Regioselective synthesis of pyrrolo[1,2-*a*]imidazoles and imidazo-[1,2-*a*]-pyridines

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Supporting Information

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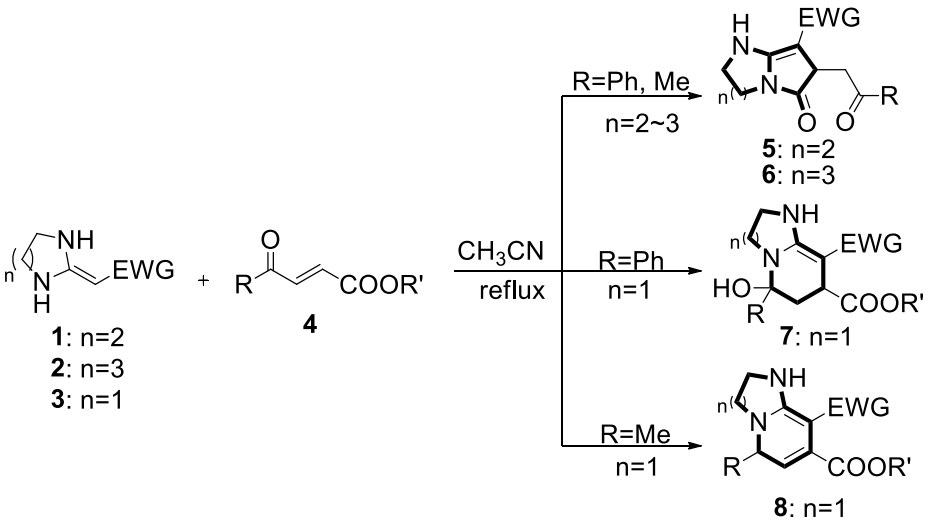
General Information

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX400 (^{1}H: 400 MHZ, ^{13}C: 100 MHZ), chemical shifts (δ) are expressed in ppm, and J values are given in Hz, and deuterated $CDCl_3$ was used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on XT-4A melting point apparatus and are uncorrected. HRMs were performed on a Agilent LC/Msd TOF instrument.

The materials were purchased from Adamas-beta Corporation Limited. All chemicals and solvents were used as received without further purification unless otherwise stated. Column chromatography was performed on silica gel (200–300 mesh).

Compounds **1**–**3** were prepared according to the literature[1]. The materials **4a**–**4b** were purchased from Adamas-beta Corporation Limited.

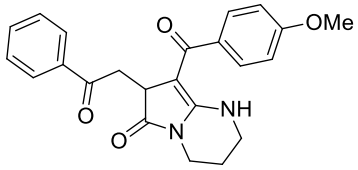
General Procedure for the Preparation of Pyrrolo[1,2-*a*]imidazole and Imidazo[1,2-*a*]-pyridines Derivatives 5~8



HKA derivatives **1**–**3** (1.0 mmol), Michael reaction acceptors **4** (1.1 mmol) and CH_3CN (10 ml) were placed into a 25 mL round-bottom flask and the mixture was stirred at reflux for 30–120 min. Completion of the reaction was monitored by TLC. The reaction mixture was then filtered to obtain the pure crude product, which was further washed with Hexane/EtOH (10:1) to give pure products **5**–**8** with a yield of 81–98%.

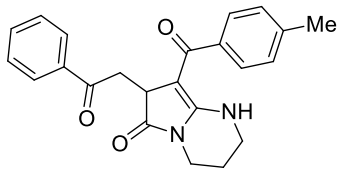
Spectroscopic Data of Pyrrolo[1,2-*a*]imidazoles 5–6

8-(4-methoxybenzoyl)-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5a)



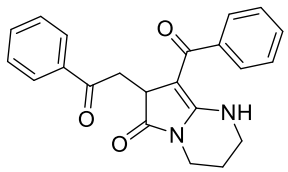
Red solid; Mp 90.5–92.9 °C; IR (KBr): 3440, 2930, 1634, 1518, 1443, 1253, 1165, 1025 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ = 1.99–2.06 (m, 2H, CH_2), 3.00–3.21 (m, 2H, $COCH_2$), 3.39–3.47 (m, 2H, CH_2N), 3.55–3.70 (m, 2H, NCH_2), 3.73 (s, 3H, OCH_3), 3.90–3.96 (m, 1H, CH), 6.70–6.87 (m, 2H, ArH), 7.14–7.29 (m, 2H, ArH), 7.31–7.41 (m, 3H, ArH), 7.41–7.51 (m, 2H, ArH), 9.89 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.1, 37.3, 38.2, 38.6, 41.1, 55.3, 88.5, 113.6, 127.9, 128.3, 128.5, 133.0, 134.1, 136.5, 158.9, 160.7, 177.4, 184.0, 197.4; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{22}N_2NaO_4$ [$(M+Na)^+$], 413.1472; found, 413.1469.

8-(4-methylbenzoyl)-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5b)



Red solid; Mp 87.9–88.5 °C; IR (KBr): 3394, 2923, 1636, 1522, 1443, 1262, 1164, 1093 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 2.03–2.09 (m, 2H, CH_2), 2.29 (s, 3H, $ArCH_3$), 2.97–3.16 (m, 2H, $COCH_2$), 3.40–3.50 (m, 2H, CH_2N), 3.61–3.74 (m, 2H, NCH_2), 3.89–3.91 (m, 1H, CH), 7.05–7.07 (m, 2H, ArH), 7.19–7.27 (m, 4H, ArH), 7.39–7.43 (m, 3H, ArH), 9.89 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.1, 21.4, 37.3, 38.2, 38.6, 41.0, 88.8, 126.7, 127.9, 128.3, 129.0, 133.0, 136.5, 138.8, 139.6, 159.0, 177.5, 184.8, 197.4; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{22}N_2NaO_3$ [$(M+Na)^+$], 397.1523; found, 397.1525.

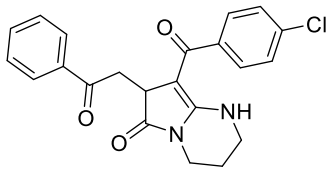
8-benzoyl-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5c)



Red solid; Mp 126.4–126.9 °C; IR (KBr): 3438, 2894, 1729, 1528, 1443, 1265, 1158, 745 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 2.07–2.14 (m, 2H, CH_2), 3.03–3.13 (m,

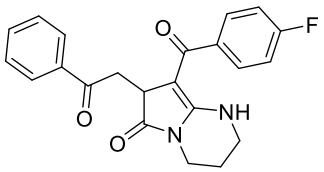
2H, $COCH_2$), 3.47–3.53 (m, 2H, CH_2N), 3.70–3.78 (m, 2H, NCH_2), 3.92–3.94 (m, 1H, CH), 7.27–7.48 (m, 10H, ArH), 9.95 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.1, 37.3, 38.1, 38.6, 40.9, 88.8, 126.5, 127.9, 128.3, 128.4, 129.5, 133.1, 136.4, 141.7, 159.1, 177.4, 184.7, 197.3; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{21}N_2O_3$ $[(M+H)^+]$, 361.1547; found, 361.1545.

8-(4-chlorobenzoyl)-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5d)



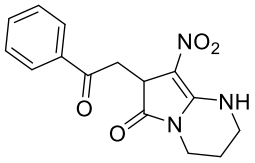
Red solid; Mp 141.9–143.0 °C; IR (KBr): 3441, 2911, 1729, 1631, 1527, 1440, 1265, 760 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.98–2.07 (m, 2H, CH_2), 3.00–3.13 (m, 2H, $COCH_2$), 3.38–3.47 (m, 2H, CH_2N), 3.60–3.72 (m, 2H, NCH_2), 3.84–3.86 (m, 1H, CH), 7.20–7.28 (m, 4H, ArH), 7.26–7.30 (m, 2H, ArH), 7.38–7.45 (m, 3H, ArH), 9.90 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.0, 37.3, 38.2, 38.7, 40.7, 88.8, 127.8, 128.1, 128.4, 128.6, 133.2, 135.4, 136.3, 140.0, 159.4, 177.2, 183.0, 197.1; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{19}ClN_2NaO_3$ $[(M+Na)^+]$, 417.0976; found, 417.0976.

8-(4-fluorobenzoyl)-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5e)



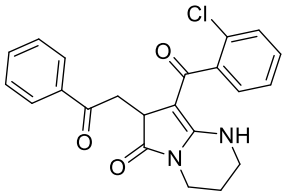
Red solid; Mp 117.6–118.7 °C; IR (KBr): 3221, 3059, 2878, 1728, 1636, 1526, 1270, 1092 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 2.00–2.10 (m, 2H, CH_2), 3.00–3.14 (m, 2H, $COCH_2$), 3.41–3.51 (m, 2H, CH_2N), 3.62–3.76 (m, 2H, NCH_2), 3.85–3.88 (m, 1H, CH), 6.92–6.97 (m, 2H, ArH), 7.19–7.27 (m, 2H, ArH), 7.34–7.46 (m, 5H, ArH), 9.88 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.1, 37.3, 38.2, 38.7, 40.8, 88.7, 115.2 (*J* = 21.3 Hz), 115.5 (*J* = 21.3 Hz), 127.8, 128.4, 128.7 (*J* = 8.2 Hz), 128.8 (*J* = 8.2 Hz), 133.2, 136.3, 137.8, 159.3, 162.1 (*J* = 247.8 Hz), 164.6 (*J* = 247.8 Hz), 177.3, 183.3, 197.1; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{19}FN_2NaO_3$ $[(M+Na)^+]$, 401.1272; found, 401.1268.

8-nitro-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5f)



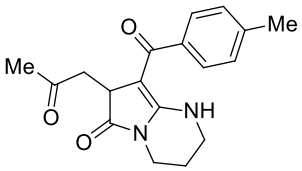
Red solid; Mp 147.4–148.1 °C; IR (KBr): 3464, 3265, 2971, 1748, 1668, 1515, 1310, 1155 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 2.00–2.13 (m, 2H, CH_2), 3.48–3.52 (m, 2H, $COCH_2$), 3.52–3.67 (m, 2H, CH_2N), 3.72–3.78 (m, 2H, CH_2N), 4.30–4.35 (m, 1H, CH), 7.34–7.38 (m, 2H, ArH), 7.45–7.48 (m, 1H, ArH), 7.80–7.83 (m, 2H, ArH), 9.13 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 19.4, 36.4, 37.3, 39.3, 39.9, 105.0, 128.1, 128.7, 133.6, 135.9, 154.2, 137.4, 197.5; HRMS (TOF ES^+): *m/z* calcd for $C_{15}H_{15}N_3NaO_4$ [$(M+Na)^+$], 324.0955; found, 324.0954.

8-(2-chlorobenzoyl)-7-(2-oxo-2-phenylethyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5g)



White solid; Mp 266.9–268.2 °C; IR (KBr): 3434, 3246, 2888, 1731, 1630, 1526, 1365, 1094 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 2.08–2.15 (m, 2H, CH_2), 2.76–2.81 (m, 1H, $COCH_2$), 3.02–3.08 (m, 1H, $COCH_2$), 3.46–3.51 (m, 2H, CH_2N), 3.55–3.58 (m, 1H, CH), 3.64–3.76 (m, 2H, NCH_2), 6.97–7.05 (m, 2H, ArH), 7.15–7.30 (m, 4H, ArH), 7.42–7.45 (m, 1H, ArH), 7.49–7.52 (m, 2H, ArH), 9.63 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.0, 37.3, 38.1, 38.7, 39.8, 90.0, 126.9, 127.8, 128.1, 128.4, 129.6, 129.7, 130.1, 133.2, 136.1, 140.9, 158.9, 177.3, 182.7, 196.6; HRMS (TOF ES^+): *m/z* calcd for $C_{22}H_{19}ClN_2NaO_3$ [$(M+Na)^+$], 417.0976; found, 417.0976.

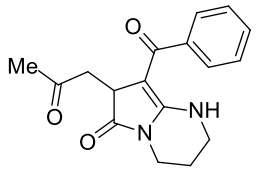
8-(4-methylbenzoyl)-7-(2-oxopropyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5h)



White solid; Mp 228.7–229.5 °C; IR (KBr): 3435, 2922, 1719, 1626, 1532, 1440, 1272, 1162 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.75 (s, 3H, $COCH_3$), 1.98–2.02 (m, 2H, CH_2), 2.30 (s, 3H, $ArCH_3$), 2.37–2.43 (m, 1H, $COCH_2$), 2.56–2.62 (m, 1H, $COCH_2$), 3.39–3.43 (m, 2H, CH_2N), 3.58–3.63 (m, 2H, NCH_2), 3.72–3.75 (m, 1H, CH), 7.10–7.12 (m, 2H, ArH), 7.31–7.33 (m, 2H, ArH), 9.88 (br, 1H, NH); ^{13}C NMR

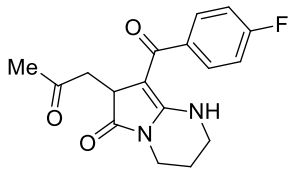
(100 MH_Z, $CDCl_3$): δ = 20.1, 21.4, 30.1, 37.3, 38.6, 40.7, 42.9, 88.5, 126.6, 129.0, 138.8, 139.7, 158.8, 177.2, 184.6, 205.6; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{20}N_2NaO_3$ [$(M+Na)^+$], 335.1366; found, 335.1365.

8-benzoyl-7-(2-oxopropyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5i)



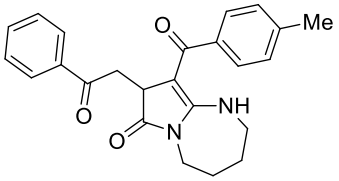
White solid; Mp 195.0–196.7 °C; IR (KBr): 3205, 3050, 2967, 1720, 1628, 1536, 1363, 1079 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.72 (s, 3H, $COCH_3$), 1.98–2.01 (m, 2H, CH_2), 2.30–2.36 (m, 1H, $COCH_2$), 2.54–2.59 (m, 1H, $COCH_2$), 3.38–3.43 (m, 2H, CH_2N), 3.58–3.63 (m, 2H, NCH_2), 3.70–3.72 (m, 1H, CH), 7.29–7.32 (m, 3H, ArH), 7.39–7.42 (m, 2H, ArH), 9.87 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.0, 30.0, 37.2, 38.6, 40.6, 42.8, 88.7, 126.4, 128.4, 129.6, 141.6, 158.9, 177.2, 184.5, 205.6; HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{18}N_2NaO_3$ [$(M+Na)^+$], 321.1210; found, 321.1210.

8-(4-fluorobenzoyl)-7-(2-oxopropyl)-1,3,4,7-tetrahydropyrrolo[1,2-*a*]pyrimidin-6(2*H*)-one (5j)



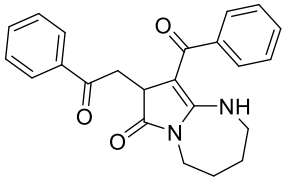
White solid; Mp 237.7–238.8 °C; IR (KBr): 3231, 3064, 2876, 1724, 1629, 1536, 1263, 1083 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.77 (s, 3H, $COCH_3$), 2.01–2.07 (m, 2H, CH_2), 2.36–2.43 (m, 1H, $COCH_2$), 2.59–2.64 (m, 1H, $COCH_2$), 3.42–3.47 (m, 2H, CH_2N), 3.61–3.66 (m, 2H, NCH_2), 3.70–3.73 (m, 1H, CH), 6.98–7.03 (m, 2H, ArH), 7.42–7.45 (m, 2H, ArH), 9.88 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 20.0, 30.0, 37.3, 38.6, 40.6, 42.9, 88.5, 115.3 (*J* = 21.4 Hz), 115.5 (*J* = 21.4 Hz), 128.7 (*J* = 8.4 Hz), 128.8 (*J* = 8.4 Hz), 137.7, 159.2, 162.2 (*J* = 248.0 Hz), 164.6 (*J* = 248.0 Hz), 177.0, 183.1, 205.4; HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{17}FN_2NaO_3$ [$(M+Na)^+$], 339.1115; found, 339.1115.

9-(4-methylbenzoyl)-8-(2-oxo-2-phenylethyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6a)



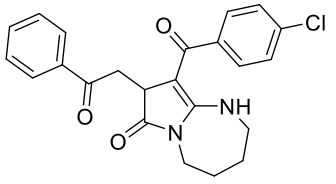
Red solid; Mp 164.0–164.9 °C; IR (KBr): 3436, 2941, 1732, 1680, 1532, 1443, 1237, 1141 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.99–2.09 (m, 4H, CH_2CH_2), 2.29 (s, 3H, $ArCH_3$), 2.96–3.09 (m, 2H, $COCH_2C$), 3.46–3.54 (m, 2H, CH_2N), 3.77–3.91 (m, 1H, NCH_2), 3.93–3.95 (m, 1H, CH), 3.96–4.00 (m, 1H, NCH_2), 7.05–7.07 (m, 2H, ArH), 7.20–7.25 (m, 4H, ArH), 7.38–7.44 (m, 2H, ArH), 10.71 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 21.4, 24.9, 27.4, 38.6, 41.1, 41.2, 42.7, 90.6, 126.6, 127.9, 128.3, 129.0, 133.0, 136.5, 138.9, 139.6, 165.2, 178.8, 185.0, 197.2; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{24}N_2NaO_3$ [$(M+Na)^+$], 411.1679; found, 411.1679.

9-benzoyl-8-(2-oxo-2-phenylethyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6b)



Red solid; Mp 159.4–160.9 °C; IR (KBr): 3454, 3054, 2903, 1735, 1617, 1447, 1275, 1142, cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.92–2.08 (m, 4H, CH_2CH_2), 2.95–2.97 (m, 2H, $COCH_2$), 3.44–3.51 (m, 2H, CH_2N), 3.78–3.85 (m, 1H, NCH_2), 3.83–3.85 (m, 1H, CH), 3.90–3.96 (m, 1H, NCH_2), 7.18–7.30 (m, 7H, ArH), 7.30–7.40 (m, 3H, ArH), 10.71 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 24.8, 27.3, 38.5, 41.0, 41.2, 42.6, 90.5, 126.5, 127.9, 128.3, 128.4, 129.4, 133.1, 136.3, 141.8, 165.3, 178.7, 184.9, 197.1; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{22}N_2NaO_3$ [$(M+Na)^+$], 397.1523; found, 397.1519.

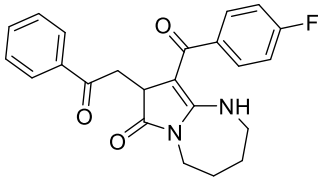
9-(4-chlorobenzoyl)-8-(2-oxo-2-phenylethyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6c)



Red solid; Mp 175.9–177.4 °C; IR (KBr): 3454, 3061, 2929, 1736, 1616, 1441, 1275, 1142 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 2.00–2.19 (m, 4H, CH_2CH_2), 3.10–3.12 (m, 2H, $COCH_2$), 3.56–3.64 (m, 2H, CH_2N), 3.87–3.93 (m, 1H, NCH_2), 3.91–3.93 (m, 1H, CH), 4.01–4.07 (m, 1H, NCH_2), 7.28–7.36 (m, 6H, ArH), 7.46–7.55 (m, 3H, ArH), 10.83 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 24.8, 27.2, 38.7, 40.9,

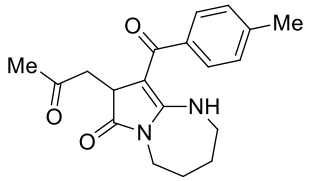
41.2, 42.7, 90.5, 127.9, 128.1, 128.4, 128.6, 133.2, 135.4, 136.2, 140.1, 165.6, 178.5, 183.2, 196.9; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{21}ClN_2O_3$ [$(M+Na)^+$], 431.1133; found, 431.1140.

9-(4-fluorobenzoyl)-8-(2-oxo-2-phenylethyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6d)



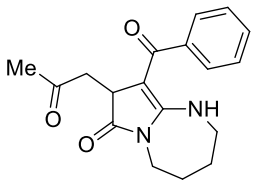
Red solid; Mp 178.3–179.0 °C; IR (KBr): 3449, 3065, 2917, 1734, 1685, 1540, 1369, 1144 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 2.02–2.11 (m, 4H, CH_2CH_2), 3.01–3.02 (m, 2H, $COCH_2$), 3.47–3.56 (m, 2H, CH_2N), 3.78–3.82 (m, 1H, NCH_2), 3.81–3.83 (m, 1H, CH), 3.84–3.99 (m, 1H, NCH_2), 6.92–6.96 (m, 2H, ArH), 7.22–7.46 (m, 7H, ArH), 10.73 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 24.8, 27.3, 38.6, 40.9, 41.2, 42.6, 90.4, 115.2 (*J* = 21.3 Hz), 115.5 (*J* = 21.3 Hz), 127.8, 128.4, 128.7 (*J* = 8.3 Hz), 128.8 (*J* = 8.3 Hz) , 133.2, 136.3, 137.9 (*J* = 2.6 Hz), 137.9 (*J* = 2.6 Hz), 162.0 (*J* = 247.7 Hz), 164.5 (*J* = 247.7 Hz), 165.5, 178.6, 183.4, 196.9; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{21}FN_2NaO_3$ [$(M+Na)^+$], 415.1428; found, 415.1429.

9-(4-methylbenzoyl)-8-(2-oxopropyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6e)



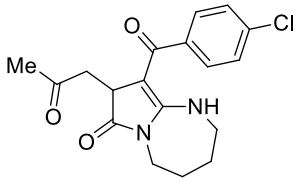
Yellow solid; Mp 202.0–203.8 °C; IR (KBr): 3445, 2940, 1722, 1618, 1541, 1437, 1265, 1151 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.75 (s, 3H, $COCH_3$), 1.87–2.06 (m, 4H, CH_2CH_2), 2.30 (s, 3H, $ArCH_3$), 2.32–2.37 (m, 1H, $COCH_2$), 2.56–2.61 (m, 1H, $COCH_2$), 3.46–3.52 (m, 2H, CH_2N), 3.71–3.73 (m, 1H, CH), 3.71–3.79 (m, 1H, NCH_2), 3.87–3.93 (m, 1H, NCH_2), 7.10–7.13 (m, 2H, ArH), 7.29–7.31 (m, 2H, ArH), 10.70 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 21.4, 24.8, 27.3, 30.0, 40.9, 41.1, 42.6, 43.2, 90.4, 126.5, 129.0, 138.9, 139.7, 165.1, 178.5, 184.9, 205.5; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{22}N_2NaO_3$[$(M+Na)^+$], 349.1523; found, 349.1527.

9-benzoyl-8-(2-oxopropyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3]diazepin-7-one (6f)



Yellow solid; Mp 169.9–170.6 °C; IR (KBr): 3445, 2933, 1723, 1619, 1543, 1444, 1262, 1148 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.73 (s, 3H, $COCH_3$), 1.89–2.04 (m, 4H, CH_2CH_2), 2.24–2.30 (m, 1H, $COCH_2$), 2.55–2.60 (m, 1H, $COCH_2$), 3.49–3.53 (m, 2H, CH_2N), 3.68–3.69 (m, 1H, CH), 3.70–3.80 (m, 1H, NCH_2), 3.87–3.93 (m, 1H, NCH_2), 7.31–7.33 (m, 3H, ArH), 7.37–7.40 (m, 2H, ArH), 10.71 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 24.8, 27.3, 29.9, 40.8, 41.1, 42.6, 43.2, 90.4, 126.4, 128.5, 129.5, 141.7, 165.2, 178.5, 184.9, 205.4; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{20}N_2NaO_3$ [$(M+Na)^+$], 335.1366; found, 335.1369.

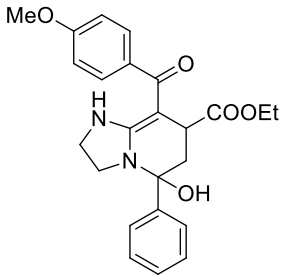
9-(4-chlorobenzoyl)-8-(2-oxopropyl)-1,2,3,4,5,8-hexahydro-7*H*-pyrrolo[1,2-*a*][1,3] diazepin-7-one (6g)



Yellow solid; Mp 242.3–243.5 °C; IR (KBr): 3452, 2943, 1727, 1619, 1543, 1267, 1152, 1089 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.78 (s, 3H, $COCH_3$), 1.88–2.07 (m, 4H, CH_2CH_2), 2.30–2.39 (m, 1H, $COCH_2$), 2.60–2.65 (m, 1H, $COCH_2$), 3.50–3.55 (m, 2H, CH_2N), 3.67–3.69 (m, 1H, CH), 3.75–3.81 (m, 1H, NCH_2), 3.88–3.94 (m, 1H, NCH_2), 7.29–7.32 (m, 2H, ArH), 7.31–7.37 (m, 2H, ArH), 10.76 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 24.7, 27.2, 30.0, 40.6, 41.1, 42.6, 43.3, 90.4, 128.0, 128.7, 135.5, 140.0, 165.5, 178.3, 183.0, 205.3; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{19}ClN_2NaO_3$ [$(M+Na)^+$], 369.0976; found, 369.0979.

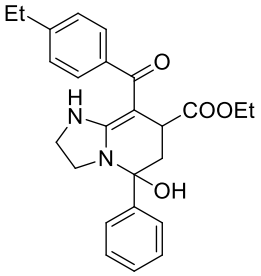
Spectroscopic Data of Imidazo[1,2-*a*]-pyridines 7–8

Ethyl 5-hydroxy-8-(4-methoxybenzoyl)-5-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine-7-carboxylate (7a)



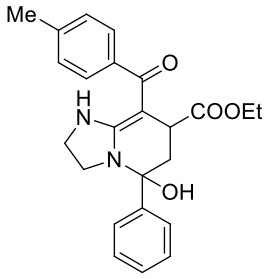
Yellow solid; Mp 80.5–81.9 °C; IR (KBr): 3427, 2971, 1729, 1599, 1384, 1247, 1168, 1027 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 0.93–0.96 (t, 3H, CCH_3), 2.25–2.27 (m, 2H, CH_2), 3.08–3.09 (m, 1H, CHCO), 3.42–3.47 (m, 2H, NCH_2), 3.50–3.53 (m, 1H, CH_2N), 3.73 (s, 3H, OCH_3), 3.76–3.80 (m, 1H, CH_2N), 3.78–3.85 (q, 2H, OCH_2), 6.19 (s, 1H, OH), 6.78–6.80 (m, 2H, ArH), 7.19–7.22 (m, 2H, ArH), 7.23–7.25 (m, 1H, ArH), 7.28–7.33 (m, 2H, ArH), 7.45–7.47 (m, 2H, ArH), 9.68 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 39.0, 40.5, 41.8, 42.9, 55.3, 61.5, 82.3, 82.7, 113.4, 126.0, 128.1, 128.1, 128.6, 135.3, 142.6, 159.7, 161.2, 178.4, 189.9; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{27}N_2O_5$ $[(M+H)^+]$, 423.1914; found, 429.1914.

Ethyl 8-(4-ethylbenzoyl)-5-hydroxy-5-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-*a*] -pyridine-7-carboxylate (7b)



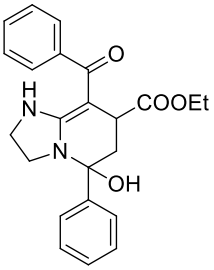
Yellow solid; Mp 91.0–91.9 °C; IR (KBr): 3291, 2968, 2353, 1728, 1599, 1512, 1387, 1169 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 0.83–0.95 (t, 3H, CCH_3), 1.11–1.17 (t, 3H, CCH_3), 2.19–2.30 (m, 2H, CH_2), 2.54–2.60 (q, 2H, $ArCH_2$), 3.08–3.10 (t, 1H, CHCO), 3.42–3.53 (m, 2H, NCH_2), 3.51–3.65 (m, 1H, CH_2N), 3.74–3.78 (q, 2H, OCH_2), 3.80–3.87 (m, 1H, CH_2N), 6.16 (s, 1H, OH), 7.08–7.18 (m, 4H, ArH), 7.24–7.36 (m, 3H, ArH), 7.31–7.47 (m, 2H, ArH), 9.72 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 15.6, 28.7, 39.0, 40.4, 41.8, 42.9, 61.4, 82.4, 82.7, 126.0, 126.4, 127.5, 128.1, 128.6, 140.1, 142.6, 144.3, 161.2, 178.5, 190.5; HRMS (TOF ES^+): *m/z* calcd for $C_{25}H_{29}N_2O_4$ $[(M+H)^+]$, 421.2122; found, 421.2123.

Ethyl 5-hydroxy-8-(4-methylbenzoyl)-5-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine-7-carboxylate (7c)



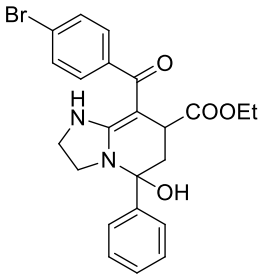
Orange solid; Mp 95.0–96.3 °C; IR (KBr): 3287, 2975, 2352, 1727, 1588, 1512, 1386, 1170 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 0.92–0.96 (t, 3H, CCH_3), 2.24–2.25 (d, 2H, CH_2), 2.27 (s, 3H, CCH_3), 3.07–3.12 (m, 1H, CHCO), 3.43–3.51 (m, 2H, NCH_2), 3.54–3.61 (m, 1H, CH_2N), 3.73–3.75 (q, 2H, OCH_2), 3.79–3.87 (m, 1H, CH_2N), 6.16 (s, 1H, OH), 7.06–7.08 (m, 2H, ArH), 7.12–7.14 (m, 2H, ArH), 7.24–7.26 (m, 1H, ArH), 7.29–7.33 (m, 2H, ArH), 7.45–7.47 (m, 2H, ArH), 9.71 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 21.3, 39.0, 40.4, 41.8, 42.9, 61.5, 82.3, 82.7, 126.0, 126.4, 128.1, 128.6, 128.7, 138.0, 139.9, 142.6, 161.2, 178.6, 190.5; HRMS (TOF ES^+): *m/z* calcd for $C_{24}H_{26}N_2NaO_4$ [$(M+Na)^+$], 429.1785; found, 429.1785.

Ethyl 8-benzoyl-5-hydroxy-5-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-*a*]pyri-dine-7-carboxylate (7d)



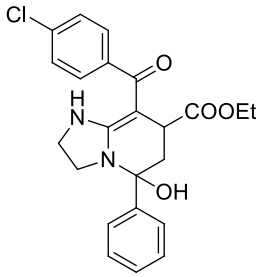
Red solid; Mp 84.9–85.7 °C; IR (KBr): 3288, 2979, 1729, 1600, 1513, 1387, 1168, 1024 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 0.91–0.94 (t, 3H, CCH_3), 2.23–2.26 (d, 2H, CH_2), 3.07–3.12 (m, 1H, CHCO), 3.42–3.56 (m, 2H, NCH_2), 3.58–3.61 (m, 1H, CH_2N), 3.70–3.75 (q, 2H, OCH_2), 3.77–3.87 (m, 1H, CH_2N), 6.17 (s, 1H, OH), 7.18–7.25 (m, 6H, ArH), 7.29–7.33 (m, 2H, ArH), 7.45–7.47 (m, 2H, ArH), 9.70 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 38.9, 40.4, 41.8, 42.9, 61.5, 82.4, 82.7, 126.0, 126.4, 128.1, 128.2, 128.3, 128.6, 142.6, 142.7, 161.3, 178.5, 190.2; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{25}N_2O_4$ [$(M+H)^+$], 393.1809; found, 393.1806.

Ethyl 8-(4-bromobenzoyl)-5-hydroxy-5-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine-7-carboxylate (7e)



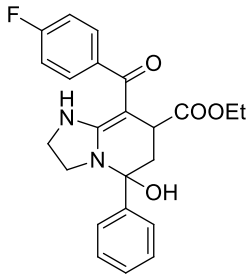
Yellow solid; Mp 200.9–202.5 °C; IR (KBr): 3295, 2974, 2887, 1694, 1591, 1515, 1398, 1226 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 0.96–0.99 (t, 3H, CCH_3), 2.26–2.28 (d, 2H, CH_2), 3.11–3.14 (m, 1H, CHCO), 3.46–3.57 (m, 2H, NCH_2), 3.59–3.70 (q, 2H, OCH_2), 3.79–3.91 (m, 2H, CH_2N), 6.17 (s, 1H, OH), 7.12–7.19 (m, 2H, ArH), 7.26–7.35 (m, 3H, ArH), 7.41–7.48 (m, 4H, ArH), 9.71 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 38.8, 40.3, 41.8, 42.9, 61.7, 82.2, 82.7, 122.3, 126.0, 128.1, 128.2, 128.6, 131.3, 141.5, 142.4, 161.3, 178.4, 188.7; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{24}BrN_2O_4$ [$(M+H)^+$], 471.0914; found, 471.0913.

Ethyl 8-(4-chlorobenzoyl)-5-hydroxy-5-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine-7-carboxylate (7f)



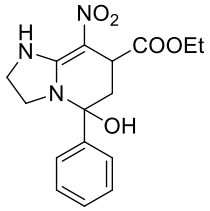
White solid; Mp 190.5–192.4 °C; IR (KBr): 3302, 2977, 2885, 1695, 1593, 1398, 1226, 1022 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.02–1.06 (t, 3H, CCH_3), 2.33–2.35 (d, 2H, CH_2), 3.17–3.22 (m, 1H, CHCO), 3.53–3.69 (m, 2H, NCH_2), 3.71–3.78 (q, 2H, OCH_2), 3.86–3.98 (m, 2H, CH_2N), 6.24 (s, 1H, OH), 7.26–7.27 (m, 3H, ArH), 7.32–7.34 (m, 2H, ArH), 7.35–7.42 (m, 2H, ArH), 7.53–7.55 (m, 2H, ArH), 9.79 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 38.9, 40.3, 41.8, 42.9, 61.7, 82.2, 82.7, 126.0, 128.0, 128.2, 128.3, 128.6, 134.1, 141.1, 142.5, 161.3, 178.4, 188.8; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{24}ClN_2O_4$ [$(M+H)^+$], 427.1419; found, 427.1417.

Ethyl 8-(4-fluorobenzoyl)-5-hydroxy-5-phenyl-1,2,3,5,6,7-hexahydroimidazo-[1,2-*a*]pyridine-7-carboxylate (7g)



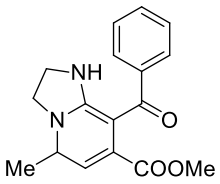
Yellow solid; Mp 115.6–117.8 °C; IR (KBr): 3256, 2976, 1730, 1590, 1510, 1381, 1162, 1026 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 0.93–0.97 (t, 3H, CCH_3), 2.25–2.26 (d, 2H, CH_2), 3.07–3.12 (m, 1H, CHCO), 3.43–3.54 (m, 2H, NCH_2), 3.56–3.69 (q, 2H, OCH_2), 3.77–3.90 (m, 2H, CH_2N), 6.17 (s, 1H, OH), 6.93–6.97 (m, 2H, ArH), 7.21–7.24 (m, 3H, ArH), 7.26–7.33 (m, 2H, ArH), 7.44–7.46 (m, 2H, ArH), 9.67 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.7, 38.9, 40.4, 41.8, 42.9, 61.6, 82.3, 82.7, 114.9 (*J* = 21.3 Hz), 115.1 (*J* = 21.3 Hz), 126.0, 128.2, 128.4 (*J* = 8.1 Hz), 128.5 (*J* = 8.1 Hz), 128.6, 138.7 (*J* = 2.9 Hz), 138.8 (*J* = 2.9 Hz), 142.5, 161.3, 161.3 (*J* = 249.9 Hz), 163.8 (*J* = 249.9 Hz), 178.3, 188.9; HRMS (TOF ES^+): *m/z* calcd for $C_{23}H_{23}FN_2NaO_4$ [$(M+Na)^+$], 433.1534; found, 433.1533.

Ethyl 5-hydroxy-8-nitro-5-phenyl-1,2,3,5,6,7-hexahydroimidazo[1,2-*a*]pyridine-7-carboxylate (7h)



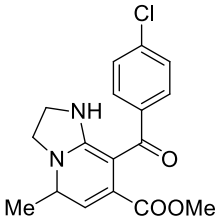
Yellow solid; Mp 193.9–194.6 °C; IR (KBr): 3335, 2978, 2354, 1684, 1501, 1253, 1129, 1018 cm^{-1}; ^{1}H NMR (400 MH_Z, $CDCl_3$): δ = 1.24–1.27 (t, 3H, CCH_3), 2.25–2.42 (m, 2H, CH_2), 3.17–3.22 (m, 1H, CHCO), 3.51–3.66 (m, 2H, NCH_2), 3.70–3.73 (q, 1H, OCH_2), 4.04–4.07 (q, 1H, OCH_2), 4.19–4.23 (m, 2H, CH_2N), 5.52 (s, 1H, OH), 7.28–7.36 (m, 3H, ArH), 7.44–7.46 (m, 2H, ArH), 8.87 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 13.0, 38.0, 38.3, 41.2, 43.1, 61.4, 82.4, 102.3, 124.9, 127.6, 127.7, 139.9, 156.6, 175.7; HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{19}N_3NaO_5$ [$(M+Na)^+$], 356.1217; found, 356.1217.

Methyl 8-benzoyl-5-methyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridine-7-carboxylate (8a)



Yellow solid; Mp 200.9–201.4 °C; IR (KBr): 3234, 2954, 2897, 1739, 1530, 1473, 1157, 1014 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.82 (s, 3H, CCH_3), 3.39 (s, 3H, OCH_3), 3.65–3.78 (m, 4H, CH_2CH_2), 4.01–4.02 (m, 1H, NCH), 4.58–4.60 (m, 1H, CCH), 7.16–7.20 (m, 2H, ArH), 7.22–7.25 (m, 3H, ArH), 9.32 (br, 1H, NH); ^{13}C NMR (100 MHZ, $CDCl_3$): δ = 17.0, 41.5, 41.7, 43.6, 50.8, 81.7, 98.1, 125.0, 127.1, 127.3, 132.4, 141.3, 157.3, 173.7, 191.3; HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{18}N_2NaO_3$ [$(M+Na)^+$], 321.1210; found, 321.1208.

Methyl 8-(4-chlorobenzoyl)-5-methyl-1,2,3,5-tetrahydroimidazo[1,2-*a*]pyridine-7-carboxylate (8b)



Yellow solid; Mp 180.3–181.1 °C; IR (KBr): 3236, 2898, 1733, 1605, 1472, 1328, 1223, 1090 cm^{-1}; ^1H NMR (400 MH_Z, $CDCl_3$): δ = 1.83 (s, 3H, CCH_3), 3.41 (s, 3H, OCH_3), 3.65–3.78 (m, 4H, CH_2CH_2), 3.96–3.98 (m, 1H, NCH), 4.60–4.62 (m, 1H, CCH), 7.12–7.14 (m, 2H, ArH), 7.19–7.23 (m, 3H, ArH), 9.30 (br, 1H, NH); ^{13}C NMR (100 MH_Z, $CDCl_3$): δ = 16.9, 41.3, 41.7, 43.6, 50.9, 81.6, 98.0, 126.6, 127.3, 132.4, 133.2, 139.7, 157.4, 173.5, 189.7; HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{17}ClN_2NaO_3$ [$(M+Na)^+$], 355.0820; found, 355.0825.

X-ray Structure and Data[2] of 5e

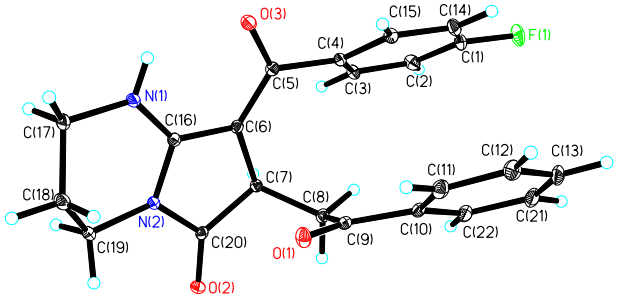


Figure S1 X-Ray crystal structure of **5e**

Table S1 Crystal data and structure refinement for **5e**

Empirical formula	C_{23} H_{21} C_{l2} F N_2 O_3
Formula weight	463.32
Temperature	100(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P 21/c
Unit cell dimensions	a = 9.9049(18) A alpha = 90 deg.
	b = 24.490(4) A beta = 96.040(3) deg.
	c = 8.7934(16) A gamma = 90 deg.
Volume	2121.2(7) A^3
Z, Calculated density	4, 1.451 Mg/m^3
Absorption coefficient	0.344 mm^-1
F(000)	960
Crystal size	1.35 x 0.40 x 0.20 mm
Theta range for data collection	1.66 to 28.00 deg.
Limiting indices	-13<=h<=13, -32<=k<=32, -11<=l<=11
Reflection collected/unique	19828 / 5114 [R(int) = 0.0344]
Completeness to theta = 28.2	99.9%
Absorption correction	Semi-empirical from equivalents
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	5114 / 0 / 280
Goodness-of-fit on F^2	1.034
Final R indices [I>2sigma(I)]	R1 = 0.0706, wR2 = 0.1748
R indices (all data)	R1 = 0.0869, wR2 = 0.1877
Largest diff. peak and hole	1.458 and -1.284 e.A^-3

Table S2 Bond lengths [A] and angles [deg] for **5e**

Cl(1)-C(23)	1.752(4)
Cl(2)-C(23)	1.735(4)
F(1)-C(1)	1.363(3)
O(1)-C(9)	1.220(3)
O(2)-C(20)	1.220(3)
O(3)-C(5)	1.260(3)
N(1)-C(16)	1.321(3)
N(1)-C(17)	1.460(3)
N(1)-H(1)	0.8800
N(2)-C(20)	1.378(3)
N(2)-C(16)	1.385(3)
N(2)-C(19)	1.465(3)
C(1)-C(14)	1.377(4)
C(1)-C(2)	1.378(4)
C(2)-C(3)	1.396(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.399(3)
C(3)-H(3)	0.9500
C(4)-C(15)	1.393(3)
C(4)-C(5)	1.501(3)
C(5)-C(6)	1.408(3)
C(6)-C(16)	1.403(3)
C(6)-C(7)	1.517(3)
C(7)-C(20)	1.523(3)
C(7)-C(8)	1.532(3)
C(7)-H(7)	1.0000
C(8)-C(9)	1.512(3)
C(8)-H(8A)	0.9900
C(8)-H(8B)	0.9900
C(9)-C(10)	1.498(3)
C(10)-C(11)	1.396(4)
C(10)-C(22)	1.397(4)
C(11)-C(12)	1.389(4)
C(11)-H(11)	0.9500
C(12)-C(13)	1.393(4)
C(12)-H(12)	0.9500
C(13)-C(21)	1.384(4)
C(13)-H(13)	0.9500
C(14)-C(15)	1.389(3)
C(14)-H(14)	0.9500
C(15)-H(15)	0.9500
C(17)-C(18)	1.523(4)
C(17)-H(17A)	0.9900
C(17)-H(17B)	0.9900
C(18)-C(19)	1.521(4)
C(18)-H(18A)	0.9900
C(18)-H(18B)	0.9900
C(19)-H(19A)	0.9900
C(19)-H(19B)	0.9900
C(21)-C(22)	1.393(4)
C(21)-H(21)	0.9500
C(22)-H(22)	0.9500
C(23)-H(23A)	0.9900
C(23)-H(23B)	0.9900
C(16)-N(1)-C(17)	123.2(2)
C(16)-N(1)-H(1)	118.4

C(17)-N(1)-H(1)	118.4
C(20)-N(2)-C(16)	110.82(19)
C(20)-N(2)-C(19)	125.5(2)
C(16)-N(2)-C(19)	123.5(2)
F(1)-C(1)-C(14)	118.6(2)
F(1)-C(1)-C(2)	118.1(2)
C(14)-C(1)-C(2)	123.3(2)
C(1)-C(2)-C(3)	118.2(2)
C(1)-C(2)-H(2)	120.9
C(3)-C(2)-H(2)	120.9
C(2)-C(3)-C(4)	120.3(2)
C(2)-C(3)-H(3)	119.9
C(4)-C(3)-H(3)	119.9
C(15)-C(4)-C(3)	119.2(2)
C(15)-C(4)-C(5)	118.0(2)
C(3)-C(4)-C(5)	122.8(2)
O(3)-C(5)-C(6)	121.7(2)
O(3)-C(5)-C(4)	117.1(2)
C(6)-C(5)-C(4)	121.1(2)
C(16)-C(6)-C(5)	120.7(2)
C(16)-C(6)-C(7)	107.1(2)
C(5)-C(6)-C(7)	131.6(2)
C(6)-C(7)-C(20)	102.85(18)
C(6)-C(7)-C(8)	119.22(19)
C(20)-C(7)-C(8)	111.70(19)
C(6)-C(7)-H(7)	107.5
C(20)-C(7)-H(7)	107.5
C(8)-C(7)-H(7)	107.5
C(9)-C(8)-C(7)	112.64(19)
C(9)-C(8)-H(8A)	109.1
C(7)-C(8)-H(8A)	109.1
C(9)-C(8)-H(8B)	109.1
C(7)-C(8)-H(8B)	109.1
H(8A)-C(8)-H(8B)	107.8
O(1)-C(9)-C(10)	121.5(2)
O(1)-C(9)-C(8)	120.3(2)
C(10)-C(9)-C(8)	118.2(2)
C(11)-C(10)-C(22)	119.8(2)
C(11)-C(10)-C(9)	118.1(2)
C(22)-C(10)-C(9)	122.0(2)
C(12)-C(11)-C(10)	119.9(3)
C(12)-C(11)-H(11)	120.1
C(10)-C(11)-H(11)	120.1
C(11)-C(12)-C(13)	120.1(3)
C(11)-C(12)-H(12)	119.9
C(13)-C(12)-H(12)	119.9
C(21)-C(13)-C(12)	120.2(3)
C(21)-C(13)-H(13)	119.9
C(12)-C(13)-H(13)	119.9
C(1)-C(14)-C(15)	117.8(2)
C(1)-C(14)-H(14)	121.1
C(15)-C(14)-H(14)	121.1
C(14)-C(15)-C(4)	121.2(2)
C(14)-C(15)-H(15)	119.4
C(4)-C(15)-H(15)	119.4
N(1)-C(16)-N(2)	119.5(2)
N(1)-C(16)-C(6)	129.5(2)

N(2)-C(16)-C(6)	110.9(2)
N(1)-C(17)-C(18)	109.8(2)
N(1)-C(17)-H(17A)	109.7
C(18)-C(17)-H(17A)	109.7
N(1)-C(17)-H(17B)	109.7
C(18)-C(17)-H(17B)	109.7
H(17A)-C(17)-H(17B)	108.2
C(19)-C(18)-C(17)	110.3(2)
C(19)-C(18)-H(18A)	109.6
C(17)-C(18)-H(18A)	109.6
C(19)-C(18)-H(18B)	109.6
C(17)-C(18)-H(18B)	109.6
H(18A)-C(18)-H(18B)	108.1
N(2)-C(19)-C(18)	108.4(2)
N(2)-C(19)-H(19A)	110.0
C(18)-C(19)-H(19A)	110.0
N(2)-C(19)-H(19B)	110.0
C(18)-C(19)-H(19B)	110.0
H(19A)-C(19)-H(19B)	108.4
O(2)-C(20)-N(2)	124.6(2)
O(2)-C(20)-C(7)	127.3(2)
N(2)-C(20)-C(7)	108.06(19)
C(13)-C(21)-C(22)	120.0(3)
C(13)-C(21)-H(21)	120.0
C(22)-C(21)-H(21)	120.0
C(21)-C(22)-C(10)	119.9(3)
C(21)-C(22)-H(22)	120.0
C(10)-C(22)-H(22)	120.0
Cl(2)-C(23)-Cl(1)	111.9(2)
Cl(2)-C(23)-H(23A)	109.2
Cl(1)-C(23)-H(23A)	109.2
Cl(2)-C(23)-H(23B)	109.2
Cl(1)-C(23)-H(23B)	109.2
H(23A)-C(23)-H(23B)	107.9

Symmetry transformations used to generate equivalent atoms:

Table S3. Hydrogen bonds for **5e** [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(17)-H(17B)...O(3)	0.97	1.98	2.387(12)	102.7
C(15)-H(15)...F(1)	0.98	2.51	2.872(4)	101.7
O(2)-H(2)...O(5)	0.82	1.94	2.753(3)	169.6
N(1)-H(1)...O(1)	0.86	2.04	2.607(4)	123.1

Symmetry transformations used to generate equivalent atoms:

X-ray Structure and Data[2] of 7e

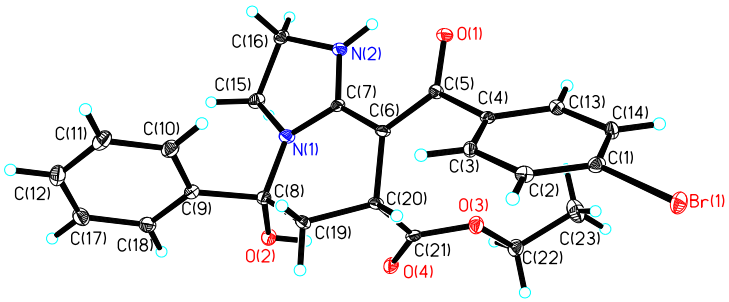


Figure S2 X-Ray crystal structure of **7e**

Table S4 Crystal data and structure refinement for **7e**

Empirical formula	$C_{27}H_{25}Cl_3F_3N_3O_5$
Formula weight	634.85
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P-1
Unit cell dimensions	a = 10.489(5) A alpha = 73.462(5) deg. b = 11.635(5) A beta = 80.503(5) deg. c = 13.375(5) A gamma = 72.854(5) deg.
Volume	1489.3(11) A^3
Z, Calculated density	2, 1.416 Mg/m^3
Absorption coefficient	0.367 mm^-1
F(000)	652
Crystal size	0.23x 0.19 x 0.14 mm
Theta range for data collection	1.89 to 26.31 deg.
Limiting indices	-12<=h<=13, -15<=k<=15, -17<=l<=17
Reflection collected/unique	10468/6121[R(int) = 0.0656]
Completeness to theta = 28.2	96.6%
Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.9745 and 0.9532
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	6121/ 0/ 374
Goodness-of-fit on F^2	1.028
Final R indices [I>2sigma(I)]	R1 = 0.1239, wR2 = 0.3167
R indices (all data)	R1 = 0.2712, wR2 = 0.4173
Extinction coefficient	0.010(5)
Largest diff. peak and hole	0.689 and -0.735 e.A^-3

Table S5 Bond lengths [A] and angles [deg] for **7e**

C(1)-O(1)	1.244(8)
C(1)-C(8)	1.390(9)
C(1)-C(2)	1.530(10)
C(2)-C(7)	1.371(10)
C(2)-C(3)	1.385(9)
C(3)-C(4)	1.369(10)
C(3)-H(3)	0.9300
C(4)-C(5)	1.352(11)
C(4)-H(4)	0.9300
C(5)-C(6)	1.405(12)
C(5)-H(5)	0.9300
C(6)-C(7)	1.355(12)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.403(10)
C(8)-C(19)	1.523(8)
C(9)-N(1)	1.320(8)
C(9)-N(2)	1.359(8)
C(10)-N(1)	1.464(9)
C(10)-C(12)	1.486(10)
C(10)-C(11)	1.503(10)
C(10)-H(10)	0.9800
C(11)-H(11A)	0.9600
C(11)-H(11B)	0.9600
C(11)-H(11C)	0.9600
C(12)-N(2)	1.483(9)
C(12)-H(12A)	0.9700
C(12)-H(12B)	0.9700
C(13)-O(2)	1.396(7)
C(13)-N(2)	1.444(8)
C(13)-C(14)	1.533(10)
C(13)-C(15)	1.534(10)
C(14)-F(3)	1.317(8)
C(14)-F(1)	1.328(10)
C(14)-F(2)	1.341(9)
C(15)-C(16)	1.506(9)
C(15)-C(19)	1.537(9)
C(15)-H(15)	0.9800
C(16)-O(3)	1.210(8)
C(16)-O(4)	1.321(8)
C(17)-C(18)	1.476(12)
C(17)-O(4)	1.477(8)
C(17)-H(17A)	0.9700
C(17)-H(17B)	0.9700
C(18)-H(18A)	0.9600
C(18)-H(18B)	0.9600
C(18)-H(18C)	0.9600
C(19)-C(26)	1.512(9)
C(19)-C(20)	1.577(9)
C(20)-O(5)	1.219(7)
C(20)-N(3)	1.332(8)
C(21)-C(22)	1.389(11)
C(21)-N(3)	1.399(8)
C(21)-C(26)	1.410(9)
C(22)-C(23)	1.385(12)
C(22)-H(22)	0.9300

C(23)-C(24)	1.394(13)
C(23)-H(23)	0.9300
C(24)-C(25)	1.403(11)
C(24)-H(24)	0.9300
C(25)-C(26)	1.346(9)
C(25)-H(25)	0.9300
C(27)-Cl(3)	1.658(17)
C(27)-Cl(2)	1.72(2)
C(27)-Cl(1)	1.85(2)
C(27)-H(27)	0.9800
N(1)-H(1)	0.8600
N(3)-H(3A)	0.8600
O(2)-H(2)	0.8200
O(1)-C(1)-C(8)	124.9(7)
O(1)-C(1)-C(2)	113.1(6)
C(8)-C(1)-C(2)	122.0(6)
C(7)-C(2)-C(3)	118.2(7)
C(7)-C(2)-C(1)	122.1(7)
C(3)-C(2)-C(1)	119.0(7)
C(4)-C(3)-C(2)	121.1(7)
C(4)-C(3)-H(3)	119.4
C(2)-C(3)-H(3)	119.4
C(5)-C(4)-C(3)	119.2(8)
C(5)-C(4)-H(4)	120.4
C(3)-C(4)-H(4)	120.4
C(4)-C(5)-C(6)	121.3(8)
C(4)-C(5)-H(5)	119.3
C(6)-C(5)-H(5)	119.3
C(7)-C(6)-C(5)	117.8(8)
C(7)-C(6)-H(6)	121.1
C(5)-C(6)-H(6)	121.1
C(6)-C(7)-C(2)	122.3(8)
C(6)-C(7)-H(7)	118.9
C(2)-C(7)-H(7)	118.9
C(1)-C(8)-C(9)	118.1(6)
C(1)-C(8)-C(19)	124.3(6)
C(9)-C(8)-C(19)	117.4(6)
N(1)-C(9)-N(2)	108.5(6)
N(1)-C(9)-C(8)	126.0(7)
N(2)-C(9)-C(8)	125.4(6)
N(1)-C(10)-C(12)	101.0(6)
N(1)-C(10)-C(11)	110.1(7)
C(12)-C(10)-C(11)	113.7(7)
N(1)-C(10)-H(10)	110.6
C(12)-C(10)-H(10)	110.6
C(11)-C(10)-H(10)	110.6
C(10)-C(11)-H(11A)	109.5
C(10)-C(11)-H(11B)	109.5
H(11A)-C(11)-H(11B)	109.5
C(10)-C(11)-H(11C)	109.5
H(11A)-C(11)-H(11C)	109.5
H(11B)-C(11)-H(11C)	109.5
N(2)-C(12)-C(10)	103.4(6)
N(2)-C(12)-H(12A)	111.1
C(10)-C(12)-H(12A)	111.1
N(2)-C(12)-H(12B)	111.1
C(10)-C(12)-H(12B)	111.1

H(12A)-C(12)-H(12B)	109.0
O(2)-C(13)-N(2)	112.1(6)
O(2)-C(13)-C(14)	104.2(6)
N(2)-C(13)-C(14)	108.2(6)
O(2)-C(13)-C(15)	114.5(6)
N(2)-C(13)-C(15)	107.3(5)
C(14)-C(13)-C(15)	110.5(6)
F(3)-C(14)-F(1)	106.6(7)
F(3)-C(14)-F(2)	105.4(7)
F(1)-C(14)-F(2)	107.1(7)
F(3)-C(14)-C(13)	112.5(7)
F(1)-C(14)-C(13)	113.5(7)
F(2)-C(14)-C(13)	111.2(7)
C(16)-C(15)-C(13)	114.4(5)
C(16)-C(15)-C(19)	110.4(5)
C(13)-C(15)-C(19)	113.7(5)
C(16)-C(15)-H(15)	105.9
C(13)-C(15)-H(15)	105.9
C(19)-C(15)-H(15)	105.9
O(3)-C(16)-O(4)	123.3(7)
O(3)-C(16)-C(15)	124.1(7)
O(4)-C(16)-C(15)	112.5(6)
C(18)-C(17)-O(4)	110.1(7)
C(18)-C(17)-H(17A)	109.6
O(4)-C(17)-H(17A)	109.6
C(18)-C(17)-H(17B)	109.6
O(4)-C(17)-H(17B)	109.6
H(17A)-C(17)-H(17B)	108.2
C(17)-C(18)-H(18A)	109.5
C(17)-C(18)-H(18B)	109.5
H(18A)-C(18)-H(18B)	109.5
C(17)-C(18)-H(18C)	109.5
H(18A)-C(18)-H(18C)	109.5
H(18B)-C(18)-H(18C)	109.5
C(26)-C(19)-C(8)	115.2(5)
C(26)-C(19)-C(15)	108.1(5)
C(8)-C(19)-C(15)	110.8(5)
C(26)-C(19)-C(20)	100.7(6)
C(8)-C(19)-C(20)	110.2(5)
C(15)-C(19)-C(20)	111.4(5)
O(5)-C(20)-N(3)	126.2(6)
O(5)-C(20)-C(19)	124.6(6)
N(3)-C(20)-C(19)	109.1(6)
C(22)-C(21)-N(3)	129.5(7)
C(22)-C(21)-C(26)	120.2(8)
N(3)-C(21)-C(26)	110.3(6)
C(23)-C(22)-C(21)	118.4(8)
C(23)-C(22)-H(22)	120.8
C(21)-C(22)-H(22)	120.8
C(22)-C(23)-C(24)	121.9(9)
C(22)-C(23)-H(23)	119.0
C(24)-C(23)-H(23)	119.0
C(23)-C(24)-C(25)	117.9(8)
C(23)-C(24)-H(24)	121.0
C(25)-C(24)-H(24)	121.0
C(26)-C(25)-C(24)	121.3(8)
C(26)-C(25)-H(25)	119.3

C(24)-C(25)-H(25)	119.3
C(25)-C(26)-C(21)	120.1(7)
C(25)-C(26)-C(19)	131.5(7)
C(21)-C(26)-C(19)	108.3(6)
Cl(3)-C(27)-Cl(2)	110.5(16)
Cl(3)-C(27)-Cl(1)	111.3(10)
Cl(2)-C(27)-Cl(1)	103.2(7)
Cl(3)-C(27)-H(27)	110.6
Cl(2)-C(27)-H(27)	110.6
Cl(1)-C(27)-H(27)	110.6
C(9)-N(1)-C(10)	113.3(6)
C(9)-N(1)-H(1)	123.4
C(10)-N(1)-H(1)	123.4
C(9)-N(2)-C(13)	120.5(6)
C(9)-N(2)-C(12)	108.7(6)
C(13)-N(2)-C(12)	123.5(6)
C(20)-N(3)-C(21)	111.5(6)
C(20)-N(3)-H(3A)	124.2
C(21)-N(3)-H(3A)	124.2
C(13)-O(2)-H(2)	109.5
C(16)-O(4)-C(17)	117.8(5)

Symmetry transformations used to generate equivalent atoms:

Table S6. Hydrogen bonds for **7e** [A and deg.].

D-H...A	d(D-H)	d(H...A)	d(D...A)	<(DHA)
C(15)-H(15)...F(2)	0.98	2.54	2.902(8)	101.6
C(12)-H(12A)...F(1)	0.97	2.39	2.795(9)	104.8
C(6)-H(6)...O(2)#1	0.93	2.49	3.400(10)	165.4
N(3)-H(3A)...O(5)#2	0.86	2.05	2.853(7)	155.4
O(2)-H(2)...F(3)	0.82	2.35	2.767(7)	112.6
N(1)-H(1)...O(1)#3	0.86	2.10	2.867(8)	148.4
N(1)-H(1)...O(1)	0.86	2.05	2.623(8)	123.2

Symmetry transformations used to generate equivalent atoms:
#1 x+1,y,z #2 -x,-y+1,-z #3 -x,-y+1,-z+1

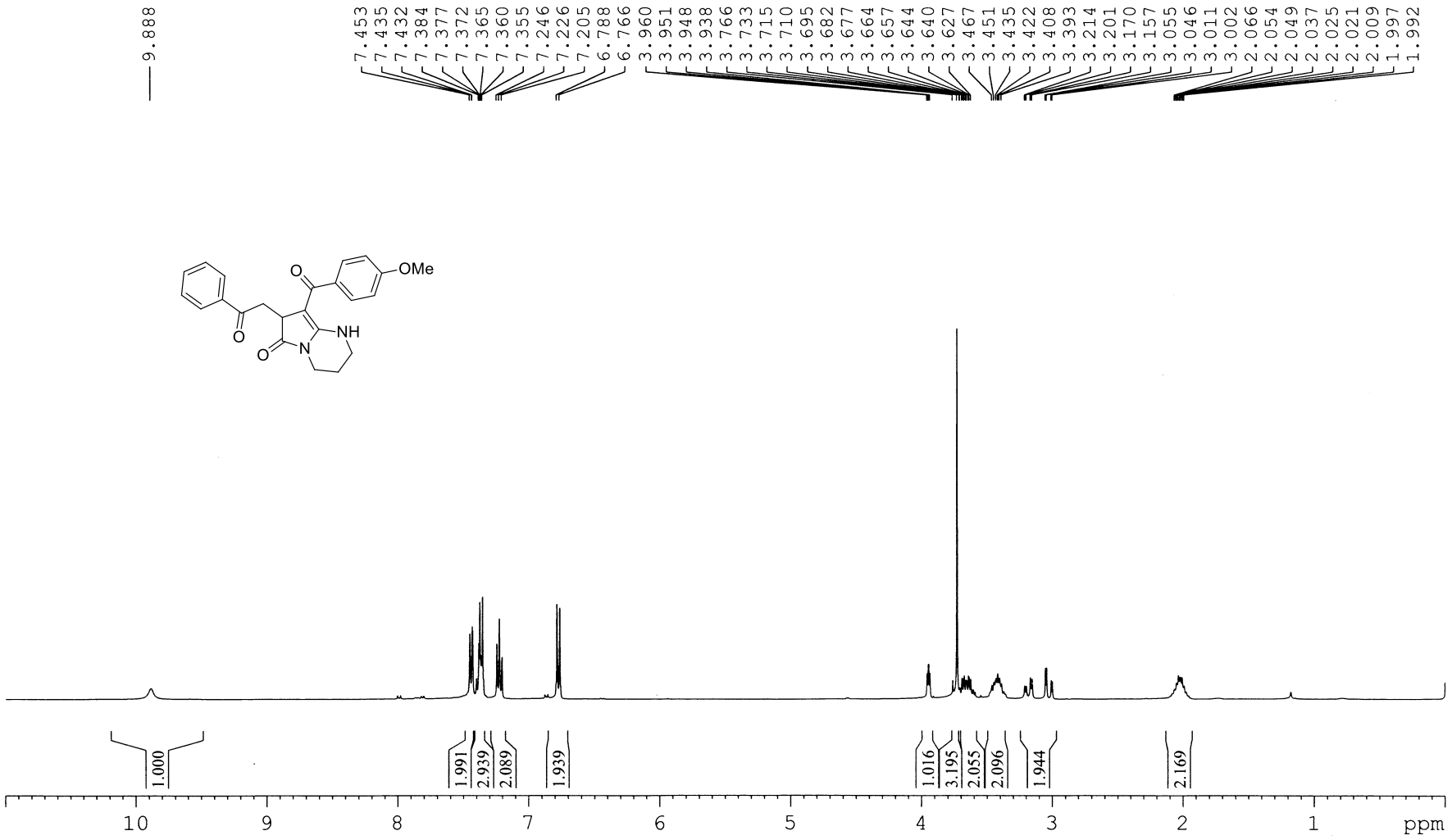


Figure 1. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5a**

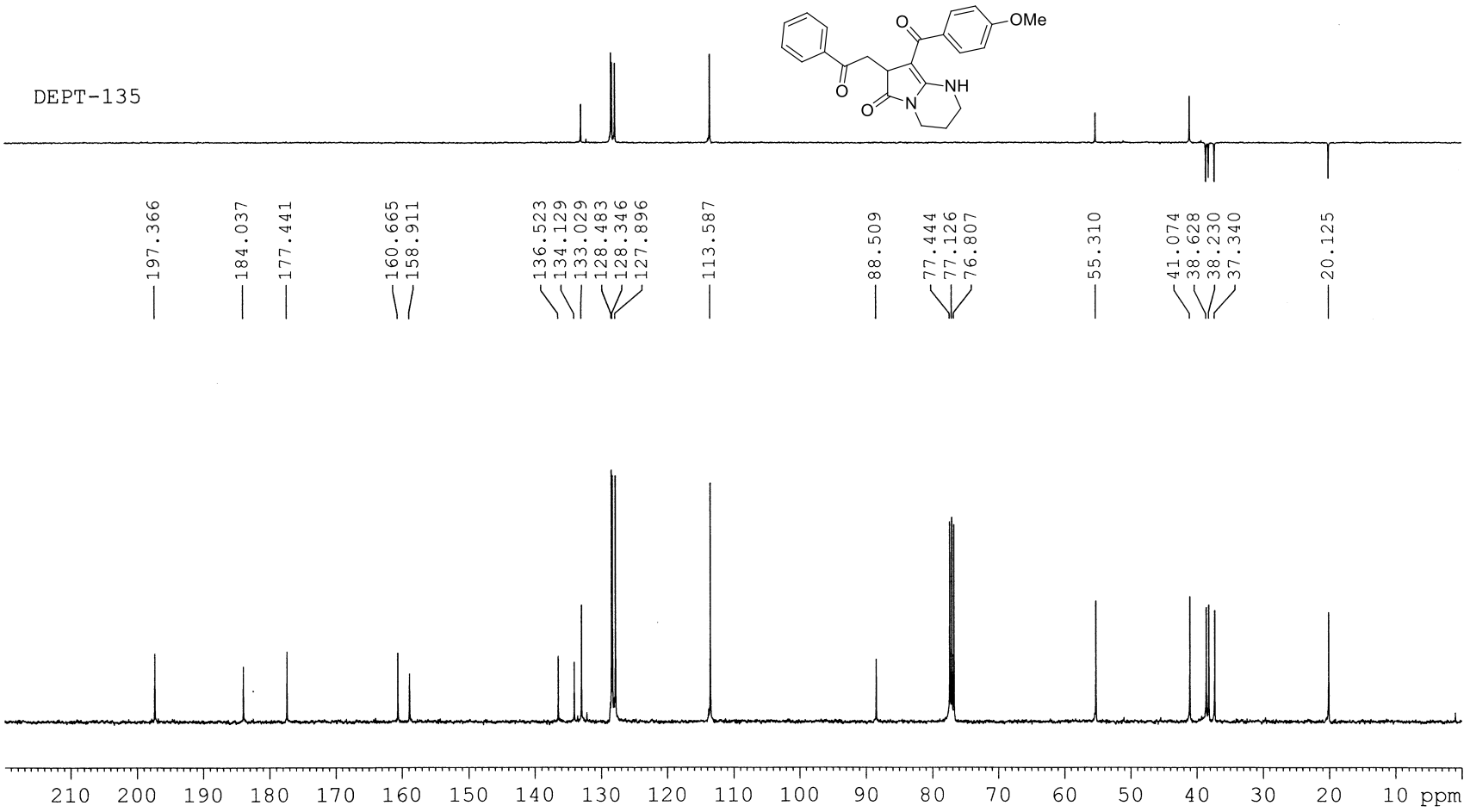


Figure 2. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5a**

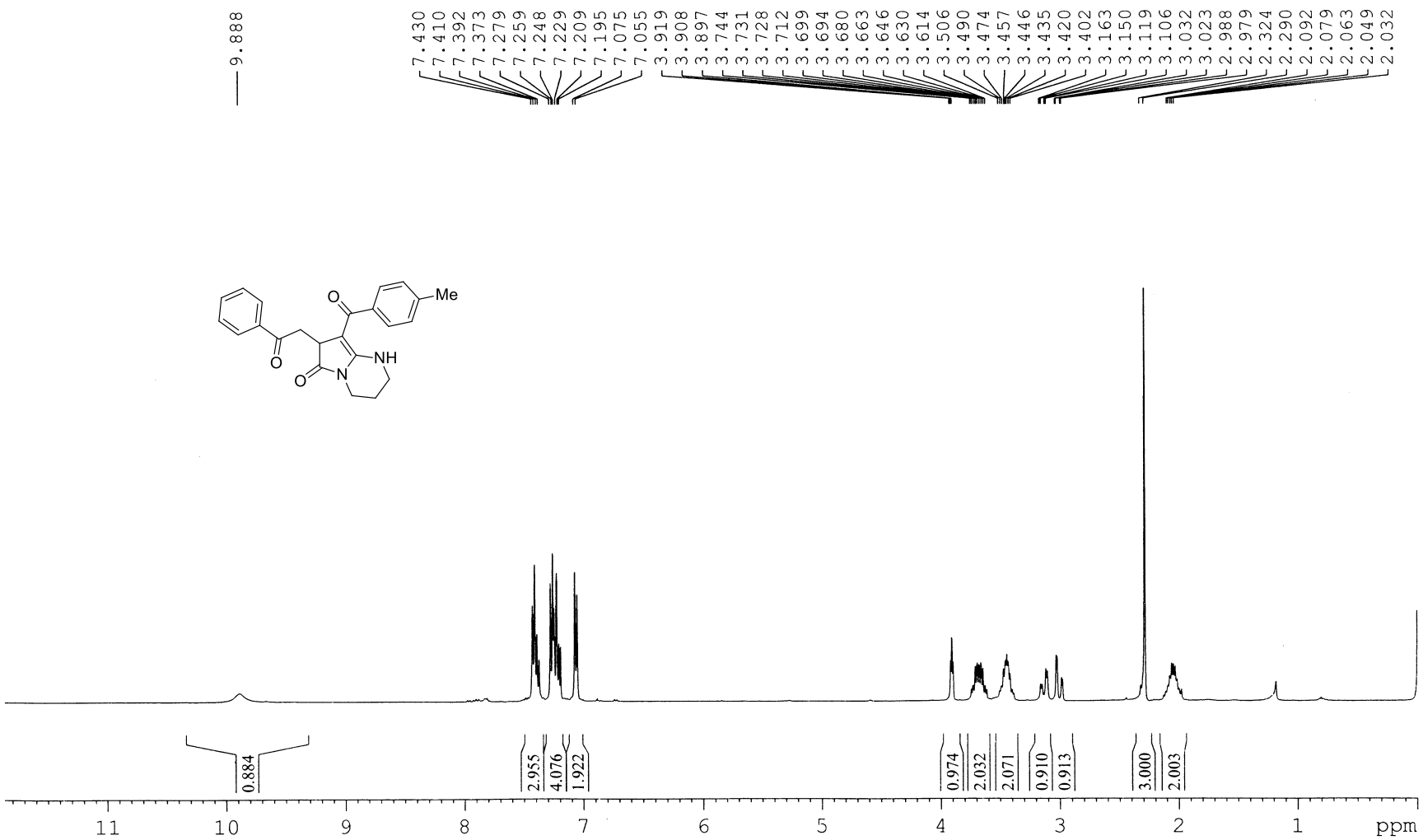


Figure 3. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5b**

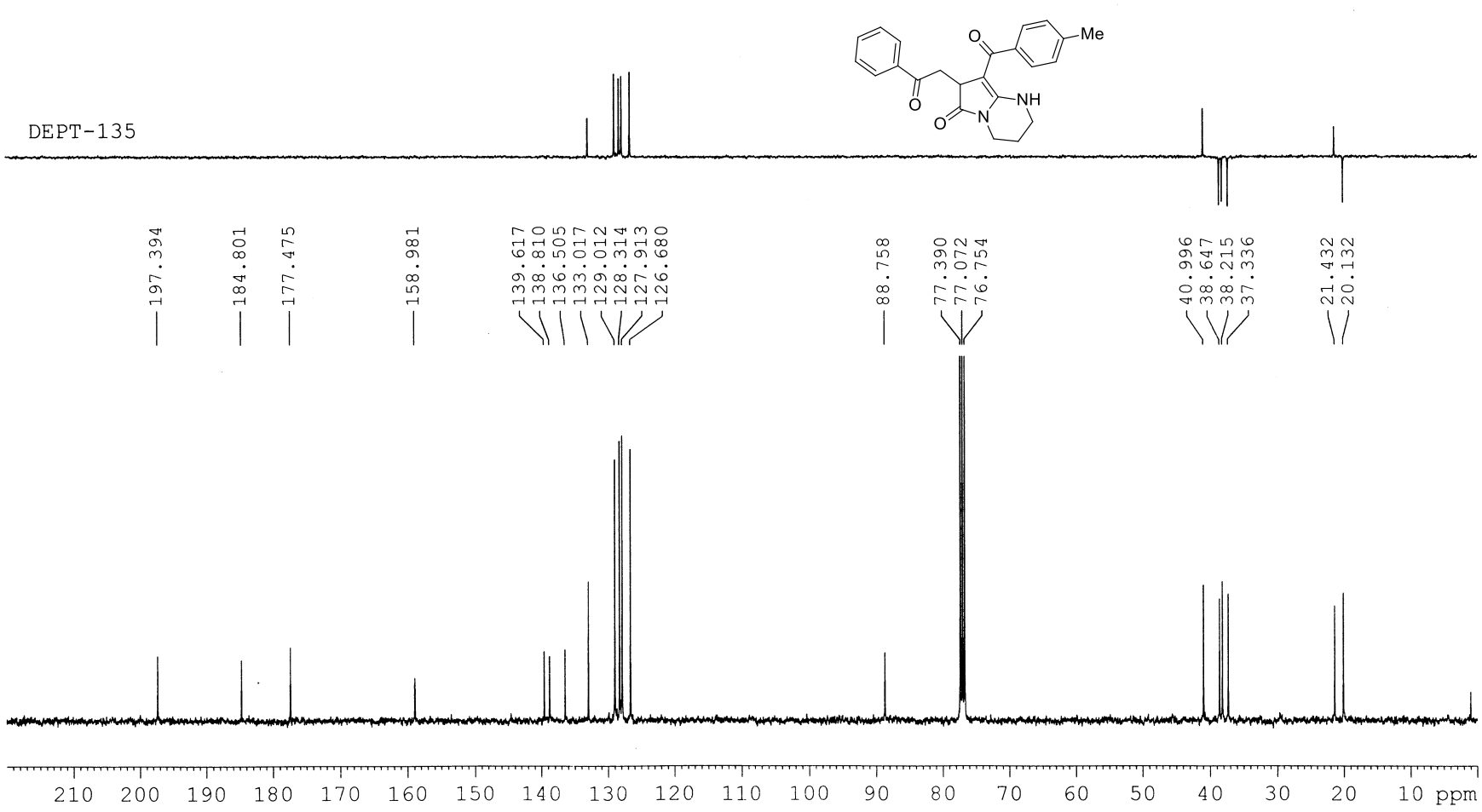


Figure 4. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5b**

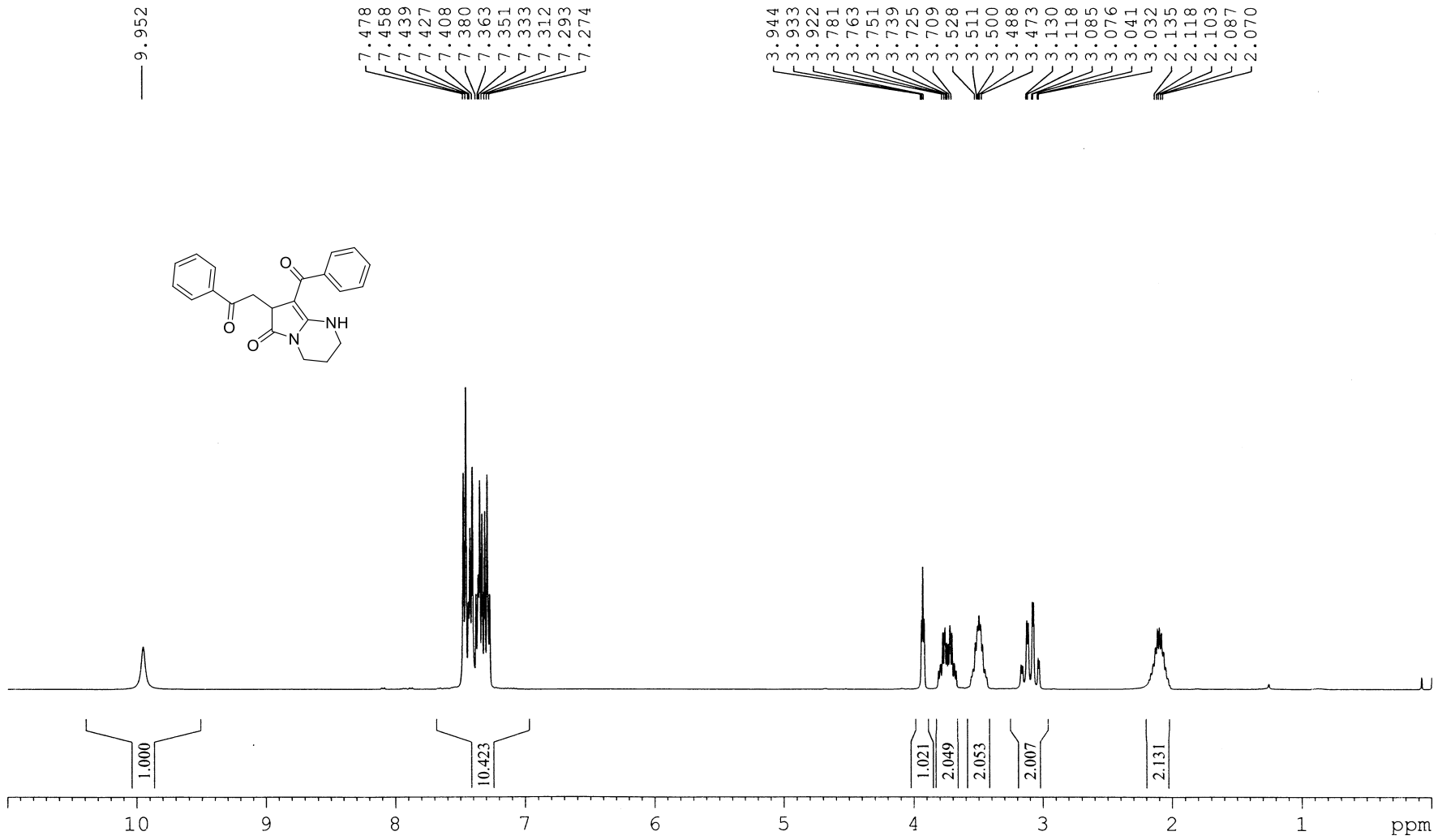


Figure 5. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5c**

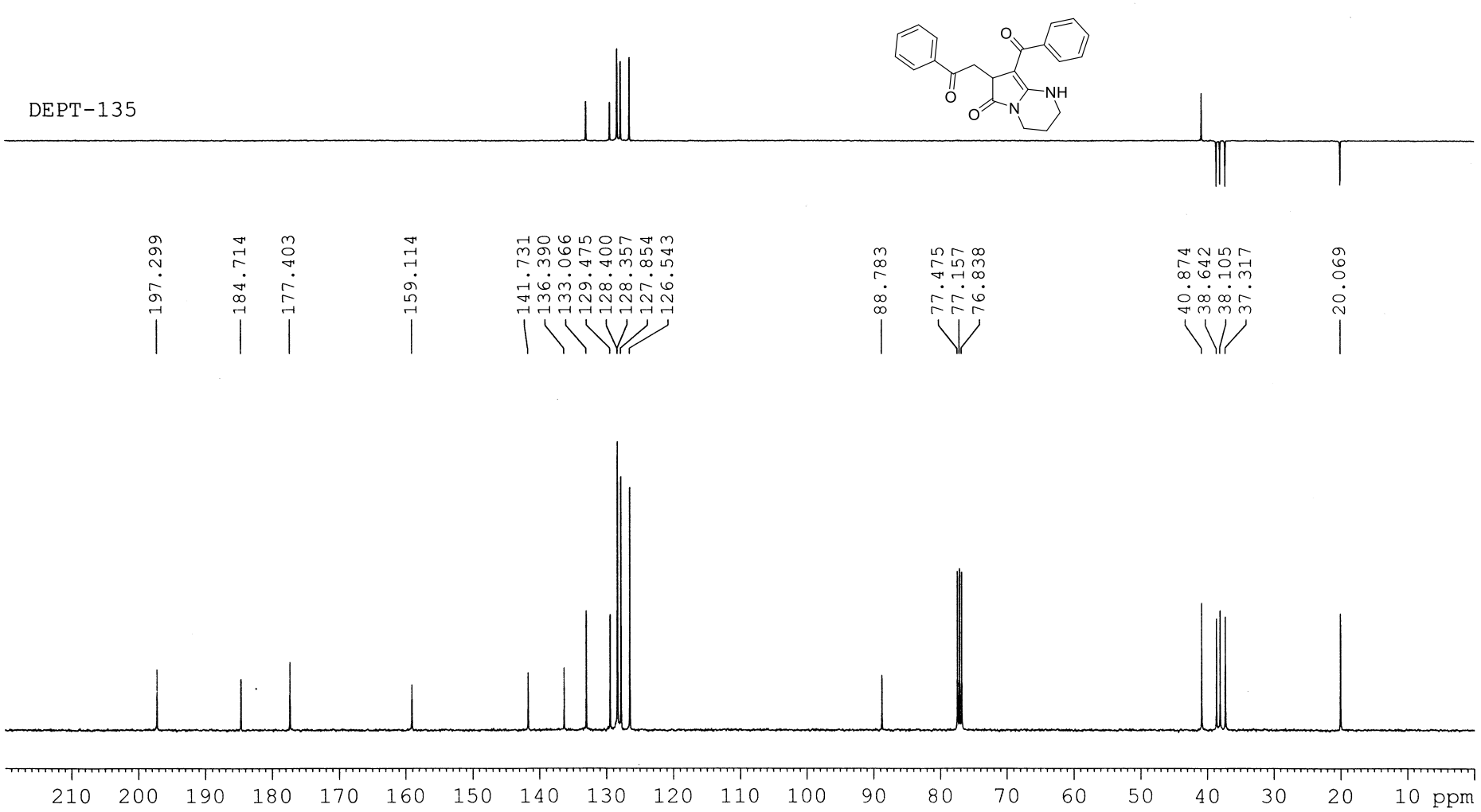


Figure 6. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5c**

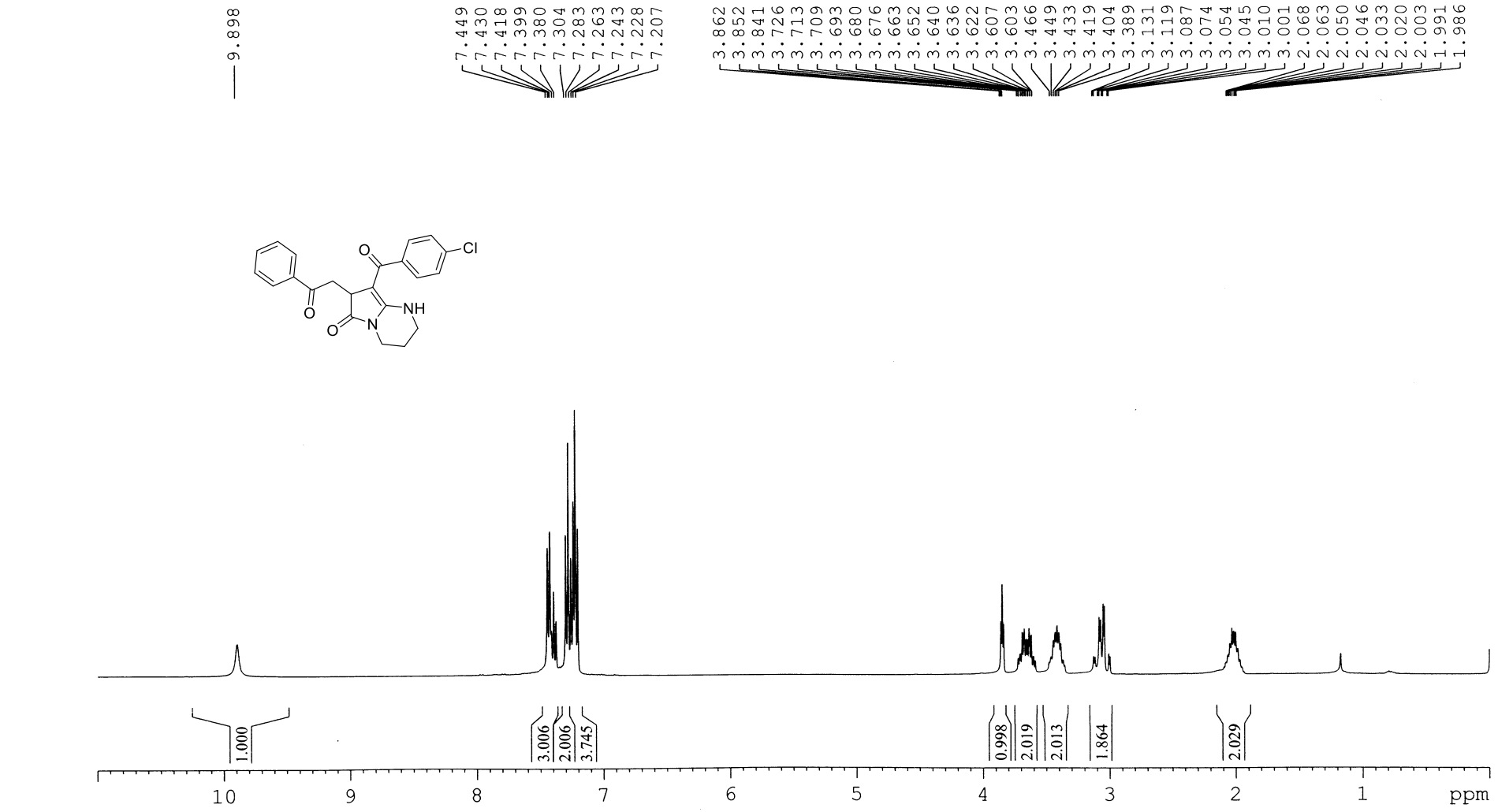


Figure 7. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5d**

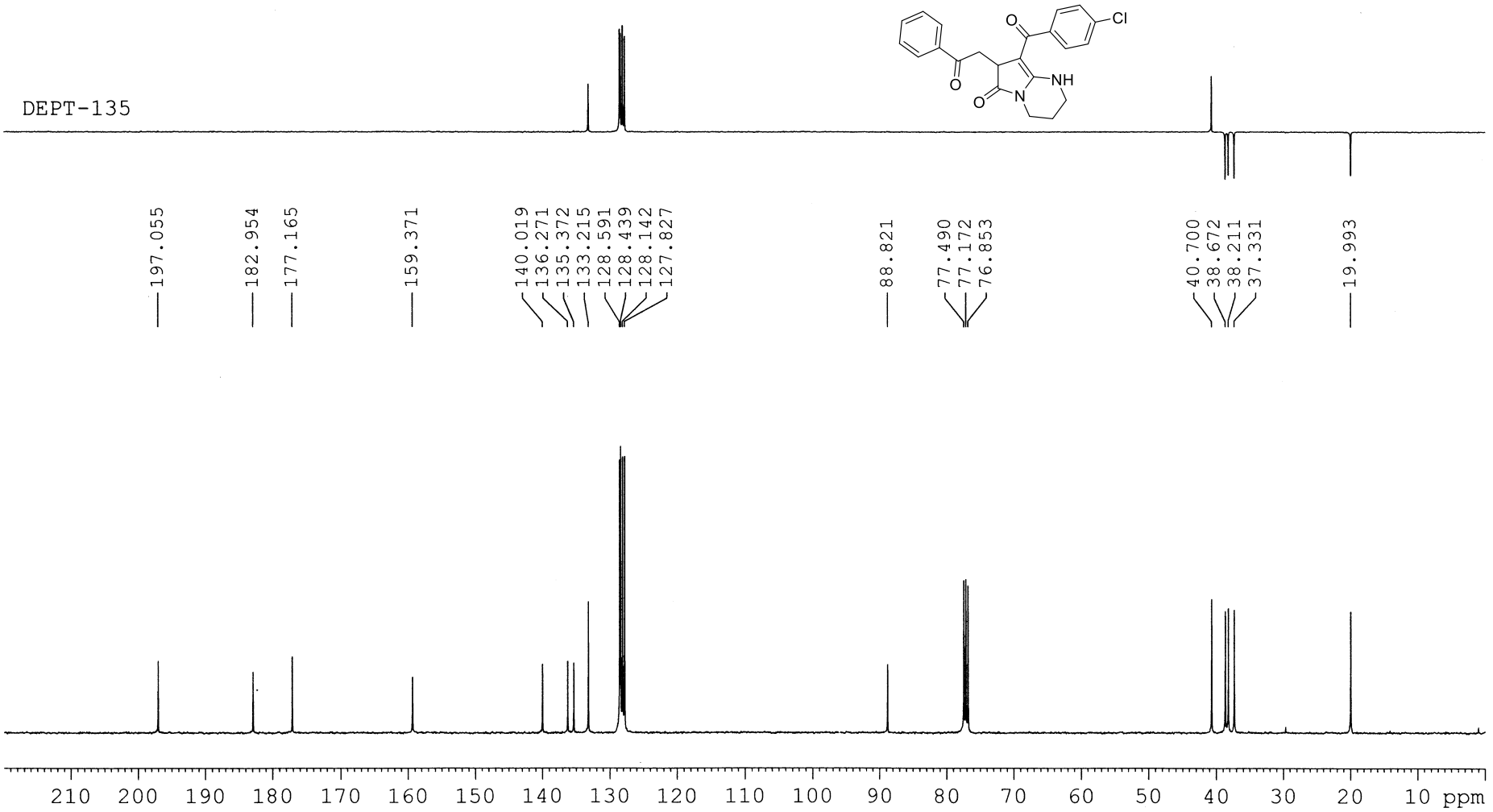


Figure 8. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5d**

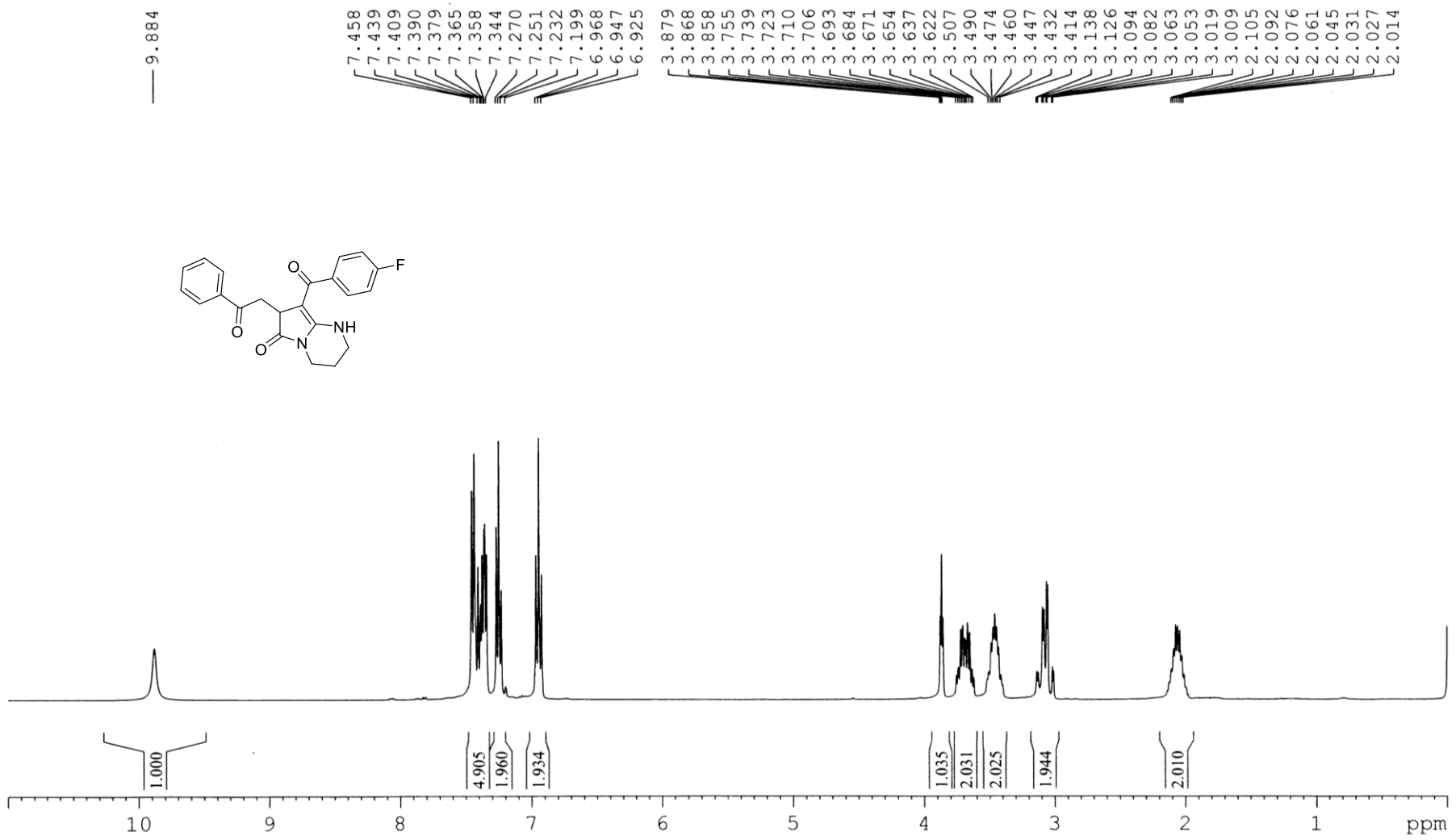


Figure 9. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5e**

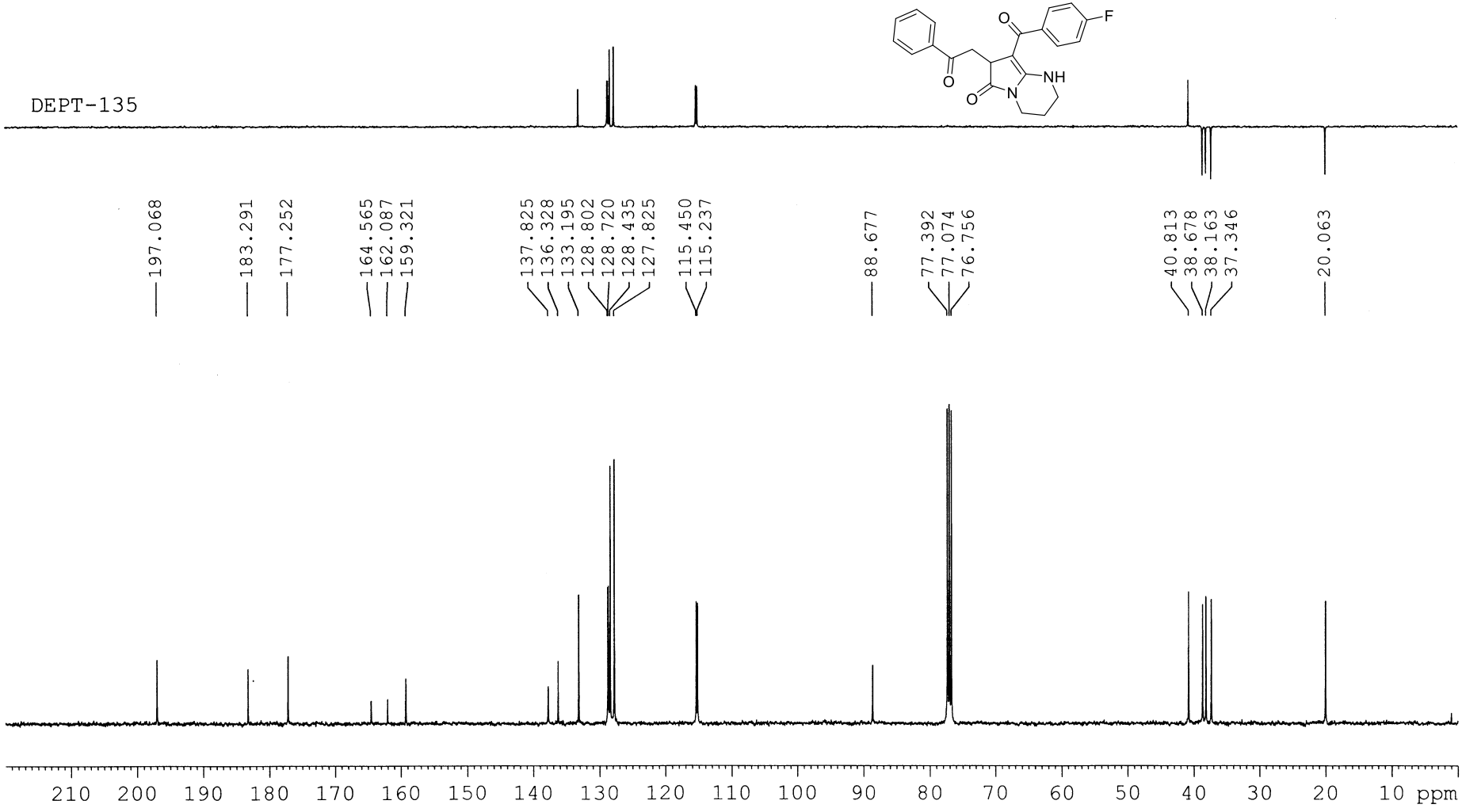


Figure 10. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5e**

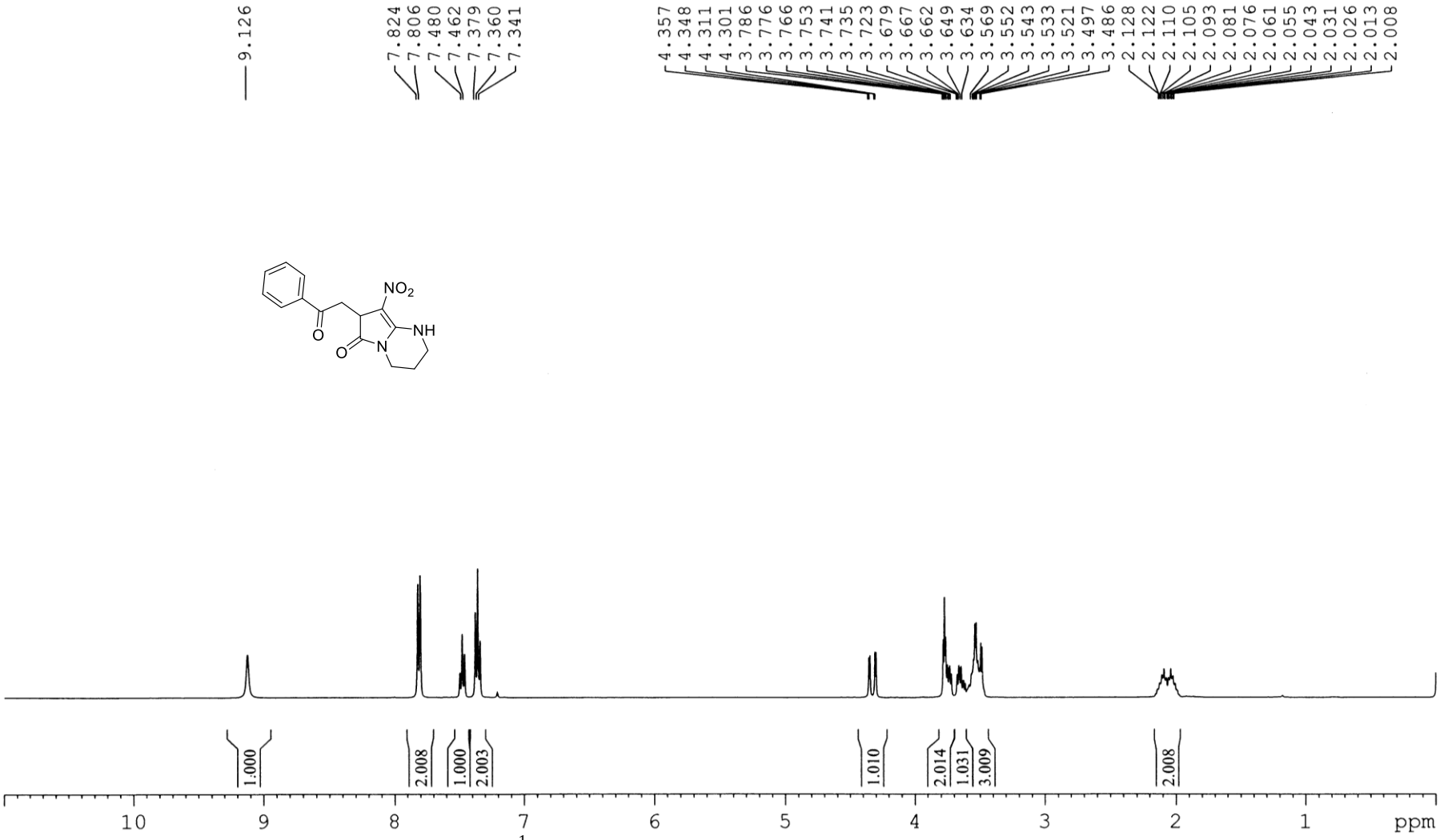


Figure 11. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5f**

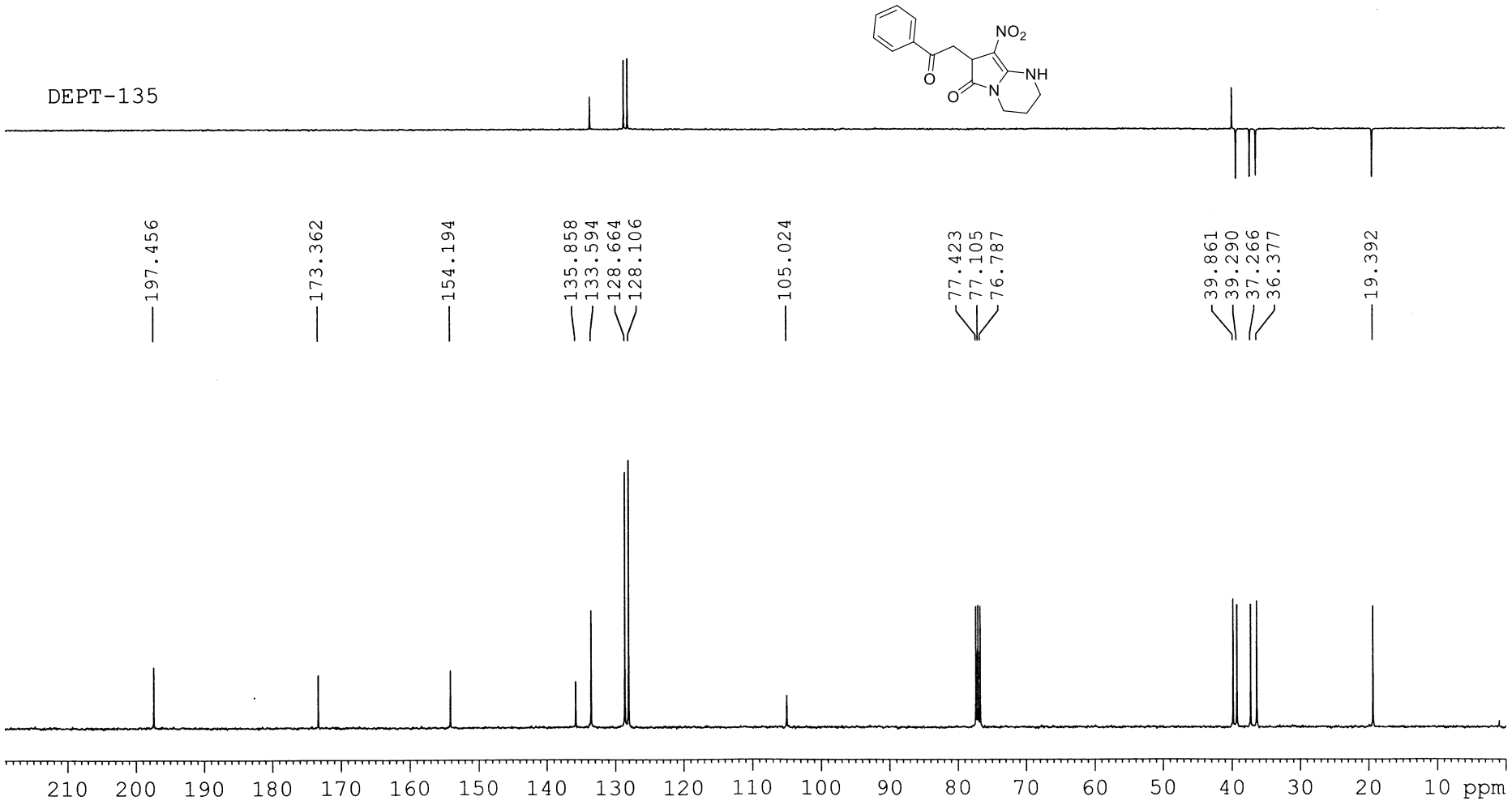


Figure 12. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5f**

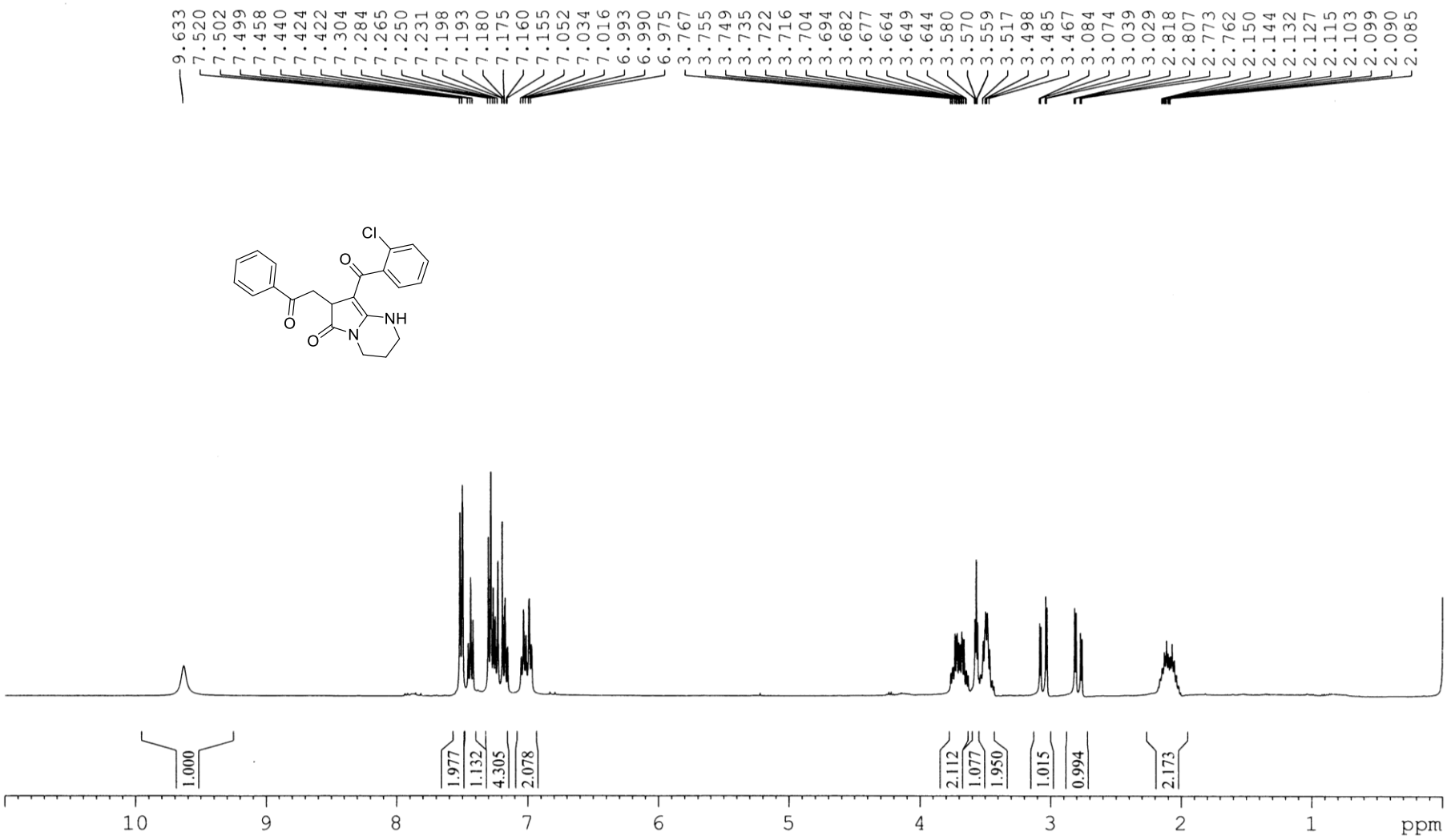


Figure 13. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5g**

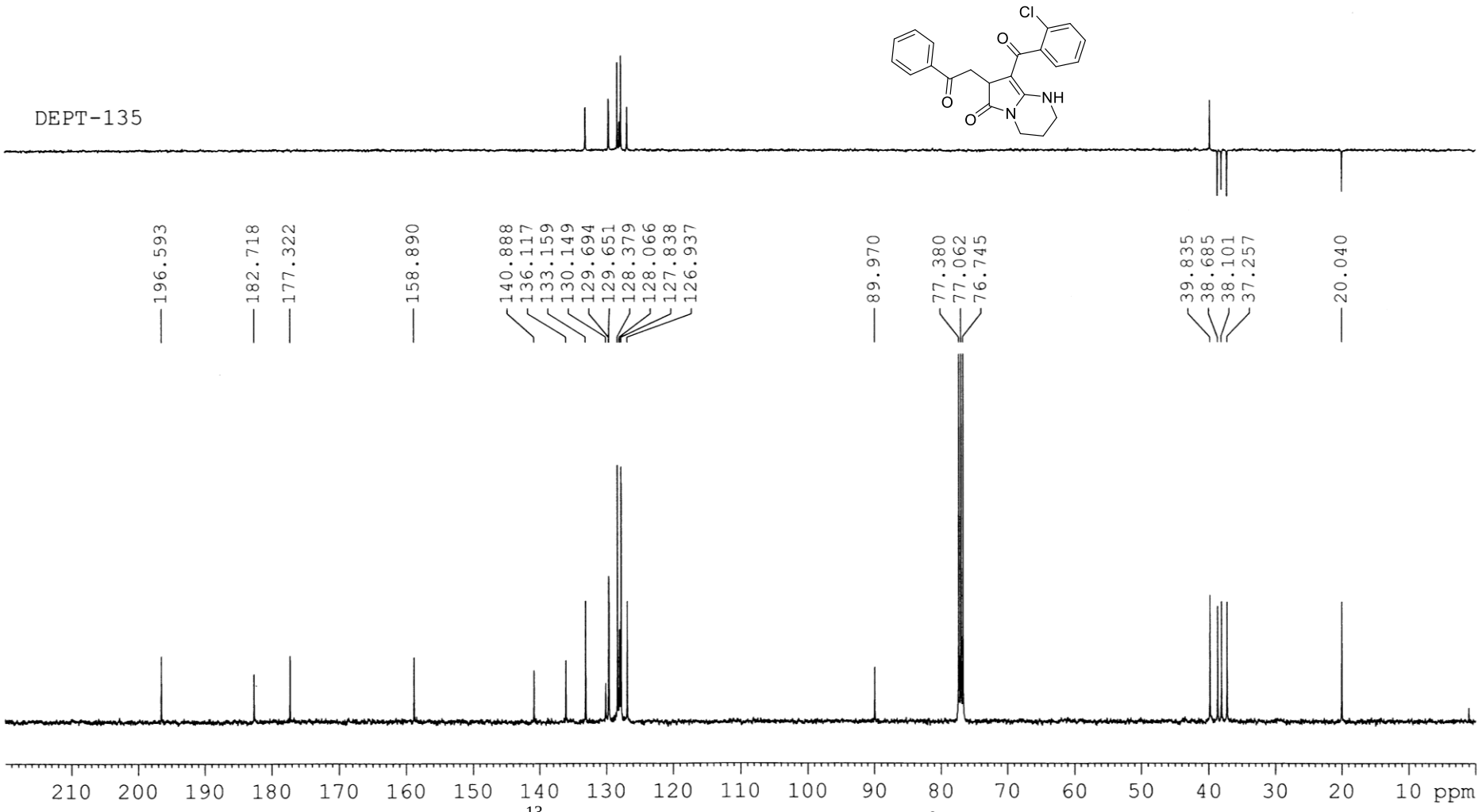


Figure 14. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5g**

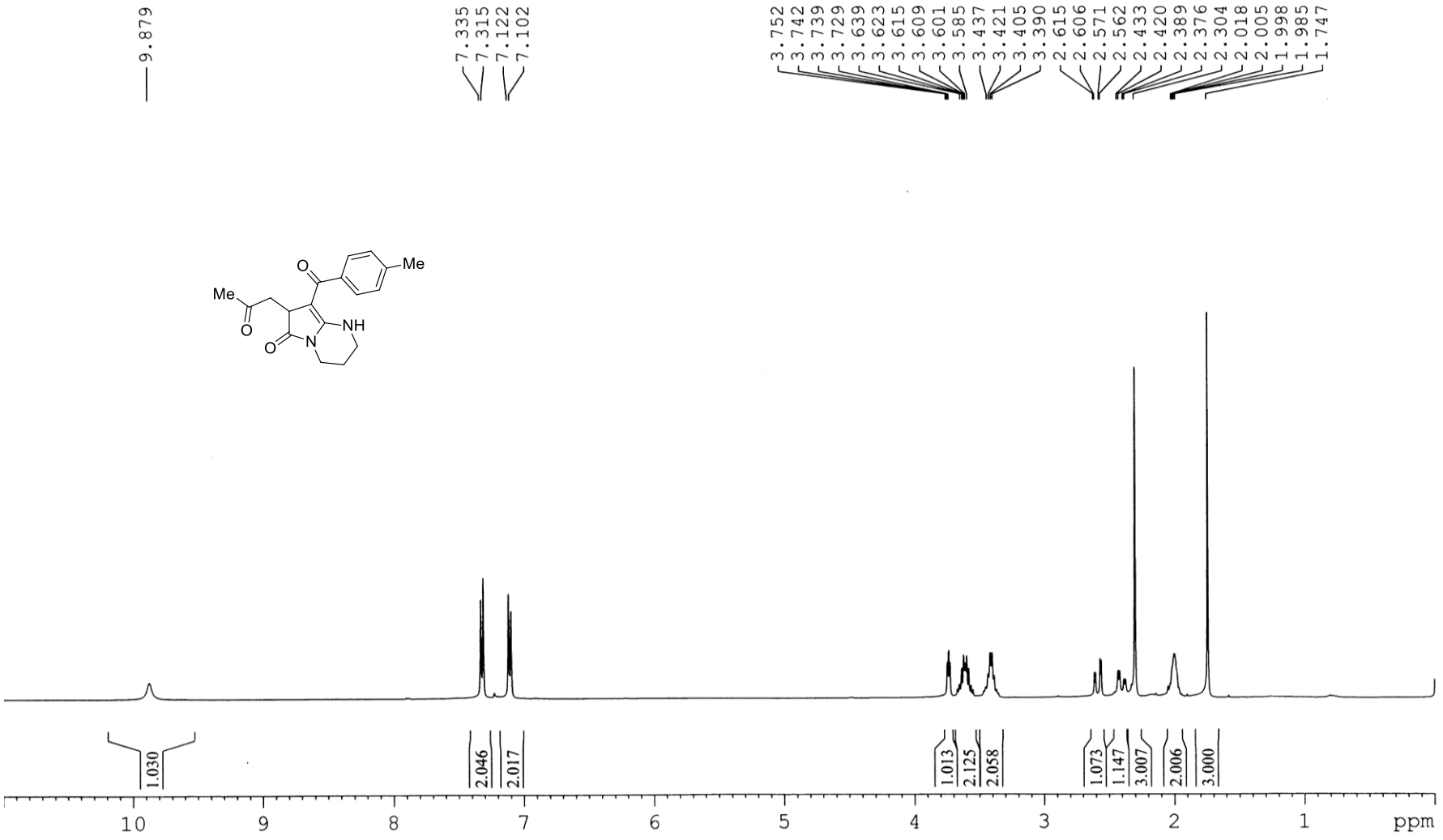


Figure 15. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5h**

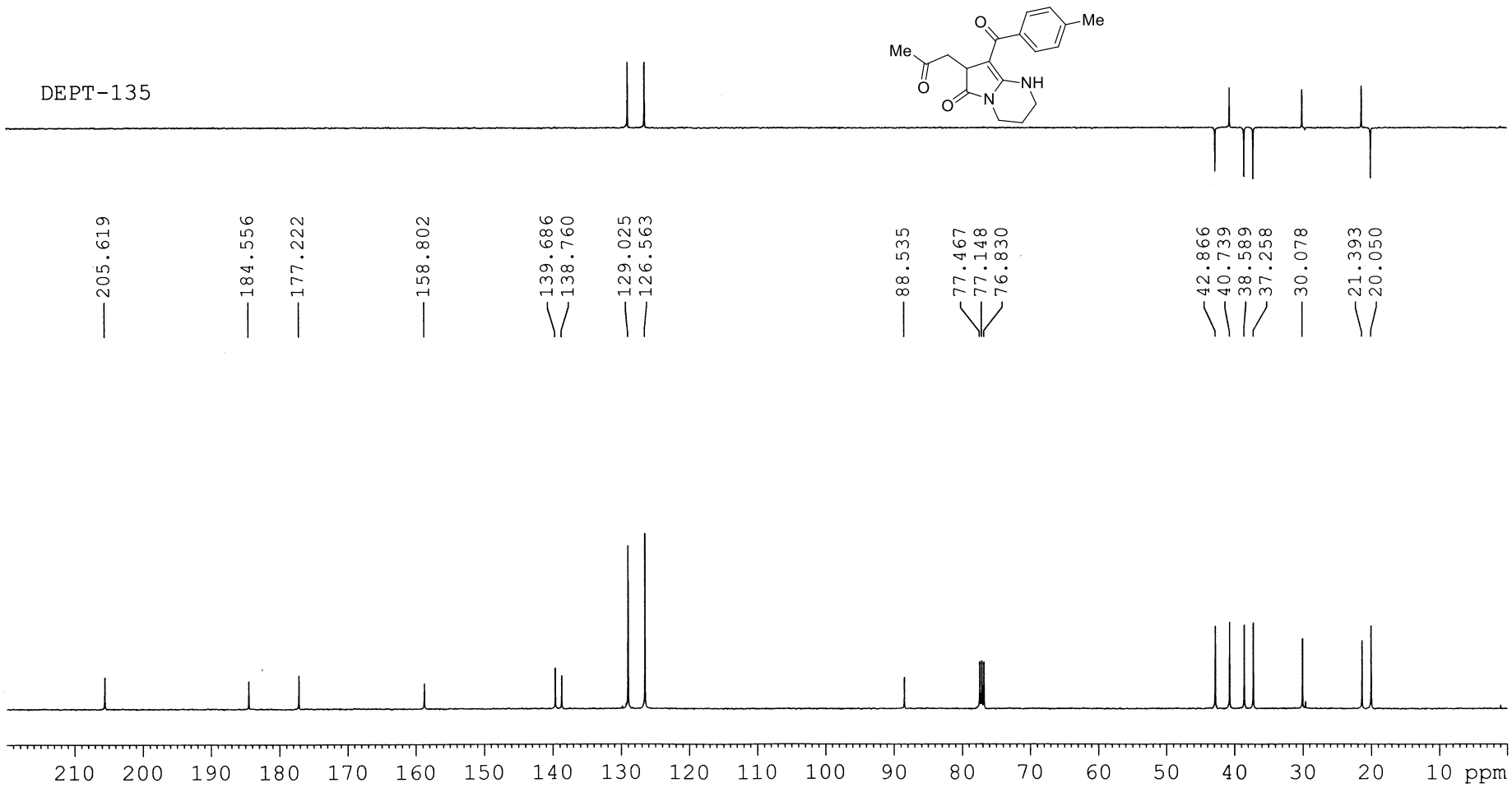


Figure 16. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5h**

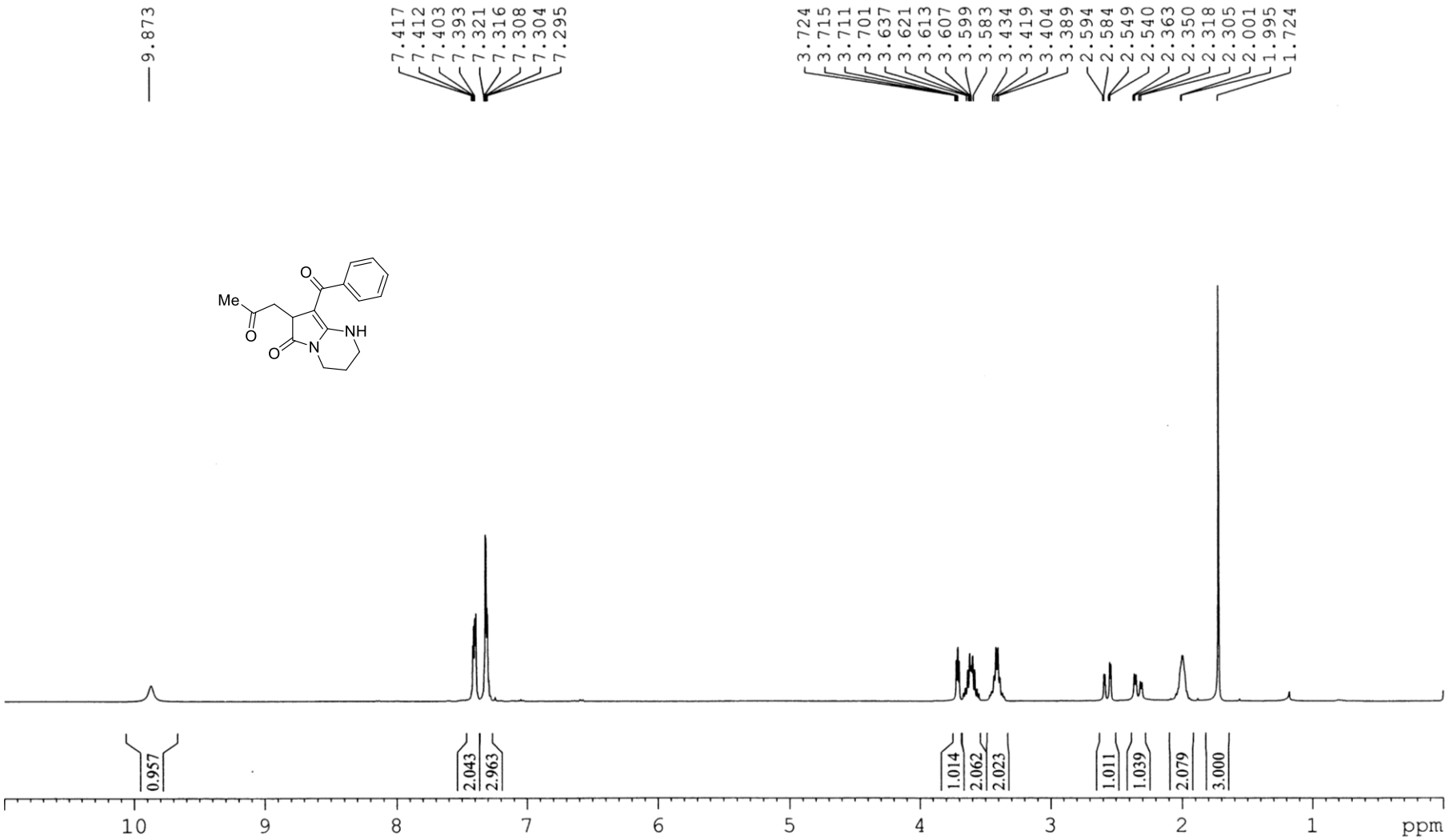


Figure 17. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5i**

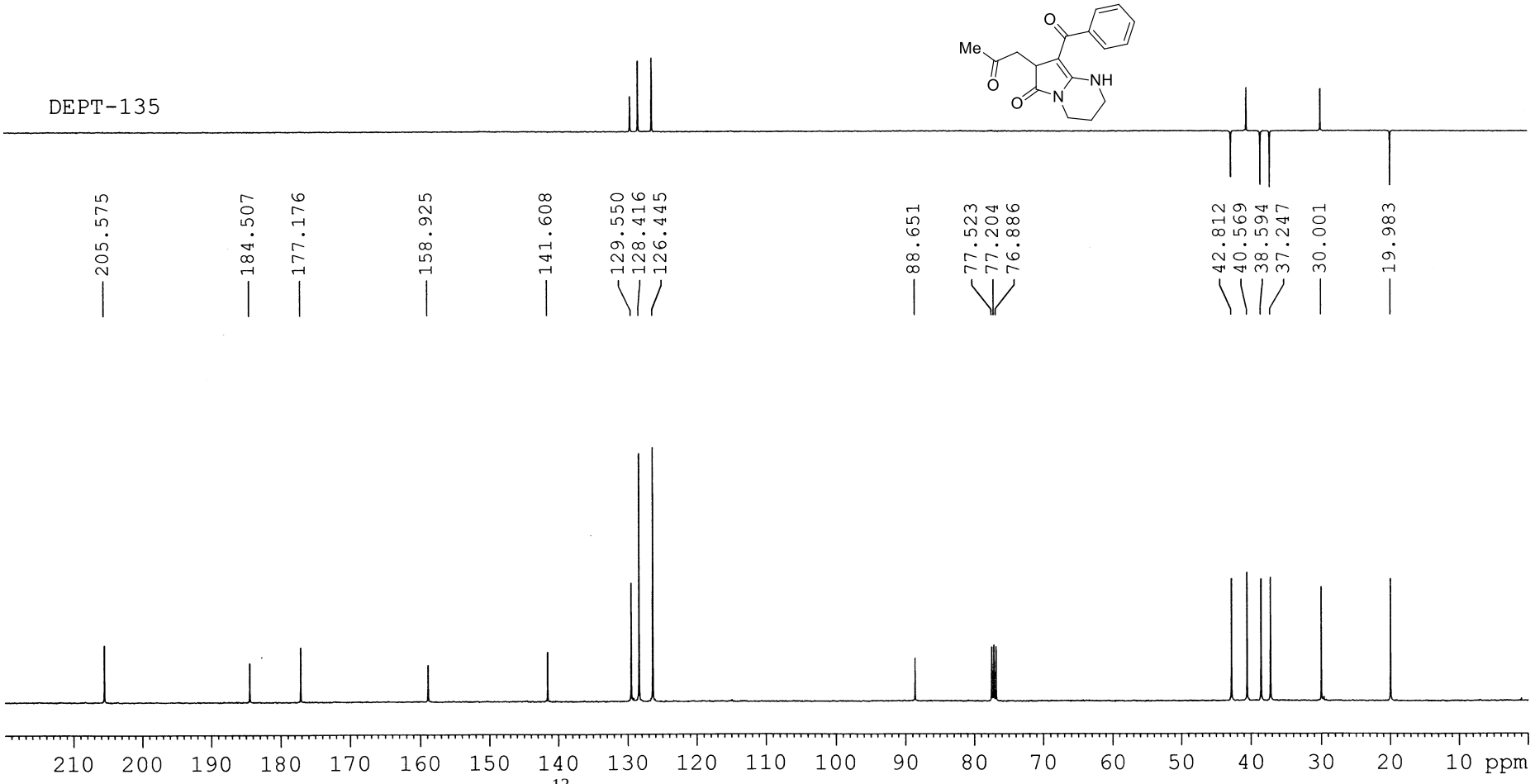


Figure 18. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5i**

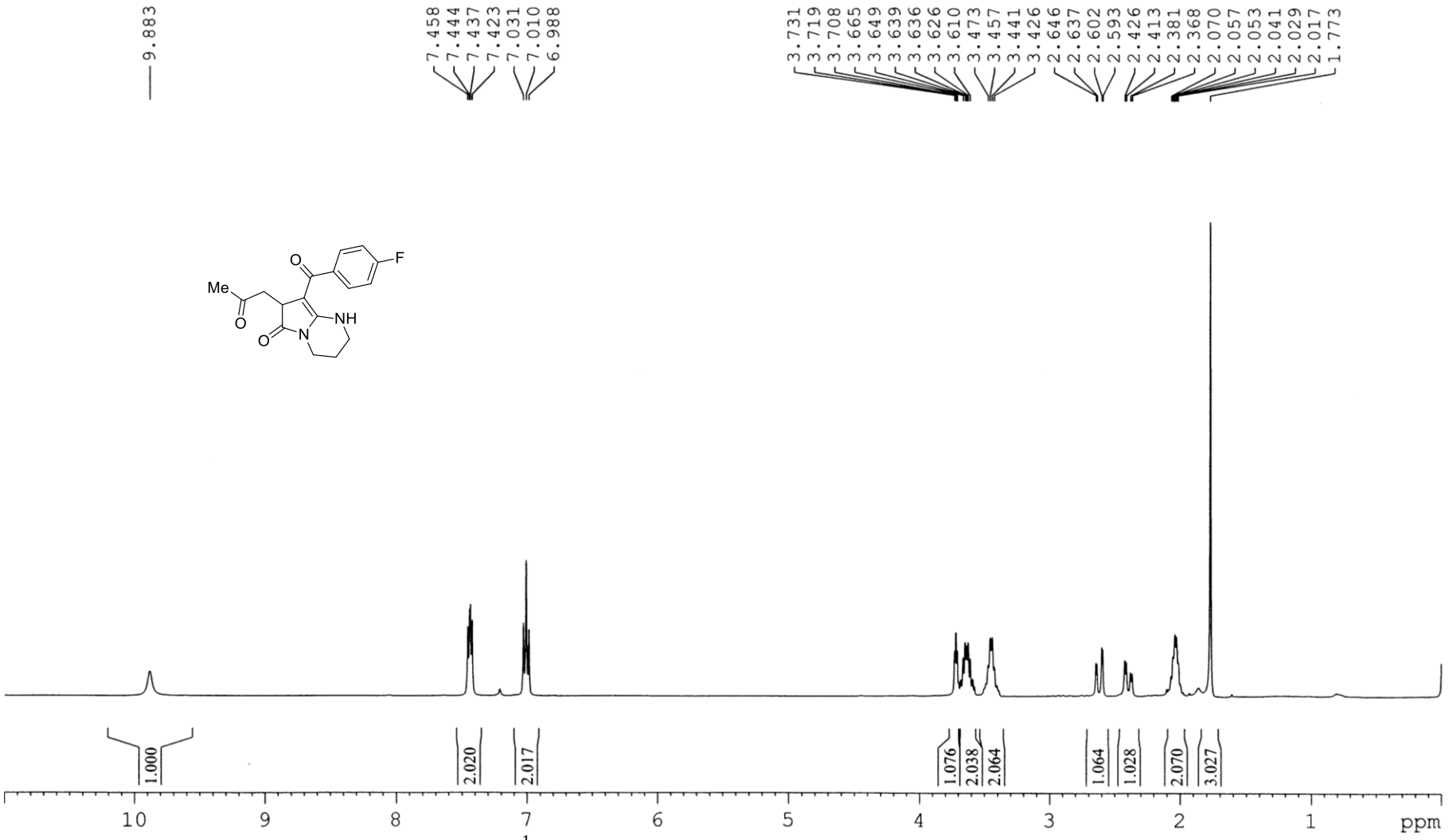


Figure 19. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **5j**

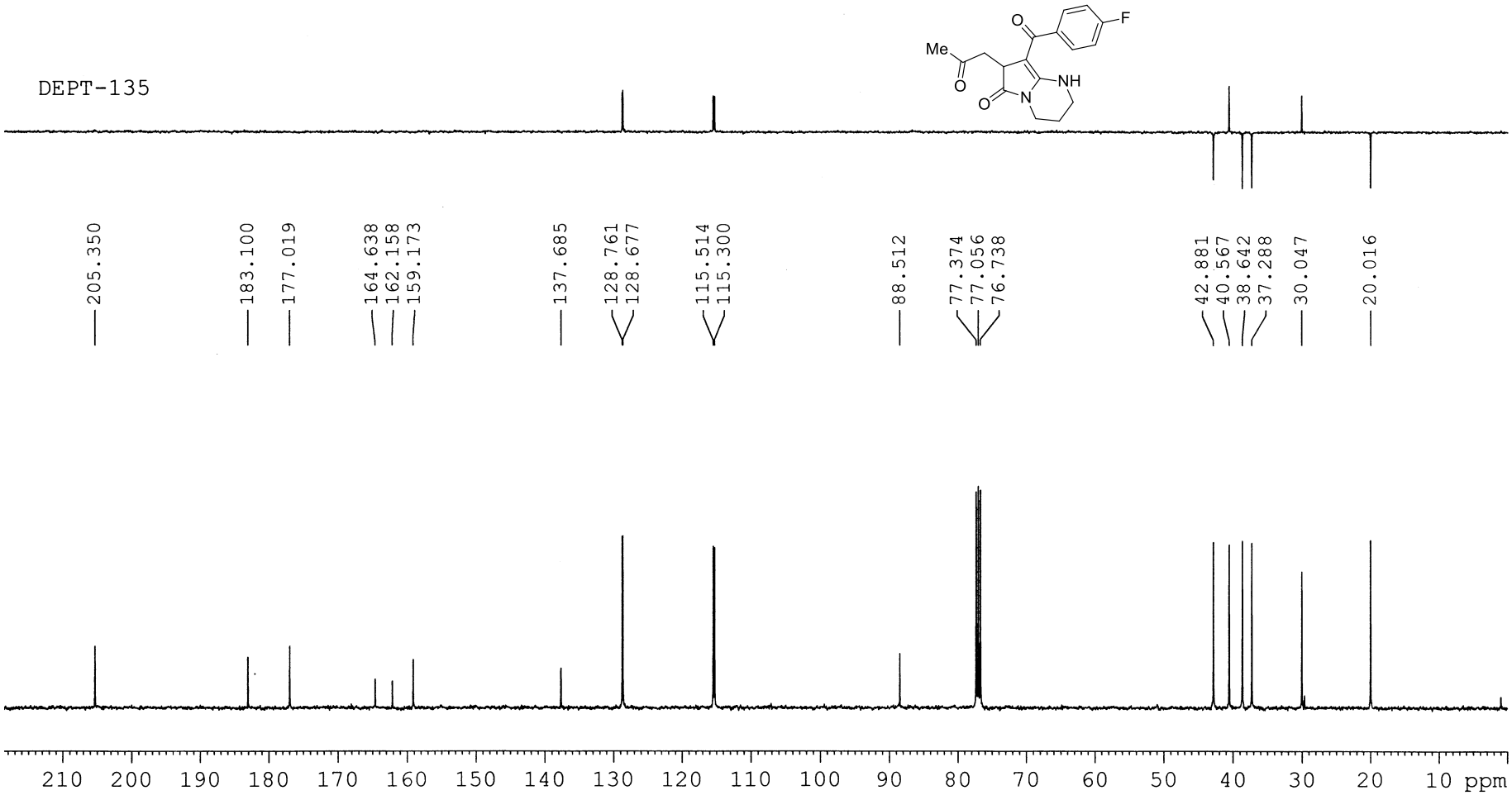


Figure 20. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **5j**

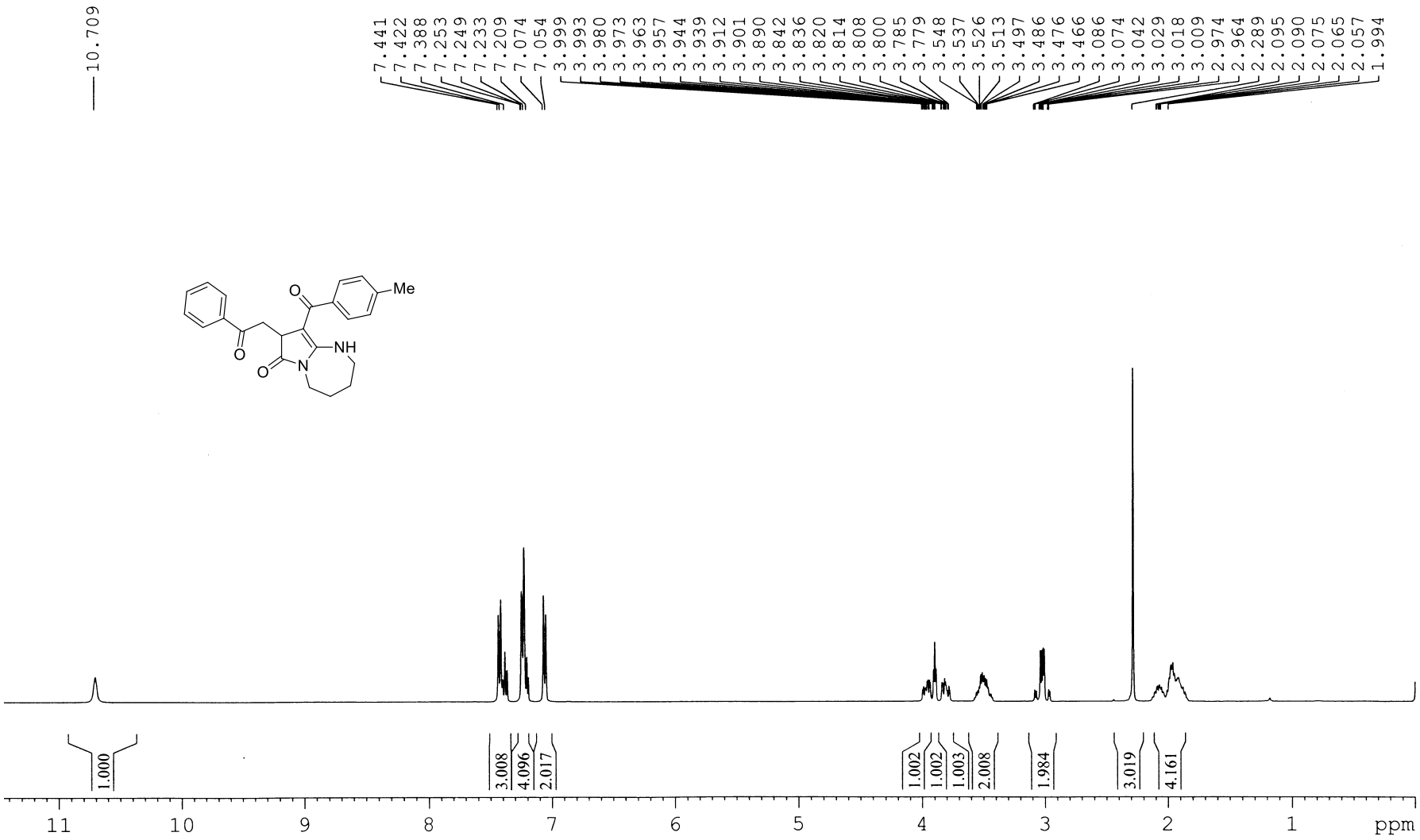


Figure 21. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6a**

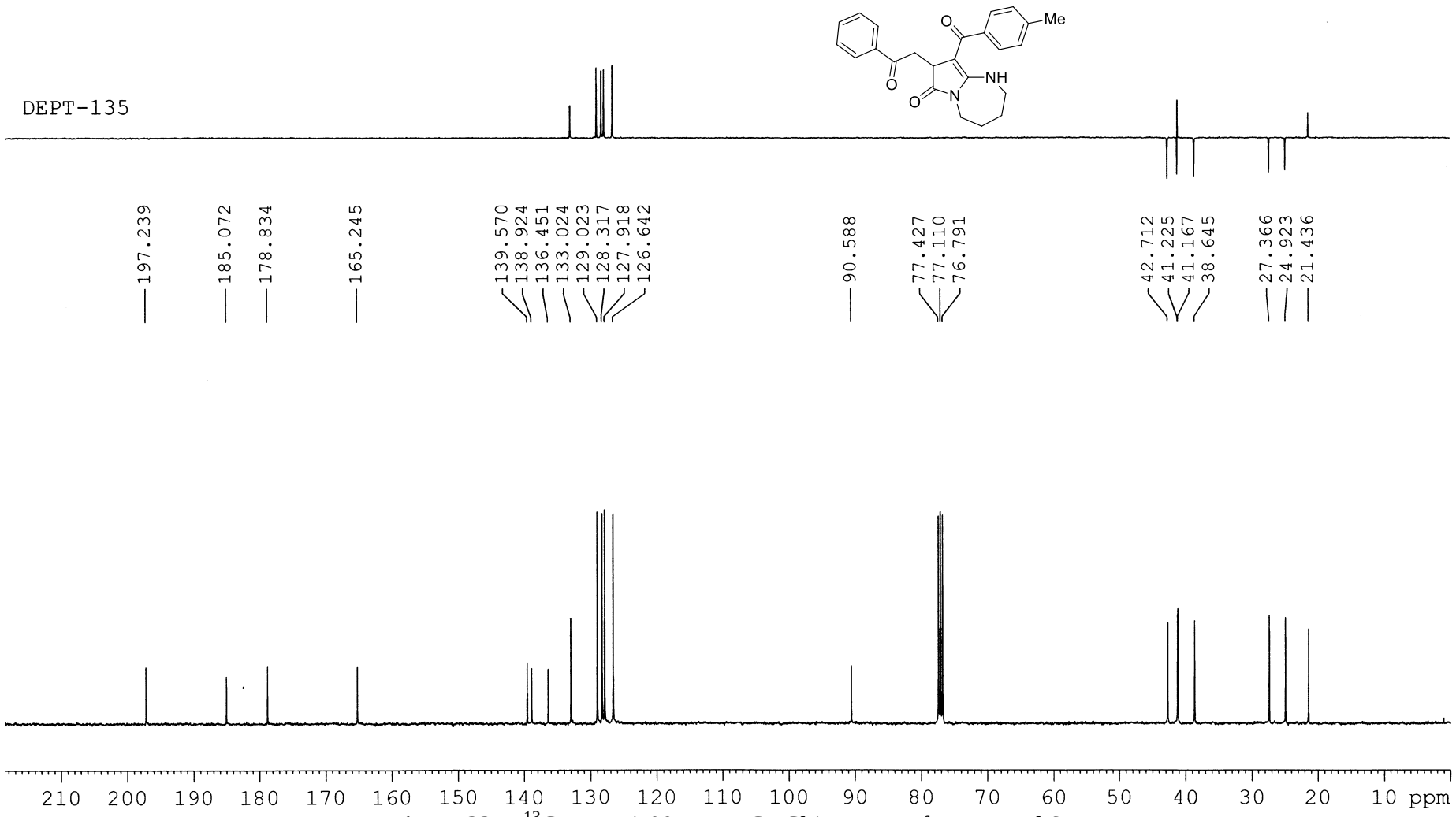


Figure 22. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6a**

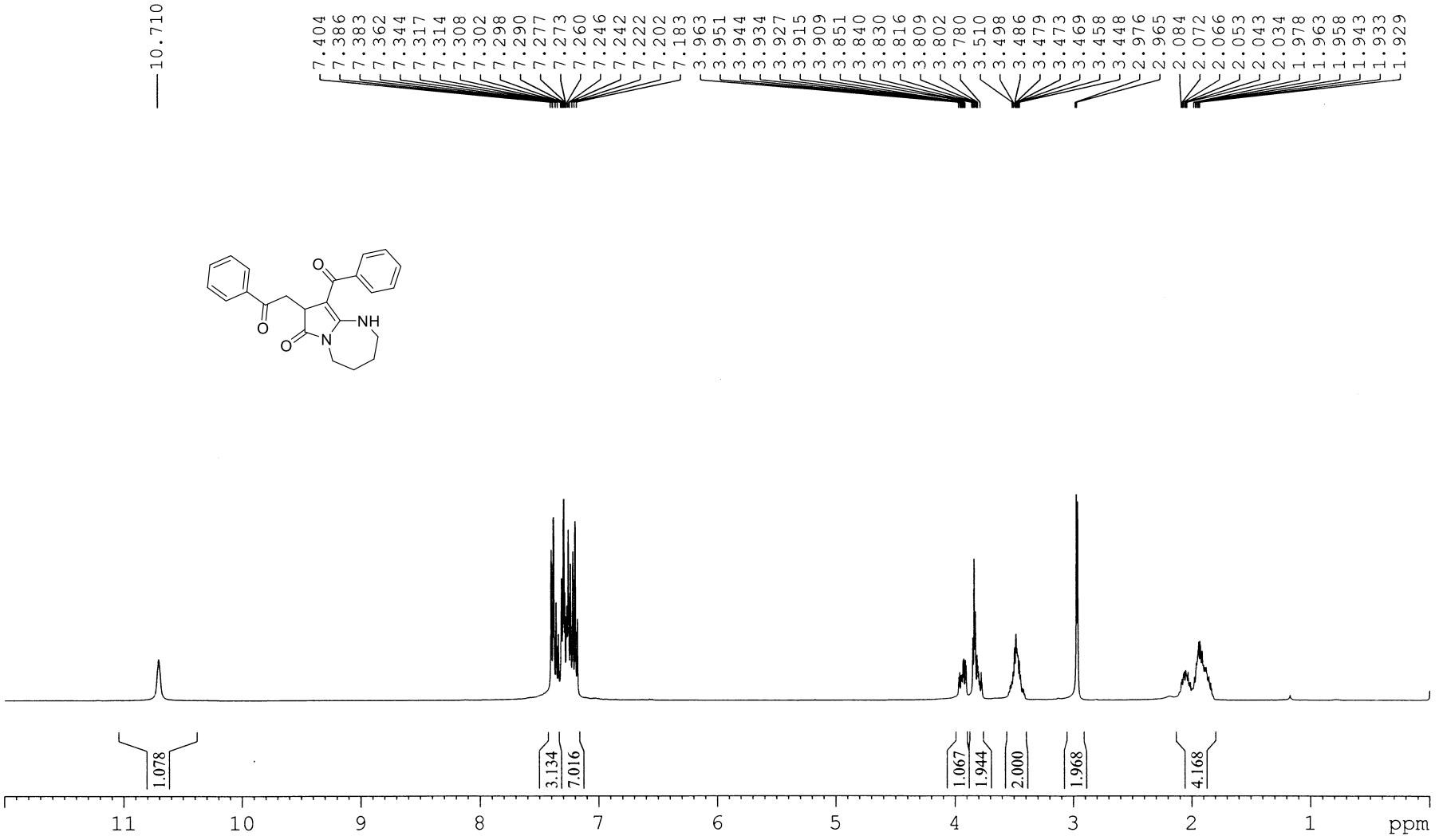


Figure 23. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6b**

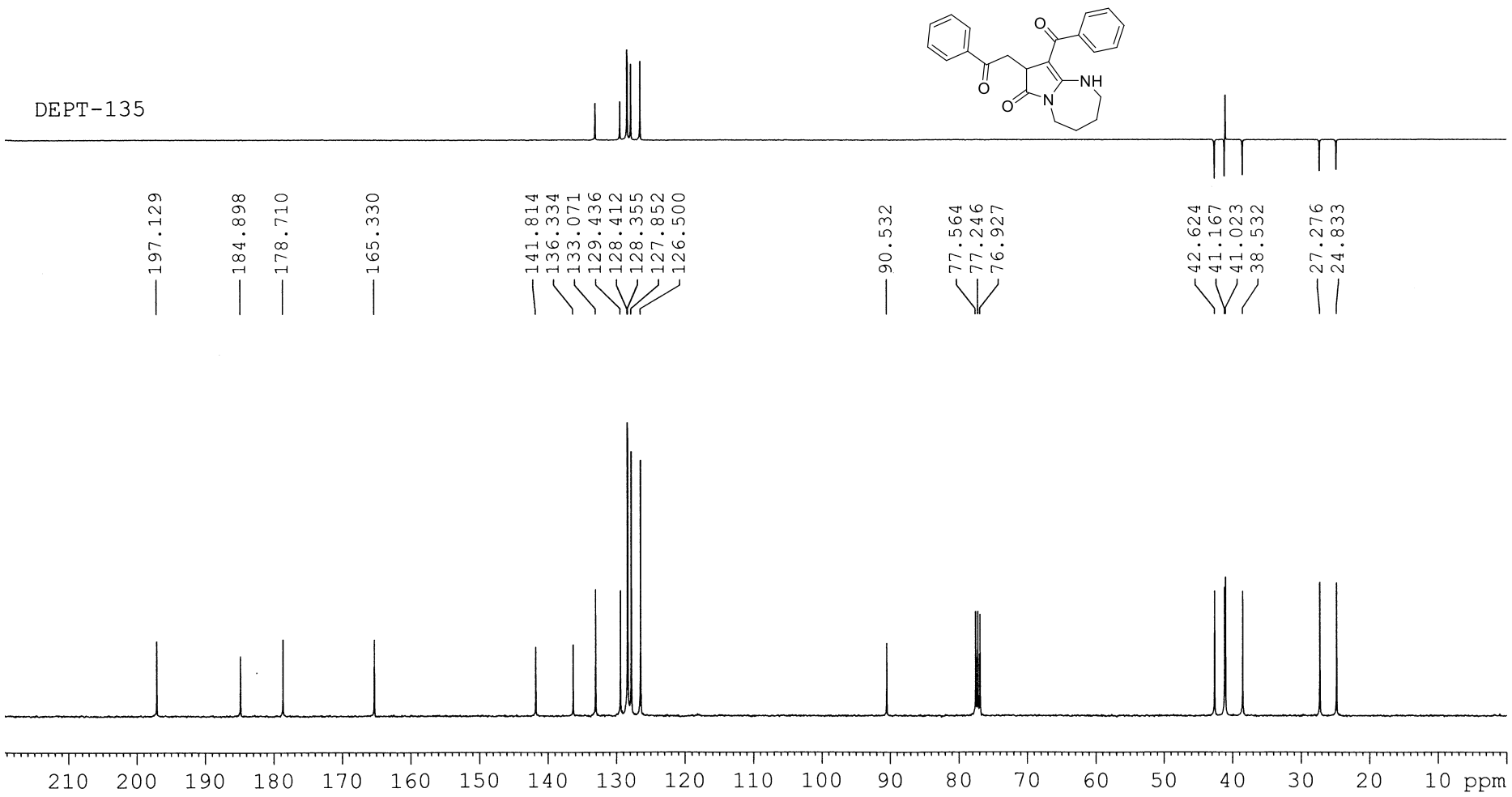


Figure 24. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6b**

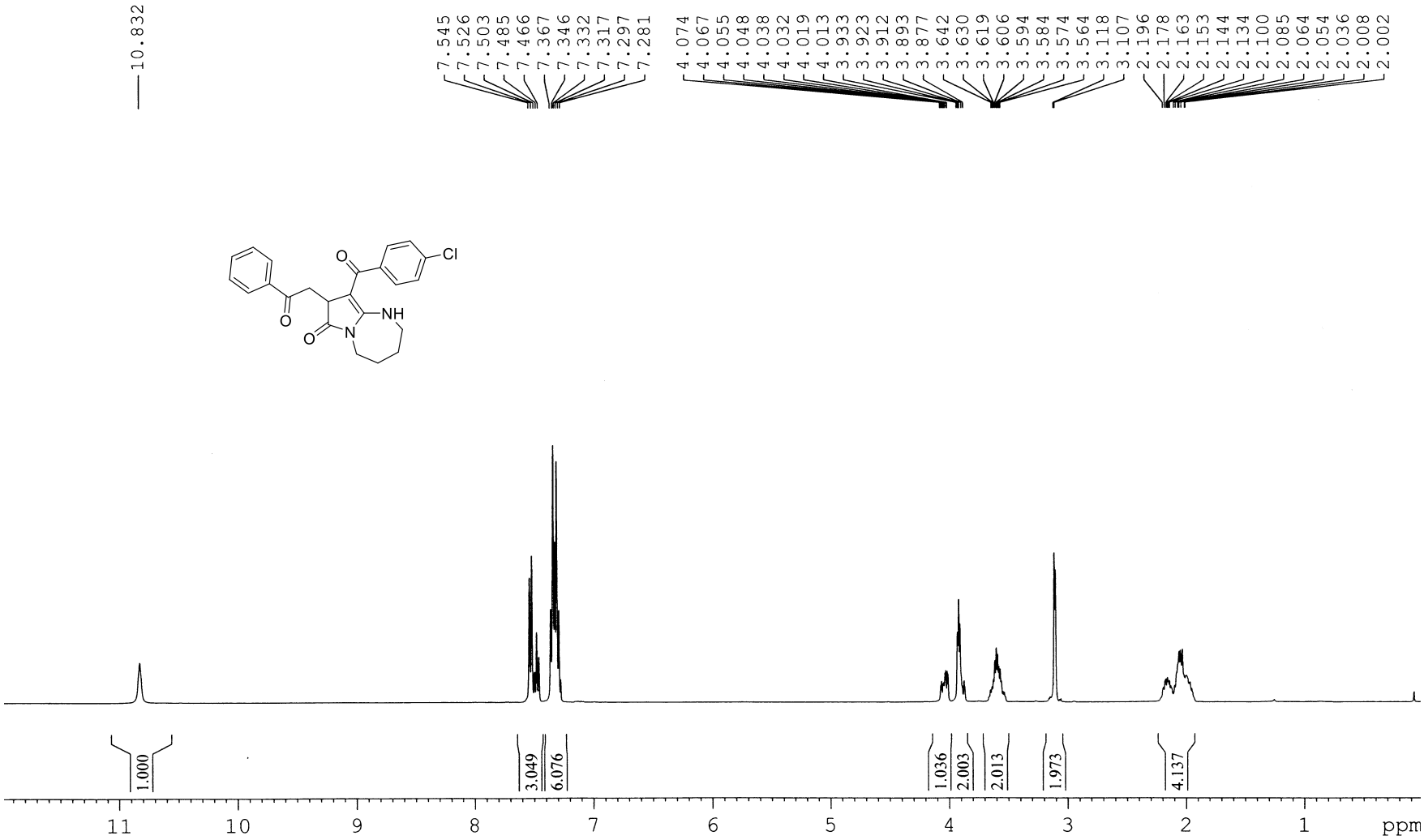


Figure 25. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6c**

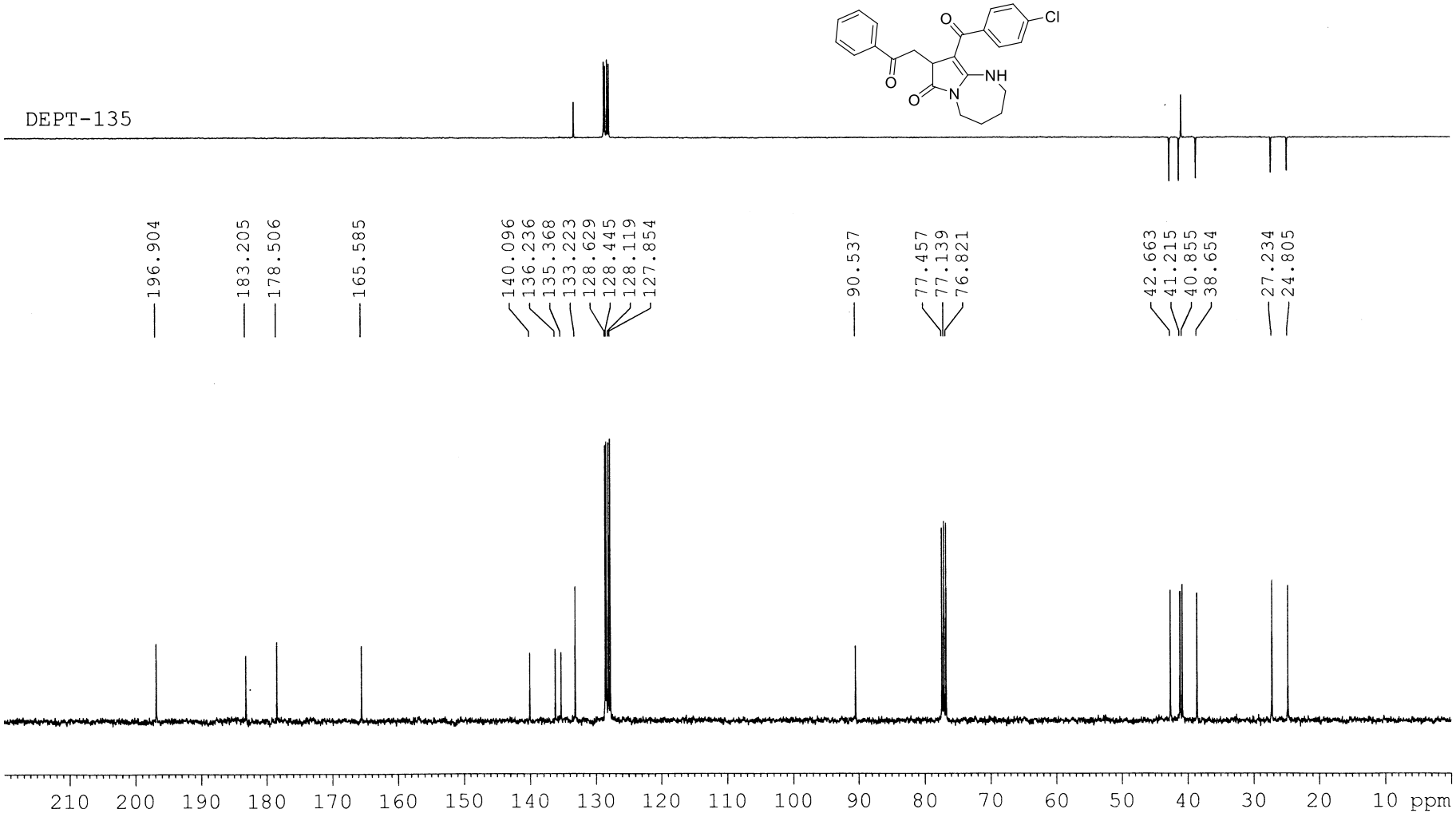


Figure 26. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6c**

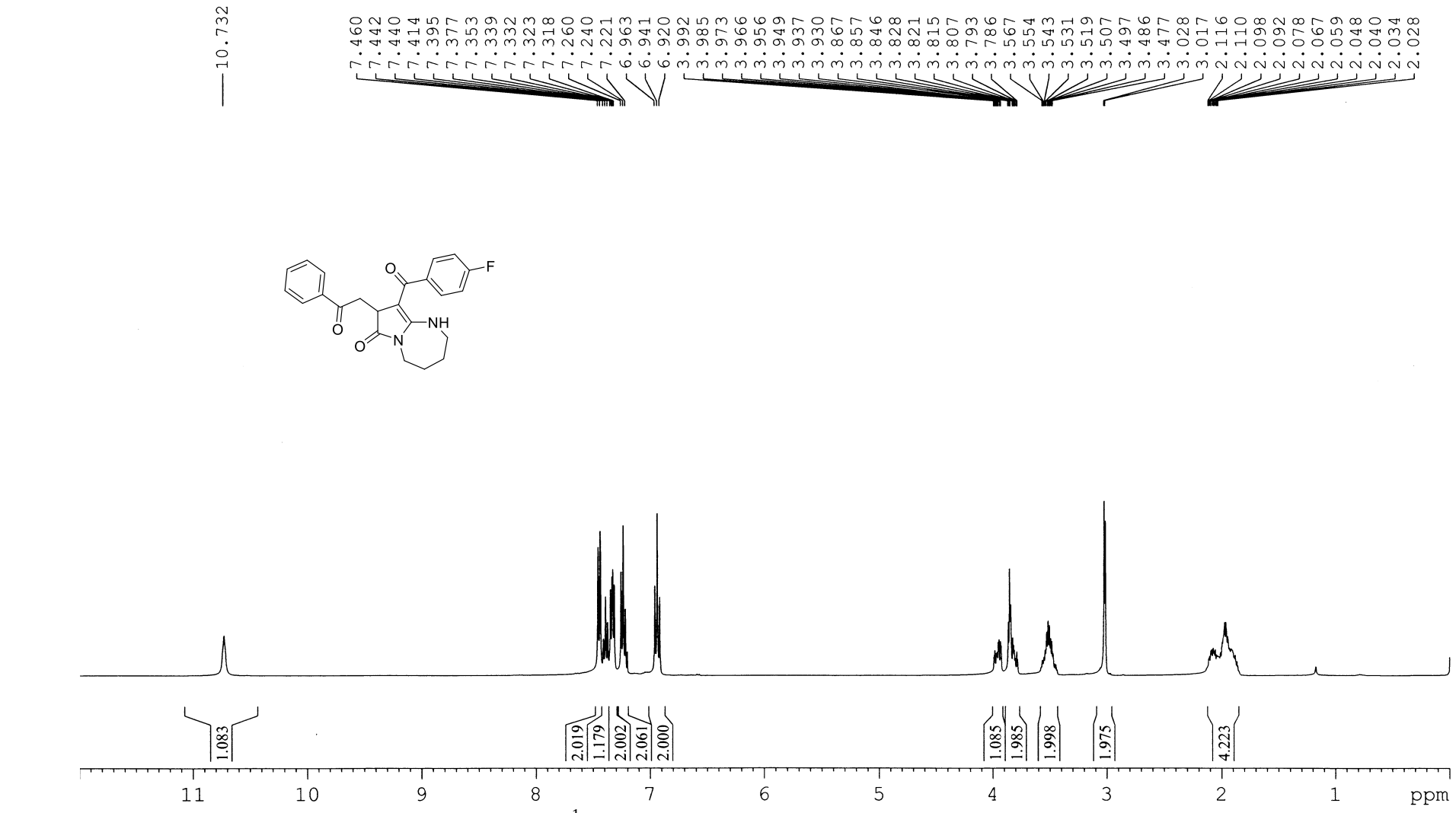


Figure 27. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6d**

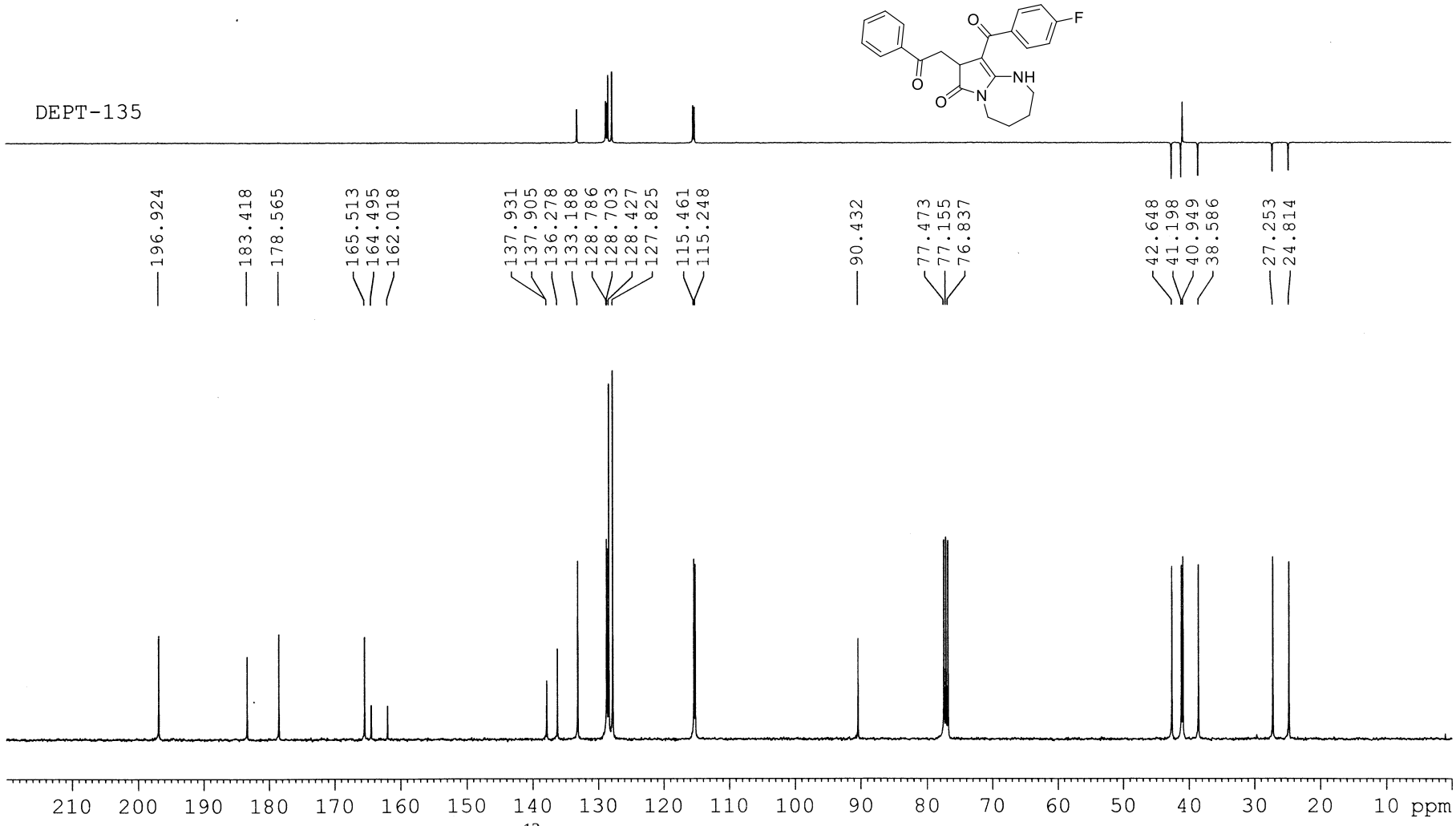


Figure 28. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6d**

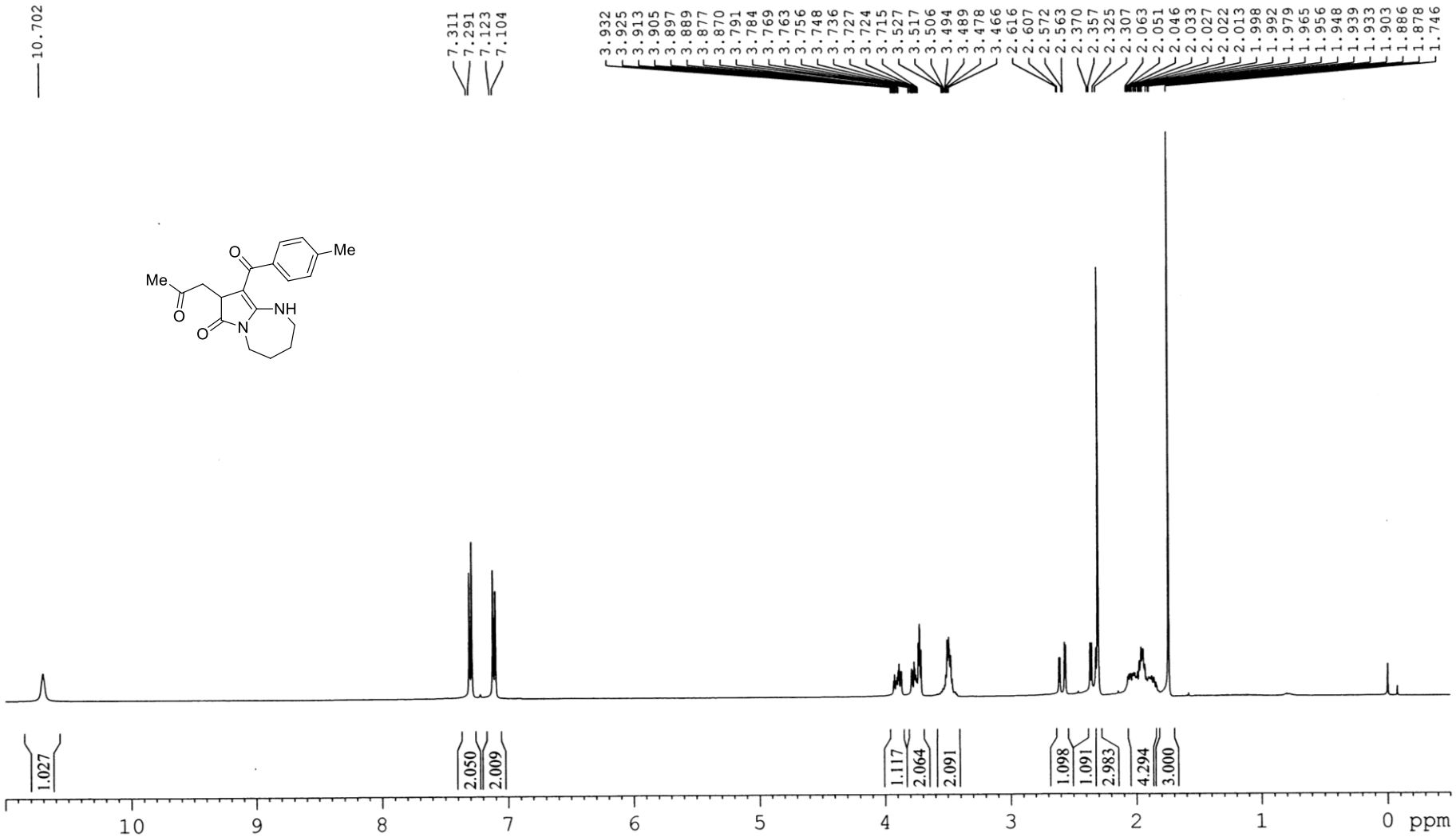


Figure 29. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6e**

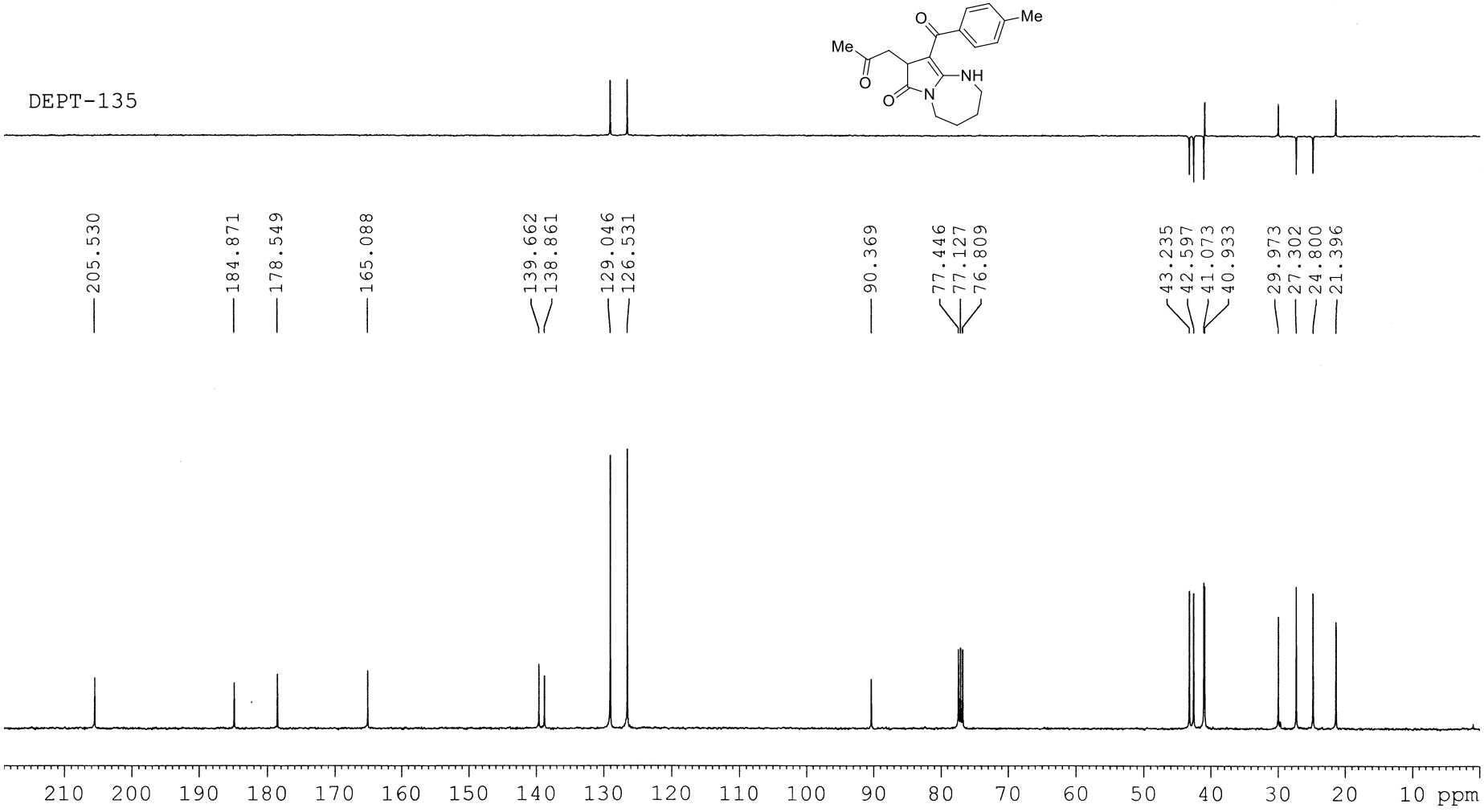


Figure 30. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6e**

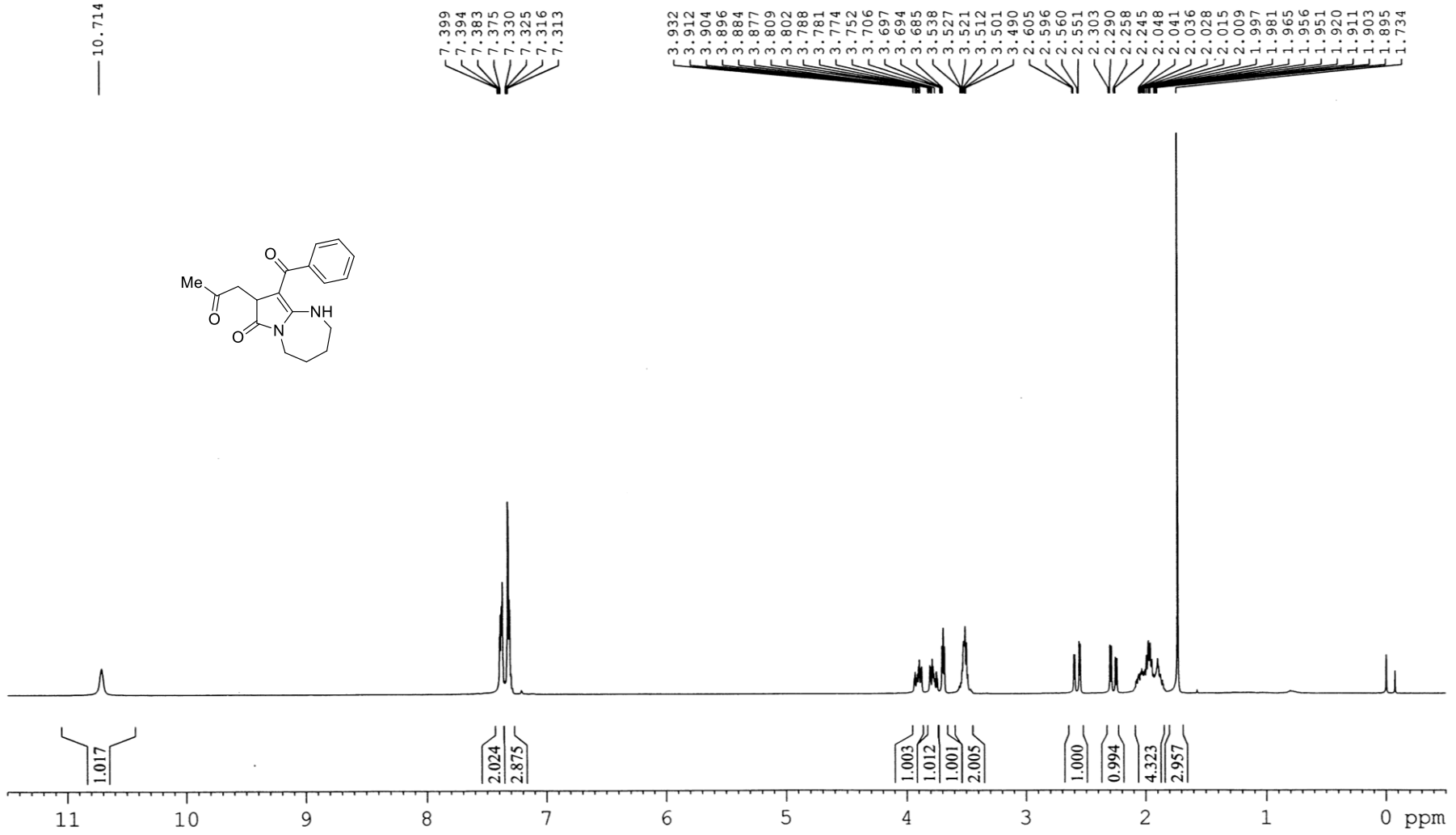


Figure 31. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6f**

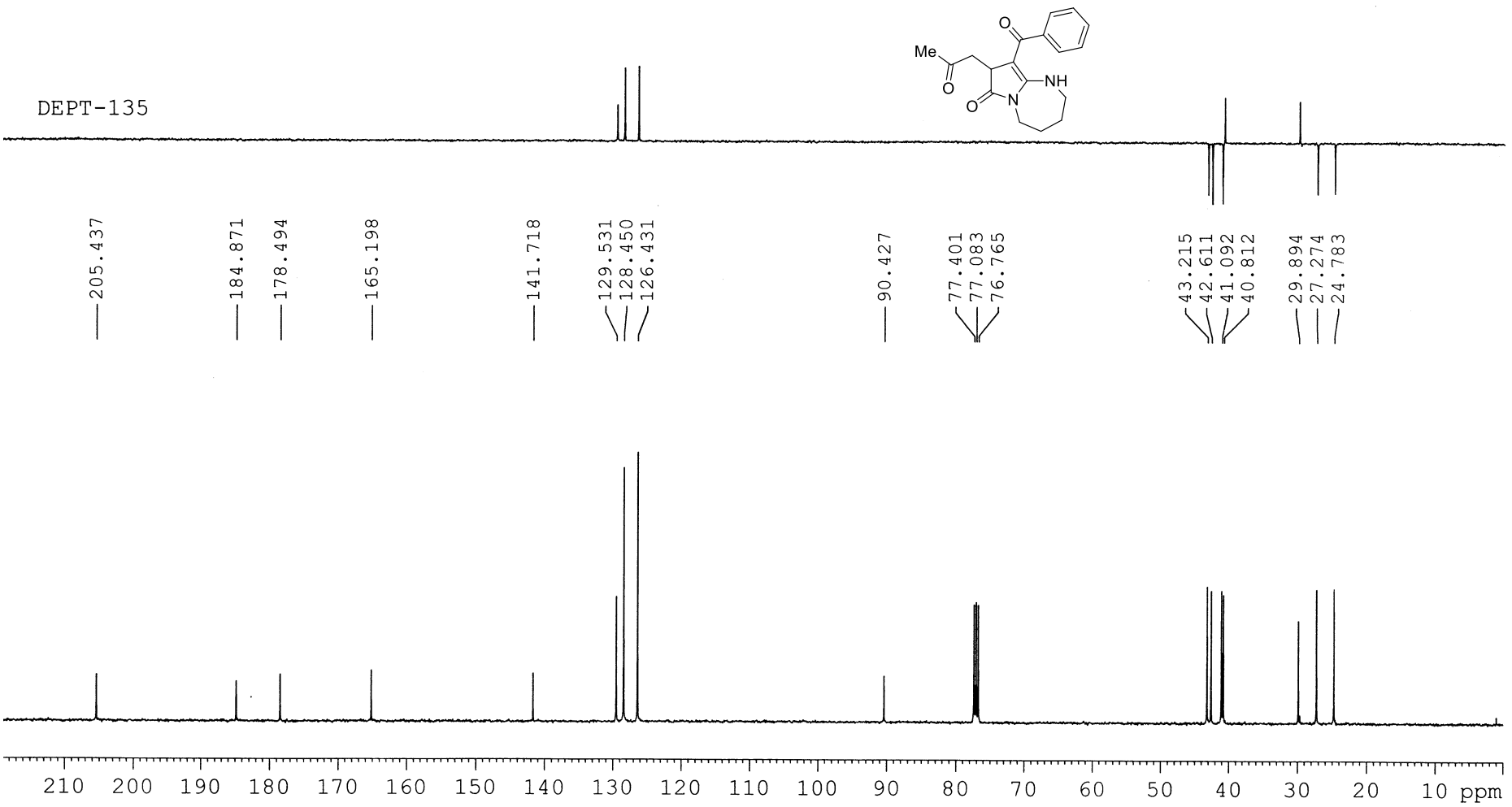


Figure 32. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6f**

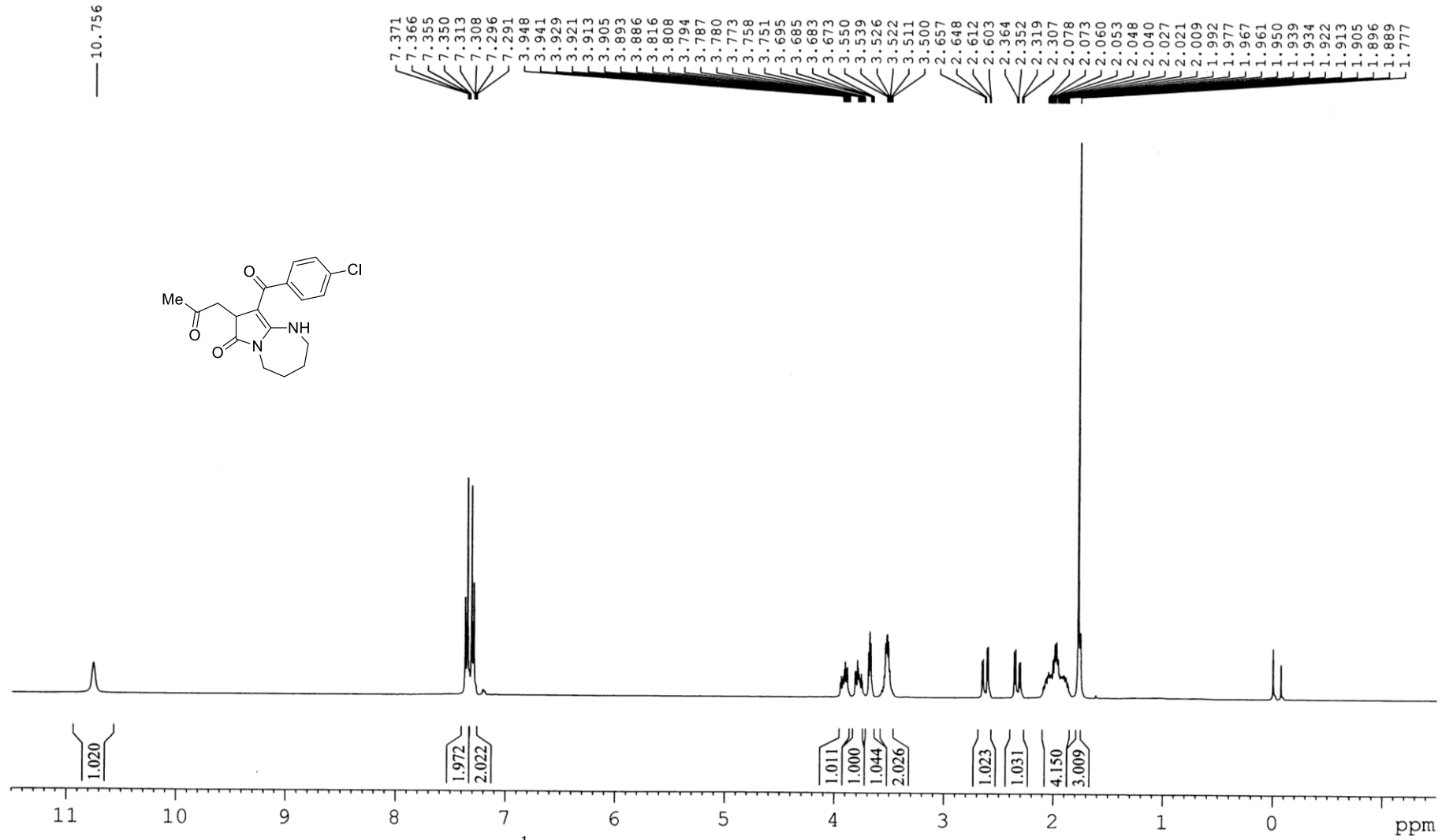


Figure 33. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **6g**

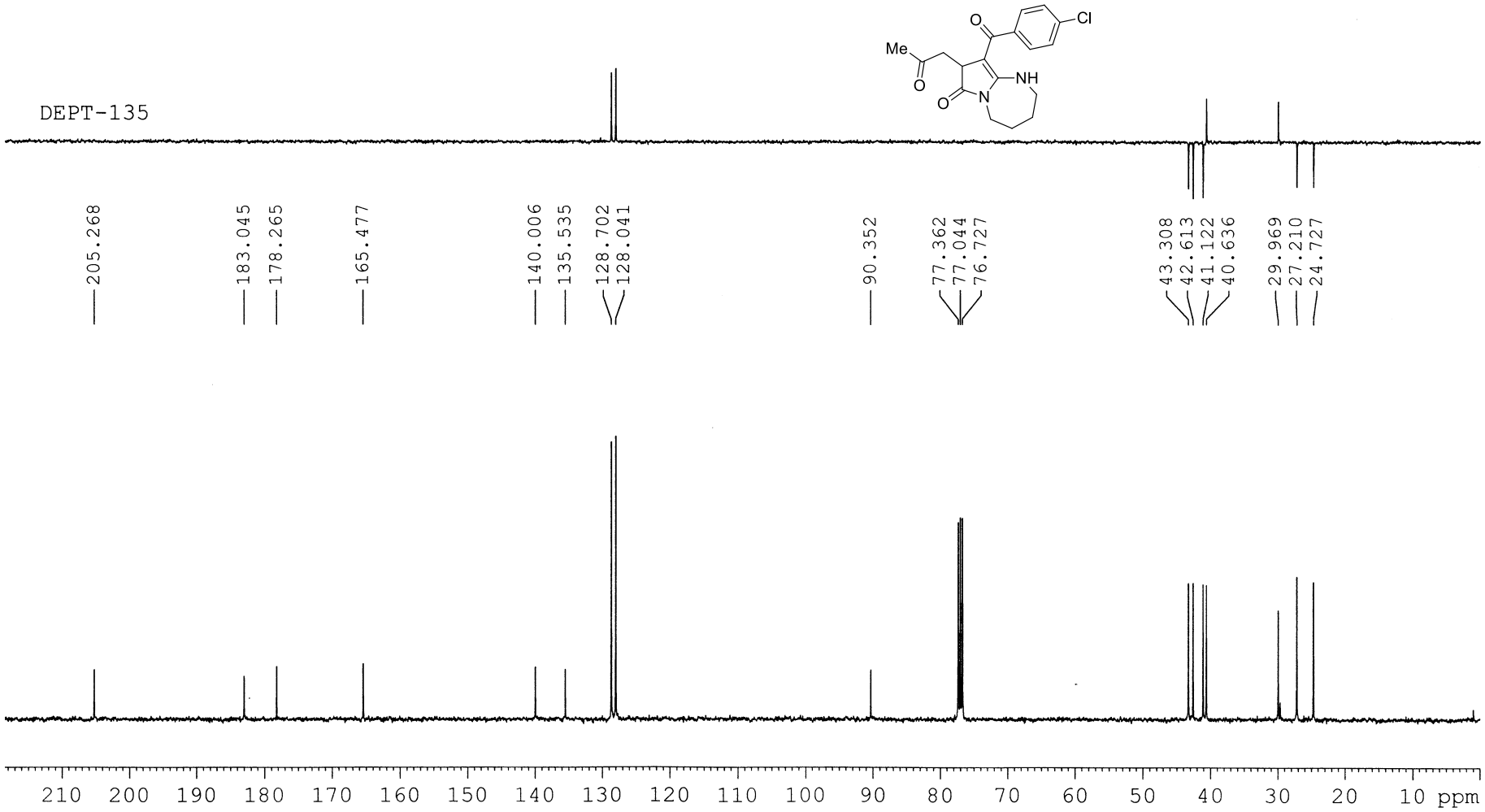


Figure 34. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **6g**

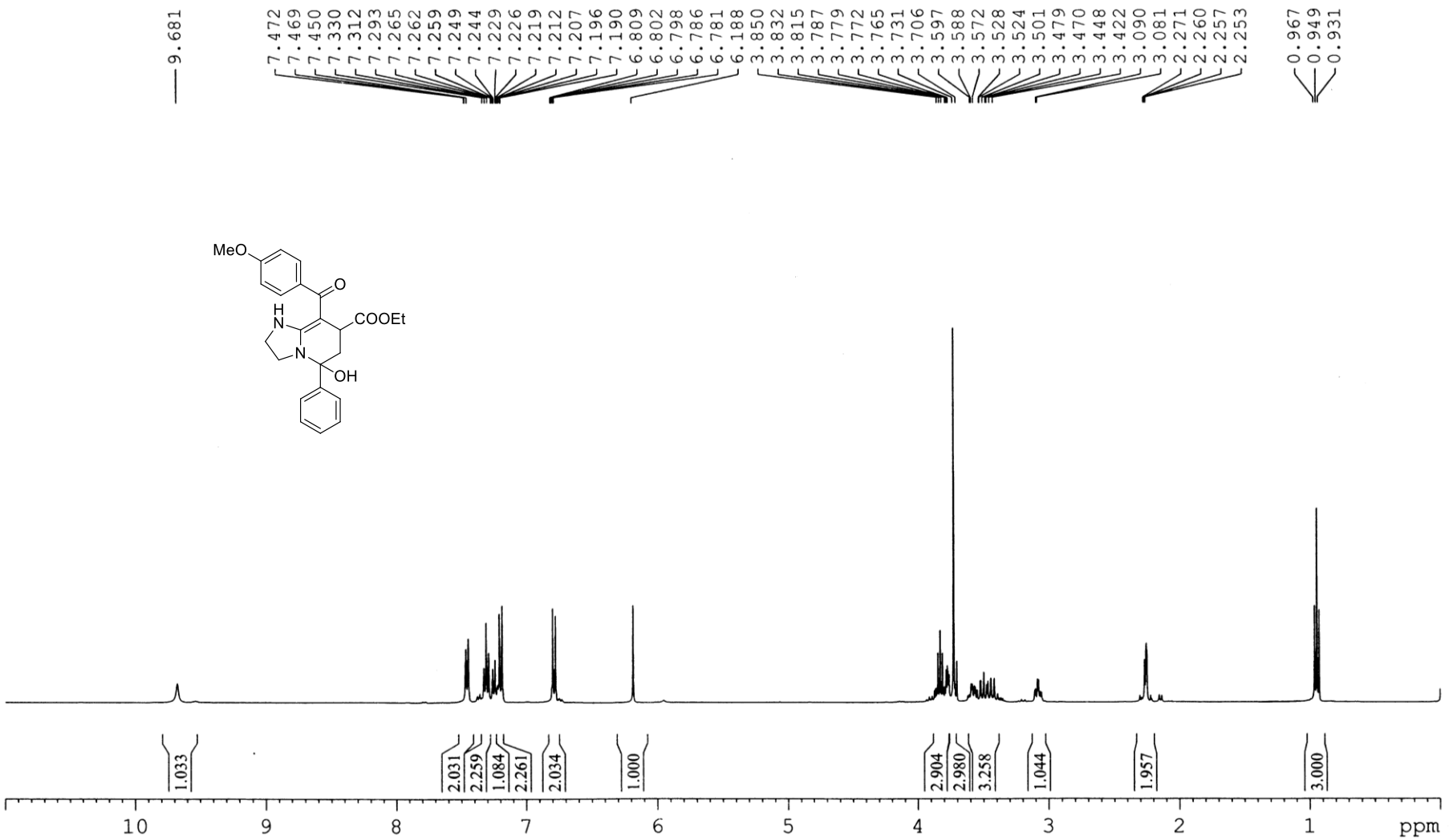


Figure 35. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7a**

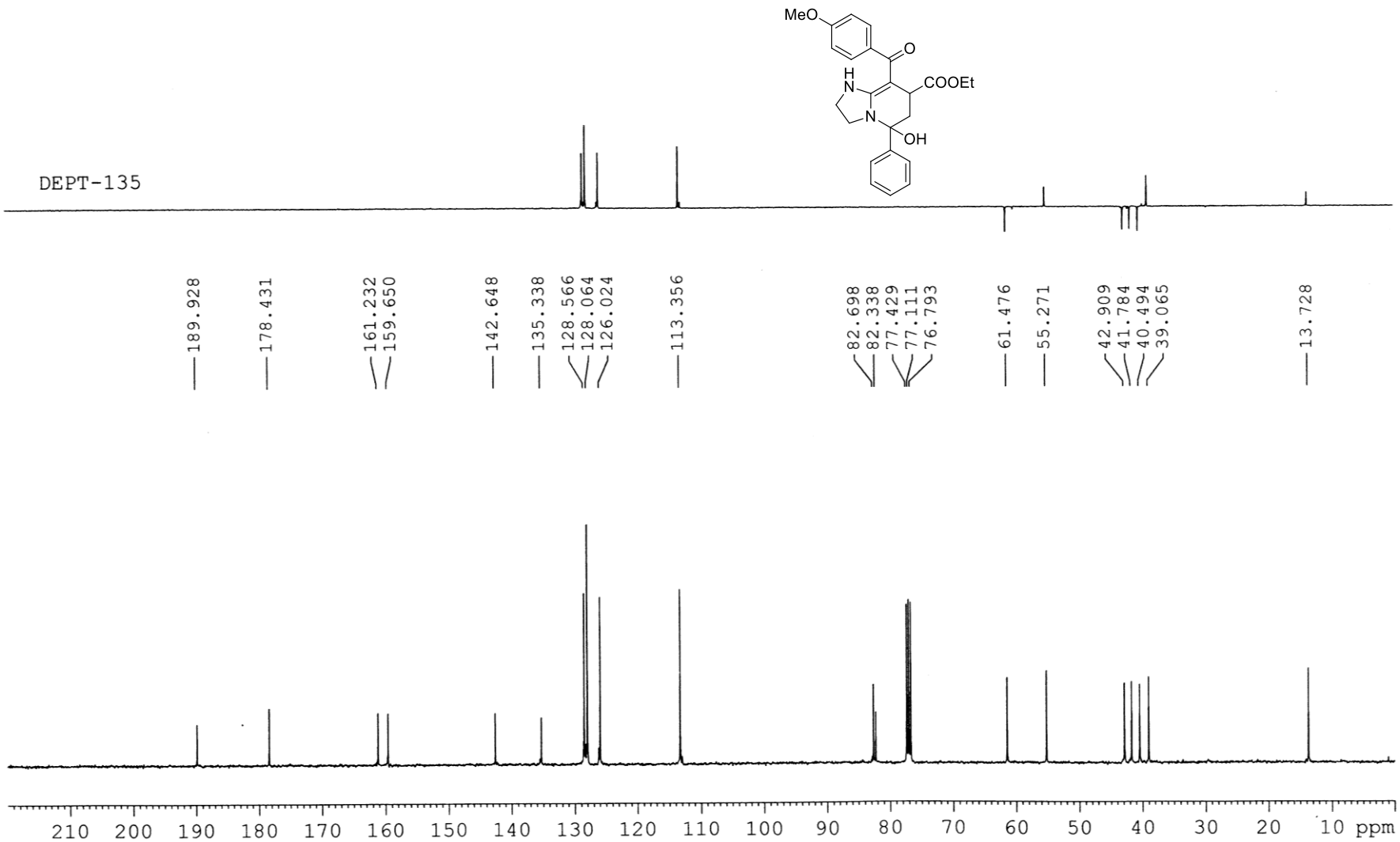


Figure 36. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7a**

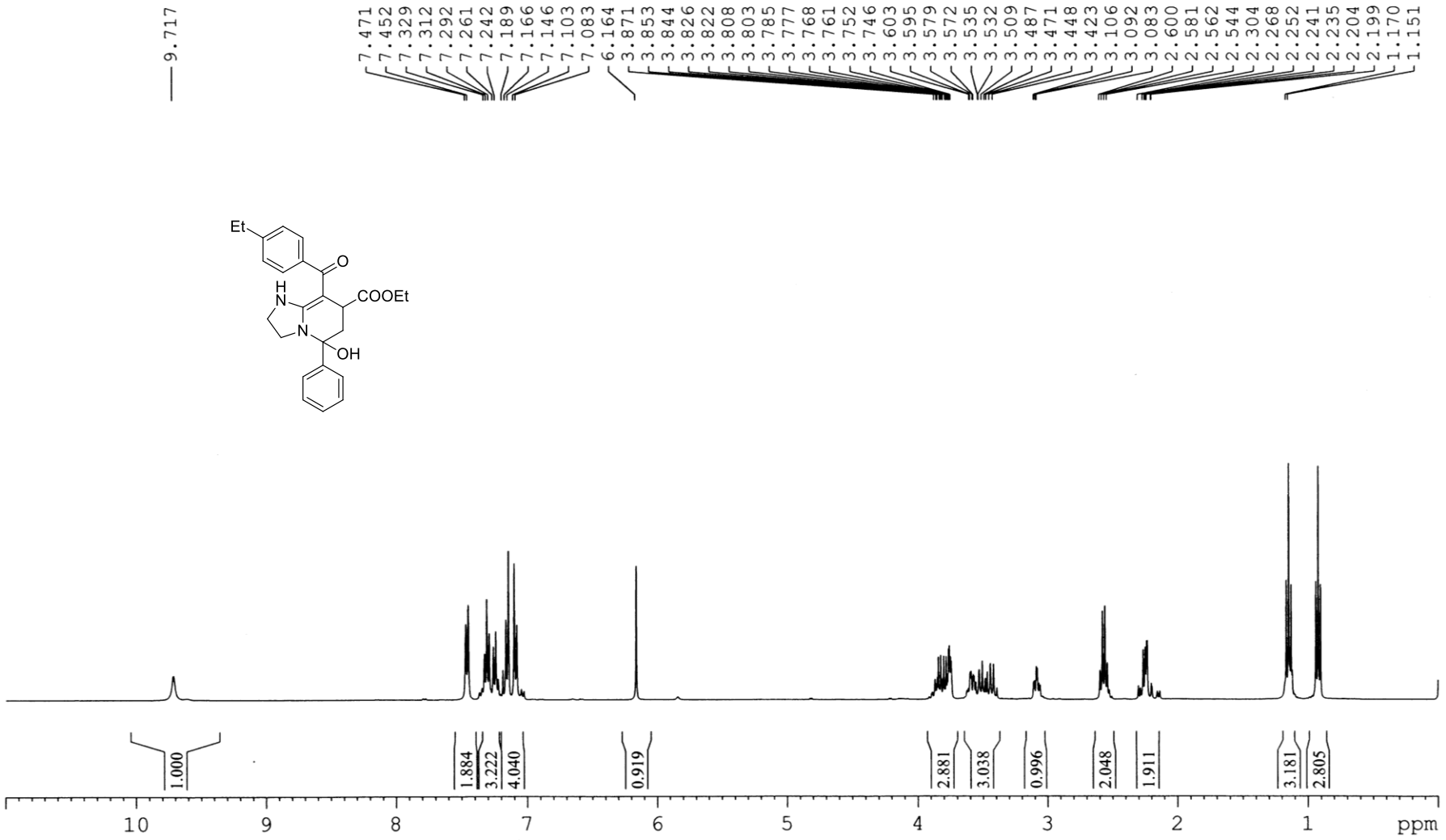


Figure 37. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7b**

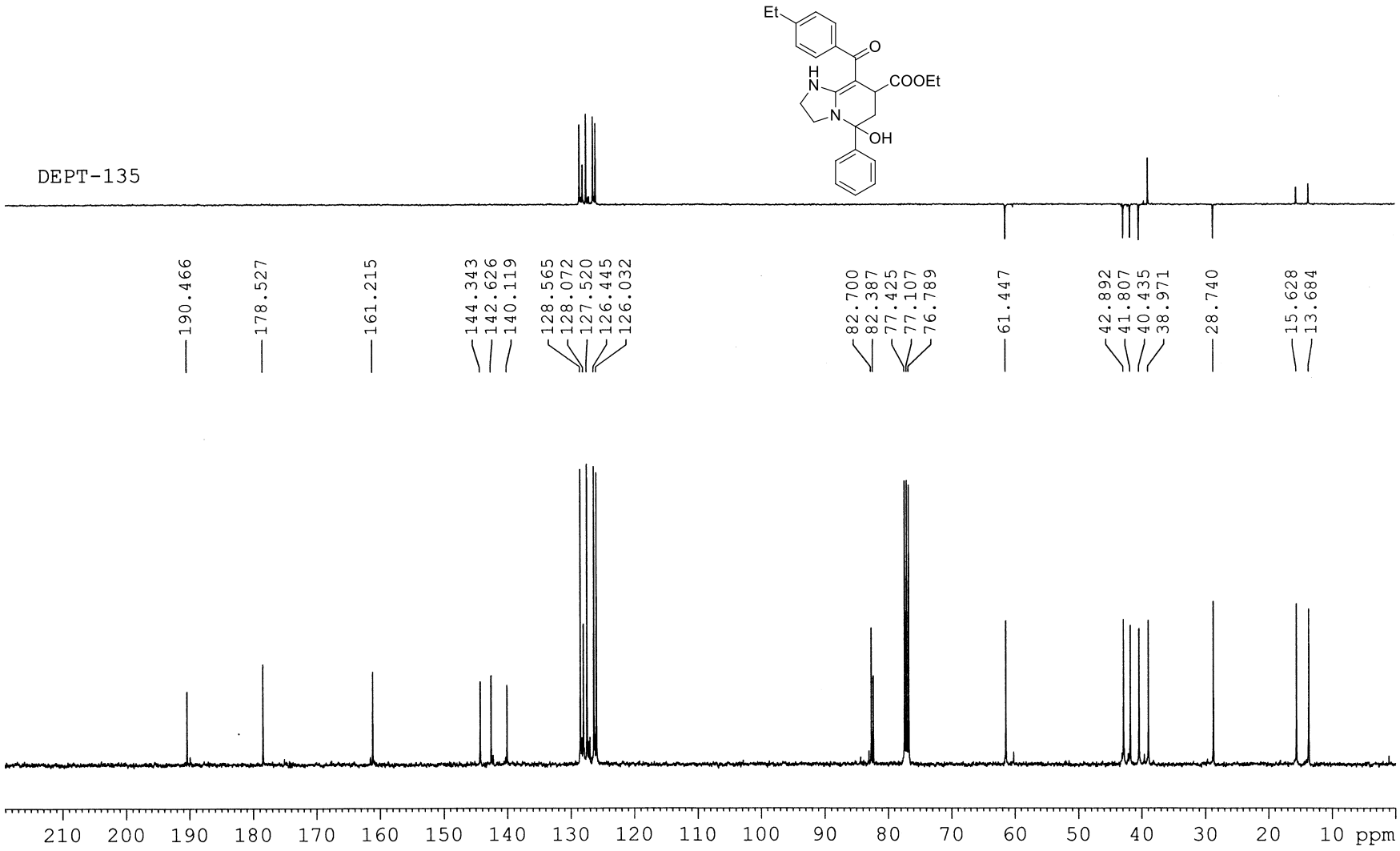


Figure 38. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7b**

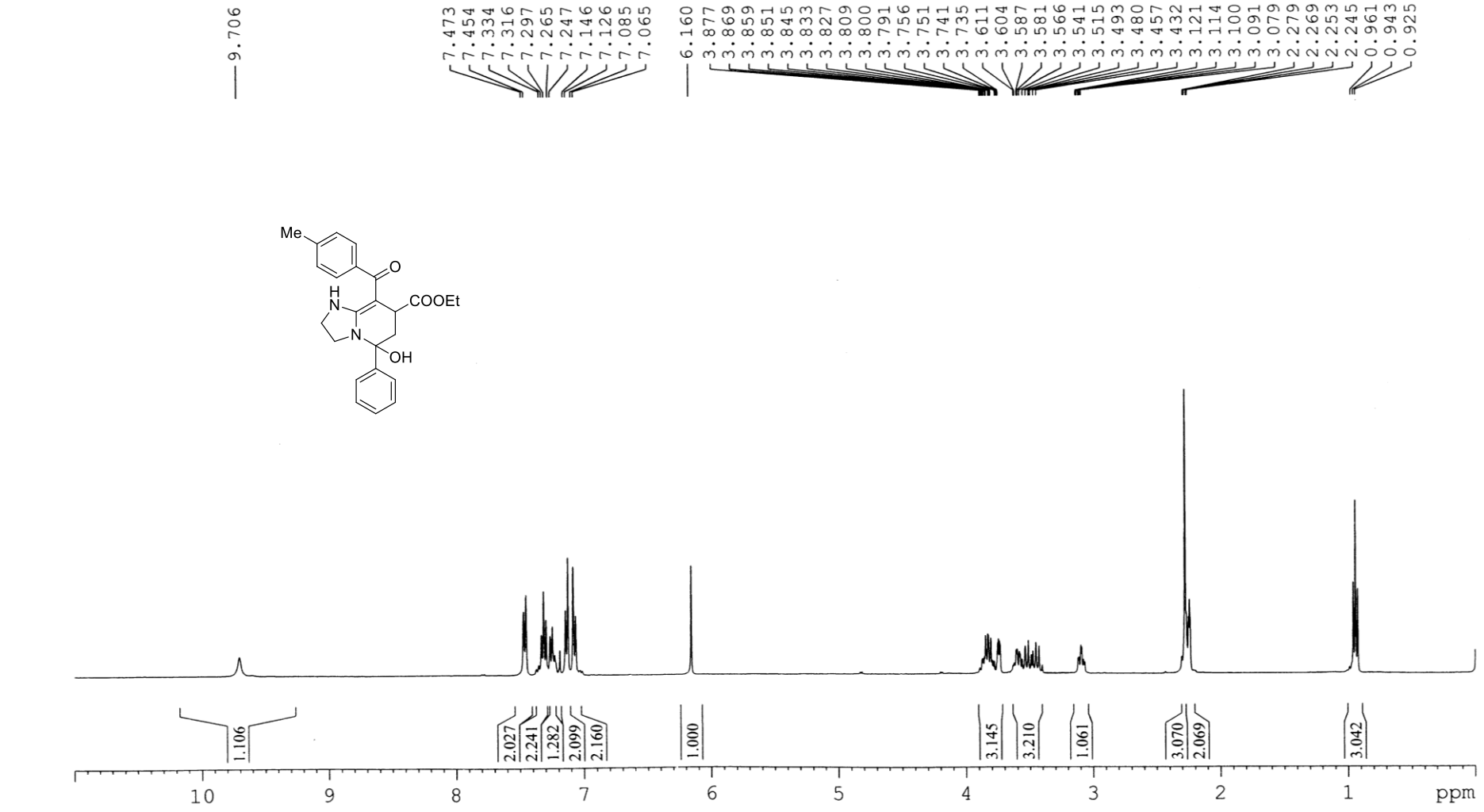


Figure 39. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7c**

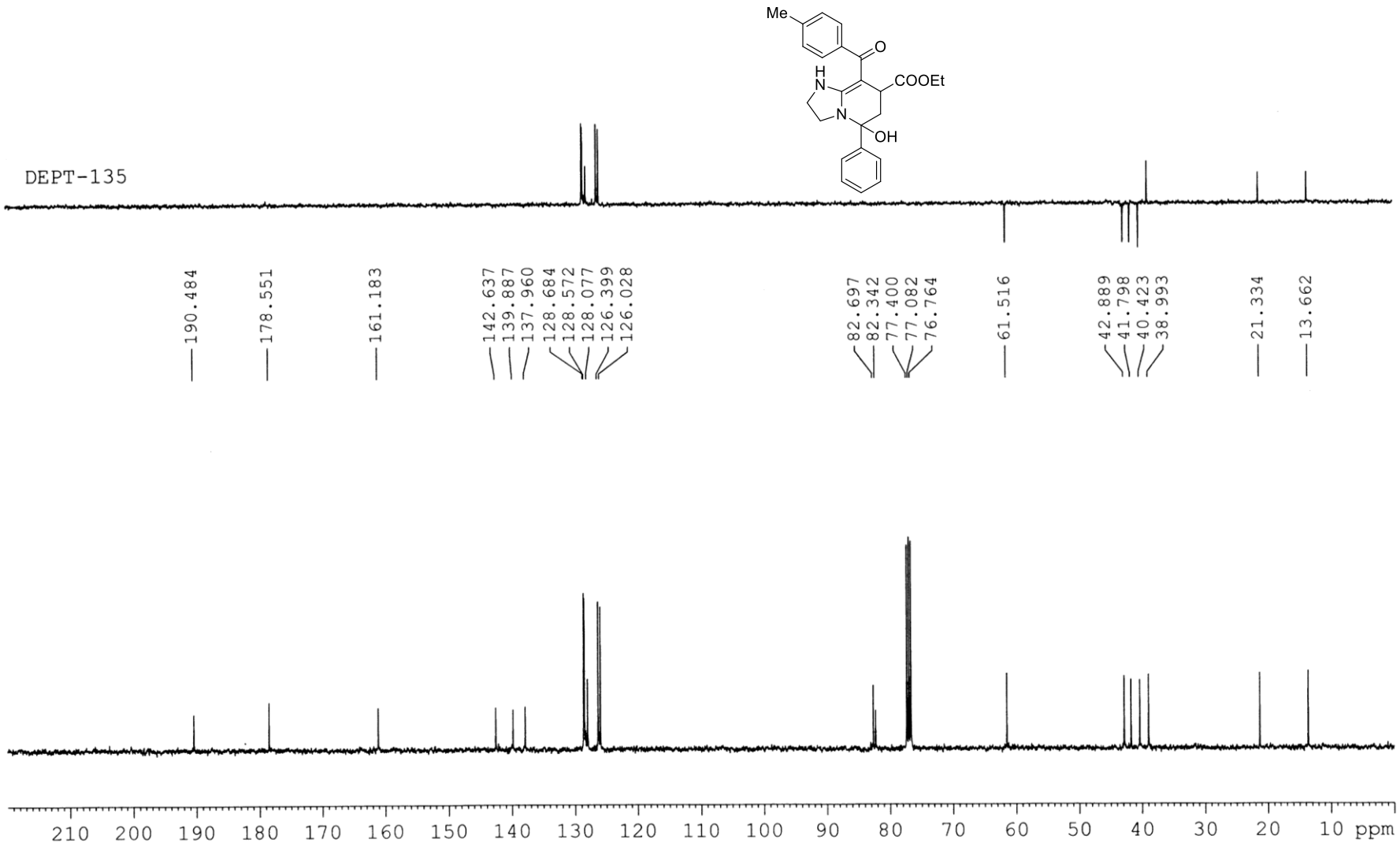


Figure 40. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7c**

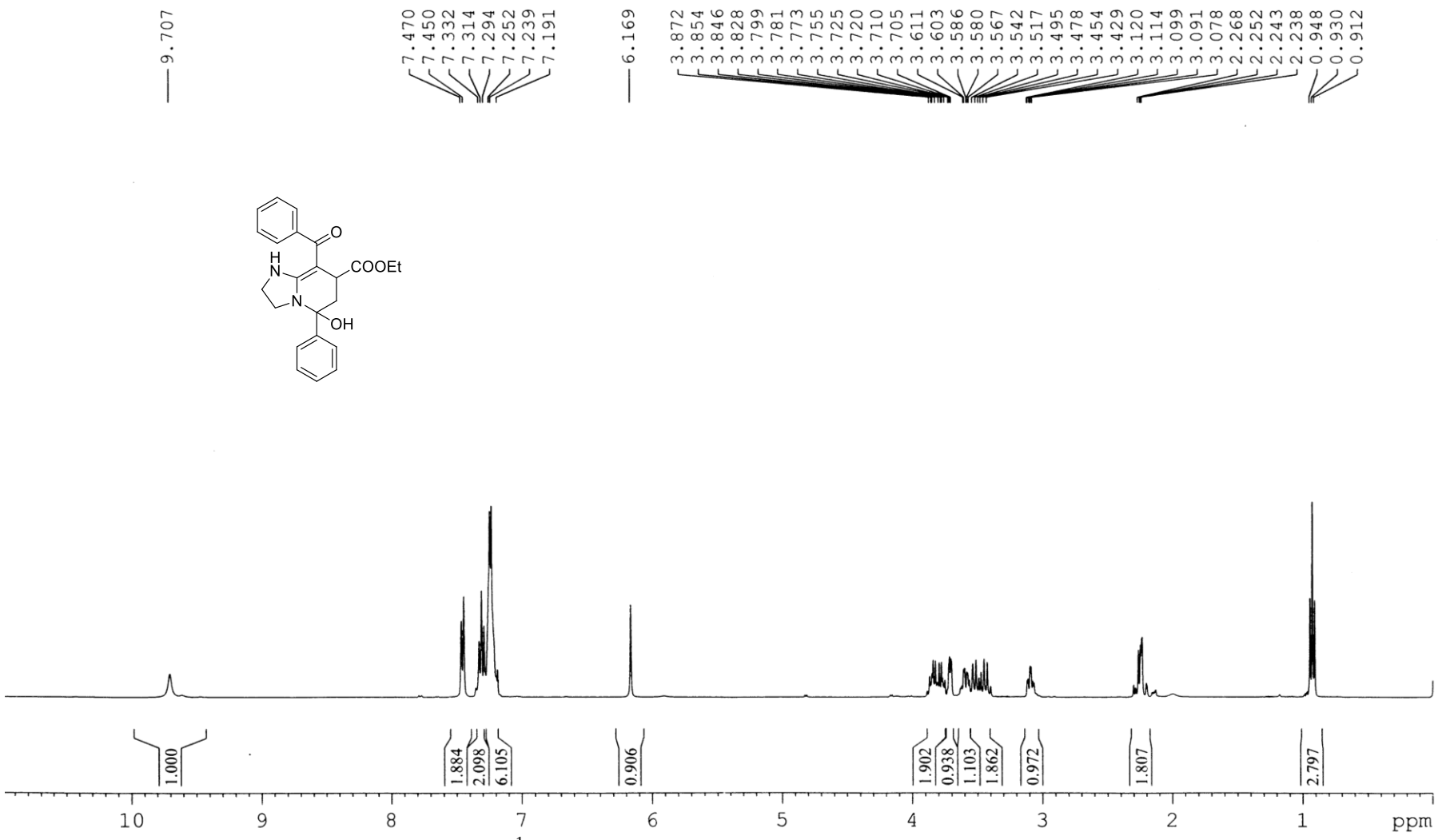


Figure 41. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7d**

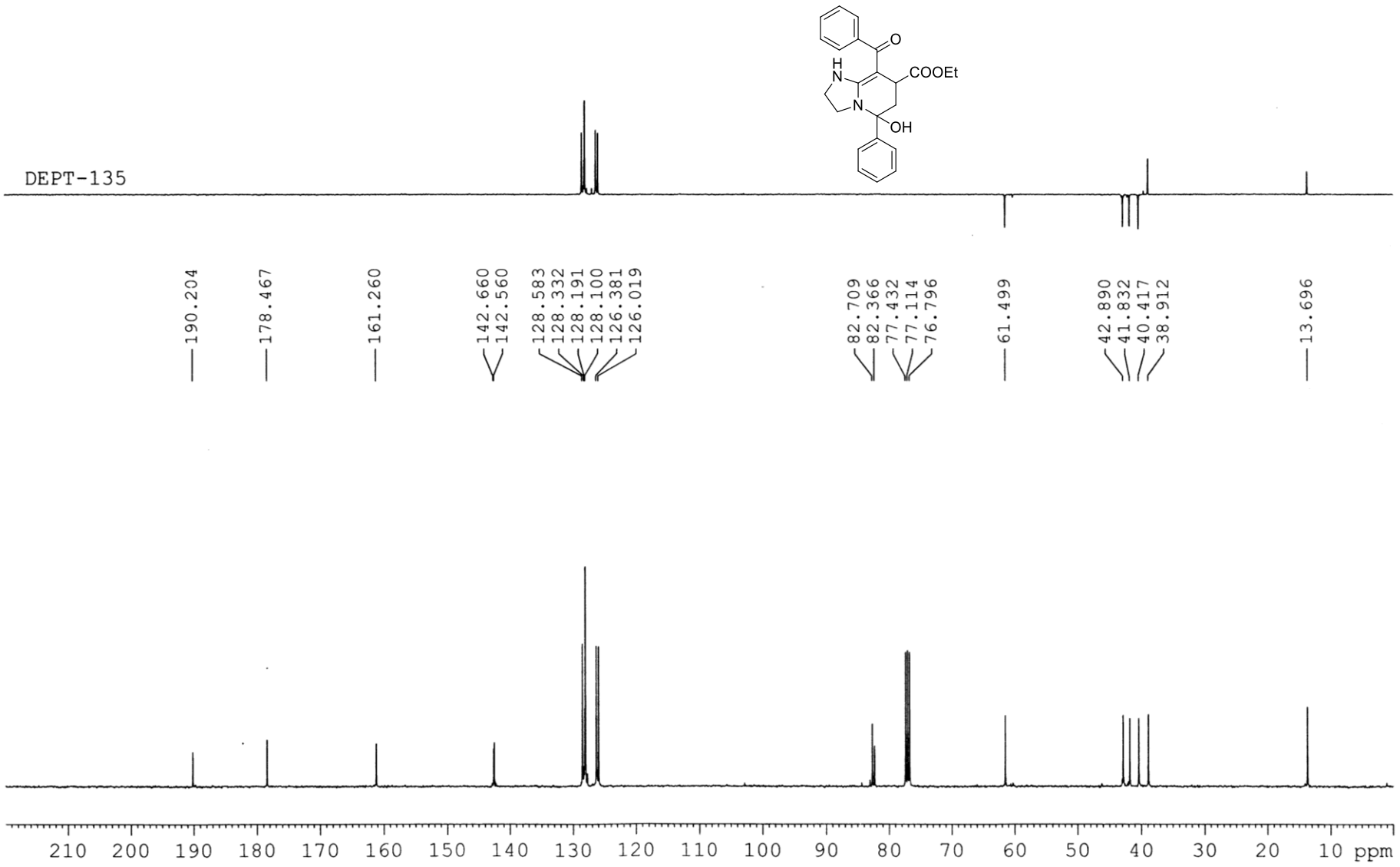


Figure 42. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7d**

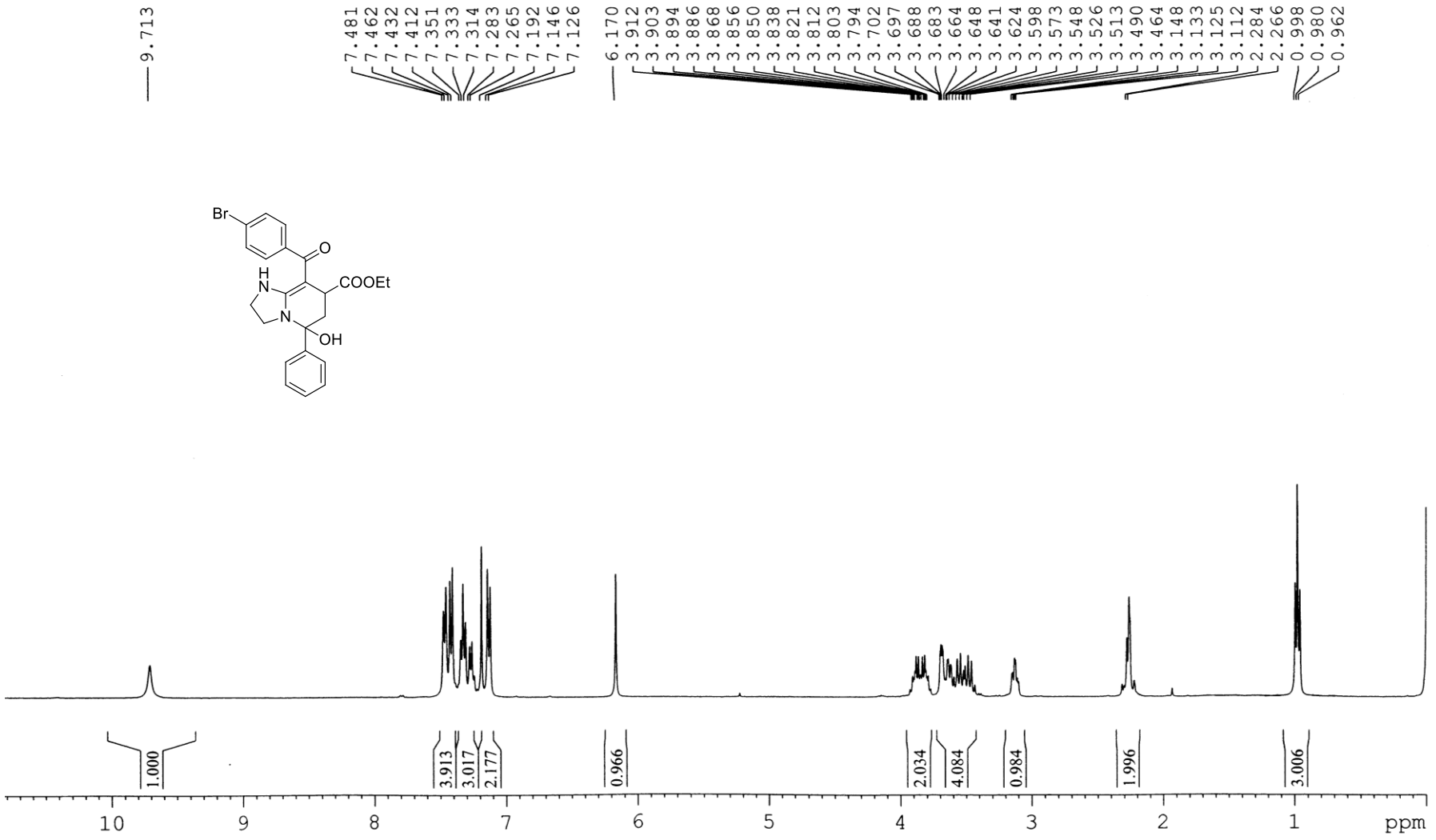


Figure 43. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7e**

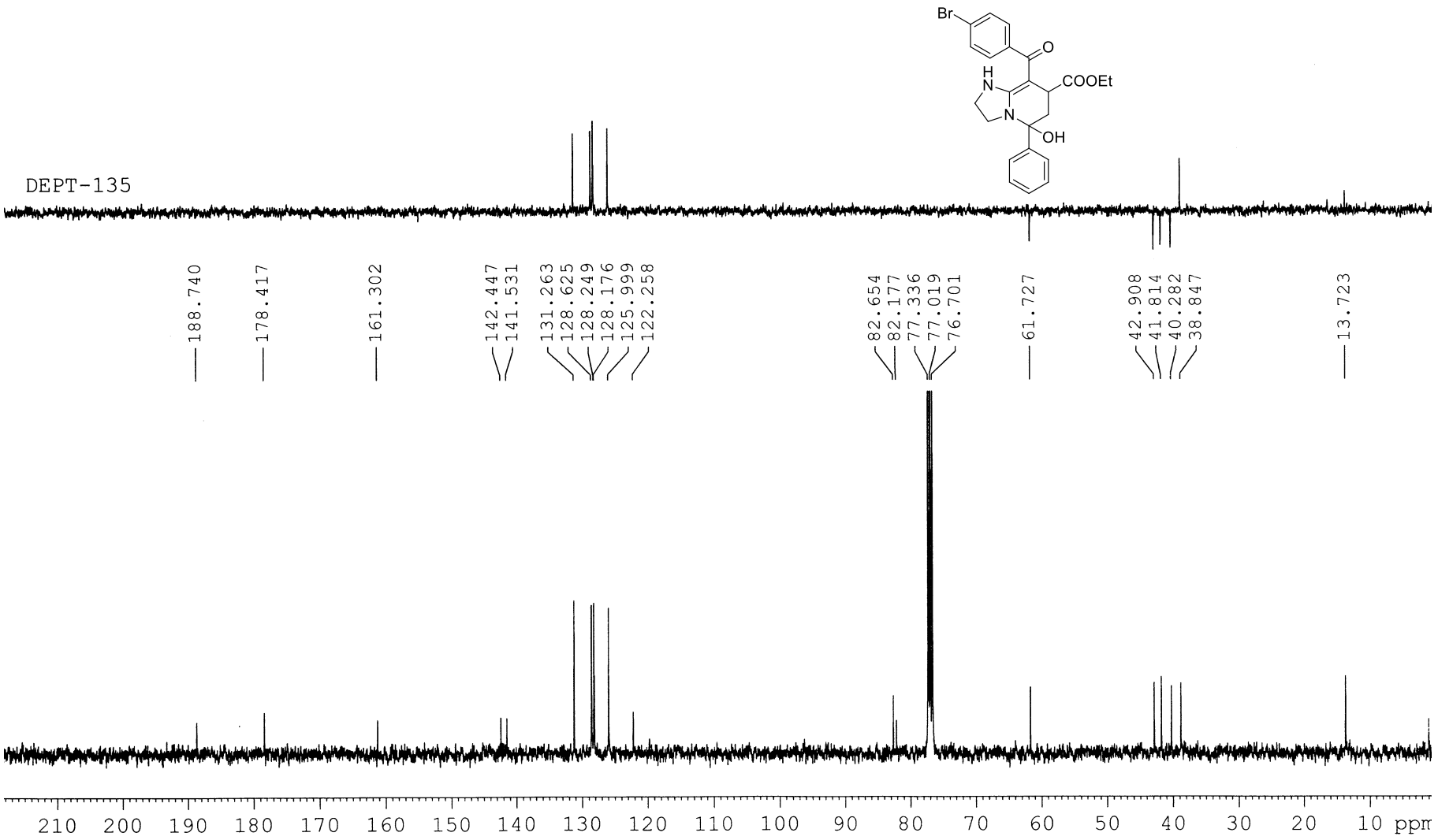


Figure 44. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7e**

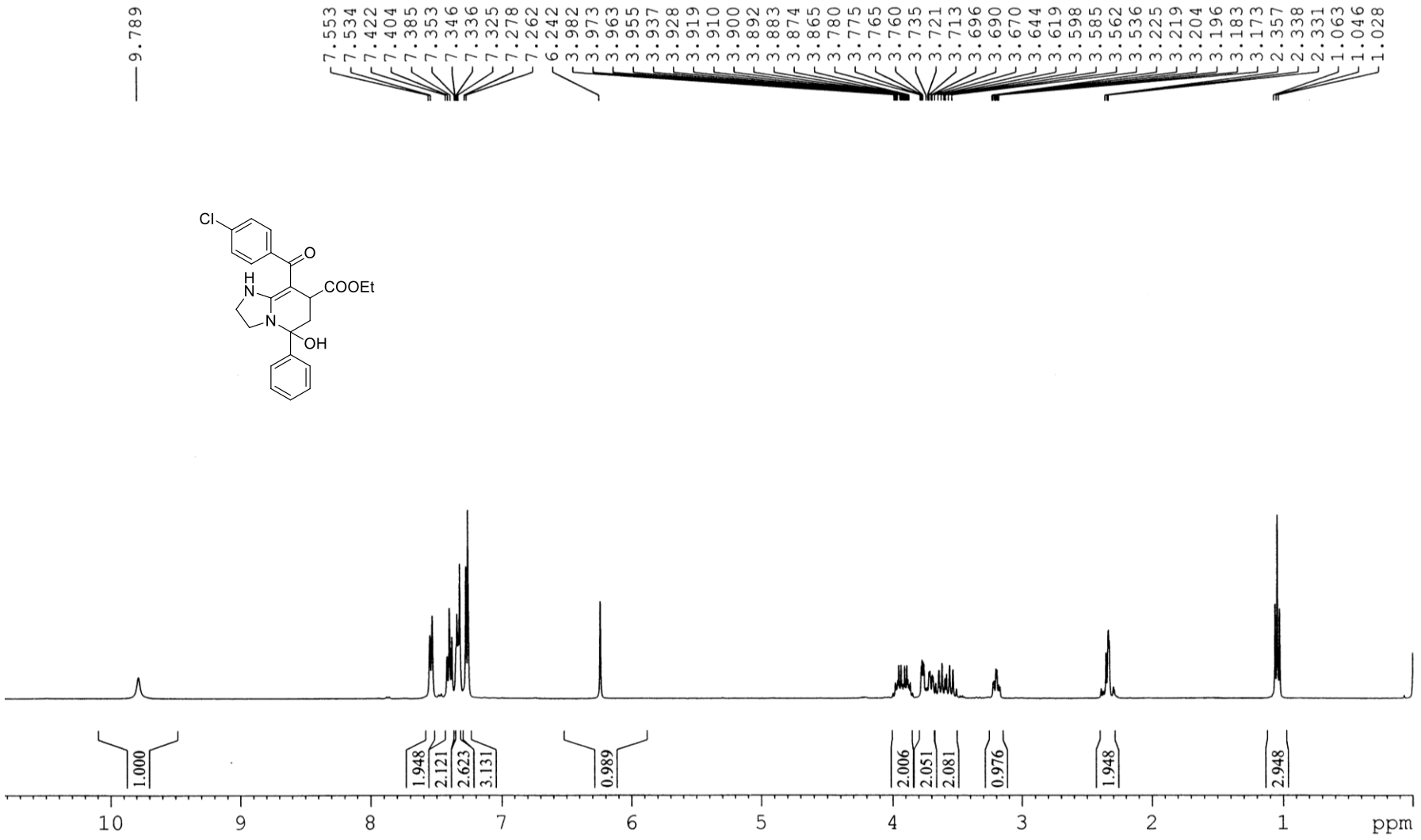


Figure 45. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7f**

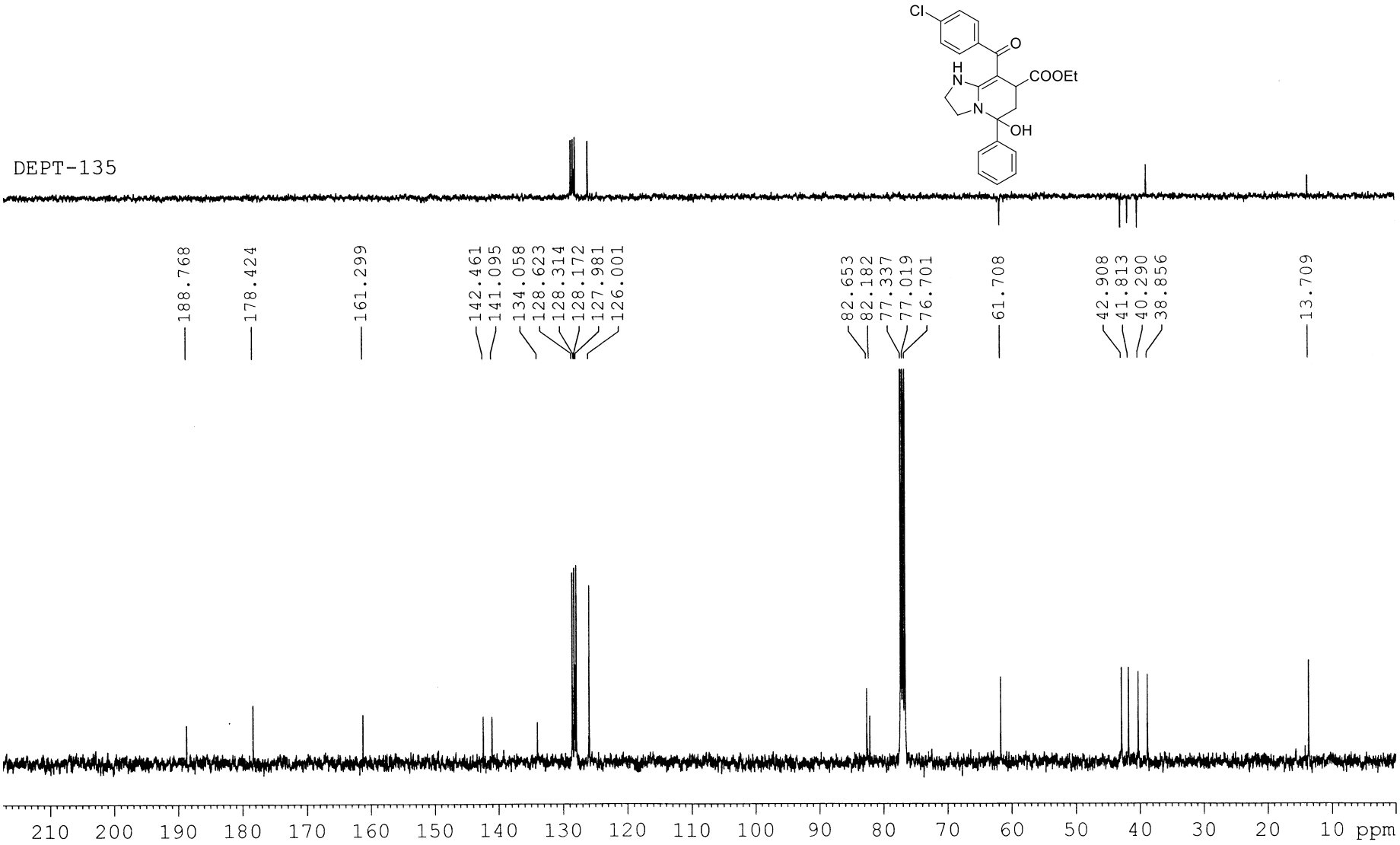


Figure 46. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7f**

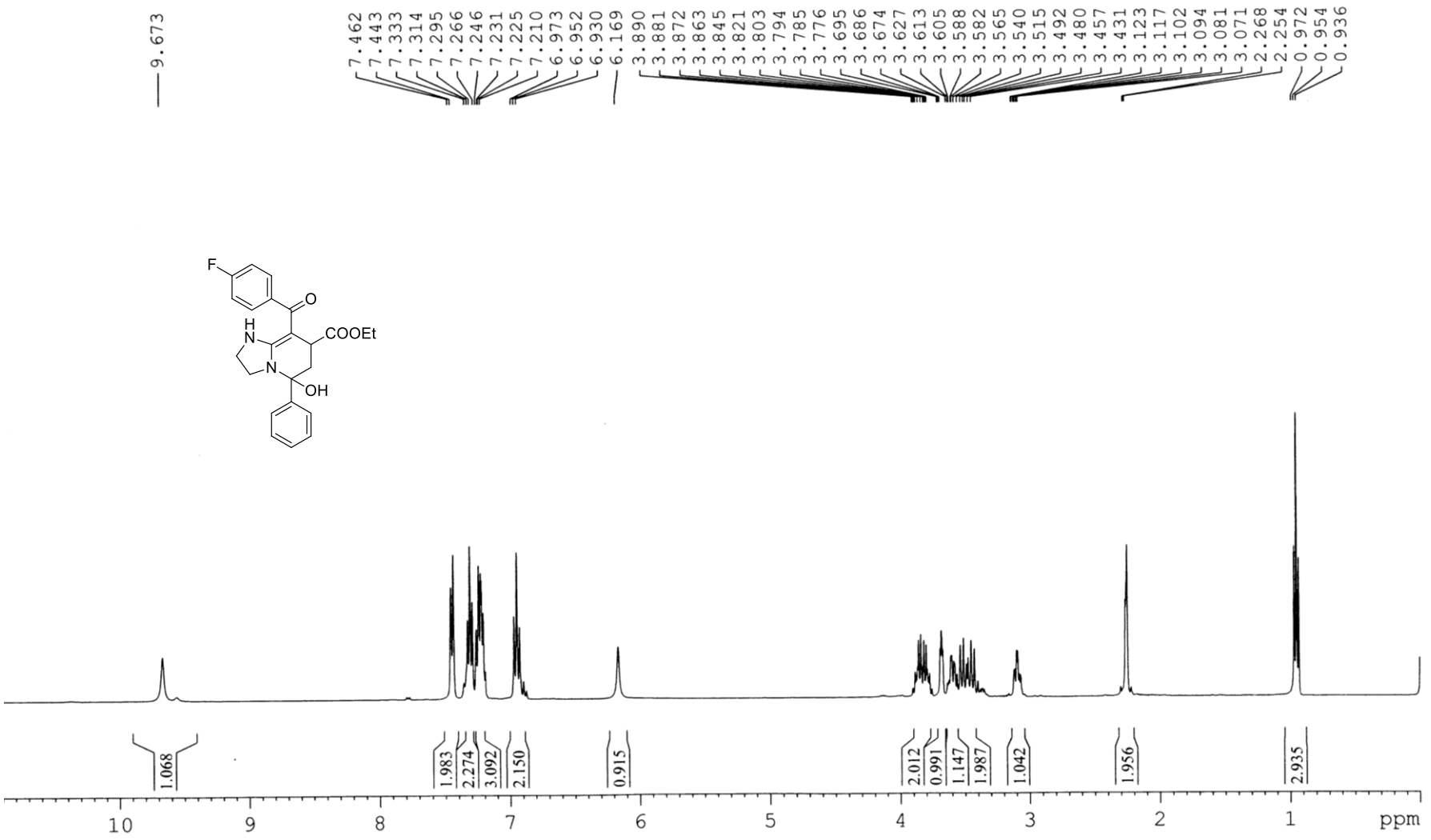


Figure 47. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7g**

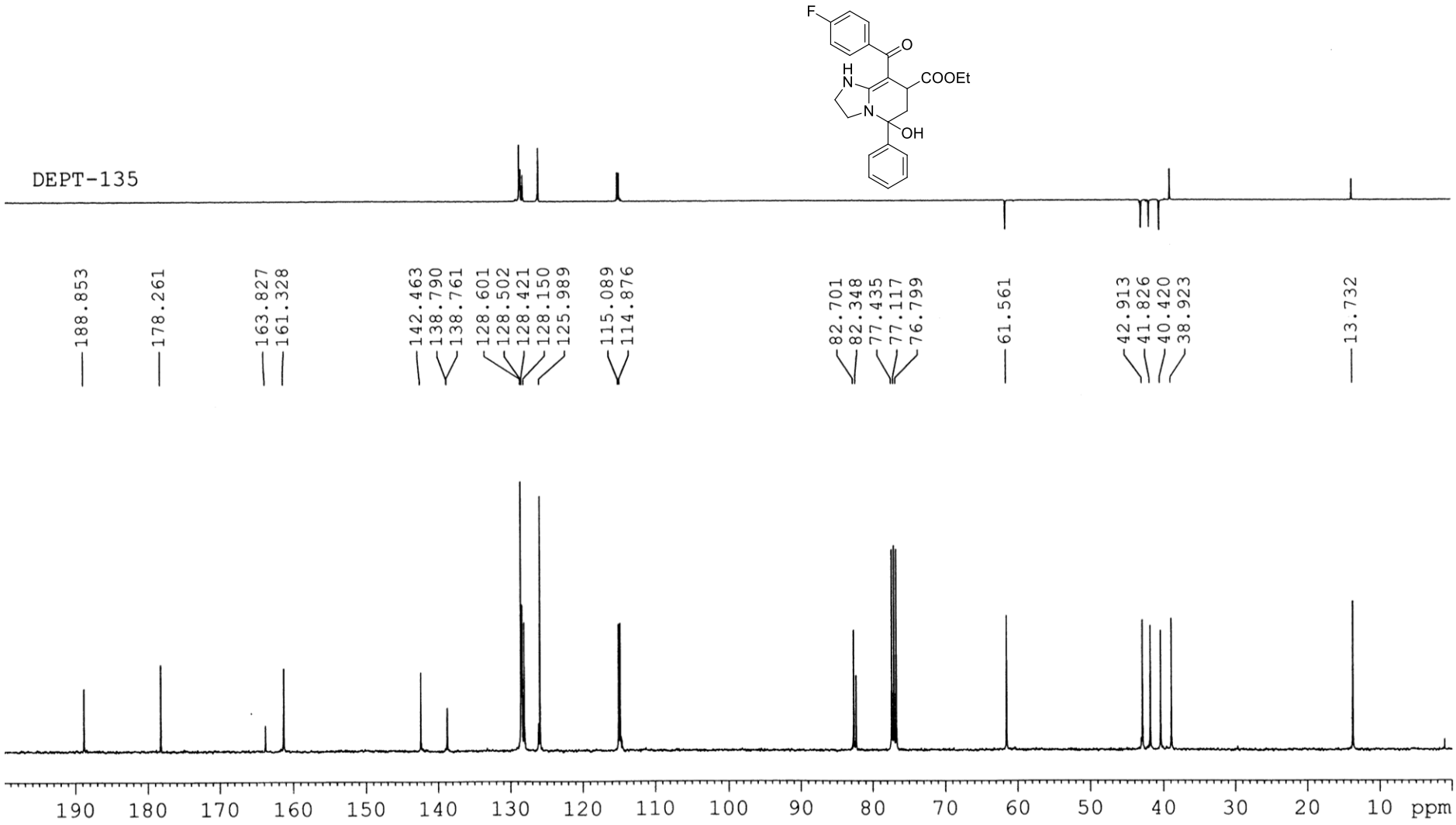


Figure 48. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7g**

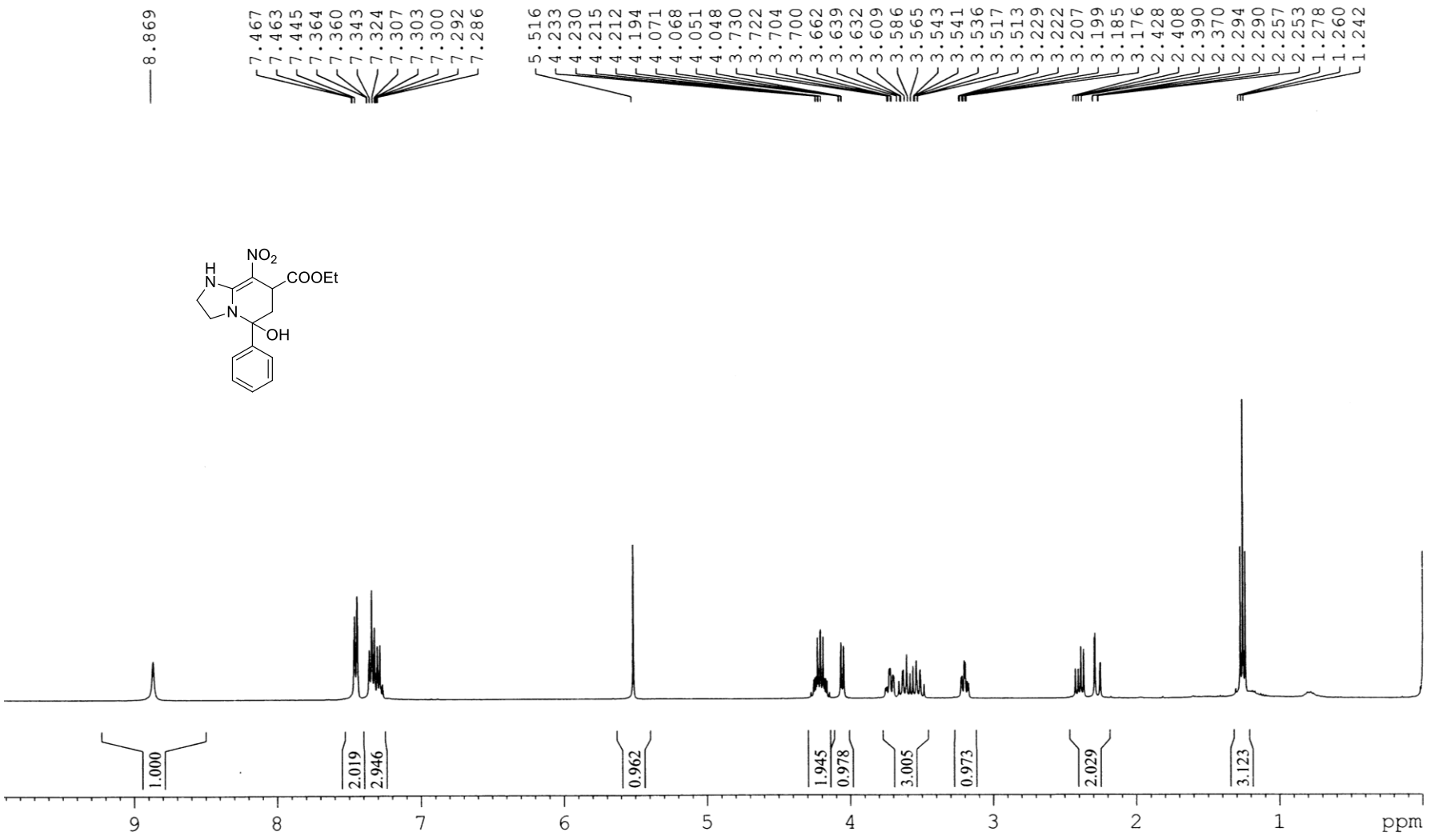


Figure 49. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **7h**

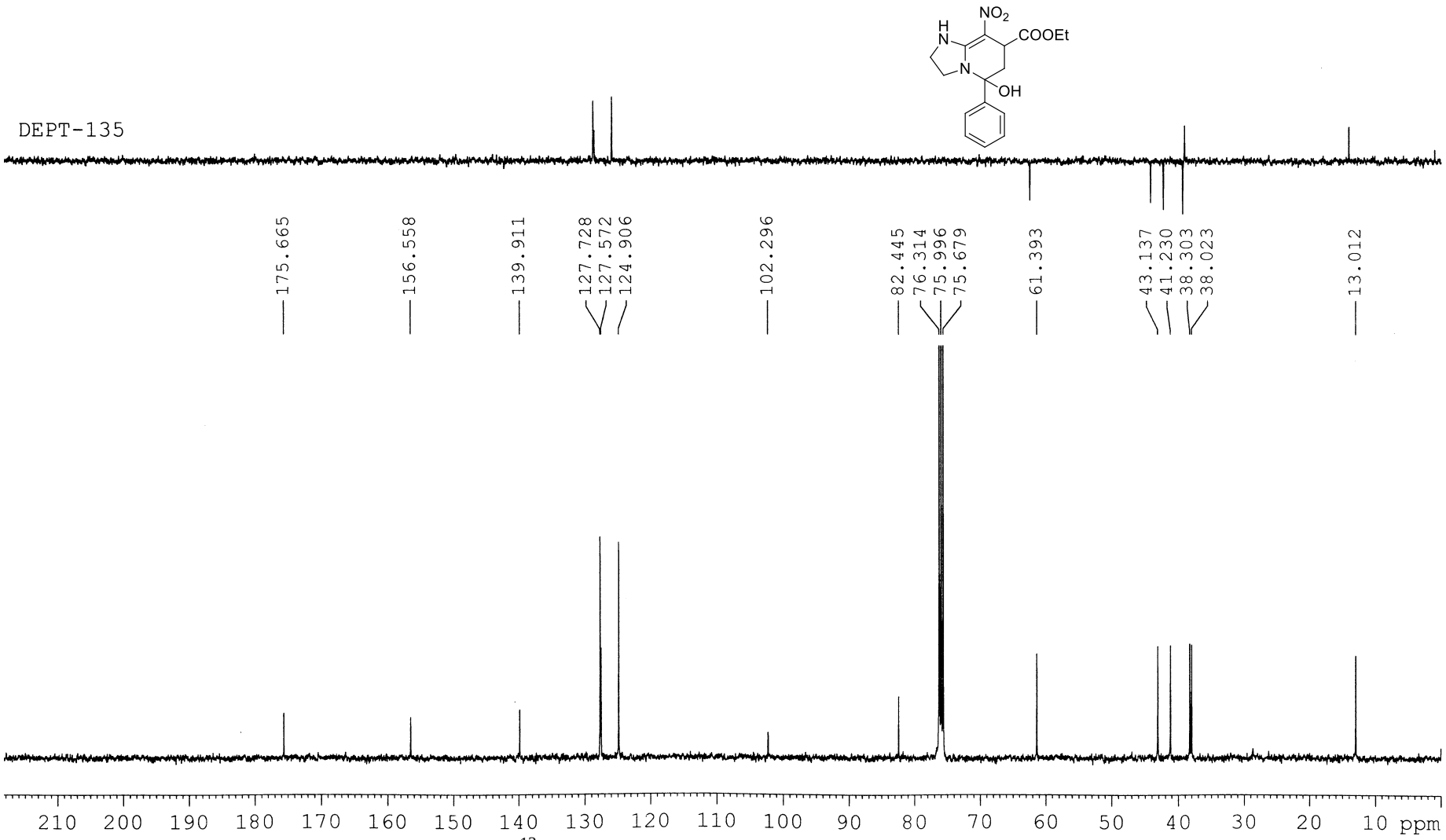


Figure 50. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **7h**

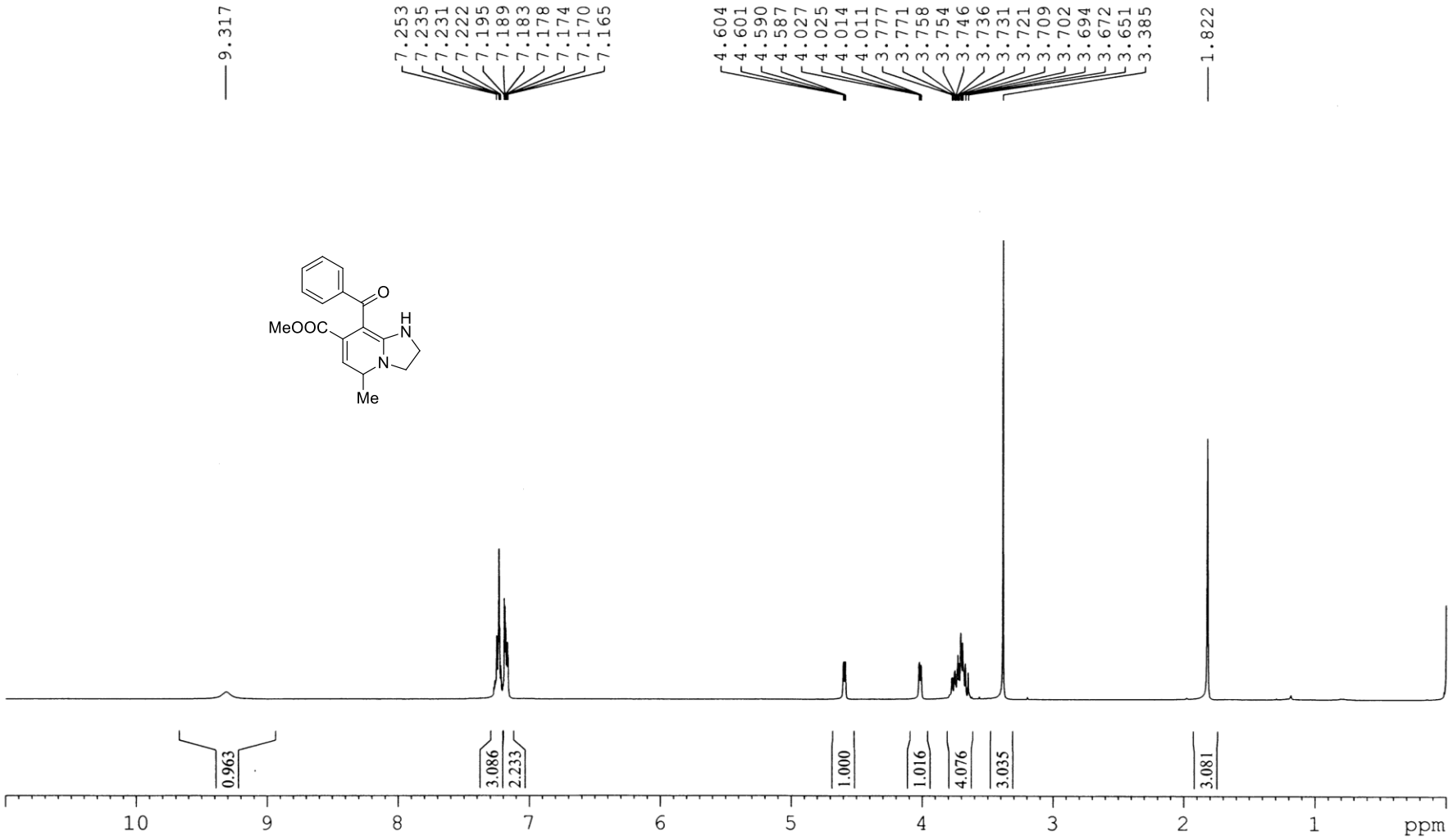


Figure 51. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **8a**

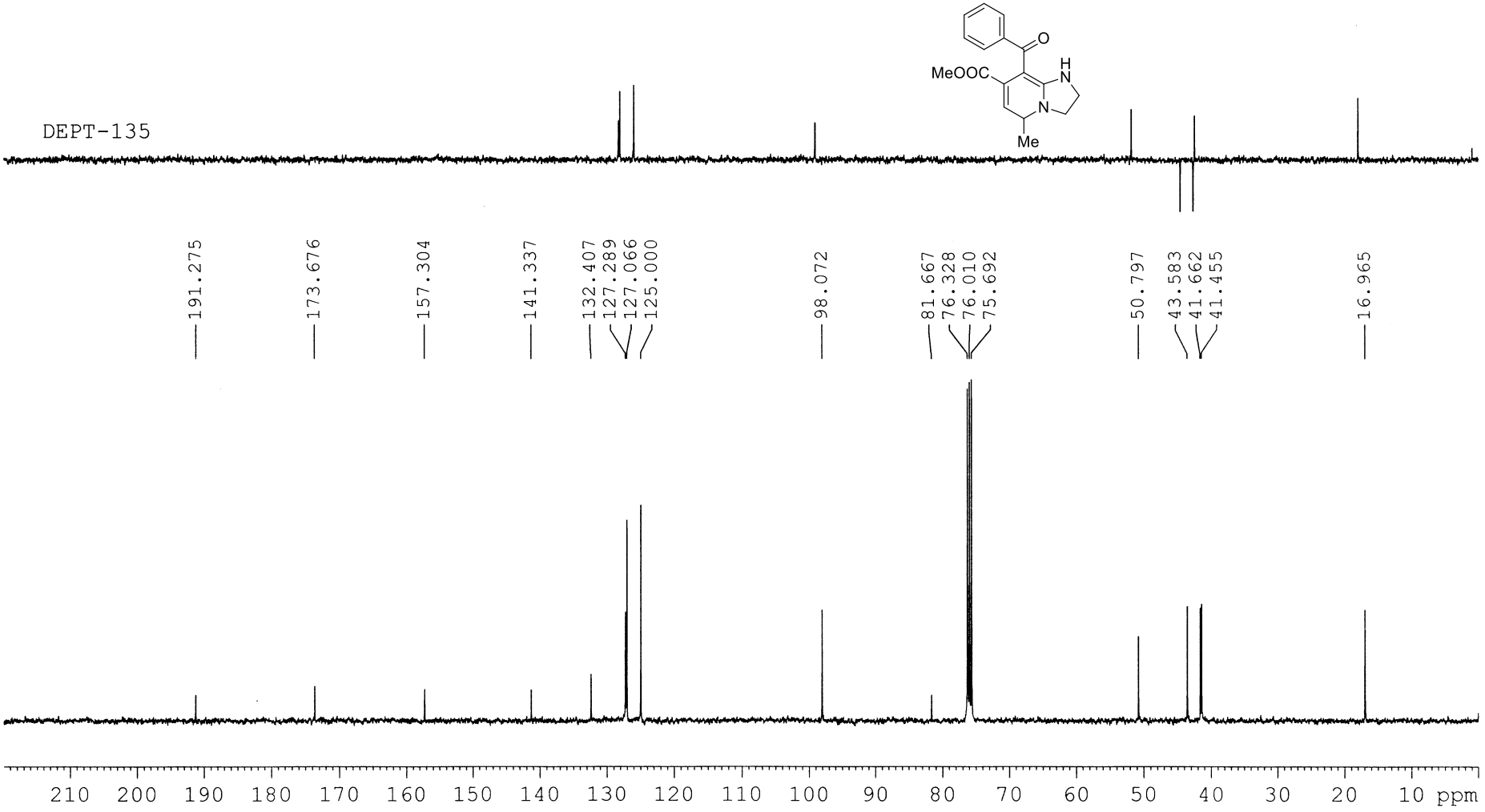


Figure 52. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **8a**

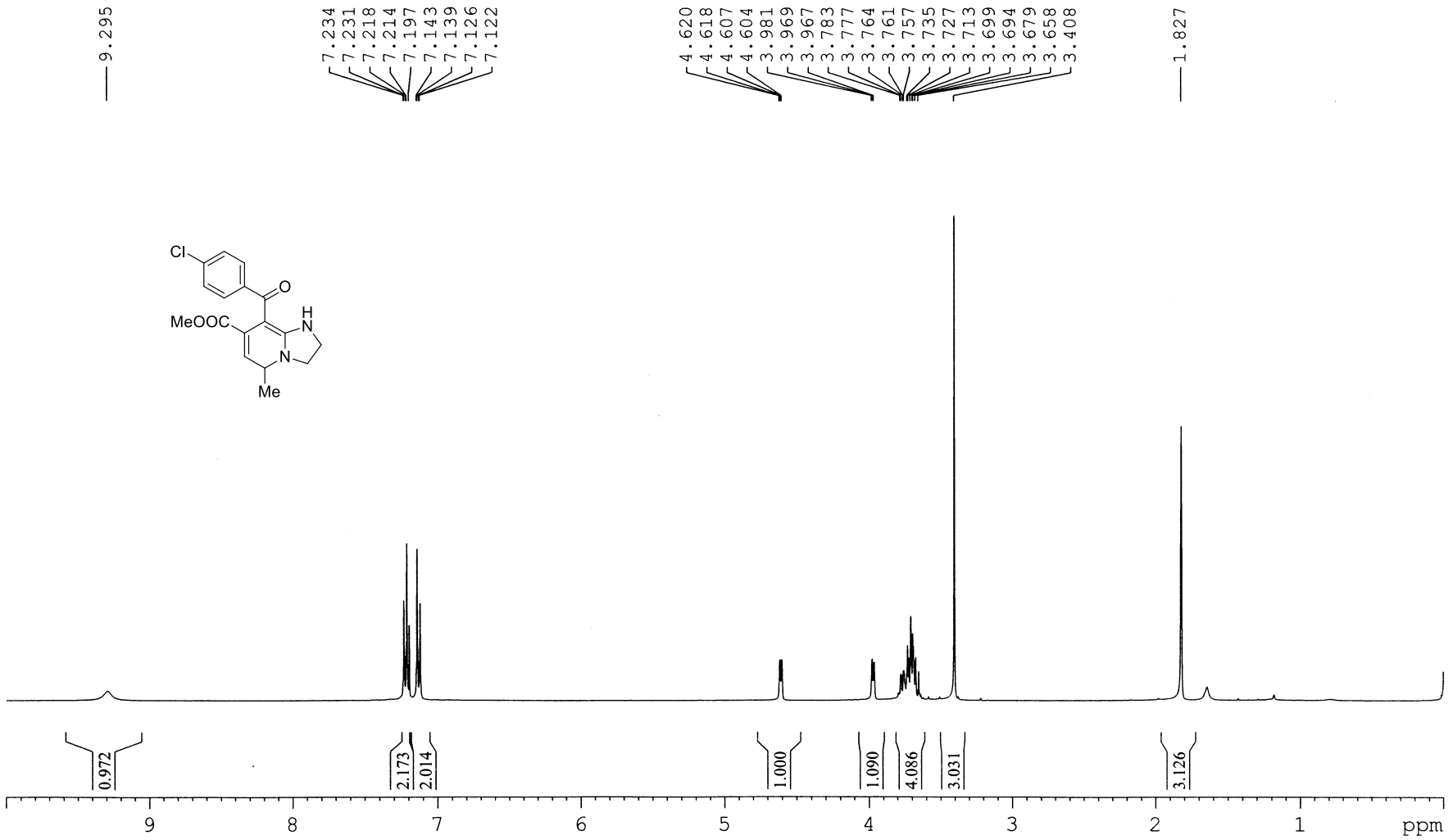


Figure 53. ^{1}H NMR (400 MHZ, $CDCl_3$) spectra of compound **8b**

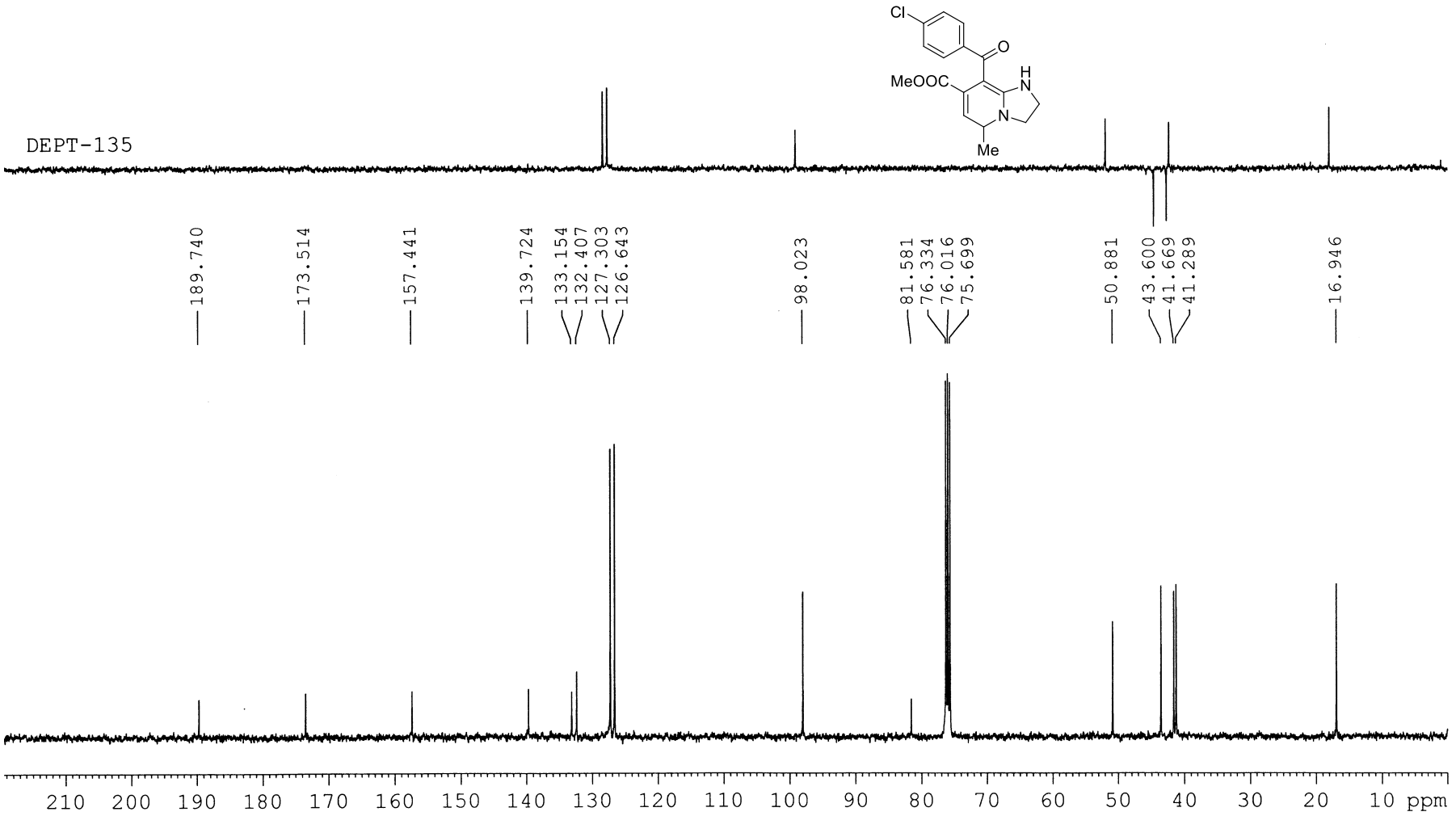


Figure 54. ^{13}C NMR (100 MHZ, $CDCl_3$) spectra of compound **8b**

References and Notes

1. (a) Huang, Z.-T.; Wang, M.-X. *Synthesis* **1992**, 12, 1273−1276. (b) Li, Z.-J.; Charles, D. *Synth. Commun.* **2001**, 31, 527−533.
2. CCDC 1052283 contain the supplementary crystallographic data for compound **5e**. CCDC 1052294 contain the supplementary crystallographic data for compound **7e**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center via www.ccdc.cam.ac.uk/data_request/cif.