(9A)	110.1
C(10)-C(9)-H(9A)	110.1
C(8)-C(9)-H(9B)	110.1
C(10)-C(9)-H(9B)	110.1
H(9A)-C(9)-H(9B)	108.4
C(12)-C(10)-C(9)	114.07(10)
C(12)-C(10)-C(11)	112.03(10)
C(9)-C(10)-C(11)	107.75(10)
C(12)-C(10)-H(10)	107.6
C(9)-C(10)-H(10)	107.6
C(11)-C(10)-H(10)	107.6
N(1)-C(11)-C(19)	108.87(10)
N(1)-C(11)-C(10)	112.96(10)
C(19)-C(11)-C(10)	115.02(9)
N(1)-C(11)-H(11)	106.5
C(19)-C(11)-H(11)	106.5
C(10)-C(11)-H(11)	106.5
N(2)-C(12)-C(13)	123.10(11)
N(2)-C(12)-C(10)	115.57(11)
C(13)-C(12)-C(10)	121.32(11)
C(14)-C(13)-C(12)	117.16(12)
C(14)-C(13)-C(18)	120.11(12)
C(12)-C(13)-C(18)	122.70(12)
C(13)-C(14)-C(15)	119.82(13)
C(13)-C(14)-H(14)	120.1

C(15)-C(14)-H(14)	120.1
C(16)-C(15)-C(14)	118.86(12)
C(16)-C(15)-C(17)	119.62(14)
C(14)-C(15)-C(17)	121.51(14)
N(2)-C(16)-C(15)	122.45(12)
N(2)-C(16)-H(16)	118.8
C(15)-C(16)-H(16)	118.8
N(3)-C(17)-C(15)	178.58(19)
C(13)-C(18)-H(18A)	109.5
C(13)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(13)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(20)-C(19)-C(24)	118.30(12)
C(20)-C(19)-C(11)	122.11(11)
C(24)-C(19)-C(11)	119.57(11)
C(21)-C(20)-C(19)	120.70(13)
C(21)-C(20)-H(20)	119.7
C(19)-C(20)-H(20)	119.7
C(22)-C(21)-C(20)	120.27(14)
C(22)-C(21)-H(21)	119.9
C(20)-C(21)-H(21)	119.9
C(21)-C(22)-C(23)	119.73(13)
C(21)-C(22)-H(22)	120.1
C(23)-C(22)-H(22)	120.1
C(22)-C(23)-C(24)	119.96(13)
C(22)-C(23)-H(23)	120.0
C(24)-C(23)-H(23)	120.0
C(23)-C(24)-C(19)	121.01(13)
C(23)-C(24)-H(24)	119.5
C(19)-C(24)-H(24)	119.5
O(1)-C(25)-H(25A)	109.5
O(1)-C(25)-H(25B)	109.5
H(25A)-C(25)-H(25B)	109.5
O(1)-C(25)-H(25C)	109.5
H(25A)-C(25)-H(25C)	109.5
H(25B)-C(25)-H(25C)	109.5

Table 4. Torsion angles [°] for mo_d8v19040_0m.

C(6)-C(1)-C(2)-C(3)	-0.6(2)
C(25)-O(1)-C(3)-C(2)	170.93(14)
C(25)-O(1)-C(3)-C(4)	-9.5(2)
C(1)-C(2)-C(3)-O(1)	-177.58(13)
C(1)-C(2)-C(3)-C(4)	2.8(2)
O(1)-C(3)-C(4)-C(5)	178.17(13)
C(2)-C(3)-C(4)-C(5)	-2.2(2)
C(3)-C(4)-C(5)-C(6)	-0.6(2)
C(4)-C(5)-C(6)-C(1)	2.7(2)
C(4)-C(5)-C(6)-C(7)	-174.52(12)
C(2)-C(1)-C(6)-C(5)	-2.1(2)
C(2)-C(1)-C(6)-C(7)	174.92(13)
C(11)-N(1)-C(7)-C(6)	178.74(11)
C(11)-N(1)-C(7)-C(8)	0.04(18)
C(5)-C(6)-C(7)-N(1)	9.16(18)
C(1)-C(6)-C(7)-N(1)	-167.88(13)
C(5)-C(6)-C(7)-C(8)	-172.11(12)
C(1)-C(6)-C(7)-C(8)	10.86(19)
N(1)-C(7)-C(8)-F(2)	-135.68(12)
C(6)-C(7)-C(8)-F(2)	45.64(15)
N(1)-C(7)-C(8)-F(1)	110.67(13)
C(6)-C(7)-C(8)-F(1)	-68.01(14)
N(1)-C(7)-C(8)-C(9)	-12.07(17)
C(6)-C(7)-C(8)-C(9)	169.25(11)
F(2)-C(8)-C(9)-C(10)	167.26(10)
F(1)-C(8)-C(9)-C(10)	-78.39(12)
C(7)-C(8)-C(9)-C(10)	43.45(14)
C(8)-C(9)-C(10)-C(12)	172.76(10)
C(8)-C(9)-C(10)-C(11)	-62.19(12)
C(7)-N(1)-C(11)-C(19)	108.23(13)
C(7)-N(1)-C(11)-C(10)	-20.84(16)
C(12)-C(10)-C(11)-N(1)	178.18(10)
C(9)-C(10)-C(11)-N(1)	51.92(13)
C(12)-C(10)-C(11)-C(19)	52.34(14)
C(9)-C(10)-C(11)-C(19)	-73.92(13)

C(16)-N(2)-C(12)-C(13)	-2.21(17)
C(16)-N(2)-C(12)-C(10)	176.67(10)
C(9)-C(10)-C(12)-N(2)	27.09(15)
C(11)-C(10)-C(12)-N(2)	-95.66(12)
C(9)-C(10)-C(12)-C(13)	-154.00(11)
C(11)-C(10)-C(12)-C(13)	83.24(14)
N(2)-C(12)-C(13)-C(14)	1.90(18)
C(10)-C(12)-C(13)-C(14)	-176.92(11)
N(2)-C(12)-C(13)-C(18)	-176.28(12)
C(10)-C(12)-C(13)-C(18)	4.90(18)
C(12)-C(13)-C(14)-C(15)	0.09(19)
C(18)-C(13)-C(14)-C(15)	178.32(13)
C(13)-C(14)-C(15)-C(16)	-1.6(2)
C(13)-C(14)-C(15)-C(17)	178.33(13)
C(12)-N(2)-C(16)-C(15)	0.52(18)
C(14)-C(15)-C(16)-N(2)	1.4(2)
C(17)-C(15)-C(16)-N(2)	-178.58(13)
N(1)-C(11)-C(19)-C(20)	-32.66(15)
C(10)-C(11)-C(19)-C(20)	95.26(14)
N(1)-C(11)-C(19)-C(24)	145.72(11)
C(10)-C(11)-C(19)-C(24)	-86.36(13)
C(24)-C(19)-C(20)-C(21)	1.91(19)
C(11)-C(19)-C(20)-C(21)	-179.68(12)
C(19)-C(20)-C(21)-C(22)	-1.6(2)
C(20)-C(21)-C(22)-C(23)	0.3(2)
C(21)-C(22)-C(23)-C(24)	0.7(2)
C(22)-C(23)-C(24)-C(19)	-0.40(19)
C(20)-C(19)-C(24)-C(23)	-0.90(18)
C(11)-C(19)-C(24)-C(23)	-179.35(11)

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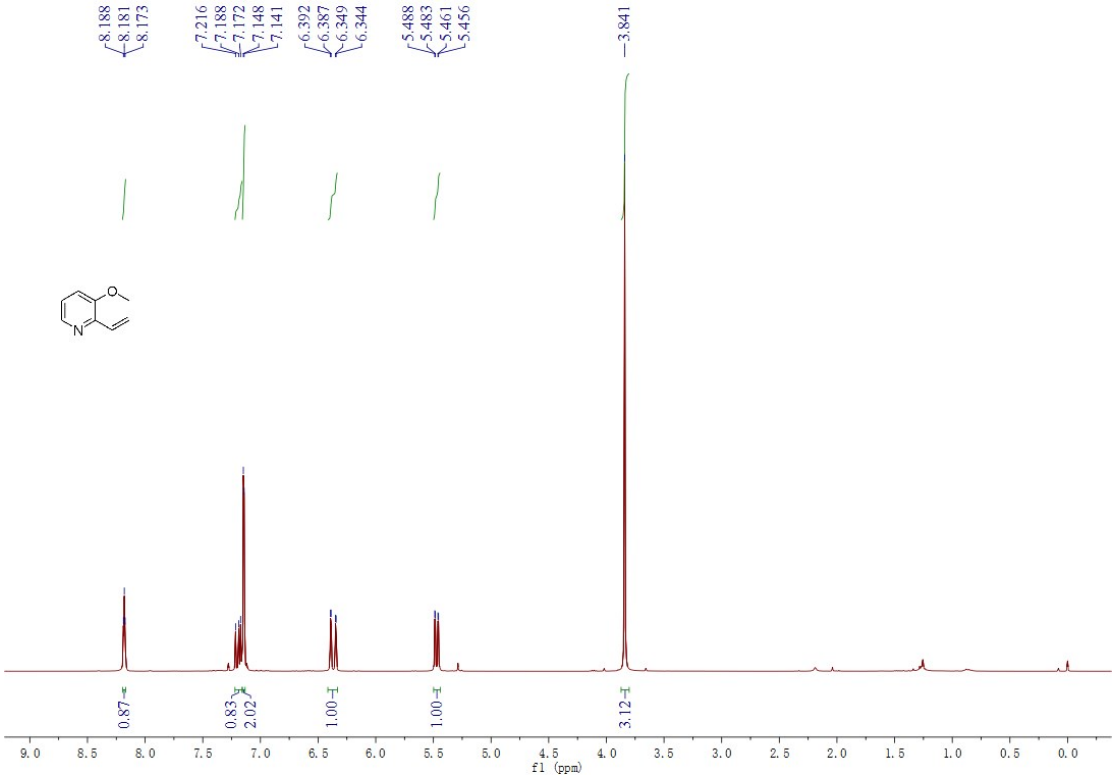
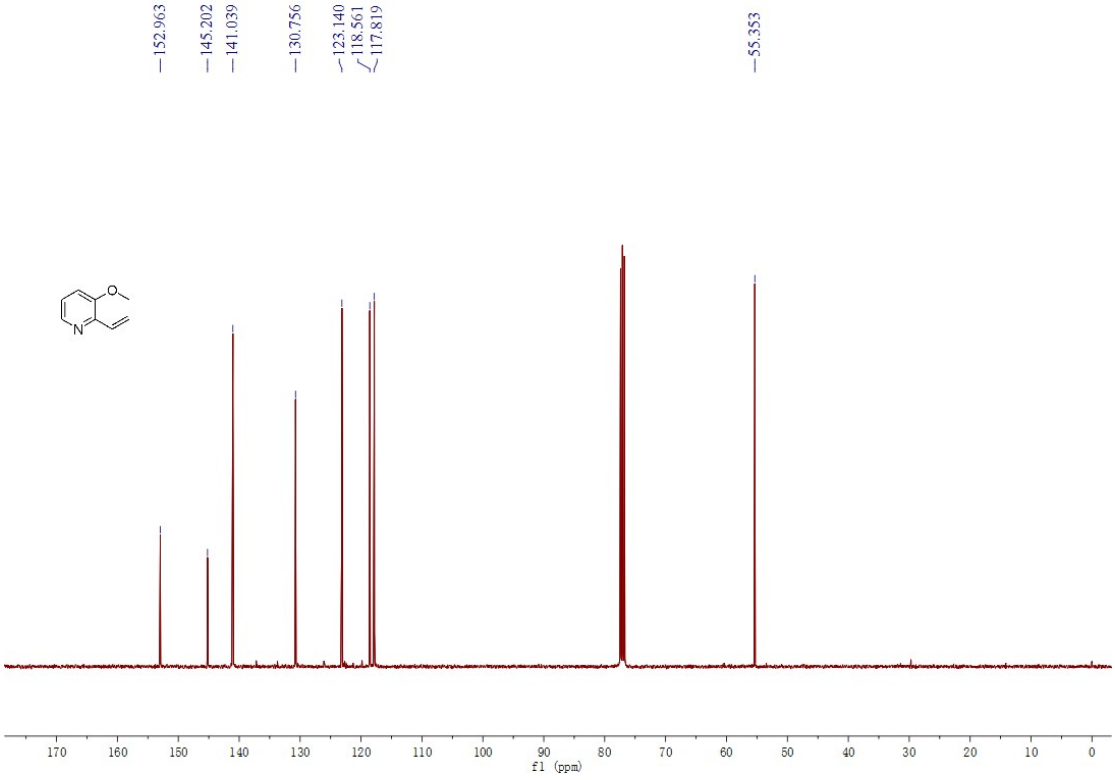
8. ^{1}H, ^{13}C and ^{19}F NMR spectra

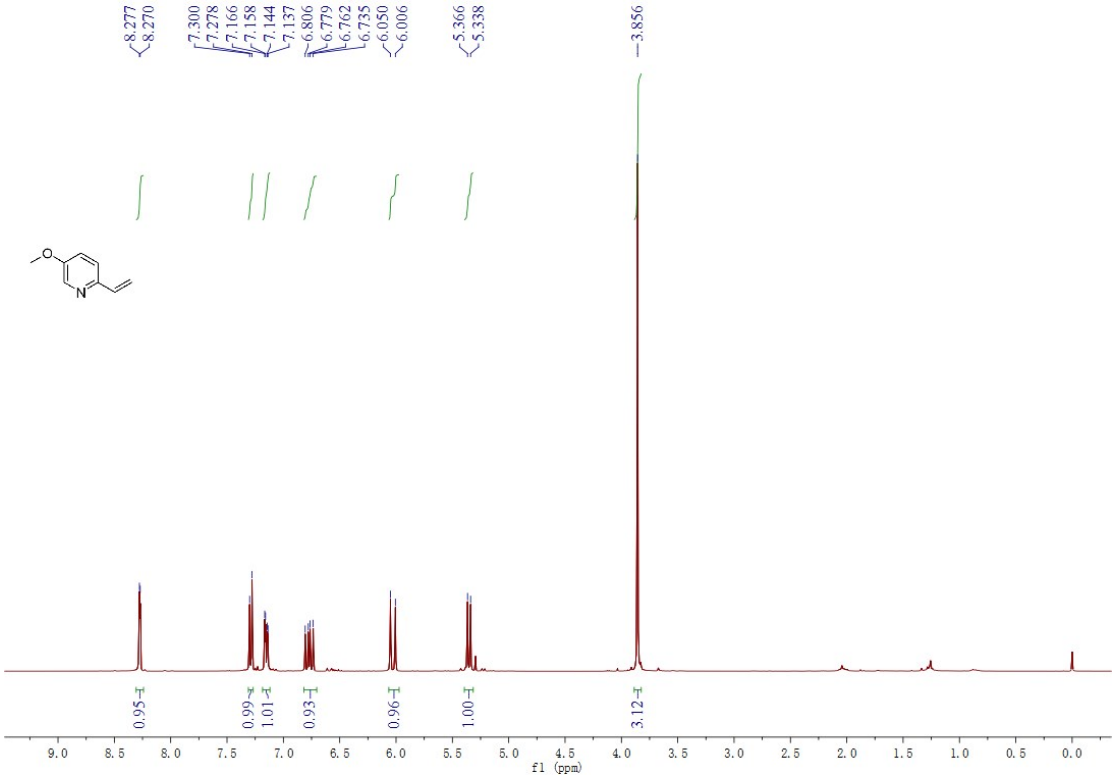
3-Methoxy-2-vinylpyridine (2b) [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



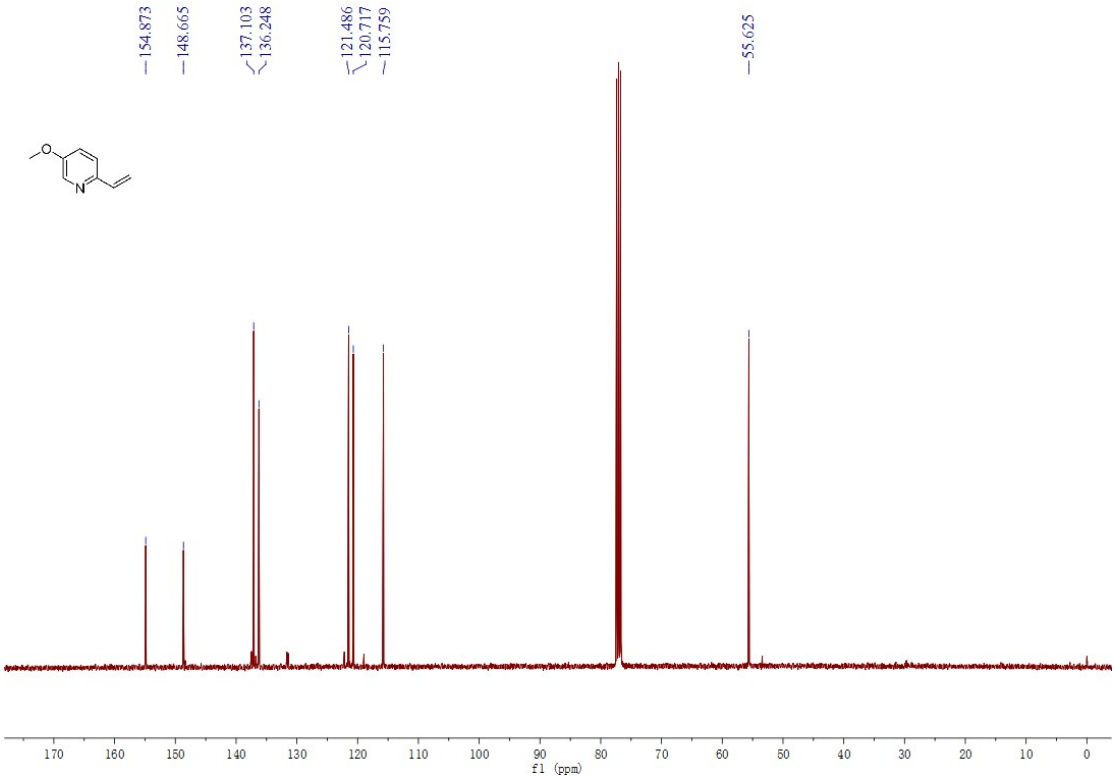
[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



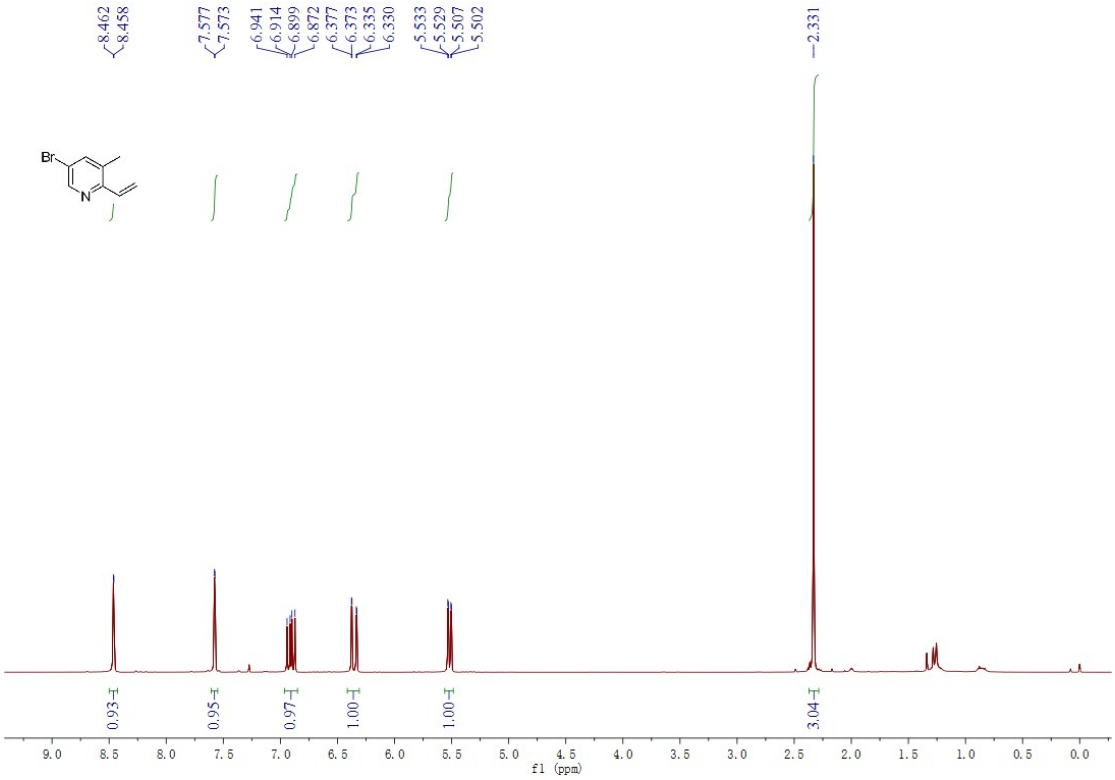
5-Methoxy-2-vinylpyridine (2c) [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



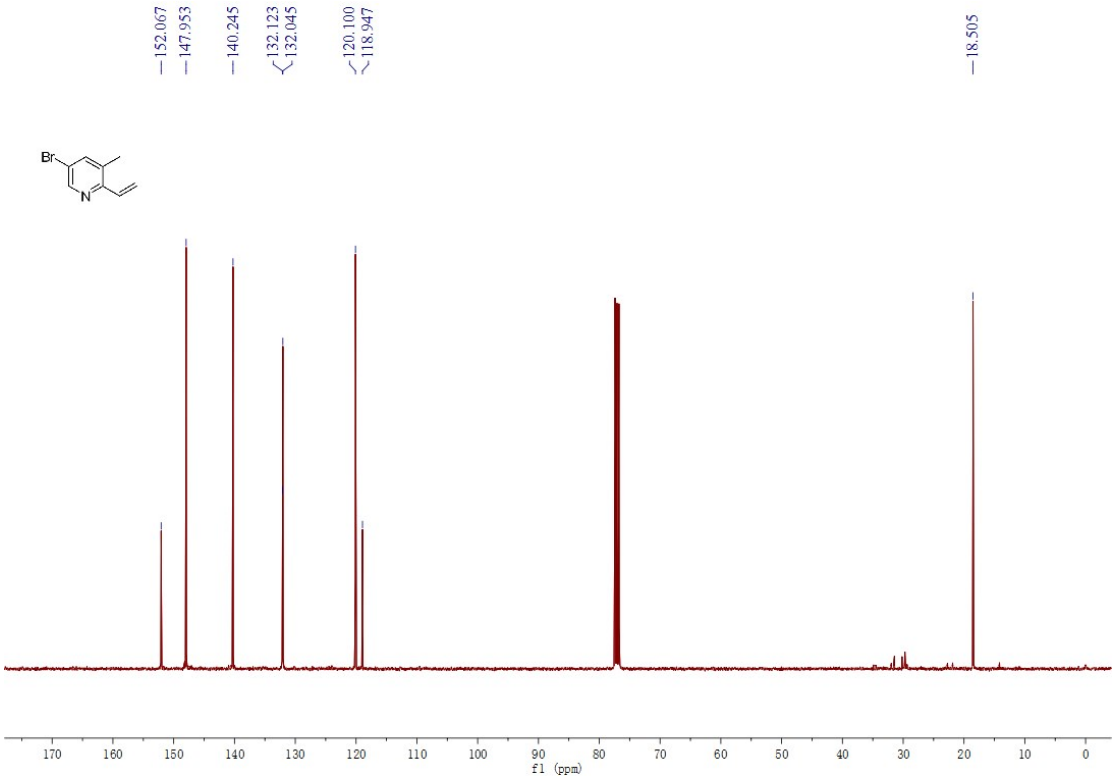
[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



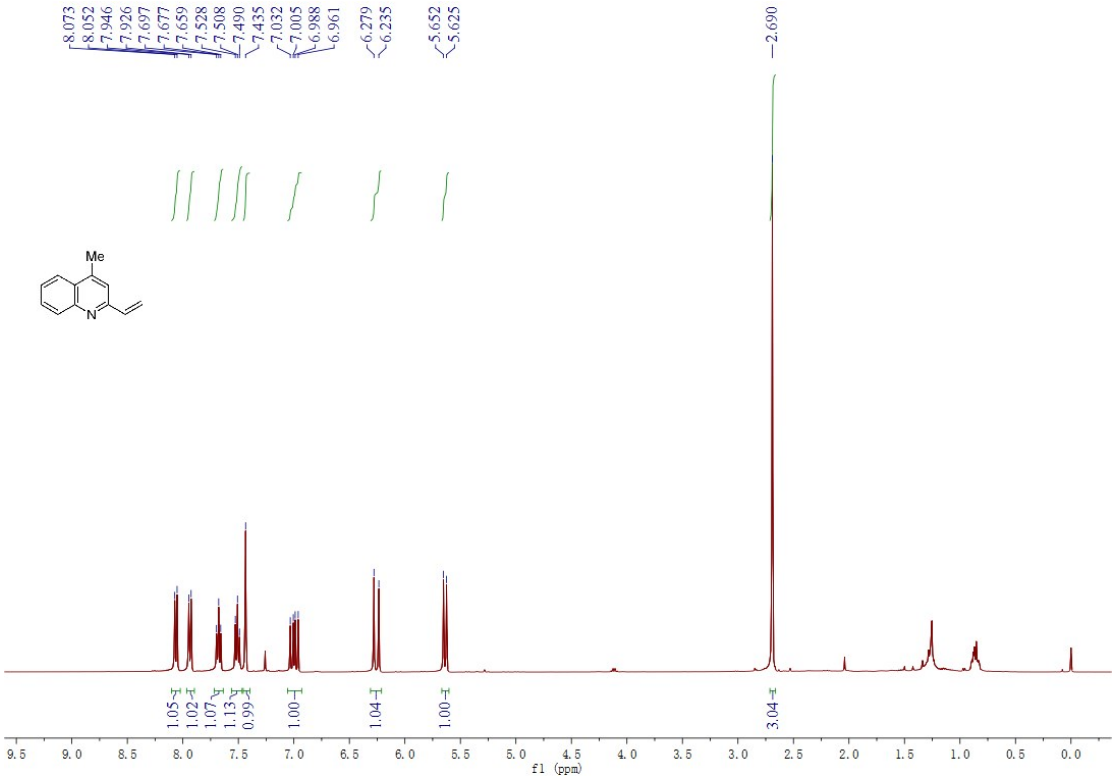
5-Bromo-3-methyl-2-vinylpyridine (2i) [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



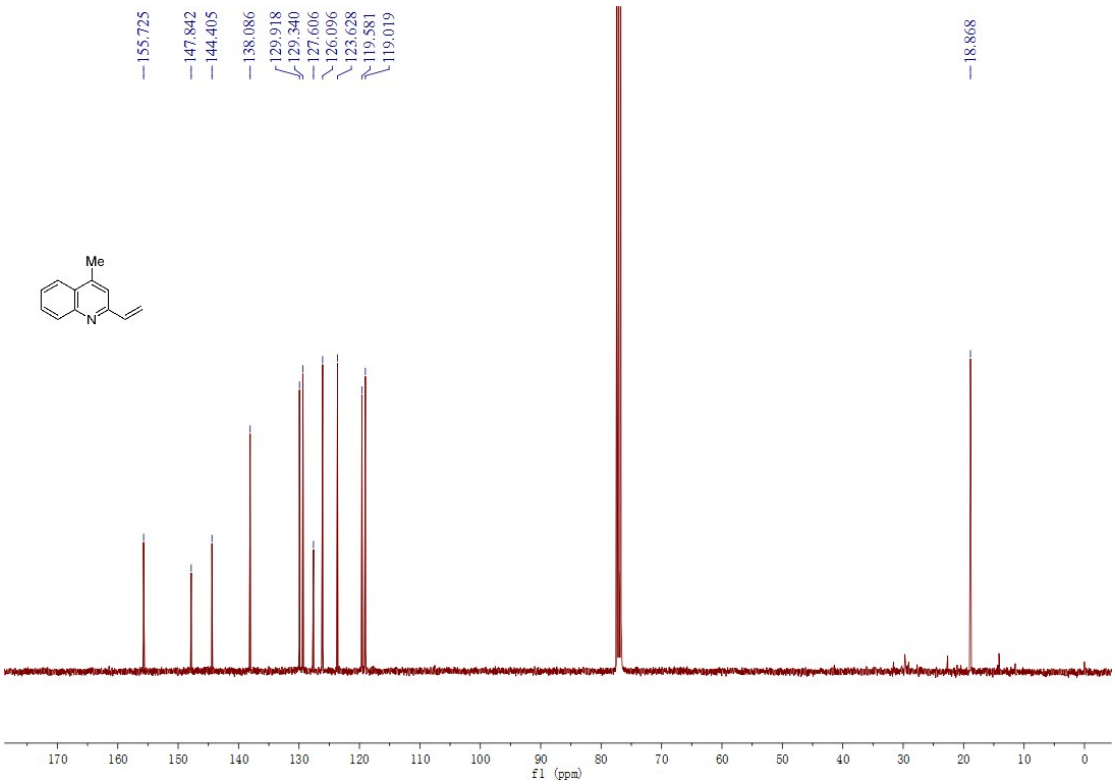
[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



4-Methyl-2-vinylquinoline (2n) [^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]

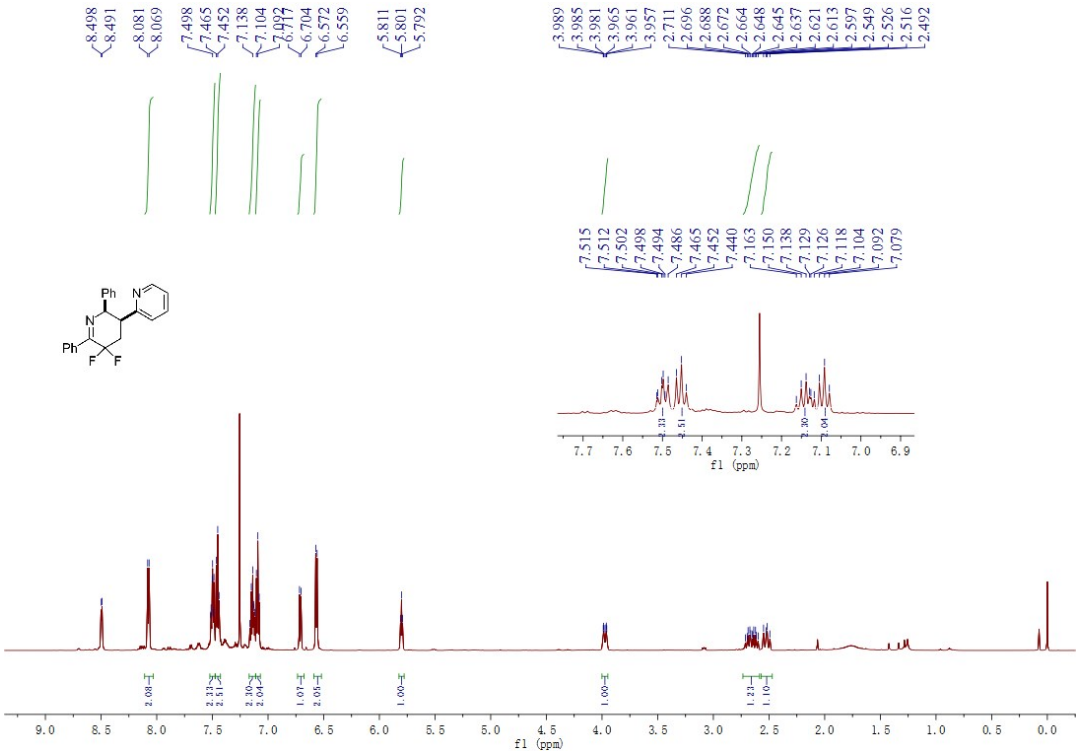


[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

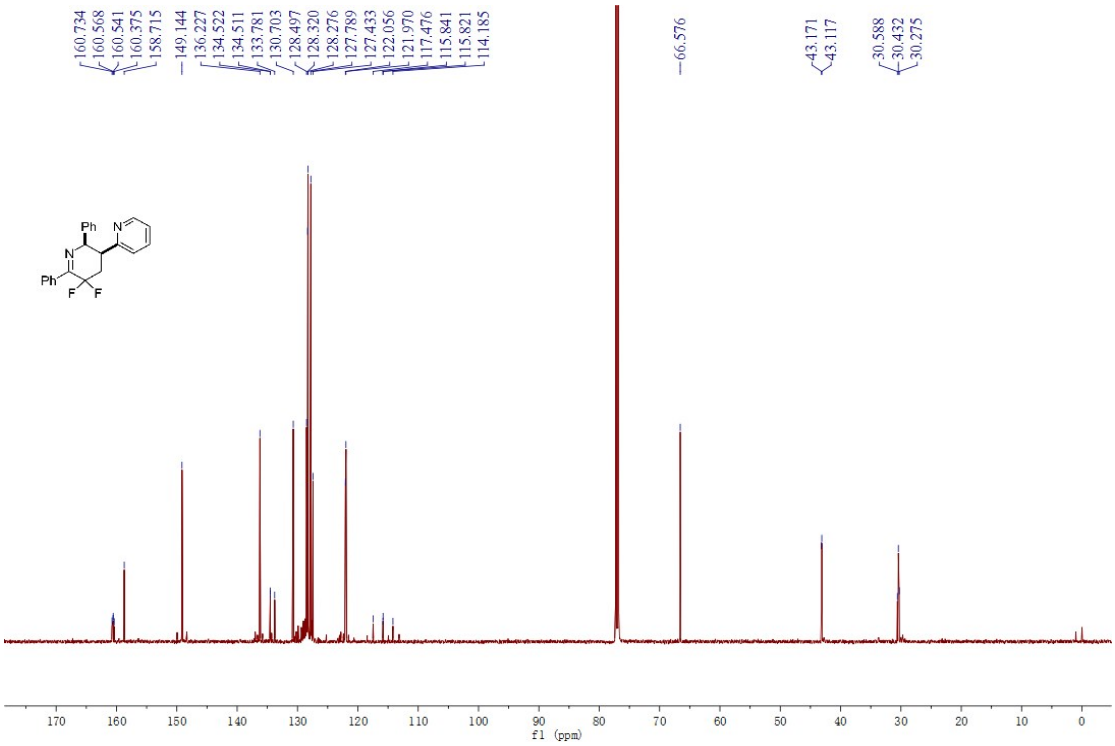


5',5'-Difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3a)

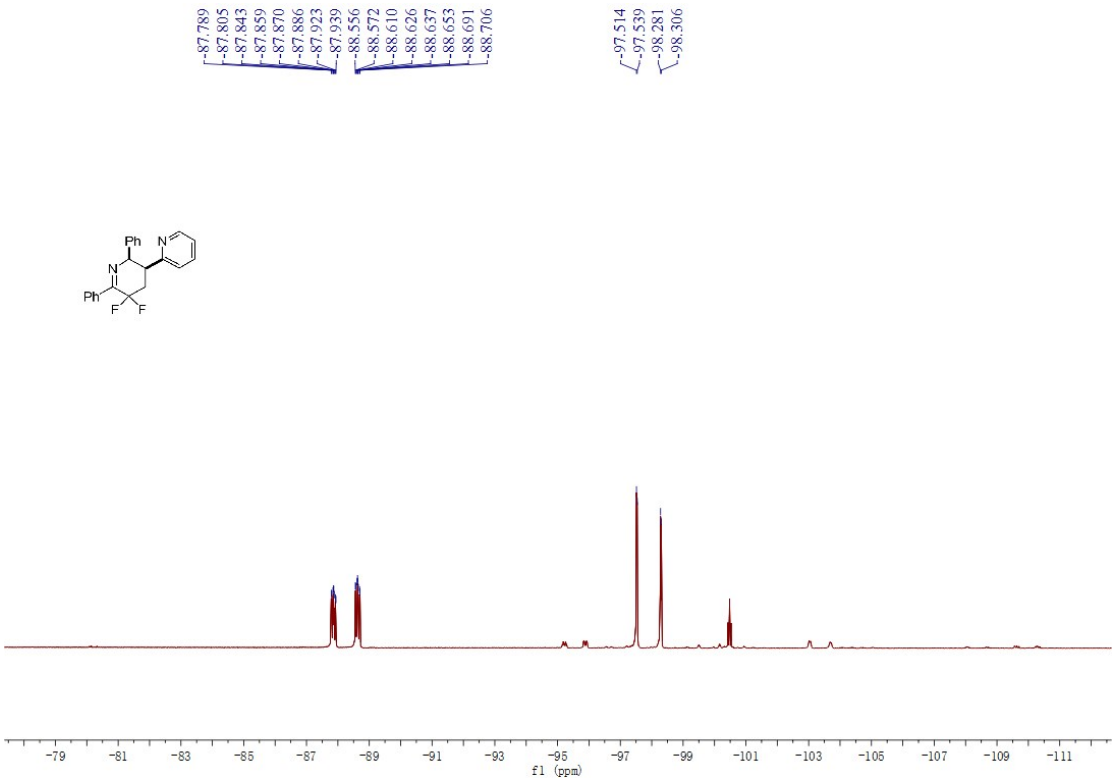
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

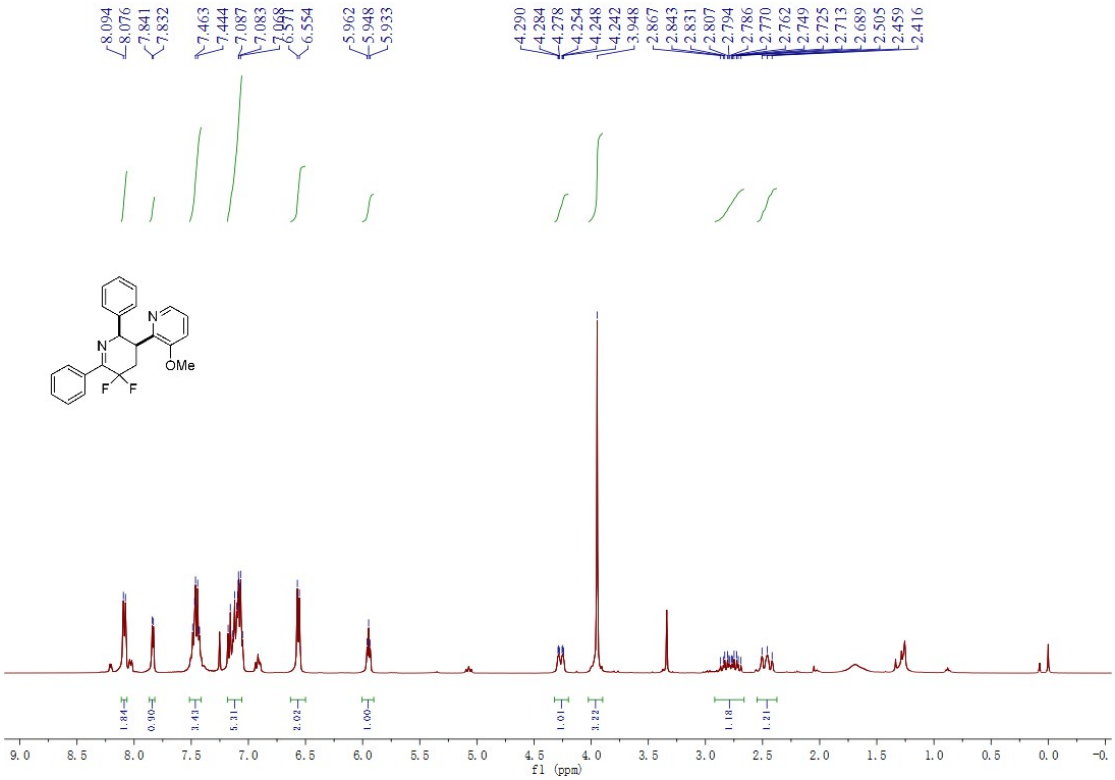


[^{19}F_NMR_375 MHz]

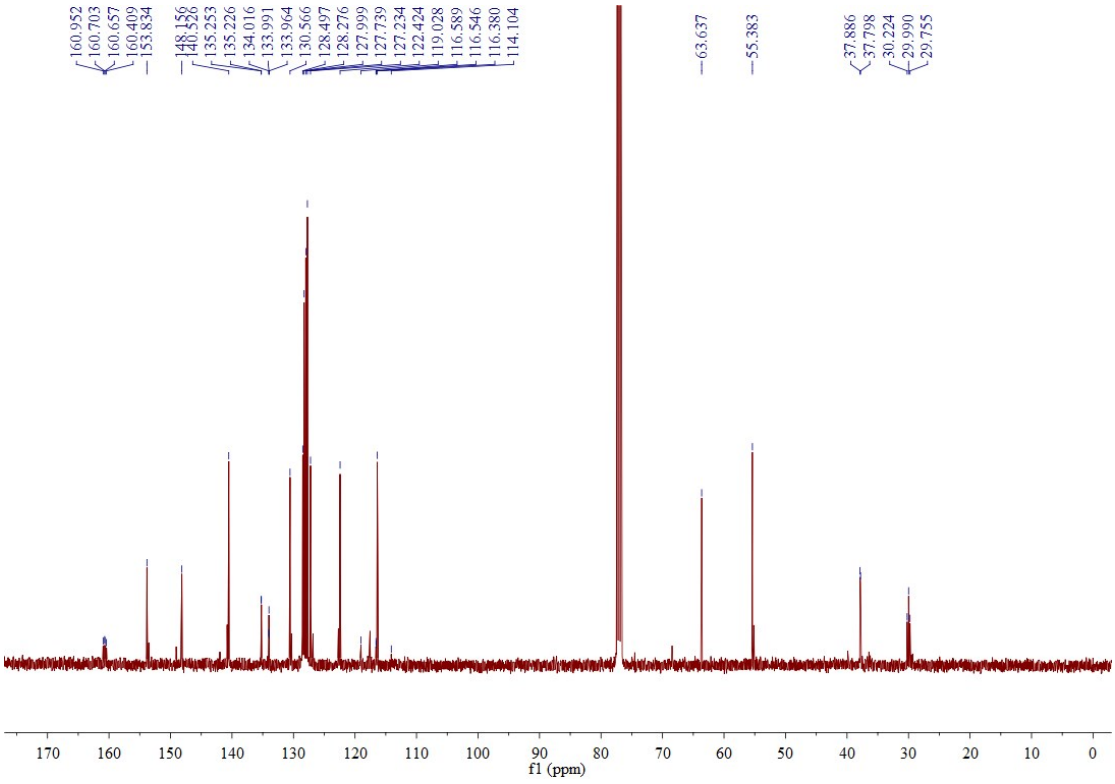


5',5'-Difluoro-3-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3b)

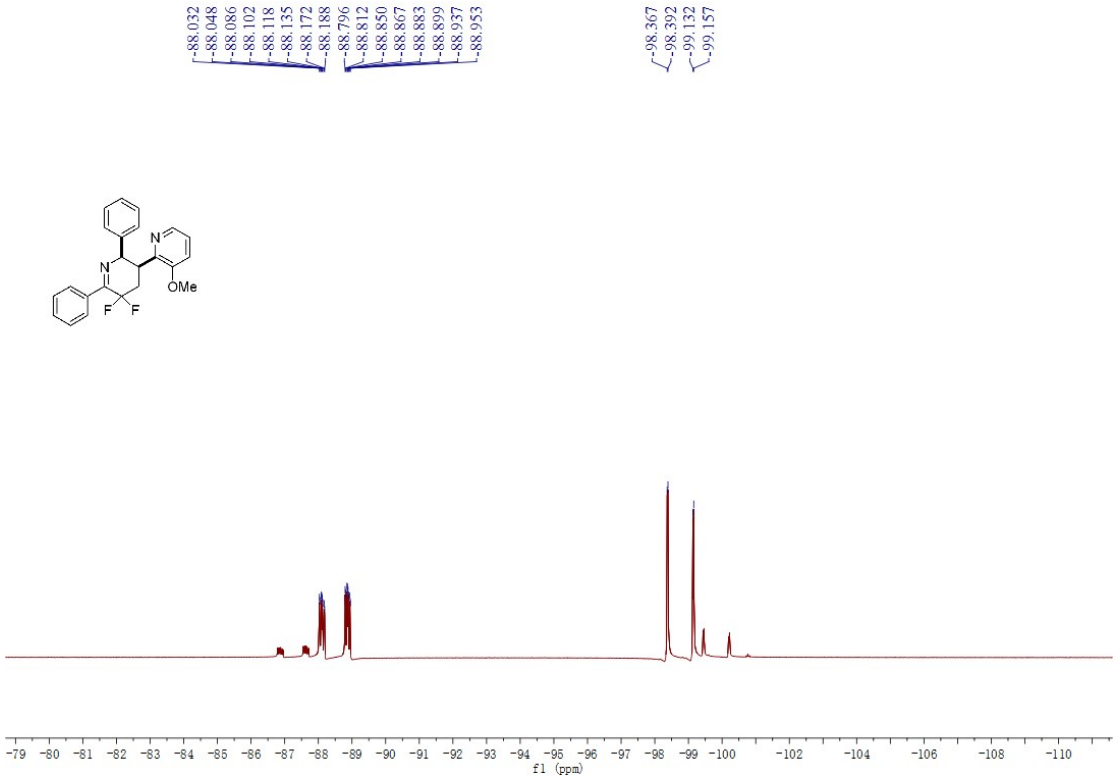
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

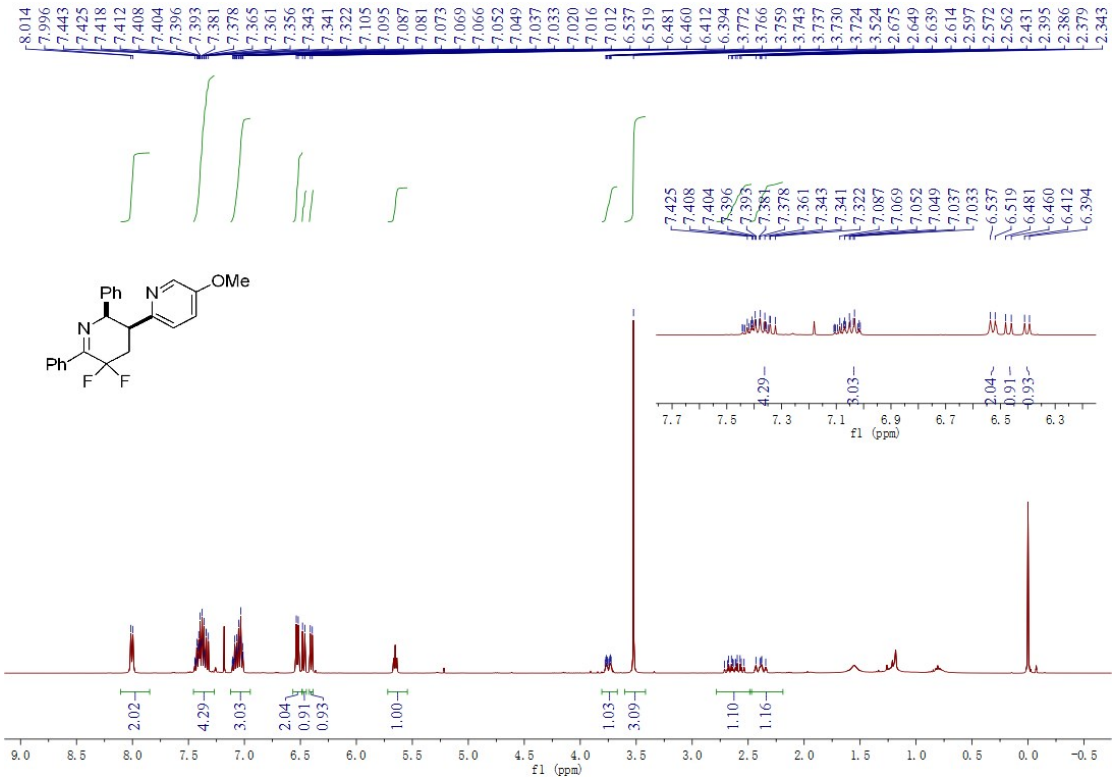


[^{19}F_NMR_375 MHz]

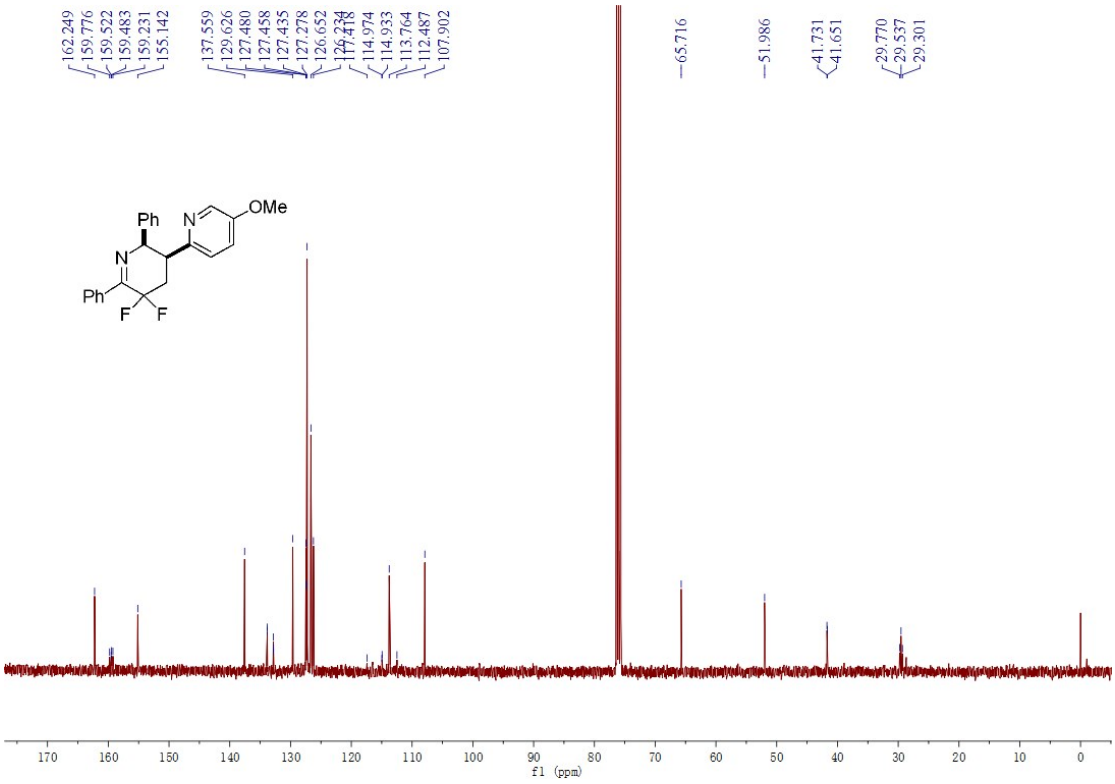


5',5'-Difluoro-4-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3c)

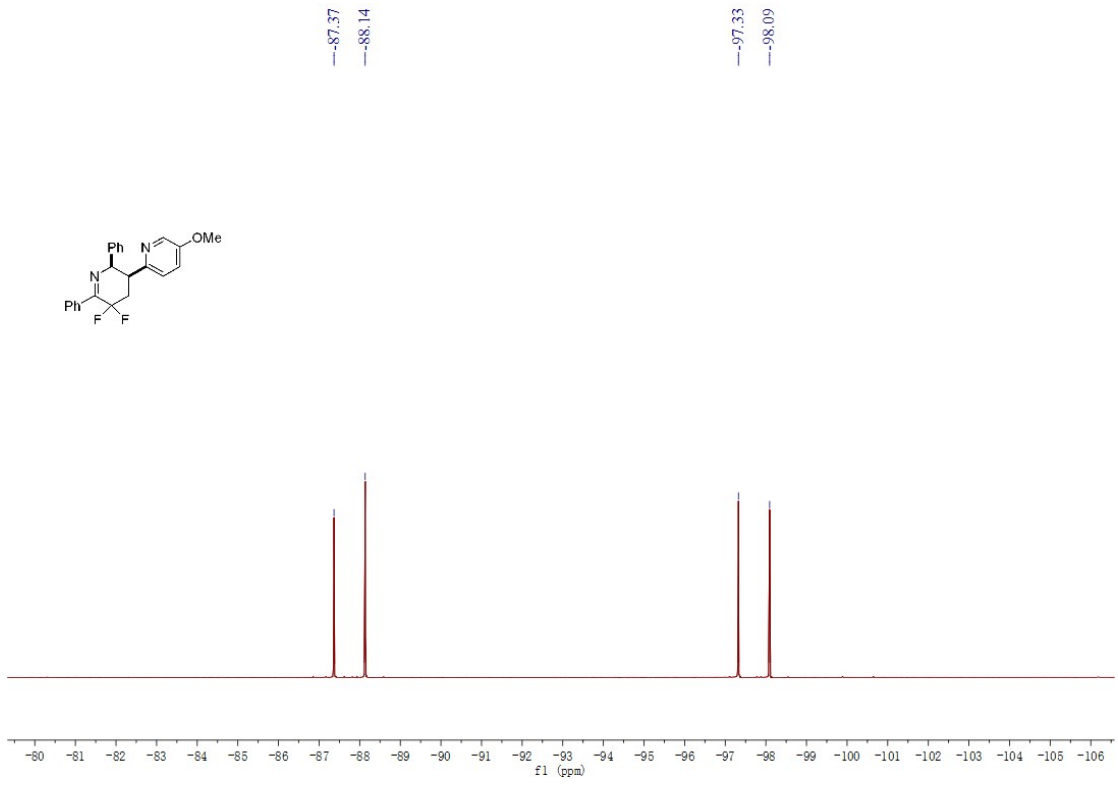
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

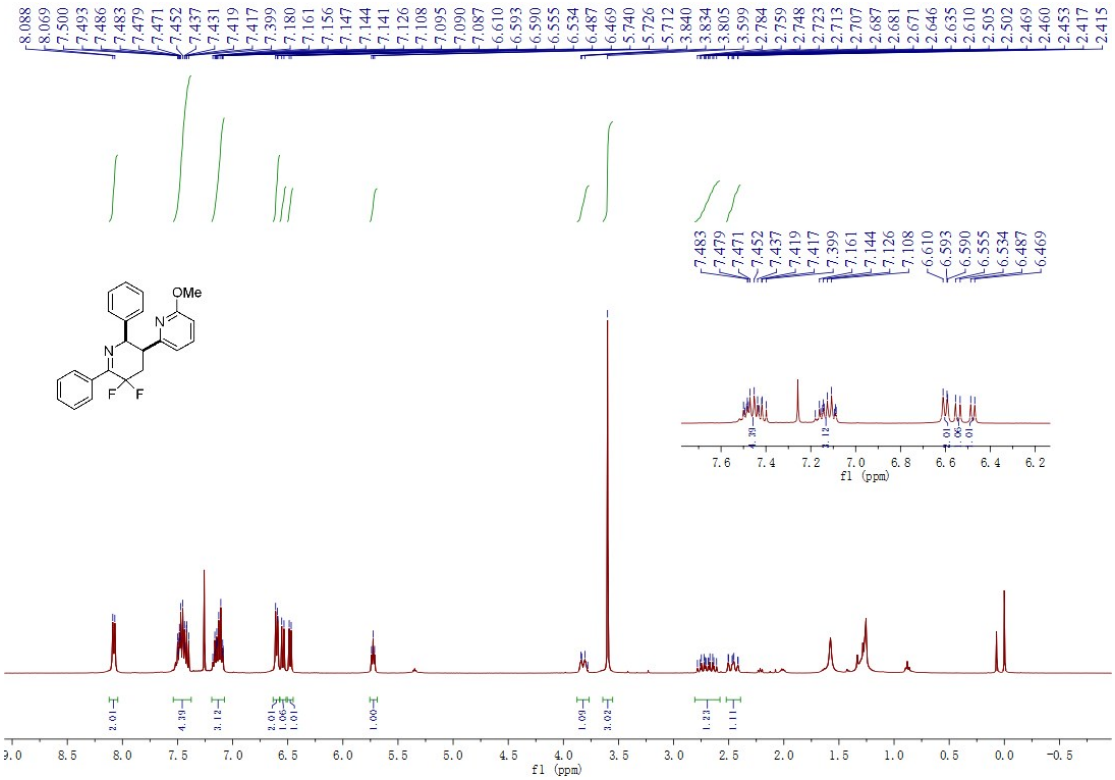


[^{19}F_NMR_375 MHz]

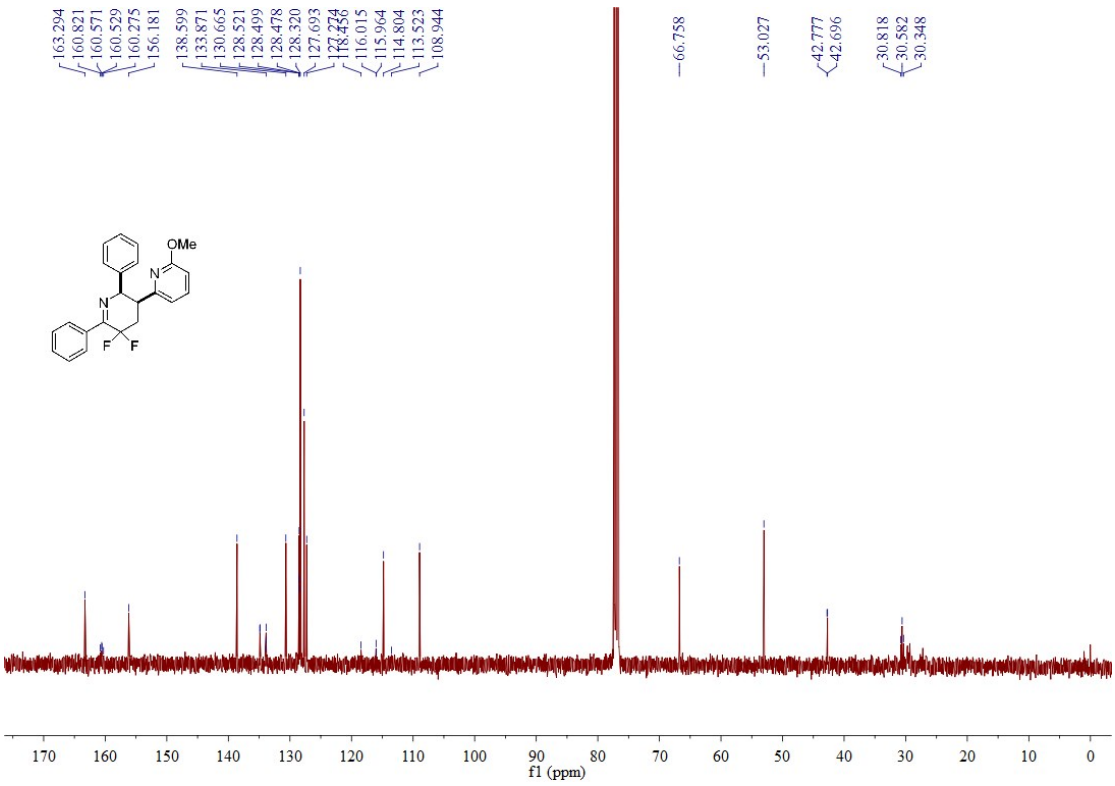


5',5'-Difluoro-6-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine

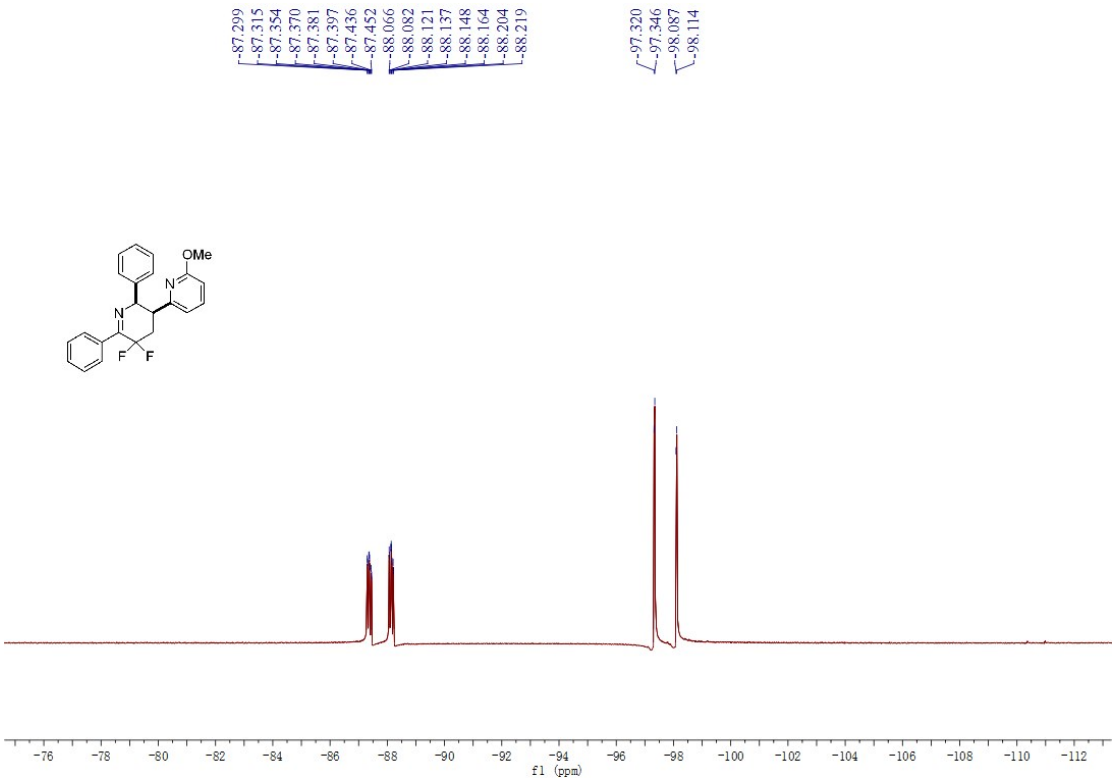
(3d)[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

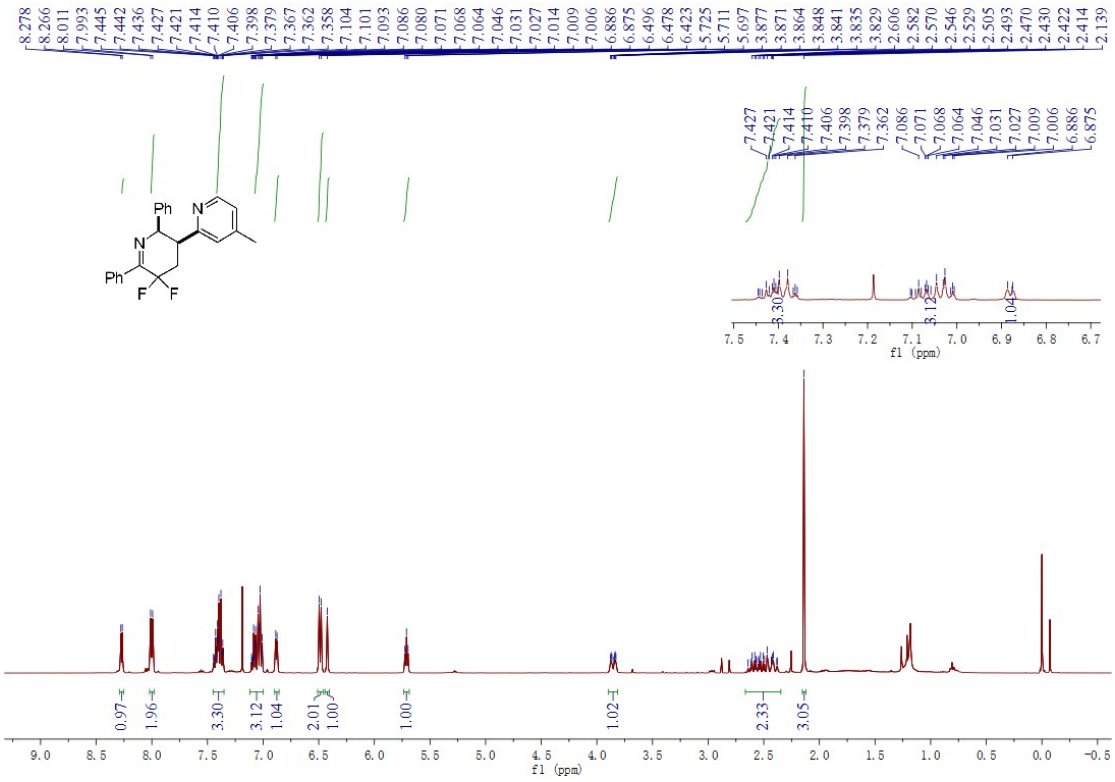


[^{19}F_NMR_375 MHz]

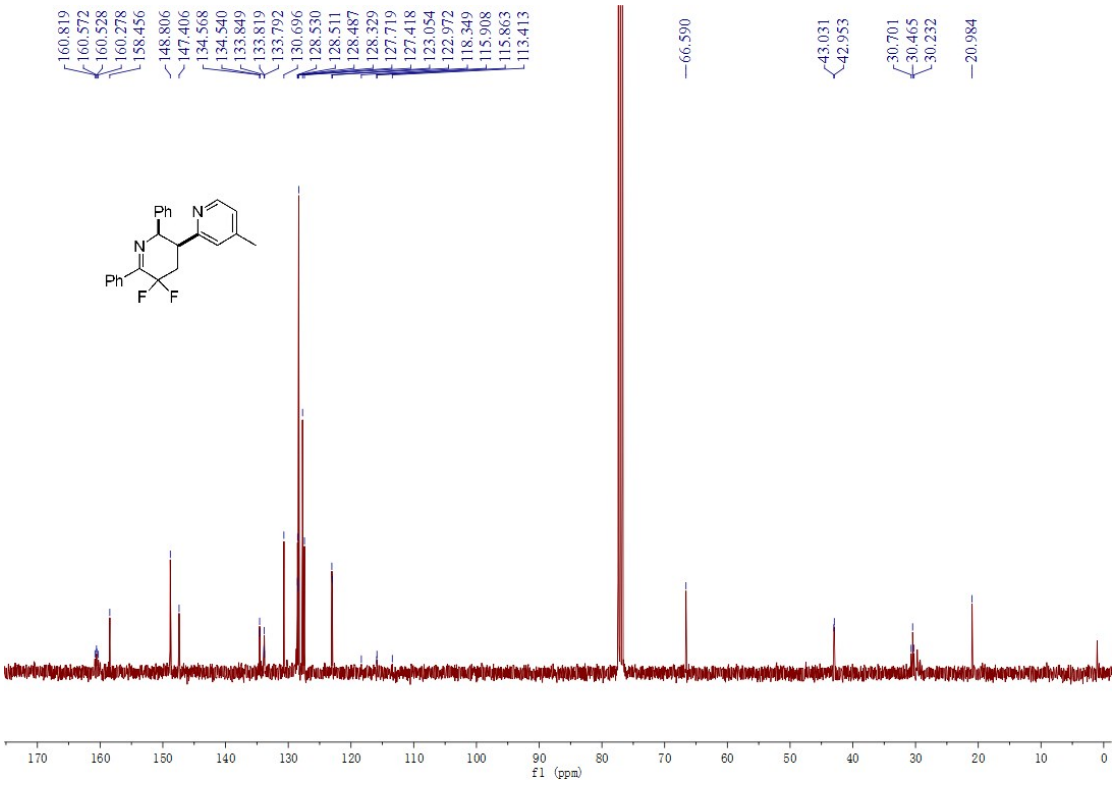


5',5'-Difluoro-5-methoxy-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3e)

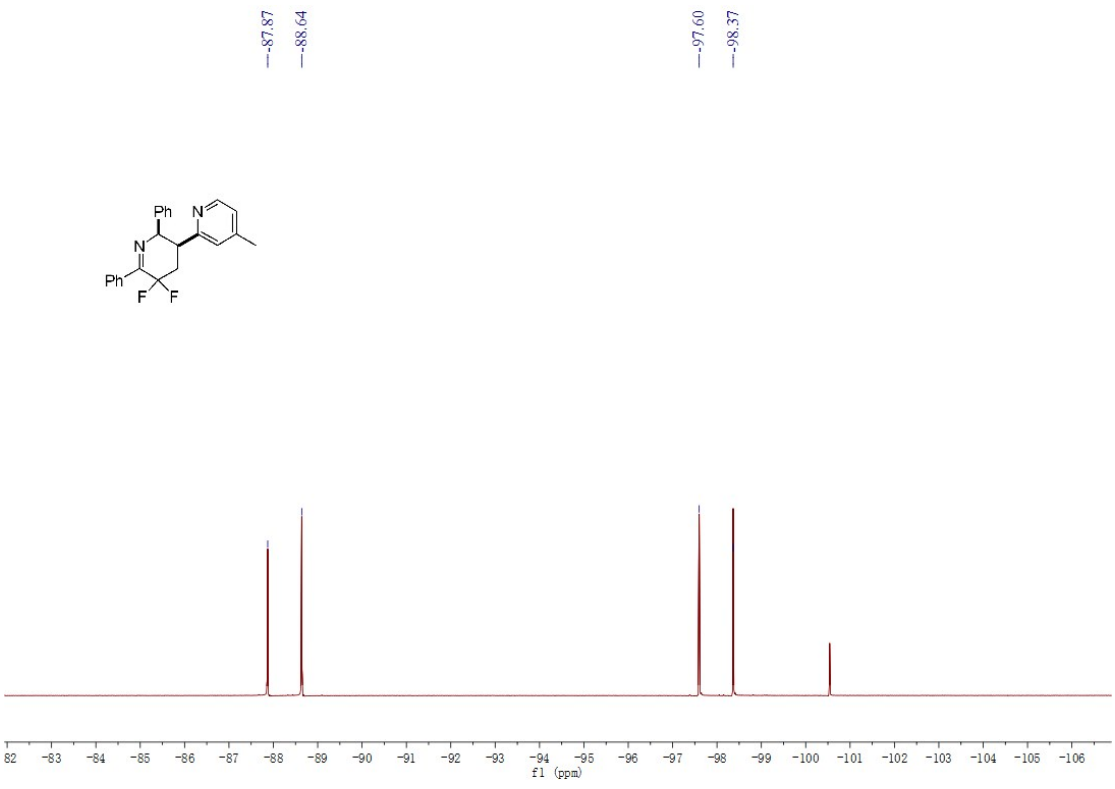
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



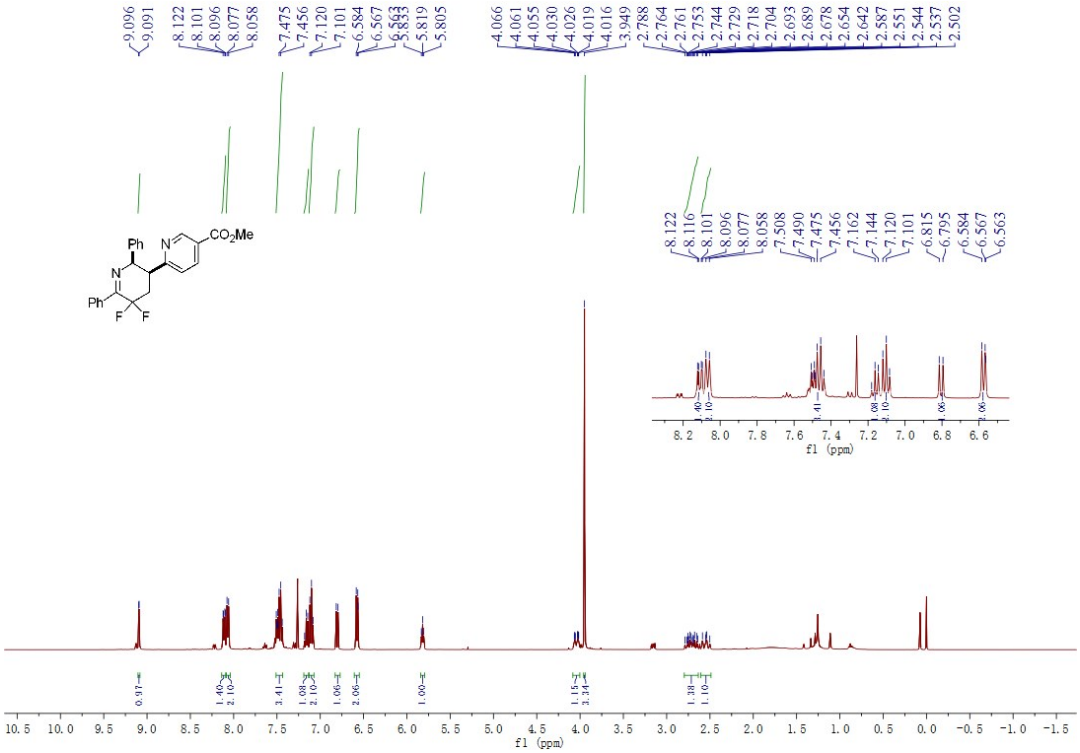
[^{19}F_NMR_375 MHz]



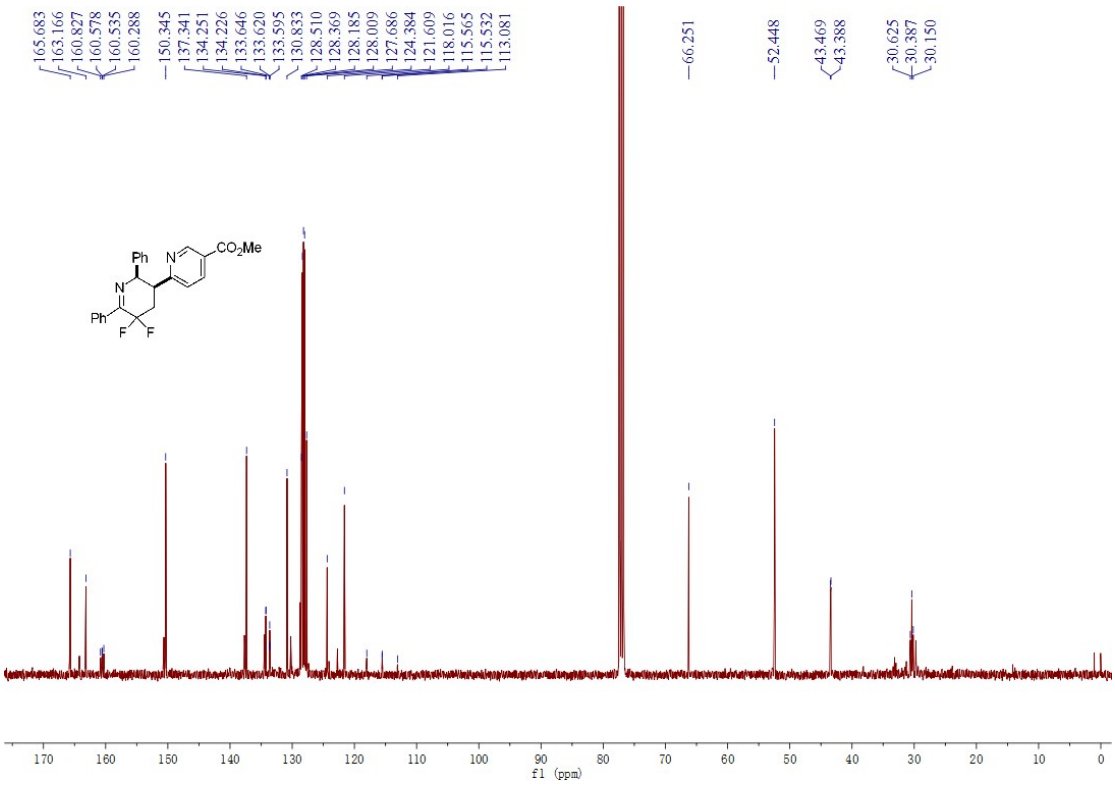
Methyl-5',5'-difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-

carboxylate (3f)

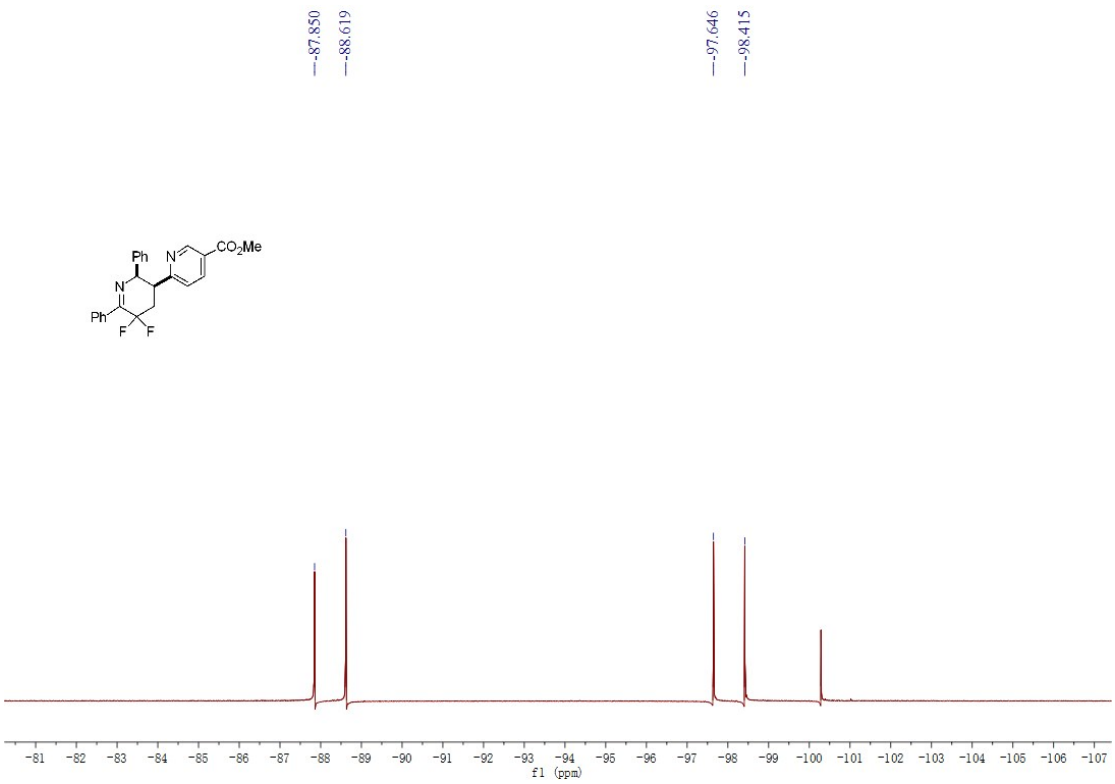
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

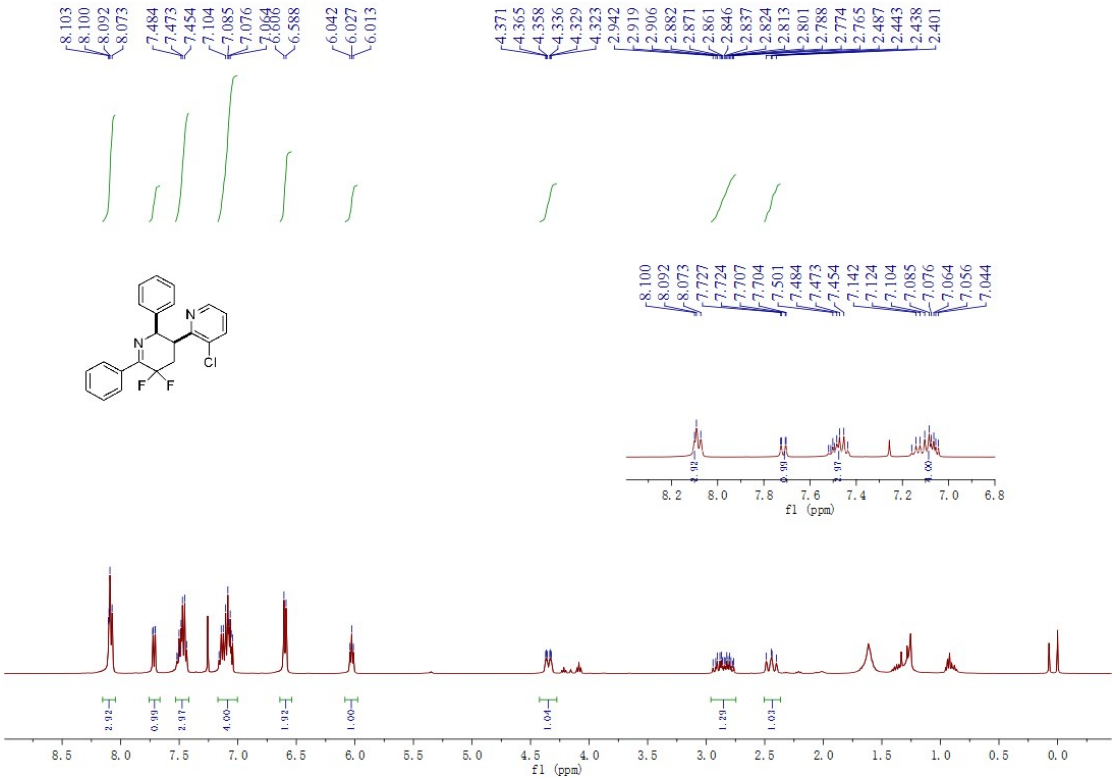


[^{19}F_NMR_375 MHz]

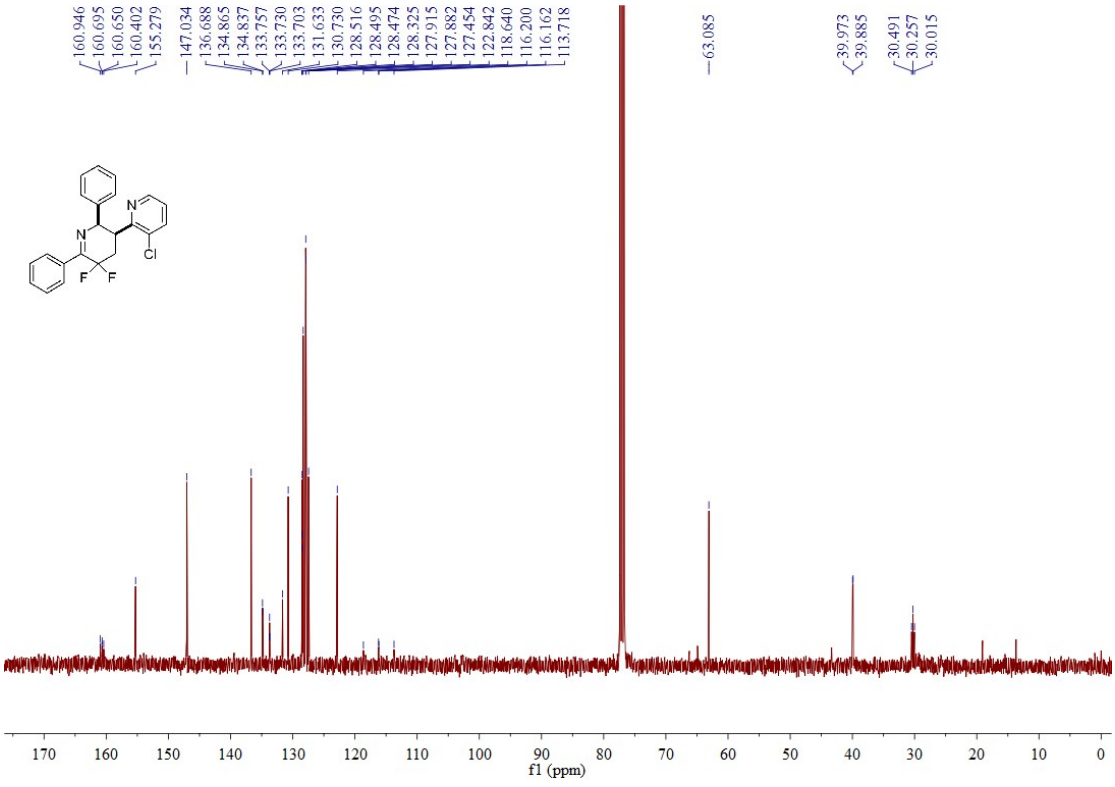


3-Chloro-5',5'-difluoro-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-bipyridine (3g)

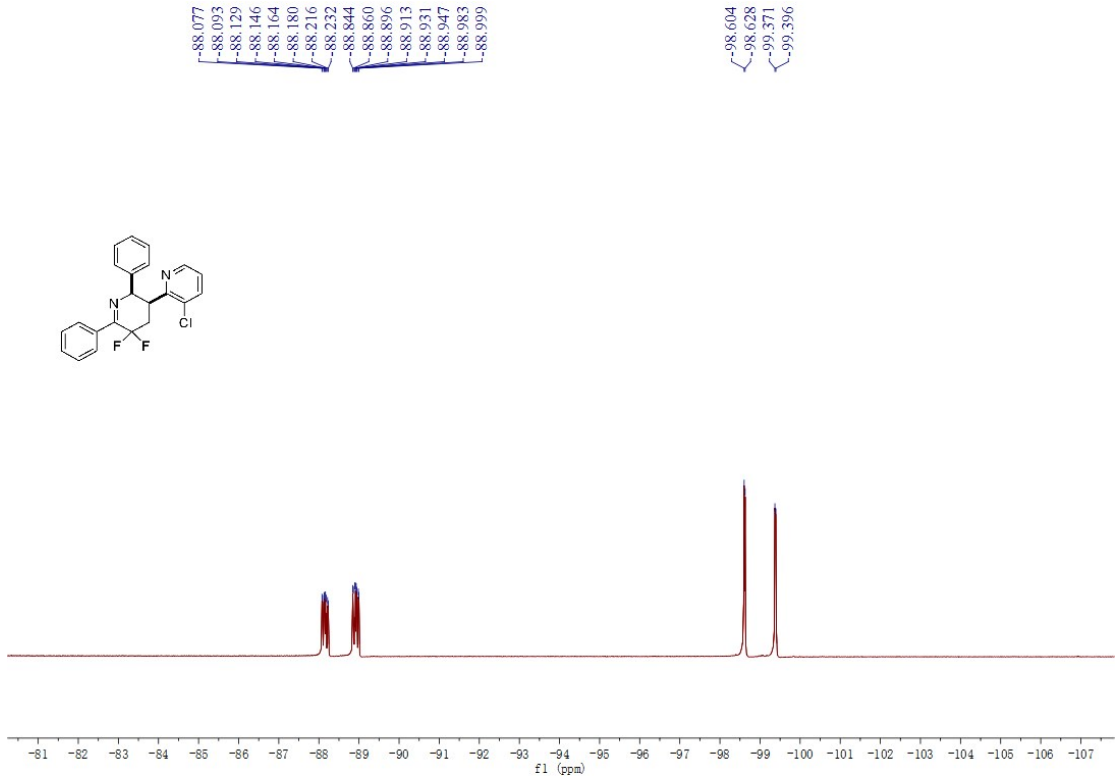
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



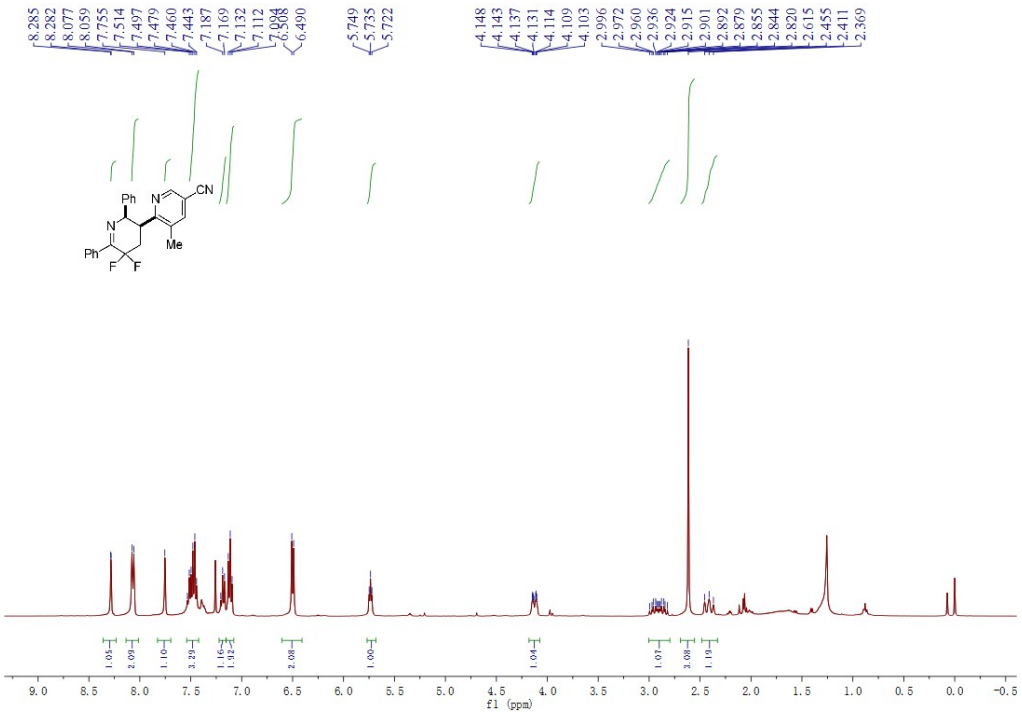
[^{19}F_NMR_375 MHz]



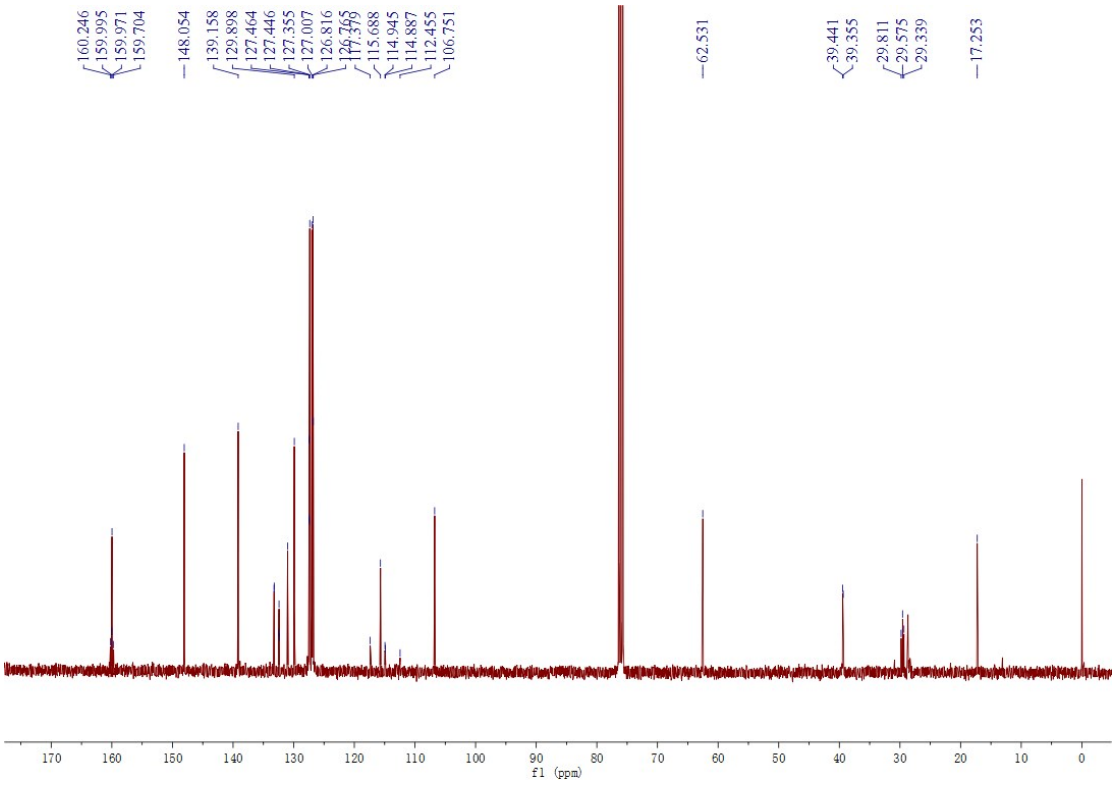
5',5'-Difluoro-3-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-

carbonitrile (3h)

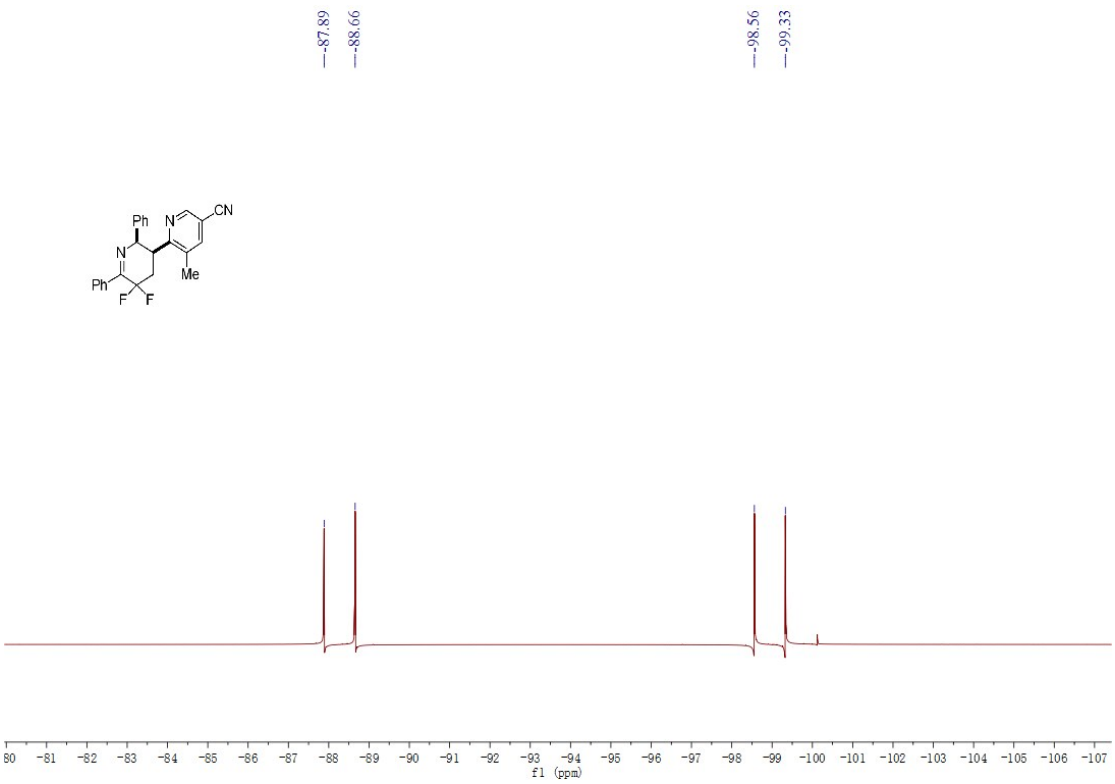
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



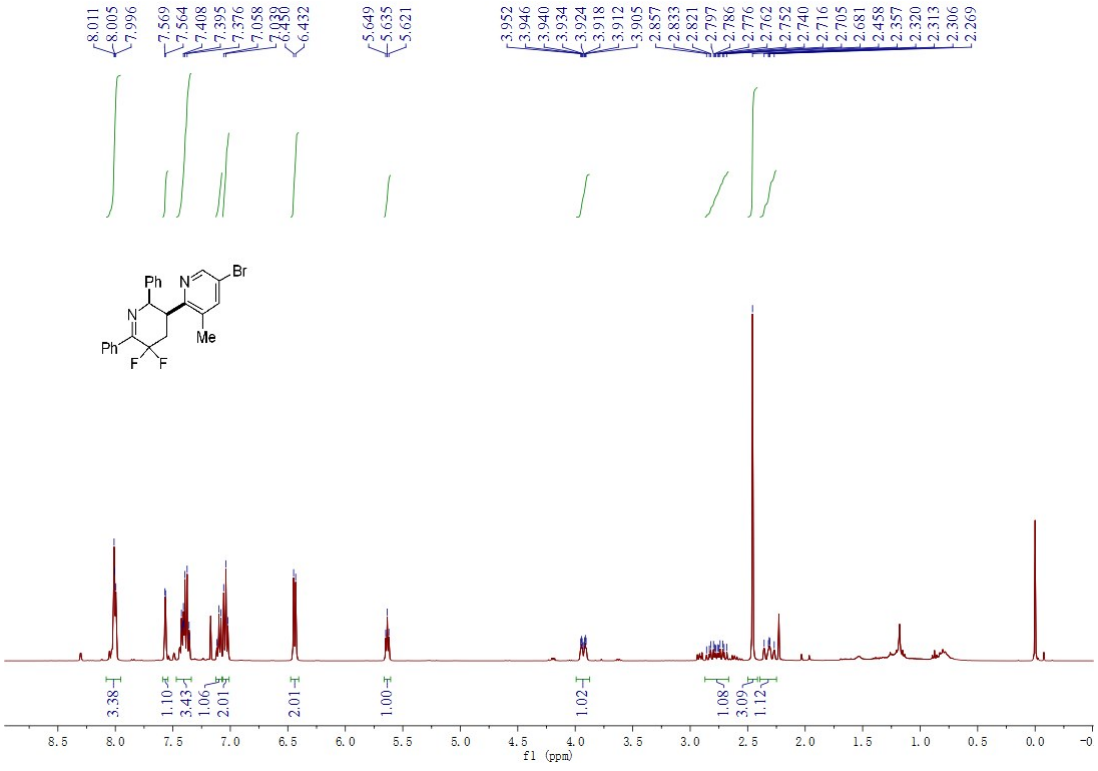
[^{19}F_NMR_375 MHz]



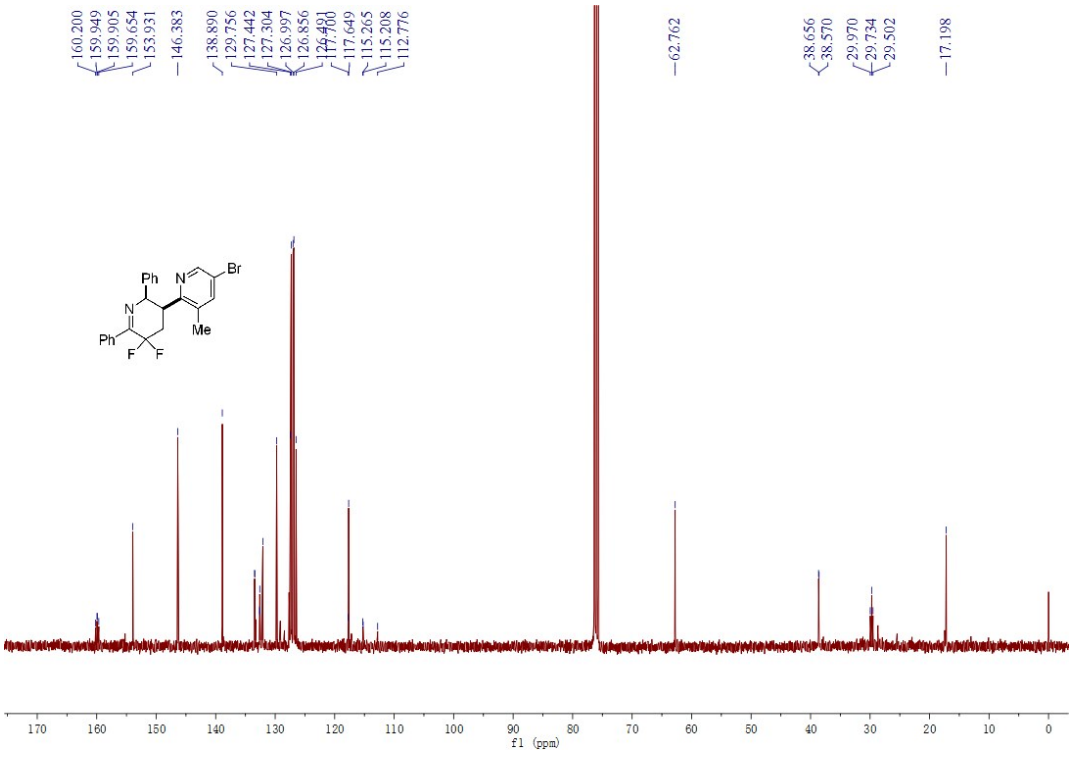
5-Bromo-5',5'-difluoro-3-methyl-2',6'-diphenyl-2',3',4',5'-tetrahydro-2,3'-

bipyridine (3i)

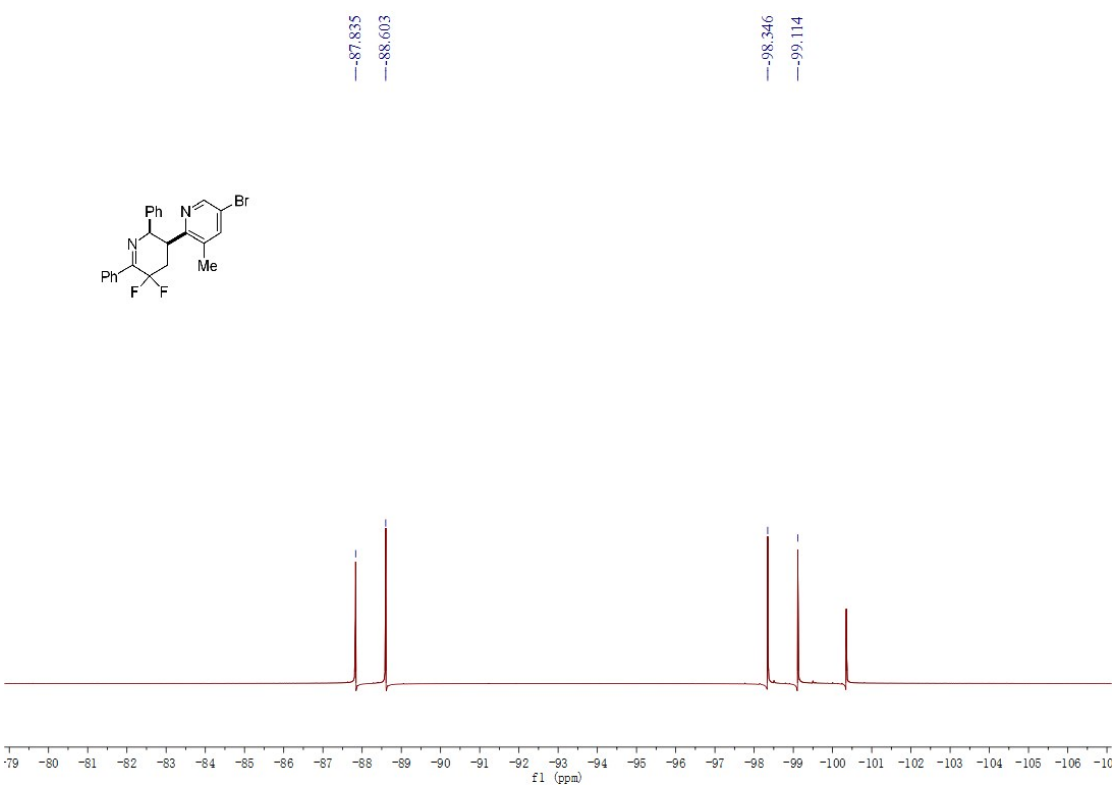
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

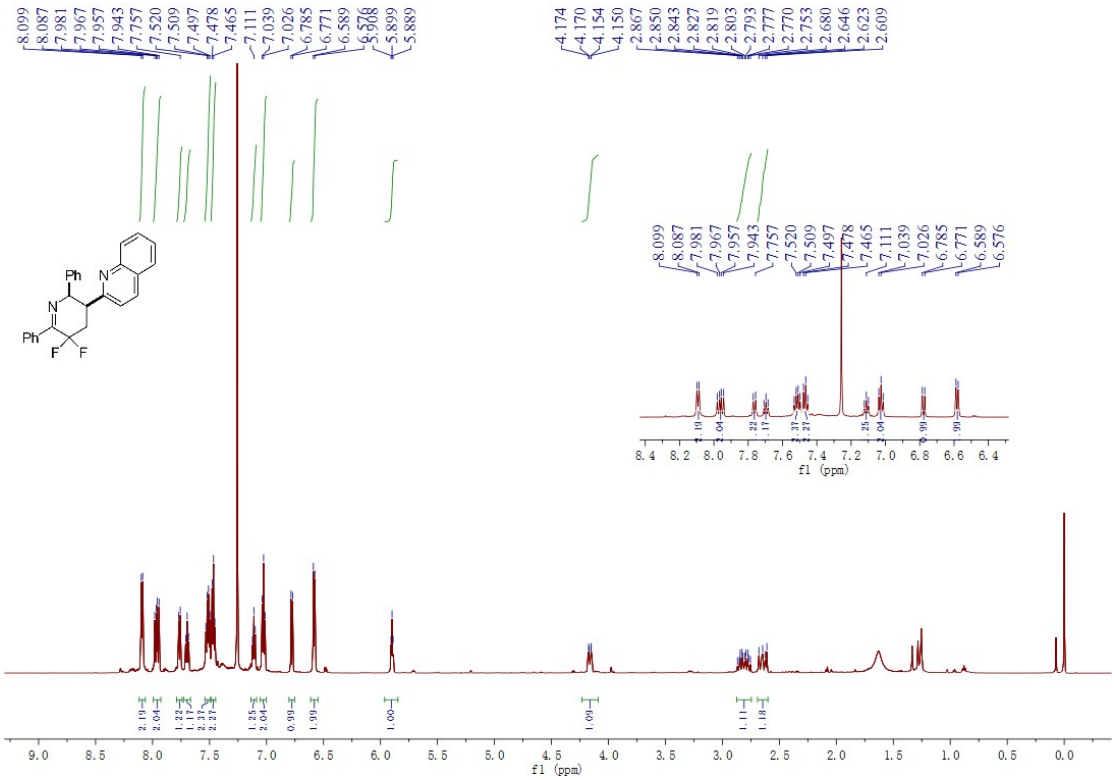


[^{19}F_NMR_375 MHz]

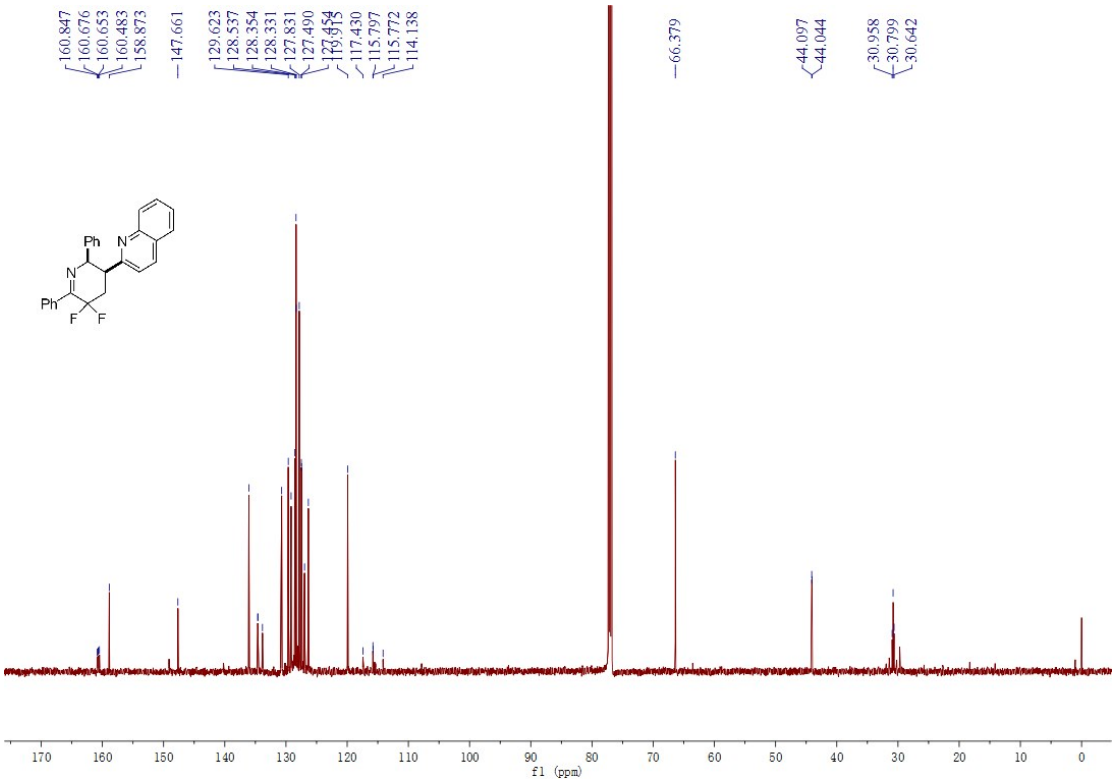


2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline (3j)

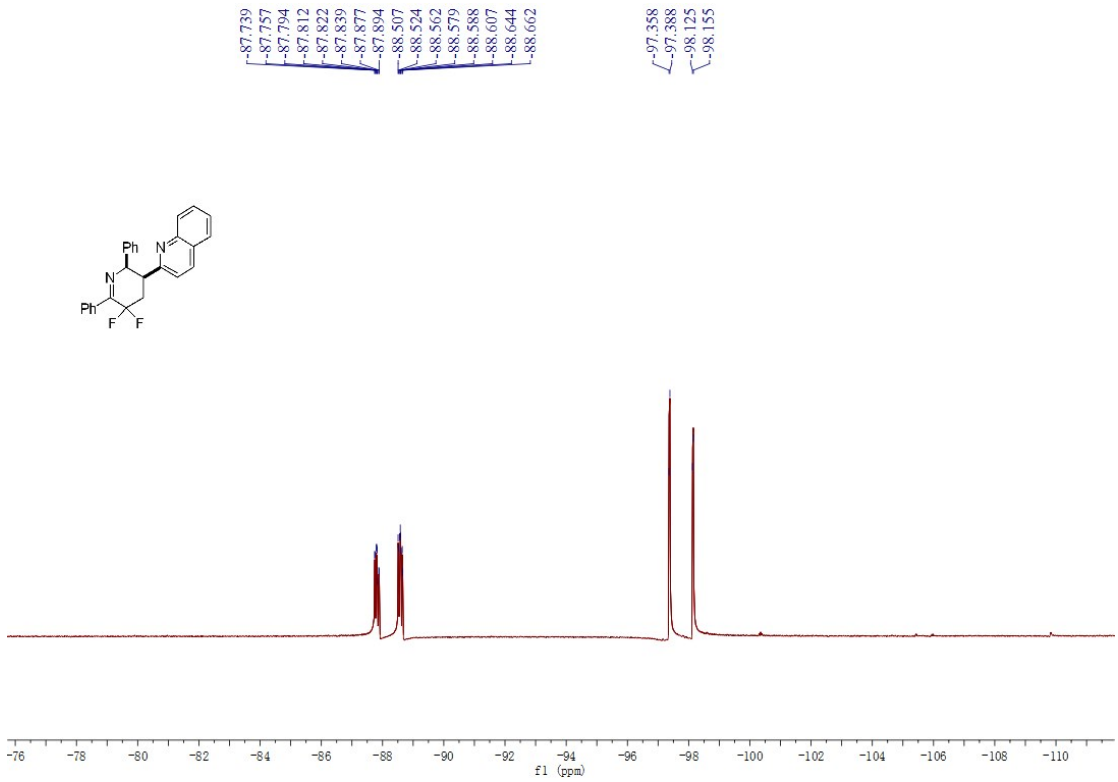
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



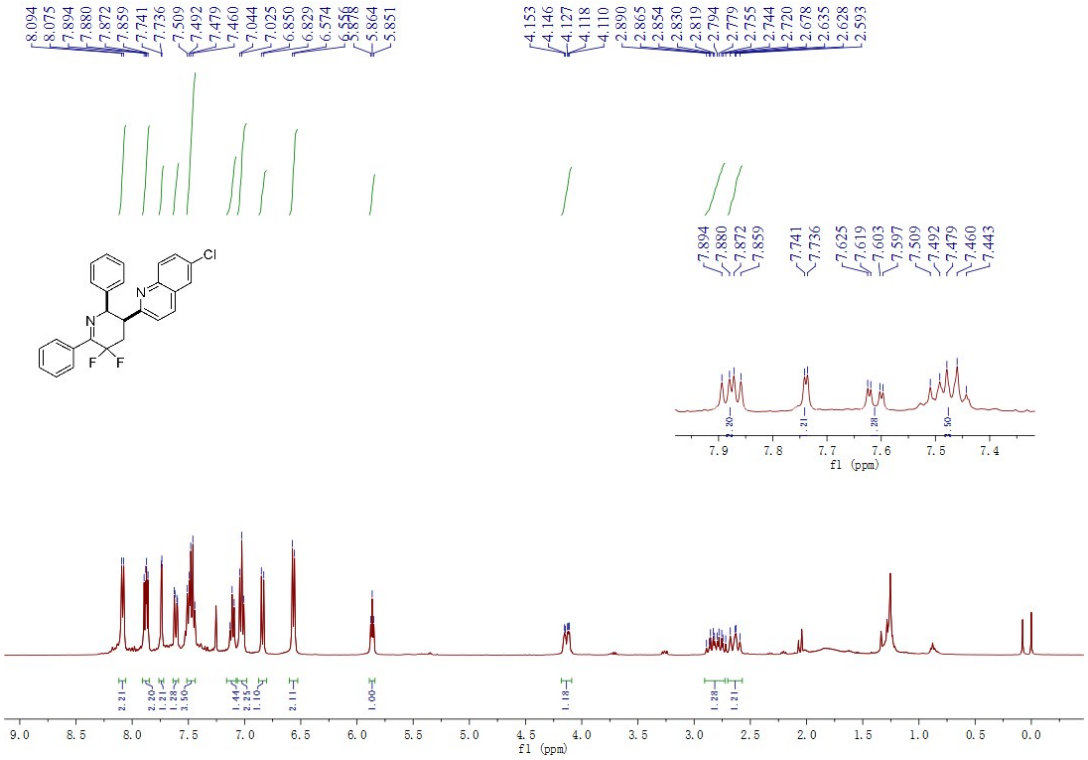
[^{19}F_NMR_375 MHz]



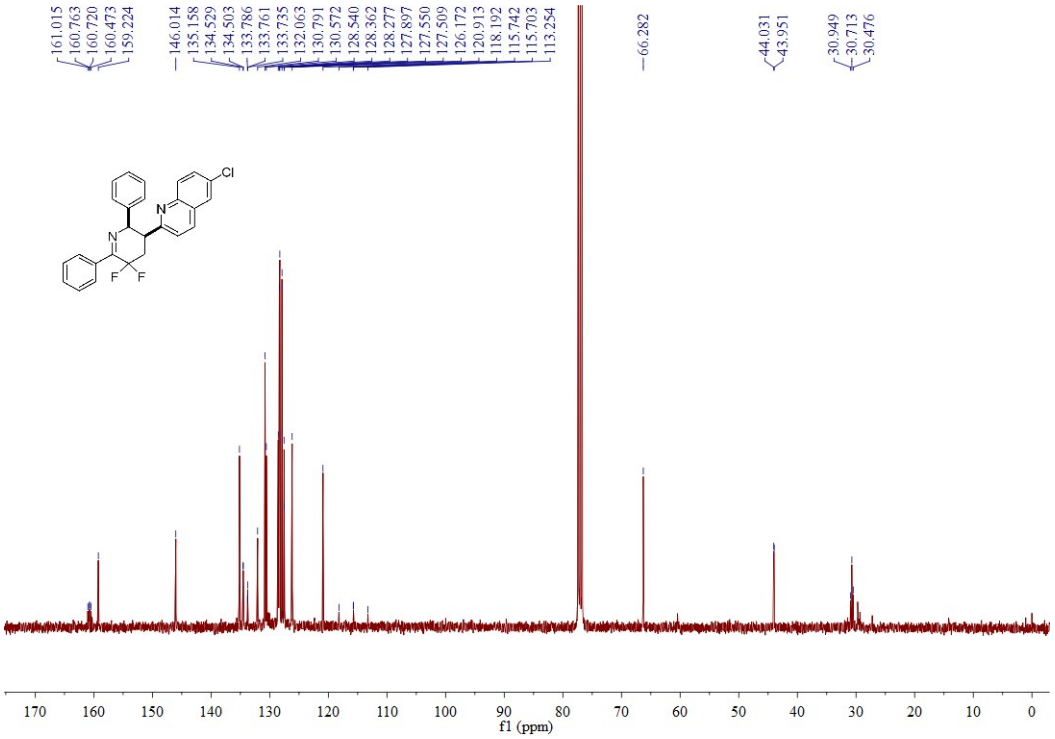
6-Chloro-2-(5,5-difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline

(3k)

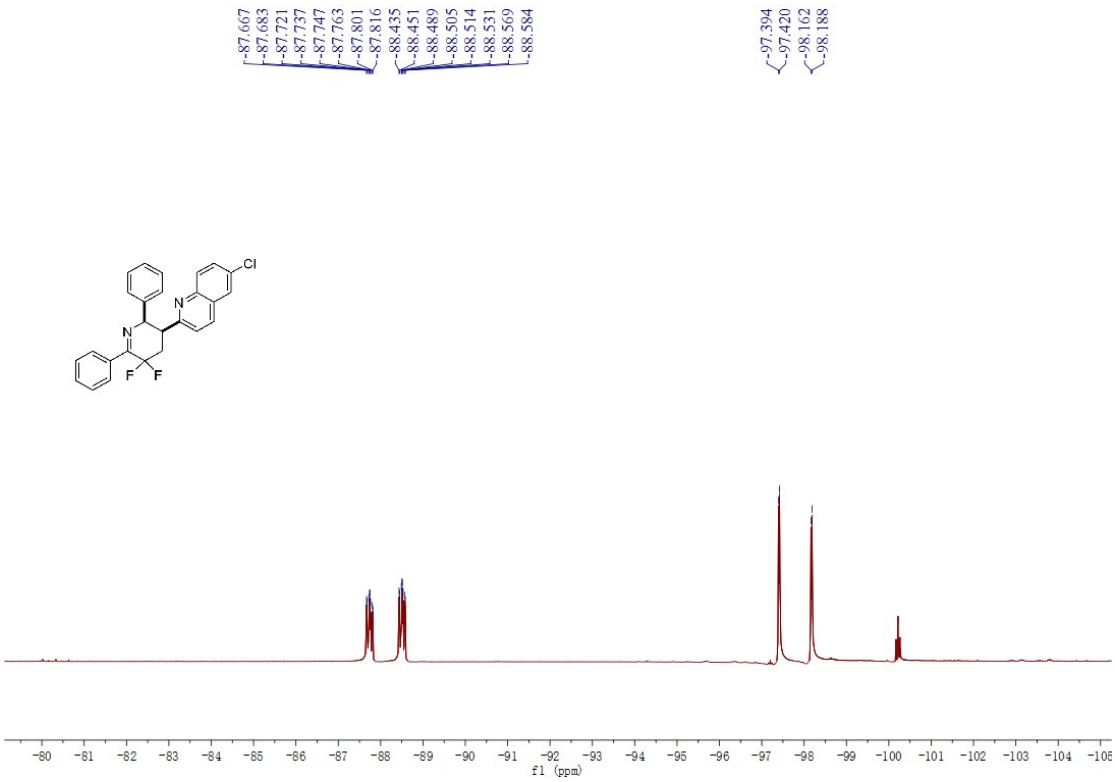
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



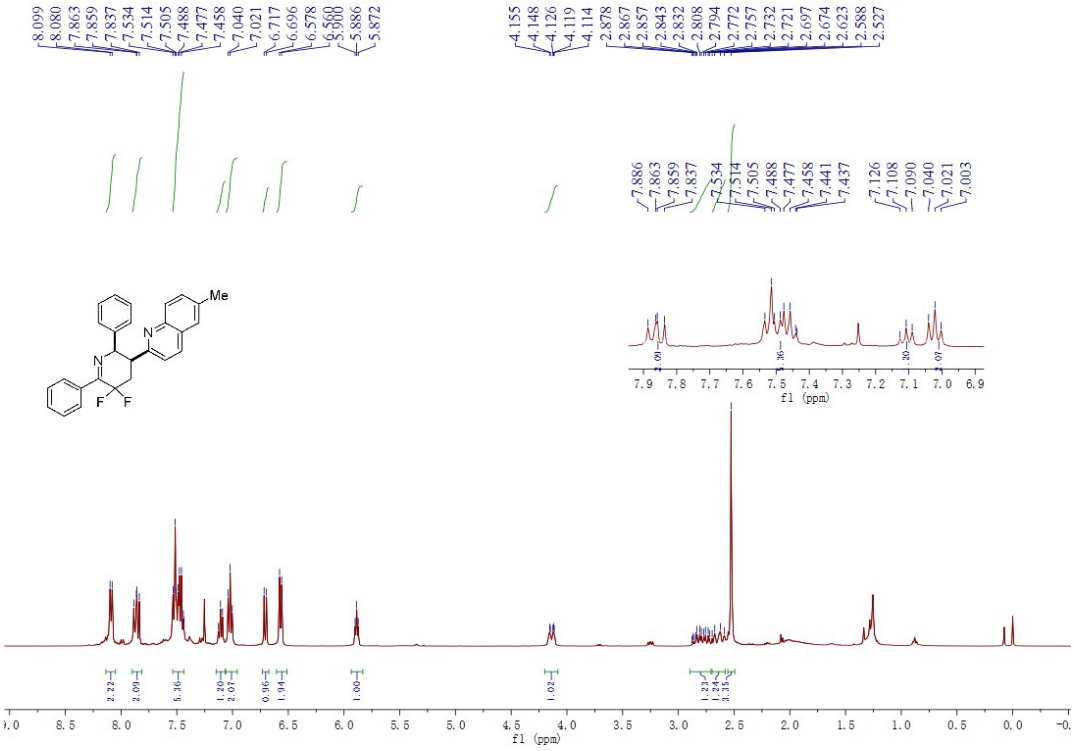
[^{19}F_NMR_375 MHz]



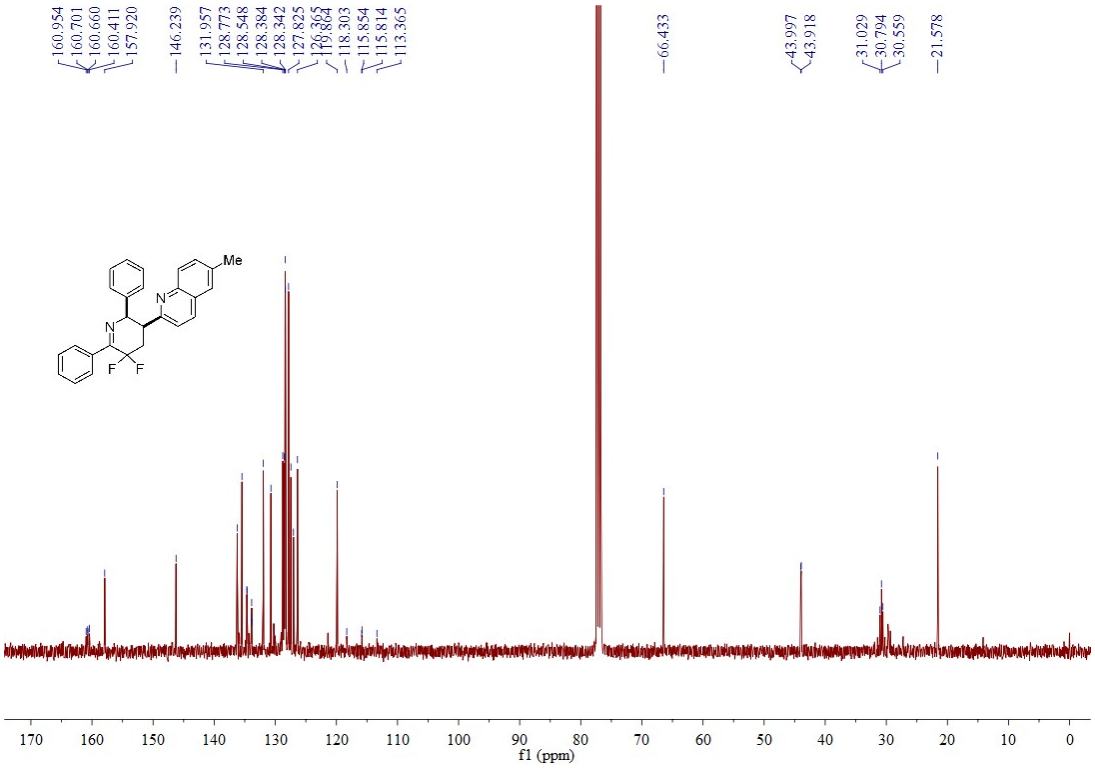
2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-6-methylquinoline

(3l)

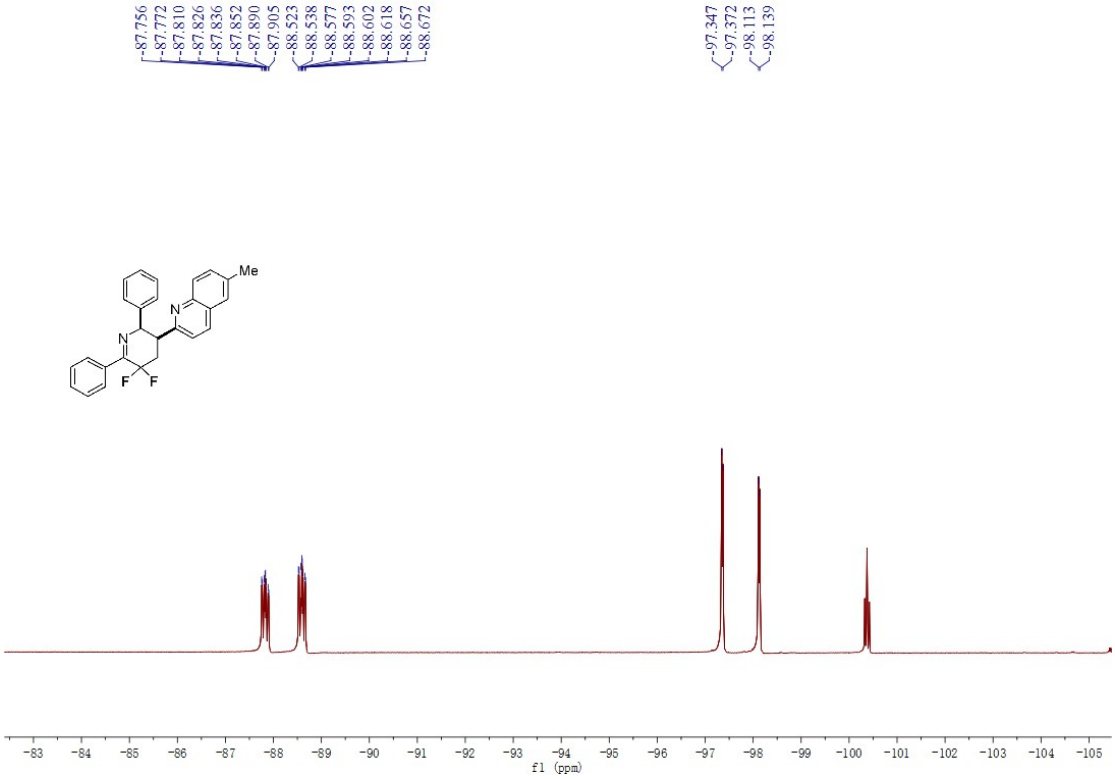
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



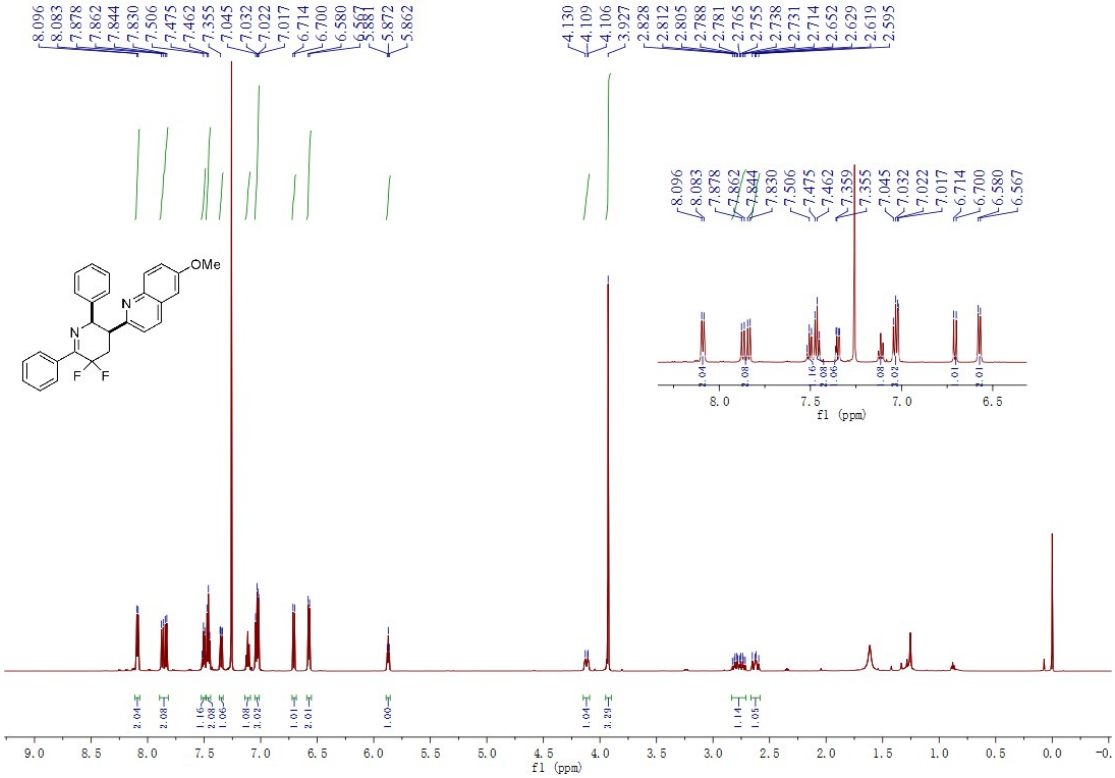
[^{19}F_NMR_375 MHz]



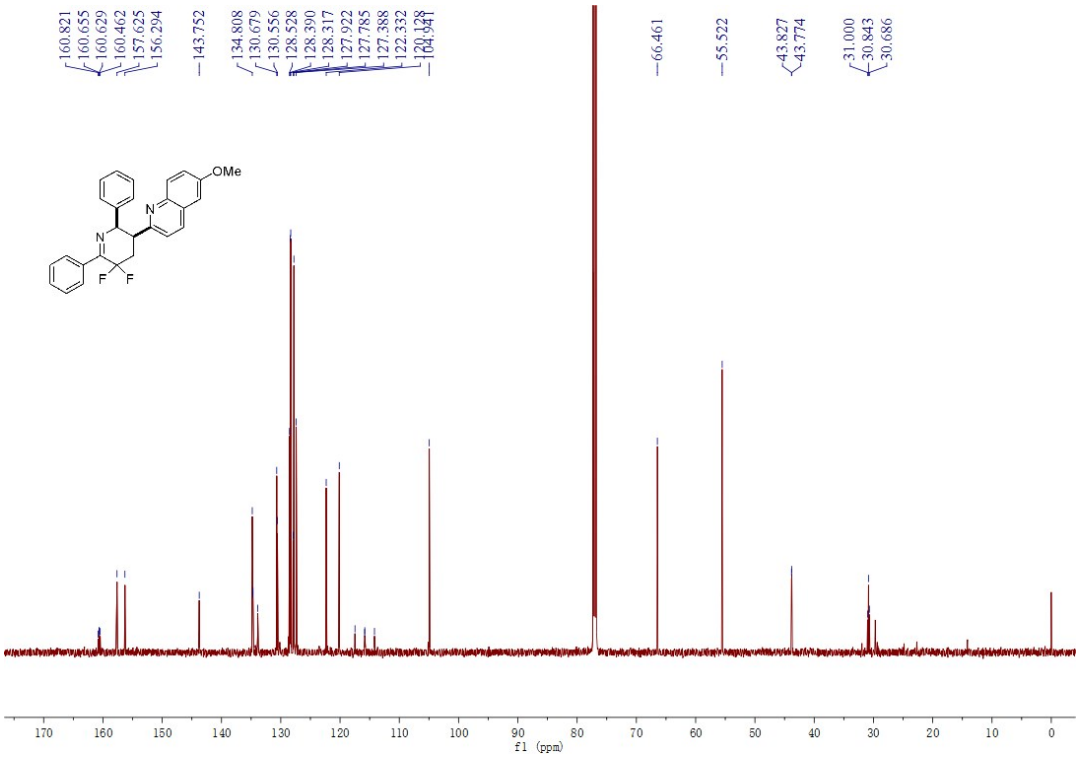
2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-6-methoxyquinoline

(3m)

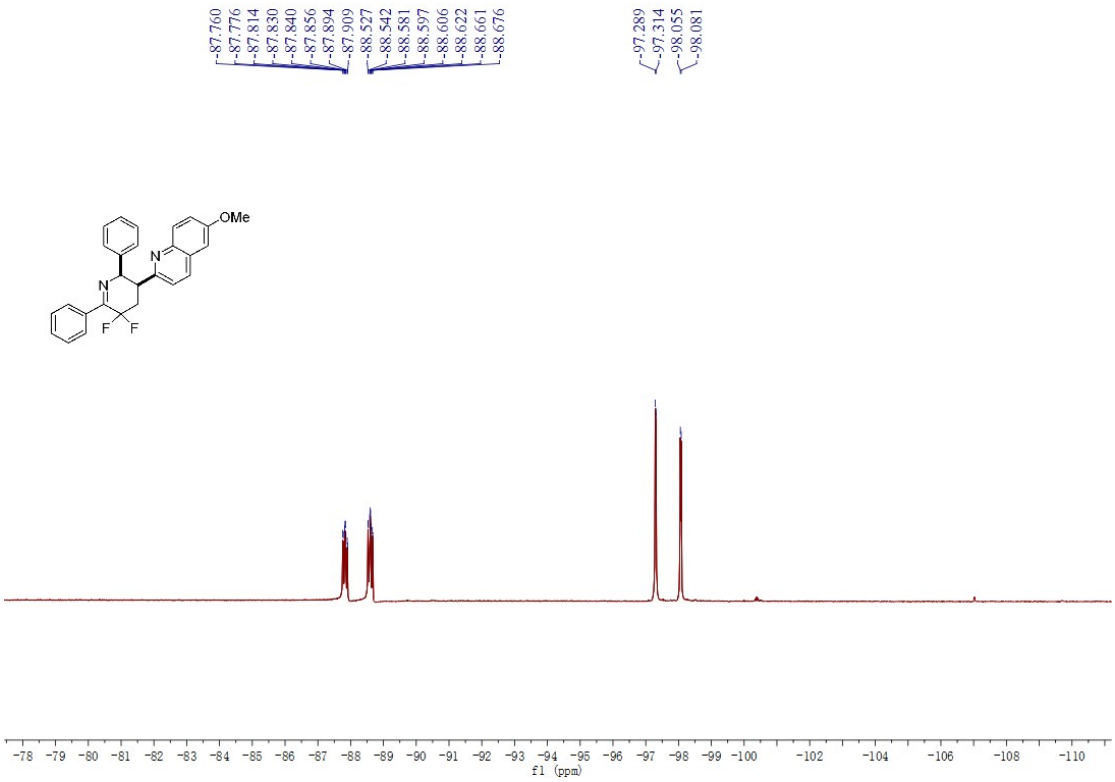
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



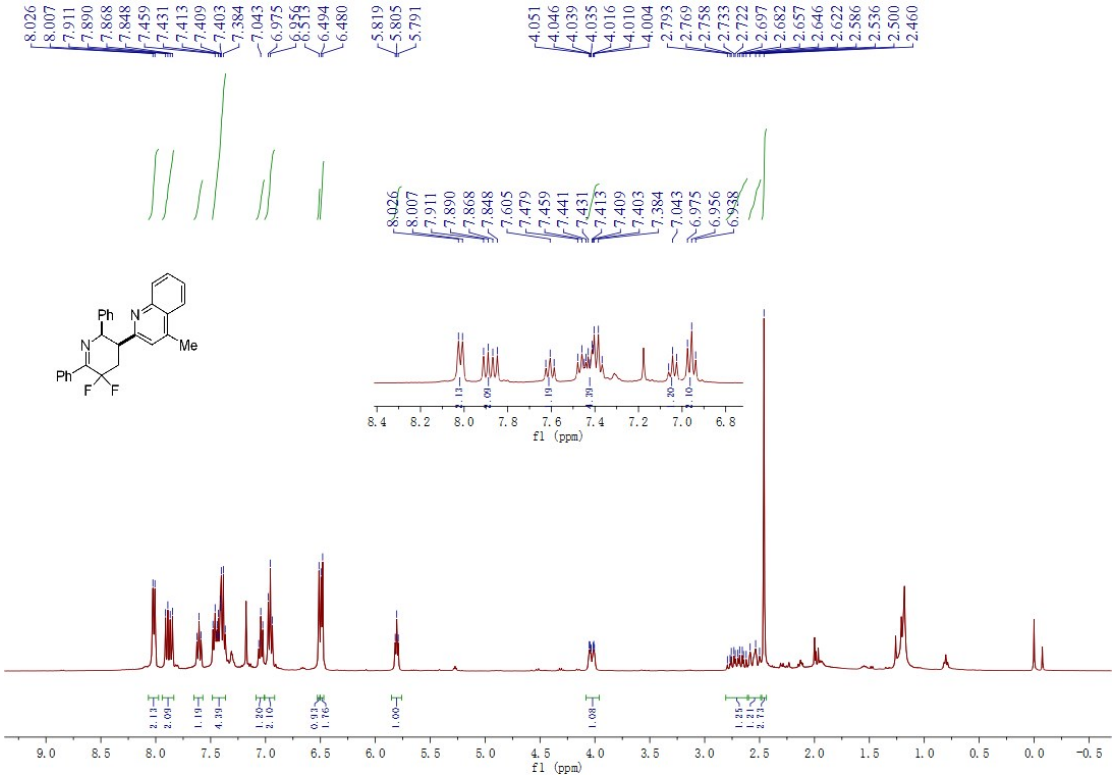
[^{19}F_NMR_375 MHz]



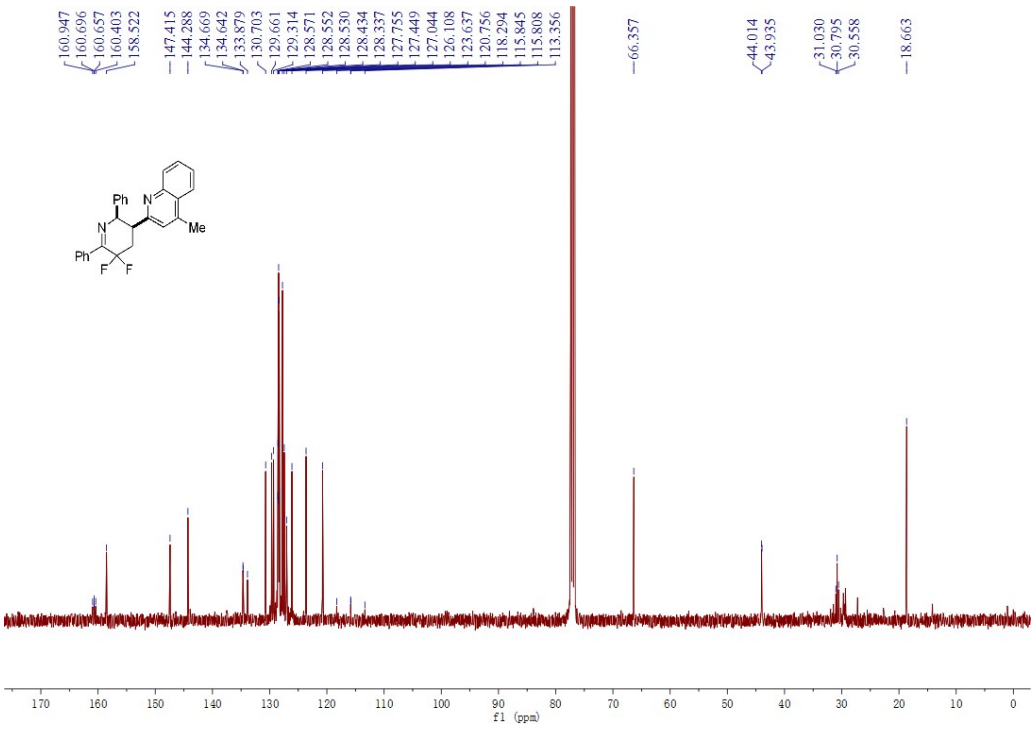
2-(5,5-Difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)-4-methylquinoline

(3n)

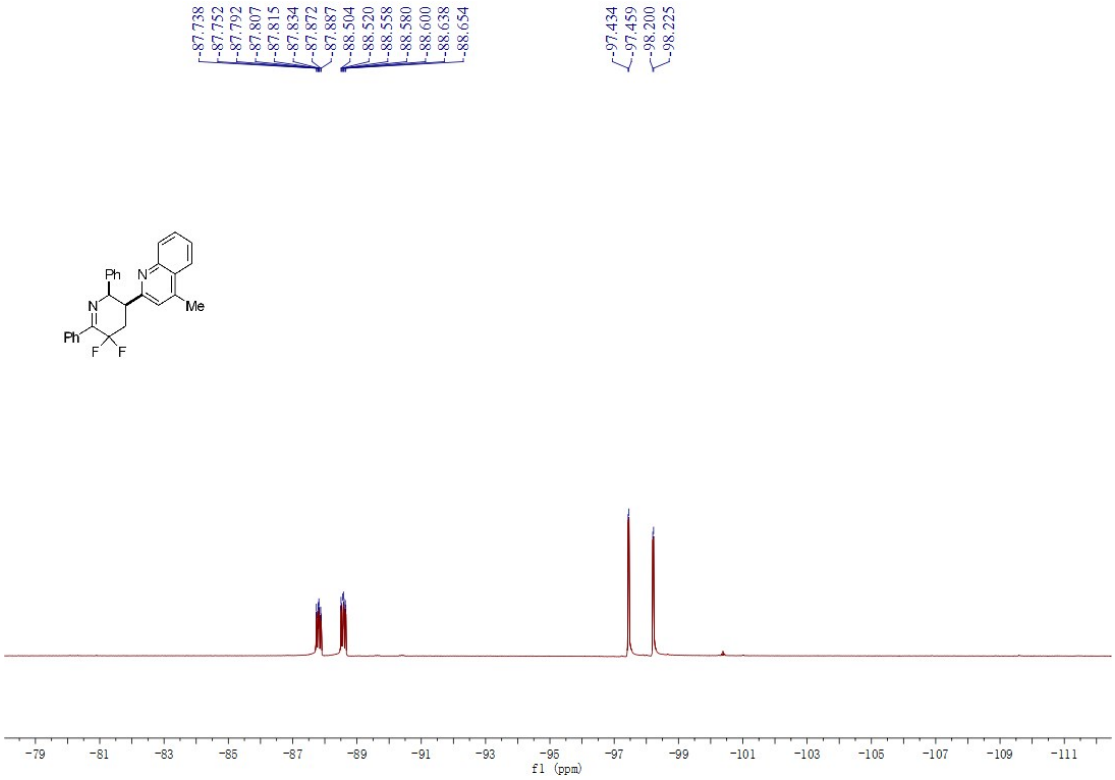
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



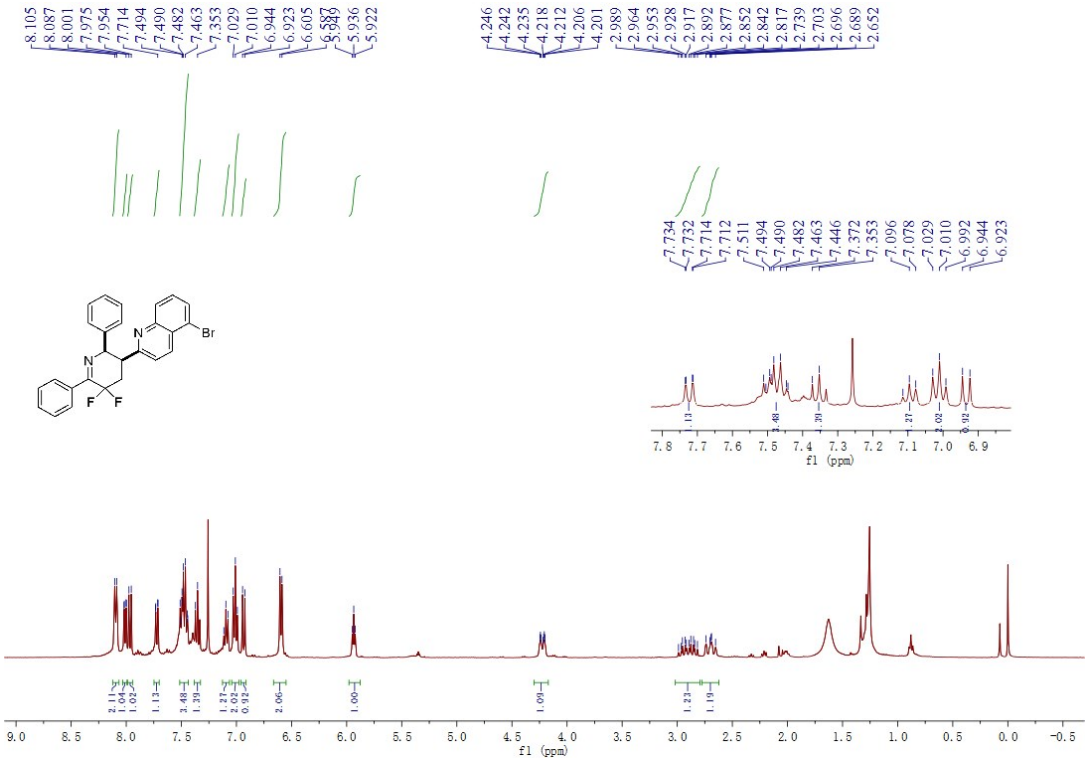
[^{19}F_NMR_375 MHz]



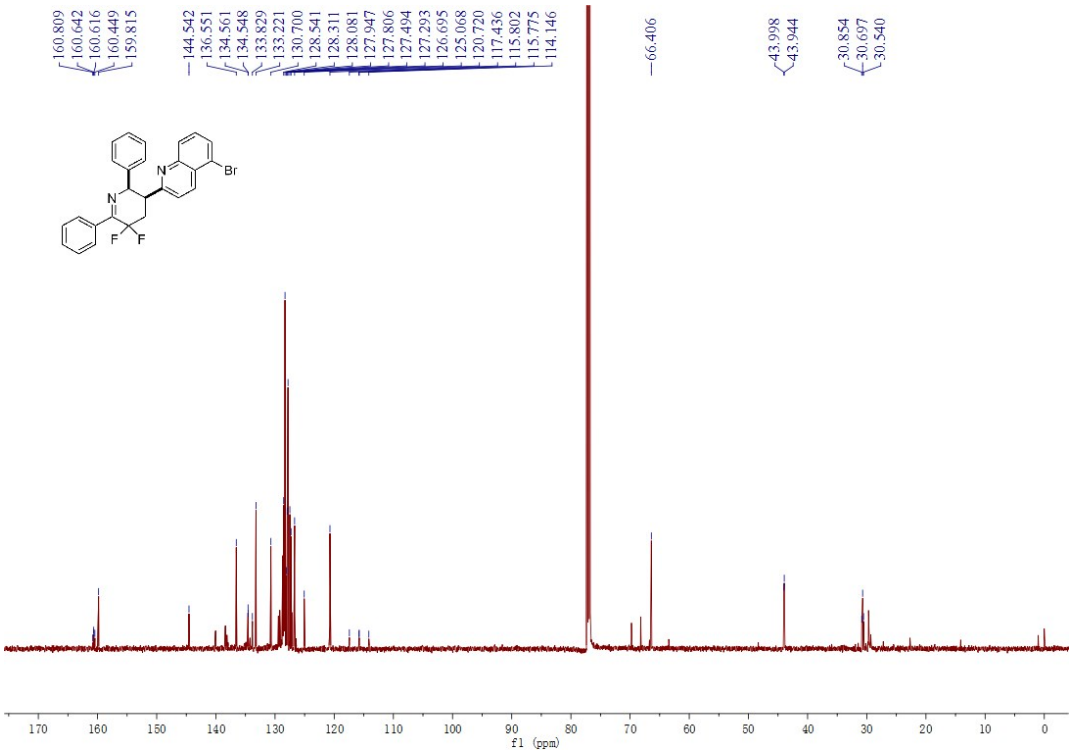
5-Bromo-2-(5,5-difluoro-2,6-diphenyl-2,3,4,5-tetrahydropyridin-3-yl)quinoline

(3o)

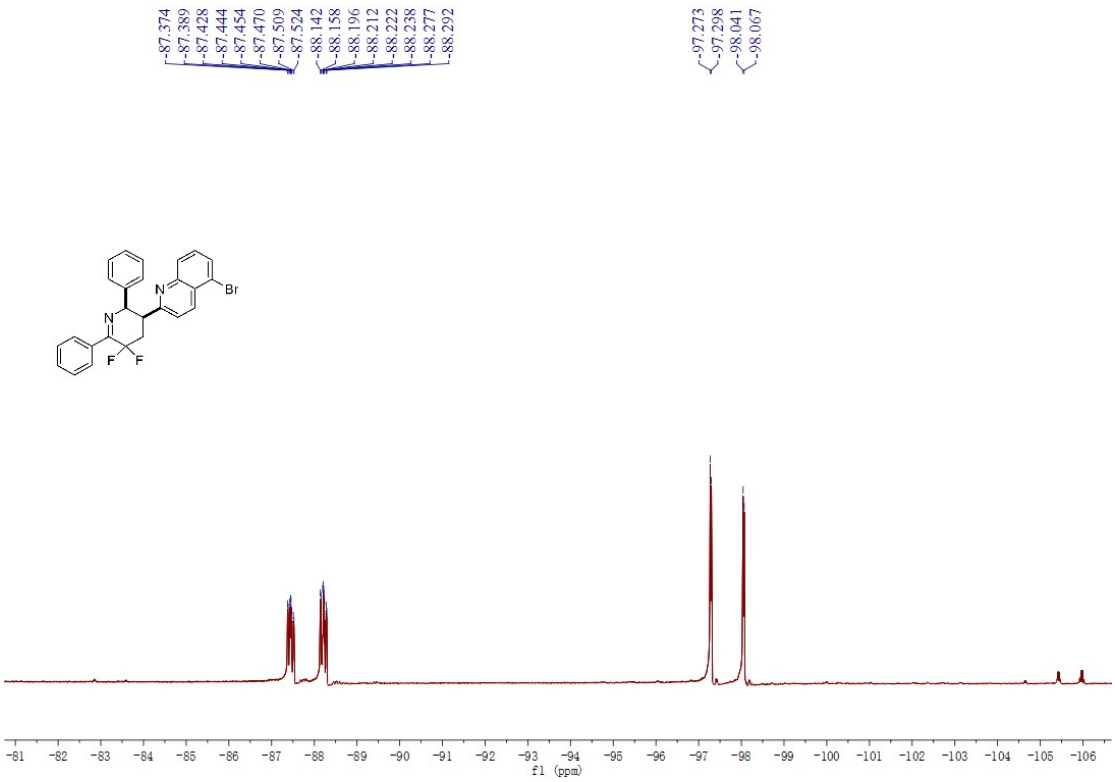
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



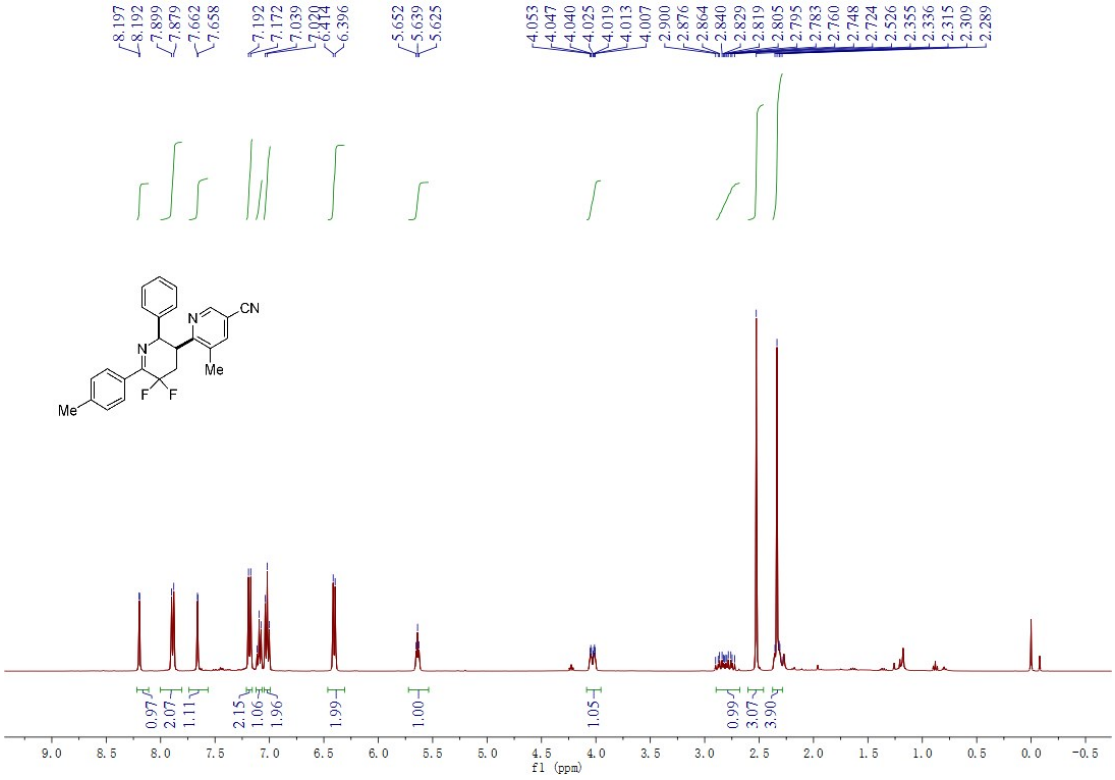
[^{19}F_NMR_375 MHz]



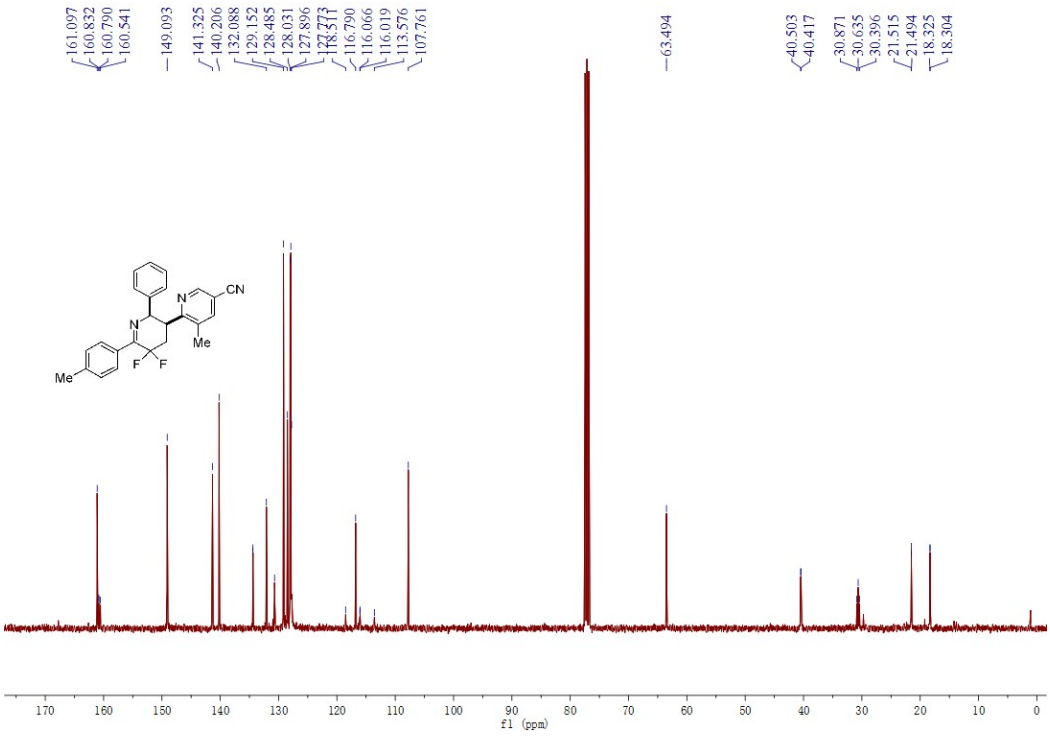
5',5'-Difluoro-3-methyl-2'-phenyl-6'-(p-tolyl)-2',3',4',5'-tetrahydro-[2,3'-

bipyridine]-5-carbonitrile (3p)

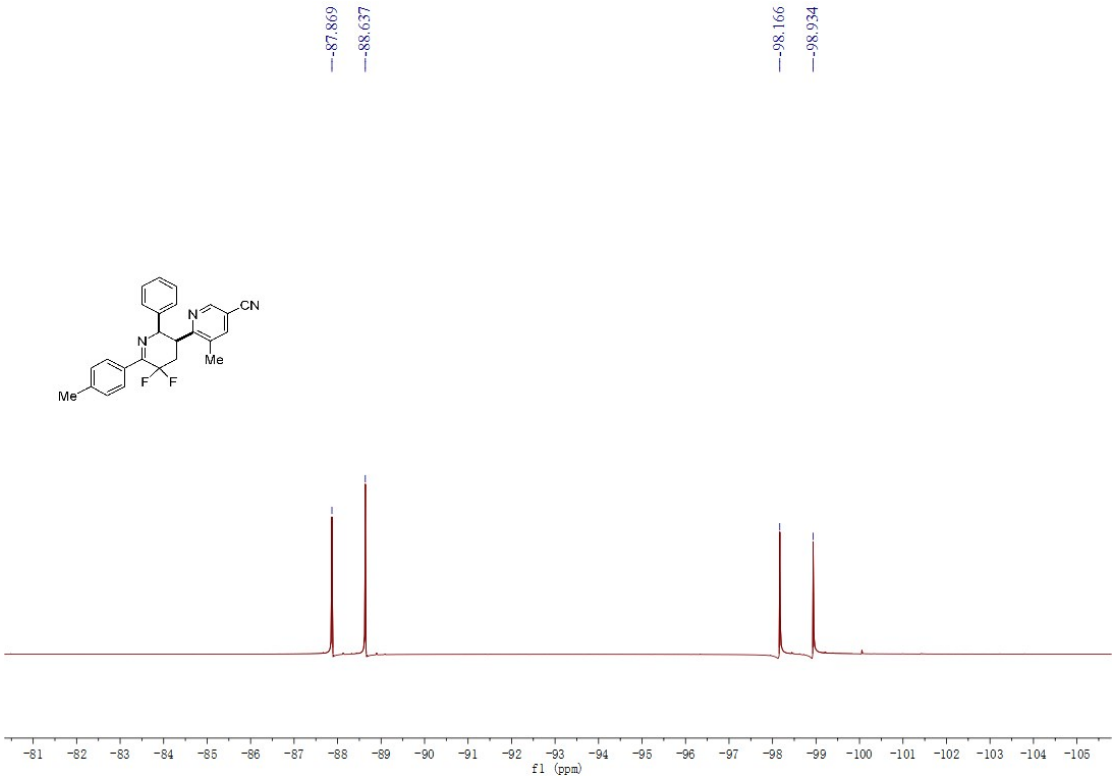
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



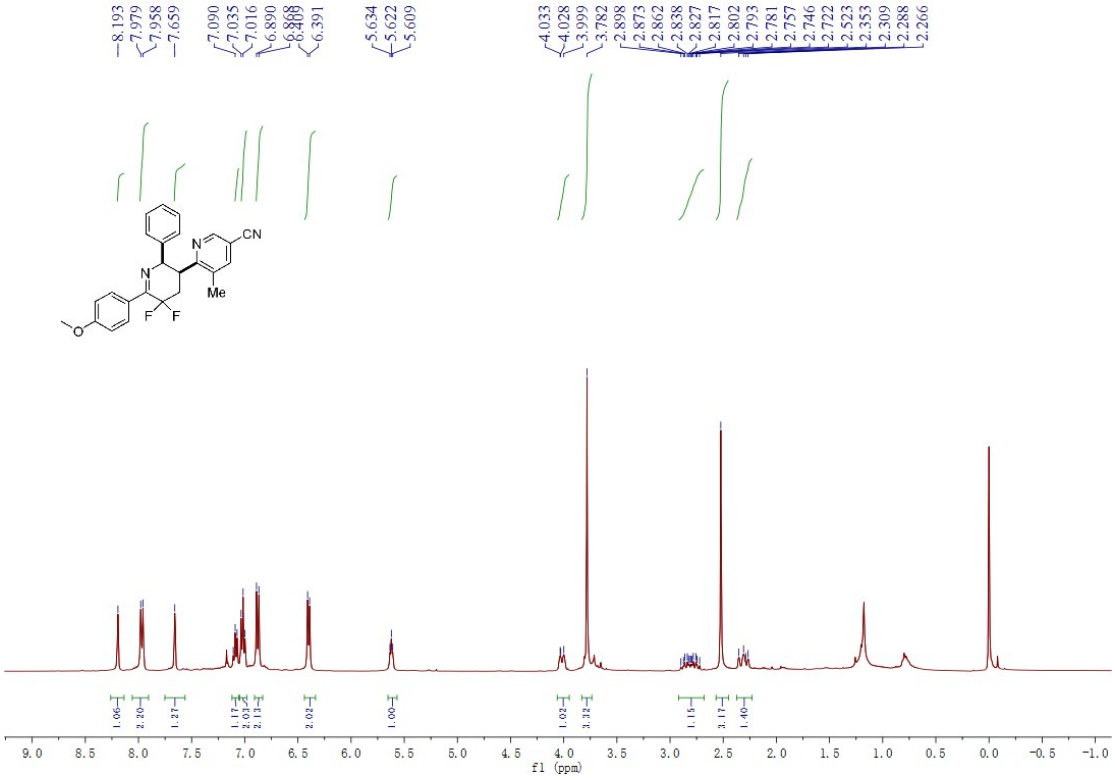
[^{19}F_NMR_375 MHz]



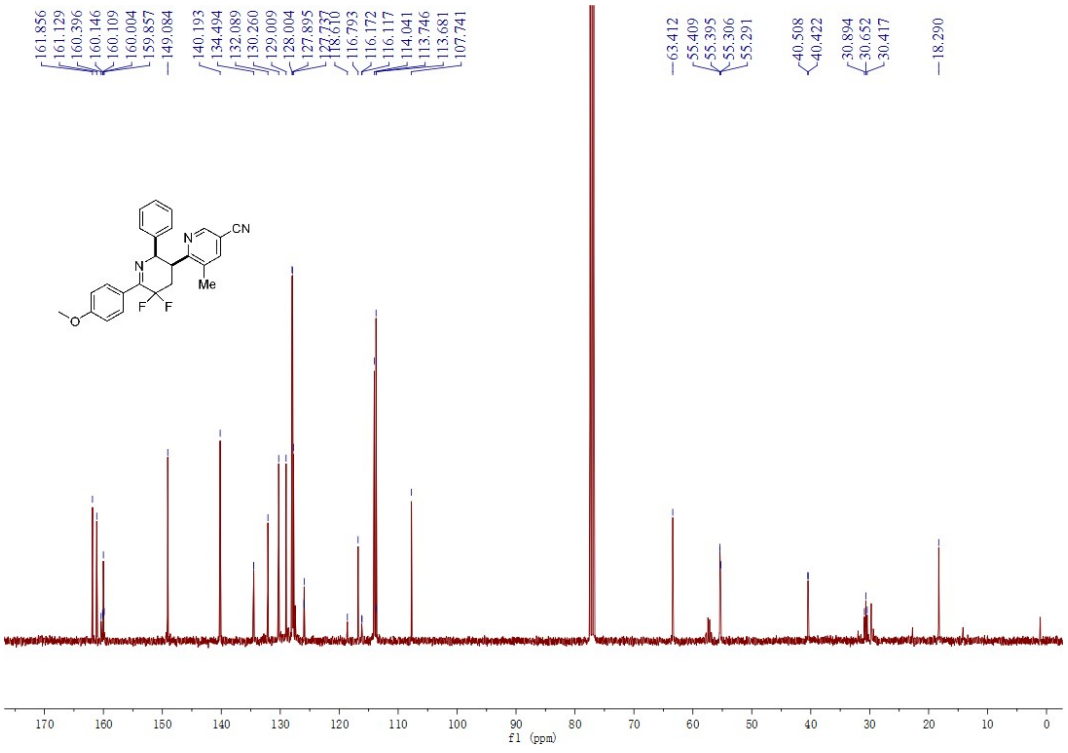
5',5'-Difluoro-6'-(4-methoxyphenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-

[2,3'-bipyridine]-5-carbonitrile (3q)

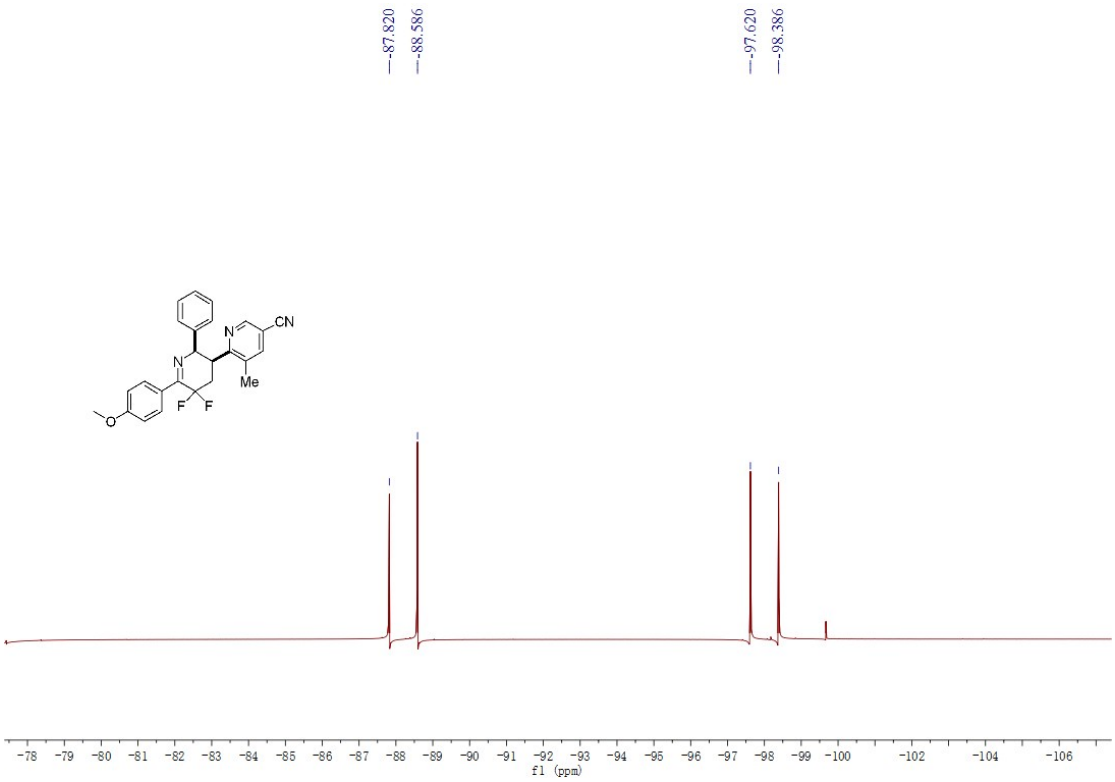
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



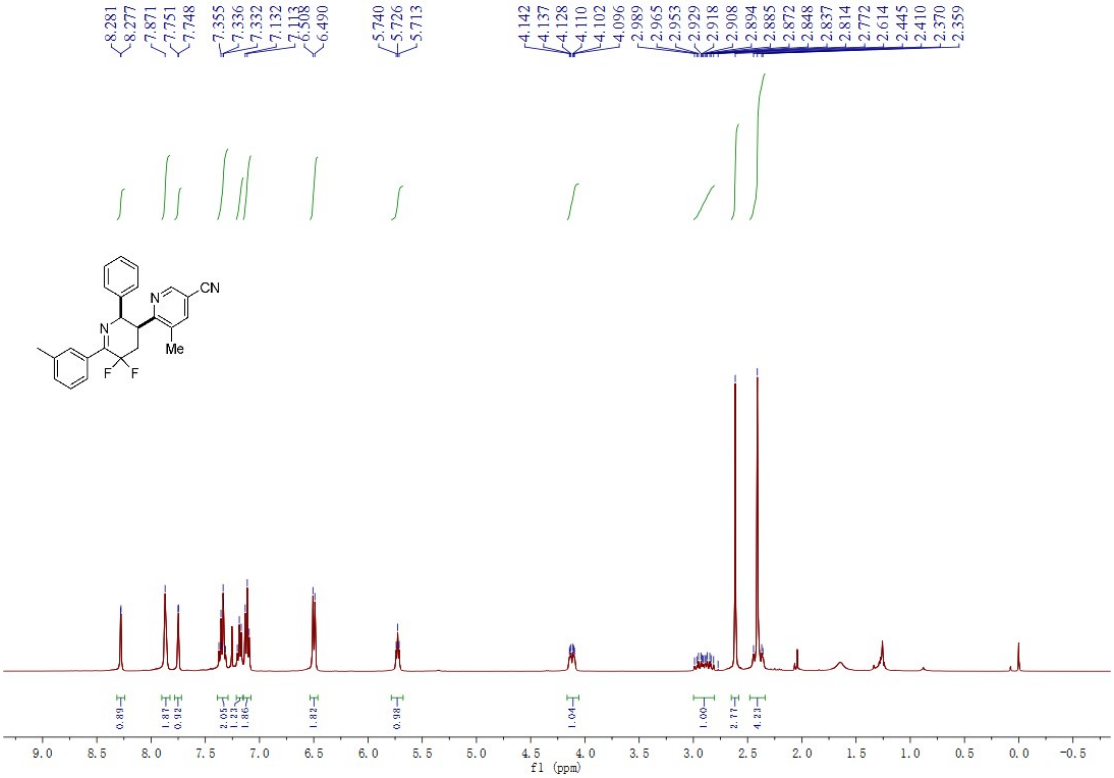
[^{19}F_NMR_375 MHz]



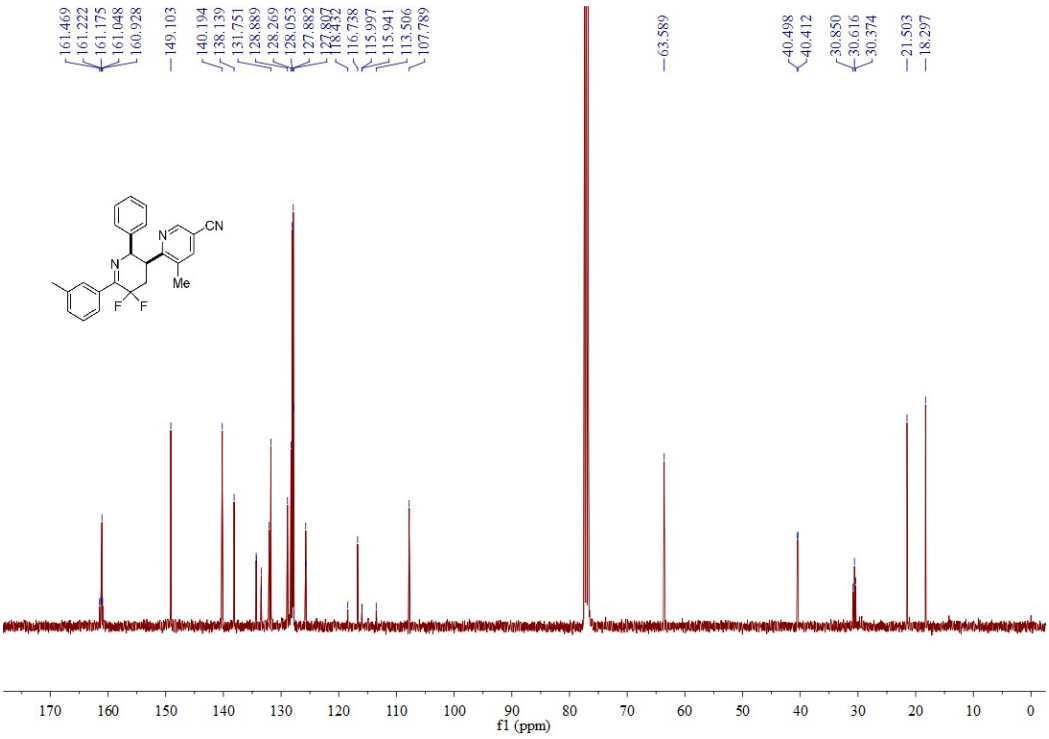
5',5'-Difluoro-3-methyl-2'-phenyl-6'-(m-tolyl)-2',3',4',5'-tetrahydro-[2,3'-

bipyridine]-5-carbonitrile (3r)

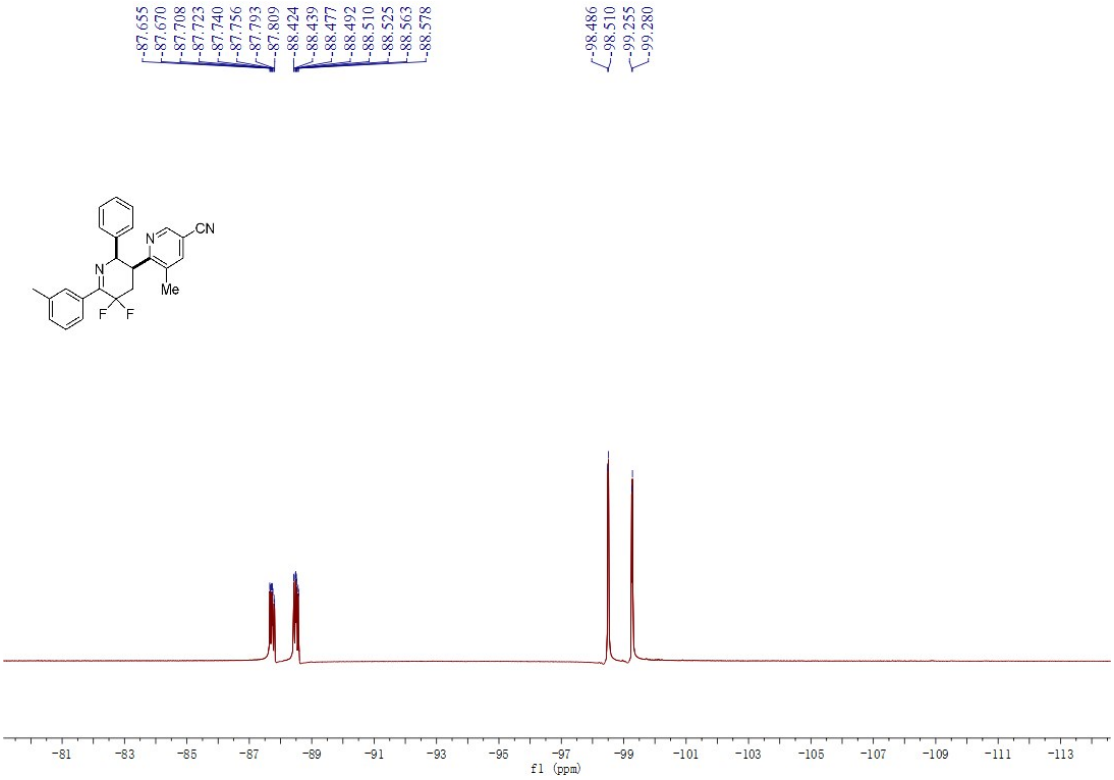
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



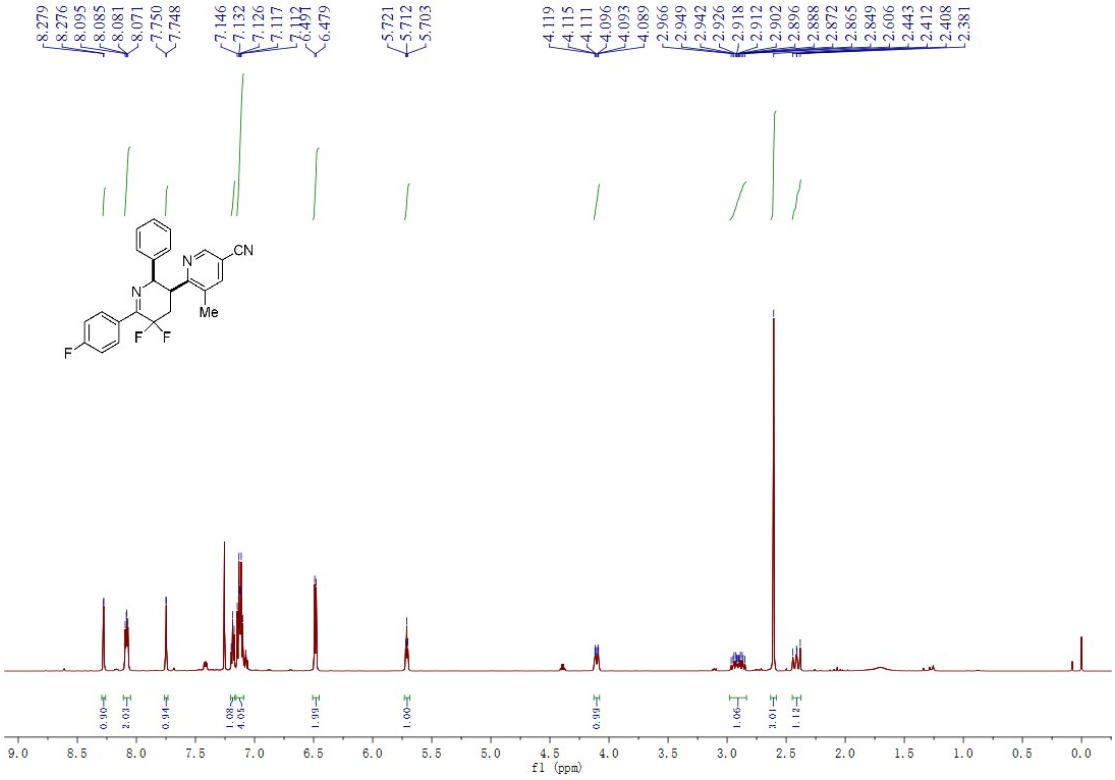
[^{19}F_NMR_375 MHz]



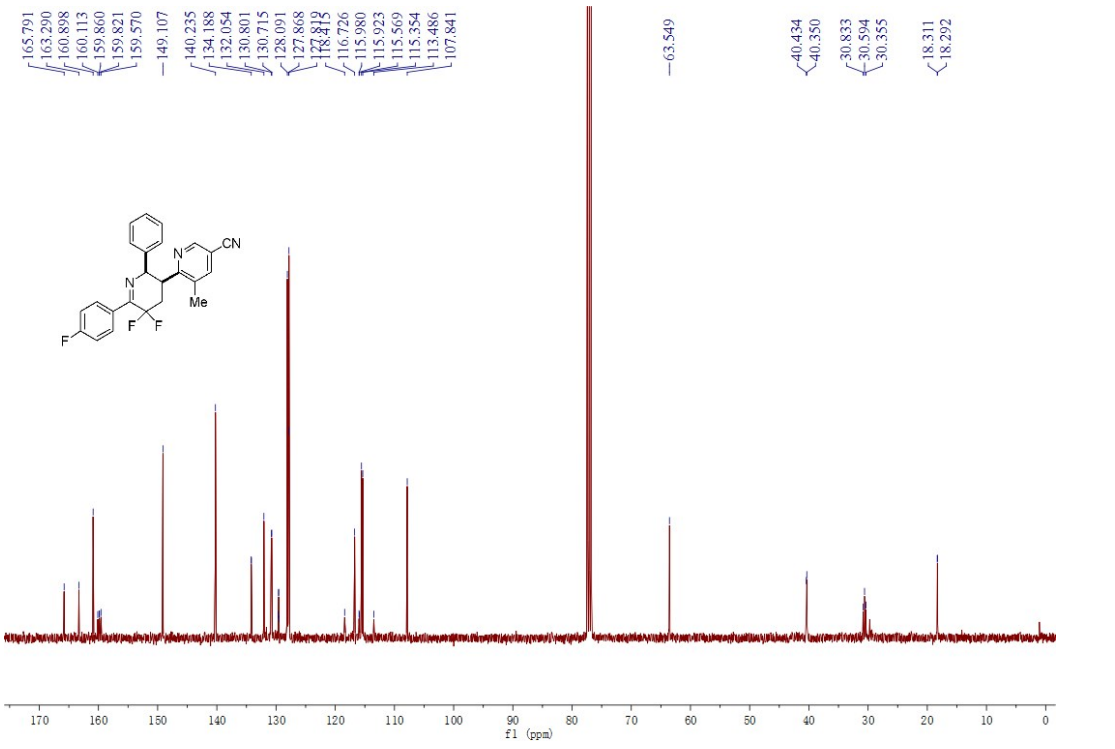
5',5'-Difluoro-6'-(4-fluorophenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-

bipyridine]-5-carbonitrile (3s)

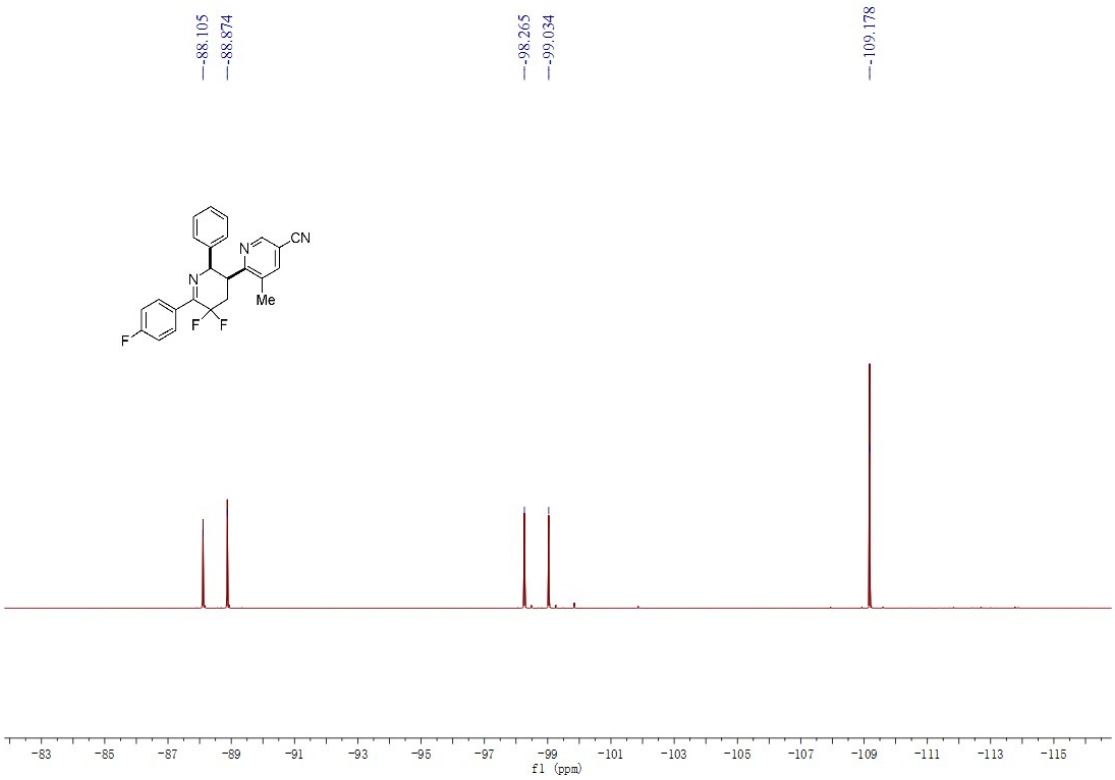
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



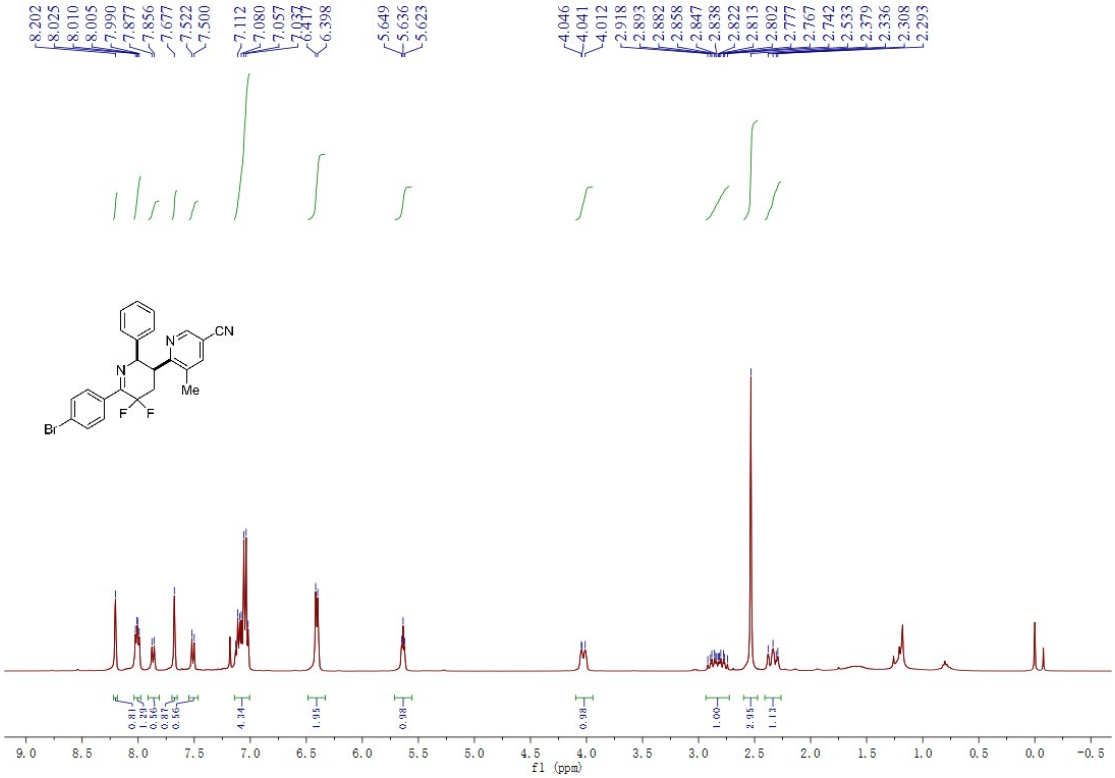
[^{19}F_NMR_375 MHz]



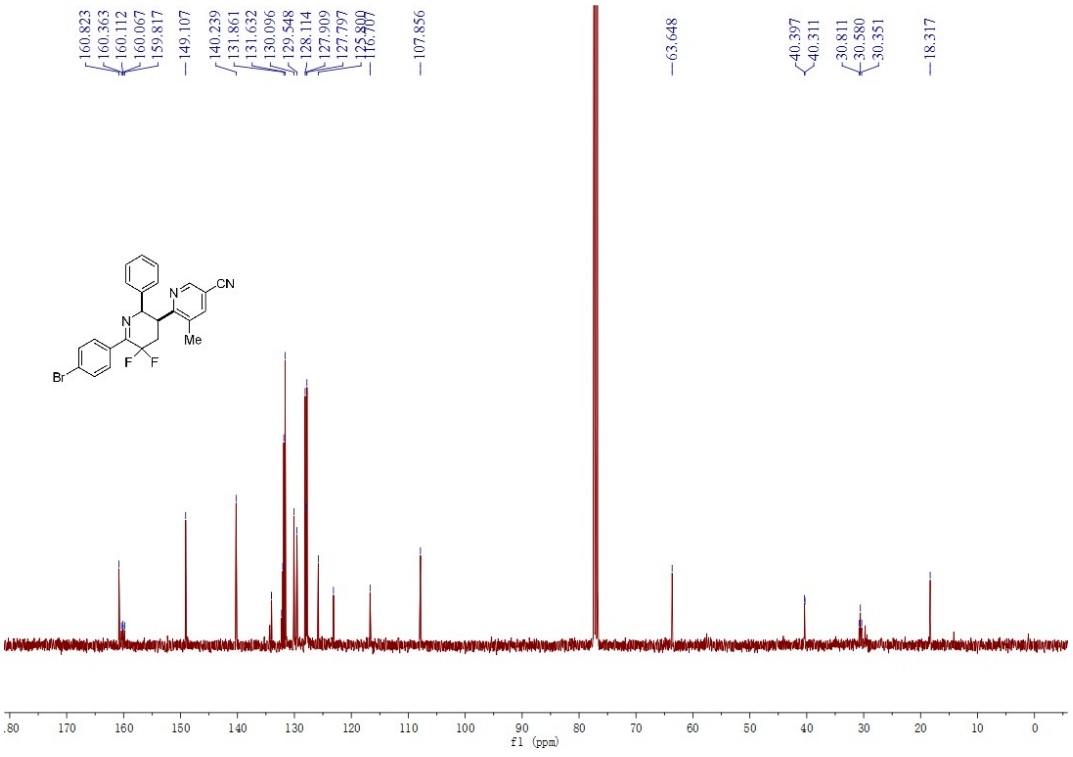
6'-(4-Bromophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-

bipyridine]-5-carbonitrile (3t)

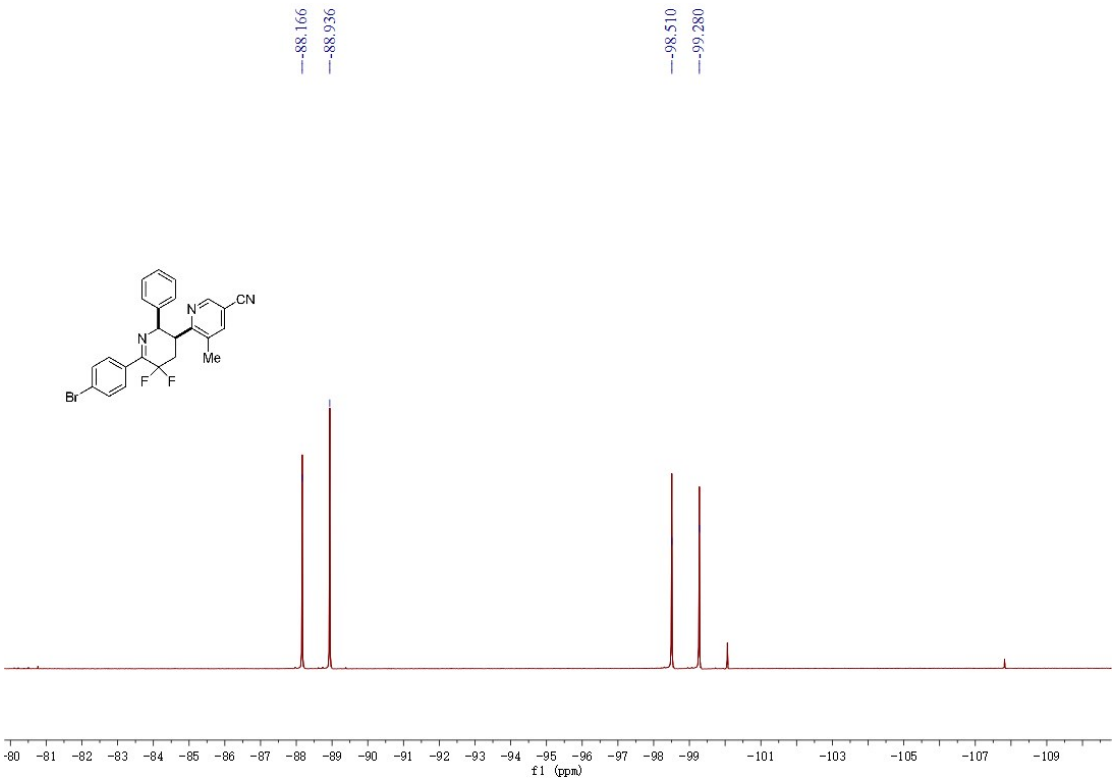
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



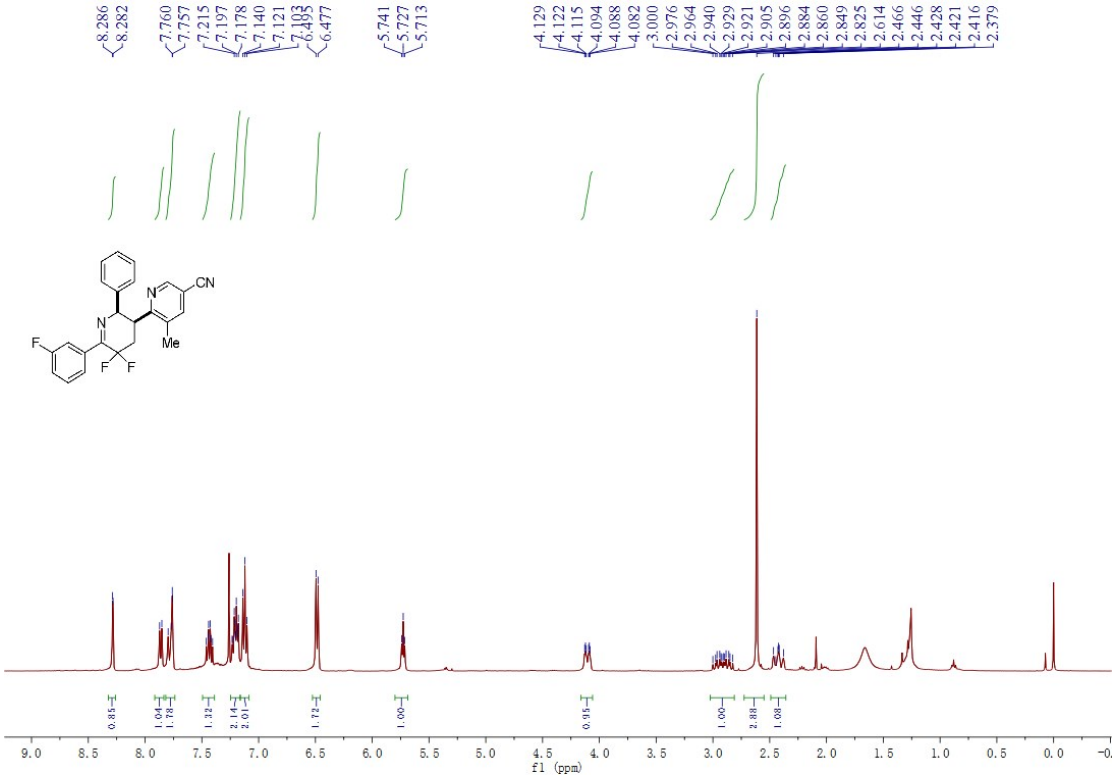
[^{19}F_NMR_375 MHz]



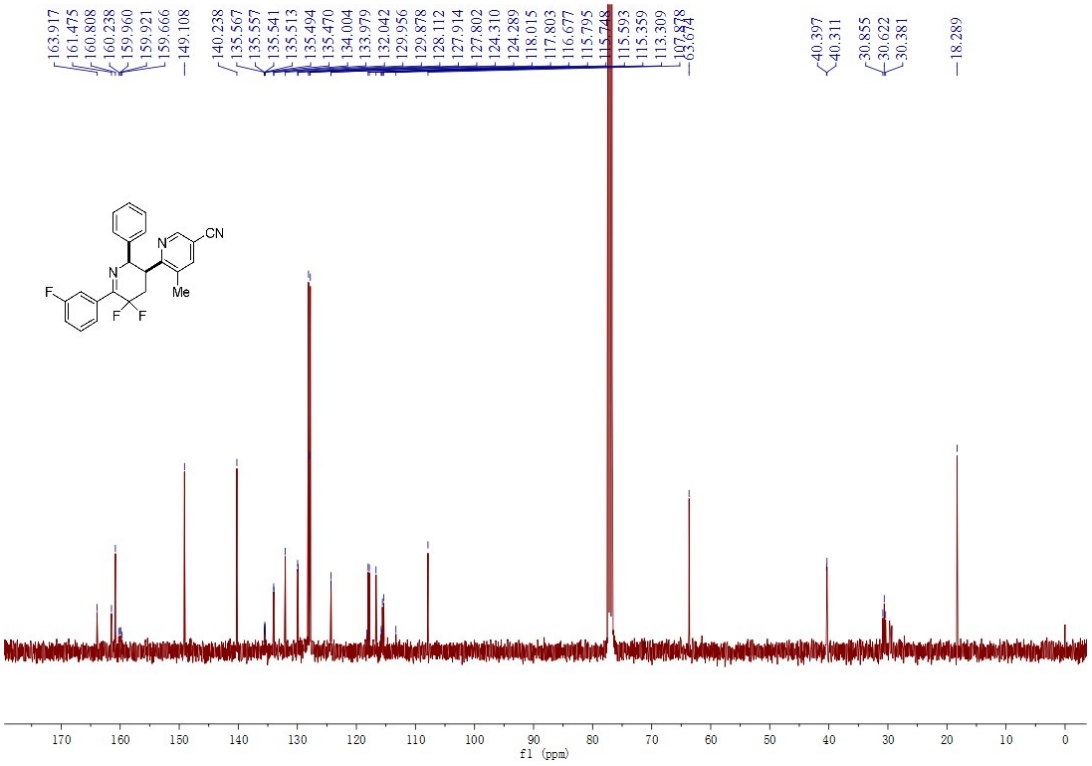
5',5'-Difluoro-6'-(3-fluorophenyl)-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-

bipyridine]-5-carbonitrile (3u)

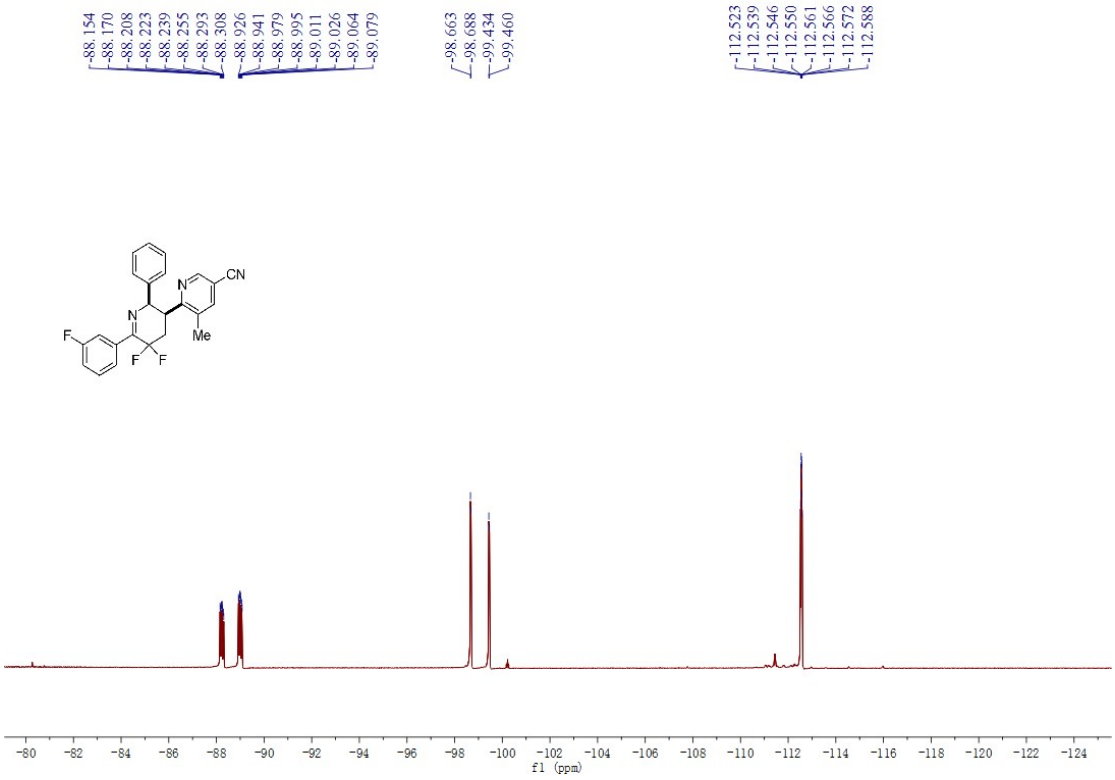
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

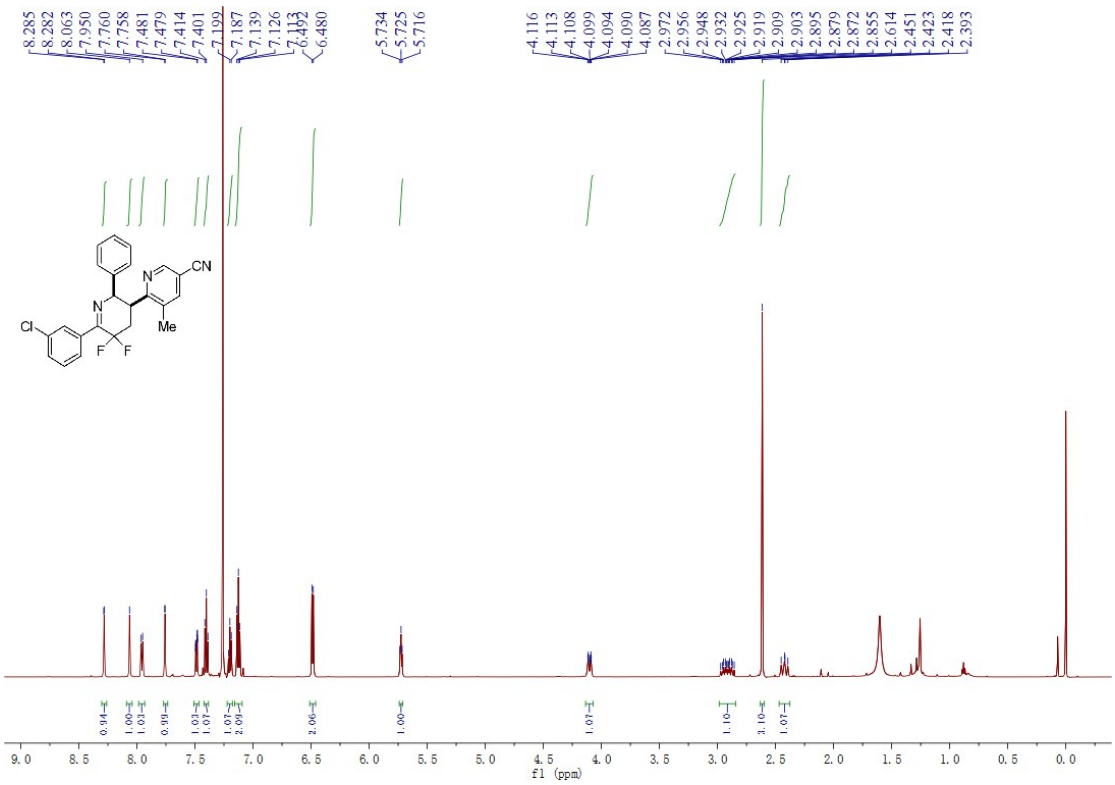


[^{19}F_NMR_375 MHz]

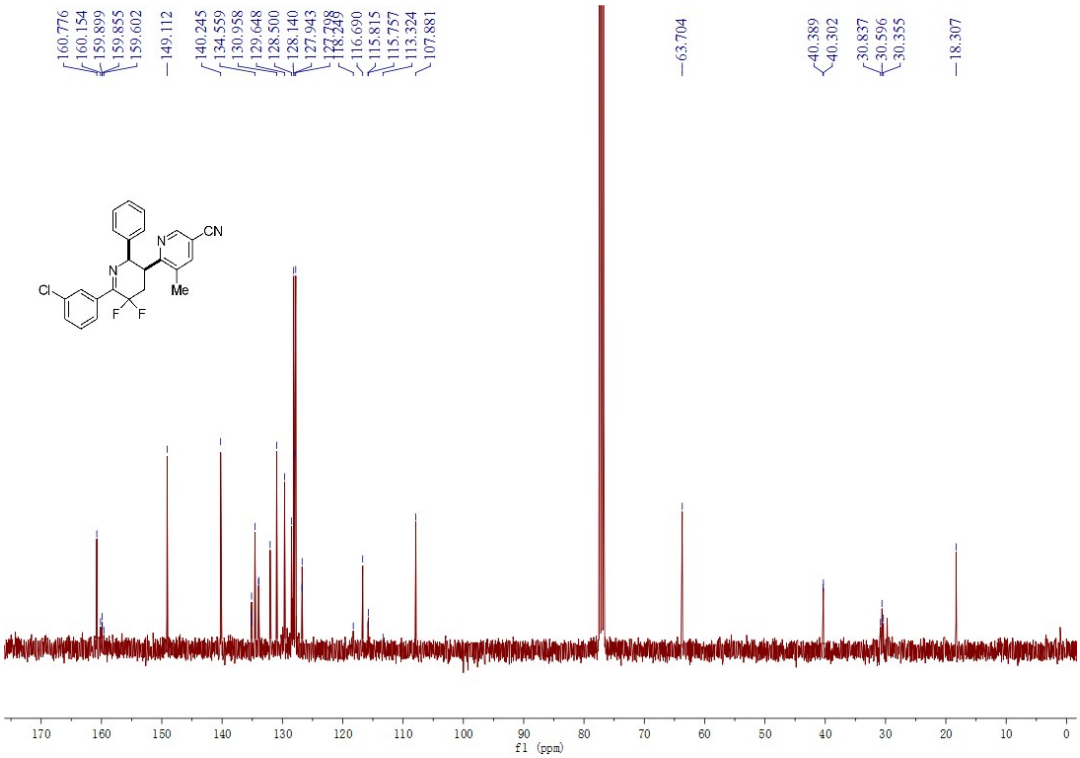


6'-(3-Chlorophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3v)

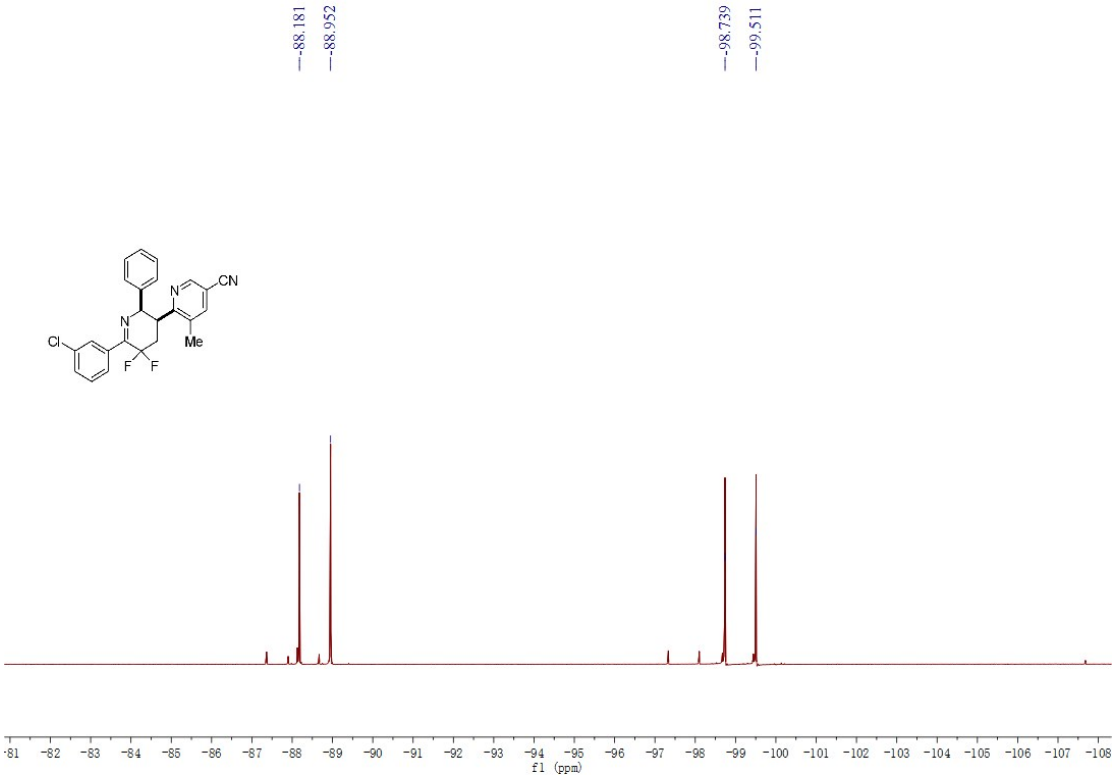
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

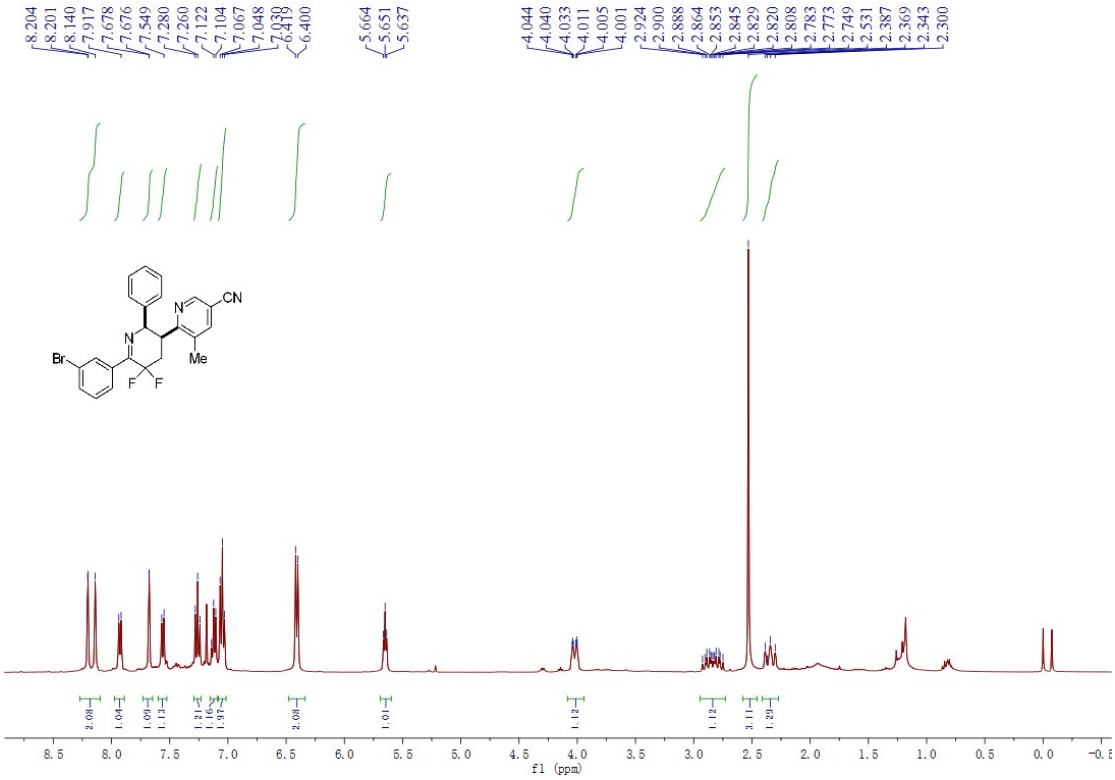


[^{19}F_NMR_375 MHz]

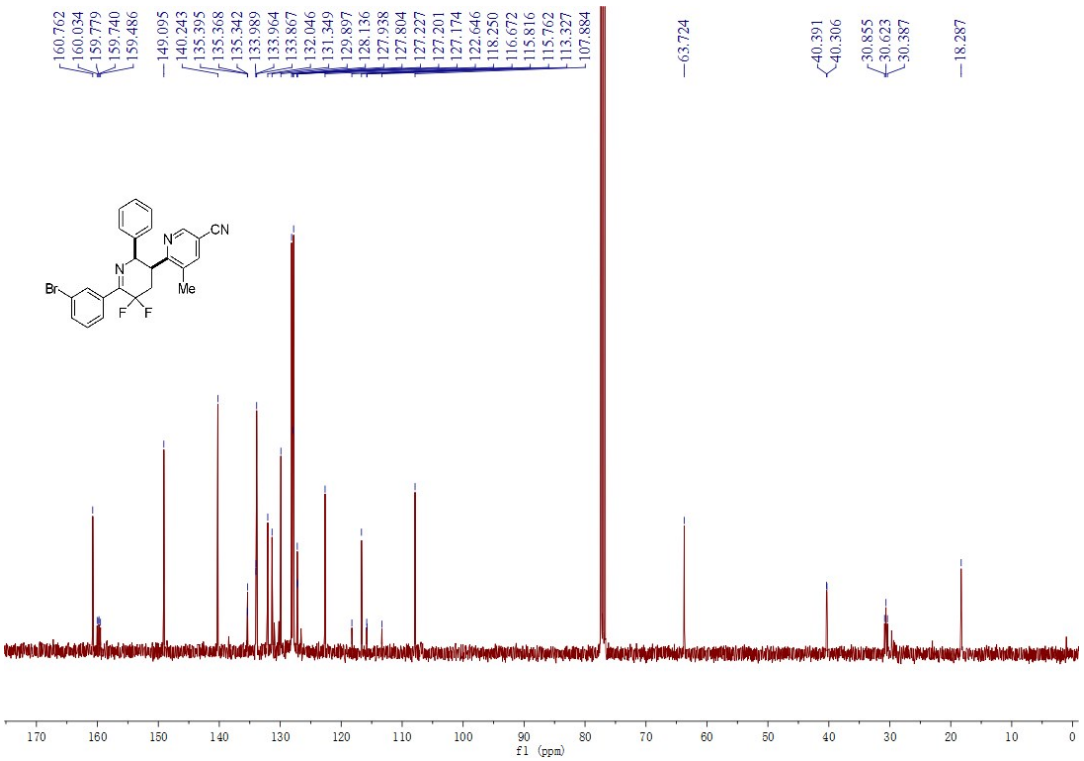


6'-(3-Bromophenyl)-5',5'-difluoro-3-methyl-2'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3w)

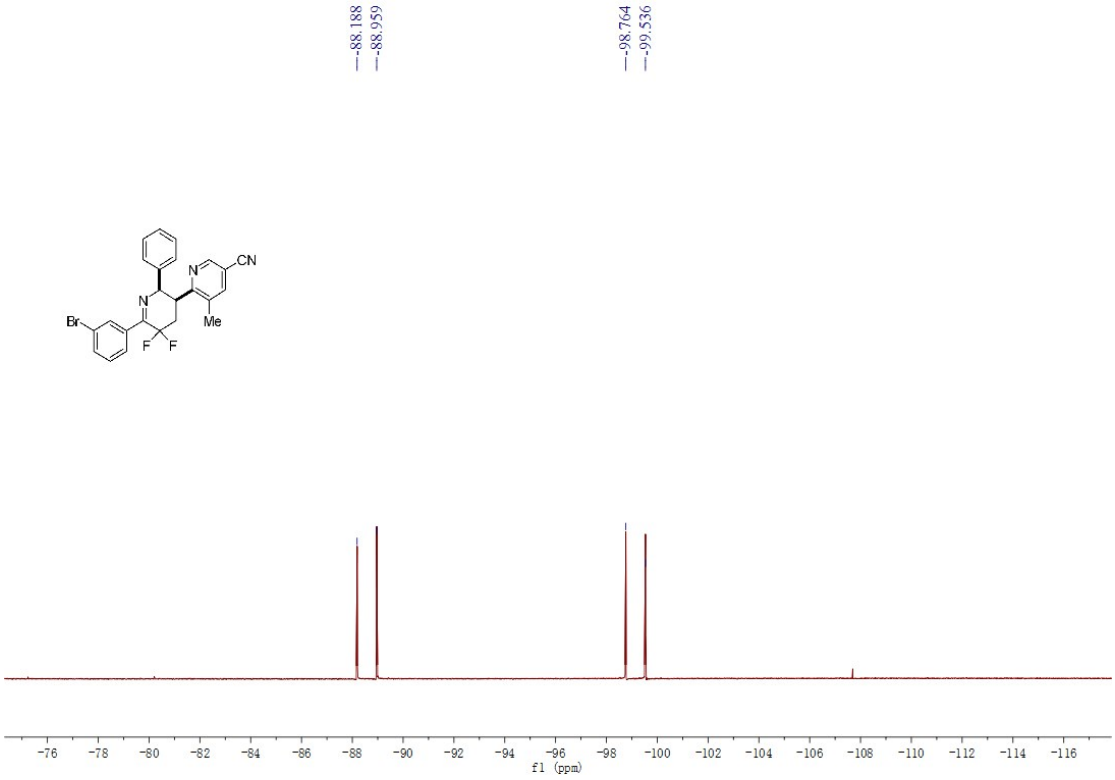
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

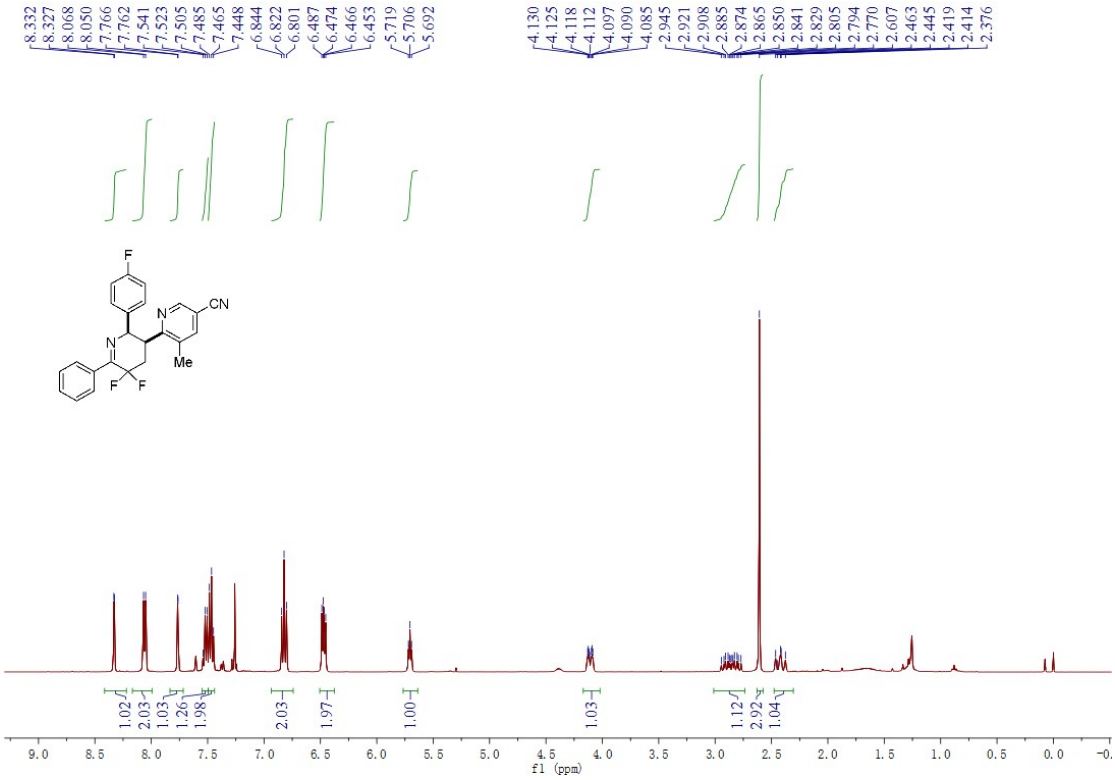


[^{19}F_NMR_375 MHz]

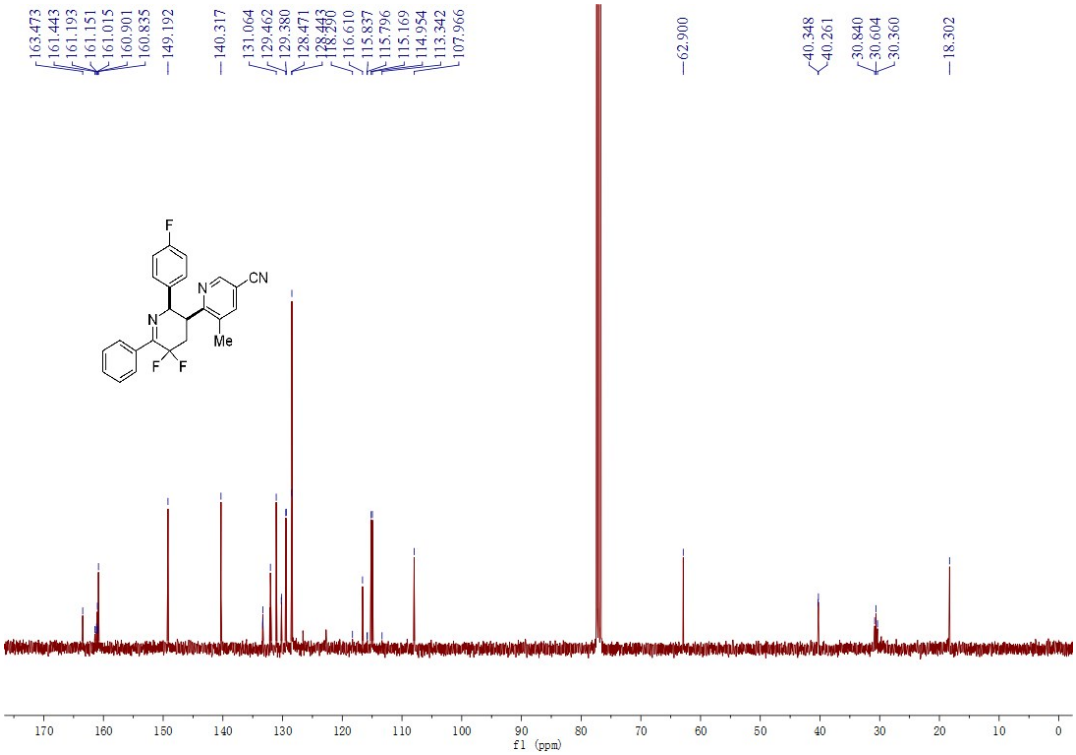


5',5'-Difluoro-2'-(4-fluorophenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3x)

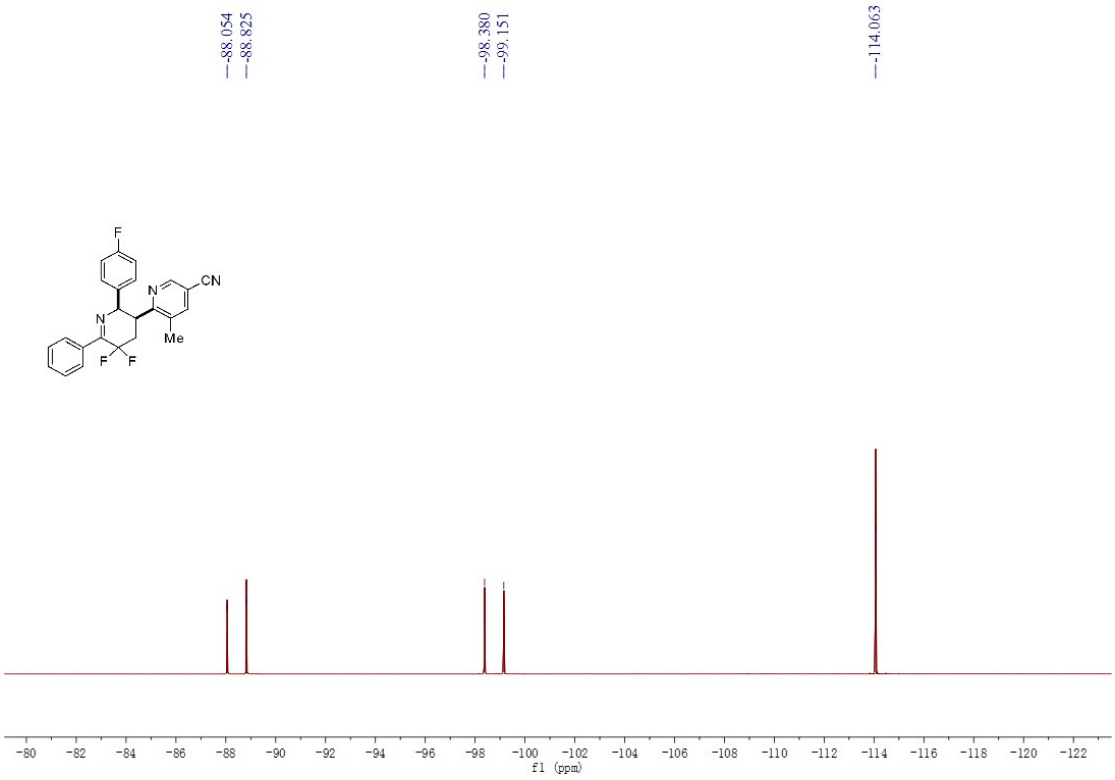
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

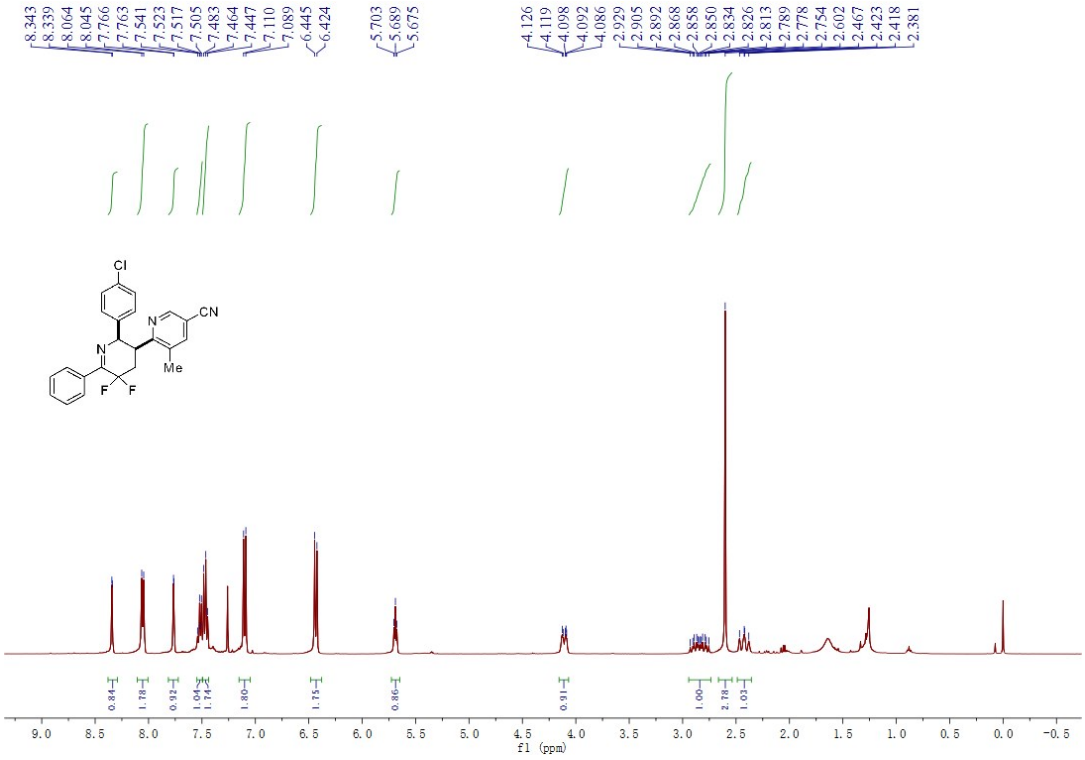


[^{19}F_NMR_375 MHz]

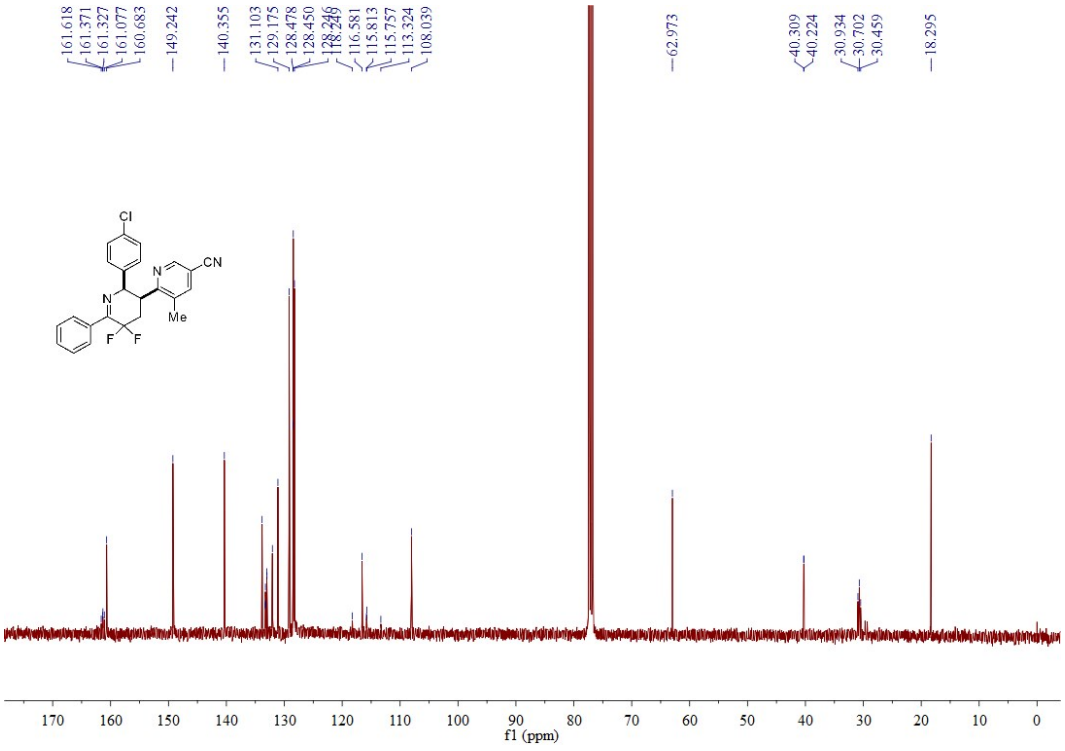


2'-(4-Chlorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3y)

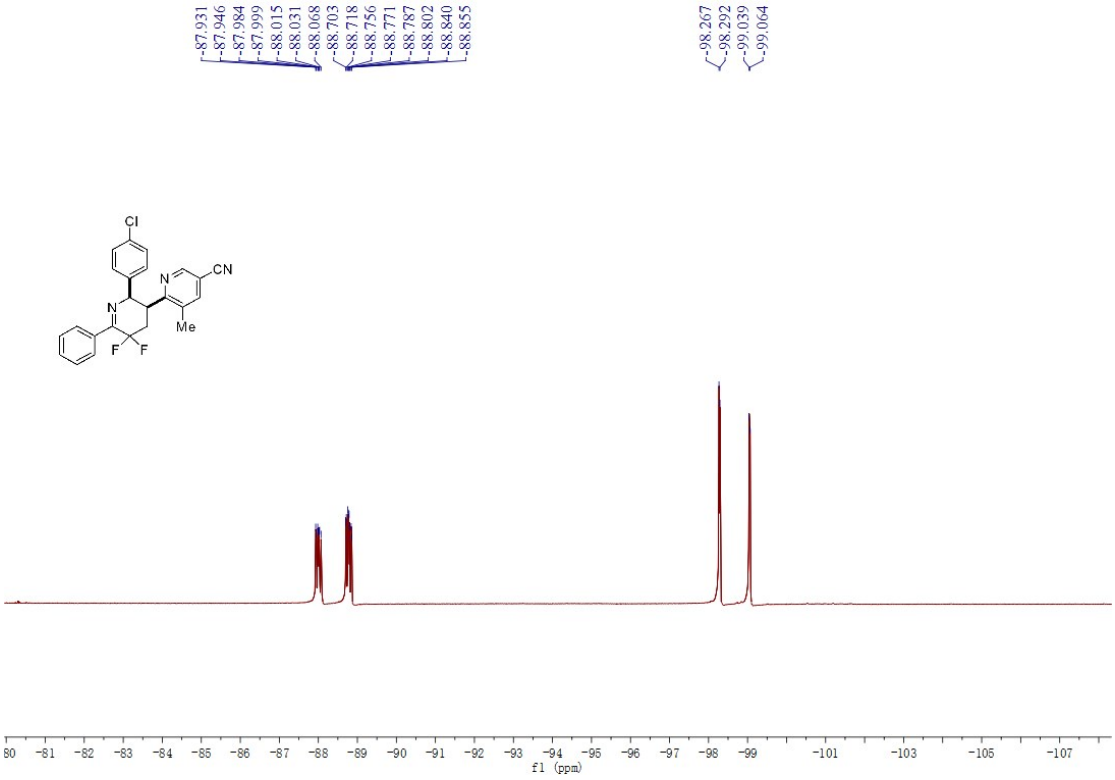
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

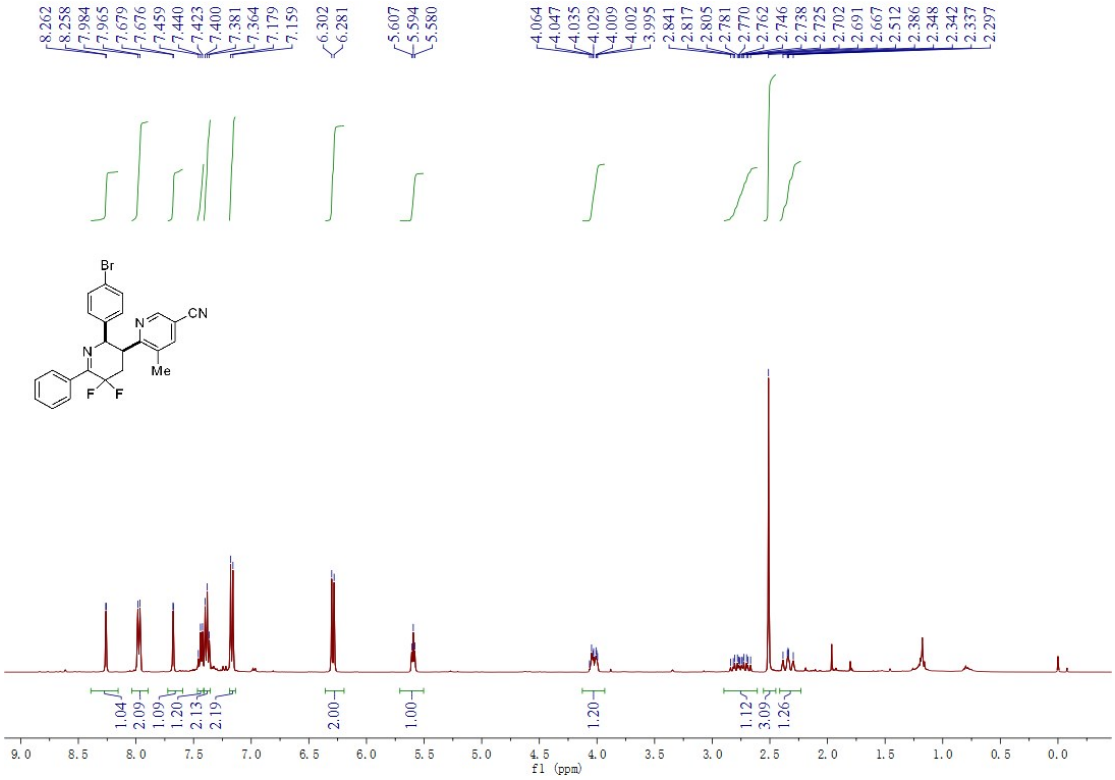


[^{19}F_NMR_375 MHz]

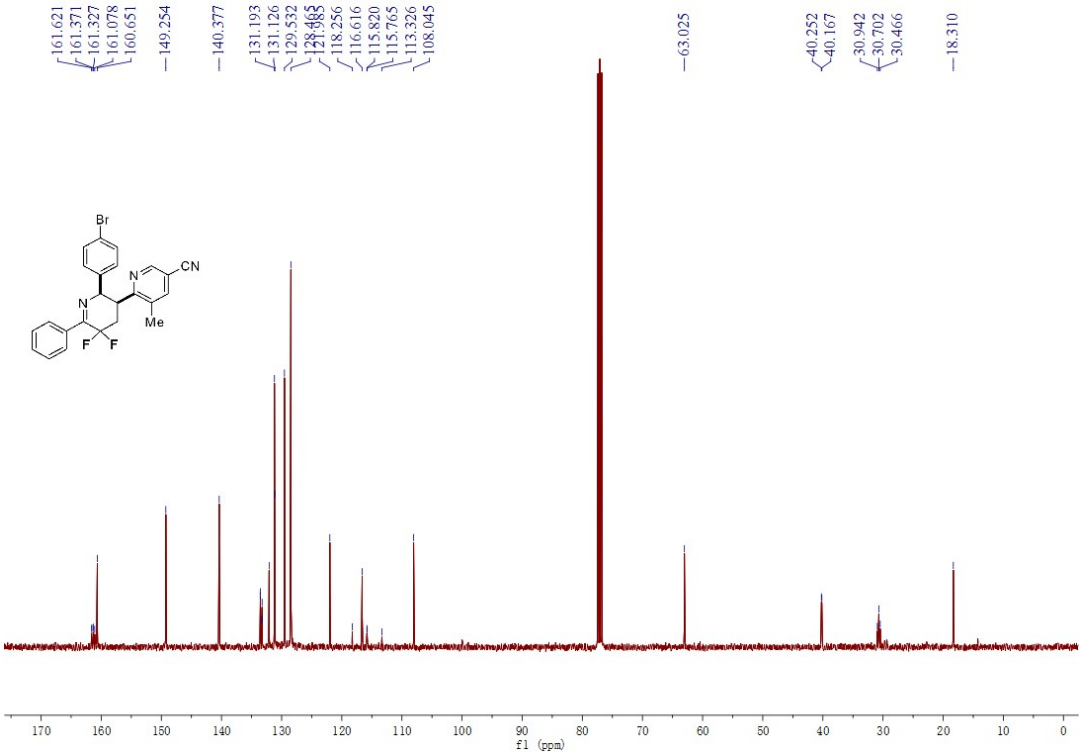


2'-(4-Bromophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3z)

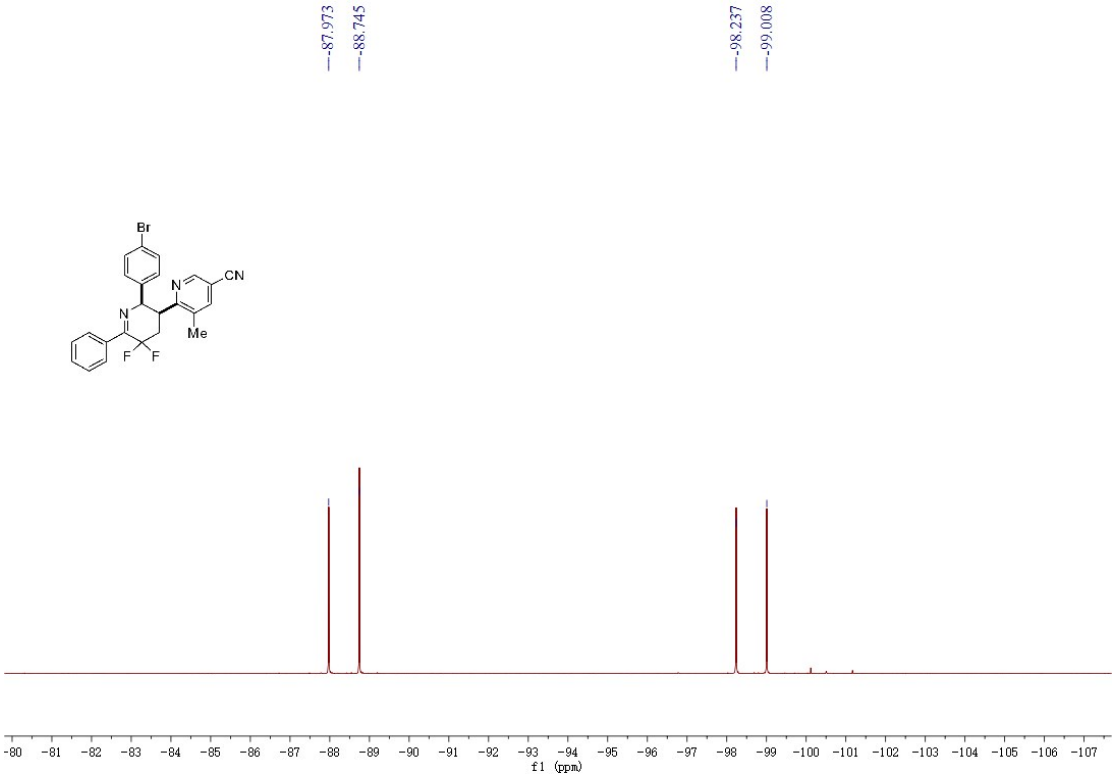
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

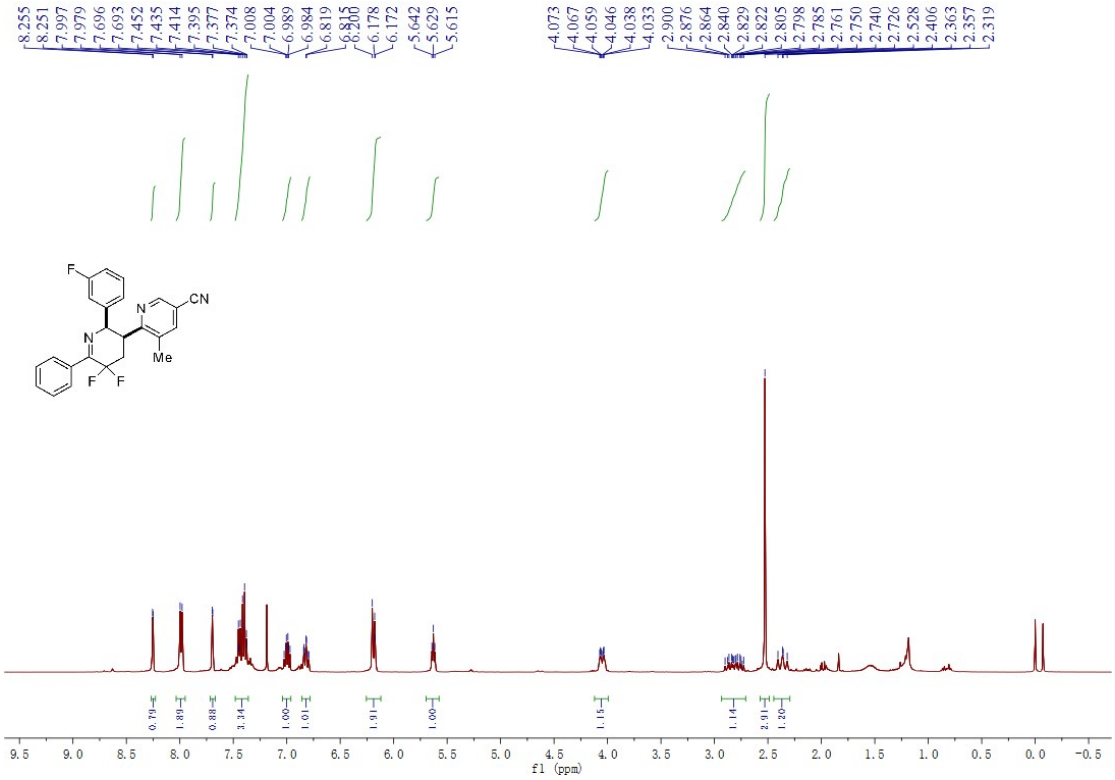


[^{19}F_NMR_375 MHz]

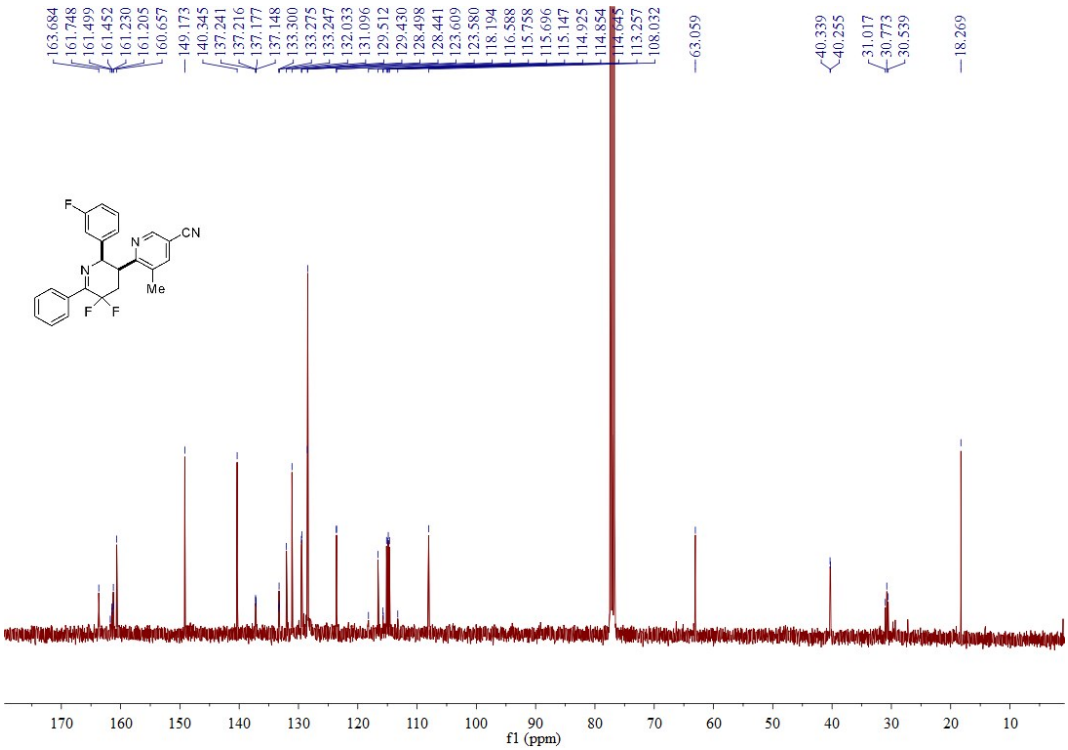


5',5'-Difluoro-2'-(3-fluorophenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3aa)

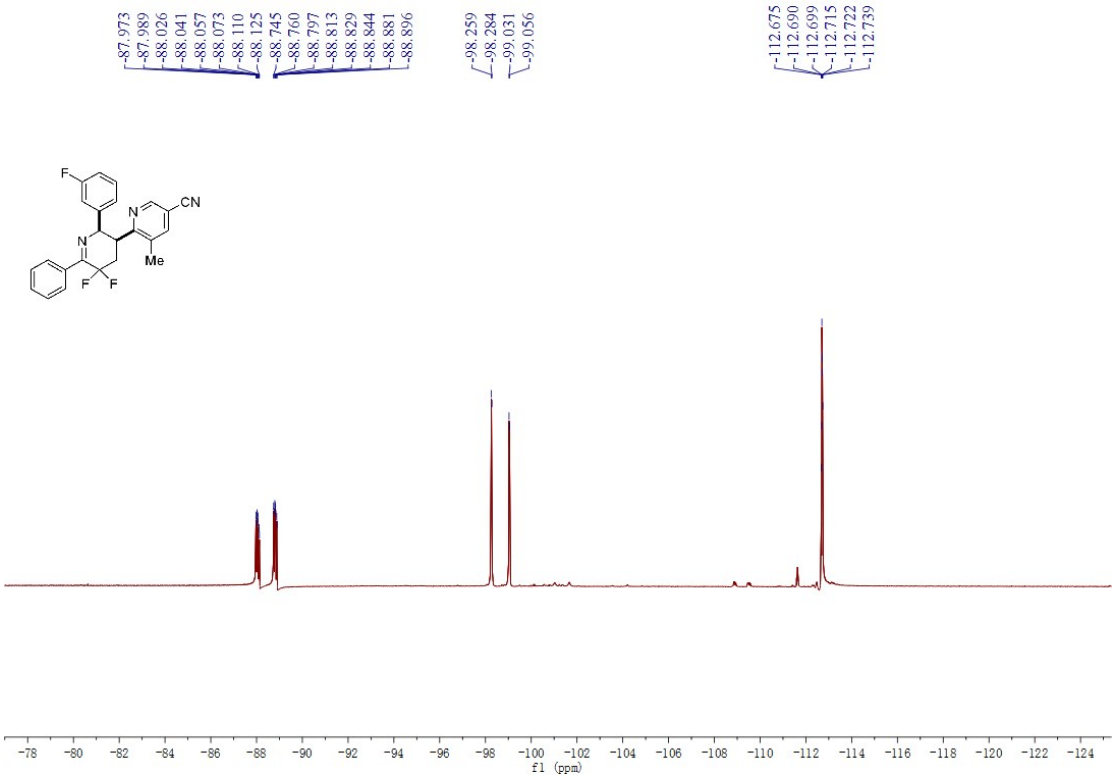
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

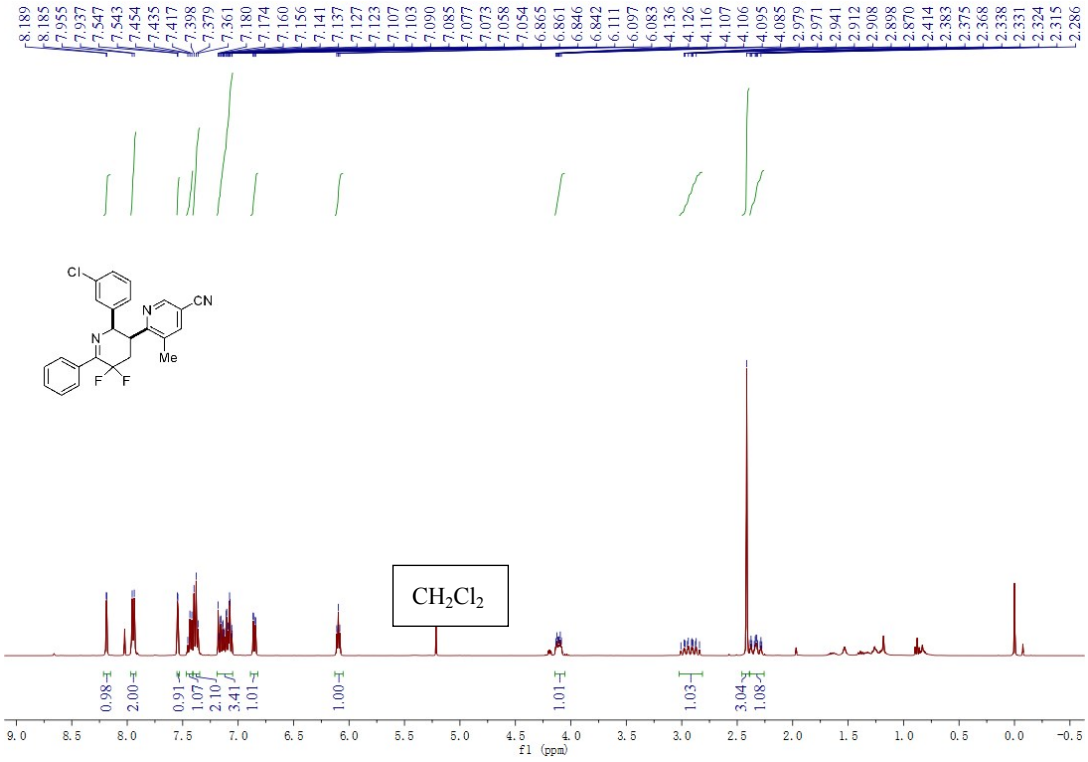


[^{19}F_NMR_375 MHz]

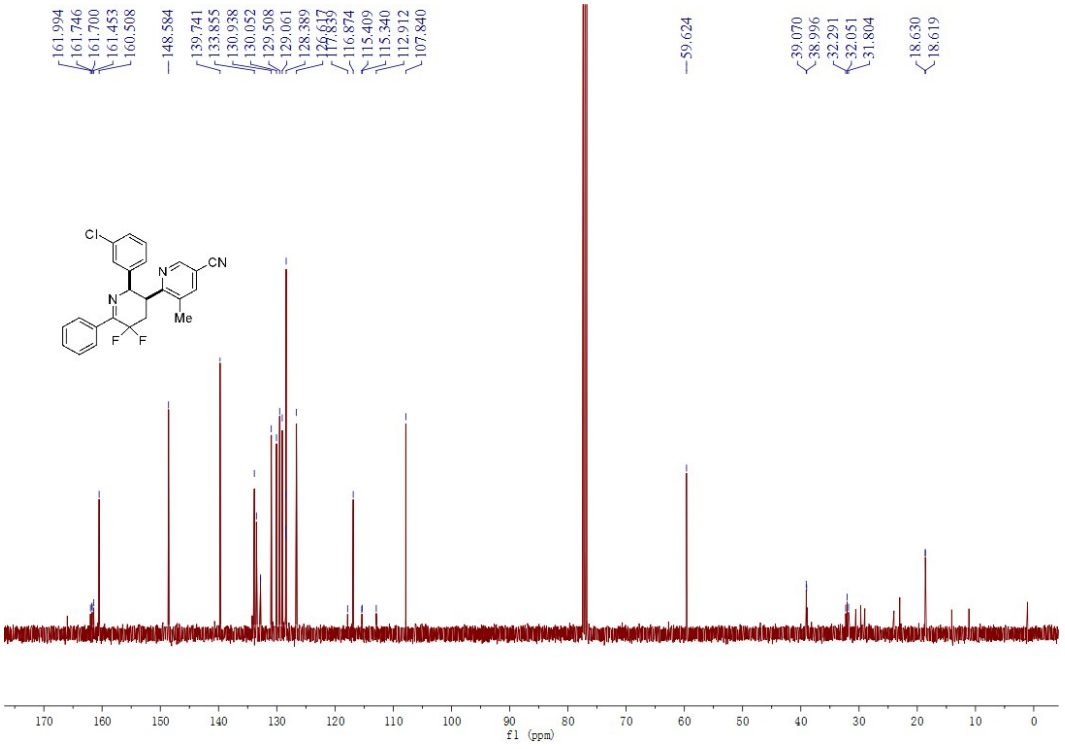


2'-(3-Chlorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3ab)

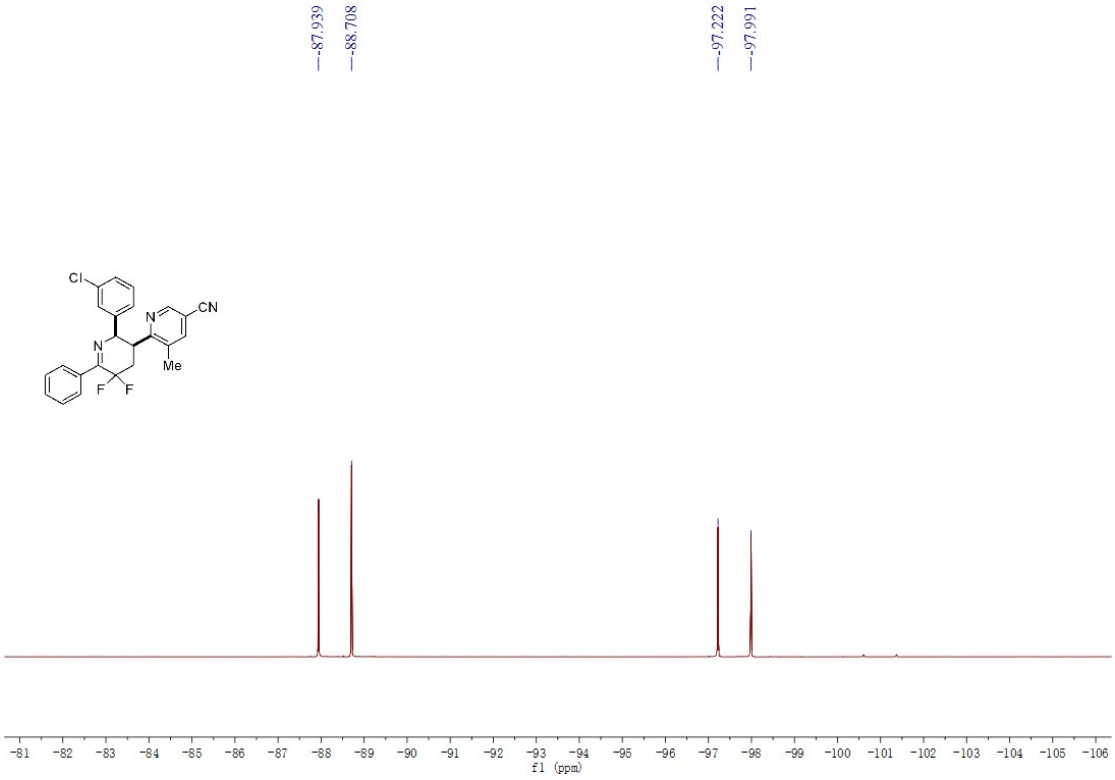
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

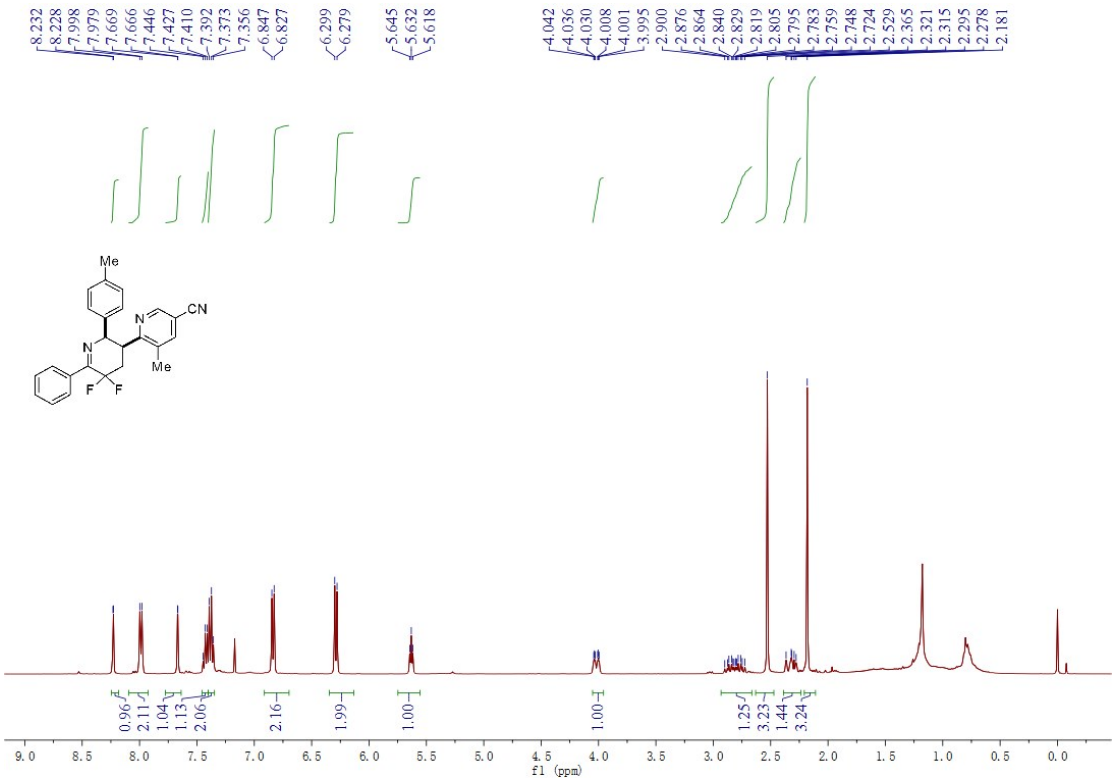


[^{19}F_NMR_375 MHz]

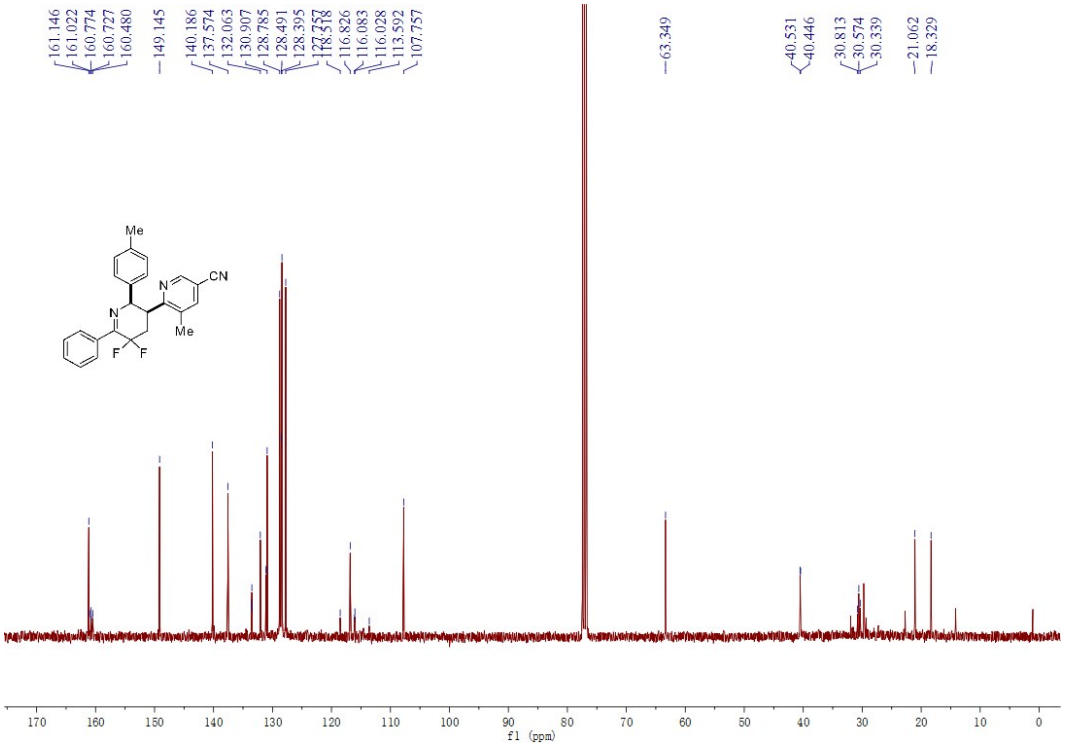


5',5'-Difluoro-3-methyl-6'-phenyl-2'-(p-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3ac)

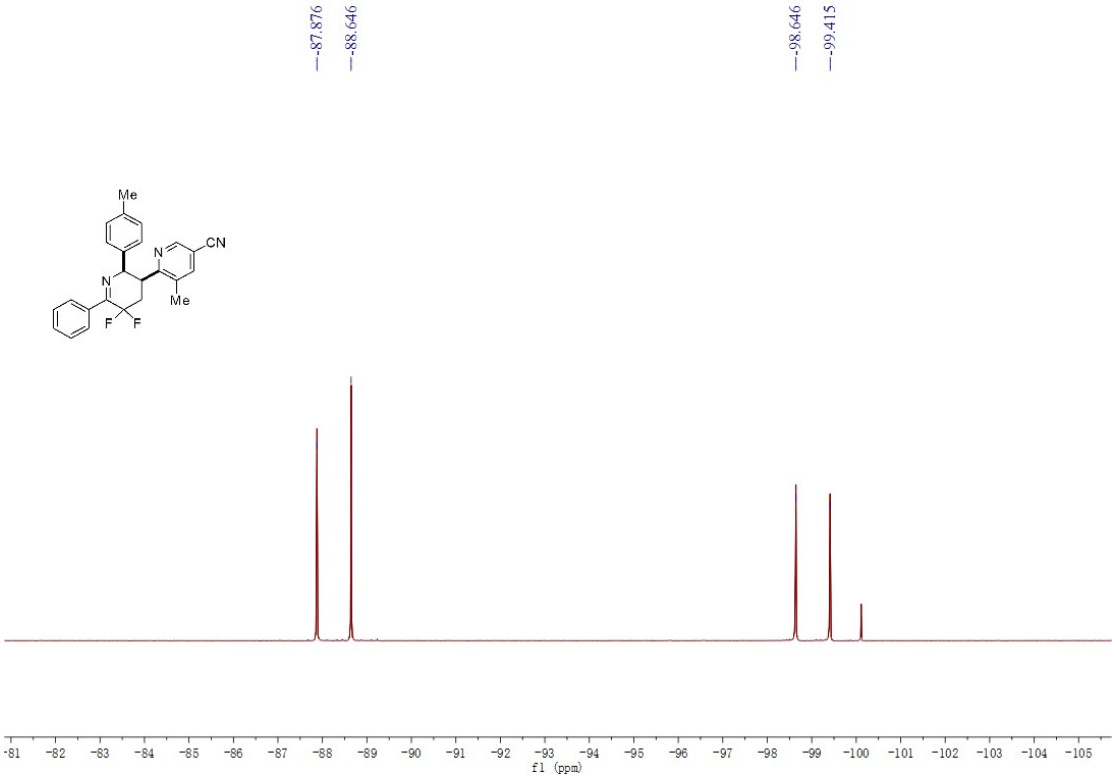
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

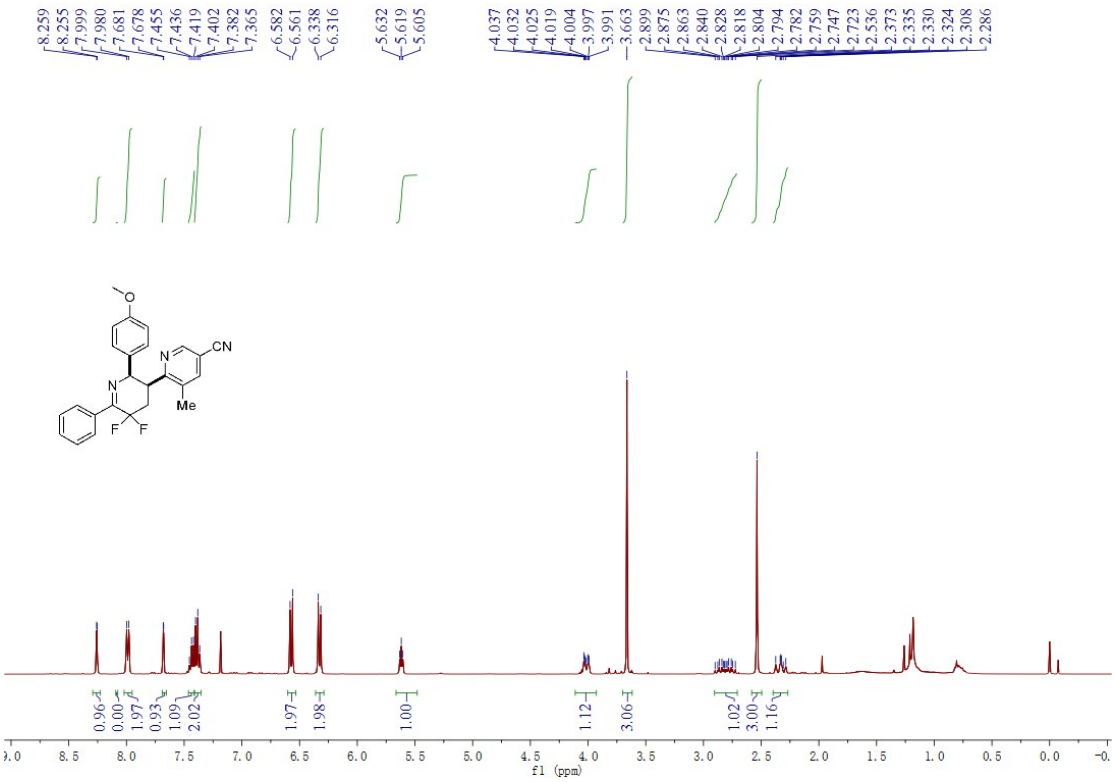


[^{19}F_NMR_375 MHz]

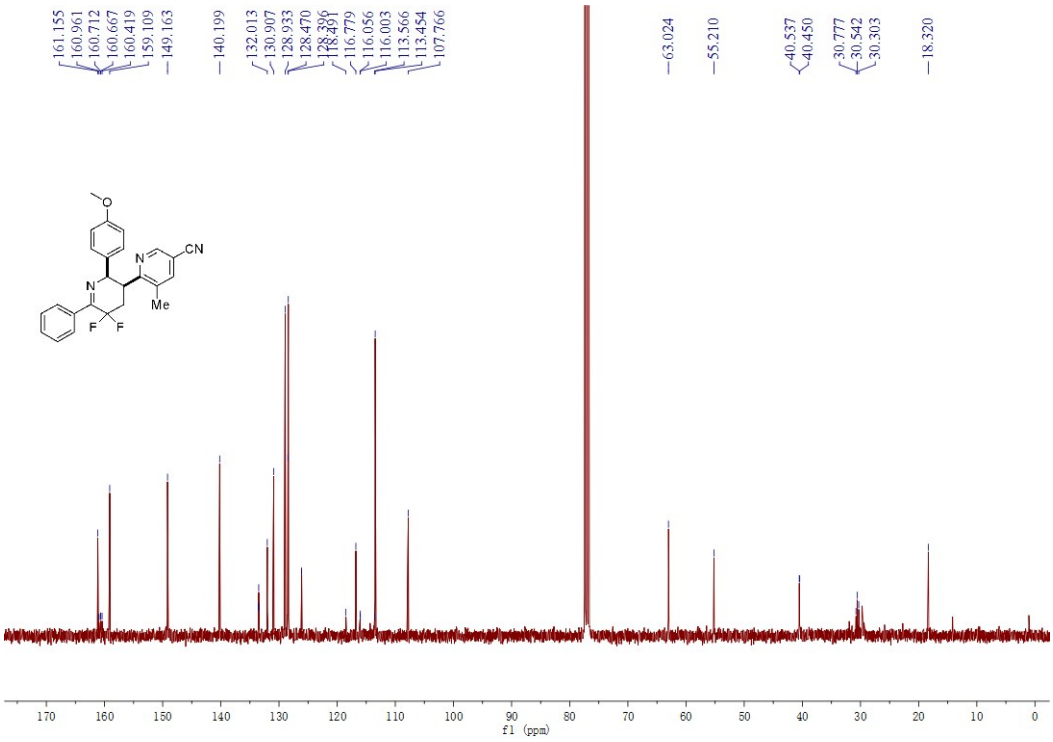


5',5'-Difluoro-2'-(4-methoxyphenyl)-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3ad)

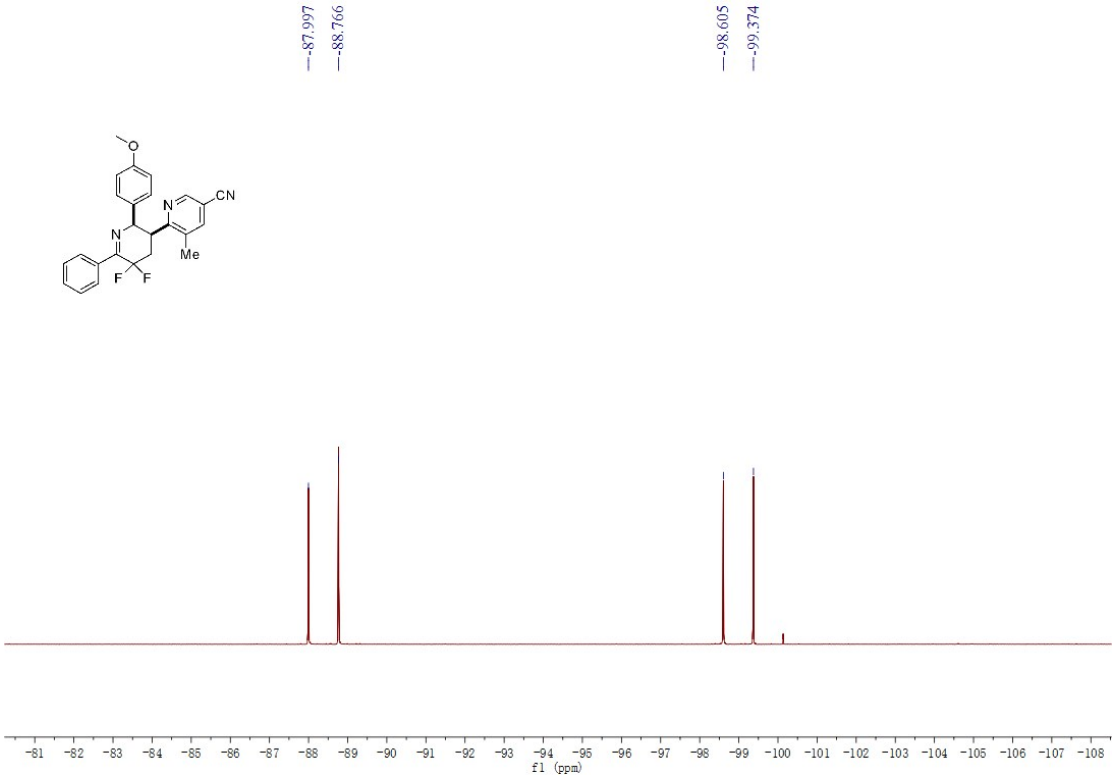
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

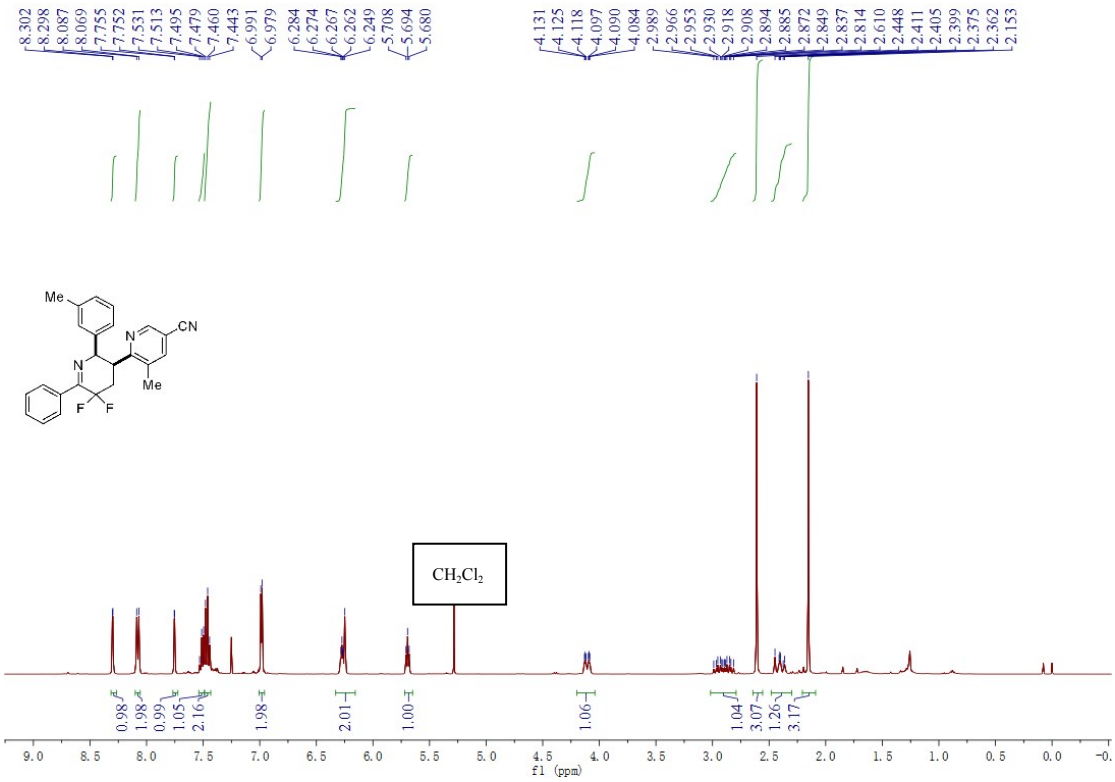


[^{19}F_NMR_375 MHz]

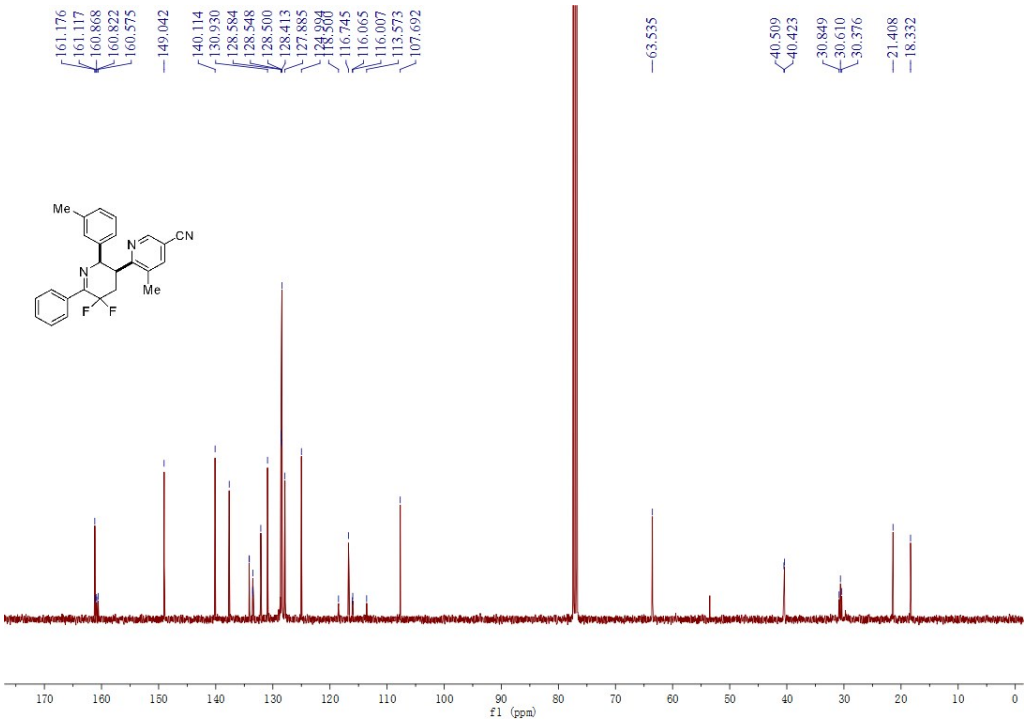


5',5'-Difluoro-3-methyl-6'-phenyl-2'-(m-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3ae)

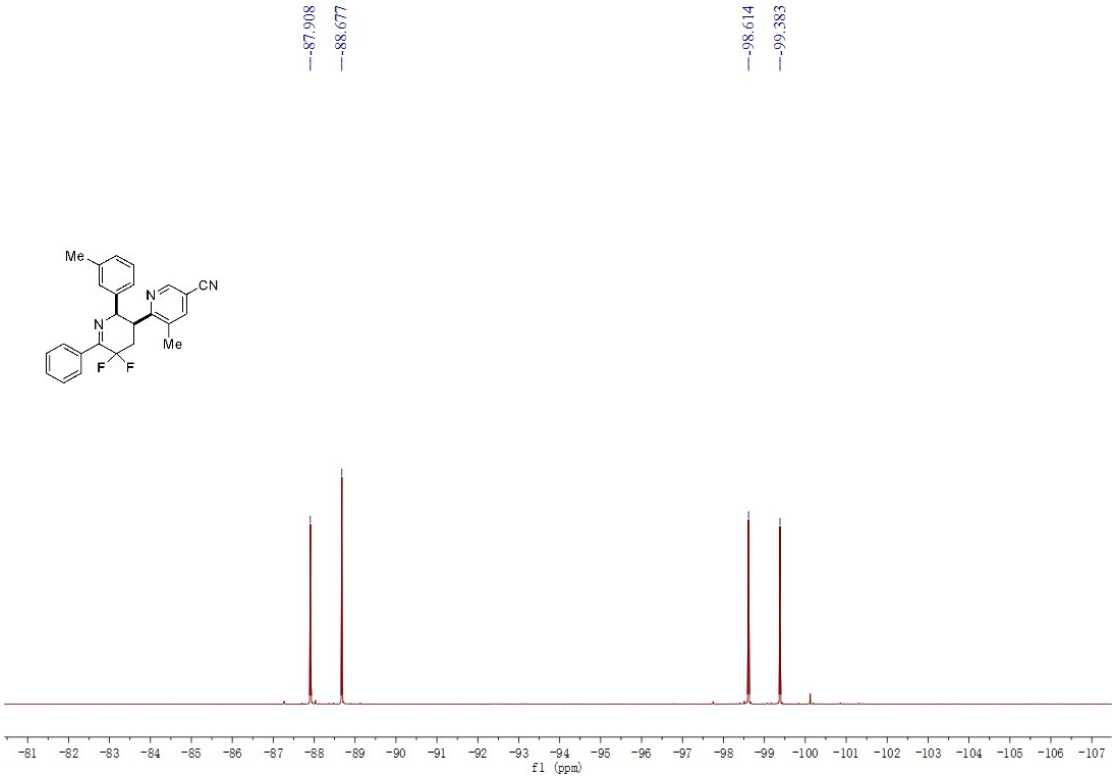
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

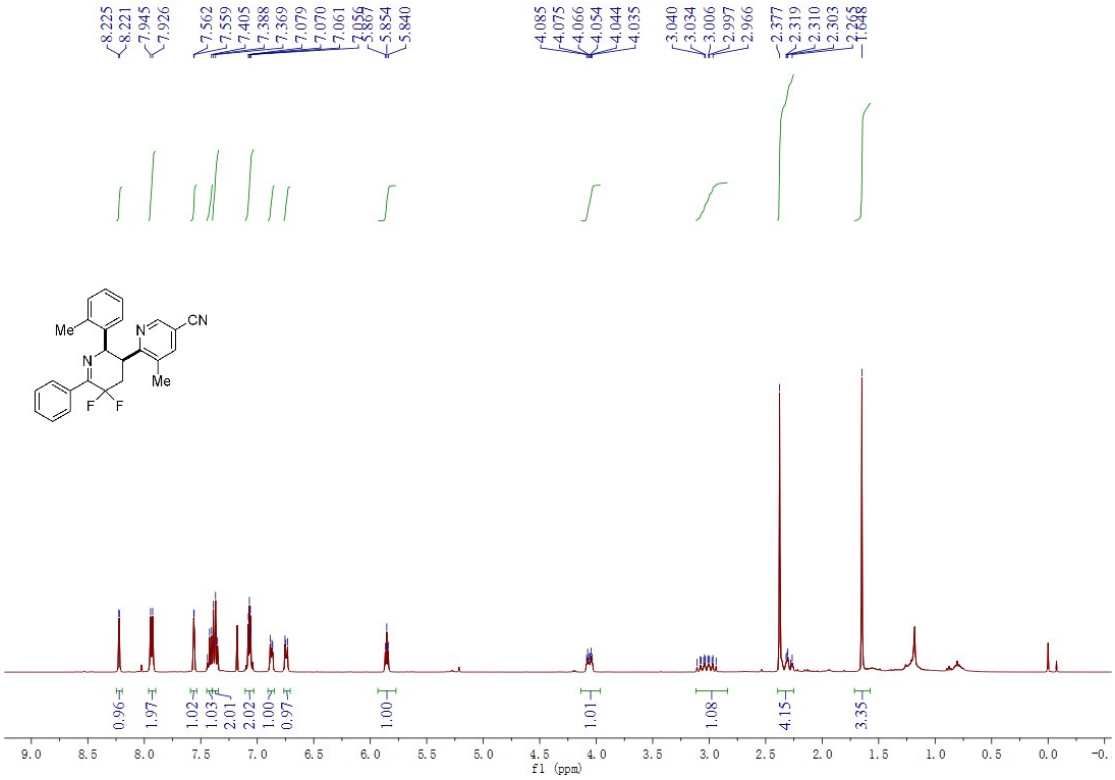


[^{19}F_NMR_375 MHz]

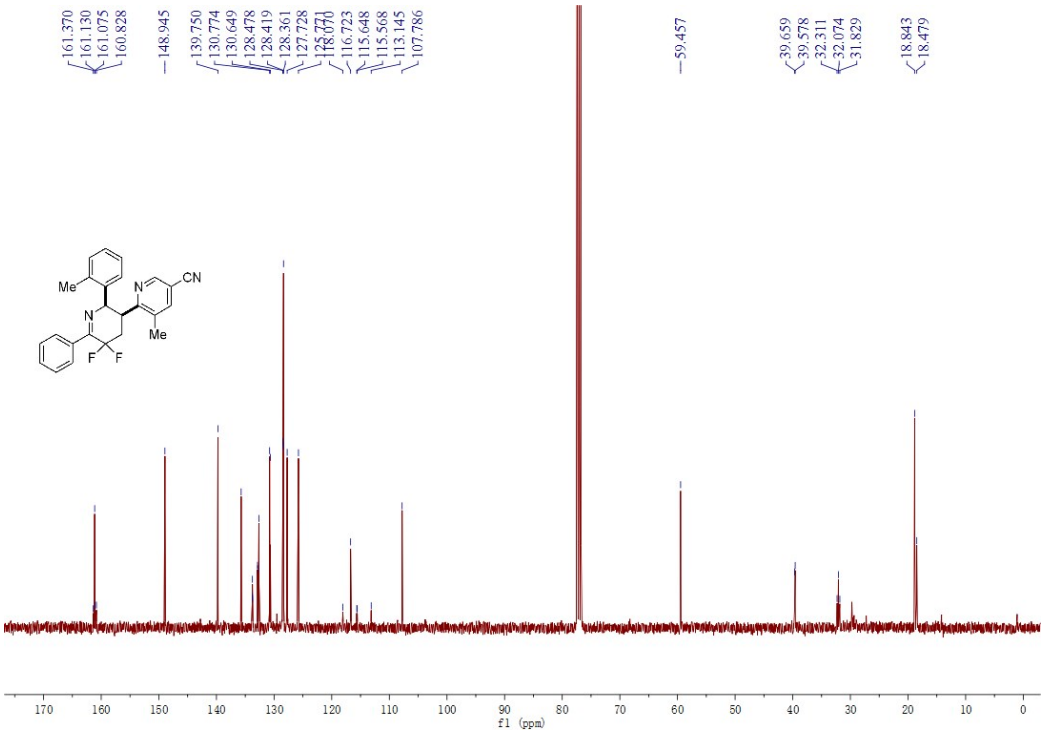


5',5'-Difluoro-3-methyl-6'-phenyl-2'-(o-tolyl)-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3af)

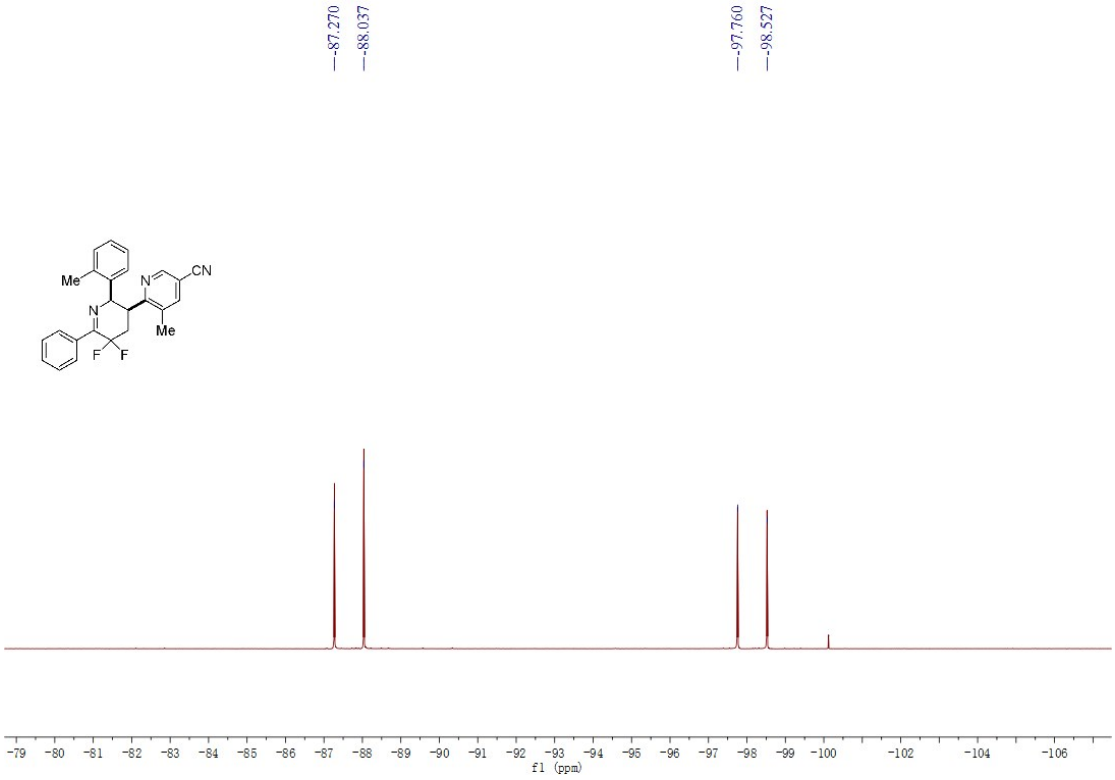
[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]

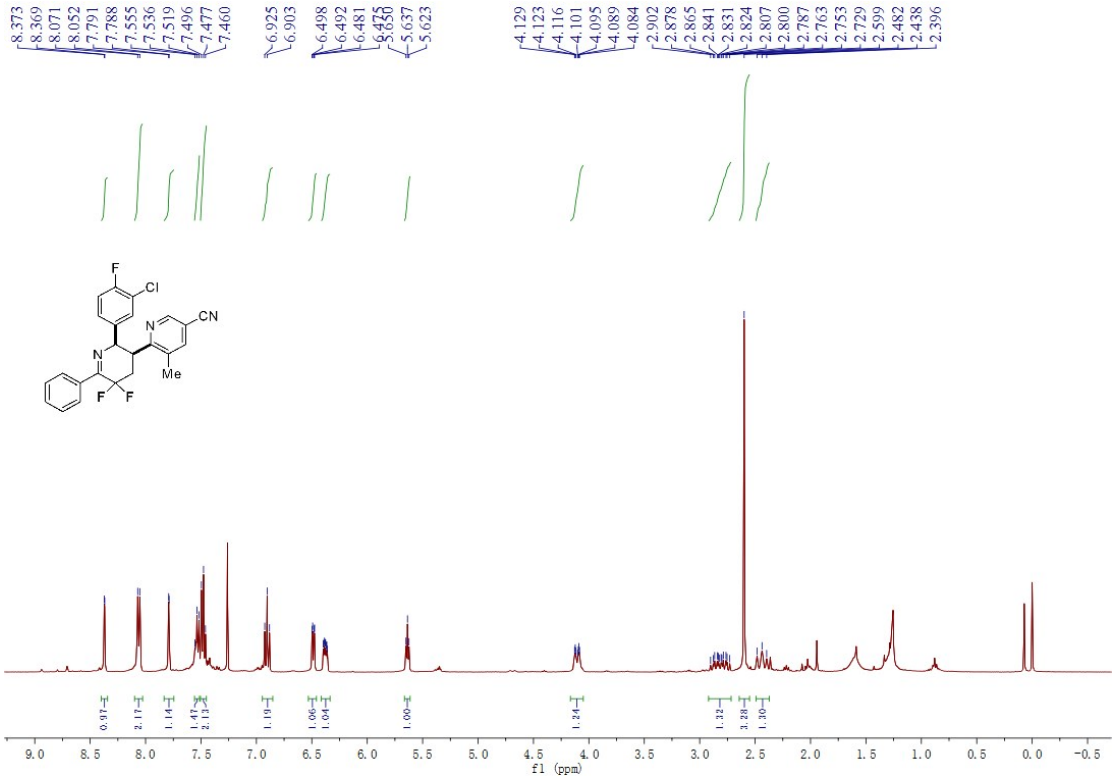


[^{19}F_NMR_375 MHz]

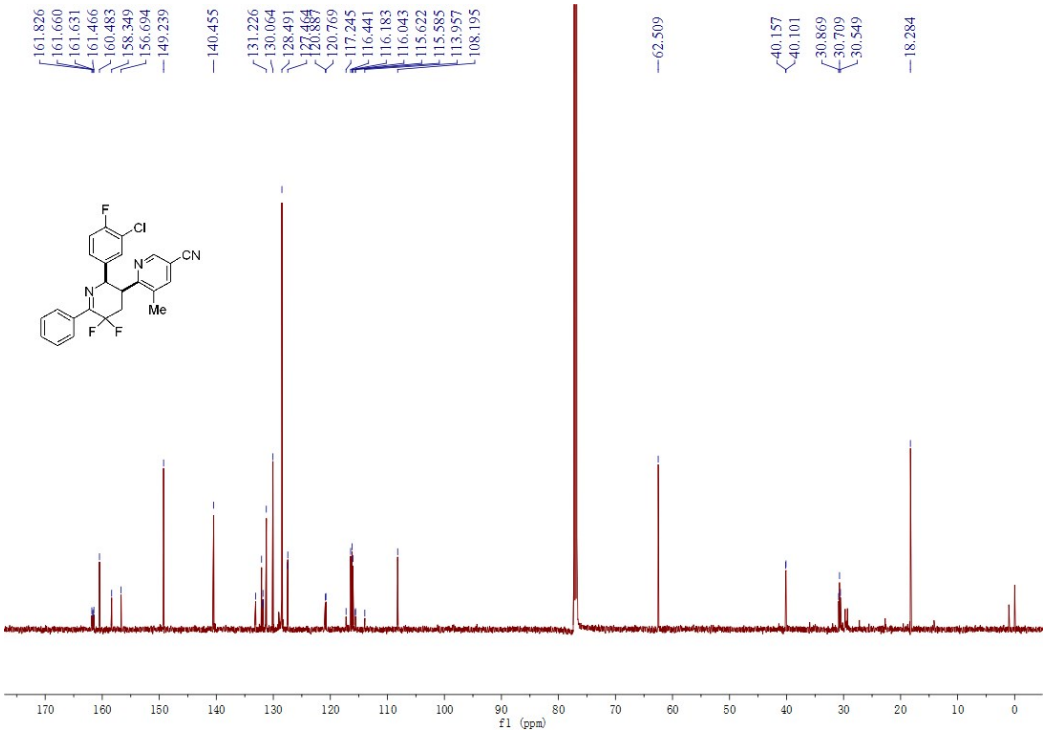


2'-(3-Chloro-4-fluorophenyl)-5',5'-difluoro-3-methyl-6'-phenyl-2',3',4',5'-tetrahydro-[2,3'-bipyridine]-5-carbonitrile (3ag)

[^{1}H_NMR_400 MHz_($CDCl_3$: 7.26 ppm)]



[^{13}C_NMR_100 MHz_($CDCl_3$: 77.00 ppm)]



[^{19}F_NMR_375 MHz]