Palladium(II)-Catalyzed Aerobic Oxidative O-H/C-H Isocyanide Insertion: Facile Access to Pyrrolo[2,1-*c*][1,4]benzoxazine Derivatives

Liangliang Luo,[a] Xiao-Pan Chen,[b] Zhao-Feng Li,[b] Yuan Zhou,[b] You-Cai Xiao,[b]* and Fen-Er Chen [b, c]*

[a] *Key Laboratory of Green Chemistry and Technology of Ministry of Education, College of Chemistry, Sichuan University, Chengdu 610064,* [b]*China Sichuan Research Center for Drug Precision Industrial Technology West China School of Pharmacy, Sichuan University, Chengdu, 610041, China. E-mail: xiaoliguo1987@scu.edu.cn,* [c]*Engineering Center of Catalysis and synthesis for Chiral Molecules, Department of chemistry, Fudan University, Shanghai, 200433, China. E-mail: rfchen@ fudan.edu.cn*

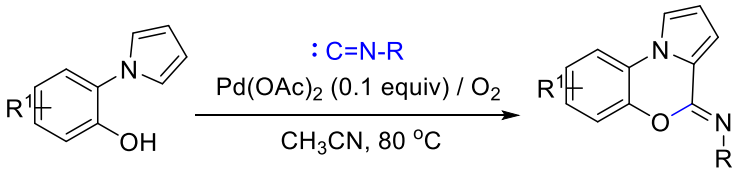
Supporting Information

Table of Contents

1. General methods

NMR data were obtained for ^{1}H at 400 MHz and for ^{13}C at 100 MHz. Chemical shifts were reported in ppm from tetramethylsilane with the solvent resonance as the internal standard in $CDCl_3$ solution. ESI HRMS was recorded on a Bruker Apex-2. Column chromatography was performed on silica gel (200-300 mesh) eluting with ethyl acetate and petroleum ether. All chemicals were used without purification as commercially available unless otherwise noted. Substrates (**1a**-**1s, 5a-5g**) were prepared according to the literature procedures.[1]

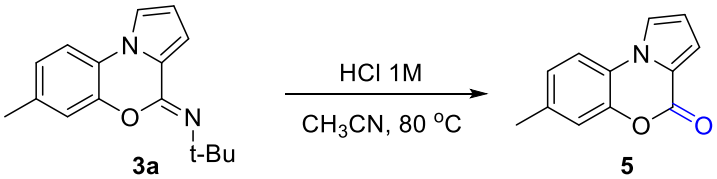
2. General Experimental Procedure A



1a- 1s **3a- 3s, 4a- 4j**

A mixture of **1a-1t,** (0.2 mmol, 1.0 equiv.), isocyanide **2a-2i** (0.4 mmol, 2.0 equiv.), $Pd(OAc)_2$ (0.02 mmol, 0.1 equiv.) in CH_3CN was stirred at 80℃ at O_2 atmosphere for 24 h, After completion monitored by TLC (by UV visualization), the solvent was evaporated under reduced pressure and the residue were separated by the flash column chromatography eluted with petroleum ether/ ethyl acetate (v/v 100:1) to afford the desired product **3a-3r, 4a-4j**.

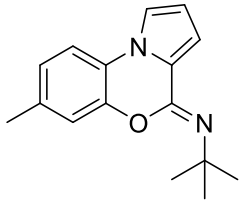
3. General Experimental Procedure B for the Synthesis of 7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-one.



3a **5**

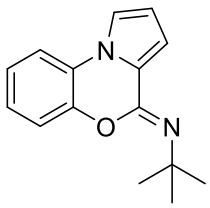
To a 10 mL round-bottom flask containing **3a** (0.5 mmol) CH_3CN (5 mL) and hydrochloric acid (1 M, 1 mL) were added. The resulting reaction mixture was stirred at 80 °C for 24 h. Progress of the reaction was monitored by TLC until the reaction was completed. The reaction mixture was quenched by addition of aq. $NaHCO_3$ solution and extracted with ethyl acetate (3 × 10 mL). The organic layer was dried (Na2SO4) and concentrated in vacuo. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate as eluent (hexane/ethyl acetate100:1) provided the product **5**.

4. Analytical data for compounds



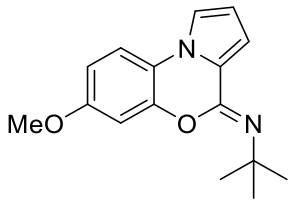
(*Z*)-*N*-(*tert*-butyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3a

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 150.3−151.5°C; 45mg (yield = 90%); **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (d, *J* = 8.1 Hz, 2H), 7.02 (s, 1H), 6.93 (d, *J* = 8.4 Hz, 2H), 6.46 (t, *J* = 3.2 Hz, 1H), 2.37 (s, 3H), 1.47 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.1, 140.5, 135.5, 124.0, 121.3, 120.9, 117.29, 115.0, 113.9, 112.5, 111.3, 54.0, 30.5, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O^+$) 255.1492, found 255.1489.



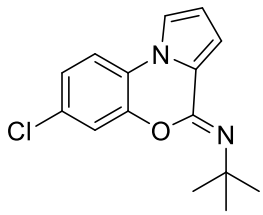
(*Z*)-*N*-(*tert*-butyl)-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3b

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 83.5−84.7°C; 34mg (yield = 71%).**^{1}H NMR** (400 MHz, $CDCl_3$)δ 7.44 (dd, *J* = 7.4, 2.0 Hz, 1H), 7.35 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.23 – 7.10 (m, 3H), 6.97 (dd, *J* = 3.8, 1.5 Hz, 1H), 6.52 – 6.45 (m, 1H), 1.48 (s, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.3, 140.3, 125.3, 123.4, 123.2, 121.4, 117.0, 115.2, 114.2, 112.8, 111.6, 54.0, 30.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{12}N_2O^+$) 241.1335, found 241.1335.



(*Z*)-N-(*tert*-butyl)-7-methoxy-4*H*-benzo[b]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3c

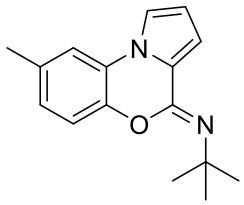
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 126.1−127.8°C; 49 mg (yield = 91 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (d, *J* = 8.9 Hz, 1H), 7.26 (dd, *J* = 3.0, 1.7 Hz, 1H), 6.92 (dd, *J* = 3.9, 1.5 Hz, 1H), 6.73 (d, *J* = 2.7 Hz, 1H), 6.68 (dd, *J* = 8.8, 2.7 Hz, 1H), 6.46 – 6.41 (m, 1H), 3.83 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 157.3, 144.1, 140.2, 120.8, 117.2, 114.8, 114.7, 112.3, 111.1, 109.6, 102.2, 55.8, 54.0, 30.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O_2^+$) 271.1441, found 271.1445.



(*Z*)-*N*-(*tert*-butyl)-7-chloro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3d

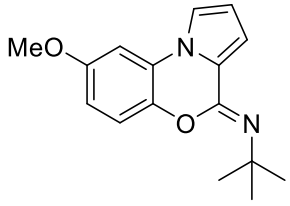
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum

ether: EtOAc) as eluent furnished the product; M. p. 129.2−130.5°C; 28 mg (yield = 52 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 8.6 Hz, 1H), 7.31 (s, 1H), 7.23 (d, *J* = 2.2 Hz, 1H), 7.11 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.95 (s, 1H), 6.50 (s, 1H), 1.46 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.6, 129.2, 122.4, 121.0, 116.3, 114.3, 114.0, 112.1, 111.0, 76.3, 76.0, 75.7, 53.2, 29.4. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}ClN_2O^+$) 275.0946, found 275.0943.



(*Z*)-*N*-(*tert*-butyl)-8-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3e

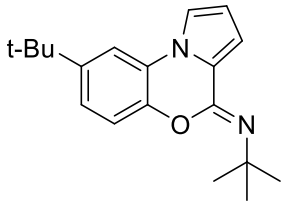
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 88.6−90.1°C 41mg (yield= 82 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.25 (d, *J* = 1.9 Hz, 1H), 7.09 (d, *J* = 8.3 Hz, 1H), 6.97 – 6.92 (m, 2H), 6.47 (dd, *J* = 3.8, 2.8 Hz, 1H), 2.39 (s, 3H), 1.46 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.3, 140.6, 133.2, 125.8, 122.8, 121.5, 116.6, 115.1, 114.5, 112.6, 111.5, 77.4, 77.0, 76.7, 53.9, 30.5, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O^+$) 255.1492, found 255.1489.



(*Z*)-*N*-(*tert*-butyl)-8-methoxy-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3f

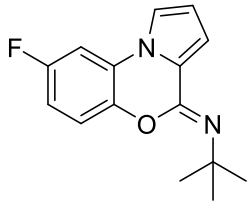
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 110.6−112.1°C; 36 mg (yield = 89 %).**^{1}H NMR** (400 MHz, $CDCl_3$)δ 7.29 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.12 (d, *J* = 8.9 Hz, 1H), 6.97 – 6.93(m, 2H), 6.69 (dd, *J* = 8.9, 2.8 Hz, 1H), 6.47 (dd, *J* = 3.8, 2.8 Hz, 1H), 3.84 (s, 3H),

1.46 (s, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 155.6, 140.6, 137.6, 123.5, 121.6, 117.5, 115.2, 112.8, 111.7, 110.2, 100.1, , 55.9, 53.9, 30.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O_2^+$) 271.1441, found 271.1438.



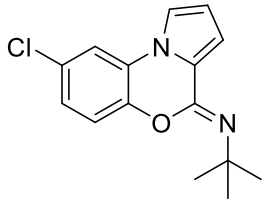
(*Z*)-*N*,8-*di*-*tert*-butyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3g

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 115.1−116.8^{o}C; 47 mg (yield = 80 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 – 7.37 (m,2H), 7.22 – 7.09 (m, 2H), 6.96 (d, *J* = 4.0 Hz, 1H), 6.53-6.41 (m, 1H), 1.47 (s, 9H), 1.36 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 145.7, 140.1, 139.6, 121.5, 121.3, 120.5, 115.4, 113.9, 111.5, 110.5, 109.9, 52.9, 33.6, 30.4, 29.4.**HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{19}H_{25}N_2O^+$) 297.1961, found 297.1961.



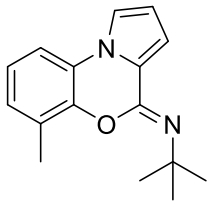
(*Z*)-*N*-(*tert*-butyl)-8-fluoro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3h

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 81.3−83.1^{o}C;28 mg (yield = 55 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.26 – 7.24 (m, 1H), 7.15 (dd, *J* = 9.0, 4.9 Hz, 2H), 6.95 (dd, *J* = 3.8, 1.5 Hz, 1H), 6.89 – 6.81 (m, 1H), 6.49 (dd, *J* = 3.8, 2.8 Hz, 1H), 1.45 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 159.5, 157.1, 139.6, 139.6, 123.8, 123.7, 121.4, 117.9, 117.8, 115.4, 113.3, 112.0, 111.8, 111.6, 101.9, 101.6, 54.1, 30.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}FN_2O^+$) 259.1241, found 259.1245.



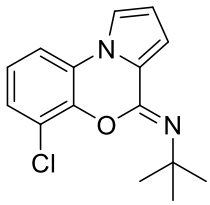
(*Z*)-*N*-(*tert*-butyl)-8-chloro-4H-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3i

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 93.2−94.7°C; 24 mg (yield = 45 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (d, *J* = 2.0 Hz, 1H), 7.32 – 7.27 (m, 1H), 7.20 – 7.08 (m, 2H), 7.01 – 6.90 (m, 1H), 6.50 (t, *J* = 3.3 Hz, 1H), 1.45 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.9, 139.3, 128.4, 125.1, 124.0, 121.3, 118.0, 115.4, 114.4, 113.4, 112.1, 54.2, 30.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}ClN_2O^+$) 275.0946, found 275.0946.



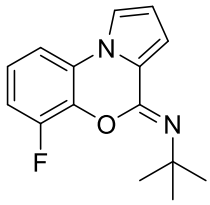
(*Z*)-*N*-(*tert*-butyl)-6-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3k

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 146.1−147.5°C; 46 mg (yield = 91 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.25 (dd, *J* = 2.8, 1.5 Hz, 1H), 7.23 – 7.18 (m, 1H), 6.94 (d, *J* = 4.7 Hz, 2H), 6.89 (d, *J* = 2.3 Hz, 1H), 6.43 – 6.39 (m, 1H), 2.39 (s, 3H), 1.44 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.0, 140.1, 126.8, 126.5, 122.9, 122.7, 121.4, 115.3, 112.7, 111.9, 111.4, 53.7, 30.1, 17.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O^+$) 255.1492, found 255.1497.



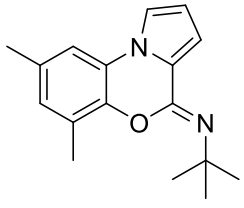
(*Z*)-*N*-(*tert*-butyl)-6-chloro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3l

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 200.5−201.8°C; 49 mg (yield = 90 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.34 (d, *J* = 8.2 Hz, 2H), 7.22 (dd, *J* = 8.1, 1.4 Hz, 1H), 7.05 (t, *J* = 8.1 Hz, 1H), 6.97 (d, *J* = 3.7 Hz, 1H), 6.53 – 6.47 (m, 1H), 1.52 (s, 9H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.0, 137.4, 124.8, 123.4, 122.1, 121.1, 120.1, 114.6, 112.3, 111.5, 111.0, 53.3, 29.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}ClN_2O^+$) 275.0946, found 275.0945.



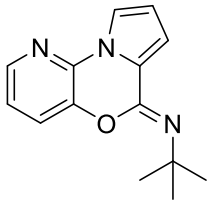
(*Z*)-*N*-(*tert*-butyl)-6-fluoro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3m

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 141.5−143.2°C; 45 mg (yield = 88 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.31 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.19 (dt, *J* = 8.2, 1.5 Hz, 1H), 7.03 (td, *J* = 8.2, 5.3 Hz, 1H), 6.99 – 6.91 (m, 2H), 6.52 – 6.47 (m, 1H), 1.49 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 150.9, 148.5, 137.5, 131.4, 131.2, 123.8, 123.8, 121.6, 121.5, 120.1, 114.7, 112.0, 111.2, 111.2, 111.0, 108.3, 108.2, 53.4, 29.2. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}FN_2O^+$) 259.1241, found 259.1244.



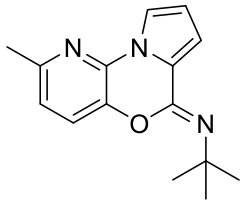
(*Z*)-*N*-(*tert*-butyl)-6,8-dimethyl-4H-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 3n

The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 109.2−111.1°C; 46 mg (yield = 85 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.32 (dd, *J* = 2.9, 1.5 Hz, 1H), 7.09 (d, *J* = 2.0 Hz, 1H), 6.95 (dd, *J* = 3.8, 1.5 Hz, 1H), 6.82 (d, *J* = 2.0 Hz, 1H), 6.51 – 6.44 (m, 1H), 2.42 (s, 3H), 2.34 (s, 3H), 1.51 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 139.4, 138.9, 131.3, 126.5, 125.0, 121.5, 120.4, 114.1, 111.5, 111.1, 110.2, 76.3, 76.0, 75.7, 52.6, 29.1, 19.9, 15.8. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{17}H_{21}N_2O^+$)269.1648, found 269.1647.



(*Z*)-*N*-(*tert*-butyl)-6*H*-pyrido[3,2-*b*]pyrrolo[1,2-*d*][1,4]oxazin-6-imine 3o

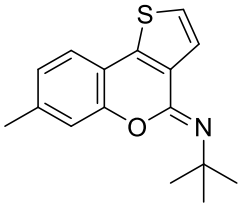
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (50:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 127.3−128.7°C; 21 mg (yield = 45 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 8.12 (dd, *J* = 4.8, 1.5 Hz, 1H), 7.80 (dd, *J* = 2.9, 1.6 Hz, 1H), 7.46 (dd, *J* = 8.1, 1.5 Hz, 1H), 7.12 (dd, *J* = 8.1, 4.8 Hz, 1H), 6.99 (s, 1H), 6.50 (t, *J* = 3.3 Hz, 1H), 1.46 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 141.2, 138.0, 137.7, 135.3, 122.7, 120.8, 119.9, 115.3, 112.2, 112.0, 53.2, 29.5. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{14}H_{16}N_3O^+$) 242.1288, found 242.1288.



(*Z*)-*N*-(*tert*-butyl)-2-methyl-6*H*-pyrido[3,2-*b*]pyrrolo[1,2-*d*][1,4]oxazin-6-imine 3p

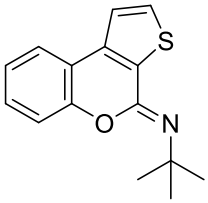
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel

column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 104.1−105.4°C; 44 mg (yield = 87 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.81 (s, 1H), 7.35 (d, *J* = 8.1 Hz, 1H), 6.95 (d, *J* = 8.2 Hz, 2H), 6.48 (t, *J* = 3.3 Hz, 1H). 2.52 (s, 3H), 1.45 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 151.6, 136.9, 135.2, 130.9, 128.9, 124.1, 121.8, 120.3, 116.3, 112.9, 54.2, 30.5, 23.6. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{18}N_3O^+$) 256.1444, found 256.1443.



(*Z*)-*N*-(*tert*-butyl)-7-methyl-4*H*-thieno[3,2-*c*]chromen-4-imine 3q

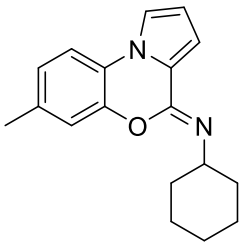
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 95.1−96.8°C; 44 mg (yield = 81 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.47 (d, *J* = 5.2 Hz, 1H), 7.43 – 7.36 (m, 2H), 7.11 (s, 2H), 2.39 (s, 3H), 1.49 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 149.8, 142.7, 136.4, 131.6, 129.6, 129.4, 128.3, 122.5, 120.7, 116.6, 114.8, 52.8, 29.2, 19.8. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{18}NOS^+$) 272.1104, found 272.1111.



(*Z*)-*N*-(*tert*-butyl)-4*H*-thieno[2,3-*c*]chromen-4-imine 3r

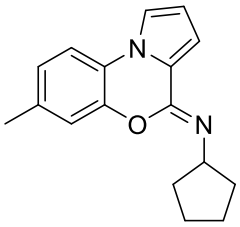
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate(10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 63.1−64.9°C; 46 mg (yield = 90 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.64 (dd, *J* = 7.7, 1.6 Hz, 1H), 7.49 (d, *J* = 5.2 Hz, 1H), 7.43 (d, *J* = 5.2 Hz, 1H), 7.35-7.27 (m, 1H), 7.22 (dd, *J* = 8.3, 1.3 Hz, 1H), 7.16 (td, *J* = 7.5, 1.3 Hz, 1H), 1.47 (s, 9H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 152.8, 143.4, 137.4, 130.7, 130.5,

128.7, 123.5, 123.3, 121.8, 118.1, 116.2, 53.91, 30.25. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{15}H_{16}NOS^+$) 258.0947, found258.0943.



(*Z*)-*N*-cyclohexyl-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4a

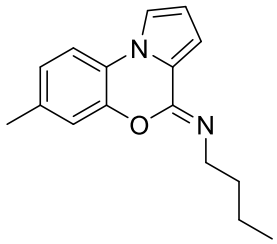
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (20:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 62.3−64.1°C; 49mg (yield = 89%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 – 7.30 (m, 2H), 7.07 – 6.98 (m, 2H), 6.92 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.47 (t, *J* = 3.3 Hz, 1H), 4.04 – 3.92 (m, 1H), 2.36 (s, 3H), 1.87 – 1.77 (m, 5H), 1.73 – 1.63 (m, 1H), 1.51 – 1.38 (m, 4H). **^{13}C NMR** ^{13}C NMR (101 MHz, $CDCl_3$) δ 143.1, 141.8, 135.5, 124.0, 121.0, 120.6, 117.2, 115.1, 113.8, 112.5, 111.1, 54.1, 34.0, 25.9, 25.2, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{18}H_{21}N_2O^+$) 281.1648, found 281.1648.



(Z)-*N*-cyclopentyl-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4b

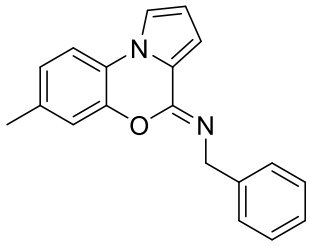
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (20:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 109.1−110.8°C;42mg (yield= 80 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.30 (m, 2H), 7.06 - 7.69 (m, 2H), 6.92 (dd, *J* = 8.2, 1.9 Hz, 1H), 6.47 (t, *J* = 3.3 Hz, 1H), 2.36 (s, 3H), 2.07-1.95 (m, 2H), 1.84 - 1.76 (m, 2H), 1.69-1.55 (m, 4H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.2, 142.6, 124.0, 120.9, 120.7,

117.3, 115.1, 113.8, 112.5, 111.1, 56.3, 34.3, 24.5, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{17}H_{19}N_2O^+$) 267.1492, found 267.1494.



(*Z*)-*N*-butyl-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4c

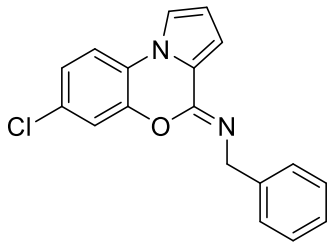
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (20:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 67.4−69.2°C; 44mg (yield = 87%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 – 7.29 (m, 2H), 7.03 (s, 1H), 6.98 (dd, *J* = 3.8, 1.5 Hz, 1H), 6.93 (d, *J* = 7.9 Hz, 1H), δ 6.50 – 6.45 (m, 1H) 3.61 (t, *J* = 7.2 Hz, 2H), 2.36 (s, 3H), 1.74 – 1.63 (m, 2H), 1.51 – 1.40 (m, 2H), 0.98 (t, *J* = 7.4 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.2, 143.1, 135.5, 124.1, 120.9, 120.5, 117.3, 115.2, 113.8, 112.6, 111.0, 45.6, 33.0, 201.0, 20.8, 14.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{16}H_{19}N_2O^+$) 255.1492, found 255.1492.



(*Z*)-N-benzyl-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4d

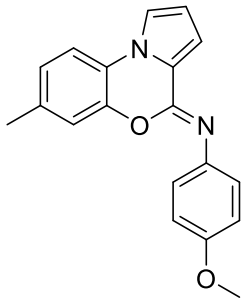
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 103.2−105.1°C; 53mg (yield = 92 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.49 (d, *J* = 7.5 Hz, 2H), 7.40 – 7.30 (m, 4H), 7.29 – 7.22 (m, 1H), 7.11 - 7.02 (m, 2H), 6.94 (d, *J* = 8.1 Hz, 1H), 6.51 (t, *J* = 3.3 Hz, 1H), 4.87 (s, 2H), 2.37 (s, 3H).**^{13}C NMR** (101 MHz, $CDCl_3$) δ 144.1, 142.9, 140.7, 135.7, 128.4, 127.9,

126.5, 124.3, 120.9, 120.4, 117.3, 115.4, 113.9, 112.8, 111.5, 49.7, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{22}H_{25}N_2O^+$)289.1335, found 289.1338.



(*Z*)-*N*-benzyl-7-chloro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4e

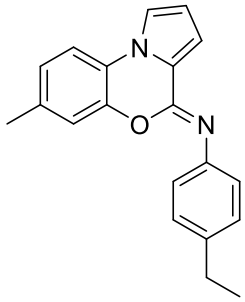
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 108.4−110.3°C 37mg (yield = 60 %).**^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.37 (d, *J* = 7.5 Hz, 2H), 7.30 – 7.22 (m, 4H), 7.17 (dd, *J* = 5.3, 3.7 Hz, 2H), 7.05 – 6.96 (m, 2H), 6.43 (t, *J* = 3.3 Hz, 1H), 4.75 (s, 2H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.5, 142.8, 140.3, 130.4, 128.4, 127.8, 126.6, 123.8, 122.1, 120.2, 117.4, 115.7, 115.0, 113.4, 112.2, 77.4, 77.1, 76.8, 49.7. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{18}H_{14}ClN_2O^+$)309.0789, found 309.0790.



(*Z*)-*N*-(4-methoxyphenyl)-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4f

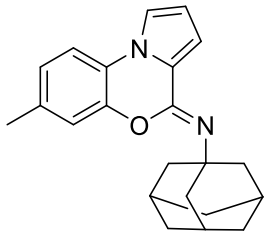
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a yellow oil; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum ether: EtOAc) as eluent furnished the product; 33mg (yield = 55%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.43 (dd, *J* = 2.8, 1.5 Hz, 1H), 7.38 (d, *J* = 8.3 Hz, 1H), 7.29 (d, *J* = 8.9 Hz, 2H), 7.20 – 7.14 (m, 1H), 6.99 (d, *J* = 6.5 Hz, 2H), 6.92 (d, *J* = 8.9 Hz, 2H), 6.58 (dd, *J* = 3.9, 2.8 Hz, 1H), 3.84 (s, 3H), 2.35 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 156.3, 142.7, 135.9,

124.8, 124.6, 121.2, 120.9, 120.4, 117.7, 116.1, 113.9, 113.8, 113.2, 112.5, 55.5, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{19}H_{17}N_2O_2^+$) 305.1285, found 305.1281.



(*Z*)-*N*-(4-ethylphenyl)-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4g

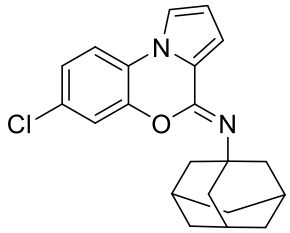
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a yellow solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (100:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 62.1−63.7°C; 27mg (yield = 45%). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.44 (dd, *J* = 2.8, 1.5 Hz, 1H), 7.37 (d, *J* = 8.2 Hz, 1H), 7.26 (s, 1H), 7.20 (s, 4H), 7.01 – 6.93 (m, 2H), 6.61 – 6.55 (m, 1H), 2.67 (q, *J* = 7.6 Hz, 2H), 2.33 (s, 3H), 1.28 (t, *J* = 7.6 Hz, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.7, 139.7, 135.9, 128.8, 128.0, 124.6, 123.4, 121.8, 120.9, 120.4, 120.1, 117.7, 116.1, 113.8, 113.2, 112.6, 110.3, 28.4, 20.9, 15.6. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{20}H_{19}N_2O^+$) 303.1492, found 303.1489.



(*Z*)-*N*-(adamantan-1-yl)-7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4h

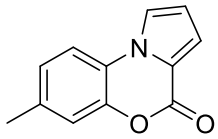
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 213.1−214.9°C; 56 mg (yield = 85 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.33 – 7.28 (m, 2H), 7.01 (d, *J* = 1.8 Hz, 1H), 6.96 – 6.88 (m, 2H), 6.45 (dd, *J* = 3.8, 2.8 Hz, 1H), 2.37 (s, 3H), 2.14 (s, 9H), 1.80 – 1.68 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 143.1, 140.1, 135.4, 123.9, 121.3, 120.9, 117.2, 115.0,

113.9, 112.5, 111.4, 54.9, 42.9, 36.8, 30.0, 21.0. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{22}H_{25}N_2O^+$)333.1961, found 333.1965.



(*Z*)-*N*-(adamantan-1-yl)-7-chloro-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-imine 4i

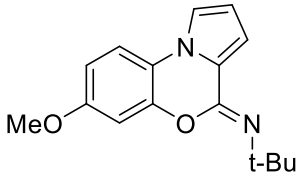
The title compound was prepared according to the general procedure A on a 0.2 mmol scale to obtain as a white solid; Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (10:1, Petroleum ether: EtOAc) as eluent furnished the product; M. p. 204.1−205.9°C; (4:1, Petroleum ether: EtOAc) 38 mg (yield = 55 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.36 (dd, *J* = 8.6, 1.8 Hz, 1H), 7.29-7.27 (m, 1H), 7.20 (d, *J* = 2.0 Hz, 1H), 7.09 (dd, *J* = 8.6, 2.2 Hz, 1H), 6.95 (dd, *J* = 3.6, 1.6 Hz, 1H), 6.48 (t, *J* = 3.3 Hz, 1H), 2.11 (s, 9H), 1.82 – 1.68 (m, 6H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 142.6, 137.6, 129.0, 122.3, 121.1, 120.1, 116.2, 114.2, 113.9, 112.1, 111.0, 76.3, 76.0, 75.7, 54.1, 41.9, 35.7, 28.9. **HRMS** (ESI, MeOH): calcd. For $[M+H]^+$($C_{21}H_{22}ClN_2O^+$)353.1415, found 353.1419.



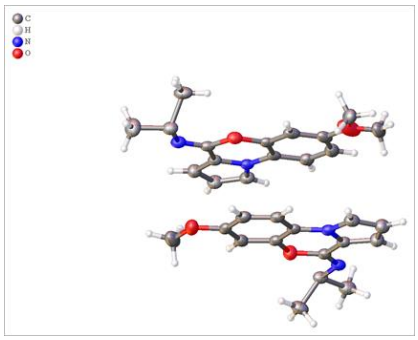
7-methyl-4*H*-benzo[*b*]pyrrolo[1,2-*d*][1,4]oxazin-4-one 5[1]

The title compound was prepared according to the general procedure B on a 0.5 mmol scale to obtain as a white solid. Purification of the residue on a silica gel column chromatography using petroleum ether/ethyl acetate (5:1, Petroleum ether: EtOAc) as eluent furnished the product; 79mg (yield = 80 %). **^{1}H NMR** (400 MHz, $CDCl_3$) δ 7.59 (dd, *J* = 2.7, 1.4 Hz, 1H), 7.47 (d, *J* = 8.3 Hz, 1H), 7.34 (dd, *J* = 4.0, 1.4 Hz, 1H), 7.17 (d, *J* = 1.8 Hz, 1H), 7.08 (dd, *J* = 8.2, 1.8 Hz, 1H), 6.66 (dd, *J* = 4.0, 2.7 Hz, 1H), 2.41 (s, 3H). **^{13}C NMR** (101 MHz, $CDCl_3$) δ 153.2, 141.9, 135.8, 124.5, 119.3, 117.5, 117.3, 116.3, 116.3, 112.9, 112.8, 20.0.

5. Crystallographic Data



3c



X-ray of **3c**

Figure 1. ORTEP of the molecular structure of **3c**

CCDC 2074200 contains the supplementary crystallographic data for compound **3c**

Empirical formula	C_8H_9NO
Formula weight	135.16
Temperature/K	120
Crystal system	monoclinic
Space group	C2/m
a/Å	22.5105(8)
b/Å	6.8064(2)
c/Å	20.6235(7)
α/°	90
β/°	117.1570(10)
γ/°	90
Volume/Å^3	2811.49(16)
Z	16
ρ_{calc}g/cm^3	1.277
μ/mm^{-1}	0.085
F(000)	1152
Crystal size/mm^3	0.32 × 0.09 × 0.05
Radiation	MoKα (λ = 0.71073)

2Θ range for data collection/°	4.068 to 54.994
Index ranges	-29 ≤ h ≤ 28, -8 ≤ k ≤ 8, -26 ≤ l ≤ 26
Reflections collected	21970
Independent reflections	3496 [R_{int} = 0.0733, R_{sigma} = 0.0440]
Data/restraints/parameters	3496/0/243
Goodness-of-fit on F^2	1.018
Final R indexes [I>=2σ (I)]	R_1 = 0.0555, wR_2 = 0.1228
Final R indexes [all data]	R_1 = 0.0923, wR_2 = 0.1449
Largest diff. peak/hole / e $Å^{-3}$ 0.40/-0.28	

These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via

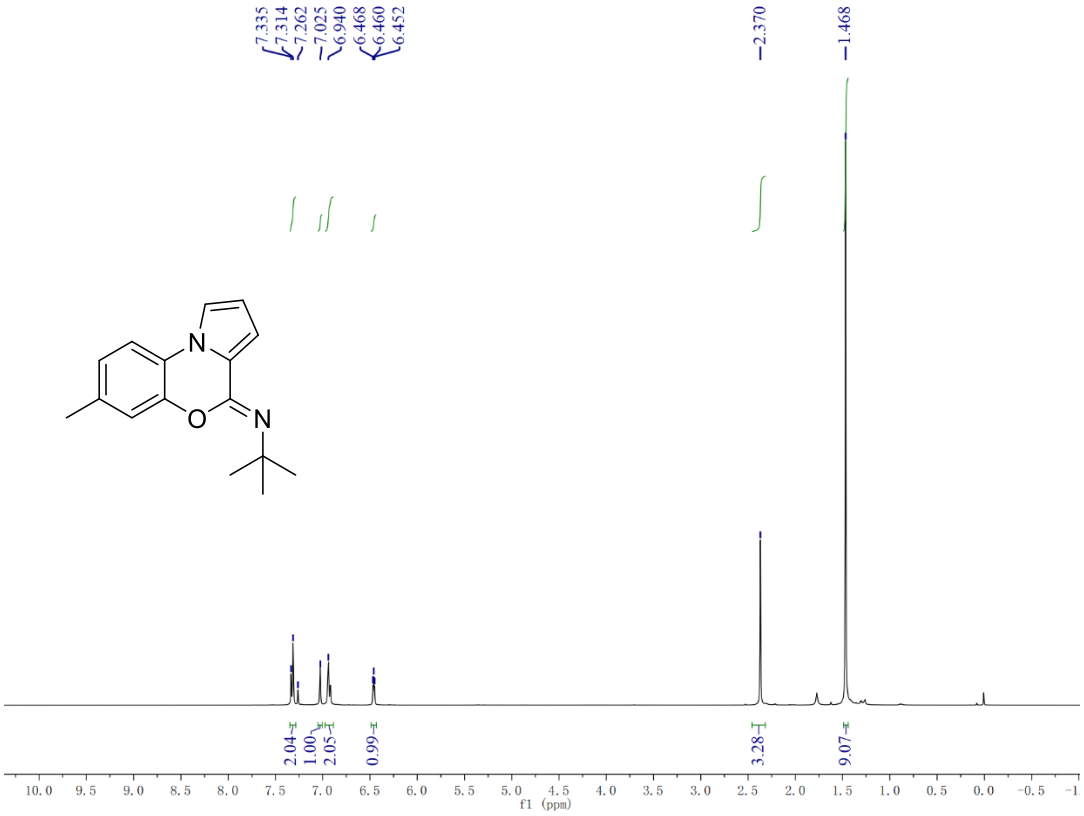
www.ccdc.cam.ac.uk/data_request/cif

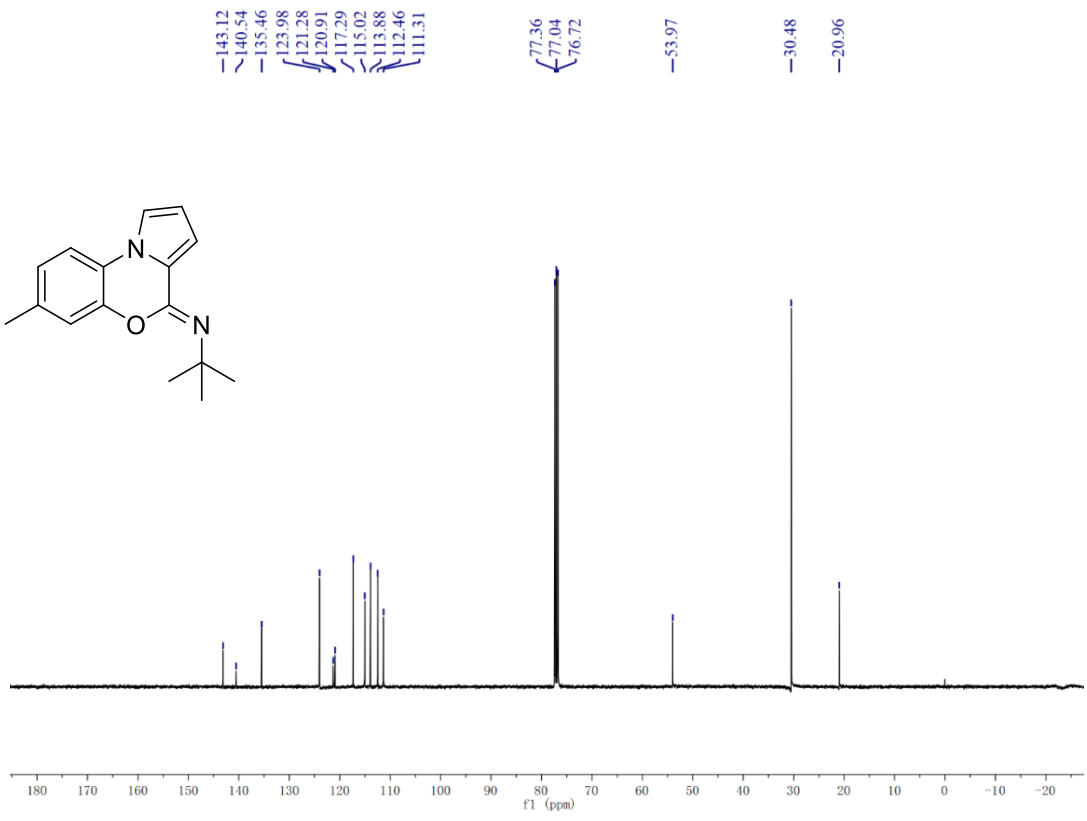
6. References

(1) L. Fu, S. D. Li, Z. H. Cai, Y. Z. Ding, X. Q. Guo, L. P. Zhou and G. Li, *Nature Catalysis*. 2018, **1**, 469–478.

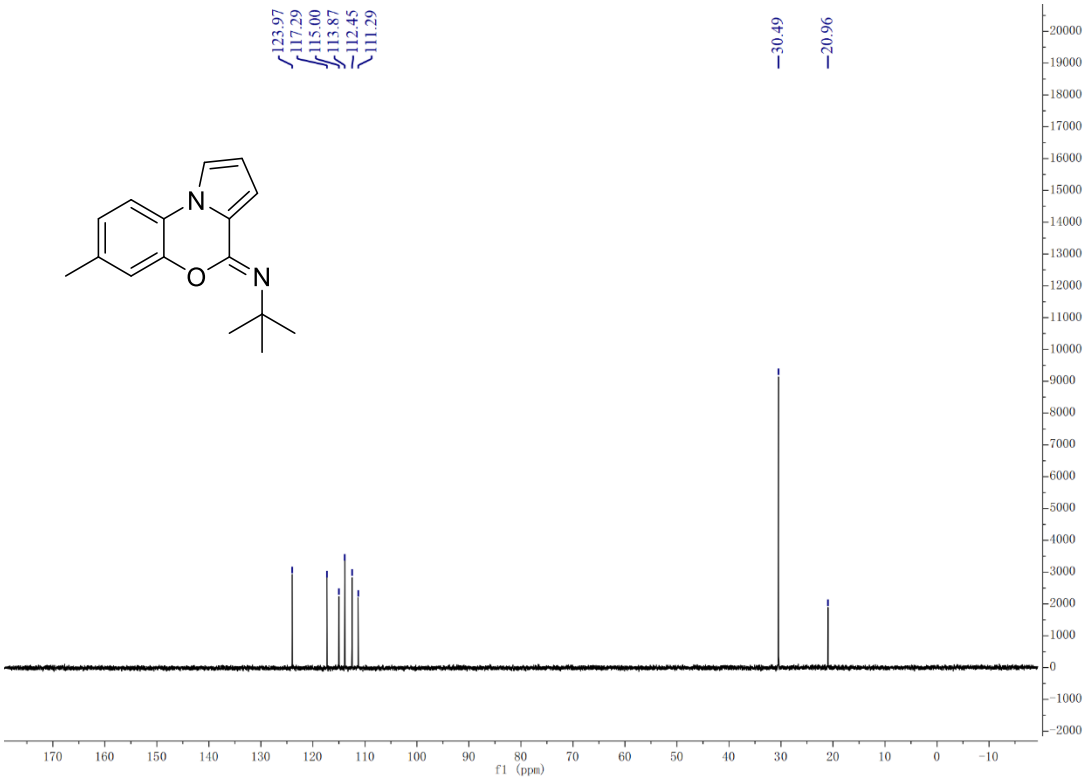
7. NMR spectra

^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3a**, Solvent: $CDCl_3$

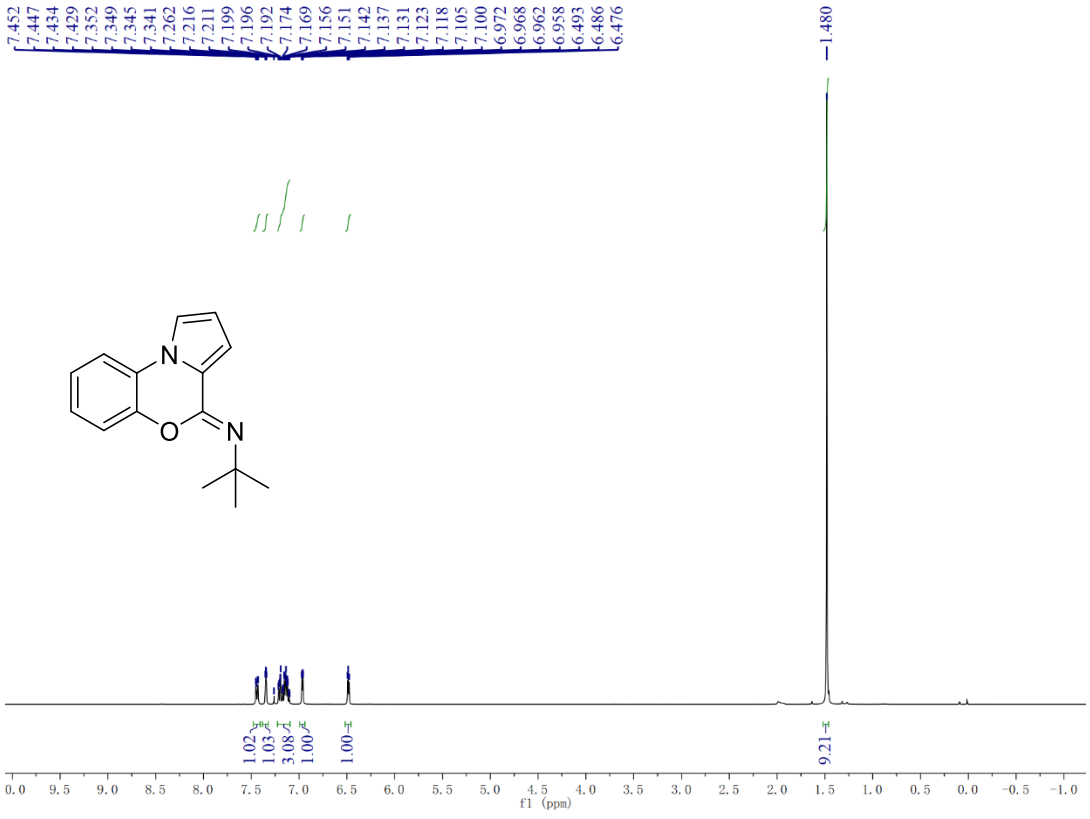


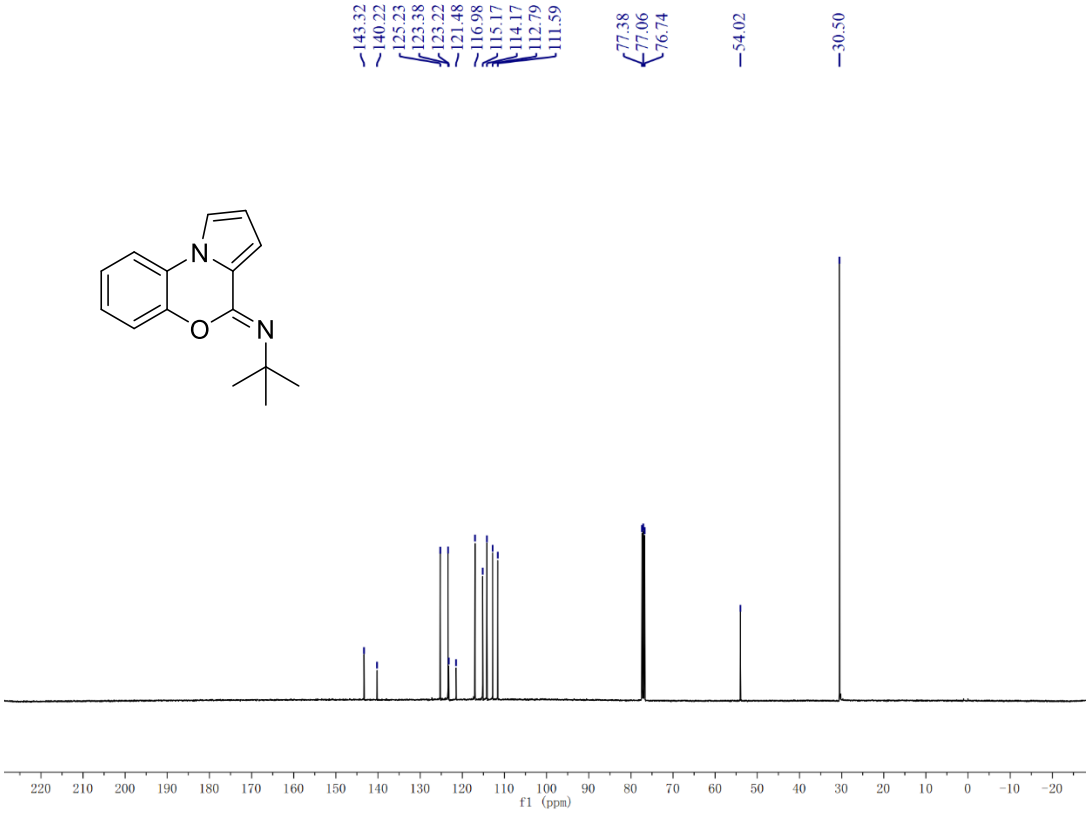


DEPT spectra of **3a**. Solvent: $CDCl_3$

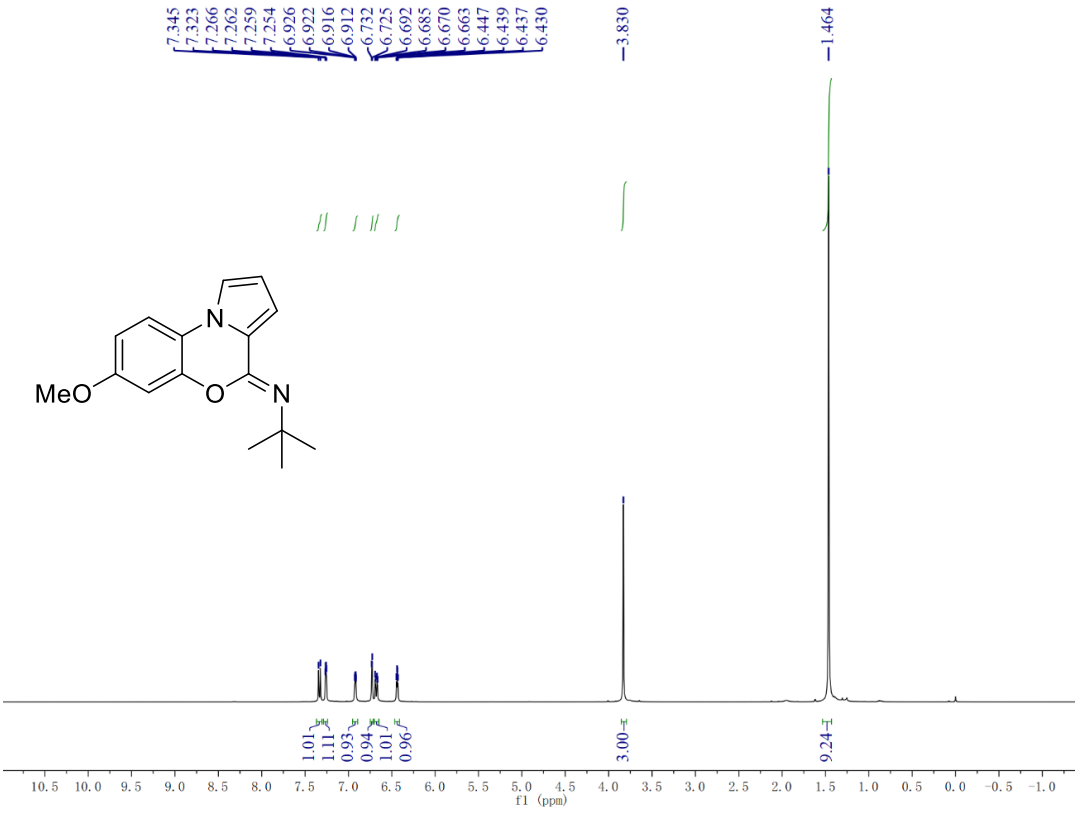


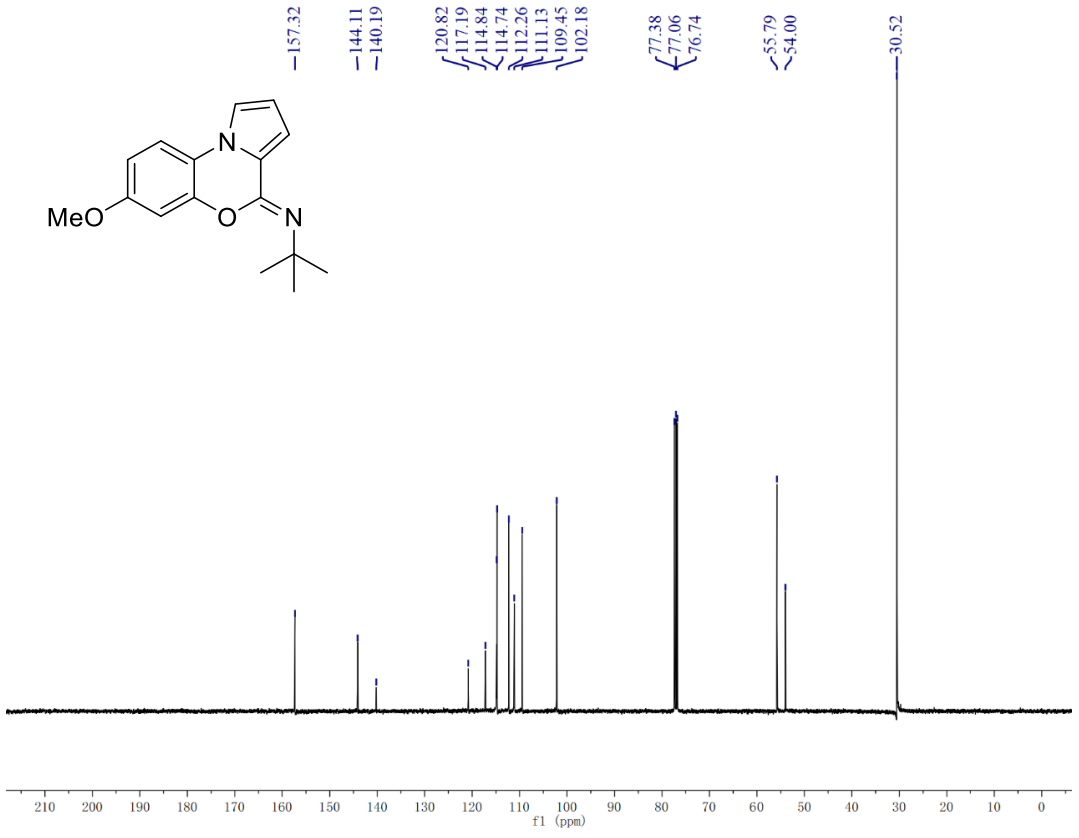
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3b**, Solvent: $CDCl_3$



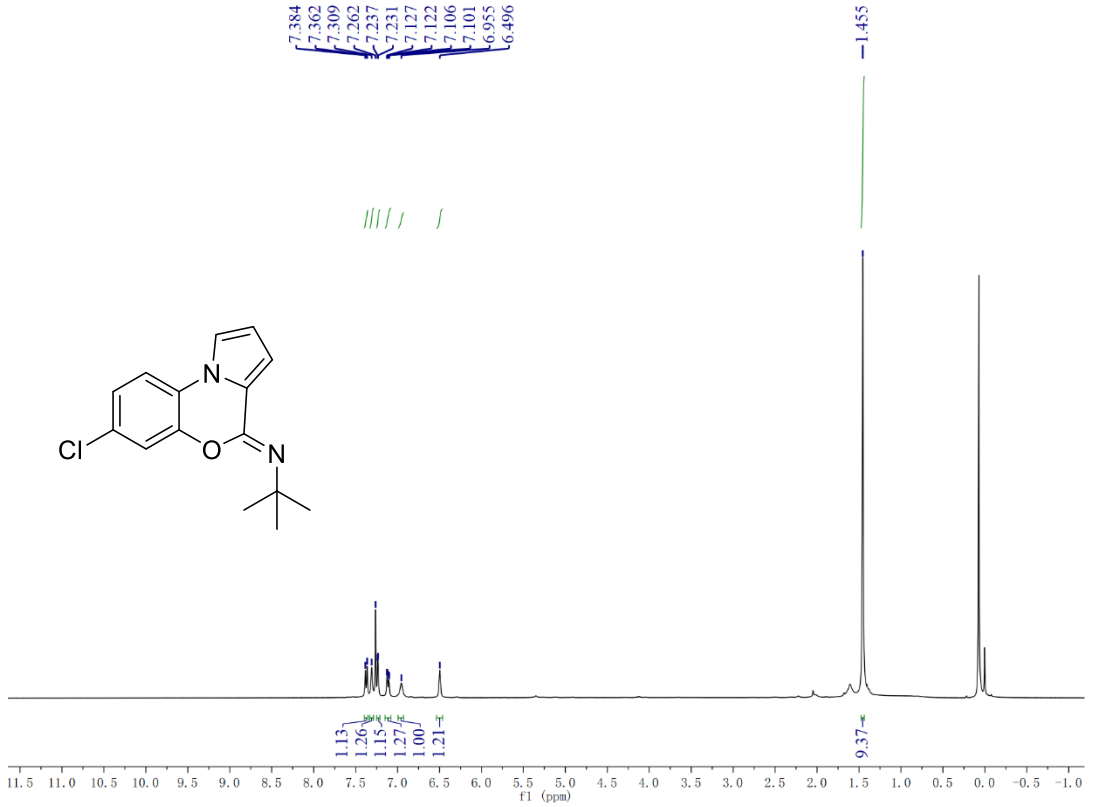


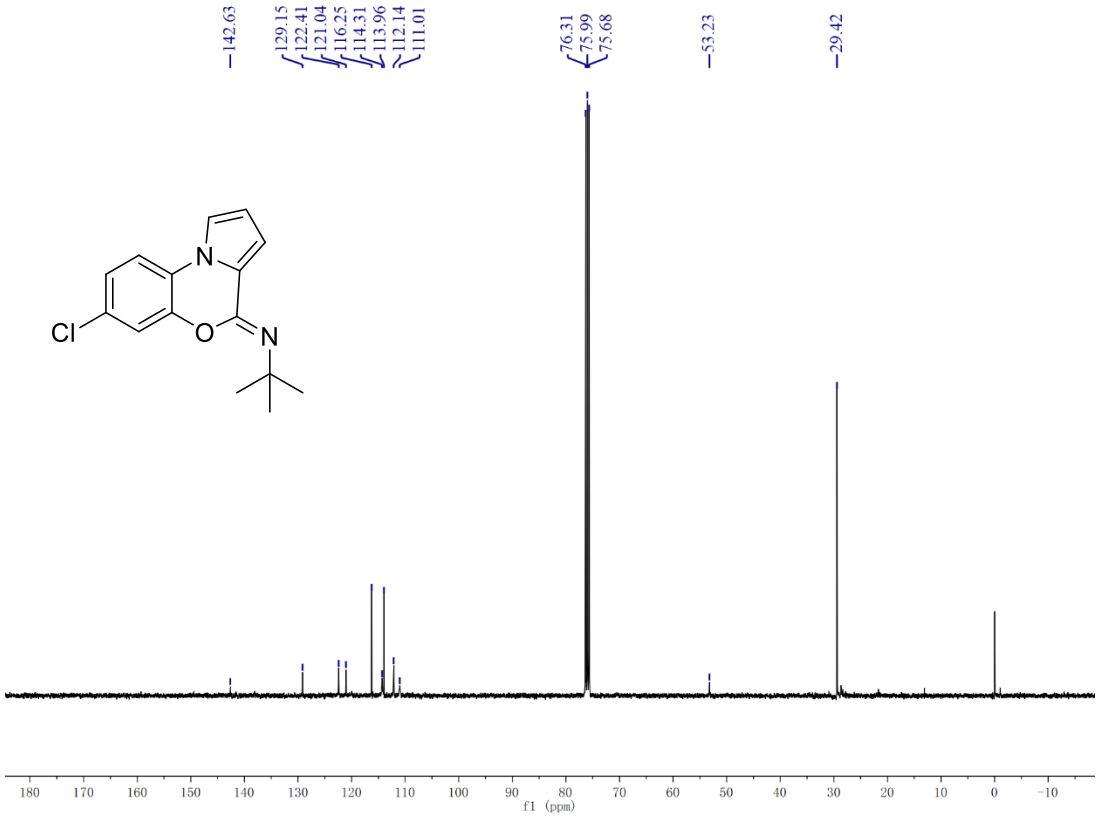
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3c**, Solvent: $CDCl_3$



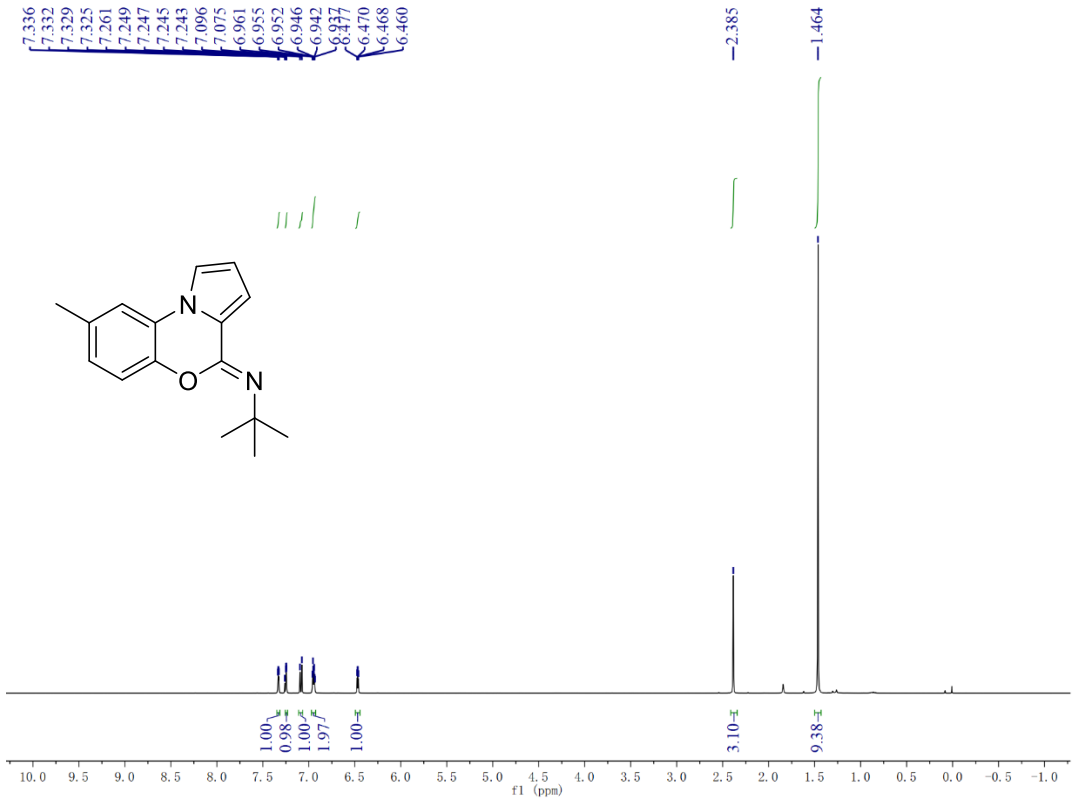


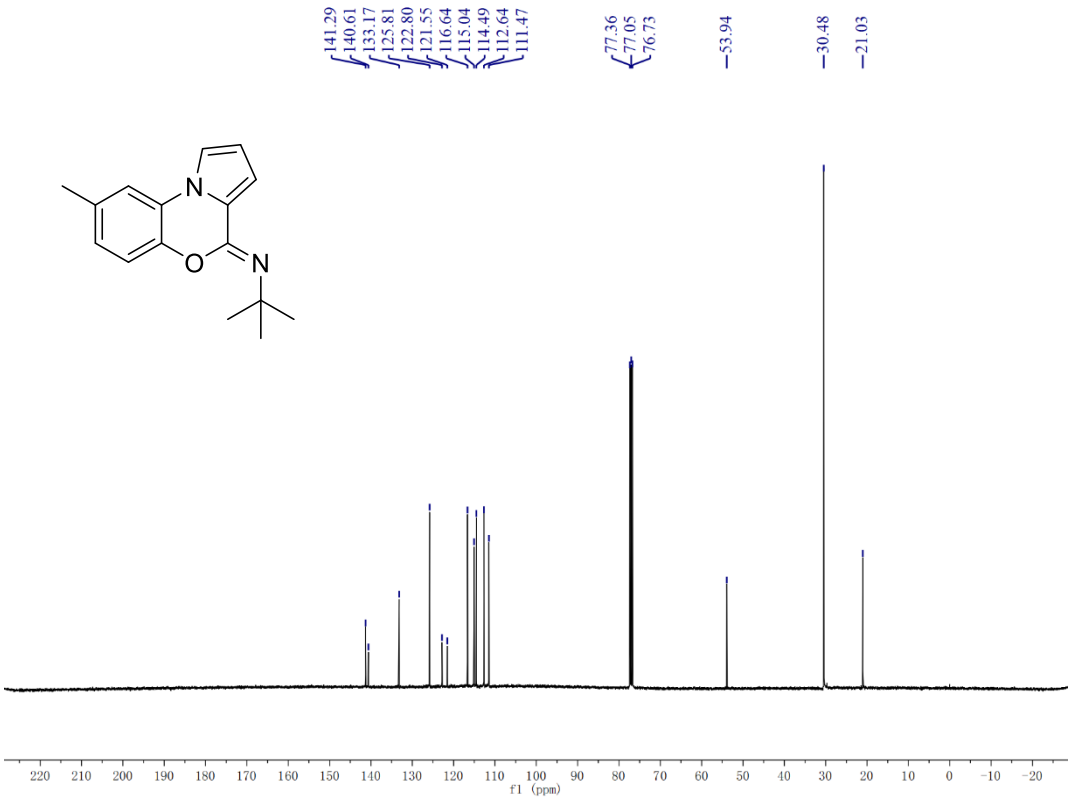
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **3d**, Solvent: $CDCl_3$



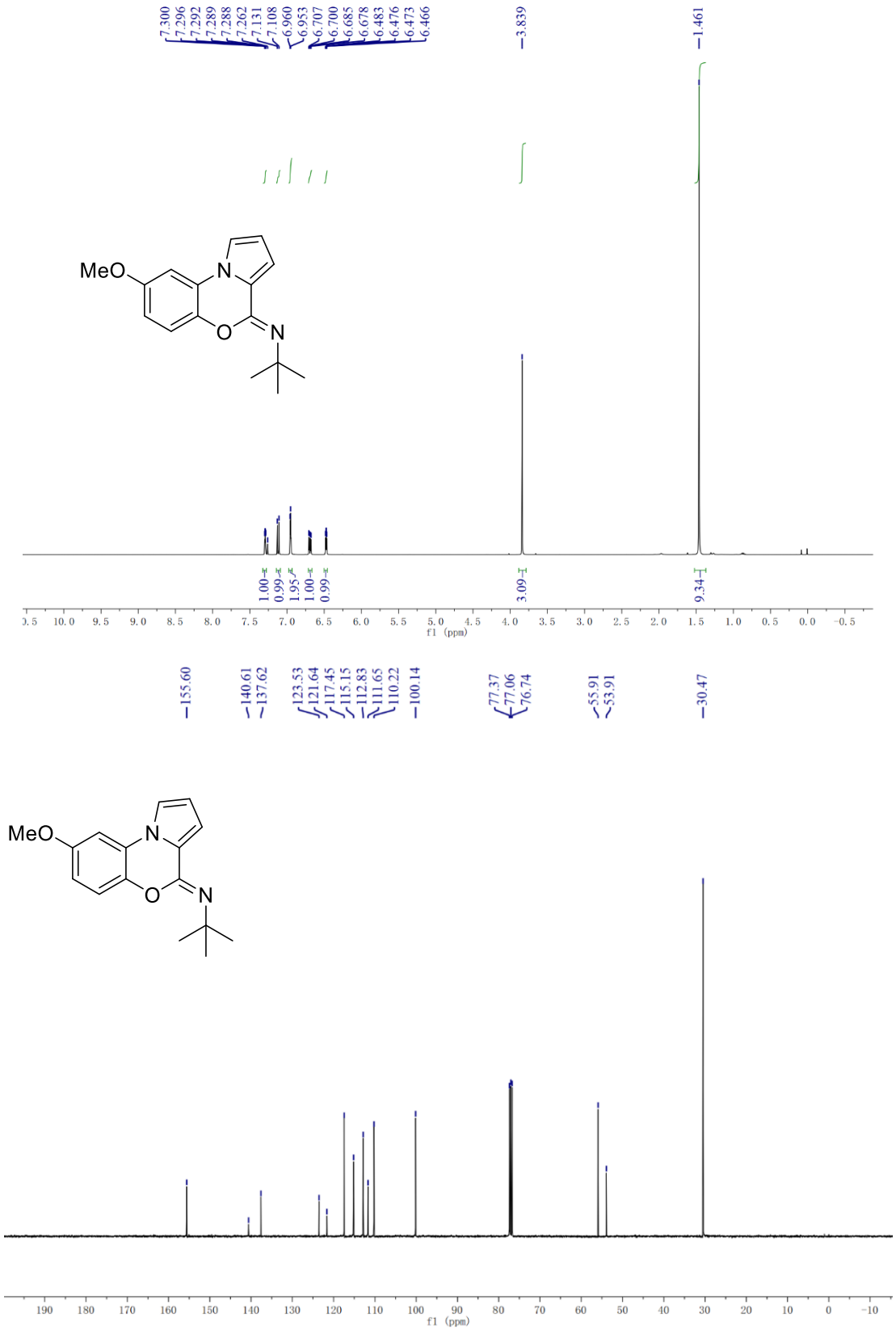


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **3e**, Solvent: $CDCl_3$

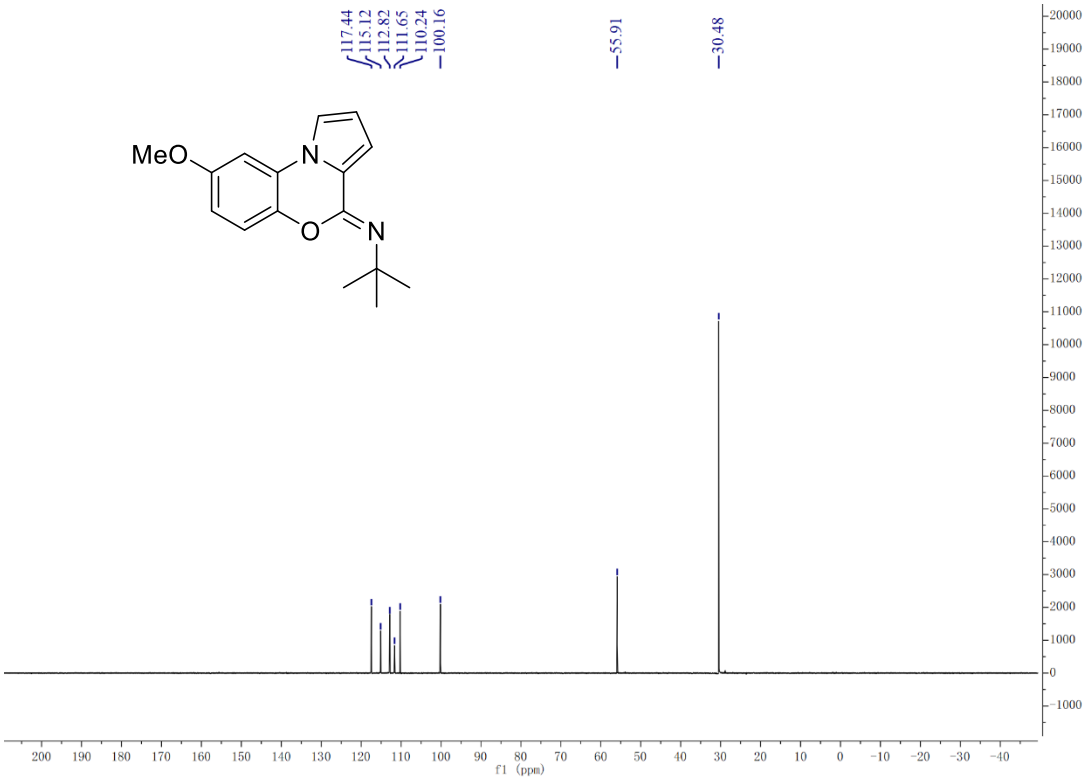




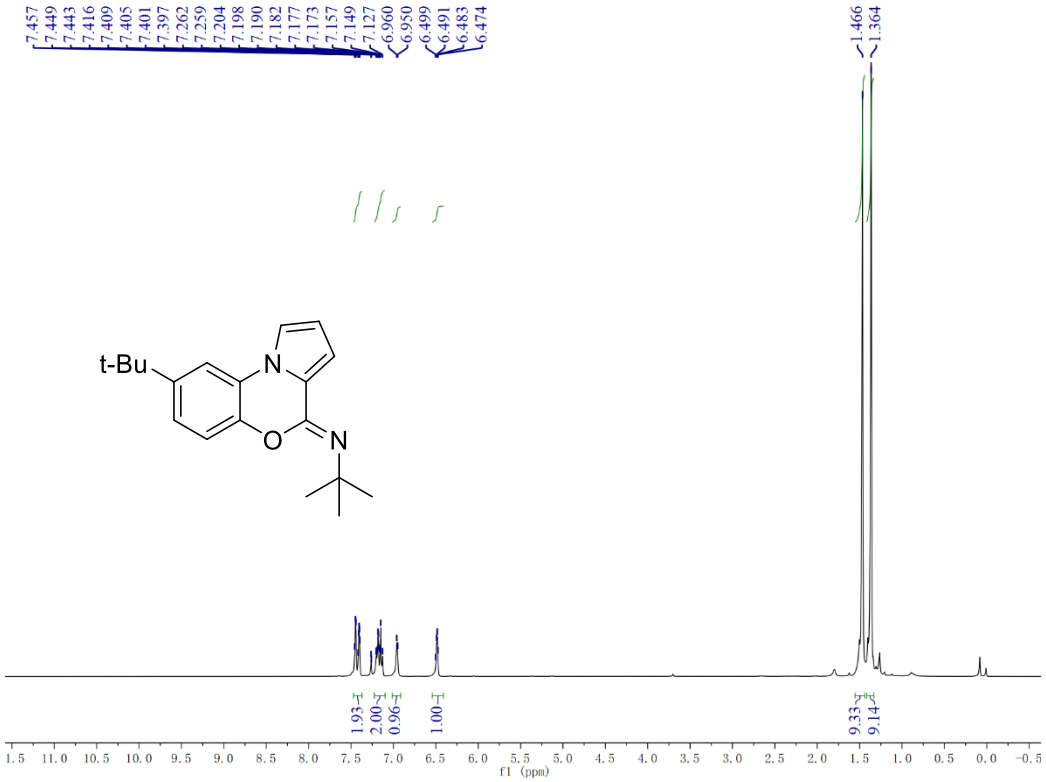
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3f**, Solvent: $CDCl_3$

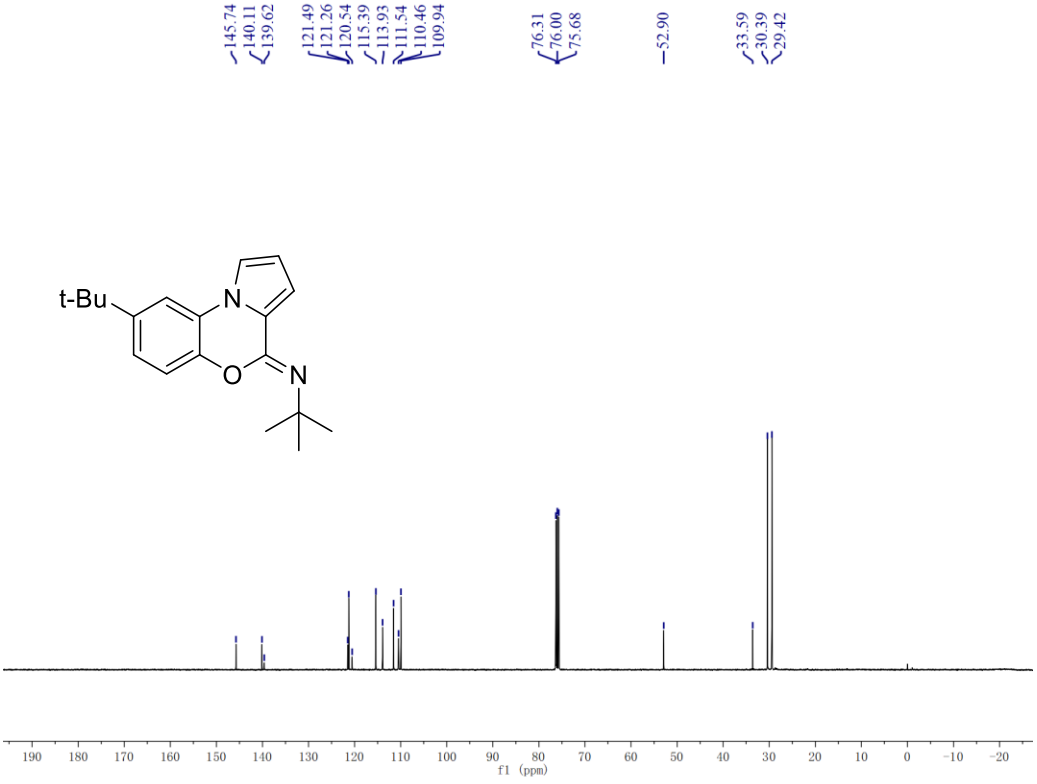


DEPT spectra of **3f**. Solvent: $CDCl_3$

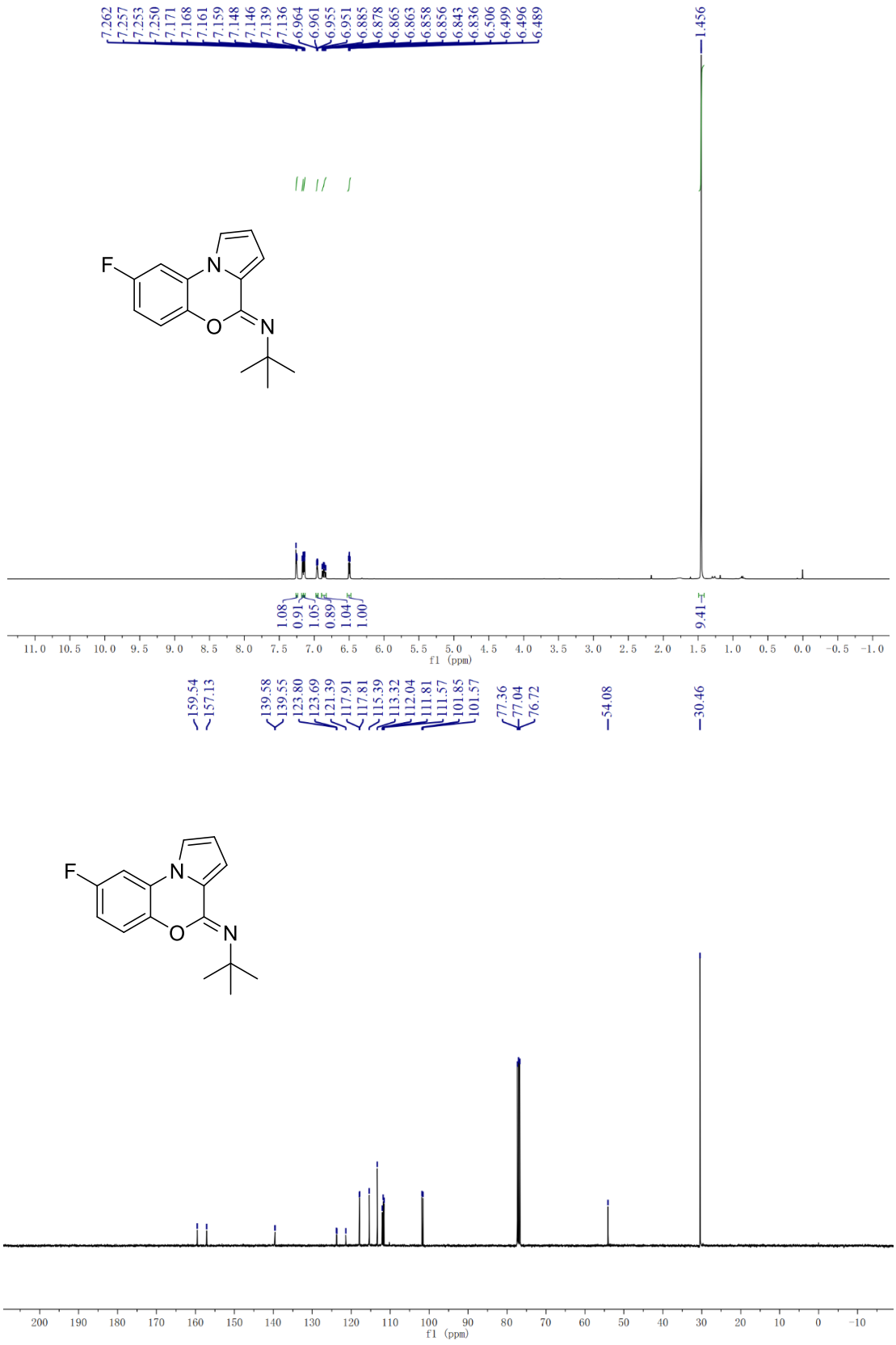


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3g**, Solvent: $CDCl_3$

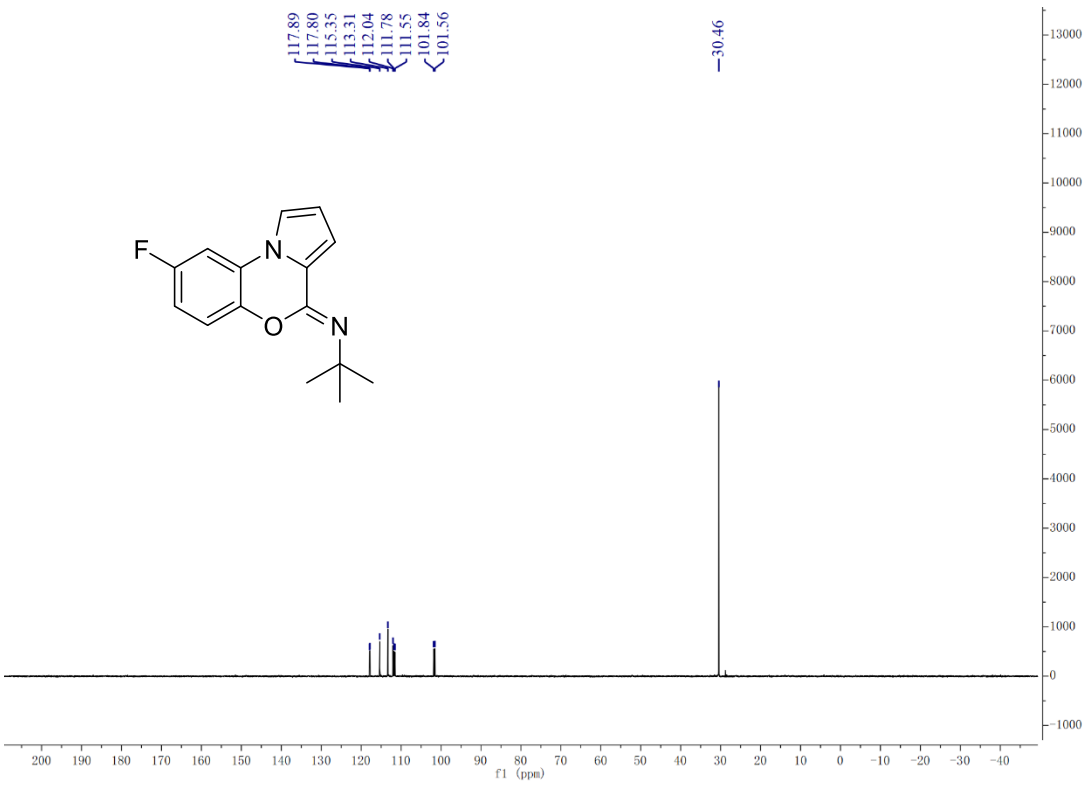




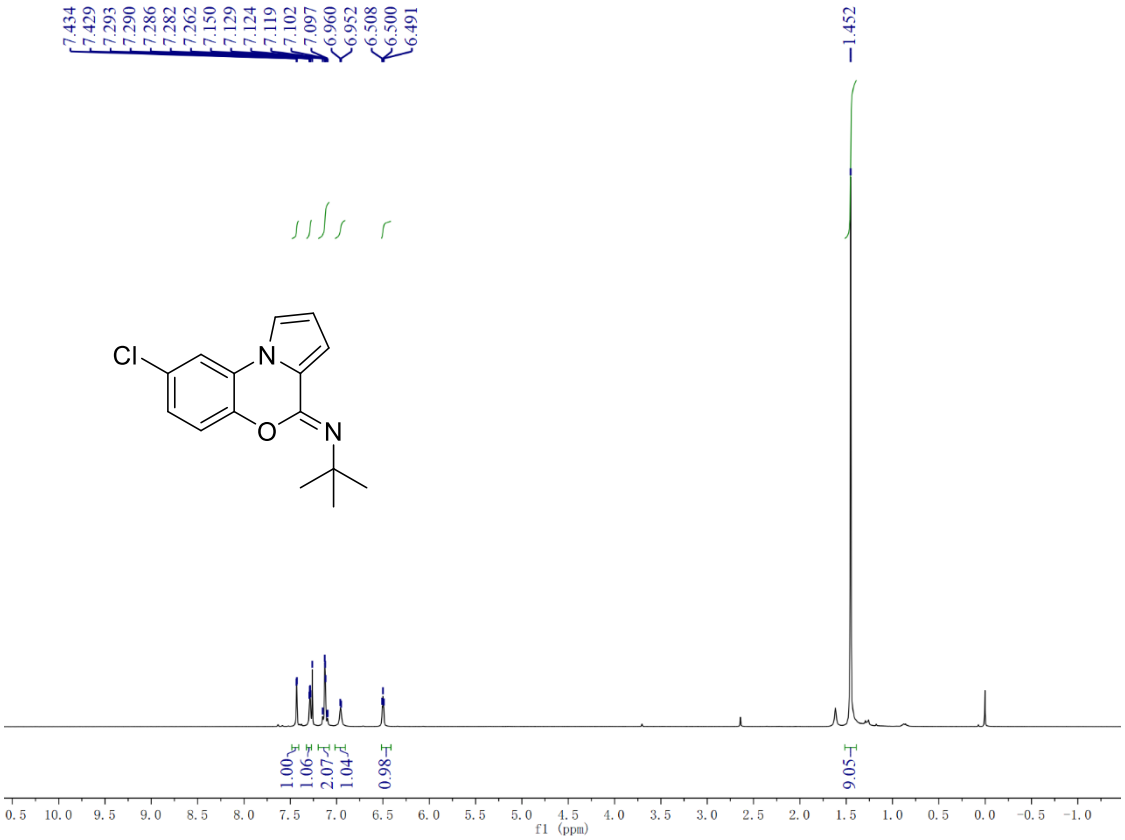
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3h**, Solvent: $CDCl_3$

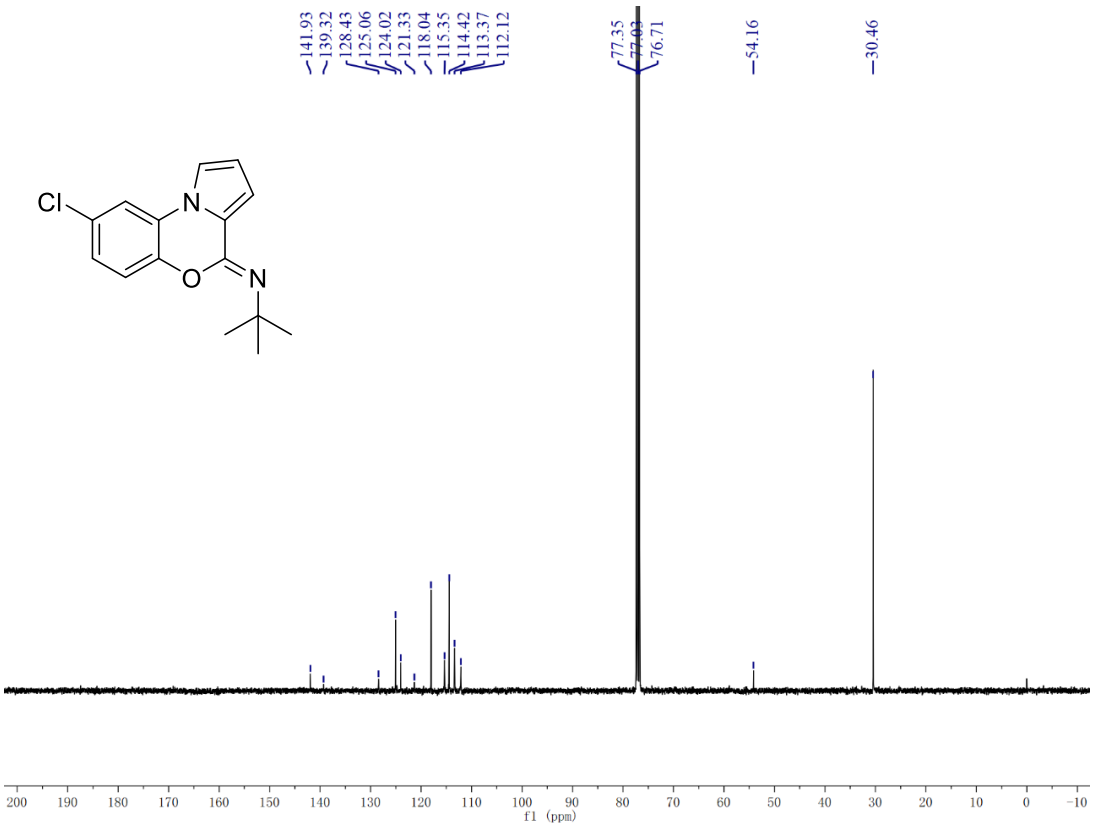


DEPT spectra of **3h**. Solvent: $CDCl_3$

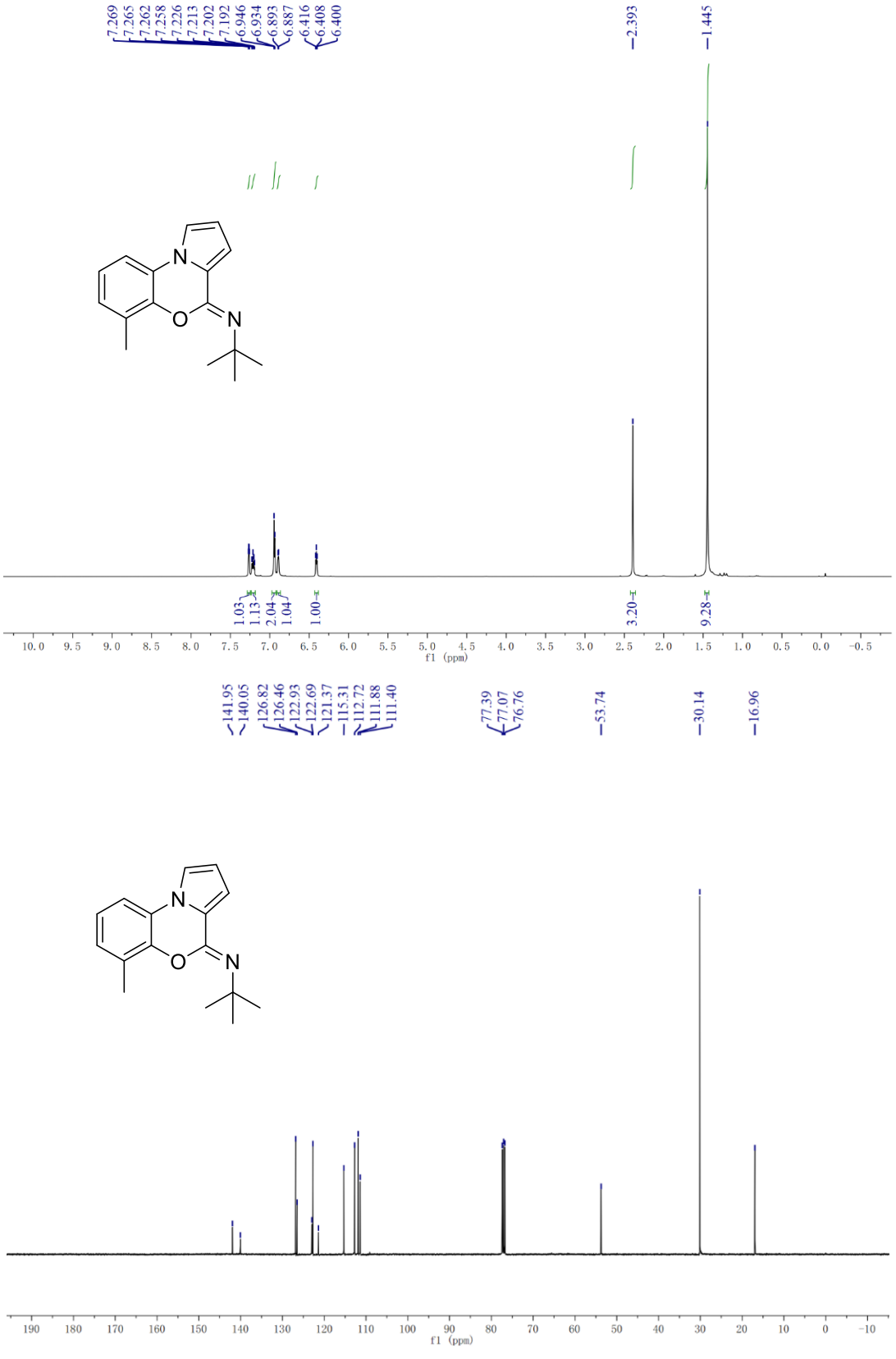


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3i**, Solvent: $CDCl_3$

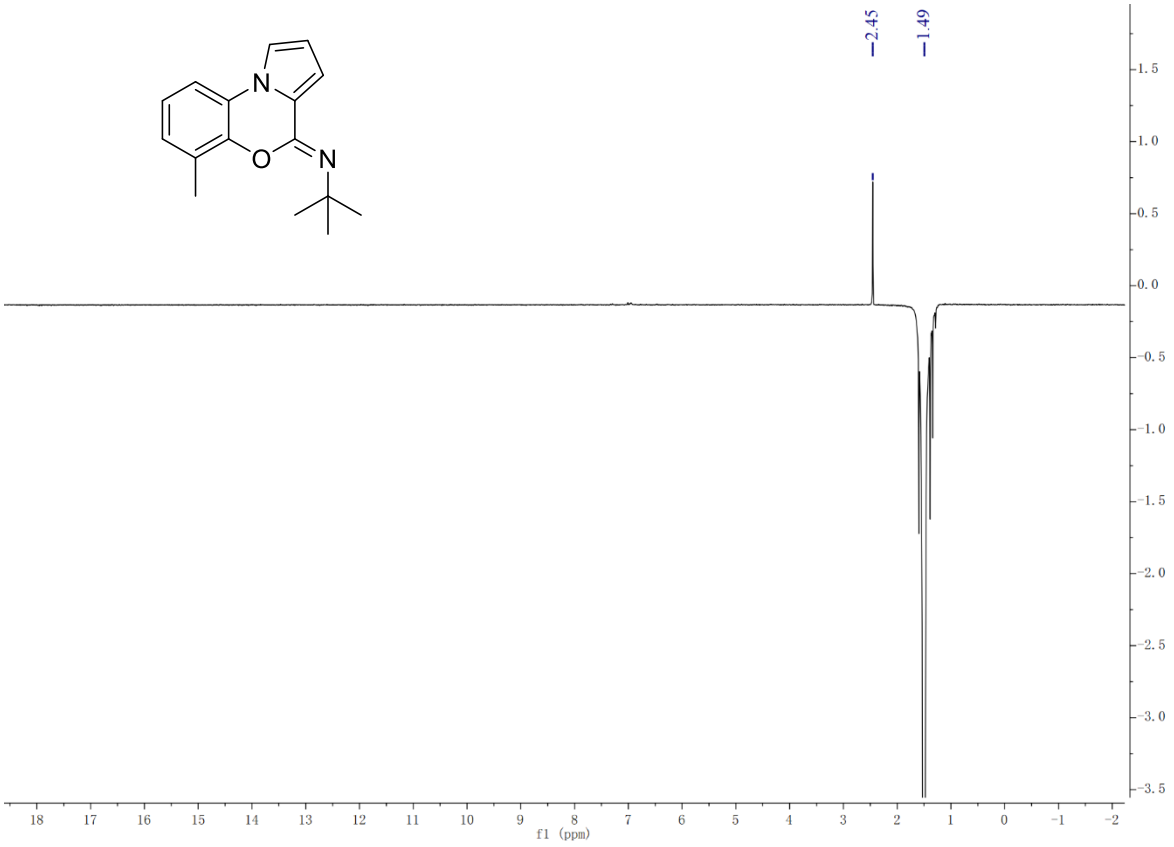


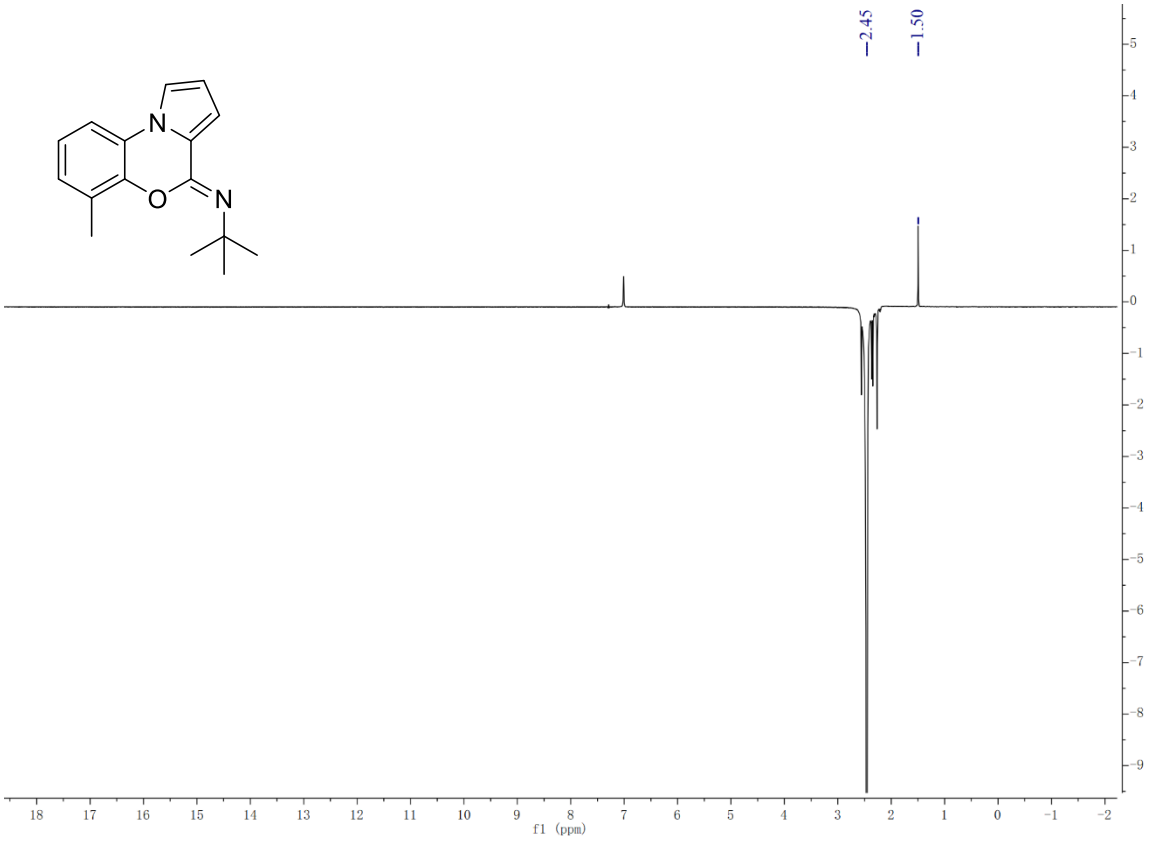


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3k**, Solvent: $CDCl_3$

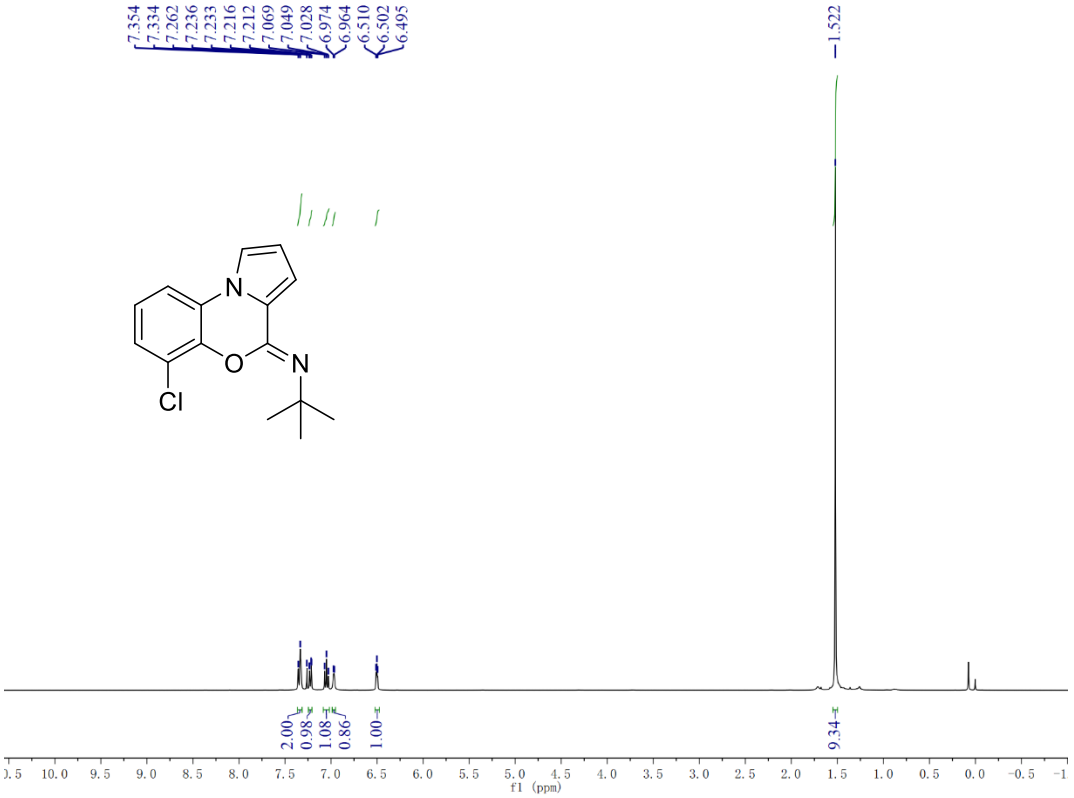


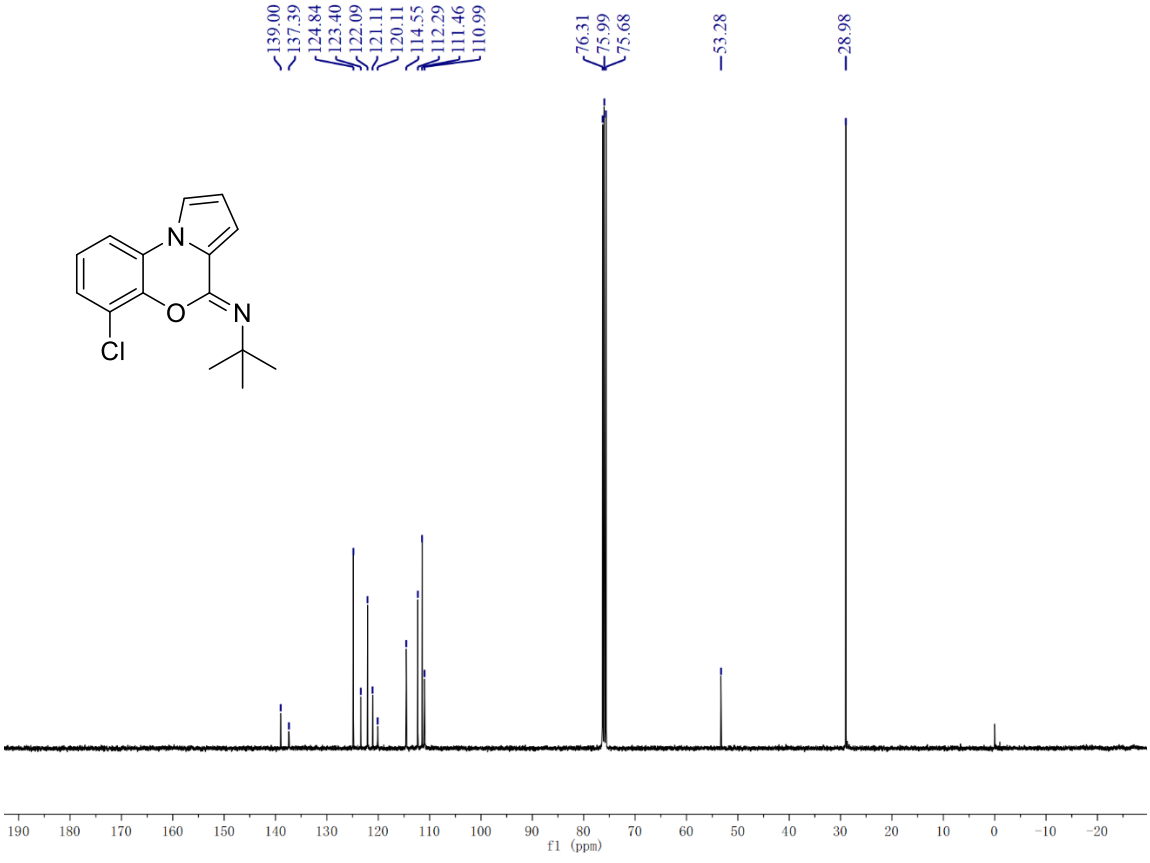
NOEDS of **3k.** Solvent: $CDCl_3$



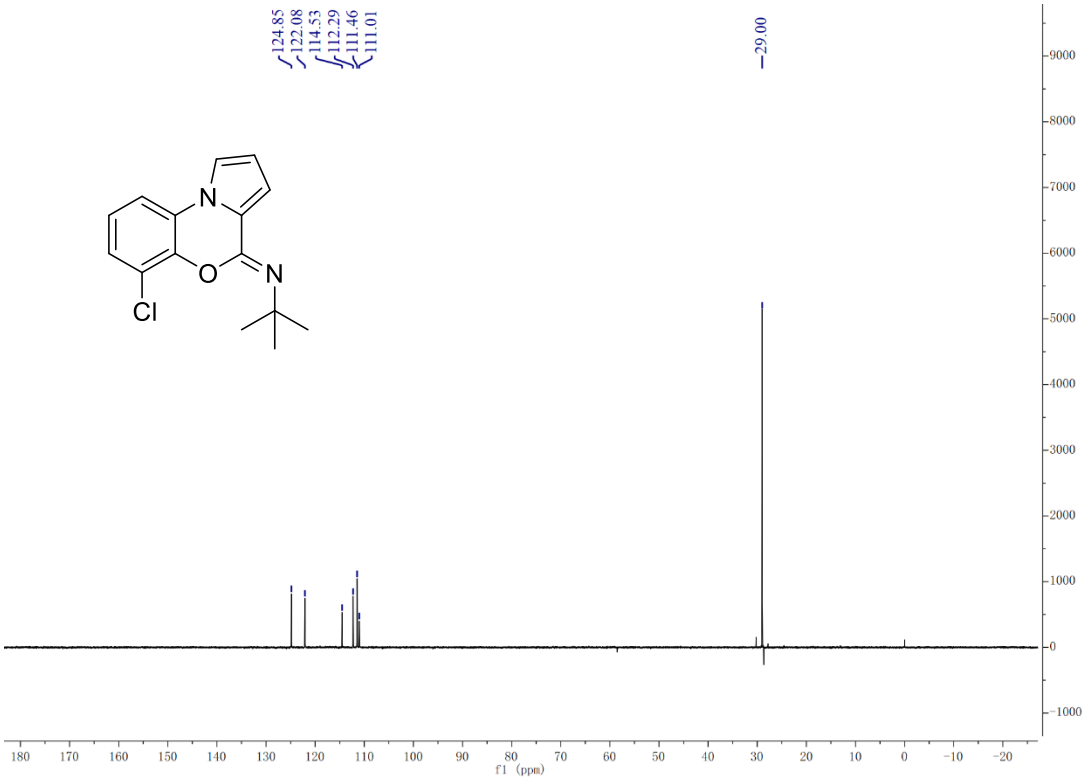


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **3l**, Solvent: $CDCl_3$

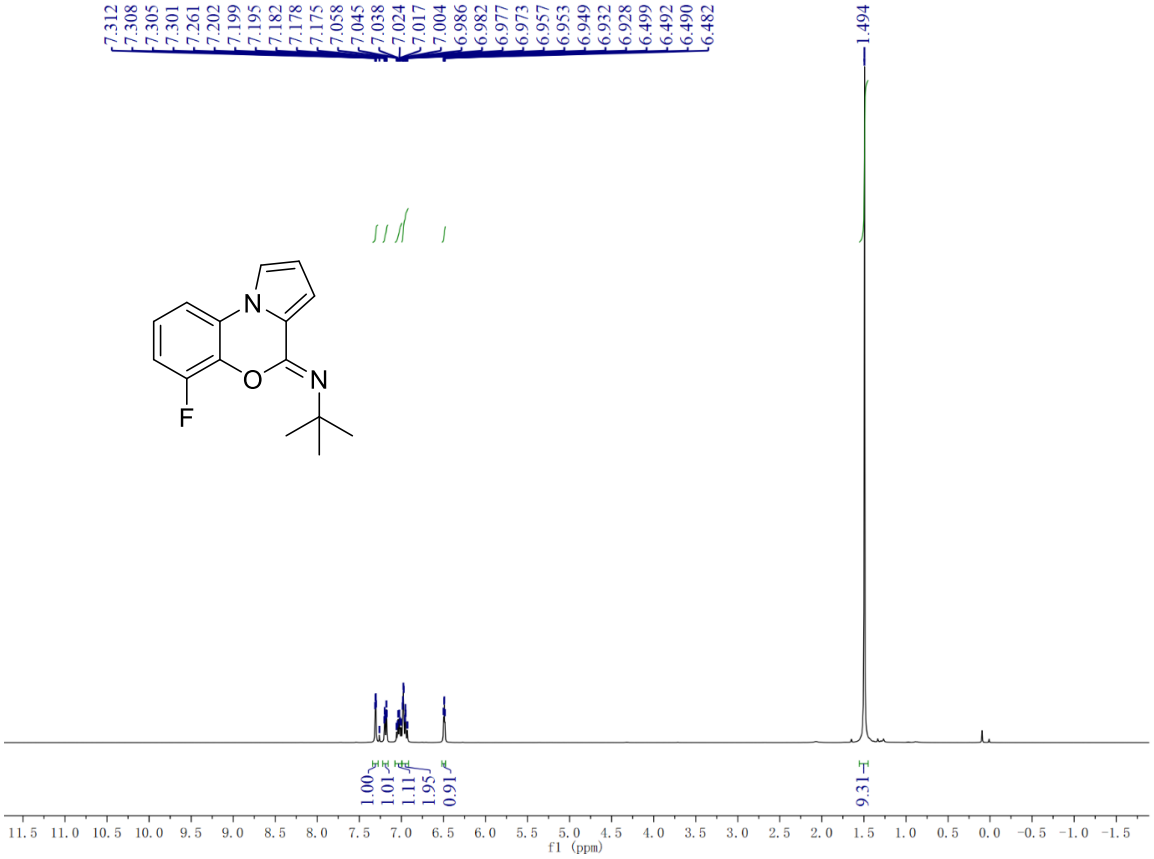


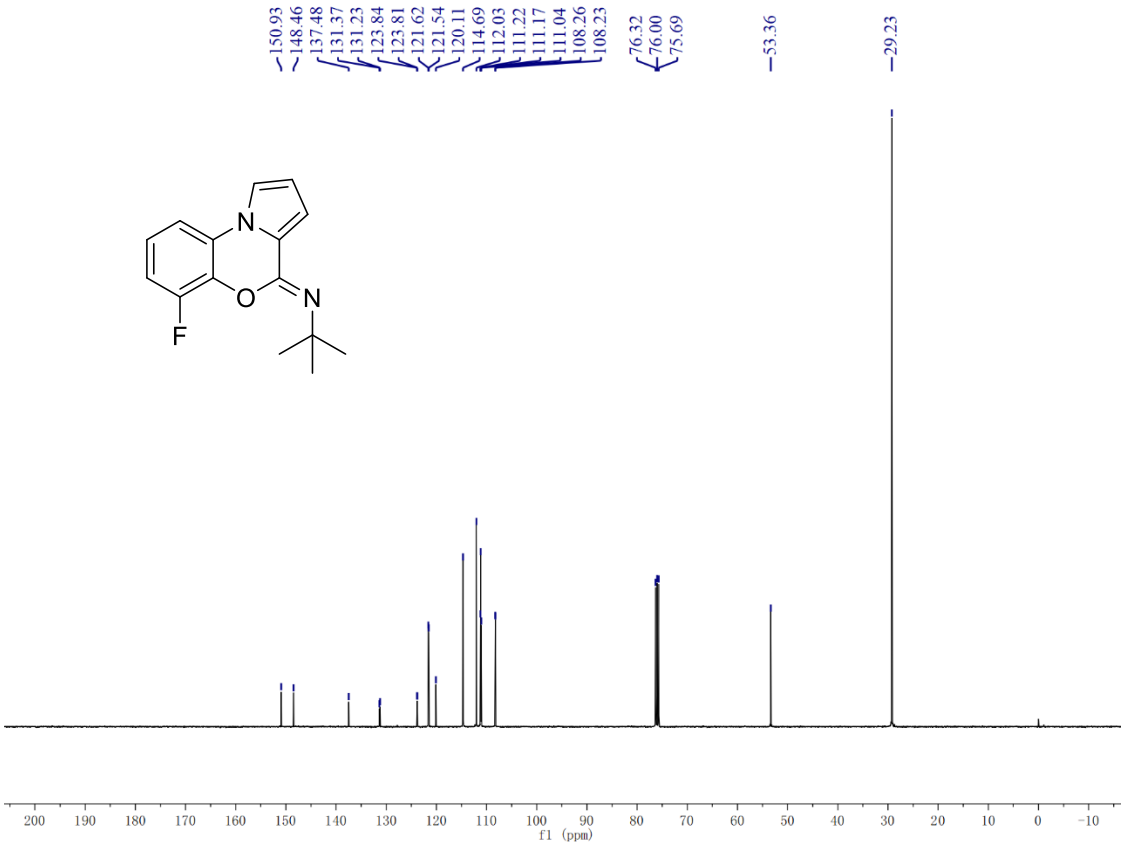


DEPT spectra of **3l.** Solvent： $CDCl_3$

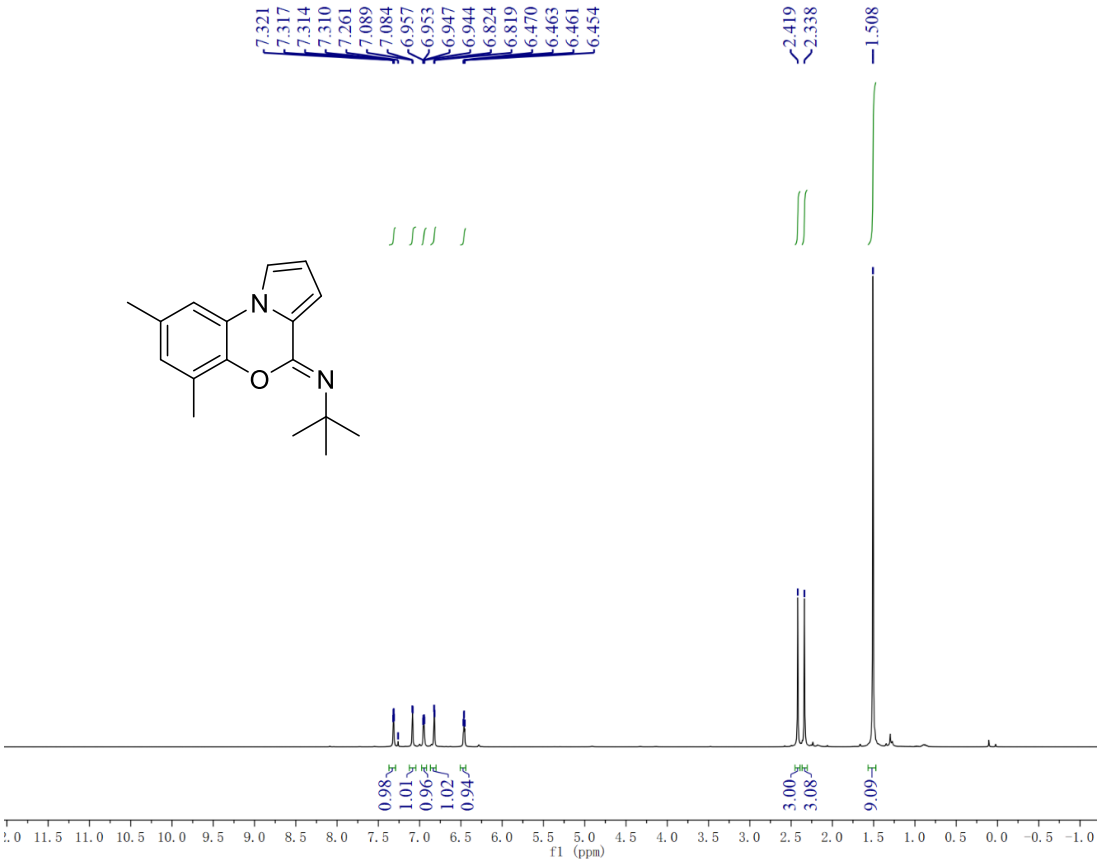


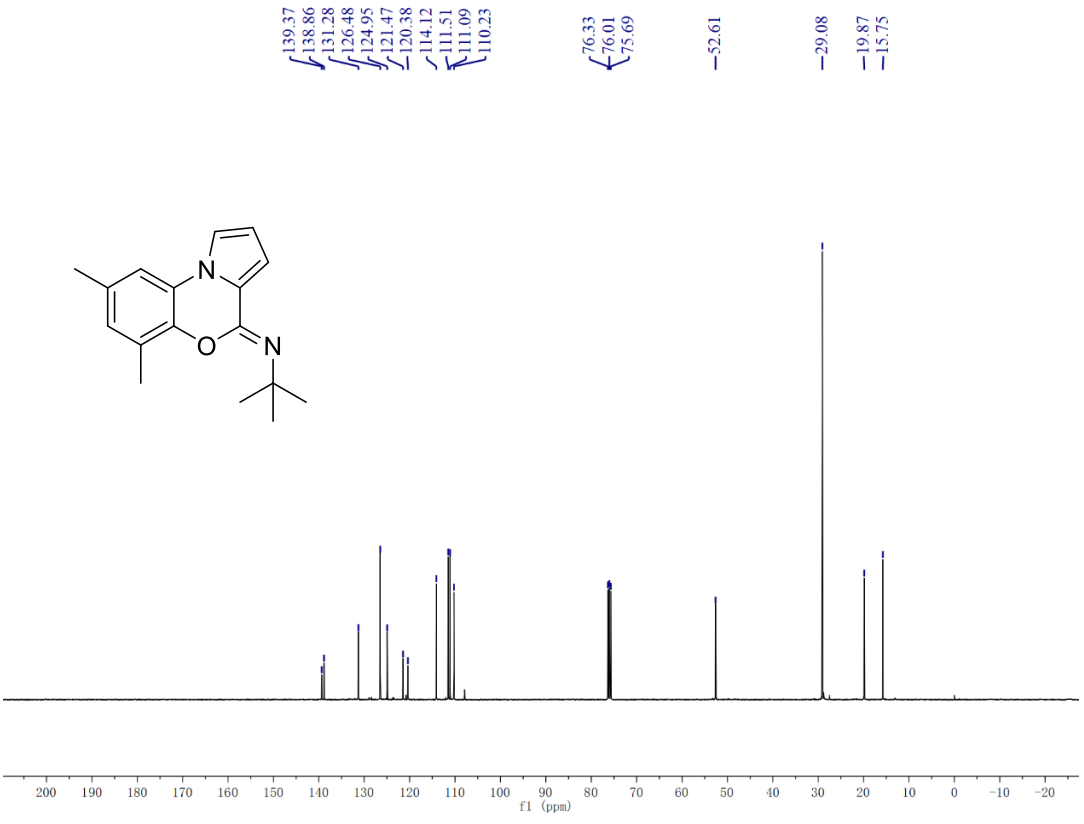
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3m**, Solvent: $CDCl_3$



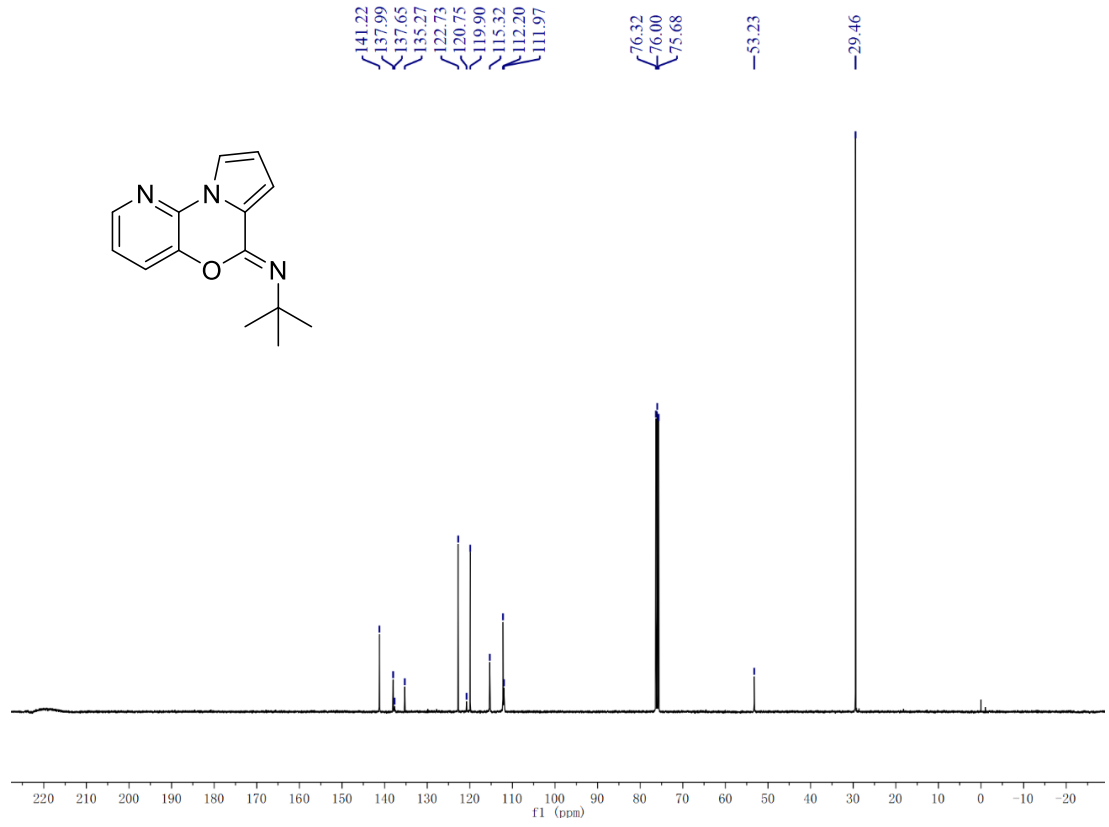


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3n**, Solvent: $CDCl_3$



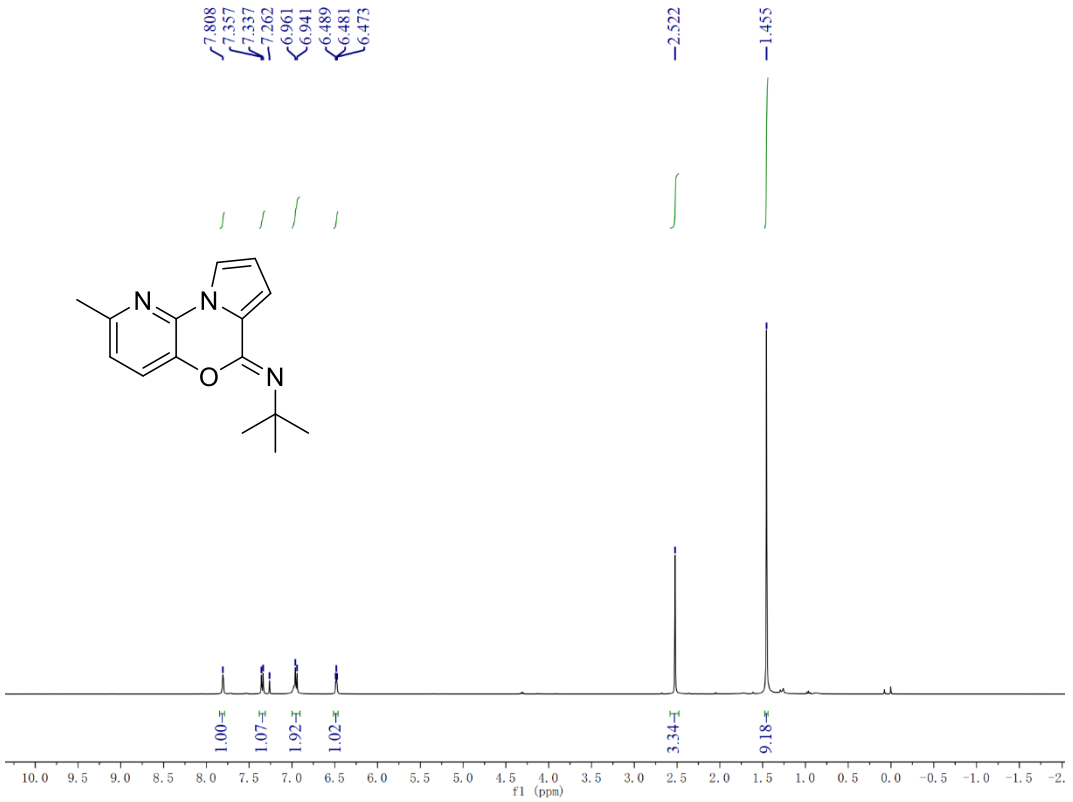


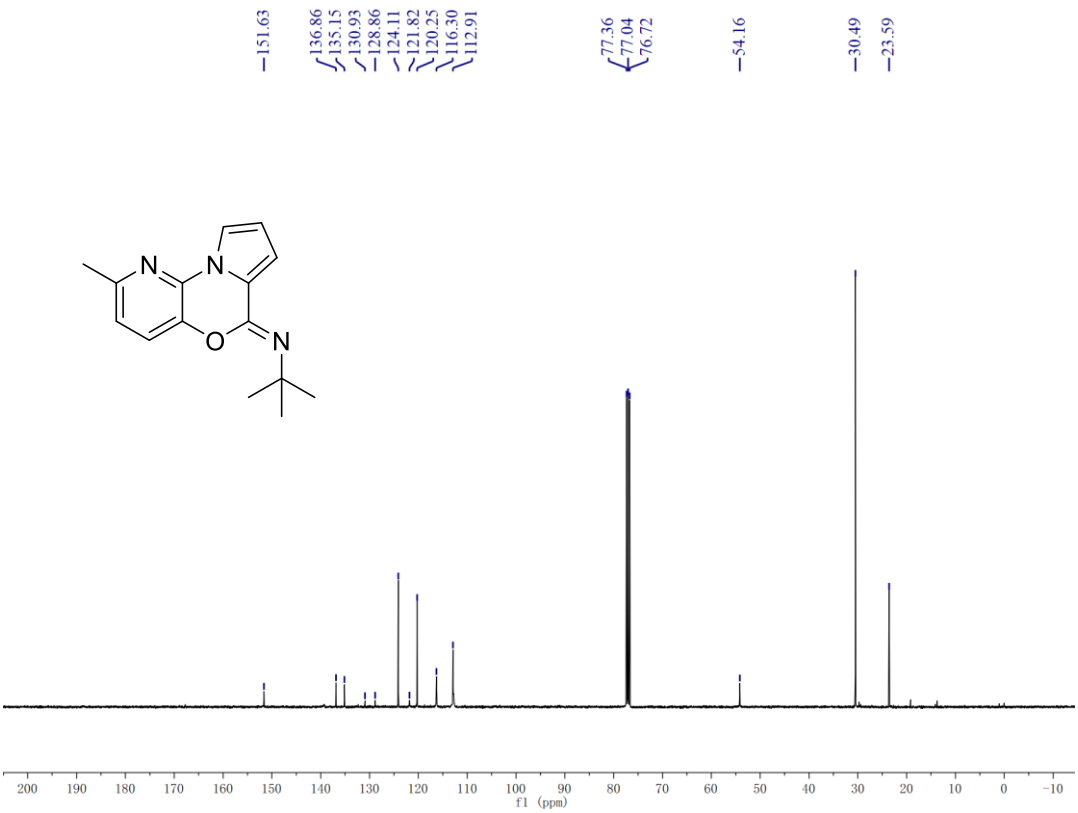
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3o**, Solvent: $CDCl_3$



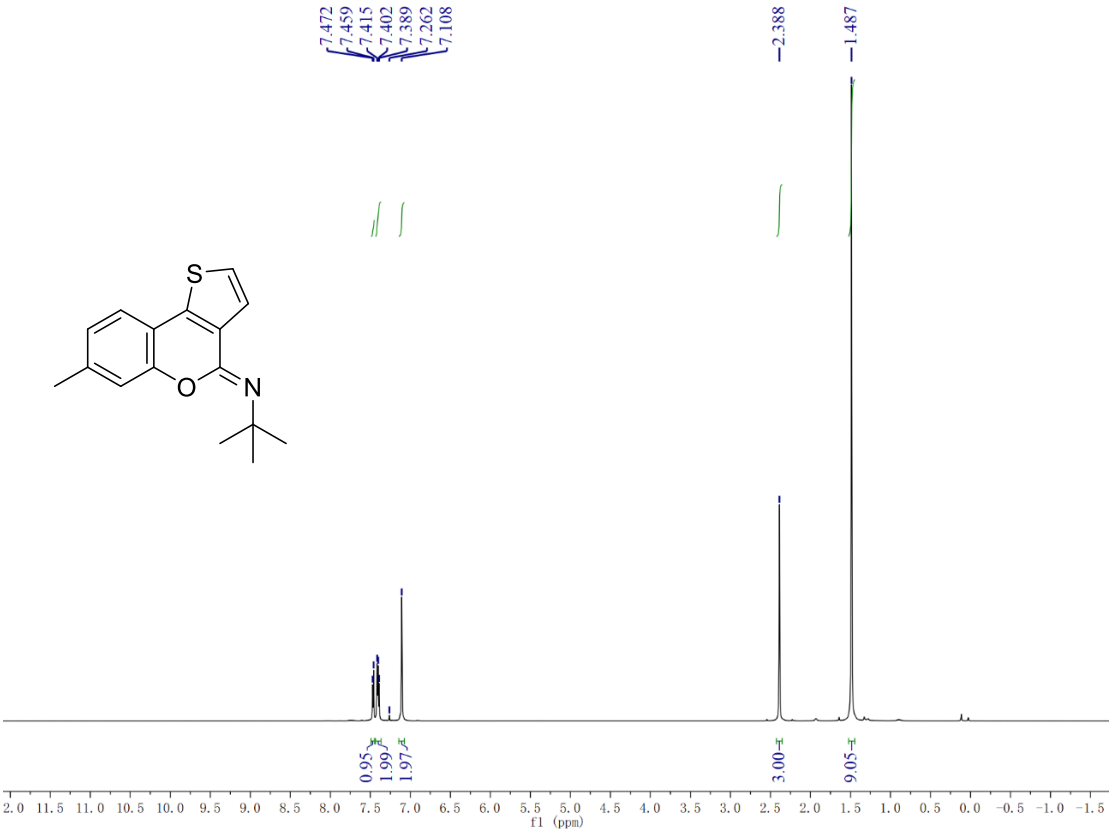
DEPT spectra of **3o.** Solvent： $CDCl_3$

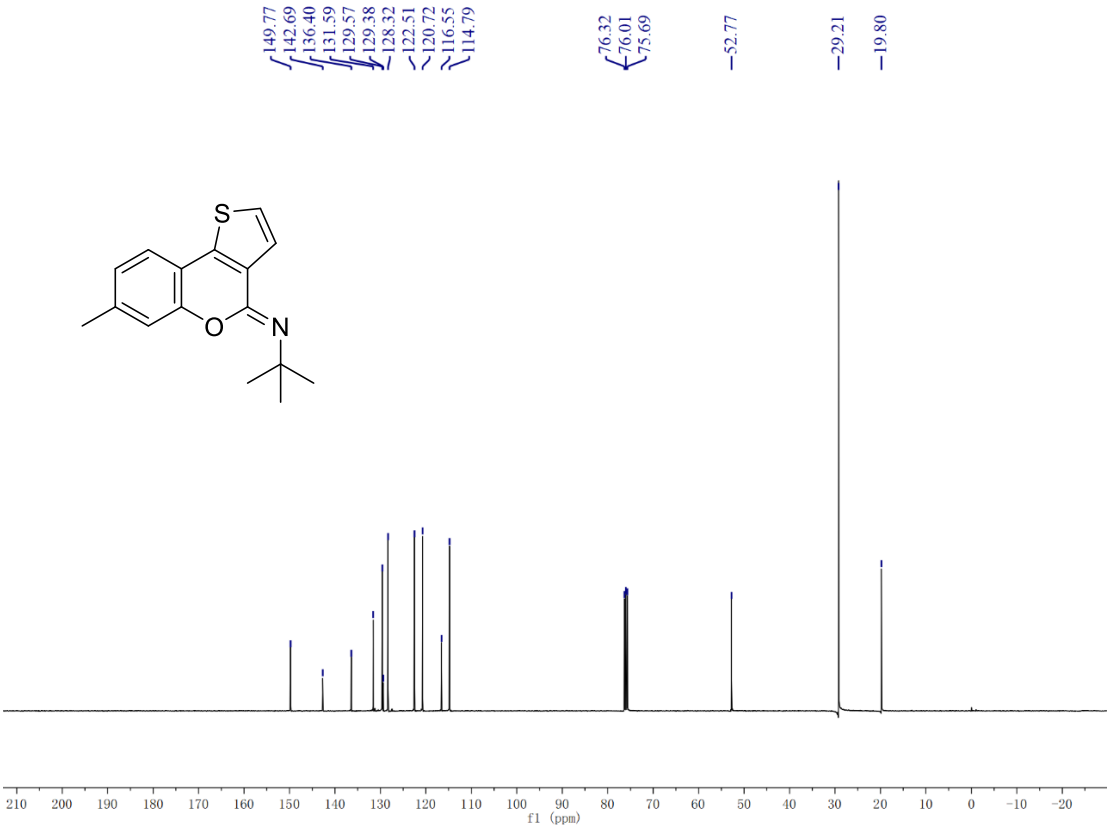
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3p**, Solvent: $CDCl_3$



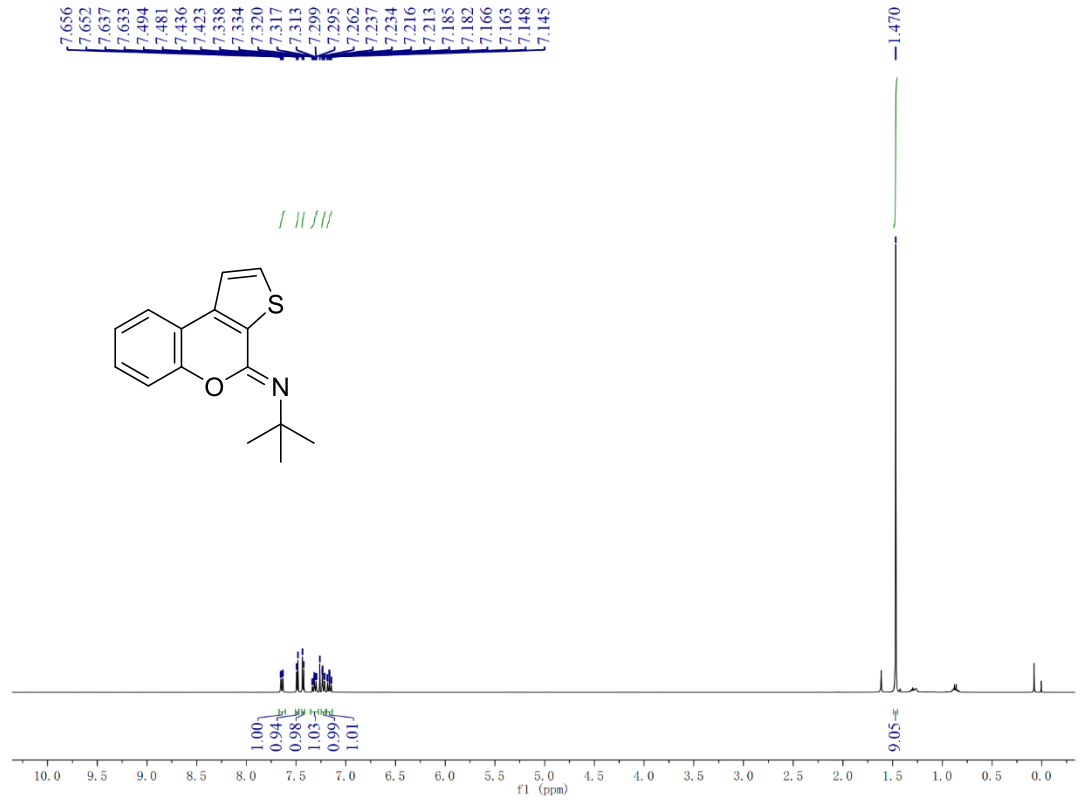


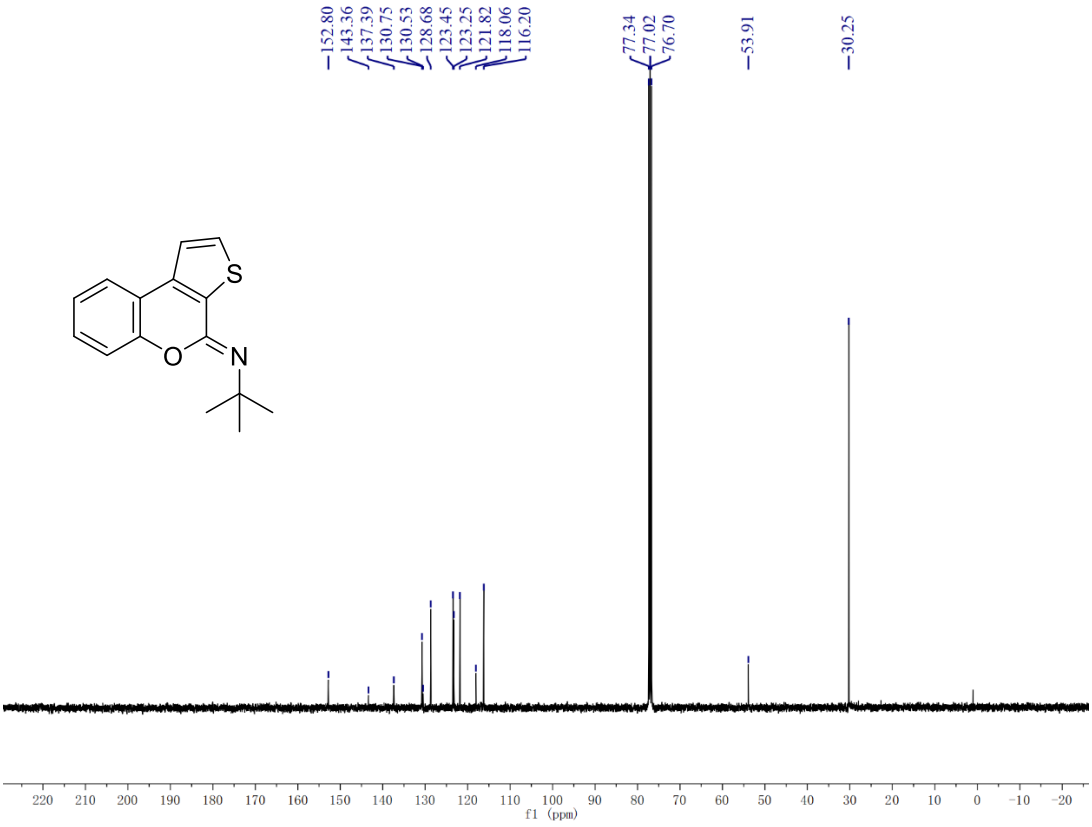
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **3q**, Solvent: $CDCl_3$



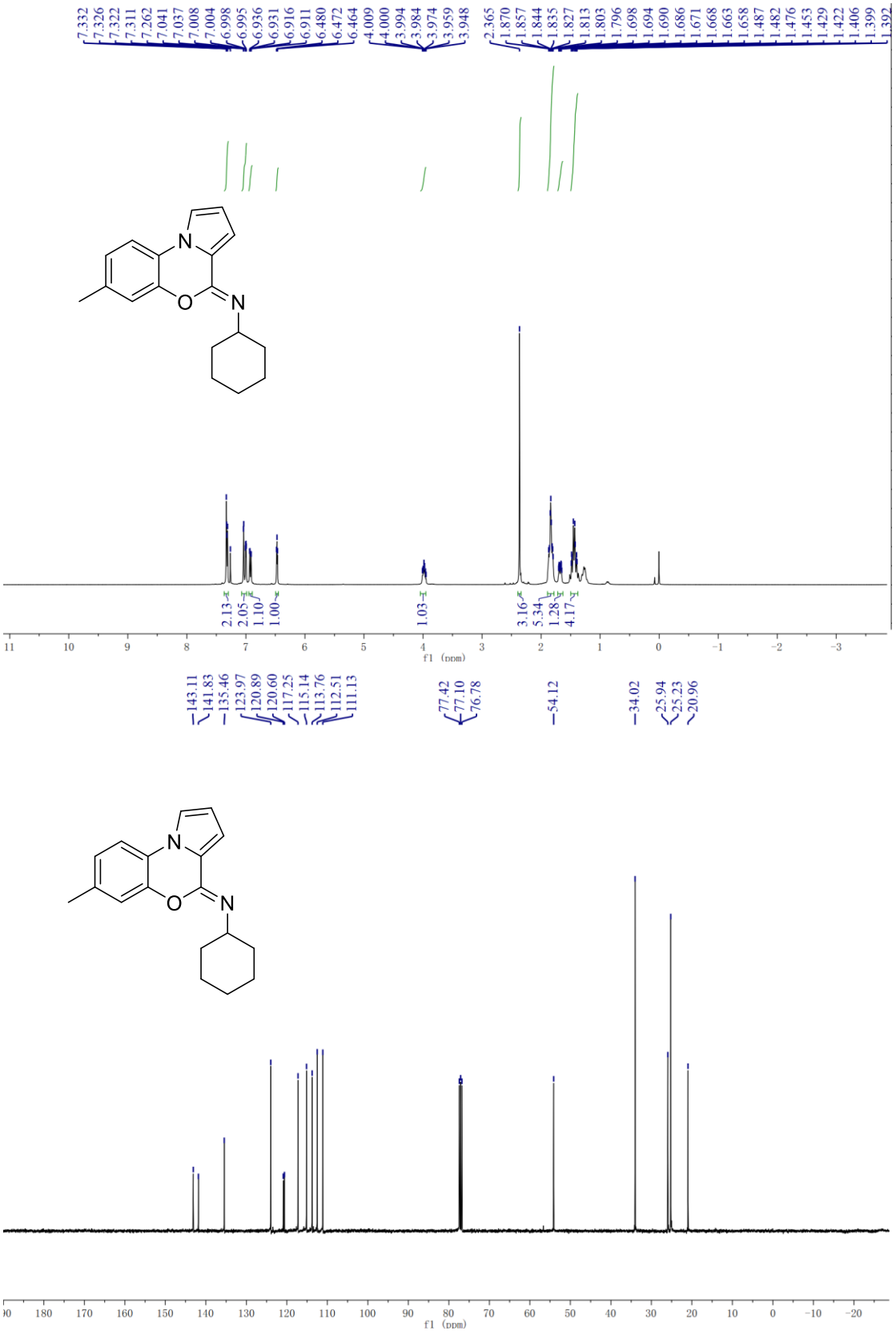


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **3r**, Solvent: $CDCl_3$

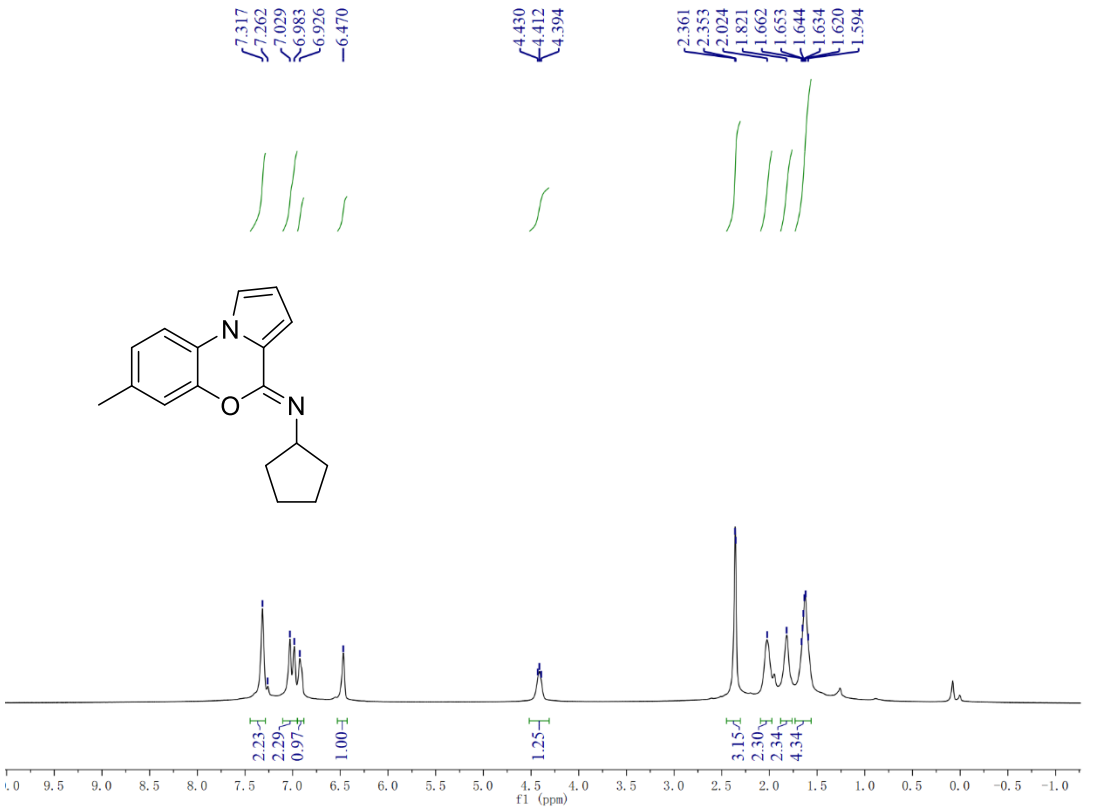


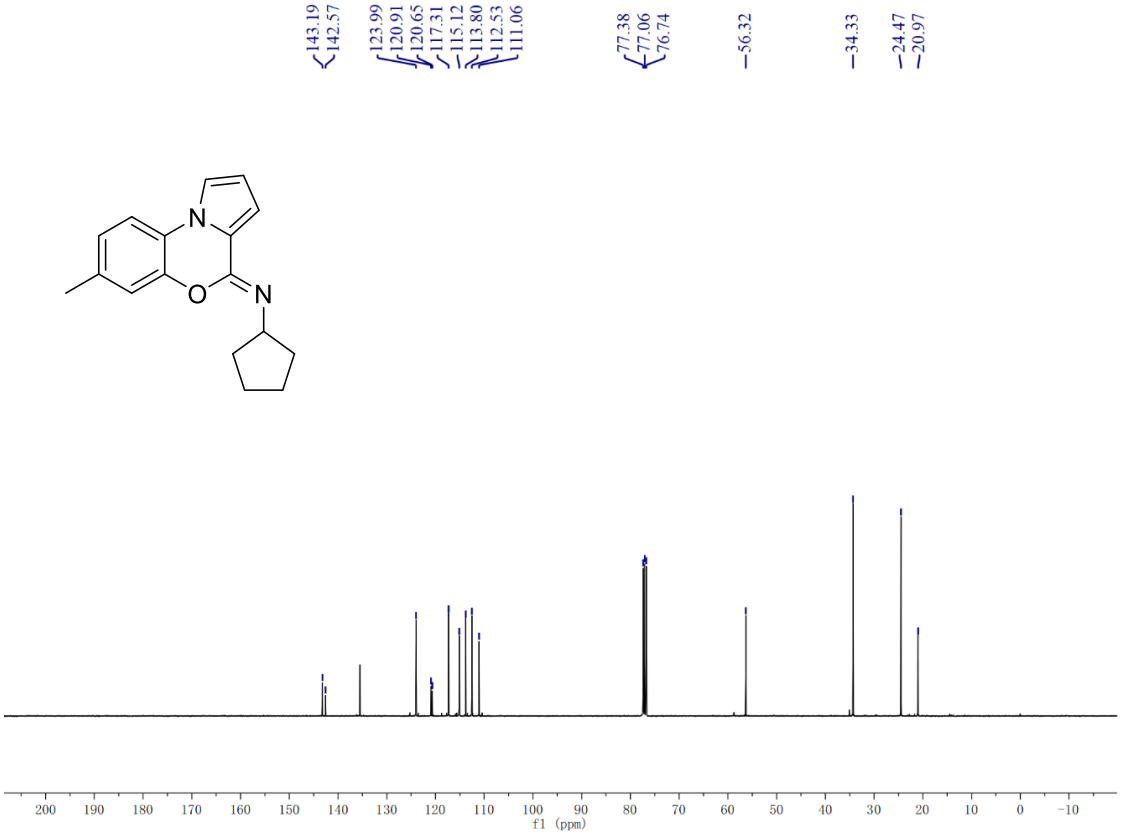


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **4a**, Solvent: $CDCl_3$

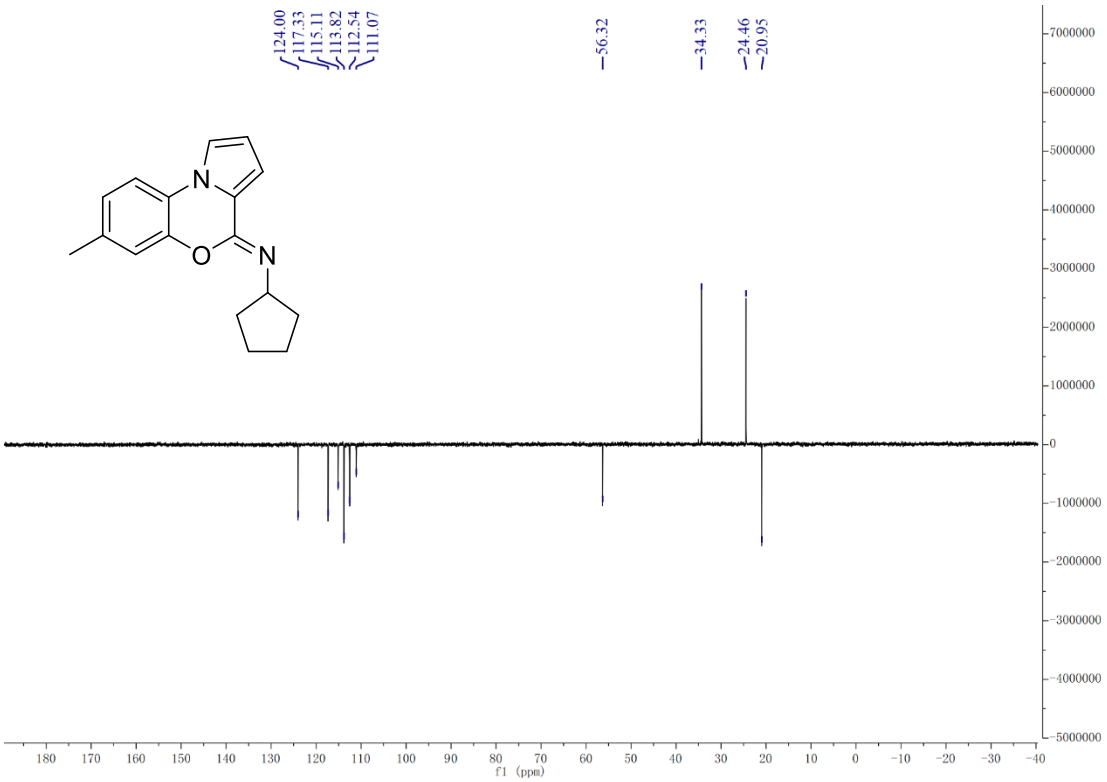


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **4b**, Solvent: $CDCl_3$

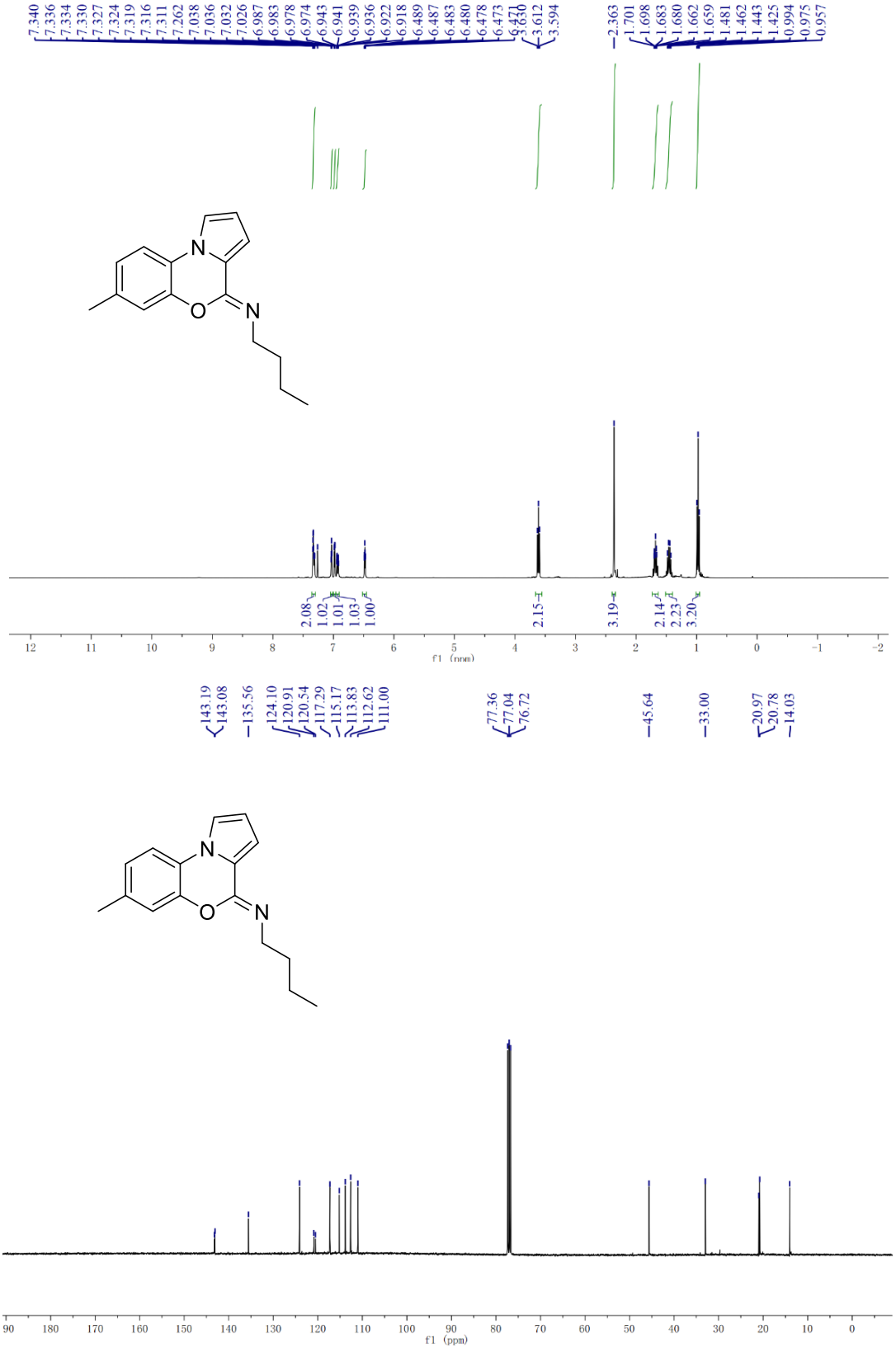




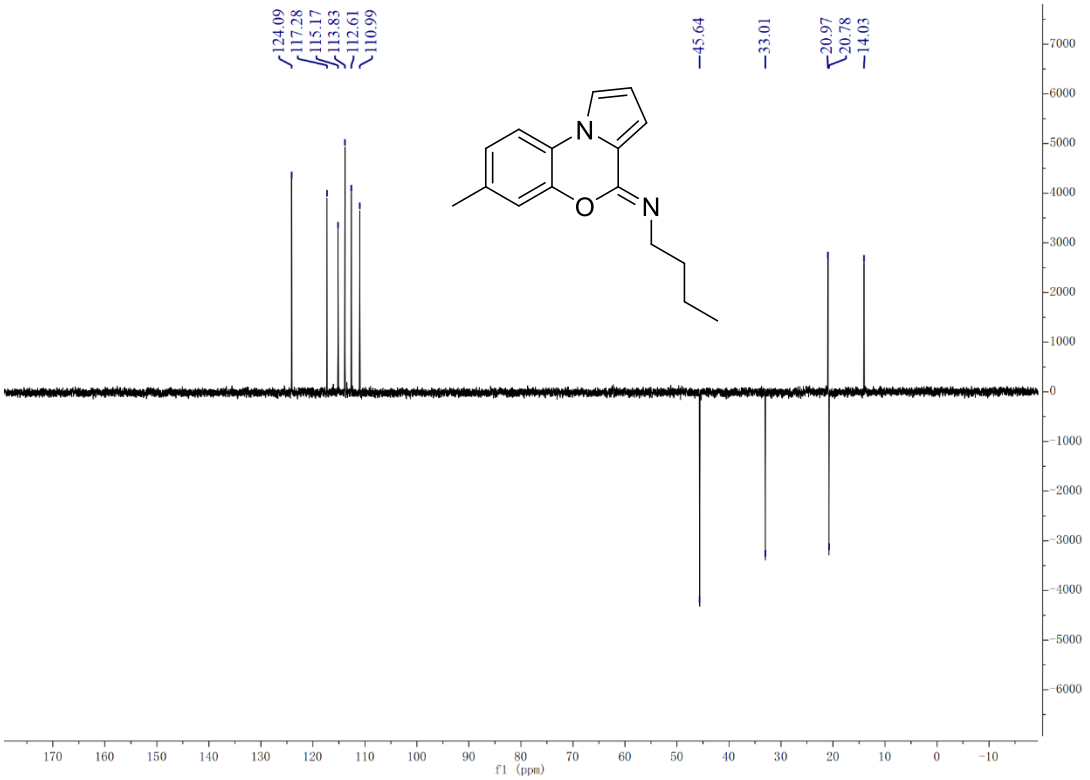
DEPT spectra of **4b.** (400 MHz, $CDCl_3$)



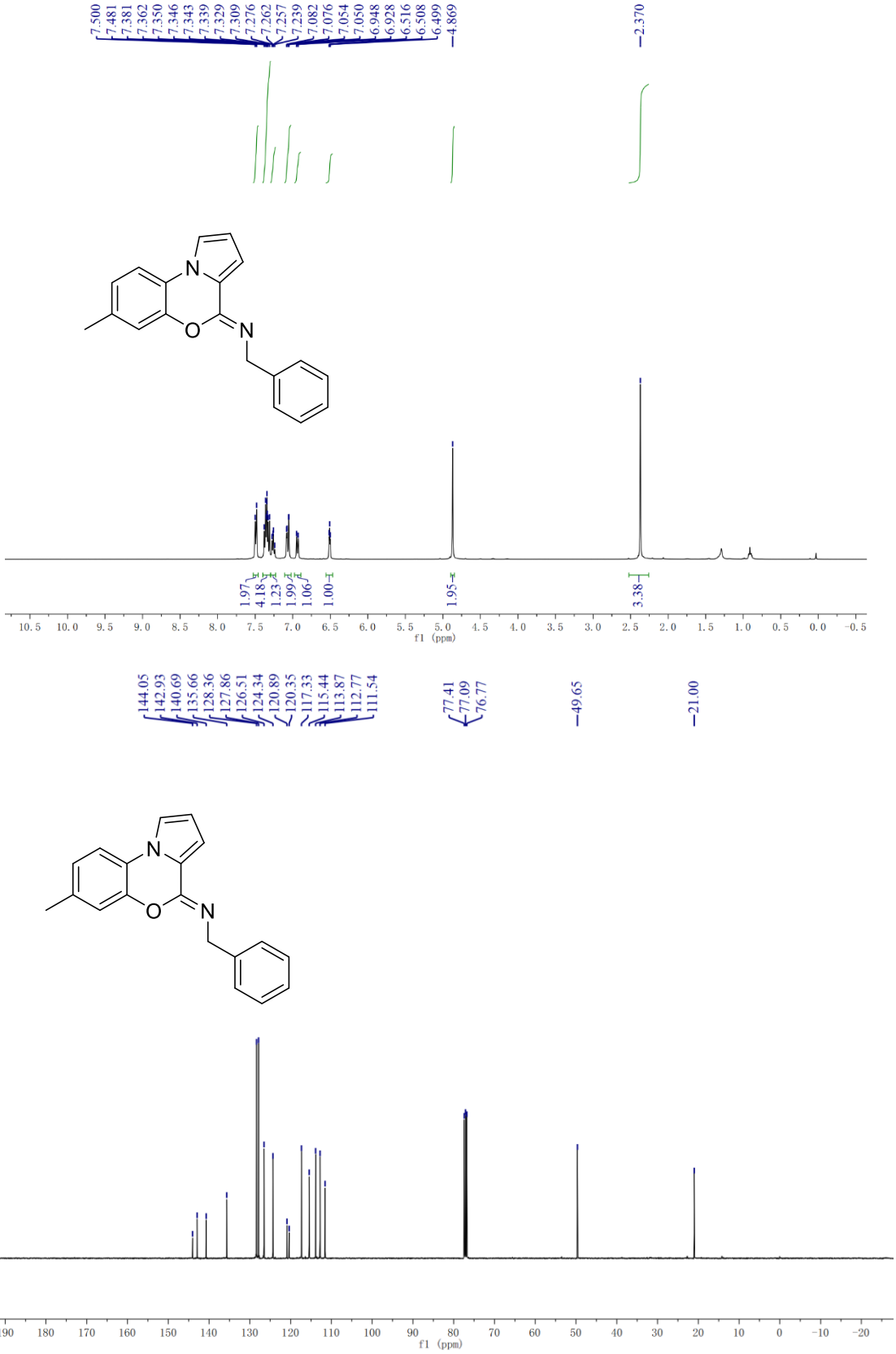
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **4c**, Solvent: $CDCl_3$



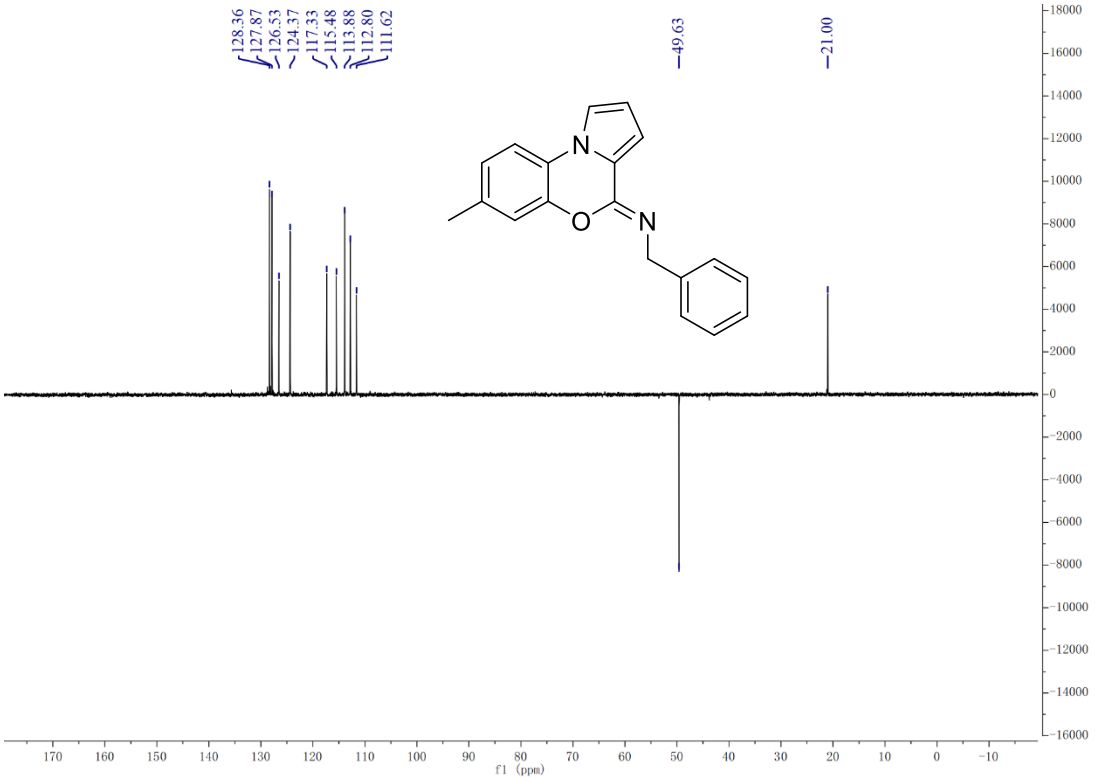
DEPT spectra of **4c**. Solvent: $CDCl_3$



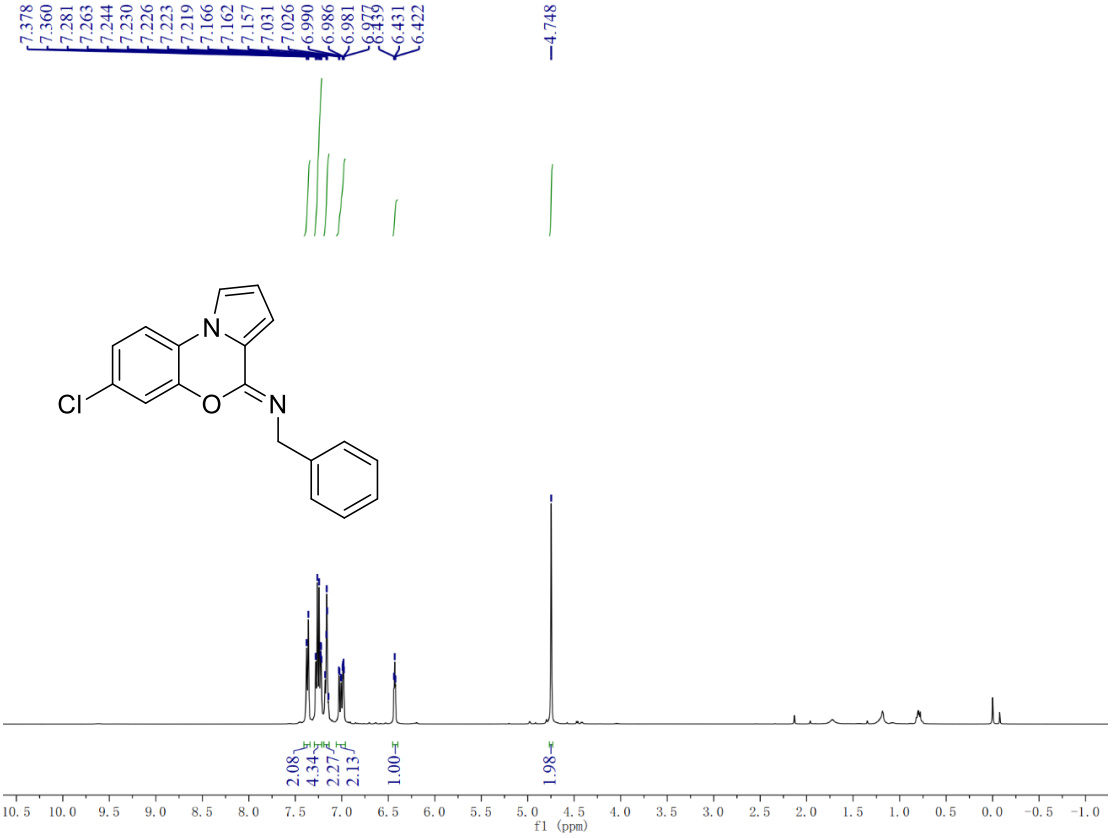
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **4d**, Solvent: $CDCl_3$

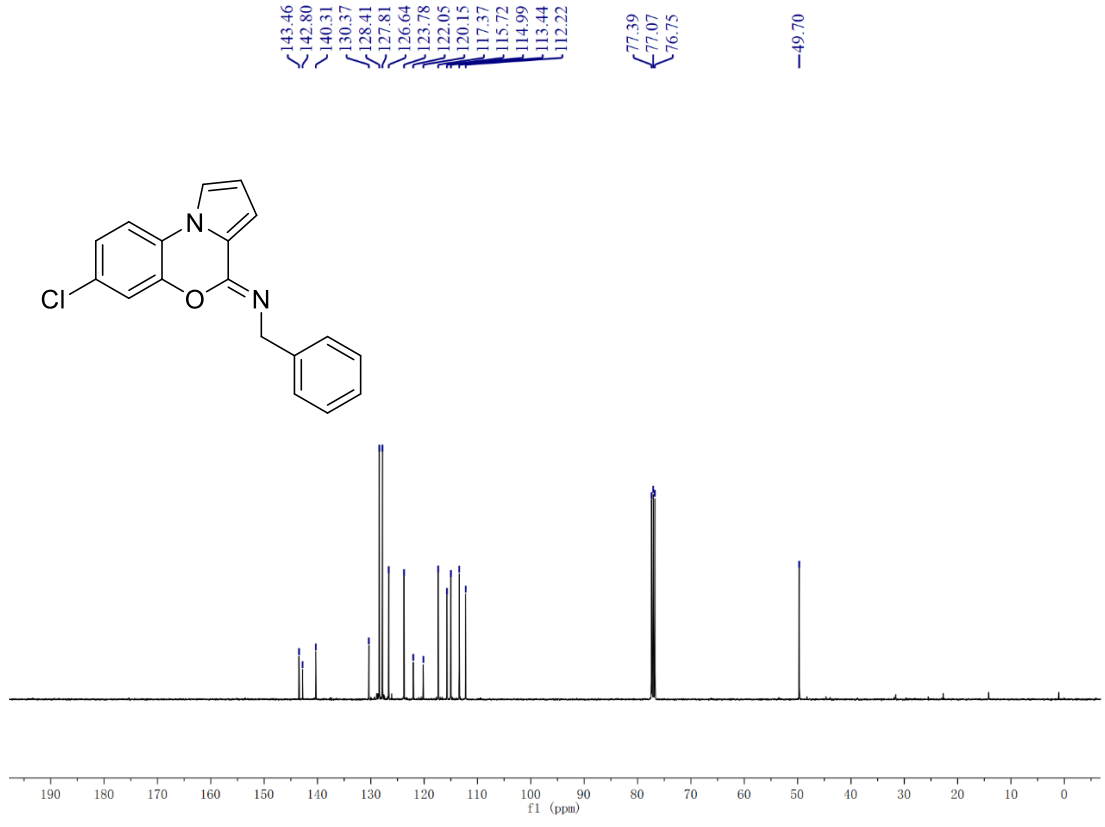


DEPT spectra of **4d**. Solvent: $CDCl_3$

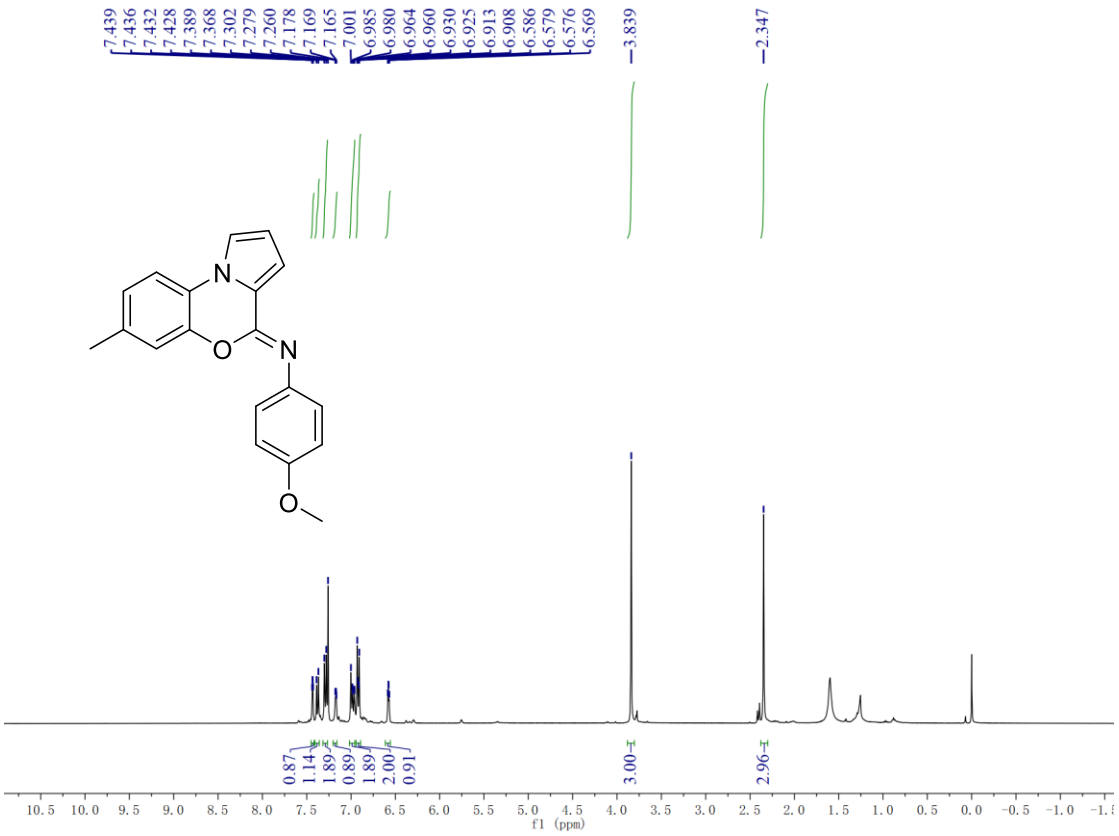


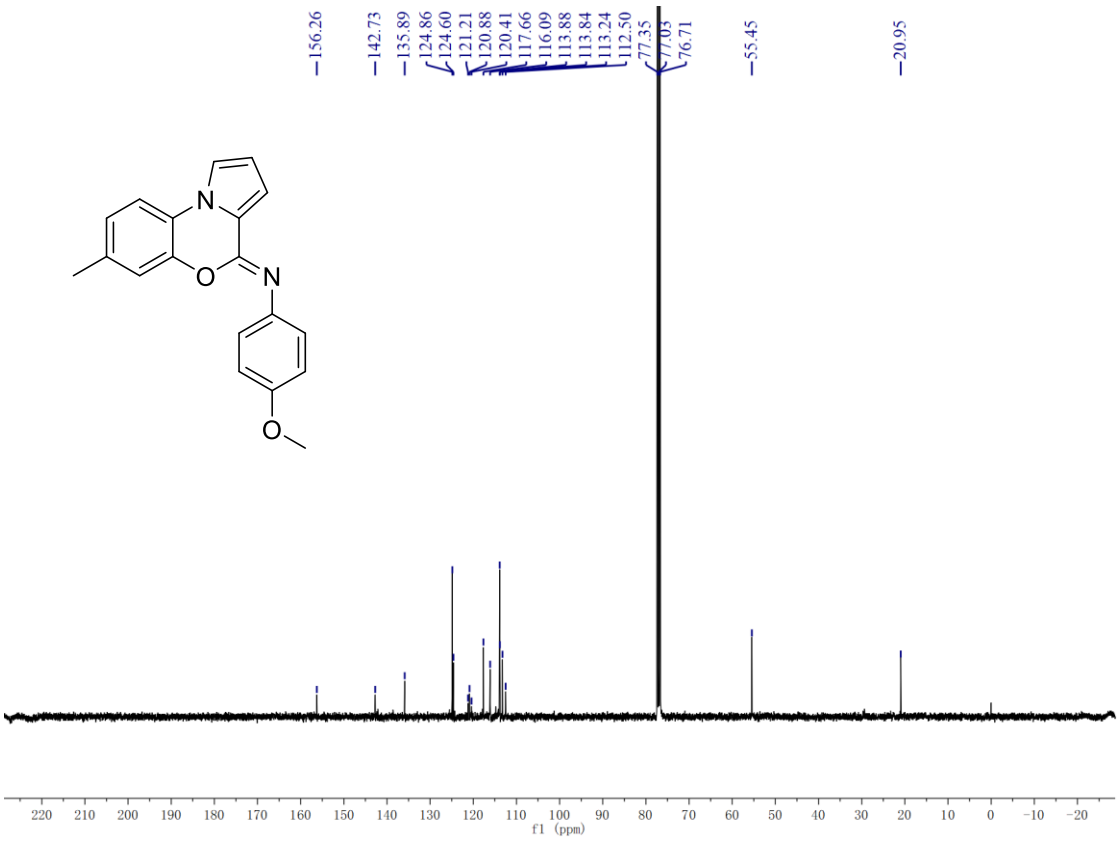
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **4e**, Solvent: $CDCl_3$



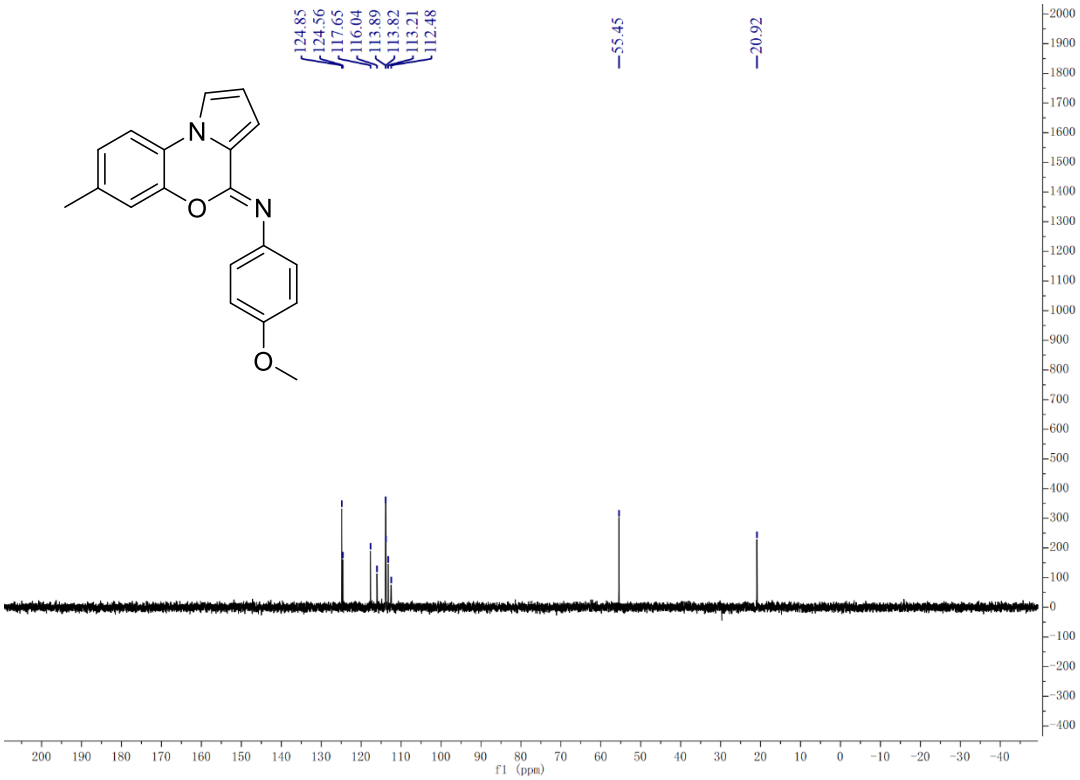


^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **4f**, Solvent: $CDCl_3$

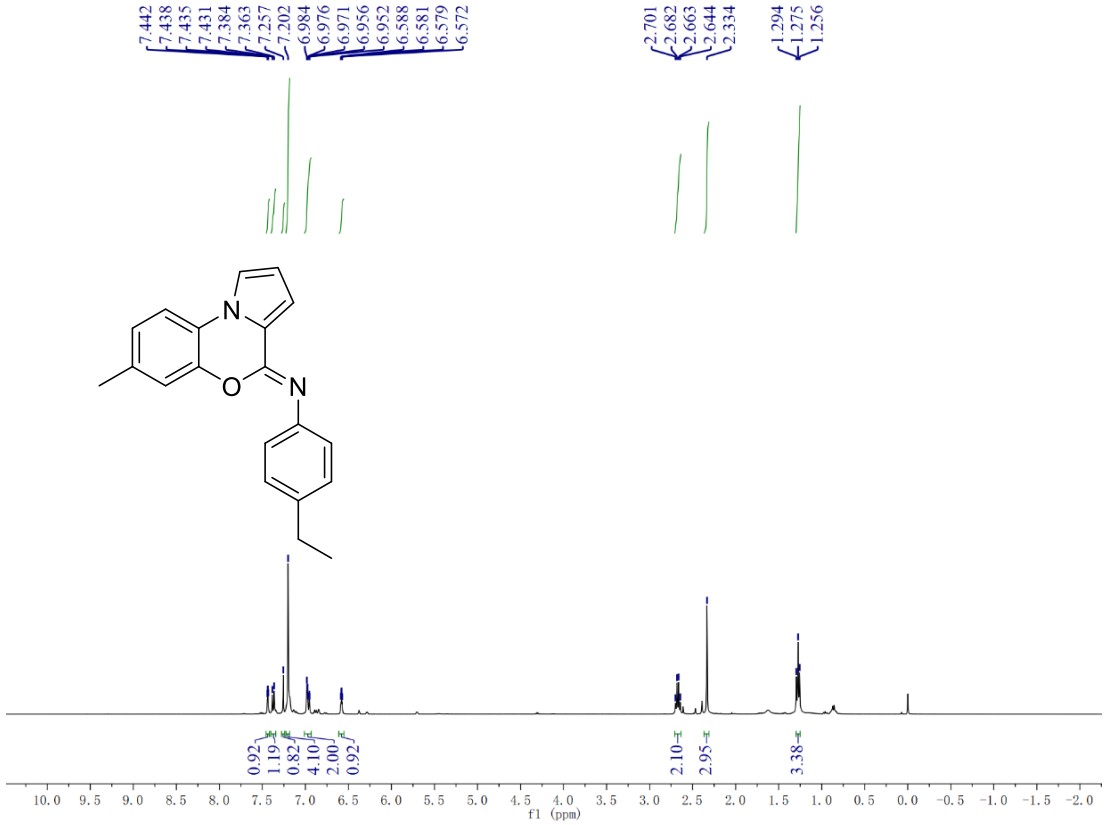


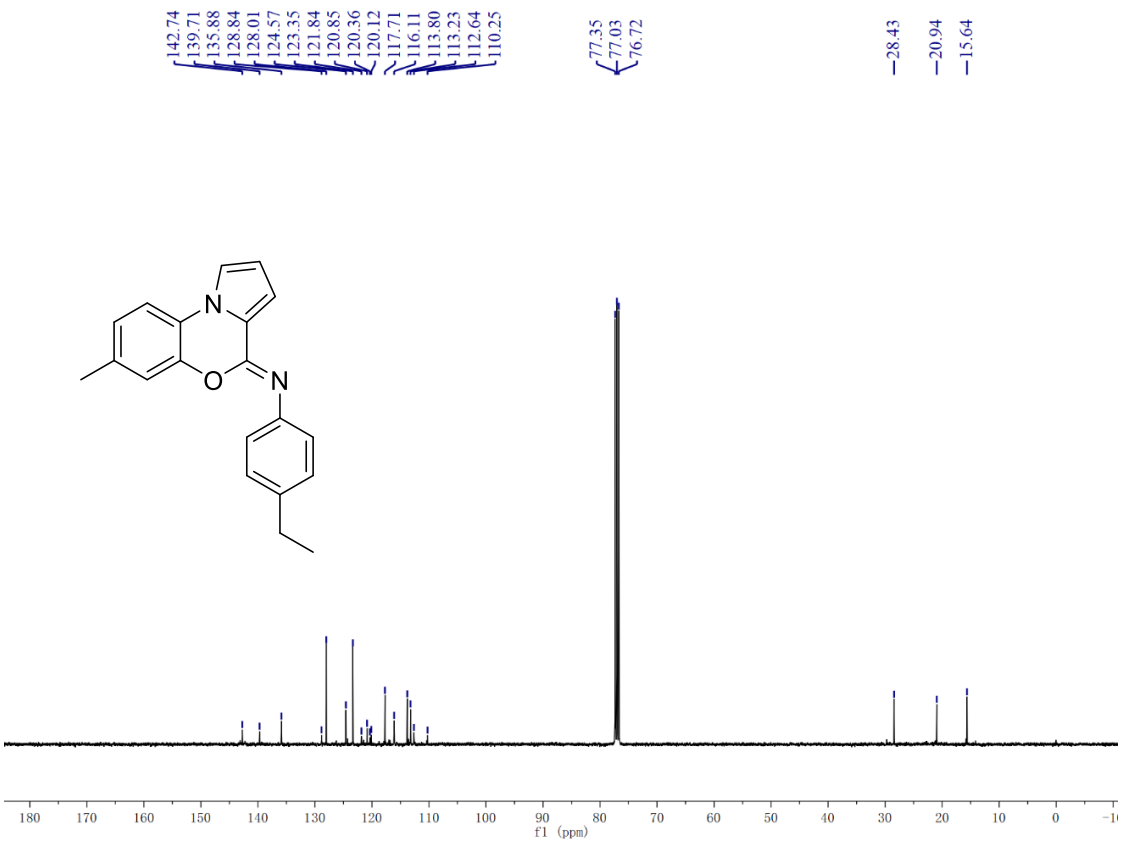


DEPT spectra of **4f.** Solvent: $CDCl_3$)

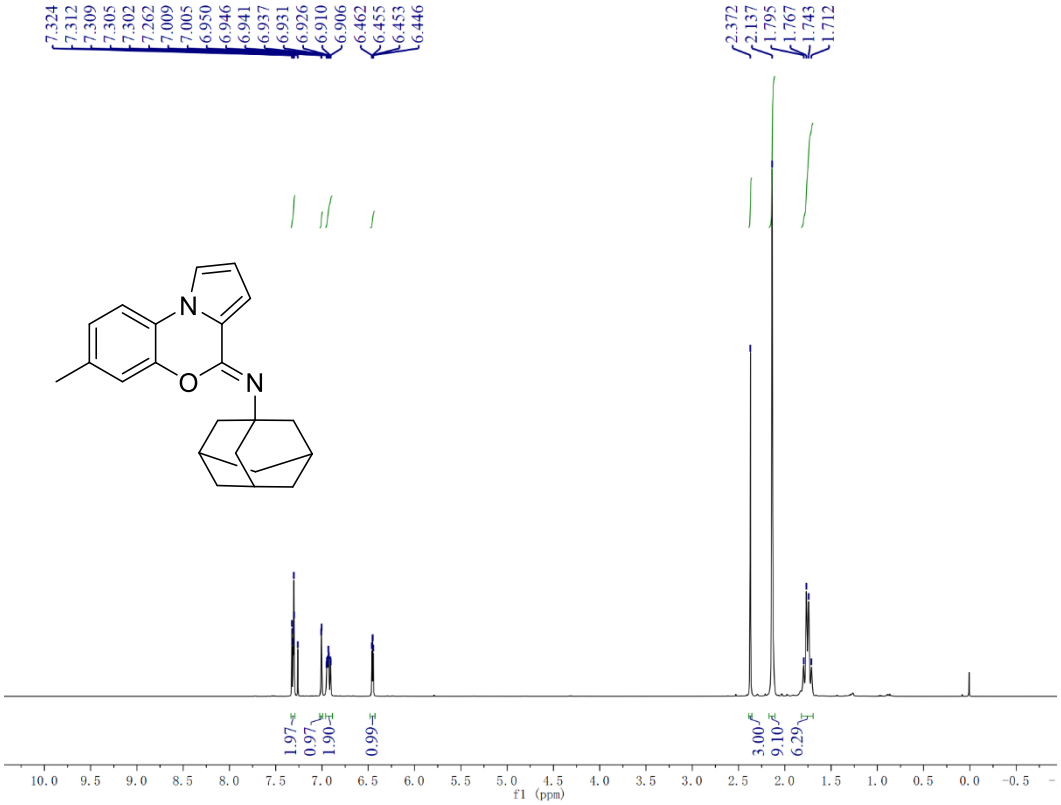


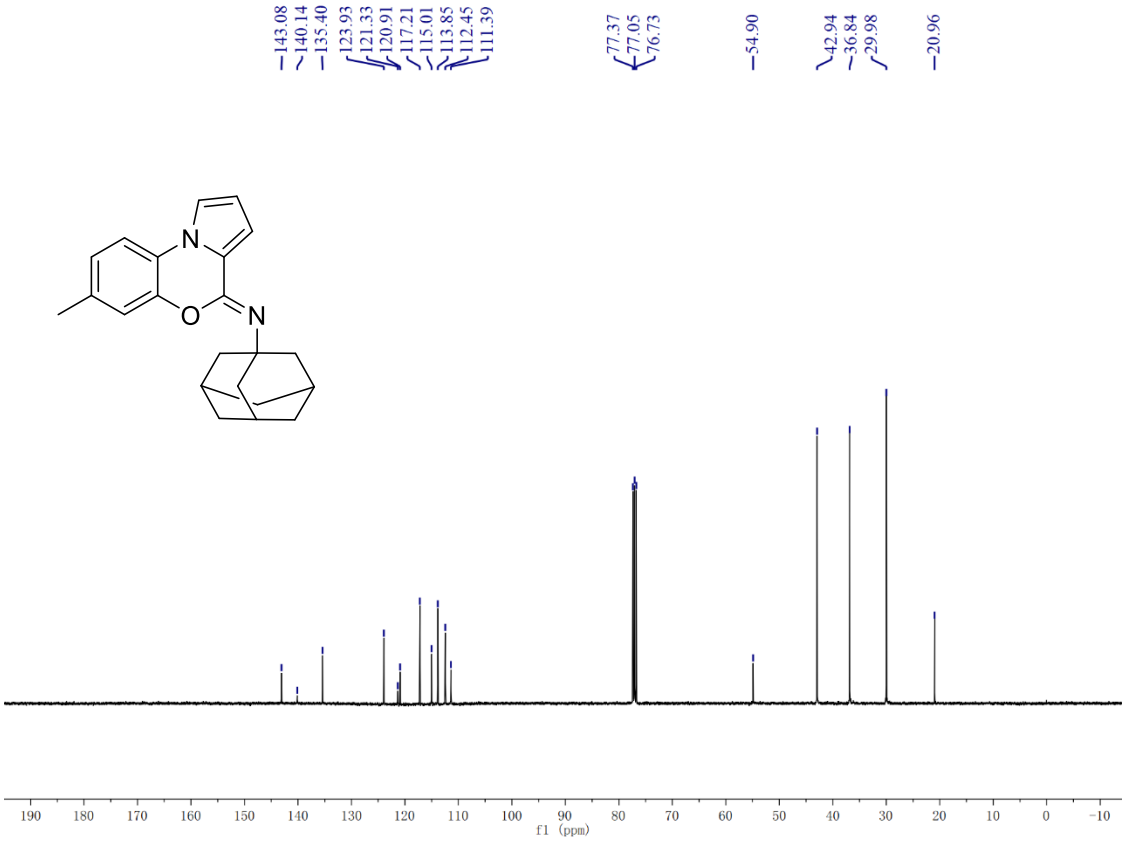
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **4g**, Solvent: $CDCl_3$





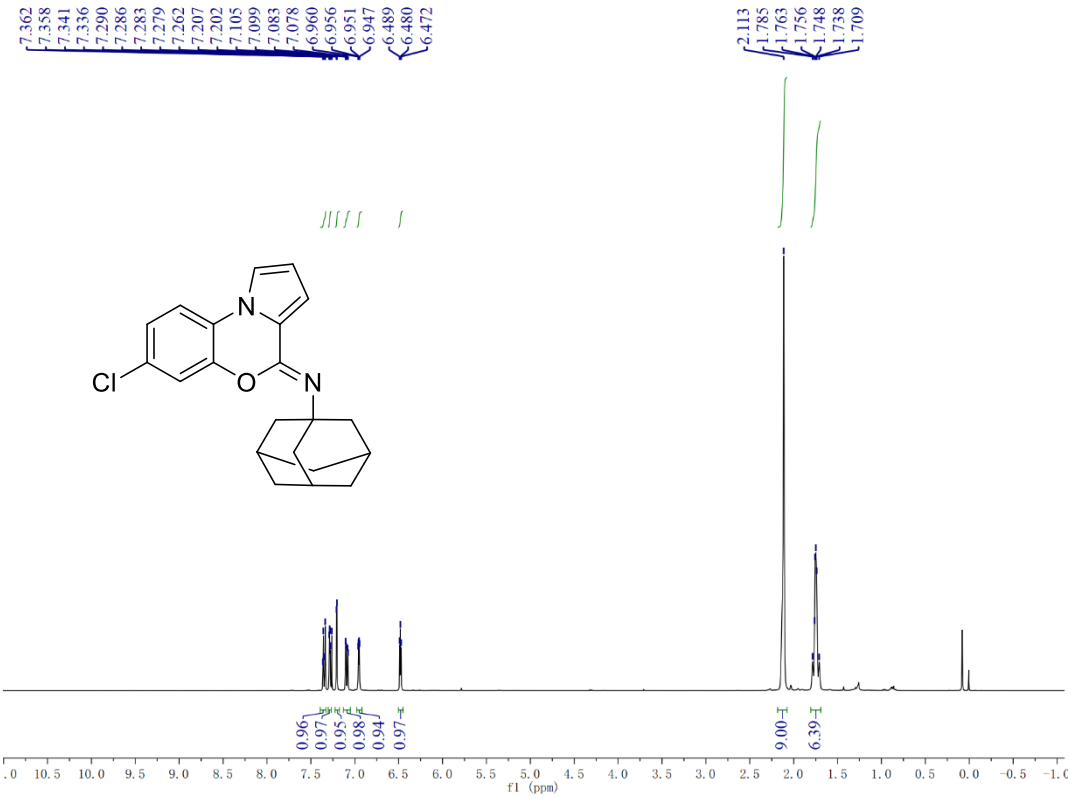
^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **4h**, Solvent: $CDCl_3$

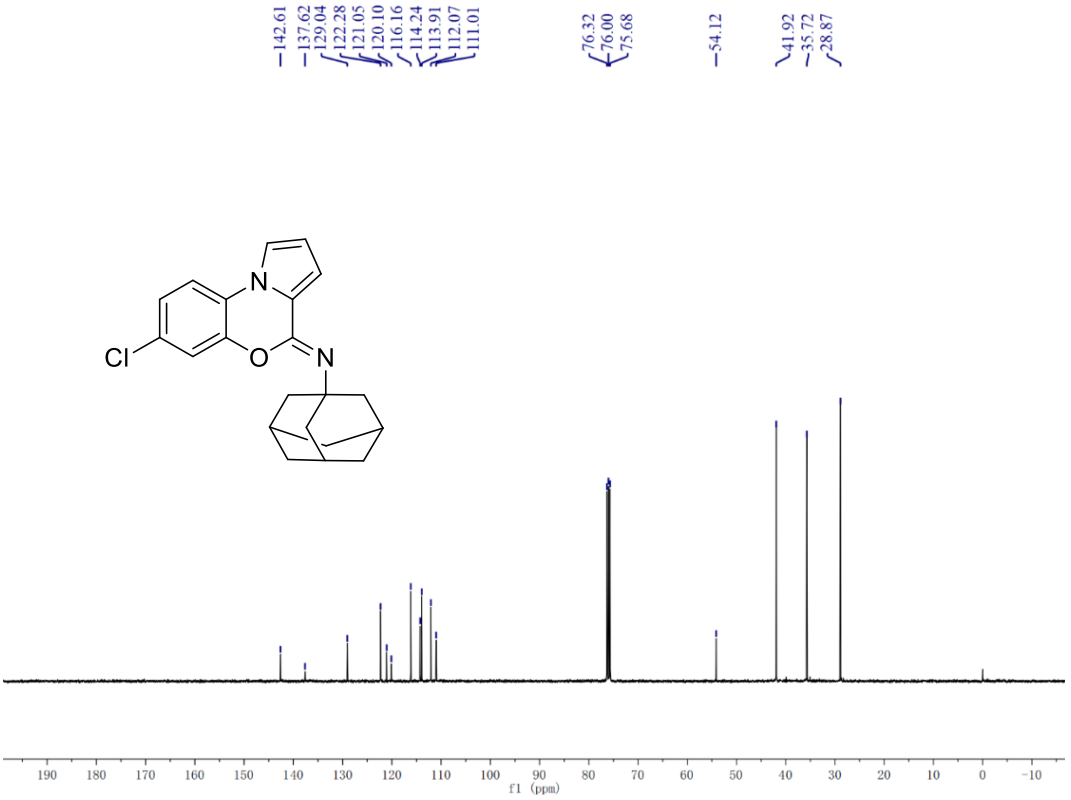




DEPT spectra of **4h**. Solvent: $CDCl_3$

^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz) of **4i**, Solvent: $CDCl_3$





^{1}H NMR (400 MHz) and **^{13}C NMR** (101 MHz)of **5**, Solvent: $CDCl_3$