Supporting Information

Photoelectrochemical Synthesis of 4-Halomethyl Benzoxazines with Halogen Anion Source

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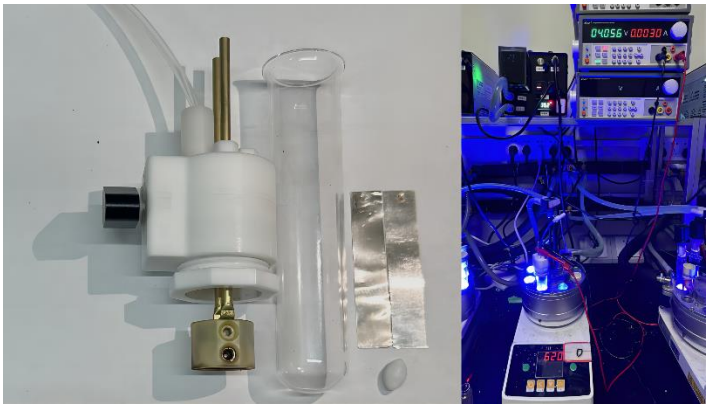
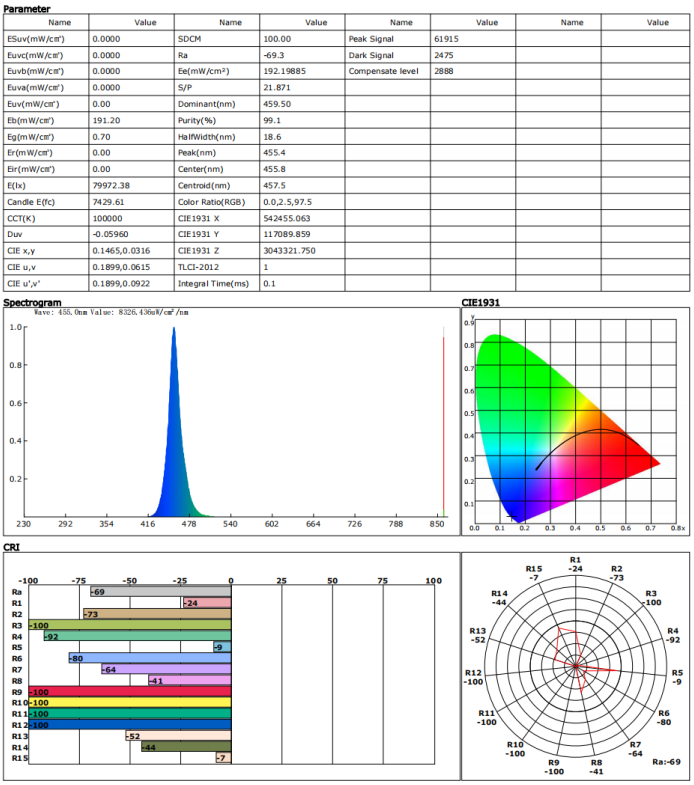
General Information

Unless otherwise noted, materials were obtained from commercial suppliers and used without further purification. Thin layer chromatography (TLC) employed glass 0.25 mm silica gel plates. Flash chromatography columns were packed with 200-300 mesh silica gel. ^{1}H NMR spectra were recorded at 400 MHz, ^{13}C NMR spectra were recorded at 101 MHz and ^{19}F NMR spectra were recorded at 500 MHz by using a Bruker Avance 500 spectrometer. Chemical shifts were calibrated using residual undeuterated solvent as an internal reference (^{1}H NMR: $CDCl_3$ 7.26 ppm, ^{13}C {1H} NMR: $CDCl_3$ 77.16 ppm), the chemical shifts (δ) were expressed in ppm, and J values were given in Hz. The following abbreviations were used to describe peak splitting patterns when appropriate: s = singlet, d = doublet, t = triplet, q = quartet, m = multiplet, dd = doublet of doublets, br = broad. HRMS were performed on a spectrometer operating on ESI-TOF.

General information for photoelectrochemical devices



The photoelectrochemical reaction system was consist of RLH-18CU purchased from Beijing Rogertech Co. ltd and DC power supply purchased from A-BF, and the reactor was designed by Beijing Rogertech Co. ltd. The spectrum of light source is as following.



Parameter

Name	Value	Name	Value	Name	Value	Name	Value
ESuv(mW/cm²)	0.0000	SDCM	100.00	Peak Signal	61915		
Euvc(mW/cm²)	0.0000	Ra	-69.3	Dark Signal	2475		
Euvb(mW/cm²)	0.0000	Ee(mW/cm²)	192.19885	Compensate level	2888		
Euva(mW/cm²)	0.0000	S/P	21.871				
Euv(mW/cm²)	0.00	Dominant(nm)	459.50				
Eb(mW/cm²)	191.20	Purity(%)	99.1				
Eg(mW/cm²)	0.70	HalfWidth(nm)	18.6				
Er(mW/cm²)	0.00	Peak(nm)	455.4				
Eir(mW/cm²)	0.00	Center(nm)	455.8				
E(lx)	79972.38	Centroid(nm)	457.5				
Candle E(fc)	7429.61	Color Ratio(RGB)	0.0,2.5,97.5				
CCT(K)	100000	CIE1931 X	542455.063				
Duv	-0.05960	CIE1931 Y	117089.859				
CIE x,y	0.1465,0.0316	CIE1931 Z	3043321.750				
CIE u,v	0.1899,0.0615	TLCI-2012	1				
CIE u',v'	0.1899,0.0922	Integral Time(ms)	0.1				

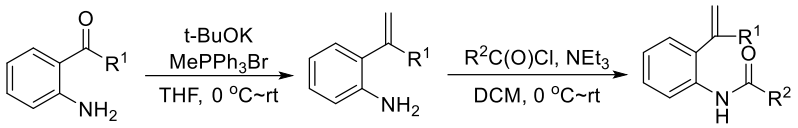
Spectrogram

CIE1931

CRI

General procedure for the synthesis of compounds 1

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 ℃. 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 ℃. After completion, the reaction mixture was purified via column chromatography to give **1a**.

Typical procedure for the synthesis of compound 3

Condition A: In an undivided flask (10 mL) equipped with a stir bar, **1** (0.2 mmol), $^{n}Bu_4NX$ (0.4 mmol), 4CzPN (0.01 mmol) and MeCN (7 mL) were added. The flask was equipped with platinum anode (10 mm × 50 mm × 0.3 mm) and platinum cathode (10 mm × 50 mm × 0.3 mm). The reaction mixture was stirred and electrolyzed at a constant current of 3 mA under radiation of 455 nm LEDs at r.t. for 12 h. After completion, the reaction medium was extracted with 5 mL ethyl acetate three times, organic phase was dried and concentrated under reduced pressure and the pure products **3** were obtained by flash chromatography on silica gel.

Condition B: In an undivided flask (10 mL) equipped with a stir bar, **1** (0.2 mmol), $^{n}Bu_4NX$ (0.4 mmol), MeCN (7 mL) were added. The flask was equipped with platinum anode (10 mm × 50 mm × 0.3 mm) and platinum cathode (10 mm × 50 mm × 0.3 mm). The reaction mixture was stirred and electrolyzed at a constant current of 6 mA and room temperature for 12 h. After completion, the reaction medium was extracted with 5 mL ethyl acetate three times, organic phase was dried and concentrated under reduced pressure and the pure products **3** were obtained by flash chromatography on silica gel.

Gram-scale synthesis of 3aa and 3rc

In an oven-dried 100-mL three-necked flask equipped with a stir bar, the platinum plate (10 mm × 50 mm × 0.3 mm) as the anode and platinum plate (10 mm × 50 mm × 0.3 mm) as cathode, **1r** (3 mmol, 1.551 g), nBu$_4$NI (6 mmol, 1.11 g), 4CzPN (0.15 mmol, 118.2 mg), and MeCN (30 mL) were added. The reaction mixture was stirred at a constant current of 3 mA and under radiation of 455 nm LEDs for 12 h. The resulting mixture was purified by HPLC to afford the desired product **3rc** (61%, 1.18 g).

In an oven-dried 100-mL three-necked flask equipped with a stir bar, the platinum plate (10 mm × 50 mm × 0.3 mm) as the anode and platinum plate (10 mm × 50 mm × 0.3 mm) as cathode, **1a** (8 mmol, 1.896 g), nBu$_4$NCl (16 mmol, 4.48 g), 4CzPN (0.4 mmol, 315.2 mg), and MeCN (50 mL) were added. The reaction mixture was stirred at a constant current of 3 mA and under radiation of 455 nm LEDs for 12 h. The resulting mixture was purified by HPLC to afford the desired product **3aa** (71%, 1.54 g).

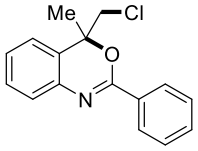
Reference

[1] Q.-H. Deng, J.-R. Chen, Q. Wei, Q.-Q. Zhao, L.-Q. Lua and W.-J. Xiao, *Chem. Commun.*, 2015, **51**, 3537.

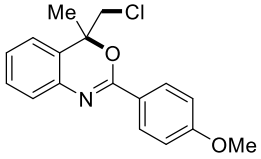
[2] F. Lu, J. Xu, H. Li, K. Wang, D. Ouyang, L. Sun, M. Huang, J. Jiang, J. Hu, H. Alhumade, L. Lu and A. Lei, *Green Chem.*, 2021, **23**, 7982.

[3] Q. Xie, H. J. Long, Q. Y. Zhang, P. Tang, J. Deng, *J. Org. Chem*. 2020, **85**, 1882.

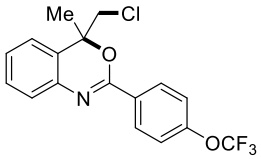
Characterization Data for Products



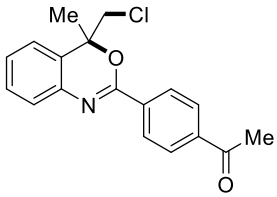
4-(chloromethyl)-4-methyl-2-phenyl-4H-benzo[d][1,3]oxazine (**3aa**)[3] colorless oil, 46.1 mg, 85% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.10 (d, J = 7.5 Hz, 2H), 7.42 (t, J = 7.2 Hz, 1H), 7.36 (t, J = 7.4 Hz, 2H), 7.29 – 7.24 (m, 2H), 7.14 (td, J = 6.9, 6.5, 2.2 Hz, 1H), 7.08 (d, J = 7.7 Hz, 1H), 3.66 (dd, J = 108.2, 11.9 Hz, 2H), 1.81 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.4, 139.3, 132.5, 131.7, 129.7, 128.4, 128.4, 127.0, 126.9, 125.6, 123.4, 79.0, 50.7, 24.1.



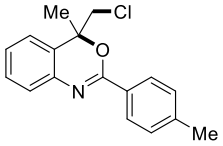
4-(chloromethyl)-2-(4-methoxyphenyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3ba**) colorless oil, 47.6 mg, 79% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, J = 8.9 Hz, 2H), 7.34 (dt, J = 15.0, 7.7 Hz, 2H), 7.21 (t, J = 7.3 Hz, 1H), 7.16 (d, J = 7.3 Hz, 1H), 6.96 (d, J = 8.9 Hz, 2H), 3.89 – 3.83 (m, 4H), 3.62 (d, J = 11.9 Hz, 1H), 1.89 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 162.6, 156.4, 139.6, 130.2, 129.7, 127.0, 126.5, 125.3, 124.9, 123.4, 113.8, 78.8, 55.5, 50.6, 23.8. HRMS: calcd for $C_{17}H_{17}ClNO_2^+$ $[M+H]^+$, 302.0942, found 302.0948.



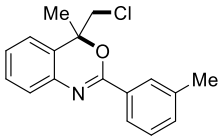
4-(chloromethyl)-4-methyl-2-(4-(trifluoromethoxy)phenyl)-4H-benzo[d][1,3]oxazine (**3ca**) colorless oil, 57.6 mg, 81% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.23 (d, J = 7.1 Hz, 2H), 7.36 (dt, J = 14.6, 7.6 Hz, 2H), 7.29 (d, J = 8.3 Hz, 2H), 7.25 (t, J = 7.4 Hz, 1H), 7.17 (d, J = 7.6 Hz, 1H), 3.75 (dd, J = 107.5, 12.0 Hz, 2H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 155.1, 151.8, 139.0, 131.0, 130.1, 129.8, 127.2, 126.9, 125.7, 123.4, 120.5 (q, J =258.8 Hz), 120.5, 79.3, 50.8, 24.1. HRMS: calcd for $C_{17}H_{14}ClF_3NO_2^+$ $[M+H]^+$, 356.0660, found 356.0657.



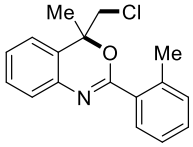
1-(4-(4-(chloromethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)phenyl)ethan-1-one (**3da**) colorless oil, 46.4 mg, 74% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, J = 8.2 Hz, 2H), 7.92 (d, J = 8.2 Hz, 2H), 7.27 (t, J = 4.4 Hz, 2H), 7.18 – 7.14 (m, 1H), 7.08 (d, J = 7.6 Hz, 1H), 3.76 (d, J = 12.0 Hz, 1H), 3.55 (d, J = 12.0 Hz, 1H), 2.55 (s, 3H), 1.81 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 197.9, 155.3, 139.2, 138.9, 136.6, 129.8, 128.4, 128.3, 127.5, 127.0, 125.9, 123.5, 79.3, 50.8, 27.0, 24.2. HRMS: calcd for $C_{18}H_{17}ClNO_2^+$ $[M+H]^+$, 314.0942, found 314.0947.



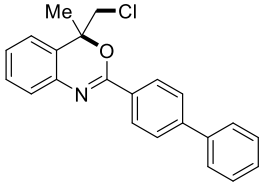
4-(chloromethyl)-4-methyl-2-(p-tolyl)-4H-benzo[d][1,3]oxazine (**3ea**) colorless oil, 45.2 mg, 79% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.09 (d, J = 8.0 Hz, 2H), 7.38 – 7.32 (m, 2H), 7.28 – 7.25 (m, 2H), 7.21 (dd, J = 6.8, 1.8 Hz, 1H), 7.17 (dd, J = 7.7, 1.4 Hz, 1H), 3.75 (dd, J = 111.0, 11.9 Hz, 2H), 2.42 (s, 3H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.6, 142.2, 139.5, 129.7, 129.2, 128.4, 127.1, 126.7, 125.5, 123.4, 78.8, 50.6, 23.9, 21.8. HRMS: calcd for $C_{17}H_{17}ClNO^+$ $[M+H]^+$, 286.0993, found 286.0999.



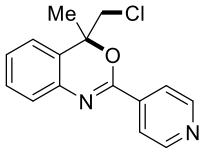
4-(chloromethyl)-4-methyl-2-(m-tolyl)-4H-benzo[d][1,3]oxazine (**3fa**) colorless oil, 38.9 mg, 68% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (s, 1H), 8.00 (d, J = 7.1 Hz, 1H), 7.39 – 7.31 (m, 4H), 7.26 – 7.21 (m, 1H), 7.17 (d, J = 7.0 Hz, 1H), 3.89 – 3.64 (m, 2H), 2.44 (s, 3H), 1.91 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.6, 139.3, 138.1, 132.6, 132.4, 129.7, 128.8, 128.3, 127.0, 126.8, 125.6, 125.5, 123.4, 79.0, 50.7, 24.1, 21.5. HRMS: calcd for $C_{17}H_{17}ClNO^+$ $[M+H]^+$, 286.0993, found 286.0987.



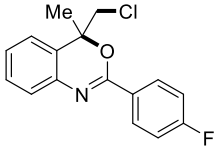
4-(chloromethyl)-4-methyl-2-(o-tolyl)-4H-benzo[d][1,3]oxazine (**3ga**) colorless oil, 40.6 mg, 71% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.91 (d, J = 7.7 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.29 – 7.23 (m, 3H), 7.16 (d, J = 7.6 Hz, 1H), 3.93 – 3.71 (m, 2H), 2.66 (s, 3H), 1.88 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 157.8, 139.1, 138.6, 132.3, 131.5, 130.6, 130.1, 129.6, 127.1, 126.3, 125.9, 125.6, 123.4, 79.5, 51.1, 24.8, 21.8. HRMS: calcd for $C_{17}H_{17}ClNO^+$ $[M+H]^+$, 286.0993, found 286.0990.



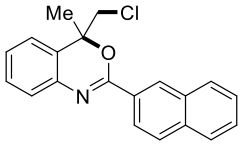
2-([1,1'-biphenyl]-4-yl)-4-(chloromethyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3ha**) colorless oil, 55.6 mg, 80% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.14 (d, J = 8.0 Hz, 2H), 7.57 (d, J = 8.0 Hz, 2H), 7.53 (d, J = 7.6 Hz, 2H), 7.35 (t, J = 7.5 Hz, 2H), 7.29 – 7.22 (m, 3H), 7.12 (dd, J = 7.8, 3.3 Hz, 1H), 7.06 (d, J = 7.6 Hz, 1H), 3.80 – 3.50 (m, 2H), 1.80 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.3, 144.4, 140.5, 139.4, 131.3, 129.7, 129.0, 128.8, 128.0, 127.4, 127.1, 127.0, 126.9, 125.6, 123.5, 79.0, 50.7, 24.0. HRMS: calcd for $C_{22}H_{19}ClNO^+$ $[M+H]^+$, 348.1150, found 348.1157.



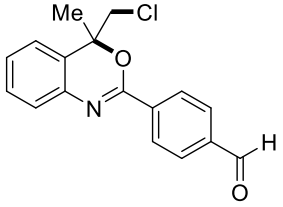
4-(chloromethyl)-4-methyl-2-(pyridin-4-yl)-4H-benzo[d][1,3]oxazine (**3ia**) colorless oil, 36.4 mg, 67% yield. petroleum ether/ethyl acetate (5:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.74 (d, J = 5.2 Hz, 2H), 8.01 (d, J = 4.9 Hz, 2H), 7.41 – 7.33 (m, 2H), 7.31 – 7.26 (m, 1H), 7.17 (d, J = 7.7 Hz, 1H), 3.91 – 3.62 (m, 2H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 154.3, 150.3, 140.0, 138.5, 129.9, 128.0, 127.0, 126.1, 123.5, 121.8, 79.6, 51.0, 24.4. HRMS: calcd for $C_{15}H_{14}ClNO^{+}$ $[M+H]^{+}$, 273.0789, found 273.0791.



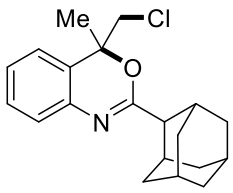
4-(chloromethyl)-2-(4-fluorophenyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3ja**) colorless oil, 34.2 mg, 59% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.24 – 8.16 (m, 2H), 7.39 – 7.31 (m, 2H), 7.27 – 7.21 (m, 1H), 7.17 – 7.11 (m, 2H), 3.92 – 3.60 (m, 2H), 1.90 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 165.2 (d, J = 252.0 Hz), 155.5, 139.2, 130.6 (d, J = 8.9 Hz), 129.8, 128.6 (d, J = 3.2 Hz), 127.0, 126.9, 125.6, 123.4, 115.5 (d, J = 21.9 Hz), 79.1, 50.7, 24.0. ^{19}F NMR (471 MHz, $CDCl_3$) δ -108.0 – -108.1 (m, 1F). HRMS: calcd for $C_{16}H_{14}FClNO^{+}$ $[M+H]^{+}$, 290.0742, found 290.0749.



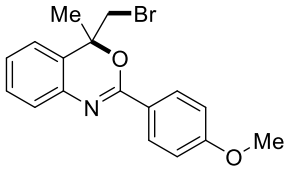
4-(chloromethyl)-4-methyl-2-(naphthalen-2-yl)-4H-benzo[d][1,3]oxazine (**3ka**) colorless oil, 46.9 mg, 73% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.54 (s, 1H), 8.15 (dd, J = 8.7, 1.8 Hz, 1H), 7.83 (d, J = 7.7 Hz, 1H), 7.74 (dd, J = 13.8, 8.1 Hz, 2H), 7.43 – 7.35 (m, 2H), 7.28 – 7.21 (m, 2H), 7.13 – 7.07 (m, 1H), 7.04 (d, J = 7.6 Hz, 1H), 3.77 – 3.53 (m, 2H), 1.80 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.5, 139.4, 135.1, 132.9, 129.8, 129.7, 129.3, 129.0, 128.1, 127.9, 127.7, 127.1, 127.0, 126.5, 125.7, 124.8, 123.5, 79.1, 50.7, 24.1. HRMS: calcd for $C_{20}H_{17}ClNO^{+}$ $[M+H]^{+}$, 322.0993, found 322.0989.



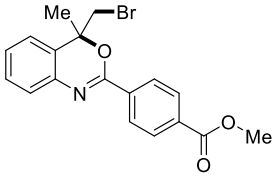
4-(4-(chloromethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzaldehyde (**3la**) colorless oil, 36.6 mg, 61% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 9.93 (s, 1H), 8.23 – 8.12 (m, 2H), 7.84 – 7.76 (m, 2H), 7.27 – 7.16 (m, 2H), 7.14 – 7.08 (m, 1H), 7.02 (d, J = 7.6 Hz, 1H), 3.73 – 3.45 (m, 2H), 1.75 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 192.0, 155.1, 138.9, 138.3, 137.9, 129.9, 129.7, 128.8, 127.7, 127.0, 126.0, 123.5, 79.5, 50.9, 24.3. HRMS: calcd for $C_{17}H_{15}ClNO_2^{+}$ $[M+H]^{+}$, 300.0786, found 300.0785.



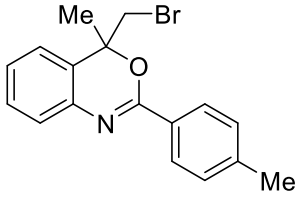
2-(adamantan-2-yl)-4-(chloromethyl)-4-methyl-4H-benzo[d][1,3]oxazine (3ma) colorless oil, 52.8 mg, 80% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.21 (d, J = 7.6 Hz, 1H), 7.14 – 7.07 (m, 2H), 7.00 (d, J = 7.6 Hz, 1H), 3.66 – 3.47 (m, 2H), 1.98 (s, 3H), 1.91 (s, 6H), 1.67 (s, 9H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 167.0, 139.2, 129.4, 126.6, 126.4, 125.2, 123.3, 78.0, 50.7, 39.3, 39.3, 36.8, 28.3, 24.2. HRMS: calcd for $C_{20}H_{25}ClNO^+$ $[M+H]^+$, 330.1619, found 330.1625.



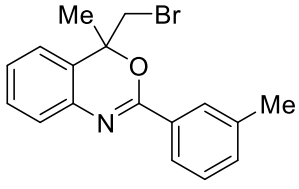
4-(bromomethyl)-2-(4-methoxyphenyl)-4-methyl-4H-benzo[d][1,3]oxazine (3bb) colorless oil, 57.5 mg, 83% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.21 – 8.15 (m, 2H), 7.38 – 7.30 (m, 2H), 7.23 – 7.14 (m, 2H), 7.01 – 6.92 (m, 2H), 3.87 (s, 3H), 3.65 (dd, J = 117.5, 11.1 Hz, 2H), ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 1.92 (s, 3H); 162.6, 156.3, 139.5, 130.3, 129.7, 127.1, 126.5, 125.3, 124.8, 123.3, 113.8, 77.9, 55.5, 39.8, 24.7. HRMS: calcd for $C_{17}H_{17}BrNO_2^+$ $[M+H]^+$, 346.0437, found 346.0440.



methyl 4-(4-(bromomethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzoate (3nb) colorless oil, 57.5 mg, 79% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.29 (d, J = 8.2 Hz, 2H), 8.13 (d, J = 8.2 Hz, 2H), 7.42 – 7.35 (m, 2H), 7.28 (td, J = 7.0, 6.4, 2.2 Hz, 1H), 7.19 (d, J = 7.6 Hz, 1H), 3.96 (s, 3H), 3.82 – 3.54 (m, 2H), 1.96 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 166.8, 155.4, 138.8, 136.5, 132.7, 129.8, 129.6, 128.3, 127.5, 127.1, 125.9, 123.4, 78.6, 52.5, 39.9, 25.1. HRMS: calcd for $C_{18}H_{17}BrNO_3^+$ $[M+H]^+$, 374.0386, found 374.0379.

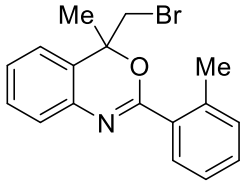


4-(bromomethyl)-4-methyl-2-(p-tolyl)-4H-benzo[d][1,3]oxazine (**3eb**) colorless oil, 54.8 mg, 83% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.11 (d, J = 7.8 Hz, 2H), 7.35 (d, J = 7.0 Hz, 2H), 7.26 (d, J = 7.8 Hz, 2H), 7.21 (t, J = 7.1 Hz, 1H), 7.16 (d, J = 7.6 Hz, 1H), 3.80 – 3.49 (m, 2H), 2.41 (s, 3H), 1.92 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 156.5, 142.2, 139.4, 129.7, 129.6, 129.2, 128.4, 127.2, 126.7, 125.5, 123.4, 78.0, 39.8, 24.9, 21.8. HRMS: calcd for $C_{17}H_{17}BrNO^+$ $[M+H]^+$, 330.0488, found 330.0492.

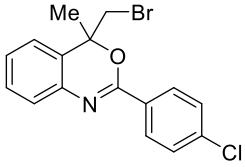


4-(bromomethyl)-4-methyl-2-(m-tolyl)-4H-benzo[d][1,3]oxazine (**3fb**) colorless oil, 49.5 mg, 75% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.02 (d, J = 16.5 Hz, 2H), 7.39 – 7.30 (m,

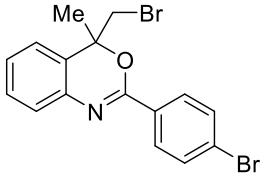
4H), 7.23 (td, *J* = 6.6, 2.2 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 3.78 – 3.54 (m, 2H), 2.43 (s, 3H), 1.93 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 156.6, 139.2, 138.1, 132.6, 132.3, 129.7, 128.9, 128.3, 127.2, 126.9, 125.6, 125.6, 123.4, 78.2, 39.9, 25.0, 21.6. HRMS: calcd for $C_{17}H_{17}BrNO^+$ $[M+H]^+$, 330.0488, found 330.0481.



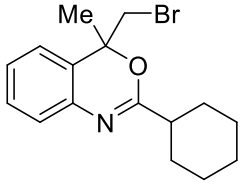
4-(bromomethyl)-4-methyl-2-(o-tolyl)-4H-benzo[d][1,3]oxazine (**3gb**) colorless oil, 46.9 mg, 71% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.94 (dd, *J* = 7.7, 1.5 Hz, 1H), 7.38 – 7.30 (m, 3H), 7.29 – 7.21 (m, 3H), 7.15 (dd, *J* = 7.6, 1.4 Hz, 1H), 3.82 – 3.61 (m, 2H), 2.66 (s, 3H), 1.90 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 157.7, 139.0, 138.6, 132.3, 131.6, 130.6, 130.1, 129.6, 127.1, 126.5, 125.8, 125.6, 123.3, 78.8, 40.1, 25.7, 21.9. HRMS: calcd for $C_{17}H_{17}BrNO^+$ $[M+H]^+$, 330.0488, found 330.0494.



4-(bromomethyl)-2-(4-chlorophenyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3ob**) colorless oil, 54.0 mg, 77% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.15 (d, *J* = 8.2 Hz, 2H), 7.42 (d, *J* = 8.2 Hz, 2H), 7.34 (dt, *J* = 14.8, 7.6 Hz, 2H), 7.23 (t, *J* = 7.4 Hz, 1H), 7.16 (d, *J* = 7.6 Hz, 1H), 3.82 – 3.46 (m, 2H), 1.92 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 155.4, 139.0, 137.9, 130.9, 129.8, 129.7, 128.7, 127.2, 127.1, 125.7, 123.4, 78.4, 39.9, 24.9. HRMS: calcd for $C_{16}H_{14}BrClNO^+$ $[M+H]^+$, 349.9942, found 349.9948.

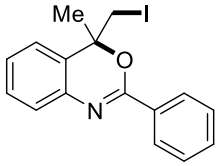


4-(bromomethyl)-2-(4-bromophenyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3pb**) colorless oil, 53.7 mg, 68% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.08 (d, *J* = 8.5 Hz, 2H), 7.59 (d, *J* = 8.4 Hz, 2H), 7.35 (dt, *J* = 14.9, 7.9 Hz, 2H), 7.24 (t, *J* = 7.4 Hz, 1H), 7.17 (d, *J* = 7.6 Hz, 1H), 3.77 – 3.50 (m, 2H), 1.92 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 155.5, 138.9, 131.7, 131.3, 129.9, 129.8, 127.2, 127.1, 126.5, 125.7, 123.4, 78.4, 39.9, 24.9. HRMS: calcd for $C_{16}H_{14}BrNO^+$ $[M+H]^+$, 393.9437, found 393.9439.

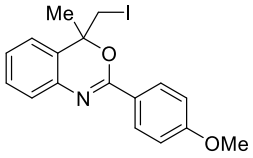


4-(bromomethyl)-2-cyclohexyl-4-methyl-4H-benzo[d][1,3]oxazine (**3qb**) colorless oil, 46.3 mg, 72% yield. petroleum ether/ethyl acetate (20:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.30 (t, *J* = 7.6 Hz, 1H), 7.18 (t, *J* = 7.1 Hz, 2H), 7.10 – 7.06 (m, 1H), 3.67 – 3.47 (m, 2H), 2.39 – 2.31 (m, 1H), 2.05 – 1.95 (m, 2H), 1.79 (s, 5H),

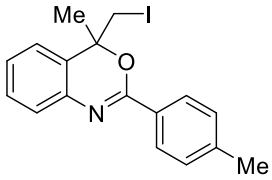
1.71 (d, *J* = 12.1 Hz, 1H), 1.64 – 1.49 (m, 2H), 1.37 – 1.23 (m, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 165.3, 138.8, 129.5, 126.6, 126.5, 125.0, 123.3, 77.6, 44.1, 40.1, 29.8, 29.7, 26.0, 26.0, 25.9, 25.4. HRMS: calcd for $C_{16}H_{21}BrNO^+$ $[M+H]^+$, 322.0801, found 322.0800.



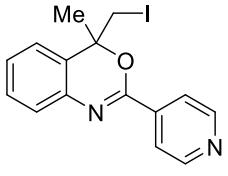
4-(iodomethyl)-4-methyl-2-phenyl-4H-benzo[d][1,3]oxazine (**3ac**) colorless oil, 66.8 mg, 92% yield. petroleum ether/ethyl acetate (10:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.17 (d, *J* = 7.4 Hz, 2H), 7.43 (t, *J* = 7.2 Hz, 1H), 7.38 (t, *J* = 7.4 Hz, 2H), 7.27 (d, *J* = 4.3 Hz, 2H), 7.14 (dt, *J* = 8.5, 4.1 Hz, 1H), 7.08 (d, *J* = 7.6 Hz, 1H), 3.49 (dd, *J* = 94.5, 11.1 Hz, 2H), 1.84 (s, 3H); $^{13}C\{^{1}H\}$ NMR (126 MHz, $CDCl_3$) δ 156.2, 138.9, 132.3, 131.7, 129.6, 128.5, 128.4, 127.1, 126.9, 125.7, 123.2, 77.6, 26.7, 15.9. HRMS: calcd for $C_{16}H_{15}INO^+$ $[M+H]^+$, 364.0193, found 364.0199.



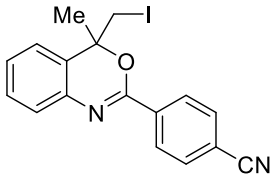
4-(iodomethyl)-2-(4-methoxyphenyl)-4-methyl-4H-benzo[d][1,3]oxazine (**3bc**) colorless oil, 68.4 mg, 87% yield, petroleum ether/ethyl acetate (8:1), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.27 – 8.17 (m, 2H), 7.37 – 7.30 (m, 2H), 7.22 – 7.14 (m, 2H), 7.00 – 6.94 (m, 2H), 3.87 (s, 3H), 3.73 – 3.39 (m, 2H), 1.92 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 162.6, 156.1, 139.2, 130.3, 129.6, 127.0, 126.5, 125.4, 124.7, 123.1, 113.7, 77.3, 55.5, 26.5, 16.0. HRMS: calcd for $C_{17}H_{17}INO_2^+$ $[M+H]^+$, 394.0298, found 394.0304.



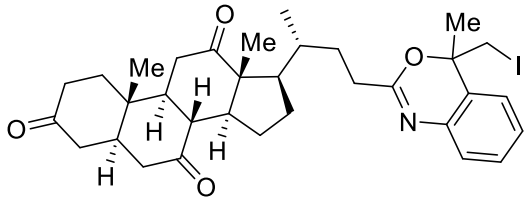
4-(iodomethyl)-4-methyl-2-(p-tolyl)-4H-benzo[d][1,3]oxazine (**3ec**) colorless oil, 68.6 mg, 91% yield, petroleum ether/ethyl acetate (20:1), ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.06 (d, *J* = 8.0 Hz, 2H), 7.28 – 7.21 (m, 2H), 7.17 (d, *J* = 8.0 Hz, 2H), 7.11 (ddd, *J* = 8.4, 5.3, 3.1 Hz, 1H), 7.06 (d, *J* = 7.7 Hz, 1H), 3.46 (dd, *J* = 98.7, 11.0 Hz, 2H), 2.32 (s, 3H), 1.82 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 155.4, 141.2, 138.1, 128.6, 128.5, 128.1, 127.5, 126.1, 125.7, 124.5, 122.1, 25.6, 20.7, 14.9. HRMS: calcd for $C_{17}H_{17}INO^+$ $[M+H]^+$, 378.0349, found 378.0344.



4-(iodomethyl)-4-methyl-2-(pyridin-4-yl)-4H-benzo[d][1,3]oxazine **(3ic)** colorless oil, 53.6 mg, 74% yield, petroleum ether/ethyl acetate (4:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.76 (d, *J* = 4.5 Hz, 2H), 8.07 (d, *J* = 4.7 Hz, 2H), 7.38 (d, *J* = 7.0 Hz, 2H), 7.28 (td, *J* = 6.9, 5.8, 1.6 Hz, 1H), 7.18 (d, *J* = 7.6 Hz, 1H), 3.72 – 3.45 (m, 2H), 1.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.1, 150.3, 139.9, 138.1, 129.8, 128.0, 127.2, 126.1, 123.2, 121.8, 78.2, 26.8, 15.8. HRMS: calcd for $C_{15}H_{14}IN_2O^+$ $[M+H]^+$, 365.0145, found 365.0147.



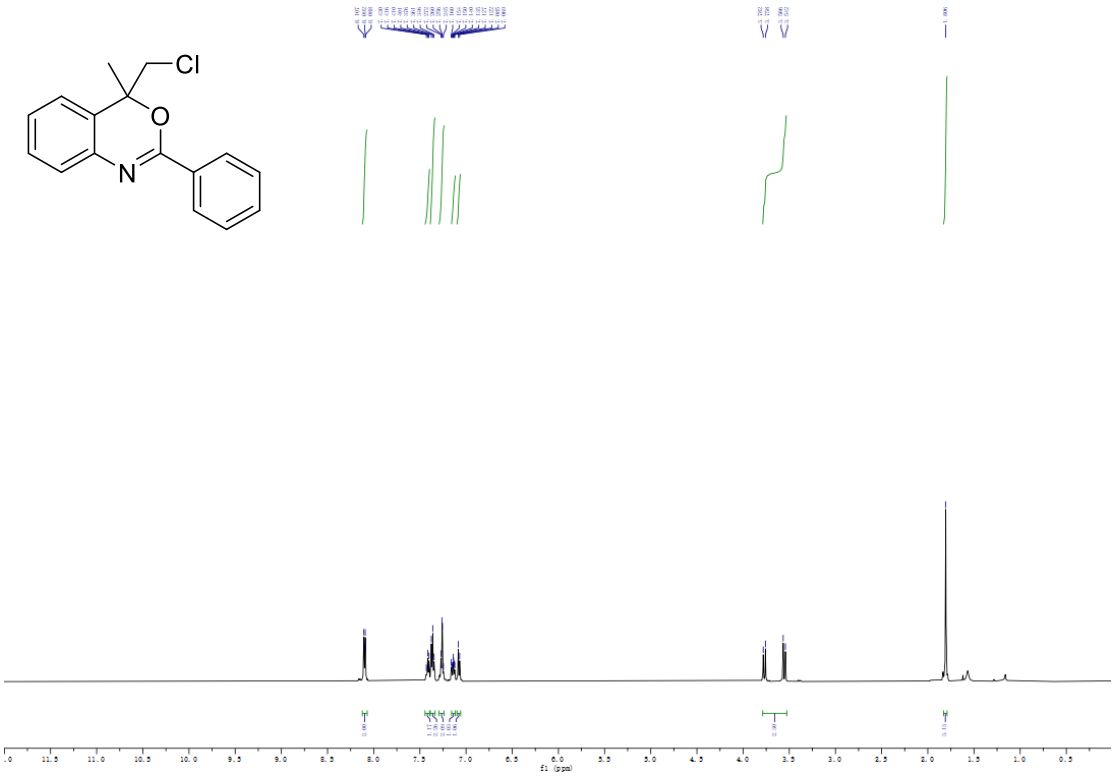
4-(4-(iodomethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)benzonitrile (**3oc**) colorless oil, 62.1 mg, 80% yield, petroleum ether/ethyl acetate (10:1). ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.35 (d, J = 8.2 Hz, 2H), 7.74 (d, J = 8.2 Hz, 2H), 7.41 – 7.33 (m, 2H), 7.30 – 7.24 (m, 1H), 7.18 (d, J = 7.6 Hz, 1H), 3.56 (dd, J = 84.9, 11.2 Hz, 2H), 1.94 (s, 3H). ^{13}C NMR (126 MHz, $CDCl_3$) δ 154.2, 138.2, 136.5, 132.1, 129.8, 128.8, 127.9, 127.1, 126.1, 123.2, 118.6, 114.8, 78.2, 26.8, 15.8. HRMS: calcd for $C_{17}H_{14}IN_2O^+$ $[M+H]^+$, 389.0145, found 389.0139.



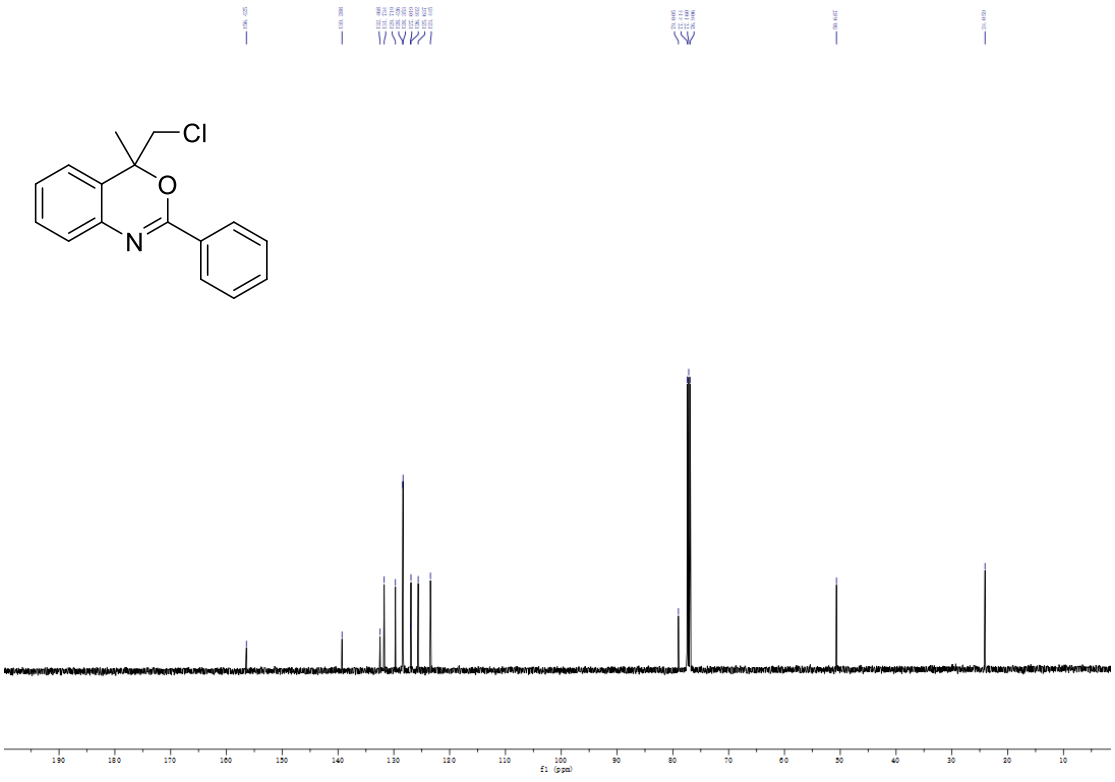
(5R,8R,9S,10S,13R,14S,17R)-17-((2R)-4-(4-(iodomethyl)-4-methyl-4H-benzo[d][1,3]oxazin-2-yl)butan-2-yl)-10,13-dimethyldodecahydro-3H-cyclopenta[a]phenanthrene-3,7,12(2H,4H)-trione (**3rc**) colorless oil, 88.8 mg, 69% yield. petroleum ether/ethyl acetate (2:1); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.26 – 7.19 (m, 1H), 7.15 – 7.08 (m, 2H), 7.00 (d, J = 7.6 Hz, 1H), 3.49 (d, J = 11.0 Hz, 1H), 3.34 (dd, J = 11.0, 4.6 Hz, 1H), 2.89 – 2.75 (m, 3H), 2.43 (tt, J = 10.2, 5.2 Hz, 1H), 2.35 – 2.20 (m, 5H), 2.19 – 2.12 (m, 2H), 2.11 – 2.05 (m, 2H), 2.05 – 1.99 (m, 2H), 1.98 – 1.85 (m, 3H), 1.73 (s, 5H), 1.59 – 1.51 (m, 1H), 1.33 (s, 5H), 1.22 – 1.17 (m, 1H), 1.02 (s, 3H), 0.85 (s, 3H); ^{13}C{^{1}H} NMR (126 MHz, $CDCl_3$) δ 212.1, 212.1(C'), 209.2, 208.9, 162.7, 162.7(C'), 138.4, 129.5, 129.5(C'), 126.7, 126.6(C'), 124.9, 124.8(C'), 123.1, 123.1(C'), 77.3, 77.3(C'), 57.0, 51.9, 49.1, 47.0, 45.9, 45.9(C'), 45.7, 45.6(C'), 45.1, 42.9, 38.8, 36.6, 36.1, 36.0, 35.9(C'), 35.4, 32.9, 32.8(C'), 31.8, 27.9, 27.8(C'), 26.9, 26.9(C'), 25.3, 22.0, 18.9, 18.9(C'), 16.3, 16.2(C'), 12.0 HRMS: calcd for $C_{33}H_{43}INO^+$ $[M+H]^+$, 644.2231, found 644.2237.

NMR Spectra for Products

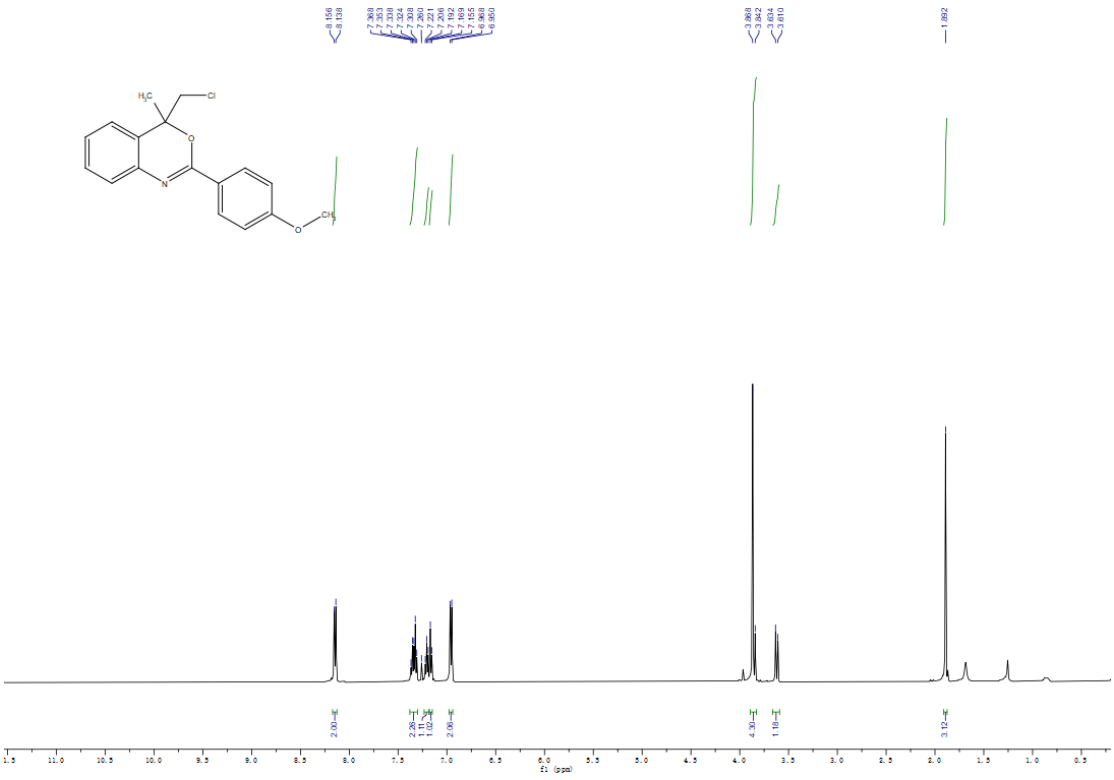
^{1}H NMR of compound **3aa**



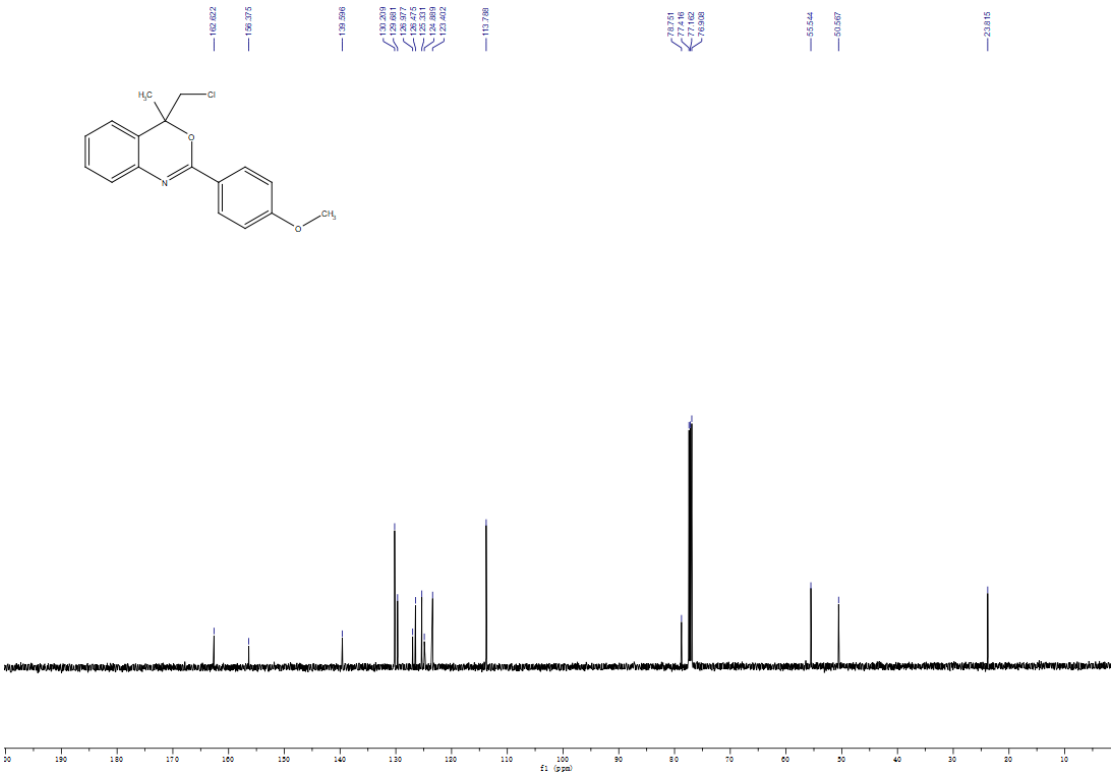
^{13}C NMR of compound **3aa**



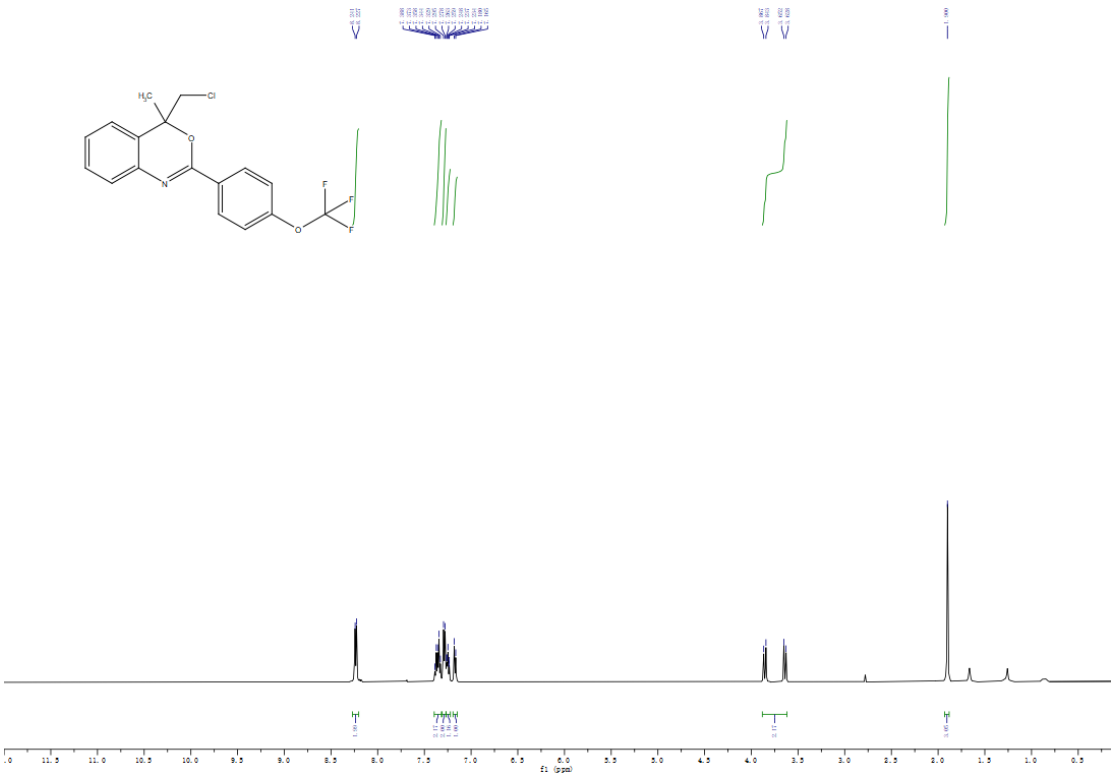
^{1}H NMR of compound **3ba**



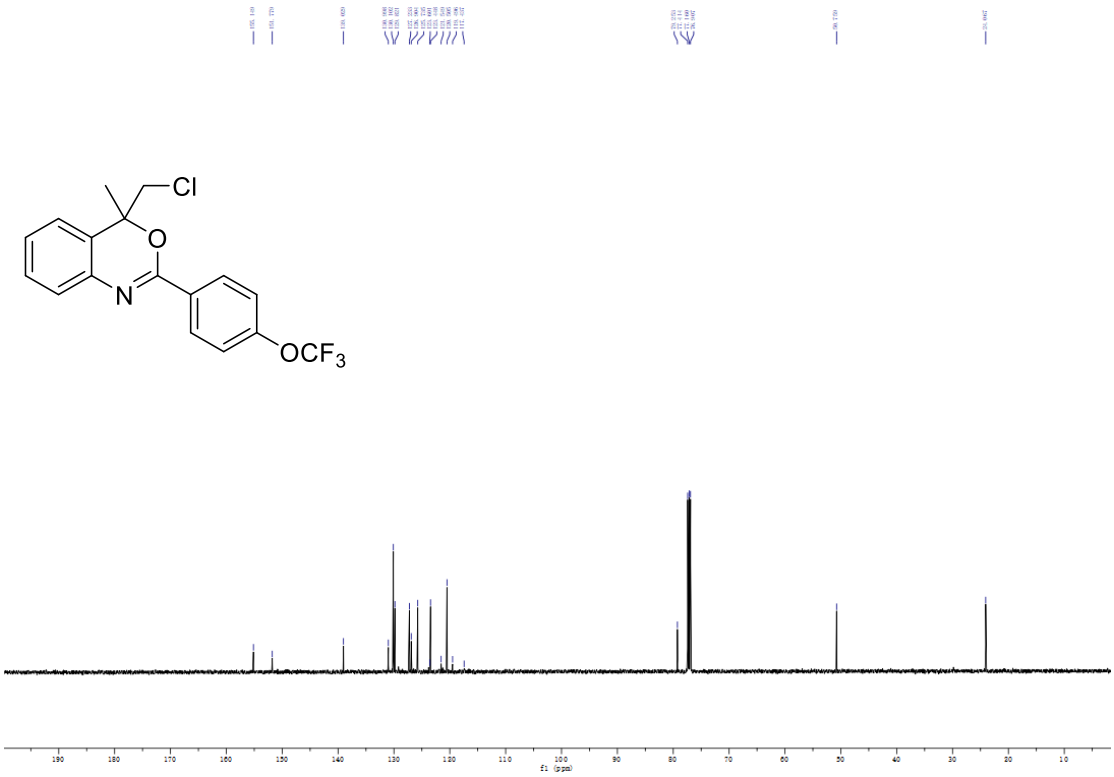
^{13}C NMR of compound **3ba**



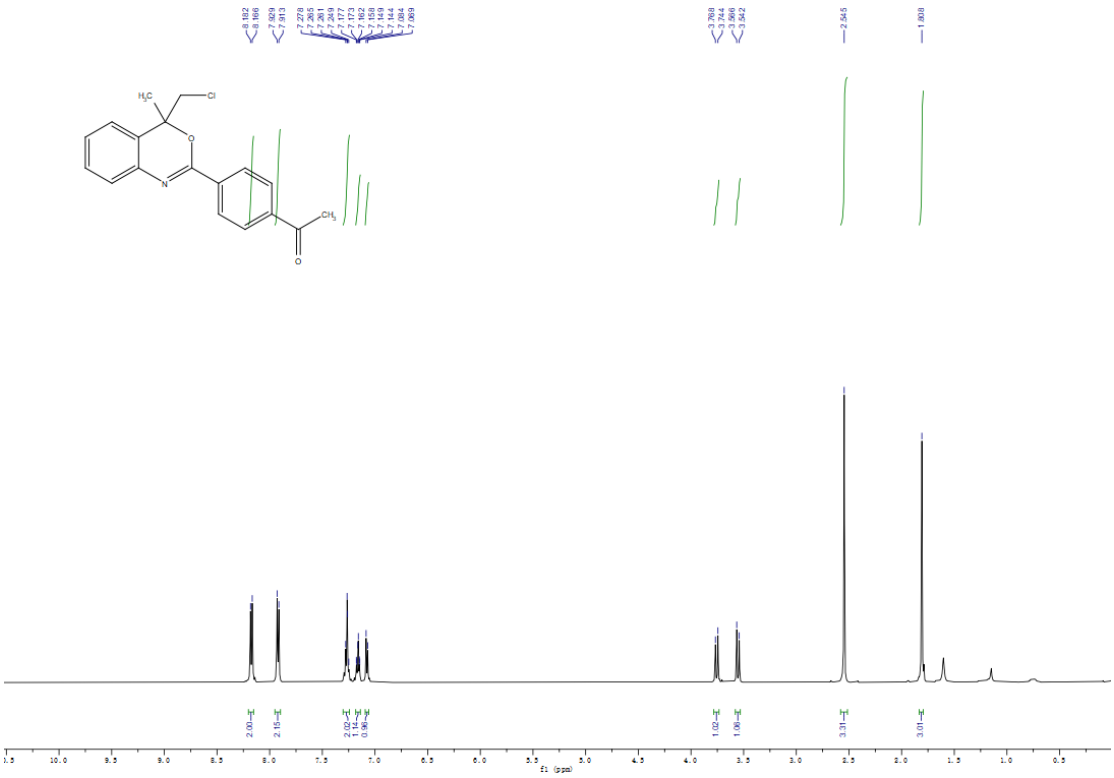
^{1}H NMR of compound **3ca**



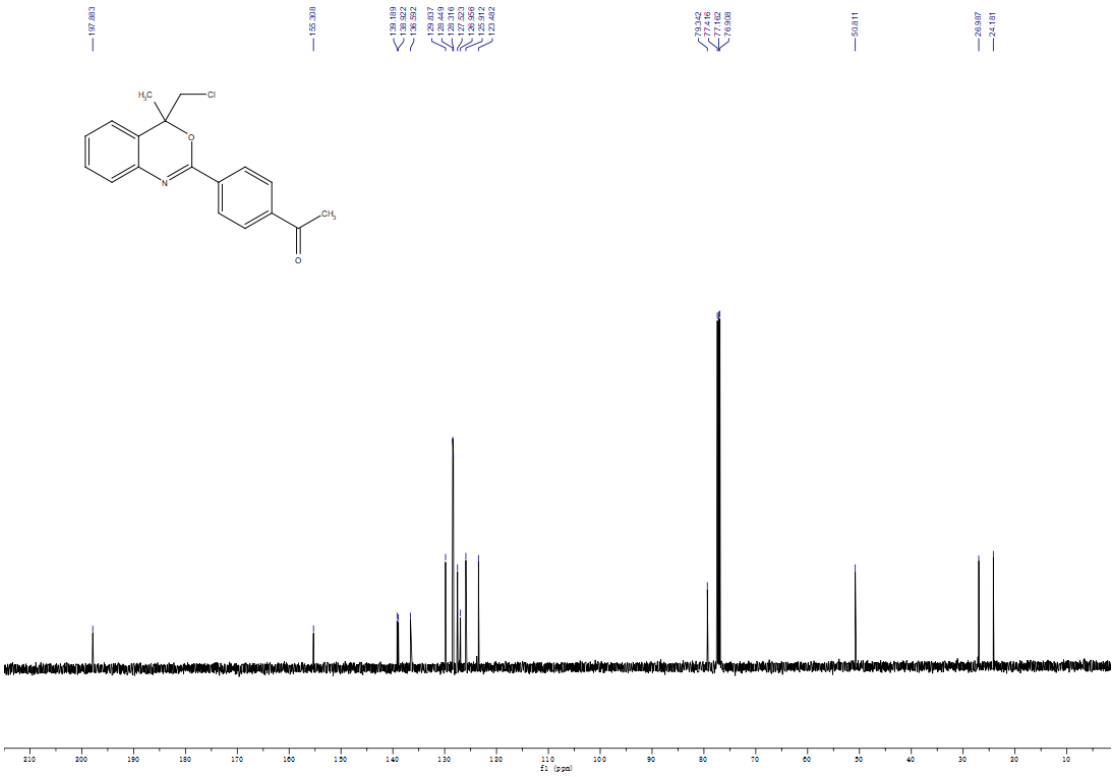
^{13}C NMR of compound **3ca**



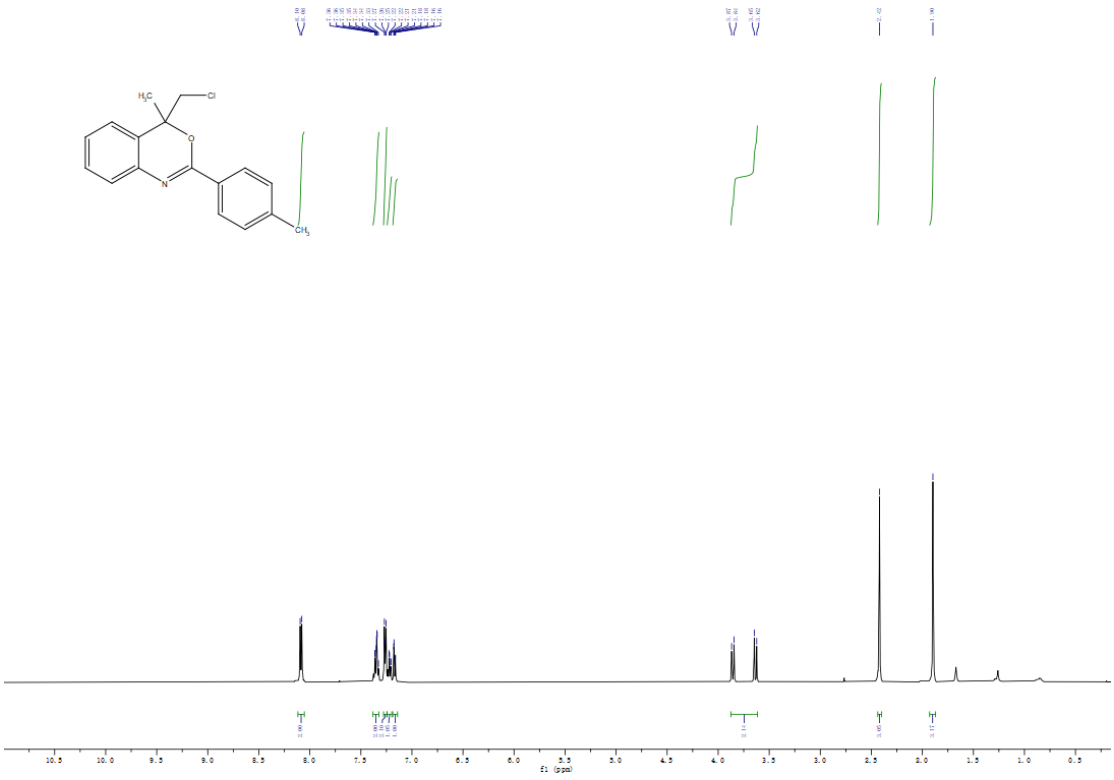
^{1}H NMR of compound **3da**



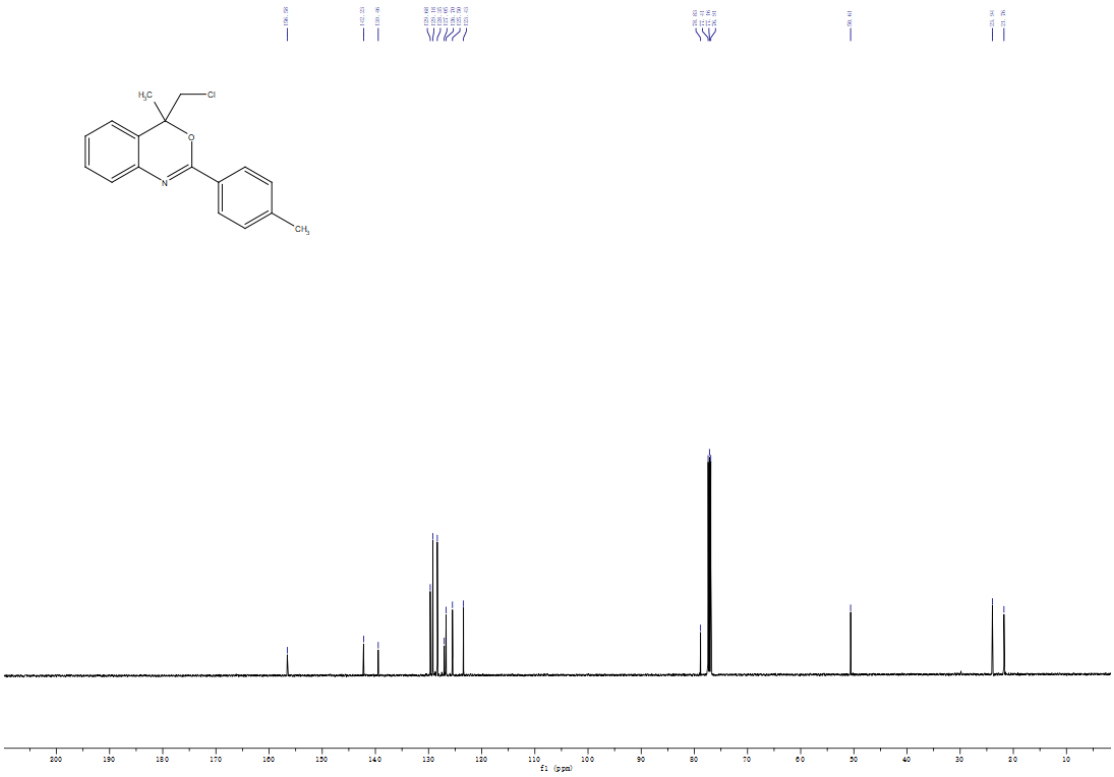
^{13}C NMR of compound **3da**



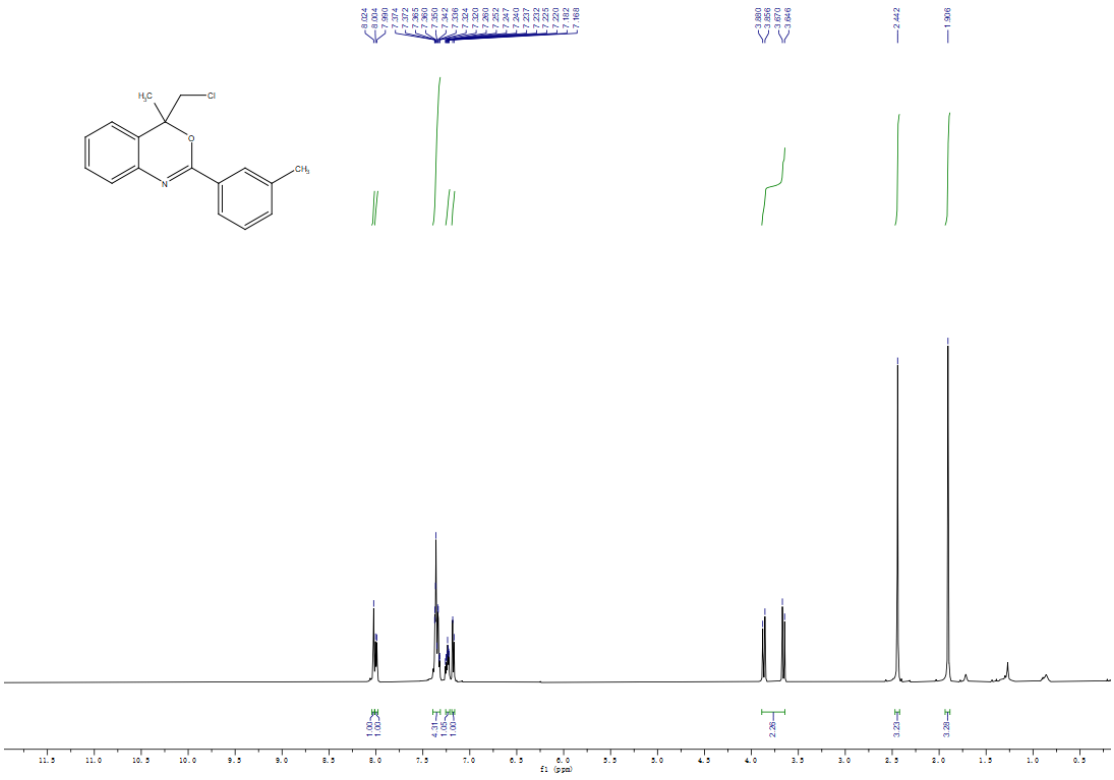
^{1}H NMR of compound **3ea**



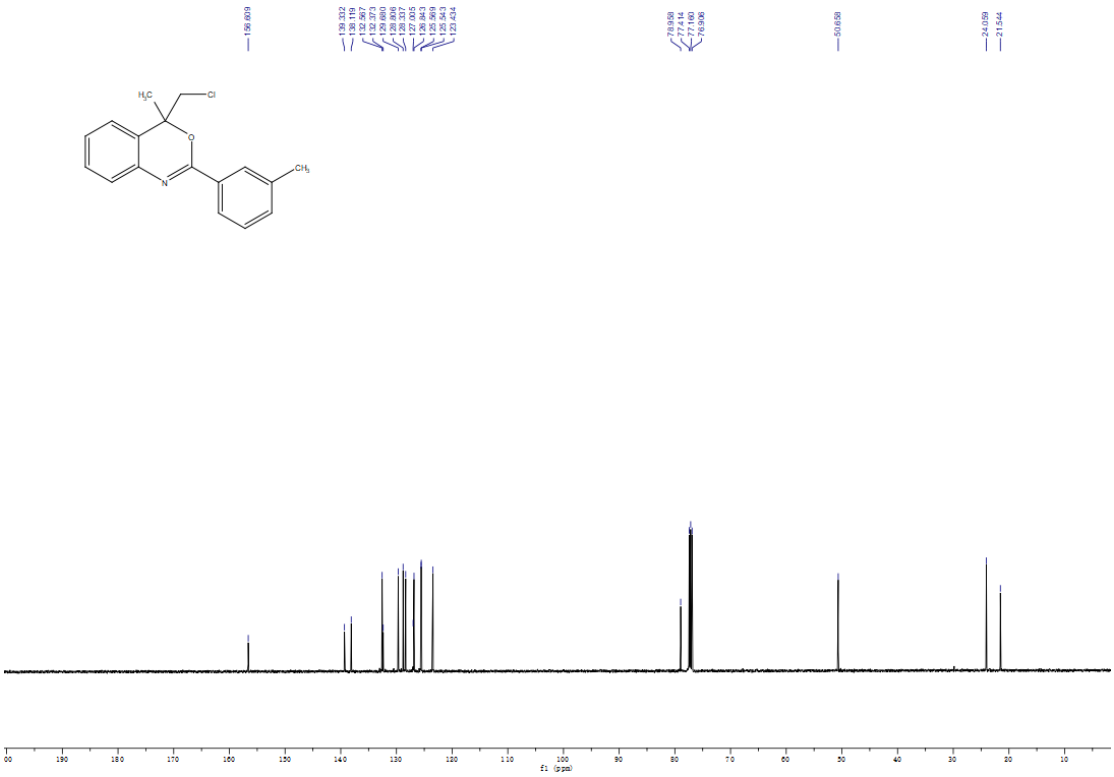
^{13}C NMR of compound **3ea**



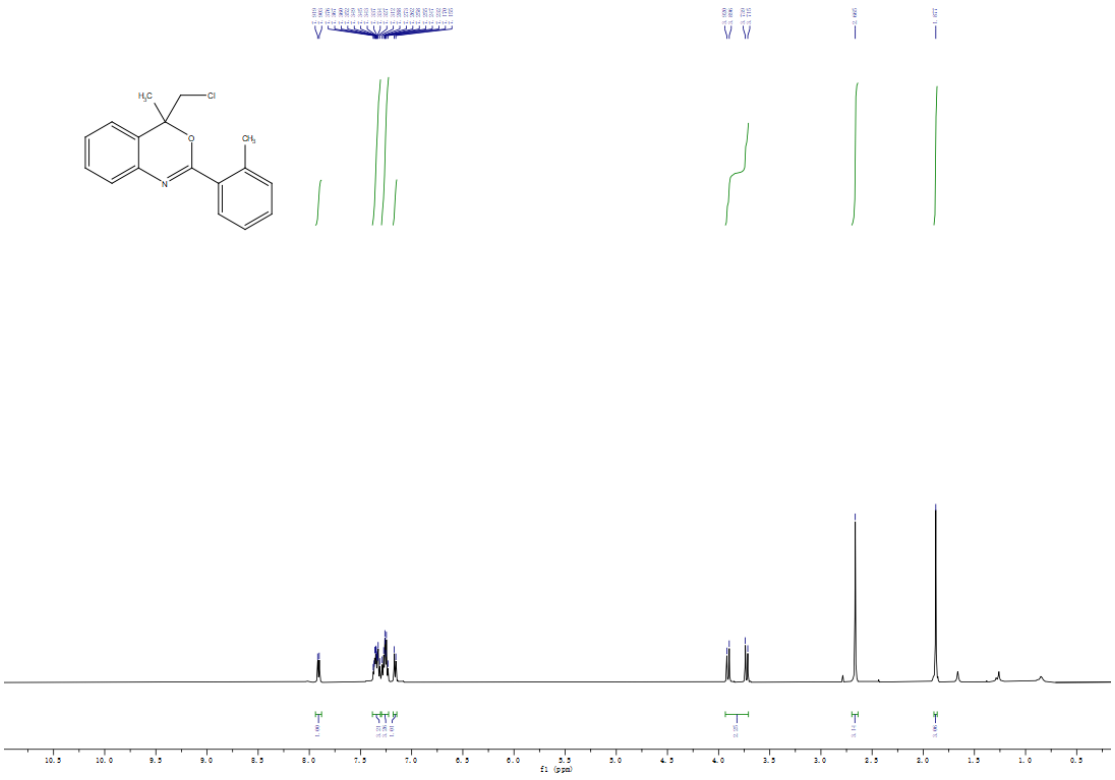
^{1}H NMR of compound **3fa**



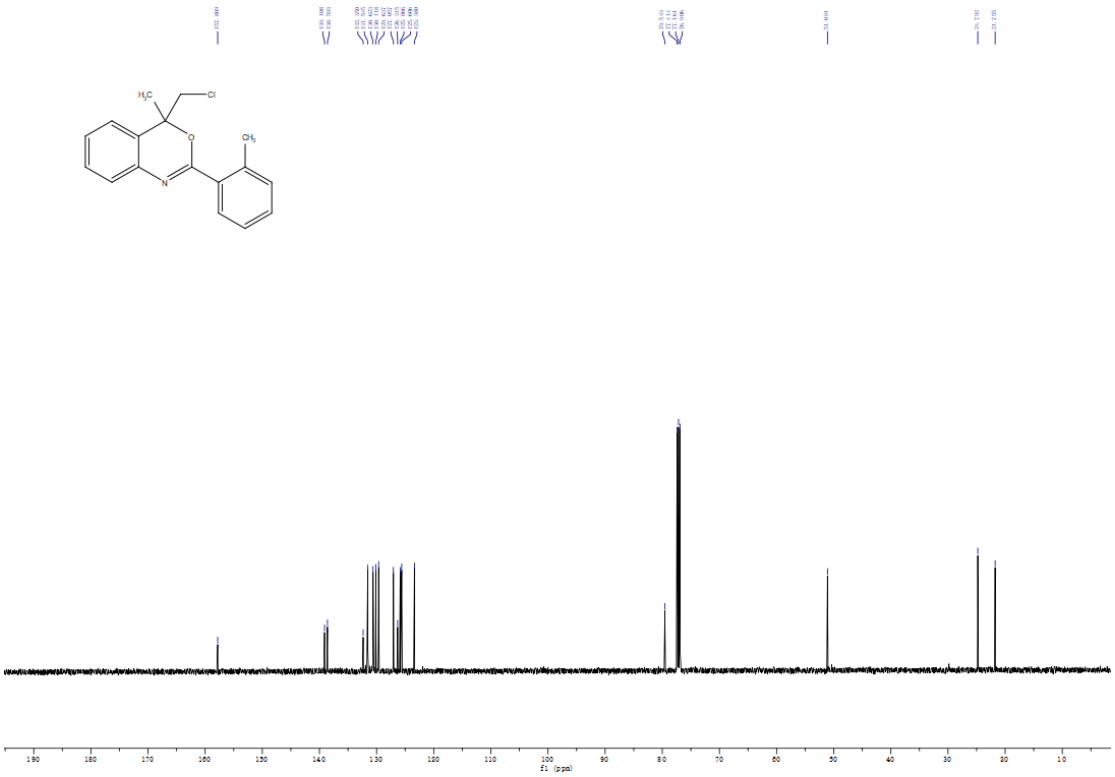
^{13}C NMR of compound **3fa**



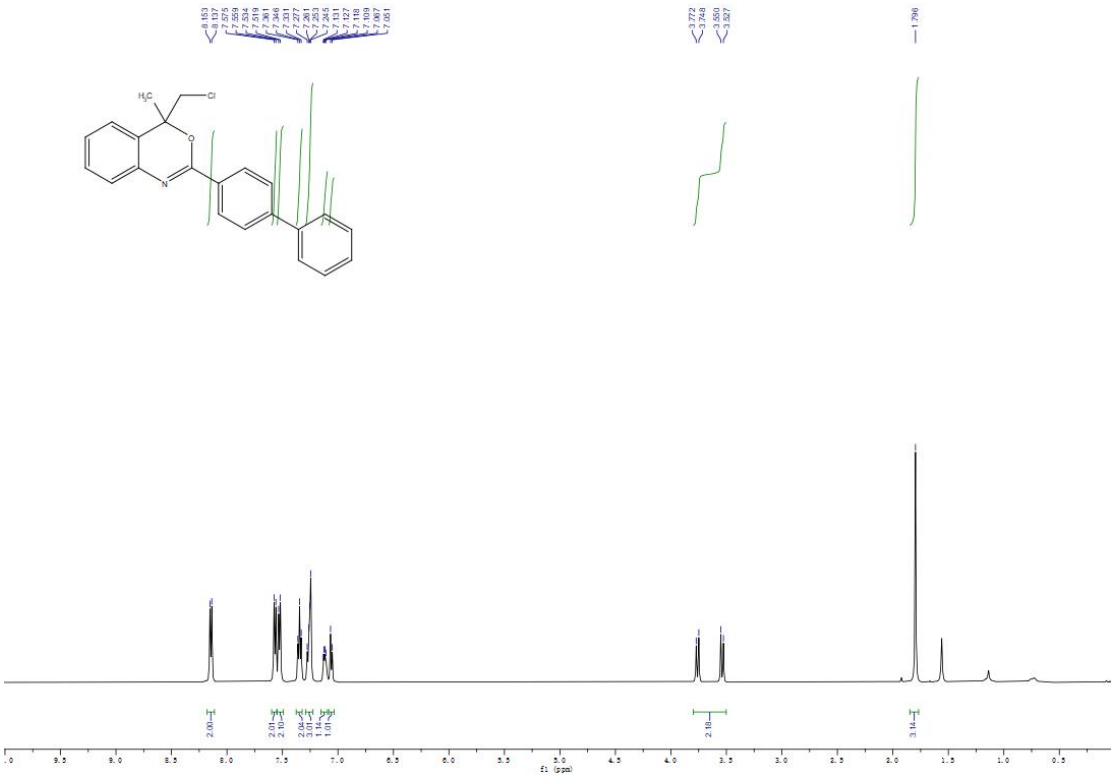
^{1}H NMR of compound **3ga**



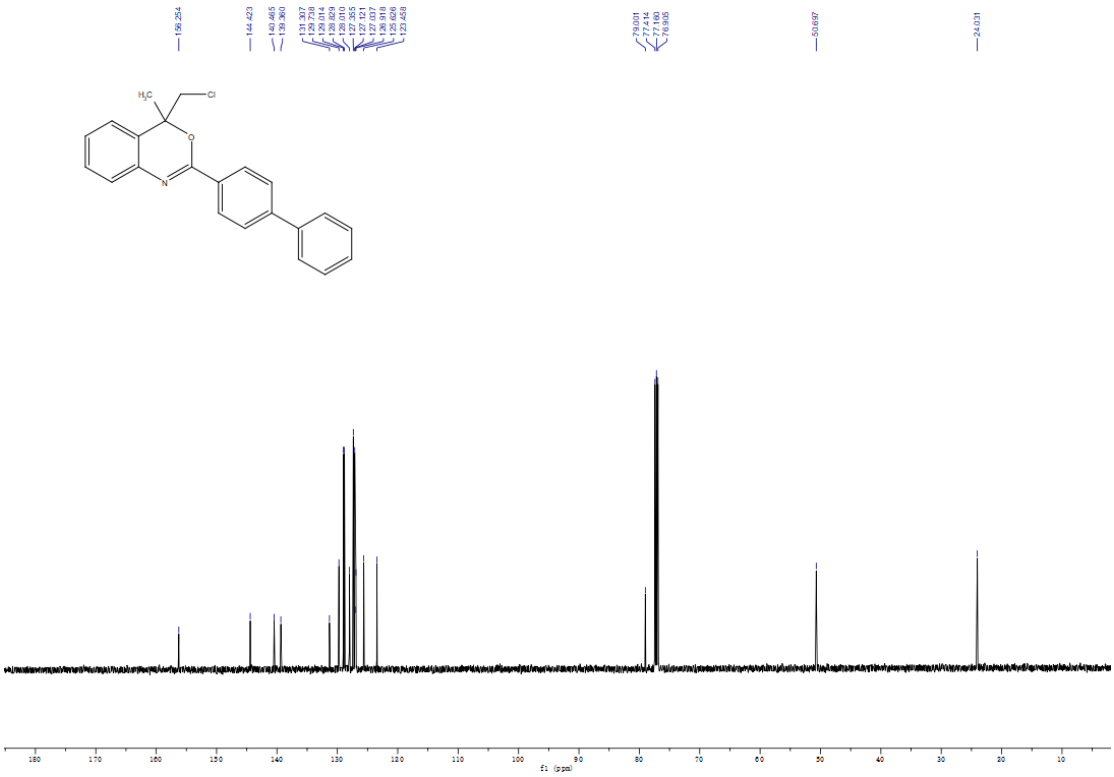
^{13}C NMR of compound **3ga**



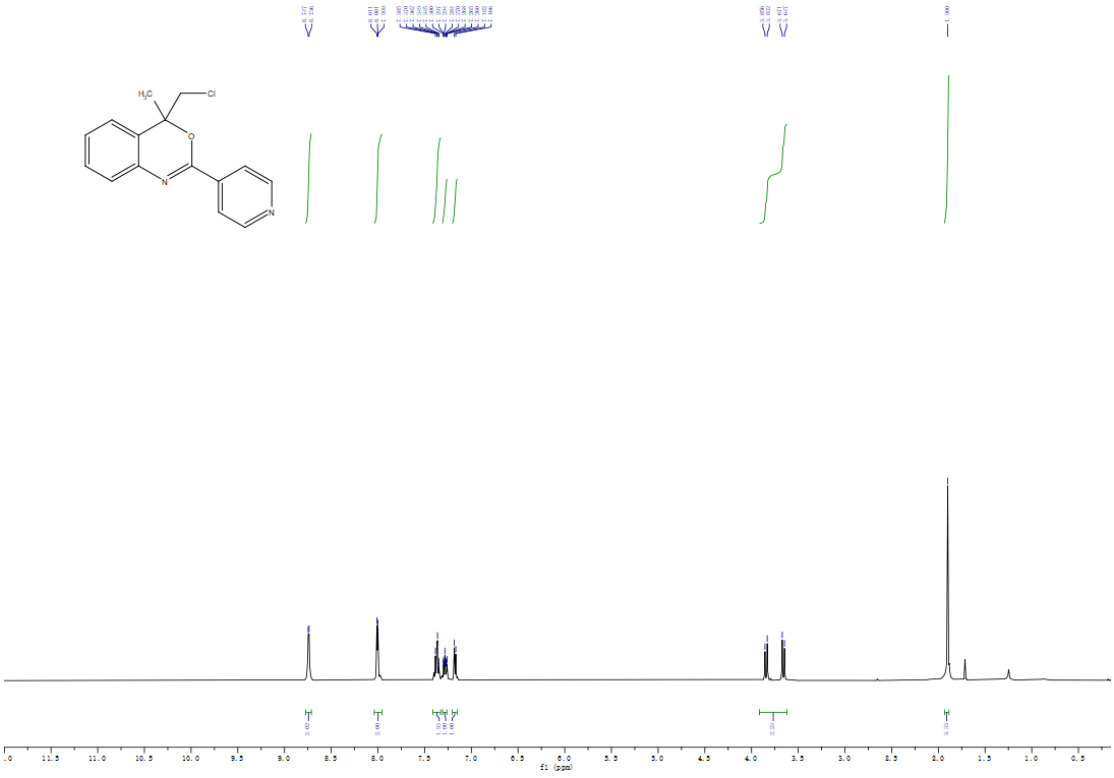
^{1}H NMR of compound **3ha**



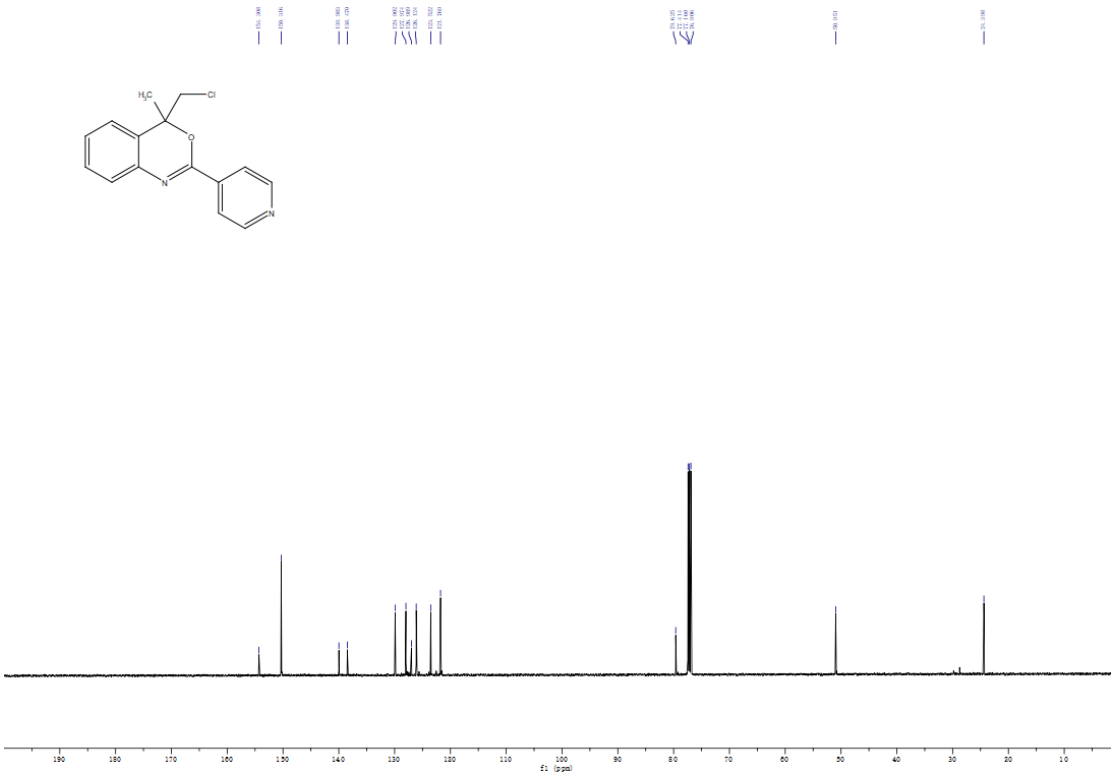
^{13}C NMR of compound **3ha**



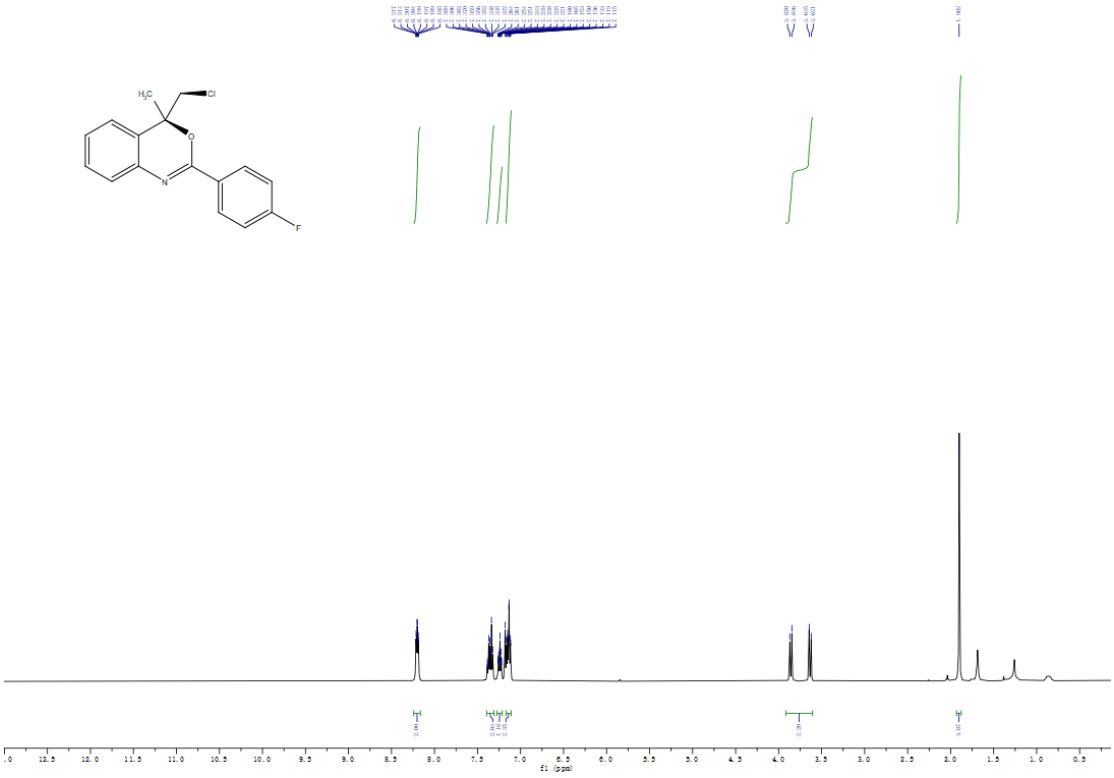
^{1}H NMR of compound **3ia**



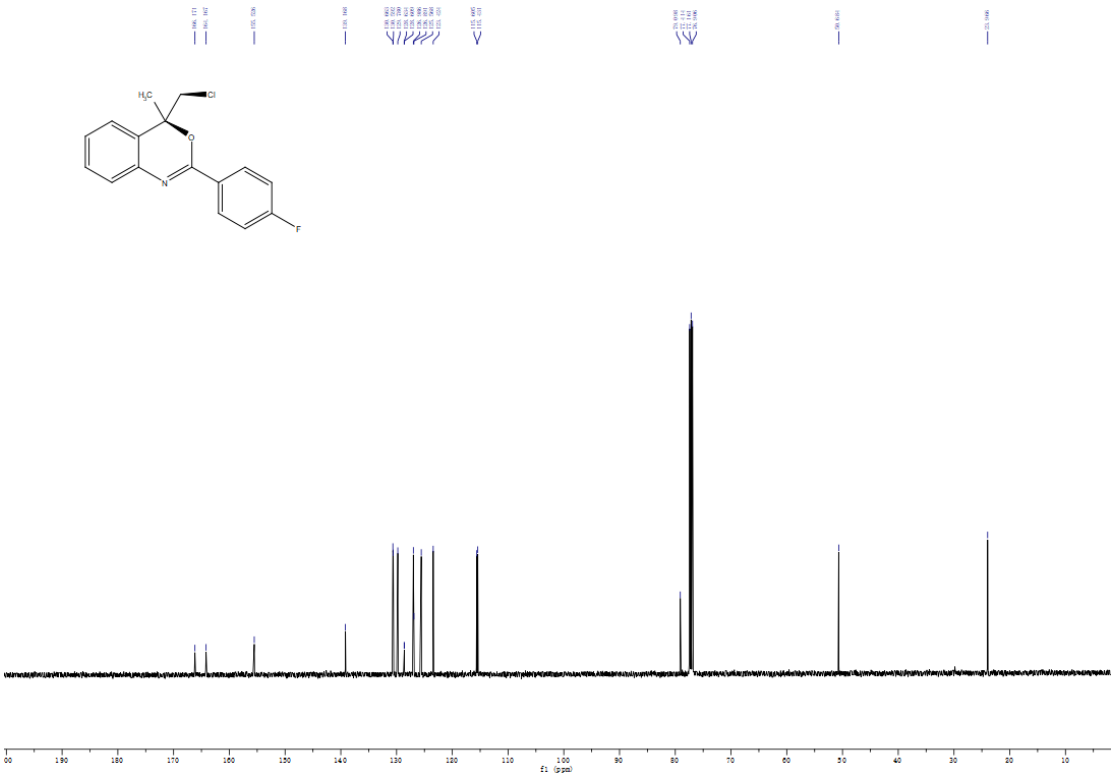
^{13}C NMR of compound **3ia**



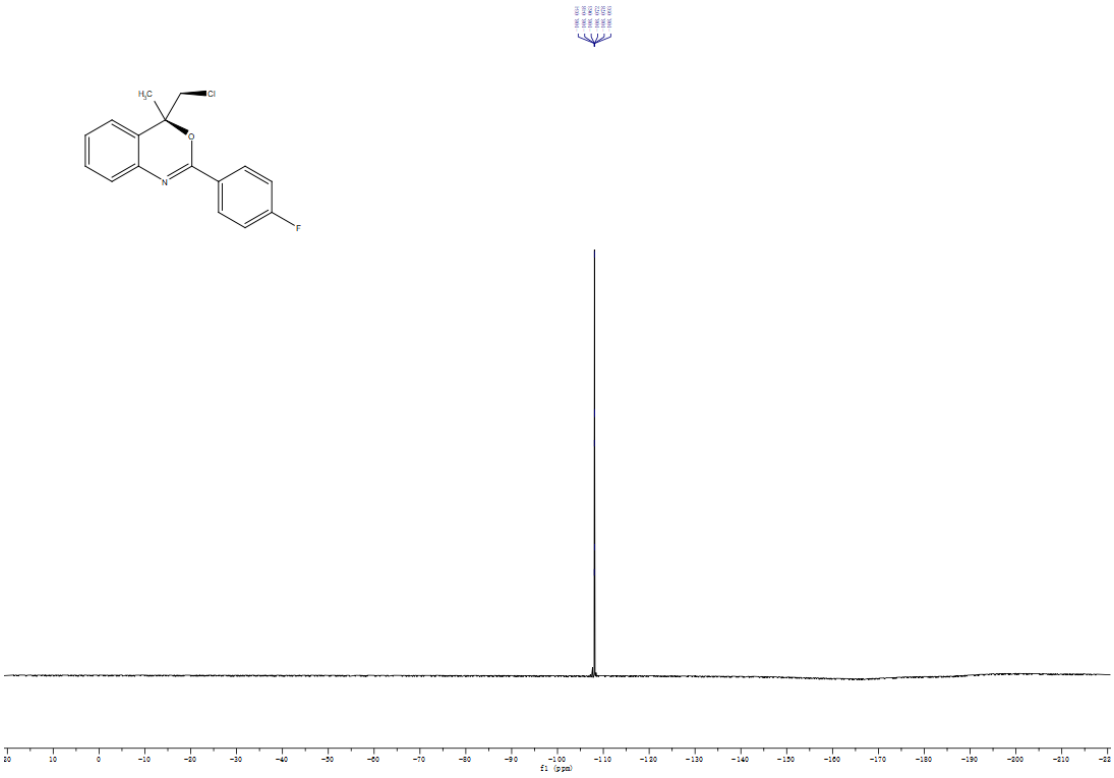
^{1}H NMR of compound **3ja**



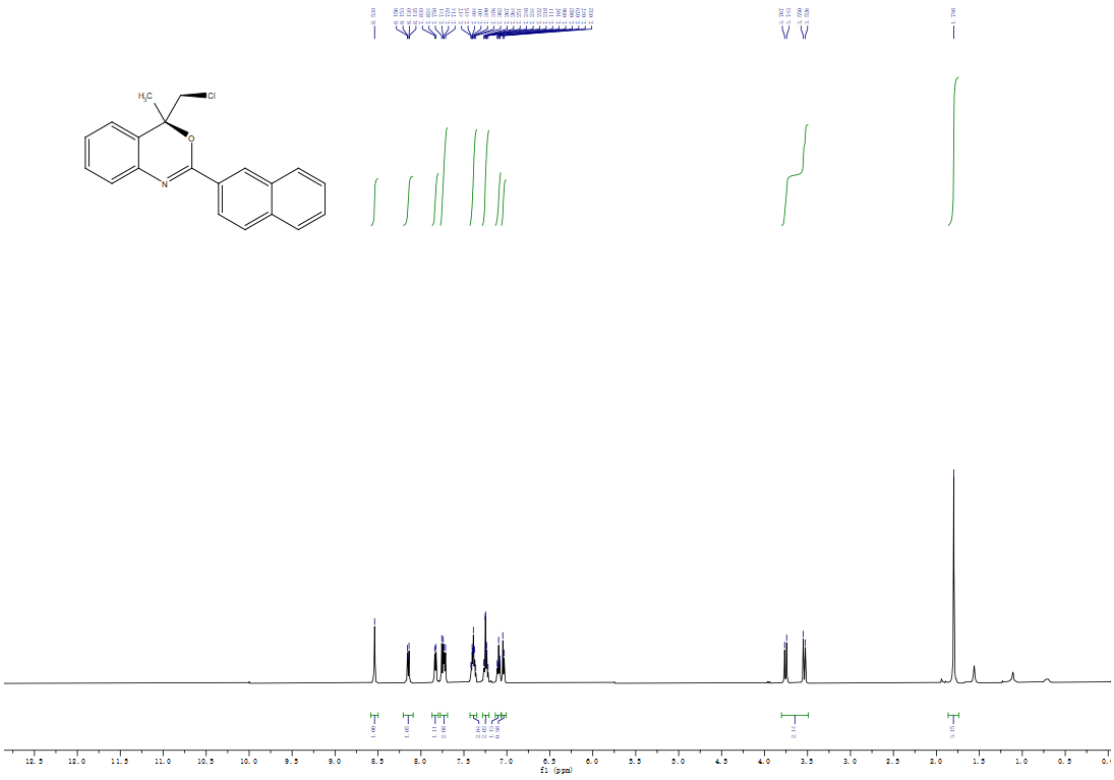
^{13}C NMR of compound **3ja**



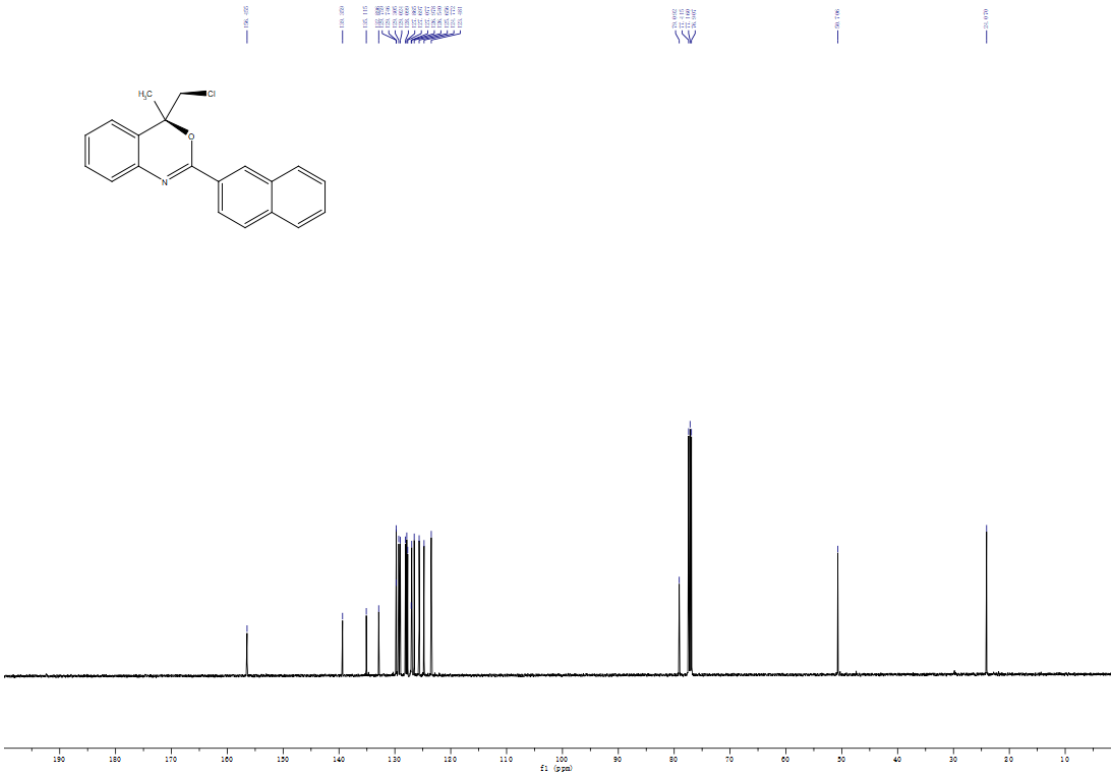
^{19}F NMR of compound **3ja**



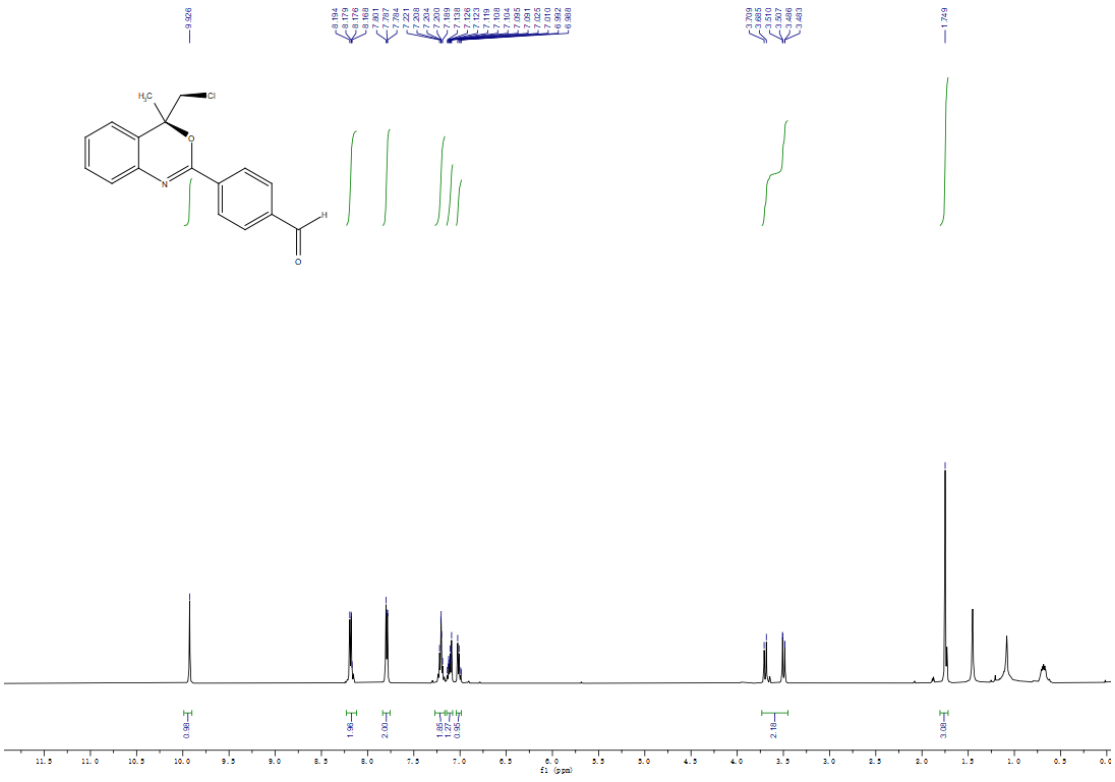
^{1}H NMR of compound **3ka**



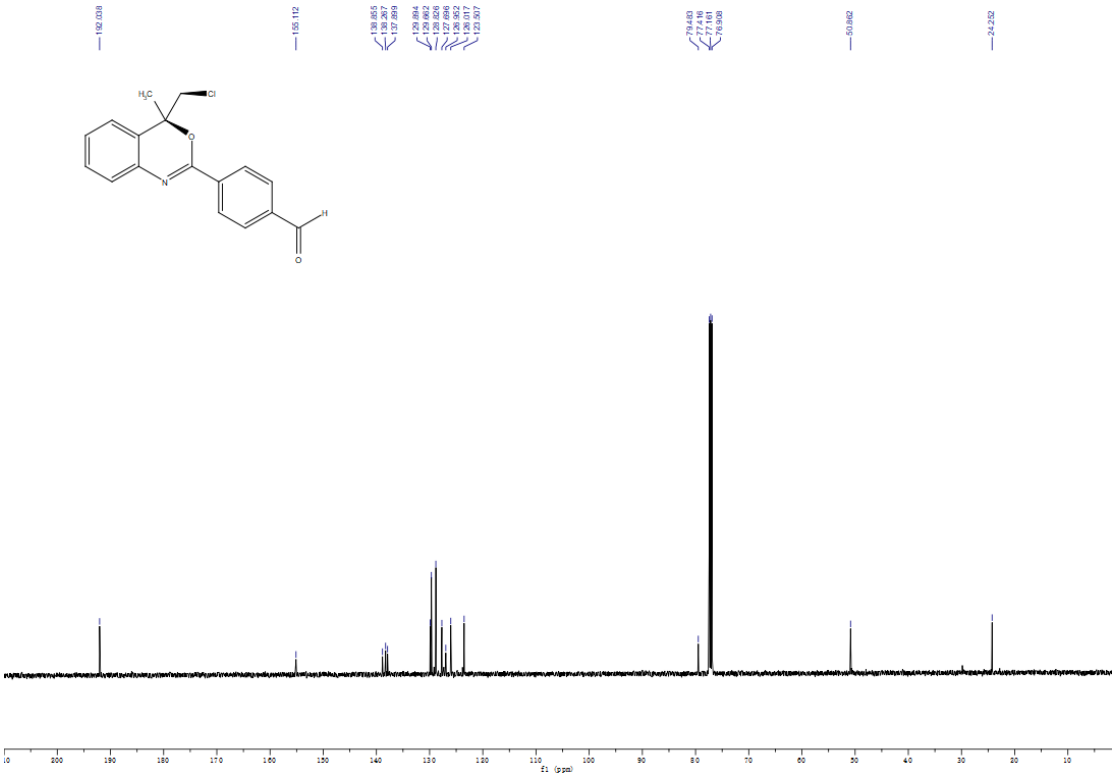
^{13}C NMR of compound **3ka**



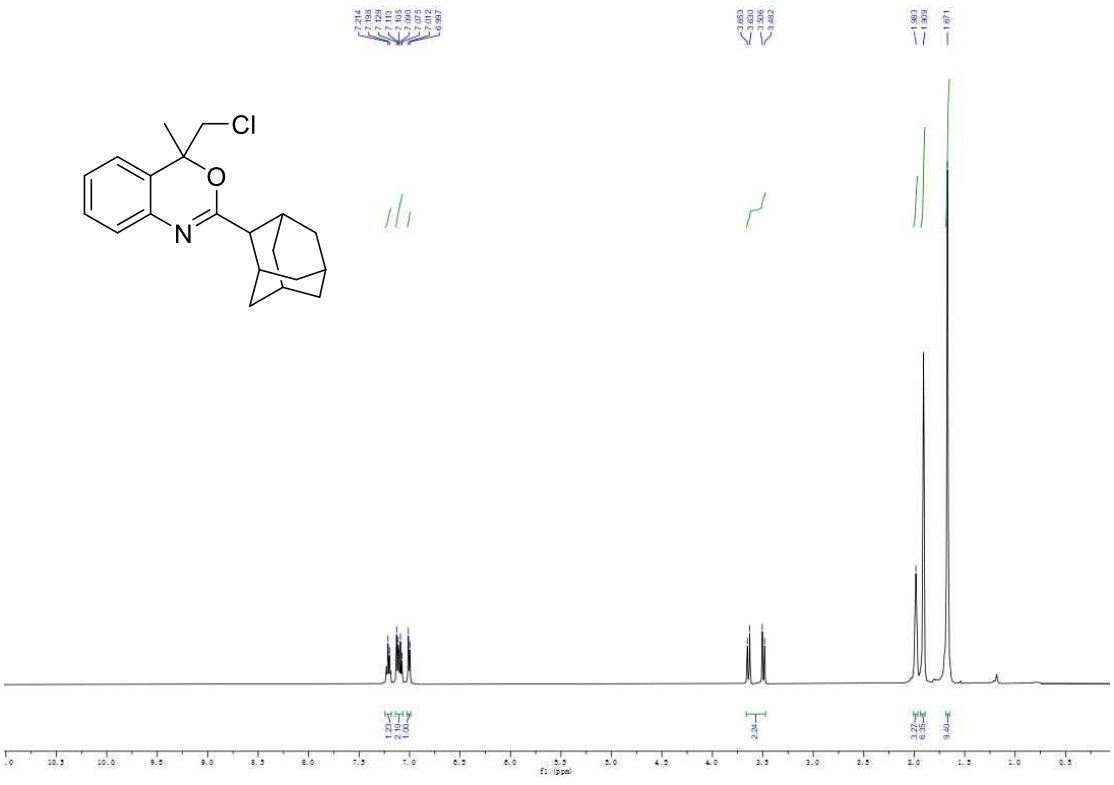
^{1}H NMR of compound **3la**



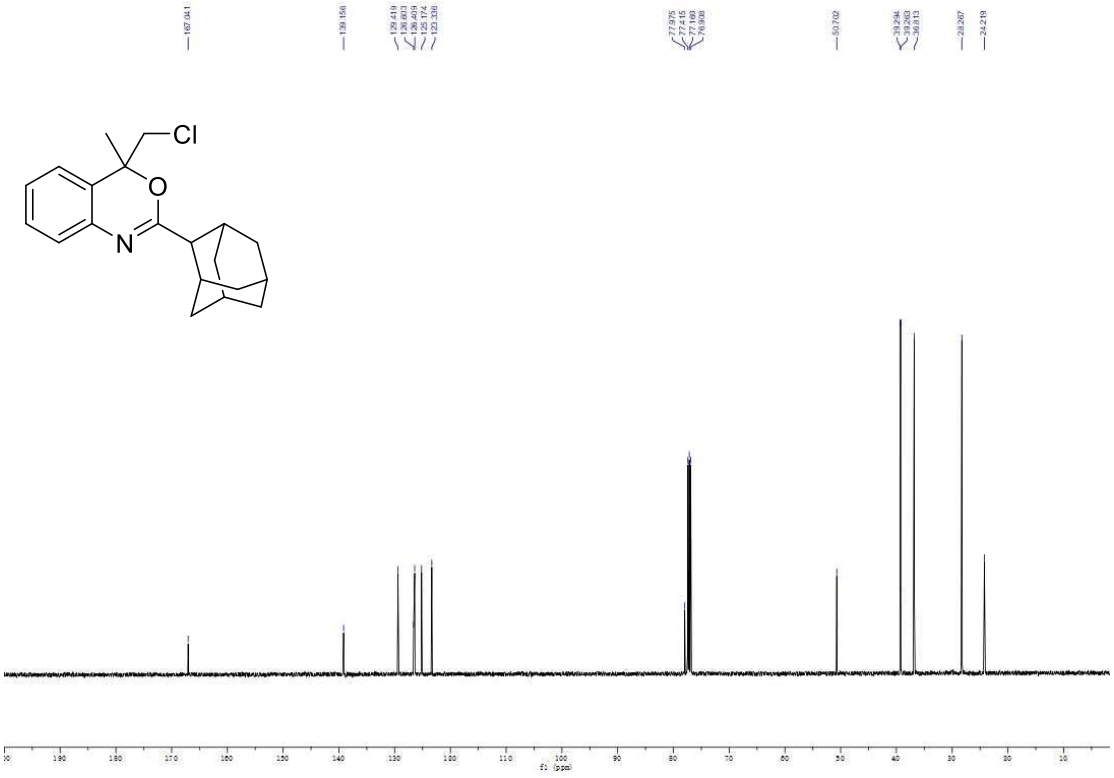
^{13}C NMR of compound **3ka**



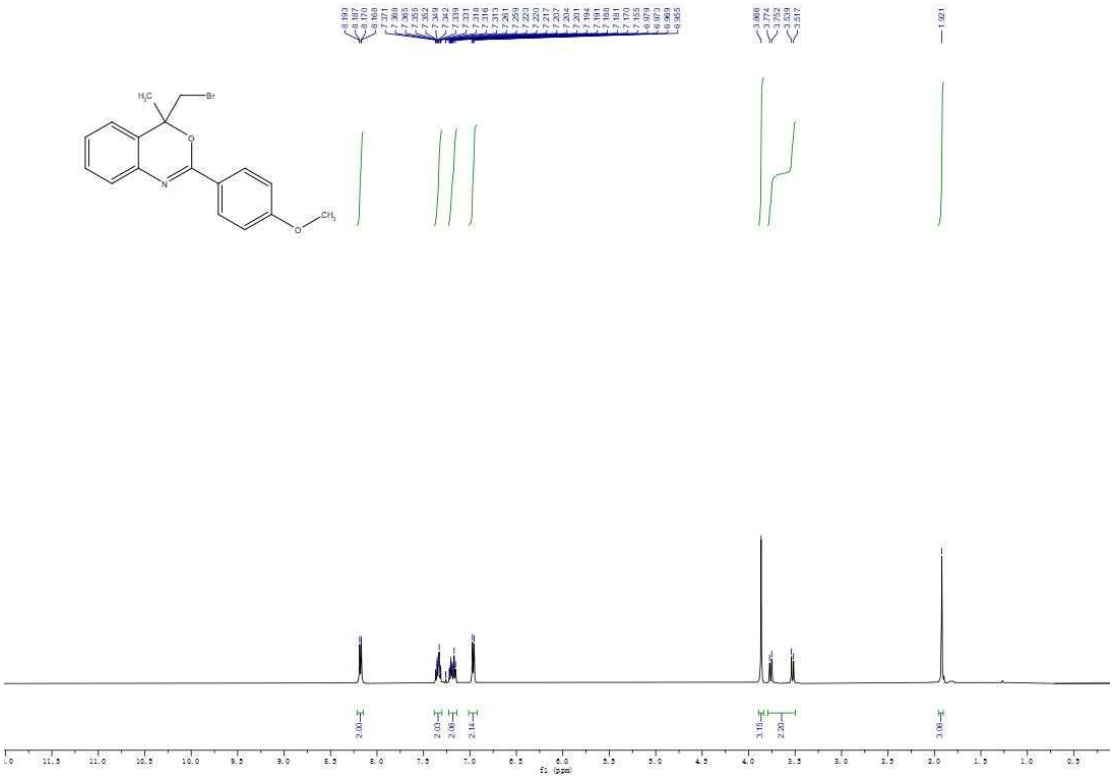
^{1}H NMR of compound **3ma**



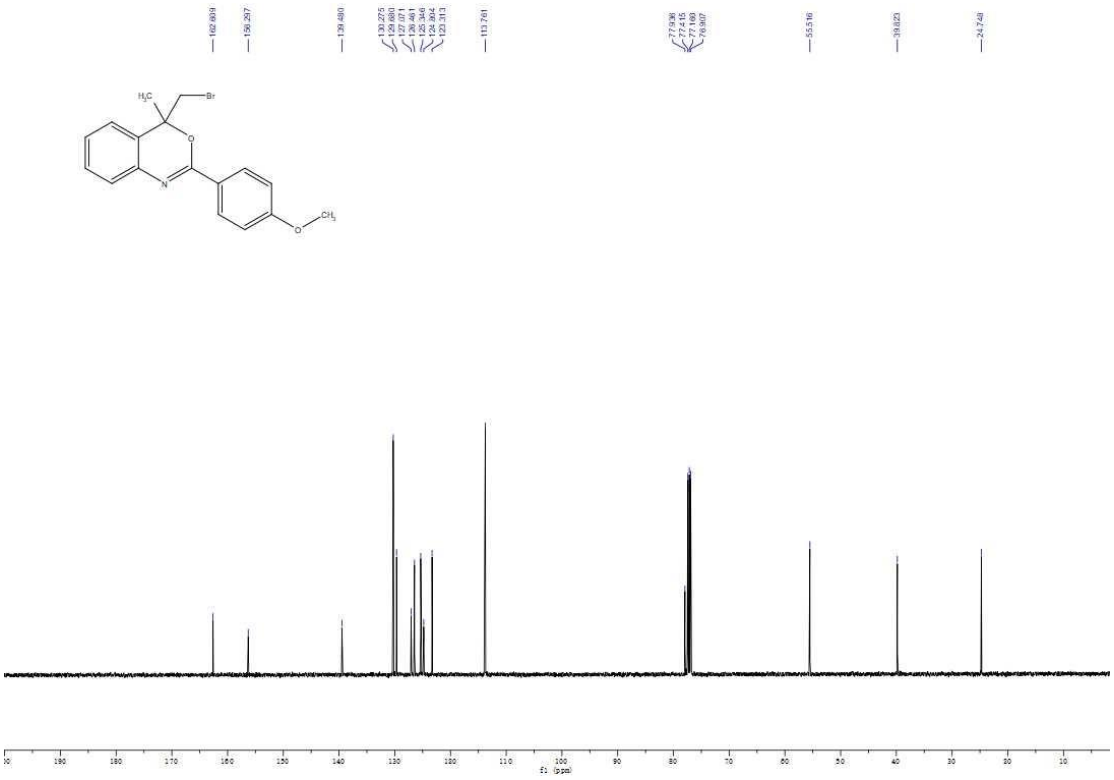
^{13}C NMR of compound **3ma**



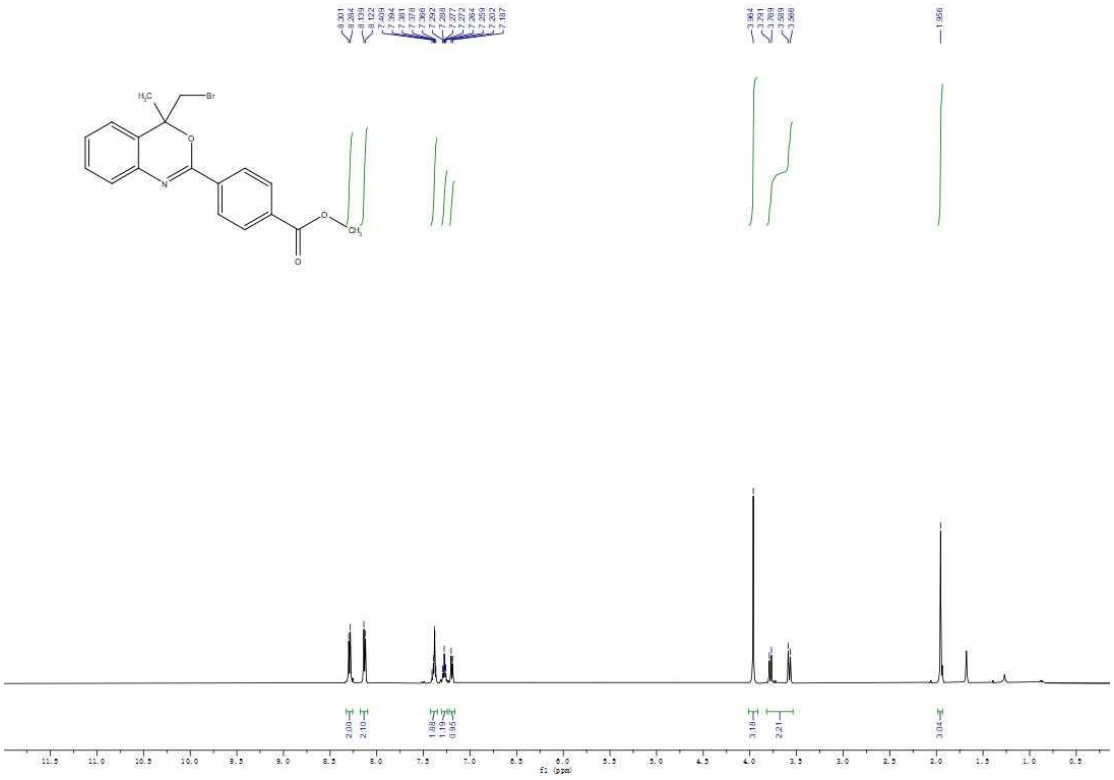
^{1}H NMR of compound **3bb**



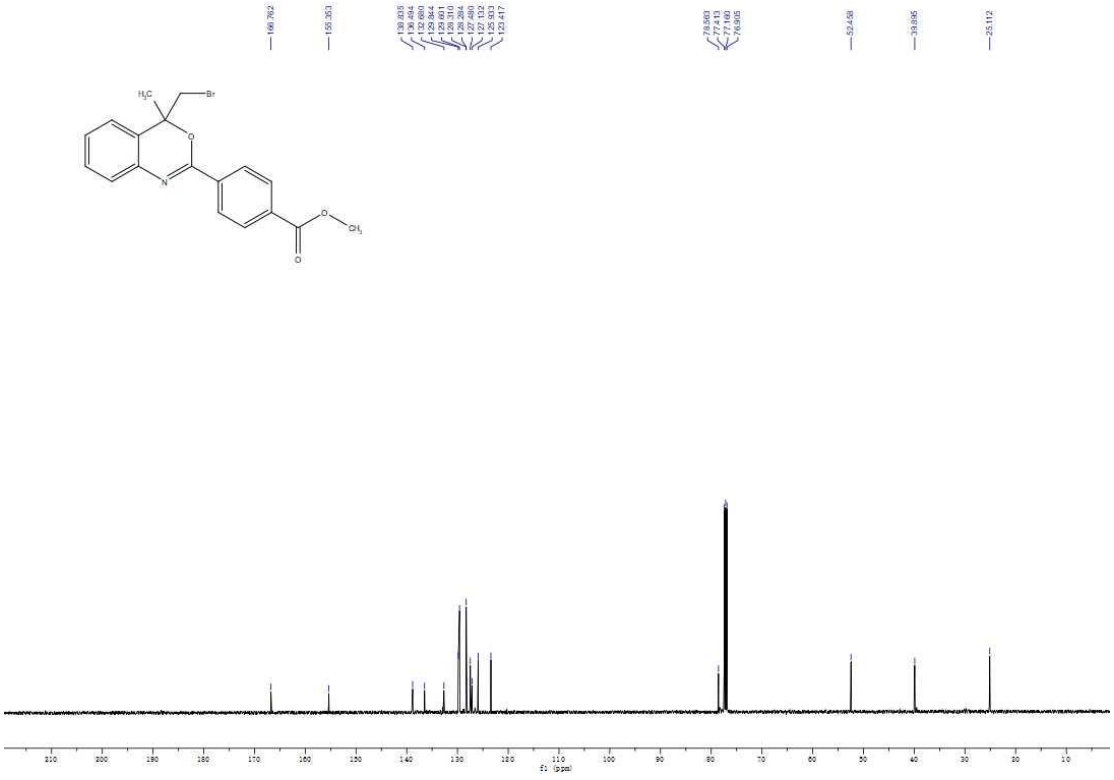
^{13}C NMR of compound **3bb**



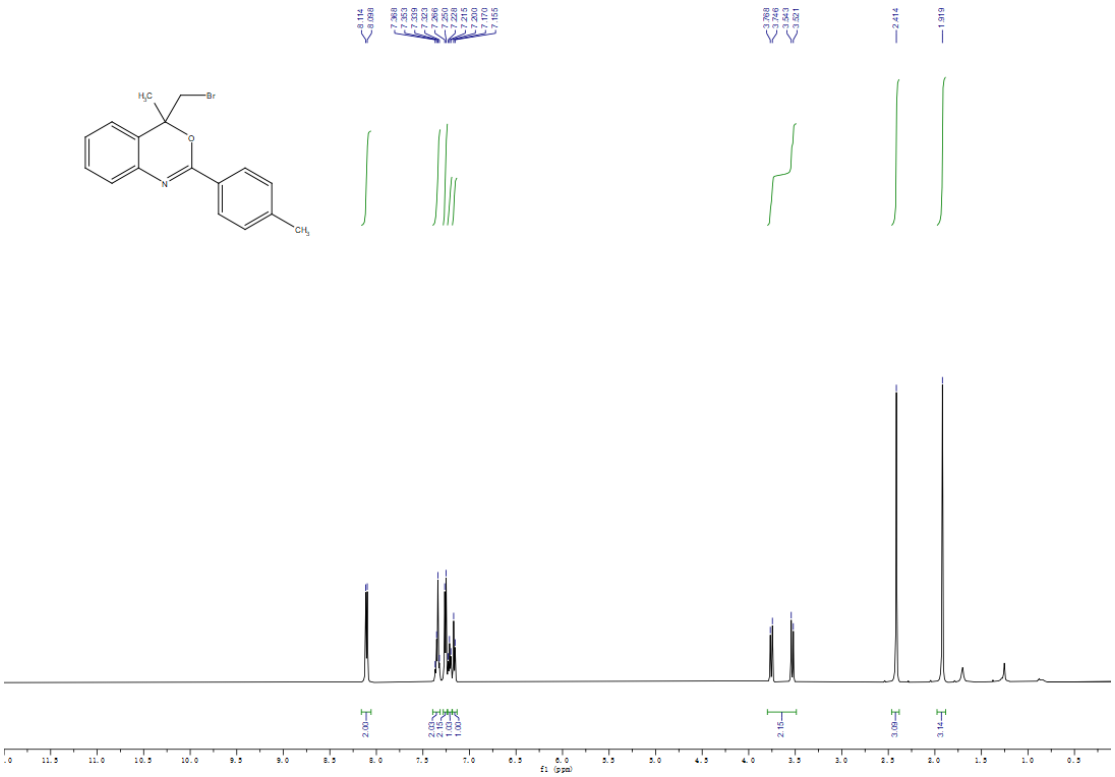
^{1}H NMR of compound **3nb**



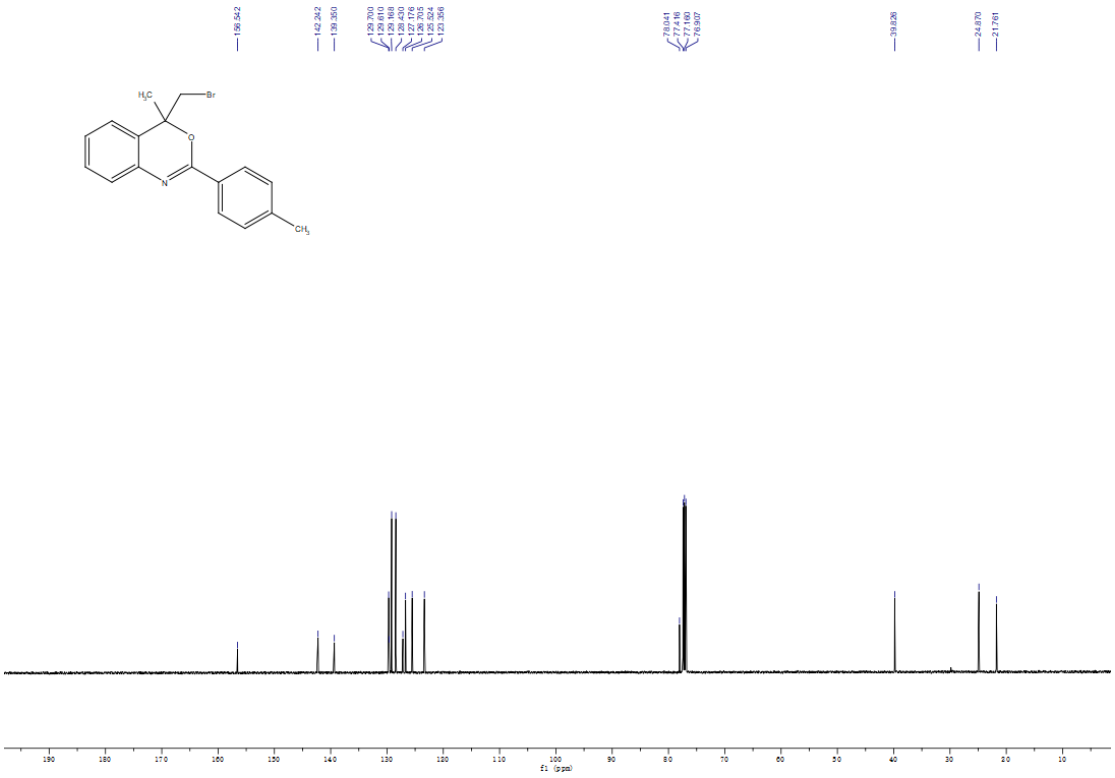
^{13}C NMR of compound **3nb**



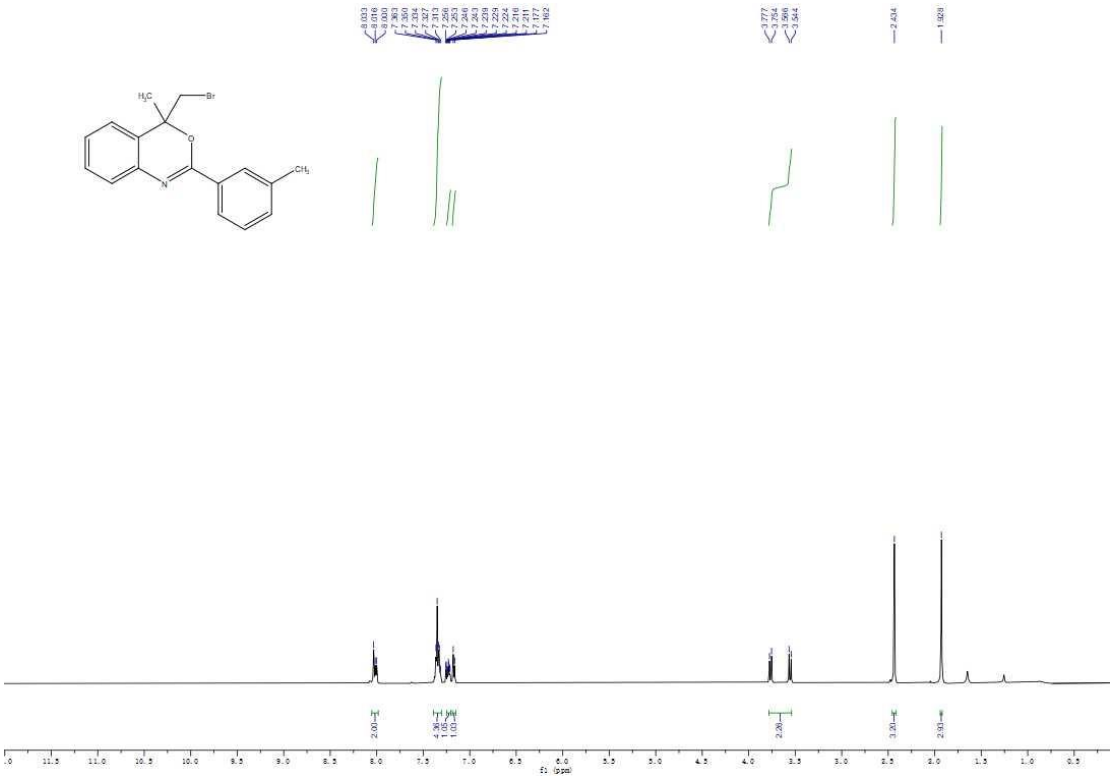
^{1}H NMR of compound **3eb**



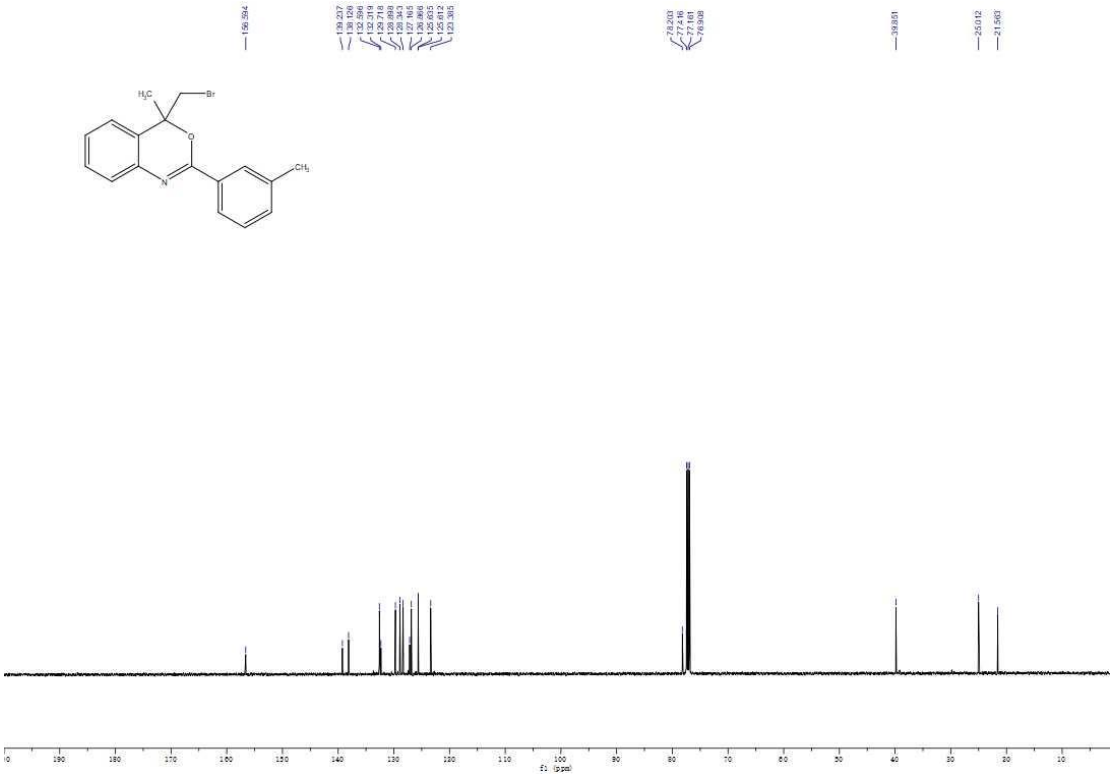
^{13}C NMR of compound **3eb**



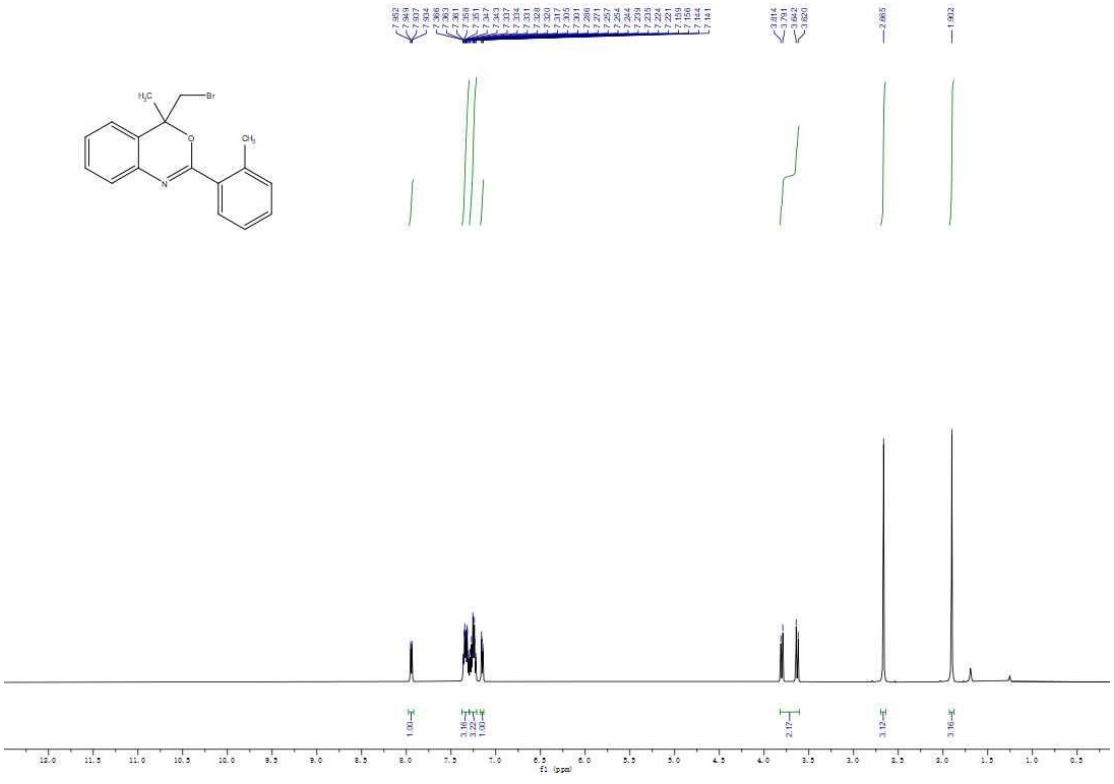
^{1}H NMR of compound **3fb**



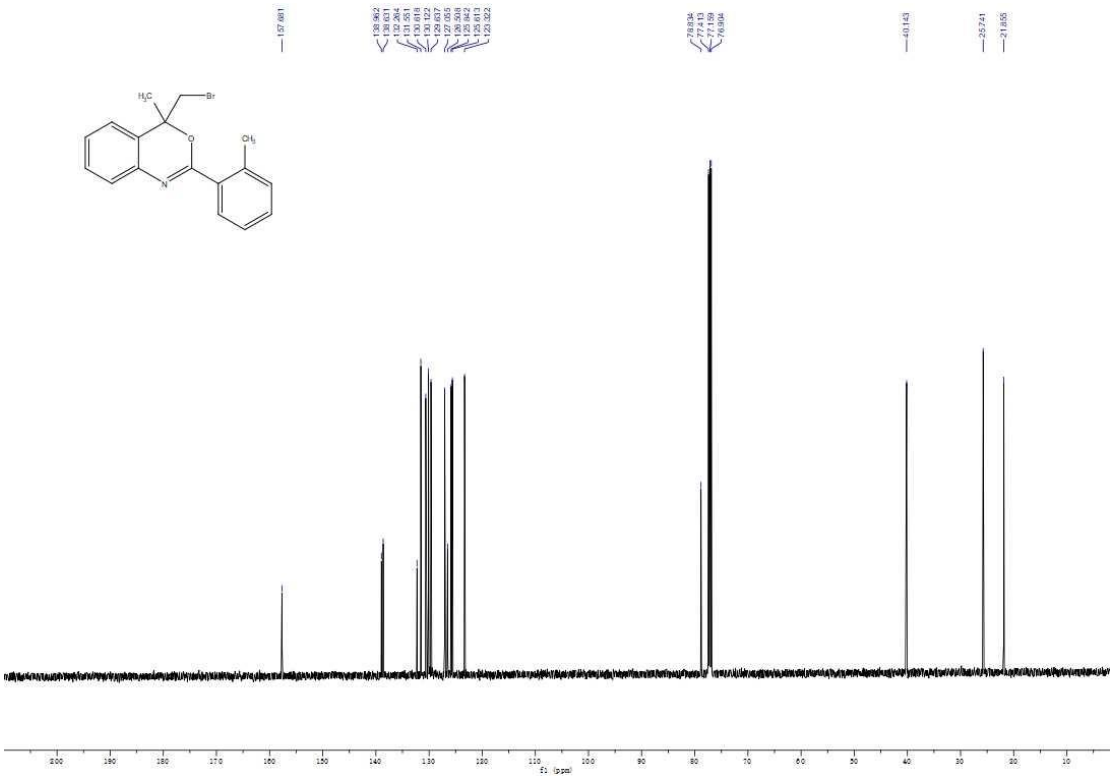
^{13}C NMR of compound **3fb**



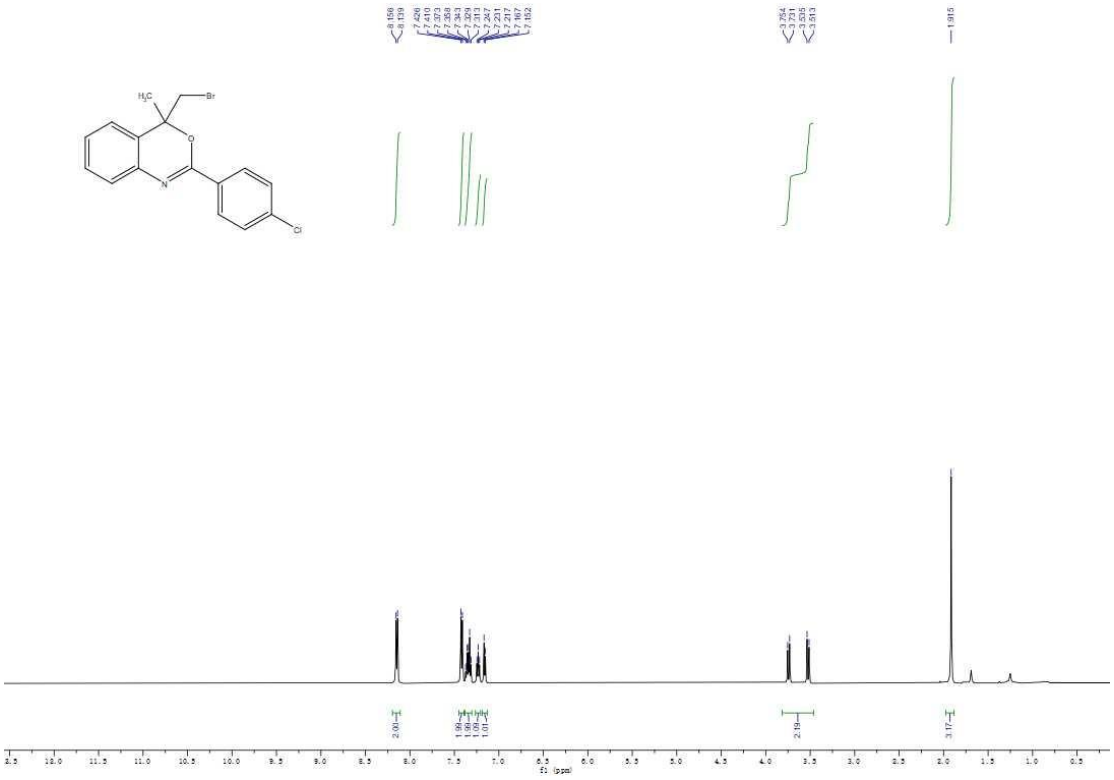
^{1}H NMR of compound **3gb**



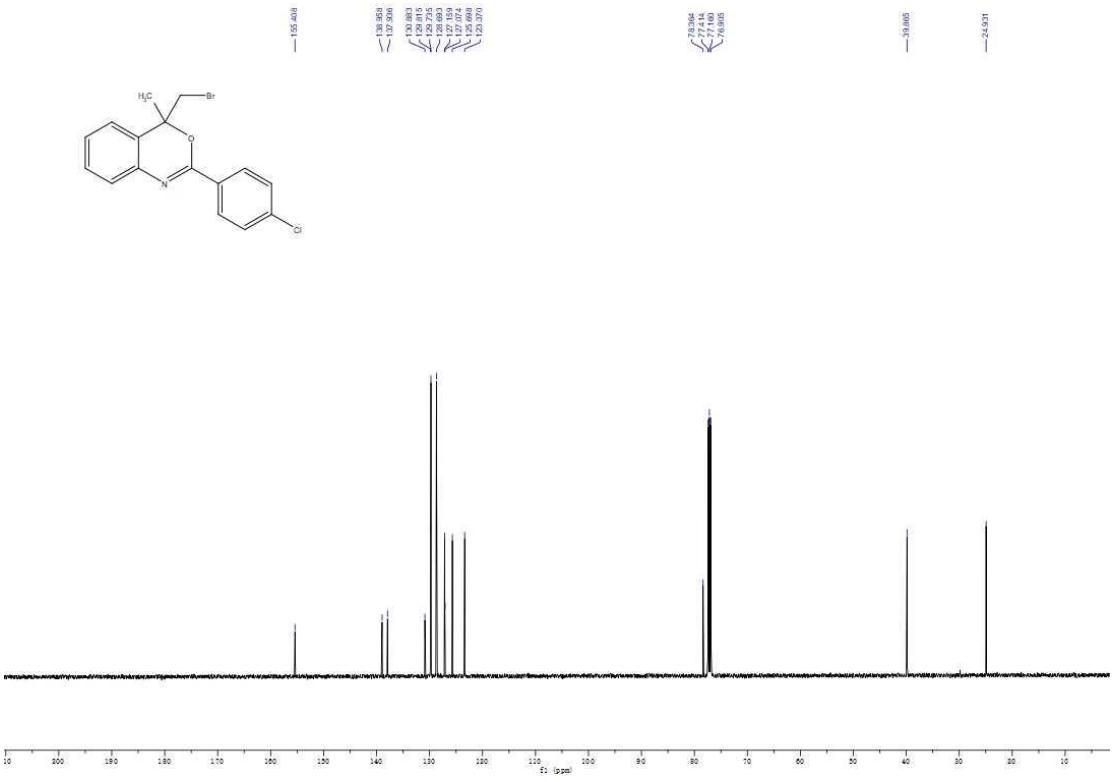
^{13}C NMR of compound **3gb**



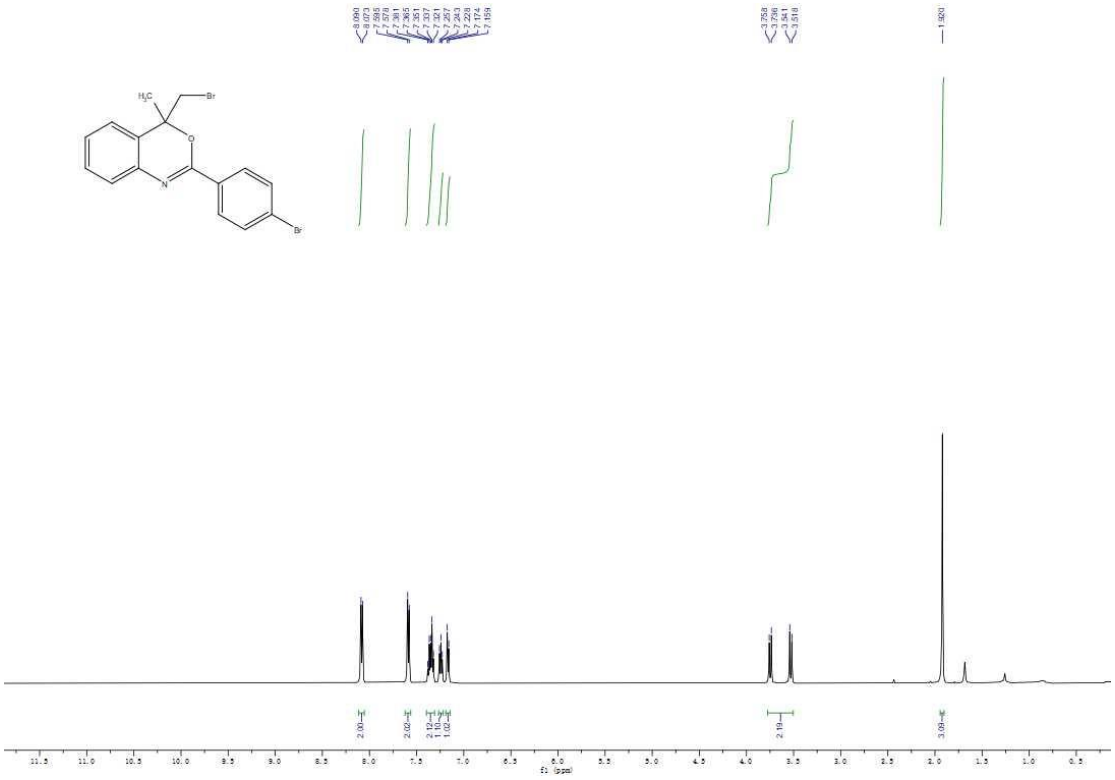
^{1}H NMR of compound **3ob**



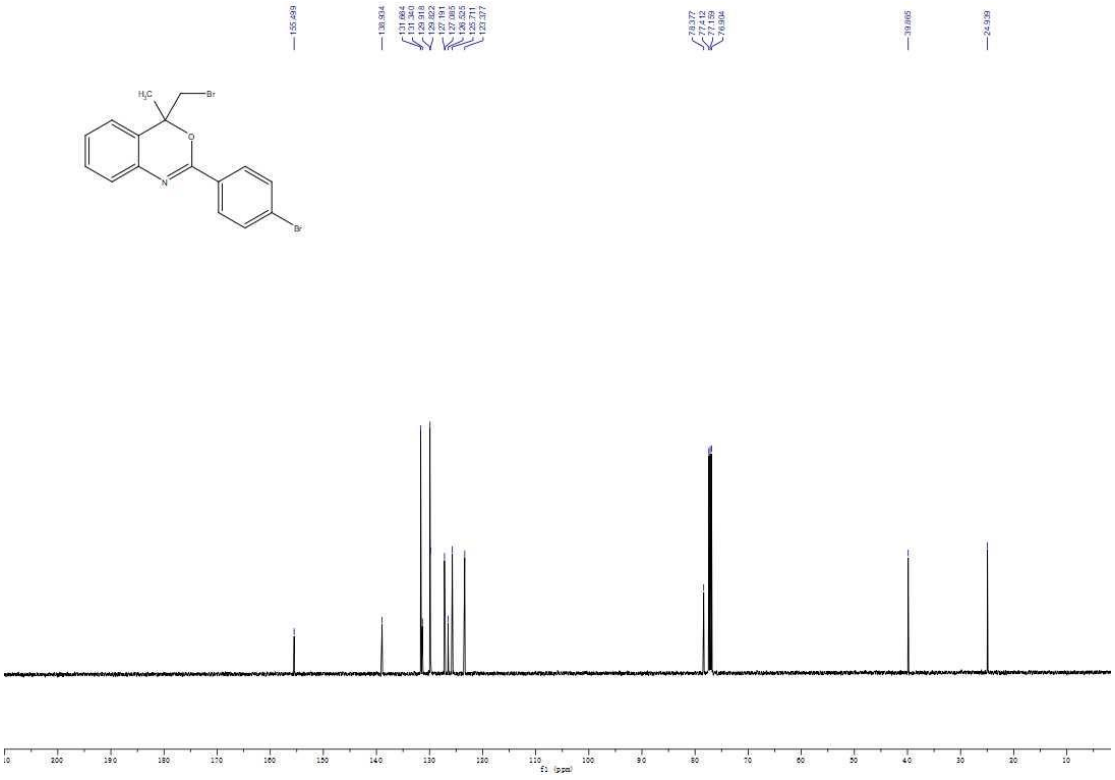
^{13}C NMR of compound **3ob**



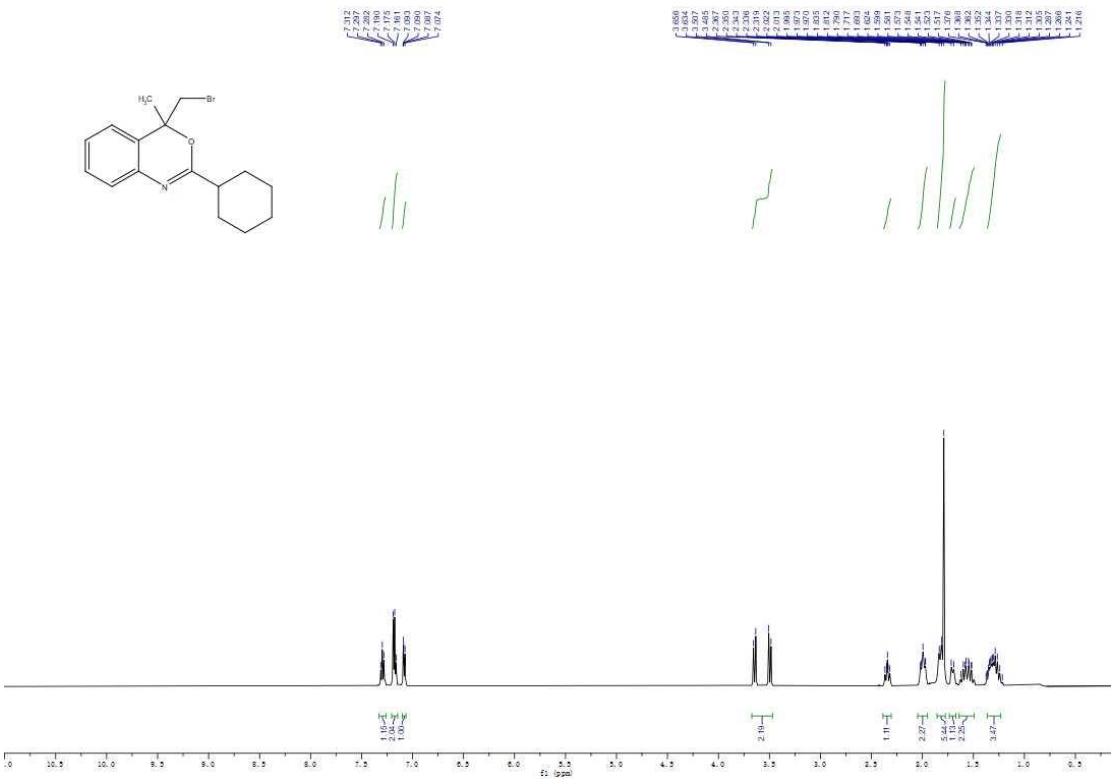
^{1}H NMR of compound **3pb**



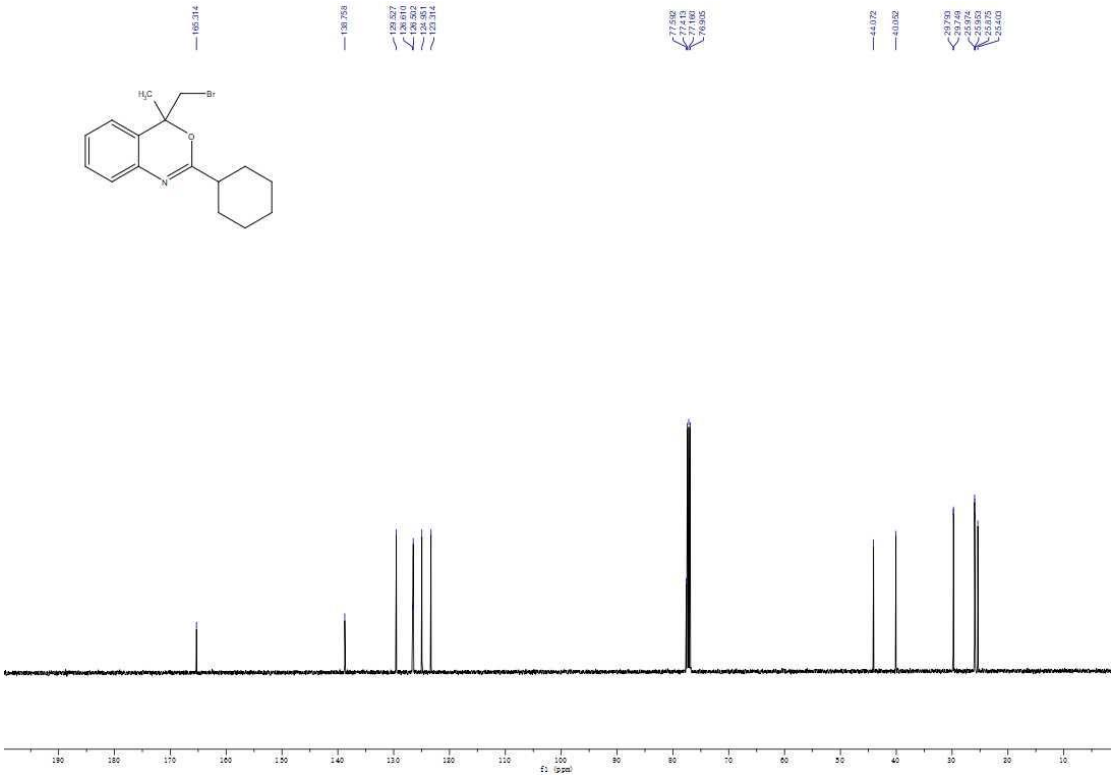
^{13}C NMR of compound **3pb**



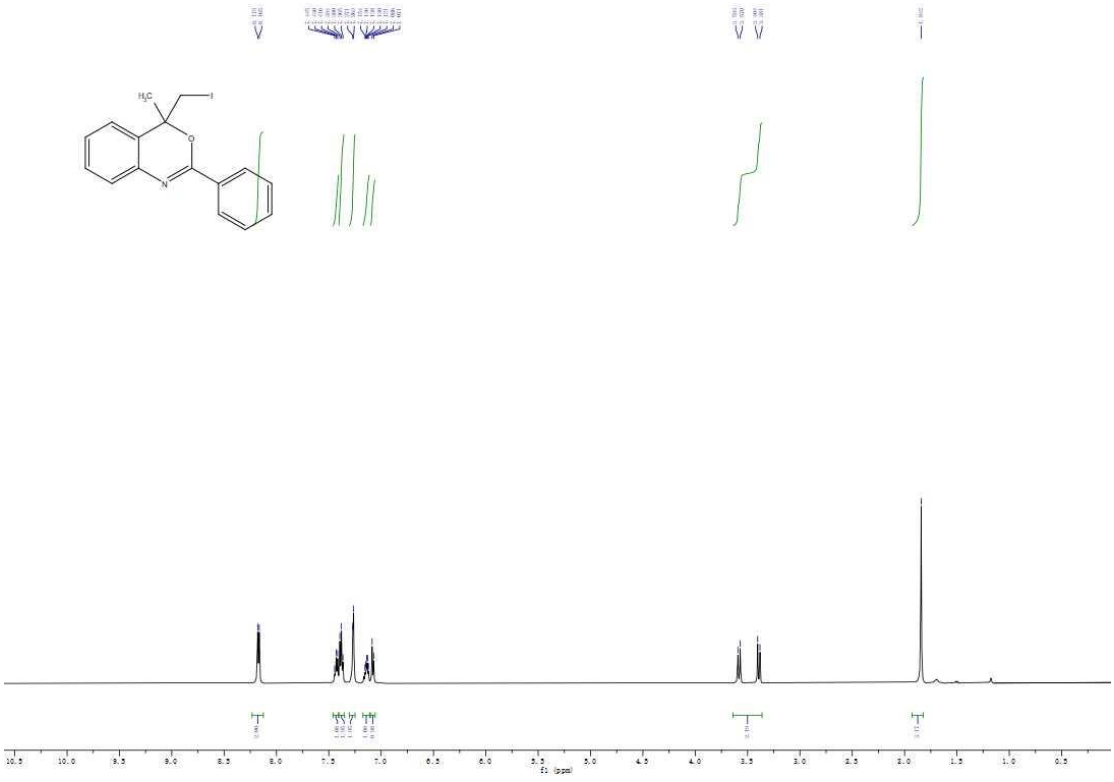
^{1}H NMR of compound **3qb**



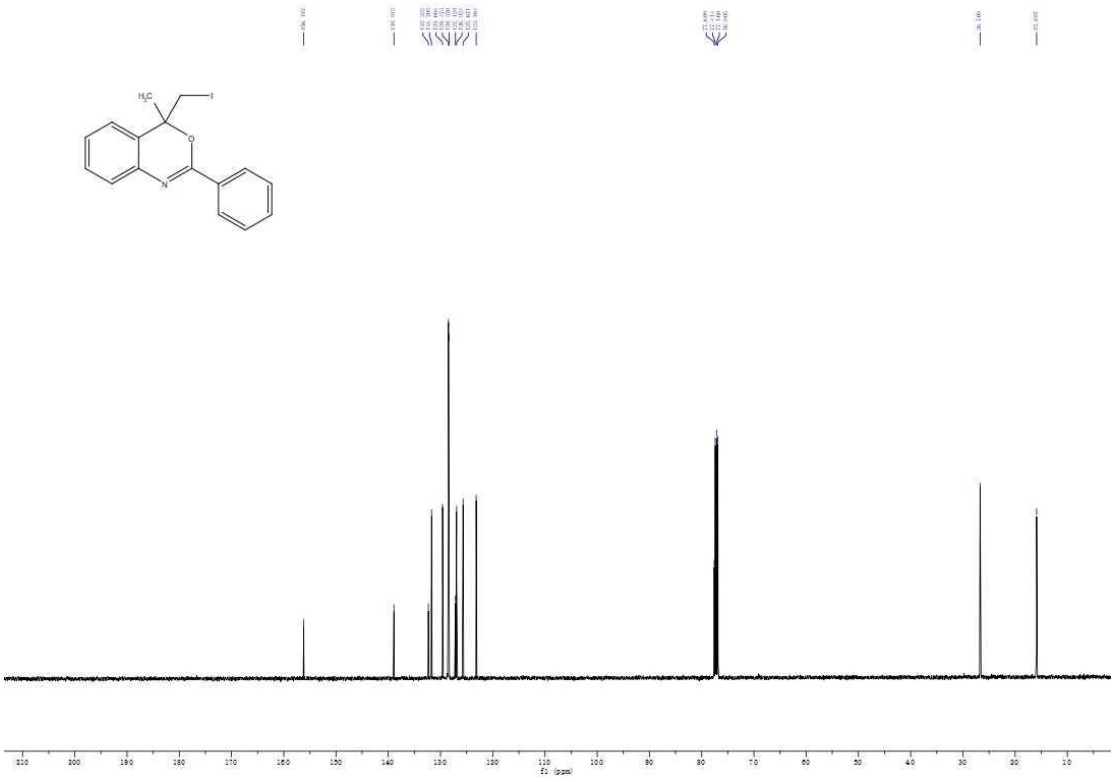
^{13}C NMR of compound **3qb**



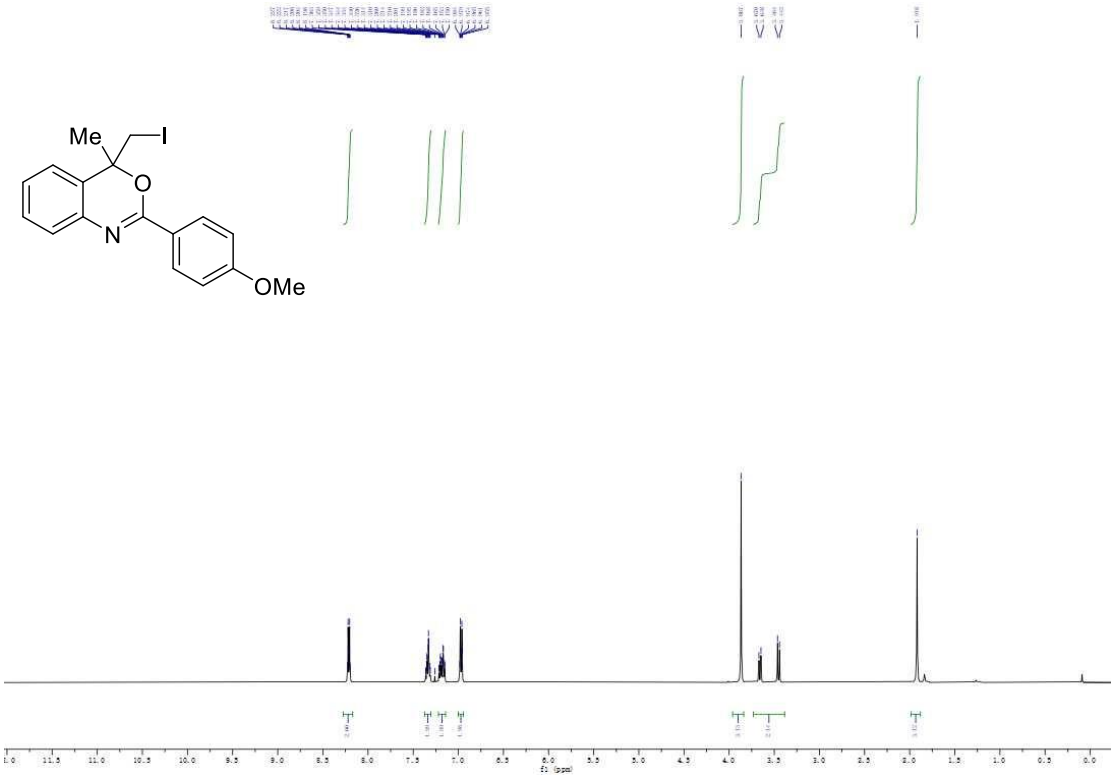
^{1}H NMR of compound **3ac**



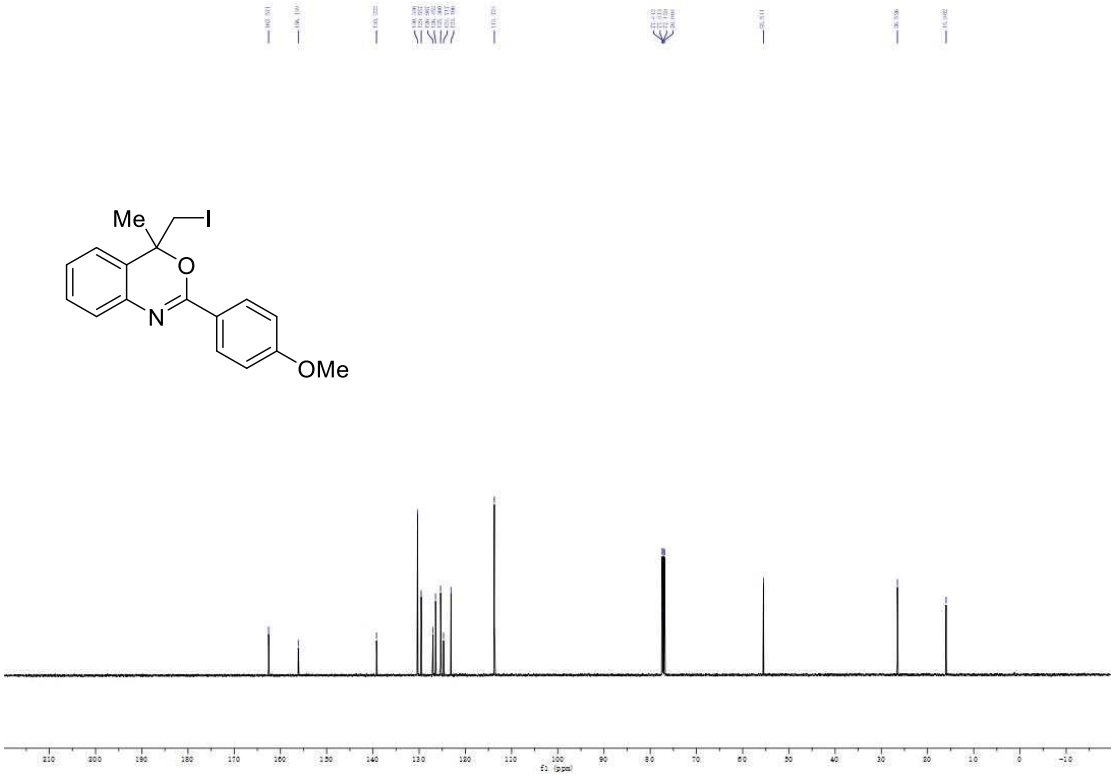
^{13}C NMR of compound **3ac**



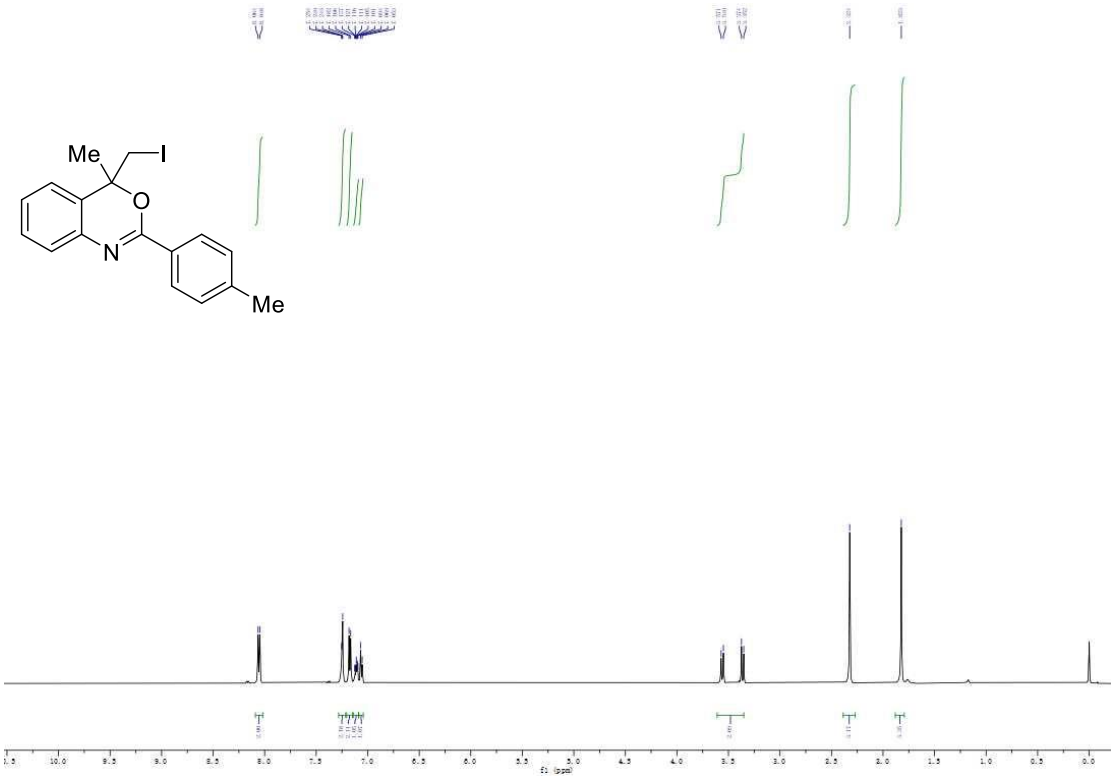
^{1}H NMR of compound **3bc**



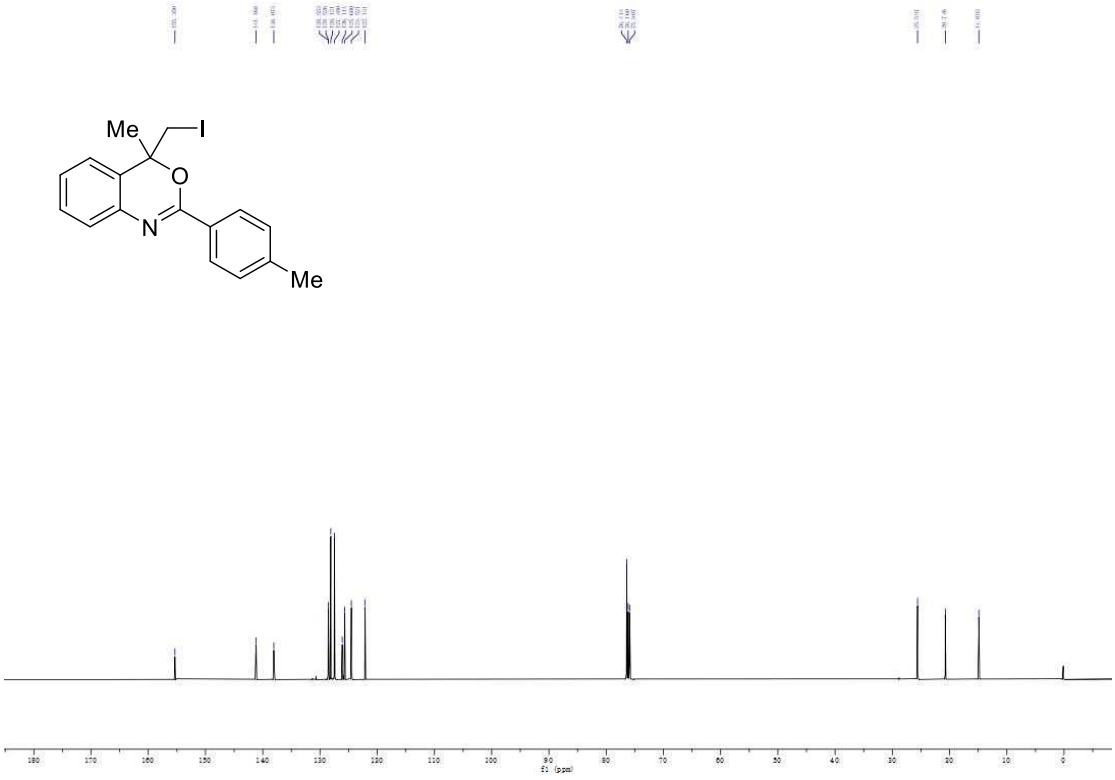
^{13}C NMR of compound **3bc**



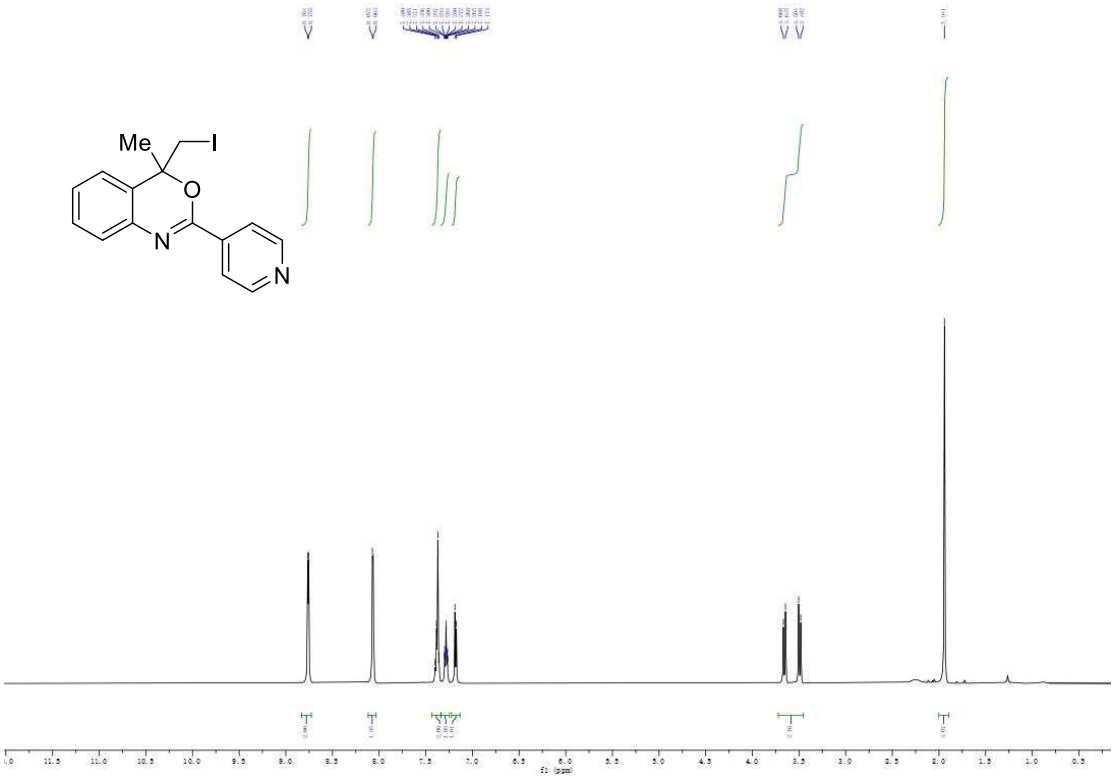
^{1}H NMR of compound **3ec**



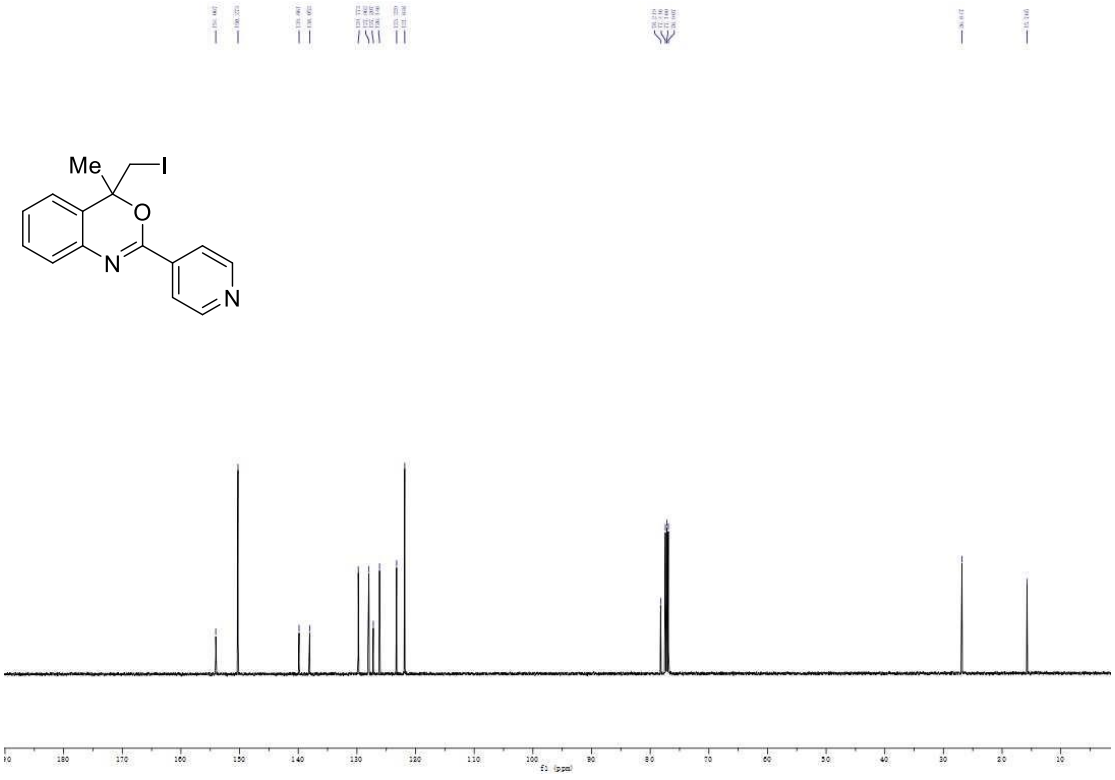
^{13}C NMR of compound **3ec**



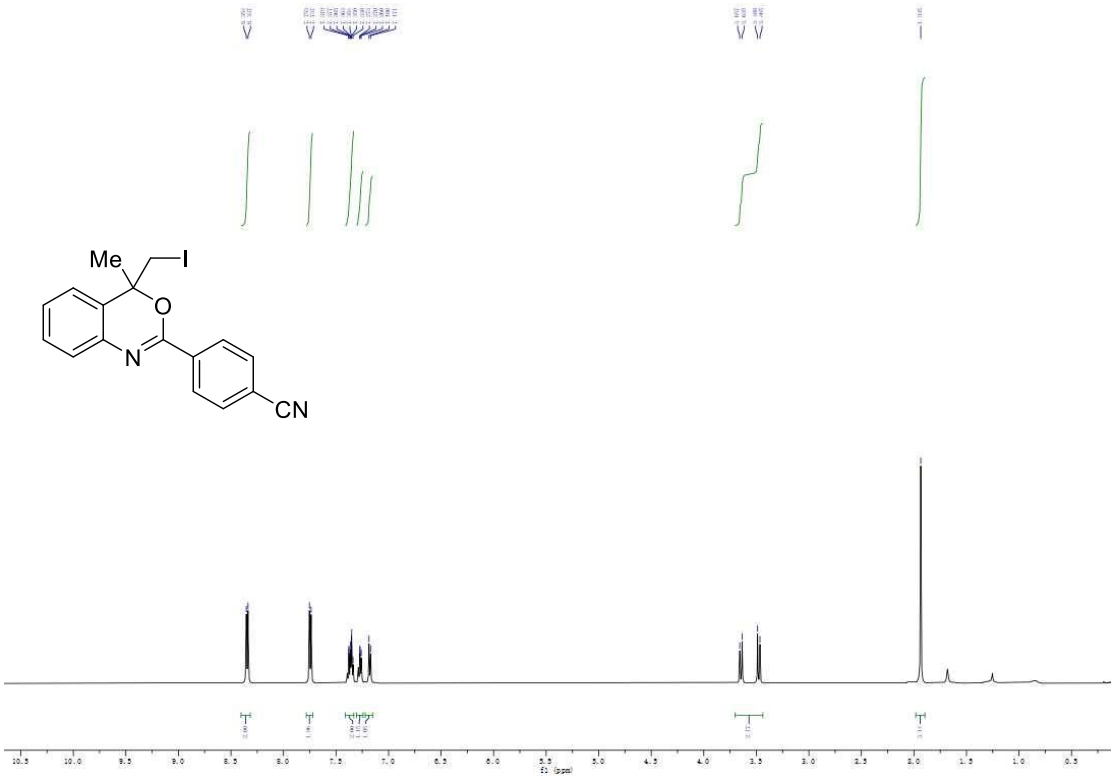
^{1}H NMR of compound **3ic**



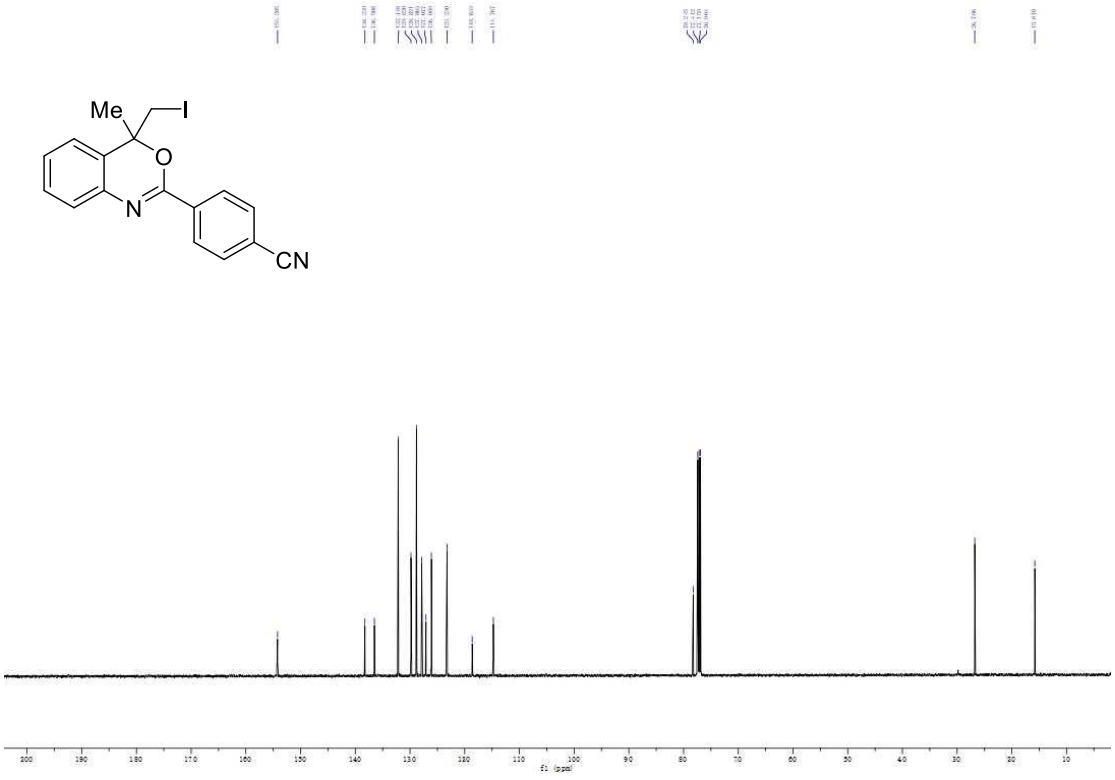
^{13}C NMR of compound **3ic**



^{1}H NMR of compound **3oc**



^{13}C NMR of compound **3oc**



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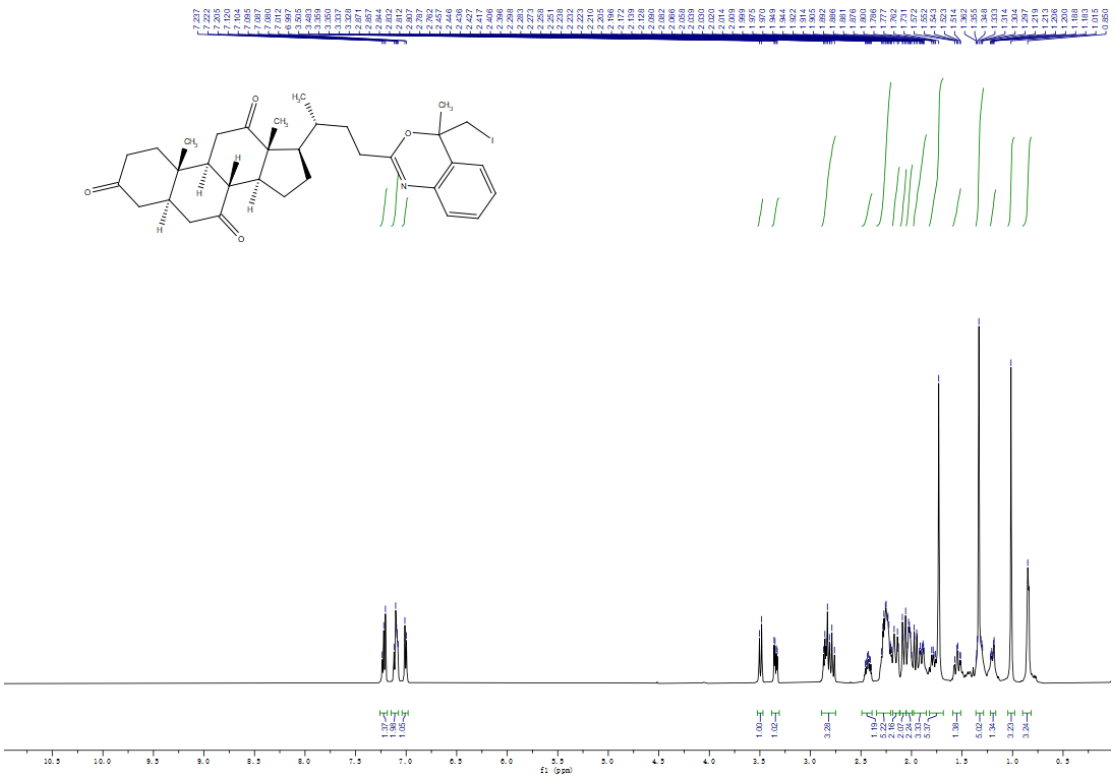

^{13}C NMR of compound **3rc**