

Supporting Information

Electrochemical oxidative radical cascade reactions for synthesis of difluoromethylated benzoxazines

Xiang Chen, Jun Jiang, Xiao-Jun Huang, and Wei-Min He*

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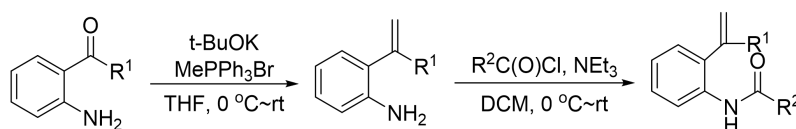
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General information

Chromatography: HaiLang Silica Flash P60 size 40~63 μm (200~300 mesh), TLC: HaiLang silica gel 60 (0.25mm). Visualization of the chromatogram was performed by UV, phosphomolybdic acid and KMnO_4 staining. Mass spectra were recorded on Bruker UltiMate3000 & Compact, Thermo ISQ LT, LTQ XL and VELOS pro & ORBITRIP mass spectrometers. ^1H , ^{13}C , ^{19}F were recorded on Bruker 500 using CDCl_3 or DMSO-d_6 as solvent. Chemical shift values are reported in ppm with the solvent resonance as the internal standard (CDCl_3 : δ 7.26 for ^1H , δ 77.16 for ^{13}C). Data are reported as follows: chemical shifts, multiplicity (s = singlet, bs = broad singlet, d = doublet, dd = doublet of doublets, t = triplet, td = triplet of doublets, m = multiplet), coupling constants (Hz), and integration. If no special description, all reactions were conducted under air atmosphere. Starting materials were purchased from adamas and used without further purification.

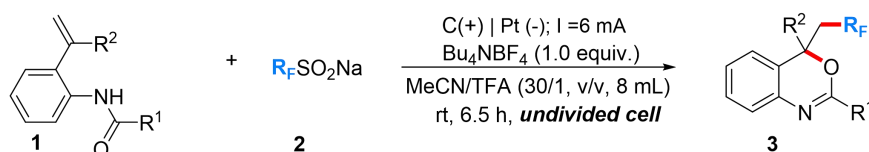
General procedure for preparation of N-acyl-(2-ene)-anilines

N-acyl-(2-ene)-anilines in the reactions were prepared with revised protocol according to the reported methods [1,2].



To a solution of methyltriphenylphosphonium bromide (5.36 g, 15.0 mmol) in dry THF (20.0 mL) under N_2 atmosphere was added t-BuOK (1.68 g, 15.0 mmol) at 0 °C. The reaction medium was allowed to RT and stir for 0.5 h. 2-aminoacetophenone (1.35 g, 10.0 mmol) was dropwise added. The reaction medium was stirred at room temperature for 12 h. Upon completion of ketone, monitored by TLC, the medium was poured into hexane, stirred for 1.0 h, plugged through a silica pad. The filtrate was concentrated under reduced pressure, the crude product was purified with column chromatography on silica gel (200~300 mesh) and PE to PE/EA (20/1, v/v) as eluent to afford corresponding styrene. To a solution of styrene (0.99 g, 7.4 mmol) and Et_3N (1.53 g, 11.1 mmol) in DCM (15.00 mL) was dropwise added the solution of acyl chloride (8.90 mmol) in dichloromethane (5.00 mL) at 0 °C. After completion, the reaction mixture was purified via column chromatography to give **1a**.

General procedure for the synthesis of difluoromethylated benzoxazines



In an undivided flask (4 mL) equipped with a stir bar, N-acyl-(2-ene)-anilines **1** (0.3 mmol), Sodium fluoromethylsulfonate **2** (0.6 mmol), Bu_4NBF_4 (0.3 mmol), MeCN/TFA (30/1, v/v, 8 mL) were added.

The flask was equipped with platinum cathode (20 mm × 10 mm × 0.1 mm) and graphite plate anode (20 mm × 10 mm × 0.1 mm). The reaction medium was stirred and electrolyzed at a constant current of 6 mA under RT for 6.5 h. After completion, the solvent was concentrated under reduced pressure, and the pure products **3** were obtained by flash chromatography on silica gel.

Investigation of reaction conditions

Table S1 reaction conditions screening

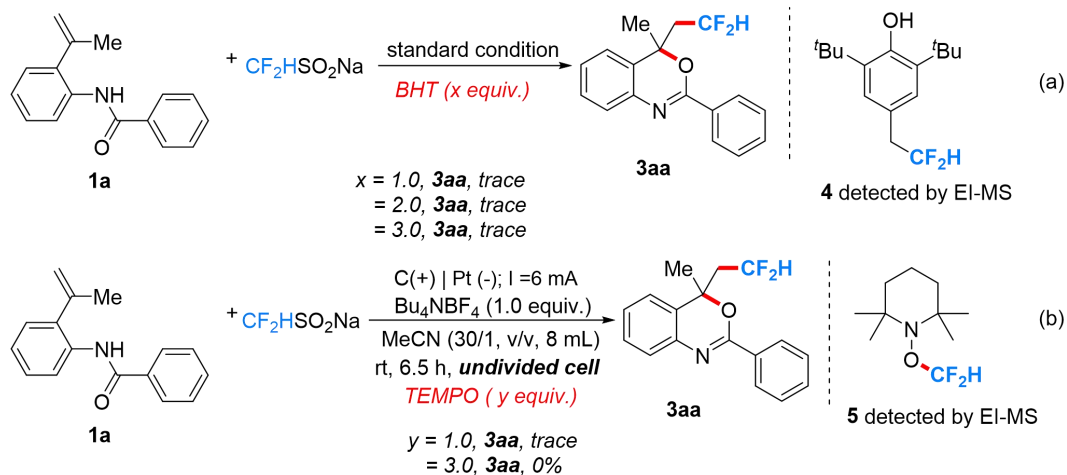
entry	1 (0.3 mmol)		2 (m equiv.)		3	
	m	x	electrolyte (y)	additive (z)	solvent	yield of 3 / %
1 ^a	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	0
2	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	38 ^b
3	2.0	Ti	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	0
4	2.0	Cu	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	12
5	2.0	Ag	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	trace
6	2.0	Ni	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	trace
7	2.0	Zn	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	0
8	2.0	Al	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN	22
9	2.0	Pt	ⁿ Bu ₄ NBF ₄ (2.0)	--	MeCN	24
10	2.0	Pt	ⁿ Bu ₄ NPF ₆ (1.0)	--	MeCN	40
11	2.0	Pt	ⁿ Bu ₄ NI (1.0)	--	MeCN	0
12	2.0	Pt	ⁿ Bu ₄ NHSO ₄ (1.0)	--	MeCN	31
13	2.0	Pt	LiClO ₄ (1.0)	--	MeCN	39
14	2.0	Pt	ⁿ Bu ₄ NOAc (1.0)	--	MeCN	17
15	2.0	Pt	KPF ₆ (1.0)	--	MeCN	17
16	2.0	Pt	Et ₄ NClO ₄ (1.0)	--	MeCN	14
17	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HFIP (7/1, v/v)	14
18	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HOAc (7/1, v/v)	52 ^b
19	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/H ₂ O (7/1, v/v)	26
20	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/DCM (7/1, v/v)	24
21	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/DMF (7/1, v/v)	14
22	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	DMSO	0
23	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	NMP	0
24	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	DMF	0
25	2.5	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HOAc (7/1, v/v)	59
26	4.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HOAc (7/1, v/v)	62
27	2.0	Pt	LiClO ₄ (1.0)	--	MeCN/HOAc (7/1, v/v)	25
28	2.0	Pt	ⁿ Bu ₄ NPF ₆ (1.0)	--	MeCN/HOAc (7/1, v/v)	44
29	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HOAc (6.5/1.5, v/v)	51
30	4.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	MeCN/HOAc (6/2, v/v)	52
31	4.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	TFA (3.0)	MeCN/HOAc (7/1, v/v)	83
32	4.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	TCA (3.0)	MeCN/HOAc (7/1, v/v)	70
33	4.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	LiClO ₄ (1.0)	MeCN/HOAc (7/1, v/v)	79
34	4.0	Pt	ⁿ Bu ₄ NBF ₄ (0.5)	LiClO ₄ (0.5)	MeCN/HOAc (7/1, v/v)	74
35	4.0	Pt	ⁿ Bu ₄ NBF ₄ (0.5)	ⁿ Bu ₄ NBF ₄ (0.5)	MeCN/HOAc (7/1, v/v)	50
36	4.0	Pt	ⁿ Bu ₄ NBF ₄ (0.5)	Fe(Cp) ₂ (0.1)	MeCN/HOAc (7/1, v/v)	56
37	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	HOAc	trace
38	2.0	Pt	ⁿ Bu ₄ NBF ₄ (1.0)	--	TFA	trace

Yields were determined by GC-MS with PhOMe as internal standard. a) CCE at 10 mA; b) isolated yield; c) 0.5 mmol scale.

Control experiments

1. Radical capturing reactions

1.1 Radical capturing experiment

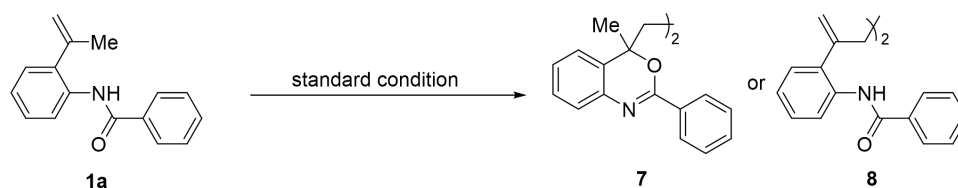


In an undivided flask (20 mL) equipped with a stir bar, N-acyl-(2-ene)-anilines **1** (0.3 mmol), Sodium fluoromethylsulfonate **2** (0.6 mmol), Bu_4NBF_4 (0.3 mmol), BHT (3.0 equiv.) or TEMPO (3.0 equiv.) MeCN/TFA (30/1, v/v, 8 mL) or MeCN (8 mL) were added. The flask was equipped with platinum cathode (20 mm \times 10 mm \times 0.1 mm) and graphite plate anode (20 mm \times 10 mm \times 1 mm). The reaction medium was stirred and electrolyzed at a constant current of 6 mA under RT for 6.5 h. After completion, compound **3** was determined with trace amount when BHT was added, and 0% yield when TEMPO as radical scavengers and MeCN as solvent were added. Compound **4** and **5** could be determined by EI-MS.



In an undivided flask (20 mL) equipped with a stir bar, N-acyl-(2-ene)-anilines **1** (0.3 mmol), Bu_4NBF_4 (0.3 mmol), TEMPO (3.0 equiv.) MeCN (8 mL) were added. The flask was equipped with platinum cathode (20 mm \times 10 mm \times 0.1 mm) and graphite plate anode (20 mm \times 10 mm \times 1 mm). The reaction medium was stirred and electrolyzed at a constant current of 6 mA under RT for 6.5 h. After completion, Compound **6** could not be observed by HRMS.

1.2 Self-coupling of 2a under standard condition



In an undivided flask (20 mL) equipped with a stir bar, N-acyl-(2-ene)-anilines **1** (0.3 mmol), Bu_4NBF_4 (0.3 mmol), MeCN/TFA (30/1, v/v, 8 mL) or MeCN (8 mL) were added. The flask was

equipped with platinum cathode (20 mm × 10 mm × 0.1 mm) and graphite plate anode (20 mm × 10 mm × 1 mm). The reaction medium was stirred and electrolyzed at a constant current of 6 mA under RT for 6.5 h. After completion, Compound **7** could not be detected by HRMS, neither as compound **8**.

2. Cyclic Voltammetry Experiments

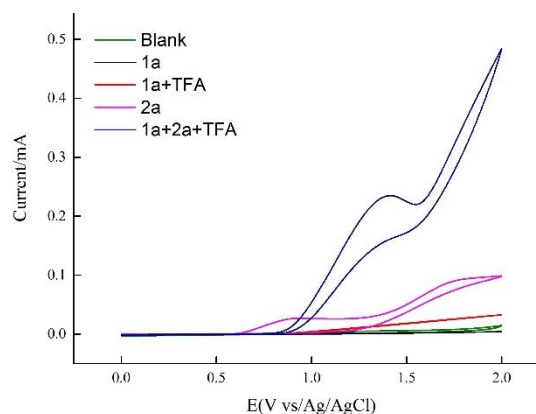


Figure S1. Cyclic Voltammogram (CV) Experiments

CV measurements were performed on a CHI 660E potentiostat, and the conditions are as follow: a glassy carbon disk working electrode (diameter, 3 mm), Pt disk and Ag/AgCl as counter and reference electrode. Cyclic voltammograms of reactants and their mixtures in 0.1 M LiClO₄ glassy carbon disk working electrode (diameter, 3 mm), Pt disk and Ag/AgCl (0.1 M in MeCN) as counter and reference electrode at 50 mV/s scan rate: 1) MeCN (8 mL) (green line), (2) 10 mM of **1a** in MeCN (8 mL) (black line), (3) 10 mM of **1a** in MeCN/TFA (30/1, v/v, 8 mL) (red line), (4) 10 mM of **2a** in MeCN (8 mL) (pink line), (5) 10 mM of **1a** and **2a** in MeCN/TFA (30/1, v/v, 8 mL) (blue line).

The radical-radical coupling mechanism

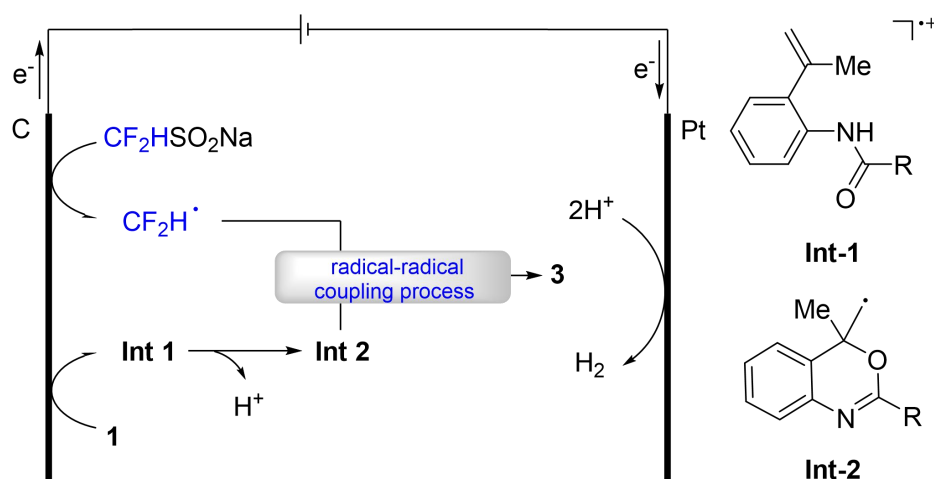


Figure S2 the radical-radical coupling mechanism

The pictures of reaction apparatuses

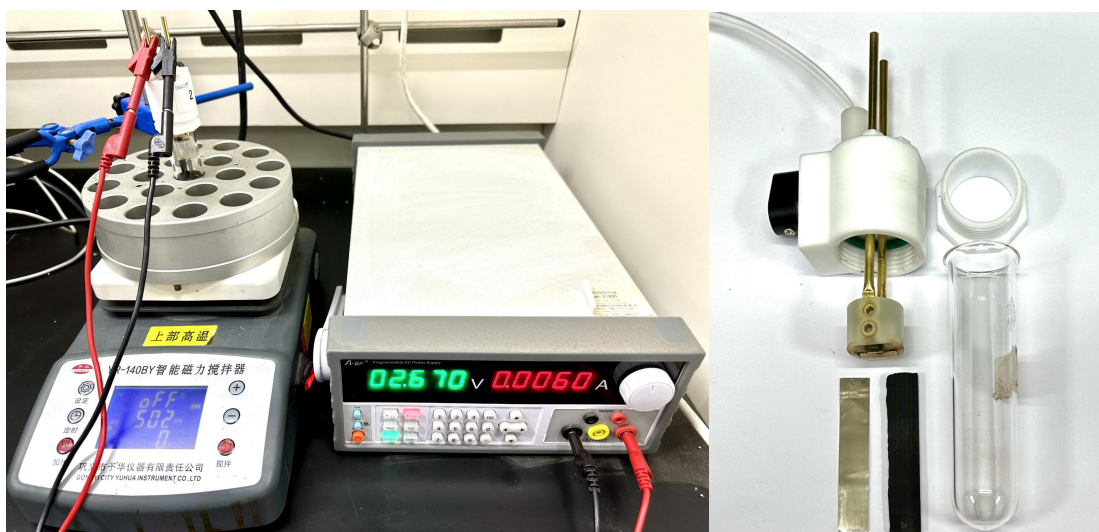
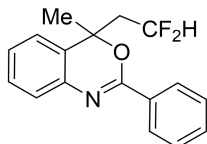


Figure S3 the pictures of reaction devices

References

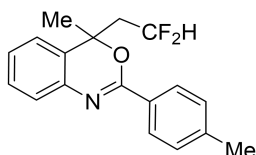
- [1] Q.-H. Deng, J.-R. Chen, Q. Wei, Q.-Q. Zhao, L.-Q. Lua and W.-J. Xiao, *Chem. Commun.*, 2015, **51**, 3537.
- [2] F. Lu, J. Xu, H. Li, K. Wang, D. Ouyang, L. Sun, M. Huang, J. Jiang, J. Hu, H. Alhumade, L. Lu and A. Lei, *Green Chem.*, 2021, **23**, 7982.

Characterization Data for Products



4-(2,2-Difluoroethyl)-4-methyl-2-phenyl-4H-benzo[d][1,3]oxazine (3aa)

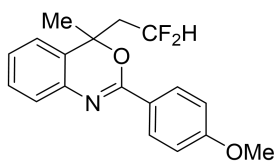
Colorless oil, 82% yield, $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.18 – 8.10 (m, 2H), 7.54 – 7.49 (m, 1H), 7.46 (dd, $J = 8.3, 6.6$ Hz, 2H), 7.34 (d, $J = 4.3$ Hz, 2H), 7.26 – 7.20 (m, 1H), 7.12 (d, $J = 7.6$ Hz, 1H), 6.15 – 5.86 (m, 1H), 2.69 – 2.44 (m, 2H), 1.79 (s, 3H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 155.9, 138.4, 132.5, 131.7, 129.3, 128.5, 128.5, 127.9, 127.1, 125.7, 122.7, 115.0 (t, $J = 239.3$ Hz), 77.6 (t, $J = 5.5$ Hz), 45.0 (t, $J = 21.3$ Hz), 27.5. $^{19}\text{F NMR}$ (471 MHz, CDCl_3) δ -112.6 (d, $J = 67.6$ Hz, 2F); HRMS: calcd for $\text{C}_{17}\text{H}_{16}\text{F}_2\text{NO}^+ [\text{M}+\text{H}]^+$, 288.1194, found 288.1189.



4-(2,2-Difluoroethyl)-4-methyl-2-(p-tolyl)-4H-benzo[d][1,3]oxazine (3ba)

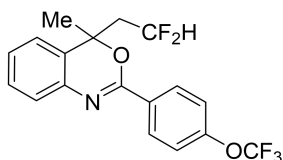
Colorless oil, 76% yield, $^1\text{H NMR}$ (500 MHz, CDCl_3) δ 8.05 – 7.99 (m, 2H), 7.36 – 7.30 (m, 2H), 7.25 (d, $J = 7.9$ Hz, 2H), 7.23 – 7.18 (m, 1H), 7.13 – 7.08 (m, 1H), 6.00 (tdd, $J = 55.8, 5.3, 3.9$ Hz, 1H), 2.66 – 2.45 (m, 2H), 2.41 (s, 3H), 1.78 (s, 4H). $^{13}\text{C NMR}$ (126 MHz, CDCl_3) δ 156.1, 142.2, 138.6,

129.7, 129.3, 129.2, 128.6, 127.9, 126.9, 125.6, 122.7, 115.1 (t, $J = 239.3$ Hz), 77.5 – 77.5 (m), 44.9 (t, $J = 21.3$ Hz), 27.4, 21.7. ^{19}F NMR (471 MHz, CDCl_3) δ -111.9 – -113.3 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{18}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 302.1351, found 302.1357.



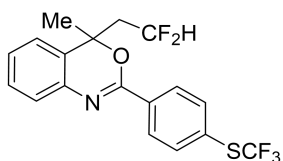
4-(2,2-Difluoroethyl)-2-(4-methoxyphenyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ca)

Colorless oil, 84% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.13 – 8.03 (m, 2H), 7.36 – 7.29 (m, 2H), 7.21 (ddd, $J = 7.6, 6.4, 2.2$ Hz, 1H), 7.11 (dd, $J = 7.4, 1.2$ Hz, 1H), 6.99 – 6.93 (m, 2H), 6.01 (tdd, $J = 55.7, 5.2, 4.0$ Hz, 1H), 3.87 (s, 3H), 2.67 – 2.43 (m, 2H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, Chloroform- d) δ 162.6, 155.9, 138.8, 129.8, 129.3, 128.5, 126.6, 125.5, 124.9, 122.7, 115.1 (t, $J = 239.3$ Hz), 113.8, 77.6 – 77.4 (m), 55.5, 44.9 (t, $J = 21.3$ Hz), 27.3. ^{19}F NMR (471 MHz, Chloroform- d) δ -110.4 – -113.6 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{18}\text{F}_2\text{NO}_2^+$ $[\text{M}+\text{H}]^+$, 318.1300, found 318.1291.



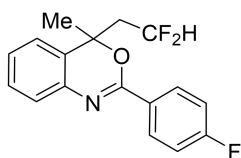
4-(2,2-Difluoroethyl)-4-methyl-2-(4-(trifluoromethoxy)phenyl)-4H-benzo[d][1,3]oxazine (3da)

Colorless oil, 83% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.22 – 8.13 (m, 2H), 7.38 – 7.31 (m, 2H), 7.28 (d, $J = 8.5$ Hz, 2H), 7.27 – 7.22 (m, 1H), 7.12 (dd, $J = 7.7, 1.2$ Hz, 1H), 5.97 (tdd, $J = 55.7, 5.2, 4.0$ Hz, 1H), 2.71 – 2.38 (m, 2H), 1.80 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.7, 151.7, 138.2, 131.0, 129.7, 129.4, 128.3, 127.4, 125.9, 122.8, 120.5 (q, $J = 258.0$ Hz), 120.5, 115.0 (t, $J = 239.4$ Hz), 78.0 (t, $J = 6.0$ Hz), 45.1 (t, $J = 21.4$ Hz), 27.7. ^{19}F NMR (471 MHz, CDCl_3) δ -57.6 (s, 3F), -112.7 – -112.7 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{15}\text{F}_5\text{NO}_2^+$ $[\text{M}+\text{H}]^+$, 372.1017, found 372.1010.



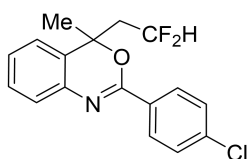
4-(2,2-Difluoroethyl)-4-methyl-2-(4-(trifluoromethylthio)phenyl)-4H-benzo[d][1,3]oxazine (3ea)

Colorless oil, 75% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.17 (d, $J = 8.2$ Hz, 2H), 7.73 (d, $J = 8.1$ Hz, 2H), 7.39 – 7.31 (m, 2H), 7.26 (td, $J = 7.0, 2.2$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.97 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.69 – 2.42 (m, 2H), 1.80 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.7, 138.1, 135.9, 134.9, 129.5 (q, $J = 308.4$ Hz), 129.5, 128.8, 128.3, 128.0 (q, $J = 2.1$ Hz), 127.7, 126.0, 122.8, 115.0 (t, $J = 239.5$ Hz), 78.1 (t, $J = 6.1$ Hz), 45.1 (t, $J = 21.4$ Hz), 27.8. ^{19}F NMR (471 MHz, CDCl_3) δ -42.1 (s, 3F), -112.6 – -112.8 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{15}\text{F}_5\text{NOS}^+$ $[\text{M}+\text{H}]^+$, 388.0789, found 388.0796.



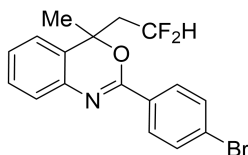
4-(2,2-Difluoroethyl)-2-(4-fluorophenyl)-4-methyl-4H-benzo[d][1,3]oxazine (3fa)

Colorless oil, 65% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.17 – 8.10 (m, 2H), 7.37 – 7.29 (m, 2H), 7.27 – 7.20 (m, 1H), 7.12 (td, $J = 8.3, 2.1$ Hz, 3H), 5.98 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.65 – 2.41 (m, 2H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 165.0 (d, $J = 252.3$ Hz), 155.0, 138.3, 130.1 (d, $J = 9.0$ Hz), 129.3, 128.6 (d, $J = 3.0$ Hz), 128.2, 127.1, 125.6, 122.7, 115.5 (d, $J = 22.0$ Hz), 114.9 (t, $J = 239.4$ Hz), 77.7 (t, $J = 6.0$ Hz), 44.9 (t, $J = 21.3$ Hz), 27.5. ^{19}F NMR (471 MHz, CDCl_3) δ -108.0 (s, 1F), -112.7 (d, $J = 30.1$ Hz, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{15}\text{F}_3\text{NO}^+ [\text{M}+\text{H}]^+$, 306.1100, found 306.1107.



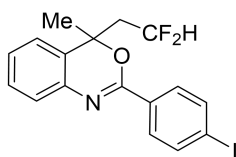
2-(4-Chlorophenyl)-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ga)

Colorless oil, 77% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.10 – 8.03 (m, 2H), 7.44 – 7.39 (m, 2H), 7.37 – 7.30 (m, 2H), 7.27 – 7.21 (m, 1H), 7.11 (dd, $J = 7.7, 1.3$ Hz, 1H), 6.14 – 5.78 (m, 1H), 2.69 – 2.38 (m, 2H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 155.0, 138.3, 137.9, 131.0, 129.4, 129.3, 128.7, 128.4, 127.3, 125.8, 122.8, 115.0 (t, $J = 239.4$ Hz), 77.9 (t, $J = 6.0$ Hz), 45.1 (t, $J = 21.4$ Hz), 27.6. ^{19}F NMR (471 MHz, CDCl_3) δ -111.3 – -113.8 (m, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{15}\text{ClF}_2\text{NO}^+ [\text{M}+\text{H}]^+$, 322.0805, found 322.0796.



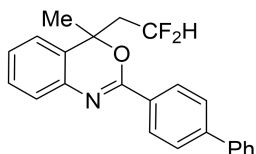
2-(4-Bromophenyl)-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ha)

Colorless oil, 79% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.91 (d, $J = 8.6$ Hz, 2H), 7.50 (d, $J = 8.6$ Hz, 2H), 7.29 – 7.22 (m, 2H), 7.19 – 7.14 (m, 1H), 7.03 (dd, $J = 7.6, 1.3$ Hz, 1H), 5.89 (tdd, $J = 55.7, 5.2, 4.0$ Hz, 1H), 2.65 – 2.25 (m, 2H), 1.71 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 155.1, 138.2, 132.5, 131.7, 131.4, 129.5, 129.4, 128.3, 127.4, 126.5, 125.8, 122.8, 115.0 (t, $J = 239.4$ Hz), 77.9 (t, $J = 6.0$ Hz), 45.0 (t, $J = 21.4$ Hz), 27.6. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 25.0$ Hz, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{14}\text{BrF}_2\text{NNaO}^+ [\text{M}+\text{Na}]^+$, 388.0119, found 388.0121.



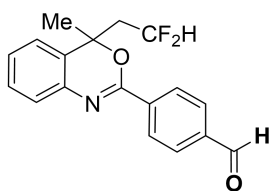
4-(2,2-Difluoroethyl)-2-(4-iodophenyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ia)

Colorless oil, 72% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.85 (d, $J = 8.6$ Hz, 2H), 7.79 (d, $J = 8.4$ Hz, 2H), 7.38 – 7.29 (m, 2H), 7.24 (td, $J = 7.6, 7.2, 2.0$ Hz, 1H), 7.11 (dd, $J = 7.7, 1.3$ Hz, 1H), 6.11 – 5.82 (m, 1H), 2.67 – 2.38 (m, 2H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 155.3, 138.2, 137.7, 132.0, 129.5, 129.4, 128.4, 127.4, 125.8, 122.8, 115.0 (t, $J = 239.5$ Hz), 98.9, 77.9 (t, $J = 6.1$ Hz), 45.0 (t, $J = 21.3$ Hz), 27.6. ^{19}F NMR (471 MHz, CDCl_3) δ -111.7 – -113.7 (m, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{15}\text{F}_2\text{INO}^+ [\text{M}+\text{H}]^+$, 414.0161, found 414.0160.



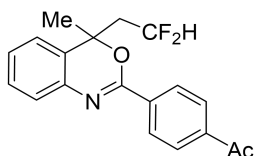
2-((1,1'-Biphenyl)-4-yl)-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ja)

Colorless oil, 74% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.20 (d, $J = 8.3$ Hz, 2H), 7.68 (d, $J = 8.3$ Hz, 2H), 7.66 – 7.62 (m, 2H), 7.47 (t, $J = 7.6$ Hz, 2H), 7.41 – 7.31 (m, 3H), 7.26 – 7.20 (m, 1H), 7.12 (d, $J = 7.6$ Hz, 1H), 6.03 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.71 – 2.43 (m, 2H), 1.81 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 155.8, 144.4, 140.3, 138.5, 131.3, 129.3, 129.0, 128.5, 128.4, 128.0, 127.3, 127.1, 127.1, 125.7, 122.7, 115.1 (t, $J = 239.4$ Hz), 77.6 (t, $J = 6.0$ Hz), 45.0 (t, $J = 21.3$ Hz), 27.5. ^{19}F NMR (471 MHz, CDCl_3) δ -111.7 – -113.6 (m, 2F). HRMS: calcd for $\text{C}_{23}\text{H}_{20}\text{F}_2\text{NO}^+ [\text{M}+\text{H}]^+$, 364.1507, found 364.1505.



4-(4-(2,2-Difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzaldehyde (3ka)

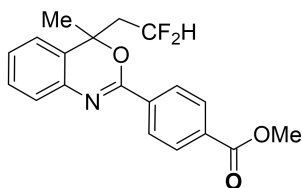
Colorless oil, 68% yield, ^1H NMR (500 MHz, CDCl_3) δ 10.09 (s, 1H), 8.29 (d, $J = 8.1$ Hz, 2H), 7.95 (d, $J = 8.1$ Hz, 2H), 7.36 (d, $J = 4.2$ Hz, 2H), 7.27 (dt, $J = 8.5, 4.2$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.98 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.66 – 2.47 (m, 2H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 191.9, 154.7, 138.3, 138.1, 138.0, 129.6, 129.5, 128.5, 128.4, 127.8, 126.2, 122.8, 115.0 (t, $J = 239.5$ Hz), 78.2 (t, $J = 6.0$ Hz), 45.3 (t, $J = 21.5$ Hz), 27.8. ^{19}F NMR (471 MHz, CDCl_3) δ -112.5 – -112.9 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{16}\text{F}_2\text{NO}_2^+ [\text{M}+\text{H}]^+$, 316.1144, found 316.1139.



1-(4-(4-(2,2-Difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)phenyl)ethan-1-one (3la)

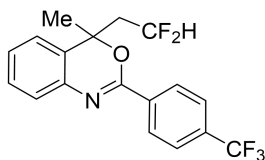
Colorless oil, 84% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.22 (d, $J = 8.3$ Hz, 2H), 8.03 (d, $J = 8.4$ Hz, 2H), 7.39 – 7.33 (m, 2H), 7.27 (ddd, $J = 8.5, 5.5, 3.2$ Hz, 1H), 7.14 (d, $J = 7.6$ Hz, 1H), 6.14 – 5.84 (m, 1H), 2.66 (s, 3H), 2.64 – 2.45 (m, 2H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 197.9, 154.9, 139.1,

138.1, 136.6, 129.5, 128.4, 128.3, 128.1, 127.7, 126.0, 122.8, 115.0 (t, $J = 239.5$ Hz), 78.0 (t, $J = 6.1$ Hz), 45.1 (t, $J = 21.4$ Hz), 27.7, 27.0. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 25.8$ Hz, 2F). HRMS: calcd for $\text{C}_{19}\text{H}_{18}\text{F}_2\text{NO}_2^+$ $[\text{M}+\text{H}]^+$, 330.1300, found 330.1303.



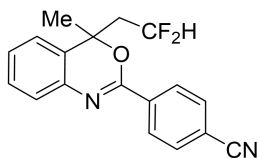
Methyl 4-(4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzoate (3ma)

Colorless oil, 80% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.20 (d, $J = 8.3$ Hz, 2H), 8.11 (d, $J = 8.3$ Hz, 2H), 7.39 – 7.33 (m, 2H), 7.26 (td, $J = 6.4, 5.6, 2.9$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.99 (tt, $J = 55.7, 4.6$ Hz, 1H), 3.95 (s, 3H), 2.69 – 2.44 (m, 2H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 166.7, 155.0, 138.1, 136.6, 132.6, 129.6, 129.5, 128.4, 127.8, 127.6, 126.0, 122.8, 115.0 (t, $J = 239.5$ Hz), 78.0 (t, $J = 6.1$ Hz), 52.5, 45.1 (t, $J = 21.3$ Hz), 27.8. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 29.6$ Hz, 2F). HRMS: calcd for $\text{C}_{19}\text{H}_{18}\text{F}_2\text{NO}_3^+$ $[\text{M}+\text{H}]^+$, 346.1249, found 346.1253.



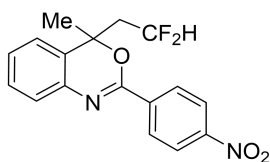
4-(2,2-Difluoroethyl)-4-methyl-2-(4-(trifluoromethyl)phenyl)-4H-benzo[d][1,3]oxazine (3na)

Colorless oil, 67% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.25 (d, $J = 8.2$ Hz, 2H), 7.71 (d, $J = 8.2$ Hz, 2H), 7.39 – 7.33 (m, 2H), 7.27 (ddd, $J = 8.5, 6.0, 2.8$ Hz, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.97 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.76 – 2.36 (m, 2H), 1.81 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.5, 138.0, 135.9, 133.1 (q, $J = 32.6$ Hz), 129.5, 128.3, 128.2, 127.7, 126.0, 124.0 (q, $J = 272.4$ Hz), 125.4 (q, $J = 3.8$ Hz), 122.8, 115.0 (t, $J = 239.5$ Hz), 78.1 (t, $J = 6.0$ Hz), 45.2 (t, $J = 21.4$ Hz), 27.8. ^{19}F NMR (471 MHz, CDCl_3) δ -62.8 (s, 3F), -112.6 – -112.9 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{15}\text{F}_5\text{NO}^+$ $[\text{M}+\text{H}]^+$, 356.1068, found 356.1073.



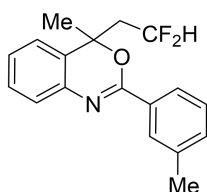
4-(4-(2,2-Difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzonitrile (3oa)

Colorless oil, 74% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.24 (d, $J = 8.3$ Hz, 2H), 7.74 (d, $J = 8.3$ Hz, 2H), 7.39 – 7.32 (m, 2H), 7.28 (td, $J = 7.6, 2.1$ Hz, 1H), 5.96 (tt, $J = 55.6, 4.6$ Hz, 1H), 2.71 – 2.43 (m, 2H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 154.0, 137.8, 136.6, 132.2, 129.6, 128.3, 128.2, 128.0, 126.1, 122.9, 118.6, 114.9 (t, $J = 239.6$ Hz), 114.7, 78.3 (t, $J = 6.0$ Hz), 45.2 (t, $J = 21.4$ Hz), 27.9. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 3.1$ Hz, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{15}\text{F}_2\text{N}_2\text{O}^+$ $[\text{M}+\text{H}]^+$, 313.1147, found 313.1150.



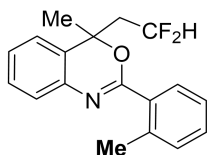
4-(2,2-Difluoroethyl)-4-methyl-2-(4-nitrophenyl)-4H-benzo[d][1,3]oxazine (3pa)

Colorless oil, 54% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.30 (s, 4H), 7.40 – 7.34 (m, 2H), 7.31 – 7.27 (m, 1H), 7.16 – 7.11 (m, 1H), 5.96 (tt, $J = 55.7, 4.6$ Hz, 1H), 2.67 – 2.45 (m, 2H), 1.83 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 153.8, 149.7, 138.4, 137.8, 129.6, 128.8, 128.2, 128.2, 126.3, 123.6, 122.9, 114.9 (t, $J = 239.6$ Hz), 78.4 (d, $J = 6.2$ Hz), 45.3 (t, $J = 21.5$ Hz), 28.0. ^{19}F NMR (471 MHz, CDCl_3) δ -112.6 – -112.9 (m, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{15}\text{F}_2\text{N}_2\text{O}_3^+$ $[\text{M}+\text{H}]^+$, 333.1045, found 333.1049.



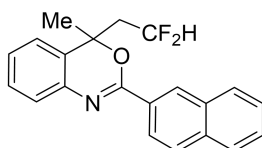
4-(2,2-Difluoroethyl)-4-methyl-2-(m-tolyl)-4H-benzo[d][1,3]oxazine (3qa)

Colorless oil, 79% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.96 (d, $J = 2.1$ Hz, 1H), 7.93 – 7.89 (m, 1H), 7.37 – 7.30 (m, 4H), 7.22 (dt, $J = 8.4, 4.3$ Hz, 1H), 7.11 (d, $J = 7.6$ Hz, 1H), 6.00 (tdd, $J = 55.7, 5.2, 3.9$ Hz, 1H), 2.67 – 2.44 (m, 2H), 2.43 (s, 3H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 156.2, 138.5, 138.2, 132.6, 132.4, 129.3, 128.5, 128.5, 128.4, 127.0, 125.7, 125.1, 122.7, 115.1 (t, $J = 239.3$ Hz), 77.6 (d, $J = 6.0$ Hz), 45.0 (t, $J = 21.3$ Hz), 27.5, 21.6. ^{19}F NMR (471 MHz, CDCl_3) δ -111.5 – -113.6 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{18}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 302.1351, found 302.1351.



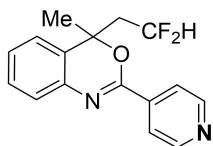
4-(2,2-Difluoroethyl)-4-methyl-2-(o-tolyl)-4H-benzo[d][1,3]oxazine (3ra)

Colorless oil, 79% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.77 (dd, $J = 7.8, 1.5$ Hz, 1H), 7.37 – 7.29 (m, 3H), 7.29 – 7.22 (m, 3H), 7.11 (dd, $J = 7.7, 1.2$ Hz, 1H), 5.96 (tdd, $J = 55.8, 5.2, 4.0$ Hz, 1H), 2.68 – 2.52 (m, 5H), 1.79 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 157.7, 138.3, 132.4, 131.6, 130.6, 129.6, 129.3, 127.8, 127.2, 125.9, 125.8, 122.7, 115.2 (d, $J = 239.7$ Hz), 78.0 (d, $J = 6.2$ Hz), 45.1 (t, $J = 21.5$ Hz), 28.1, 21.7. ^{19}F NMR (471 MHz, CDCl_3) δ -112.5 – -112.9 (m, 2F). HRMS: calcd for $\text{C}_{18}\text{H}_{18}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 302.1351, found 302.1349.



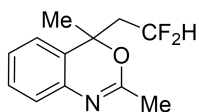
4-(2,2-Difluoroethyl)-4-methyl-2-(naphthalen-2-yl)-4H-benzo[d][1,3]oxazine (3sa)

Colorless oil, 59% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.59 (d, $J = 1.6$ Hz, 1H), 8.26 (dd, $J = 8.7, 1.6$ Hz, 1H), 7.98 (dd, $J = 7.3, 2.0$ Hz, 1H), 7.90 (dd, $J = 12.0, 8.4$ Hz, 2H), 7.56 (tt, $J = 7.2, 5.4$ Hz, 2H), 7.41 – 7.34 (m, 2H), 7.28 – 7.23 (m, 1H), 7.15 (d, $J = 7.6$ Hz, 1H), 6.22 – 5.91 (m, 1H), 2.74 – 2.47 (m, 2H), 1.86 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 156.0, 138.6, 135.1, 132.9, 129.8, 129.4, 129.2, 128.6, 128.5, 128.2, 127.9, 127.8, 127.2, 126.6, 125.8, 124.5, 122.8, 115.1 (t, $J = 239.4$ Hz), 77.8 (d, $J = 6.0$ Hz), 45.0 (t, $J = 21.3$ Hz), 27.6. ^{19}F NMR (471 MHz, CDCl_3) δ -112.4 – -112.8 (m, 2F). HRMS: calcd for $\text{C}_{21}\text{H}_{18}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 338.1351, found 338.1361.



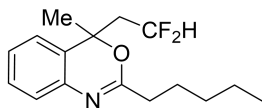
4-(2,2-Difluoroethyl)-4-methyl-2-(pyridin-4-yl)-4H-benzo[d][1,3]oxazine (3ta)

Colorless oil, 69% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.75 (s, 2H), 7.95 (d, $J = 5.2$ Hz, 2H), 7.35 (d, $J = 3.2$ Hz, 2H), 7.30 – 7.26 (m, 1H), 7.13 (d, $J = 7.6$ Hz, 1H), 5.96 (tt, $J = 55.5, 4.6$ Hz, 1H), 2.71 – 2.41 (m, 2H), 1.81 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 153.9, 150.3, 140.1, 137.7, 129.5, 128.4, 128.1, 126.3, 122.9, 121.5, 114.9 (t, $J = 239.6$ Hz), 78.3 (t, $J = 6.0$ Hz), 45.4 (t, $J = 21.6$ Hz), 27.9. ^{19}F NMR (471 MHz, CDCl_3) δ -112.1 – -113.4 (m, 2F). HRMS: calcd for $\text{C}_{16}\text{H}_{15}\text{F}_2\text{N}_2\text{O}^+$ $[\text{M}+\text{H}]^+$, 289.1147, found 289.1151.



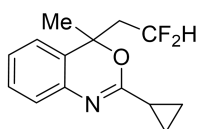
4-(2,2-Difluoroethyl)-2,4-dimethyl-4H-benzo[d][1,3]oxazine (3ua)

Colorless oil, 86% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.31 – 7.25 (m, 1H), 7.21 – 7.11 (m, 2H), 7.04 (d, $J = 7.6$ Hz, 1H), 5.88 (tt, $J = 56.2, 4.4$ Hz, 1H), 2.42 (dq, $J = 52.1, 15.0, 4.5$ Hz, 2H), 2.12 (s, 3H), 1.70 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.5, 137.9, 129.3, 127.6, 126.9, 124.9, 122.8, 115.1 (t, $J = 239.1$ Hz), 77.2 (t, $J = 6.2$ Hz), 45.7 (t, $J = 21.2$ Hz), 28.0, 21.8. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 12.3$ Hz, 2F). HRMS: calcd for $\text{C}_{12}\text{H}_{14}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 226.1038, found 226.1041.



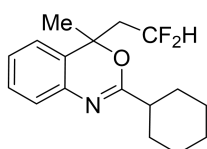
4-(2,2-Difluoroethyl)-4-methyl-2-pentyl-4H-benzo[d][1,3]oxazine (3va)

Colorless oil, 80% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.30 – 7.25 (m, 1H), 7.20 – 7.14 (m, 2H), 7.04 (d, $J = 7.5$ Hz, 1H), 5.89 (tdd, $J = 55.8, 5.5, 3.7$ Hz, 1H), 2.56 – 2.37 (m, 2H), 2.37 – 2.32 (m, 2H), 1.82 – 1.63 (m, 5H), 1.41 – 1.32 (m, 4H), 0.95 – 0.87 (m, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 162.3, 137.9, 129.2, 127.8, 126.8, 125.0, 122.7, 115.1 (t, $J = 239.1$ Hz), 77.0 (dd, $J = 7.1, 5.2$ Hz), 45.3 (t, $J = 21.3$ Hz), 35.5, 31.6, 28.0, 26.0, 22.5, 14.1. ^{19}F NMR (471 MHz, CDCl_3) δ -112.7 (d, $J = 69.3$ Hz, 2F). HRMS: calcd for $\text{C}_{16}\text{H}_{22}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 282.1664, found 282.1667.



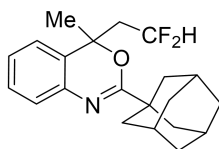
2-Cyclopropyl-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3wa)

Colorless oil, 83% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.27 (td, $J = 7.6, 1.4$ Hz, 1H), 7.14 (t, $J = 7.1$ Hz, 2H), 7.05 – 6.98 (m, 1H), 5.84 (tdd, $J = 55.8, 5.3, 3.8$ Hz, 1H), 2.57 – 2.29 (m, 2H), 1.71 (tt, $J = 8.3, 4.8$ Hz, 1H), 1.63 (s, 3H), 1.04 (dt, $J = 6.9, 3.3$ Hz, 2H), 0.87 (dq, $J = 7.1, 3.7$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 162.5, 138.3, 129.3, 127.8, 126.3, 124.5, 122.6, 115.1 (t, $J = 239.1$ Hz), 45.0 (t, $J = 21.4$ Hz), 27.7, 14.7, 7.0, 6.9. ^{19}F NMR (471 MHz, CDCl_3) δ -112.4 – -112.8 (m, 2F). HRMS: calcd for $\text{C}_{14}\text{H}_{16}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 252.1194, found 252.1191.



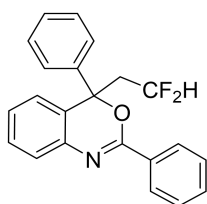
2-Cyclohexyl-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3xa)

Colorless oil, 62% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.31 – 7.24 (m, 1H), 7.20 – 7.14 (m, 2H), 7.03 (d, $J = 7.6$ Hz, 1H), 5.90 (tdd, $J = 55.9, 5.3, 3.9$ Hz, 1H), 2.58 – 2.35 (m, 2H), 2.30 (tt, $J = 11.8, 3.5$ Hz, 1H), 1.98 – 1.90 (m, 2H), 1.81 (dq, $J = 11.6, 4.5, 4.1$ Hz, 2H), 1.73 – 1.68 (m, 1H), 1.65 (s, 3H), 1.55 – 1.44 (m, 2H), 1.35 – 1.22 (m, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 164.9, 138.1, 129.2, 128.0, 126.7, 125.1, 122.7, 76.8 (dd, $J = 7.2, 5.0$ Hz), 44.0, 29.6, 27.8, 25.9, 25.9, 25.9. ^{19}F NMR (471 MHz, CDCl_3) δ -111.8 – -113.4 (m, 2F). HRMS: calcd for $\text{C}_{17}\text{H}_{22}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 294.1664, found 294.1660.



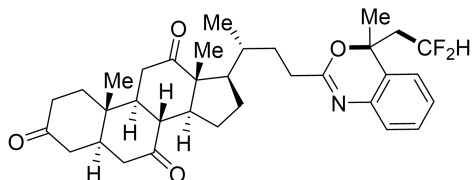
2-(Adamantan-1-yl)-4-(2,2-difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ya)

Colorless oil, 81% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.26 (t, $J = 7.6$ Hz, 1H), 7.16 (dd, $J = 19.4, 7.5$ Hz, 2H), 7.01 (d, $J = 7.6$ Hz, 1H), 5.91 (tt, $J = 56.0, 4.6$ Hz, 1H), 2.56 – 2.38 (m, 2H), 2.06 (s, 3H), 1.94 (d, $J = 3.0$ Hz, 6H), 1.79 – 1.71 (m, 6H), 1.62 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 166.5, 138.5, 129.1, 128.3, 126.6, 125.4, 122.5, 115.2 (t, $J = 239.0$ Hz), 76.5 (dd, $J = 7.2, 5.2$ Hz), 44.9 (t, $J = 21.3$ Hz), 39.2, 39.1, 36.8, 28.3, 27.7. ^{19}F NMR (471 MHz, CDCl_3) δ -112.0 – -112.8 (m, 2F). HRMS: calcd for $\text{C}_{21}\text{H}_{26}\text{F}_2\text{NO}^+$ $[\text{M}+\text{H}]^+$, 346.1977, found 346.1969.



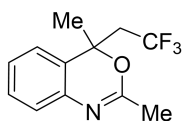
4-(2,2-Difluoroethyl)-2,4-diphenyl-4H-benzo[d][1,3]oxazine (3za)

Colorless oil, 87% yield, ^1H NMR (500 MHz, CDCl_3) δ 8.28 – 8.20 (m, 2H), 7.51 (t, $J = 7.2$ Hz, 1H), 7.46 (dd, $J = 8.3, 6.4$ Hz, 2H), 7.39 – 7.35 (m, 2H), 7.34 – 7.31 (m, 2H), 7.30 – 7.21 (m, 5H), 6.05 (tt, $J = 55.6, 4.3$ Hz, 1H), 3.01 (td, $J = 15.1, 4.3$ Hz, 2H). ^{13}C NMR (126 MHz, CDCl_3) δ 156.0, 142.1, 139.2, 132.2, 131.8, 129.6, 128.7, 128.5, 128.5, 128.0, 126.8, 126.6, 125.9, 125.6, 124.5, 115.4 (t, $J = 240.0$ Hz), 81.0 (t, $J = 6.5$ Hz), 44.9 (t, $J = 22.4$ Hz). ^{19}F NMR (471 MHz, Chloroform-*d*) δ -110.2 – -112.3 (m, 2F). HRMS: calcd for $\text{C}_{22}\text{H}_{18}\text{F}_2\text{NO}^+ [\text{M}+\text{H}]^+$, 350.1351, found 350.1344.



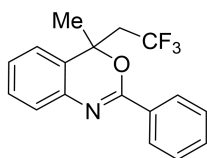
(5R,8R,9S,10S,13R,14S,17R)-17-((R)-4-((S)-4-(2,2-Difluoroethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)butan-2-yl)-10,13-dimethyldodecahydro-3H-cyclopenta[a]phenanthrene-3,7,12(2H,4H)-trione (3Aa)

Colorless oil, 64% yield, dr = 1:1, ^1H NMR (500 MHz, CDCl_3) δ 7.29 – 7.25 (m, 1H), 7.20 – 7.13 (m, 2H), 7.03 (d, $J = 7.6$ Hz, 1H), 6.01 – 5.75 (m, 1H), 2.95 – 2.82 (m, 3H), 2.56 – 2.39 (m, 3H), 2.34 (ddt, $J = 18.1, 9.0, 4.9$ Hz, 4H), 2.28 – 2.20 (m, 3H), 2.18 – 2.12 (m, 2H), 2.11 – 2.02 (m, 3H), 2.00 – 1.94 (m, 1H), 1.86 (tt, $J = 11.6, 4.9$ Hz, 2H), 1.67 (d, $J = 2.9$ Hz, 4H), 1.62 (td, $J = 14.4, 4.7$ Hz, 1H), 1.48 (q, $J = 10.9, 7.8$ Hz, 1H), 1.40 (s, 3H), 1.36 (tt, $J = 5.8, 2.2$ Hz, 2H), 1.08 (s, 3H), 0.91 (d, $J = 6.6$ Hz, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 212.0, 209.1, 208.8, 162.5, 162.4 (C'), 138.0, 129.2, 127.8, 127.8 (C'), 126.8, 125.0, 122.7, 115.6 (d, $J = 239.6$ Hz), 115.6 (d, $J = 239.6$ Hz, C') 57.1, 51.9, 49.2, 47.0, 45.9, 45.9 (C'), 45.7, 45.5 (t, $J = 21.5$ Hz), 45.1, 42.9, 38.8, 36.6, 36.2, 36.0, 36.0 (C'), 35.4, 32.7, 31.7, 31.7 (C'), 28.1, 28.0 (C'), 27.8, 27.8 (C'), 25.3, 22.0, 18.9, 18.9 (C'), 12.0. ^{19}F NMR (471 MHz, CDCl_3) δ -111.9 – -113.6 (m, 2F). HRMS: calcd for $\text{C}_{34}\text{H}_{44}\text{F}_2\text{NO}_4^+ [\text{M}+\text{H}]^+$, 568.3233, found 568.3241.



2,4-Dimethyl-4-(2,2,2-trifluoroethyl)-4H-benzo[d][1,3]oxazine (3tb)

Colorless oil, 79% yield, ^1H NMR (500 MHz, CDCl_3) δ 7.32 – 7.26 (m, 1H), 7.21 – 7.11 (m, 2H), 7.06 (dd, $J = 7.6, 1.4$ Hz, 1H), 2.79 – 2.67 (m, 1H), 2.54 – 2.43 (m, 1H), 2.13 (s, 3H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, CDCl_3) δ 159.5, 137.8, 129.4, 127.5, 126.8, 125.1 (q, $J = 279.1$ Hz), 124.8, 122.8, 76.3 (q, $J = 2.0$ Hz), 44.3 (q, $J = 26.9$ Hz), 27.1 (q, $J = 1.7$ Hz), 21.6. ^{19}F NMR (471 MHz, CDCl_3) δ 60.4 (t, $J = 279.1$ Hz, 3F). HRMS: calcd for $\text{C}_{12}\text{H}_{13}\text{F}_3\text{NO}^+ [\text{M}+\text{H}]^+$, 244.0944, found 244.0946.

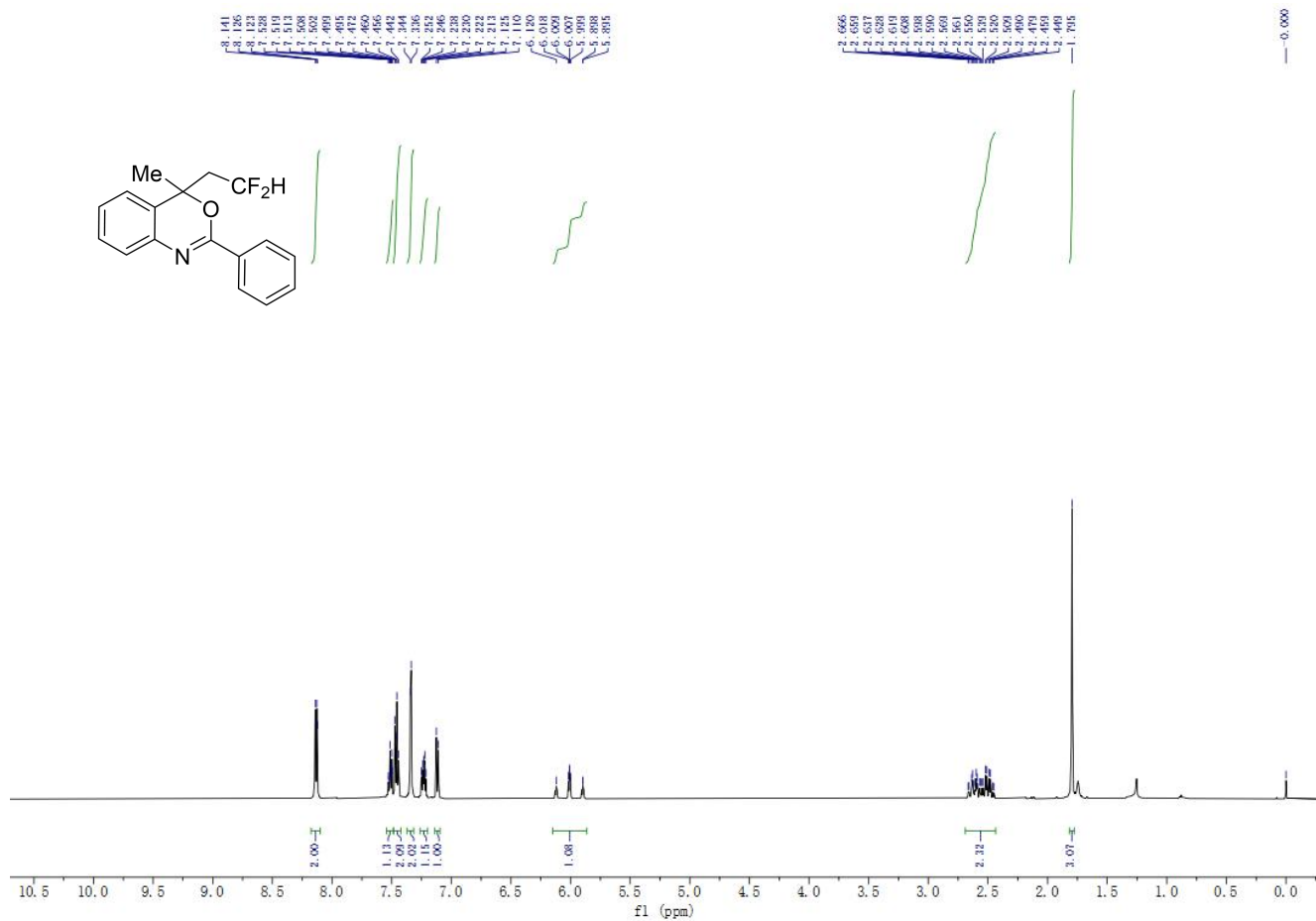


4-Methyl-2-phenyl-4-(2,2,2-trifluoroethyl)-4H-benzo[d][1,3]oxazine (3ab)

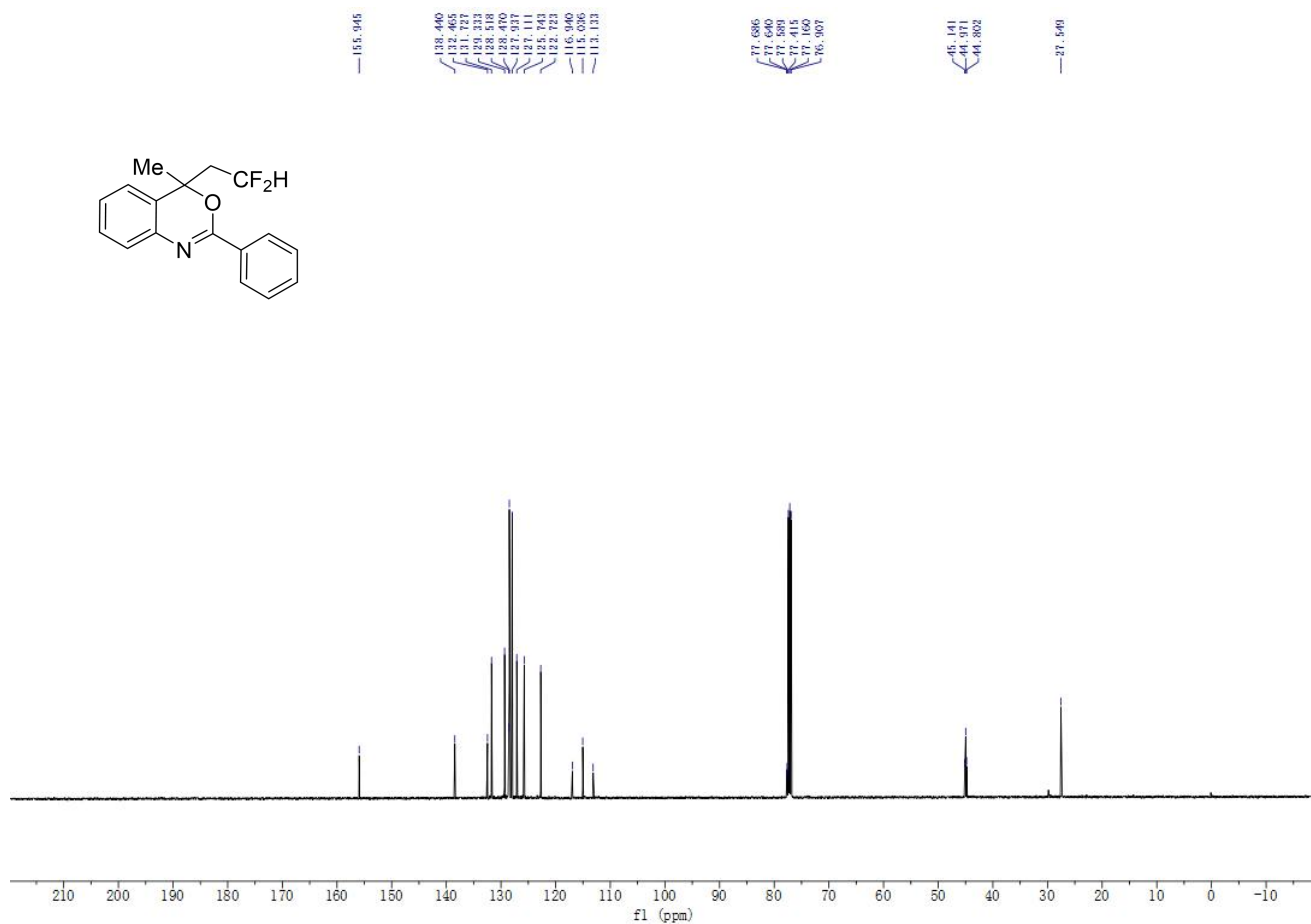
Colorless oil, 71% yield, ^1H NMR (500 MHz, Chloroform-*d*) δ 8.19 – 8.14 (m, 2H), 7.50 (dd, J = 8.5, 6.0 Hz, 1H), 7.45 (dd, J = 8.4, 6.6 Hz, 2H), 7.34 (d, J = 3.6 Hz, 2H), 7.23 (ddd, J = 10.9, 5.5, 3.0 Hz, 1H), 7.13 (d, J = 7.6 Hz, 1H), 2.90 – 2.56 (m, 2H), 1.92 (s, 3H). ^{13}C NMR (126 MHz, Chloroform-*d*) δ 155.8, 138.4, 132.3, 131.7, 129.5, 128.4, 128.1, 127.1, 125.3 (q, J = 279.2 Hz), 125.7, 122.7, 76.7 (q, J = 2.1 Hz), 43.7 (q, J = 27.1 Hz), 26.4 (q, J = 1.9 Hz). ^{19}F NMR (471 MHz, Chloroform-*d*) δ -59.9 (s, 3F). HRMS: calcd for $\text{C}_{17}\text{H}_{15}\text{F}_3\text{NO}^+$ $[\text{M}+\text{H}]^+$, 306.1100, found 306.1107.

NMR spectra for compounds

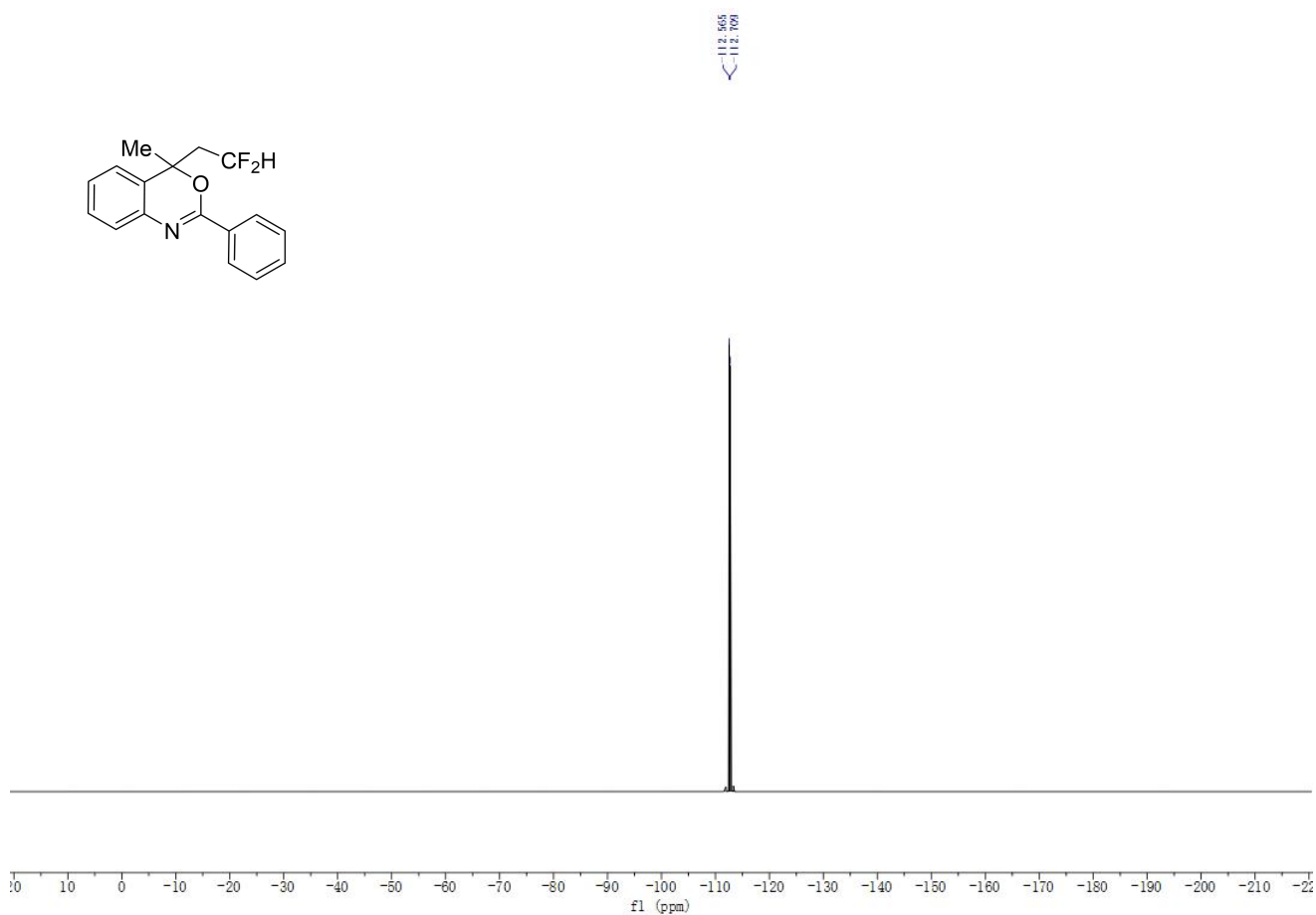
¹H NMR Spectrum of **3aa**



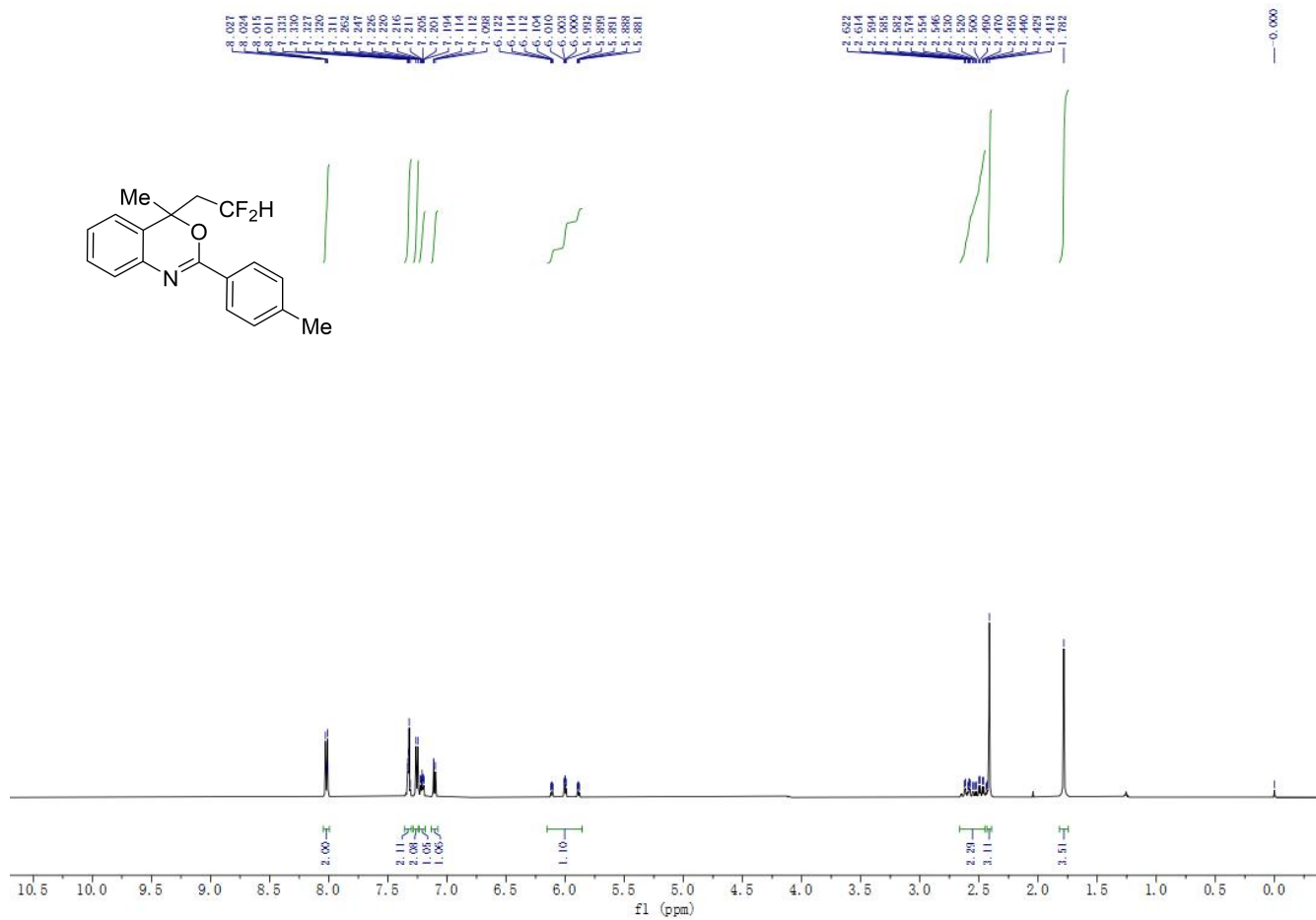
¹³C NMR Spectrum of **3aa**



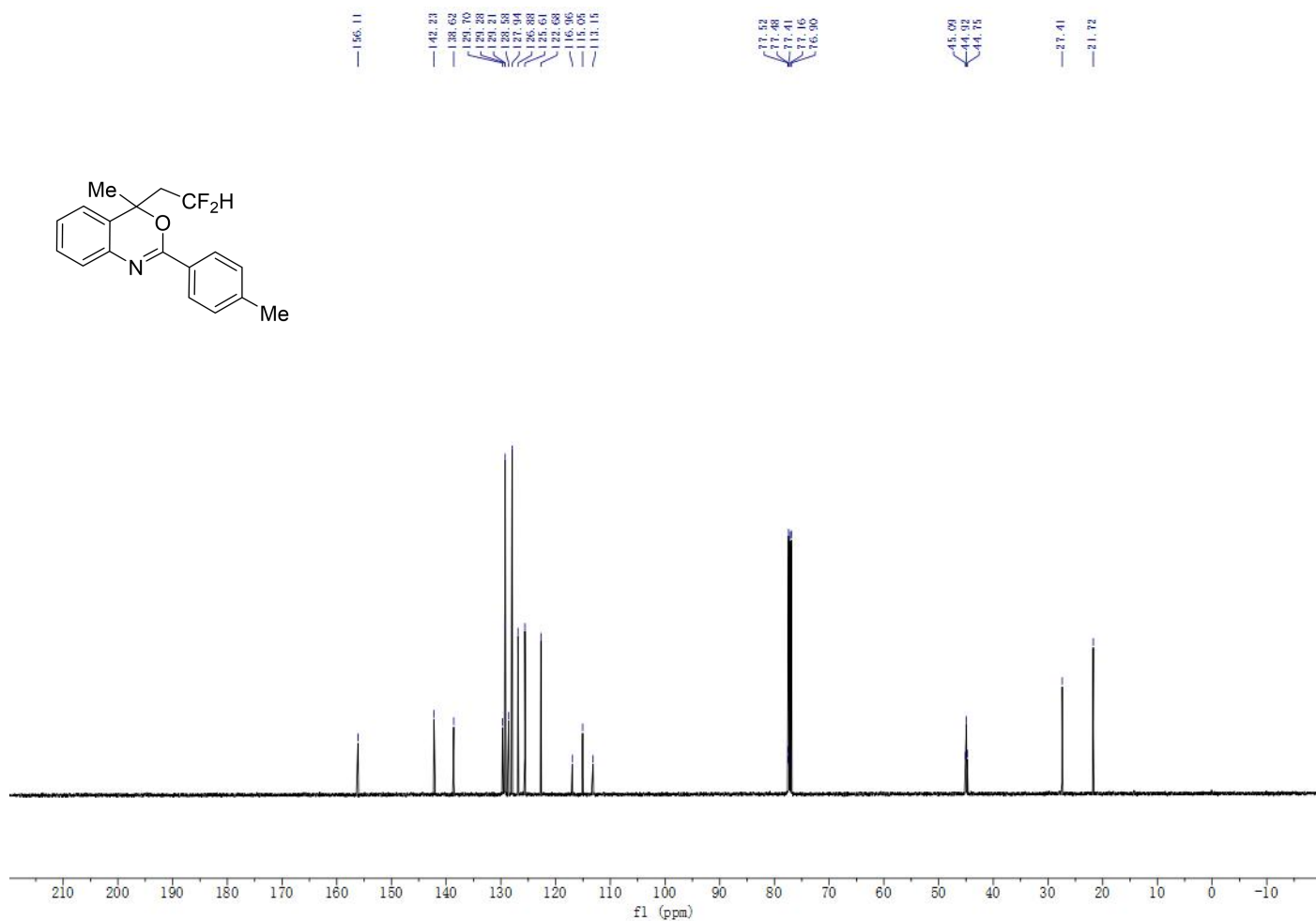
¹⁹F NMR Spectrum of 3aa



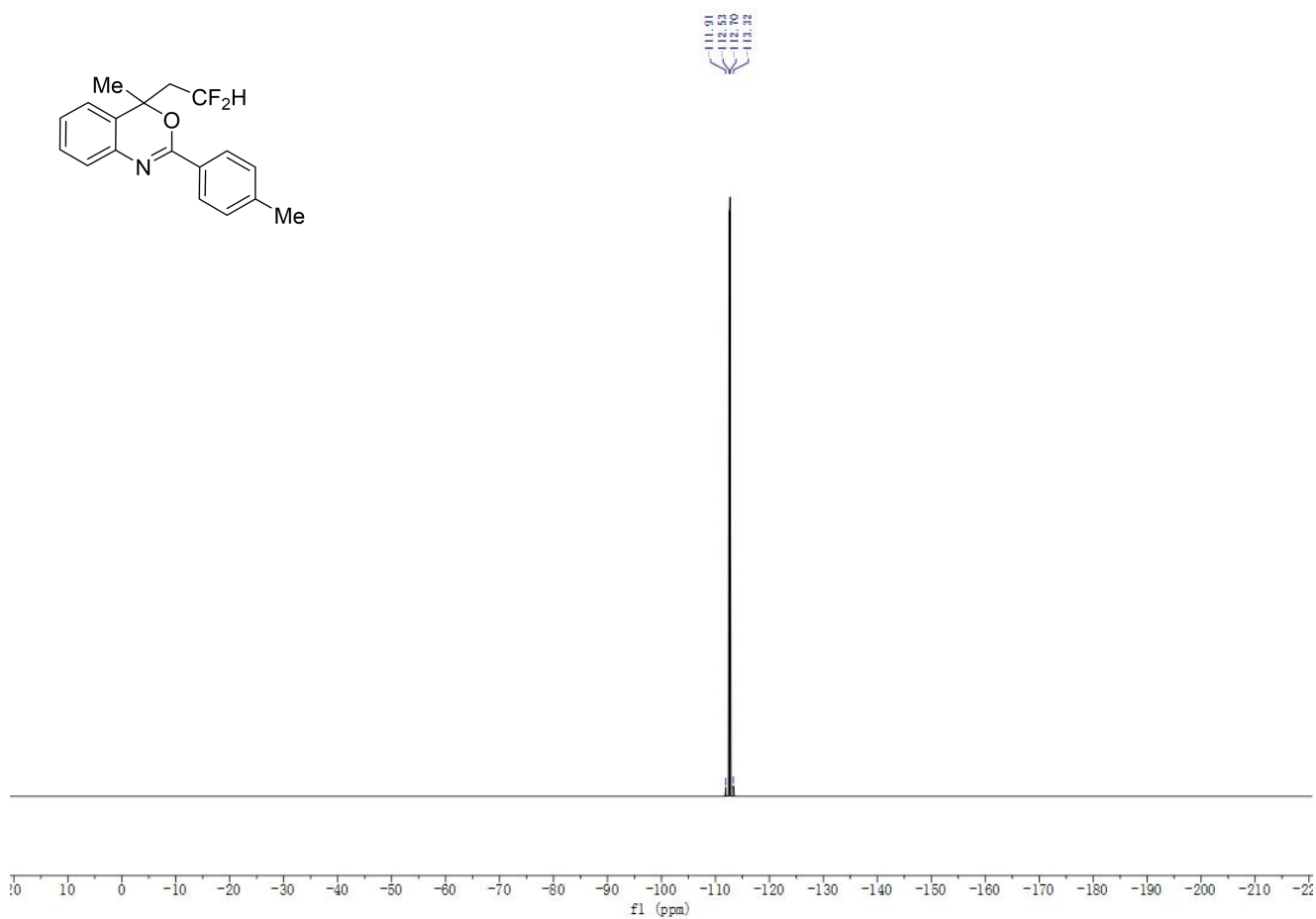
¹H NMR Spectrum of 3ba



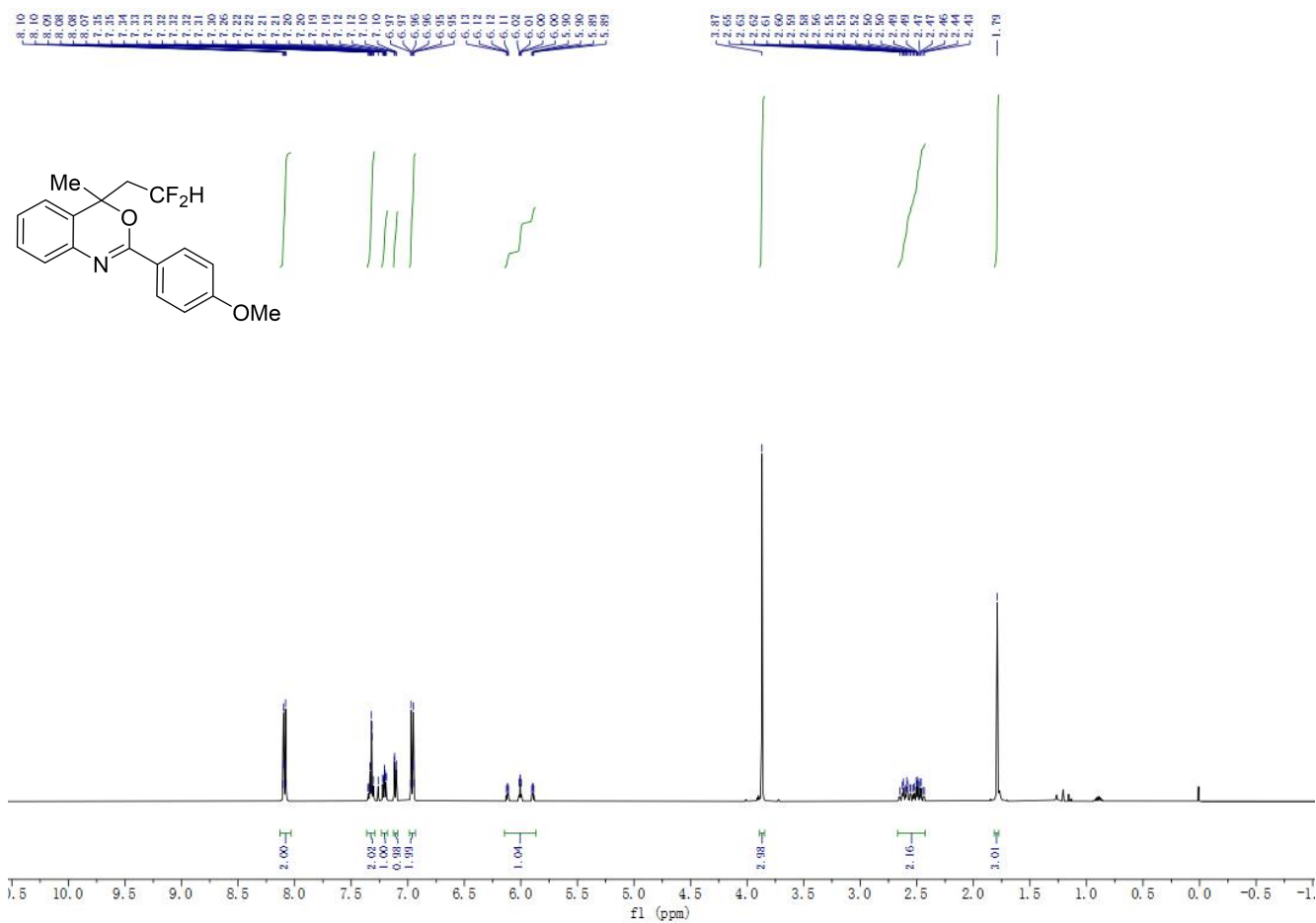
¹³C NMR Spectrum of **3ba**



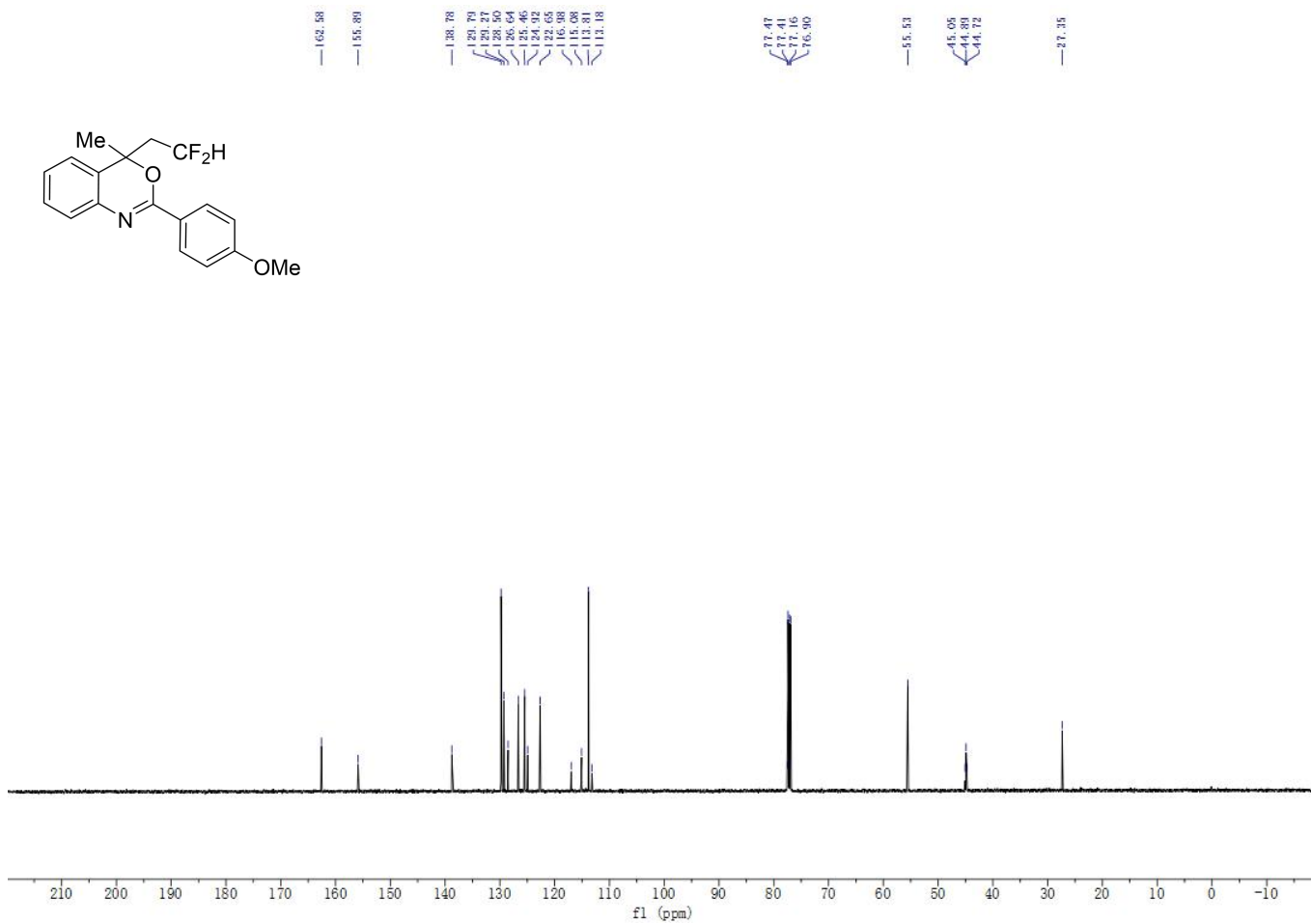
¹⁹F NMR Spectrum of **3ba**



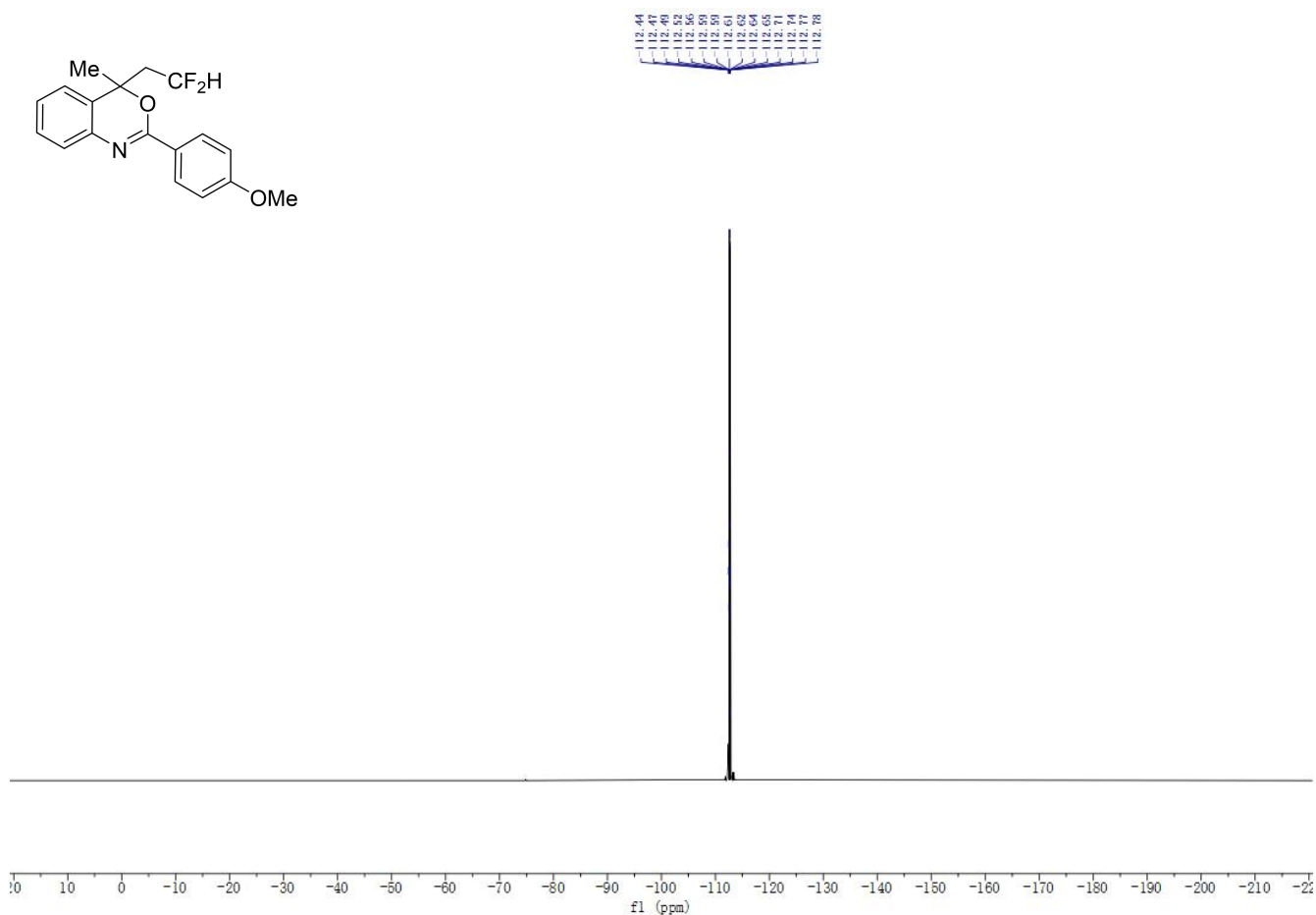
¹H NMR Spectrum of 3ca



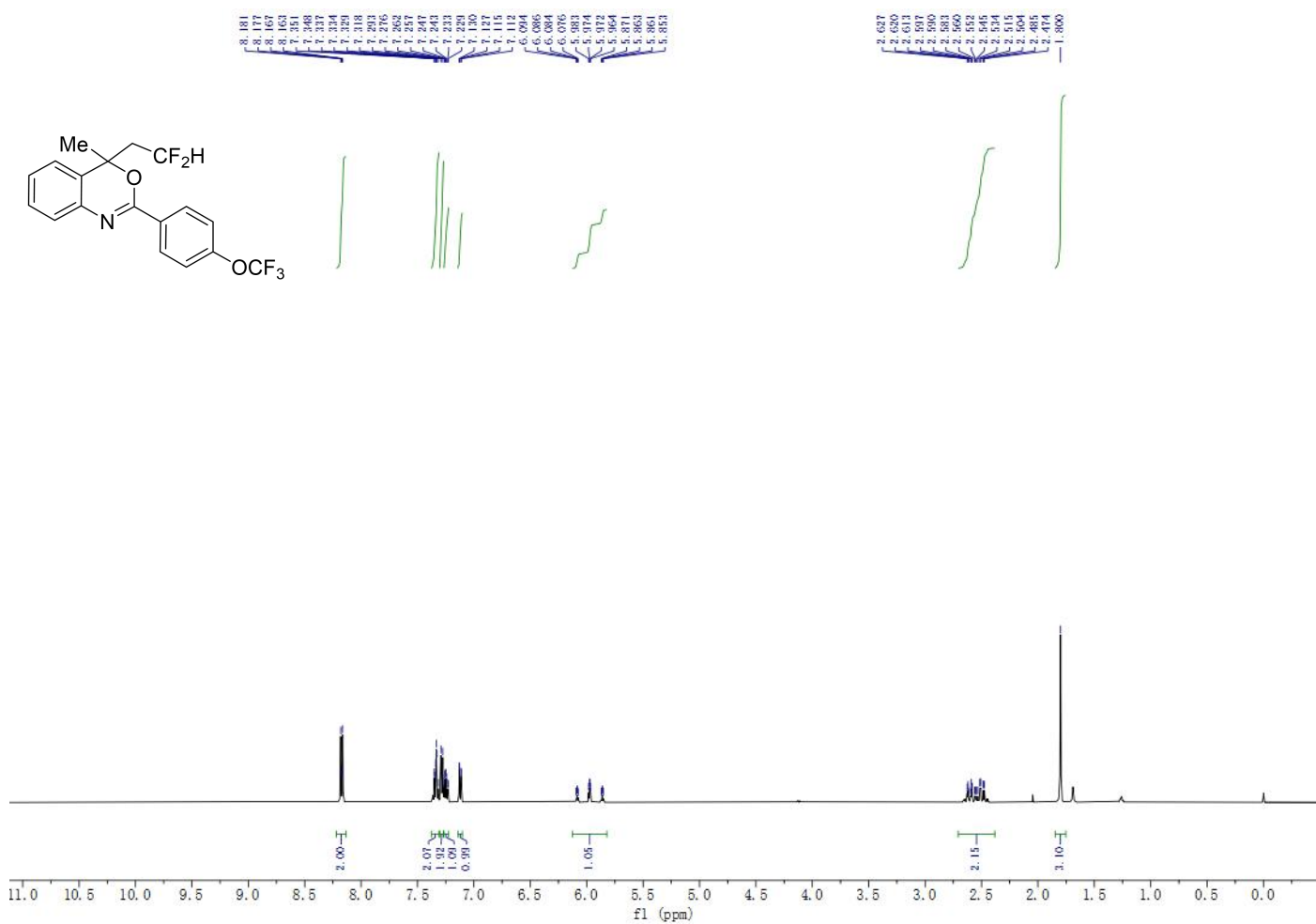
¹³C NMR Spectrum of 3ca



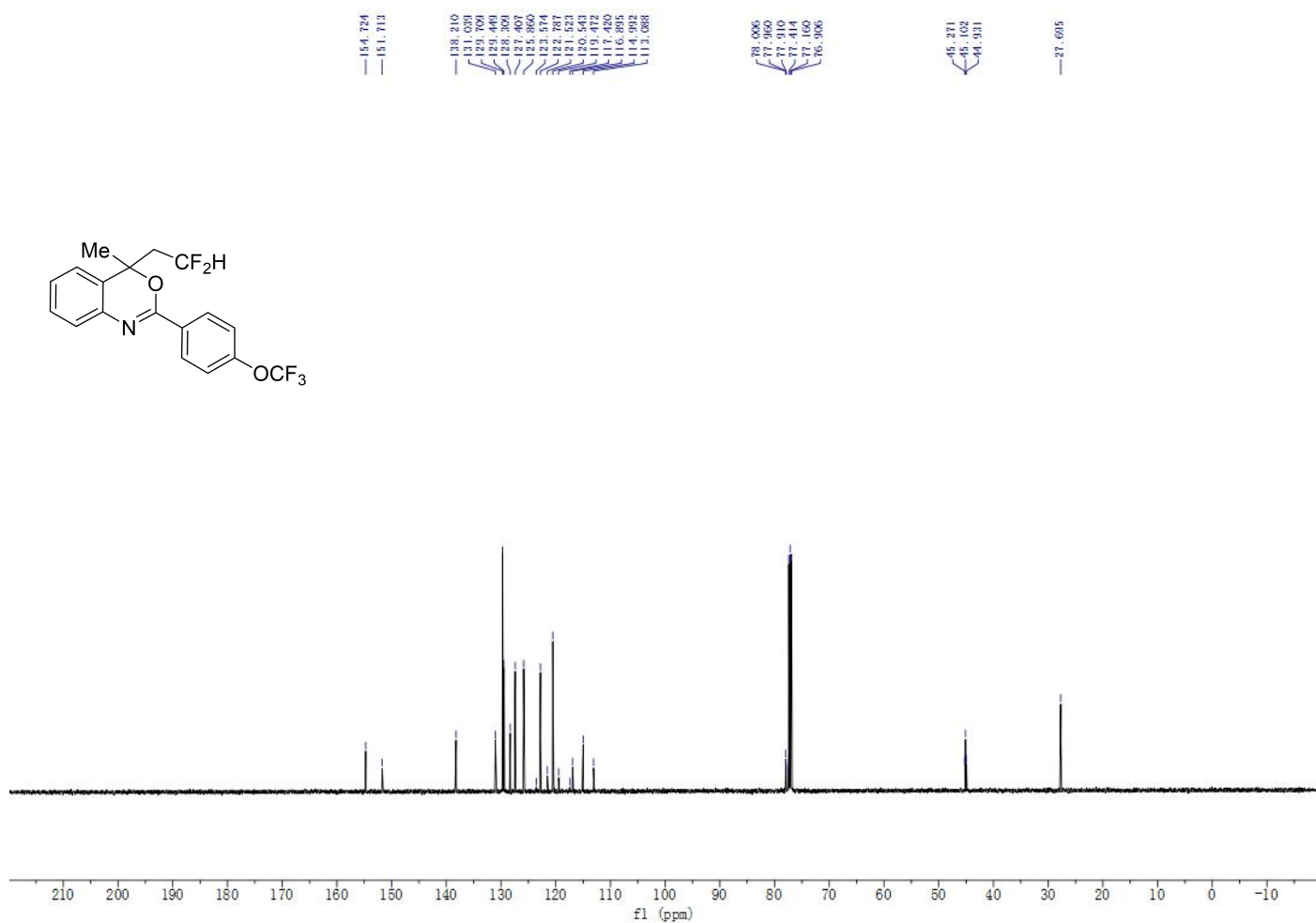
¹⁹F NMR Spectrum of 3ca



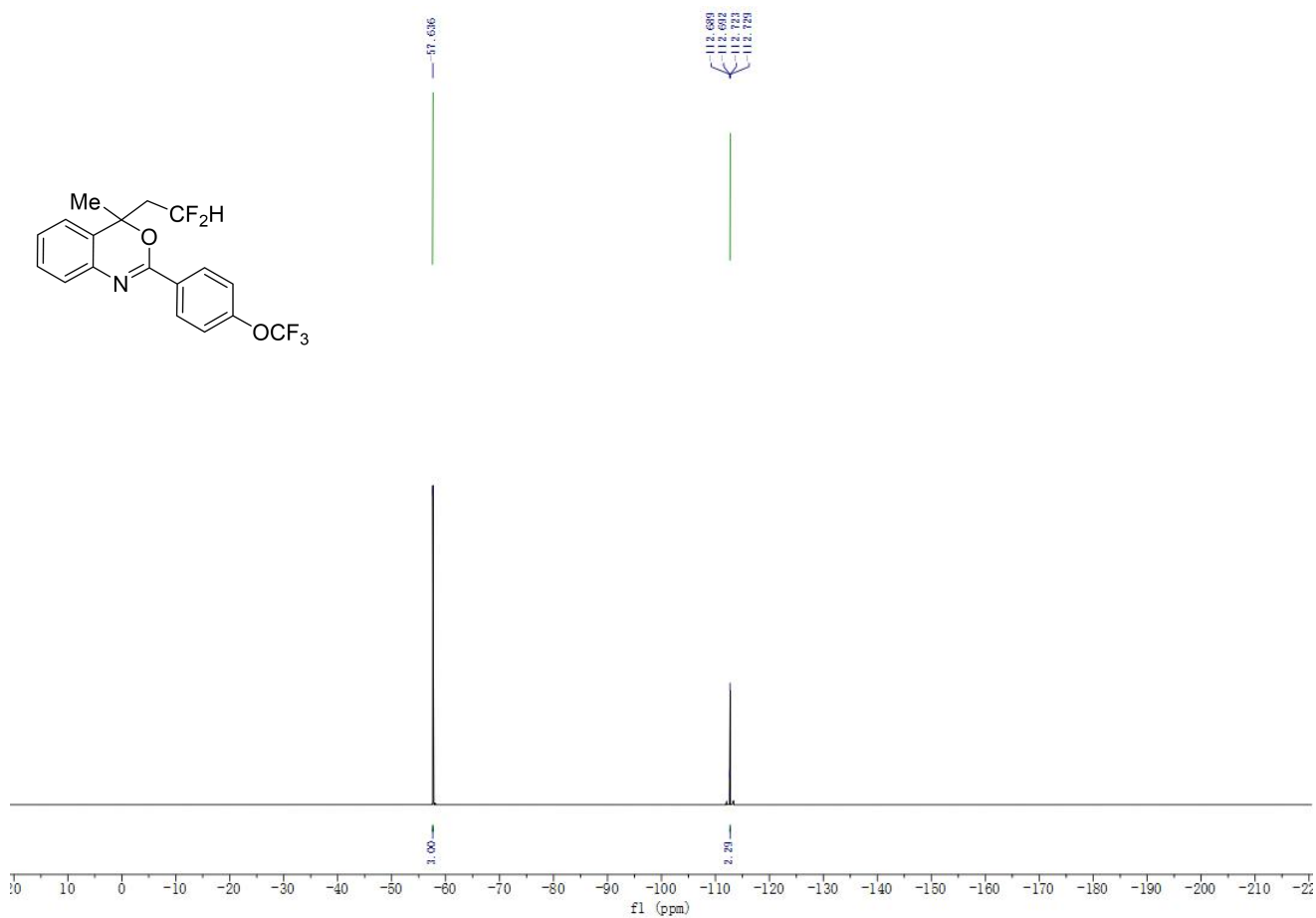
¹H NMR Spectrum of 3da



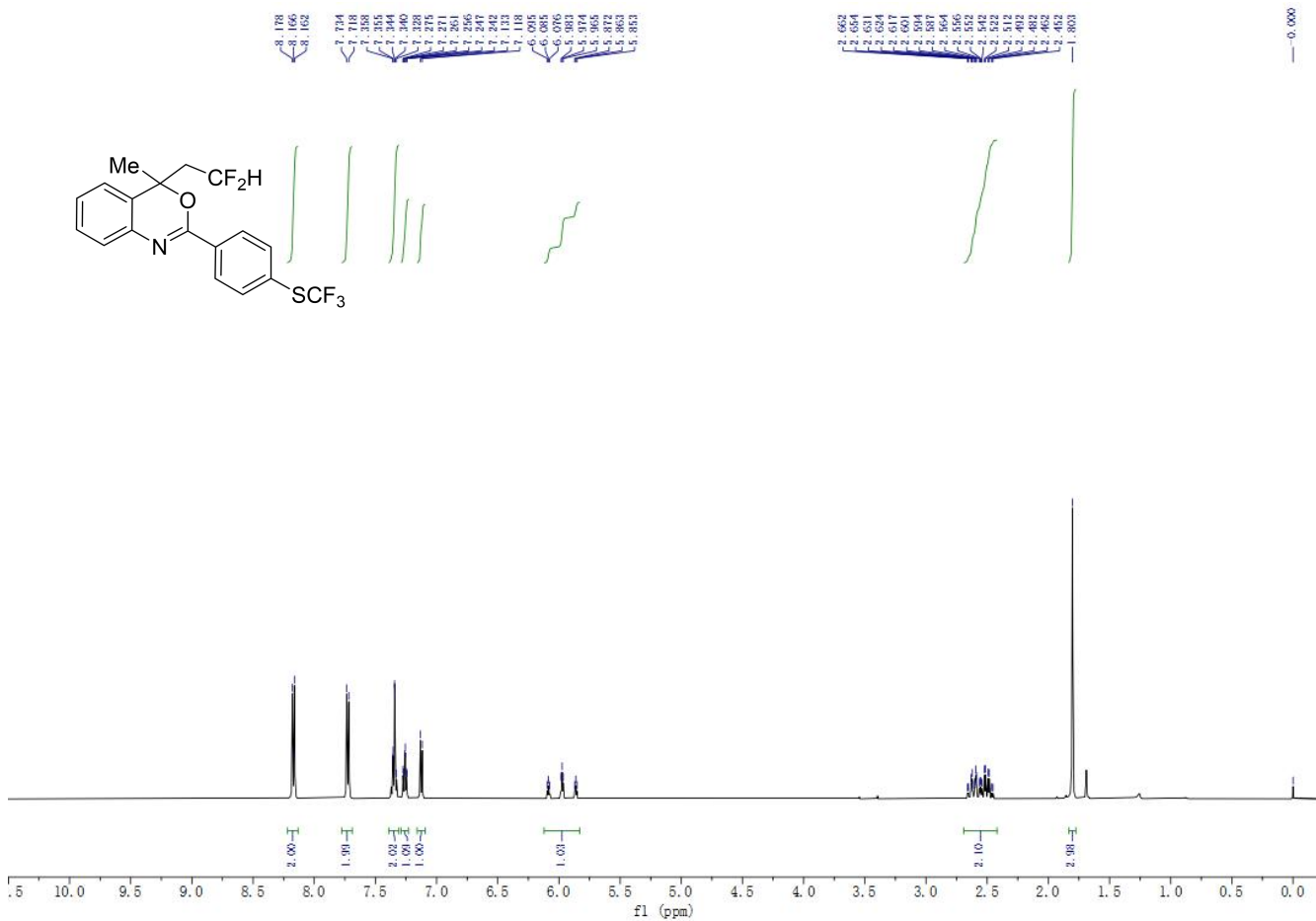
¹³C NMR Spectrum of **3da**



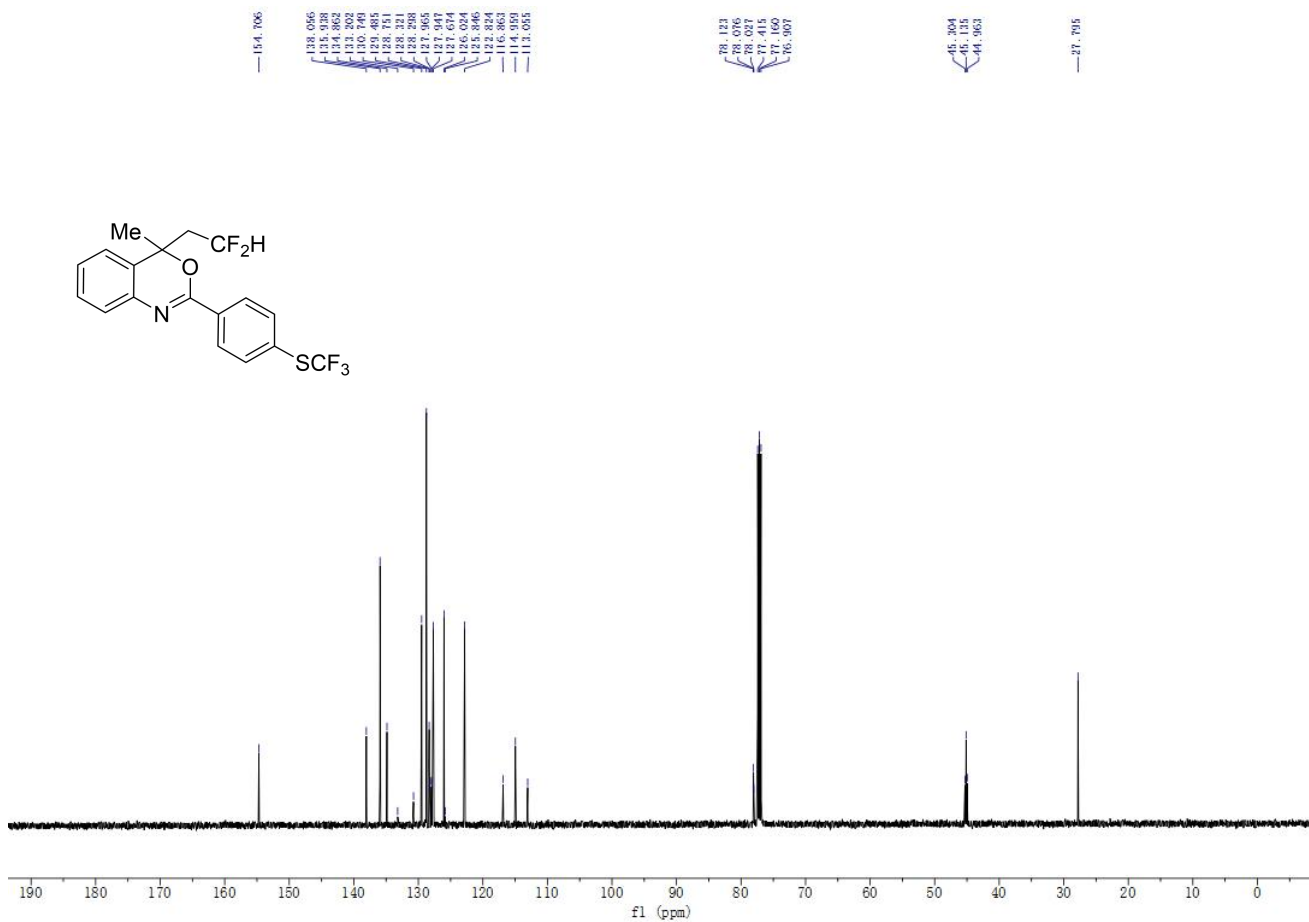
¹⁹F NMR Spectrum of **3da**



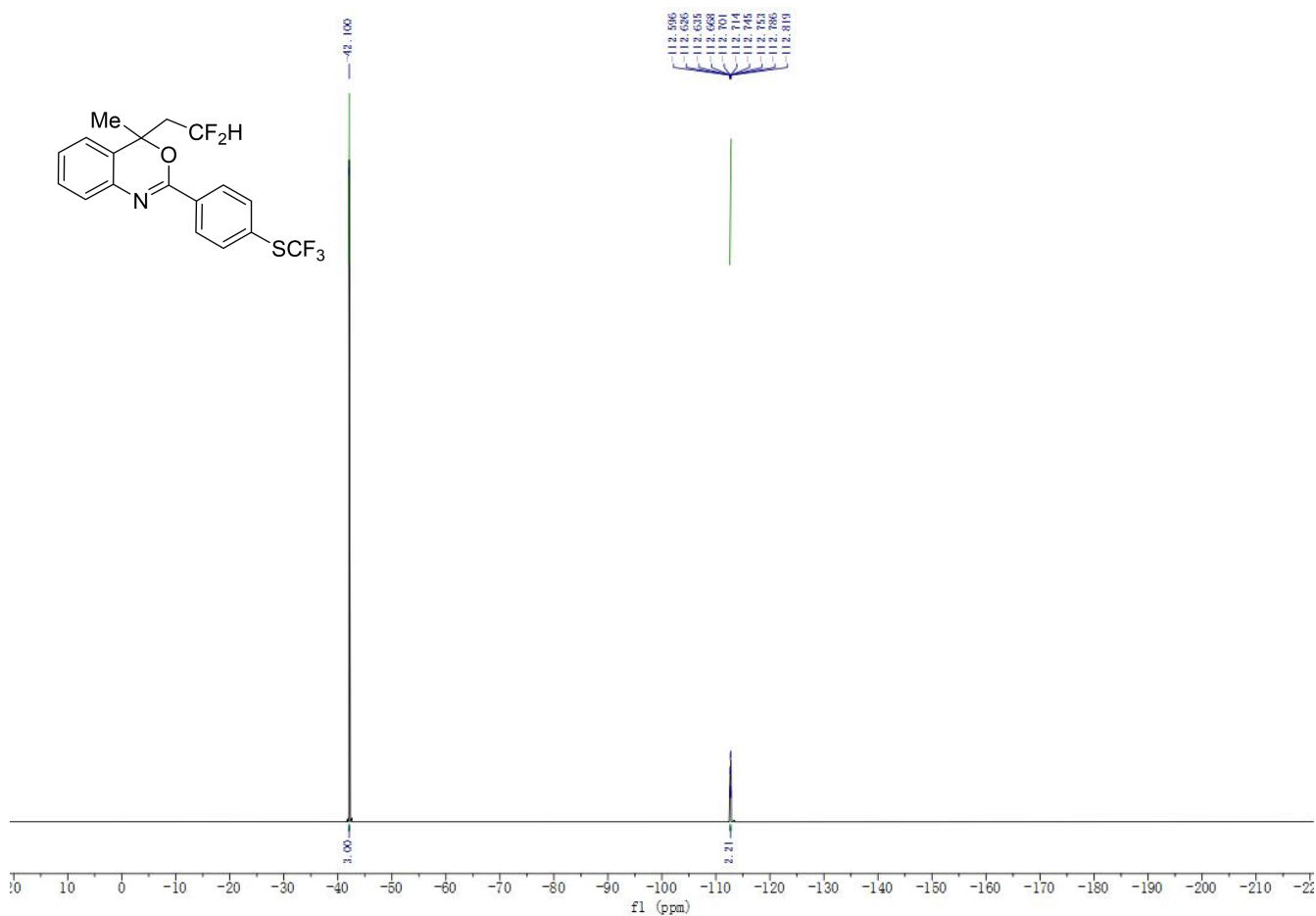
¹H NMR Spectrum of **3ea**



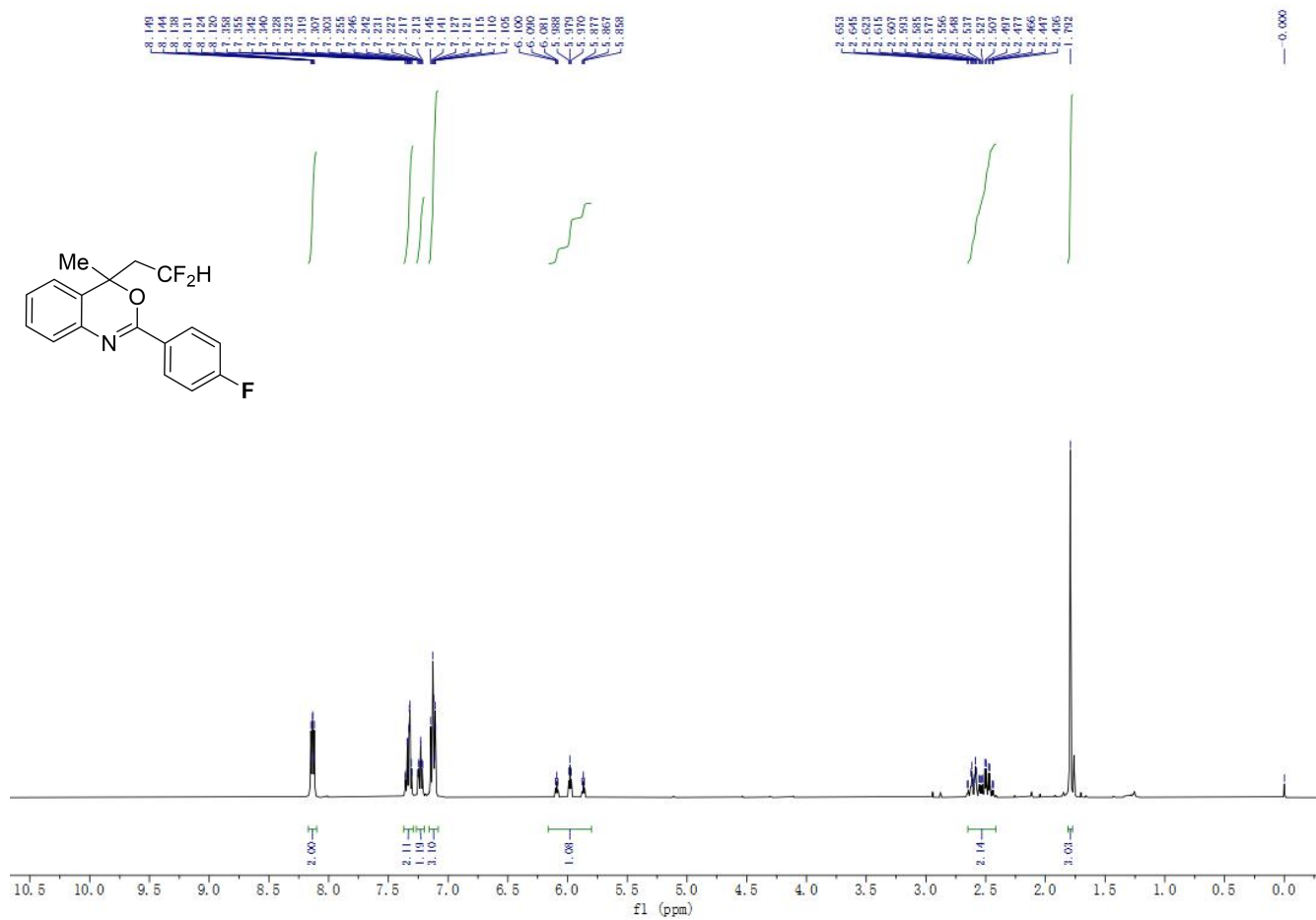
¹³C NMR Spectrum of **3ea**



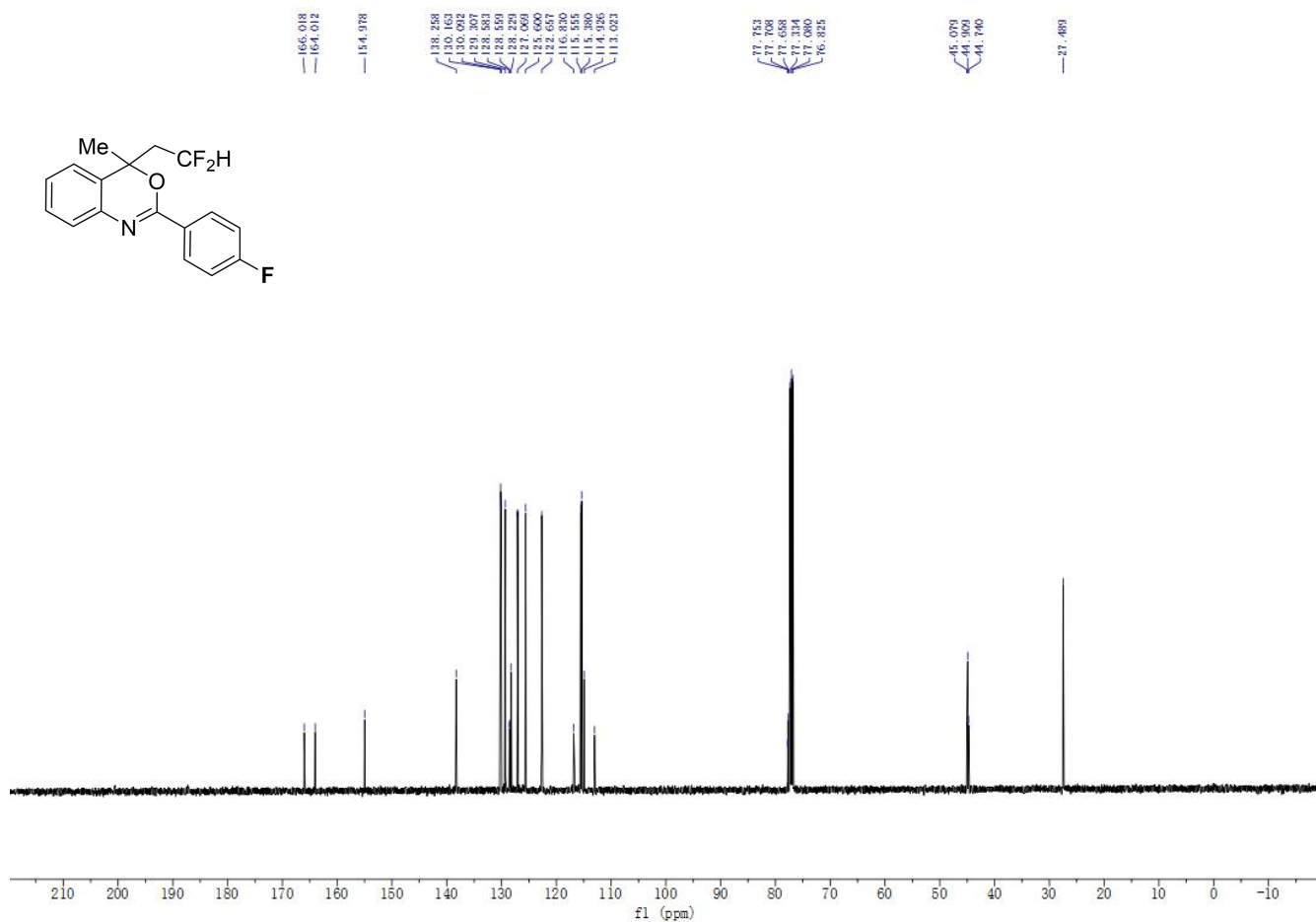
¹⁹F NMR Spectrum of 3ea



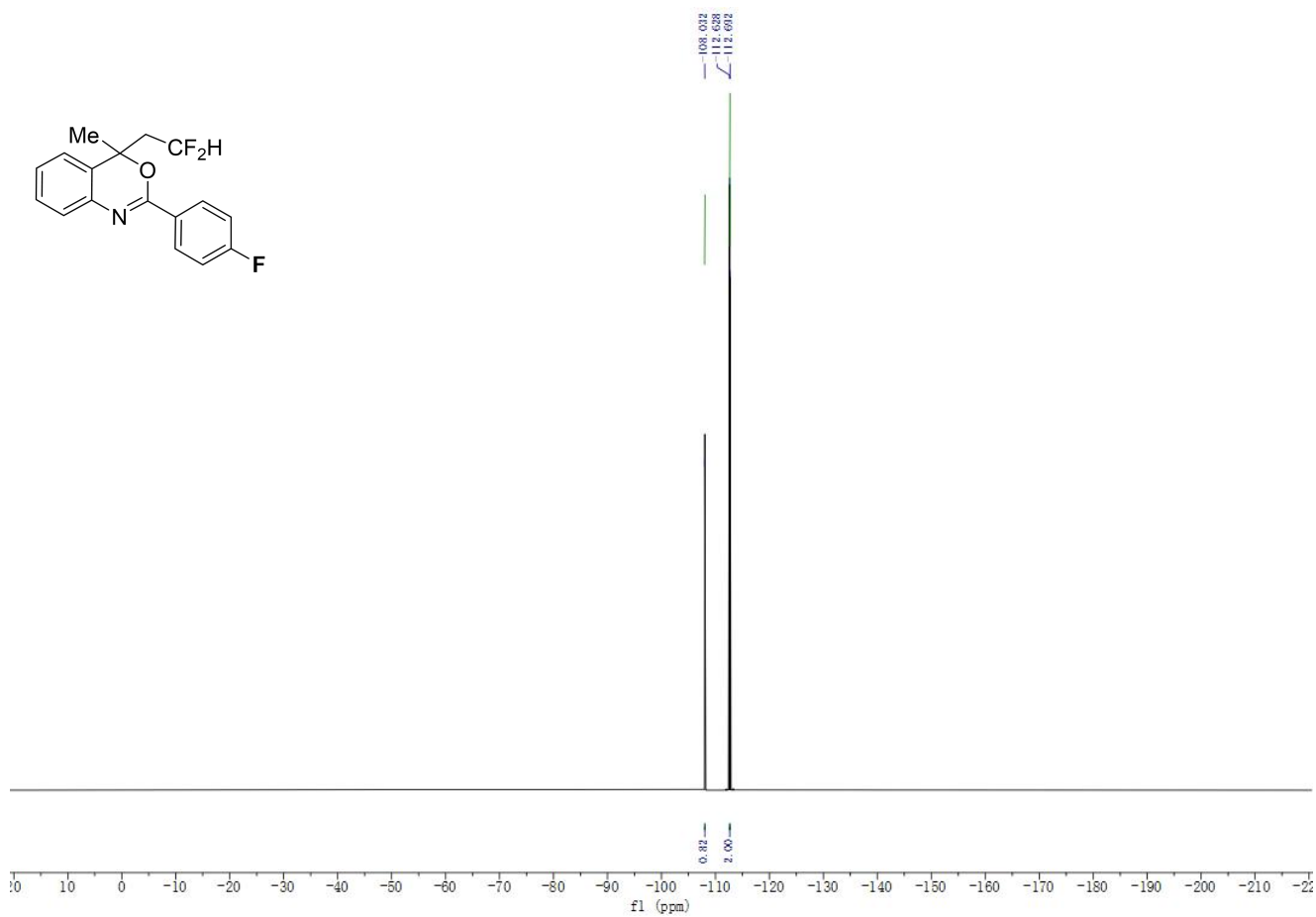
¹H NMR Spectrum of 3fa



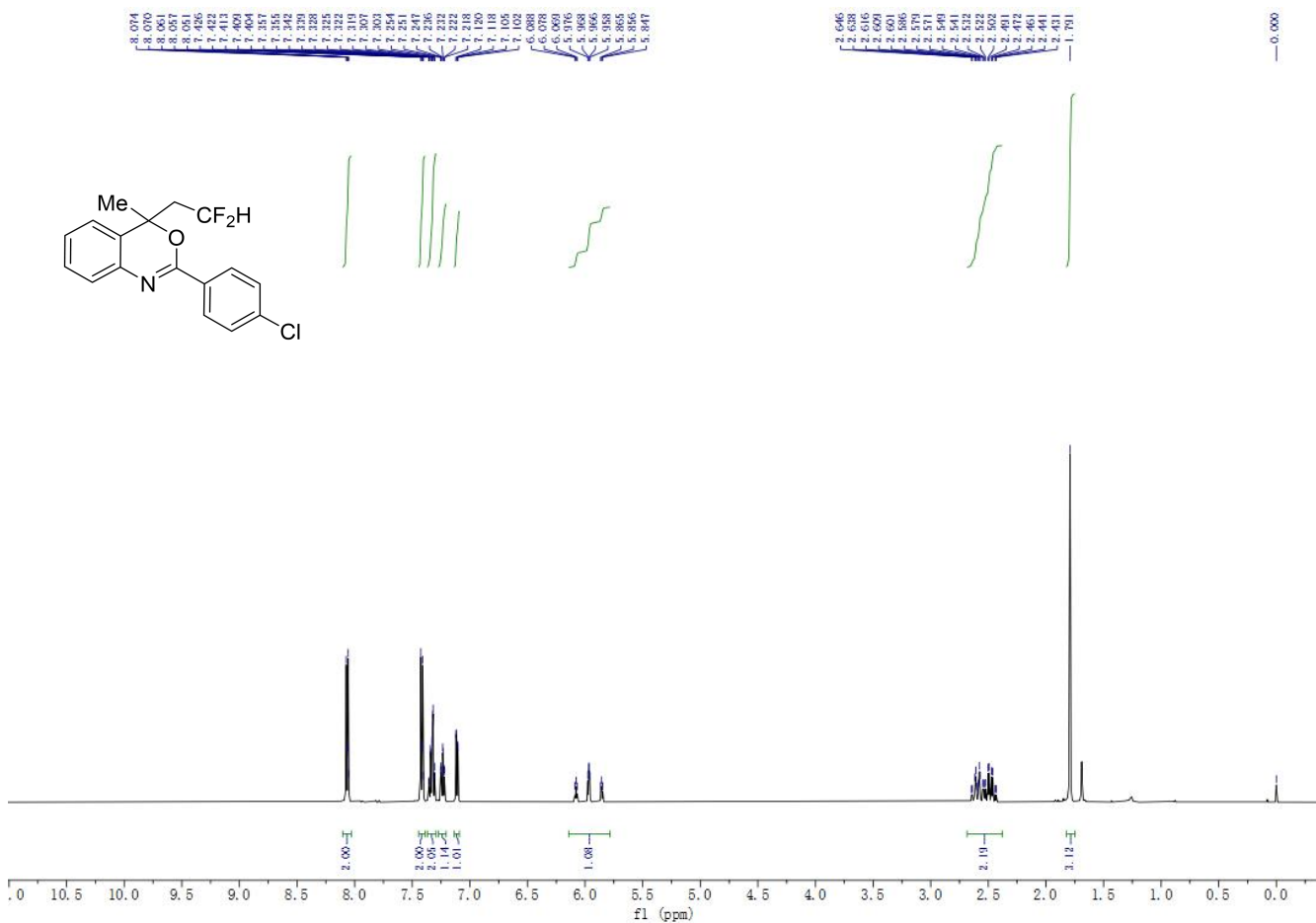
¹³C NMR Spectrum of 3fa



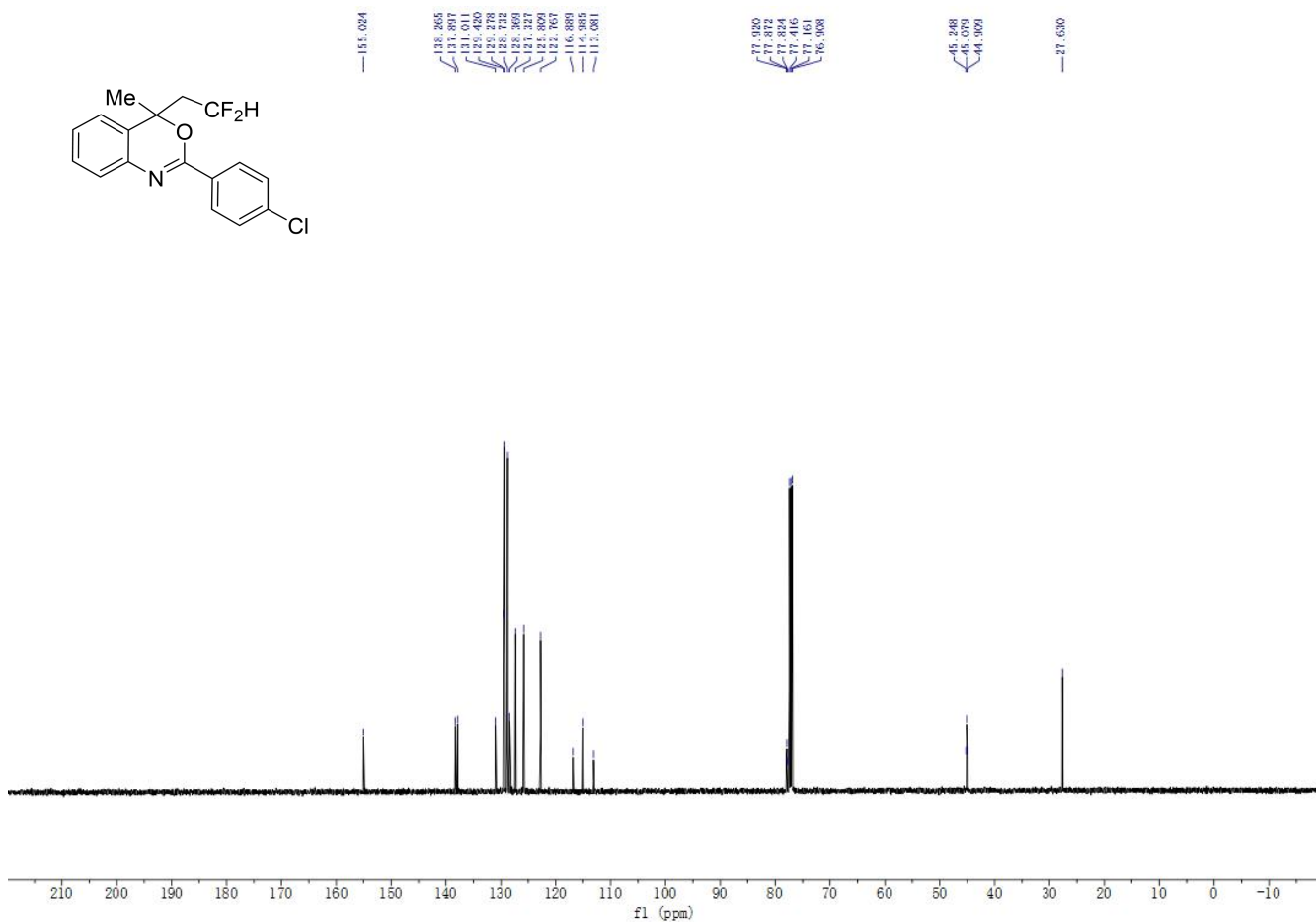
¹⁹F NMR Spectrum of 3fa



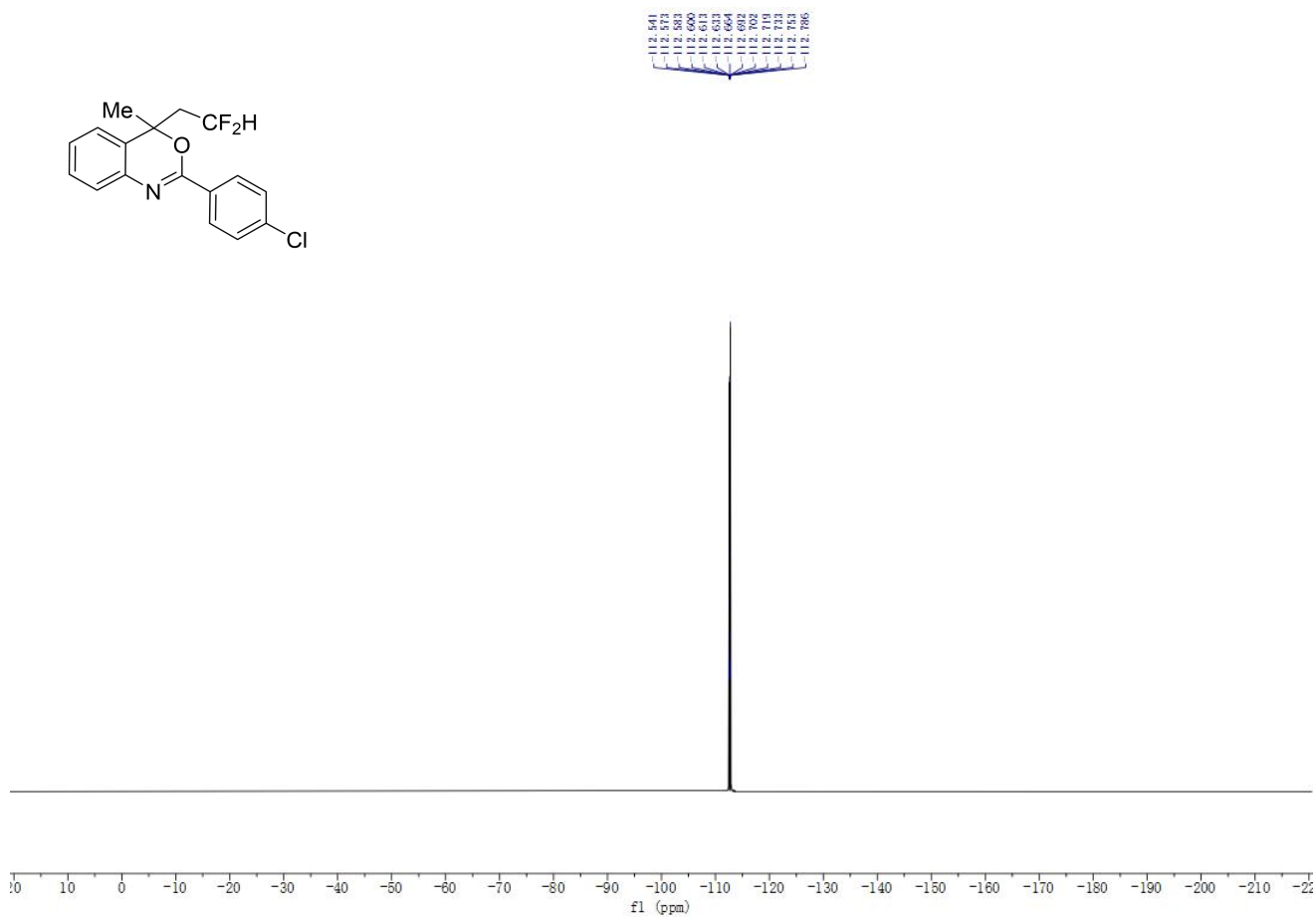
¹H NMR Spectrum of **3ga**



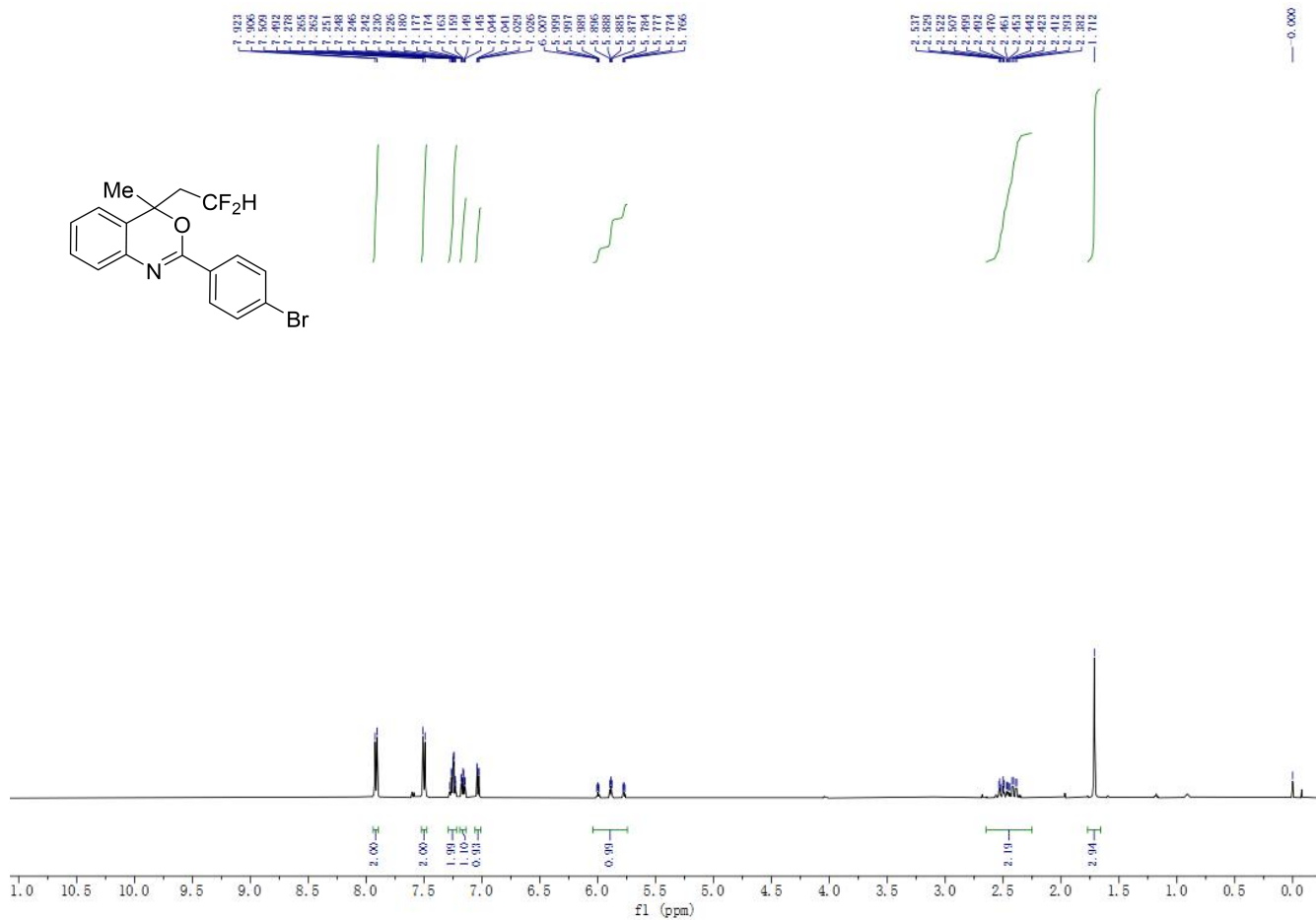
¹³C NMR Spectrum of **3ga**



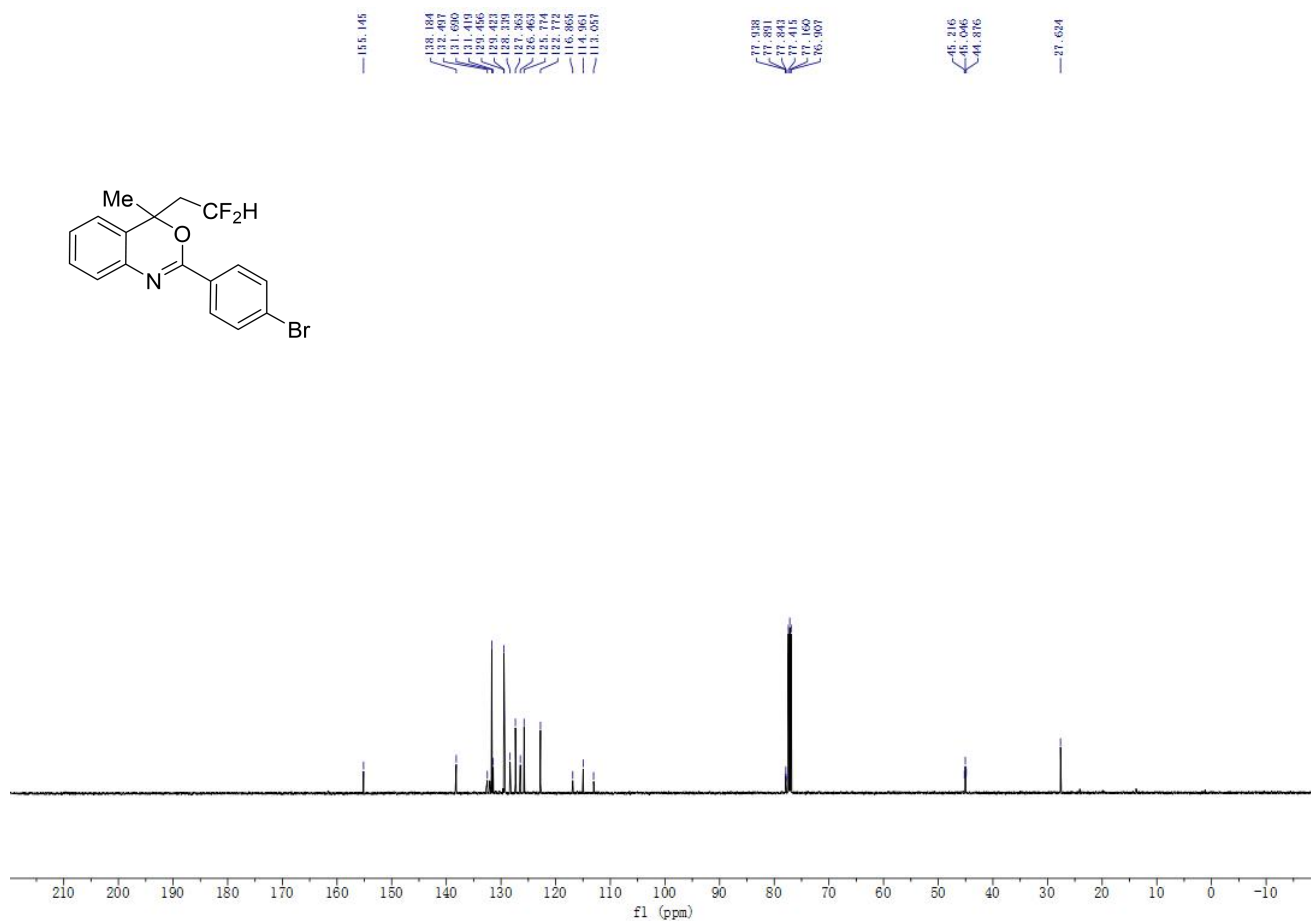
¹⁹F NMR Spectrum of 3ga



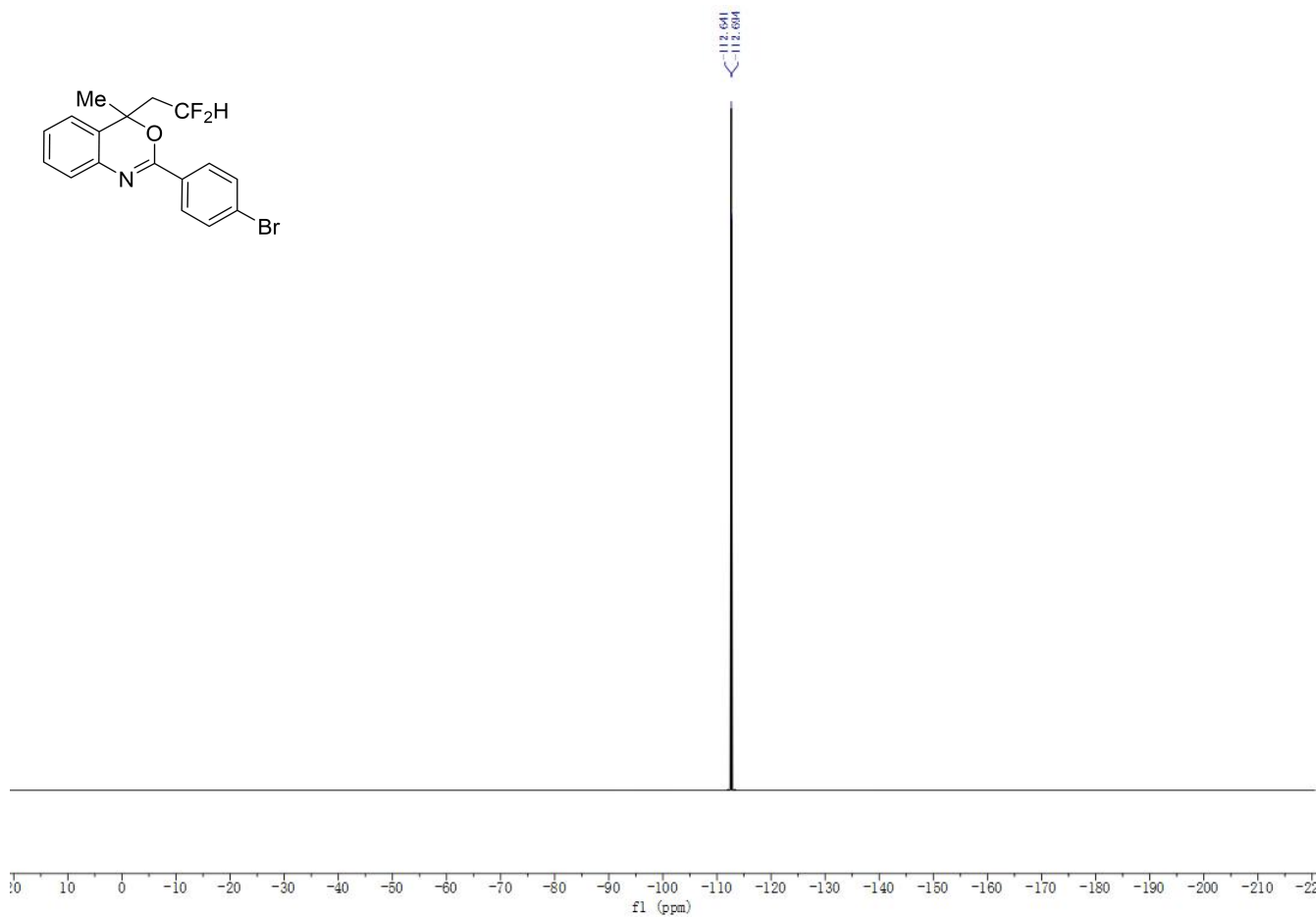
¹H NMR Spectrum of 3ha



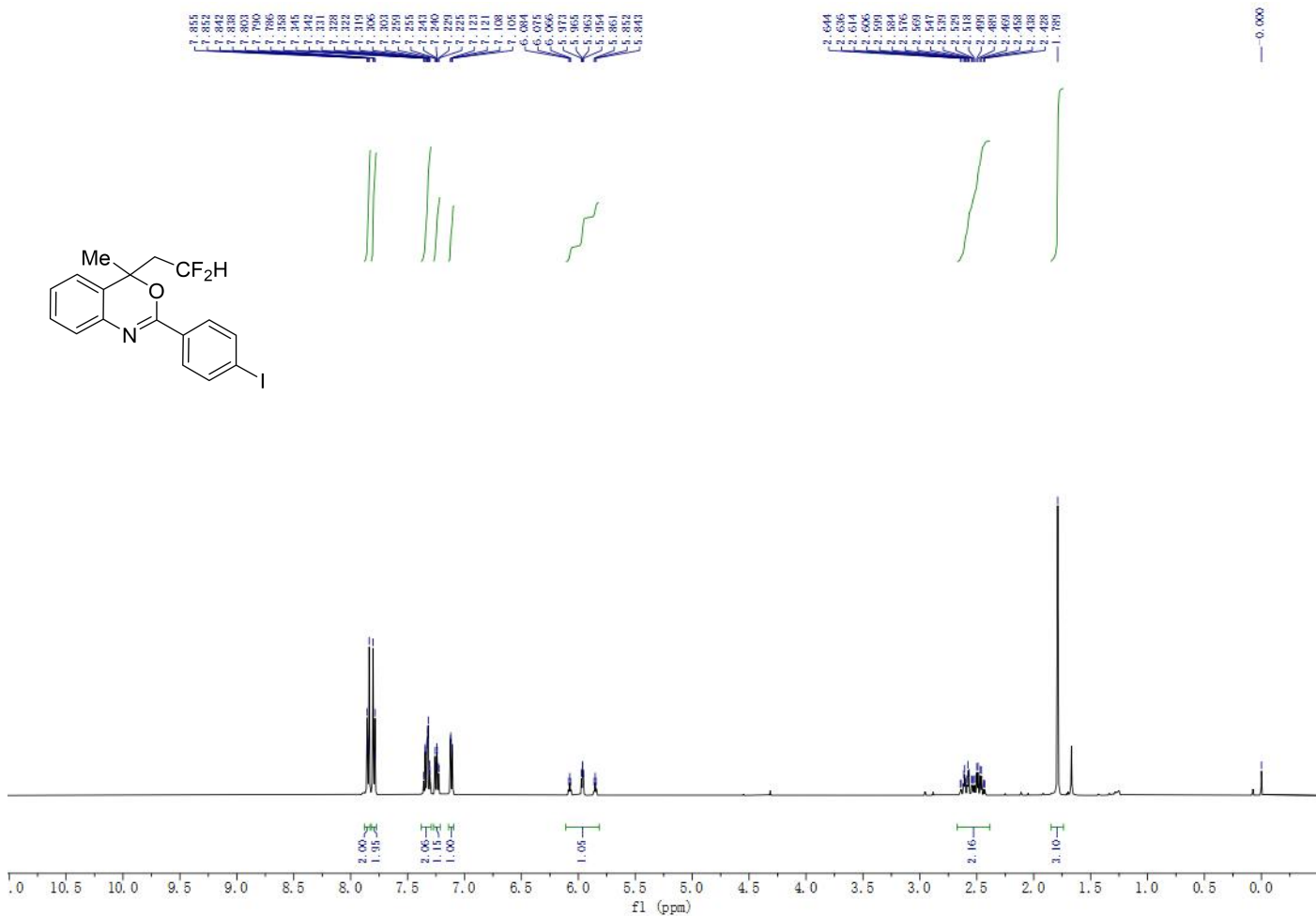
¹³C NMR Spectrum of **3ha**



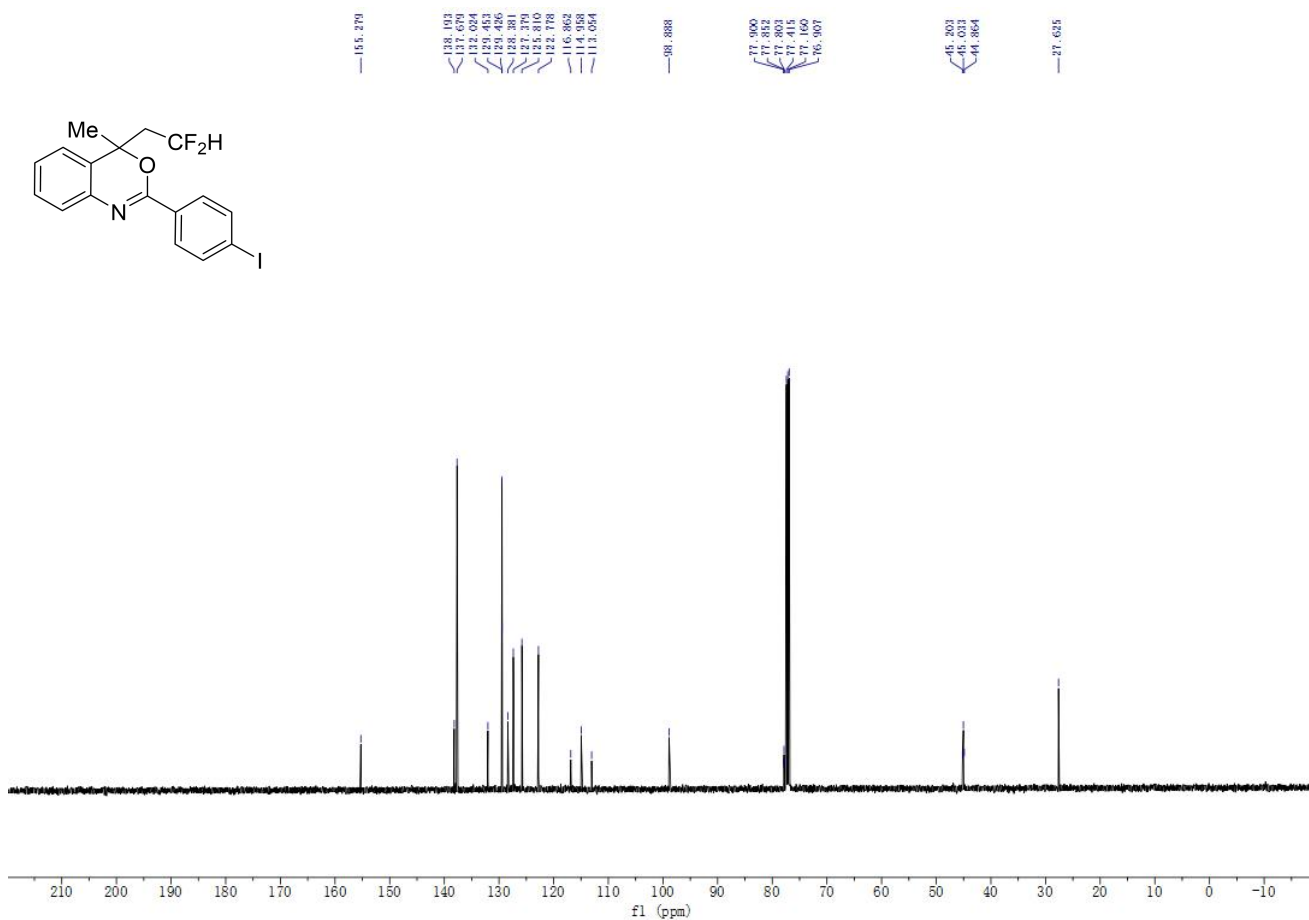
¹⁹F NMR Spectrum of **3ha**



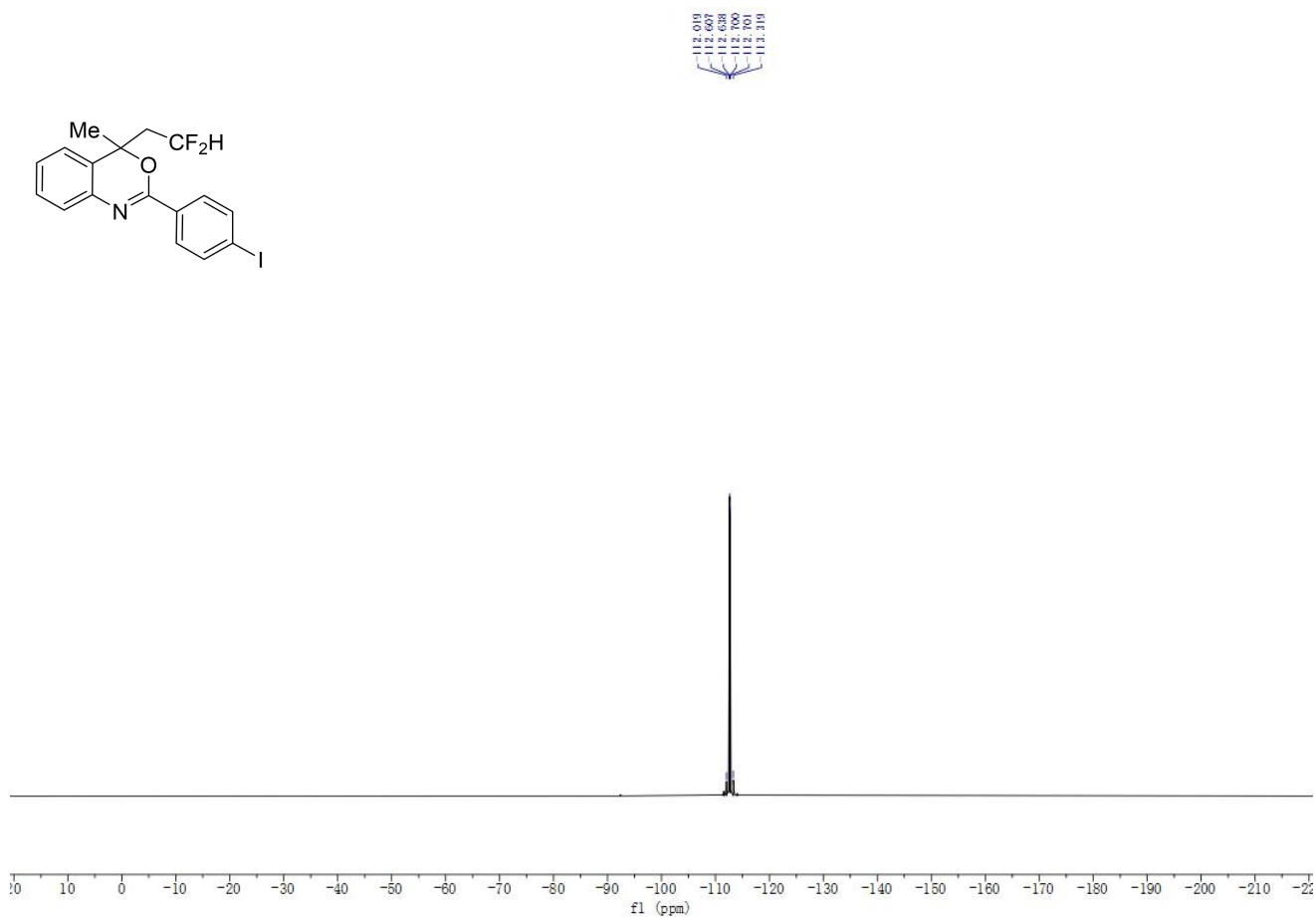
¹H NMR Spectrum of **3ia**



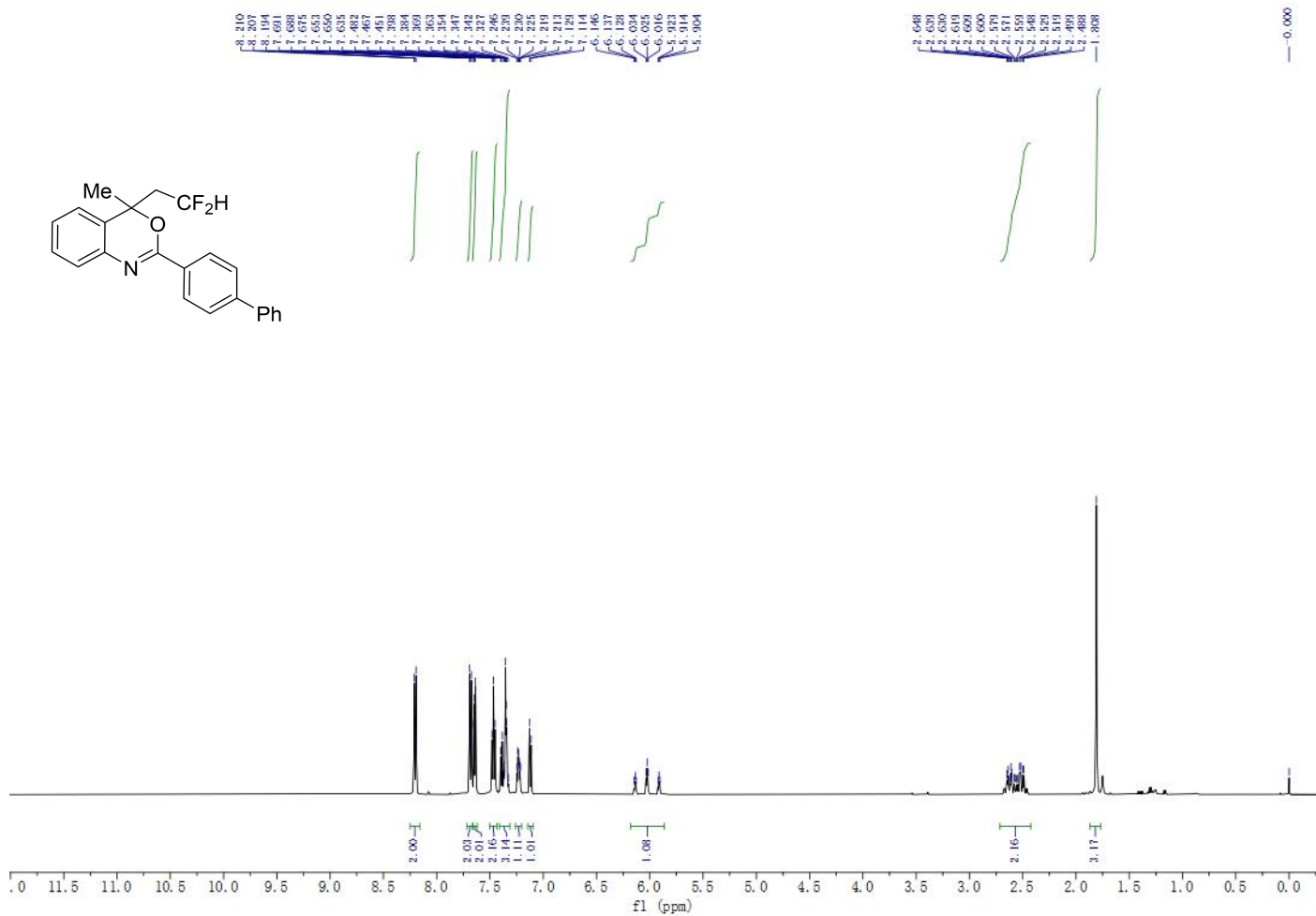
¹³C NMR Spectrum of **3ia**



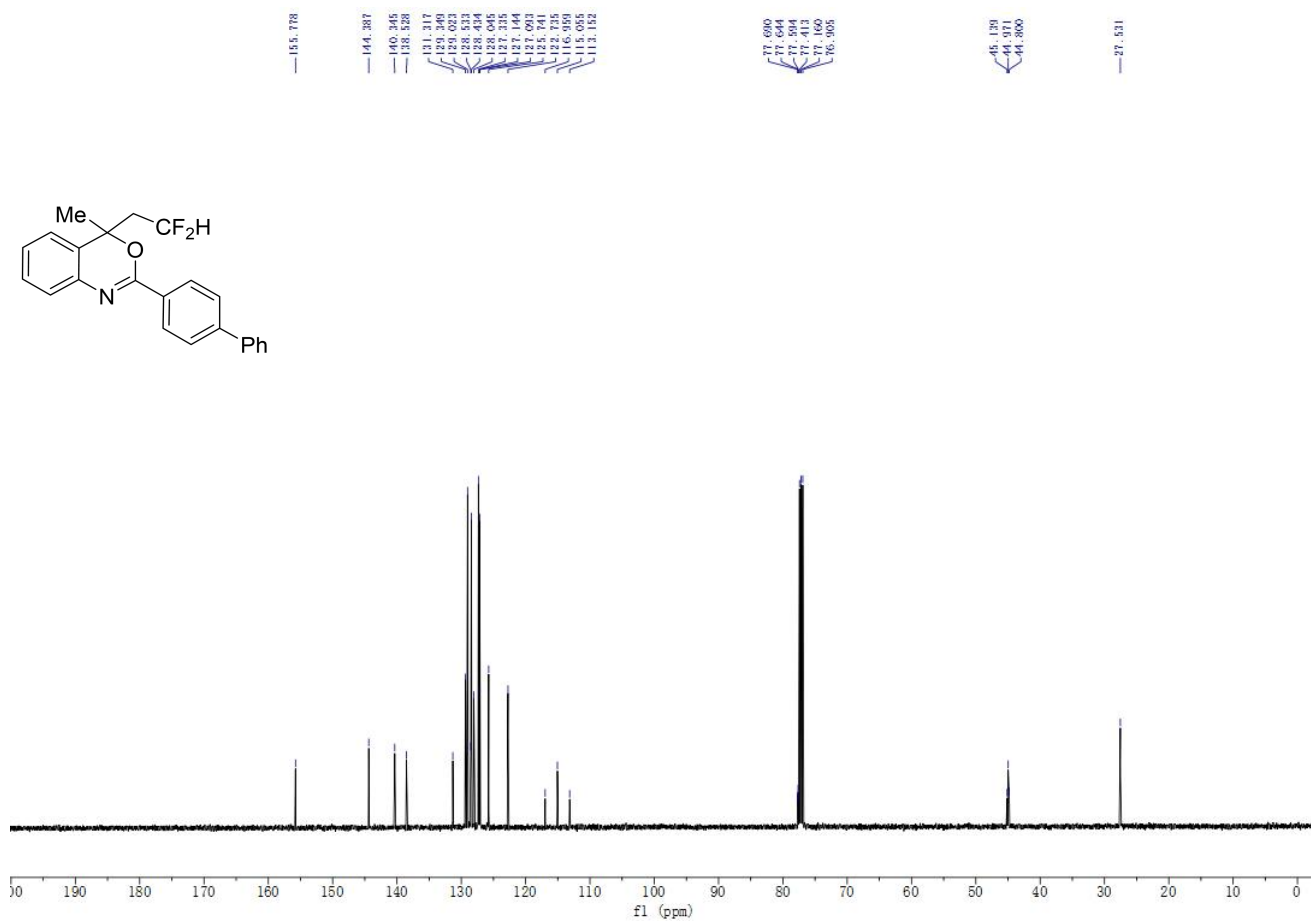
¹⁹F NMR Spectrum of **3ia**



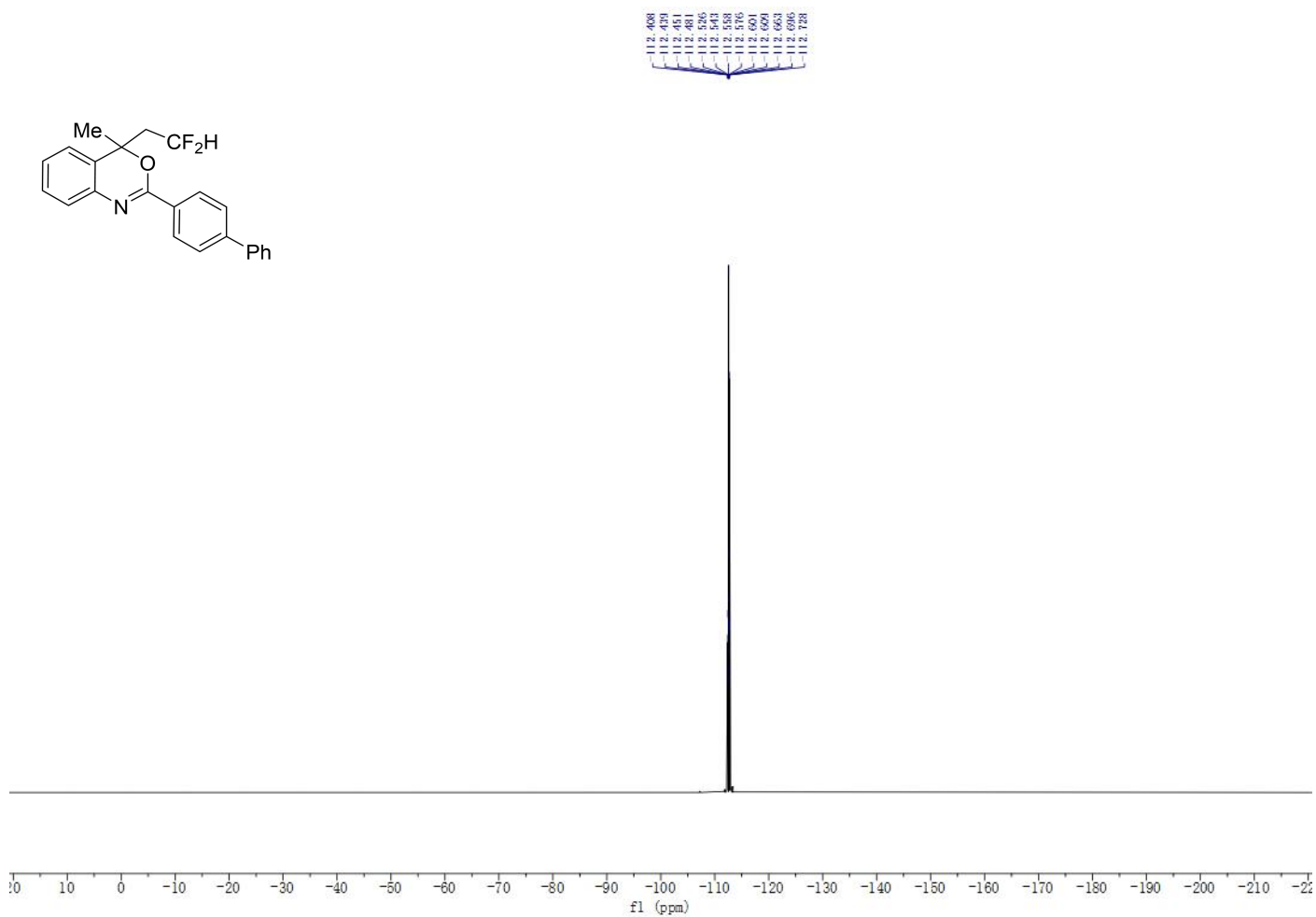
¹H NMR Spectrum of **3ja**



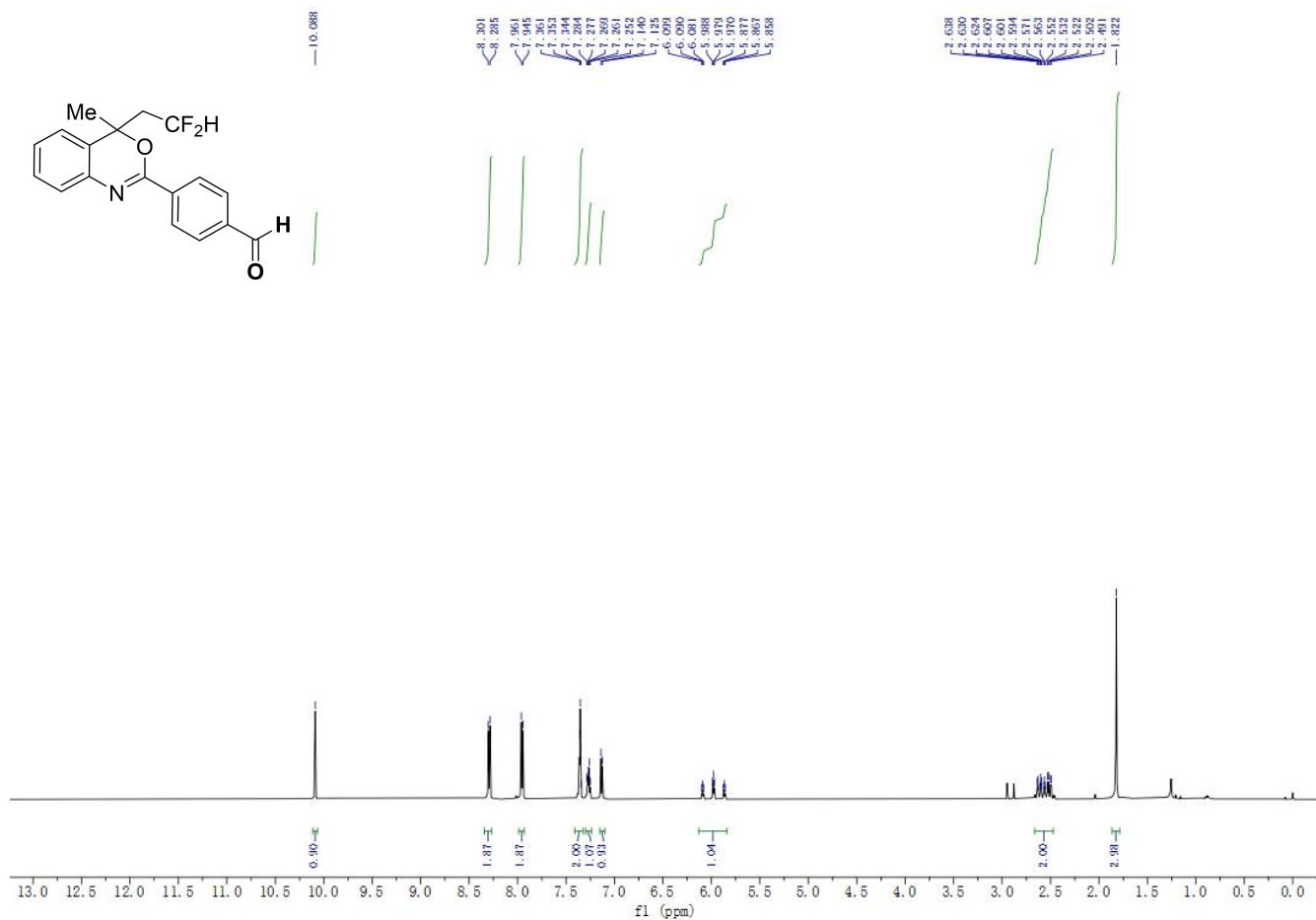
¹³C NMR Spectrum of 3ja



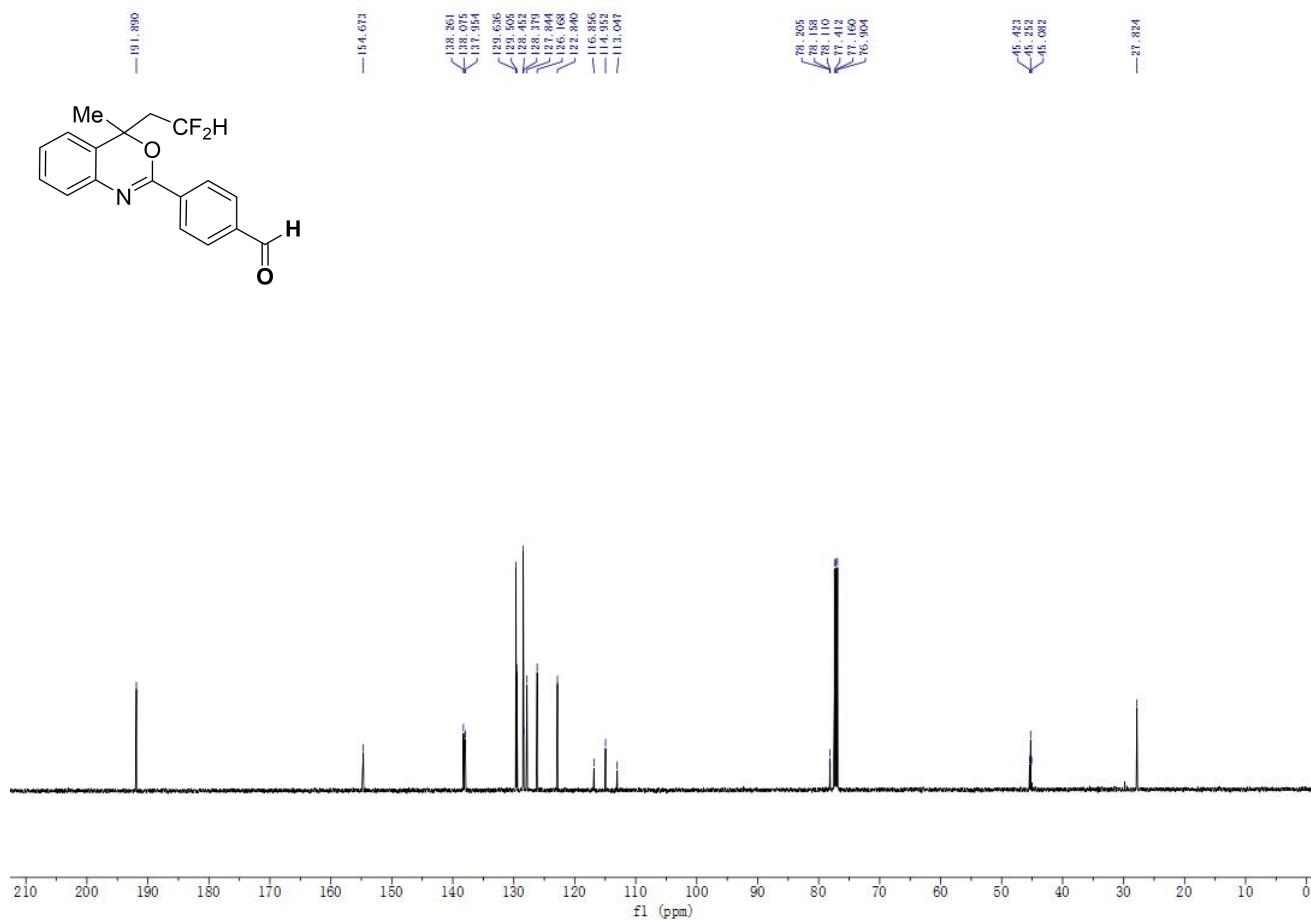
¹⁹F NMR Spectrum of 3ja



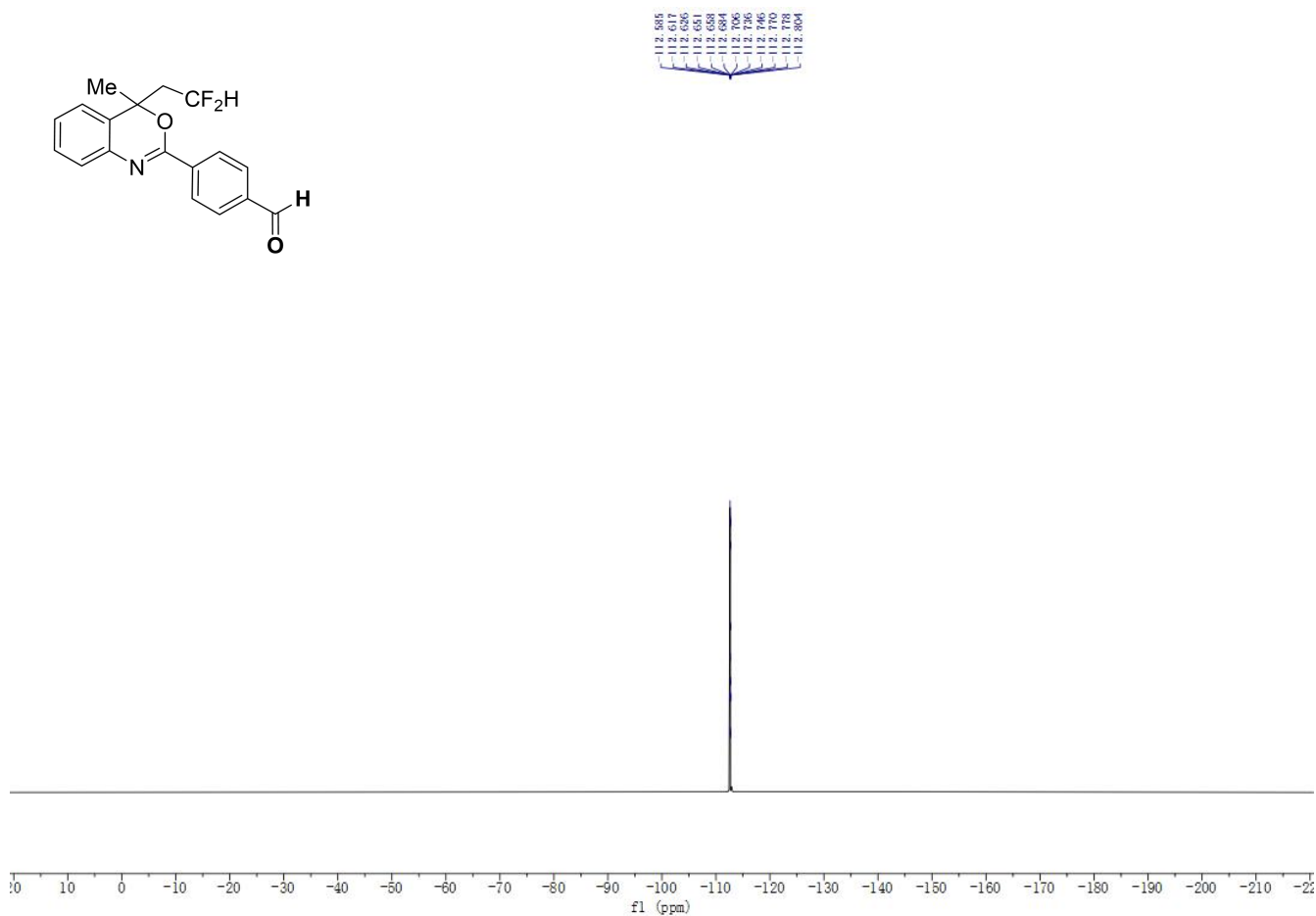
¹H NMR Spectrum of **3ka**



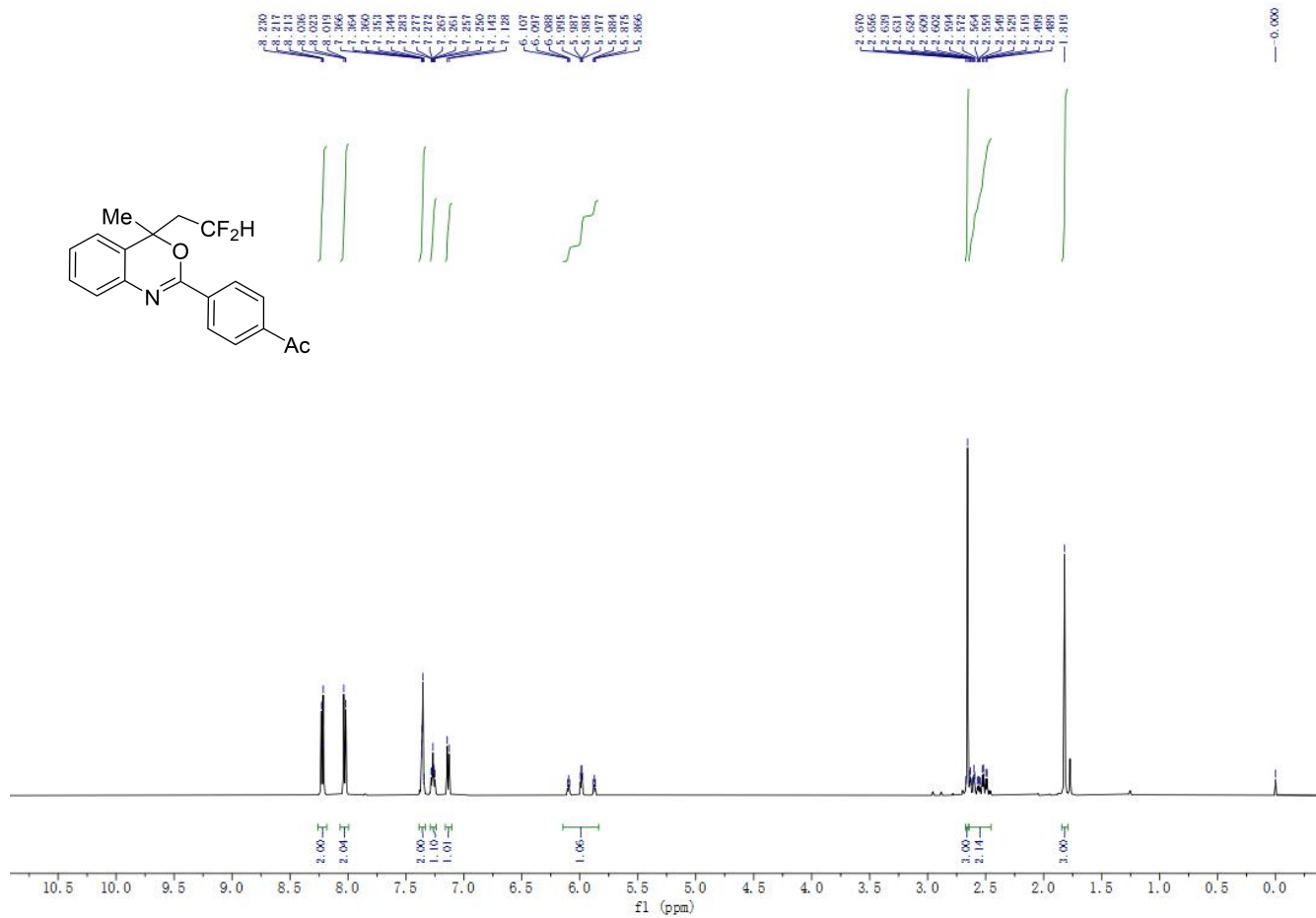
¹³C NMR Spectrum of **3ka**



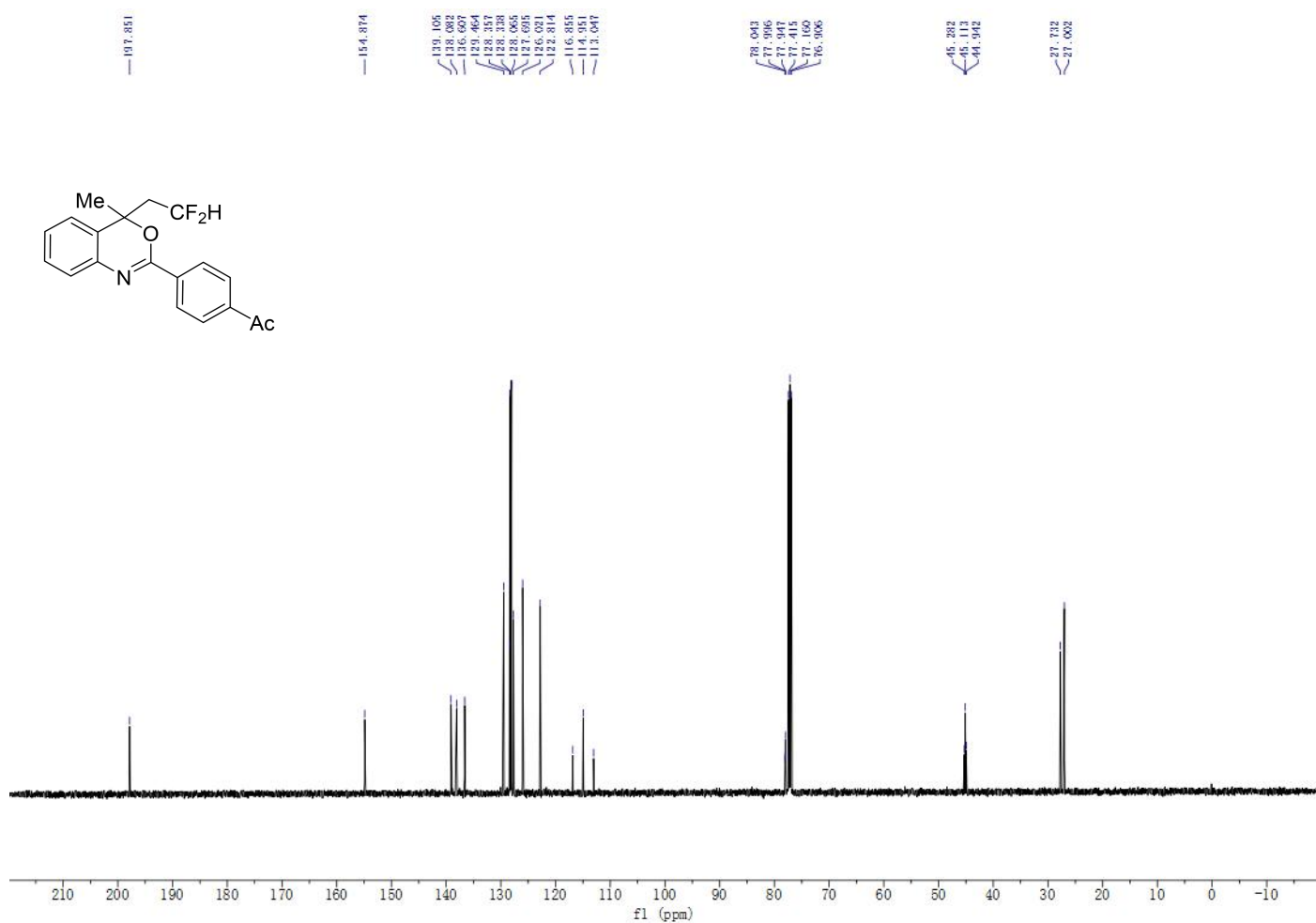
¹⁹F NMR Spectrum of **3ka**



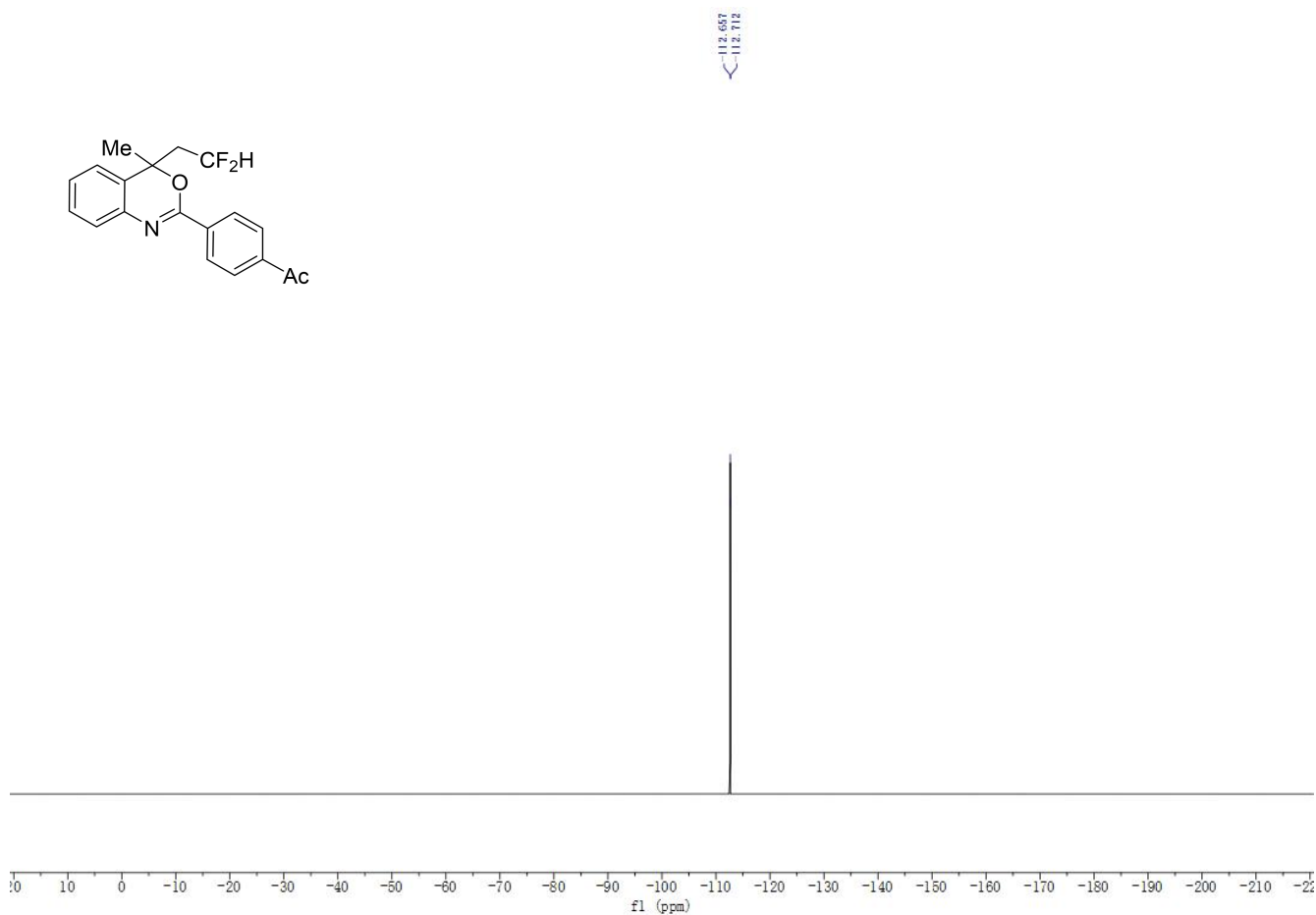
¹H NMR Spectrum of **3la**



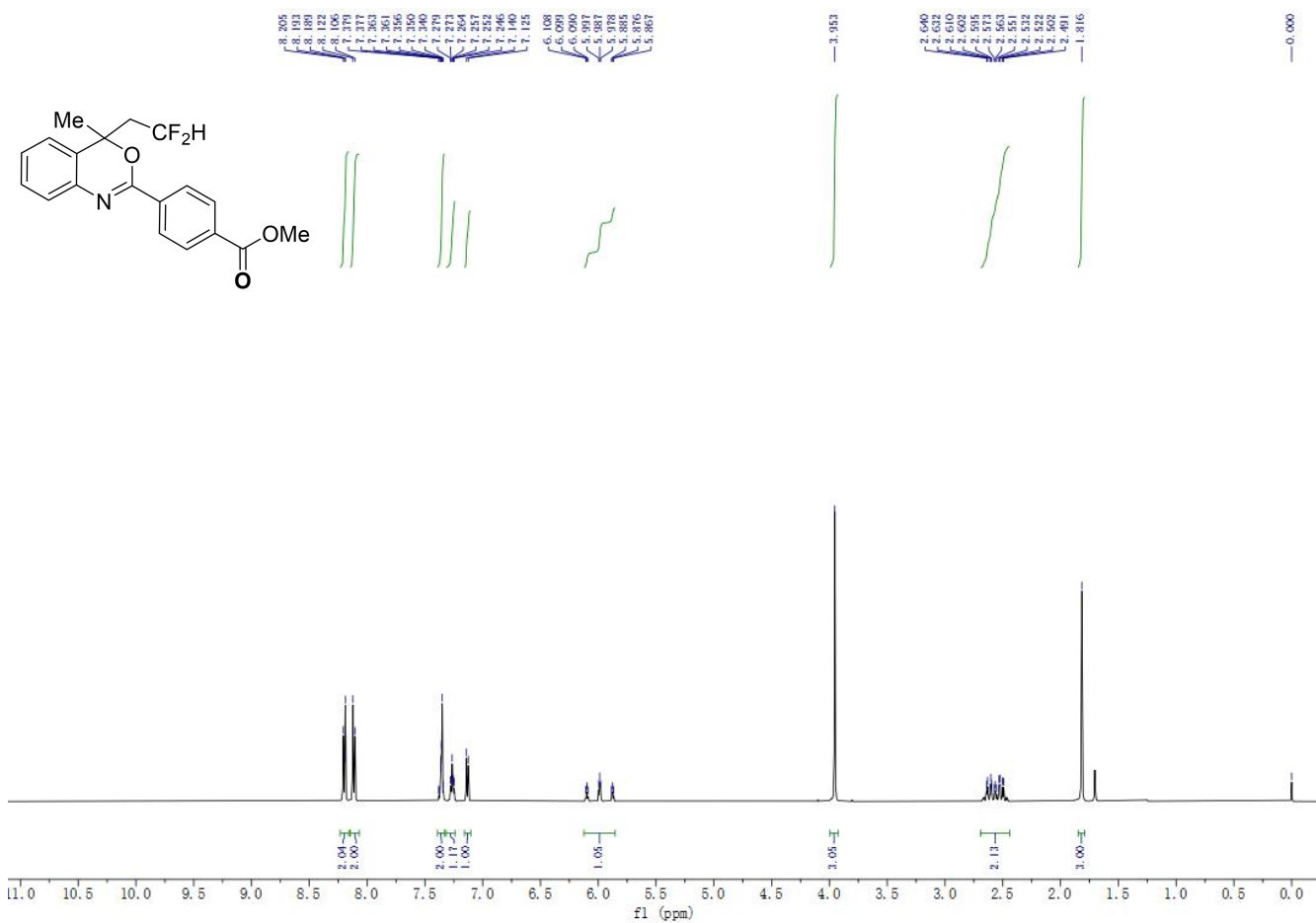
¹³C NMR Spectrum of 31a



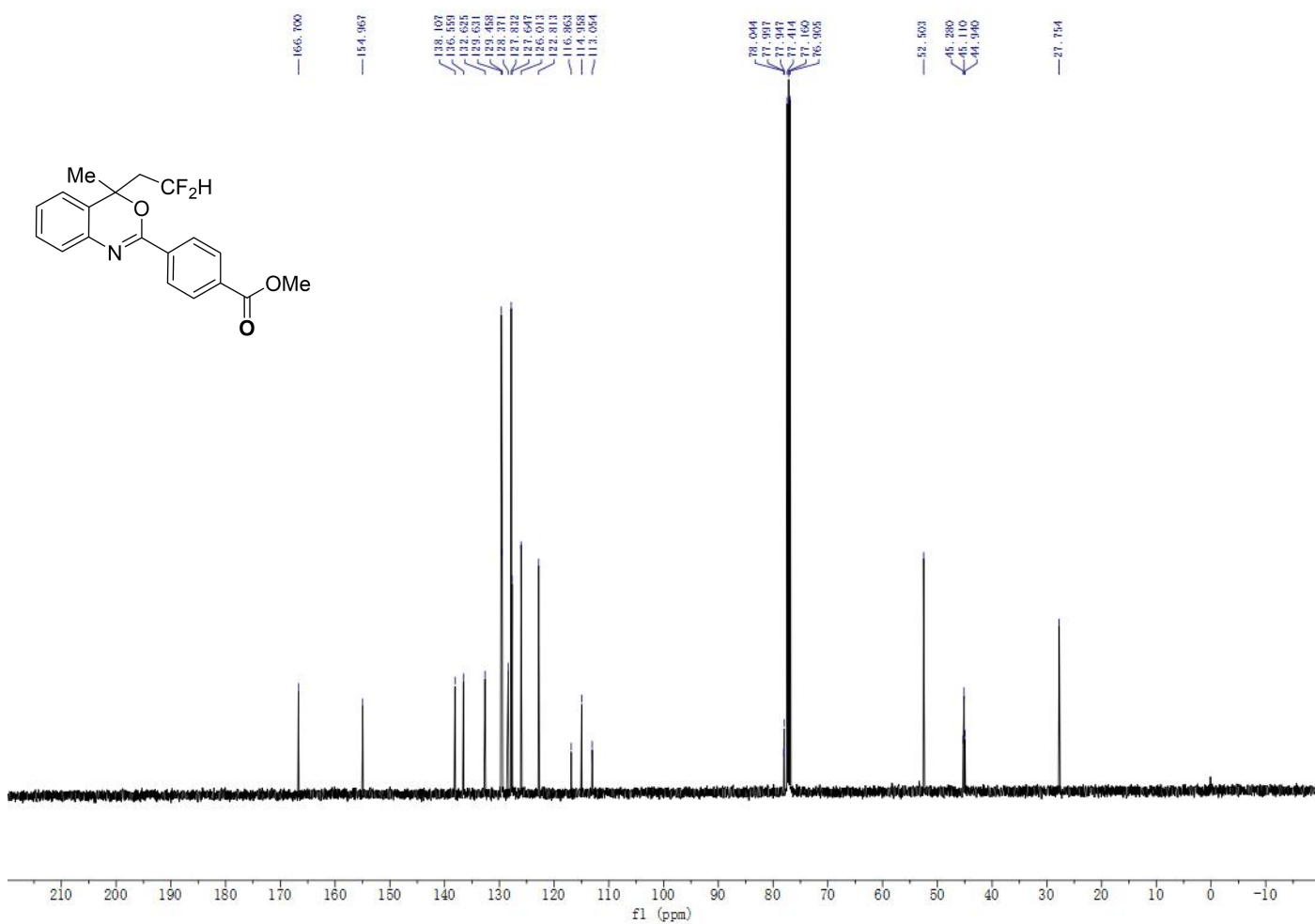
¹⁹F NMR Spectrum of 31a



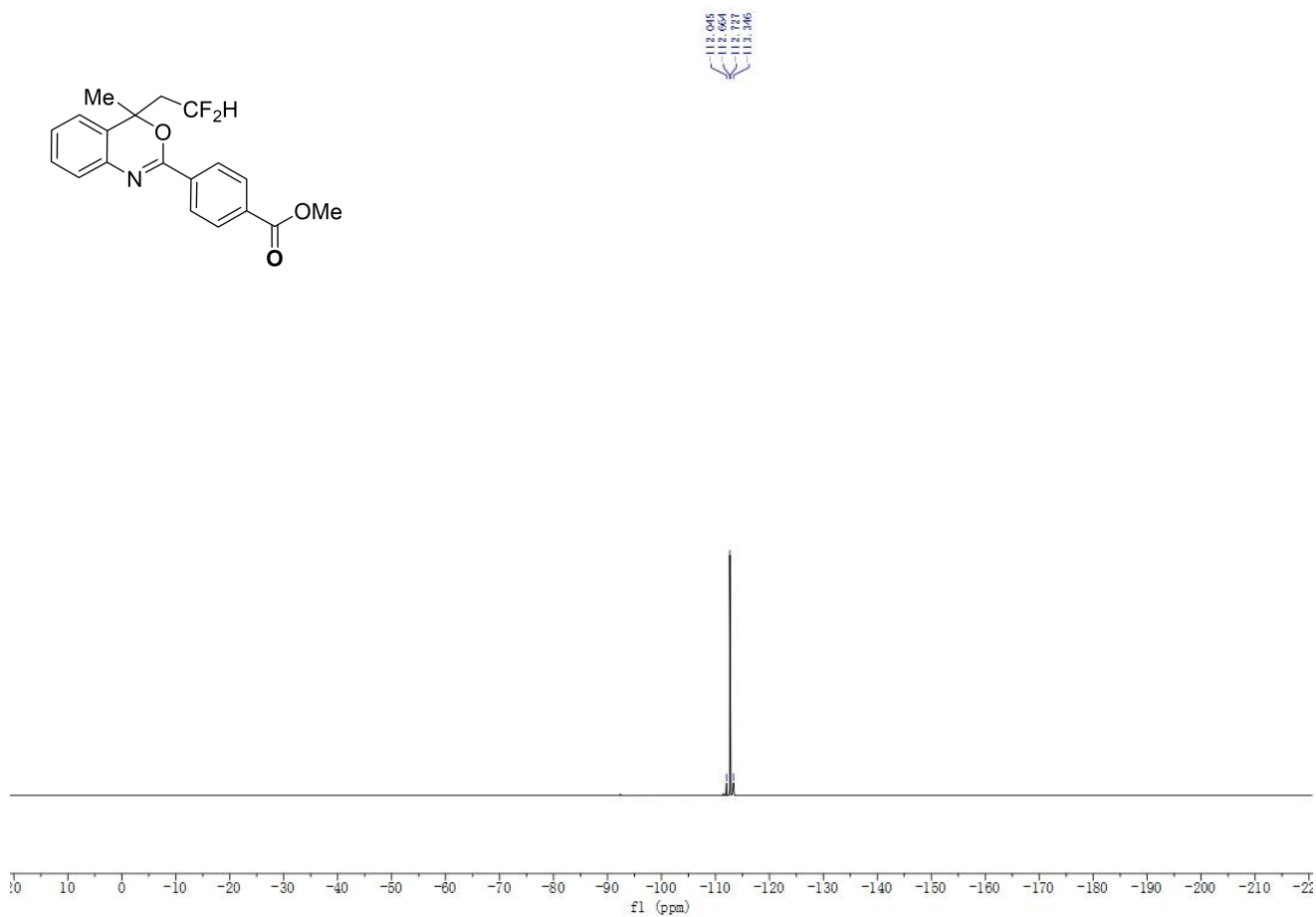
¹H NMR Spectrum of **3ma**



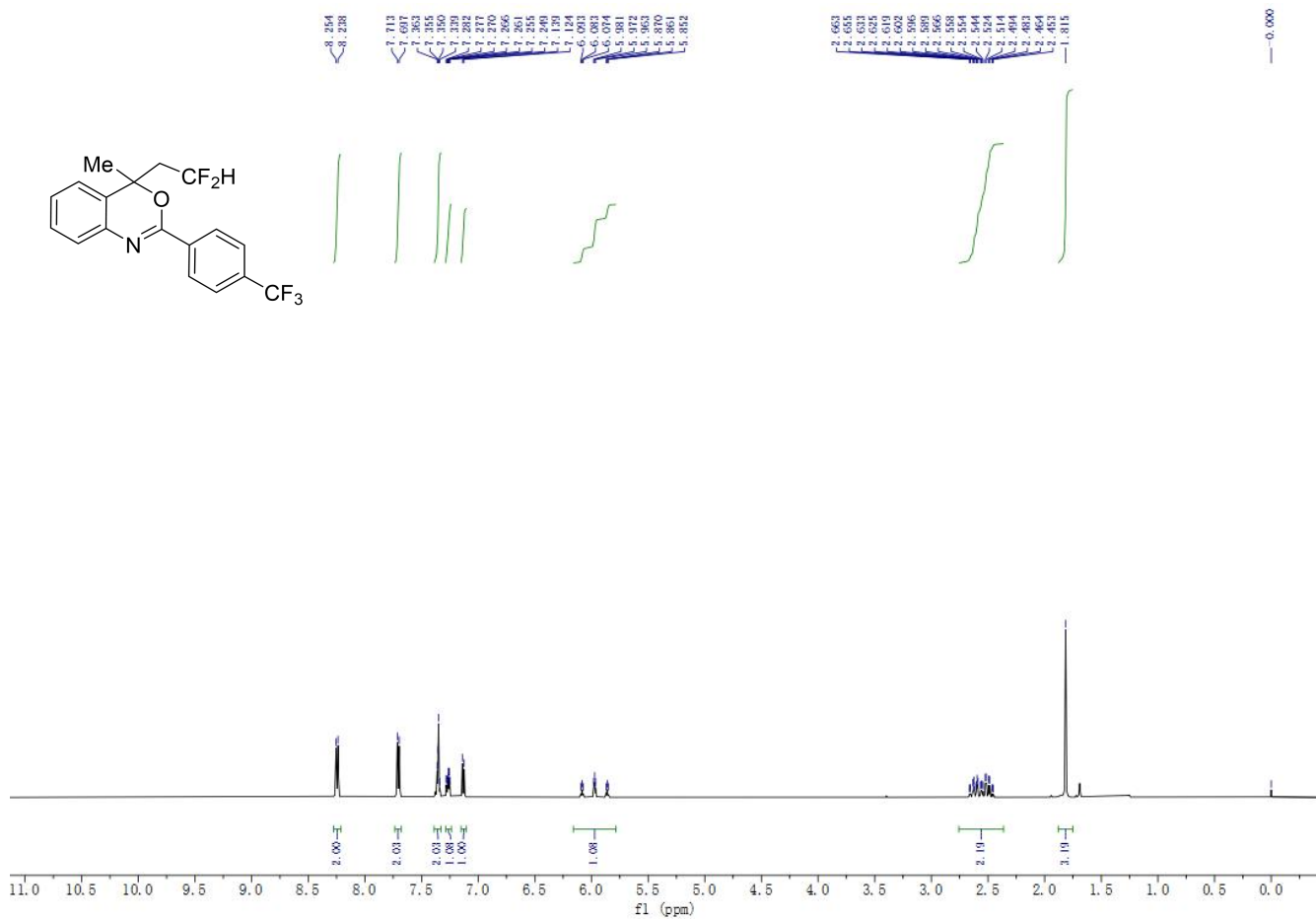
¹³C NMR Spectrum of **3ma**



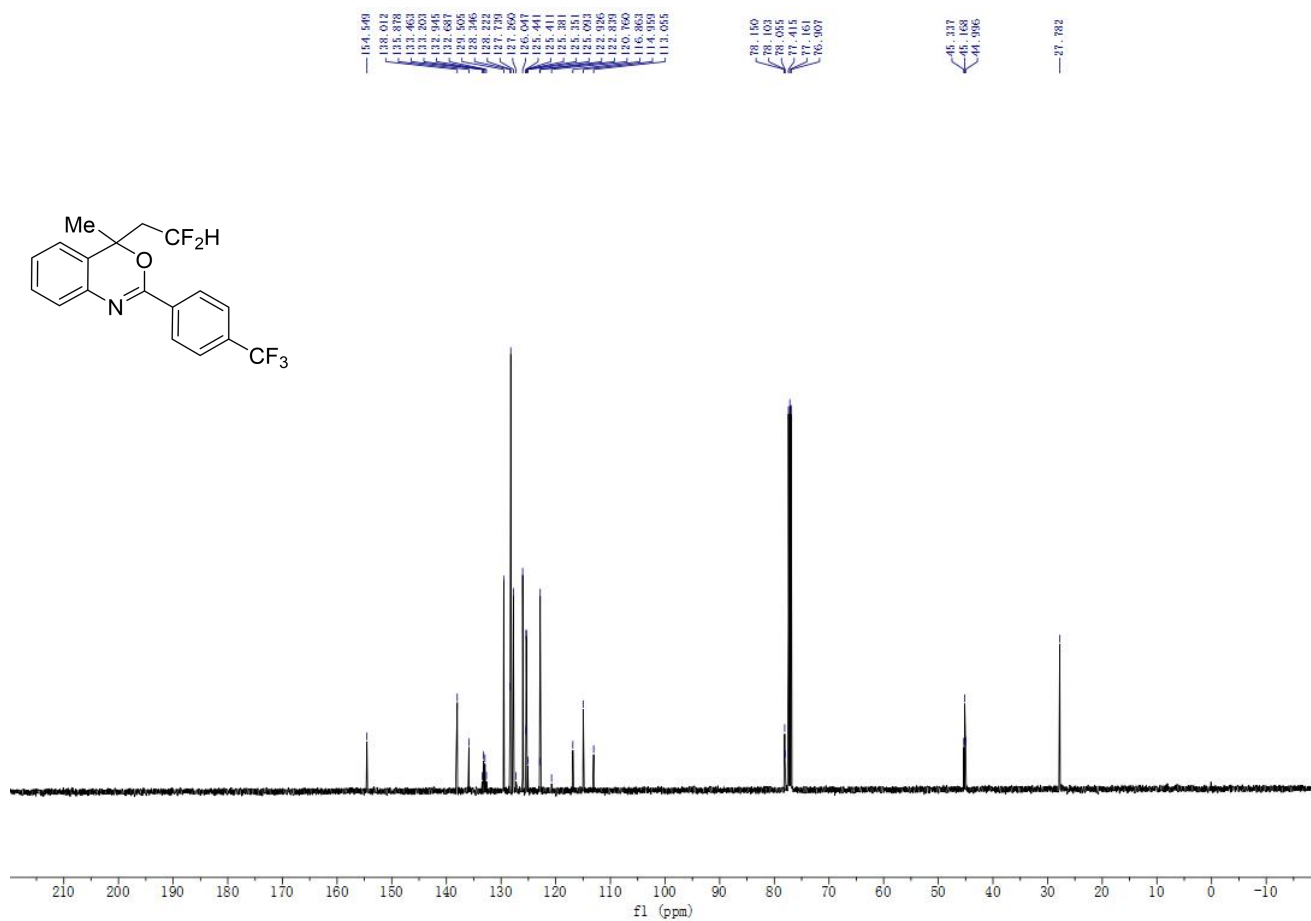
¹⁹F NMR Spectrum of **3ma**



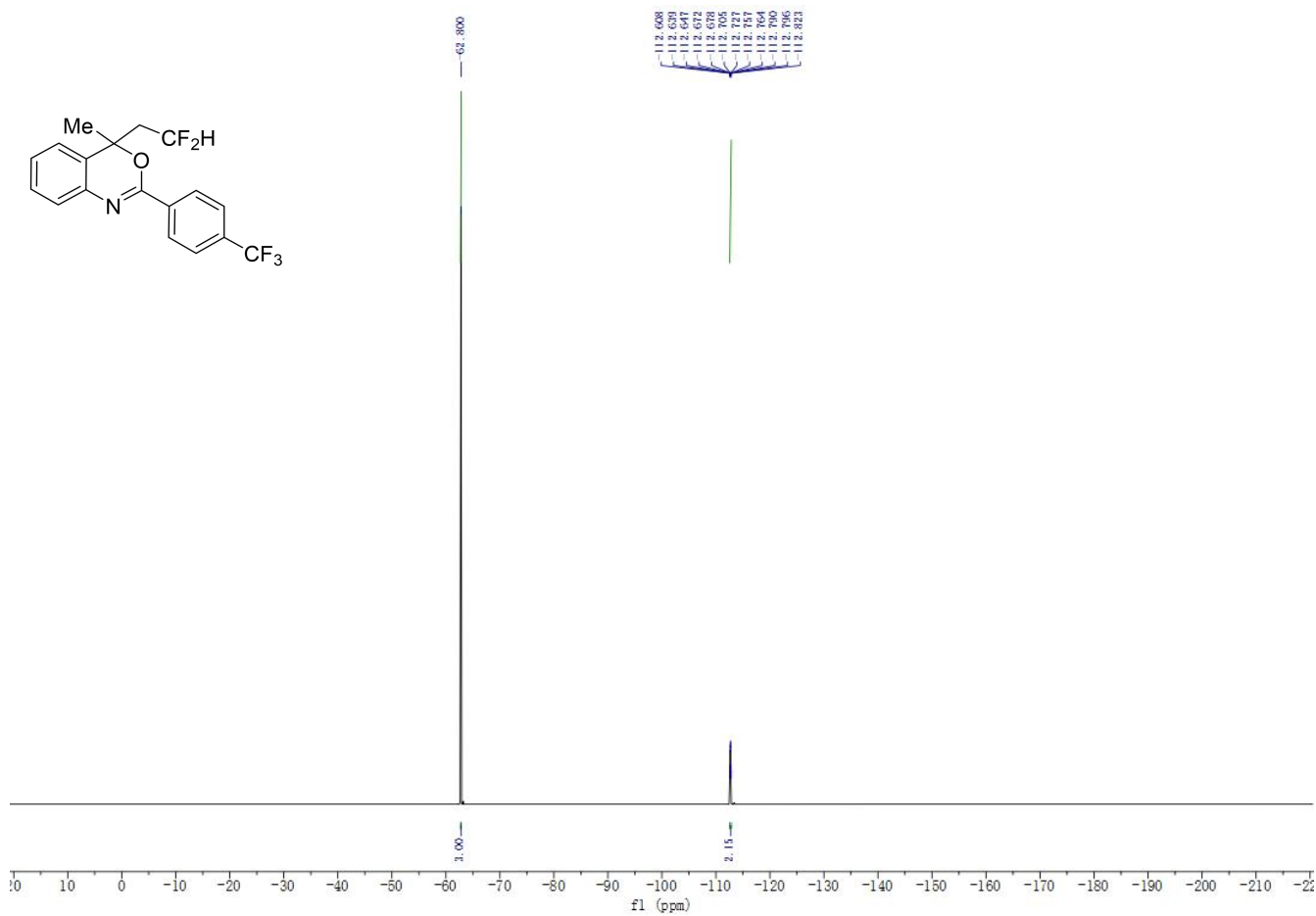
¹H NMR Spectrum of **3na**



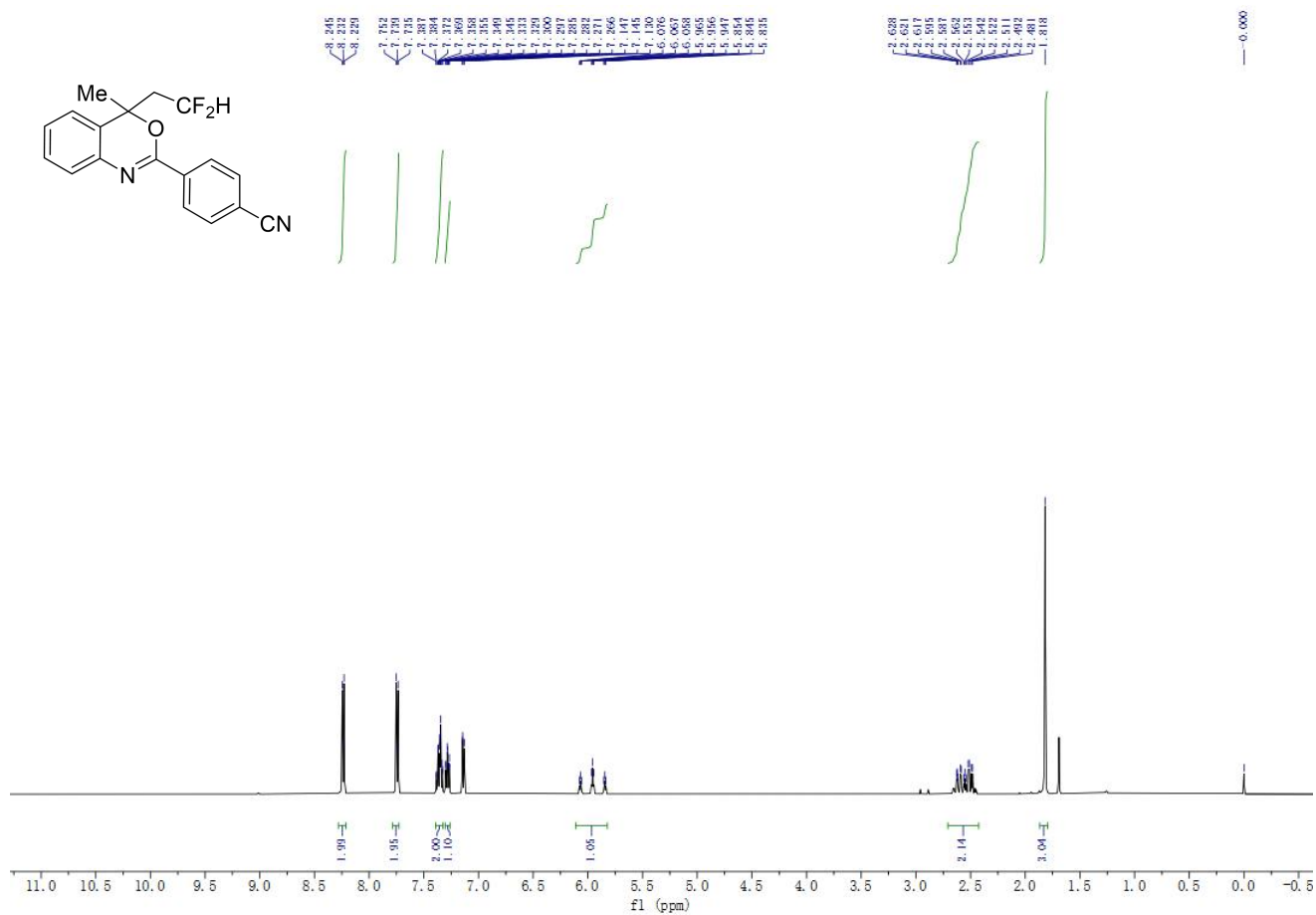
¹³C NMR Spectrum of 3na



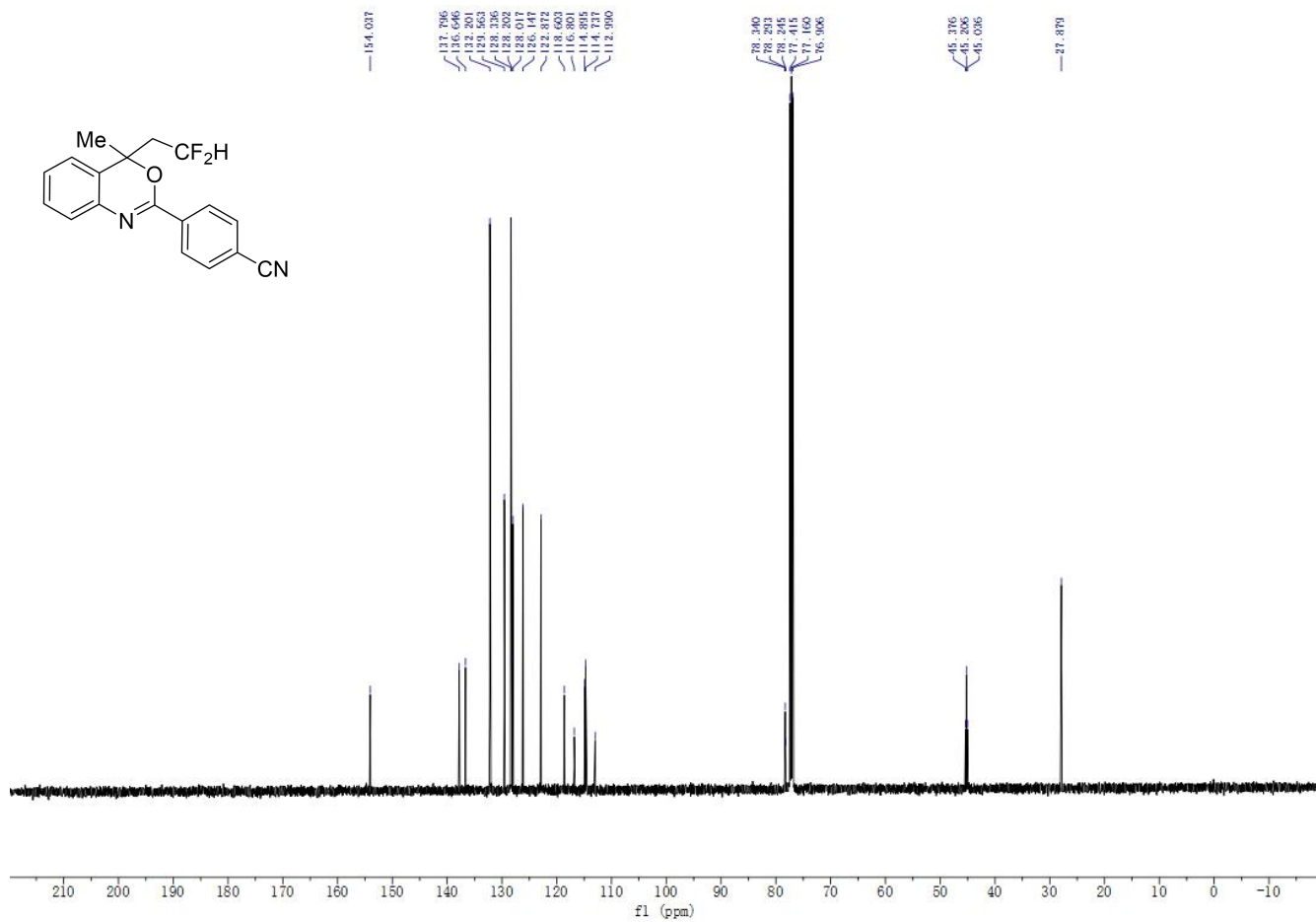
¹⁹F NMR Spectrum of 3na



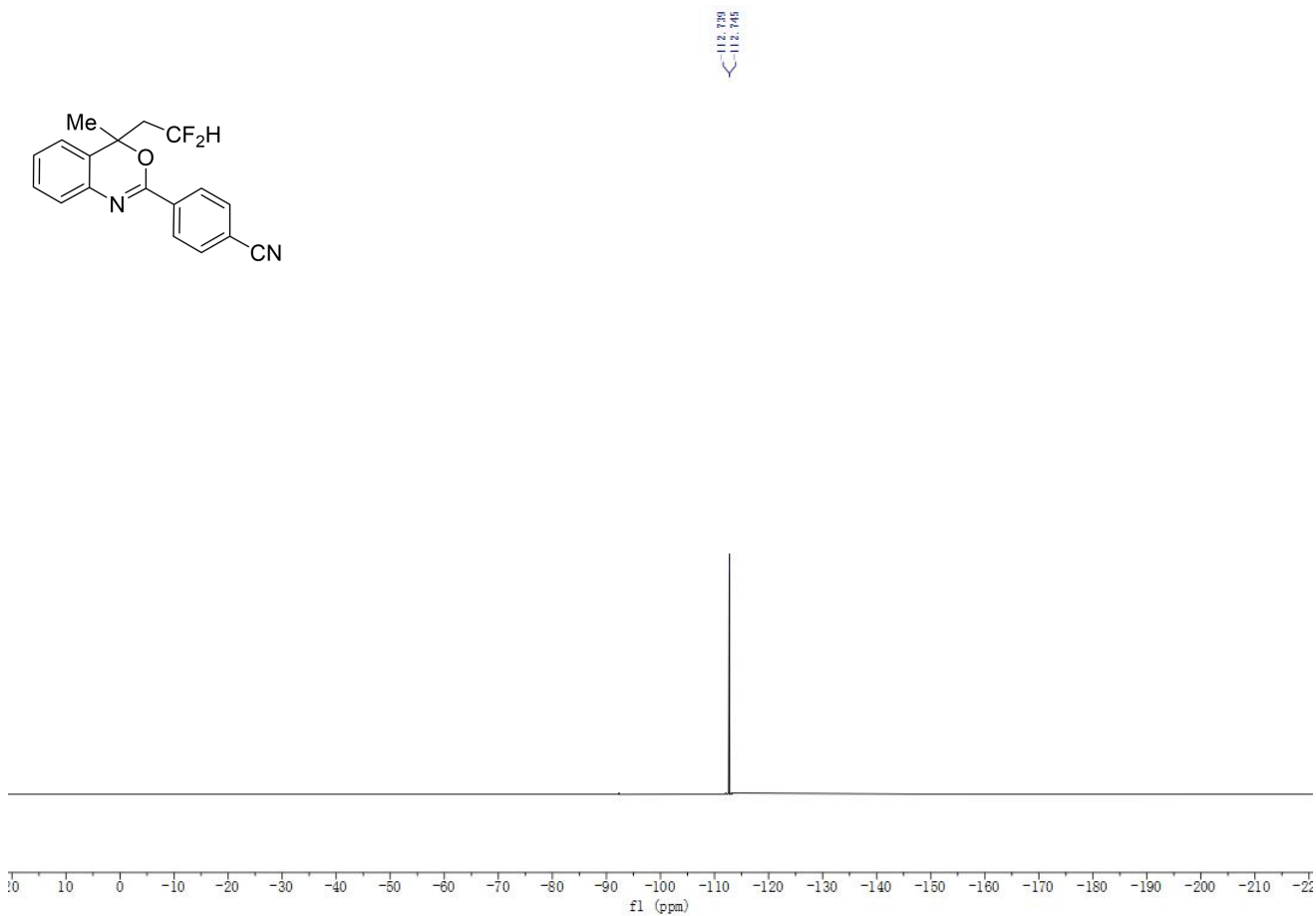
¹H NMR Spectrum of **30a**



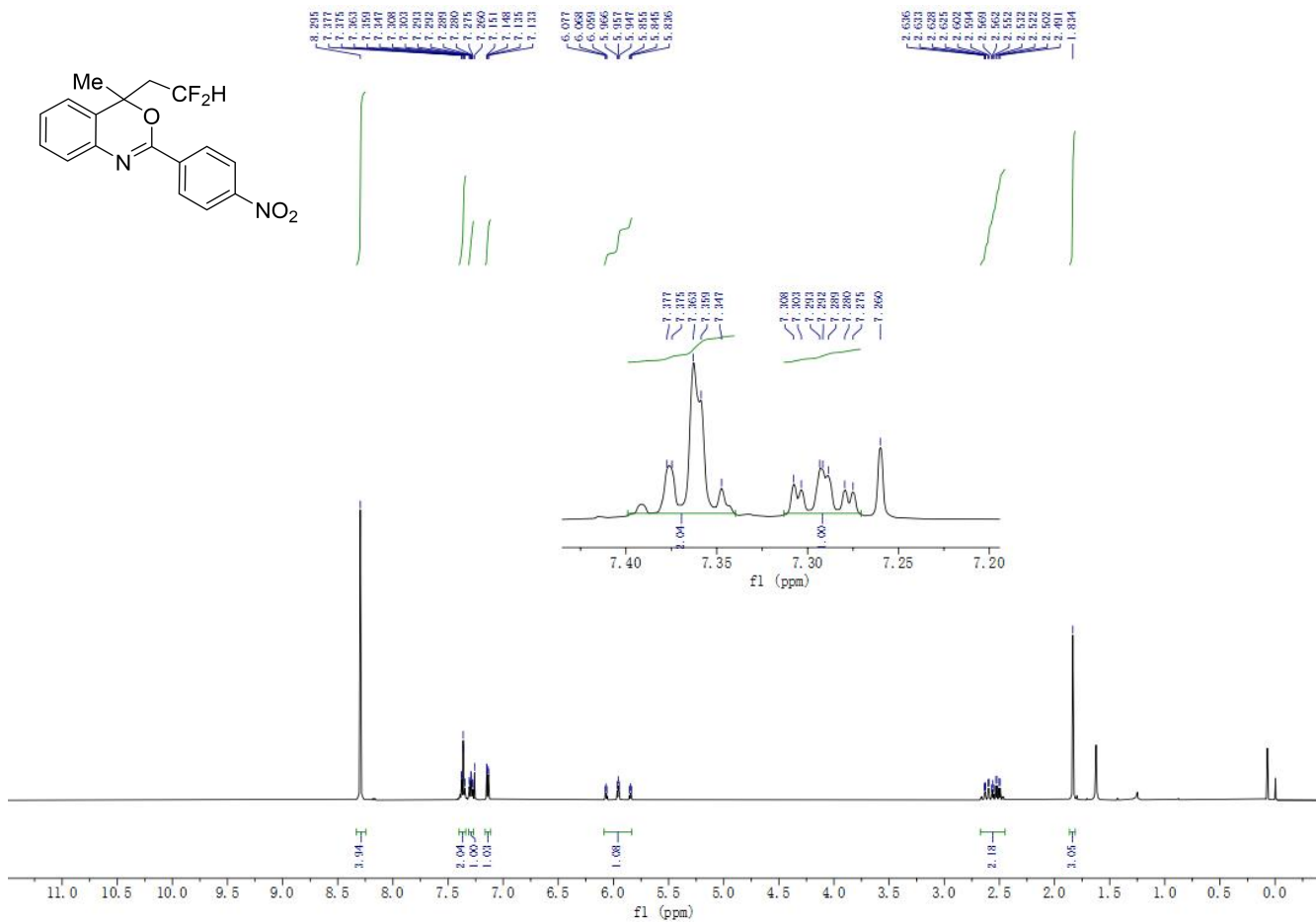
¹³C NMR Spectrum of **30a**



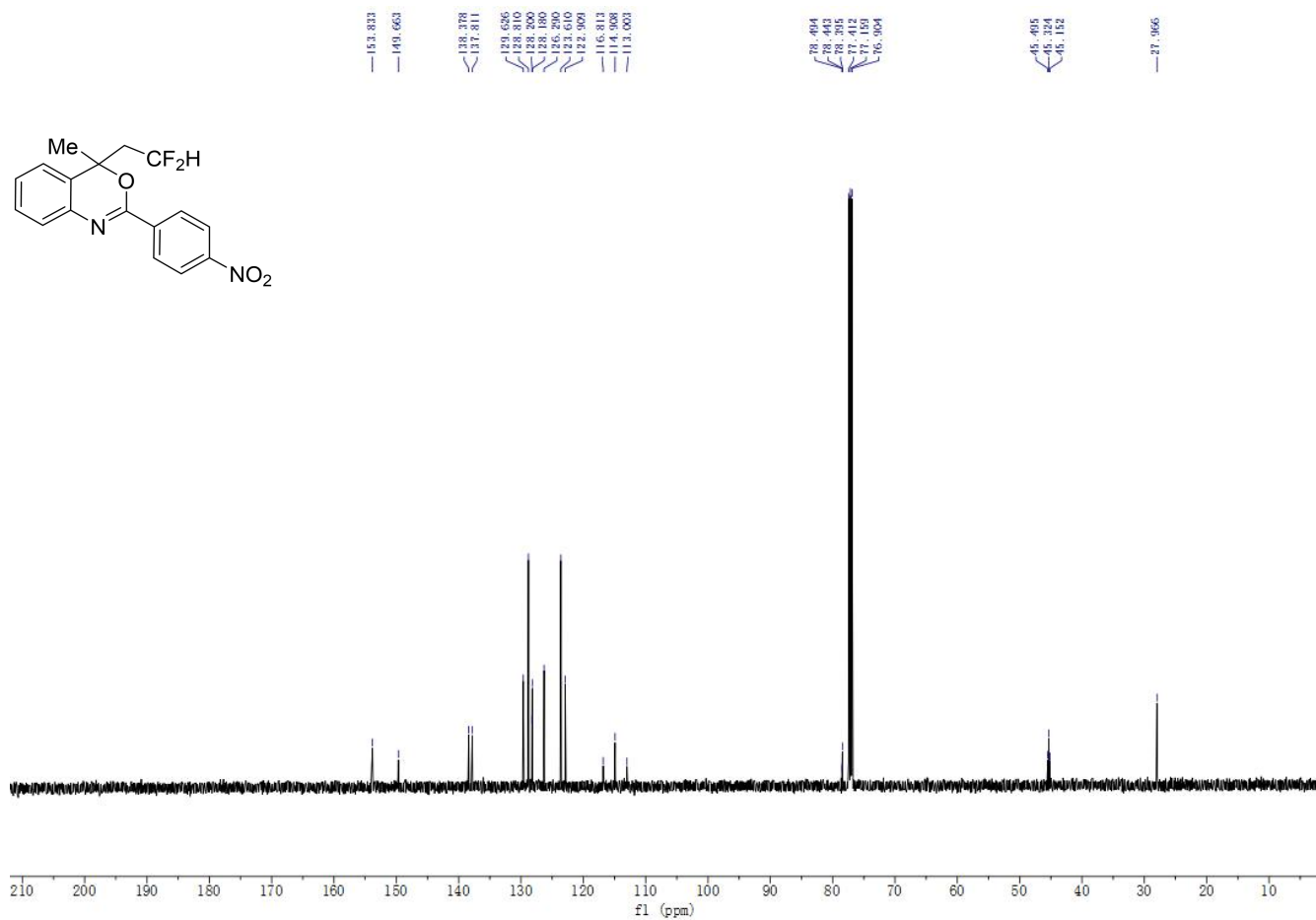
¹⁹F NMR Spectrum of **30a**



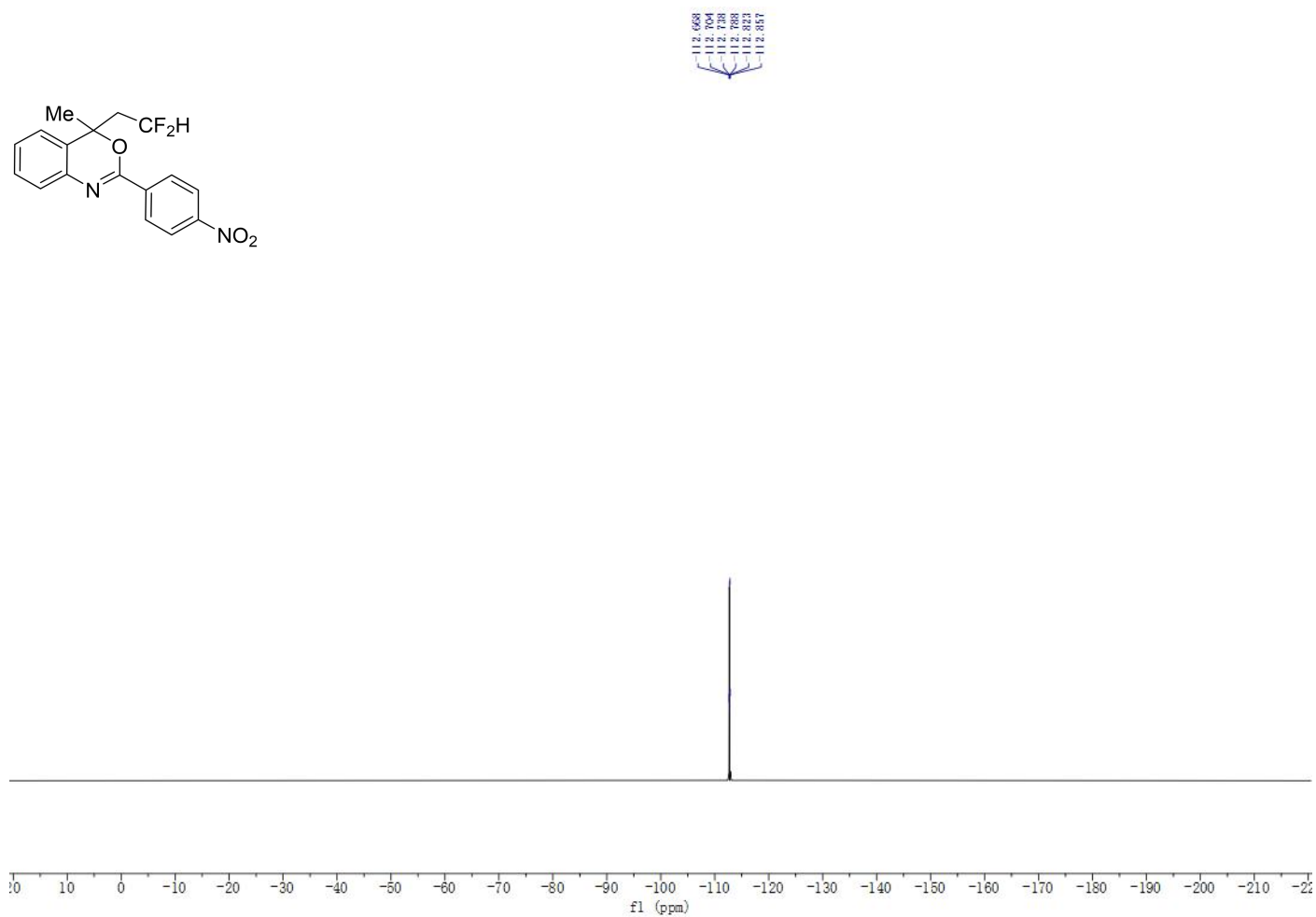
¹H NMR Spectrum of **3pa**



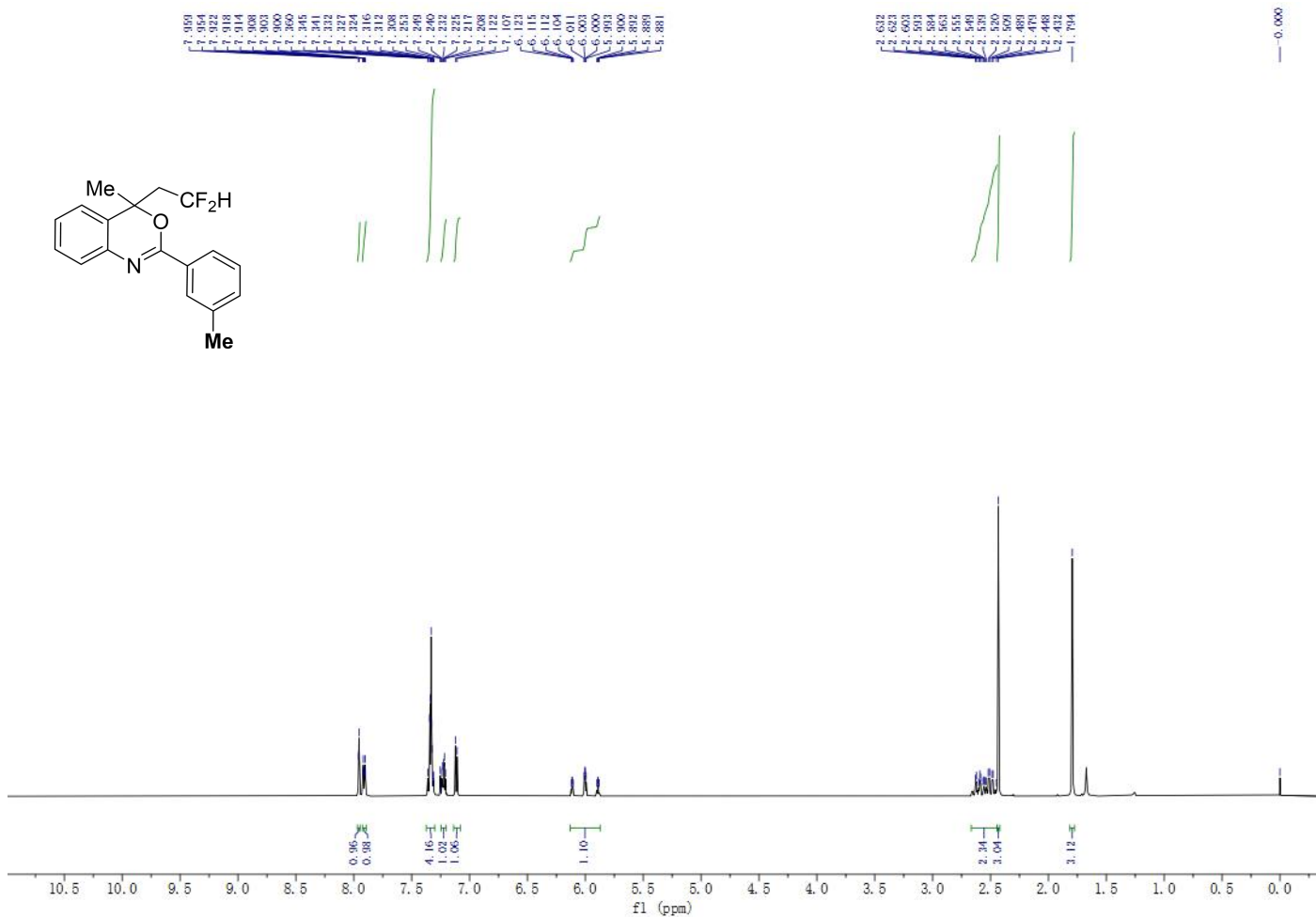
¹³C NMR Spectrum of 3pa



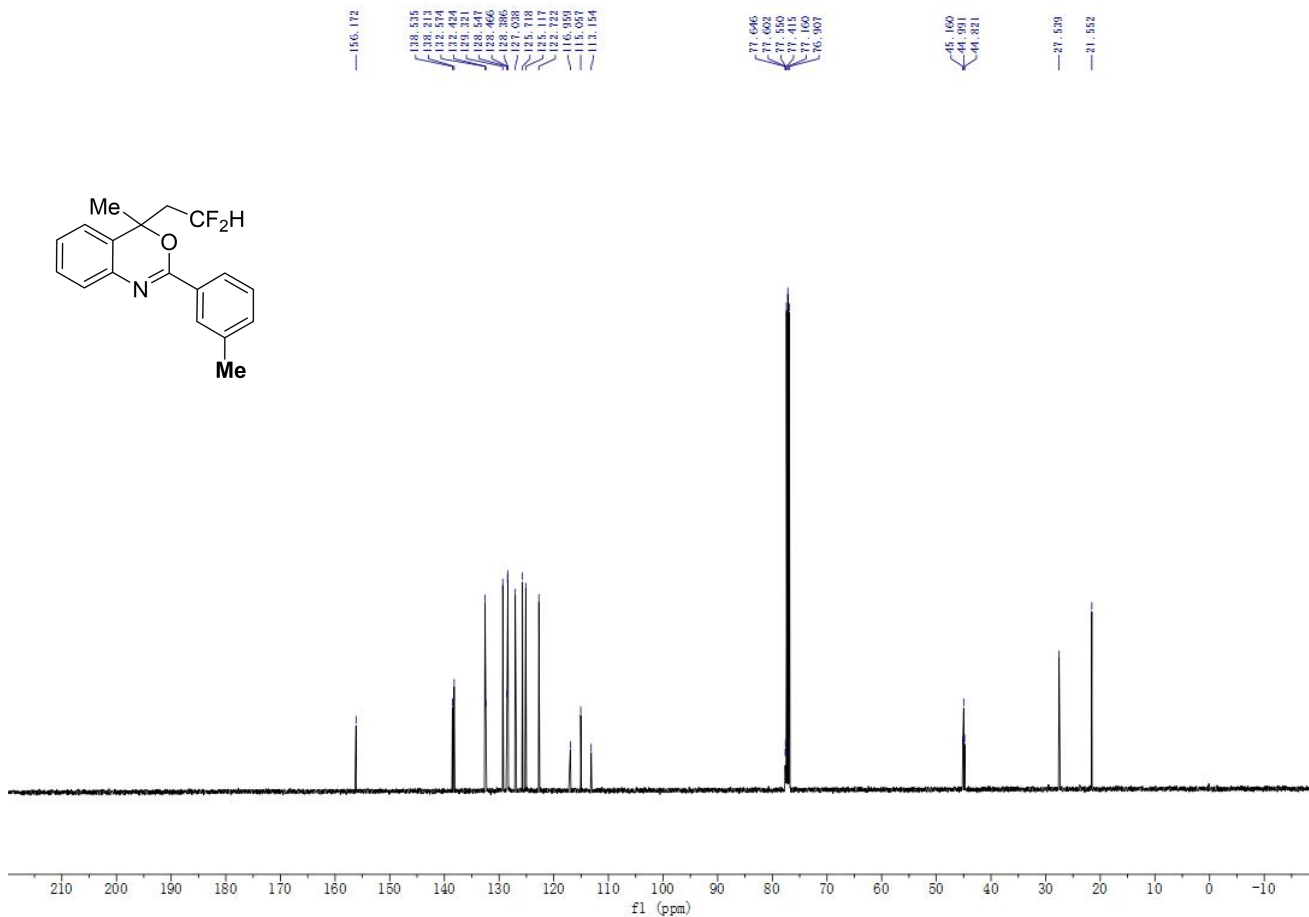
¹⁹F NMR Spectrum of 3pa



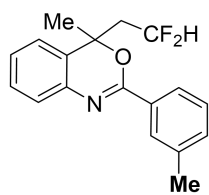
¹H NMR Spectrum of **3qa**



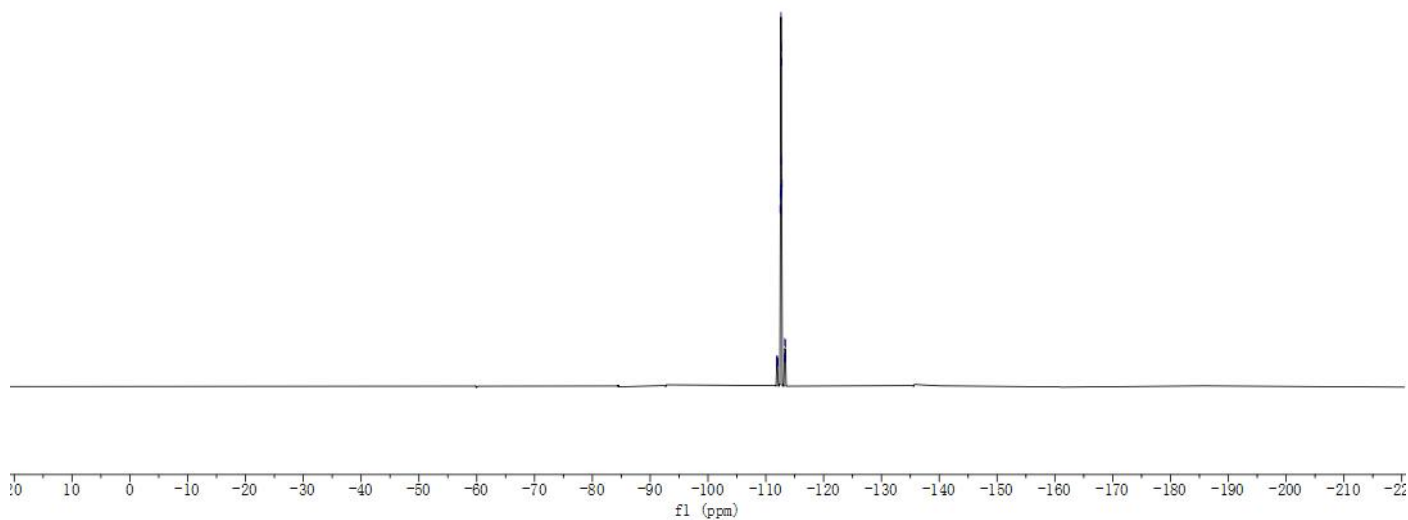
¹³C NMR Spectrum of **3qa**



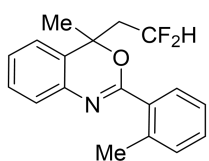
¹⁹F NMR Spectrum of **3qa**



111.859
111.880
111.901
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¹H NMR Spectrum of **3ra**

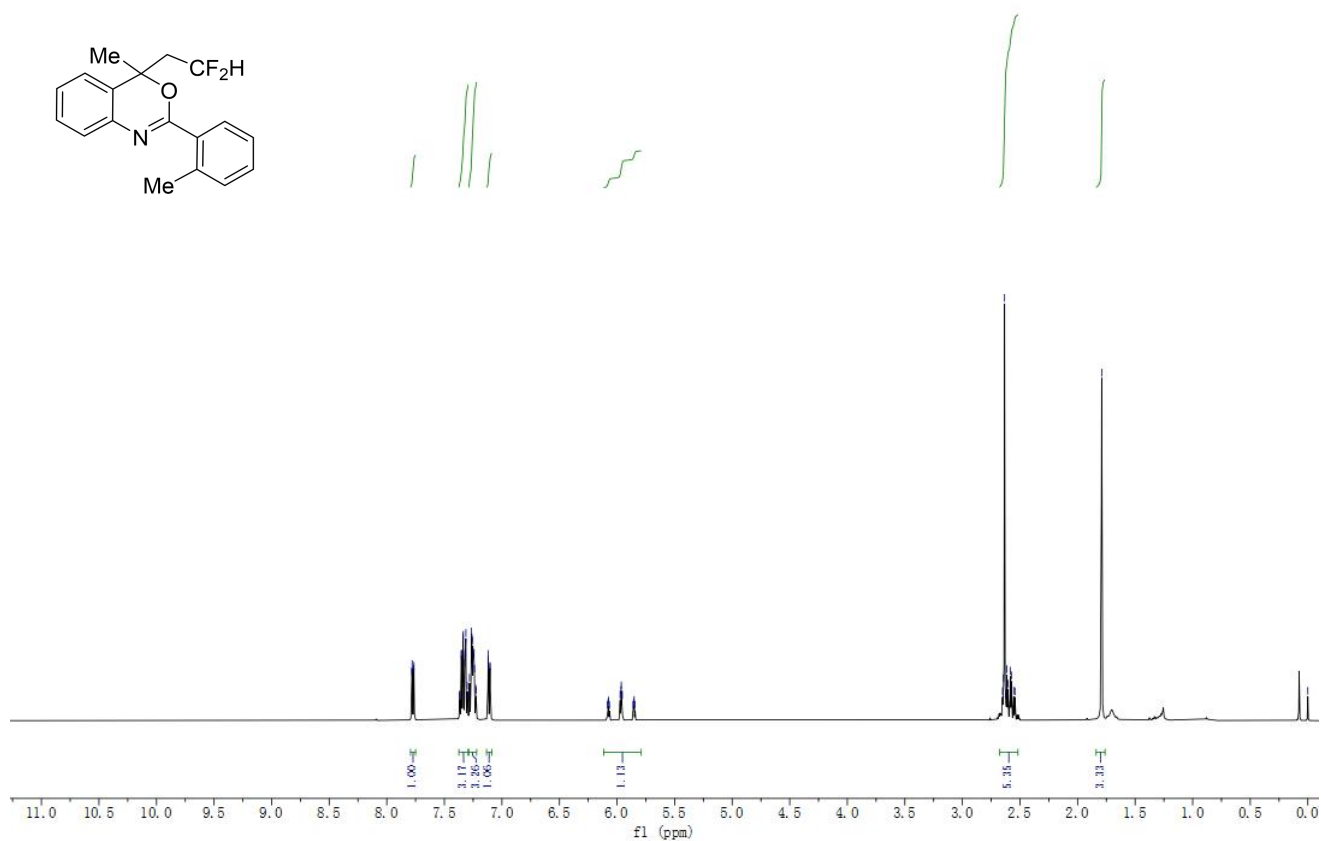


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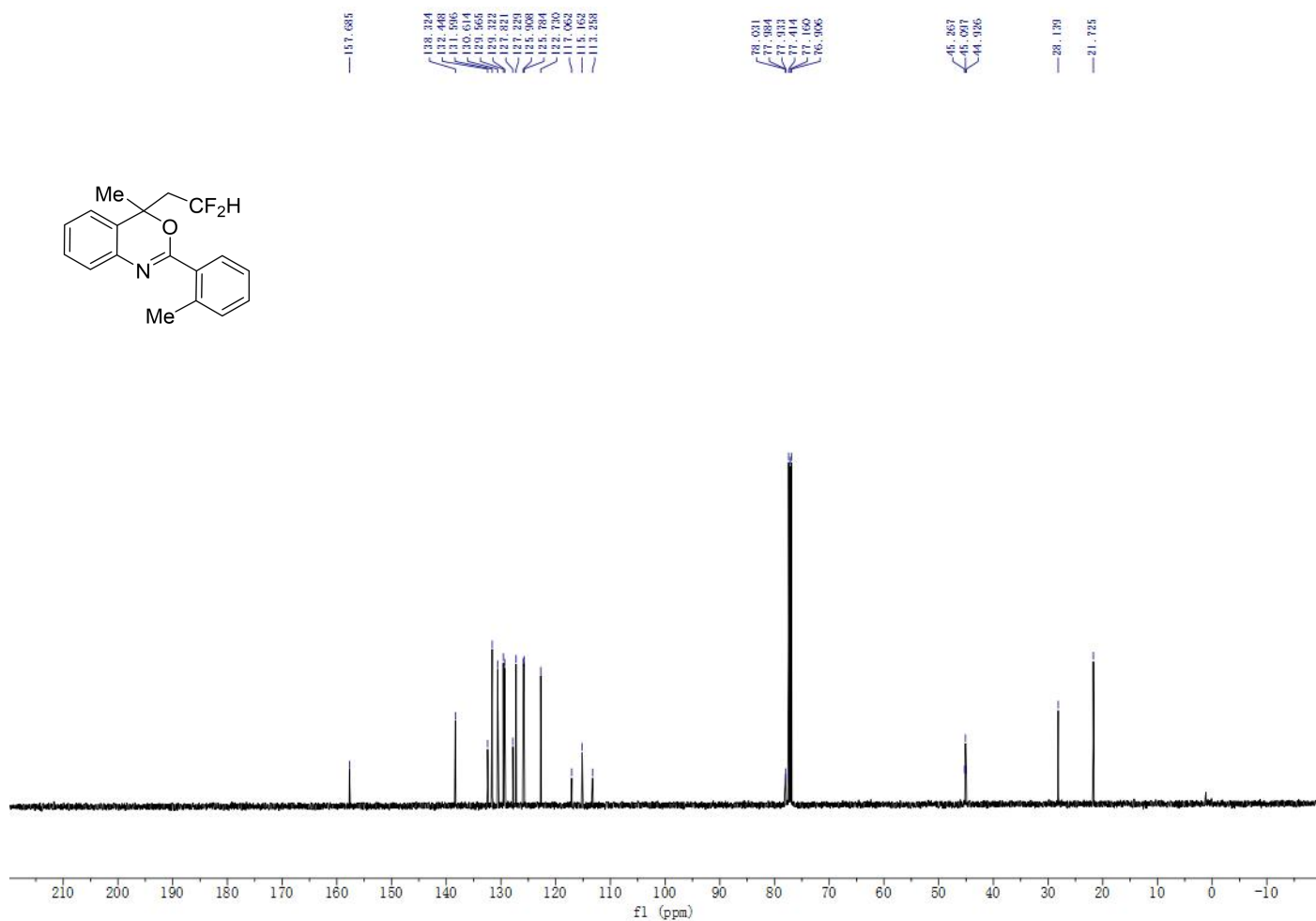
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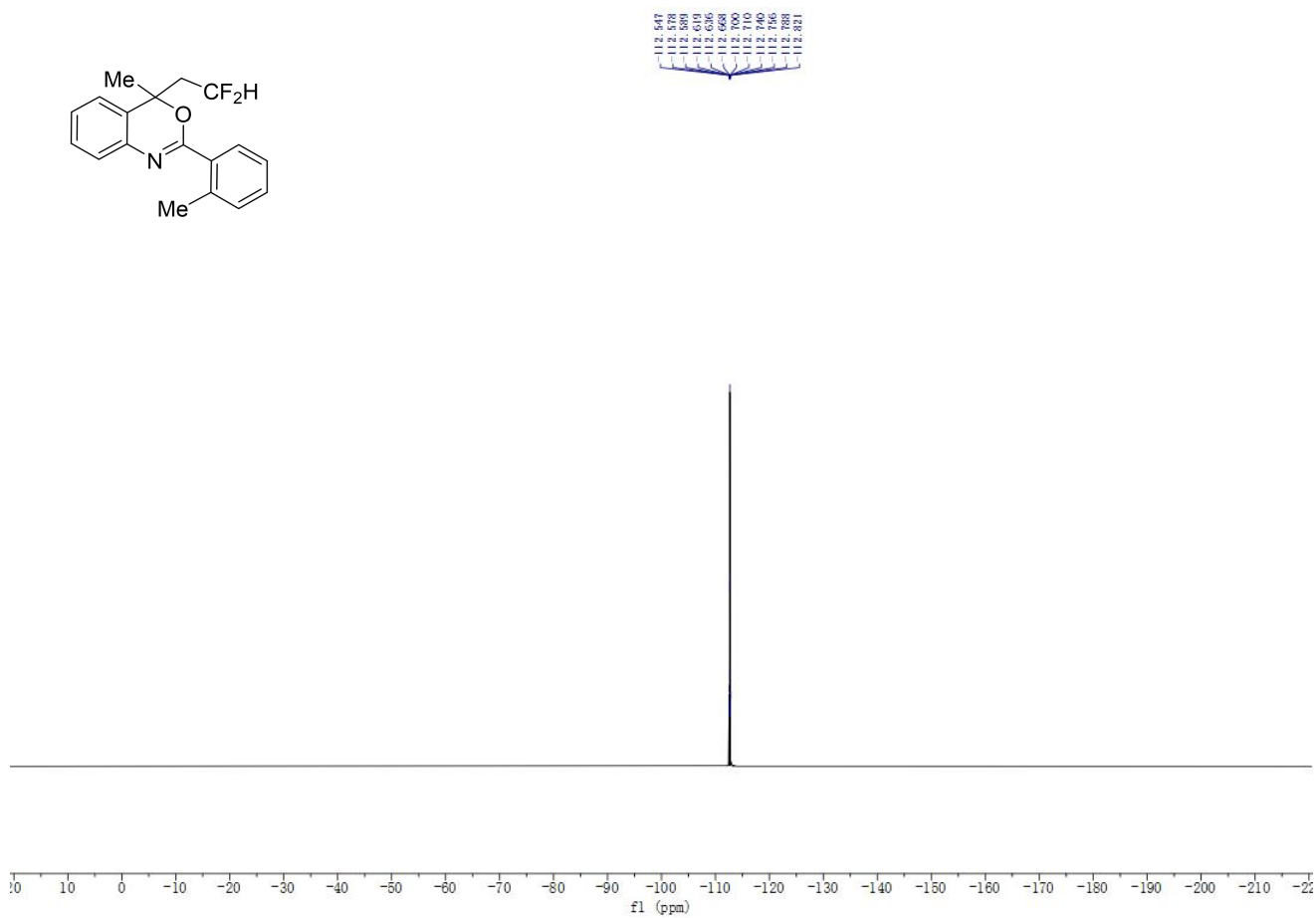
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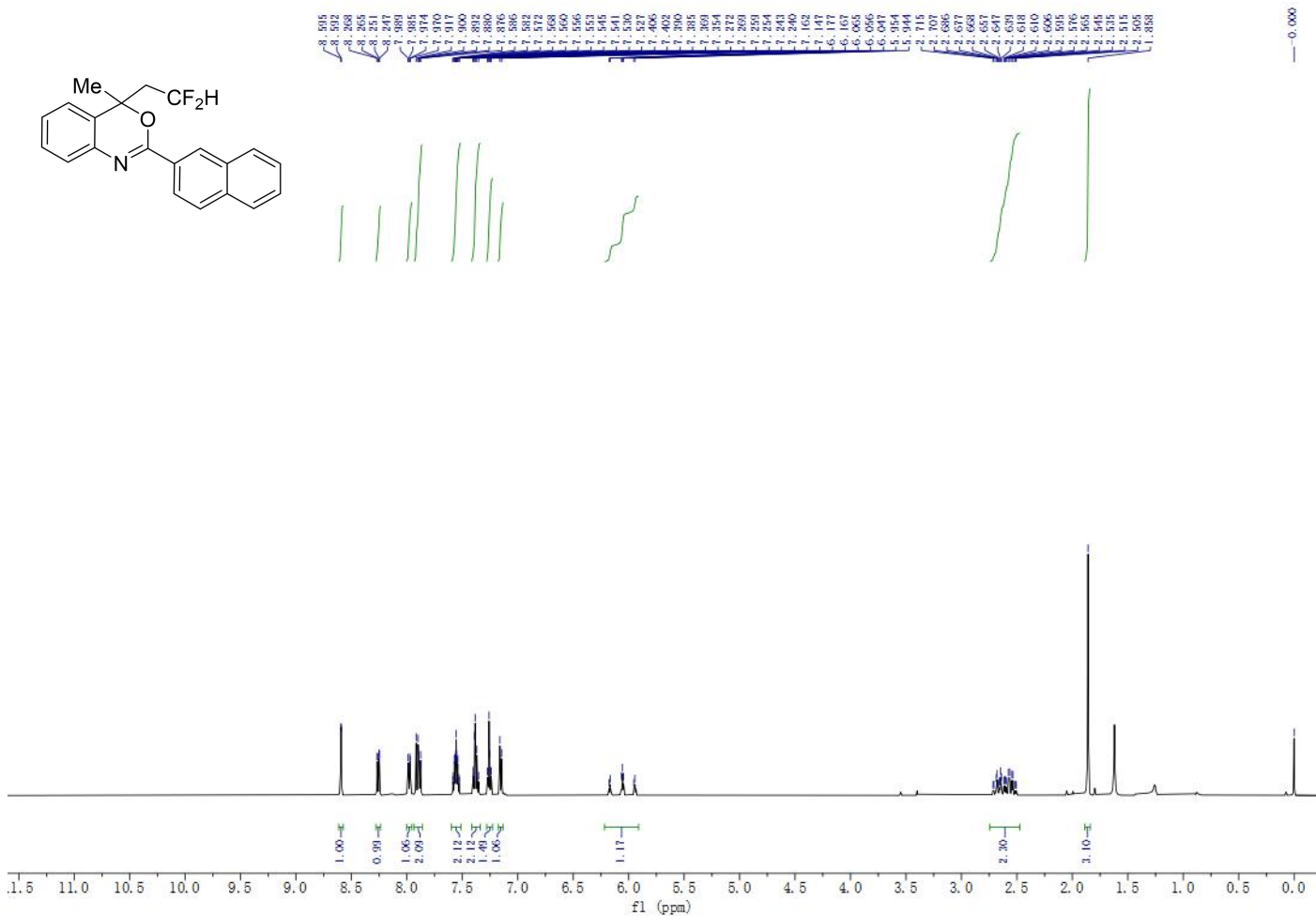
¹³C NMR Spectrum of **3ra**



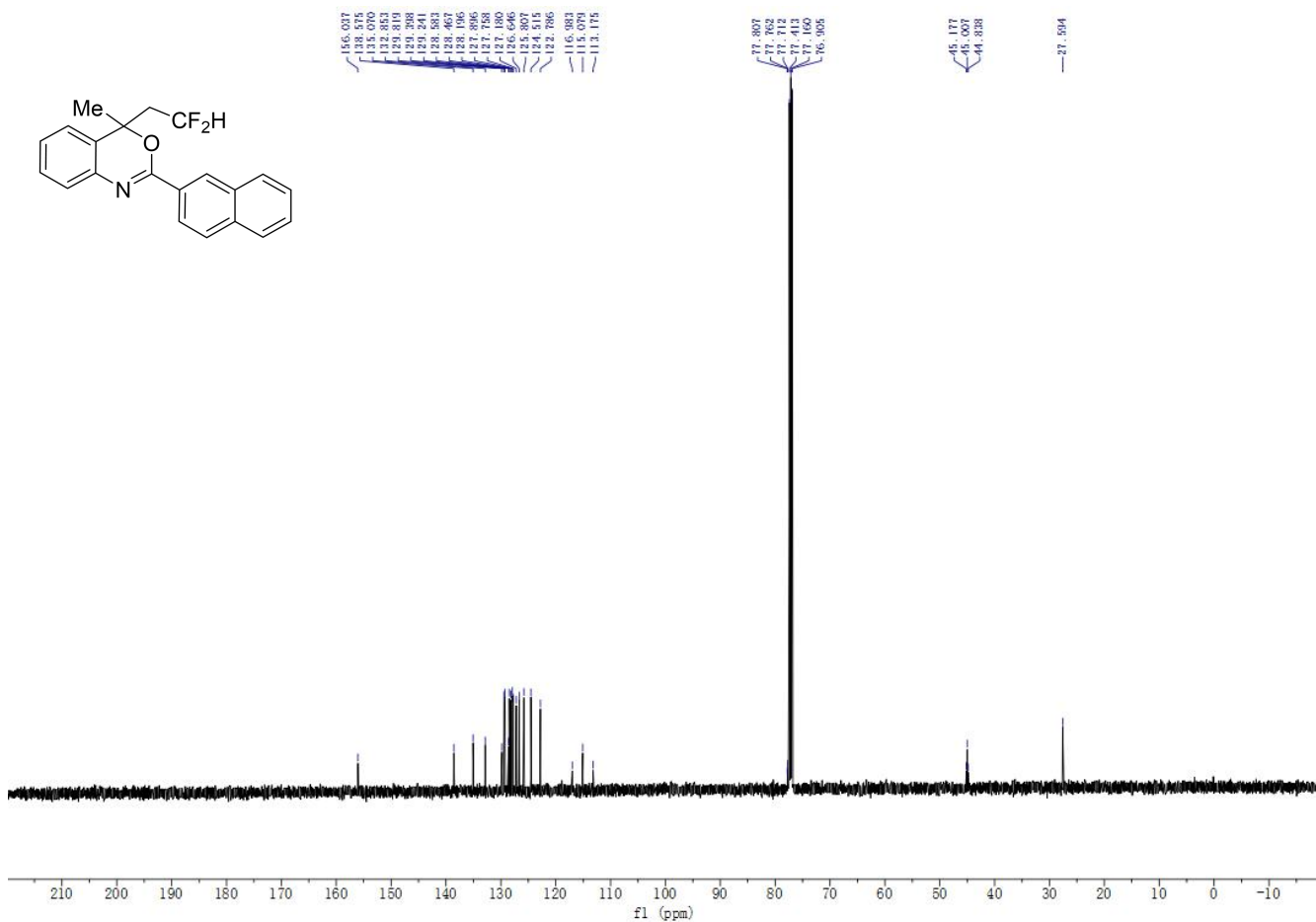
¹⁹F NMR Spectrum of **3ra**



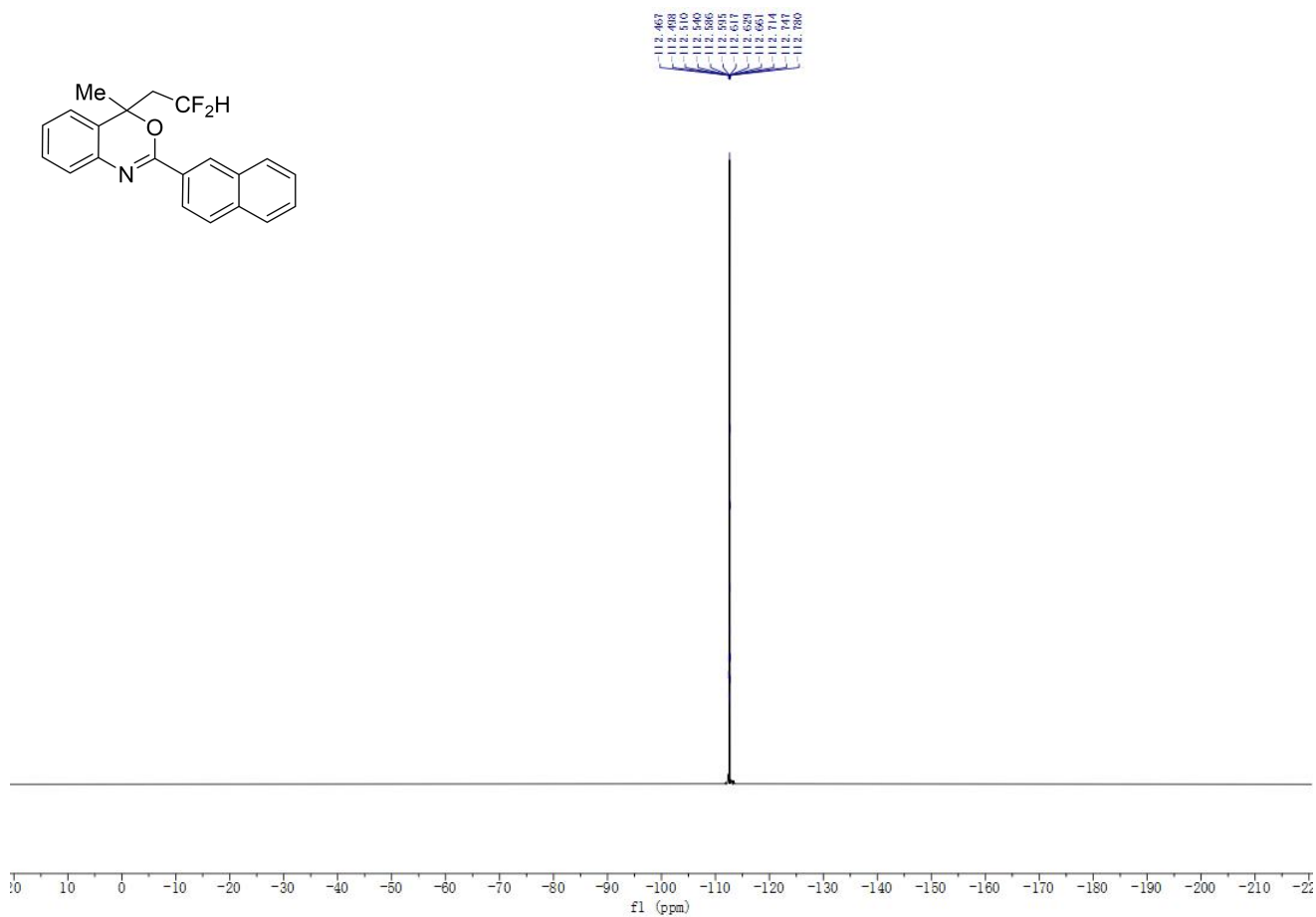
¹H NMR Spectrum of **3sa**



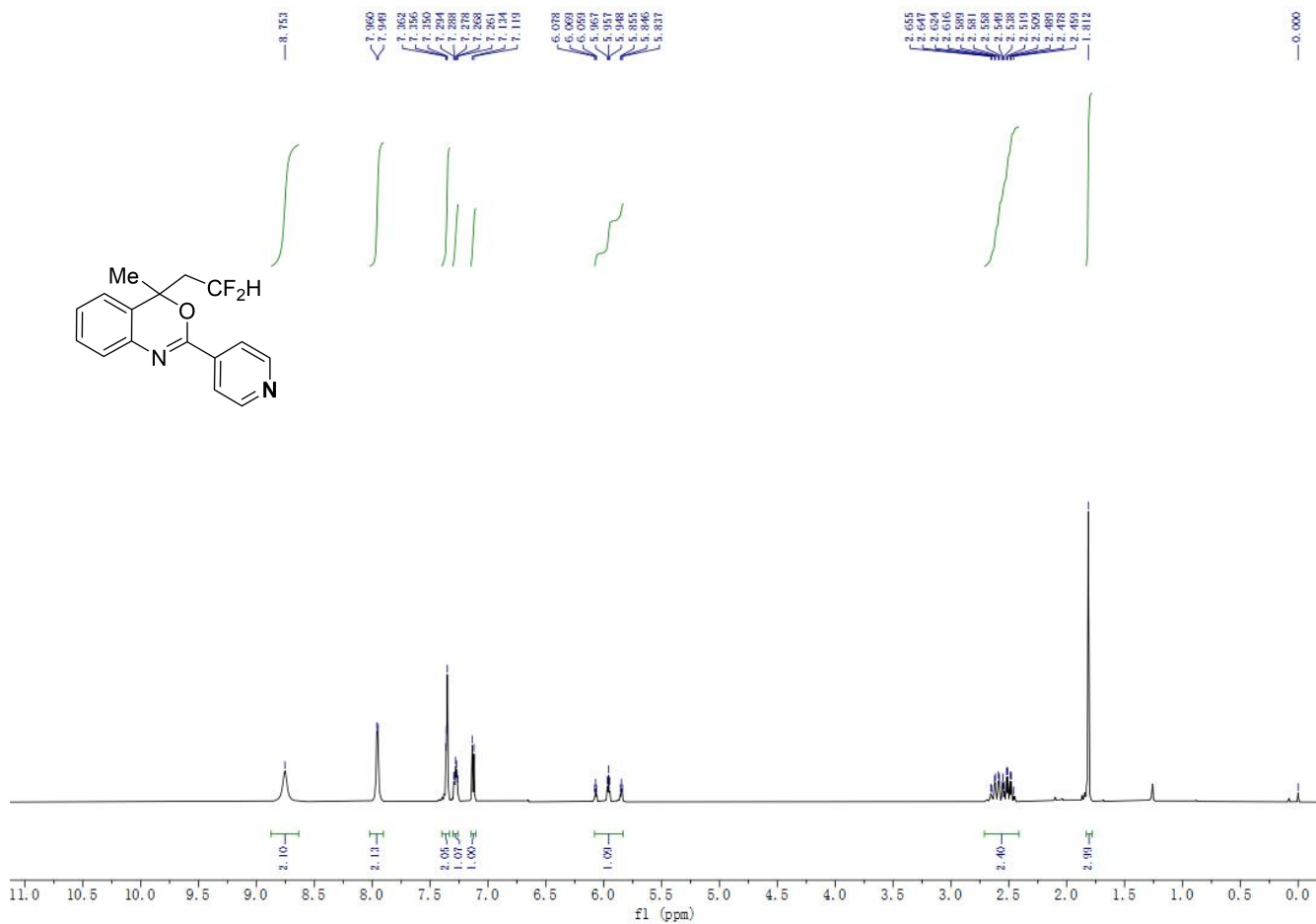
¹³C NMR Spectrum of **3sa**



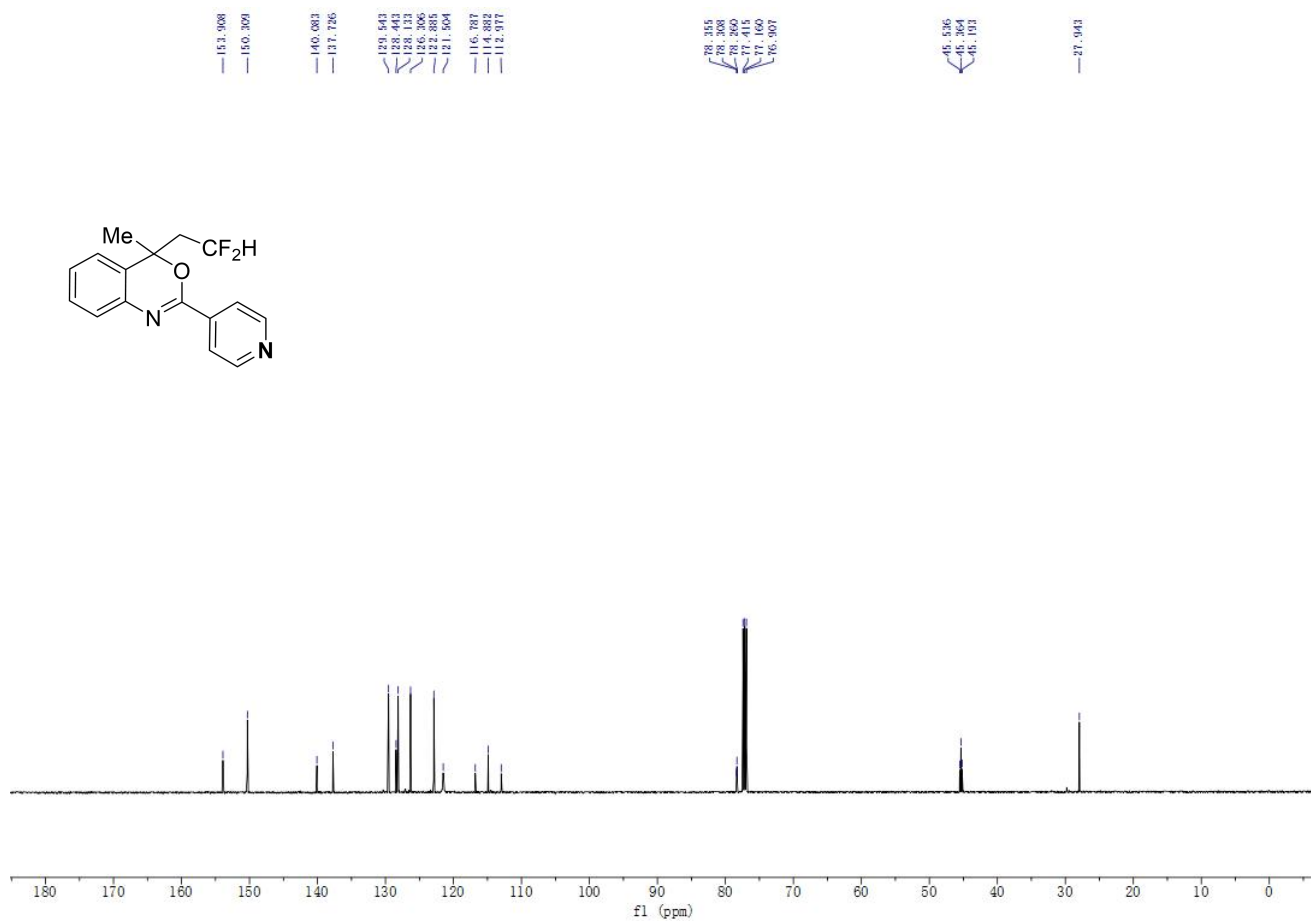
¹⁹F NMR Spectrum of **3sa**



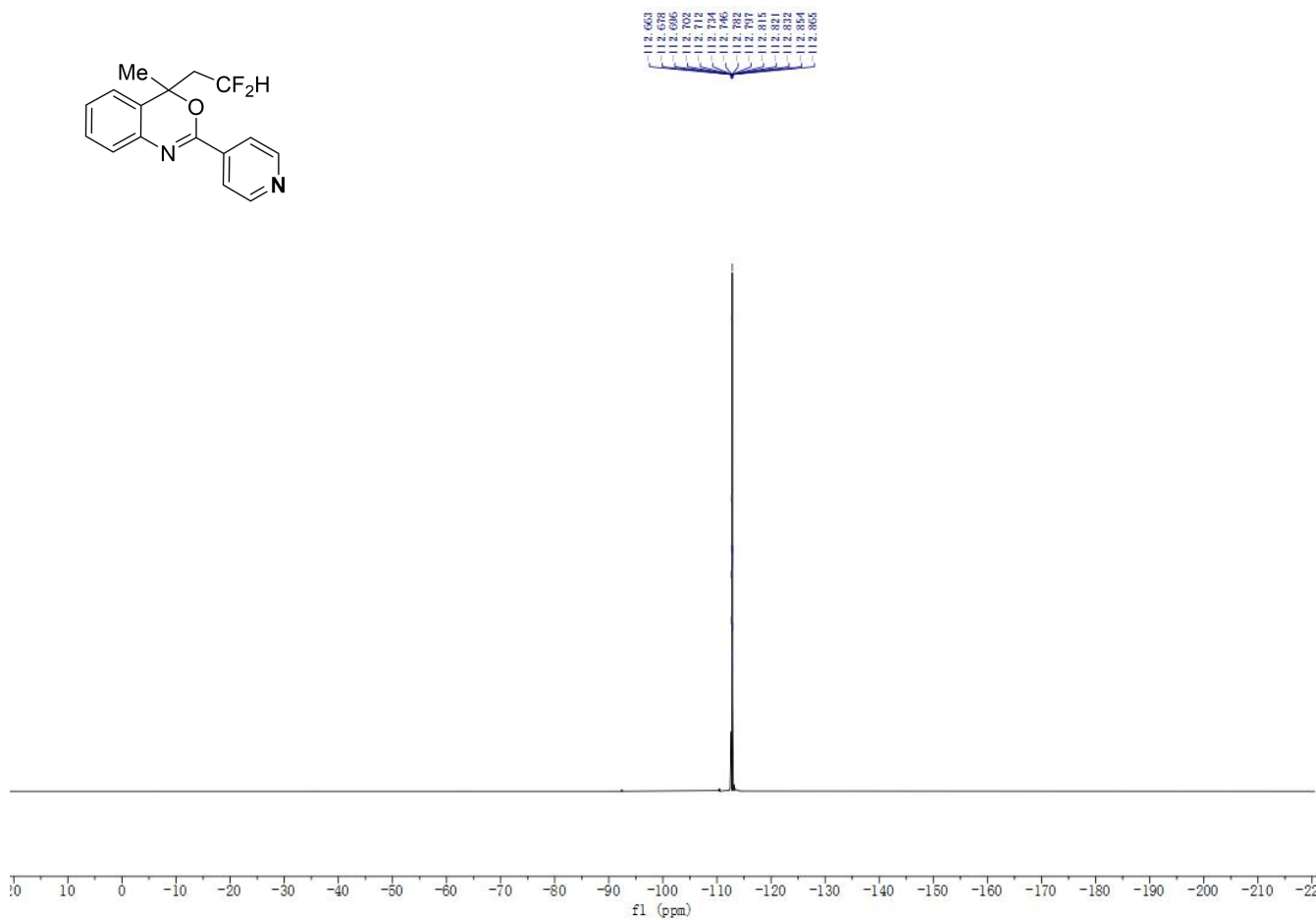
¹H NMR Spectrum of **3ta**



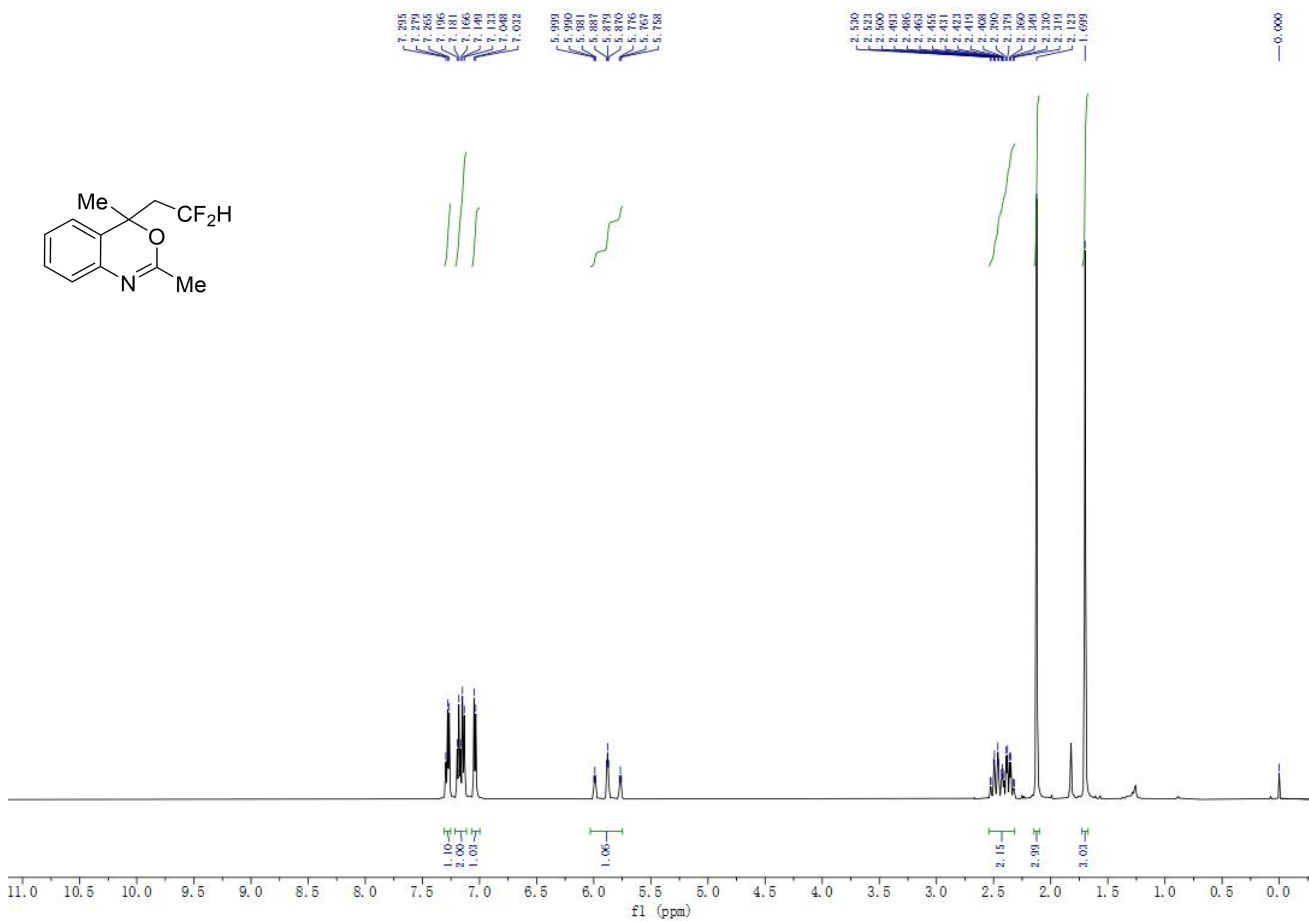
¹³C NMR Spectrum of 3ta



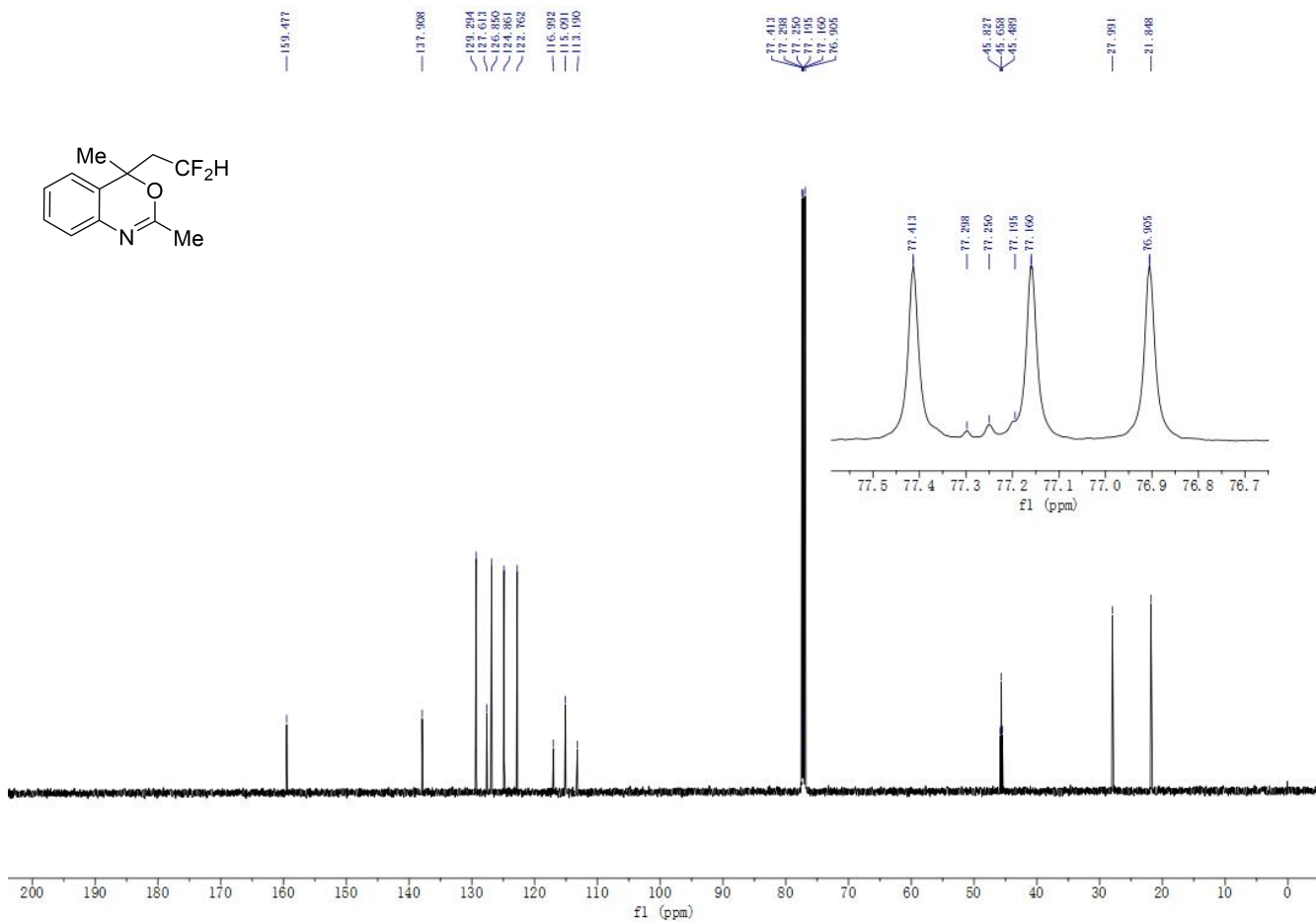
¹⁹F NMR Spectrum of 3ta



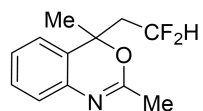
¹H NMR Spectrum of **3ua**



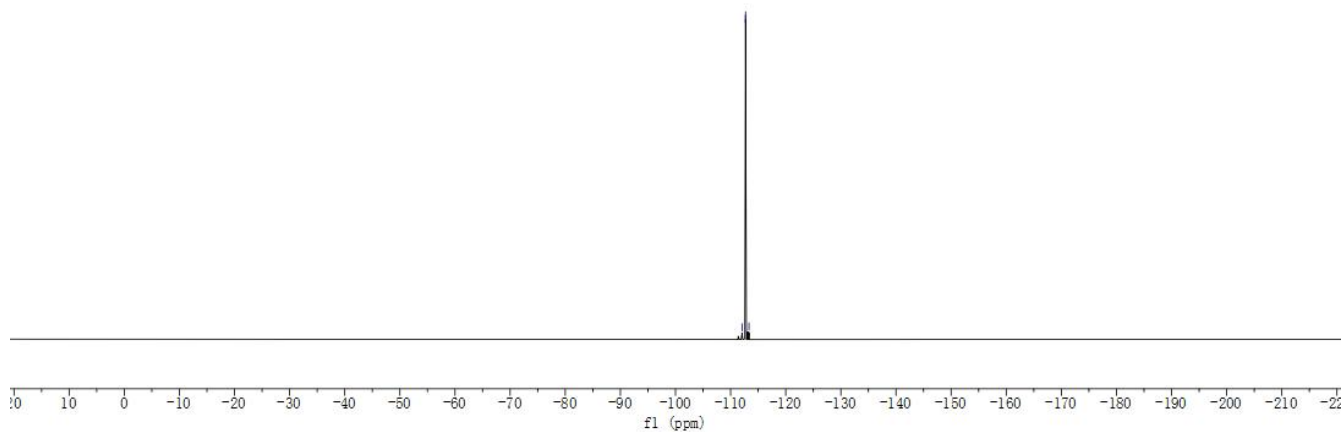
¹³C NMR Spectrum of **3ua**



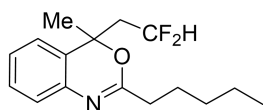
^{19}F NMR Spectrum of **3ua**



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113.330



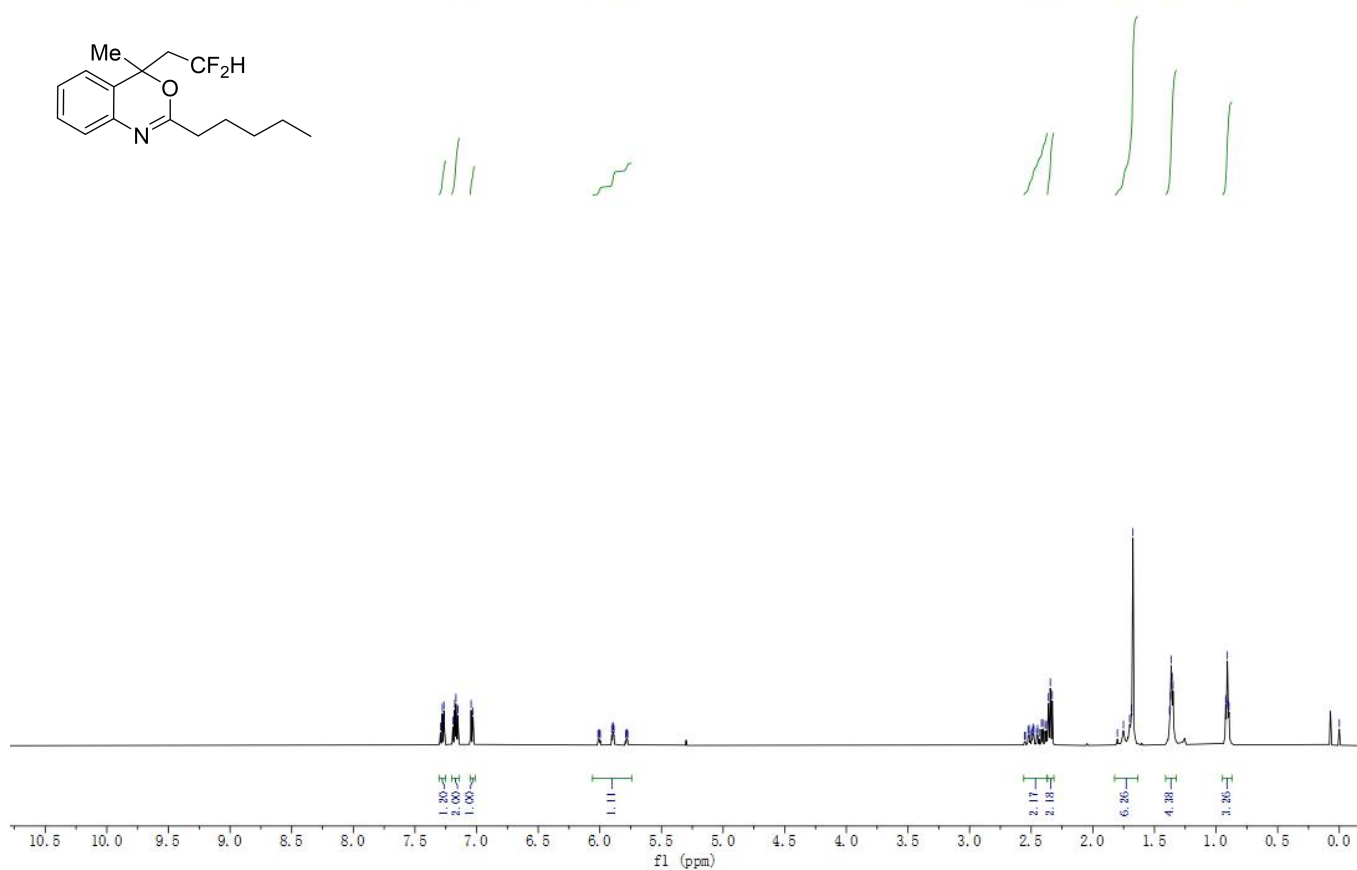
^1H NMR Spectrum of **3va**



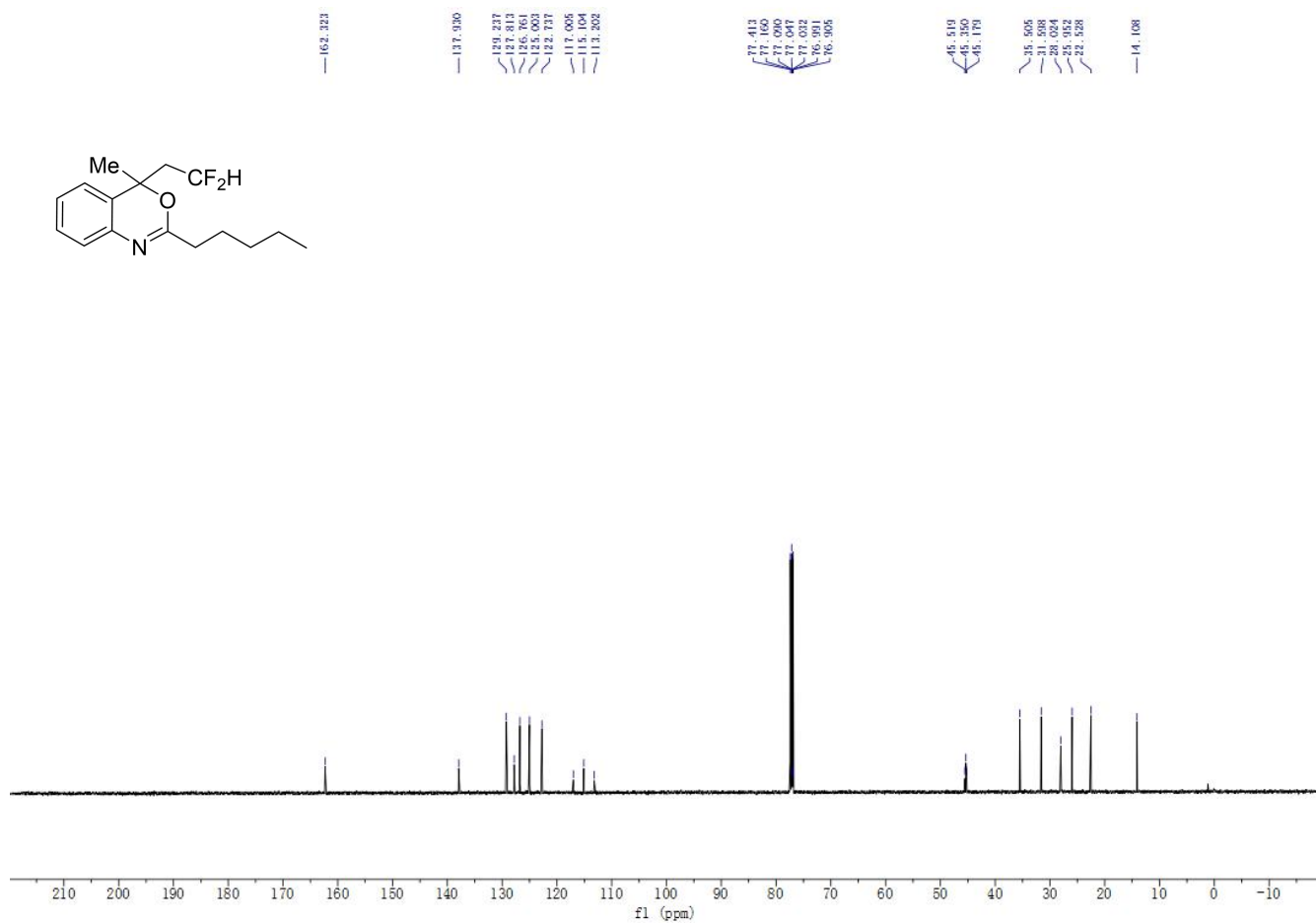
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5.784
5.771

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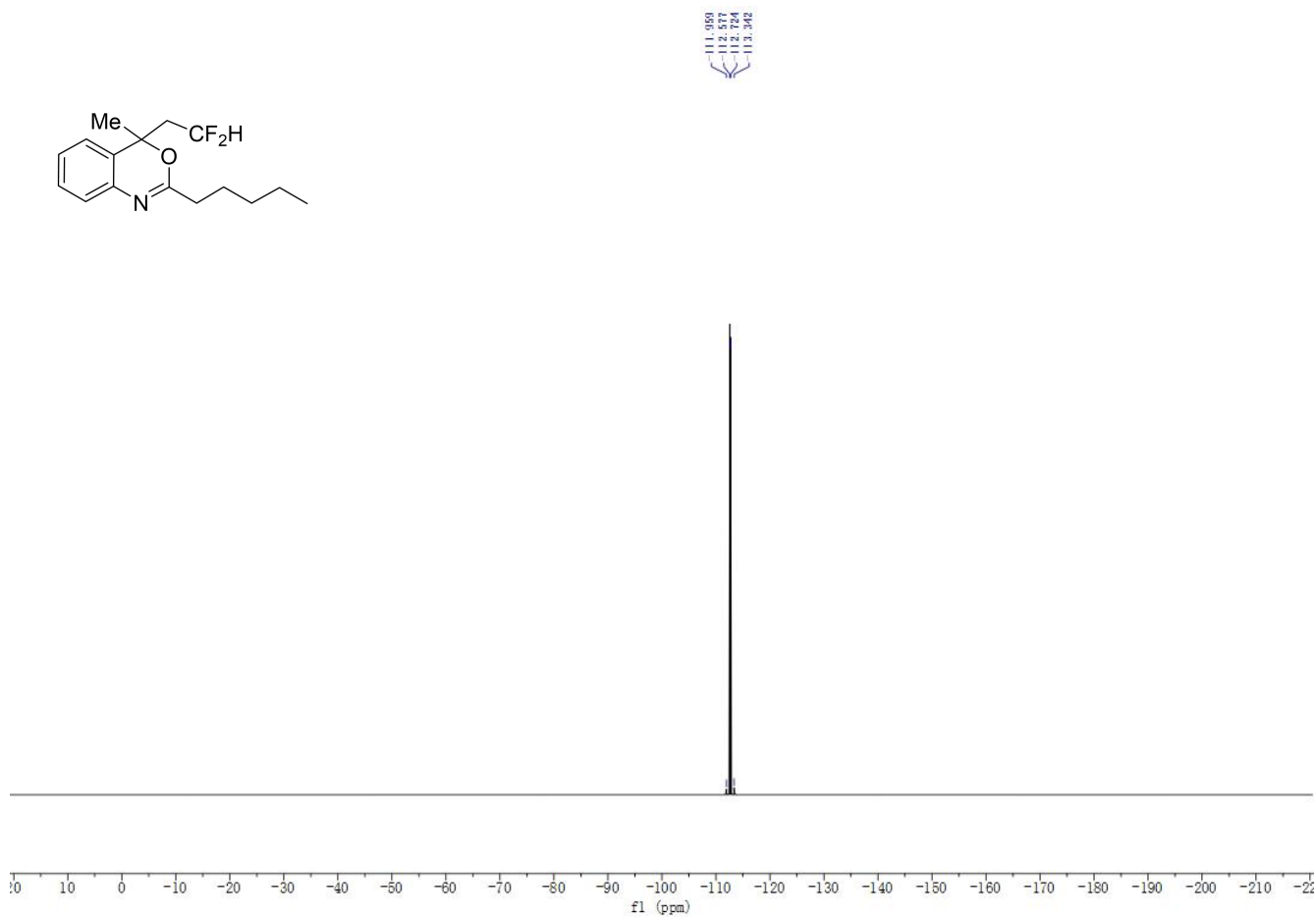
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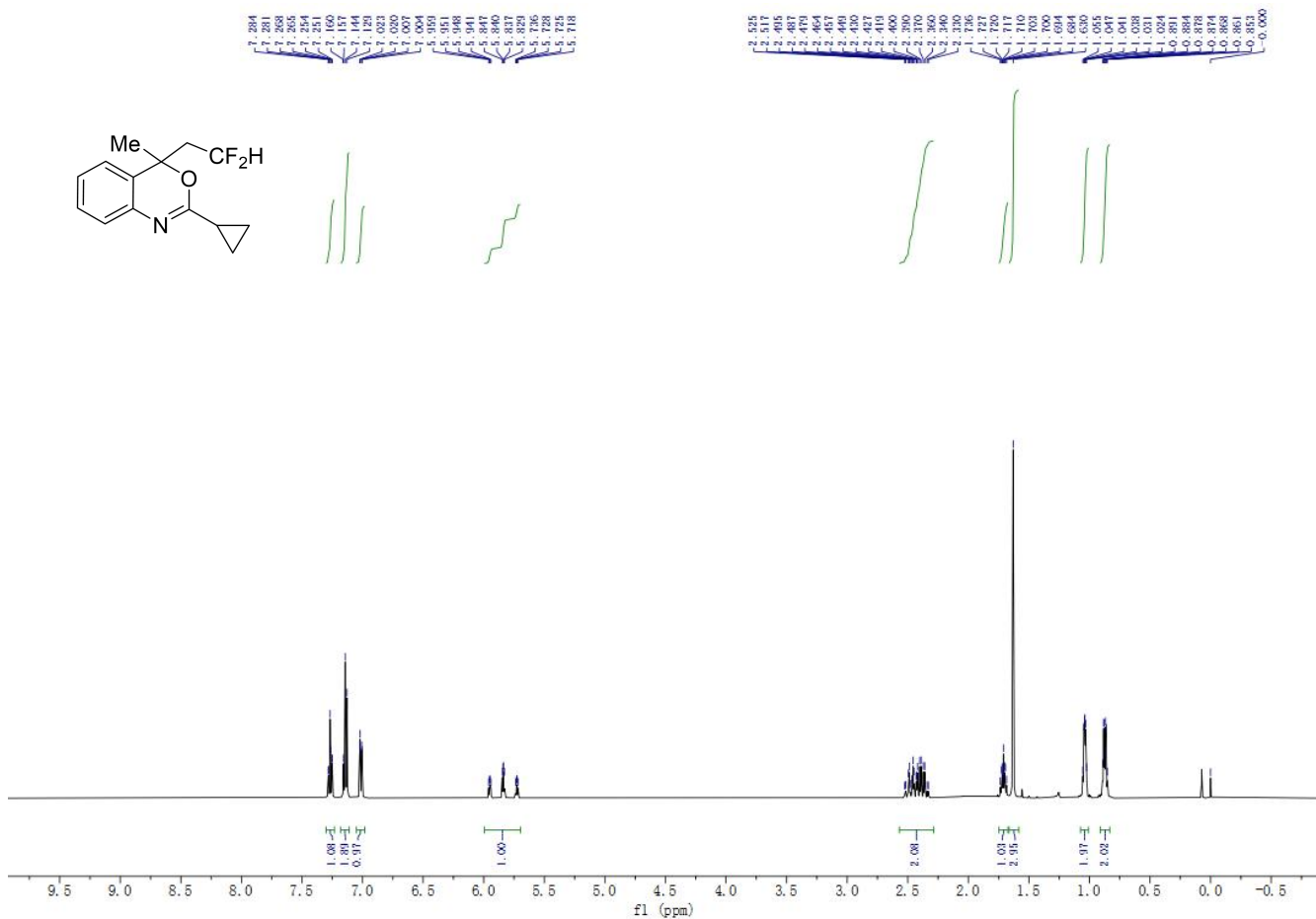
¹³C NMR Spectrum of 3va



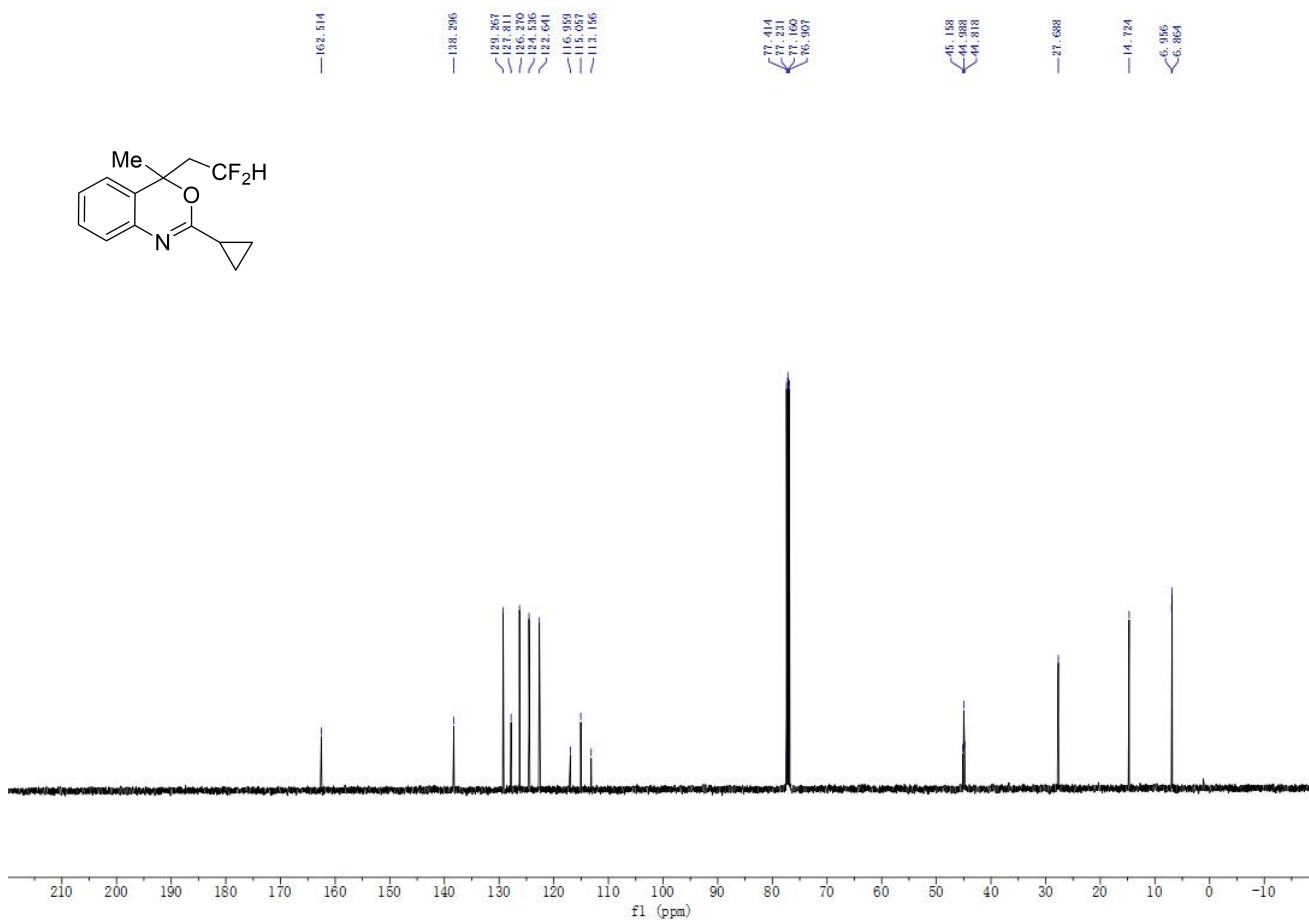
¹⁹F NMR Spectrum of 3va



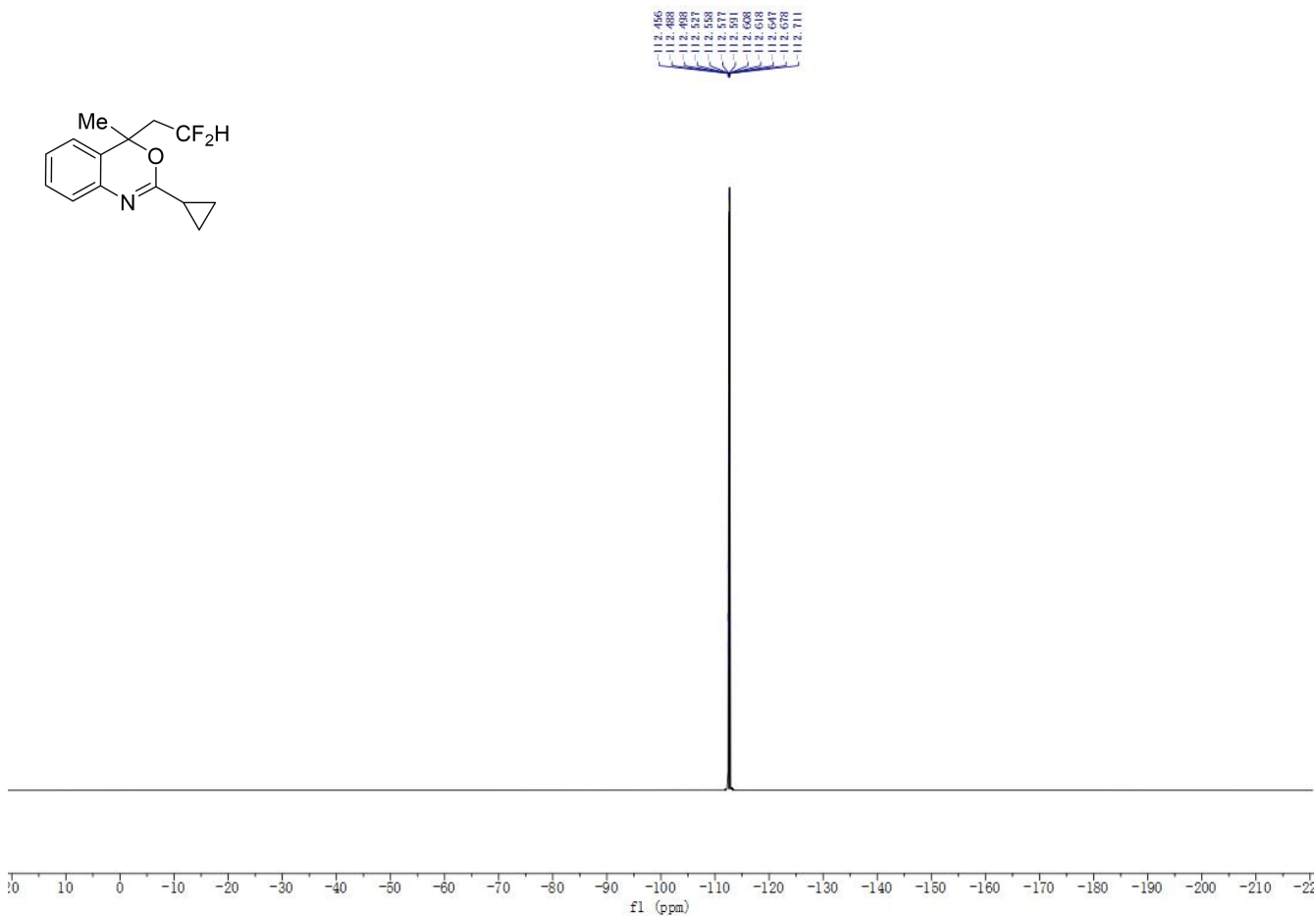
¹H NMR Spectrum of **3wa**



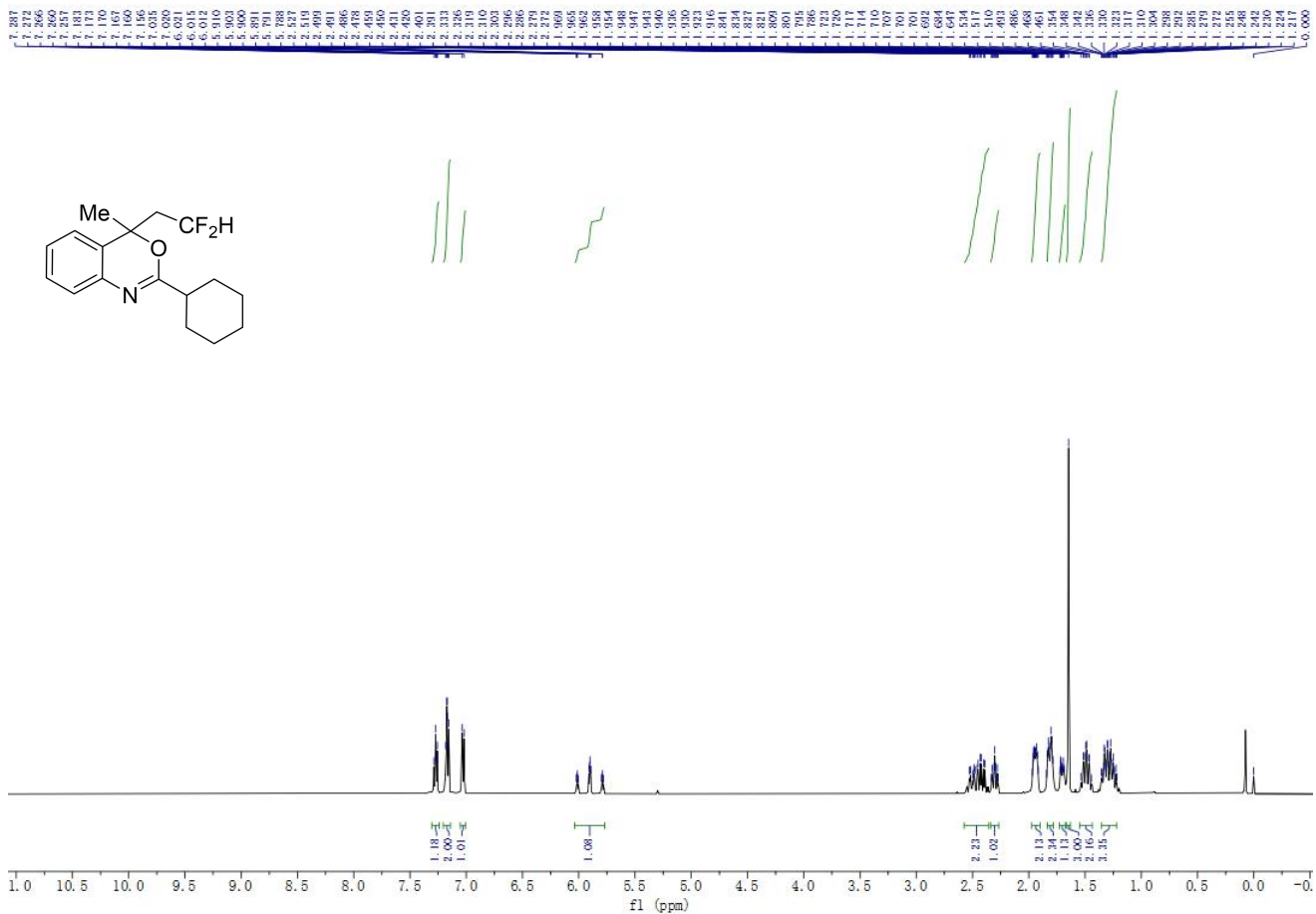
¹³C NMR Spectrum of **3wa**



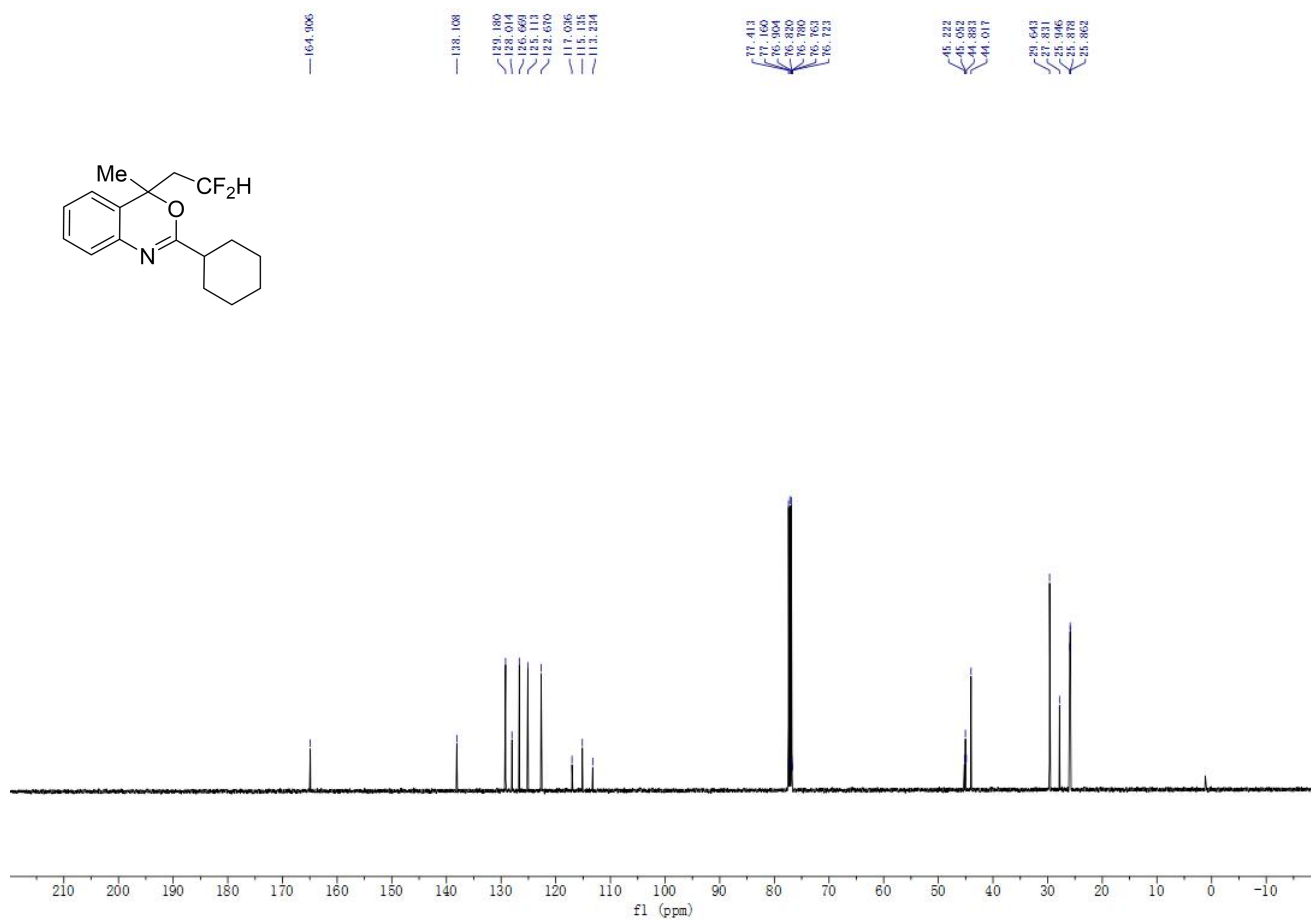
¹⁹F NMR Spectrum of **3wa**



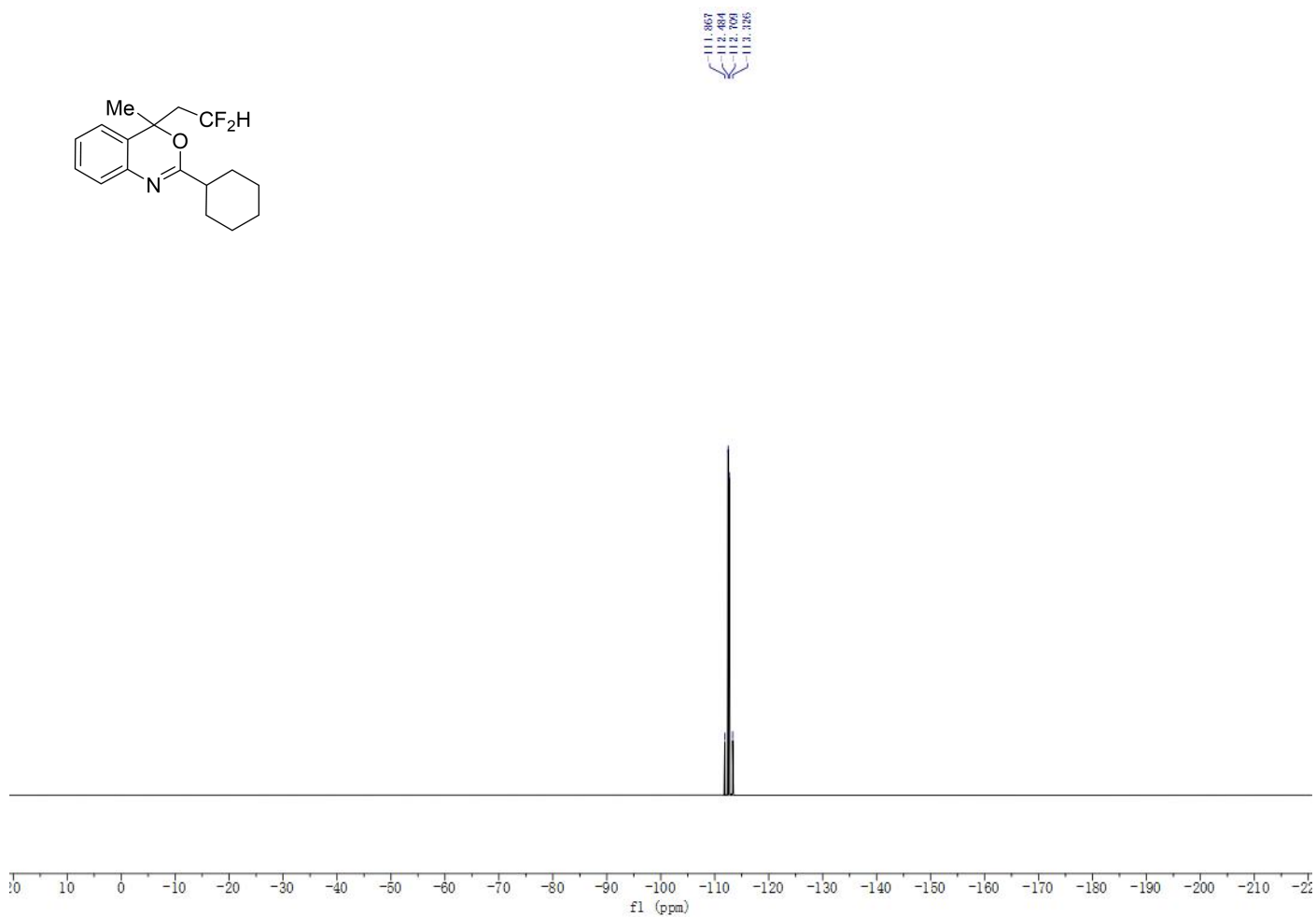
¹H NMR Spectrum of **3xa**



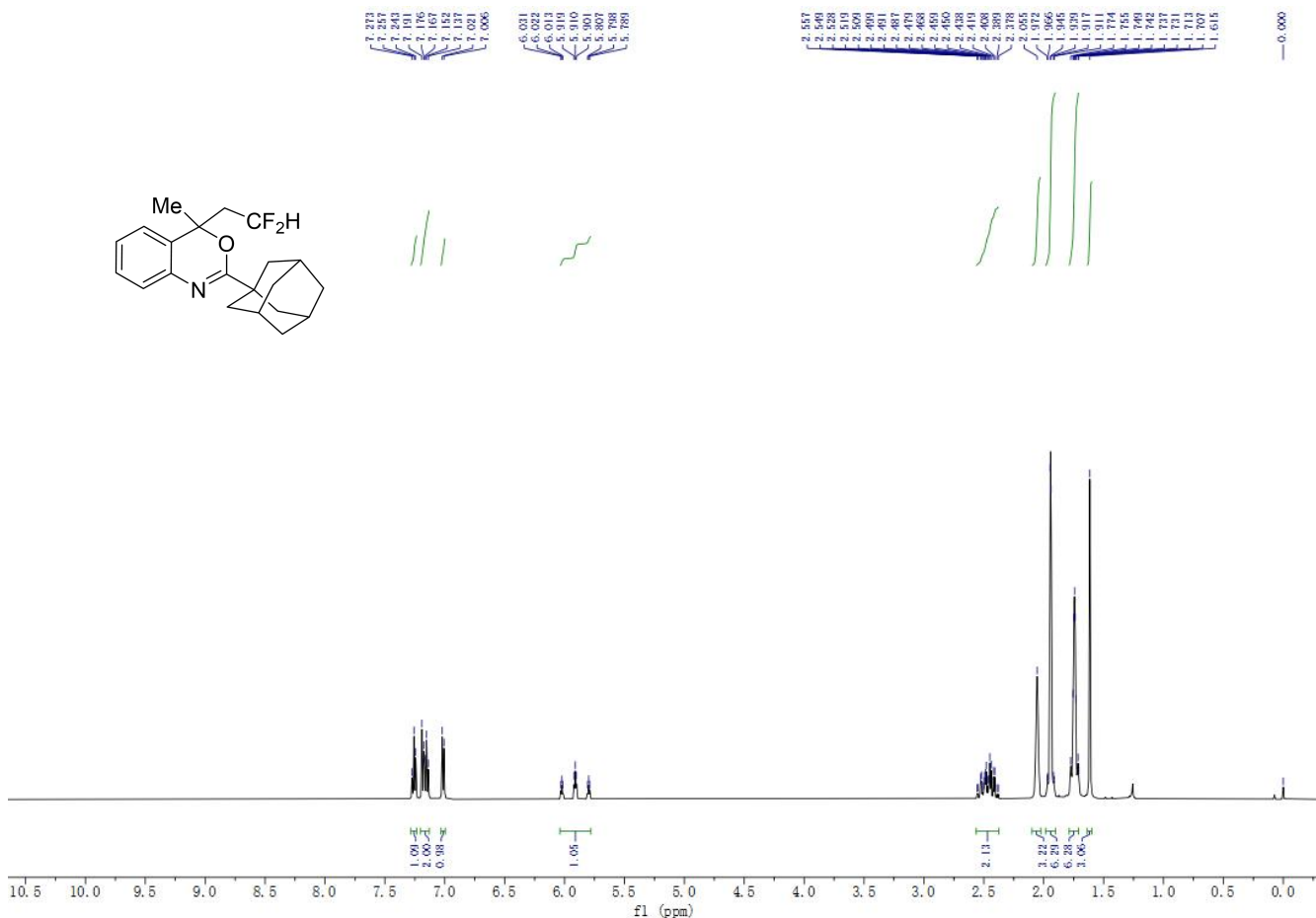
¹³C NMR Spectrum of 3xa



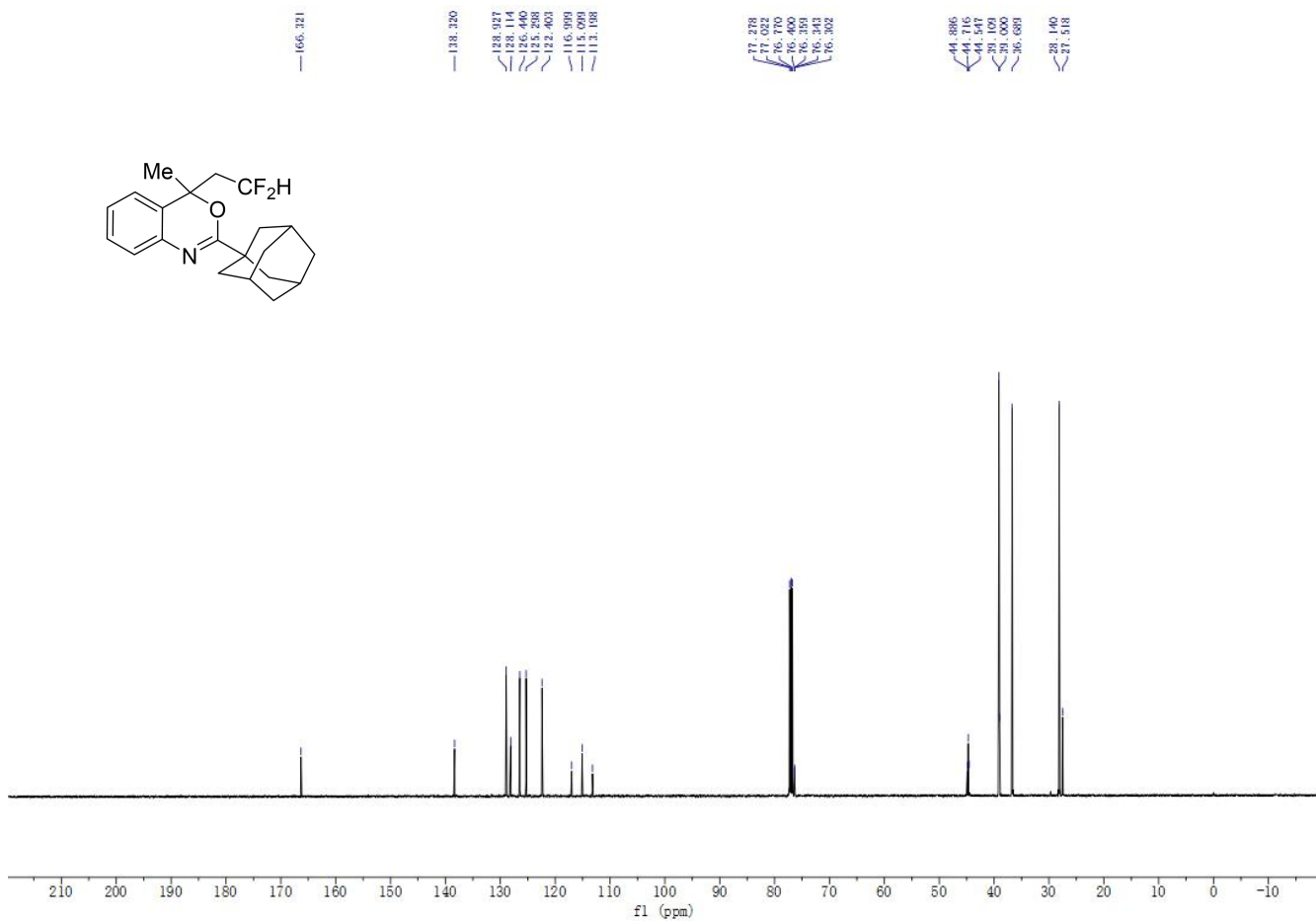
¹⁹F NMR Spectrum of 3xa



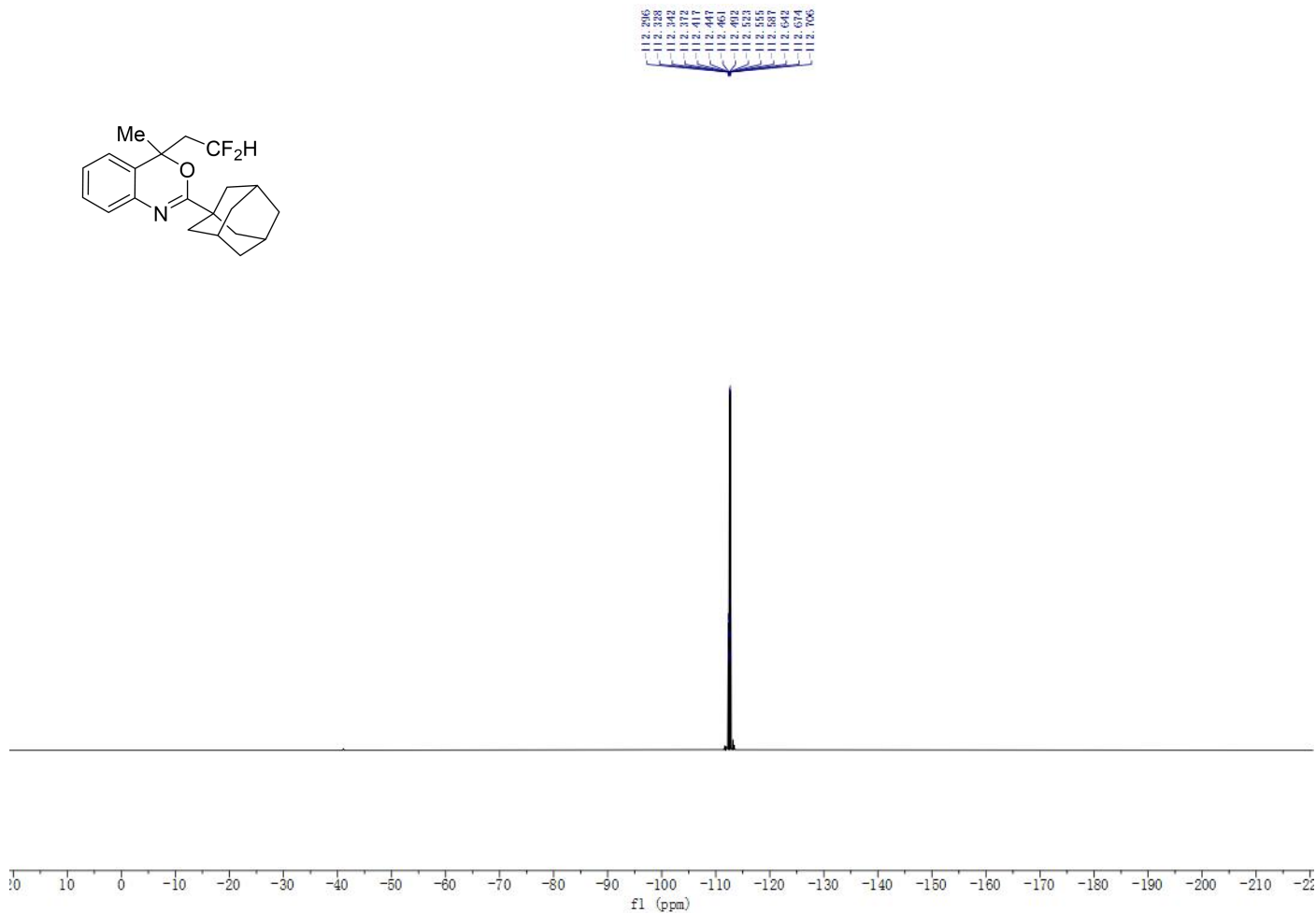
¹H NMR Spectrum of 3ya



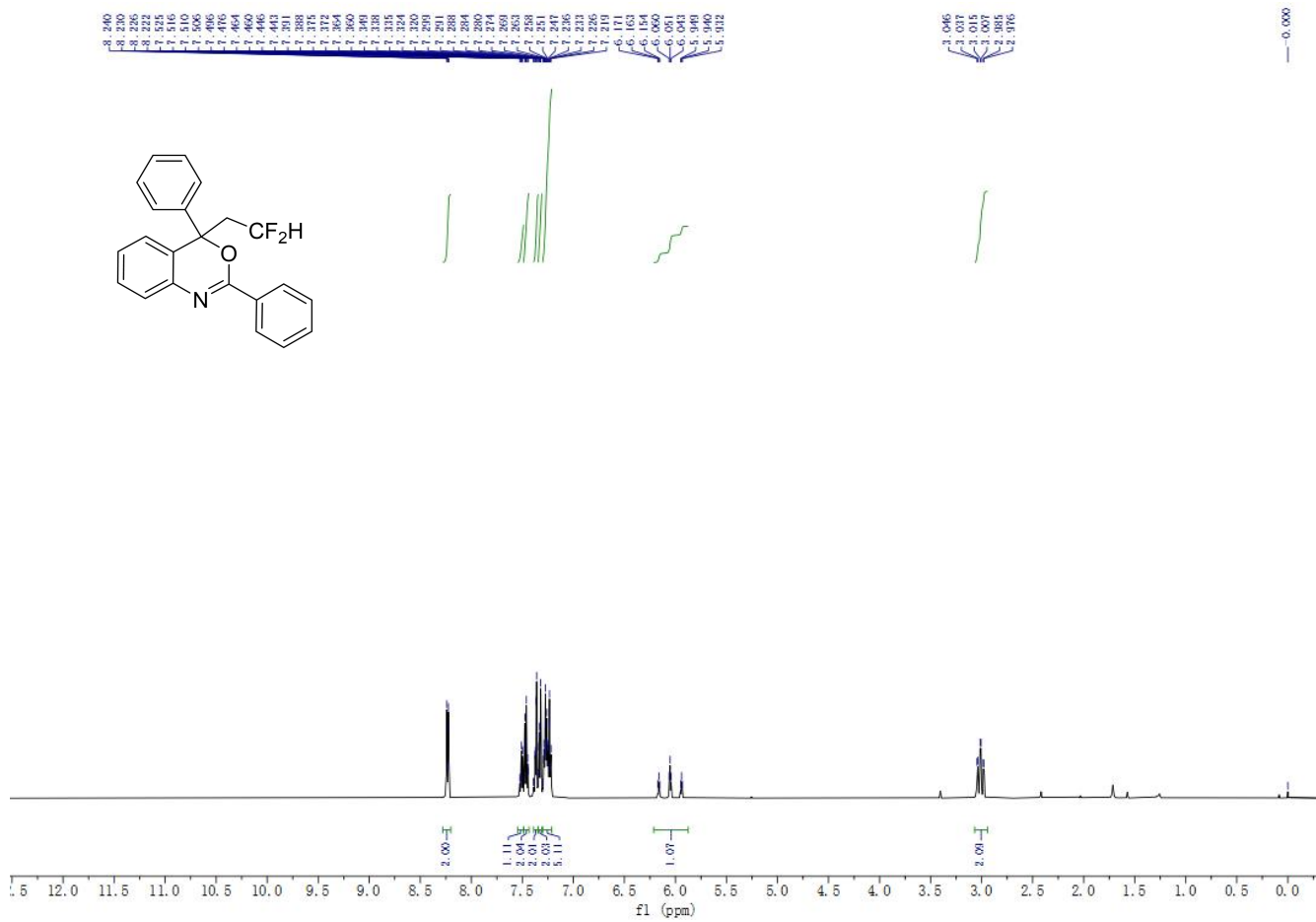
¹³C NMR Spectrum of 3ya



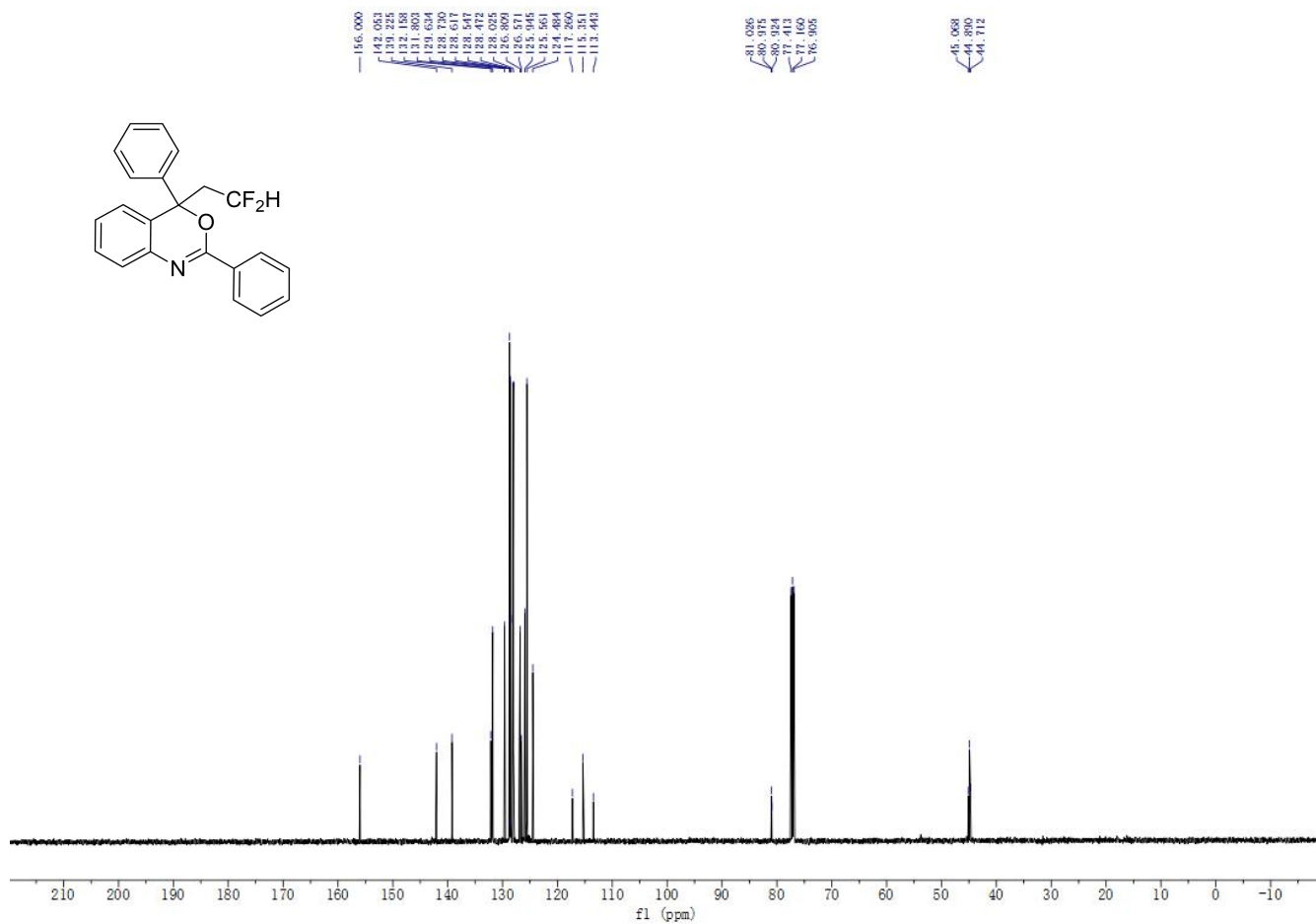
¹⁹F NMR Spectrum of 3ya



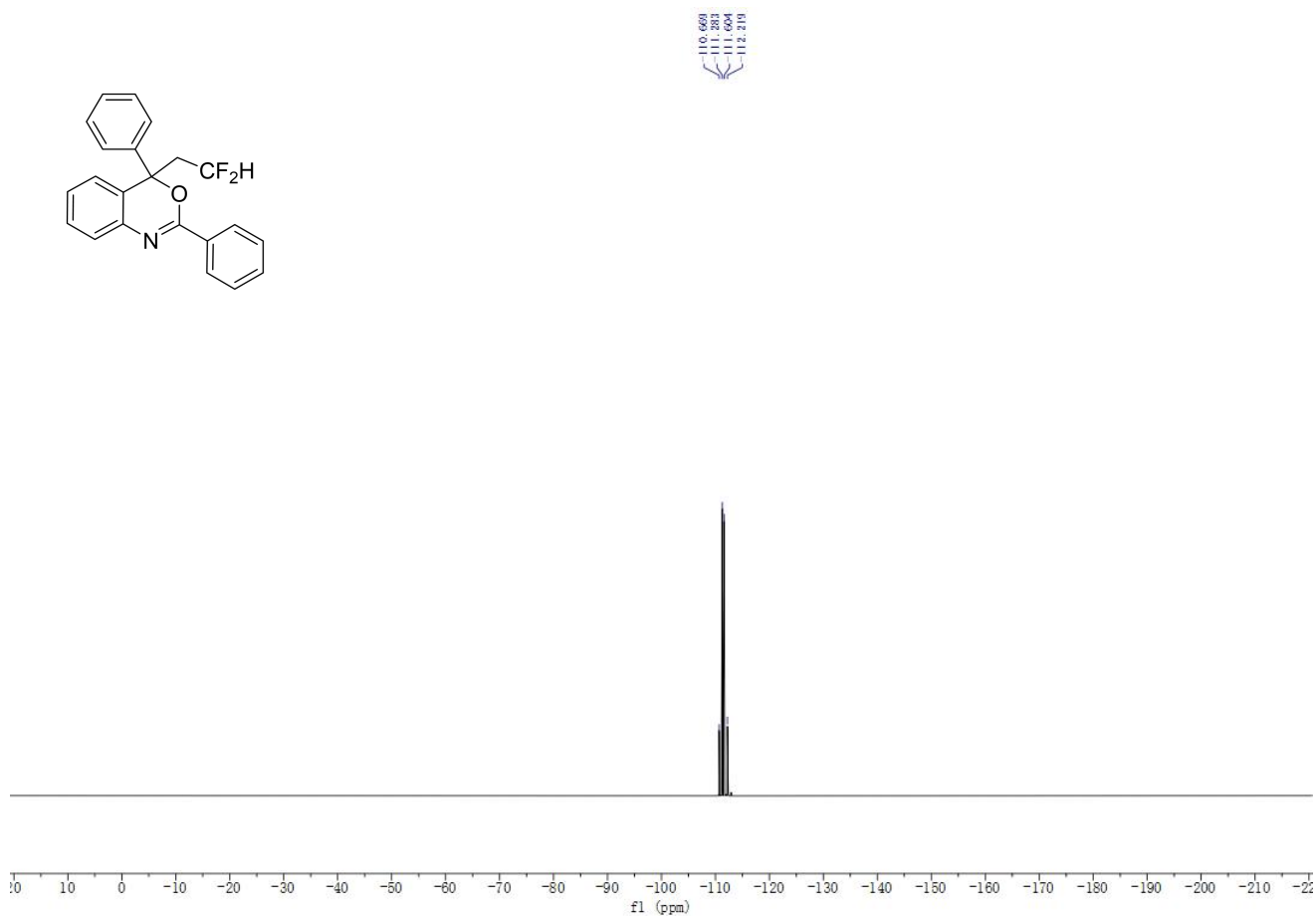
¹H NMR Spectrum of **3a**



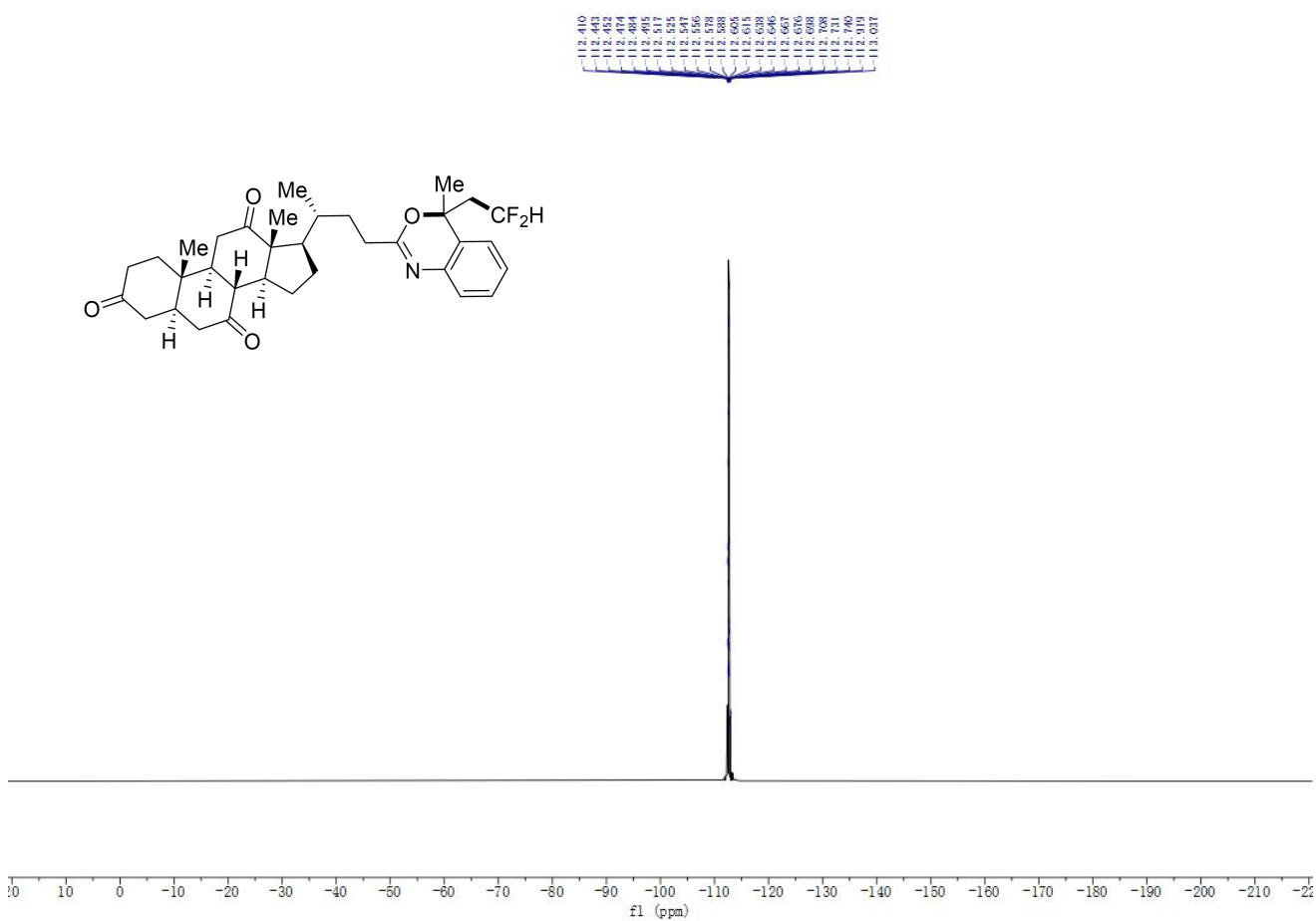
¹³C NMR Spectrum of **3za**



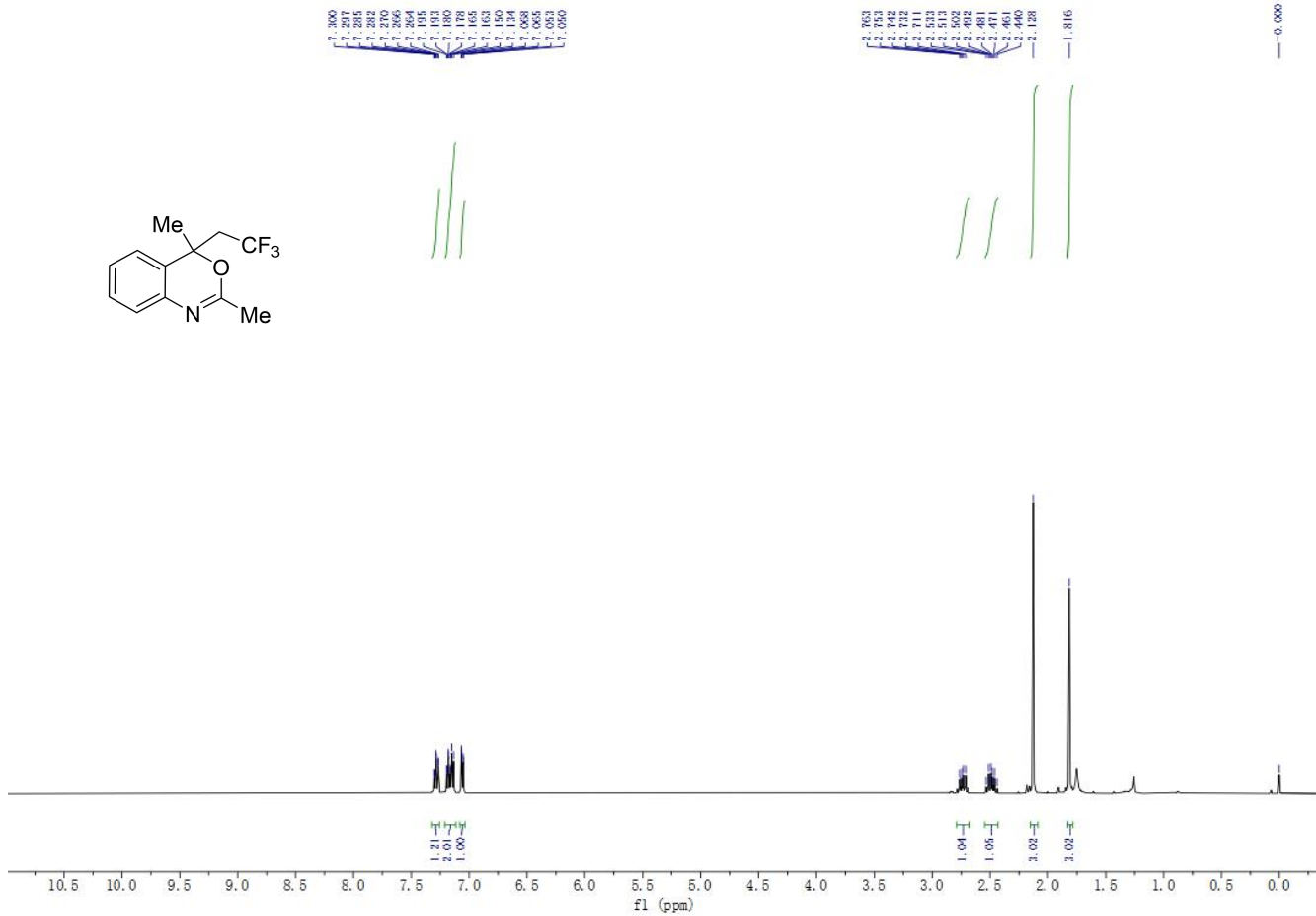
¹⁹F NMR Spectrum of **3za**



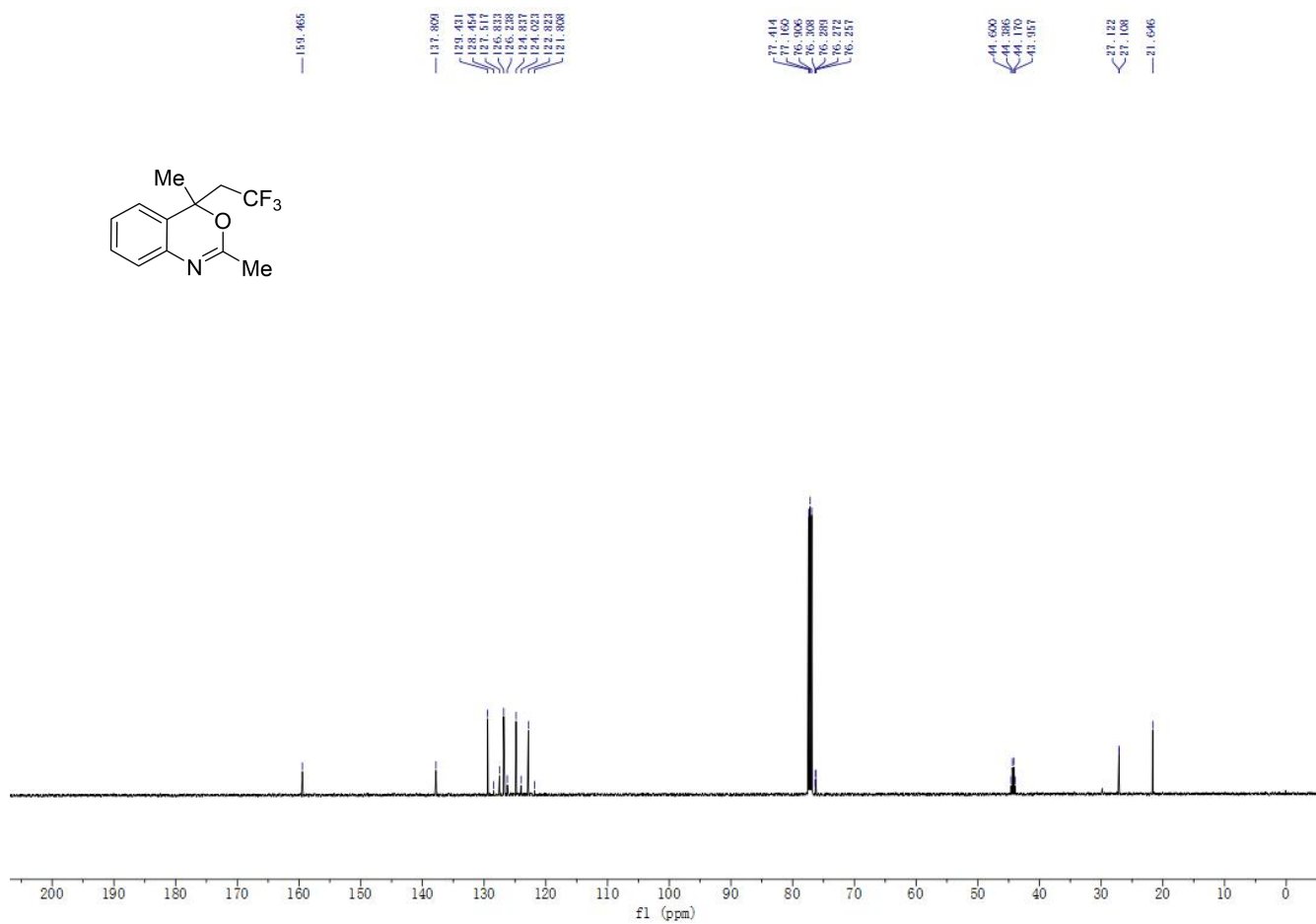
¹⁹F NMR Spectrum of **3Aa**



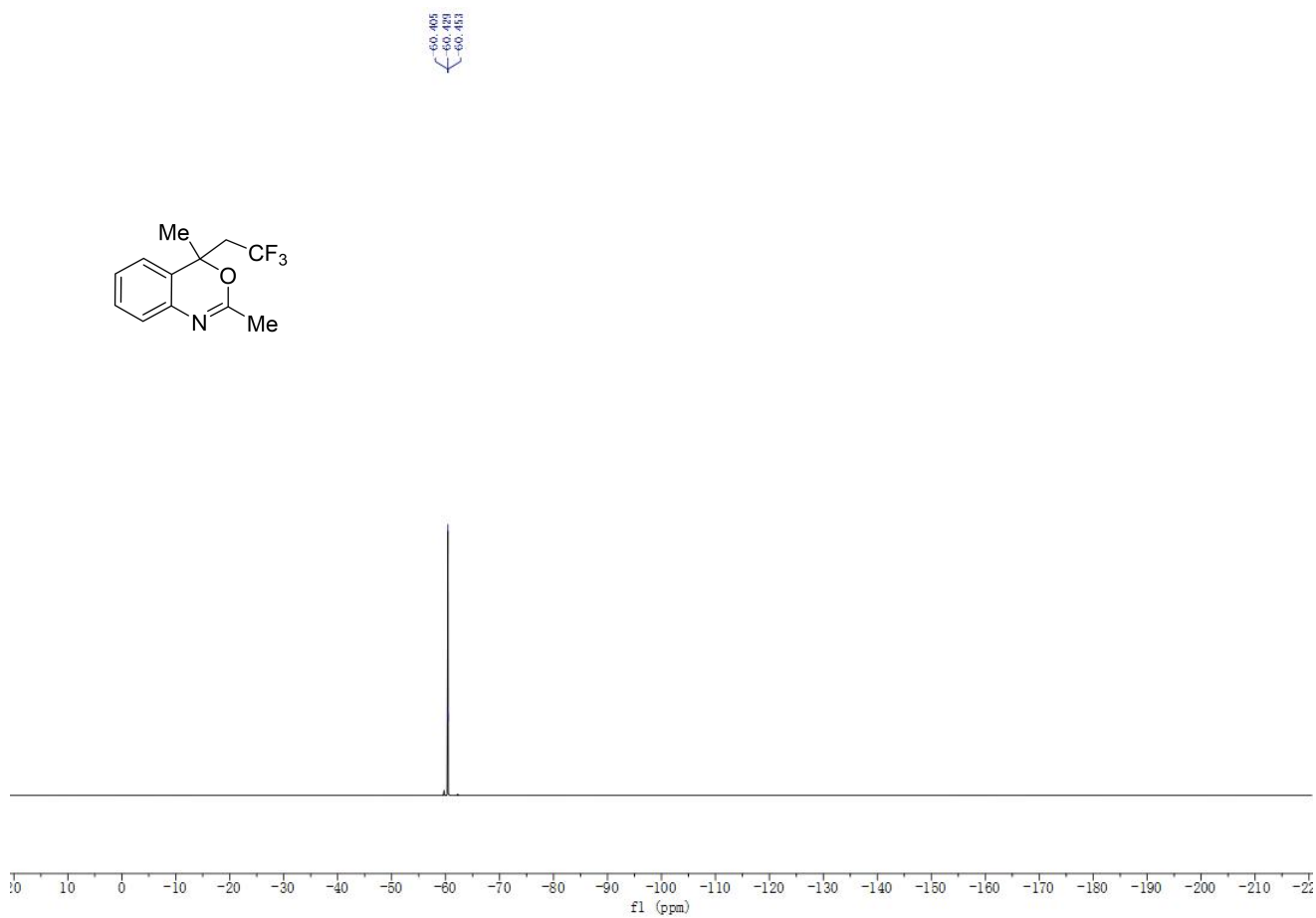
¹H NMR Spectrum of **3tb**



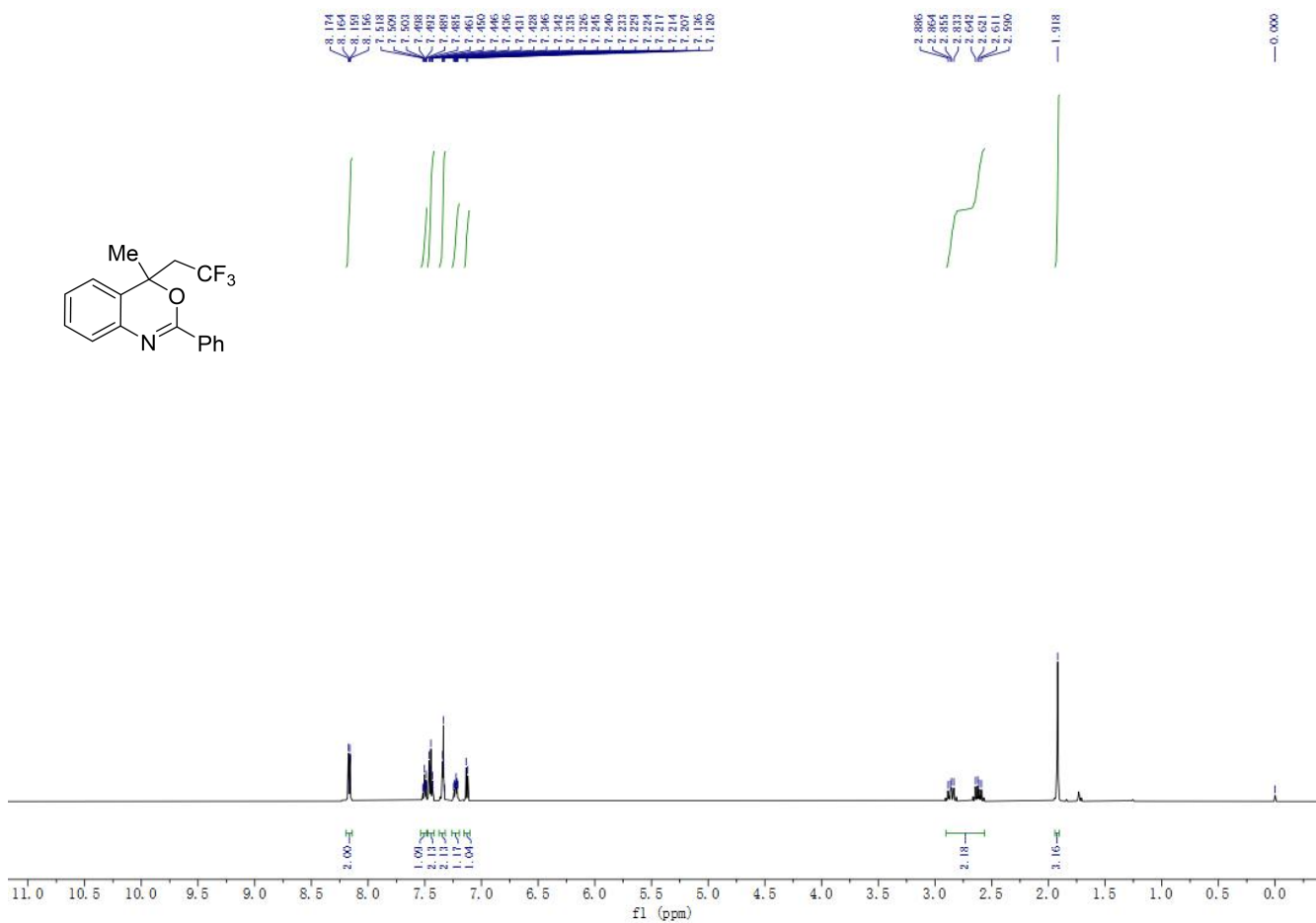
¹³C NMR Spectrum of **3tb**



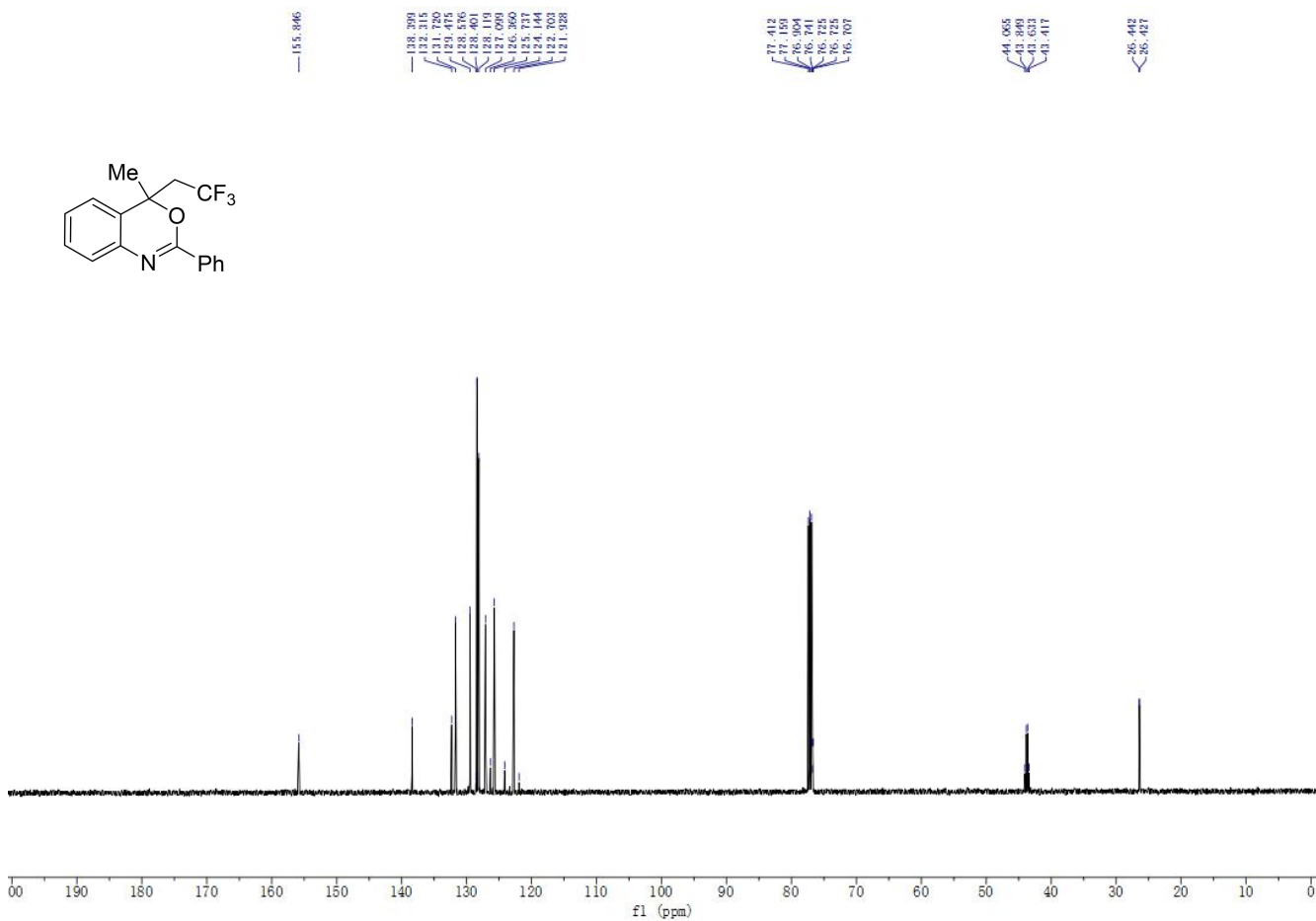
¹⁹F NMR Spectrum of **3tb**



¹H NMR Spectrum of **3ab**



¹³C NMR Spectrum of **3ab**



¹⁹F NMR Spectrum of **3ab**

— 59.875

