Electronic Supplementary Material (ESI) for New Journal of Chemistry.

Supporting Information

One-pot synthesis of multisubstituted spirocyclopropanes mediated by α-picoline

Huifang Ma, Jie Liang, Keyume Ablajan*

State Key Laboratory of Chemistry and Utilization of Carbon Based Energy Resources, College of Chemistry
Xinjiang University
Urumqi, Xinjiang 830017 China

E-mail: *ablajan209@hotmail.com, ablajan209@xju.edu.cn*

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1. General information

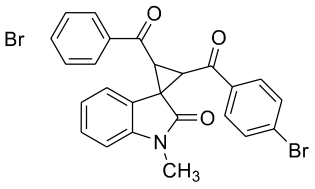
All the reagents and solvents were purchased from Aladdin, TCI, and were used without further purification. The progress of the reaction was examined by thin-layer chromatography (TLC). Column chromatography was carried out for product isolation, using silica gel (200−400 mesh). Infrared (IR) spectra were recorded on a Bruker Equinox 55 spectrophotometer using samples as KBr pellets. NMR spectra (^{1}H NMR at 400 MHz, ^{13}C NMR at 100 MHz) were recorded on a Bruker Inova-400 instrument using tetramethylsilane (TMS) as an internal standard. High-resolution mass spectrometry (HRMS) data were obtained using a Micromass Q-TOF Global Tandem Mass Spectrometer.

2. General procedure for the synthesis of compound **3**

To a reaction vial containing isatin (0.25 mmol) and α-bromo(chloro)acetophenone (0.5 mmol) in CH_3CN (2.0 mL), the catalst α-picoline (0.25 mmol, 1 equiv.) and base Et_3N (0.05 mmol, 20 mol%) were added at room temperature. The mixture was stirred for 12 h under reflux. The reaction was monitored by thin layer chromatography (TLC) until completion. Then, solvent was evaporated under vacuum. The crude mixture was purified by silica gel column chromatography (*n*-hexane /EtOAc 4:1 v/v) to afford the desired pure product **3**.

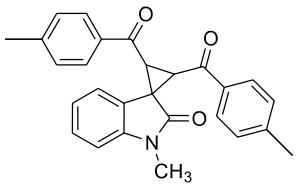
3. Characterization Data (compounds **3a-3i**)

3.1 1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((4-bromophenyl)methanone) **(***trans*-**3a)**



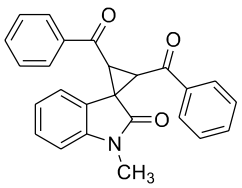
Orange solid; Yield 85% (114 mg); m.p. 170–172 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.82 (d, *J*=8.0 Hz, 2H), 7.65 (d, *J*=8.0 Hz, 2H), 7.57 (d, *J*=8.0 Hz, 2H), 7.52 (d, *J*=8.0 Hz, 2H), 7.35–7.29 (m, 2H), 7.09-7.03 (m, 1H), 6.89 (d, *J*=8.0 Hz, 1H), 4.34 (d, *J*=8.0 Hz, 1H), 4.09 (d, *J*=8.0 Hz, 1H), 3.19 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.09, 189.32, 170.91, 144.17, 135.25, 134.77, 132.10, 130.04, 129.82, 129.35, 128.96, 128.83, 123.38, 122.91, 122.30, 108.51, 40.79, 39.15, 38.34, 26.80 ppm. IR (thin film): 3050, 2927, 2848, 1720, 1685, 1492, 1368, 1250, 1130, 1042, 910, 823, 740, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{25}H_{17}Br_2NO_3$: 537.9653; found: 537.9654.

3.2 (1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis(p-tolylmethanone) (*trans*-**3b**)



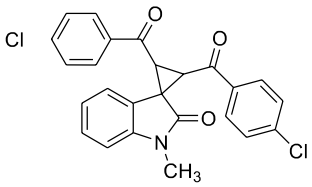
Orange solid; Yield 62% (63 mg); m.p. 128–130 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.86 (d, *J*=8.0 Hz, 2H), 7.70 (d, *J*=8.0 Hz, 2H), 7.34 (d, *J*=8.0 Hz, 1H), 7.30-7.25 (m, 1H), 7.19 (d, *J*=8.0 Hz, 2H), 7.14 (d, *J*=8.0 Hz, 2H), 7.06-6.99 (m, 1H), 6.84 (d, *J*=8.0 Hz, 1H), 4.39 (d, *J*=8.0 Hz, 1H), 4.13 (d, *J*=8.0 Hz, 1H), 3.16 (s, 3H), 2.34 (s, 6H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.70, 190.01, 171.29, 144.82, 144.39, 144.19, 134.28, 133.78, 129.38, 128.75, 128.53, 128.38, 124.11, 122.69, 122.39, 108.21, 40.73, 39.48, 38.64, 26.71, 21.66 ppm. IR (thin film): 3055, 2928, 2842, 1713, 1690, 1503, 1340, 1265, 1128, 1050, 908, 814, 728, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{27}H_{23}NO_3$: 410.1756; found: 410.1758.

3.3 (1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis(phenylmethanone) **(***trans*-**3c)**



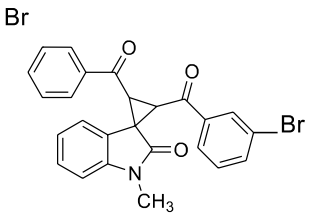
Orange solid; Yield 78% (74 mg); m.p. 159–161 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07–7.93 (m, 2H), 7.89–7.75 (m, 2H), 7.56–7.48 (m, 2H), 7.45–7.40 (m, 2H), 7.39–7.33 (m, 3H), 7.33-7.28 (m, 1H), 7.09-7.02 (m, 1H), 6.87 (d, *J*=8.0 Hz, 1H), 4.43 (d, *J*=8.0 Hz, 1H), 4.15 (d, *J*=8.0 Hz, 1H), 3.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.20, 190.33, 171.20, 144.24, 136.69, 136.13, 133.83, 133.55, 128.73, 128.64, 128.54, 128.45, 123.93, 122.79, 122.45, 108.32, 40.90, 39.50, 38.64, 26.75 ppm. IR (thin film): 3056, 2930, 2856, 1710, 1695, 1510, 1350, 1265, 1130, 1056, 910, 820, 729, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{25}H_{19}NO_3$: 382.1443; found: 382.1439.

3.4 (1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((4-chlorophenyl)methanone) **(***trans*-**3d)**



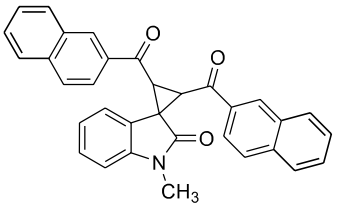
Orange solid; Yield 74% (83 mg); m.p. 164–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.90 (d, *J*=8.0 Hz, 2H), 7.73 (d, *J*=8.0 Hz, 2H), 7.39 (d, *J*=8.0 Hz, 2H), 7.35-7.28 (m, 4H), 7.08–7.03 (m, 1H), 6.88 (d, *J*=8.0 Hz, 1H), 4.34 (d, *J*=8.0 Hz, 1H), 4.10 (d, *J*=8.0 Hz, 1H), 3.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.89, 189.12, 170.94, 144.18, 140.53, 140.15, 134.86, 134.39, 129.98, 129.74, 129.11, 128.81, 123.43, 122.91, 122.32, 108.50, 40.80, 39.20, 38.38, 26.79 ppm. IR (thin film): 3052, 2928, 2847, 1728, 1679, 1488, 1372, 1245, 1156, 1050, 903, 820, 750, 470 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{25}H_{17}Cl_2NO_3$: 450.0663; found: 450.0665.

3.5 (1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((3-bromophenyl)methanone) **(***trans*-**3e)**



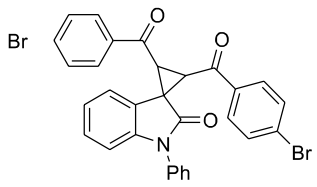
Orange solid; Yield 80% (107 mg); m.p. 165–166 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.08 (t, *J*=4.0 Hz, 1H), 7.97 (t, *J*=4.0 Hz, 1H), 7.90–7.83 (m, 1H), 7.73–7.51 (m, 3H), 7.37-7.26 (m, 3H), 7.21 (t, *J*=8.0 Hz, 1H), 7.10-7.01 (m, 1H), 6.93–6.83 (m, 1H), 4.33 (d, *J*=8.0 Hz, 1H), 4.08 (d, *J*=8.0 Hz, 1H), 3.18 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.85, 189.01, 170.82, 144.21, 138.20, 137.64, 136.76, 136.47, 131.44, 131.36, 130.31, 130.29, 128.90, 127.28, 126.88, 123.26, 123.21, 123.18, 122.97, 122.45, 108.54, 41.03, 39.26, 38.21, 26.79 ppm. IR (thin film): 3048, 2926, 2840, 1724, 1680, 1495, 1370, 1243, 1126, 1040, 915, 820, 735, 475 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{25}H_{17}Br_2NO_3$: 537.9653; found: 537.9654.

3.6 (1'-Methyl-2'-oxospiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis(naphthalen-2-ylmethanone) **(***trans*-**3f)**



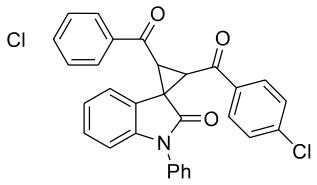
Orange solid; Yield 78% (94 mg); m.p. 181–182 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.55 (s, 1H), 8.27 (s, 1H), 8.05 (m, 1H), 8.00–7.90 (m, 2H), 7.90–7.73 (m, 4H), 7.70 (d, *J*=8.0 Hz, 1H), 7.64–7.40 (m, 5H), 7.31 (m, 1H), 7.14–7.04 (m, 1H), 6.86 (d, *J*=8.0 Hz, 1H), 4.66 (d, *J*=8.0 Hz, 1H), 4.35 (d, *J*=8.0 Hz, 1H), 3.14 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 192.07, 190.45, 171.27, 144.30, 135.86, 135.80, 134.07, 133.61, 132.37, 132.36, 130.92, 130.48, 129.82, 129.65, 128.92, 128.65, 128.59, 127.75, 127.71, 126.94, 126.71, 124.04, 123.91, 123.81, 122.84, 122.62, 108.32, 41.17, 39.94, 38.68, 26.77 ppm. IR (thin film): 3055, 2925, 2854, 1714, 1666, 1466, 1348, 1279, 1124, 1045, 905, 818, 728, 470 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{33}H_{23}NO_3$: 482.1756; found: 482.1761.

3.7 (2'-Oxo-1'-phenylspiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((4-bromophenyl)methanone) **(***trans*-**3g)**



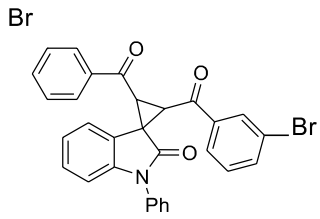
Orange solid; Yield 70% (105 mg); m.p. 168–169 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.89 (d, *J*=8.0 Hz, 2H), 7.69 (d, *J*=8.0 Hz, 2H), 7.60 (d, *J*=8.0 Hz, 2H), 7.54 (d, *J*=8.0 Hz, 2H), 7.49-7.32 (m, 5H), 7.19 (d, *J*=8.0 Hz, 2H), 7.10 (t, *J*=8.0 Hz, 1H), 6.89 (d, *J*=8.0 Hz, 1H), 4.39 (d, *J*=8.0 Hz, 1H), 4.13 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 191.09, 189.47, 170.47, 144.07, 135.28, 134.91, 133.83, 132.19, 132.13, 130.13, 129.85, 129.59, 129.49, 129.00, 128.75, 128.30, 126.31, 123.45, 123.34, 122.63, 109.87, 40.89, 39.96, 38.73 ppm. IR (thin film): 3046, 2940, 2865, 1722, 1680, 1575, 1320, 1225, 1185, 1050, 975, 839, 753, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z $[M+H]^+$ calcd for $C_{30}H_{19}Br_2NO_3$: 599.9810; found: 599.9813.

3.8 (2'-Oxo-1'-phenylspiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((4-chlorophenyl)methanone) **(***trans*-**3h)**



Orange solid; Yield 65% (83 mg); m.p. 145–146 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.97 (d, *J*=8.0 Hz, 2H), 7.77 (d, *J*=8.0 Hz, 2H), 7.43 (m, 5H), 7.40–7.34 (m, 4H), 7.19 (d, *J*=8.0 Hz, 2H), 7.10 (t, *J*=8.0 Hz, 1H), 6.90 (d, *J*=8.0 Hz, 1H), 4.40 (d, *J*=8.0 Hz, 1H), 4.13 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.87, 189.23, 170.47, 144.06, 140.66, 140.20, 134.89, 134.51, 133.84, 130.05, 129.76, 129.57, 129.17, 129.12, 129.03, 129.00, 128.71, 128.27, 126.29, 123.42, 123.37, 122.64, 109.84, 40.89, 40.00, 38.76 ppm. IR (thin film): 3050, 2956, 2860, 1718, 1656, 1598, 1345, 1210, 1169, 1068, 980, 820, 753, 470 cm^{-1}; HRMS (TOF MS ES$^+$): m/z $[M+H]^+$ calcd for $C_{30}H_{19}Cl_2NO_3$: 512.0820; found: 512.0821.

3.9 (2'-Oxo-1'-phenylspiro[cyclopropane-1,3'-indoline]-2,3-diyl)bis((3-bromophenyl)methanone) **(***trans*-**3i)**



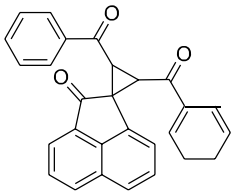
Orange solid; Yield 72% (108 mg); m.p. 152–154 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.17–8.11 (m, 1H), 8.02–7.90 (m, 2H), 7.66 (m, 3H), 7.47–7.38 (m, 3H), 7.34 (m, 2H), 7.28–7.25 (m, 1H), 7.24-7.23 (m, 1H), 7.22–7.17 (m, 2H), 7.13–7.06 (m, 1H), 6.89 (d, *J*=8.0 Hz, 1H), 4.37 (d, *J*=8.0 Hz, 1H), 4.10 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 190.86, 189.17, 170.38, 144.15, 138.22, 137.73, 136.85, 136.49, 133.82, 131.53, 131.46, 130.37, 130.30, 129.59, 128.82, 128.32, 127.33, 126.84, 126.39, 123.49, 123.24, 123.18, 123.16, 122.71, 109.87, 41.04, 39.98, 38.59 ppm. IR (thin film): 3045, 2942, 2870, 1725, 1676, 1583, 1335, 1218, 1176, 1046, 970, 842, 756, 465 cm^{-1}; HRMS (TOF MS ES$^+$): m/z $[M+H]^+$ calcd for $C_{30}H_{19}Br_2NO_3$: 599.9810; found: 599.9813.

4. General procedure for the synthesis of compounds **5a-5f**

To a reaction vial containing acenaphthoquinone (0.25 mmol) and α-bromo(chloro)acetophenone (0.5 mmol) in CH_3CN (2.0 mL), the additive α-picoline (0.25 mmol, 1 equiv.) and base Et_3N (0.05 mmol, 20 mol%) were added at room temperature. The mixture was stirred for 12 h under reflux. The reaction was monitored by thin layer chromatography (TLC) until completion. Then, solvent was evaporated under vacuum. The crude mixture was purified by silica gel column chromatography (*n*-hexane /EtOAc 4:1 v/v) to afford the desired pure product **5**.

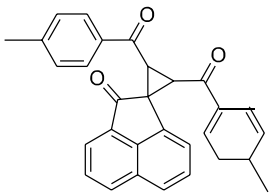
5. Characterization Data (compound **5a-5f**)

5.1 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis(phenylmethanone) **(***trans*-**5a)**



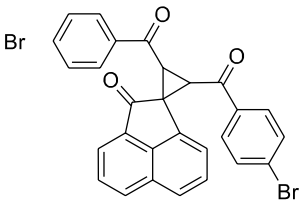
Orange solid; Yield 88% (88 mg); m.p. 83–85 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.10-8.08 (m, 1H), 8.00–7.88 (m, 3H), 7.86-7.75 (m, 3H), 7.71-7.67 (m, 1H), 7.63–7.55 (m, 2H), 7.50–7.40 (m, 2H), 7.35 (t, *J*=7.7 Hz, 2H), 7.30–7.25 (m, 2H), 4.58 (d, *J*=8.0 Hz, 1H), 4.35 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.82, 192.88, 190.79, 141.79, 136.79, 136.24, 133.86, 133.72, 133.48, 132.01, 131.85, 130.33, 128.76, 128.68, 128.52, 128.36, 127.94, 124.97, 122.43, 119.74, 47.00, 40.33, 38.80 ppm. IR (thin film): 3058, 2924, 2853, 1715, 1669, 1595, 1325, 1209, 1175, 1095, 981, 826, 778, 469 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{28}H_{18}O_3$: 403.1338; found: 403.1329.

5.2 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis(p-tolylmethanone) **(***trans*-**5b)**



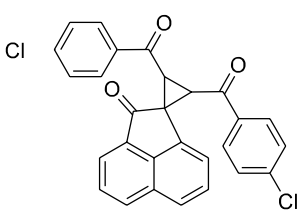
Orange solid; Yield 72% (77 mg); m.p. 120–121 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.07 (d, *J*=8.1 Hz, 1H), 7.91 (d, *J*=7.0 Hz, 1H), 7.88–7.77 (m, 3H), 7.75–7.63 (m, 3H), 7.61–7.51 (m, 2H), 7.14 (d, *J*=8.0 Hz, 2H), 7.05 (d, *J*=8.0 Hz, 2H), 4.55 (d, *J*=8.0 Hz, 1H), 4.32 (d, *J*=8.0 Hz, 1H), 2.30 (s, 3H), 2.27 (s, 3H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.97, 192.39, 190.48, 144.72, 144.33, 141.73, 134.39, 134.08, 133.89, 131.93, 131.91, 130.30, 129.35, 128.74, 128.65, 128.47, 127.87, 124.82, 122.33, 119.68, 46.86, 40.34, 38.82, 21.62, 21.59 ppm. IR (thin film): 3050, 2926, 2860, 1720, 1656, 1586, 1330, 1225, 1180, 1076, 975, 830, 780, 472 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{30}H_{22}O_3$: 431.1647; found: 431.1649.

5.3 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis((4-bromophenyl)methanone) **(***trans*-**5c)**



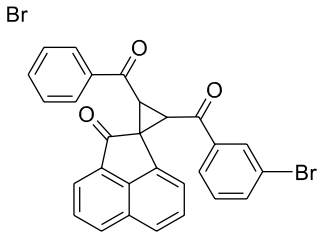
Orange solid; Yield 81% (113 mg); m.p. 130–131 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J*=8.0 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.85 (d, *J*=8.0 Hz, 1H), 7.78-7.75 (m, 2H), 7.73-7.68 (m, 1H), 7.66–7.61 (m, 2H), 7.61–7.57 (m, 1H), 7.54-7.51 (m, 1H), 7.50–7.45 (m, 2H), 7.43–7.35 (m, 2H), 4.47 (d, *J*=8.0 Hz, 1H), 4.26 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.56, 191.79, 189.79, 141.80, 135.36, 134.88, 133.29, 132.24, 132.06, 131.59, 130.37, 129.93, 129.74, 129.24, 128.90, 128.74, 128.10, 125.25, 122.66, 119.67, 46.89, 39.94, 38.49 ppm. IR (thin film): 3045, 2923, 2853, 1720, 1685, 1581, 1325, 1210, 1173, 1067, 981, 819, 743, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{28}H_{16}Br_2O_3$: 558.9544; found: 558.9545

5.3 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis((4-chlorophenyl)methanone) **(***trans*-**5d)**



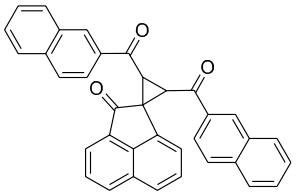
Orange solid; Yield 76% (89 mg); m.p. 197–199 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.11 (d, *J*=8.0 Hz, 1H), 7.93 (d, *J*=8.0 Hz, 1H), 7.89–7.81 (m, 3H), 7.76–7.66 (m, 3H), 7.63–7.56 (m, 1H), 7.55-7.51 (m, 1H), 7.32 (d, *J*=8.0 Hz, 2H), 7.25 (s, 1H), 7.23 (s, 1H), 4.48 (d, *J*=8.0 Hz, 1H), 4.27 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.58, 191.60, 189.59, 141.80, 140.44, 140.09, 134.98, 134.50, 133.34, 132.24, 131.61, 130.37, 129.88, 129.68, 129.07, 128.75, 128.10, 125.23, 122.65, 119.69, 46.90, 40.01, 38.54 ppm. IR (thin film): 3046, 2921, 2856, 1715, 1670, 1586, 1318, 1220, 1168, 1062, 976, 821, 750, 472 cm^{-1}; HRMS (TOF MS ES$^+$): m/z [M+H]$^+$ calcd for $C_{28}H_{16}Cl_2O_3$: 471.0556; found: 471.0554

5.6 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis((3-bromophenyl)methanone) **(*trans*-5e)**



Orange solid; Yield 80% (111 mg); m.p. 135–136 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.12 (d, *J*=8.0 Hz, 1H), 8.08 (t, *J*=1.8 Hz, 1H), 8.00 (t, *J*=1.8 Hz, 1H), 7.94 (d, *J*=8.0 Hz, 1H), 7.90–7.76 (m, 2H), 7.74-7.68 (m, 1H), 7.67–7.47 (m, 5H), 7.24-7.19 (m, 1H), 7.10 (t, *J*=8.0 Hz, 1H), 4.49 (d, *J*=8.0 Hz, 1H), 4.27 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.43, 191.52, 189.41, 141.87, 138.30, 137.76, 136.67, 136.41, 133.17, 132.25, 131.54, 131.36, 131.31, 130.37, 130.28, 130.23, 128.77, 128.08, 127.17, 126.82, 125.29, 123.20, 123.16, 122.69, 119.84, 47.10, 40.07, 38.38 ppm. IR (thin film): 3045, 2922, 2855, 1718, 1686, 1579, 1326, 1215, 1170, 1068, 976, 820, 745, 468 cm^{-1}; HRMS (TOF MS ES$^+$): m/z $[M+H]^+$ calcd for $C_{28}H_{16}Br_2O_3$: 558.9544; found: 558.9545

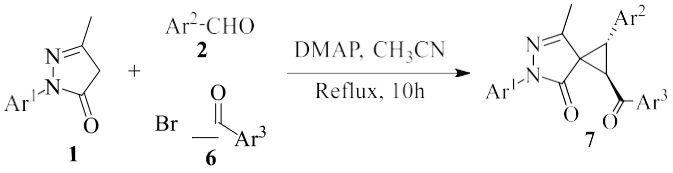
5.7 (2-Oxo-2H-spiro[acenaphthylene-1,1'-cyclopropane]-2',3'-diyl)bis(naphthalen-2-ylmethanone) **(*trans*-5f)**



Orange solid; Yield 75% (94 mg); m.p. 72–73 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.50 (s, 1H), 8.30 (s, 1H), 8.12–8.01 (m, 2H), 7.97–7.89 (m, 2H), 7.89–7.69 (m, 7H), 7.68-7.60 (m, 2H), 7.59–7.45 (m, 4H), 7.42–7.35 (m, 1H), 4.81 (d, *J*=8.0 Hz, 1H), 4.55 (d, *J*=8.0 Hz, 1H) ppm. ^{13}C NMR (100 MHz, $CDCl_3$) δ 196.95, 192.74, 190.89, 141.85, 135.79, 135.72, 134.15, 133.97, 133.70, 132.30, 132.02, 131.85, 130.81, 130.40, 130.33, 129.76, 129.59, 128.85, 128.78, 128.61, 128.57, 127.93, 127.66, 126.87, 126.63, 125.00, 123.84, 123.73, 122.48, 119.87, 47.26, 40.72, 38.87 ppm. IR (thin film): 3054, 2924, 2855, 1713, 1666, 1463, 1354, 1271, 1181, 1094, 968, 823, 728, 470 cm^{-1}; HRMS (TOF MS ES$^+$): m/z $[M+H]^+$ calcd for $C_{36}H_{22}O_3$: 503.1647; found: 503.1655

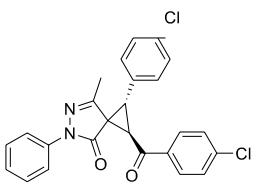
5. General procedure for the synthesis of compounds 9a-9h

A mixture of α-bromo(chloro)acetophenone (2.0 mmol), pyrazolone (2.0 mmol), aromatic aldehyde (2.0 mmol) and α-picoline (2.0 mmol) in acetonitrile (5 mL) was stirred at room temperature for 30 min. Subsequently, Et_3N (10 mol%) was added to the solution and further refluxed for 8h. After completion of the reaction, as monitored by TLC, the mixture was cooled to room temperature and the solvent was evaporated under reduced pressure. Finally, compounds **9a**–**9h** were separated by purification through column chromatography (silica-gel 300−400 mesh) using dichloromethane and petroleum ether (5:1, v/v) as the eluent.



Ar^1= C_6H_5 (**1a**), 4-Me-C_6H_4 (**1b**), 4-Cl-C_6H_4 (**1c**), 2-Cl-C_6H_4 (**1d**)
Ar^2= 4-Cl-C_6H_4 (**2a**), 4-Br-C_6H_4 (**2b**), 2-NO_2-C_6H_4 (**2c**)
Ar^3= 4-Cl-C_6H_4 (**6a**), C_6H_5 (**6b**), 4-Me-C_6H_4 (**6c**), 4-MeO-C_6H_4 (**6d**)

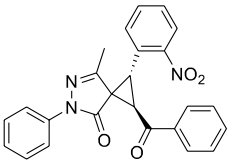
(1R,2S)-1-(4-Chlorobenzoyl)-2-(4-chlorophenyl)-7-methyl-5-phenyl-5,6-diazaspiro[2.4]hept-6-en-4-one **(9a):**



The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether =5:1) to afford the product **9a** (77% yield) as a light yellow solid. ^{1}H NMR (400 MHz, CDCl3): δ 7.78 (dd, *J* = 13.8, 8.1 Hz, 4H), 7.35 (m, *J* = 20.9, 15.2, 8.5 Hz, 8H), 7.15 (t, *J* = 7.4 Hz, 1H), 4.09 (d, *J* = 8.5 Hz, 1H), 3.81 (d, *J* = 8.6 Hz, 1H), 1.59 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ 188.62,

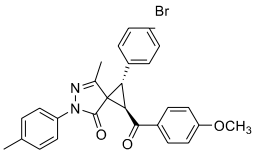
167.80, 155.42, 140.52, 138.04, 134.68, 134.07, 131.34, 130.51, 129.66, 129.02, 128.81, 125.12, 118.41, 44.55, 39.20, 38.74, 15.11 ppm; IR (thin film): 3059, 3020, 2963, 2923, 2849, 1703, 1592, 1524, 1458, 1344, 1212, 1156, 993, 845, 728, 685, 502 cm^{-1}; HRMS (TOF MS ES$^+$) m/z $[M+H]^+$ calcd. for $C_{25}H_{18}Cl_2N_2O_2$ 449.0818, found 449.0814.

(1R,2S)-1-Benzoyl-7-methyl-2-(2-nitrophenyl)-5-phenyl-5,6-diazaspiro[2.4]hept-6-en-4-one **(9b):**



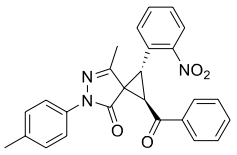
The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether =5:1) to afford the product **9b** (84% yield) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.07–7.94 (m, 3H), 7.90–7.79 (m, 2H), 7.67–7.54 (m, 3H), 7.48 (t, *J* = 6.3 Hz, 3H), 7.33 (t, *J* = 7.9 Hz, 2H), 7.13 (t, *J* = 7.4 Hz, 1H), 4.51 (d, *J* =8.7 Hz, 1H), 4.27–4.18 (m, 1H), 2.07 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.45, 167.43, 156.84, 149.08, 138.17, 135.82, 134.58, 133.38, 132.21, 129.31, 128.82, 128.59, 128.19, 125.18, 118.77, 46.33, 41.66, 35.93, 14.83 ppm; IR (thin film): 3067, 3017, 2959, 2921, 2858, 1700, 1597, 1525, 1451, 1344, 1215, 1161, 998, 848, 724, 686, 505 cm^{-1}; HRMS (TOF MS ES$^+$) m/z $[M+H]^+$ calcd. for $C_{25}H_{19}N_3O_4$ 426.1448, found 426.1444.

(1R,2S)-1-(4-Bromophenyl)-2-(4-methoxybenzoyl)-7-methyl-5-(p-tolyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9c):**



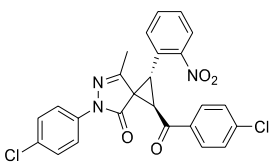
The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether =5:1) to afford the product **9d** (67% yield) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.95 (d, *J* = 9.0 Hz, 2H), 7.73 (d, *J* = 8.5 Hz, 2H), 7.45 (d, *J* = 8.5 Hz, 2H), 7.28–7.08 (m, 4H), 6.94 (d, *J* = 8.9 Hz, 2H), 4.14 (s, 2H), 3.86 (s, 3H), 2.31 (s, 3H), 1.97 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 189.77, 167.19, 164.58, 156.27, 135.84, 134.70, 131.43, 131.03, 130.65, 129.30, 128.96, 122.23, 118.51, 114.34, 55.61, 46.23, 41.16, 38.14, 20.92, 14.89 ppm; IR (thin film): 3064, 3021, 2965, 2927, 2842, 1708, 1592, 1527, 1456, 1354, 1232, 1150, 995, 845, 722, 685, 505 cm^{-1}; HRMS (TOF MS ES$^+$) m/z $[M+H]^+$ calcd. for $C_{27}H_{23}BrN_2O_3$ 503.0964, found 503.0961.

(1R,2S)-1-Benzoyl-7-methyl-2-(2-nitrophenyl)-5-(p-tolyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9d):**



The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether =5:1) to afford the product **9d** (89% yield) as a light yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.12–7.91 (m, 3H), 7.76–7.41 (m, 8H), 7.14 (d, *J* = 8.3 Hz, 2H), 4.50 (d, *J* = 8.7 Hz, 1H), 4.19 (d, *J* = 8.7 Hz, 1H), 2.31 (s, 3H), 2.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.49, 167.20, 156.62, 149.10, 135.77, 134.86, 134.54, 133.31, 132.15, 129.45, 129.08, 128.58, 128.25, 125.19, 118.85, 46.26, 41.60, 35.79, 20.94, 14.77 ppm; IR (thin film): 3066, 3011, 2954, 2923, 2856, 1710, 1678, 1514, 1434, 1343, 1214, 1159, 988, 818, 725, 685, 506 cm^{-1}; HRMS (TOF MS ES$^+$) m/z $[M+H]^+$ calcd. for $C_{26}H_{21}N_3O_4$ 440.1604, found 440.1599.

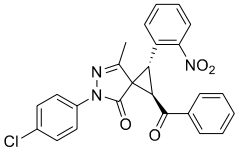
(1R,2S)-1-(4-Chlorobenzoyl)-5-(4-chlorophenyl)-7-methyl-2-(2-nitrophenyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9e):**



The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2: petroleum ether =5:1) to afford the product **9e** (72% yield) as a yellow solid. ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.09 (d, *J* = 8.2 Hz, 1H), 7.92 (d, *J* = 8.8 Hz, 2H), 7.77 (d, *J* = 9.2 Hz, 2H), 7.71–7.65 (m, 1H), 7.53 (dd, *J* = 24.0, 8.3 Hz, 4H), 7.30 (d, *J* = 9.2 Hz, 2H), 4.50 (d, *J* = 8.6 Hz, 1H), 4.13 (d, *J* = 8.6 Hz, 1H), 2.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 190.16, 167.21, 156.91, 149.03, 141.38, 136.55, 134.00, 133.39, 132.02, 130.33, 129.91, 129.59, 128.82, 127.83, 125.31, 119.85, 46.27, 41.46, 36.02, 14.76 ppm; IR (thin film):

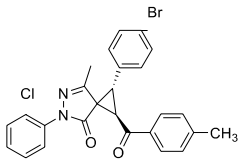
3064, 3021, 2965, 2927, 2842, 1708, 1592, 1527, 1456, 1354, 1232, 1150, 995, 845, 722, 685, 505 cm^{-1}; HRMS (TOF MS ES^+) m/z $[M+H]^+$ calcd. for $C_{25}H_{17}Cl_2N_3O_4$ 494.0668, found 494.0666.

1R,2S)-1-Benzoyl-5-(4-chlorophenyl)-7-methyl-2-(2-nitrophenyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9f):**



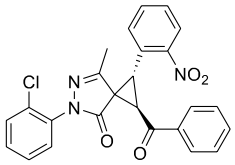
The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether =5:1) to afford the product **9f** (84% yield) as a light yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.07–7.94 (m, 3H), 7.82–7.73 (m, 2H), 7.61 (dt, *J* = 16.3, 7.4 Hz, 3H), 7.47 (dd, *J* = 17.7, 10.1 Hz, 3H), 7.26 (d, *J* = 8.9 Hz, 2H), 4.49 (d, *J* = 8.7 Hz, 1H), 4.21 (d, *J* = 8.7 Hz, 1H), 2.05 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.26, 167.38, 157.20, 149.03, 136.72, 135.75, 134.61, 133.40, 132.17, 130.09, 129.46, 129.20, 128.68, 128.05, 125.19, 119.83, 46.29, 41.66, 36.09, 14.82 ppm; IR (thin film): 3065, 3032, 2954, 2929, 2865, 1713, 1589, 1532, 1423, 1355, 1220, 1152, 995, 843, 730, 675, 501 cm^{-1}; HRMS (TOF MS ES^+) m/z $[M+H]^+$ calcd. for $C_{25}H_{18}ClN_3O_4$ 460.1064, found 460.1061.

(1R,2S)-1-(4-Bromophenyl)-5-(2-chlorophenyl)-7-methyl-2-(4-methylbenzoyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9g):**



The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2: petroleum ether =5:1) to afford the product **9g** (74% yield) as a light yellow solid. ^1H NMR (400 MHz, CDCl3): δ 7.92 (d, *J* = 8.2 Hz, 2H), 7.51–7.39 (m, 3H), 7.37 (dd, *J* = 6.1, 3.4 Hz, 1H), 7.35–7.19 (m, 6H), 4.18 (s, 2H), 2.44 (s, 3H), 1.93 (s, 3H) ppm; ^{13}C NMR (100 MHz, CDCl3): δ 191.03, 168.02, 156.43, 145.76, 134.52, 133.37, 131.78, 131.38, 131.05, 130.37, 129.84, 129.07, 128.79, 128.26, 127.50, 122.31, 45.00, 41.42, 37.90, 21.81, 14.86 ppm; IR (thin film): 3063, 3024, 2981, 2952, 2842, 1715, 1685, 1583, 1525, 1441, 1423, 1350, 1213, 1159, 982, 846, 724, 683, 544cm^{-1}; HRMS (TOF MS ES+) m/z [M+H]+ calcd. for C26H20BrClN2O2 507.0469, found 507.0467.

(1R,2S)-1-Benzoyl-5-(2-chlorophenyl)-7-methyl-2-(2-nitrophenyl)-5,6-diazaspiro[2.4]hept-6-en-4-one **(9h):**



The reaction was performed following general procedure, the crude product was purified by flash chromatography on silica gel (eluted with CH_2Cl_2:petroleum ether = 5:1) to afford the product **9h** (89% yield) as a light yellow solid. ^1H NMR (400 MHz, $CDCl_3$): δ 8.15–7.94 (m, 3H), 7.68–7.40 (m, 7H), 7.35 (s, 1H), 7.27 (ddd, *J* = 12.0, 5.7, 3.6 Hz, 2H), 4.54 (d, *J* = 8.6 Hz, 1H), 4.18 (d, *J* = 8.6 Hz, 1H), 2.00 (s, 3H) ppm; ^{13}C NMR (100 MHz, $CDCl_3$): δ 191.46, 168.06, 156.94, 149.04, 135.71, 134.53, 133.39, 132.27, 131.73, 130.21, 129.95, 129.37, 129.12, 128.64, 128.29, 127.61, 125.16, 44.71, 42.15, 35.48, 14.66 ppm; IR (thin film): 3064, 3020, 2988, 2958, 2855, 1720, 1680, 1580, 1523, 1482, 1433, 1345, 1210, 1162, 988, 845, 727, 687, 536 cm^{-1}; HRMS (TOF MS ES+) m/z $[M+H]^+$ calcd. for $C_{25}H_{18}ClN_3O_4$ 460.1058, found 460.1054.

6. ^{1}H and ^{13}C NMR spectra

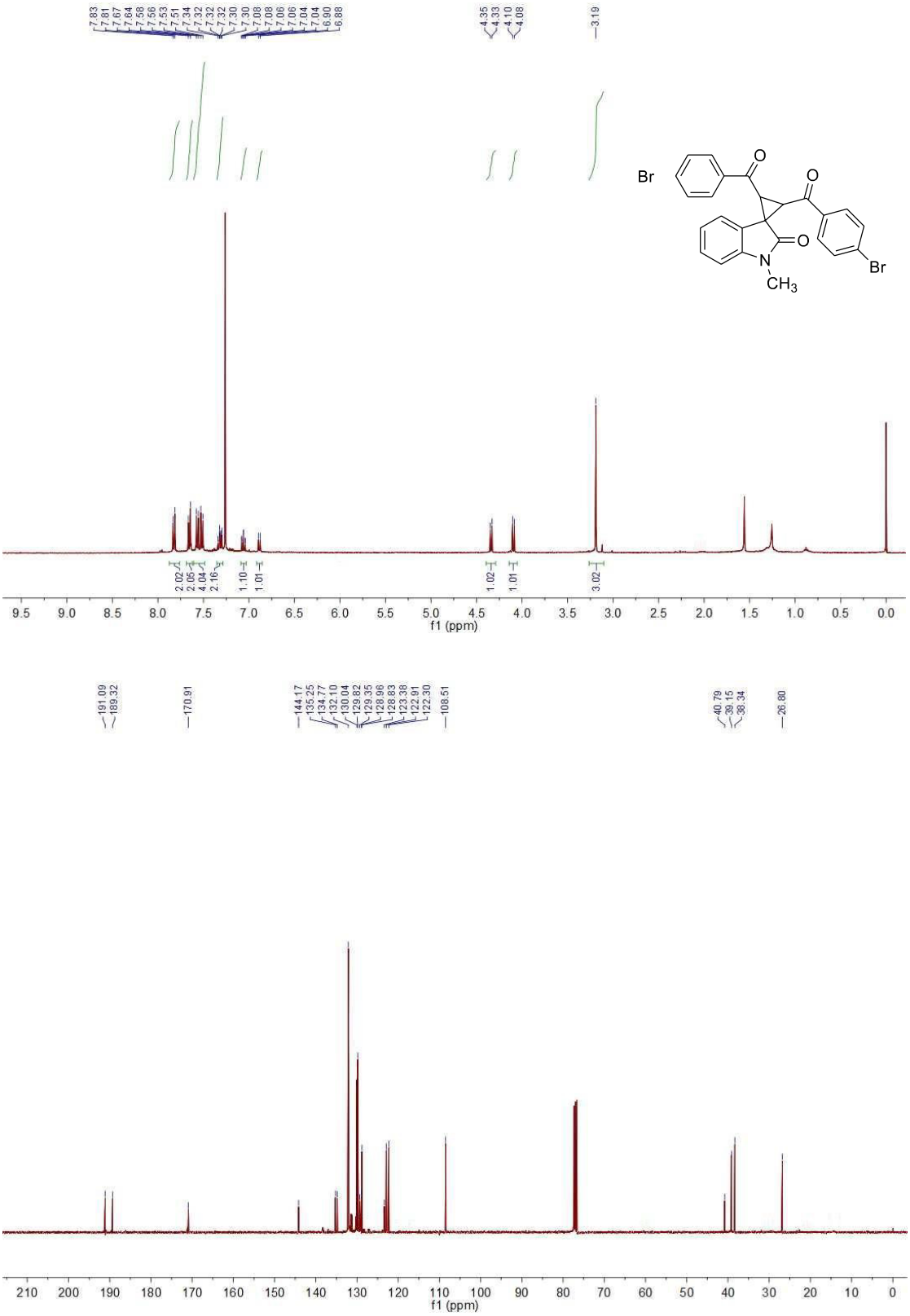


Figure 1. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3a** (100 MHz, $CDCl_3$).

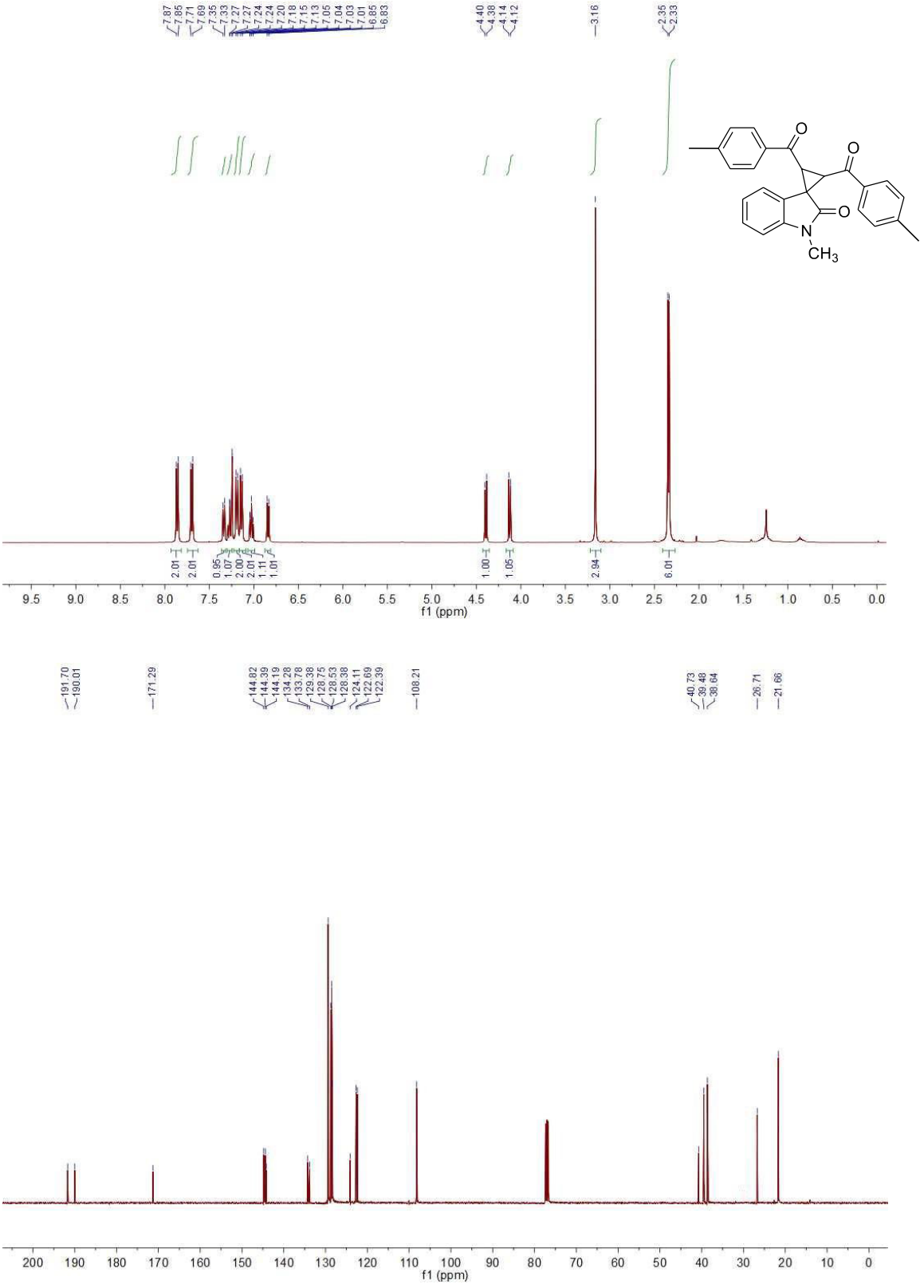


Figure 2. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3b** (100 MHz, $CDCl_3$).

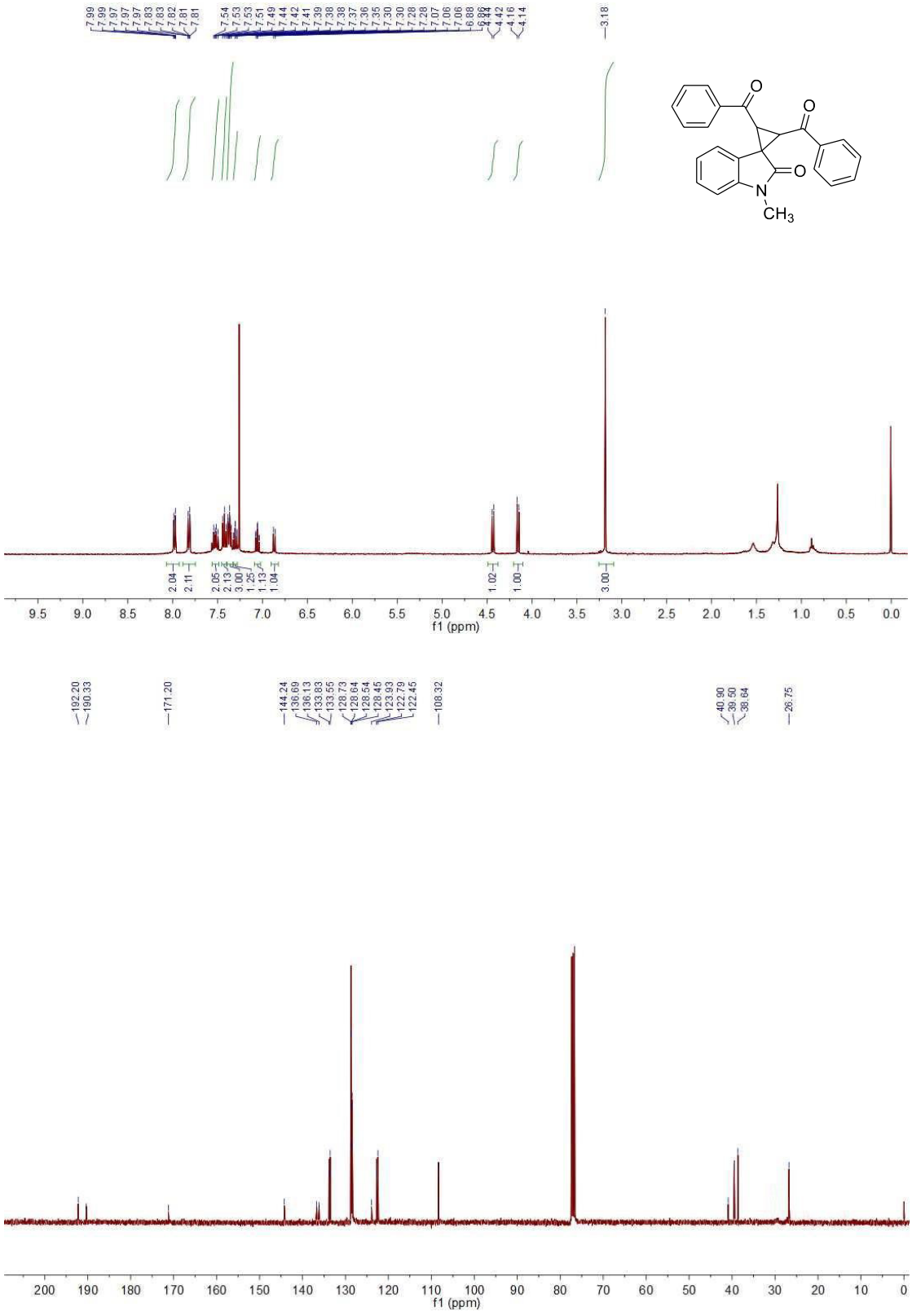


Figure 3. ^{1}H NMR (400 MHz, CDCl3) and ^{13}C NMR spectra of compound **3c** (100 MHz, CDCl3).

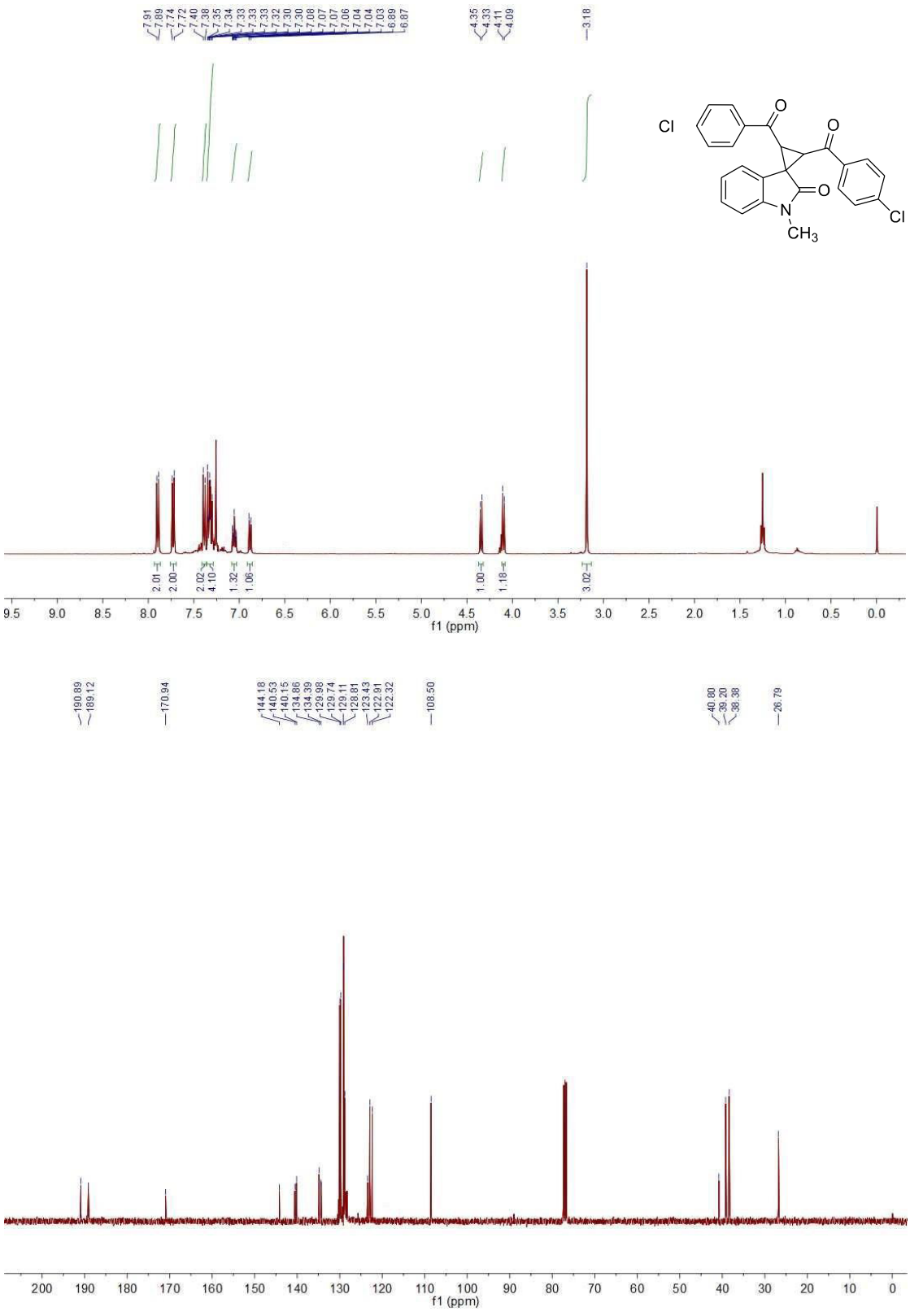


Figure 4. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3d** (100 MHz, $CDCl_3$).

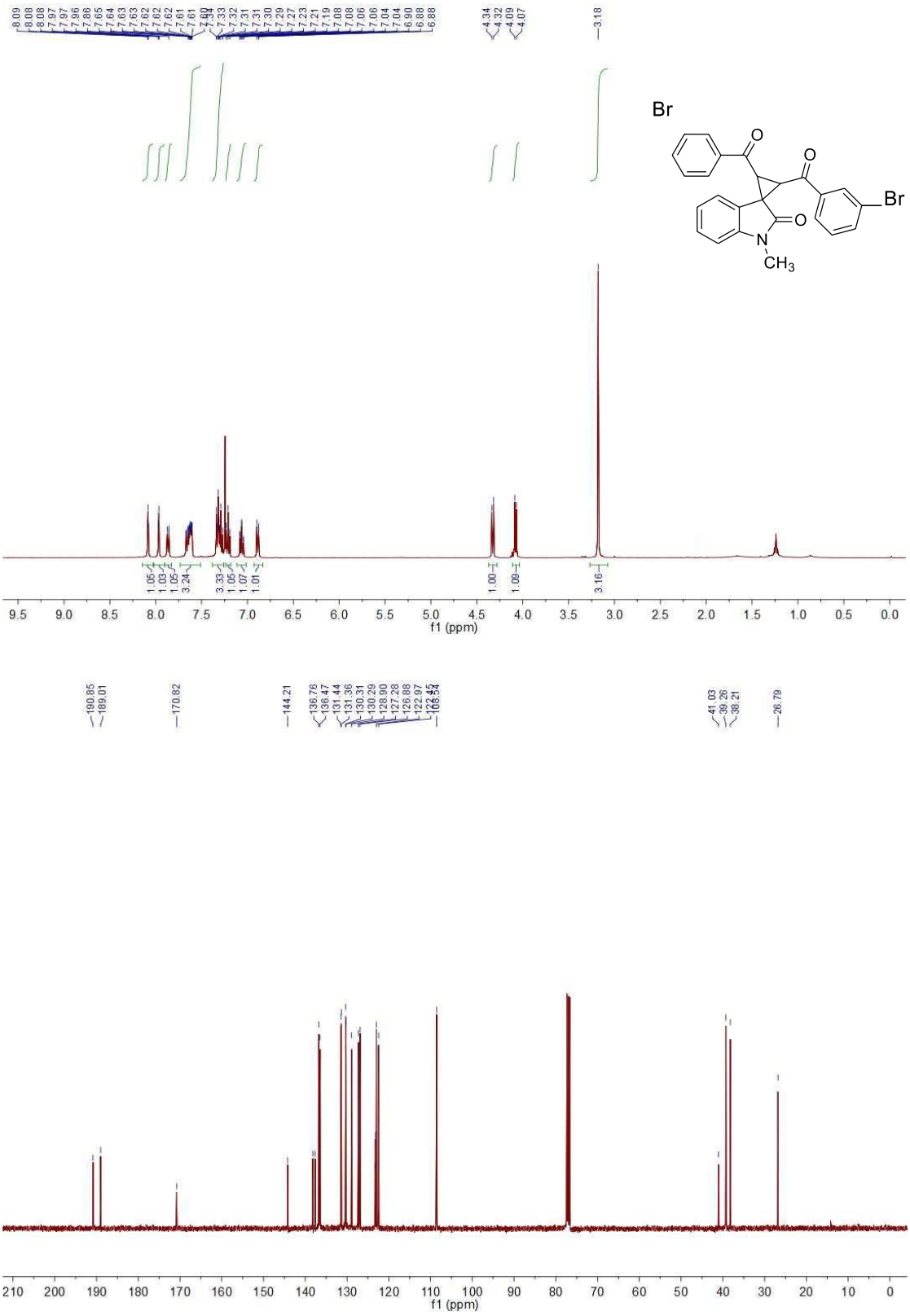


Figure 5. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3e** (100 MHz, $CDCl_3$).

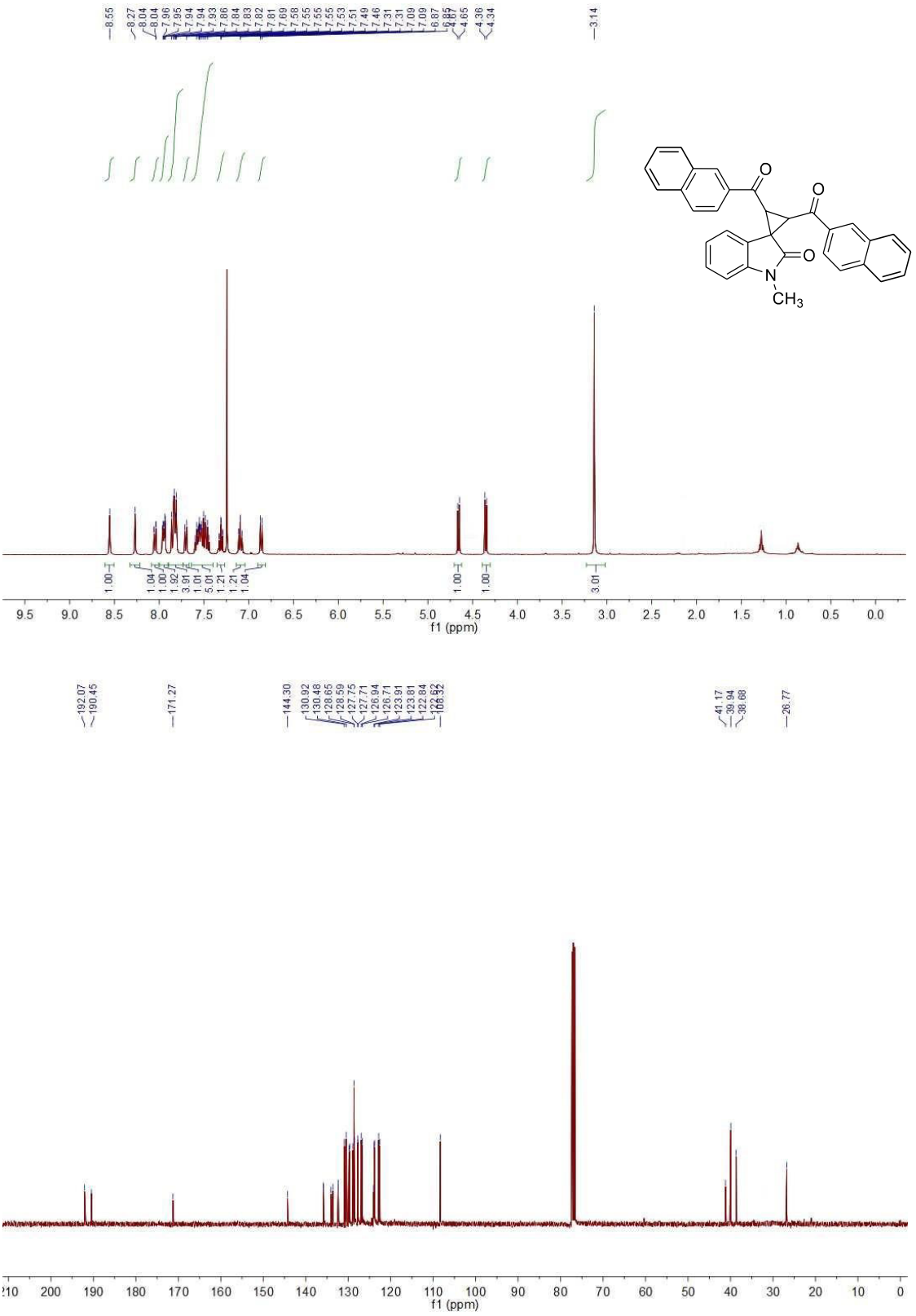


Figure 6. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3f** (100 MHz, $CDCl_3$).

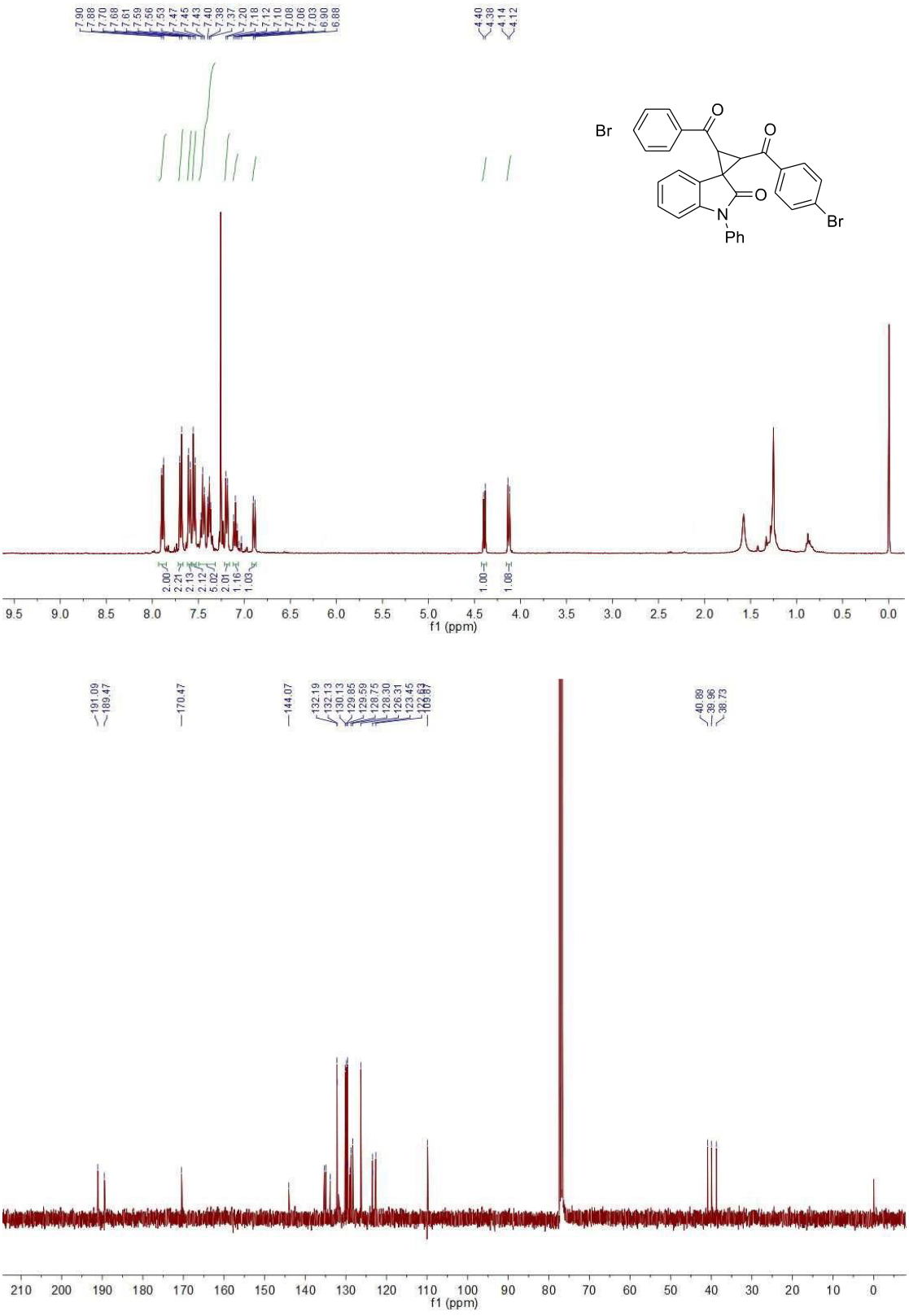


Figure 7. ^{1}H NMR of **4g** (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3g** (100 MHz, $CDCl_3$).

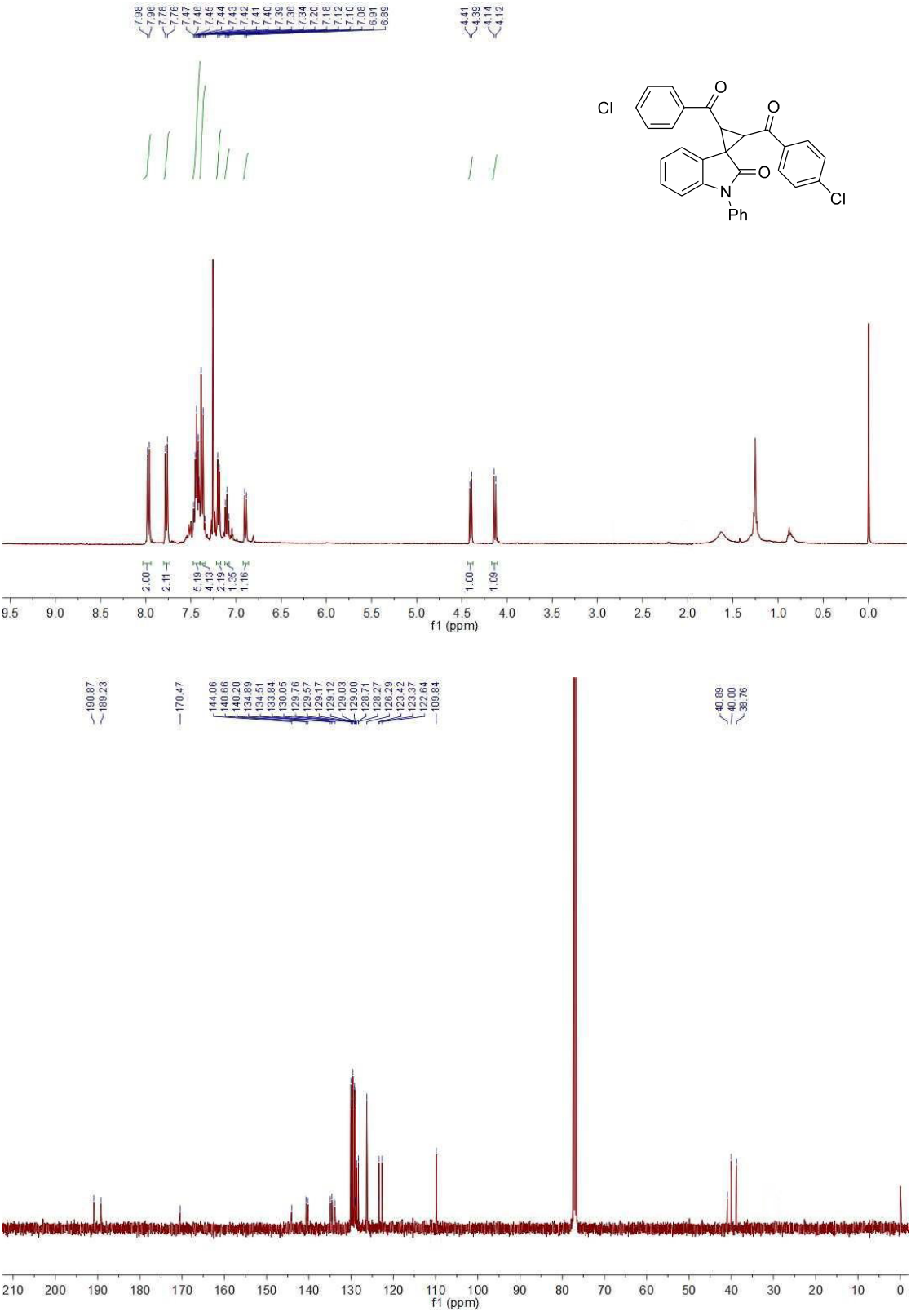


Figure 8. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3h** (100 MHz, $CDCl_3$).

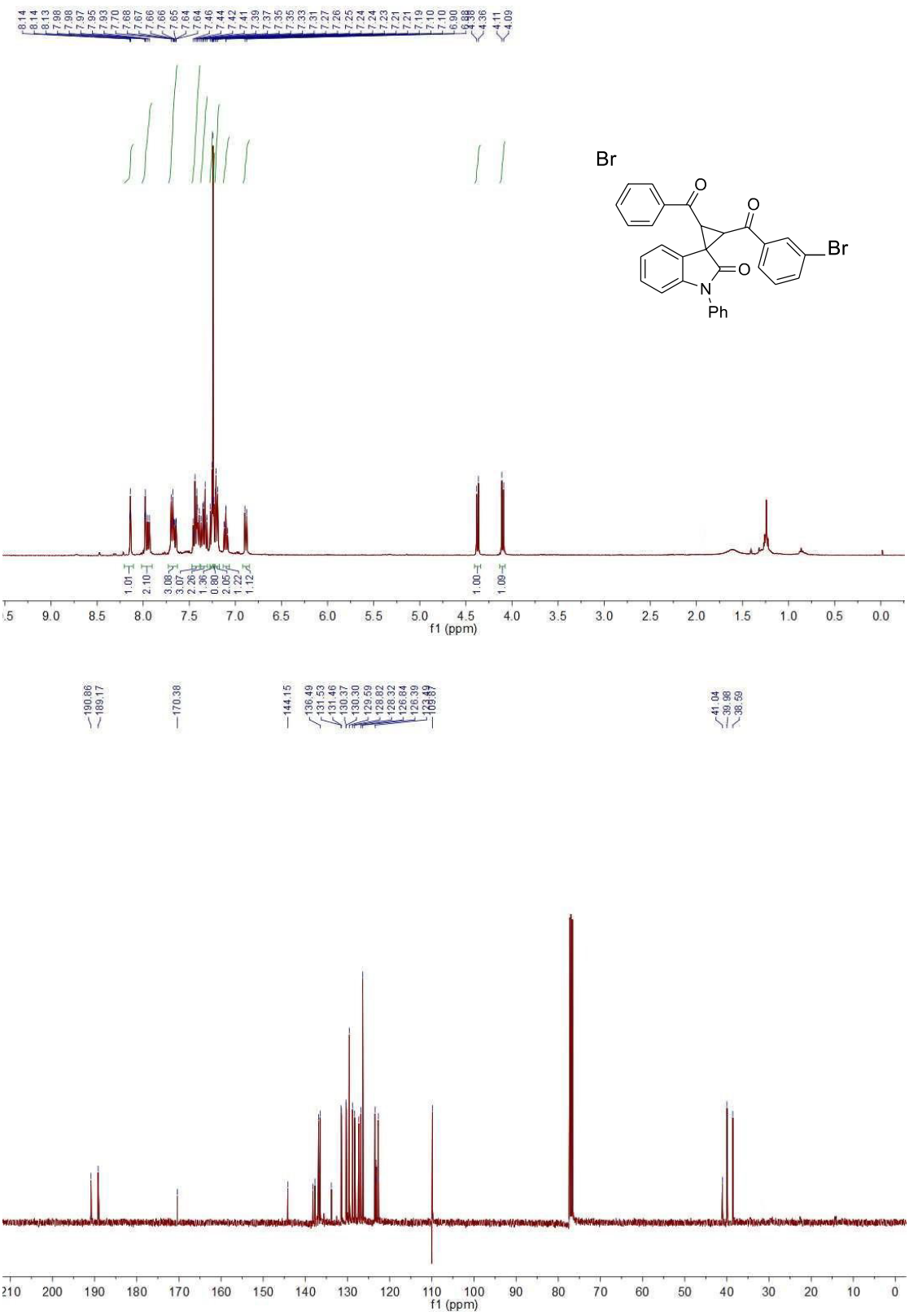


Figure 9. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **3i** (100 MHz, $CDCl_3$).

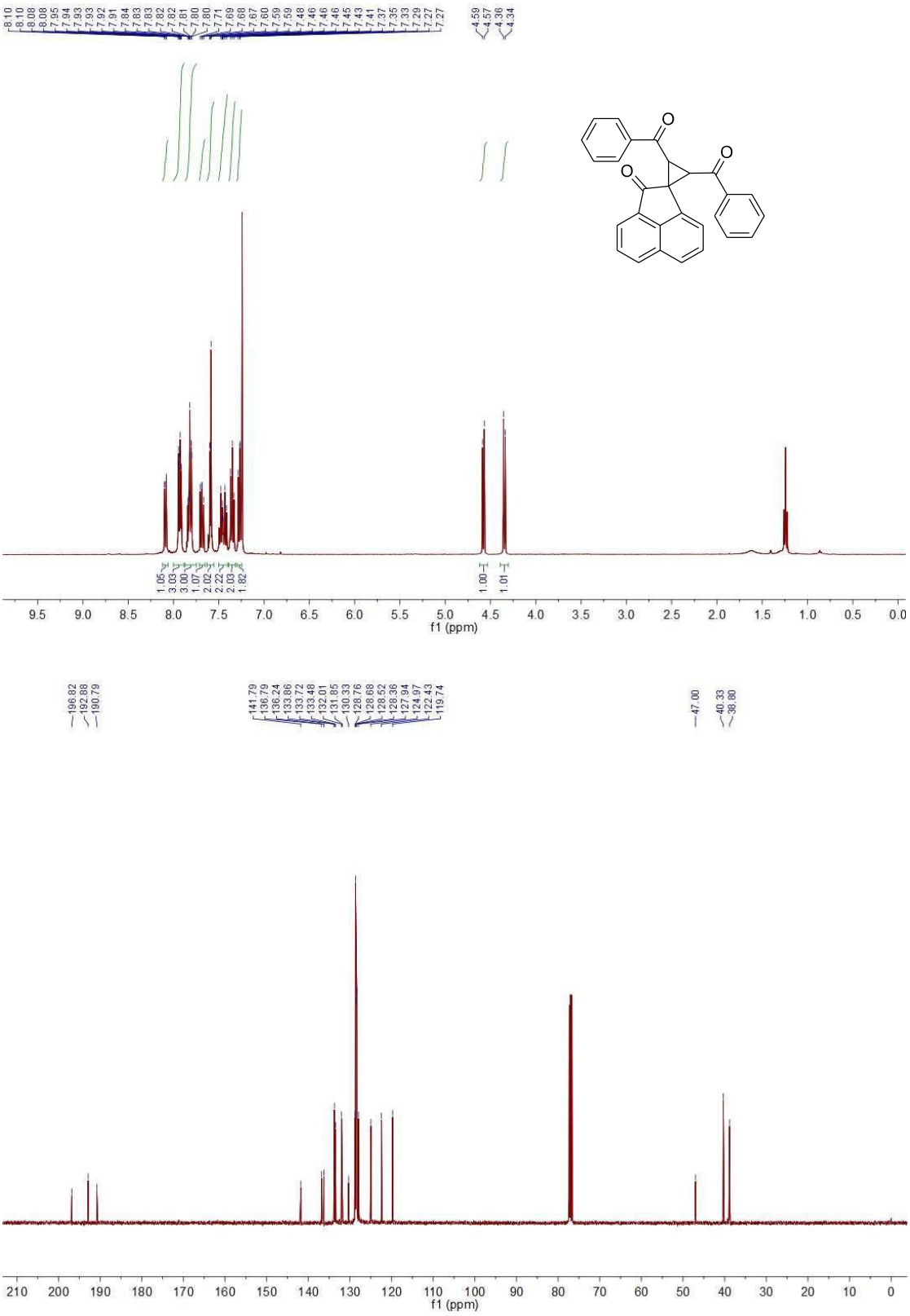


Figure 10. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **5a** (100 MHz, $CDCl_3$).

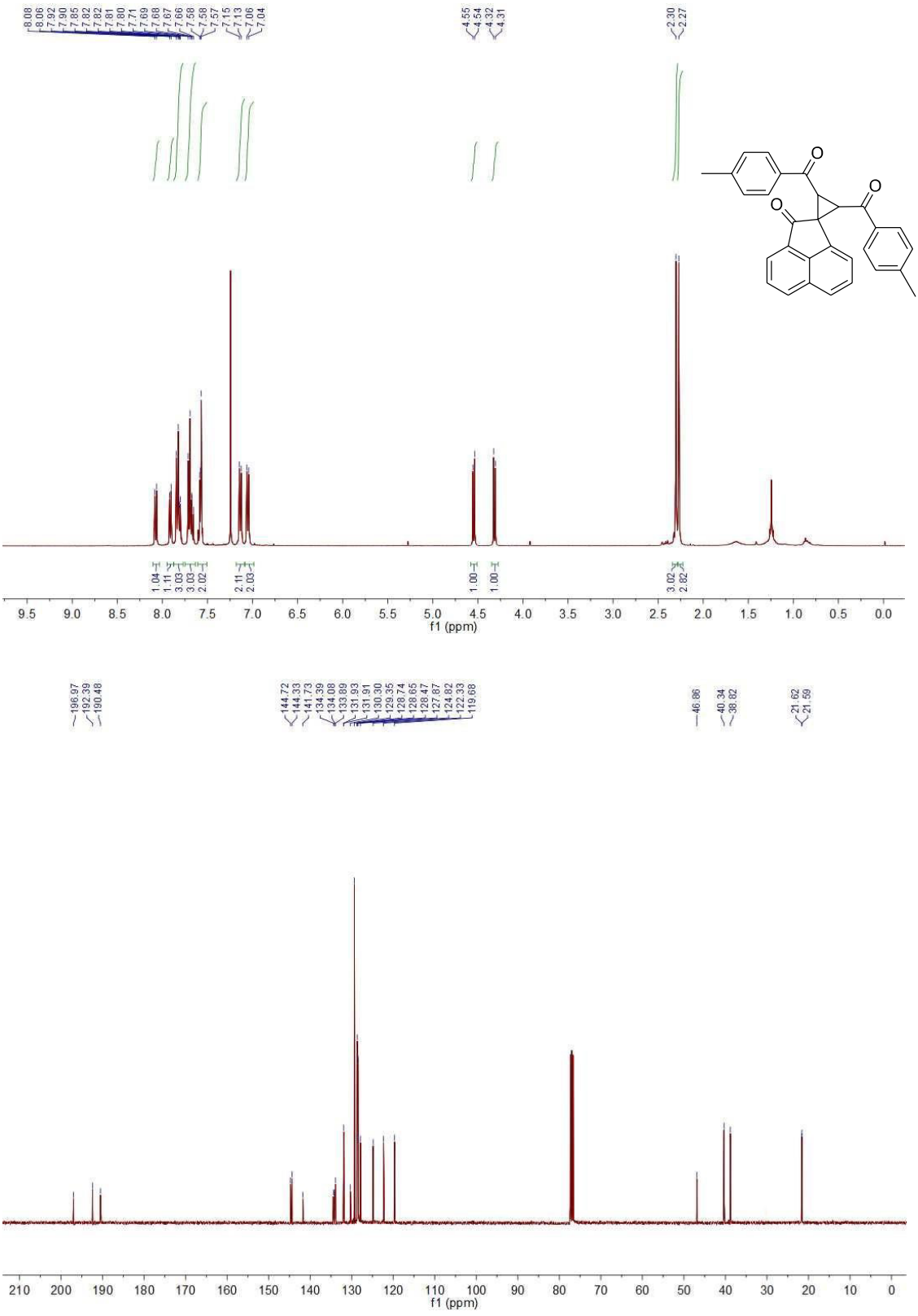


Figure 11. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **5b** (100 MHz, $CDCl_3$).

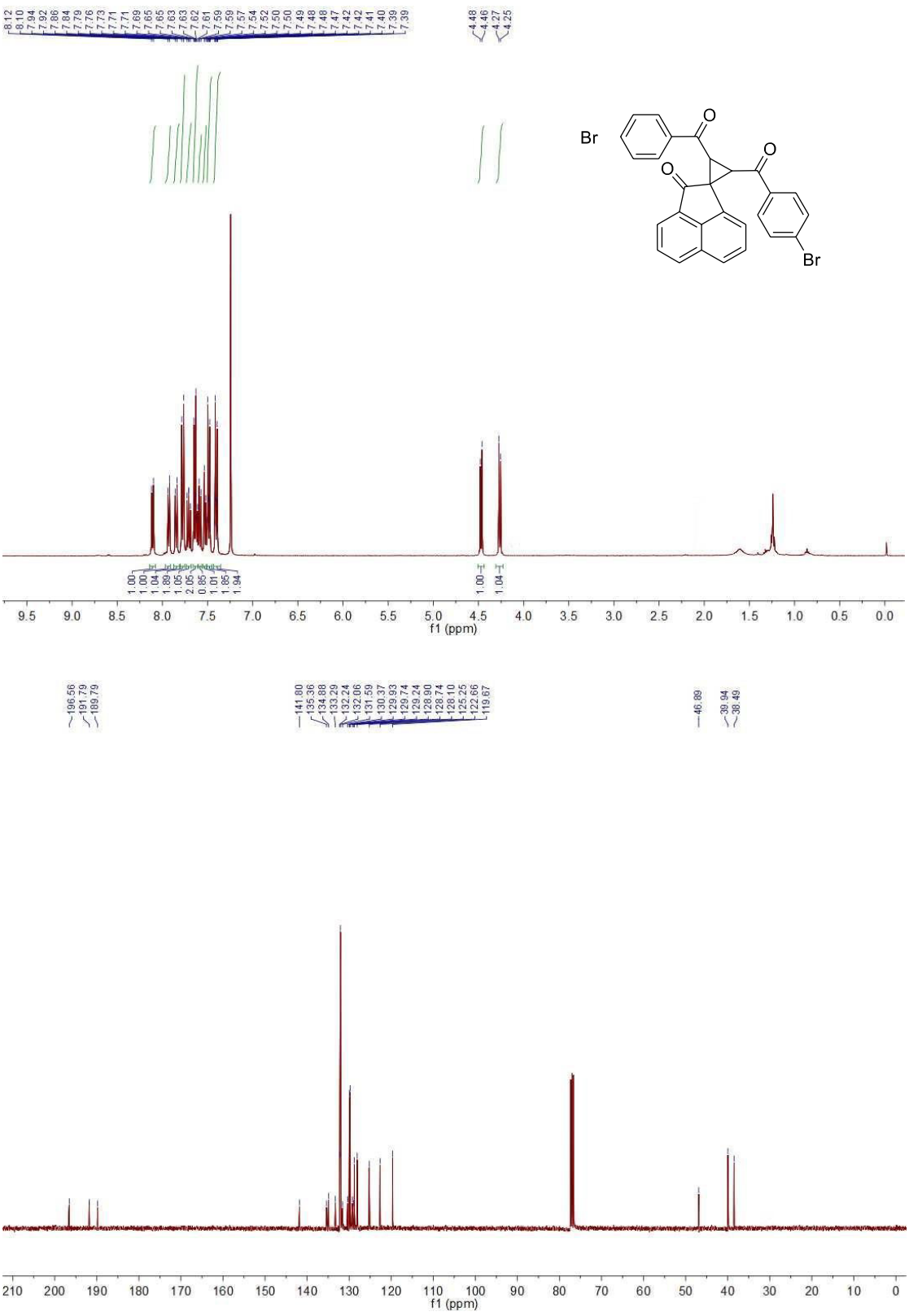


Figure 12. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **5c** (100 MHz, $CDCl_3$).

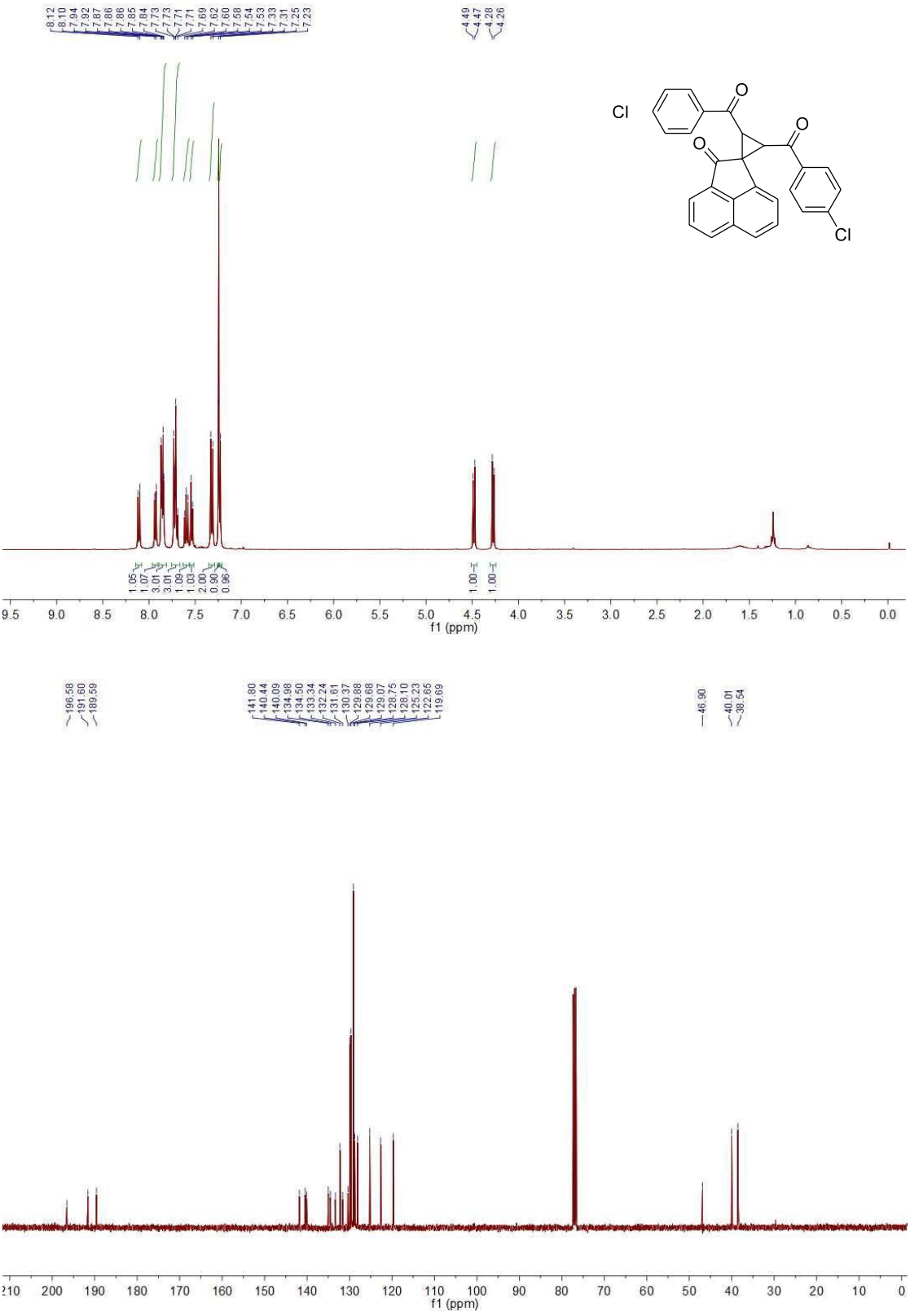


Figure 13. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **5d** (100 MHz, $CDCl_3$).

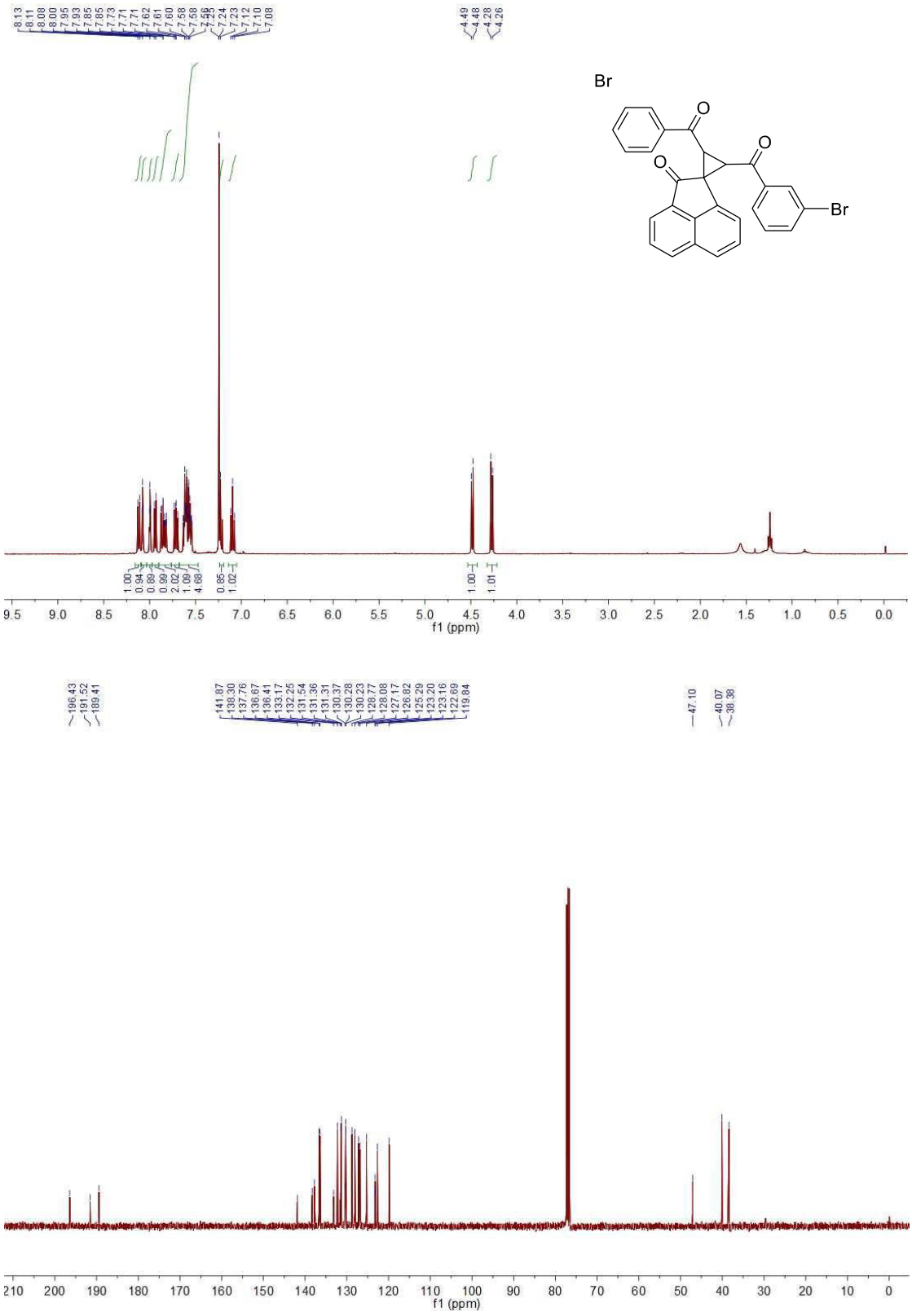


Figure 14. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR spectra of compound **5e** (100 MHz, $CDCl_3$).

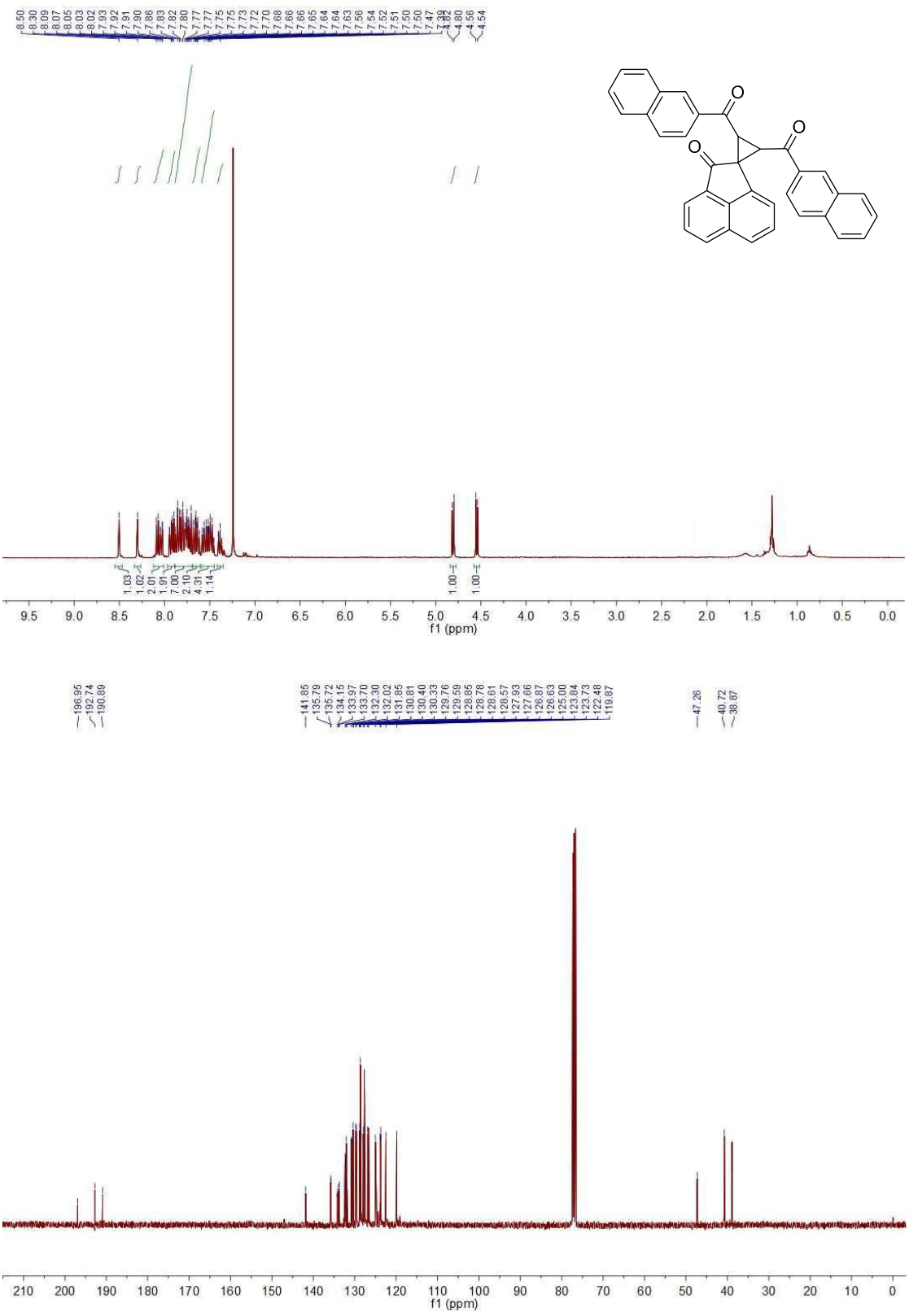


Figure 15. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **5f**.

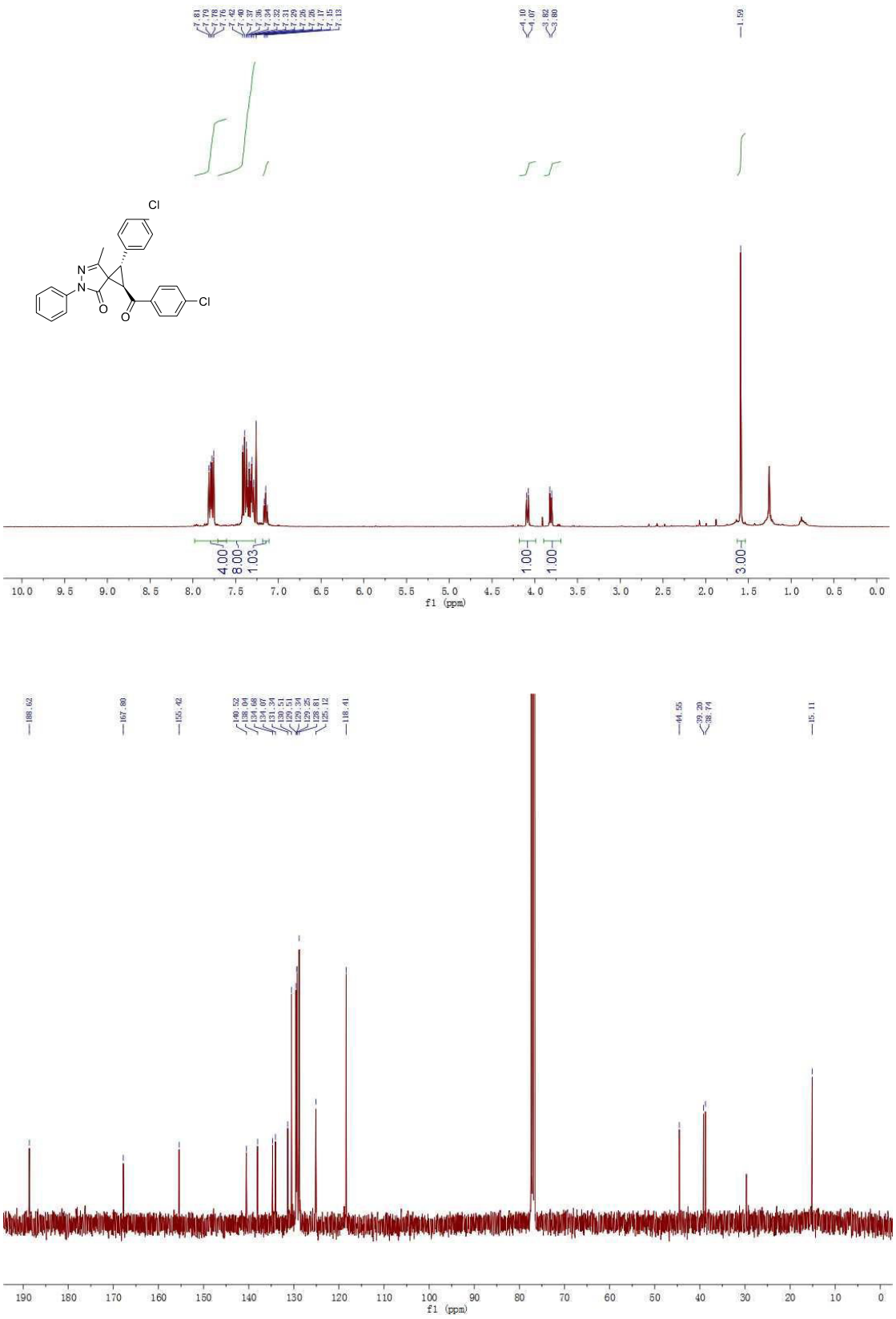


Figure 16. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9a**

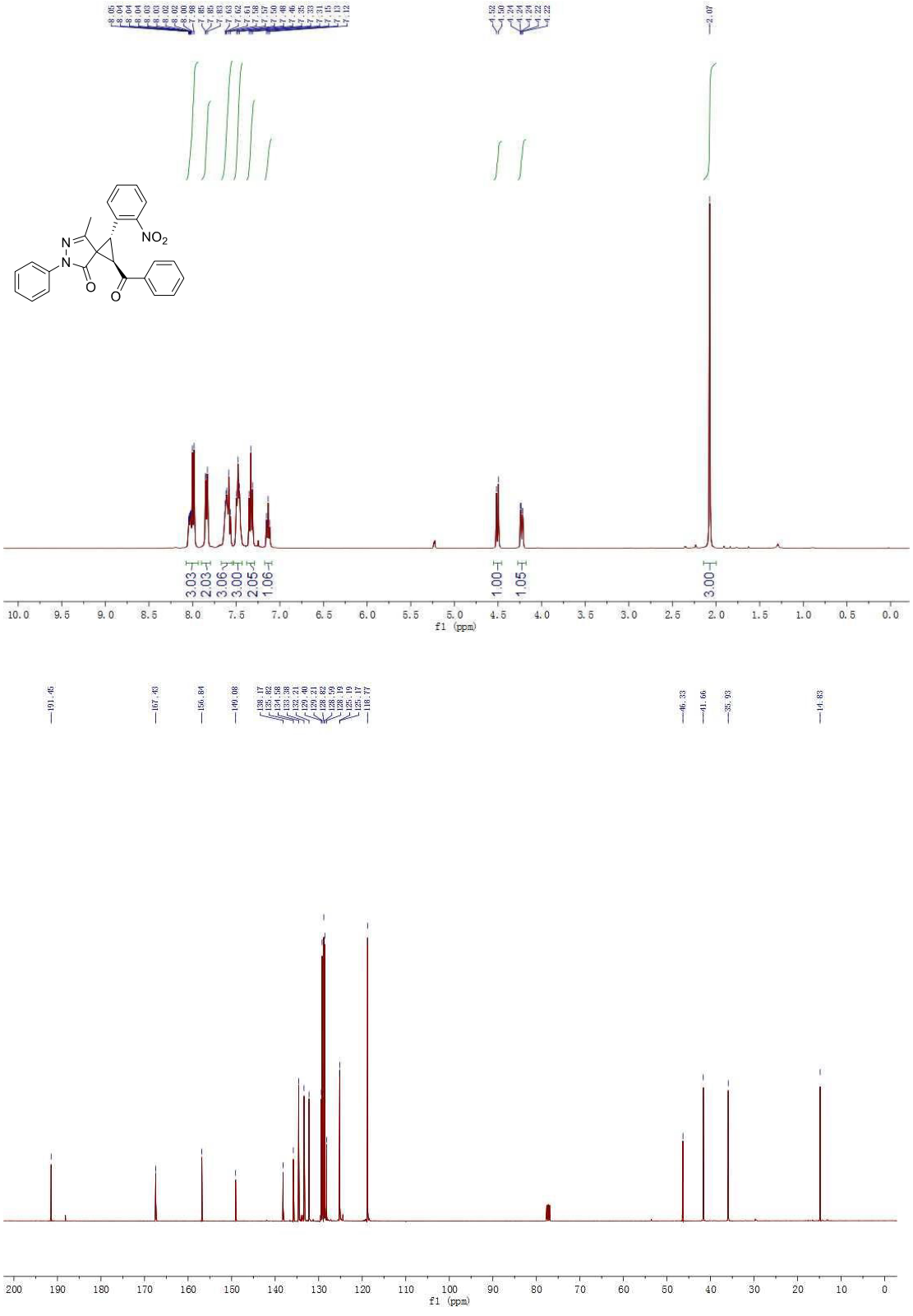


Figure 17. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9b**

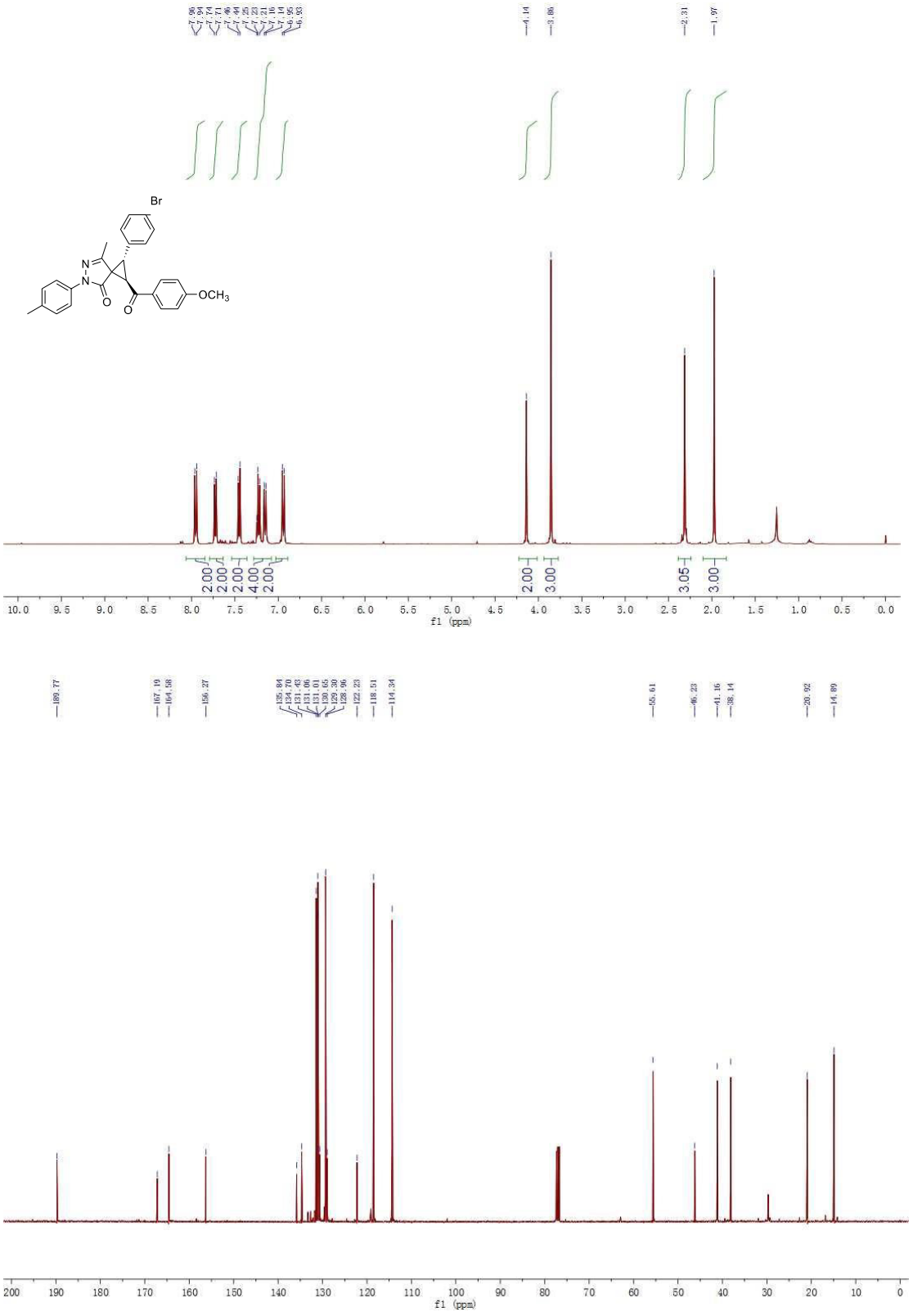


Figure 18. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9c**

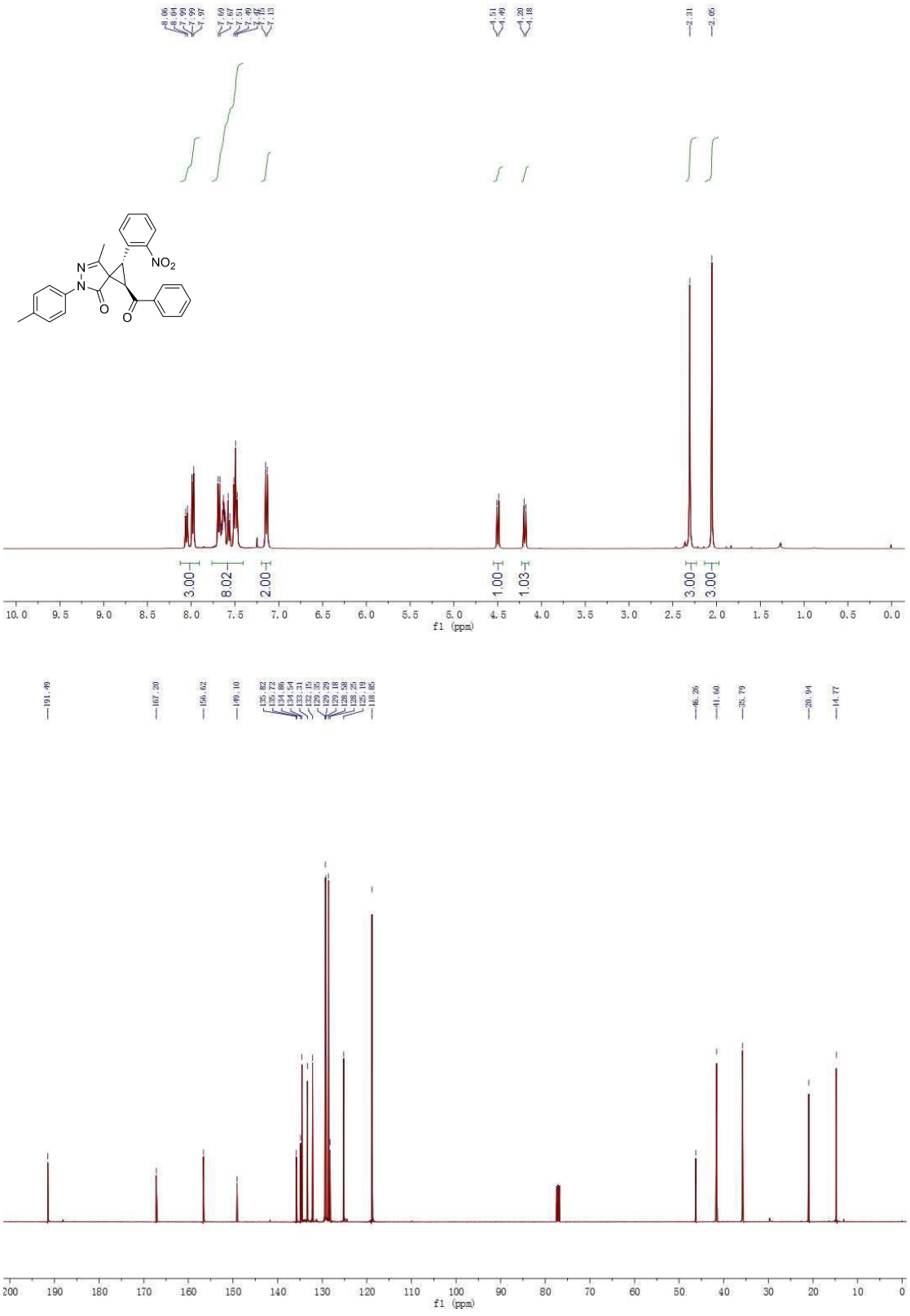


Figure 19. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9d**

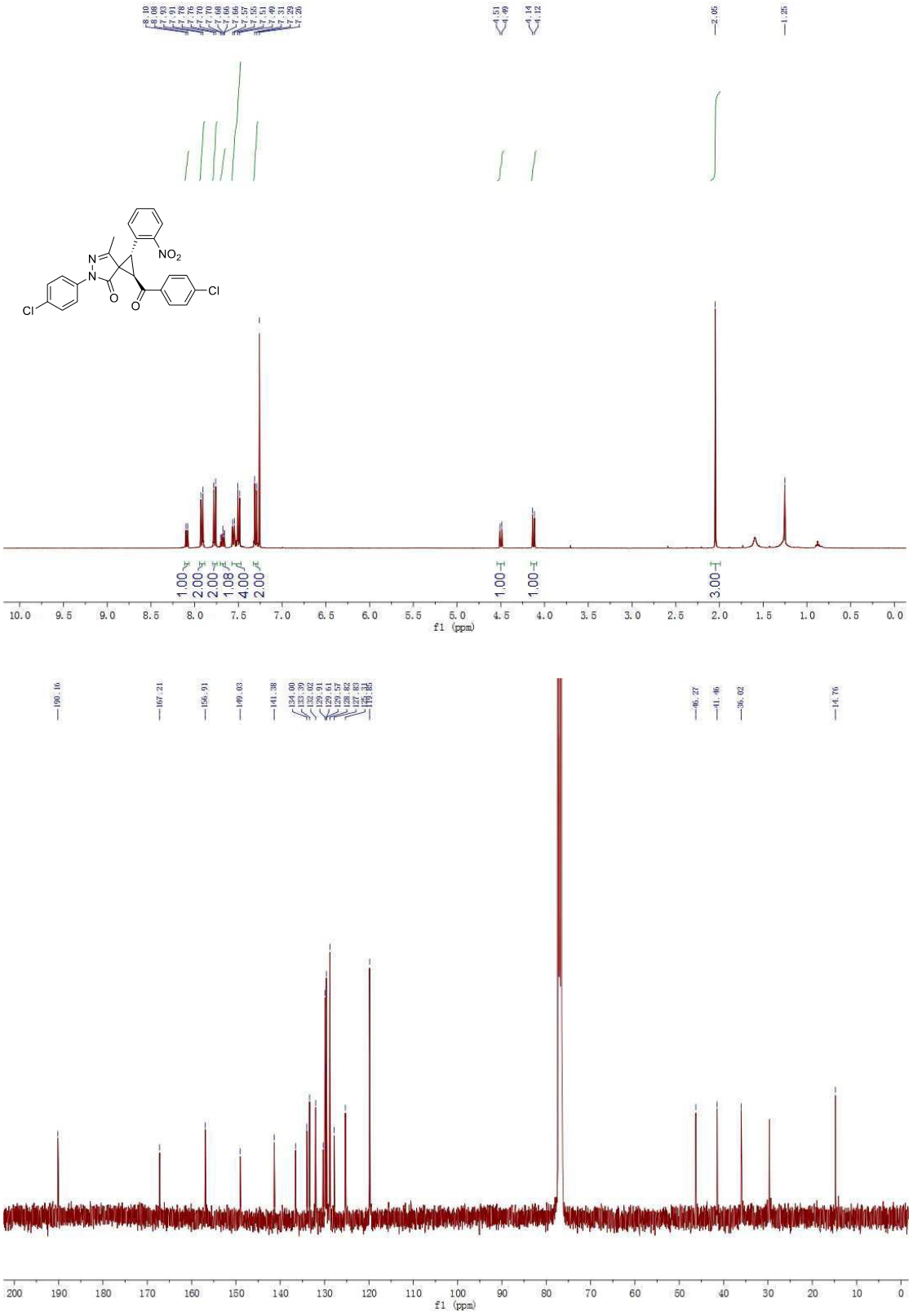


Figure 20. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9e**

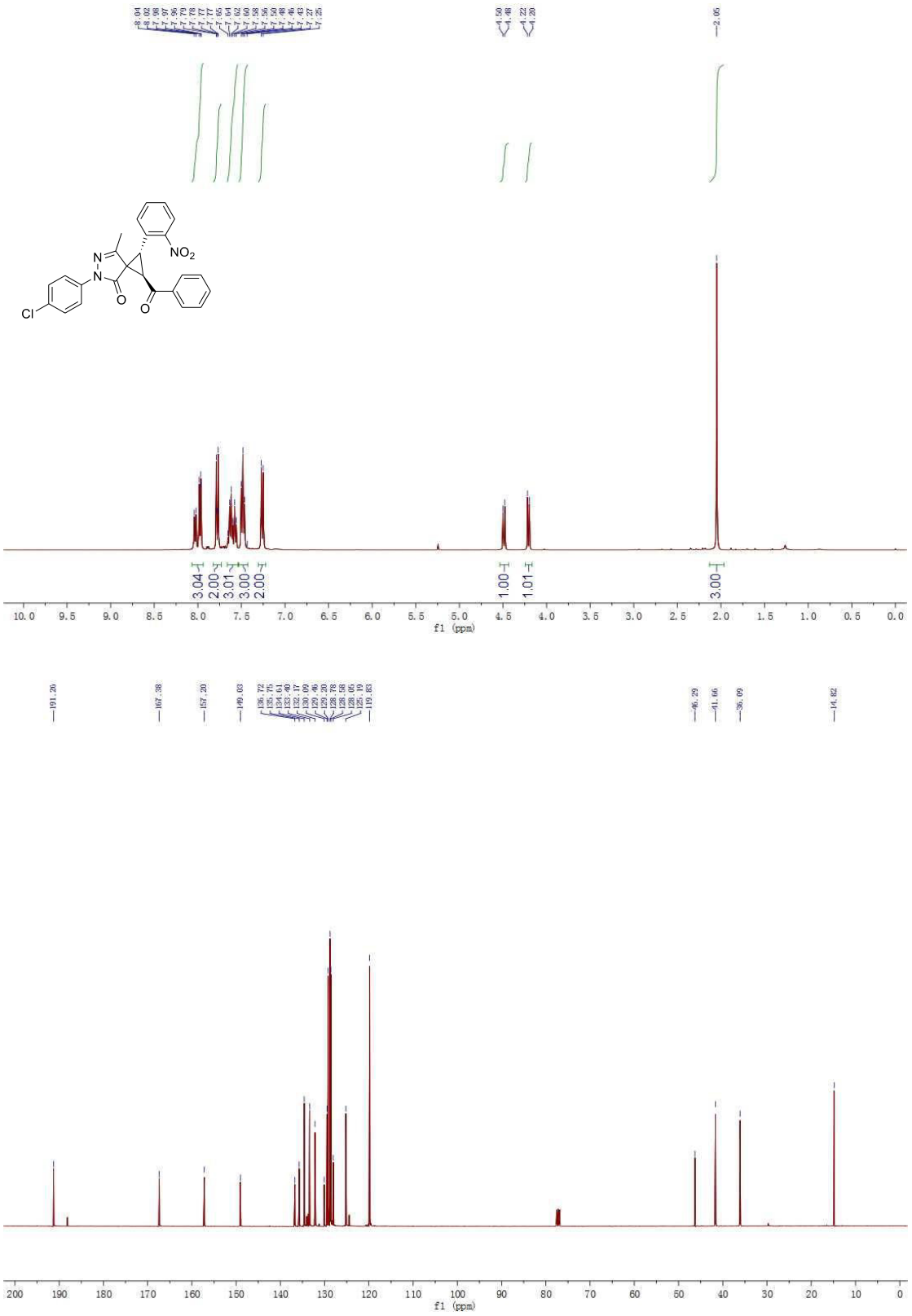


Figure 21. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9f**

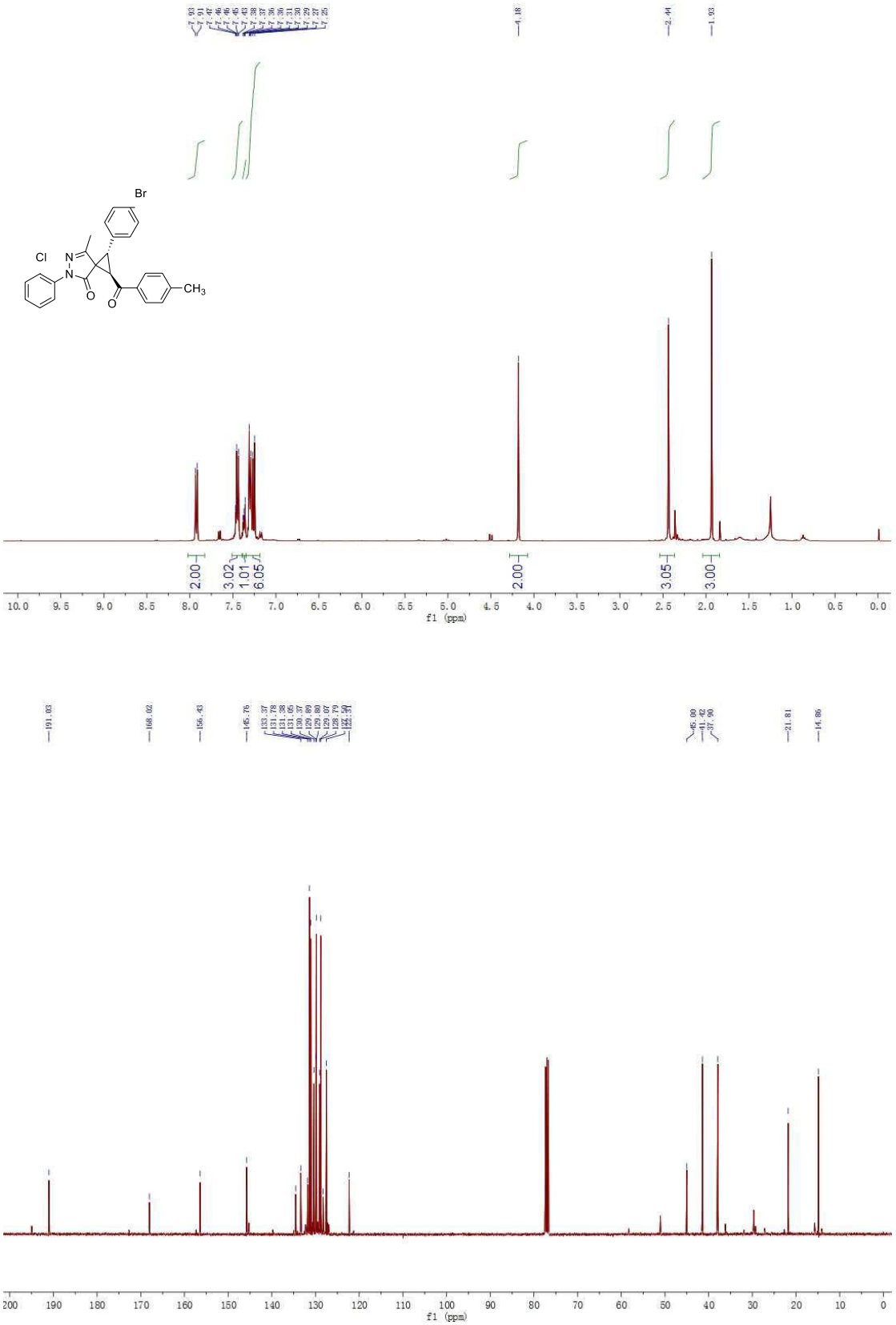


Figure 22. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9g**

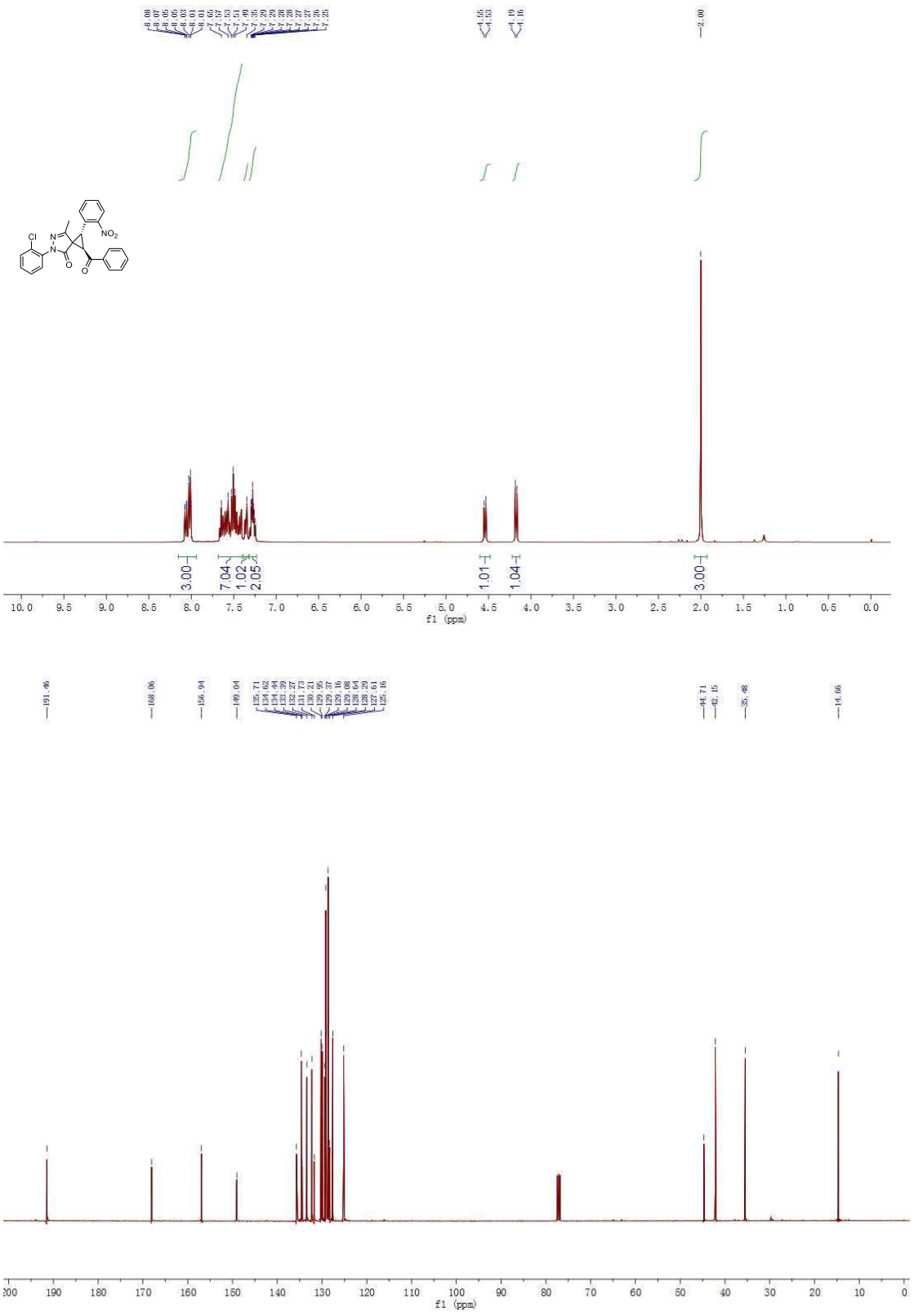
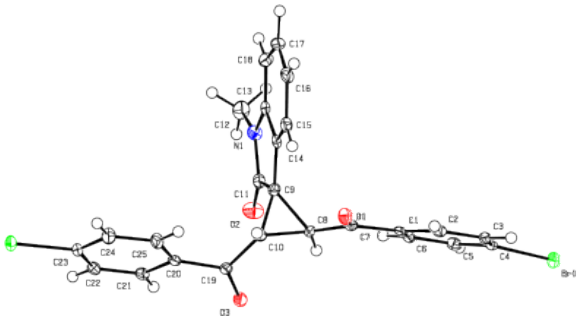


Figure 22. ^{1}H NMR (400 MHz, $CDCl_3$) and ^{13}C NMR (100 MHz, $CDCl_3$) spectra of compound **9h**

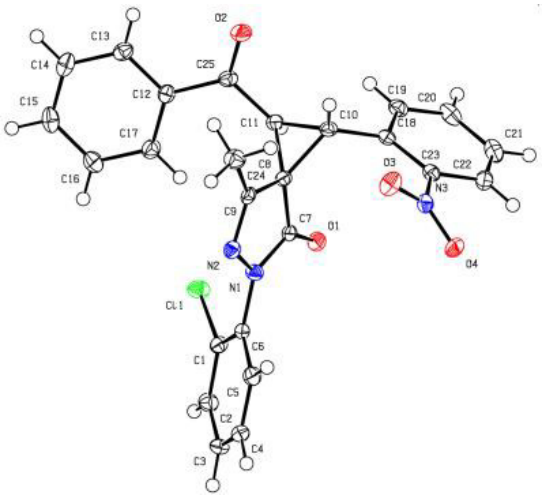
X-ray crystal data

X-ray crystal structure for compound **3a**



Identification code	**3a**
Empirical formula	$C_{25}H_{17}Br_2NO_3$
Formula weight	539.21
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	7.0127(4)
b/Å	10.5218(6)
c/Å	14.9131(8)
α/°	78.549(5)
β/°	83.673(5)
γ/°	76.958(5)
Volume/Å^3	1048.19(11)
Z	2
ρ_{calc}g/cm^3	1.708
μ/mm^{-1}	3.895
F(000)	536.0
Crystal size/mm^3	0.12 × 0.11 × 0.09
Radiation	MoKα (λ=0.71073)
2Θ range for data collection/°	4.48 to 49.98
Index ranges	-8 ≤ h ≤ 8, -12 ≤ k ≤ 12, -17 ≤ l ≤ 17
Reflections collected	11956
Independent reflections	3711 [R_{int}=0.0457, R_{sigma}=0.0484]
Data/restraints/parameters	3711/0/281
Goodness-of-fit on F^2	1.039
Final R indexes [I>=2σ (I)]	R_1=0.0317, wR_2=0.0674
Final R indexes [all data]	R_1=0.0383, wR_2=0.0705
Largest diff. peak/hole / e Å^{-3}	0.43/-0.54

X-ray crystal structure for compound **9h**



Identification code	exp_809
Empirical formula	$C_{25}H_{18}ClN_3O_4$
Formula weight	459.87
Temperature/K	100.00(10)
Crystal system	triclinic
Space group	P-1
a/Å	7.5127(4)
b/Å	9.5403(5)
c/Å	14.8625(7)
α/°	95.201(4)
β/°	95.657(4)
γ/°	92.809(4)
Volume/Å^3	1053.89(9)
Z	2
ρ_{calc}g/cm^3	1.449
μ/mm^{-1}	0.221
F(000)	476.0
Crystal size/mm^3	0.18 × 0.14 × 0.12
Radiation	MoKα (λ = 0.71073)
2Θ range for data collection/°	7.142 to 59.144
Index ranges	-9 ≤ h ≤ 9, -12 ≤ k ≤ 9, -18 ≤ l ≤ 20
Reflections collected	8667
Independent reflections	4943 [R_{int} = 0.0274, R_{sigma} = 0.0572]
Data/restraints/parameters	4943/0/299
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2σ (I)]	R_1 = 0.0457, wR_2 = 0.0930
Final R indexes [all data]	R_1 = 0.0600, wR_2 = 0.1024
Largest diff. peak/hole / e Å^{-3}	0.30/-0.29