Supporting Information

Efficient and facile synthesis of fused benzimidazole-diazepinones and dibenzimidazole-diazepines via a UDC strategy and the hydroamination of an alkyne†

Shi-Qiang Li, [a]§ *Hongyan Gao,* [b]§ *Jie Lei,*[a] *Jun Wang,*[a] *Jia Xu* [a] *Zhong-Zhu Chen**[a] *and Zhi-Gang Xu**[a]

[a]*International Academy of Targeted Therapeutics and Innovation, Chongqing University of Arts and Sciences, 319 Honghe Ave., Yongchuan, Chongqing, China 402160.*

[b]*Department of Medical Administration, General Hospital of Beijing Military Command, China 100700*

§*These authors contributed equally to this work.*

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General Experimental

All reagents were purchased from commercial suppliers and used without purification unless otherwise stated. Column chromatography was performed with silica gel (300-400 mesh) produced by Qingdao Marine Chemical Factory, Qingdao (China). HPLC-MS analyses were performed on a Shimadzu-2020 LC-MS instrument using th e following conditions: Shim-pack VP-ODS C18 column (reverse phase, 150 x 2.0 m m); 20% acetonitrile and 80% water over 6.0 min; flow rate of 0.4 mL/min. NMR spectra were recorded on Bruker AVANCE III 400MHz instrument with TMS as in-ternal standard.

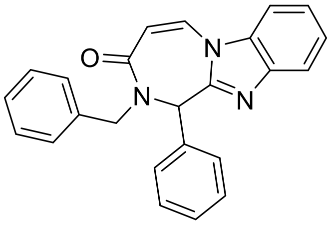
Experimental Sections

General procedures for compounds **12** and **17**.

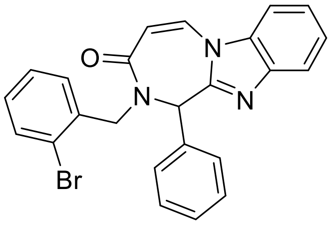
A solution of benzaldehyde (0.50 mmol), benzylamine (0.50 mmol), propiolic acid (0.50 mmol), 2-(*N*-Boc-amino)-phenyl-isocyanide (0.50 mmol) was stirred overnight in MeOH (2.0 mL) at room temperature. The reaction mixture was monitored by TLC. When no isonitrile was left, the solvent was removed under nitrogen blowing and the crude residue was dissolved in 10%TFA/DCE (3.0 mL) and treated in microwave at 160^{o}C for 30 min. After the microwave vial was cooled to room temperature, the solvent was removed under reduced pressure and then diluted with EtOAc (15 mL) and washed with sat. Na_2CO_3 and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (20-100%) to afford the relative targeted product **12**.

Benzaldehyde (0.50 mmol), N-Boc-protected-phenylenediamine (0.50 mmol), propiolic acid (0.50 mmol), 2-(*N*-Boc-amino)-phenyl-isocyanide (0.50 mmol) were mixed and stirred overnight in MeOH (2.0 mL) at room temperature. The reaction mixture was monitored by TLC. When no isonitrile was left, the solvent was removed under nitrogen blowing and the crude residue was dissolved in 10%TFA/DCE (3.0 mL) and treated in microwave at 160^{o}C for 30 min. After the microwave vial was cooled to room temperature, the solvent was removed under reduced pressure and then diluted with EtOAc (15.0 mL) and washed with sat. Na_2CO_3 and brine. The organic layer was dried over $MgSO_4$ and concentrated. The residue was purified by silica gel column chromatography using a gradient of ethyl acetate/hexane (20-100%) to afford the relative targeted product **17**.

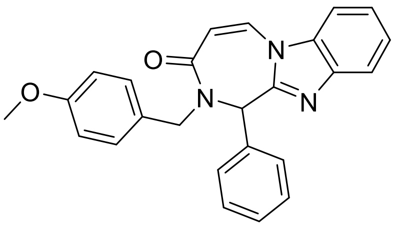
NMR Characterization Data and Figures of Products



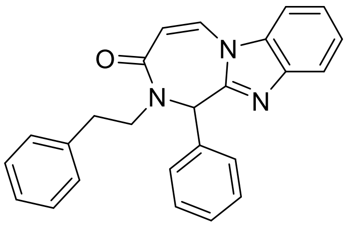
Compound **7** light yellow solid, yield 82%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.80-7.72 (m, 1H), 7.34 (q, *J* = 4.5 Hz, 5H), 7.26-7.13 (m, 3H), 7.09 (q, *J* = 6.8 Hz, 6.2 Hz, 3H,), 6.90 (d, *J* = 9.8 Hz, 1 H), 6.75 (d, *J* = 7.2 Hz, 2H), 6.21 (s, 1H), 5.82 (d, *J* = 9.8 Hz, 1H), 5.00 (d, *J* = 9.4 Hz, 1H), 4.82 (d, *J* = 10.5, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 151.7, 141.4, 135.9, 134.8, 133.3, 129.0, 128.9, 128.6, 128.18, 128.1, 125.5, 124.8, 124.5, 124.3, 120.5, 115.2, 109.8, 59.4, 53.5. LC-MS calculated for $C_{24}H_{19}N_3O$ $[M+H]^+$, 366; found 366.



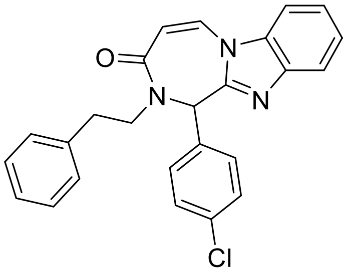
Compound **12a** yellow solid, yield 69%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.78 (m, 1H), 7.51 (d, *J* = 7.9, 1H), 7.41 (dt, *J* = 6.0 Hz, 3.2 Hz, 3H), 7.32 (d, *J* = 7.6 Hz, 1H,), 7.21 (dd, *J* = 6.5 Hz, 5.9 Hz, 4H), 7.12 (t, *J* = 7.6, 1H), 7.06-6.88 (m, 3H), 6.27 (s, 1H), 5.89 (d, *J* = 9.9 Hz, 1H), 5.56 (d, *J* = 8.2 Hz, 1H), 4.78 (d, *J* = 9.2 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 151.6, 141.9, 135.0, 133.4, 133.1, 130.6, 129.6, 128.8, 128.1, 127.7, 125.5, 124.7, 124.3, 123.9, 120.7, 114.4, 109.7, 109.6, 59.8, 53.4. LC-MS calculated for $C_{24}H_{19}BrN_3O$ $[M+H]^+$, 444; Found 444.



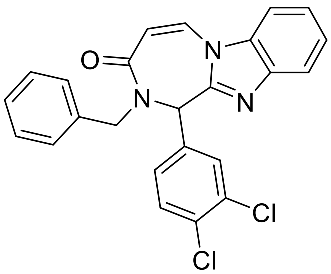
Compound **12b** white solid, yield 66%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.87-7.78 (m, 1H), 7.45-7.31 (m, 5H), 7.16 (d, *J* = 7.5 Hz, 3H), 6.96 (d, *J* = 9.8 Hz, 1H), 6.83 (d, *J* = 8.6 Hz, 4H), 6.21 (s, 1H), 5.85 (d, *J* = 9.8 Hz, 1H), 4.92 (d, *J* = 7.0 Hz, 2H), 3.75 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.45, 159.48, 151.84, 142.13, 135.18, 133.49, 130.39, 128.55, 128.10, 127.94, 125.50, 124.57, 124.38, 124.18, 120.69, 114.85, 114.29, 109.66, 59.46, 55.23, 52.90. LC-MS calculated for $C_{25}H_{21}N_3O_2$ $[M+H]^+$, 396; found 396.



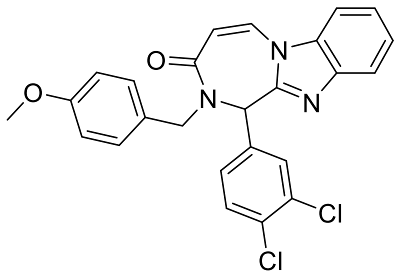
Compound **12c** white solid, yield 74%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.92-7.79 (m, 1H), 7.43 (d, *J* = 6.3 Hz, 3H), 7.25 (t, *J* = 3.1 Hz, 3H,), 7.19-7.06 (m, 5H), 7.04-6.96 (m, 2 H), 6.94 (d, *J* = 9.8 Hz, 1H), 6.26 (s, 1H), 5.82 (d, *J* = 9.8 Hz, 1H), 4.54-4.37 (m, 1H), 3.79-3.61 (m, 1H), 3.19-3.03 (m, 1H), 2.98-2.87 (, m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.2, 151.9, 141.7, 137.9, 135.2, 133.3, 128.8, 128.7, 128.4, 128.2, 126.5, 125.5, 124.7, 124.4, 124.2, 120.4, 115.2, 109.7, 60.7, 52.7, 34.4. LC-MS calculated for $C_{25}H_{21}N_3O$ $[M+H]^+$, 380; found 380.



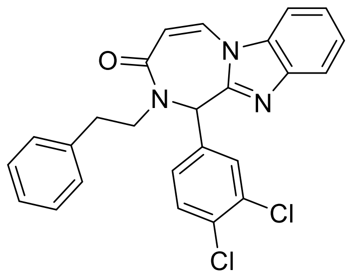
Compound **12d** white solid, yield 64%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.81 (dt, *J* =4.3 Hz, 4.2 Hz, 1H), 7.46 (s, 3H), 7.30-7.19 (m, 3H), 7.15-7.03 (m, 5H), 6.97 (d, *J* = 9.8 Hz, 1H), 6.90 (d, *J* = 8.3 Hz, 1H), 6.41 (s, 1H), 5.89 (d, *J* = 9.8 Hz, 1H), 4.55-4.35 (m, 1H), 3.76-3.58 (m, 1H), 3.09 (dd, *J* = 8.5 Hz , 4.2 Hz, 1H), 2.96-2.89 (m, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 154.8, 151.2, 137.7, 134.4, 133.3, 132.7, 129.4, 129.1, 128.8, 128.4, 126.8, 126.6, 125.3, 124.9, 124.2, 119.9, 115.7, 109.9, 59.7, 52.9, 34.2. LC-MS calculated for $C_{25}H_{20}ClN_3O$ $[M+H]^+$, 414; found 414.



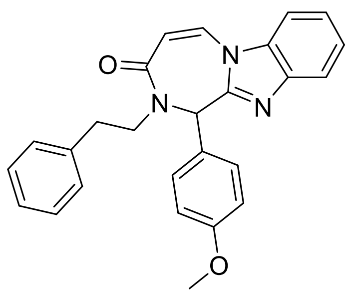
Compound **12e** light yellow solid, yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88-7.81 (m, 1H), 7.49-7.41 (m, 5H), 7.32 (d, *J* = 7.1 Hz, 3H), 7.20 (, d, *J* = 8.4 Hz, 1H), 7.04 (d, *J* = 9.8 Hz, 1H), 6.85 (s, 1H), 6.62-6.53 (m, 1H), 6.18 (s, 1H), 5.92 (d, *J* = 9.8 Hz, 1H), 5.10 (d, *J* = 14.4 Hz, 1H), 4.81 (d, *J* = 14.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.1, 150.6, 141.8, 135.6, 135.3, 133.4, 133.1, 132.81, 132.5, 130.4, 129.1, 129.1, 128.5, 127.6, 125.0, 124.8, 124.7, 120.8, 114.7, 109.8, 58.7, 53.4. LC-MS calculated for $C_{24}H_{17}Cl_2N_3O$ $[M+H]^+$, 434; found 434.



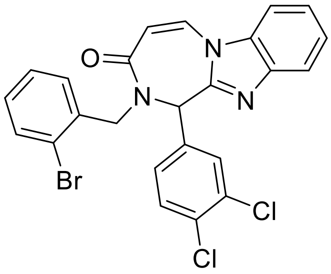
Compound **12f** white solid, yield 63%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.85 (s, 1H), 7.42 (d, *J* = 24.9 Hz, 5H), 7.20 (d, *J* = 8.4 Hz, 1H), 7.03 (d, *J* = 9.8 Hz, 1H), 6.94-6.75 (m, 3H), 6.55 (s, 1H), 6.26 (s, 1H), 5.94 (d, *J* = 9.8 Hz, 1H), 5.07 (d, *J* = 10.3 Hz, 1H), 4.70 (d, *J* = 10.3 Hz, 1H), 3.78 (s, 3H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 164.9, 159.8, 150.7, 141.2, 135.3, 133.2, 132.5, 130.5, 127.6, 127.6, 125.2, 125.0, 124.7, 124.5, 120.5, 115.3, 114.5, 109.9, 58.1, 55.3, 52.8. LC-MS calculated for $C_{25}H_{19}Cl_2N_3O_2$ $[M+H]^+$, 464; found 464.



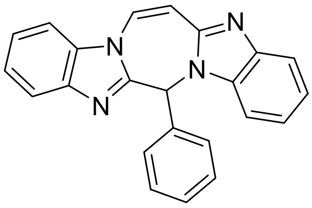
Compound **12g** white solid, yield 68%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.90-7.84 (m, 1H), 7.48 (d, *J* = 5.9 Hz, 3H), 7.33 (d, *J* = 8.4 Hz, 1H), 7.13 -7.03 (m, 6H), 7.01 (d, *J* = 9.7 Hz, 1H,), 6.80 (d, *J* = 8.4 Hz, 1H), 6.31 (s, 1H), 5.91 (d, *J* = 9.7 Hz, 1 H,), 4.46 (s, 1H), 3.66 (s, 1H), 3.13-3.00 (m, 1H), 2.96-2.86 (m, 1 H). ^{13}C NMR (100 MHz, CDCl$_3$): δ 164.8, 150.6, 140.7, 137.5, 135.3, 133.5, 132.8, 130.7, 128.7, 128.4, 127.5, 126.6, 125.4, 124.9, 124.8, 124.2, 120.3, 115.5, 109.9, 59.6, 52.9, 34.2. LC-MS calculated for $C_{25}H_{19}Cl_2N_3O$ $[M+H]^+$, 484; found 484.



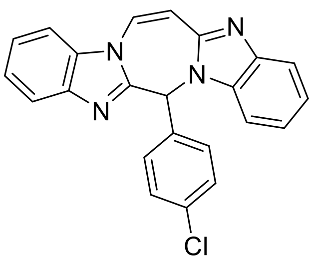
Compound **12h** white solid, yield 66%. ^{1}H NMR (400 MHz, CDCl$_3$): δ 7.90-7.84 (m, 1H), 7.44 (s, 3H), 7.18-7.04 (m, 5H), 6.96 (d, *J* = 9.8 Hz, H), 6.90 (d, *J* = 8.8 Hz, 2H), 6.77 (d, *J* = 6.7 Hz, 2H), 6.23 (s, 1H), 5.86 (, d, *J* = 9.8 Hz, 1H), 4.48-4.41 (m, 1H), 3.75 (s, 3H), 3.71-3.60 (m, 1H), 3.16-3.03 (m, 1H), 2.97-2.84 (m, 1 H). ^{13}C NMR (100 MHz, CDCl$_3$) δ 165.2, 159.4, 151.9, 141.2, 137.8, 133.1, 128.8, 128.4, 126.7, 126.7, 126.4, 124.7, 124.4, 123.9, 120.3, 115.3, 114.1, 109.7, 60.2, 55.2, 52.7, 34.4. LC-MS calculated for $C_{26}H_{23}N_3O_2$ $[M+H]^+$, 410; found 410.



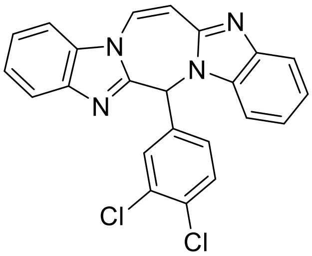
Compound **12i** white solid, yield 73%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.89-7.78 (m, 1 H), 7.52 (s, 1 H), 7.50-7.37 (m, 4H), 7.32-7.21 (m, 2H), 7.21-7.11 (m, 1H), 7.08 (d, *J* = 9.8 Hz, 1H), 7.00 (s, 1H), 6.74 (d, *J* = 9.5 Hz, 1H), 6.30 (s, 1H), 5.95 (d, *J* = 9.8 Hz, 1H), 5.40 (d, *J* = 7.9 Hz, 1H), 4.89 (d, *J* = 9.0 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) δ 165.4, 150.4, 141.3, 135.2, 134.6, 133.3, 133.2, 133.1, 132.6, 131.2, 130.6, 130.0, 128.0, 127.5, 125.1, 124.8, 124.7, 124.0, 120.6, 114.5, 109.8, 77.3, 76.7, 76.7, 58.4, 52.9. LC-MS calculated for $C_{26}H_{14}BrCl_2N_3O$ $[M+H]^+$, 512; found 512.



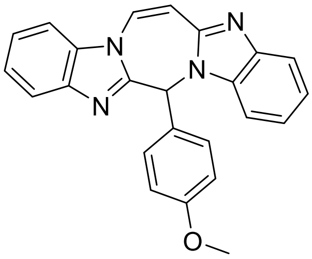
Compound **17a** white solid, yield 58%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.99-7.85 (m, 2H), 7.71-7.65 (m, 1H), 7.53-7.43 (m, 6H), 7.36 (d, *J* = 9.7 Hz, 1H), 7.21 (dt, *J* = 10.9 Hz, 7.1 Hz, 3H), 6.91 (d, *J* = 9.7 Hz, 1H), 6.62 (d, *J* = 7.7 Hz, 2H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.5, 147.6, 142.1, 140.4, 134.2, 129.7, 129.6, 129.3, 128.3, 126.3, 125.1, 124.8, 124.5, 120.8, 119.2, 114.4, 114.2, 109.9, 106.2, 57.3. LC-MS calculated for $C_{23}H_{16}N_4$ $[M+H]^+$, 349; found 349.



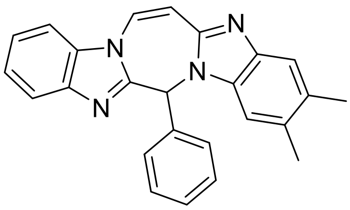
Compound **17b** white solid, yield 61%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.98 (d, *J* = 5.7 Hz, 1H), 7.90 (d, *J* = 6.6 Hz, 1H), 7.70 (s, 1H), 7.55-7.46 (m, 6H), 7.41 (d, *J* = 9.4 Hz, 1H), 7.17 (d, *J* = 8.5 Hz, 2 H), 6.98 (d, *J* = 9.5 Hz, 1H), 6.56 (d, *J* = 8.2 Hz, 2 H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 147.9, 147.2, 142.0, 139.6, 135.2, 134.1, 133.8, 132.5, 129.5, 126.6, 125.6, 125.5, 125.4, 125.3, 124.8, 120.9, 119.0, 110.0, 109.7, 105.6, 56.8. LC-MS calculated for $C_{23}H_{15}ClN_4$ $[M+H]^+$, 383; found 383.



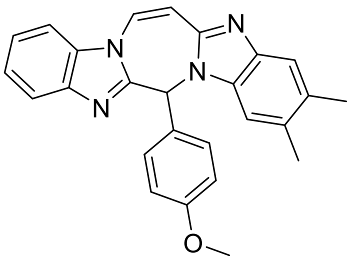
Compound **17c** white solid, yield 62%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.93-7.85 (m, 2H), 7.61 (d, *J* = 7.0 Hz, 1H), 7.52 (d, *J* = 4.4 Hz, 1H), 7.45 (t, *J* = 6.1 Hz, 5H), 7.31 (d, *J* = 9.7 Hz, 1H), 7.26-7.22 (m, 1H), 6.79 (d, *J* = 11.3 Hz, 2H), 6.39 (d, *J* = 8.4 Hz, 1H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.06, 147.72, 142.63, 141.87, 134.93, 134.58, 134.19, 133.59, 133.32, 131.02, 127.40, 125.28, 124.90, 124.65, 124.57, 124.34, 123.61, 120.80, 120.18, 110.00, 109.26, 108.02, 56.02. LC-MS calculated for $C_{23}H_{14}Cl_2N_4$ $[M+H]^+$, 417; found 417.



Compound **17d** white solid, yield 65%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.88 (d, *J* = 6.8 Hz, 2H), 7.63 (d, *J* = 5.7 Hz, 1H), 7.53-7.47 (m, 1H), 7.45-7.37 (m, 5H), 7.26 (d, *J* = 2.3Hz, 1H), 6.70 (dd, *J* = 10.5 Hz, 9.3 Hz, 3H), 6.53 (d, *J* = 8.5 Hz, 2H), 3.68 (s, 3H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.7, 149.4, 148.2, 143.2, 142.2, 135.1, 134.3, 126.9, 126.5, 124.7, 124.3, 124.2, 123.7, 123.2, 120.7, 120.1, 114.2, 109.8, 109.3, 108.3, 56.6, 55.2. LC-MS calculated for $C_{23}H_{14}Cl_2N_4$ $[M+H]^+$, 379; found 379.

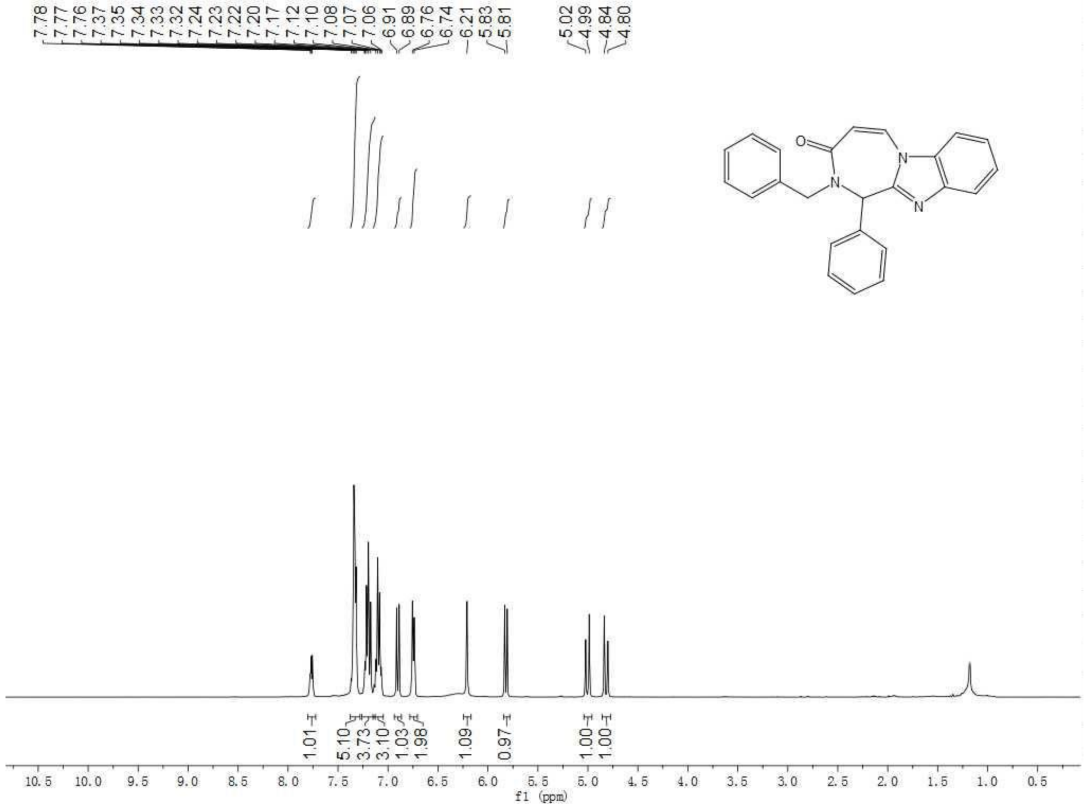


Compound **17e** white solid, yield 56%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.90 (s, 1H), 7.75 (s, 1H), 7.53-7.49 (m, 1H), 7.46 (d, *J* = 8.9 Hz, 4H), 7.38 (d, *J* = 8.9 Hz, 1H), 7.26-7.19 (m, 3H), 7.05 (d, *J* = 4.0 Hz, 1H), 6.62 (d, *J* = 7.5 Hz, 2H), 2.44 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 148.1, 142.3, 135.8, 135.4, 134.2, 133.9, 132.2, 129.2, 129.0, 125.5, 125.3, 125.1, 124.6, 120.9, 118.1, 109.9, 104.7, 57.5, 20.8, 20.3. LC-MS calculated for $C_{25}H_{20}N_4$ $[M+H]^+$, 377; found 377.



Compound **17f** white solid, yield 67%. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.91-7.85 (m, 1H), 7.68 (s, 1H), 7.53-7.48 (m, 1H), 7.46-7.40 (m, 3H), 7.34 (s, 1H), 7.30 (d, *J* = 9.6 Hz, 1H), 6.86 (d, *J* = 9.7 Hz, 1H), 6.69 (d, *J* = 8.9 Hz, 2H), 6.53 (d, *J* = 8.5 Hz, 2H), 3.69 (s, 3H), 2.42 (s, 6H). ^{13}C NMR (100 MHz, $CDCl_3$): δ 159.8, 149.0, 142.3,134.9, 134.5, 133.9, 133.0, 126.7, 126.5, 124.9, 124.3, 123.9, 120.8, 119.1, 114.4, 109.7, 106.7, 55.9, 55.3, 20.8, 20.3. LC-MS calculated for $C_{26}H_{22}N_4O$ $[M+H]^+$, 407; found 407.

Figure 1. ^{1}H NMR and ^{13}C NMR spectrum of **7**.



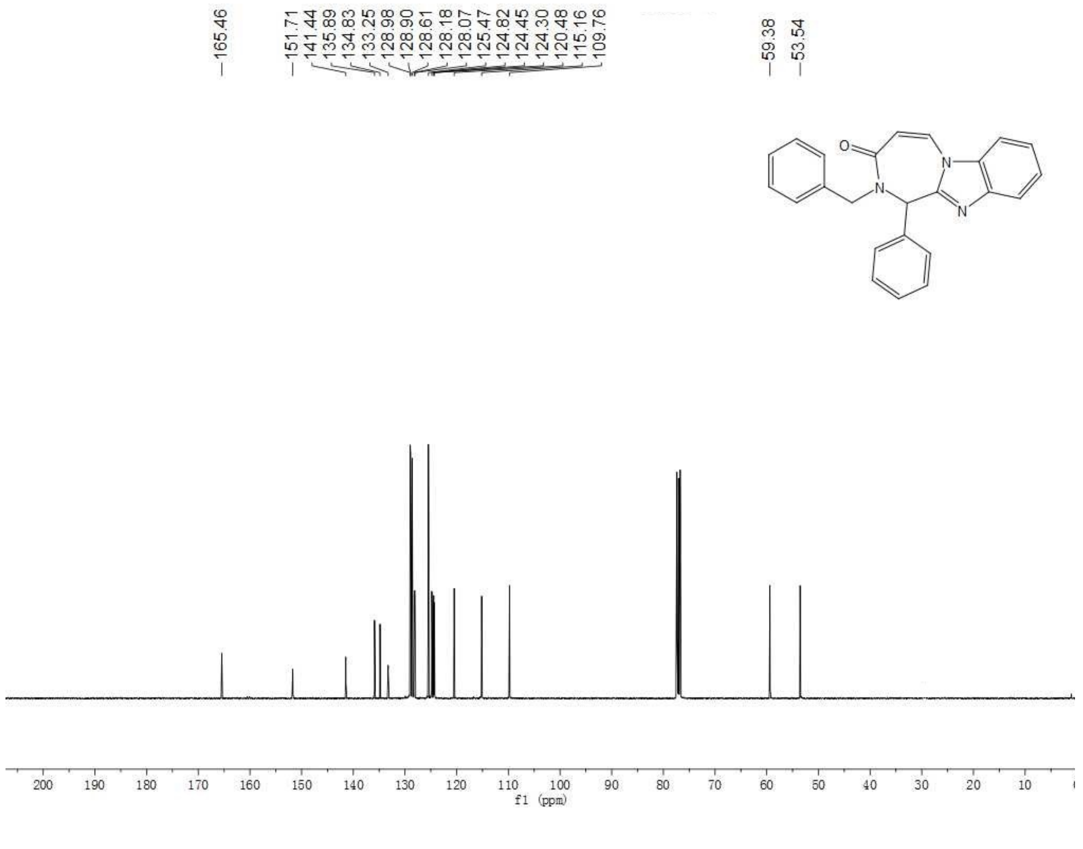
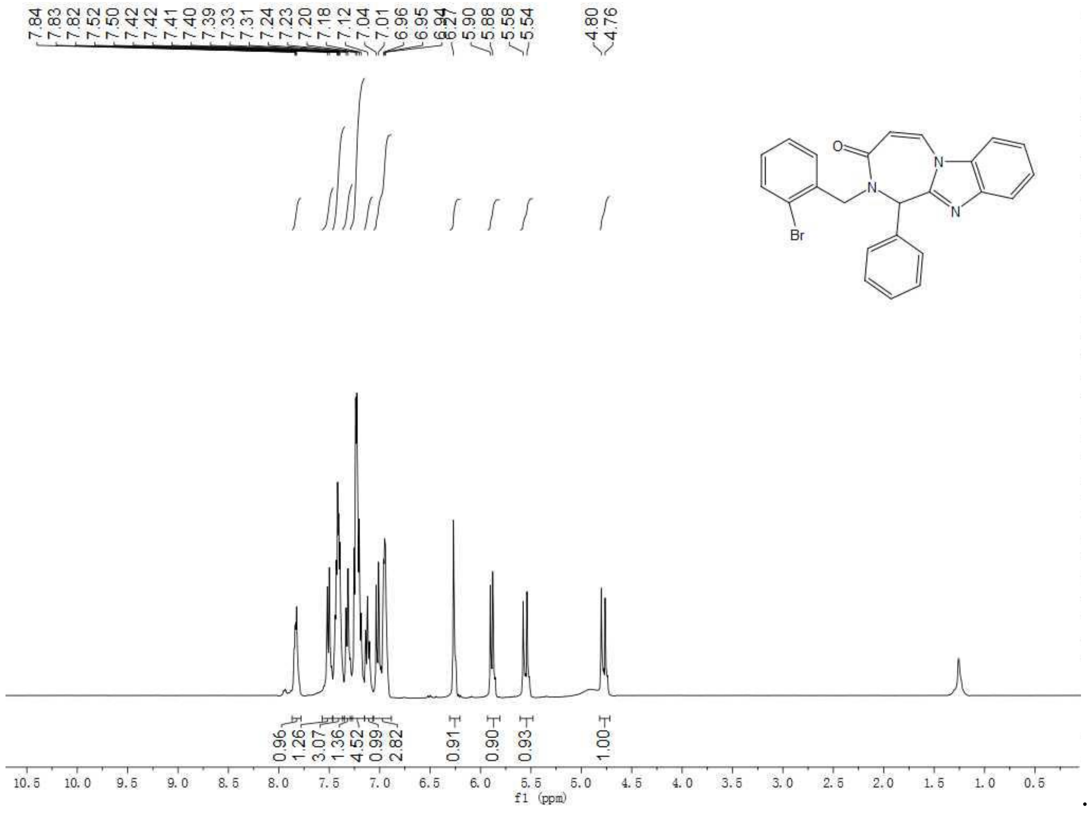


Figure 2. ^{1}H NMR and ^{13}C NMR spectrum of **12a**.



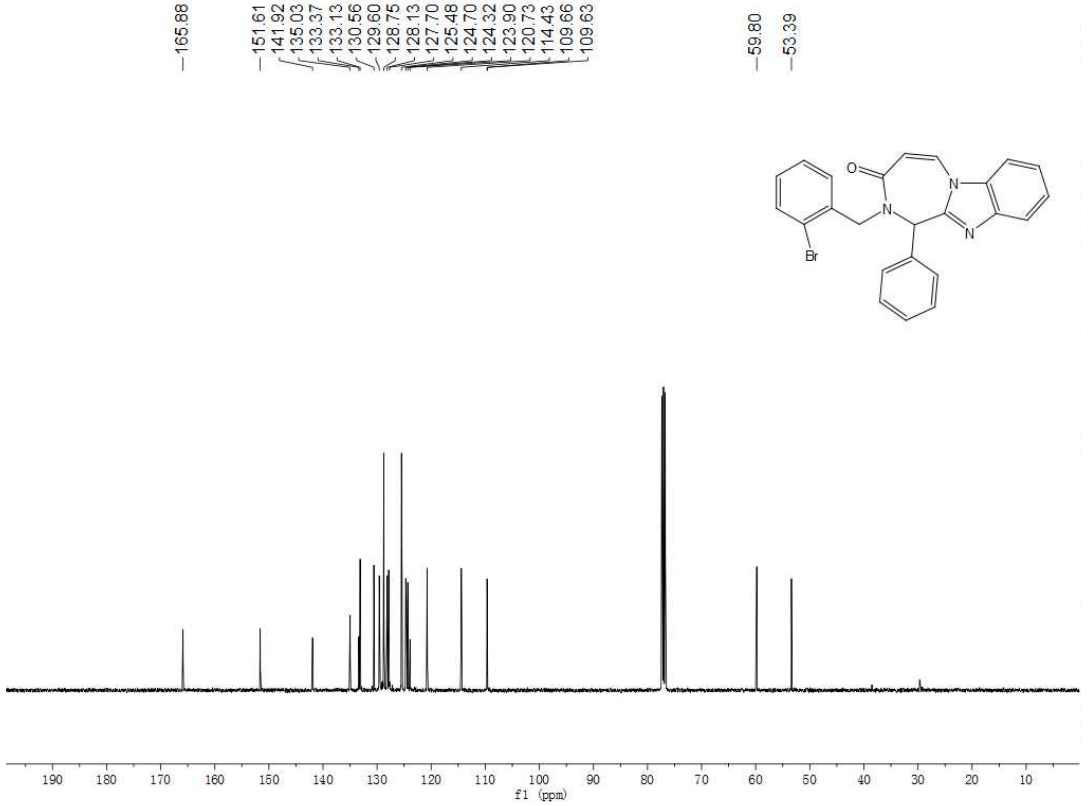
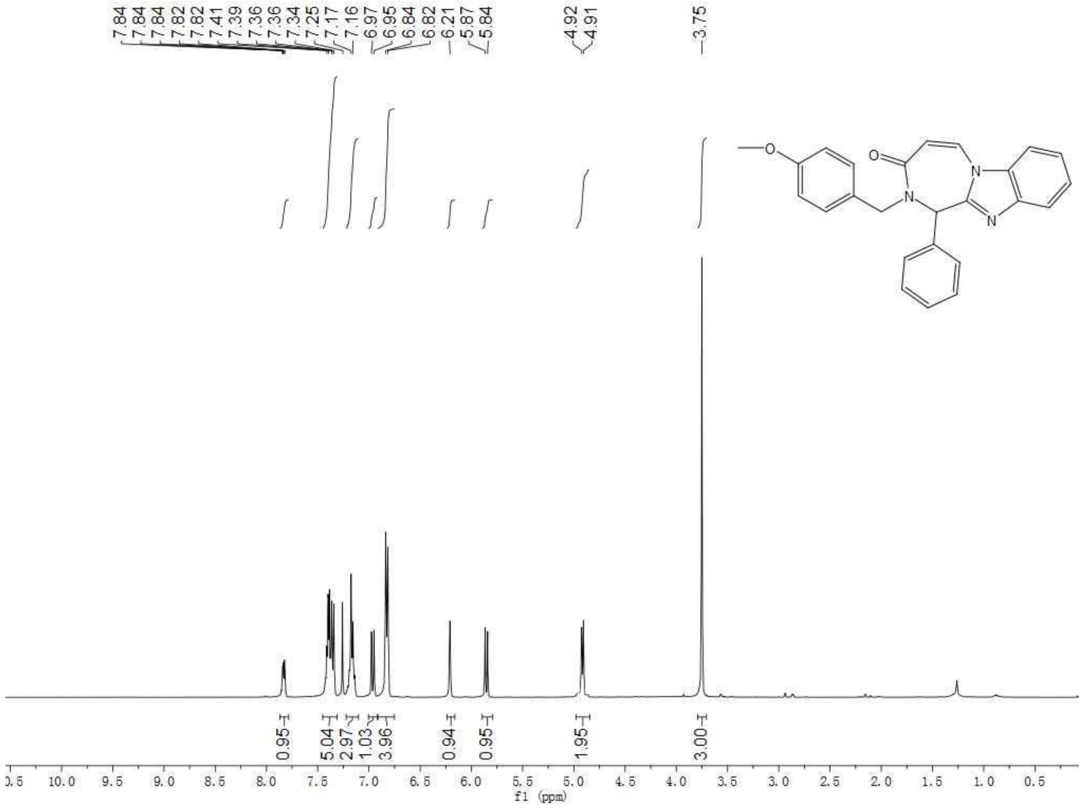


Figure 3. ^{1}H NMR and ^{13}C NMR spectrum of **12b**.



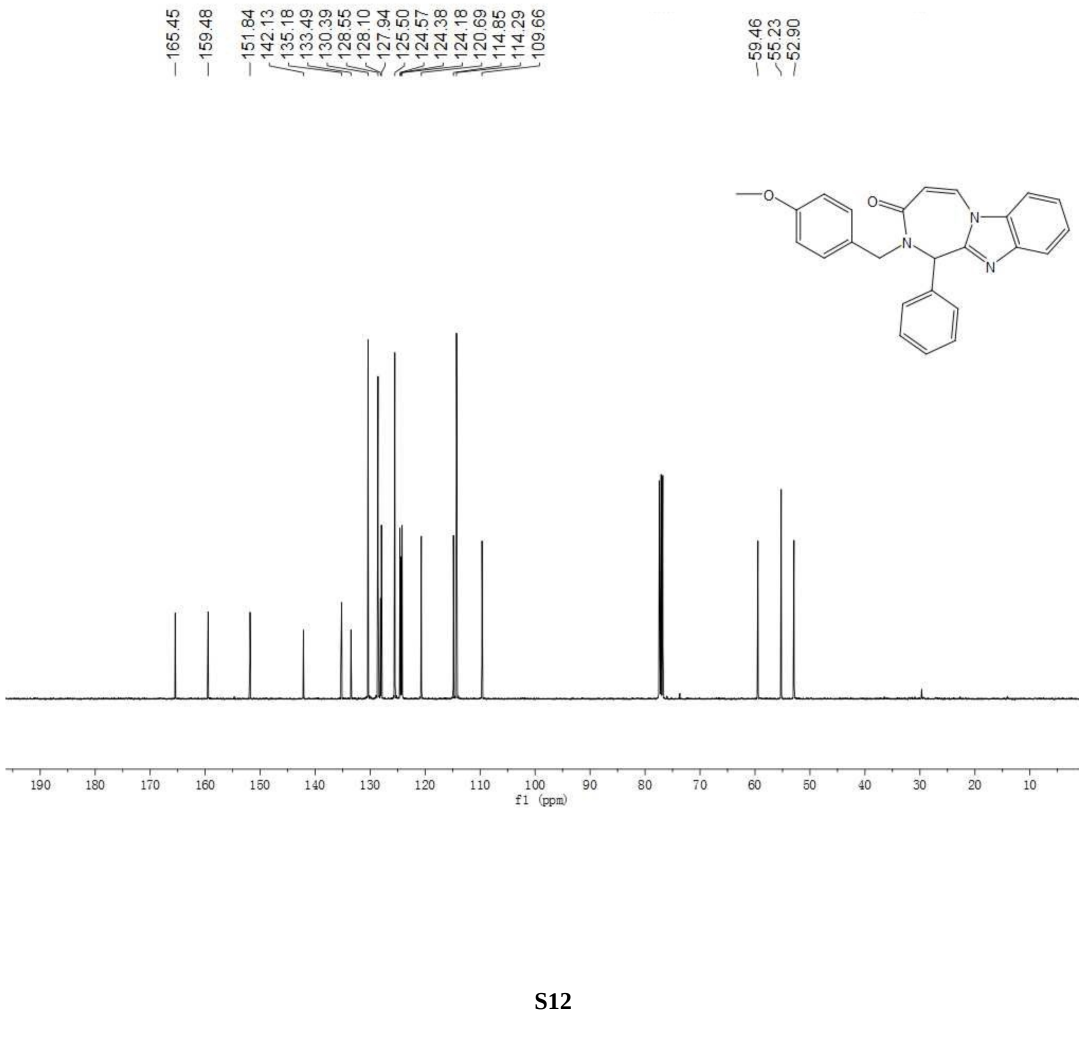
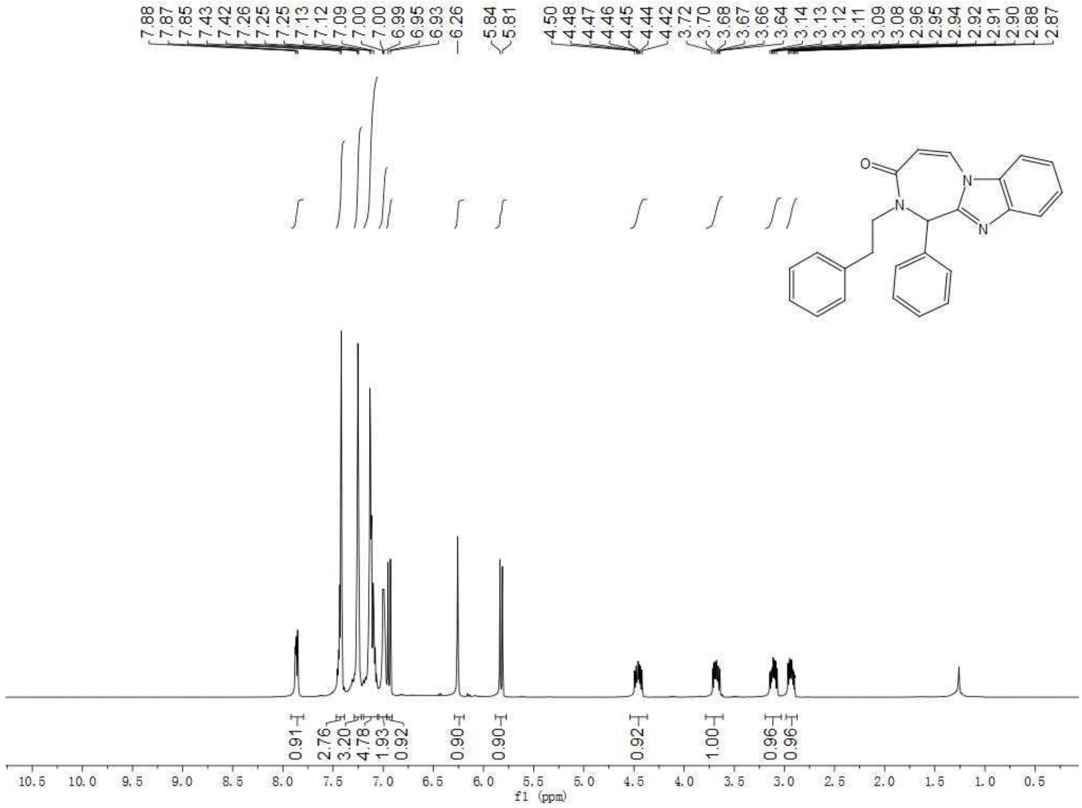


Figure 4. ^{1}H NMR and ^{13}C NMR spectrum of **12c**.



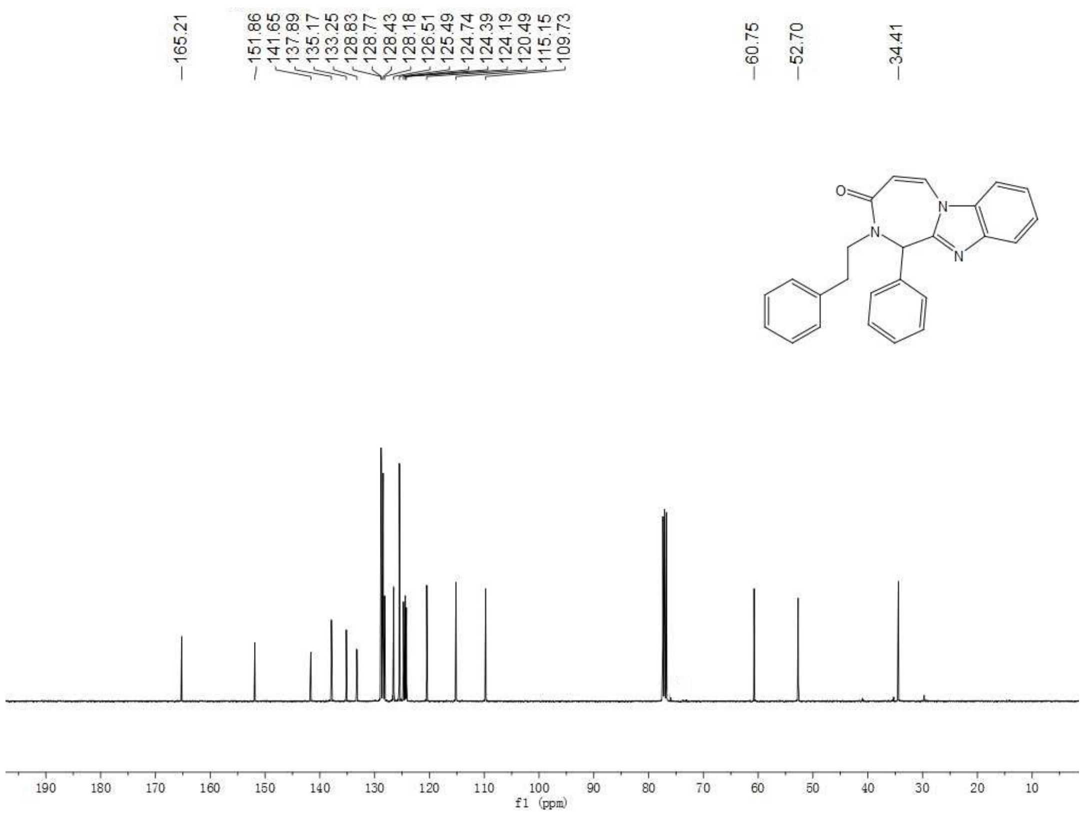
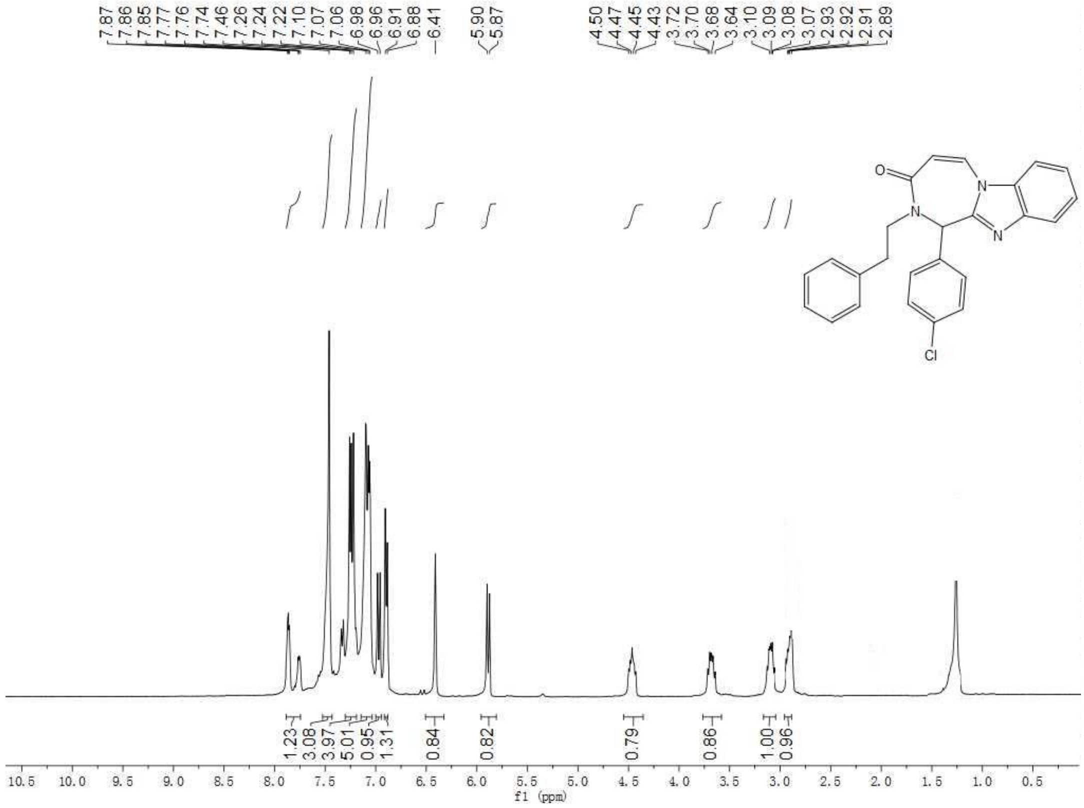


Figure 5. ^{1}H NMR and ^{13}C NMR spectrum of **12d**.



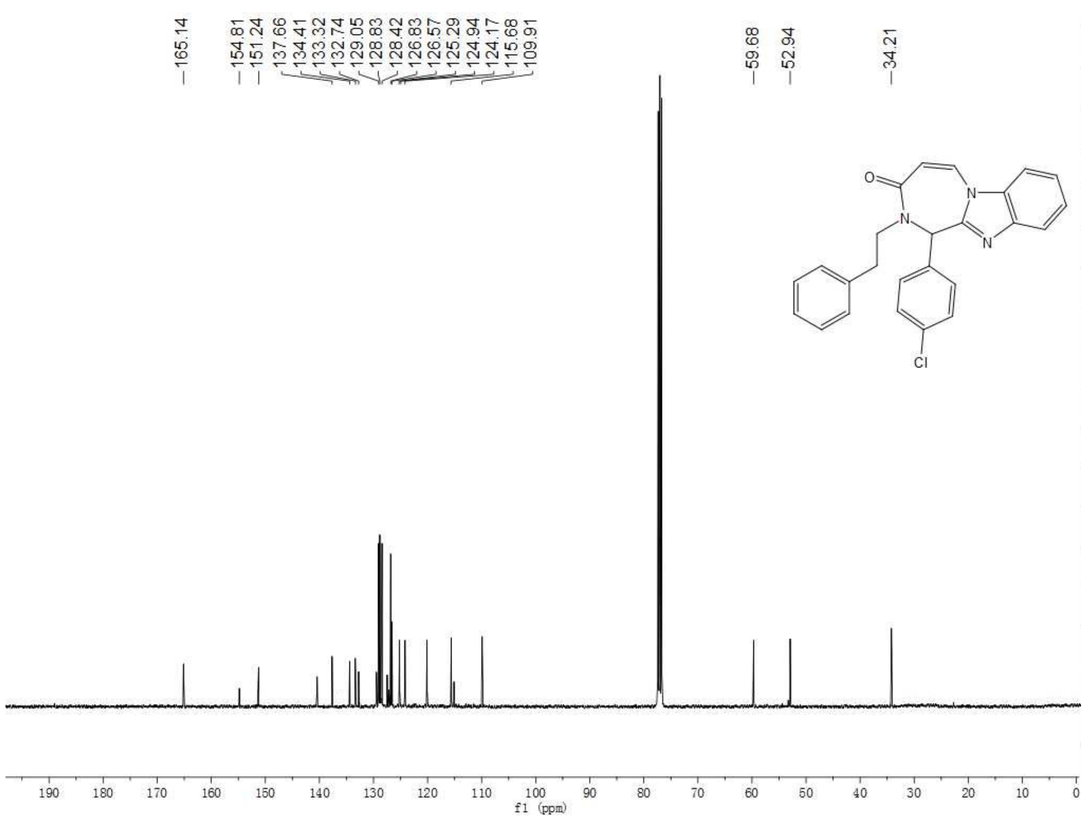
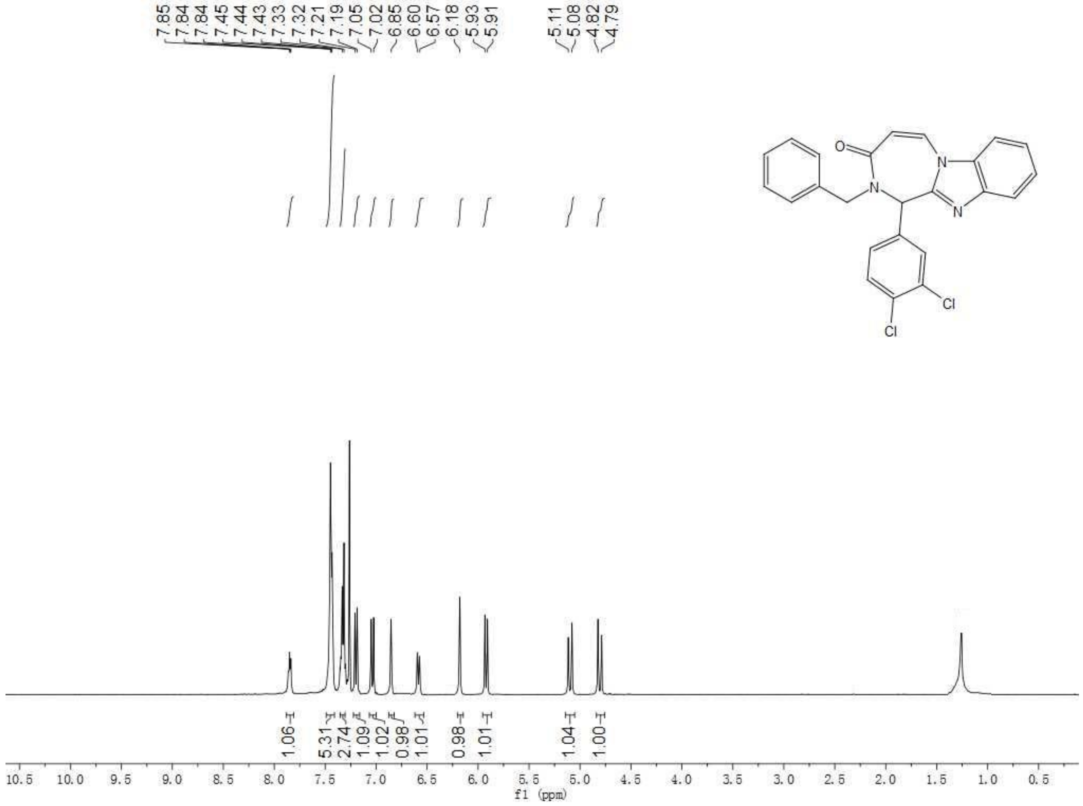


Figure 6. ^{1}H NMR and ^{13}C NMR spectrum of **12e**.



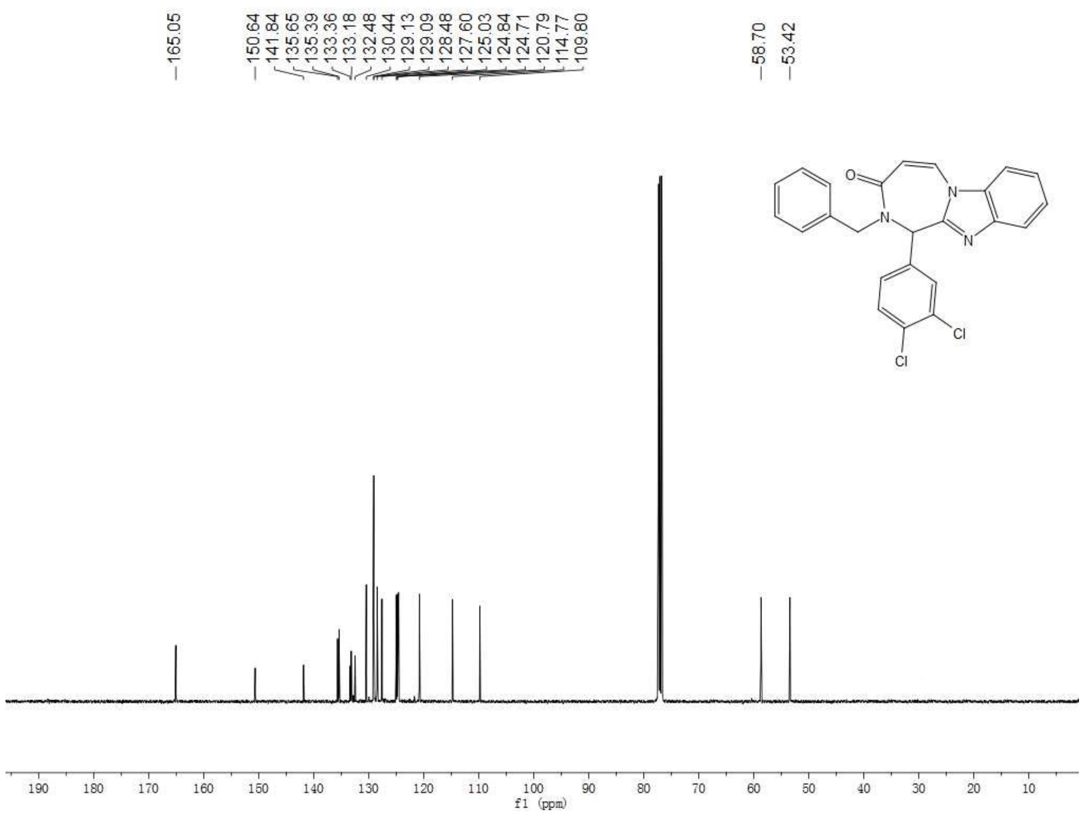
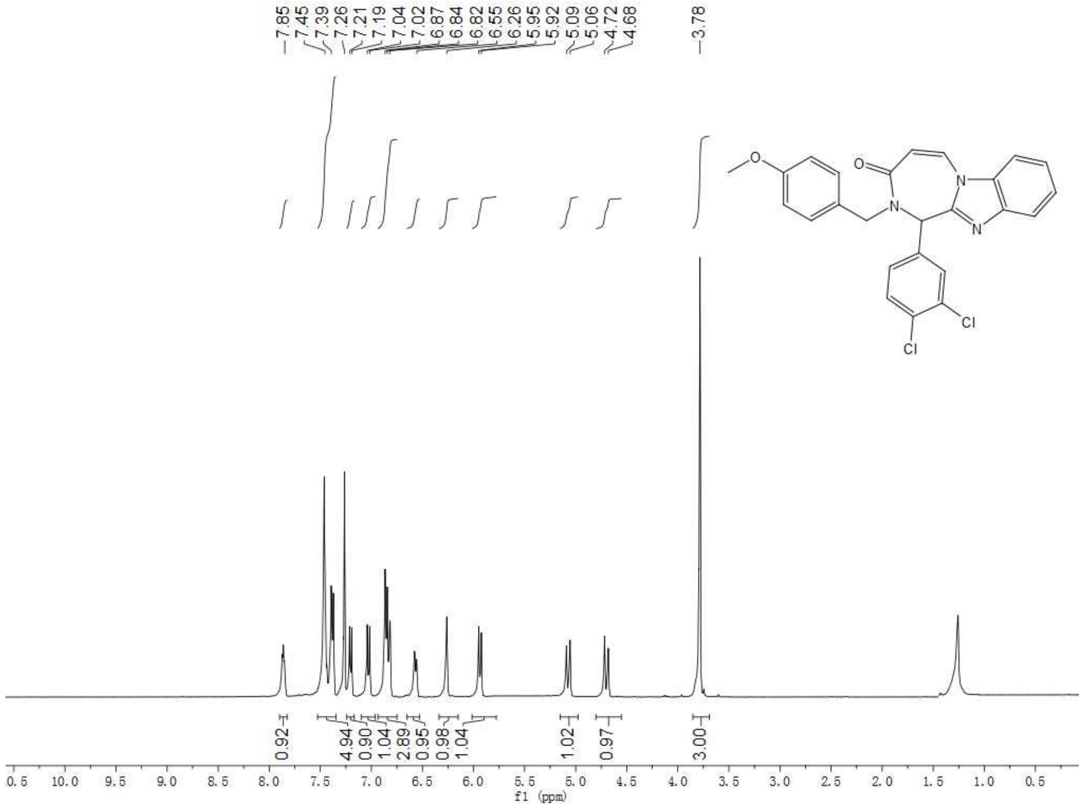


Figure 7. ^{1}H NMR and ^{13}C NMR spectrum of **12f**.



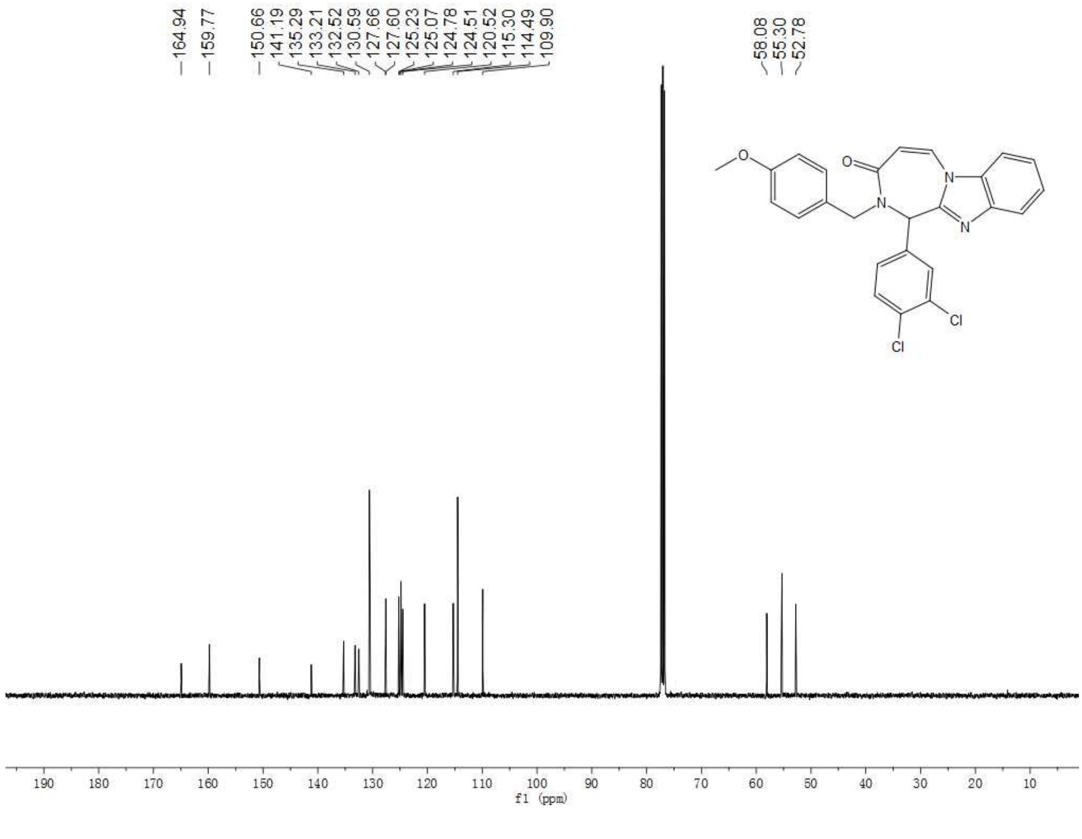
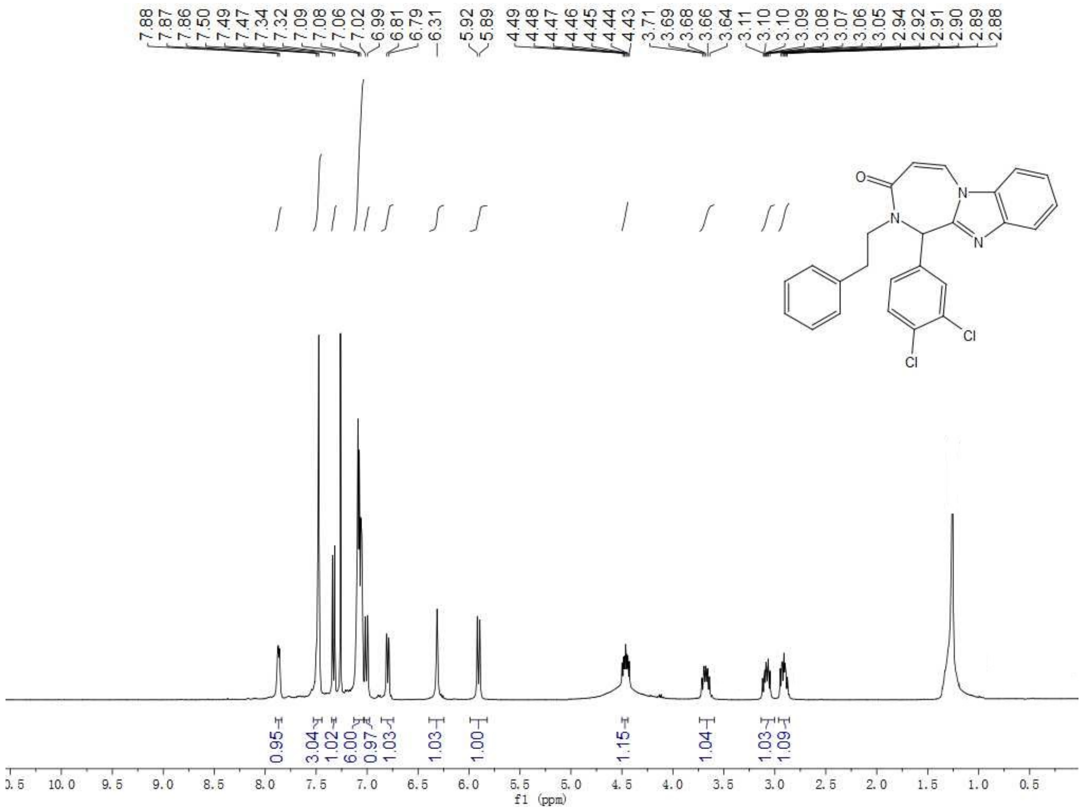


Figure 8. ^{1}H NMR and ^{13}C NMR spectrum of **12g**.



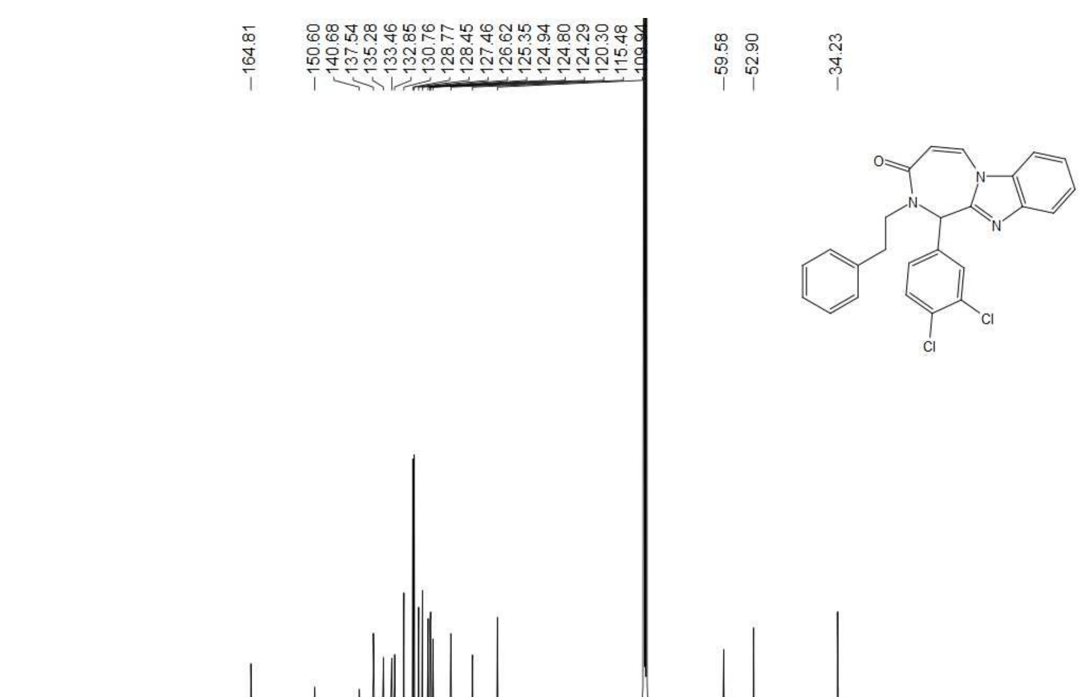
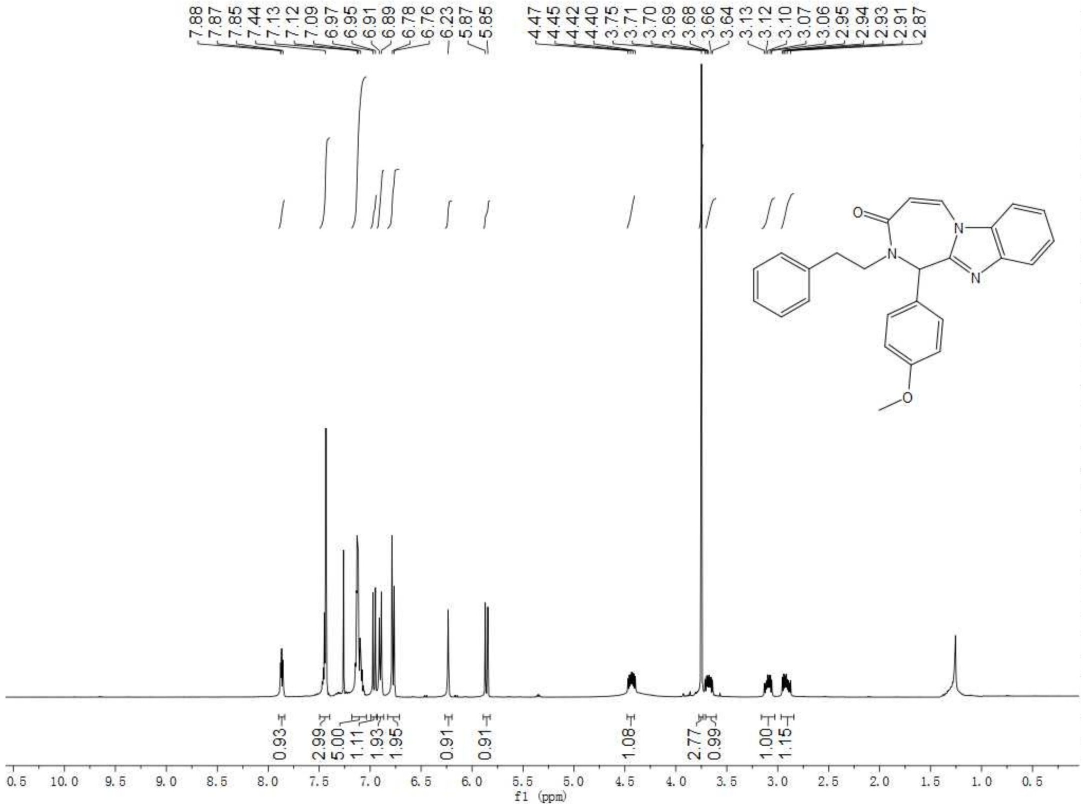


Figure 9. ^{1}H NMR and ^{13}C NMR spectrum of **12h**.



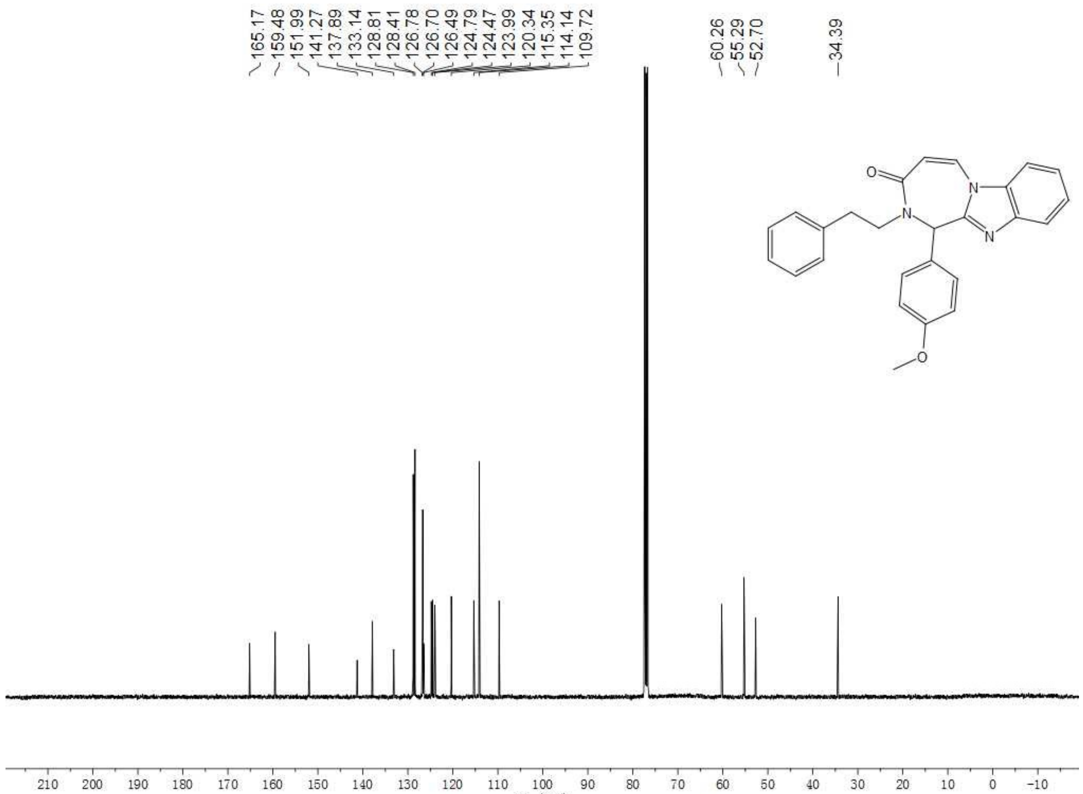
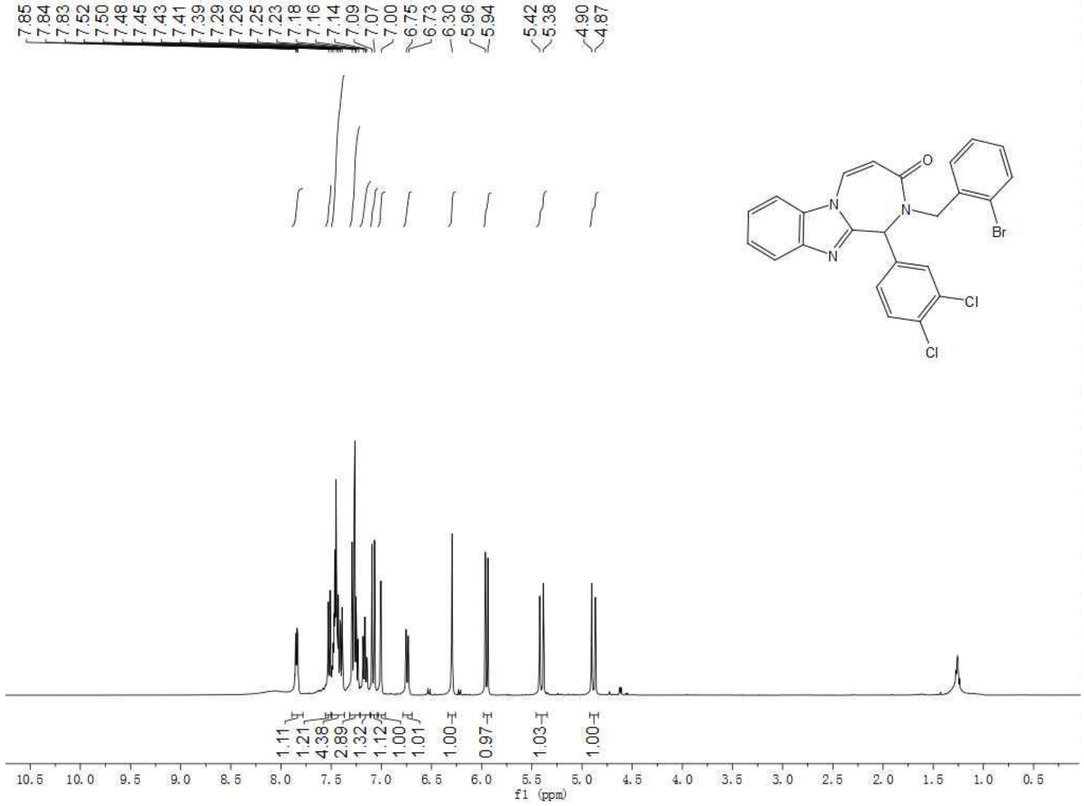


Figure 10. ^{1}H NMR and ^{13}C NMR spectrum of **12i**.



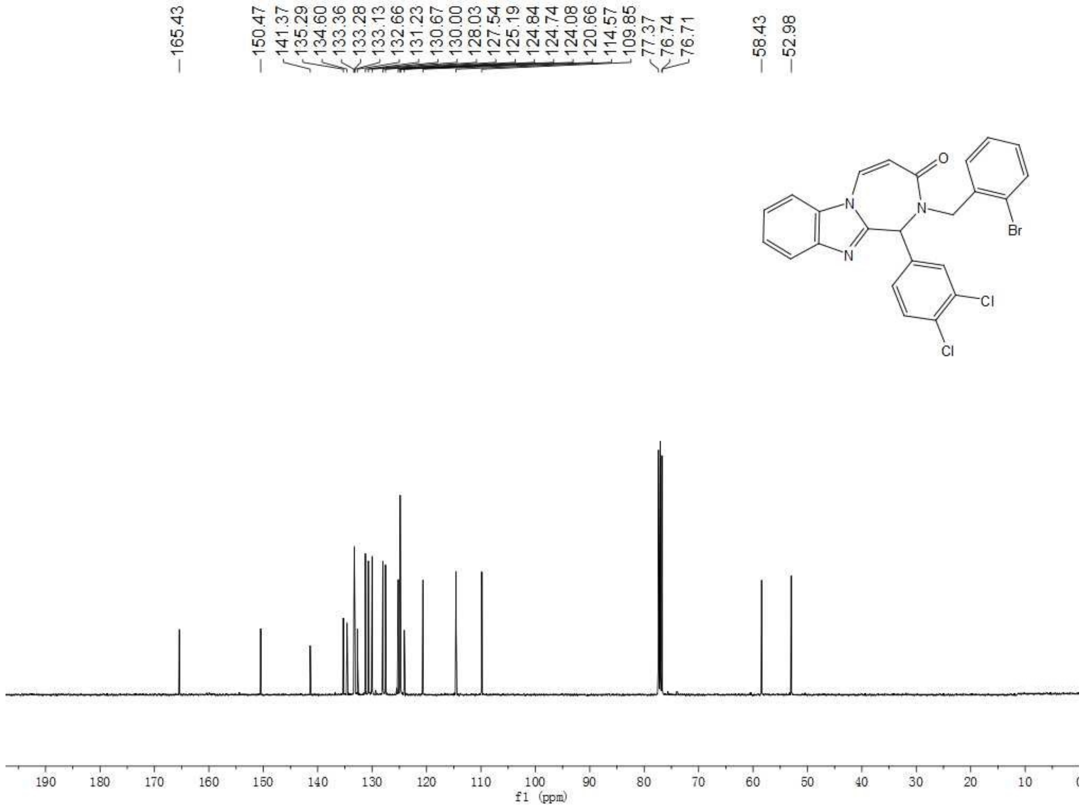
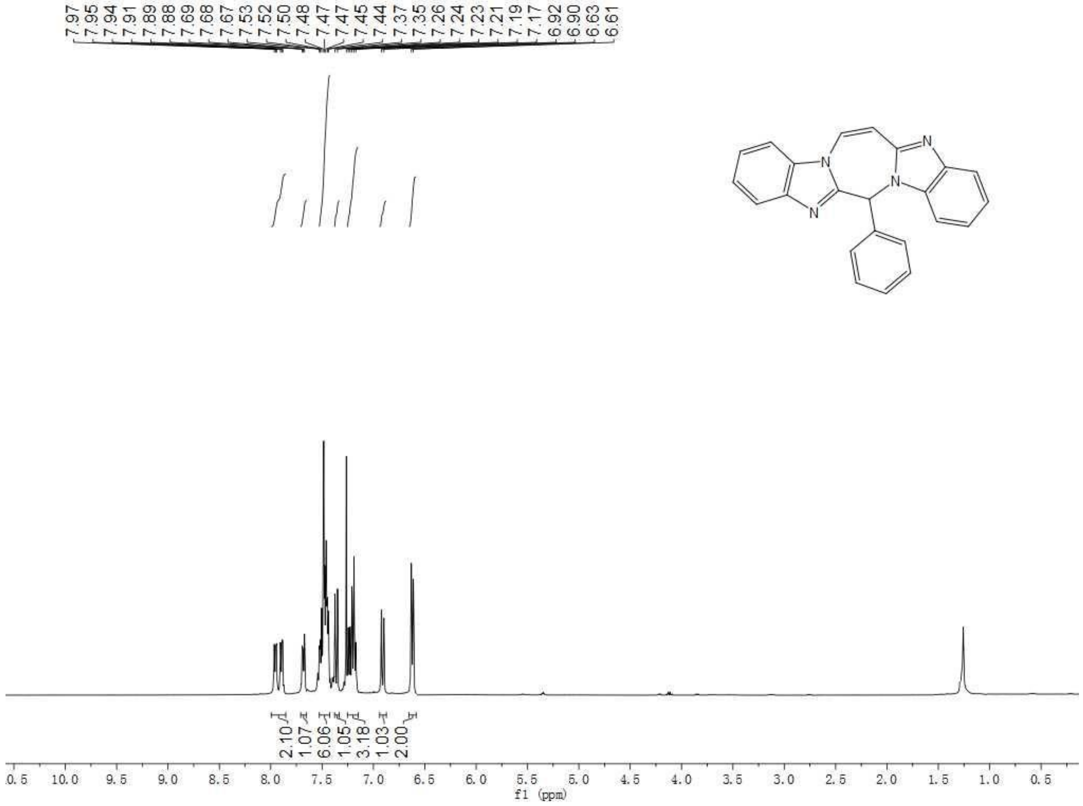


Figure 11. ^{1}H NMR and ^{13}C NMR spectrum of **17a**.



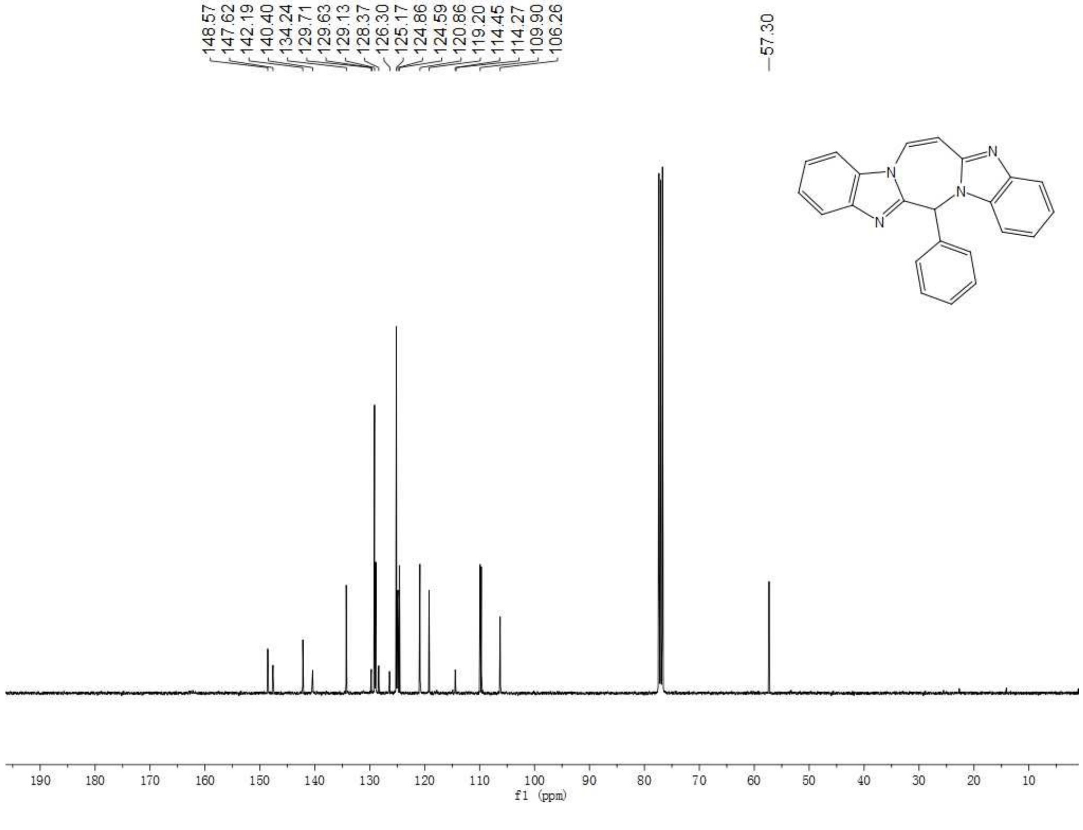
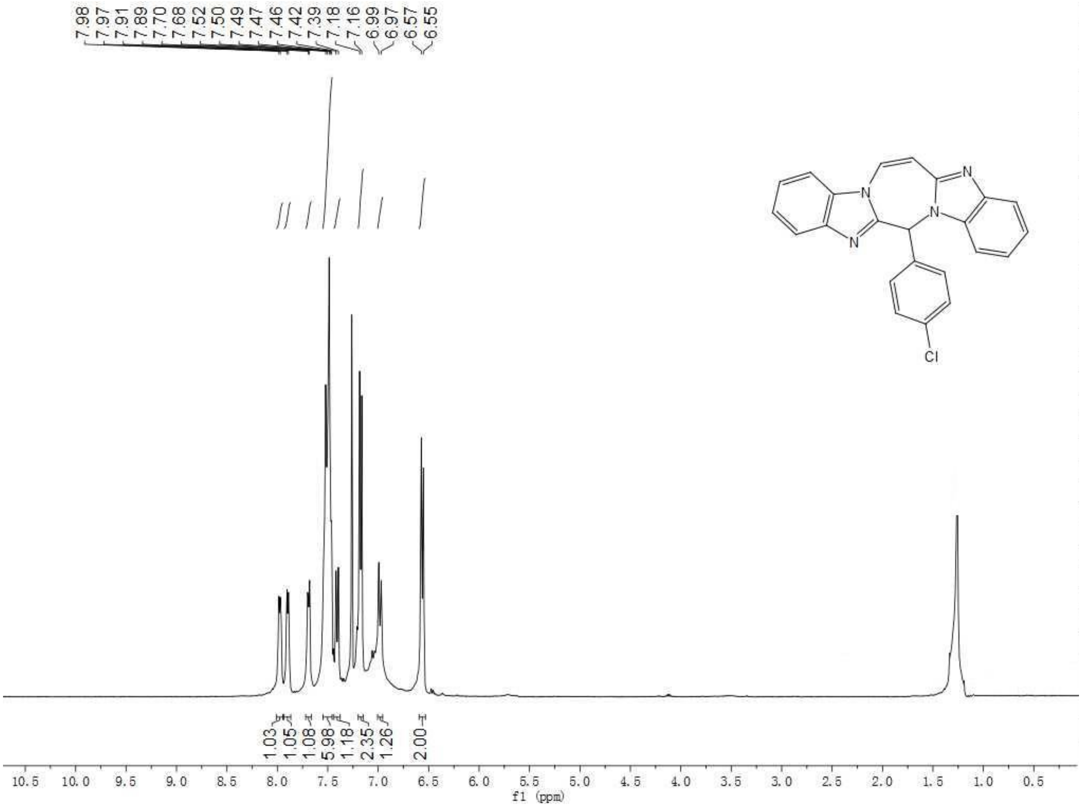


Figure 12. ^{1}H NMR and ^{13}C NMR spectrum of **17b**.



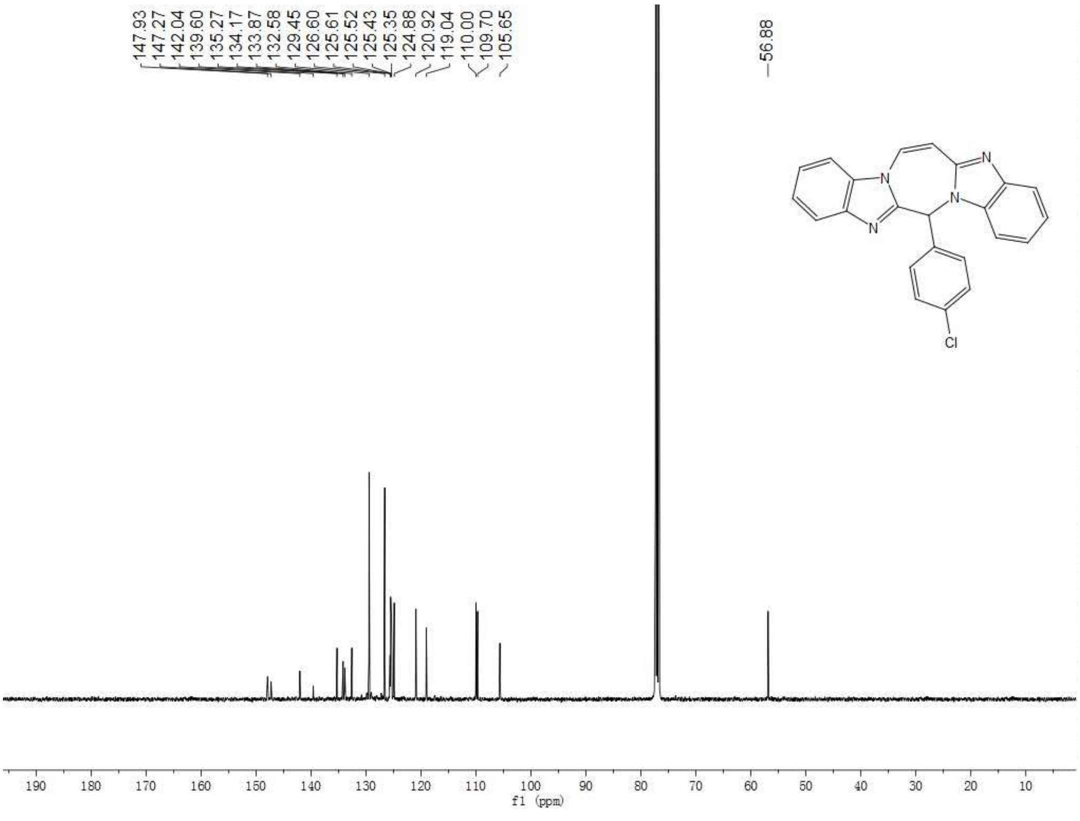
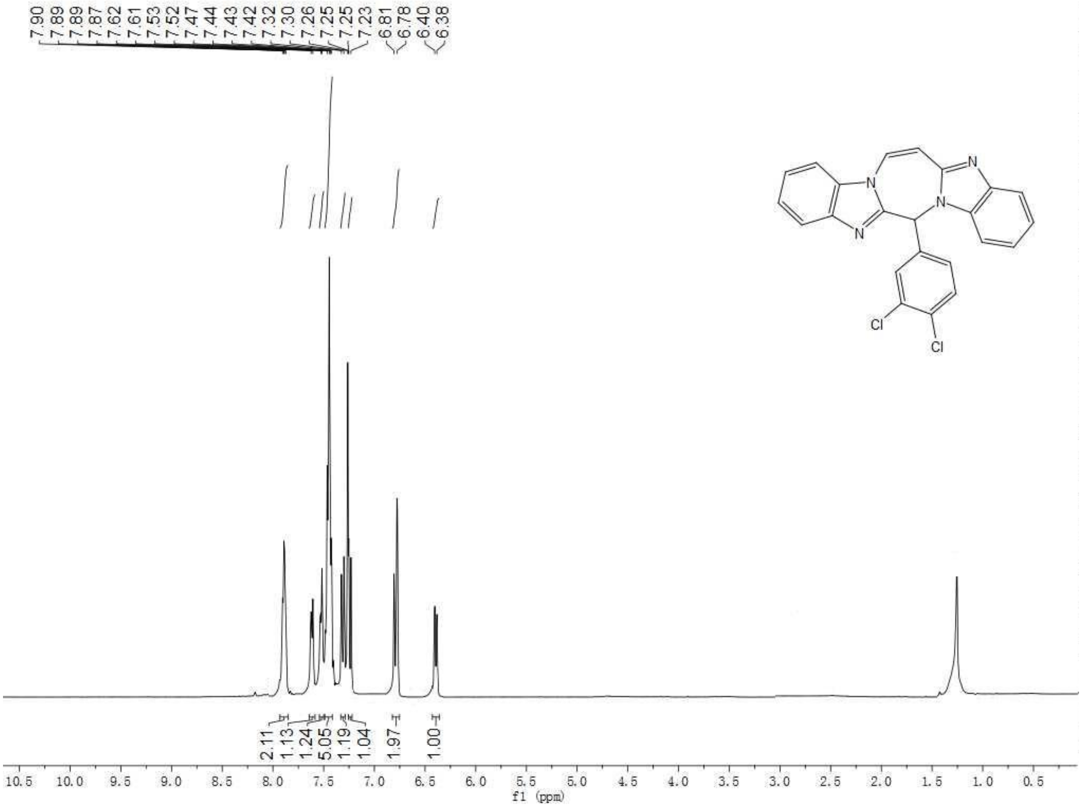


Figure 13. ^{1}H NMR and ^{13}C NMR spectrum of **17c**.



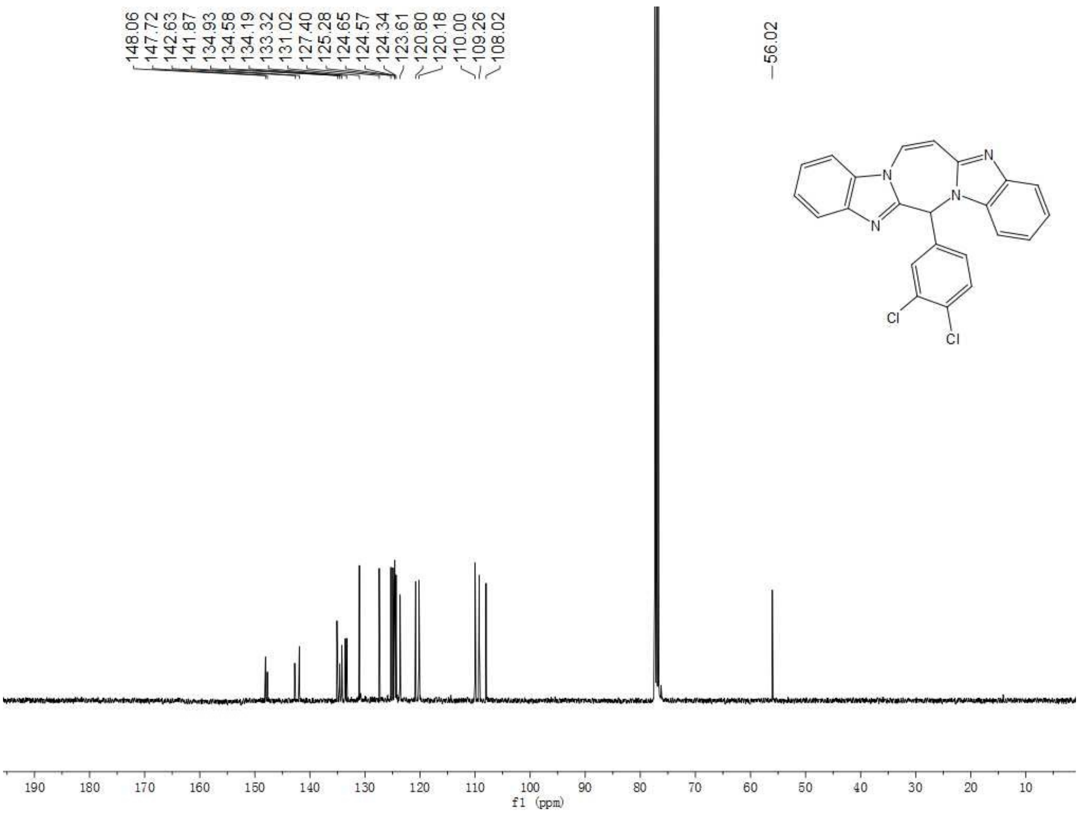
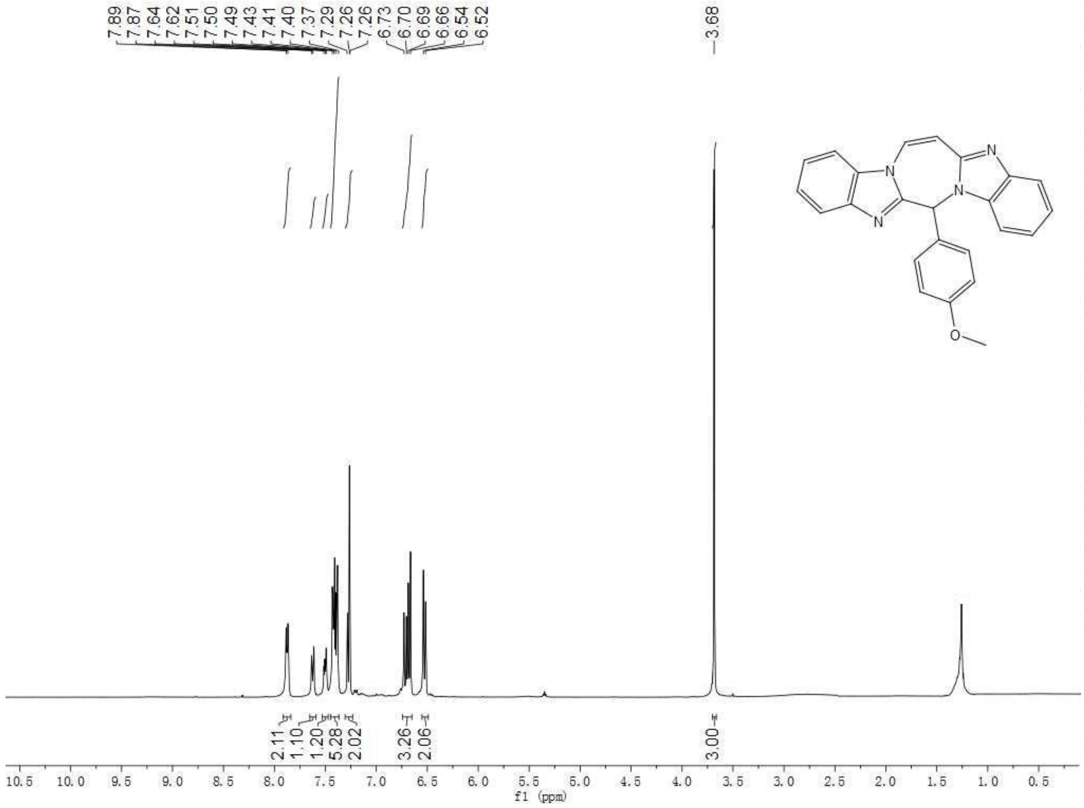


Figure 14. ^{1}H NMR and ^{13}C NMR spectrum of **17d**.



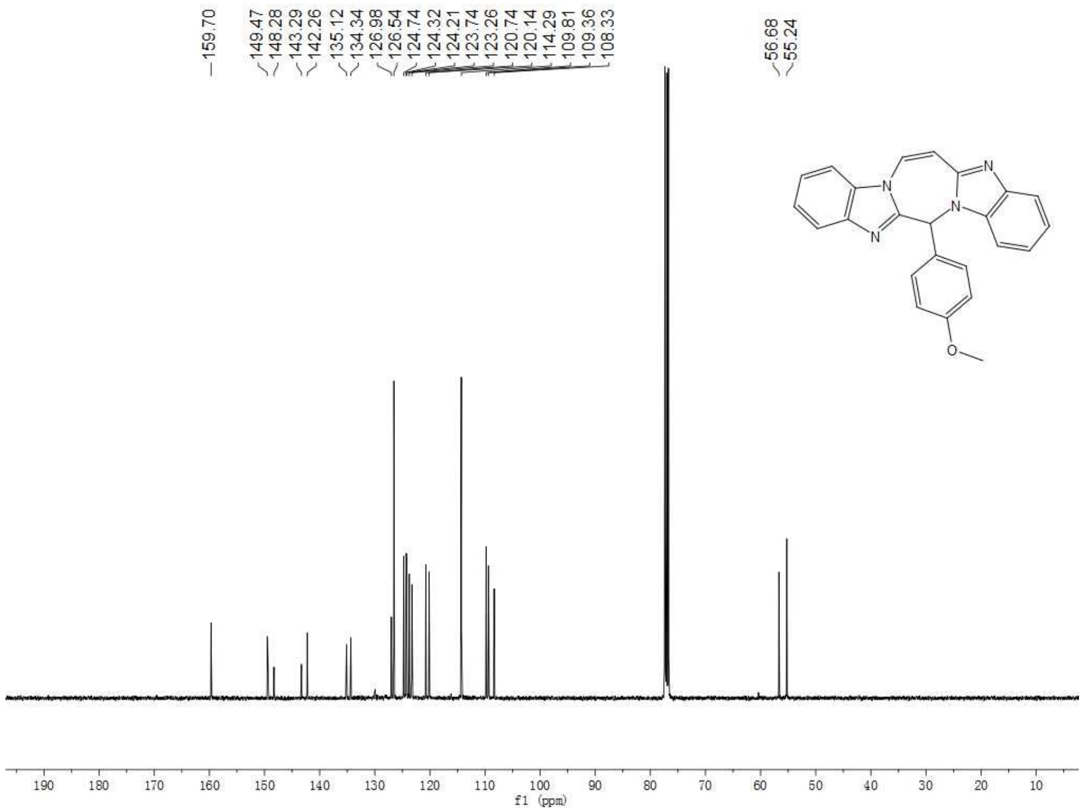


Figure 15. ^{1}H NMR and ^{13}C NMR spectrum of **17e**.

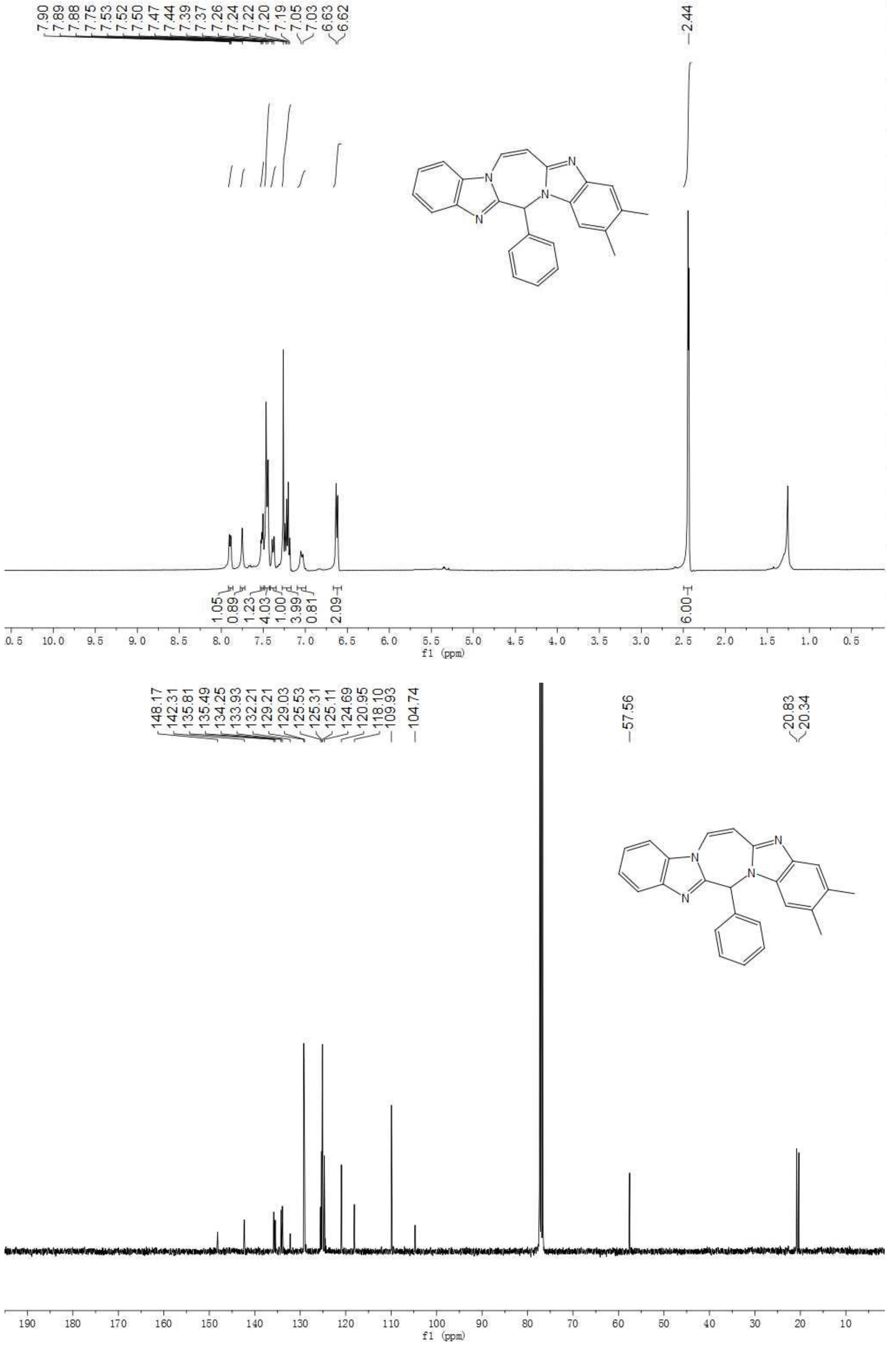


Figure 16. ^{1}H NMR and ^{13}C NMR spectrum of **17f**.