Rh(III)-catalyzed regioselective C−H activation/[3+2] cyclization of KHAs with iodonium ylides accessing pyrimido[1,2-*a*]indole derivatives†

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Supporting Information

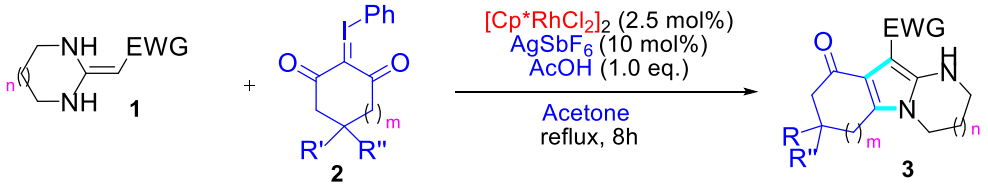
1. General Information.

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX500 or DRX600, chemical shifts (δ) are expressed in ppm, and J values are given in Hz, and deuterated $CDCl_3$ was used as solvent. 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. X-ray diffraction was obtained by APEX DUO.

All chemicals and solvents were used as received without further purification unless otherwise stated. All chemicals were purchased from Adamas-beta. Column chromatography was performed on silica gel (Qingdao, 200–300 mesh). HKAs 1 were prepared according to the literature[1]. Iodonium ylides were prepared according to the literature[2].

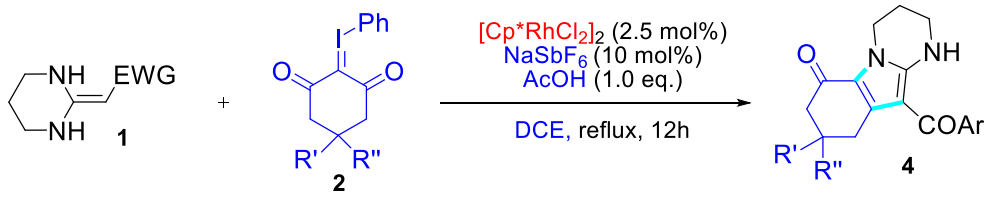
2. General Procedure for the Preparation of 3-5

2.1 Synthesis of pyrimido[1,2-a]indole derivatives (PIIDOs) 3.



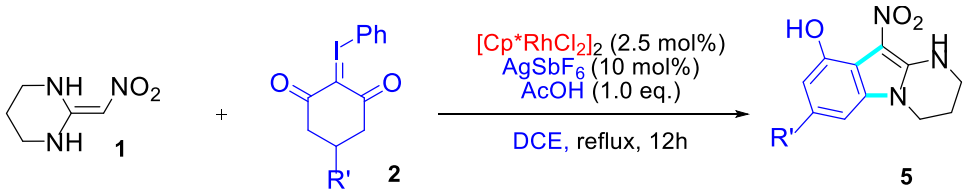
Enaminones (**1**, 1.1 mmol), iodonium ylides (**2**, 1.0 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $AgSbF_6$ (10.0 mol%), and acetic acid (HOAc, 1.0 mmol) were combined in a 25 mL round-bottom flask. The mixture was stirred and heated under reflux in acetone (5 mL) for 8 hours, or until the iodonium ylides were completely consumed. Subsequently, the mixture was allowed to cool to room temperature, followed by the addition of dichloromethane (DCM, 15 mL×2). The organic phase was washed with a sodium chloride (NaCl) solution (10 mL), dried over sodium sulfate (Na_2SO_4), concentrated, and purified by flash column chromatography to yield compound **3**.

2.2 Synthesis of pyrimido[1,2-a]indole derivatives (PIIDOs) 4.



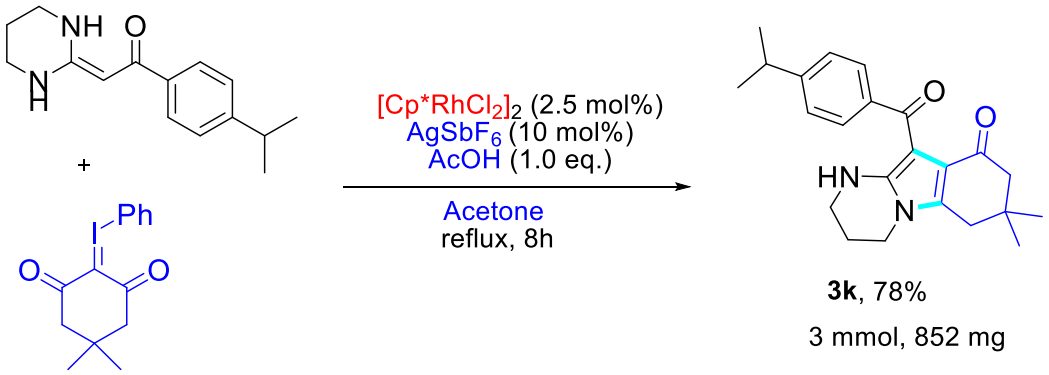
Enaminones (**1**, 1.1 mmol), iodonium ylides (2, 1.0 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $NaSbF_6$ (10.0 mol%), and acetic acid (1.0 mmol) were added to a 25 mL round-bottom flask. The mixture was stirred and heated under reflux in dichloroethane (5 mL) for 12 hours, or until the iodonium ylides were completely consumed. Following this, the mixture was cooled to room temperature, and dichloromethane (DCM, 15 mL × 2) was added. The organic layer was washed with a sodium chloride (NaCl) solution (10 mL), dried over sodium sulfate (Na_2SO_4), concentrated, and purified by flash column chromatography to yield compounds **4**.

2.3 Synthesis of pyrimido[1,2-a]indole derivatives (PIIDOs) 5.



Enaminones (**1**, 1.1 mmol), iodonium ylides (2, 1.0 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $AgSbF_6$ (10.0 mol%), and acetic acid (1.0 mmol) were added to a 25 mL round-bottom flask. The mixture was stirred and heated under reflux in dichloroethane (5 mL) for 12 hours, or until the iodonium ylides were completely consumed. Following this, the mixture was cooled to room temperature, and dichloromethane (DCM, 15 mL × 2) was added. The organic layer was washed with a sodium chloride (NaCl) solution (10 mL), dried over sodium sulfate (Na_2SO_4), concentrated, and purified by flash column chromatography to yield compounds **5**.

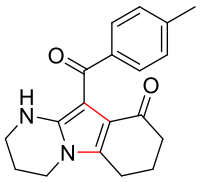
2.4 Synthesis of pyrimido[1,2-a]indole derivatives (PIIDOs) 3k.



Enaminones (**1**, 3.3 mmol), iodonium ylides (**2**, 3.0 mmol), $[Cp^*RhCl_2]_2$ (2.5 mol%), $AgSbF_6$ (10.0 mol%), and acetic acid (HOAc, 3.0 mmol) were combined in a 25 mL round-bottom flask. The mixture was stirred and heated under reflux in acetone (10 mL) for 8 hours, or until the iodonium ylides were completely consumed. Subsequently, the mixture was allowed to cool to room temperature, followed by the addition of dichloromethane (DCM, 60 mL×2). The organic phase was washed with a sodium chloride (NaCl) solution (30 mL), dried over sodium sulfate (Na_2SO_4), concentrated, and purified by flash column chromatography to yield compound **3k** 852 mg, yield is 78%.

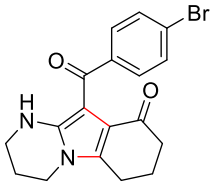
3. Spectroscopic Data.

10-(4-methylbenzoyl)-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3a)



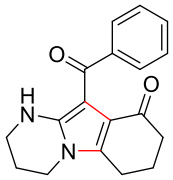
Yellow solid (70%, 215mg); Mp: 231.7-232.7 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.00-2.05 (m, 2H, CH_2), 2.19 (t, J = 6.12 Hz, 2H, CH_2), 2.32 (s, 3H, CH_3), 2.70 (t, J = 6.12 Hz, 2H, CH_2), 3.34-3.36 (m, 2H, CH_2), 3.88 (t, J = 5.94 Hz, 2H, CH_2), 7.08 (d, J = 7.92 Hz, 2H, ArH), 7.38 (d, J = 7.98 Hz, 2H, ArH), 7.78 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 21.1, 21.1, 21.5, 22.6, 38.3, 38.4, 40.7, 96.6, 116.1, 128.1, 128.9, 139.6, 140.0, 142.1, 148.8, 187.9, 189.9. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{20}O_2N_2Na$ [$(M+Na)^+$], 331.1417; found, 331.1416.

10-(4-bromobenzoyl)-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3b)



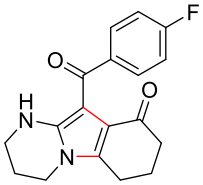
Yellow solid (85%, 316mg); Mp: 288.2-289.2 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 2.10-2.15 (m, 2H, CH_2), 2.17-2.22 (m, 2H, CH_2), 2.34 (t, J = 6.00 Hz, 2H, CH_2), 2.66 (t, J = 6.15 Hz, 2H, CH_2), 3.48-3.50 (m, 2H, CH_2), 3.86 (t, J = 6.00 Hz, 2H, CH_2), 7.43-7.47 (m, 4H, ArH), 7.94 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 21.0, 21.4, 22.5, 38.0, 38.2, 40.5, 97.4, 116.3, 124.5, 129.9, 130.5, 141.3, 141.4, 149.3, 188.9, 190.8. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{17}O_2N_2$ [(M+Na)$^+$], 395.0366; found, 395.0365.

10-benzoyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3c)



Yellow solid (82%, 241mg); Mp: 233.1-234.1 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6): δ = 2.09-2.13 (m, 2H, CH_2), 2.17-2.21 (m, 2H, CH_2), 2.32 (t, J = 6.12 Hz, 2H, CH_2), 2.65 (t, J = 6.12 Hz, 2H, CH_2), 3.47-3.50 (m, 2H, CH_2), 3.85 (t, J = 6.00 Hz, 2H, CH_2), 7.33 (t, J = 7.68 Hz, 2H, ArH), 7.40 (t, J = 7.26 Hz, 1H, ArH), 7.56 (t, J = 7.08 Hz, 2H, ArH), 7.92 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$-d_6): δ = 21.1, 21.4, 22.6, 38.2, 40.5, 97.6, 116.6, 127.3, 128.1, 130.0, 140.8, 142.6, 149.0, 190.5, 190.6. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{19}O_2N_2$ [(M+H)$^+$], 295.1441; found, 295.1440.

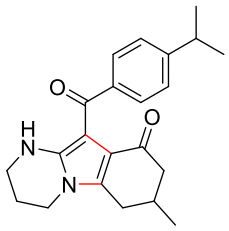
10-(4-fluorobenzoyl)-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3d)



Yellow solid (85%, 265mg); Mp: 196.8-197.8 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.99-2.04 (m, 2H, CH_2), 2.18 (t, J = 6.05 Hz, 2H, CH_2), 2.69 (t, J = 6.10 Hz, 2H, CH_2), 3.36-3.38 (m, 2H, CH_2), 3.88 (t, J = 5.95 Hz, 2H, CH_2), 7.06-7.10 (m, 2H, ArH), 7.48-7.51 (m, 2H, ArH), 7.88 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.0, 21.1, 22.5, 38.3, 38.3, 40.2, 114.3 (d, J = 21.3 Hz), 131.0 (d, J = 8.8 Hz), 131.0 (d, J = 8.8 Hz), 139.4 (d, J = 3.8 Hz), 142.6, 149.1, 163.4 (d, J = 245.0 Hz), 186.5, 190.0; ^{19}F NMR (470 MHz, DMSO-d_6): δ = -111.9. HRMS (TOF

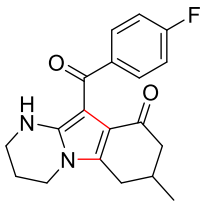
ES$^+$): *m/z* calcd for $C_{18}H_{17}O_2N_2Na$ [(M+Na)$^+$], 335.1166; found, 335.1165.

10-(4-isopropylbenzoyl)-7-methyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3e)



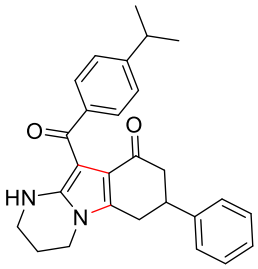
Yellow solid (84%, 294mg); Mp: 227.9-228.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 1.26 (t, J = 5.95 Hz, 6H, $2CH_3$), 2.09-2.18 (m, 4H, $1CH_3$, $1CH_2$), 2.33-2.37 (m, 2H, CH_2), 2.63-2.68 (m, 2H, CH_2), 2.89-2.95 (m, 1H, CH_2), 3.45-3.47 (m, 2H, CH_2), 3.83-3.87 (m, 2H, CH_2), 7.18 (d, J = 8.10 Hz, 2H, ArH), 7.54 (d, J = 8.20 Hz, 2H, ArH), 7.87 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 21.2, 21.4, 22.6, 23.8, 34.0, 38.2, 38.2, 40.5, 97.5, 116.7, 125.3, 128.6, 139.9, 140.6, 140.7, 148.9, 150.9, 190.1, 190.5. HRMS (TOF ES$^+$): *m/z* calcd for $C_{22}H_{27}O_2N_2$ [(M+H)$^+$], 351.2067; found, 351.2063.

10-(4-fluorobenzoyl)-7-methyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3f)



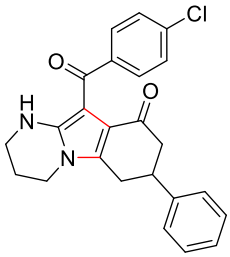
Yellow solid (85%, 277mg); Mp: 267.7-268.7 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.07 (d, J = 6.30 Hz, 3H, CH_3), 1.98-2.09 (m, 3H, $2CH_2$), 2.16-2.20 (m, 1H, CH_2), 2.25-2.36 (m, 2H, CH_2), 2.82-2.85 (m, 1H, CH), 3.35-3.39 (m, 2H, CH_2), 3.82-3.93 (m, 2H, CH_2), 7.06-7.10 (m, 2H, ArH), 7.47-7.50 (m, 2H, ArH), 7.86 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.0, 21.3, 29.1, 30.5, 38.3, 40.2, 46.8, 96.5, 114.3 (d, J = 21.3 Hz), 115.4, 131.0 (d, J = 8.8 Hz), 139.4 (d, J = 2.5 Hz), 142.1, 149.3, 163.4 (d, J = 245.0 Hz), 186.5, 189.9; ^{19}F NMR (470 MHz, DMSO-d_6): δ = -111.9. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{20}O_2N_2F$[(M+H)$^+$], 327.1503; found, 327.1501.

10-(4-isopropylbenzoyl)-7-phenyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3g)



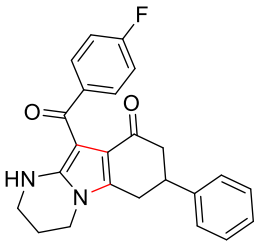
Yellow solid (79%, 325mg); Mp:197.9-198.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 1.24-1.27 (m, 6H, $2CH_3$), 2.16 (t, J = 5.75 Hz, 2H, $1CH_2$), 2.63 (t, J = 2.90 Hz, 2H, CH_2), 2.79-2.84 (m, 1H, CH), 2.91-2.99 (m, 2H, CH_2), 3.44-3.54 (m, 3H, $1CH_2$, $1CH_2$), 3.78-3.86 (m, 2H, CH_2), 7.20 (d, J = 8.15 Hz, 2H, ArH), 7.26 (d, J = 5.90 Hz, 1H, ArH), 7.30 (d, J = 7.55 Hz, 2H, ArH), 7.35 (t, J = 7.45 Hz, 2H, ArH), 7.56 (d, J = 8.20 Hz, 2H, ArH), 7.88 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 21.2, 23.8, 23.9, 29.4, 34.0, 38.2, 40.6, 41.1, 45.2, 97.4, 116.4, 125.4, 126.8, 127.1, 128.7, 128.8, 139.8, 143.2, 149.2, 151.0, 189.3, 190.2. HRMS (TOF ES$^+$): *m/z* calcd for $C_{27}H_{29}O_2N_2$ [(M+H)$^+$], 413.2224; found, 413.2222.

10-(4-chlorobenzoyl)-7-phenyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3h)



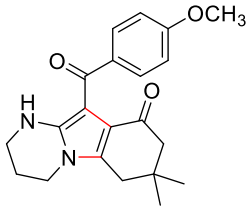
Yellow solid (85%, 343mg); Mp: 198.7-199.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6): δ = 2.03 (t, J = 5.70 Hz, 2H, CH_2), 2.31-2.34 (m, 1H, CH_2), 2.59-2.63 (m, 1H, CH_2), 2.85-2.89 (m, 1H, CH_2), 3.03-3.06 (m, 1H, CH_2), 3.36-3.40 (m, 2H, CH_2), 3.45-3.49 (m, 1H, CH), 3.83-3.86 (m, 1H, CH_2), 3.93-3.96 (m, 1H, CH_2), 7.25 (t, J = 7.32 Hz, 1H, ArH), 7.33-7.36 (m, 6H, ArH), 7.46-7.48 (m, 2H, ArH), 7.95 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$-d_6): δ = 20.9, 28.9, 38.3, 40.2, 40.5, 45.3, 96.5, 115.4, 127.1, 127.5, 127.6, 128.9, 130.4, 134.6, 141.7, 142.0, 144.1, 149.5, 186.5, 189.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{22}ClO_2N_2$ [(M+H)$^+$], 405.1364; found, 405.1364.

10-(4-fluorobenzoyl)-7-phenyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3i)



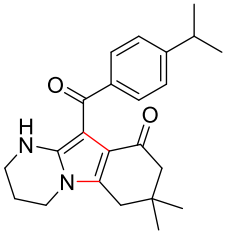
Yellow solid (86%, 333mg); Mp: 256.4-257.4 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.03 (s, 2H, CH_2), 2.33 (d, J = 13.75 Hz, 1H, CH_2), 2.62 (t, J = 15.60 Hz, 1H, CH_2), 2.87-2.90 (m, 1H, CH_2), 3.03-3.07 (m, 1H, CH_2), 3.36 (s, 2H, CH_2), 3.48 (d, J = 10.75 Hz, 1H, CH_2), 3.84 (t, J = 5.80 Hz, 1H, CH_2), 3.95 (t, J = 6.15 Hz, 1H, CH_2), 7.11 (t, J = 8.55 Hz, 2H, ArH), 7.26 (t, J = 6.90 Hz, 1H, ArH), 7.34-7.41 (m, 4H, ArH), 7.53 (d, J = 5.70 Hz, 2H, ArH), 7.92 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.0, 28.9, 38.3, 39.8, 40.2, 45.5, 96.5, 114.3 (d, J = 21.3 Hz), 115.5, 127.1, 127.5, 128.9, 131.0 (d, J = 8.8 Hz), 139.3, 141.8, 144.1, 149.4, 163.5 (d, J = 245.0 Hz), 186.6, 189.0; ^{19}F NMR (470 MHz, DMSO-d_6): δ = -111.7. HRMS (TOF ES$^+$): m/z calcd for $C_{24}H_{22}O_2N_2F$ [(M+H)$^+$], 389.1660; found, 389.1664.

10-(4-methoxybenzoyl)-7,7-dimethyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3j)



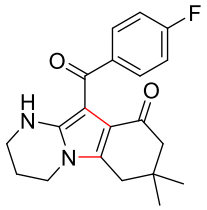
Yellow solid (88%, 309mg); Mp: 221.7-222.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6): δ = 1.13 (s, 6H, $2CH_3$), 2.19 (t, J = 5.76 Hz, 2H, CH_2), 2.26 (s, 2H, CH_2), 2.54 (s, 2H, CH_2), 3.46-3.48 (m, 2H, CH_2), 3.83 (t, J = 6.06 Hz, 5H, $1CH_2$, $1CH_3$), 6.82-6.84 (m, 2H, ArH), 7.56-7.58 (m, 2H, ArH), 5.60 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$-d_6): δ = 21.2, 28.7, 35.0, 35.4, 38.2, 40.5, 52.7, 55.2, 97.2, 112.5, 115.5, 130.5, 134.9, 139.1, 148.9, 161.3, 189.4, 190.6. HRMS (TOF ES$^+$): m/z calcd for $C_{21}H_{25}O_3N_2$ [(M+H)$^+$], 353.1860; found, 353.1861.

10-(4-isopropylbenzoyl)-7,7-dimethyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3k)



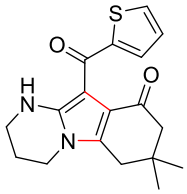
Yellow solid (82%, 298mg); Mp: 225.2-226.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.07 (d, J = 11.9 Hz, 6H, 2CH_3), 1.15-1.21 (m, 6H, 2CH_3), 1.99-2.04 (m, 2H, CH_2), 2.12 (s, 2H, CH_2), 3.03-3.07 (m, 1H, CH_2), 2.61 (s, 2H, CH_2), 2.87-2.92 (m, 1H, CH), 3.33-3.37 (m, 2H, CH_2), 3.86 (t, J = 5.95 Hz, 2H, CH_2), 7.13 (d, J = 8.15 Hz, 2H, ArH), 7.26 (t, J = 6.90 Hz, 1H, ArH), 7.38 (d, J = 8.20 Hz, 2H, ArH), 7.78 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.1, 24.2, 28.7, 33.8, 34.8, 35.0, 38.3, 40.2, 52.7, 60.2, 96.4, 114.7, 125.4, 129.0, 140.3, 140.4, 149.0, 150.4, 187.8, 189.9. HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{29}O_2N_2$ [(M+H)$^+$], 365.2224; found, 365.2221.

10-(4-fluorobenzoyl)-7,7-dimethyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3l)



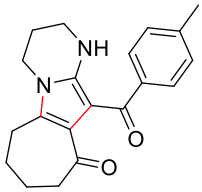
Yellow solid (89%, 302mg); Mp: 244.4-245.4 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.06 (s, 6H, 2CH_3), 2.03 (t, J = 5.60 Hz, 2H, CH_2), 2.12 (s, 2H, CH_2), 2.50-2.52 (m, 2H, CH_2), 3.87 (d, J = 5.90 Hz, 2H, CH_2), 7.07-7.10 (m, 2H, ArH), 7.45-7.48 (m, 2H, ArH), 7.86 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.0, 28.7, 34.7, 35.0, 38.2, 39.9, 52.7, 96.4, 114.2, 114.4, 130.9 (d, J = 8.8 Hz), 139.4 130.9 (d, J = 2.5 Hz), 140.9, 149.3, 163.4 (d, J = 245.0 Hz), 186.6, 190.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{22}O_2N_2F$ [(M+H)$^+$], 341.1660; found, 341.1655.

10-(4-fluorobenzoyl)-7,7-dimethyl-1,3,4,6,7,8-hexahydropyrimido[1,2-*a*]indol-9(2*H*)-one (3m)



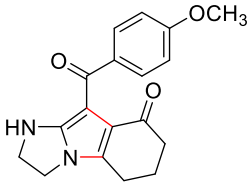
Yellow solid (72%, 236mg); Mp: 246.4-247.4 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.09 (s, 6H, 2CH_3), 2.00-2.03 (m, 2H, CH_2), 2.21 (s, 2H, CH_2), 2.62 (s, 2H, CH_2), 3.86 (d, J = 5.90 Hz, 2H, CH_2), 7.00-7.01 (m, 1H, ArH), 7.14-7.15 (m, 1H, ArH), 7.59 (s, 1H, NH), 7.64-7.65 (m, 1H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.1, 28.8, 34.8, 35.0, 38.3, 39.9, 52.7, 96.3, 114.7, 127.4, 130.3, 131.3, 141.3, 146.9, 148.9, 179.4, 190.2. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{21}O_2N_2S$ [(M+H)$^+$], 329.1318; found, 329.1316.

11-(4-methylbenzoyl)-1,2,3,4,6,7,8,9-octahydro-10*H*-cyclohepta[4,5]pyrrolo[1,2-*a*]pyrimidin-10-one (3n)



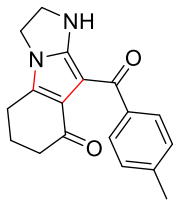
Yellow solid (20%, 64mg); Mp: 198.7-199.7 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6): δ = 1.86-1.92 (m, 4H, 2CH_2), 2.17 (t, J = 5.76 Hz, 2H, CH_2), 2.33 (s, 3H, CH_3), 2.53 (t, J = 6.54 Hz, 2H, CH_2), 2.74 (t, J = 5.76 Hz, 2H, CH_2), 3.41-3.44 (m, 2H, CH_2), 3.80 (t, J = 6.06 Hz, 2H, CH_2), 7.10 (d, J = 7.92 Hz, 2H, ArH), 7.43 (d, J = 7.98 Hz, 2H, ArH), 7.58 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$-d_6): δ = 21.5, 21.5, 22.4, 25.0, 25.7, 37.9, 40.5, 44.2, 99.4, 121.3, 127.7, 128.3, 132.8, 139.8, 139.9, 147.8, 190.0, 197.6. HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{23}O_2N_2$ [(M+H)$^+$], 323.1754; found, 323.1760.

9-(4-methoxybenzoyl)-1,2,3,5,6,7-hexahydro-8*H*-imidazo[1,2-*a*]indol-8-one (3o)



Yellow solid (80%, 248mg); Mp: 273.9-274.9 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.98-2.03 (m, 2H, CH_2), 2.21 (t, J = 6.00 Hz, 2H, CH_2), 2.71 (t, J = 6.05 Hz, 2H, CH_2), 3.79 (s, 3H, OCH_3), 3.90 (t, J = 7.90 Hz, 2H, CH_2), 4.04-4.07 (m, 2H, CH_2), 6.71 (s, 1H, NH), 6.85-6.87 (m, 2H, ArH), 7.55-7.58 (m, 2H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 21.7, 23.0, 38.3, 42.4, 49.1, 55.6, 95.5, 113.0, 119.8, 131.2, 133.9, 139.1, 154.4, 161.6, 187.2, 190.1. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{19}O_3N_2$ [(M+H)$^+$], 311.1390; found, 311.1388.

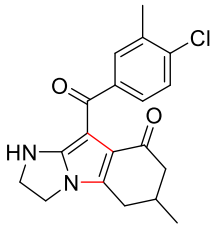
6-methyl-9-(4-methylbenzoyl)-1,2,3,5,6,7-hexahydro-8*H*-imidazo[1,2-*a*]indol-8-one (3p)



Yellow solid (70%, 205mg); Mp: 232.7-233.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 2.11 (t, J = 6.30 Hz, 2H, CH_2), 2.36 (t, J = 4.80 Hz, 5H, CH_3, CH_2), 2.68 (t, J = 6.20 Hz, 2H, CH_2), 4.00-4.07 (m, 4H, 2CH_2), 5.60 (s, 1H, NH), 7.15 (d, J = 7.85 Hz, 2H, ArH), 7.57 (d, J = 8.10 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 21.7, 22.0, 22.9, 38.2, 42.4, 48.9, 97.0, 120.2,

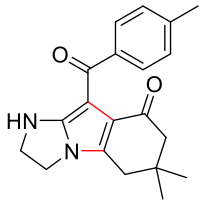
128.1, 128.9, 138.1, 138.3, 140.0, 154.7, 190.3, 191.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{19}O_2N_2$ [(M+H)$^+$], 295.1441; found, 295.1440.

9-(4-chloro-3-methylbenzoyl)-6-methyl-1,2,3,5,6,7-hexahydro-8*H*-imidazo[1,2-*a*]indol-8-one (3q)



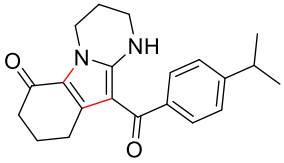
Yellow solid (86%, 294mg); Mp: 244.6-245.6 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.07 (d, J = 6.54 Hz, 3H, CH_3), 2.00-2.05 (m, 1H, CH_2), 2.17-2.20 (m, 1H, CH_2), 2.27-2.33 (m, 4H, 1CH_3, 1CH), 2.36-2.41 (m, 1H, CH_2), 2.79-2.83 (m, 1H, CH_2), 3.92-3.96 (m, 2H, CH_2), 4.02-4.09 (m, 2H, CH_2), 6.95 (s, 1H, NH), 7.32 (s, 2H, ArH), 7.48 (s, 1H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.0, 21.2, 29.6, 30.9, 42.3, 46.7, 49.1, 95.3, 119.0, 128.2, 131.5, 134.6, 135.5, 139.2, 140.6, 155.2, 187.0, 190.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{19}O_2N_2ClNa$ [(M+Na)$^+$], 365.1027; found, 365.1031.

6,6-dimethyl-9-(4-methylbenzoyl)-1,2,3,5,6,7-hexahydro-8*H*-imidazo[1,2-*a*]indol-8-one (3r)



Yellow solid (80%, 257mg); ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 0.81 (s, 6H, 2CH_3), 1.92 (s, 2H, CH_2), 2.06 (s, 3H, CH_3), 2.29 (s, 2H, CH_2), 2.66 (s, 2H, CH_2), 3.74-3.78 (m, 4H, 2CH_2), 5.68 (s, 1H, NH), 6.81 (d, J = 7.90 Hz, 2H, ArH), 7.22 (d, J = 8.05 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 21.4, 28.3, 35.2, 35.5, 42.1, 48.7, 52.4, 96.1, 118.5, 127.8, 128.6, 136.7, 138.2, 140.4, 154.6, 189.2, 190.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{23}O_2N_2$ [(M+H)$^+$], 323.1754; found, 323.1753.

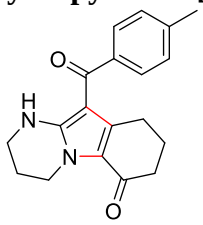
10-(4-isopropylbenzoyl)-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4a)



Yellow solid (48%, 161mg); Mp: 242.9–243.9 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 1.28 (d, J = 6.90 Hz, 6H, 2CH_3), 1.82 (t, J = 6.15 Hz, 2H, CH_2), 2.11 (t, J = 5.75 Hz, 2H, CH_2), 2.20 (t, J

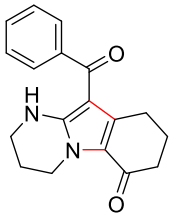
= 5.95 Hz, 2H, CH_2), 2.37 (t, *J* = 6.00 Hz, 2H, CH_2), 2.96 (t, *J* = 6.90 Hz, 1H, CH), 3.47-3.49 (m, 2H, CH_2), 4.39 (t, *J* = 5.95 Hz, 2H, CH_2), 7.27 (d, *J* = 7.15 Hz, 2H, ArH), 7.42-7.44 (m, 2H, ArH), 7.76 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 20.9, 23.9, 24.7, 25.2, 34.1, 38.1, 38.2, 42.5, 103.8, 121.9, 126.2, 127.6, 138.5, 139.3, 149.8, 151.6, 187.0, 192.2. HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{24}O_2N_2Na$ [$(M+Na)^+$], 359.1730; found, 359.1735.

10-(4-methylbenzoyl)-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4b)



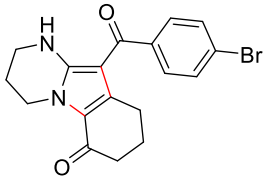
Yellow solid (52%, 160mg); Mp: 225.8–226.8 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.70-1.74 (m, 2H, CH_2), 1.95-1.99 (m, 2H, CH_2), 2.08 (t, *J* = 6.00 Hz, 2H, CH_2), 2.24 (t, *J* = 5.94 Hz, 2H, CH_2), 2.37 (s, 3H, CH_3), 3.36-3.39 (m, 2H, CH_2), 4.22 (t, *J* = 5.88 Hz, 2H, CH_2), 7.26 (d, *J* = 7.80 Hz, 2H, ArH), 7.35 (d, *J* = 7.98 Hz, 2H, ArH), 7.89 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.8, 21.5, 24.6, 25.1, 38.1, 42.8, 103.4, 121.5, 127.7, 129.1, 137.6, 139.6, 140.4, 149.5, 185.7, 190.6. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{20}O_2N_2Na$ [$(M+Na)^+$], 331.1417; found, 331.1413.

10-benzoyl-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4c)



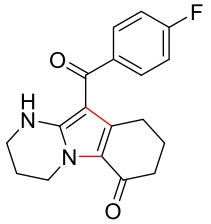
Yellow solid (65%, 191mg); Mp: 200.6–201.6 °C; ^{1}H NMR (600 MHz, $CDCl_3$-d_6): δ = 1.17-1.83 (m, 2H, CH_2), 2.05-2.14 (m, 4H, $2CH_2$), 2.36 (t, *J* = 6.18 Hz, 2H, CH_2), 3.48-3.50 (m, 2H, CH_2), 4.39 (t, *J* = 5.94 Hz, 2H, CH_2), 7.41-7.48 (m, 5H, ArH), 7.79 (s, 1H, NH); ^{13}C NMR (150 MHz, $CDCl_3$-d_6): δ = 20.9, 24.6, 25.0, 38.1, 38.2, 42.5, 103.8, 122.1, 127.3, 128.2, 130.3, 138.3, 141.8, 149.8, 187.0, 190.1. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{19}O_2N_2$ [$(M+H)^+$], 295.1441; found, 295.1443.

10-(4-bromobenzoyl)-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4d)



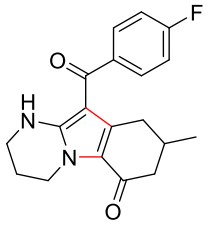
Yellow solid (66%, 245mg); Mp: 231.7–232.7 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 1.81-1.86 (m, 2H, CH_2), 2.05-2.15 (m, 4H, $2CH_2$), 2.38 (t, J = 6.05 Hz, 2H, CH_2), 3.48-3.50 (m, 2H, CH_2), 4.38 (t, J = 5.95 Hz, 2H, CH_2), 7.35-7.39 (m, 2H, ArH), 7.53-7.58 (m, 2H, ArH), 7.77 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 20.9, 24.5, 25.2, 38.1, 38.1, 42.5, 103.6, 122.2, 124.8, 129.1, 131.4, 137.8, 140.5, 149.9, 187.2, 190.6. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{17}O_2N_2BrNa$ [(M+Na)$^+$], 395.0366; found, 395.0364.

10-(4-fluorobenzoyl)-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4e)



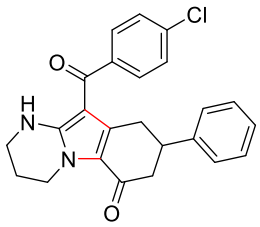
Yellow solid (68%, 212mg); Mp: 206.8–207.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 1.82-1.86 (m, 2H, CH_2), 2.10-2.17 (m, 4H, $2CH_2$), 2.38 (t, J = 6.10 Hz, 2H, CH_2), 3.48-3.50 (m, 2H, CH_2), 4.39 (t, J = 5.95 Hz, 2H, CH_2), 7.09-7.14 (m, 2H, ArH), 7.48-7.52 (m, 2H, ArH), 7.74 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 20.9, 24.6, 25.2, 38.1, 38.2, 42.5, 103.7, 115.2 (d, J = 22.5 Hz), 122.1, 129.7 (d, J = 7.5 Hz), 137.9 (d, J = 3.8 Hz), 137.9, 149.8, 164.0 (d, J = 248.8 Hz), 187.1, 190.7; ^{19}F NMR (470 MHz, $CDCl_3$-d_6): δ = -109.6. HRMS (TOF ES$^+$): *m/z* calcd for $C_{18}H_{17}O_2N_2FNa$ [(M+Na)$^+$], 335.1173; found, 335.1175.

10-(4-fluorobenzoyl)-8-methyl-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4f)



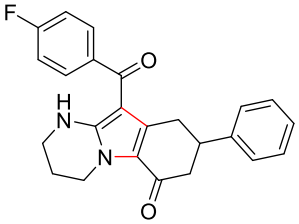
Yellow solid (62%, 202mg); Mp: 222.6–223.6 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 0.92 (d, J = 6.25 Hz, 3H, CH_3), 1.94 (t, J = 9.20 Hz, 1H, CH_2), 2.06-2.18 (m, 5H, CH_2), 2.36-2.40 (m, 1H, CH), 3.46-3.51 (m, 2H, CH_2), 4.36-4.40 (m, 2H, CH_2), 7.10-7.13 (m, 2H, ArH), 7.50-7.52 (m, 2H, ArH), 7.72 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 20.9, 21.0, 32.3, 33.3, 38.1, 42.4, 46.4, 103.6, 115.2 (d, J = 10.2 Hz), 121.9, 129.8 (d, J = 8.8 Hz), 137.3, 137.8 (d, J = 3.8 Hz), 150.0, 164.1 (d, J = 248.8 Hz), 186.8, 190.6; ^{19}F NMR (470 MHz, $CDCl_3$-d_6): δ = -109.5. HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{19}O_2N_2FNa$ [(M+Na)$^+$], 349.1323; found, 349.1324.

10-(4-chlorobenzoyl)-8-phenyl-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4g)



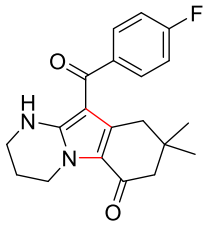
Yellow solid (66%, 266mg); Mp: 242.9–243.8 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 1.96-2.01 (m, 2H, CH_2), 2.13-2.16 (m, 1H, CH_2), 2.35-2.38 (m, 1H, CH_2), 2.50-2.56 (m, 1H, CH_2), 2.66-2.70 (m, 1H, CH_2), 3.16-3.20 (m, 1H, CH_2), 3.37-3.43 (m, 2H, CH_2), 4.25 (t, J = 6.36 Hz, 2H, CH_2), 7.15-7.18 (m, 3H, ArH), 7.25 (t, J = 7.44 Hz, 2H, ArH), 7.46-7.50 (m, 4H, ArH), 7.97 (s, 1H, NH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 20.7, 32.3, 38.2, 42.3, 42.7, 45.1, 103.3, 121.6, 127.0, 127.2, 128.7, 128.9, 129.7, 135.4, 136.3, 140.8, 144.3, 149.9, 184.7, 189.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{22}ClO_2N_2$ [(M+H)$^+$], 405.1364; found, 405.1364.

10-(4-fluorobenzoyl)-8-phenyl-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4h)



Yellow solid (69%, 267mg); Mp: 226.8–227.8 °C; ^{1}H NMR (500 MHz, $CDCl_3$-d_6): δ = 2.05-2.17 (m, 2H, CH_2), 2.35-2.39 (m, 1H, CH_2), 2.52-2.71 (m, 3H, CH_2), 3.19-3.25 (m, 1H, CH), 3.46-3.55 (m, 2H, CH_2), 4.38-4.45 (m, 2H, CH_2), 7.05-7.11 (m, 4H, ArH), 7.19-7.22 (m, 1H, ArH), 7.28 (t, J = 7.25 Hz, 2H, ArH), 7.50-7.54 (m, 2H, ArH), 7.74 (s, 1H, NH); ^{13}C NMR (125 MHz, $CDCl_3$-d_6): δ = 20.9, 32.3, 38.2, 42.5, 42.8, 45.3, 103.7, 115.3 (d, J = 21.3 Hz), 121.9, 126.7, 126.8, 128.6, 129.8 (d, J = 7.5 Hz), 136.8, 137.6 (d, J = 2.5 Hz), 143.4, 150.2, 163.2 (d, J = 248.8 Hz), 185.7, 190.5; ^{19}F NMR (470 MHz, $CDCl_3$-d_6): δ = -109.0. HRMS (TOF ES$^+$): *m/z* calcd for $C_{24}H_{21}O_2N_2FNa$ [(M+Na)$^+$], 411.1479; found, 411.1476.

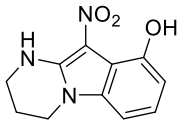
10-(4-fluorobenzoyl)-8,8-dimethyl-1,2,3,4,8,9-hexahydropyrimido[1,2-*a*]indol-6(7*H*)-one (4i)



Yellow solid (70%, 238mg); Mp: 216.2–217.2 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 0.83 (s, 6H, $2CH_3$), 1.98 (d, J = 9.25 Hz, 4H, $2CH_2$), 2.14 (s, 2H, CH_2), 4.21 (t, J = 5.80 Hz, 2H, CH_2),

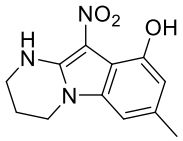
7.28-7.31 (m, 2H, ArH), 7.51-7.53 (m, 2H, ArH), 7.89 (s, 1H, NH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 20.7, 28.4, 35.6, 38.1, 38.7, 42.6, 51.8, 103.7, 115.6, 115.7 (d, J = 21.3 Hz), 120.7, 130.4 (d, J = 8.8 Hz), 135.4, 138.6 (d, J = 2.5 Hz), 149.8, 163.7 (d, J = 246.3 Hz), 185.1, 189.2; ^{19}F NMR (470 MHz, DMSO-d_6): δ = -110.1. HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{22}O_2N_2F$ [(M+H)$^+$], 341.1660; found, 341.1670.

10-nitro-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-9-ol (5a)



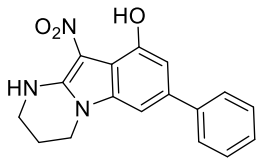
Yellow solid (42%, 97mg); Mp: 303.9–304.9 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.19-2.23 (m, 2H, CH_2), 3.62-3.64 (m, 2H, CH_2), 2.95 (t, J = 5.88 Hz, 2H, CH_2), 6.53 (d, J = 8.16 Hz, 1H, ArH), 6.60 (d, J = 7.86 Hz, 1H, ArH), 7.06 (t, J = 7.98 Hz, 1H, ArH), 9.15 (s, 1H, OH); ^{13}C NMR (150 MHz, DMSO-d_6): δ = 19.5, 38.6, 40.0, 100.2, 106.2, 110.7, 112.2, 126.7, 135.8, 148.8, 150.4. HRMS (TOF ES$^+$): *m/z* calcd for $C_{11}H_{11}O_3N_3Na$ [(M+Na)$^+$], 256.0693; found, 256.0696.

7-methyl-10-nitro-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-9-ol (5b)



Yellow solid (30%, 74mg); Mp: 269.3–270.3 °C; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 2.09 (t, J = 5.52 Hz, 2H, CH_2), 2.28 (s, 3H, CH_3), 3.51 (s, 2H, CH_2), 3.92 (t, J = 5.82 Hz, 2H, CH_2), 6.35 (s, 1H, ArH), 6.55 (s, 1H, ArH), 9.24 (s, 1H, NH), 11.22 (s, 1H, OH); ^{13}C NMR (150 MHz, DMSO-d_6): δ =19.3, 21.8, 38.8, 40.0, 101.6, 103.7, 111.3, 136.4, 137.3, 149.0, 149.9. HRMS (TOF ES$^+$): *m/z* calcd for $C_{12}H_{14}O_3N_3$ [(M+H)$^+$], 248.1030; found, 248.1028.

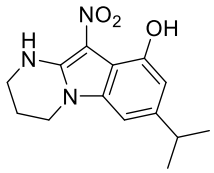
10-nitro-7-phenyl-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-9-ol (5c)



Yellow solid (35%, 108mg); Mp: 268.4–269.4 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 2.13 (d, J = 5.55 Hz, 2H, CH_2), 3.54 (s, 2H, CH_2), 4.02 (t, J = 5.80 Hz, 2H, CH_2), 6.83 (d, J = 1.30 Hz, 1H, ArH), 7.07 (d, J = 1.25 Hz, 1H, ArH), 7.37 (d, J = 7.35 Hz, 1H, ArH), 7.45 (t, J = 7.45 Hz, 2H, ArH), 7.71 (t, J = 7.25 Hz, 2H, ArH), 9.32 (s, 1H, NH), 11.3 (s, 1H, OH); ^{13}C NMR (125 MHz, DMSO-d_6): δ = 19.3, 38.9, 40.0, 99.7, 105.4, 108.8, 112.0, 127.1, 128.0, 129.3, 136.9,

139.5, 140.3, 149.2, 150.3. HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{15}O_3N_3Na$ $[(M+Na)^+]$, 332.1006; found, 332.1003.

7-isopropyl-10-nitro-1,2,3,4-tetrahydropyrimido[1,2-*a*]indol-9-ol (5d)



Yellow solid (20%, 55mg); Mp: 239.3–240.3 °C; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 1.21 (d, J = 6.90 Hz, 6H, $2CH_3$), 2.13 (s, 2H, CH_2), 2.83-2.88 (m, 1H, CH), 3.56 (s, 2H, CH_2), 3.93 (t, J = 5.70 Hz, 2H, CH_2), 6.39 (s, 1H, ArH), 6.55 (s, 1H, ArH), 9.21 (s, 1H, NH), 11.16 (s, 1H, OH); ^{13}C NMR (125 MHz, DMSO-d_6): δ =19.4, 24.3, 34.2, 38.7, 40.0, 98.7, 104.1, 108.8, 112.0, 148.6, 149.0, 150.0. HRMS (TOF ES^+): *m/z* calcd for $C_{14}H_{18}O_3N_3$ $[(M+H)^+]$, 276.1343; found, 276.1342.

4 X-ray Structure and Data[3]

4.1 X-ray Structure and Data of 3d

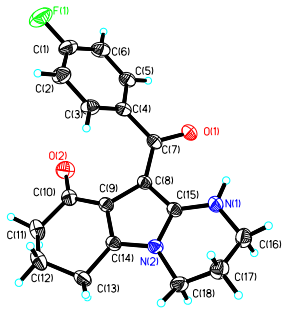


Figure S1. X-Ray crystal structure of **3d**

Table S1. Crystal data and structure refinement for **3d**

Identification code	mo-240227B
Empirical formula	$C_{18}H_{17}FN_2O_2$
Formula weight	312.33 g/mol
Wavelength	0.71073 Å
Crystal system, space group	Triclinic, P -1
Unit cell dimensions	a = 8.5103(2) Å α = 86.6800(10)°. b = 10.3560(3) Å β= 88.9640(10)°. c = 17.9206(4) Å γ= 75.0740(10)°.
Volume	1523.53(7) $Å^3$
Z, Calculated density	4, 1.362 g/cm^3
Absorption coefficient	0.098 mm^{-1}
F(000)	656
Crystal size	0.220 x 0.240 x 0.260 mm
Theta range for data collection	2.04 to 28.38°
Limiting indices	-11<=h<=11, -13<=k<=13, -23<=l<=23
Reflections collected	55404
Independent reflections	7604 [R(int) = 0.0609]
Max. and min. transmission	0.7457 and 0.7263
Structure solution technique	direct methods
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)
Refinement method	Full-matrix least-squares on F^2
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)
Function minimized	$\Sigma w(Fo^2 - Fc^2)^2$
Data / restraints / parameters	7604 / 0 / 415
Goodness-of-fit on F^2	1.085
Final R indices [I>2sigma(I)]	R1 = 0.0622, wR2 = 0.1143
R indices (all data)	R1 = 0.0994, wR2 = 0.1314
Weighting scheme	$w=1/[\sigma^2(Fo^2)+(0.0324P)^2+0.8106P]$ where $P=(Fo^2+2Fc^2)/3$
Largest diff. peak and hole	0.194 and -0.191 $eÅ^{-3}$
R.M.S. deviation from mean	0.039 $eÅ^{-3}$

Table S2. Bond lengths (Å) for **3d**

O4-C25	1.250(2)	O1-C7	1.247(2)
O2-C10	1.224(2)	N2-C14	1.377(3)
N2-C15	1.373(2)	N2-C18	1.466(2)
F2-C19	1.367(2)	O3-C33	1.226(3)
F1-C1	1.363(3)	N4-C27	1.375(2)
N4-C31	1.373(2)	N4-C30	1.464(2)
N3-H3	0.860000	N3-C27	1.340(2)
N3-C28	1.452(2)	N1-H1	0.860000
N1-C15	1.340(2)	N1-C16	1.453(3)
C26-C27	1.401(3)	C26-C25	1.434(3)
C26-C32	1.455(3)	C9-C14	1.369(3)
C9-C8	1.456(3)	C9-C10	1.452(3)
C14-C13	1.488(3)	C4-C7	1.495(3)
C4-C5	1.387(3)	C4-C3	1.388(3)
C22-C25	1.497(3)	C22-C21	1.387(3)
C22-C23	1.388(3)	C8-C15	1.403(3)
C8-C7	1.430(3)	C10-C11	1.511(3)
C32-C33	1.451(3)	C32-C31	1.370(3)
C5-H5	0.930000	C5-C6	1.377(3)
C21-H21	0.930000	C21-C20	1.385(3)
C33-C34	1.516(3)	C31-C36	1.489(3)
C3-H3A	0.930000	C3-C2	1.384(3)
C23-H23	0.930000	C23-C24	1.384(3)
C13-H13A	0.970000	C13-H13B	0.970000
C13-C12	1.519(3)	C30-H30A	0.970000
C30-H30B	0.970000	C30-C29	1.510(3)
C29-H29A	0.970000	C29-H29B	0.970000
C29-C28	1.511(3)	C18-H18A	0.970000
C18-H18B	0.970000	C18-C17	1.509(3)
C20-H20	0.930000	C20-C19	1.363(3)
C28-H28A	0.970000	C28-H28B	0.970000
C2-H2	0.930000	C2-C1	1.368(3)
C6-H6	0.930000	C6-C1	1.371(3)
C16-H16A	0.970000	C16-H16B	0.970000
C16-C17	1.514(3)	C36-H36A	0.970000
C36-H36B	0.970000	C36-C35	1.524(3)
C17-H17A	0.970000	C17-H17B	0.970000
C19-C24	1.363(3)	C12-H12A	0.970000
C12-H12B	0.970000	C12-C11	1.511(3)
C24-H24	0.930000	C34-H34A	0.970000
C34-H34B	0.970000	C34-C35	1.512(4)
C11-H11A	0.970000	C11-H11B	0.970000
C35-H35A	0.970000	C35-H35B	0.970000

4.2 X-ray Structure and Data of 4h

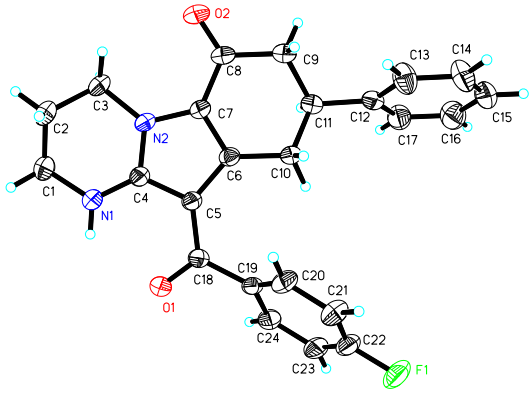


Figure S2. X-Ray crystal structure of **4h**

Table S3. Crystal data and structure refinement for **4h**

Identification code	mo-240227A
Empirical formula	$C_{24}H_{21}FN_2O_2$
Formula weight	388.43 g/mol
Wavelength	0.71073 Å
Crystal system, space group	monoclinic, P 1 21/n 1
Unit cell dimensions	a = 14.4294(6) Å α = 90°. b = 18.3423(10) Å β= 0.1700(10)°. c = 14.5578(6) Å γ= 90°.
Volume	3853.0(3) $Å^3$
Z, Calculated density	1.339 g/cm^3
Absorption coefficient	0.092 mm^{-1}
F(000)	1632
Crystal size	0.200 x 0.240 x 0.260 mm
Theta range for data collection	2.22 to 28.40°
Limiting indices	-19<=h<=18, -24<=k<=24, -19<=l<=19
Reflections collected	85595
Independent reflections	9588 [R(int) = 0.1034]
Max. and min. transmission	0.7457 and 0.7124
Structure solution technique	direct methods
Structure solution program	SHELXT 2018/2 (Sheldrick, 2018)
Refinement method	Full-matrix least-squares on F2
Refinement program	SHELXL 2018/3 (Sheldrick, 2015)
Function minimized	$\Sigma w(Fo^2 - Fc^2)^2$
Data / restraints / parameters	9588 / 50 / 521
Goodness-of-fit on F^2	1.082
Final R indices [I>2sigma(I)]	R1 = 0.0845, wR2 = 0.1539
R indices (all data)	R1 = 0.1521, wR2 = 0.1864
Weighting scheme	$w=1/[\sigma^2(Fo^2)+(0.0462P)^2+3.1389P]$ where $P=(Fo^2+2Fc^2)/3$
Largest diff. peak and hole	0.413 and -0.356 $eÅ^{-3}$
R.M.S. deviation from mean	0.044 $eÅ^{-3}$

Table S4. Bond lengths (Å) for **4h**.

F1-C22	1.362(3)	O1-C18	1.237(3)
O2-C8	1.225(3)	N1-H1	0.860000
N1-C1	1.456(4)	N1-C4	1.325(3)
N2-C3	1.467(3)	N2-C4	1.346(3)
N2-C7	1.405(3)	C1-H1A	0.970000
C1-H1B	0.970000	C1-C2	1.503(5)
C2-H2A	0.970000	C2-H2B	0.970000
C2-C3	1.503(4)	C3-H3A	0.970000
C3-H3B	0.970000	C4-C5	1.434(4)
C5-C6	1.429(4)	C5-C18	1.439(3)
C6-C7	1.376(3)	C6-C10	1.501(4)
C7-C8	1.441(4)	C8-C9	1.503(4)
C9-H9A	0.970000	C9-H9B	0.970000
C9-C11	1.522(4)	C10-H10A	0.970000
C10-H10B	0.970000	C10-C11	1.533(4)
C11-H11	0.980000	C11-C12	1.513(4)
C12-C13	1.376(4)	C12-C17	1.377(4)
C13-H13	0.930000	C13-C14	1.387(4)
C14-H14	0.930000	C14-C15	1.357(5)
C15-H15	0.930000	C15-C16	1.361(5)
C16-H16	0.930000	C16-C17	1.380(5)
C17-H17	0.930000	C18-C19	1.494(4)
C19-C20	1.382(4)	C19-C24	1.389(4)
C20-H20	0.930000	C20-C21	1.384(4)
C21-H21	0.930000	C21-C22	1.368(4)
C22-C23	1.359(5)	C23-H23	0.930000
C23-C24	1.376(4)	C24-H24	0.930000
F2-C45	1.360(3)	O3-C32	1.229(3)
O4-C48	1.238(3)	N3-C25	1.467(3)
N3-C28	1.352(3)	N3-C31	1.402(3)
N4-H4	0.860000	N4-C27	1.449(4)
N4-C28	1.330(3)	C25-H25A	0.970000
C25-H25B	0.970000	C25-H25C	0.970000
C25-H25D	0.970000	C25-C26	1.456(6)
C25-C26A	1.581(11)	C26-H26A	0.970000
C26-H26B	0.970000	C26-C27	1.476(6)
C27-H27A	0.970000	C27-H27B	0.970000
C27-H27C	0.970000	C27-H27D	0.970000
C27-C26A	1.346(11)	C28-C29	1.425(3)
C29-C30	1.424(4)	C29-C48	1.436(4)
C30-C3	1.371(3)	C30-C35	1.500(4)
C31-C32	1.439(4)	C32-C33	1.501(4)
C33-H33A	0.970000	C33-H33B	0.970000

C33-C34	1.502(4)	C34-H34	0.980000
C34-C35	1.503(4)	C34-C36	1.513(3)
C35-H35A	0.970000	C35-H35B	0.970000
C36-C37	1.390000	C36-C41	1.390000
C37-H37	0.930000	C37-C38	1.390000
C38-H38	0.930000	C38-C39	1.390000
C39-H39	0.930000	C39-C40	1.390000
C40-H40	0.930000	C40-C41	1.390000
C41-H41	0.930000	C42-C43	1.389(4)
C42-C47	1.377(4)	C42-C48	1.493(4)
C43-H43	0.930000	C43-C44	1.384(4)
C44-H44	0.930000	C44-C45	1.359(5)
C45-C46	1.354(4)	C46-H46	0.930000
C46-C47	1.380(4)	C47-H47	0.930000
C26A-H26C	0.970000	C26A-H26D	0.970000

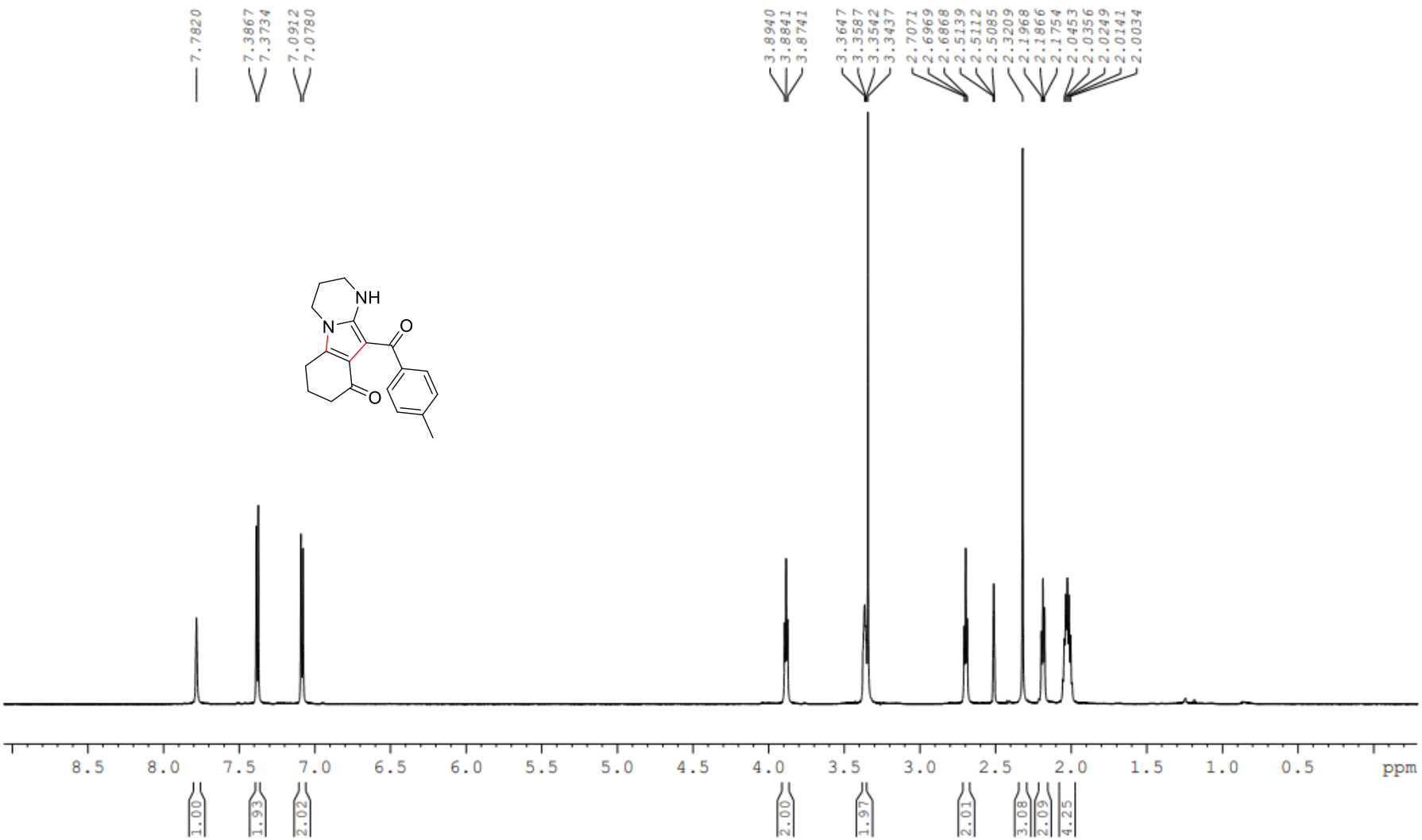


Figure S3. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3a**

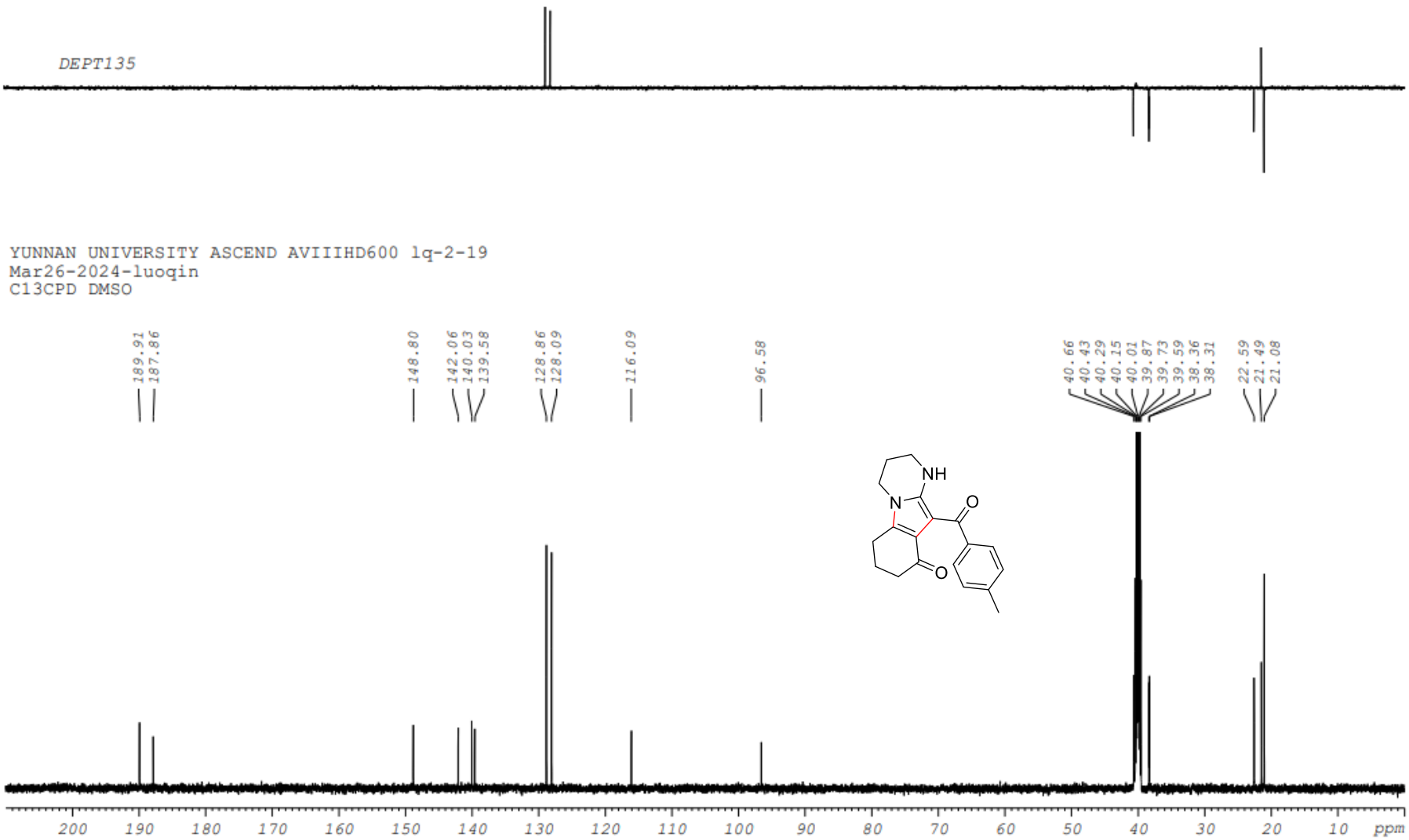


Figure S4. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3a**

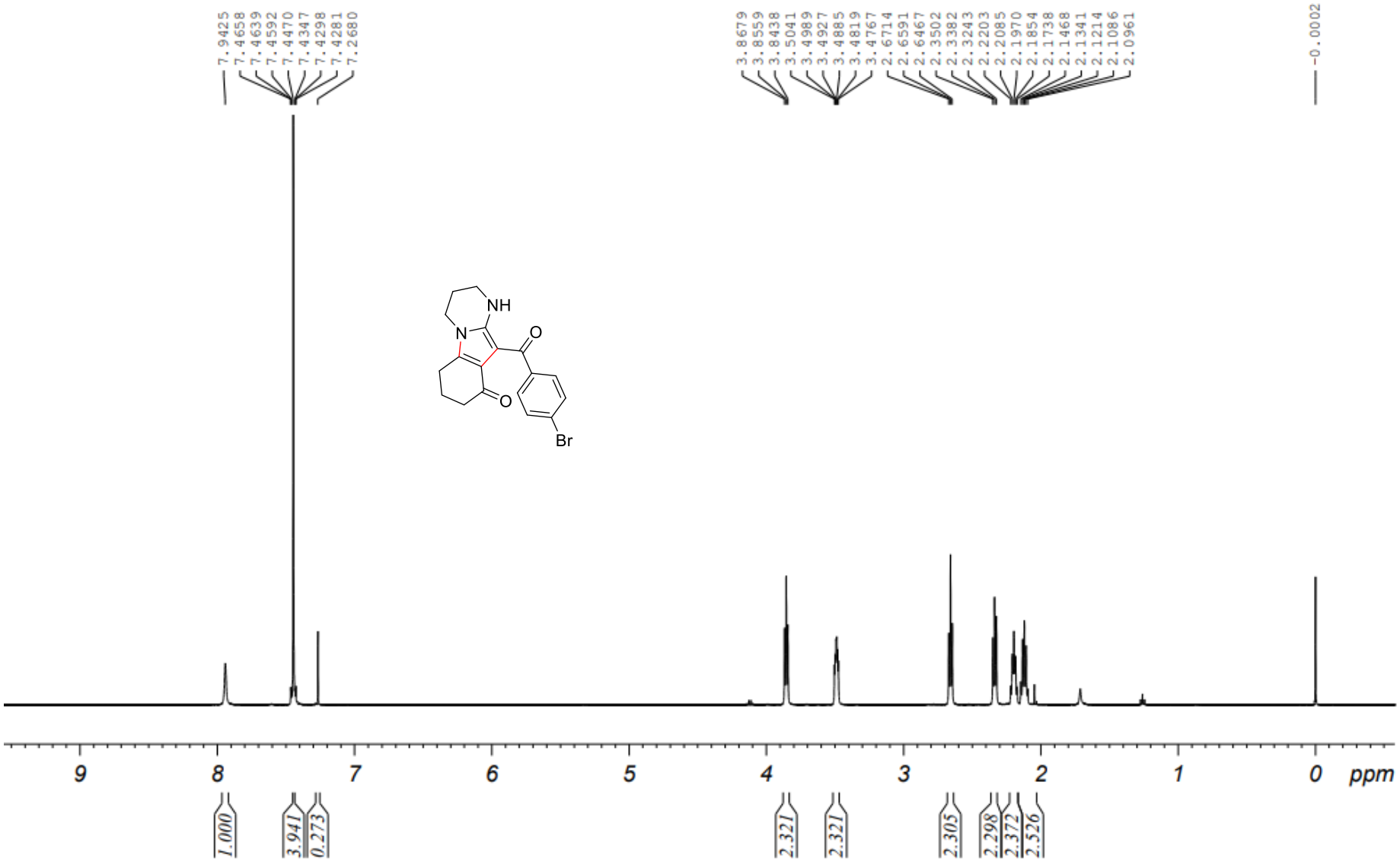


Figure S5. ^{1}H NMR (500 MHz, $CDCl_3$-d_6) spectra of compound **3b**

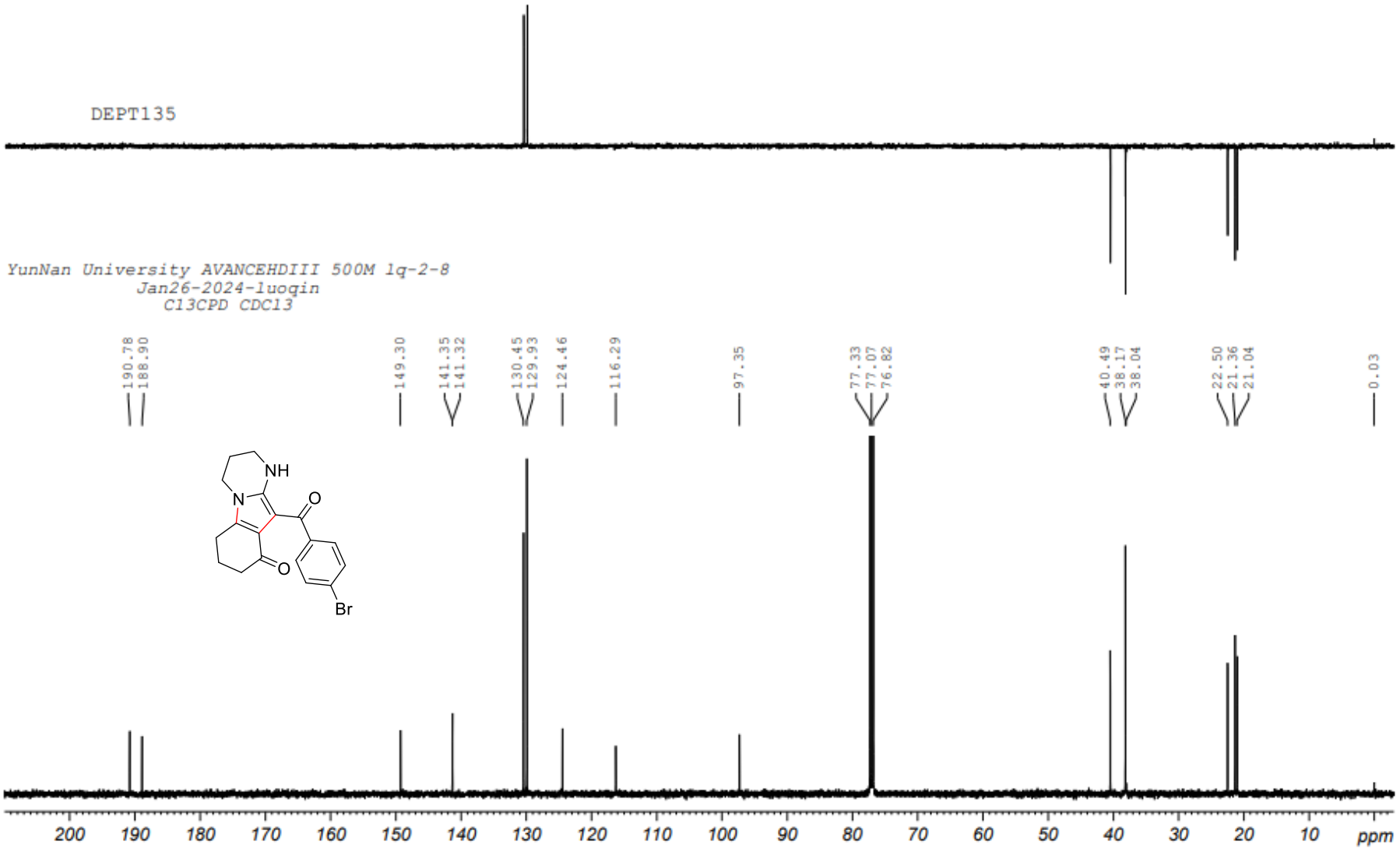


Figure S6. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **3b**

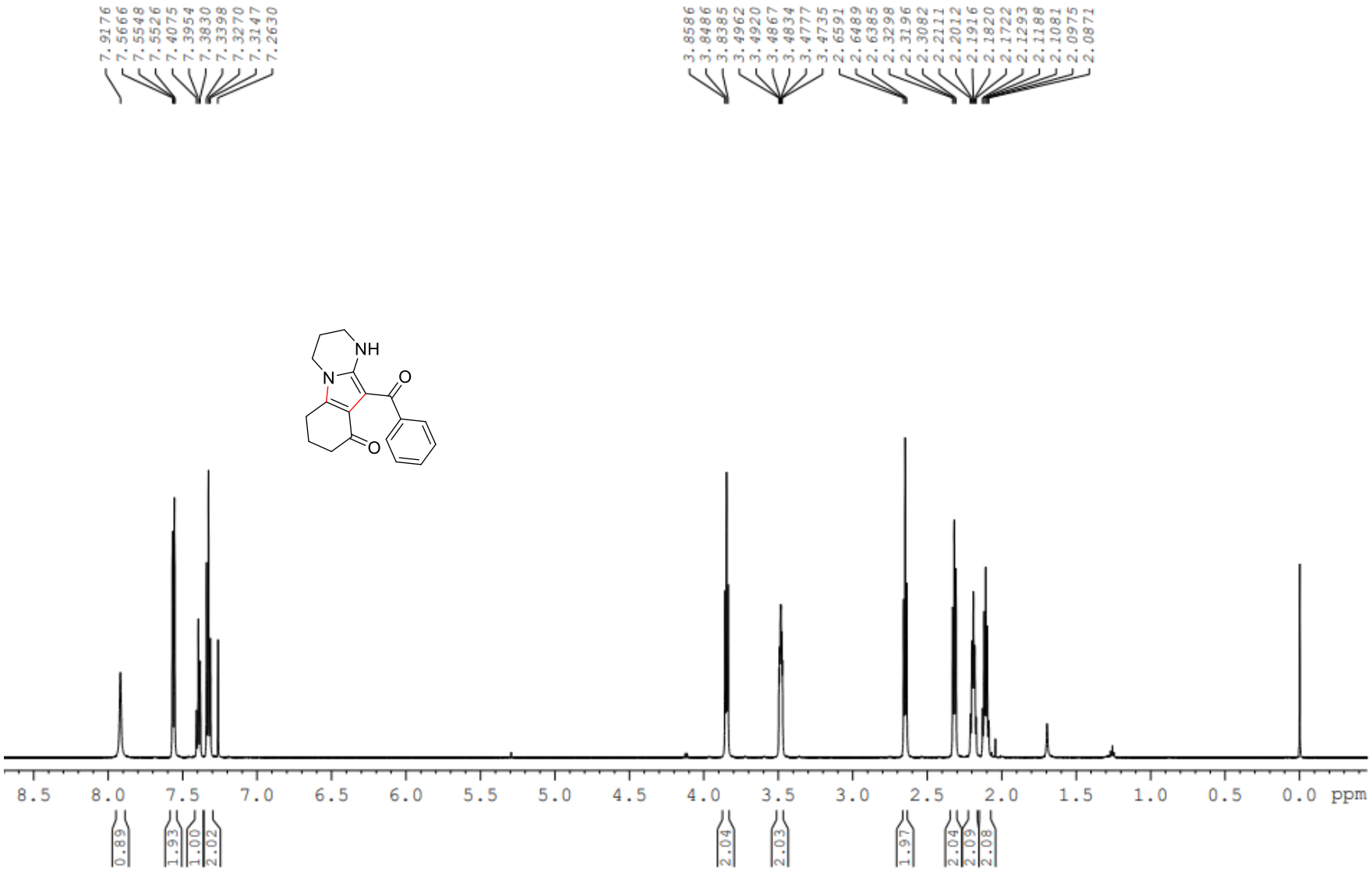


Figure S7. ^{1}H NMR (600 MHz, $CDCl_3$-d_6) spectra of compound **3c**

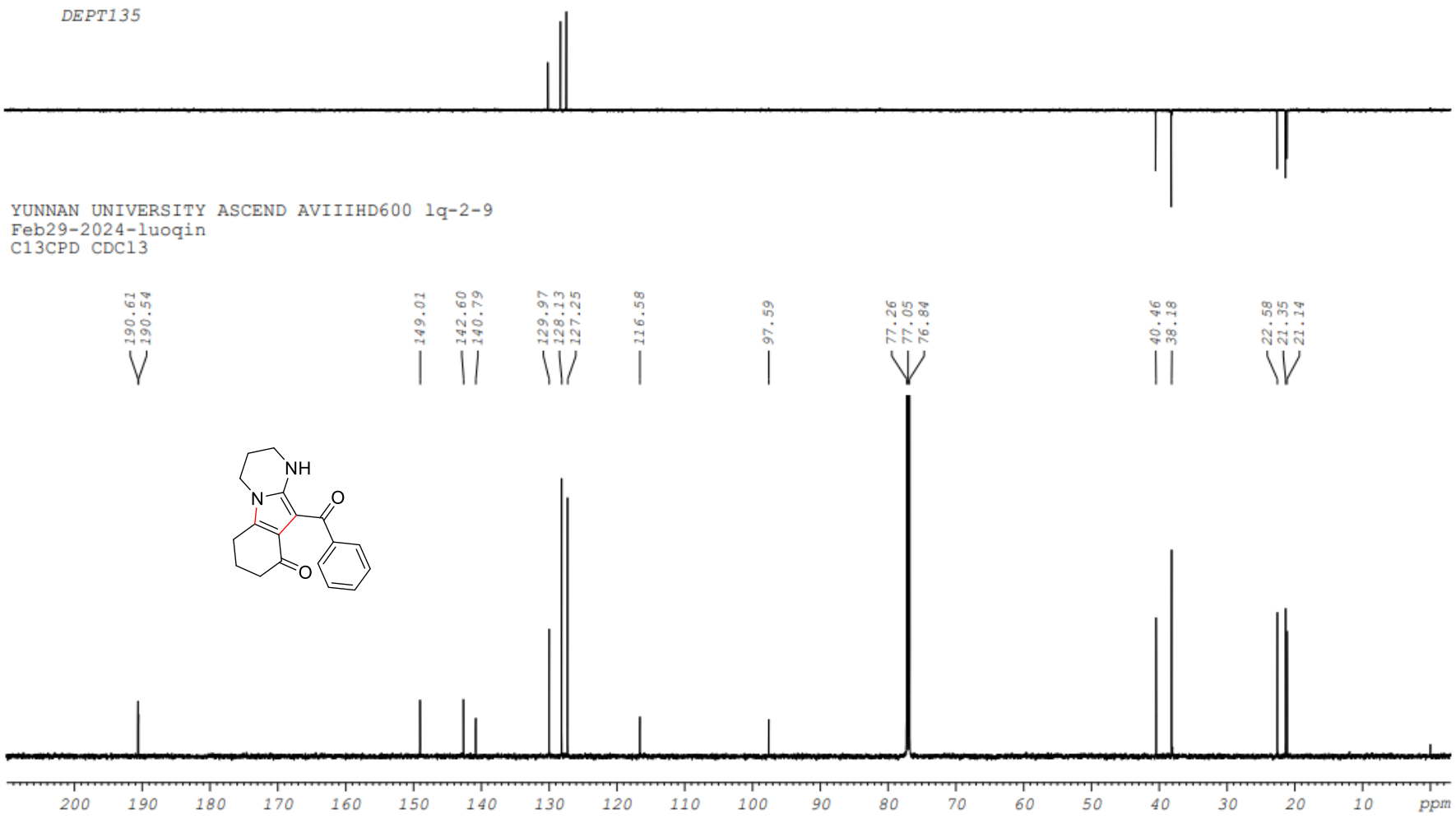


Figure S8. ^{13}C NMR (150 MHz, $CDCl_3$-d_6) spectra of compound **3c**

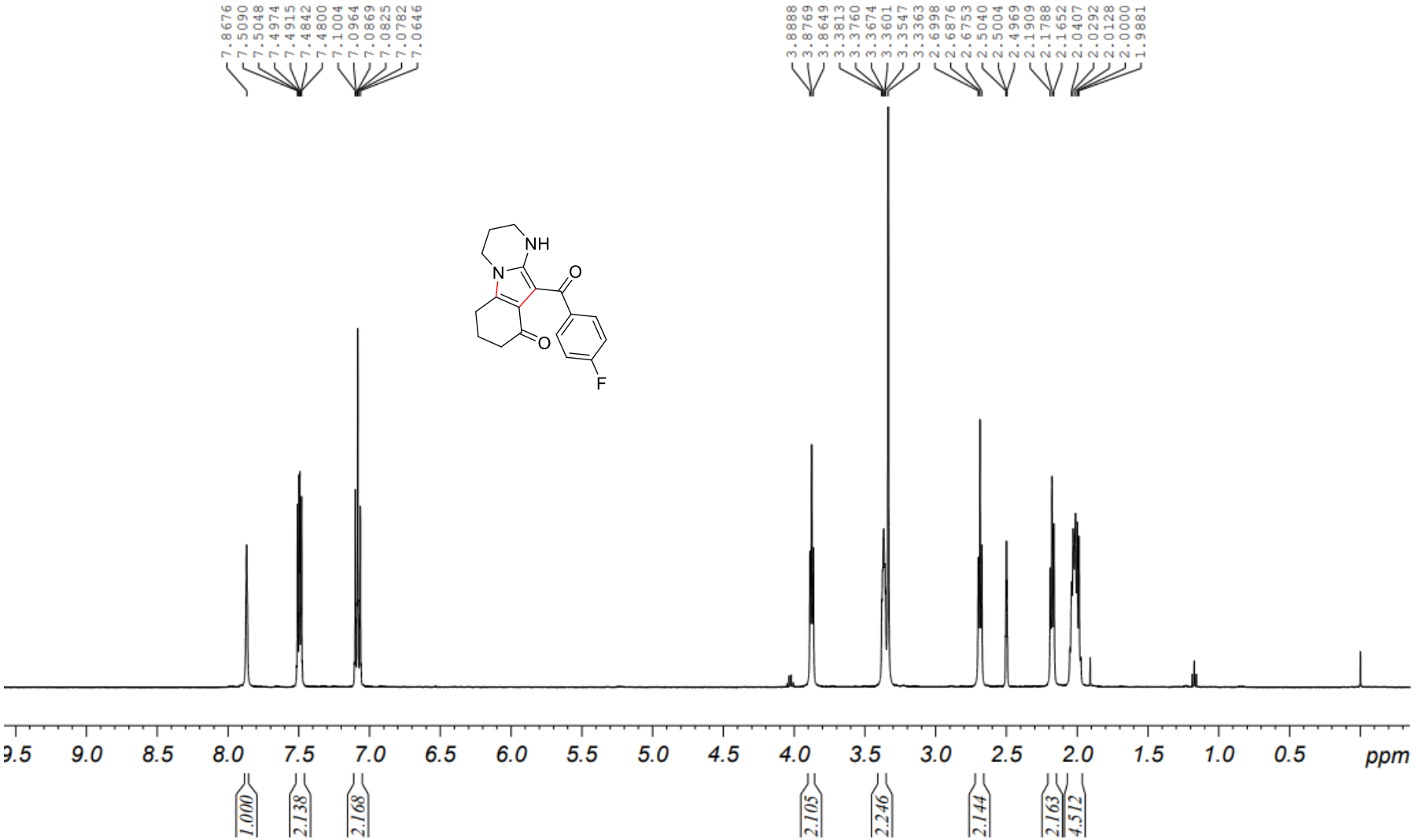


Figure S9. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3d**

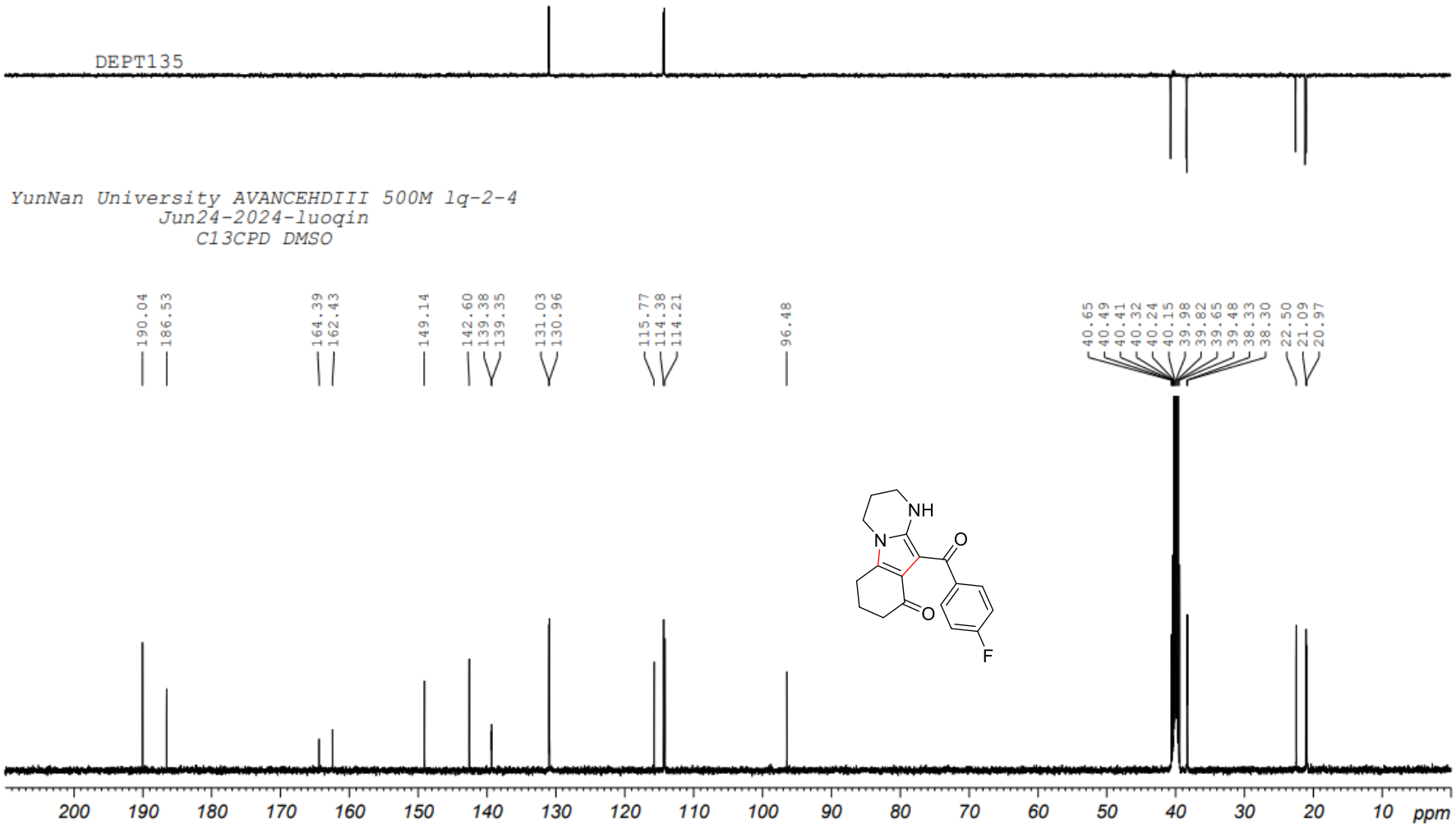


Figure S10. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3d**

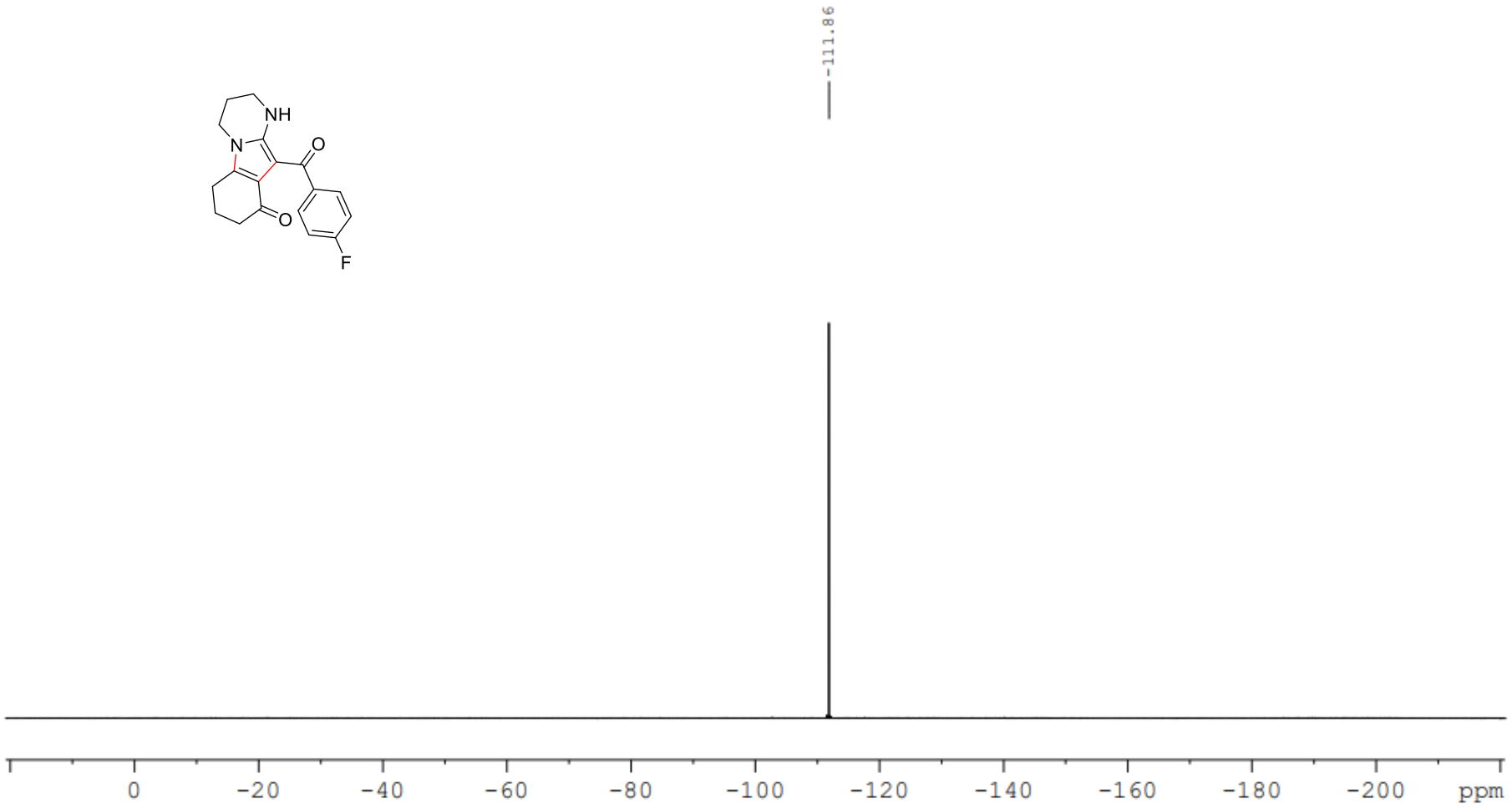


Figure S11. ^{19}F NMR (475 MHz, DMSO-d_6) spectra of compound **3d**

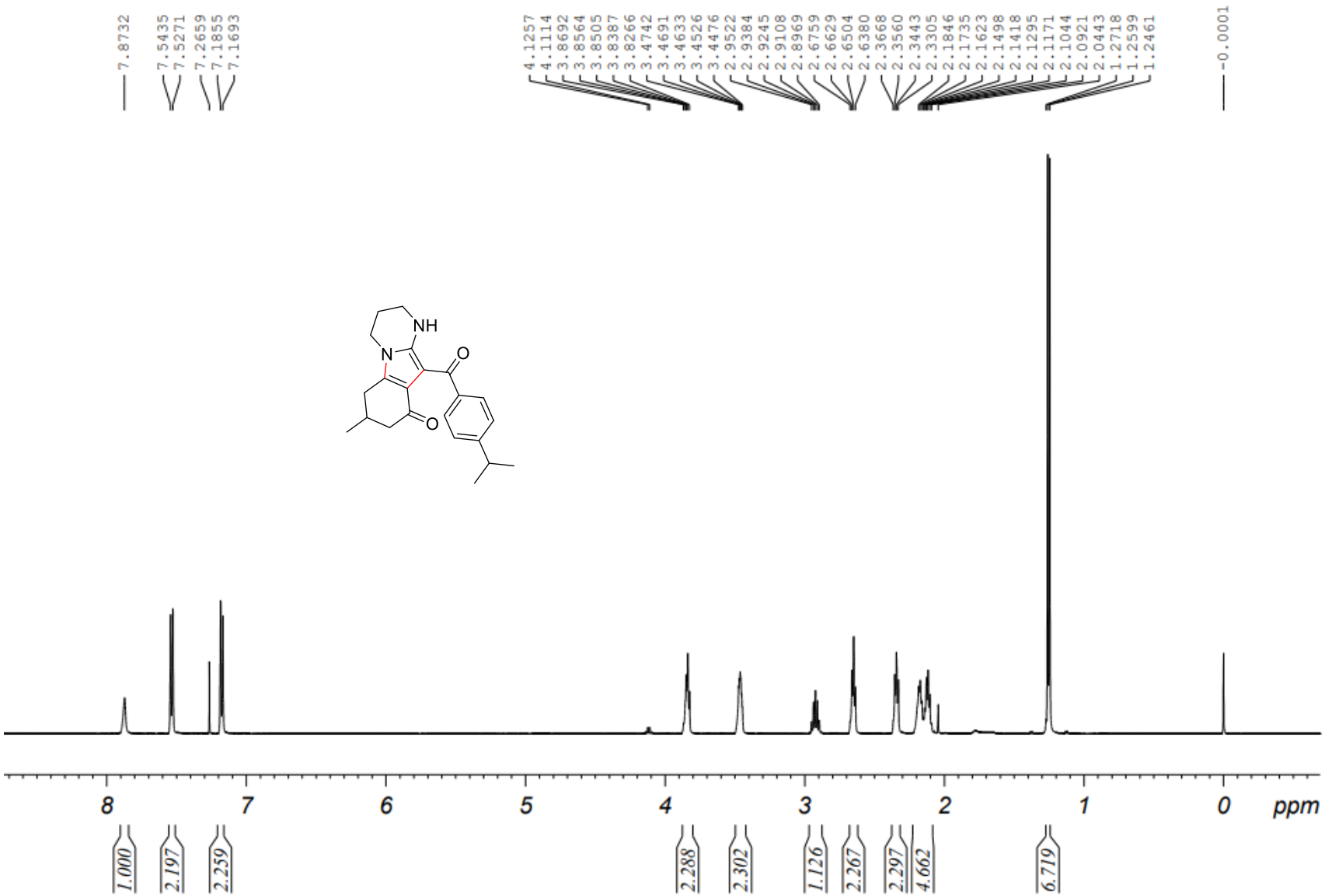


Figure S12. ^{1}H NMR (500 MHz, $CDCl_3$-d_6) spectra of compound **3e**

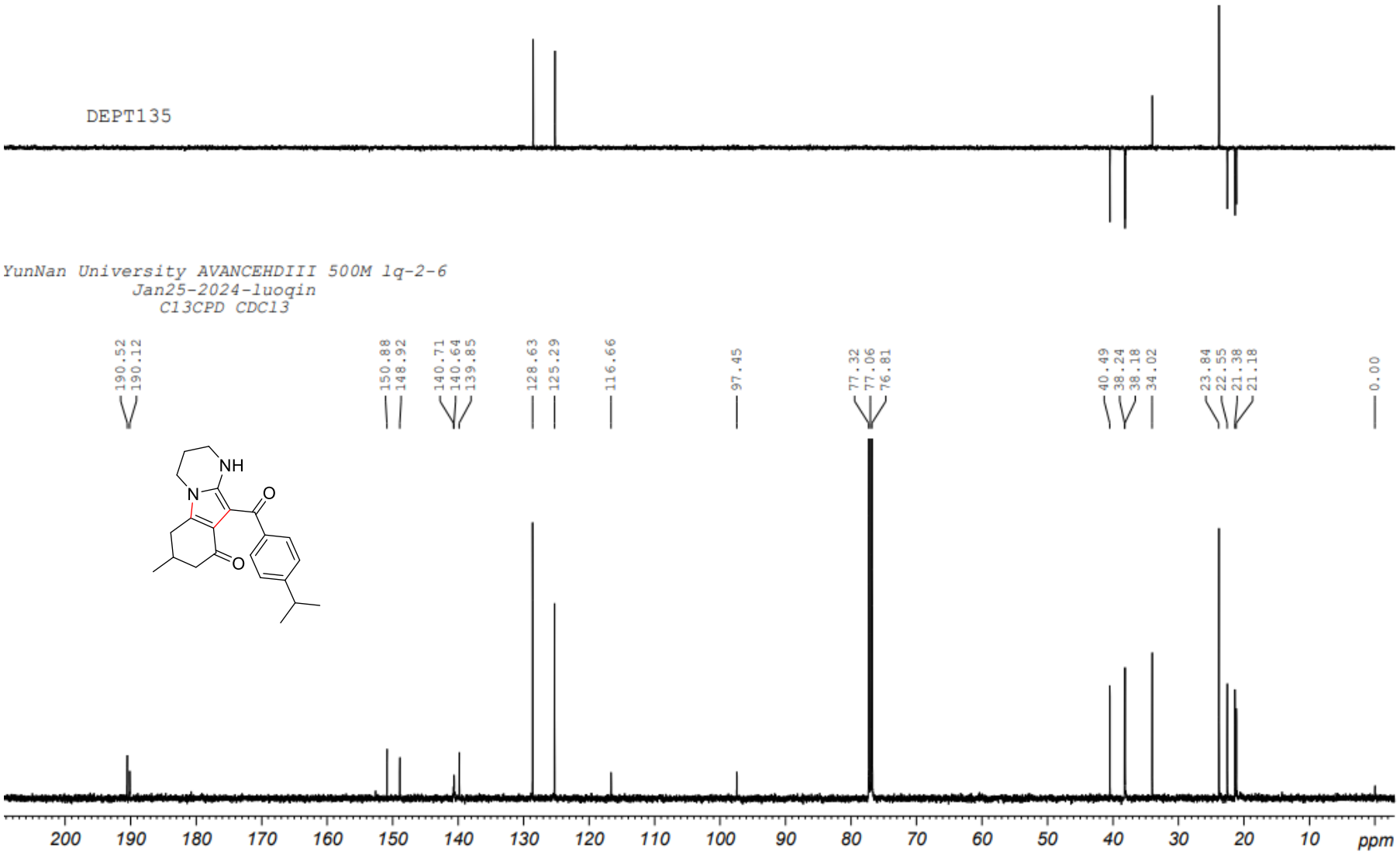


Figure S13. ^{13}C NMR (125 MHz, $CDCl_3$-d_6) spectra of compound **3e**

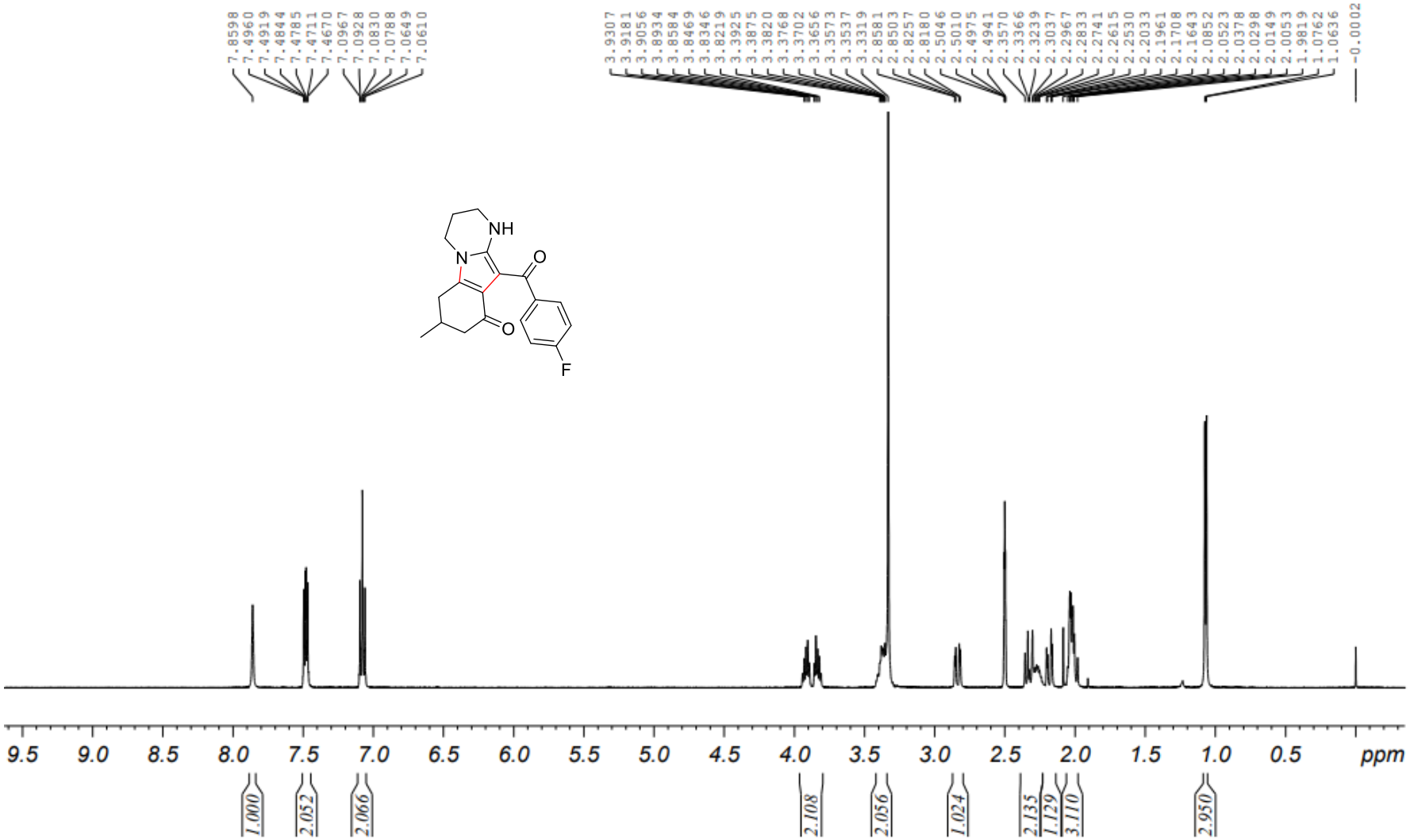


Figure S14. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3f**

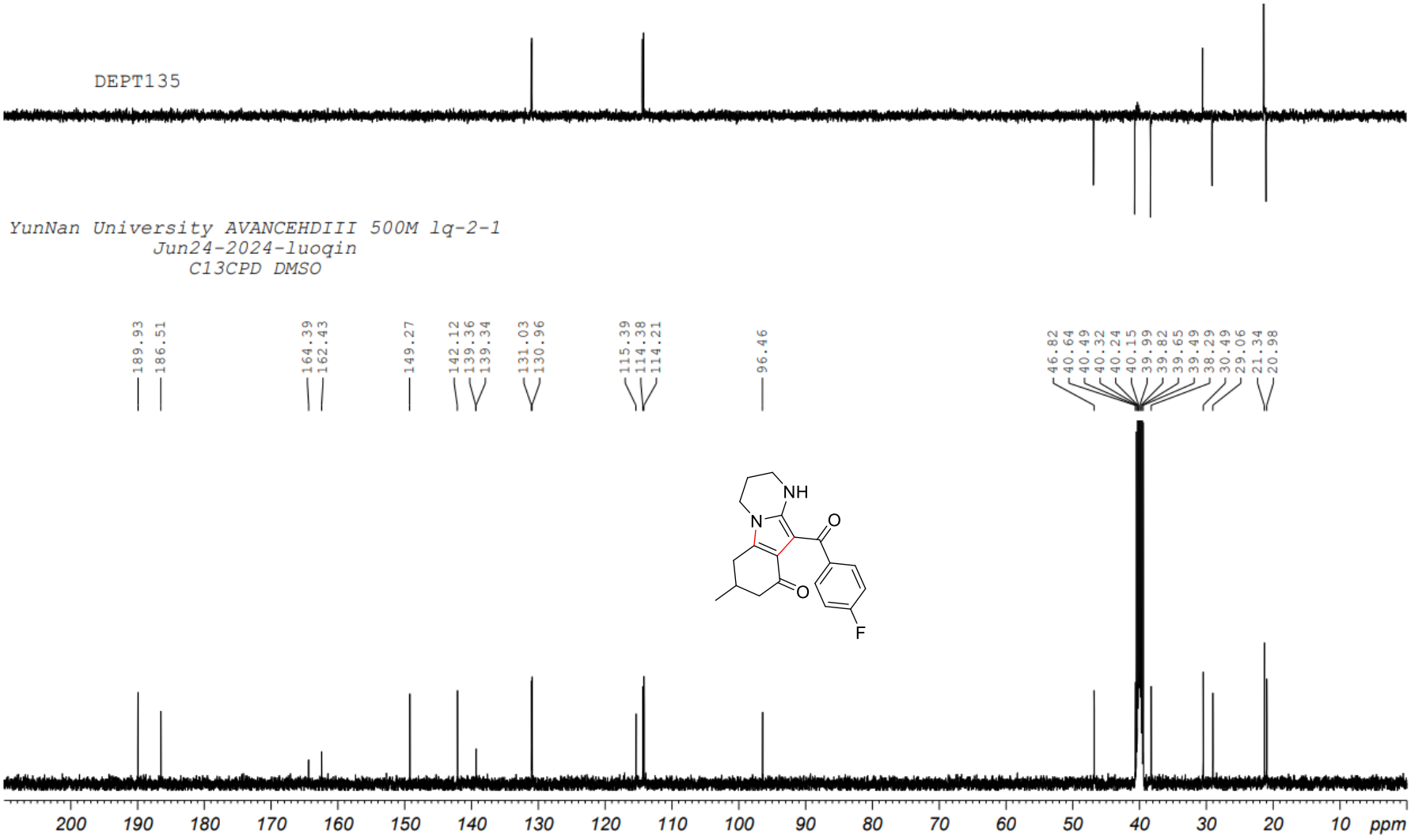


Figure S15. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3f**

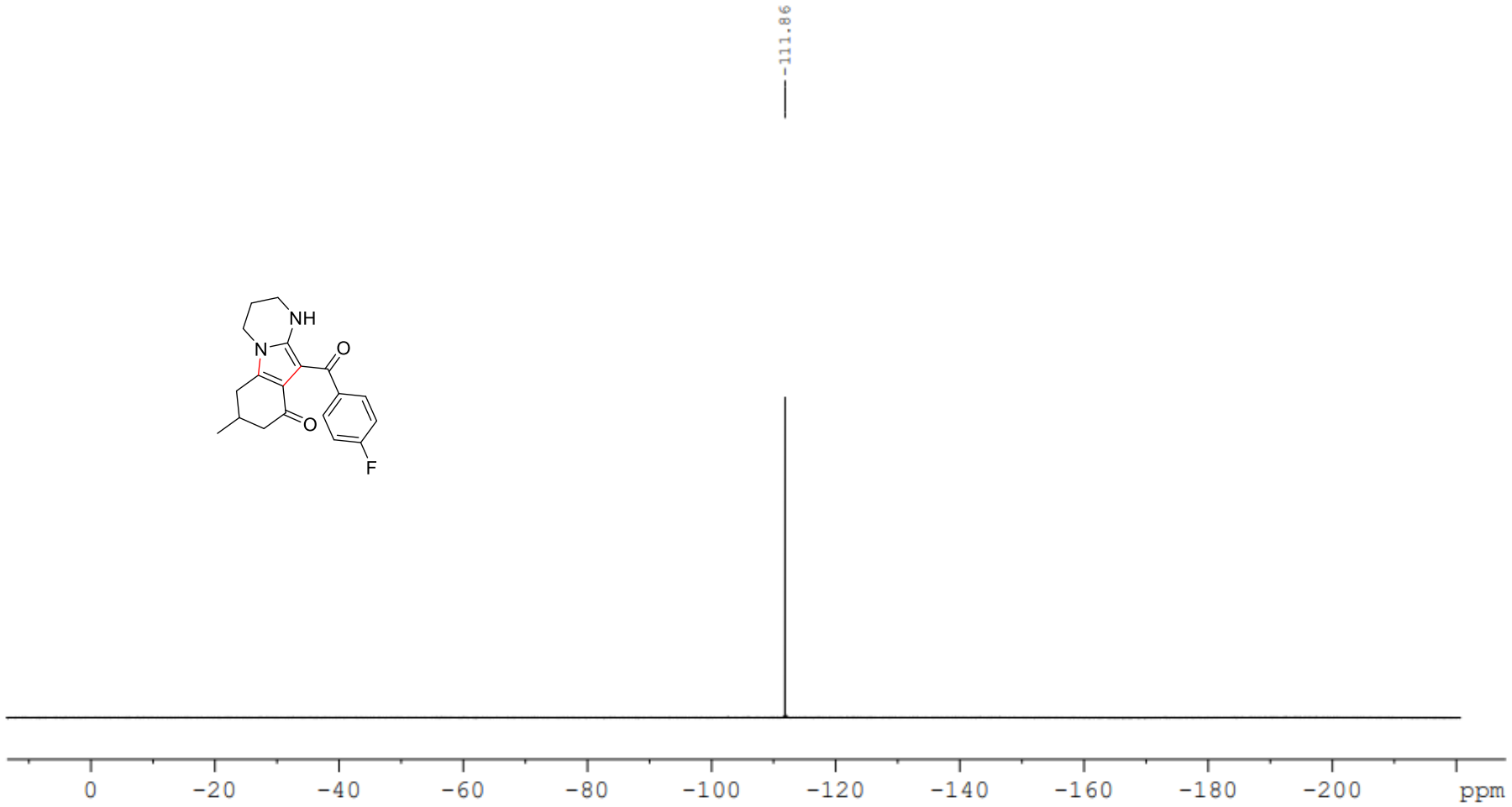


Figure S16. ^{19}F NMR (475 MHz, DMSO-d_6) spectra of compound **3f**

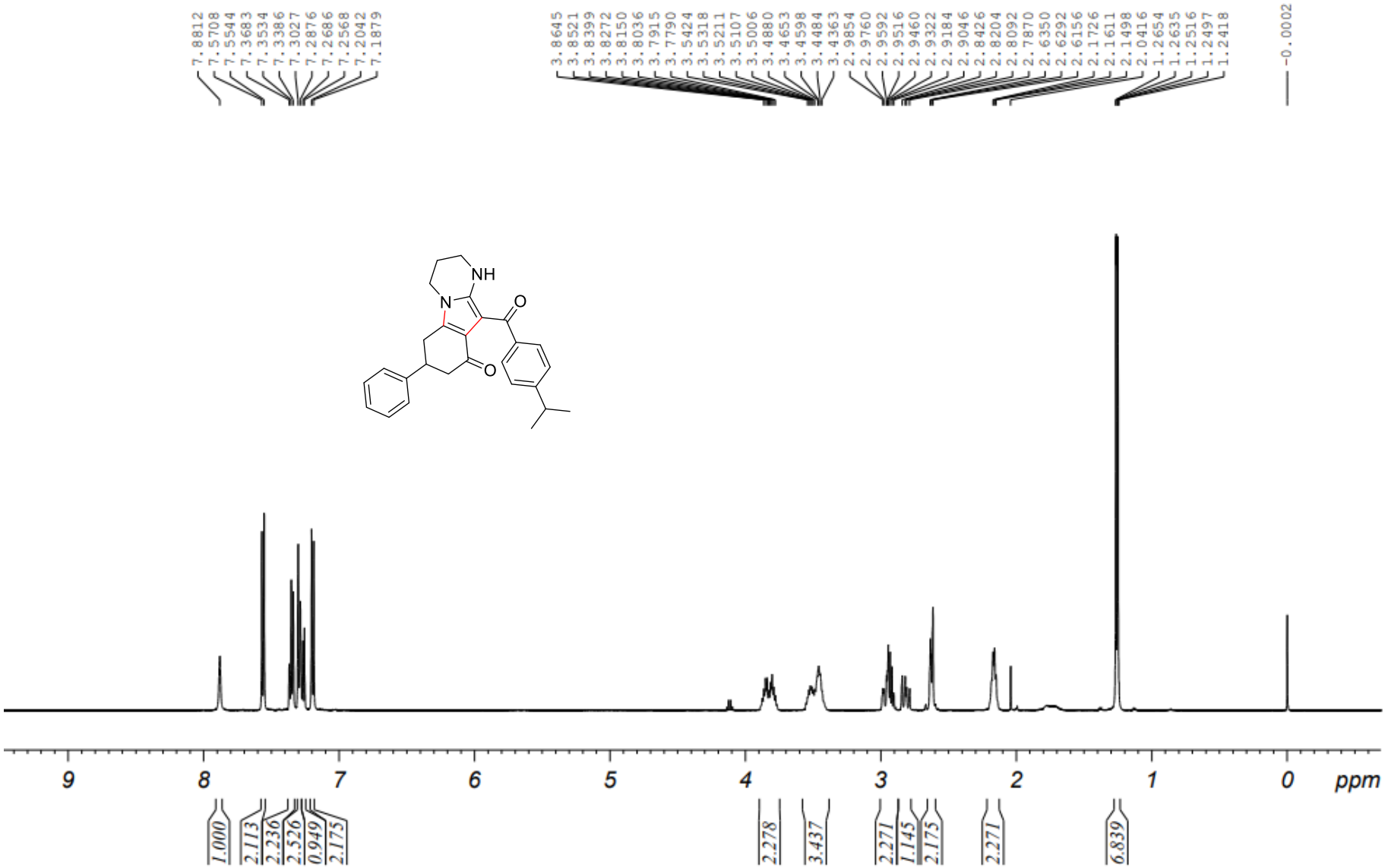


Figure S17. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **3g**

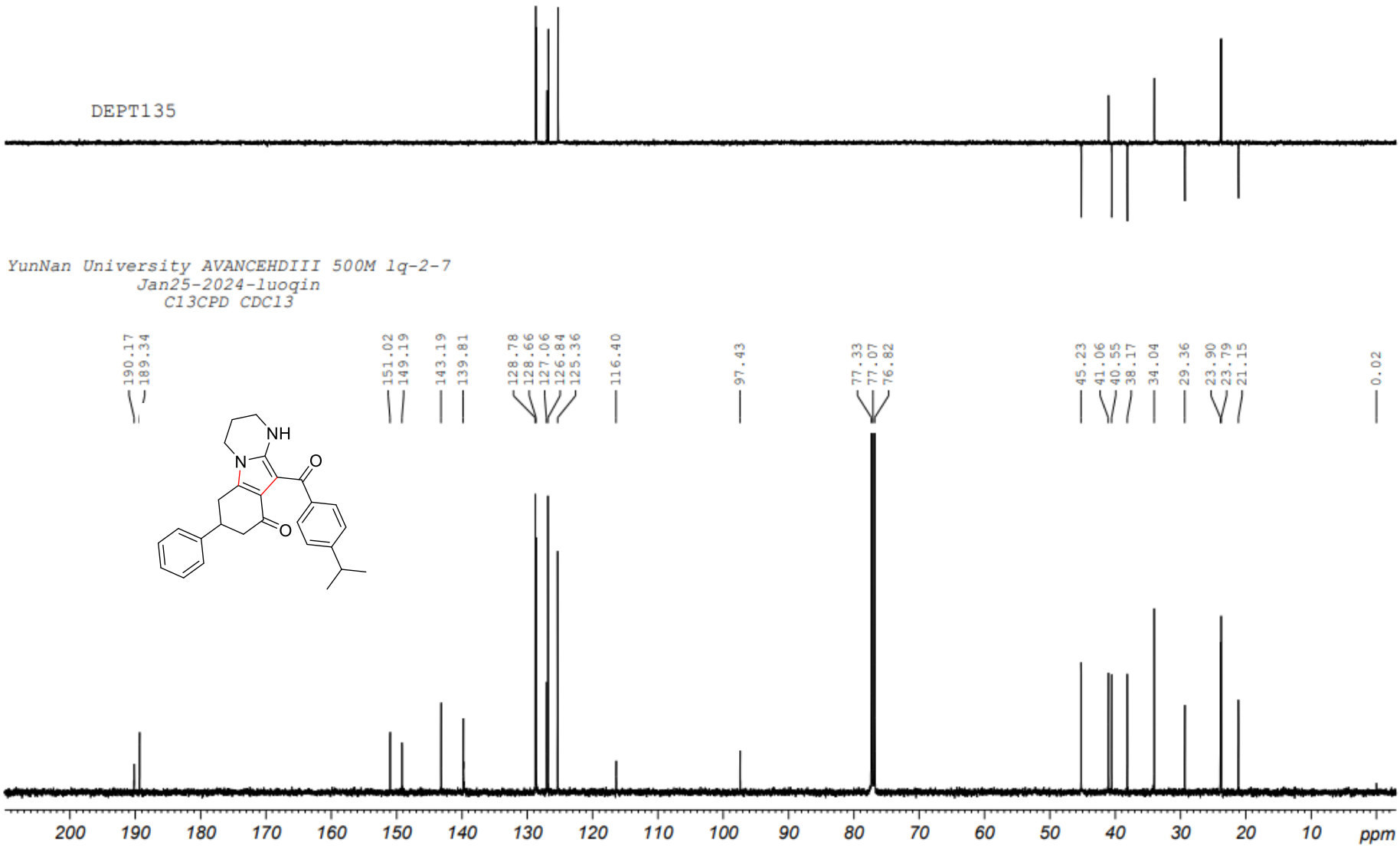


Figure S18. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **3g**

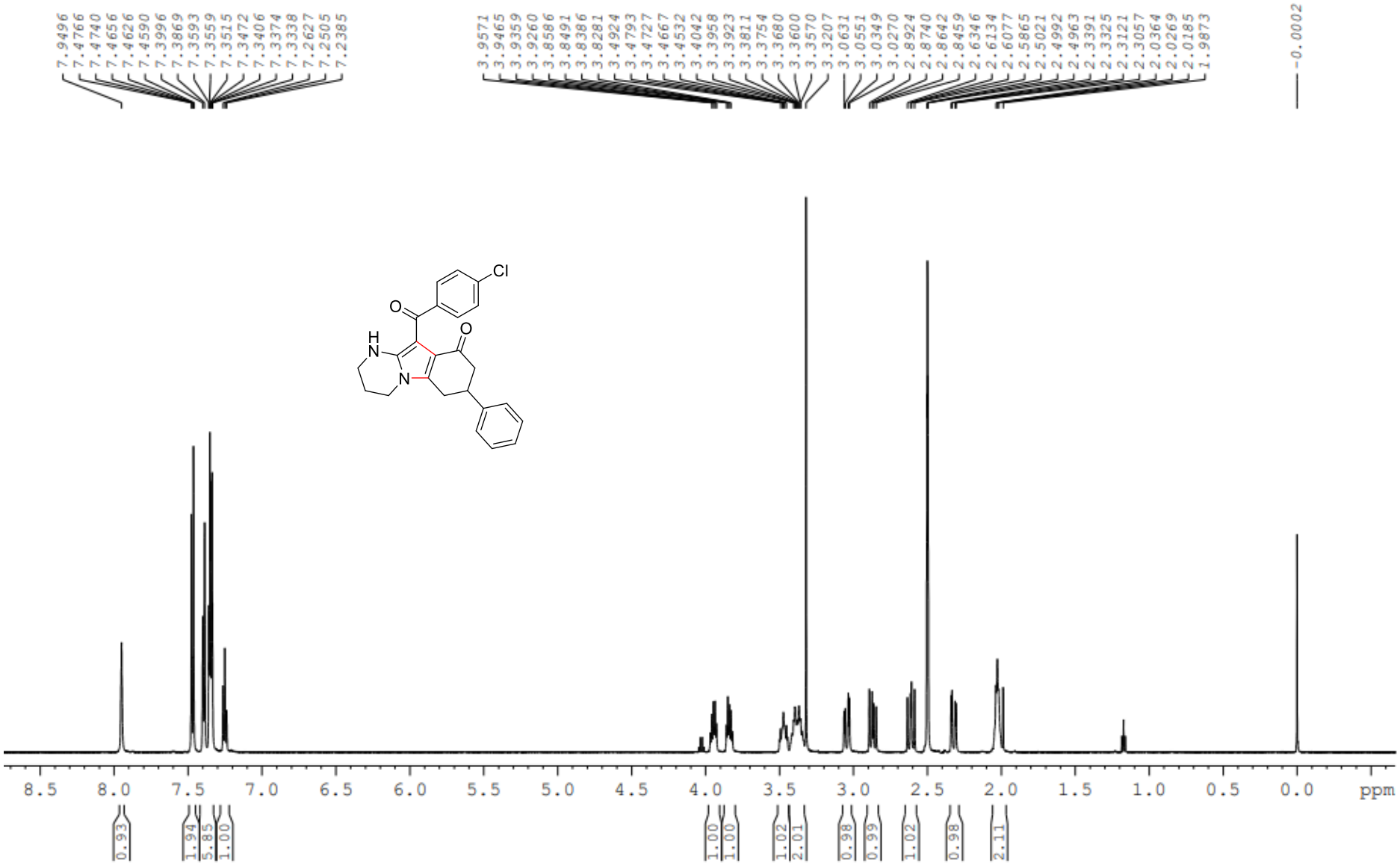


Figure S19. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **3h**

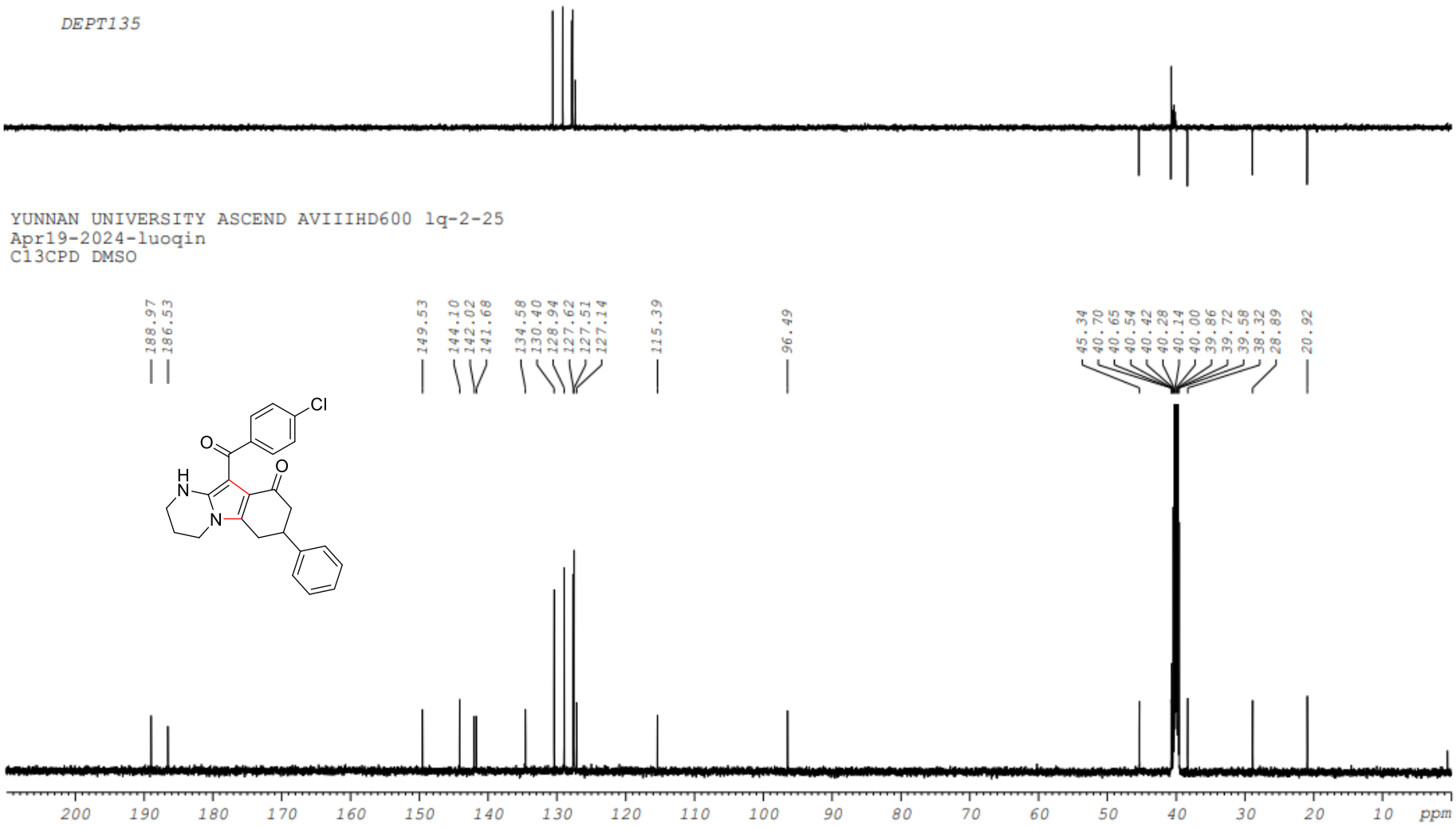


Figure S20. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **3h**

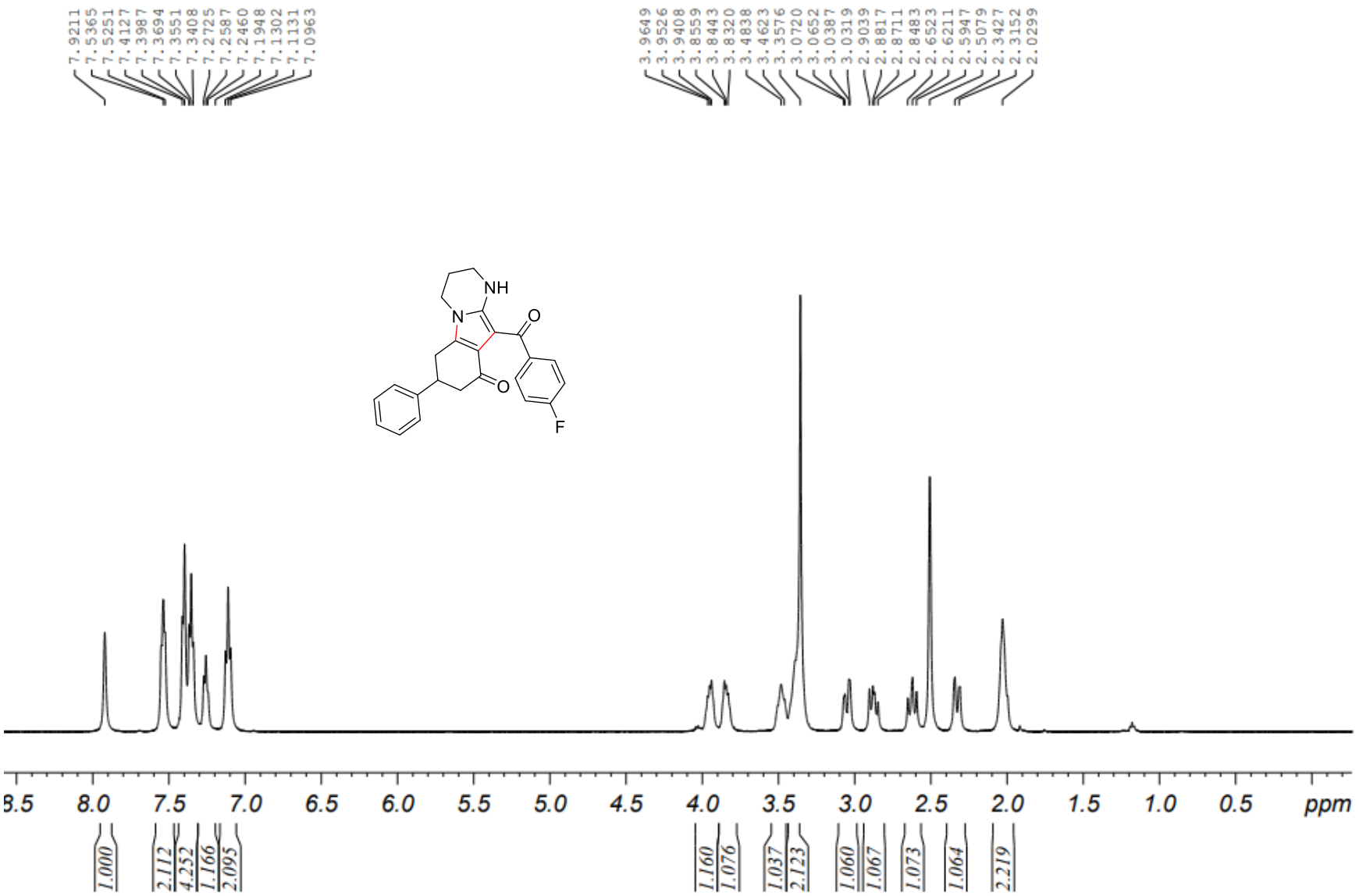


Figure S21. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **3i**

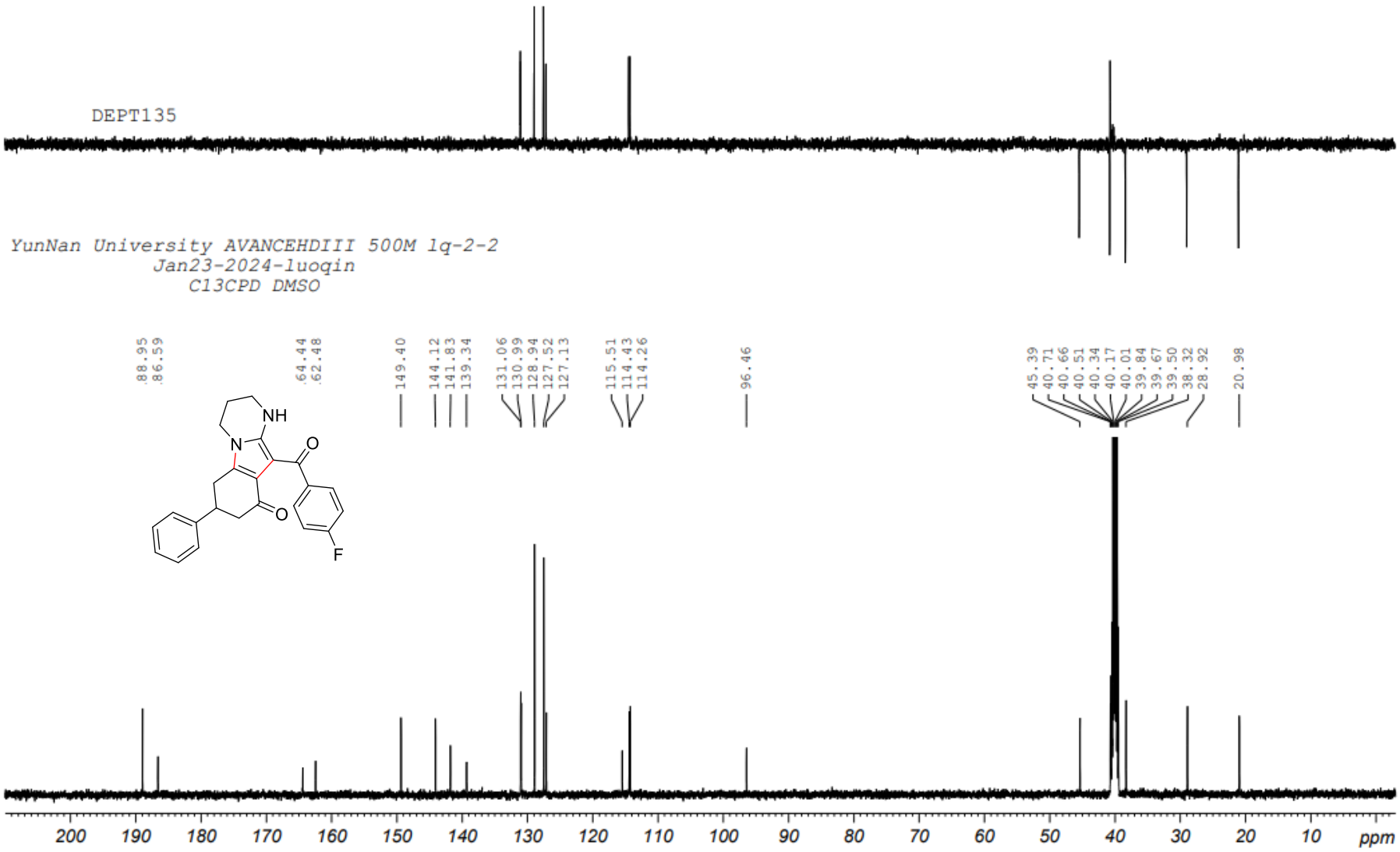


Figure S22. ^{13}C NMR (125 MHz,DMSO-d_6) spectra of compound **3i**

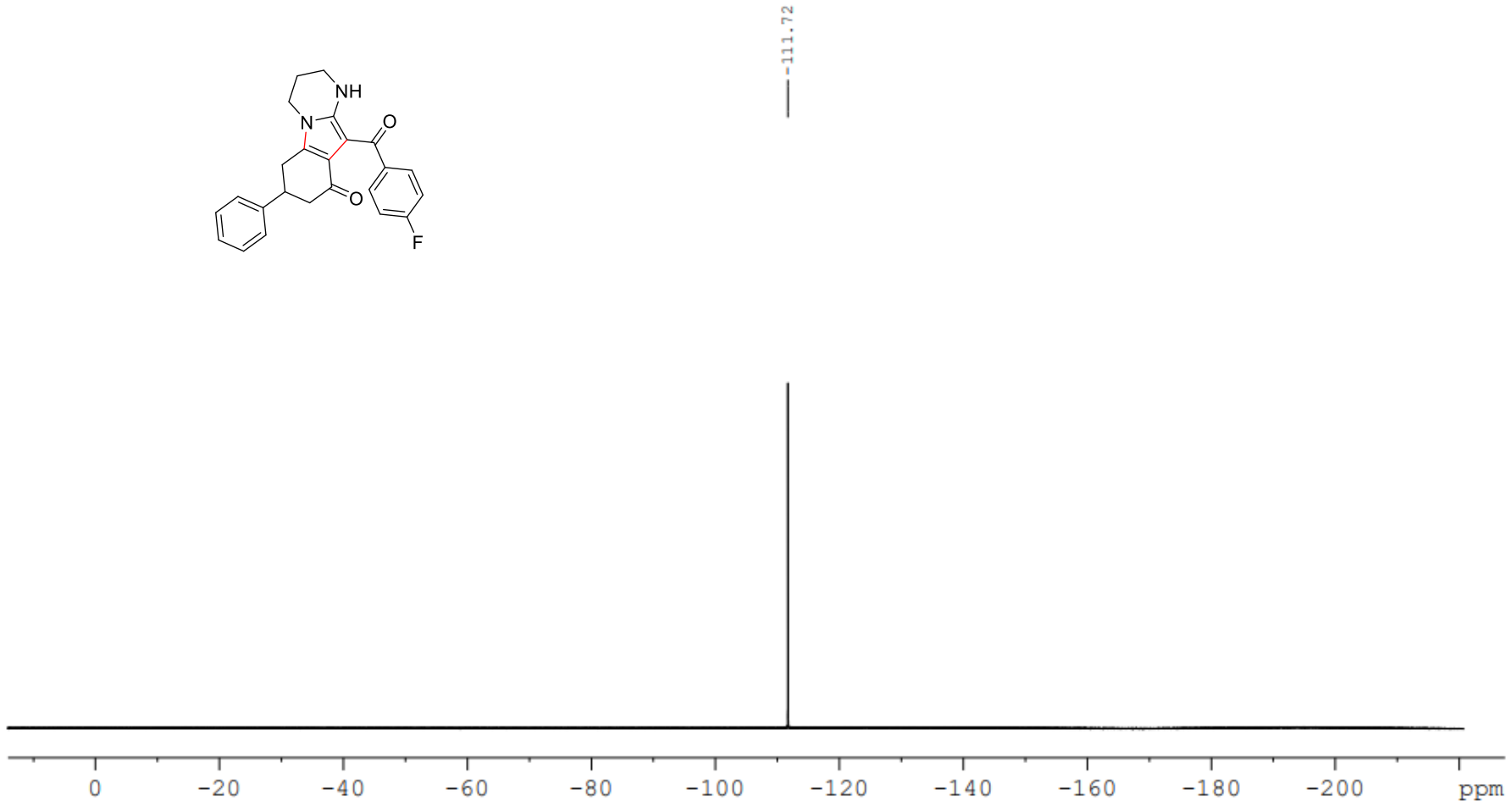


Figure S23. ^{19}F NMR (475 MHz, DMSO-d_6) spectra of compound **3i**

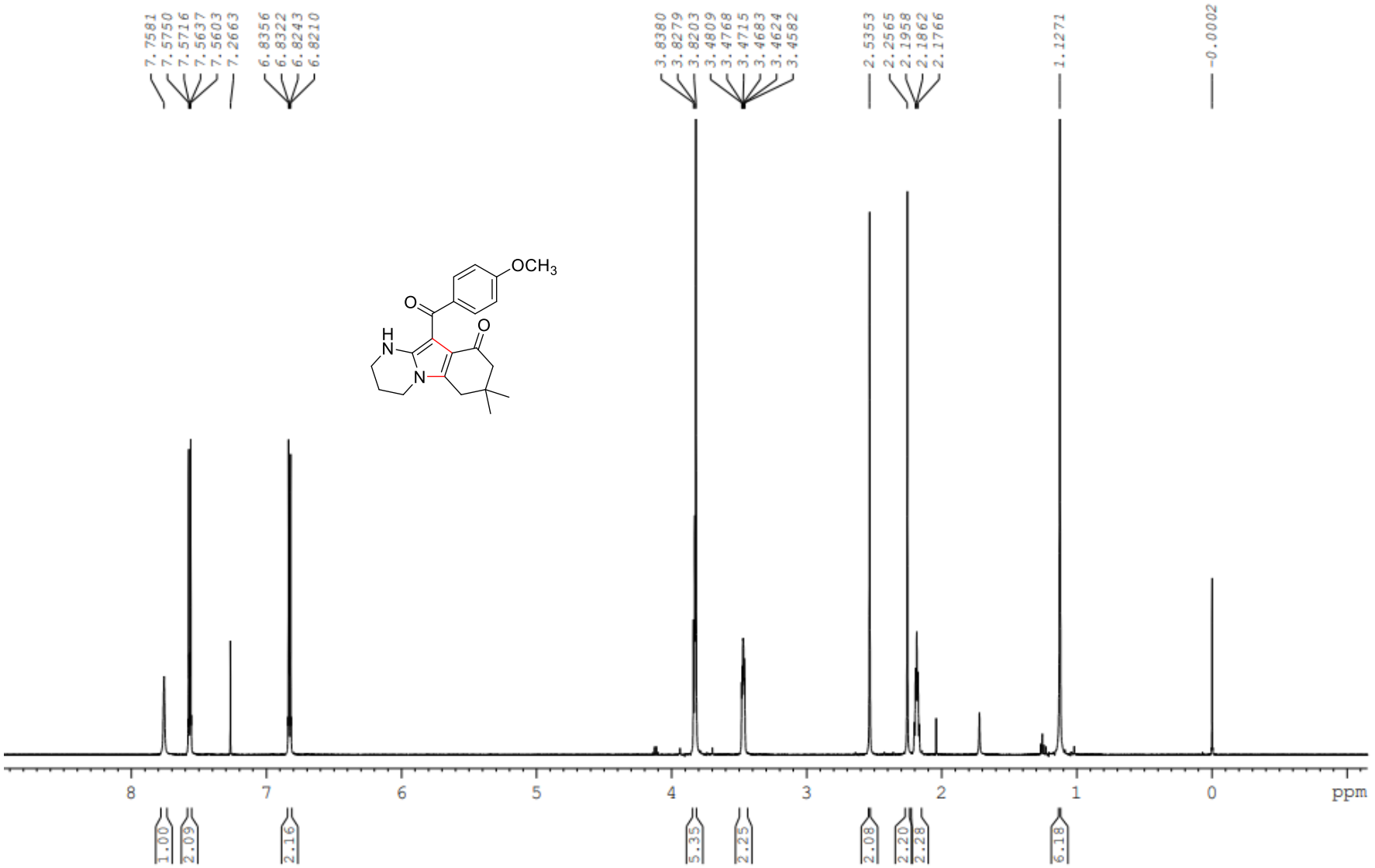


Figure S24. ^{1}H NMR (600 MHz,$CDCl_3$-d_6) spectra of compound **3j**

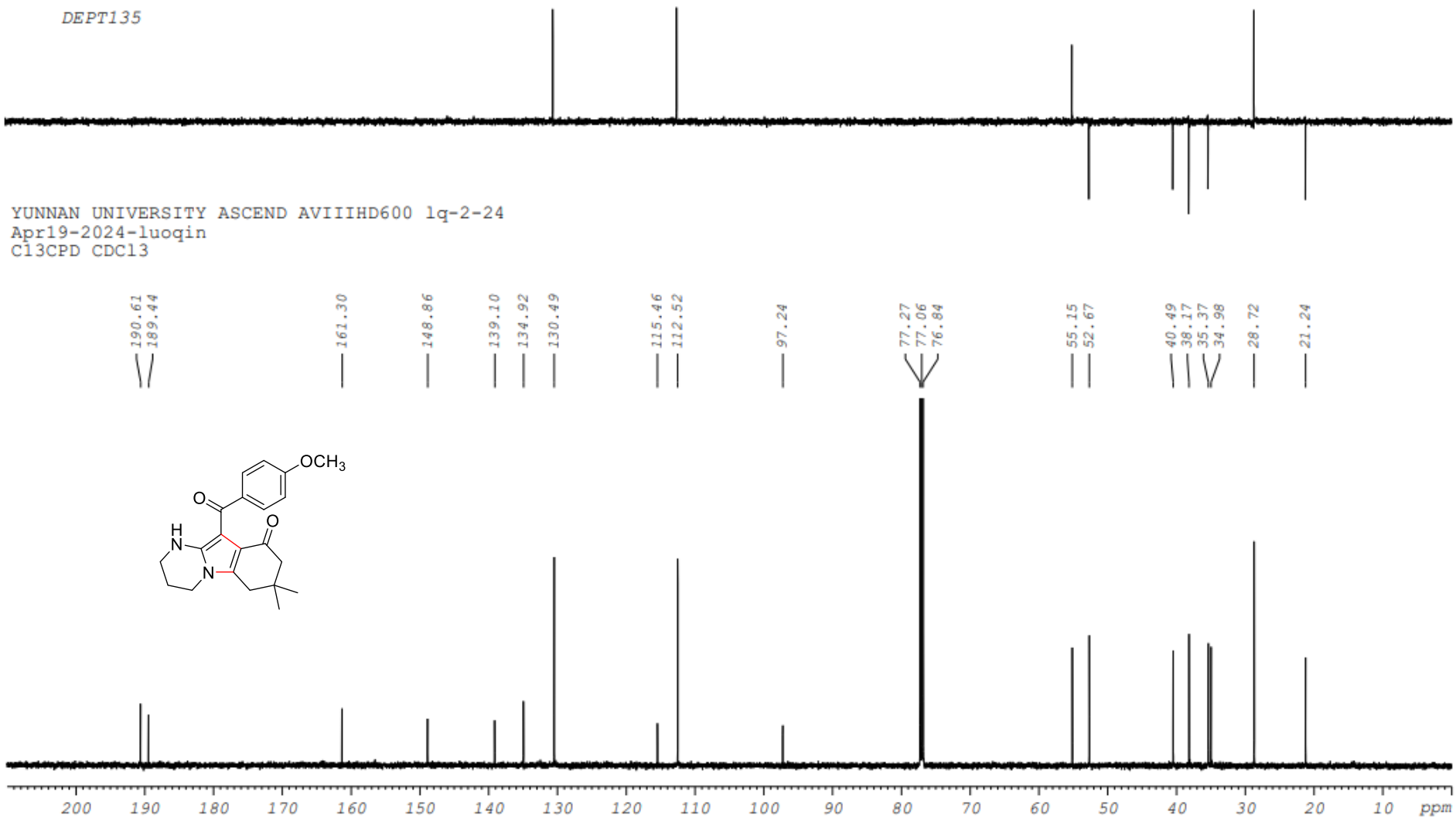


Figure S25. ^{13}C NMR (150 MHz,$CDCl_3$-d_6) spectra of compound **3j**

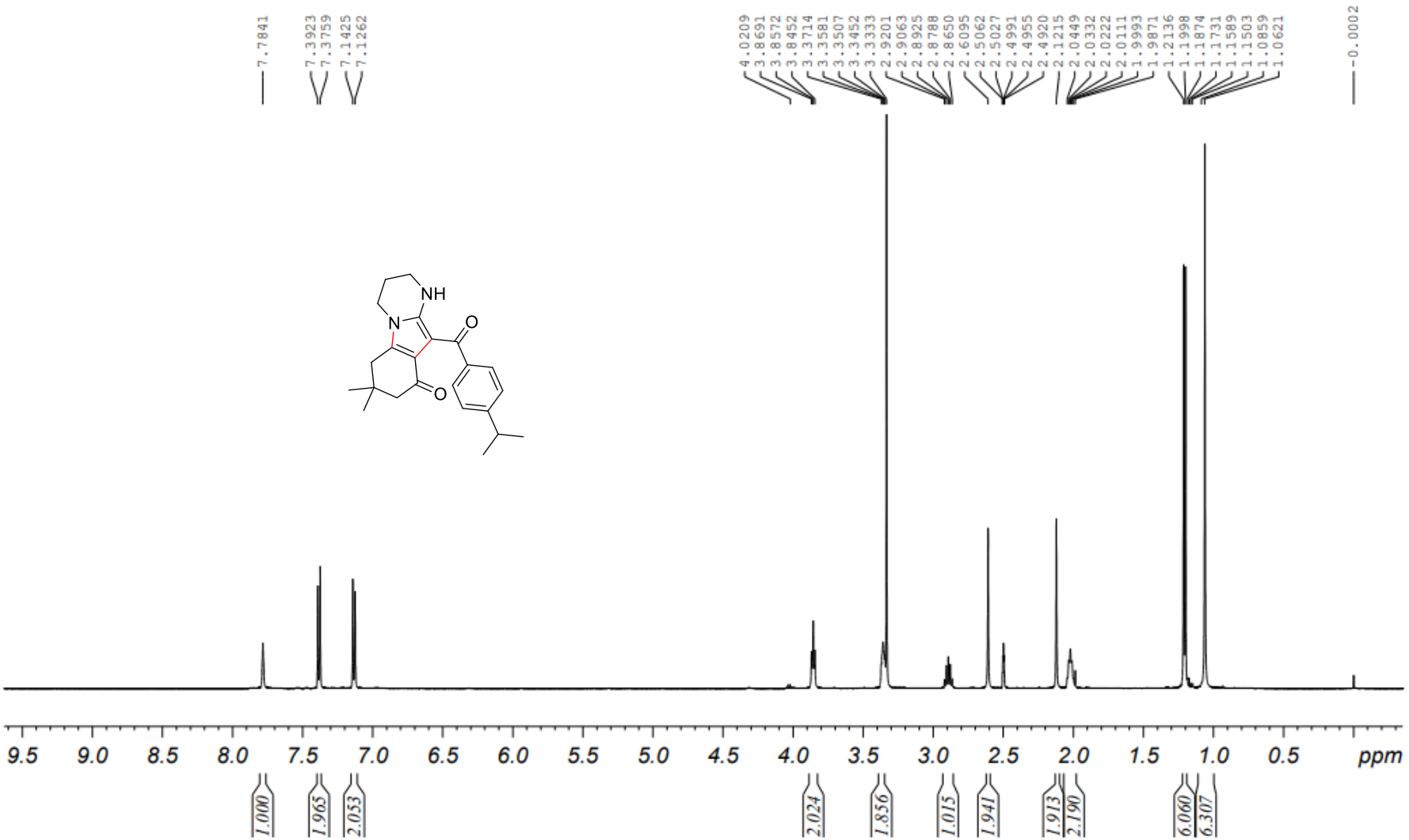


Figure S26. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **3k**

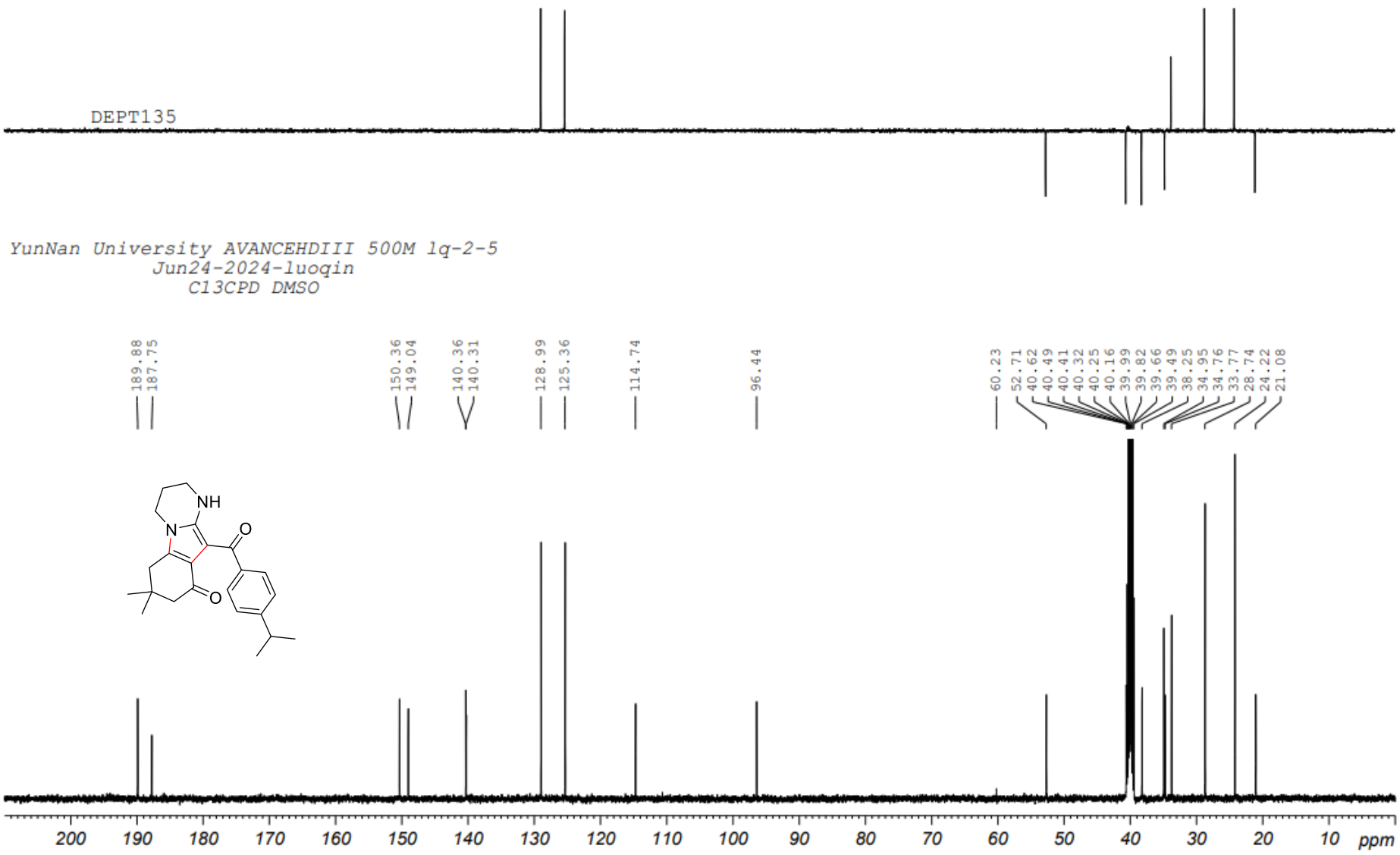


Figure S27. ^{13}C NMR (125 MHz,DMSO-d_6) spectra of compound **3k**

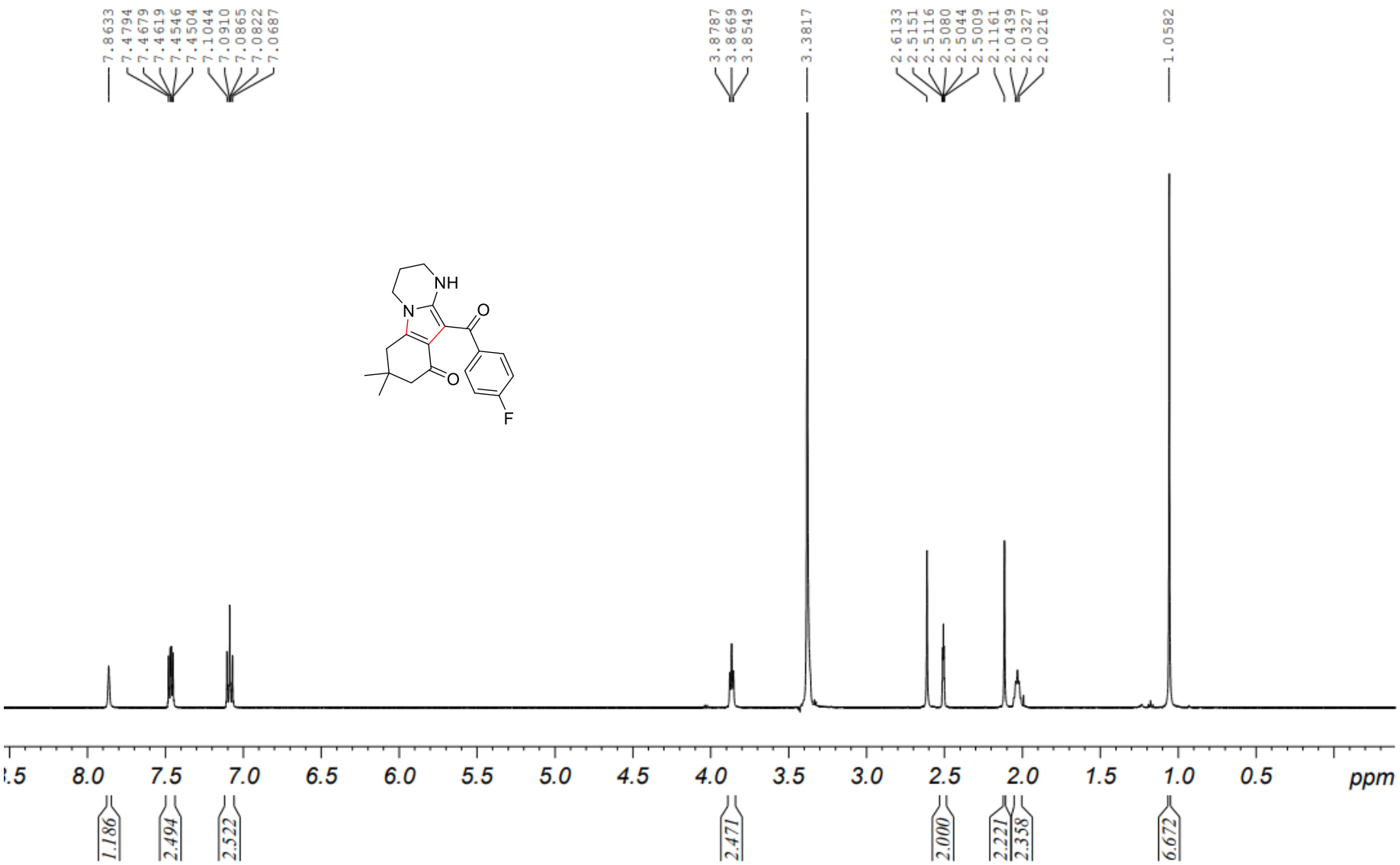


Figure S28. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **3l**

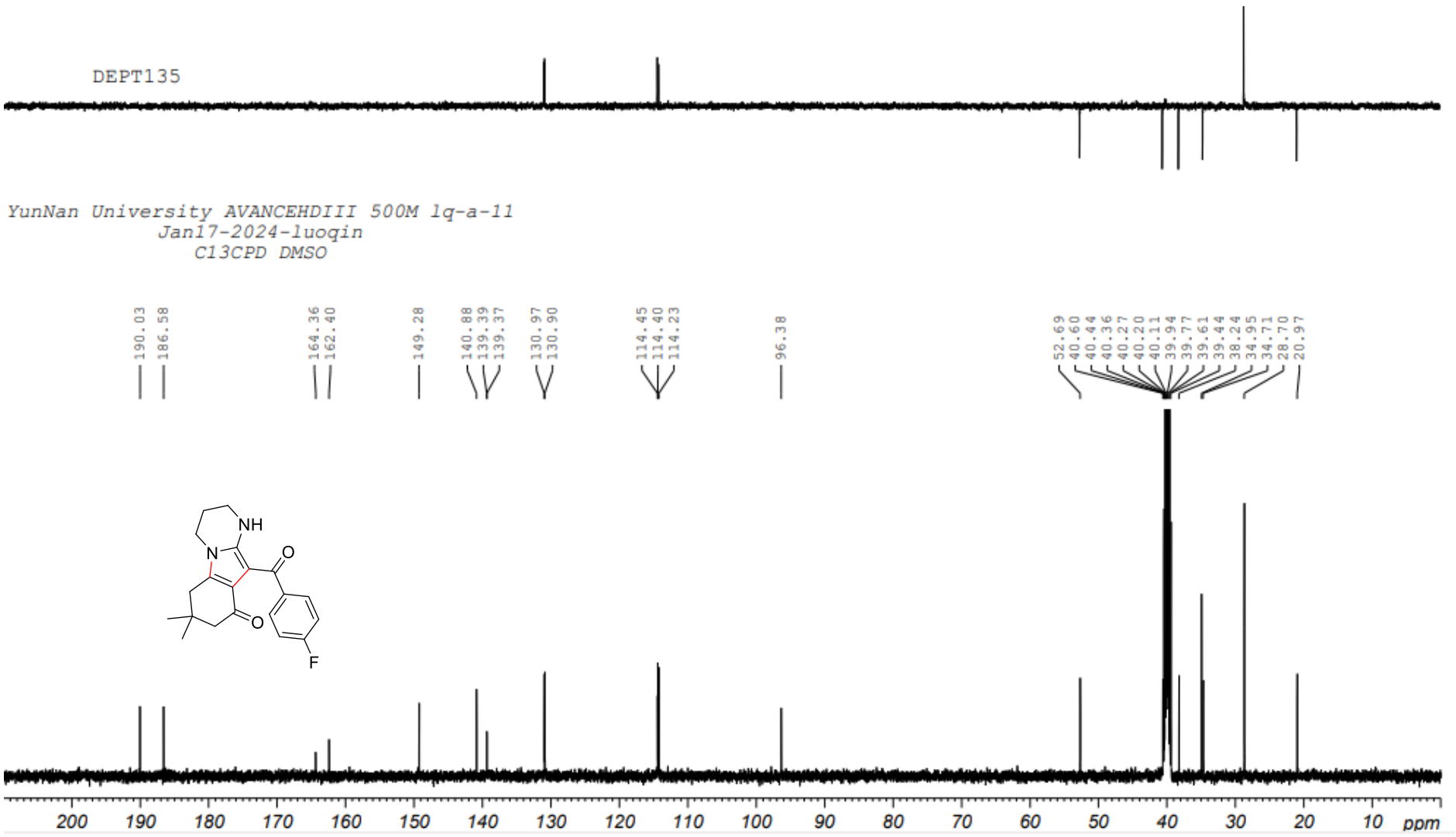


Figure S29. ^{13}C NMR (125 MHz,DMSO-d_6) spectra of compound **3l**

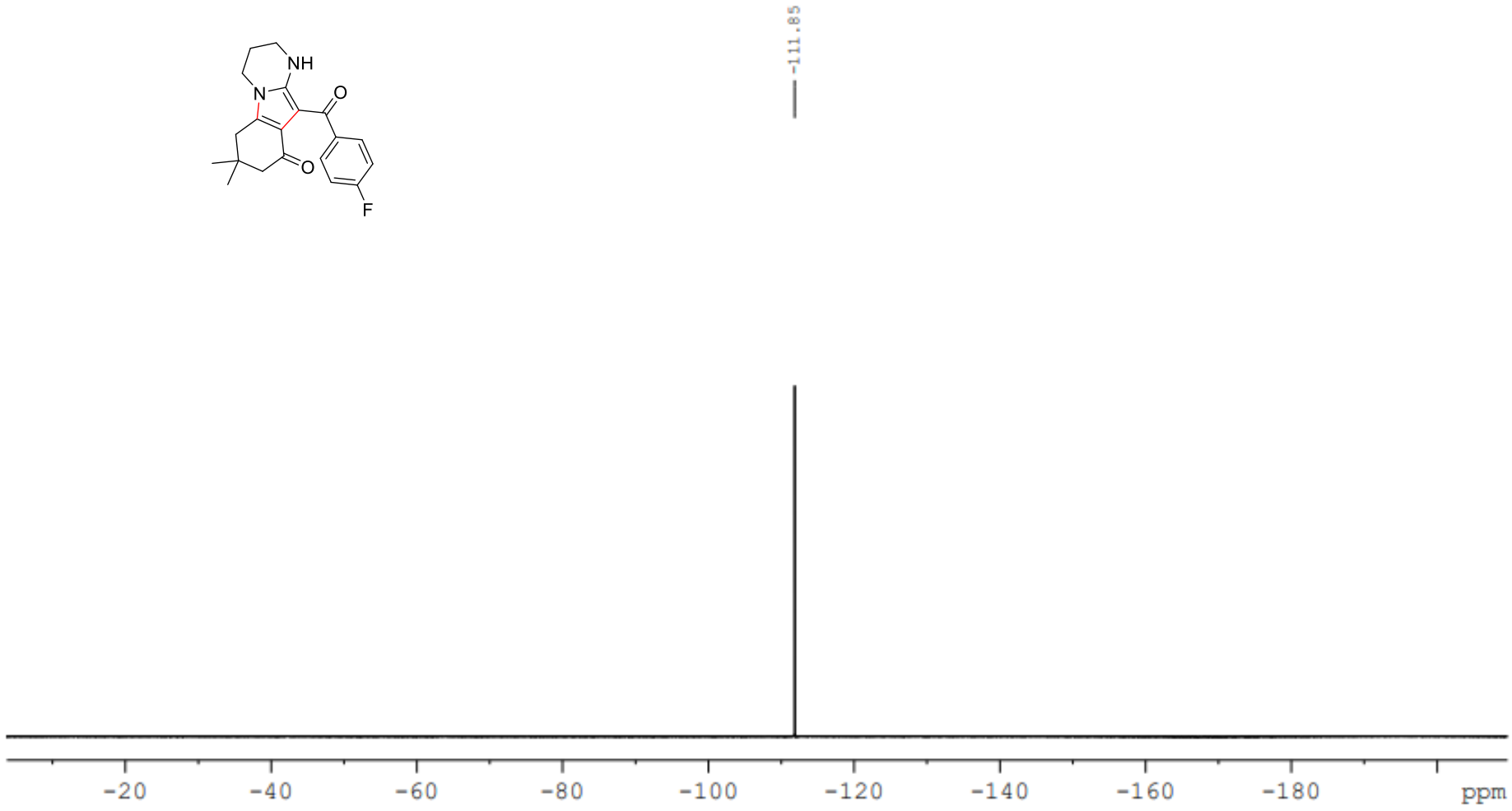


Figure S30. ^{19}F NMR (475 MHz, DMSO-d_6) spectra of compound **3l**

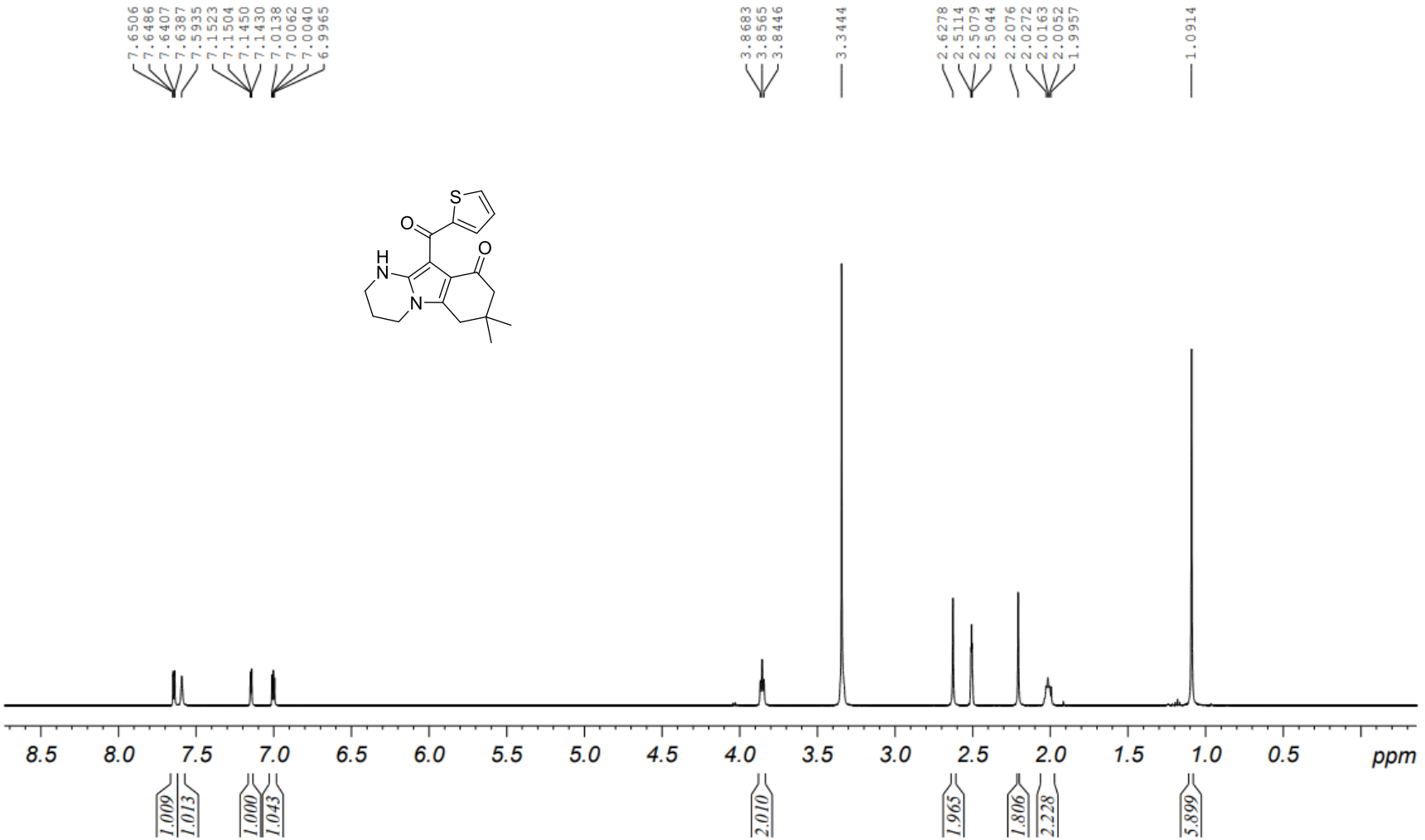


Figure S31. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **3m**

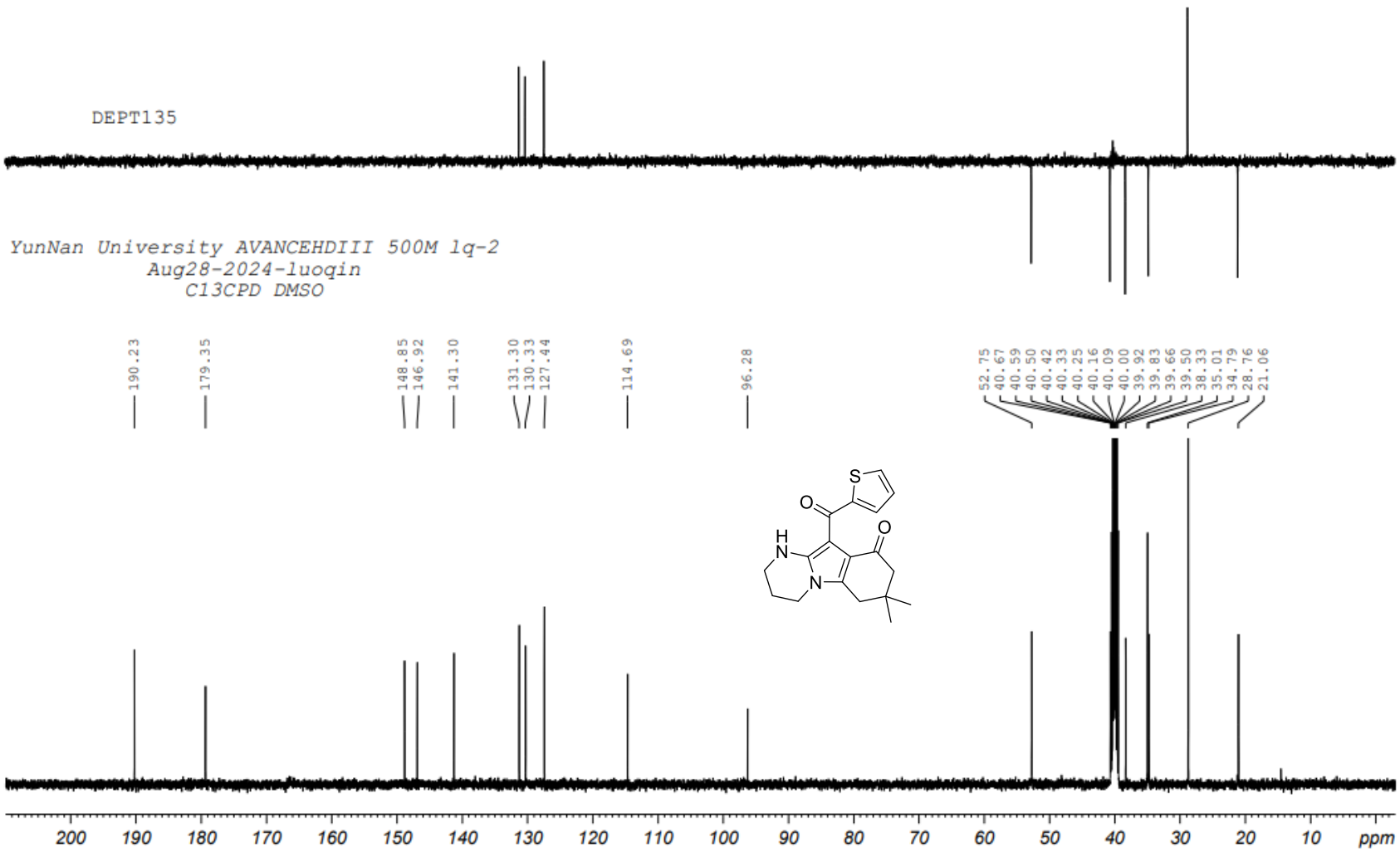


Figure S32. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **3m**

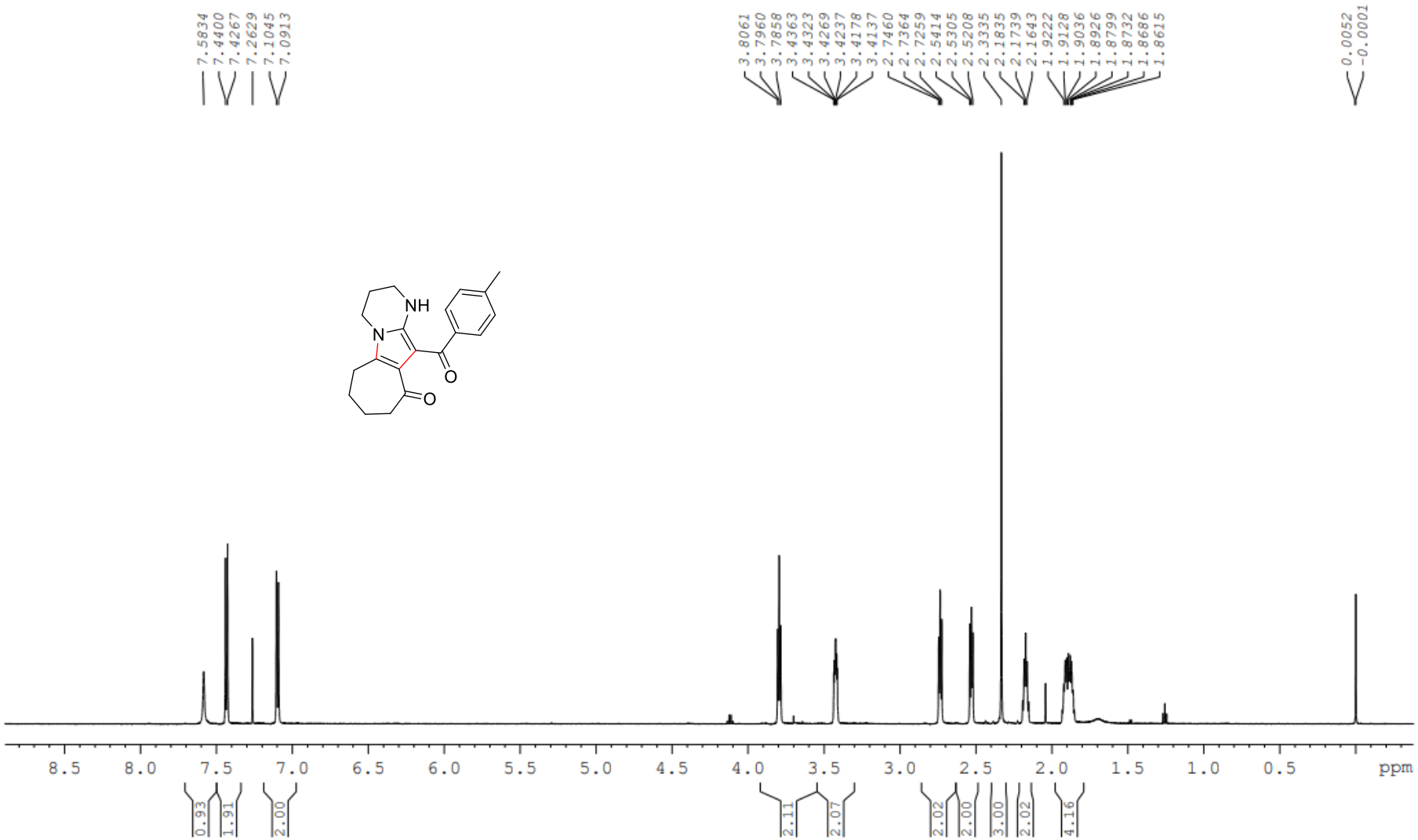


Figure S33. ^{1}H NMR (600 MHz,$CDCl_3$-d_6) spectra of compound **3n**

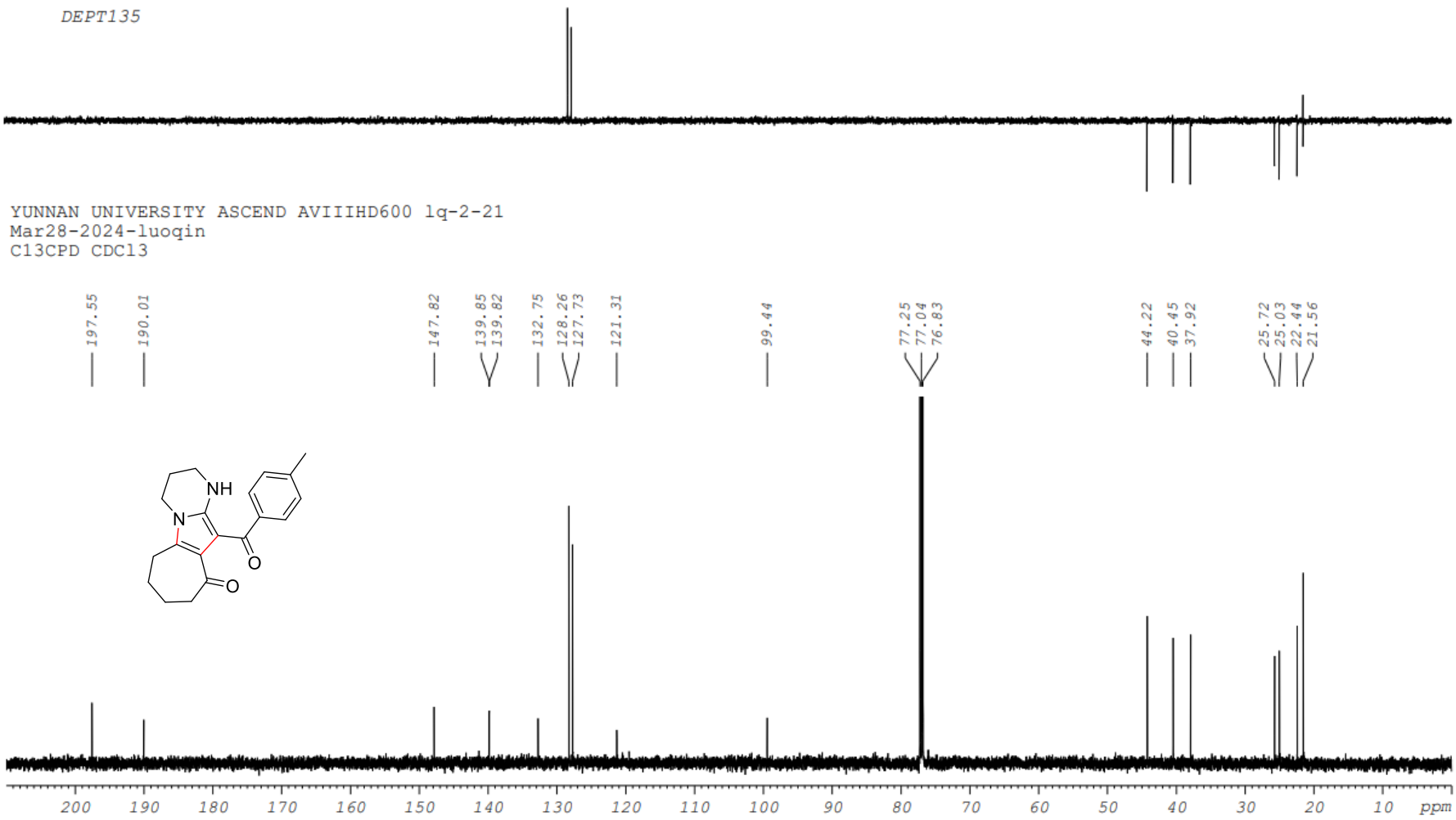


Figure S34. ^{13}C NMR (150 MHz,$CDCl_3$-d_6) spectra of compound **3n**

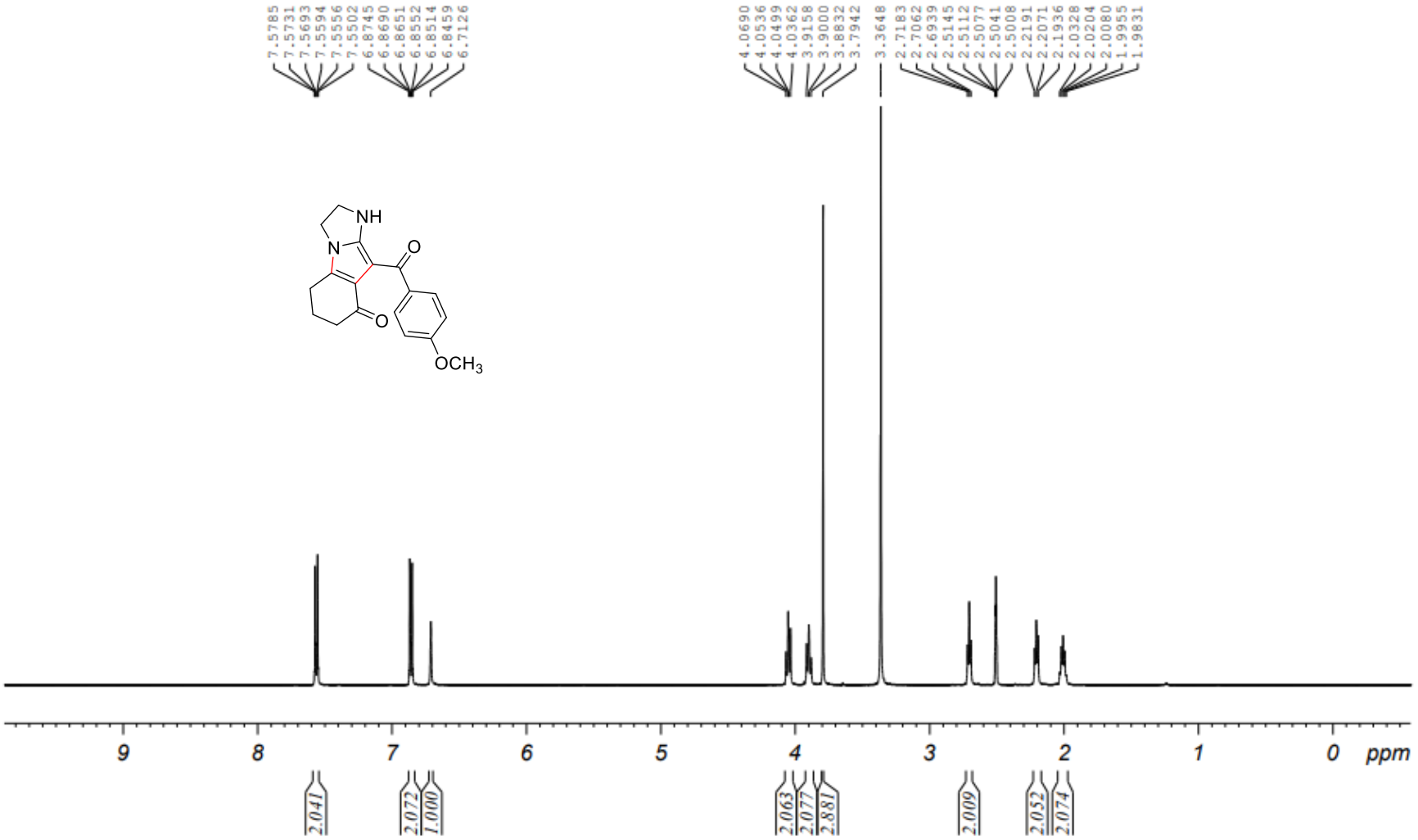


Figure S35. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3o**

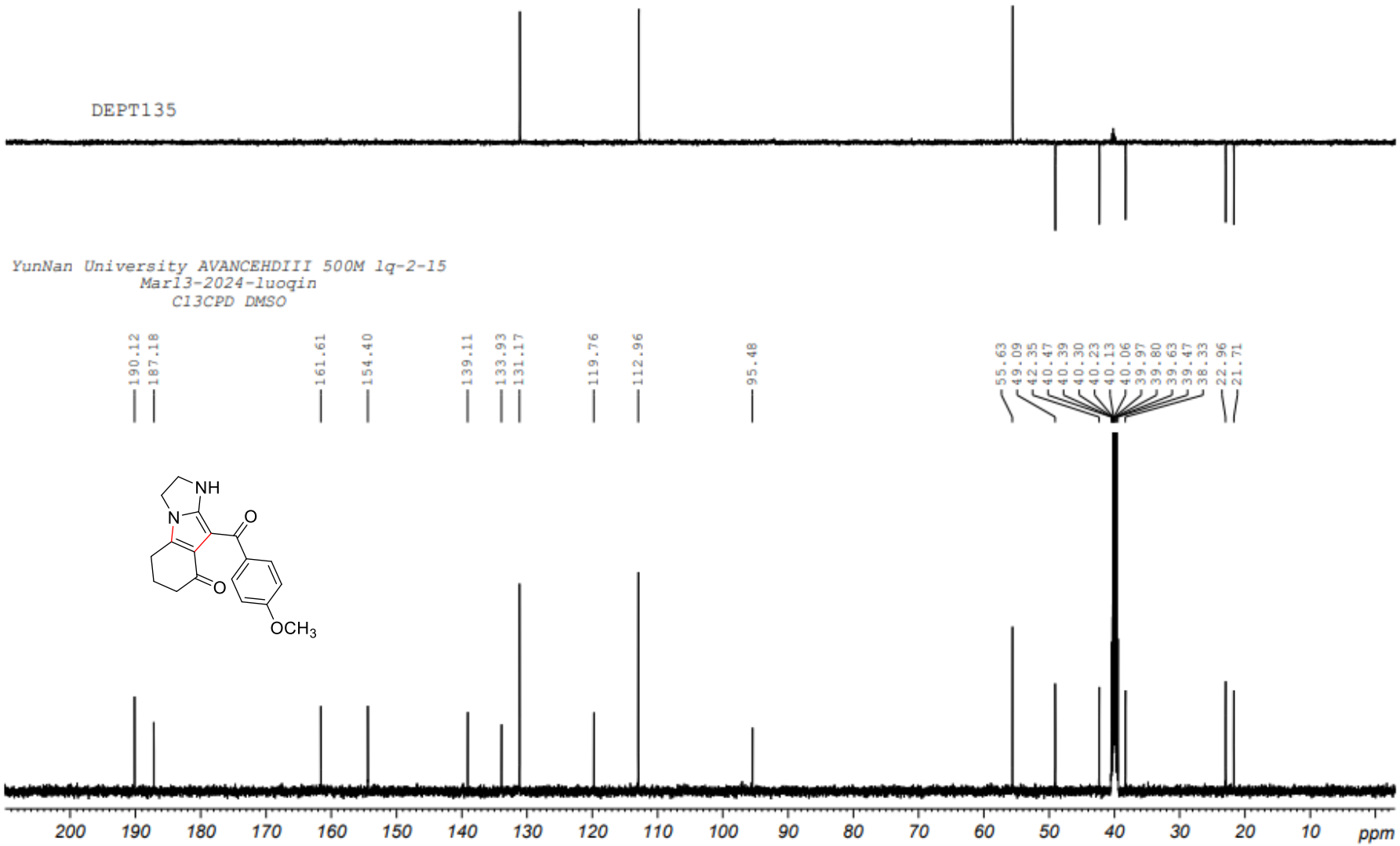


Figure S36. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3o**

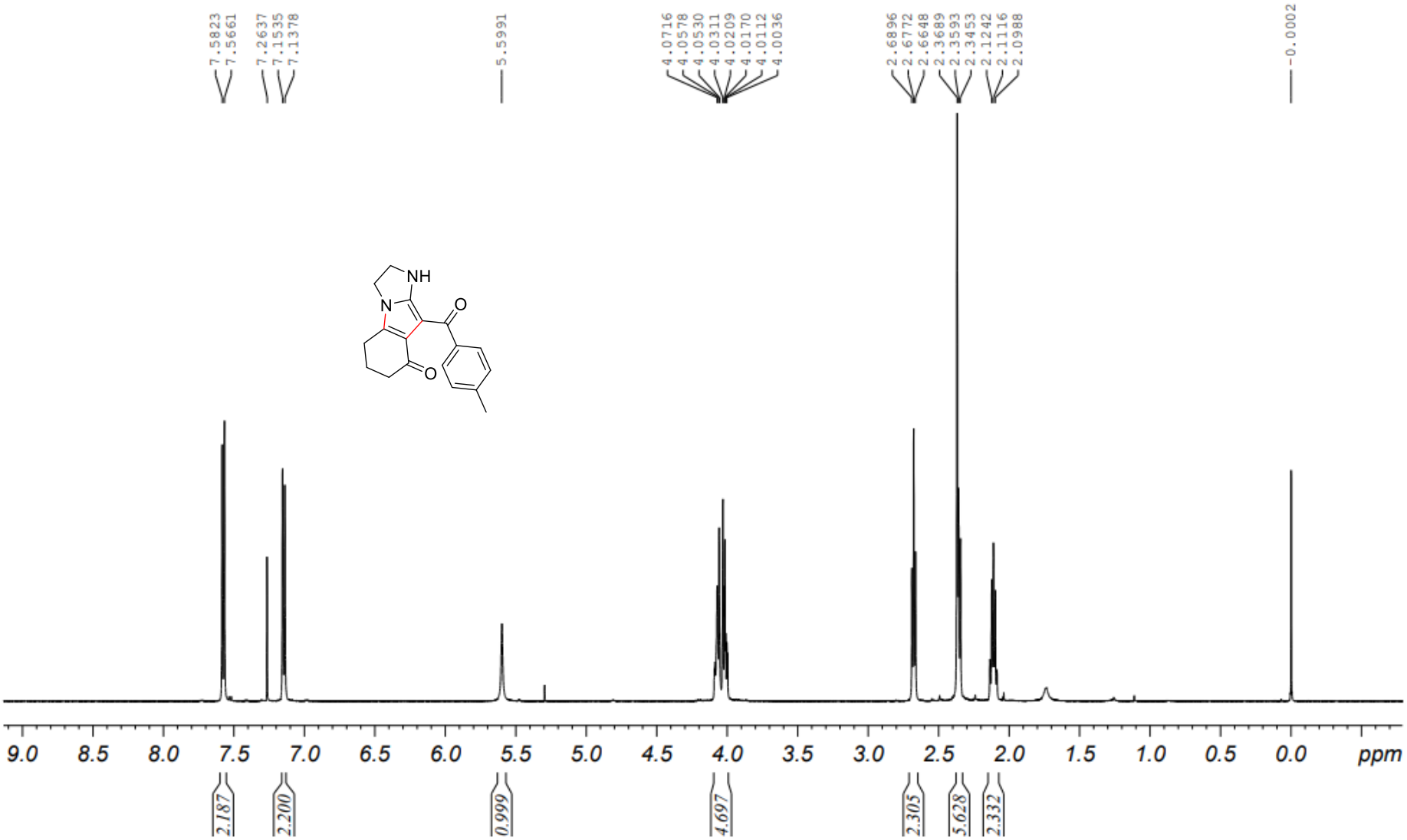


Figure S37. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **3p**

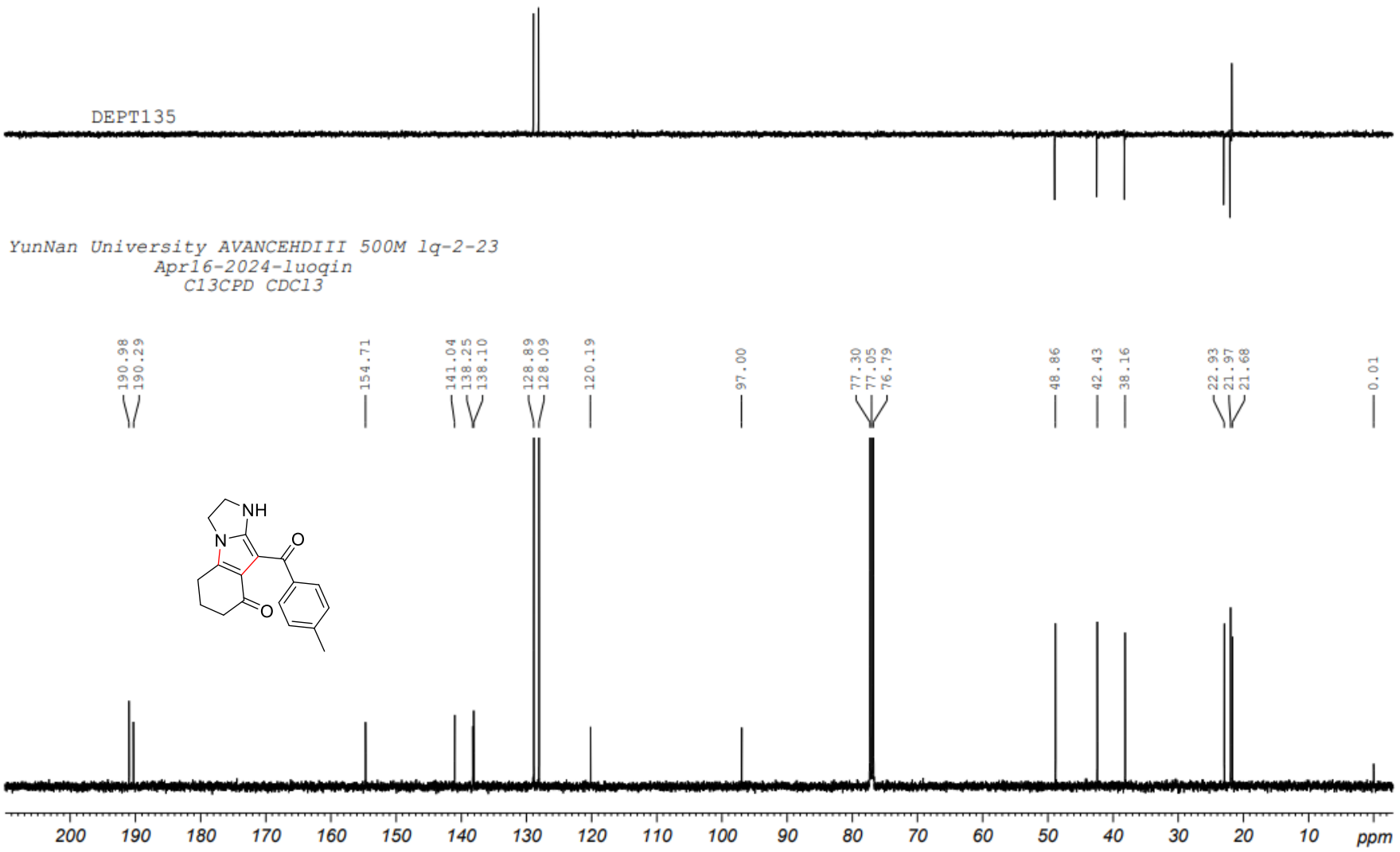


Figure S38. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **3p**

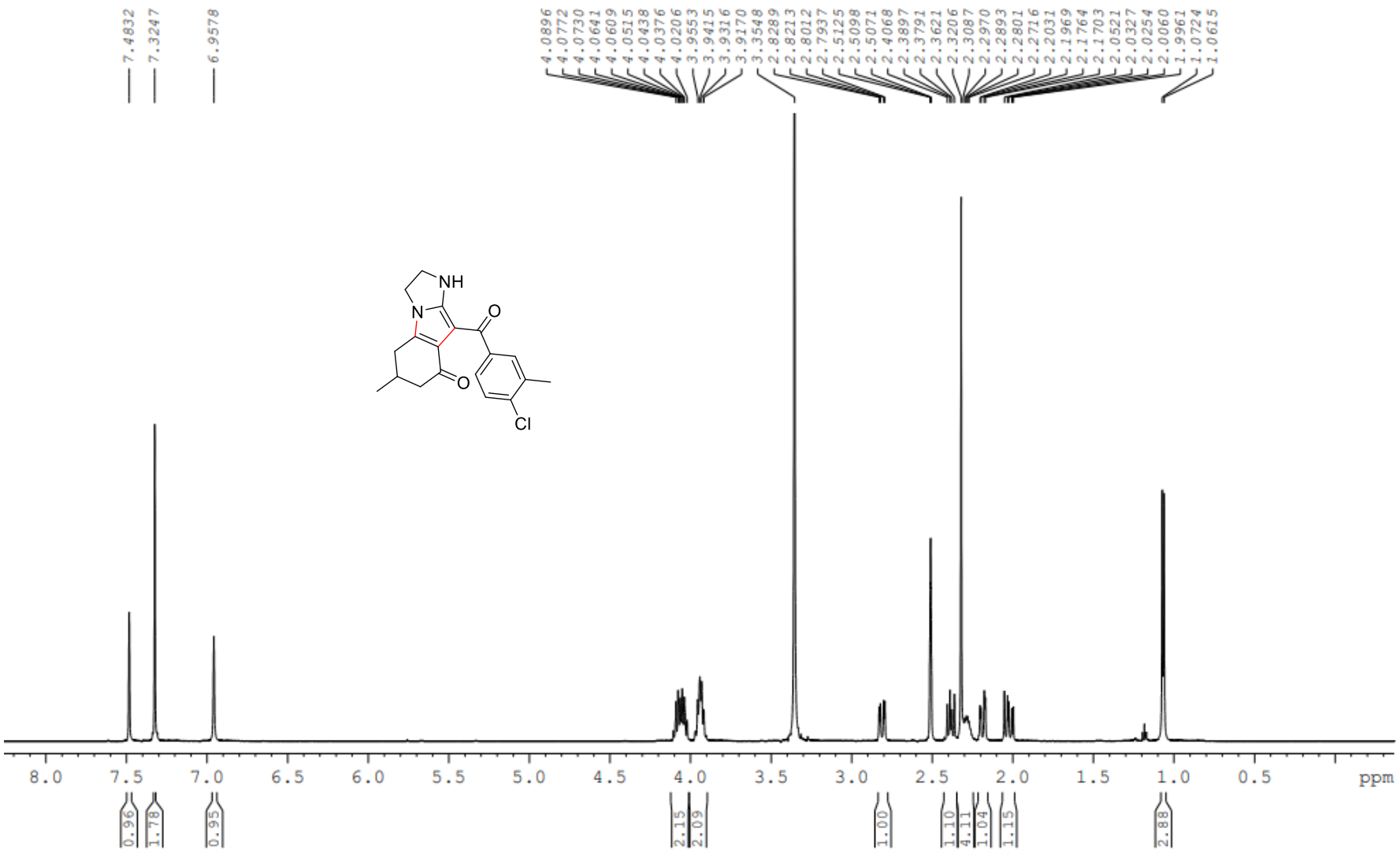


Figure S39. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **3q**

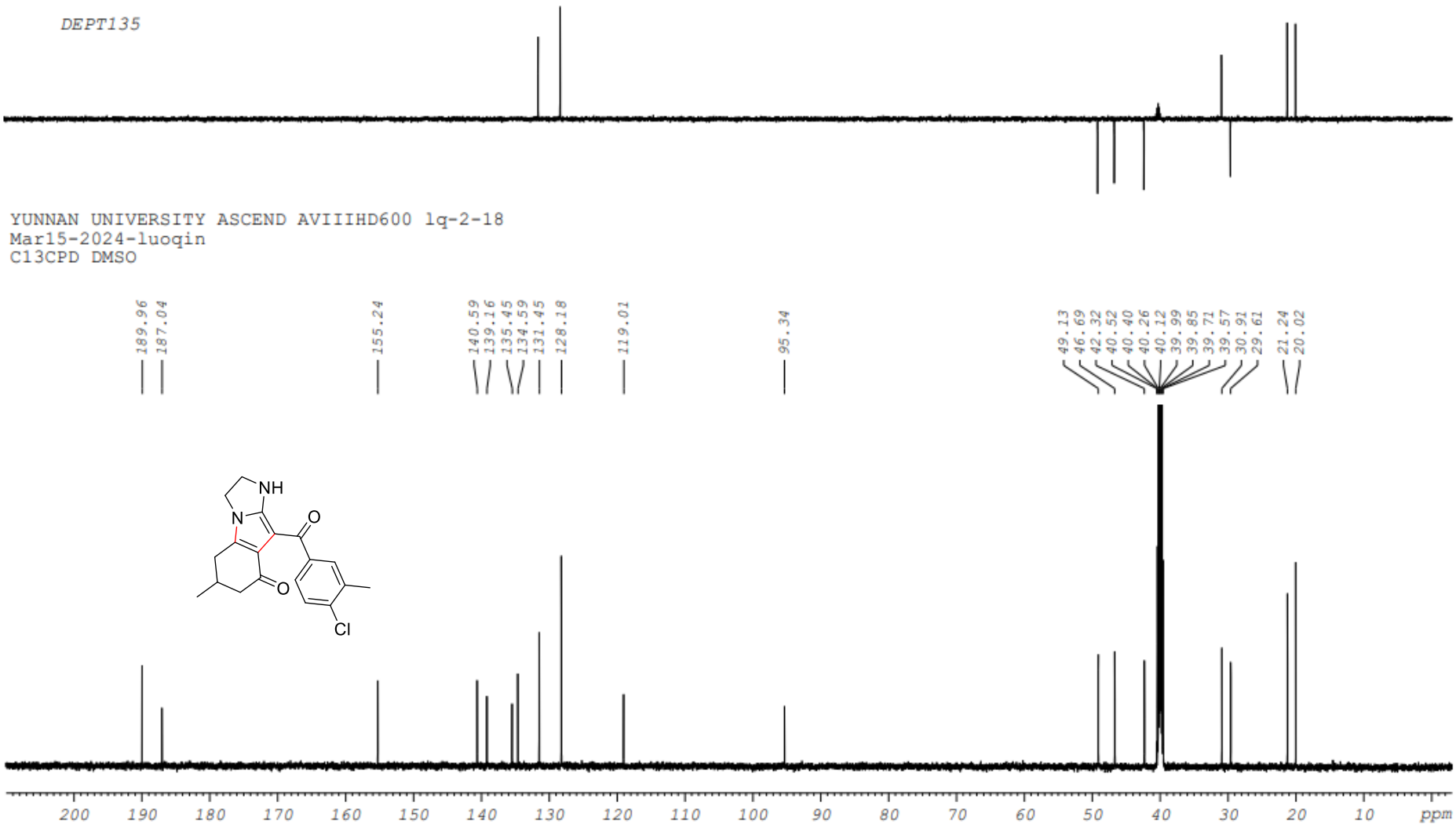


Figure S40. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **3q**

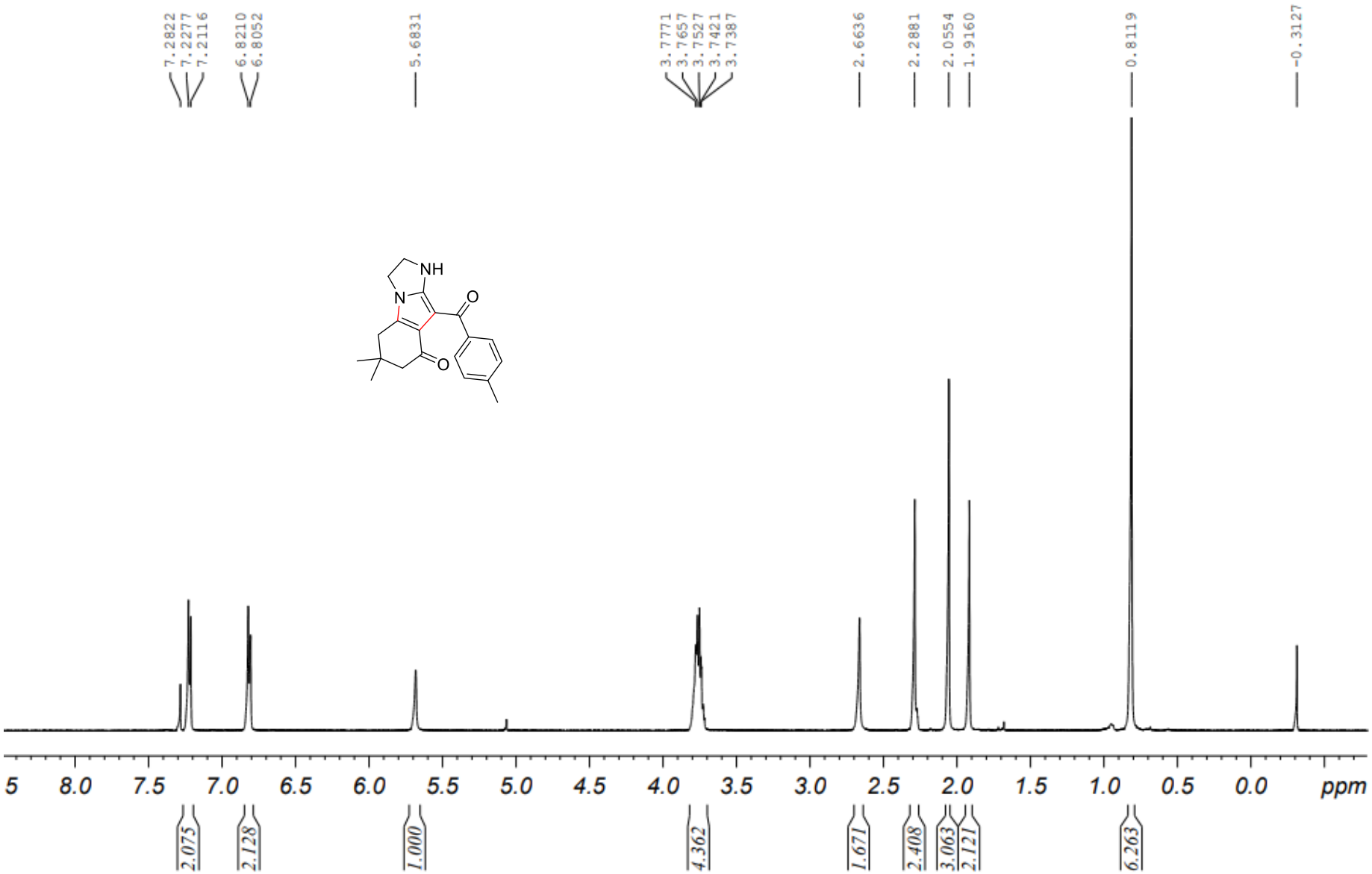


Figure S41. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **3r**

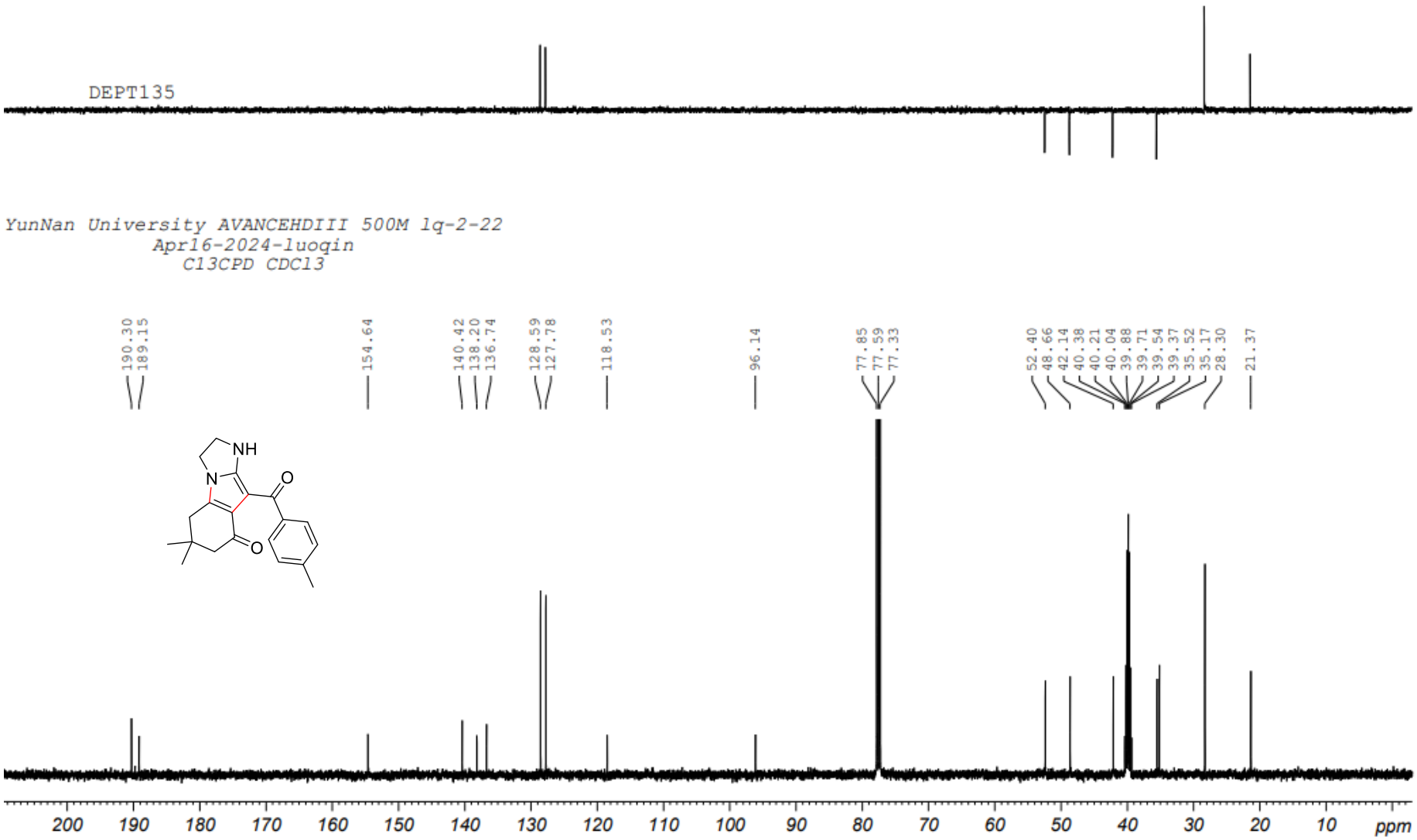


Figure S42. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **3r**

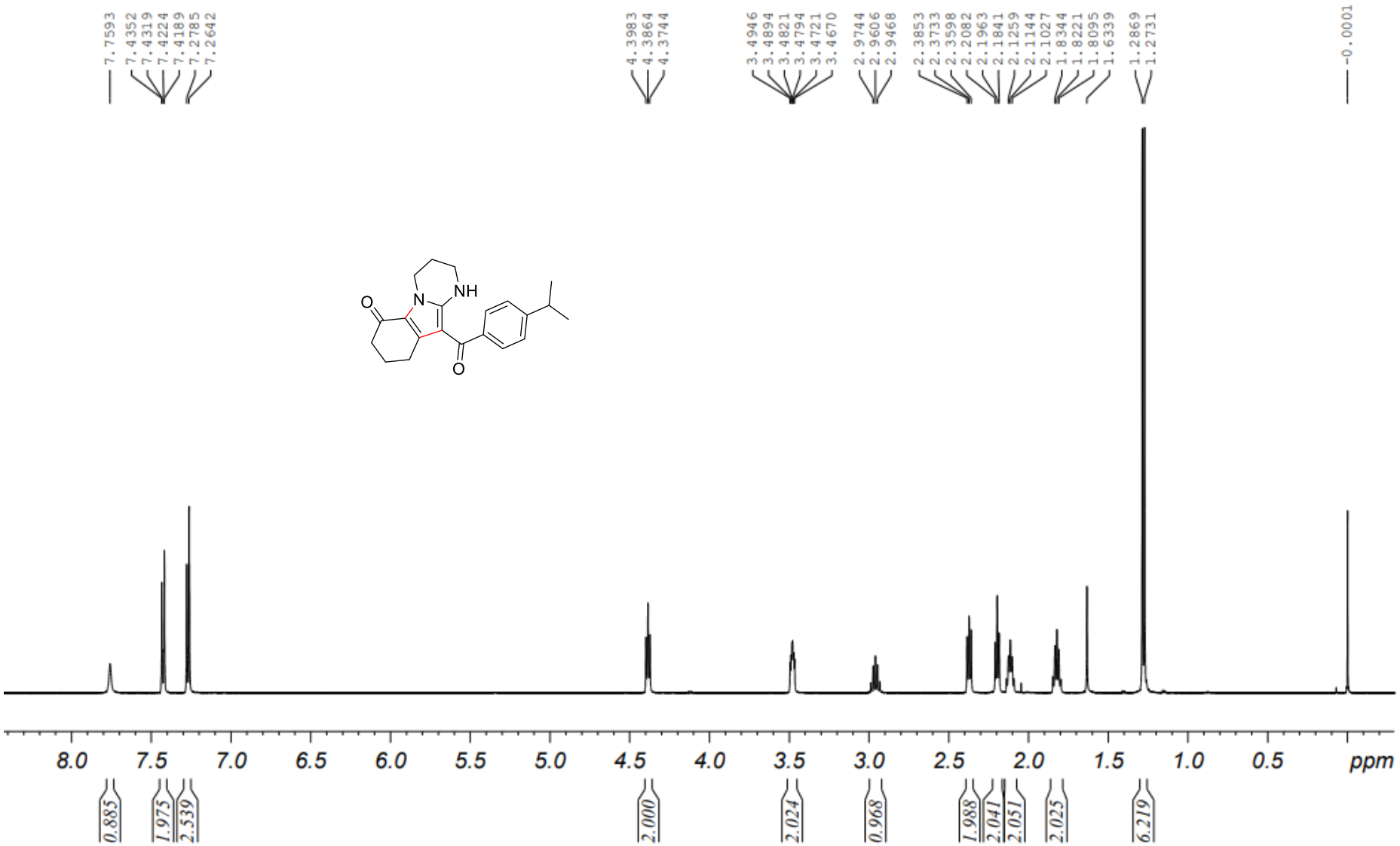


Figure S43. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **4a**

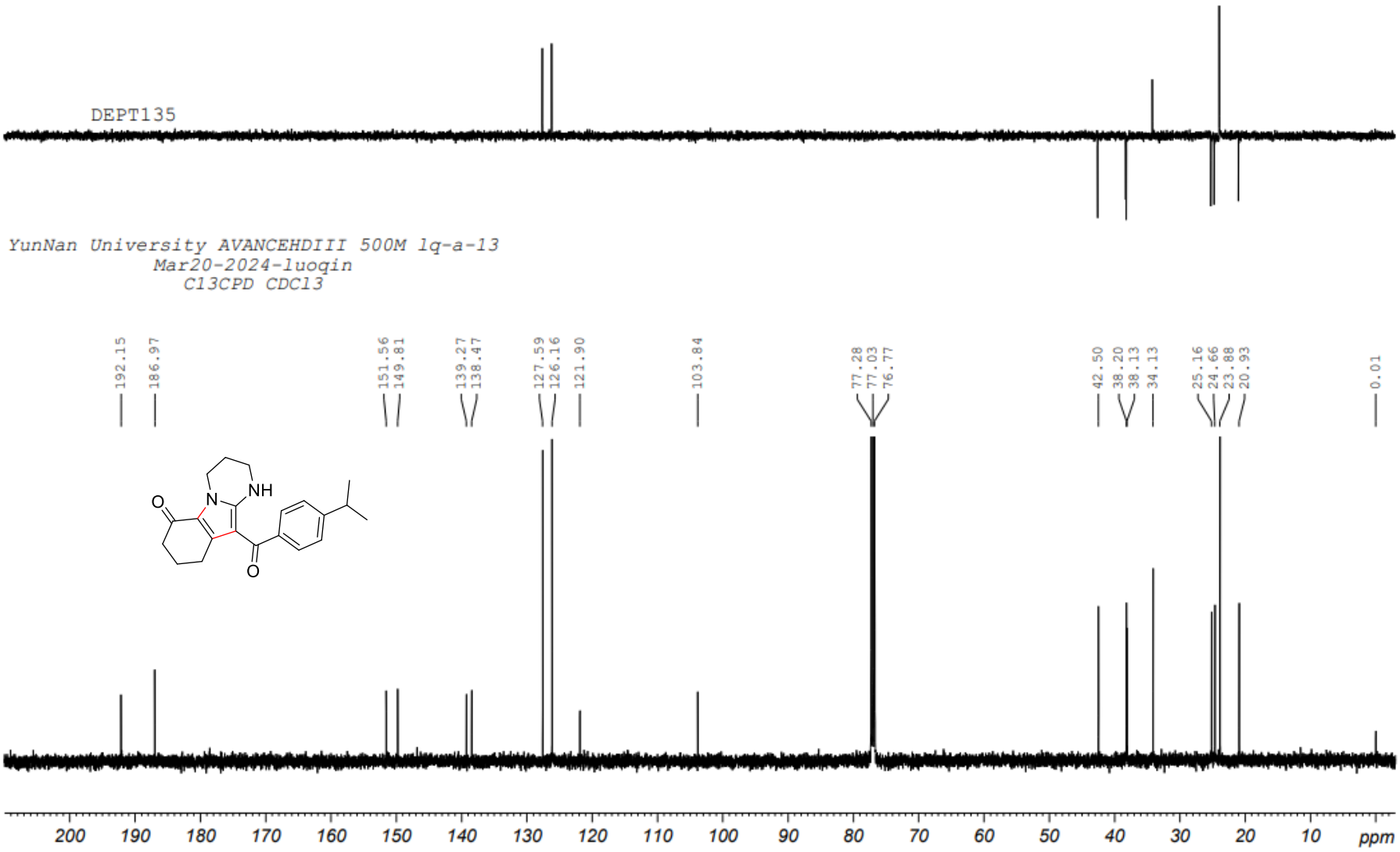


Figure S44. ^{13}C NMR (150 MHz,$CDCl_3$-d_6) spectra of compound **4a**

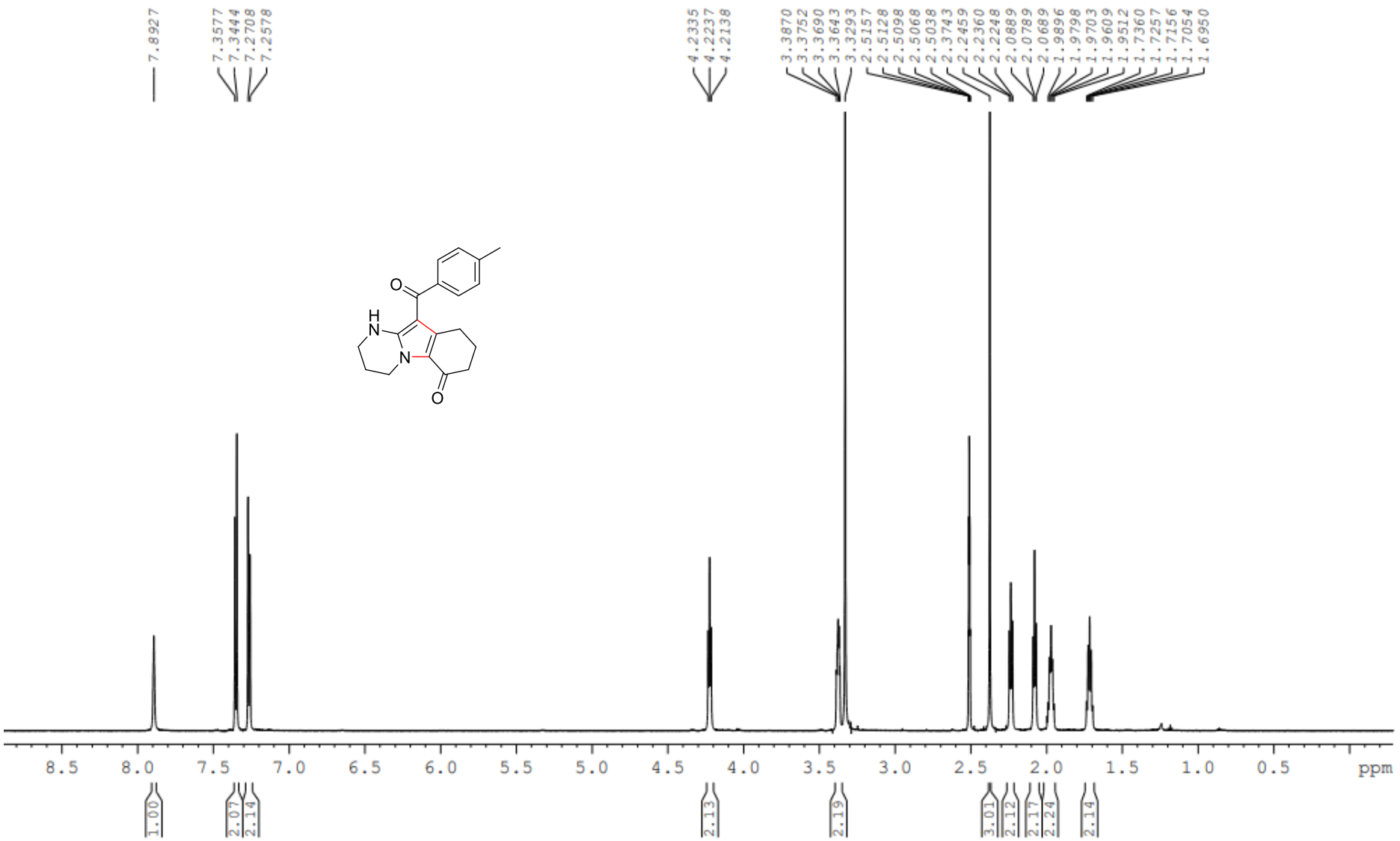


Figure S45. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **4b**

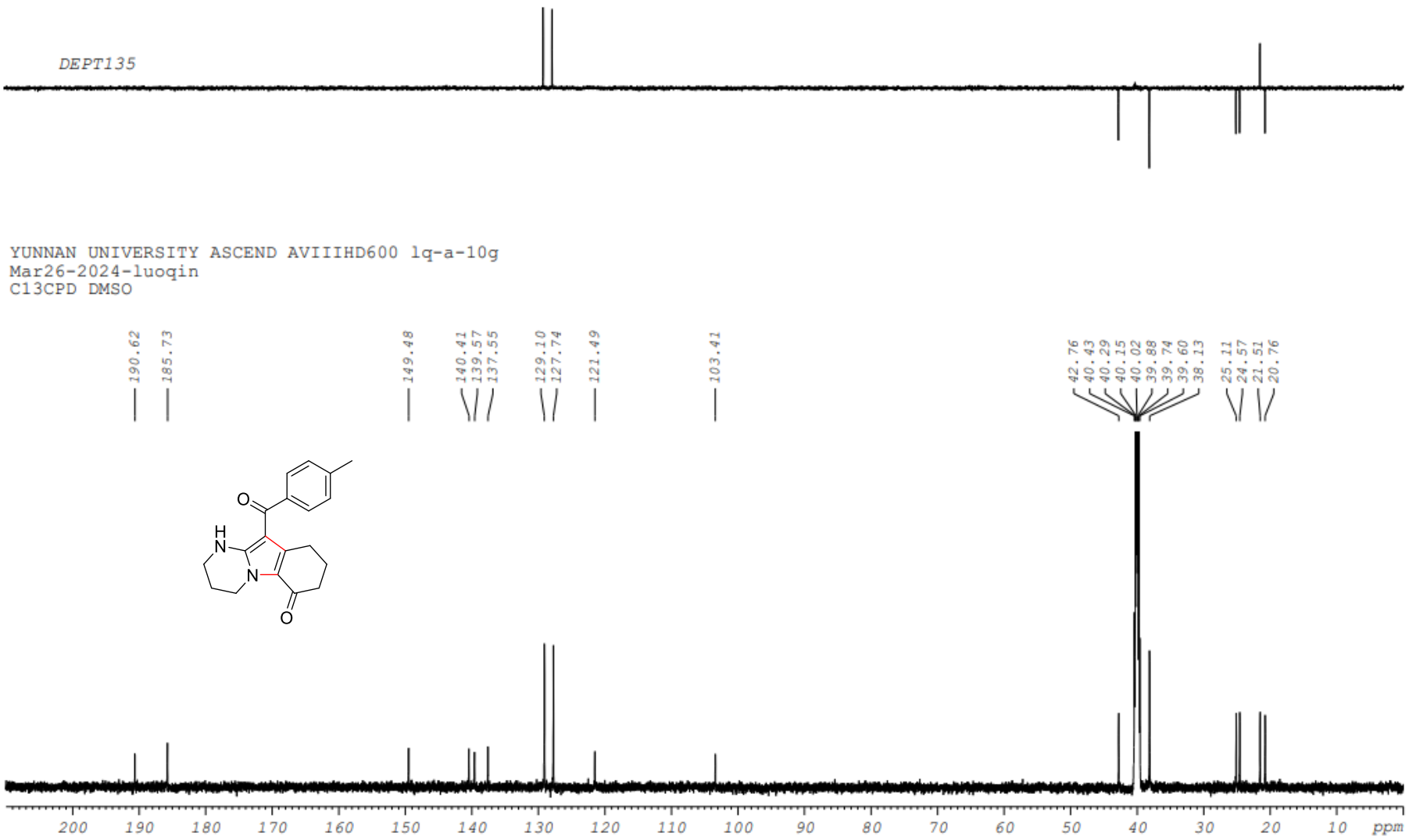


Figure S46. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **4b**

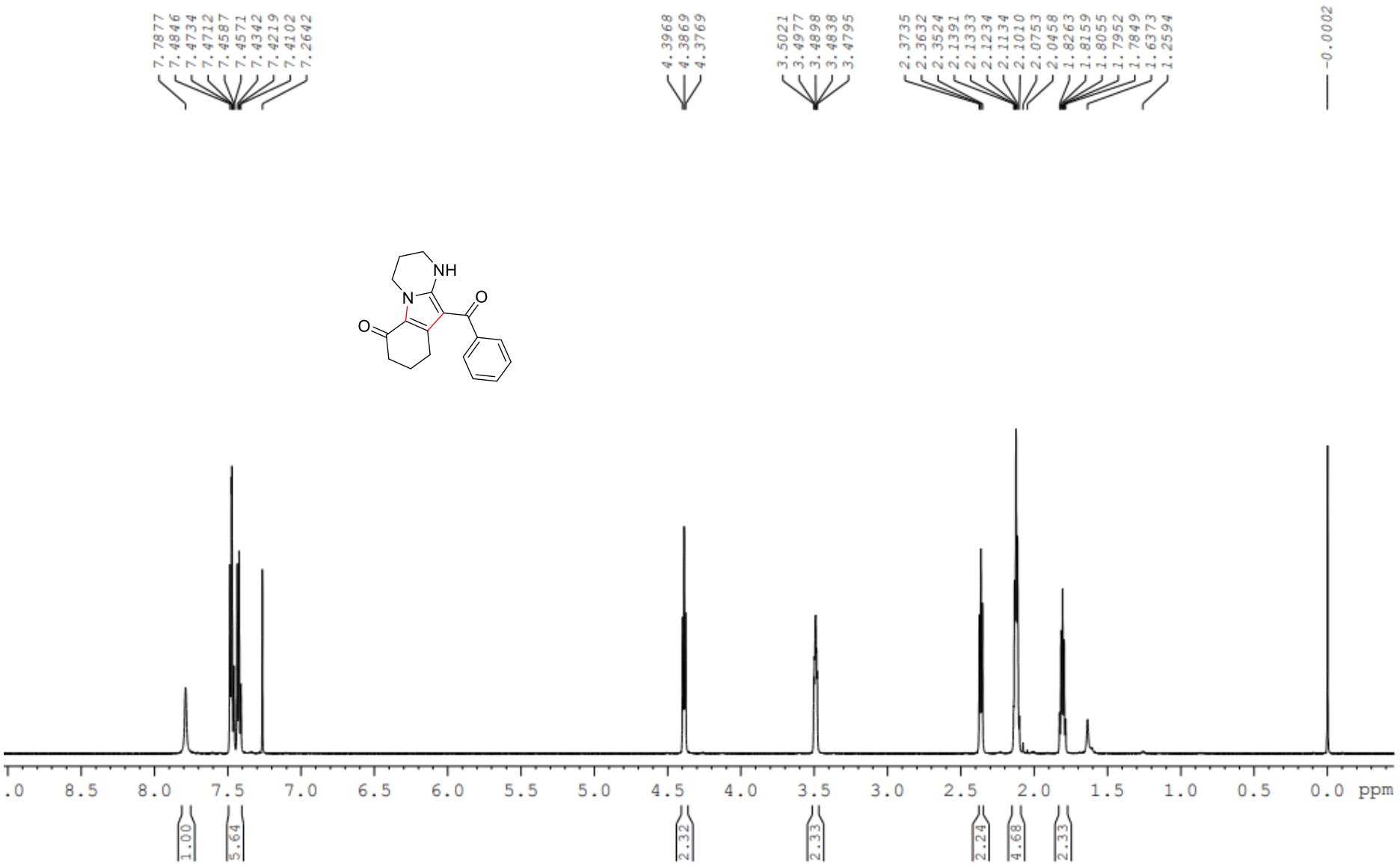


Figure S47. ^{1}H NMR (600 MHz,$CDCl_3$-d_6) spectra of compound **4c**

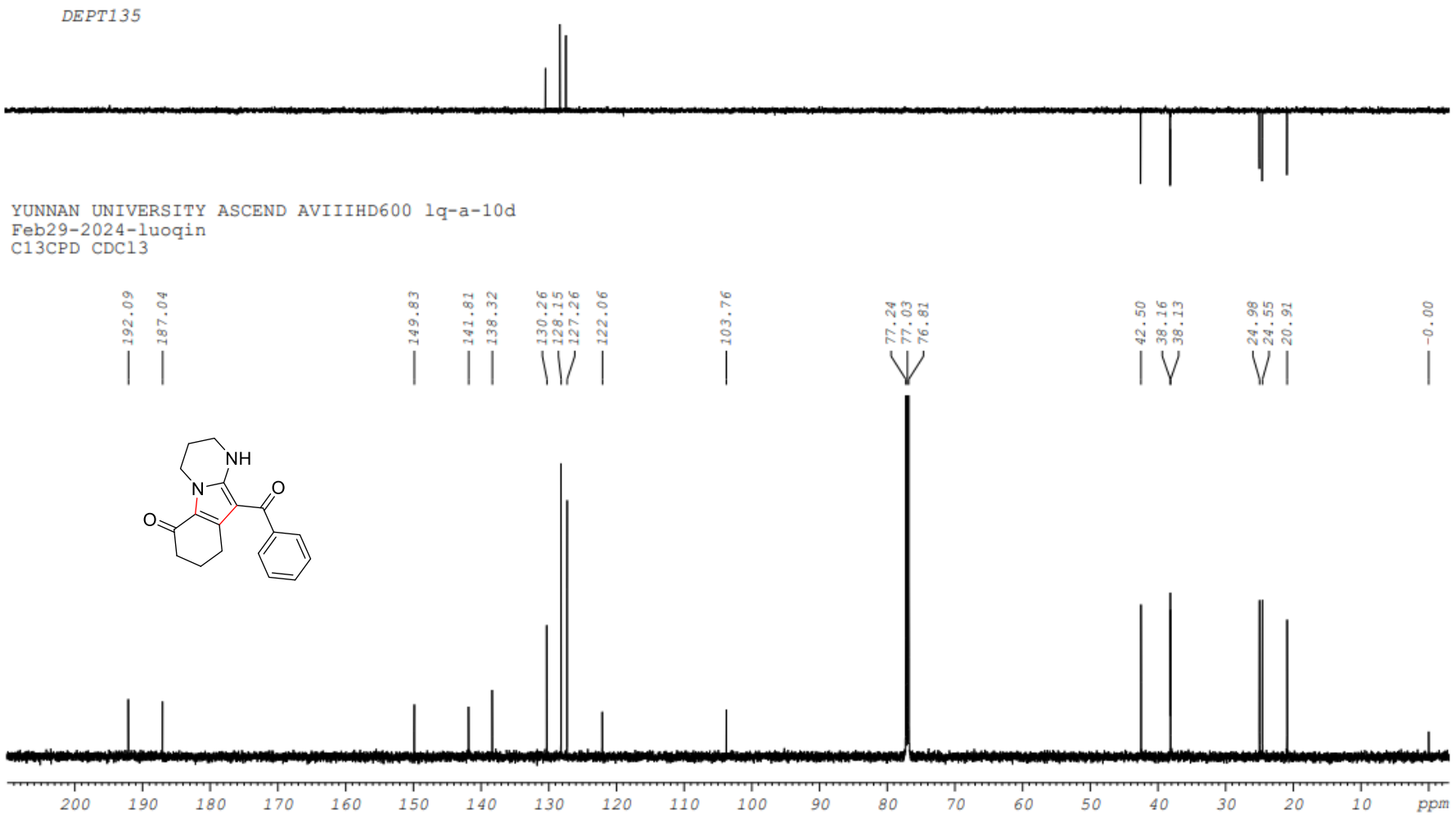


Figure S48. ^{13}C NMR (150 MHz,$CDCl_3$-d_6) spectra of compound **4c**

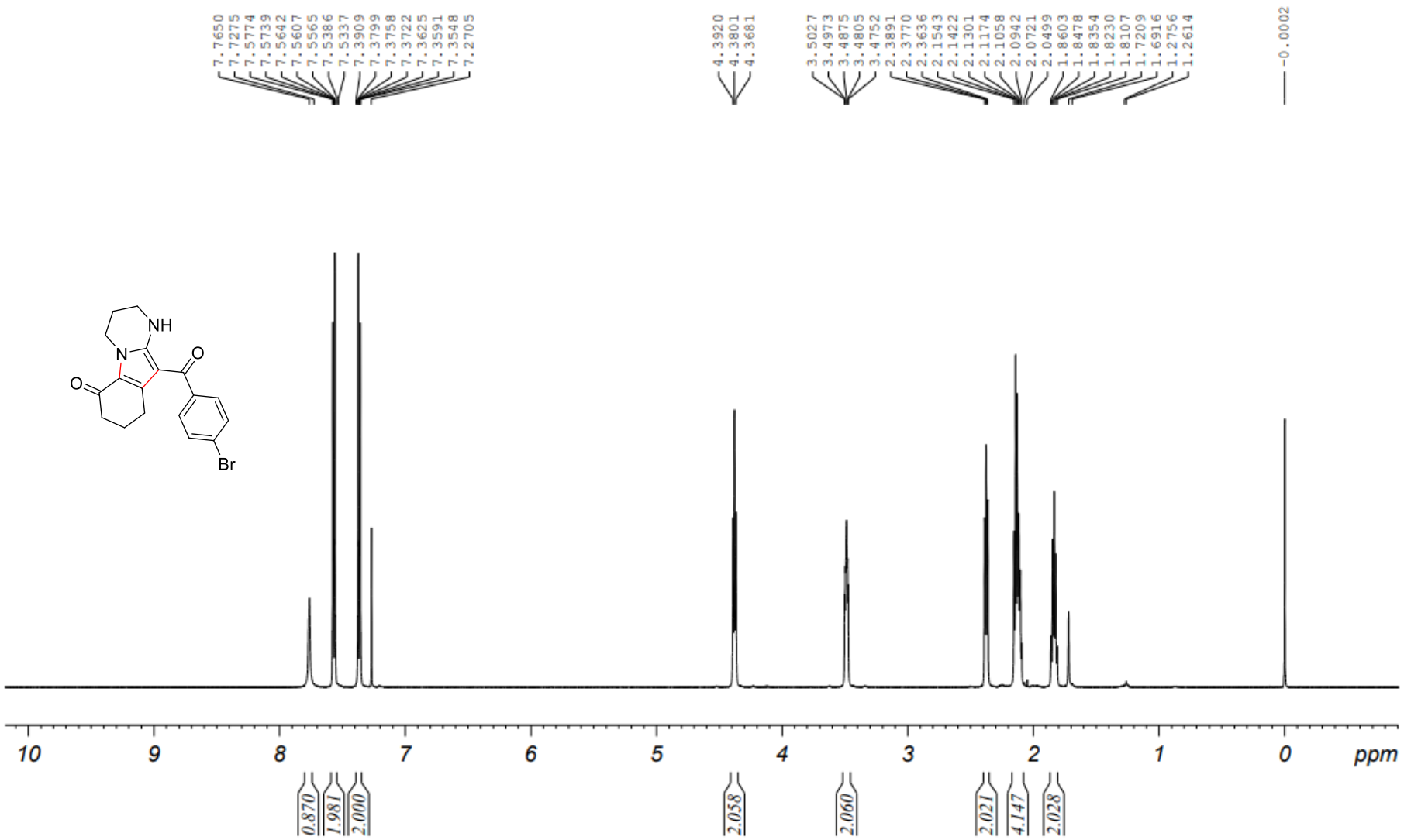


Figure S49. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **4d**

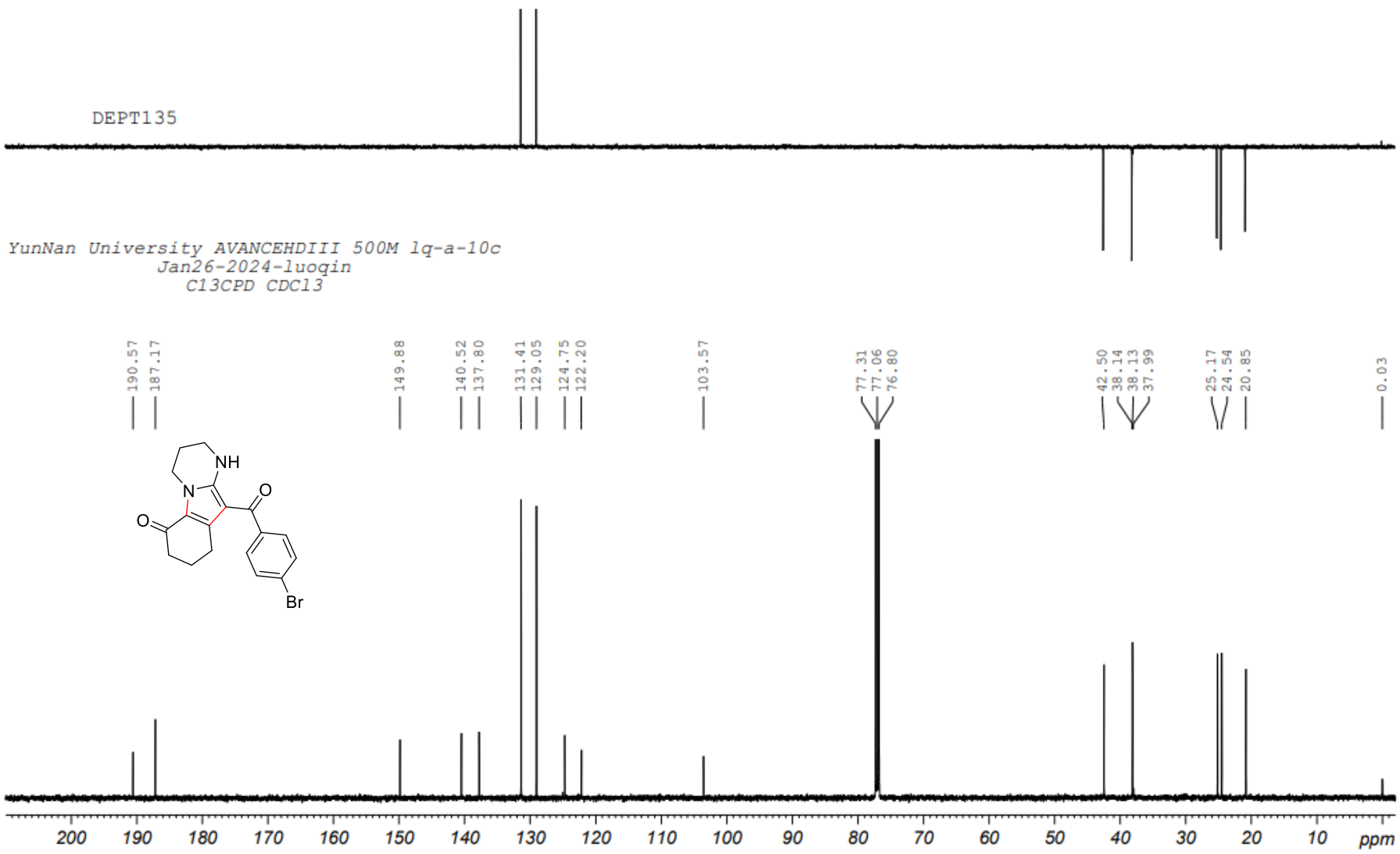


Figure S50. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **4d**

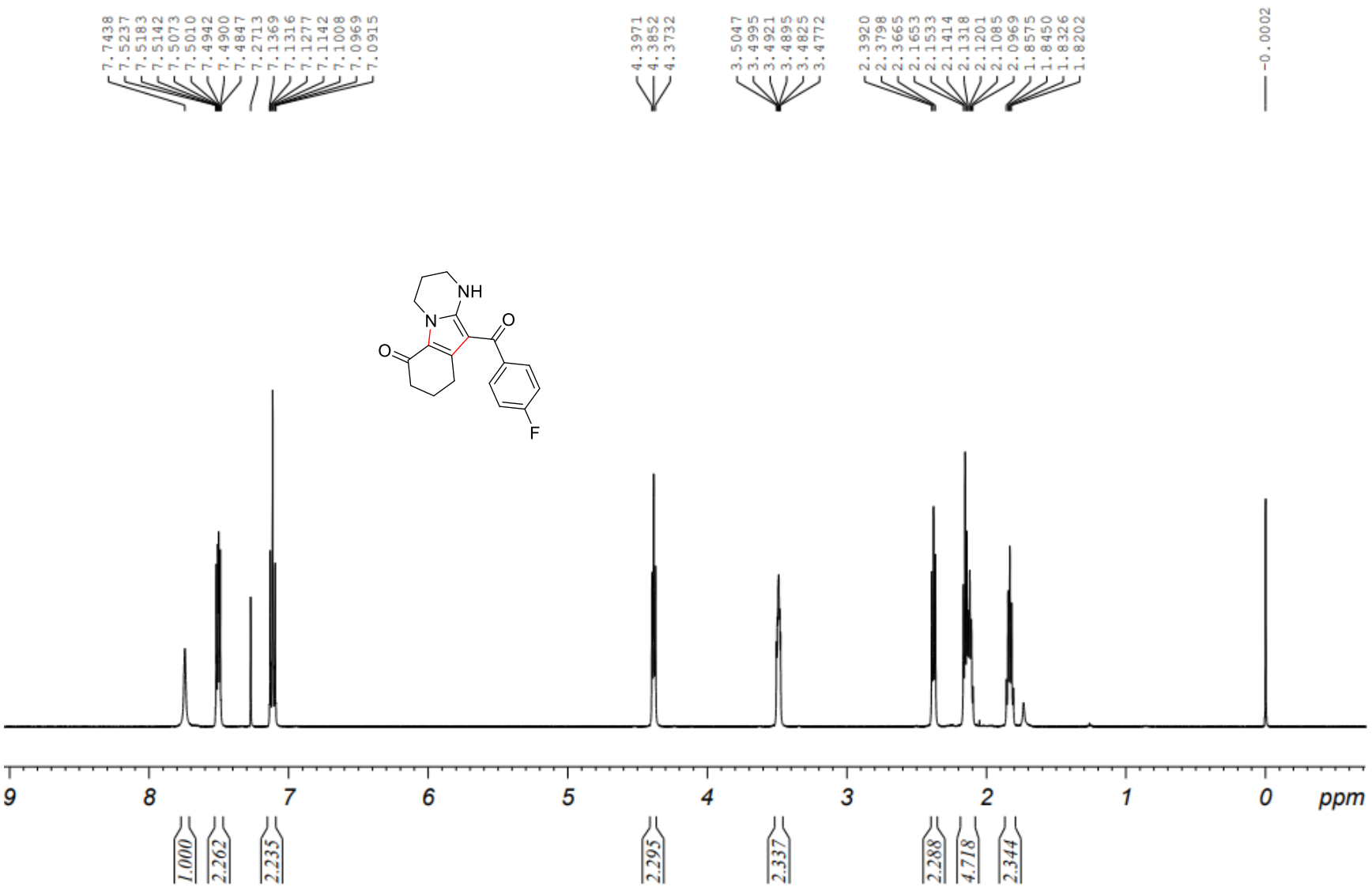


Figure S51. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **4e**

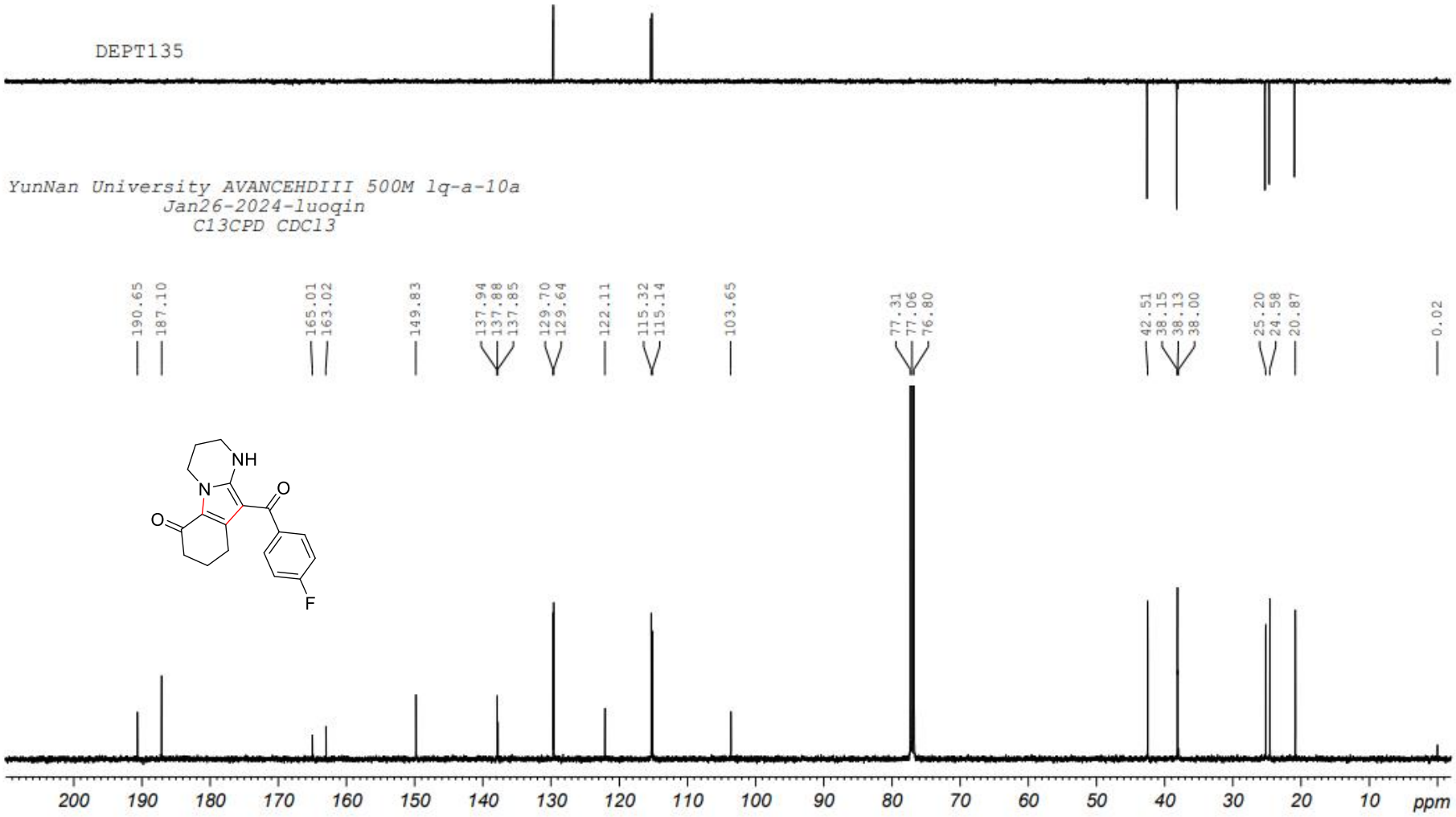


Figure S52. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **4e**

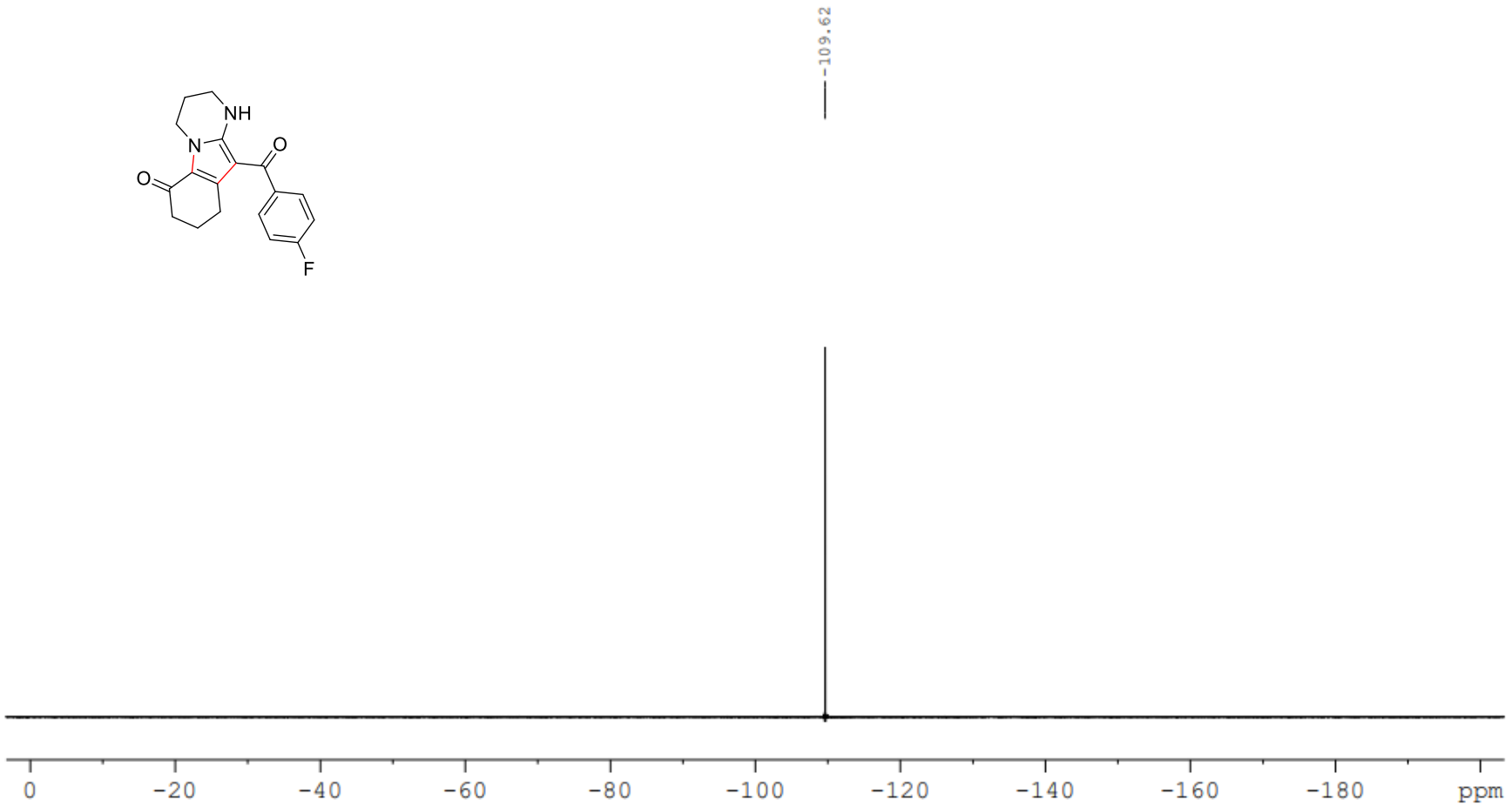


Figure S53. ^{19}F NMR (475 MHz, $CDCl_3$-d_6) spectra of compound **4e**

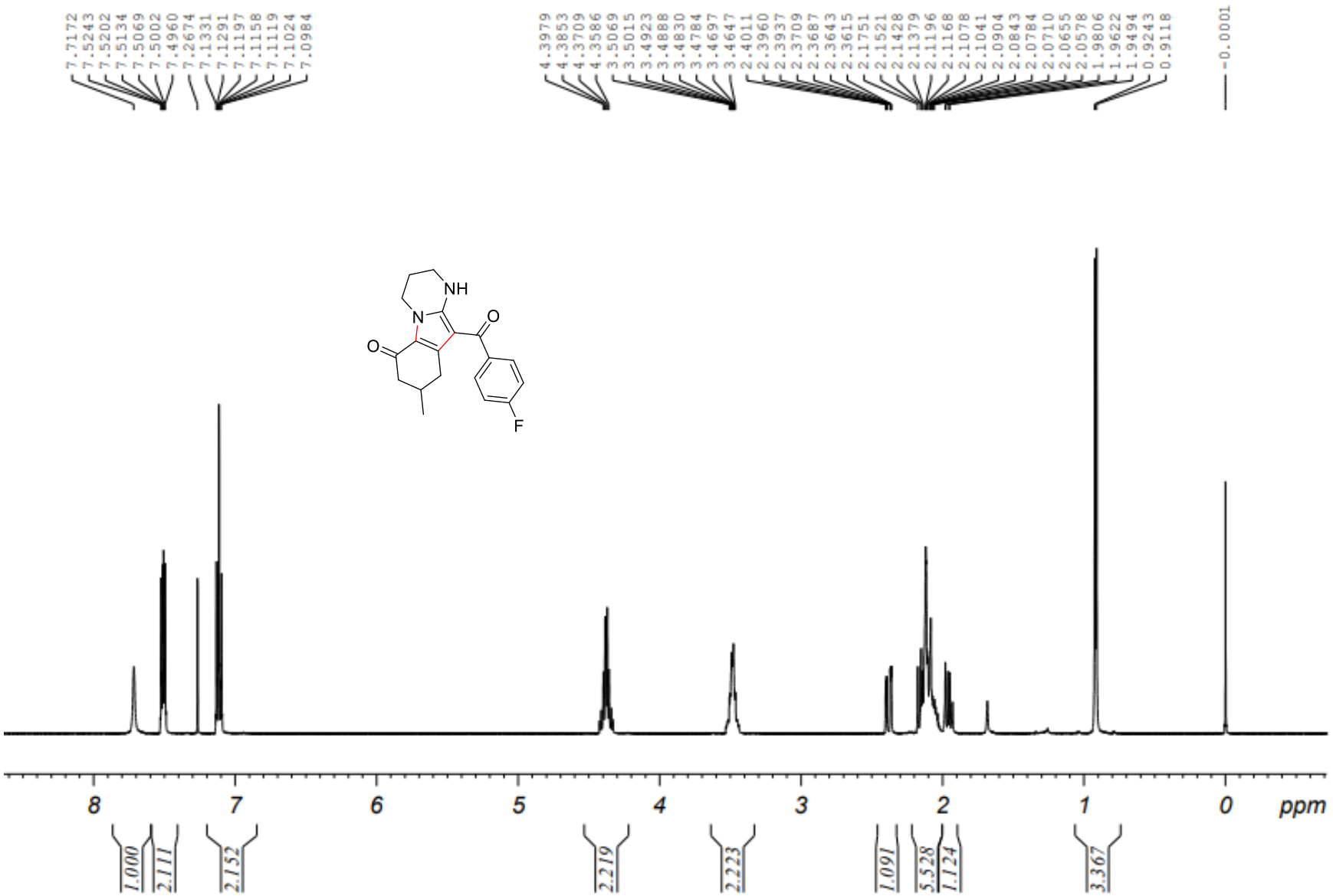


Figure S54. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **4f**

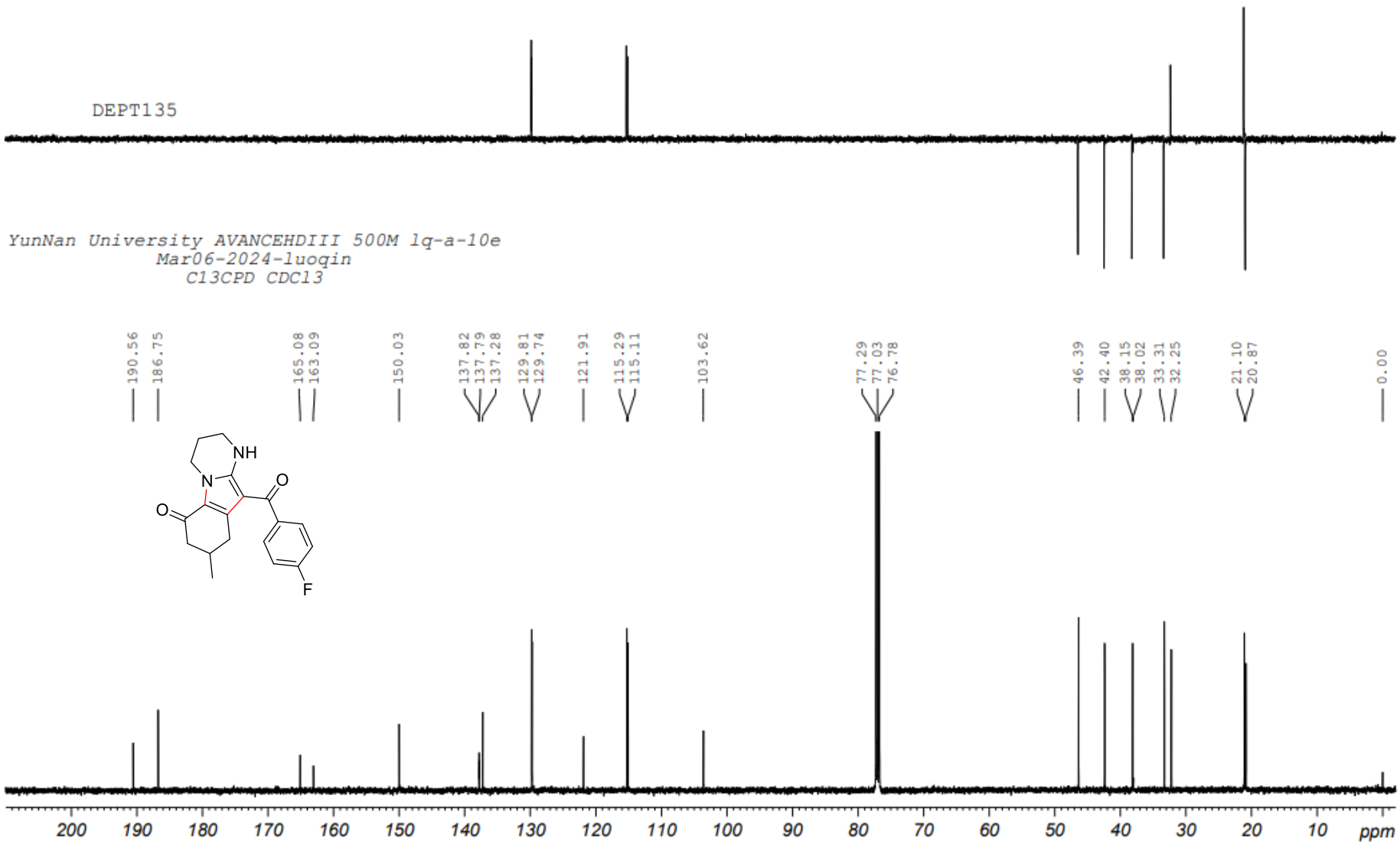


Figure S55. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **4f**

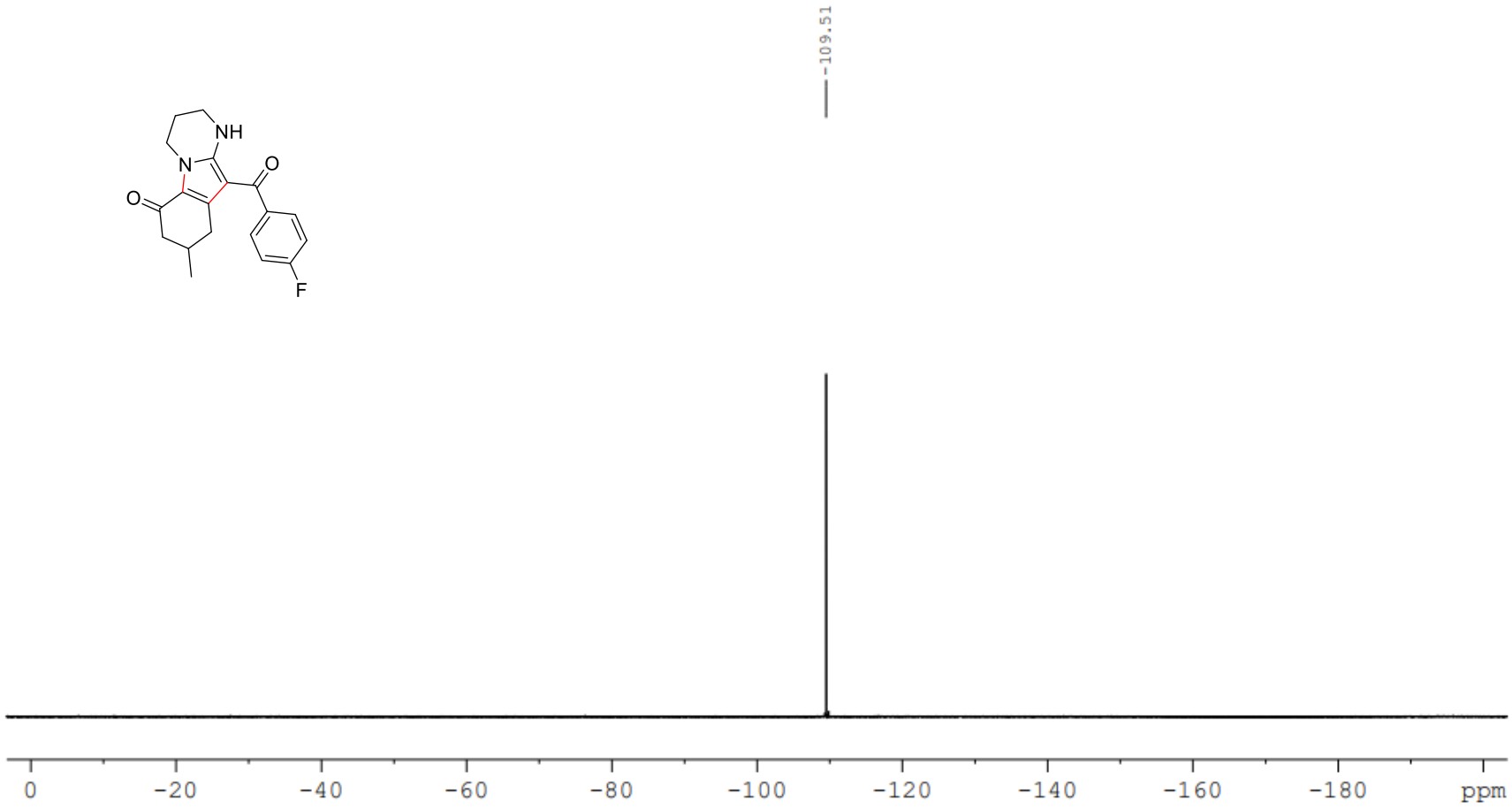


Figure S56. ^{19}F NMR (475 MHz, $CDCl_3$-d_6) spectra of compound **4f**

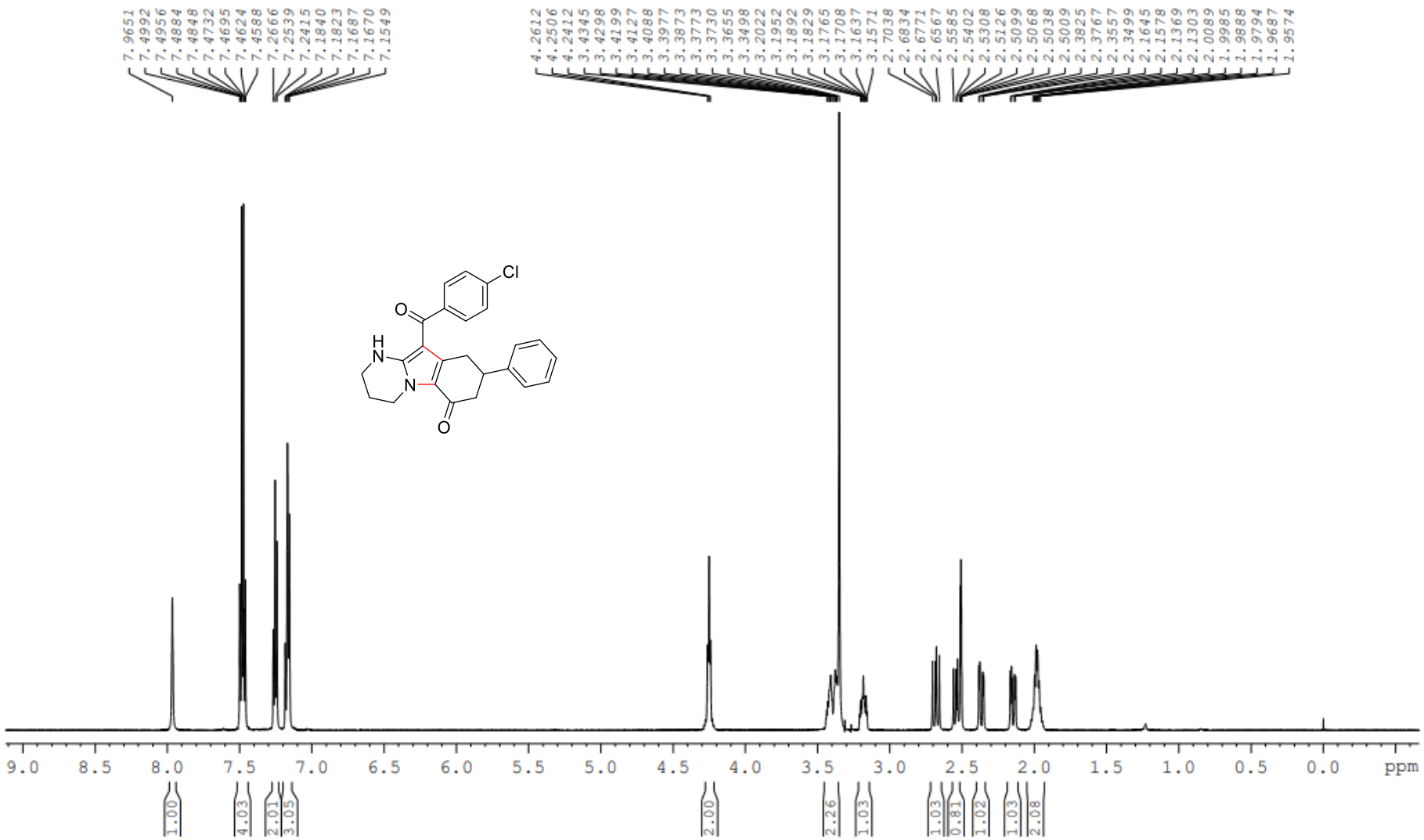


Figure S57. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **4g**

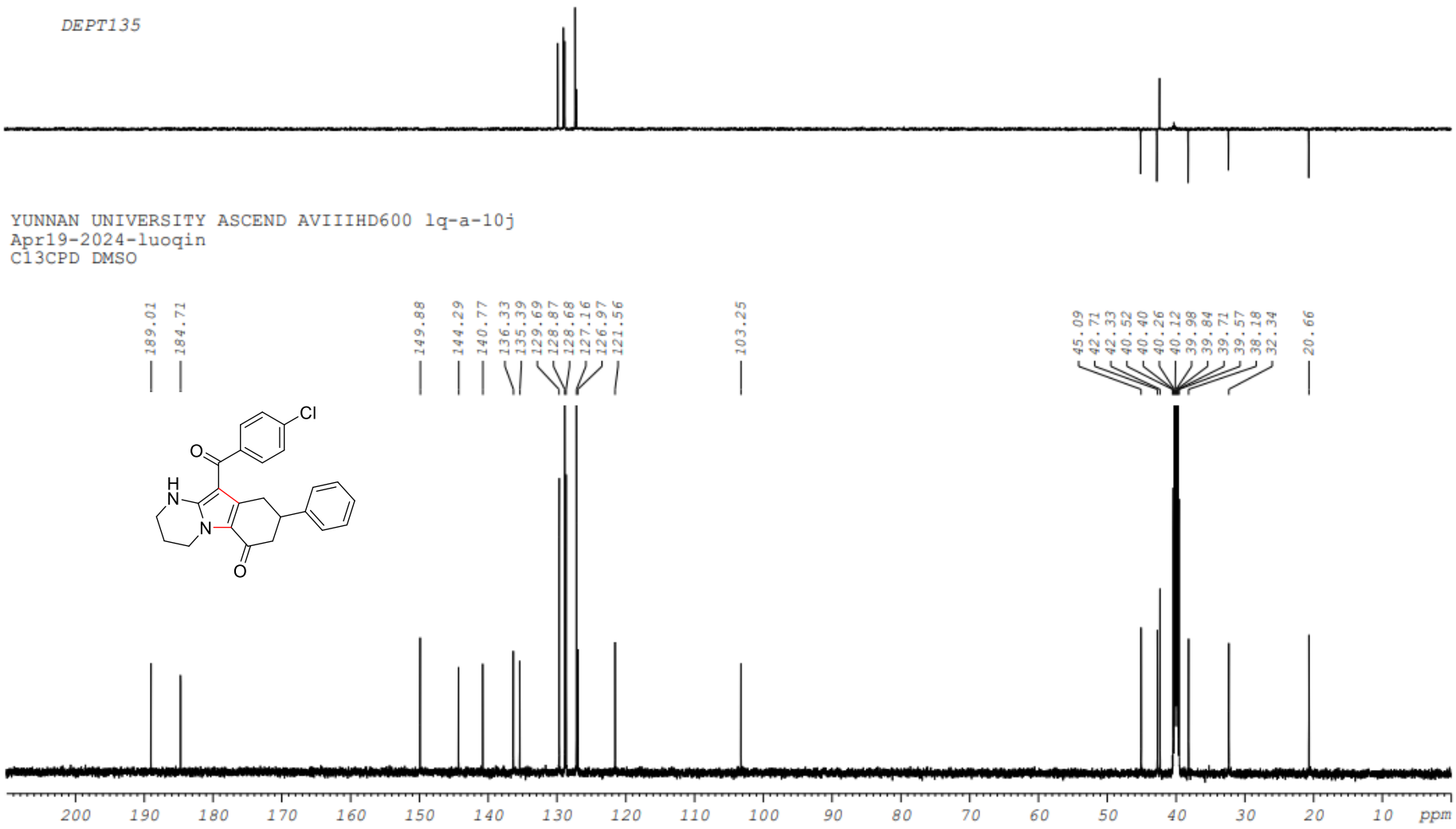


Figure S58. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **4g**

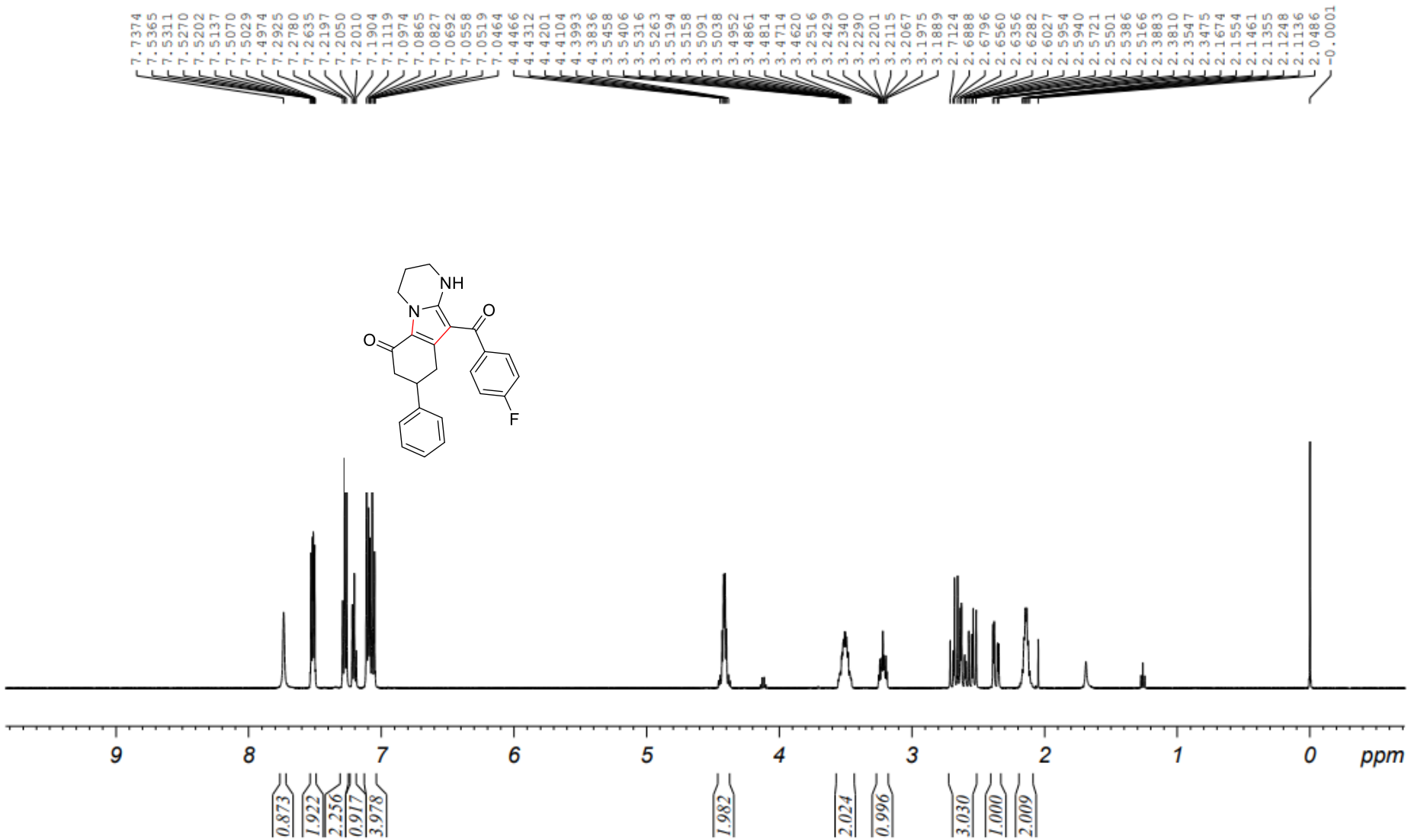


Figure S59. ^{1}H NMR (500 MHz,$CDCl_3$-d_6) spectra of compound **4h**

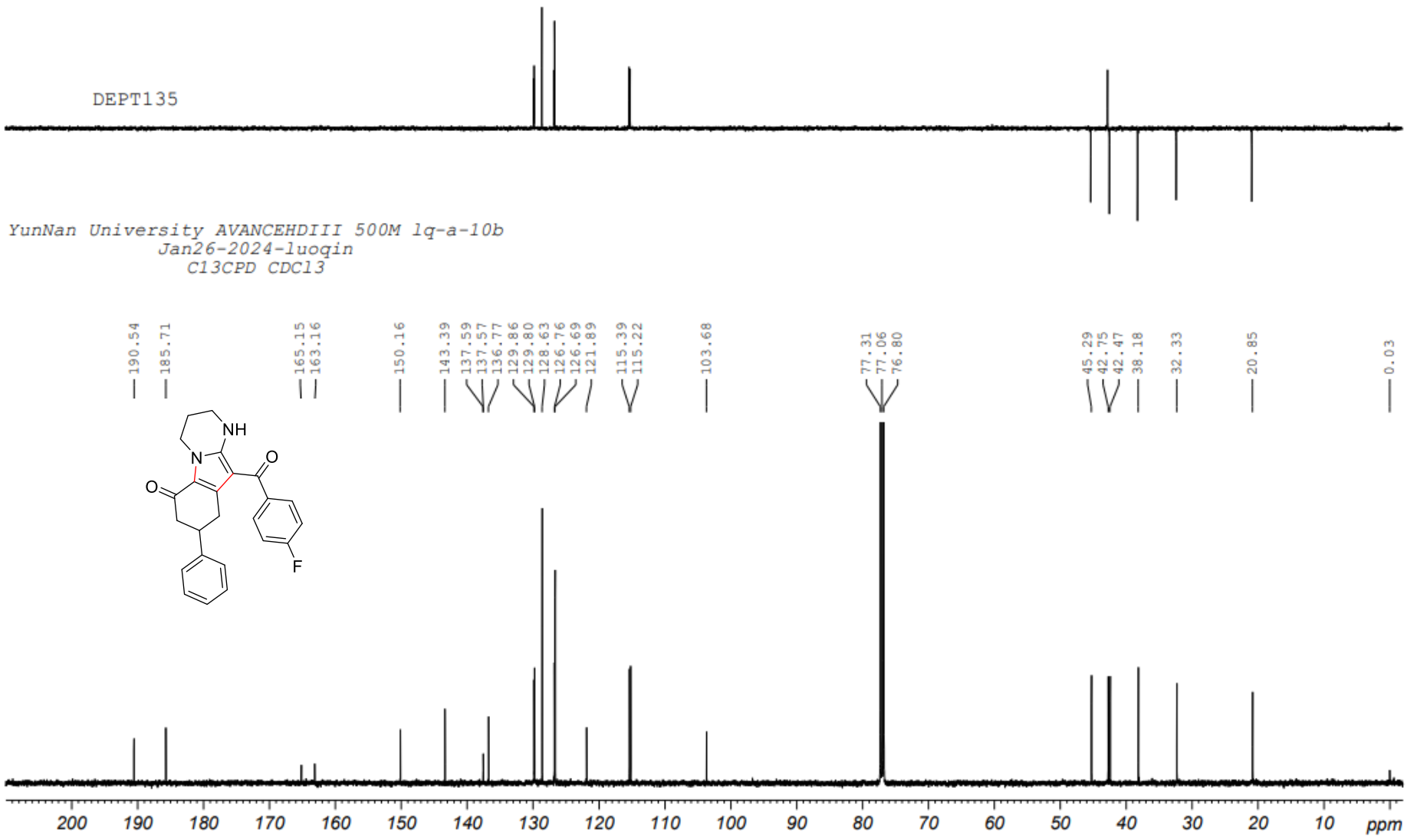


Figure S60. ^{13}C NMR (125 MHz,$CDCl_3$-d_6) spectra of compound **4h**

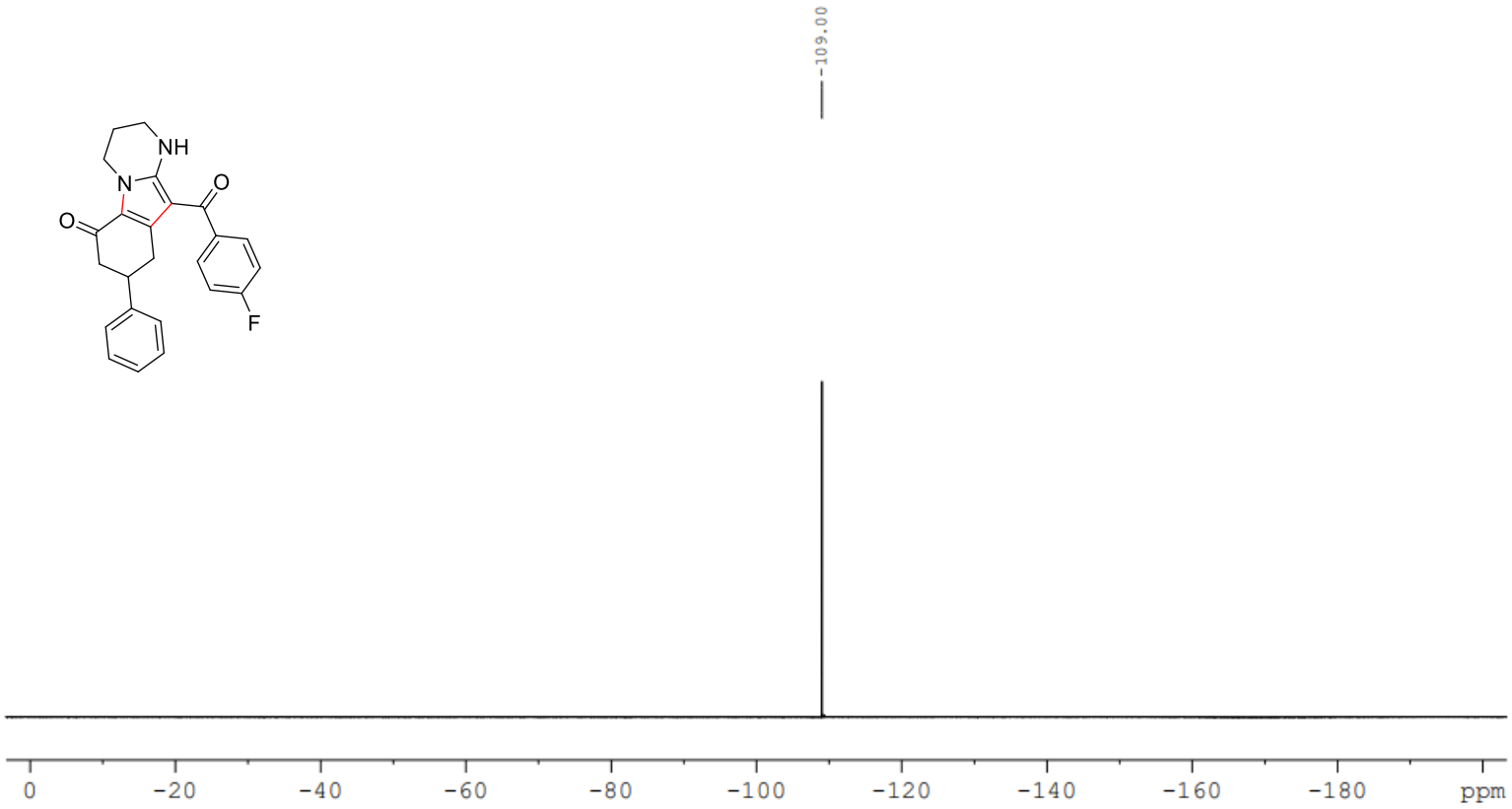


Figure S61. ^{19}F NMR (475 MHz, $CDCl_3$-d_6) spectra of compound **4h**

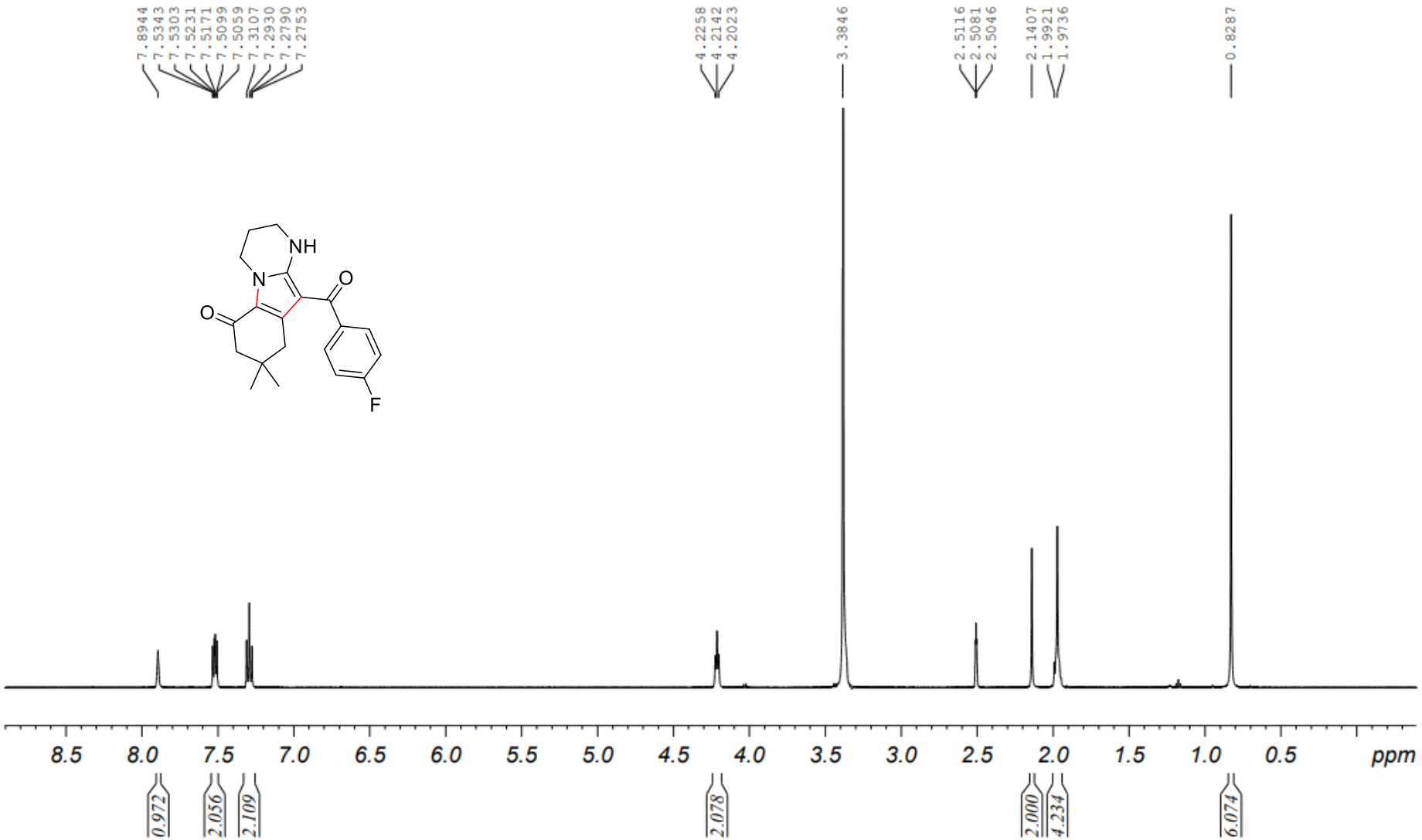


Figure S62. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **4i**

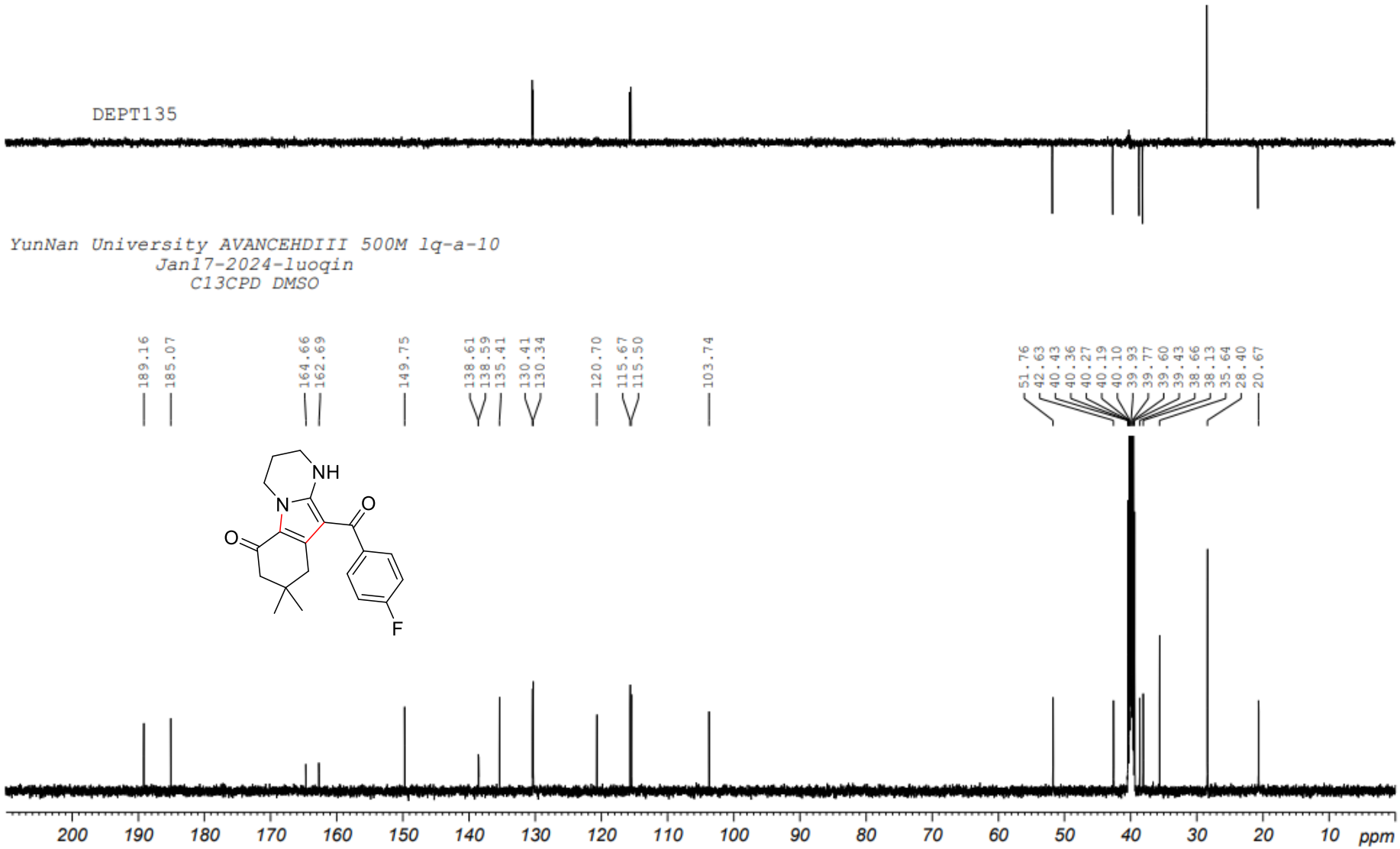


Figure S63. ^{13}C NMR (125 MHz,DMSO-d_6) spectra of compound **4i**

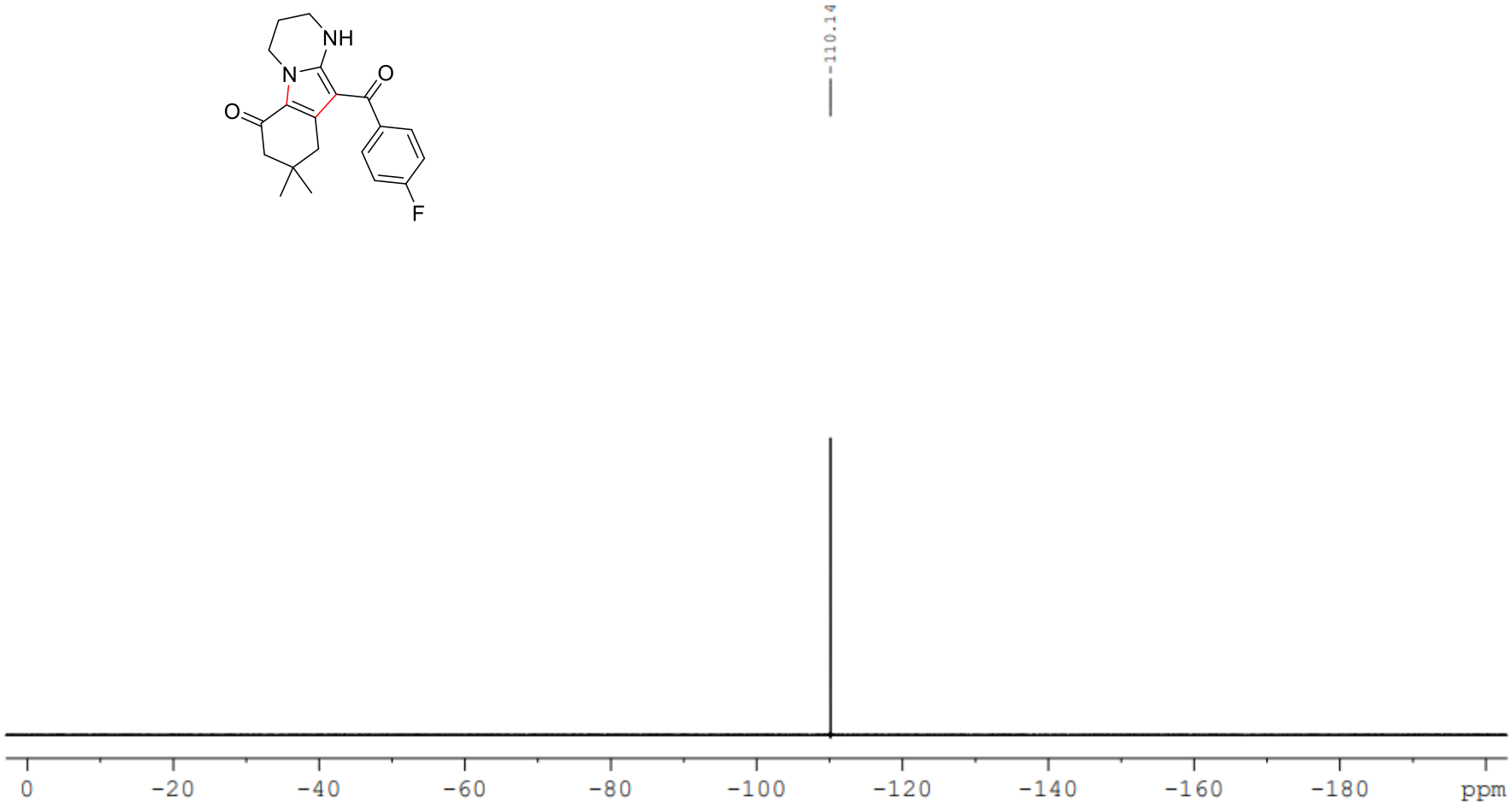


Figure S64. ^{19}F NMR (475 MHz, DMSO-d_6) spectra of compound **4i**

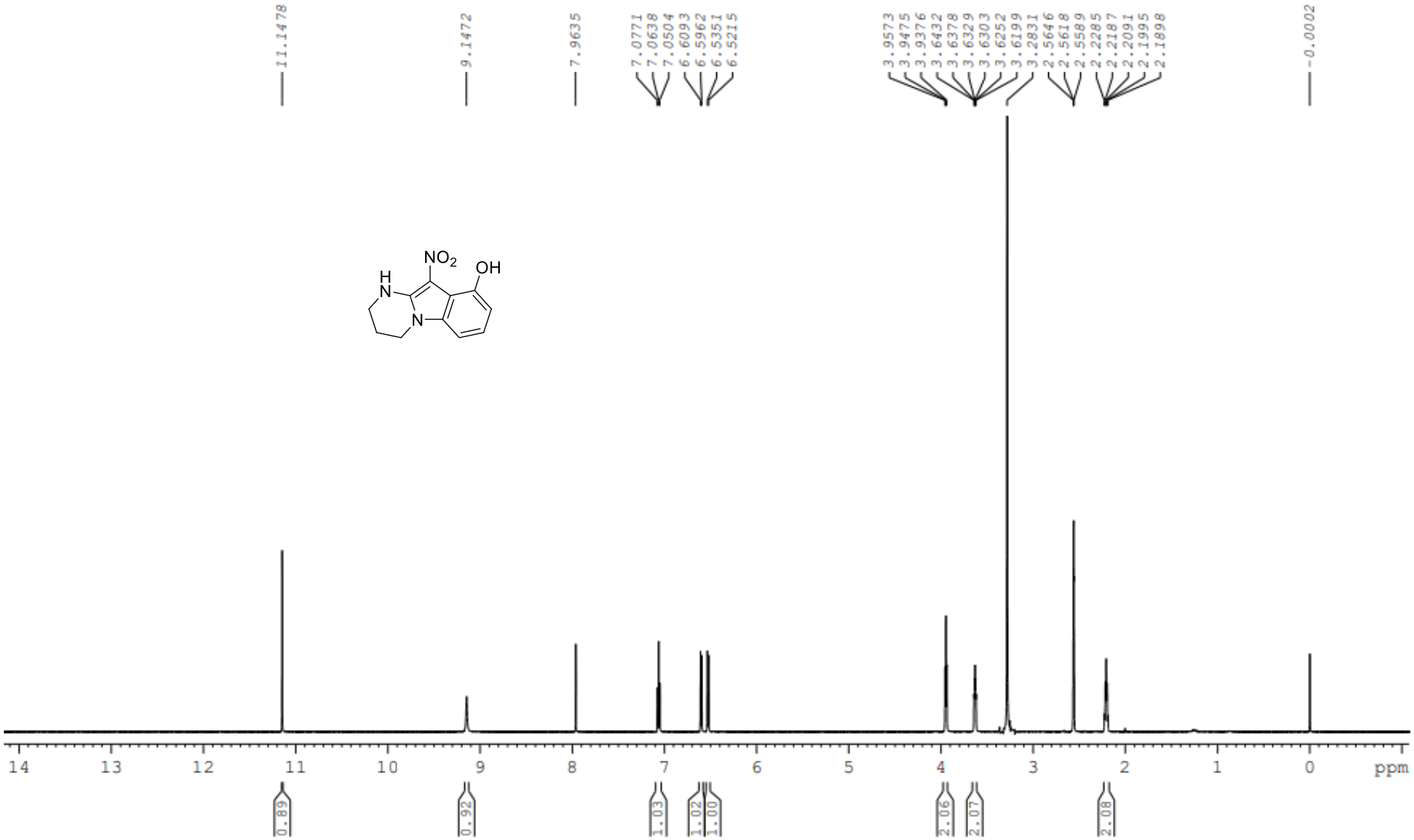


Figure S65. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **5a**

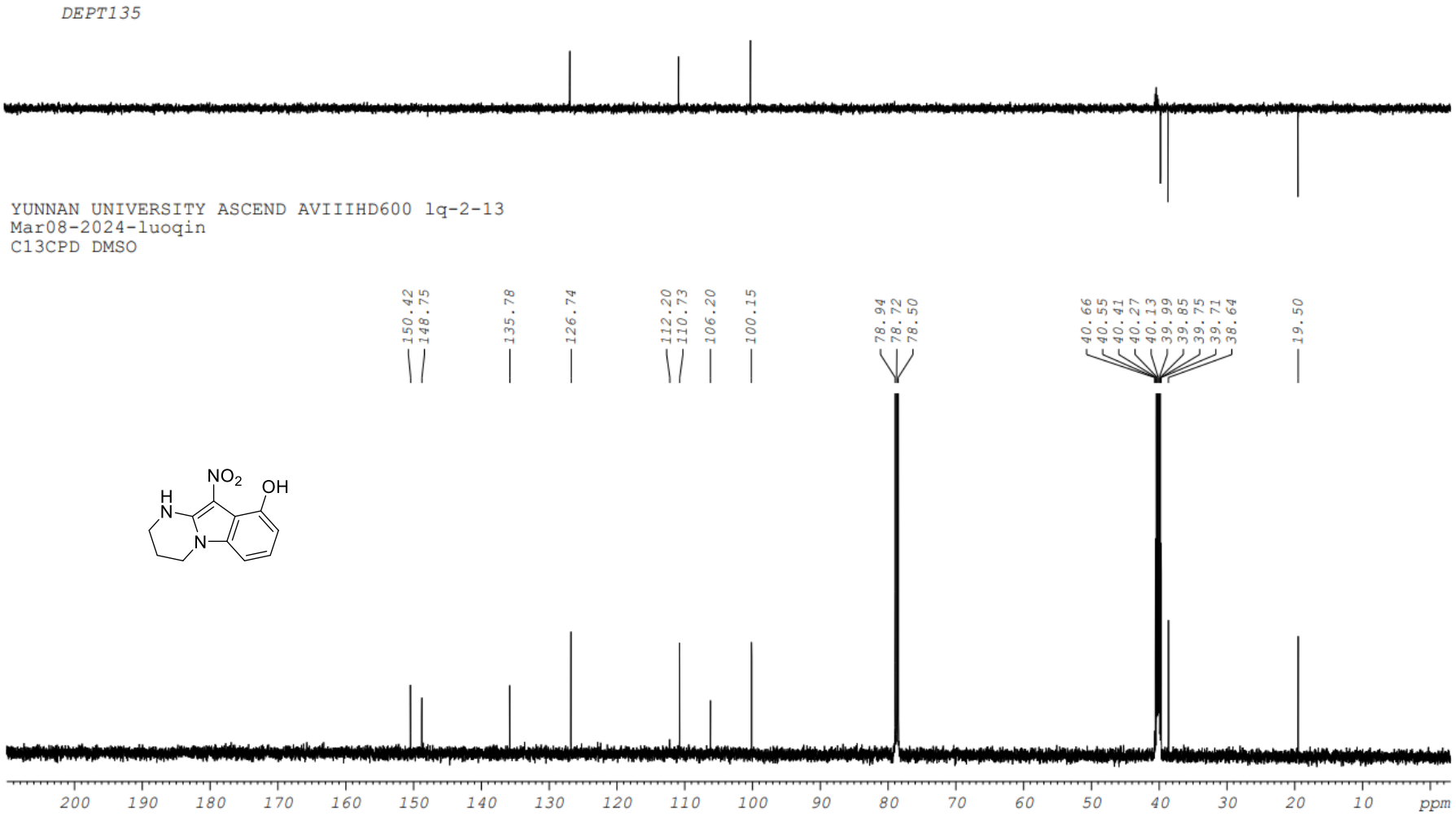


Figure S66. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **5a**

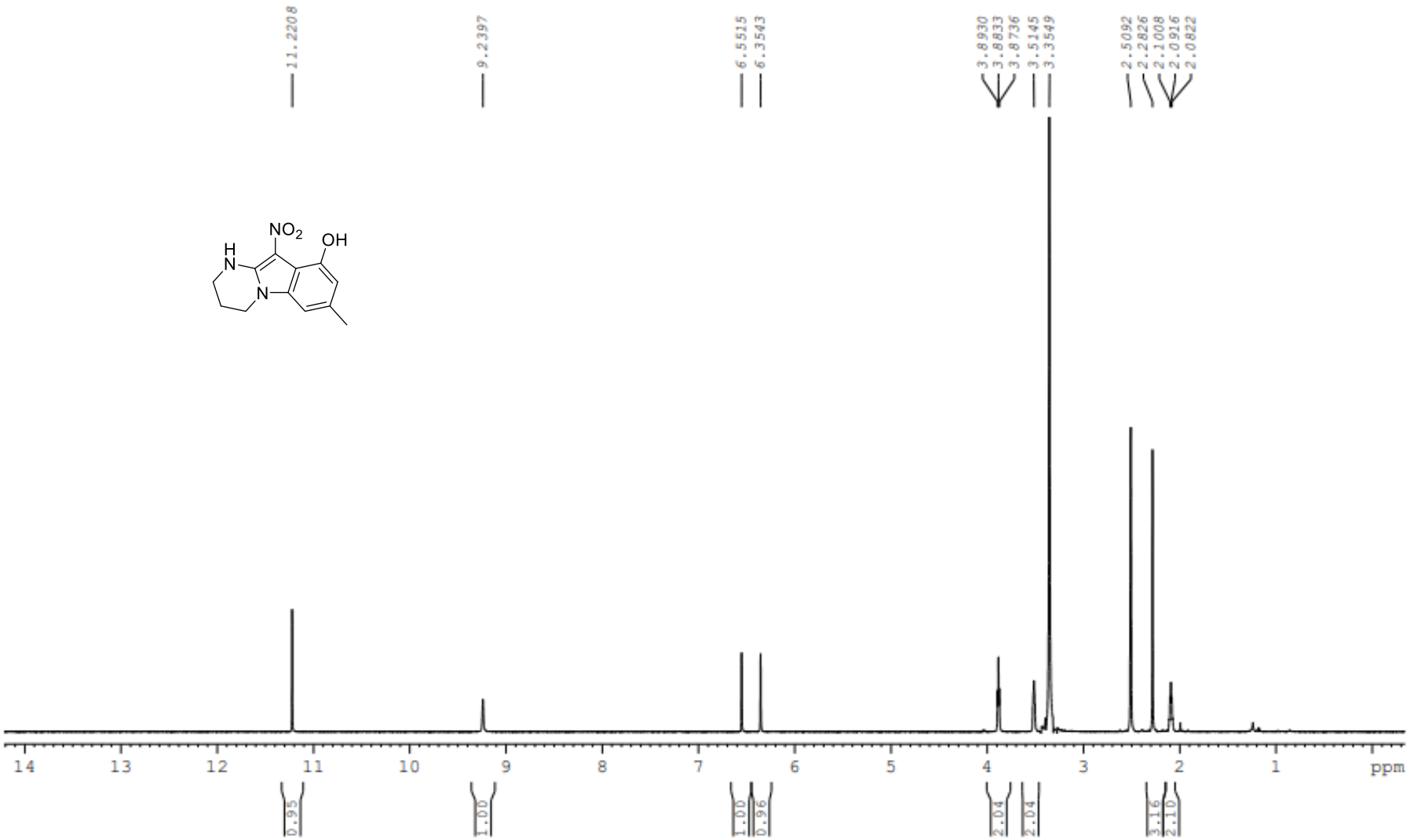


Figure S67. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **5b**

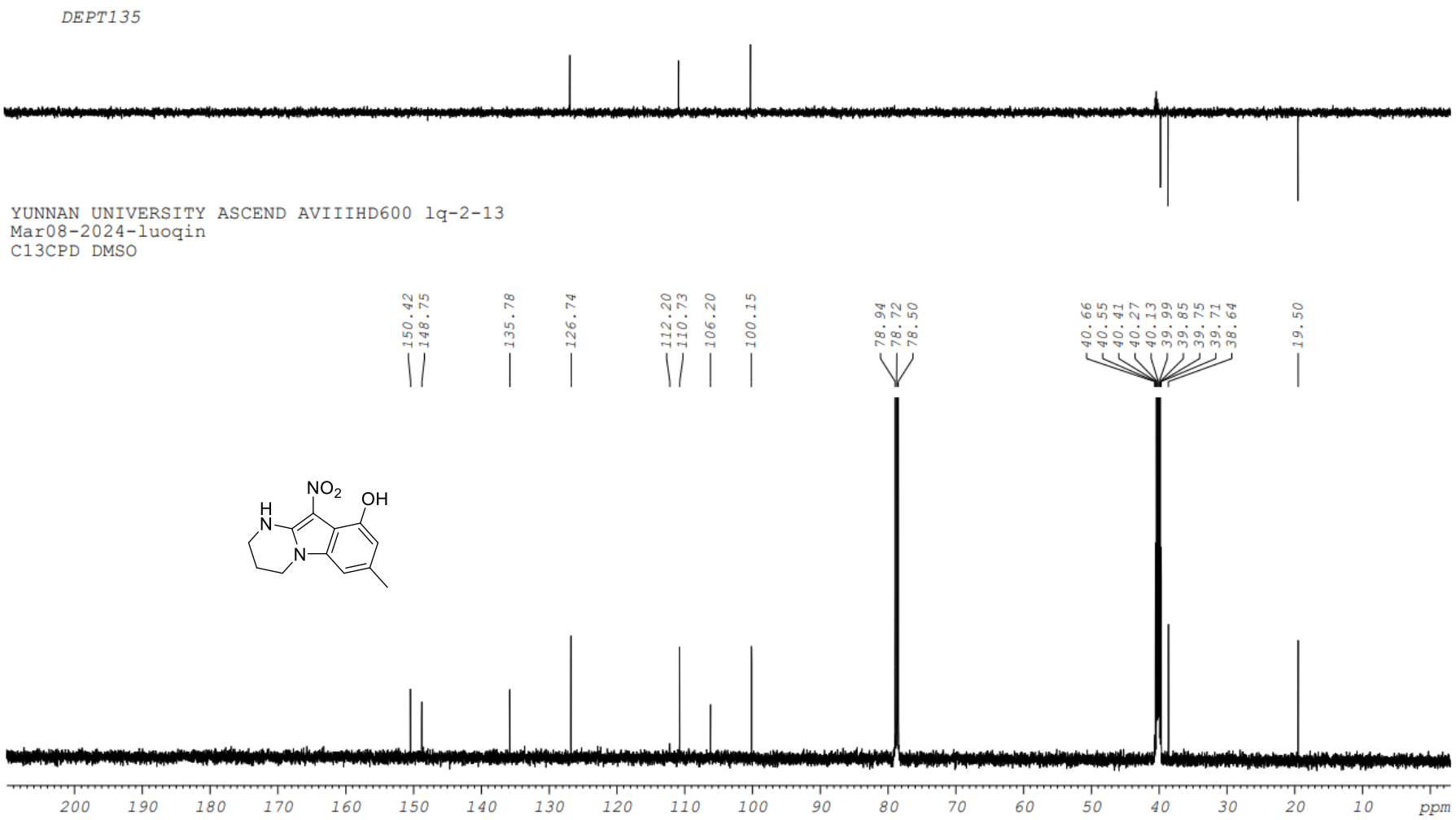


Figure S68. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **5b**

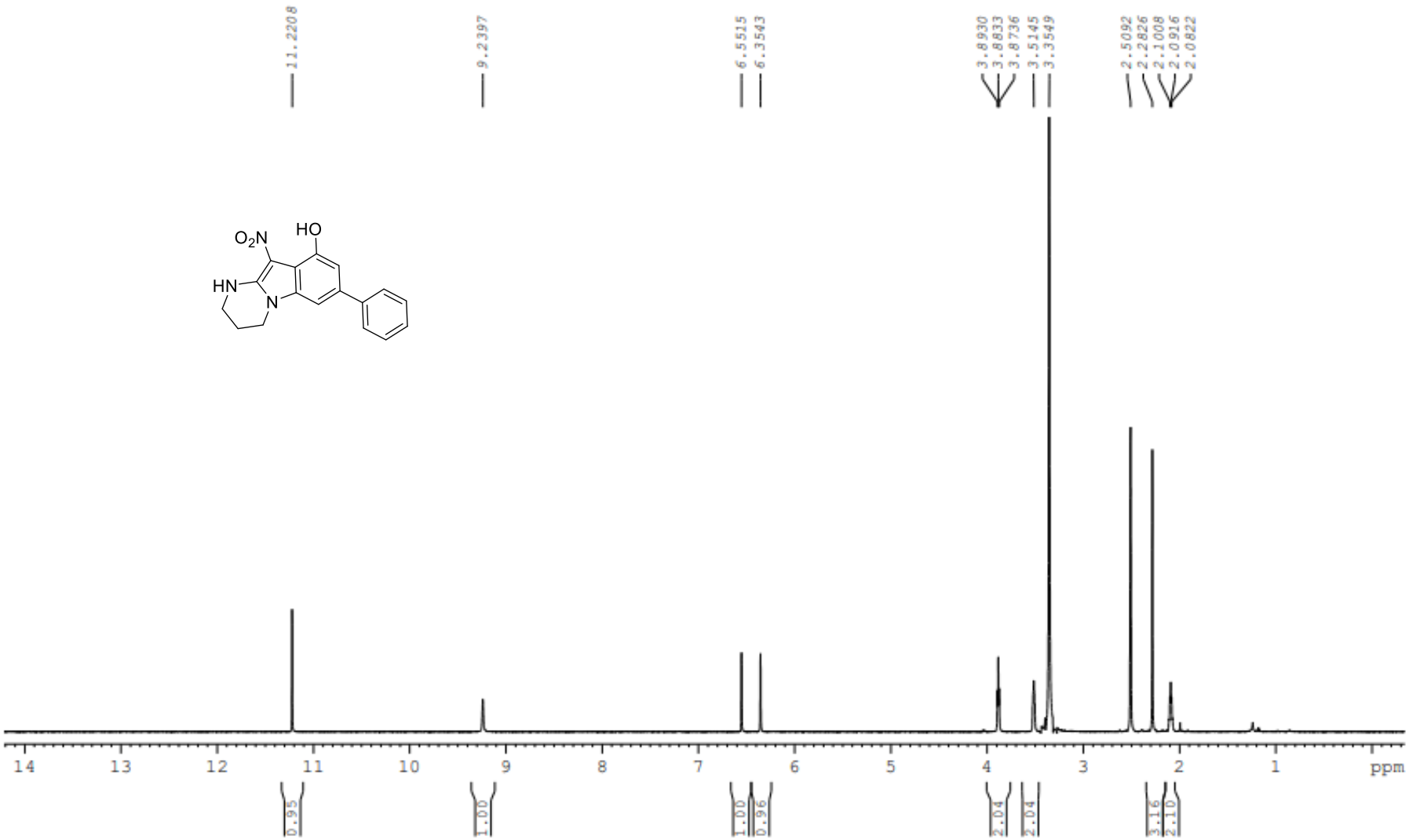


Figure S69. ^{1}H NMR (600 MHz,DMSO-d_6) spectra of compound **5c**

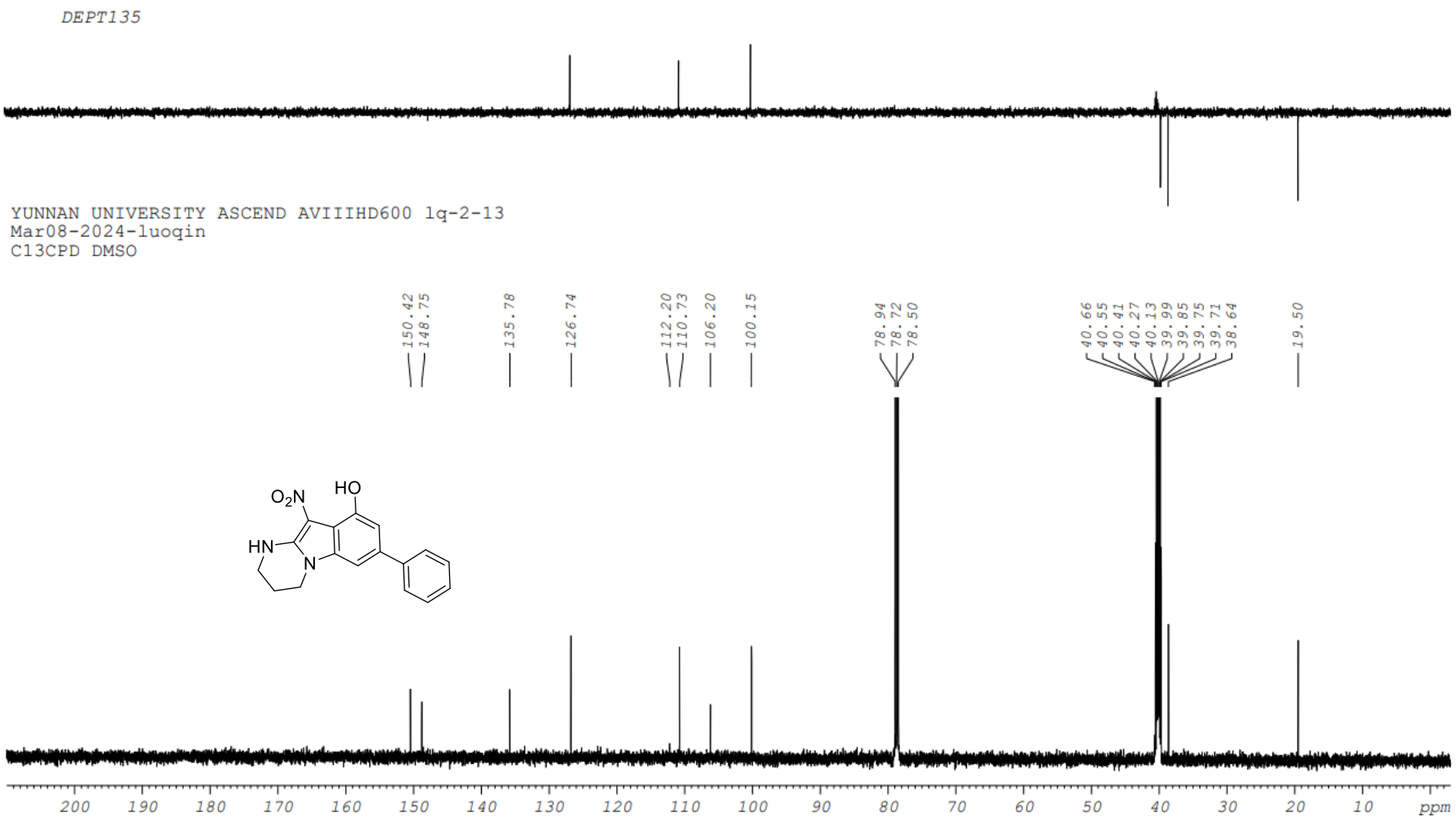


Figure S70. ^{13}C NMR (150 MHz,DMSO-d_6) spectra of compound **5c**

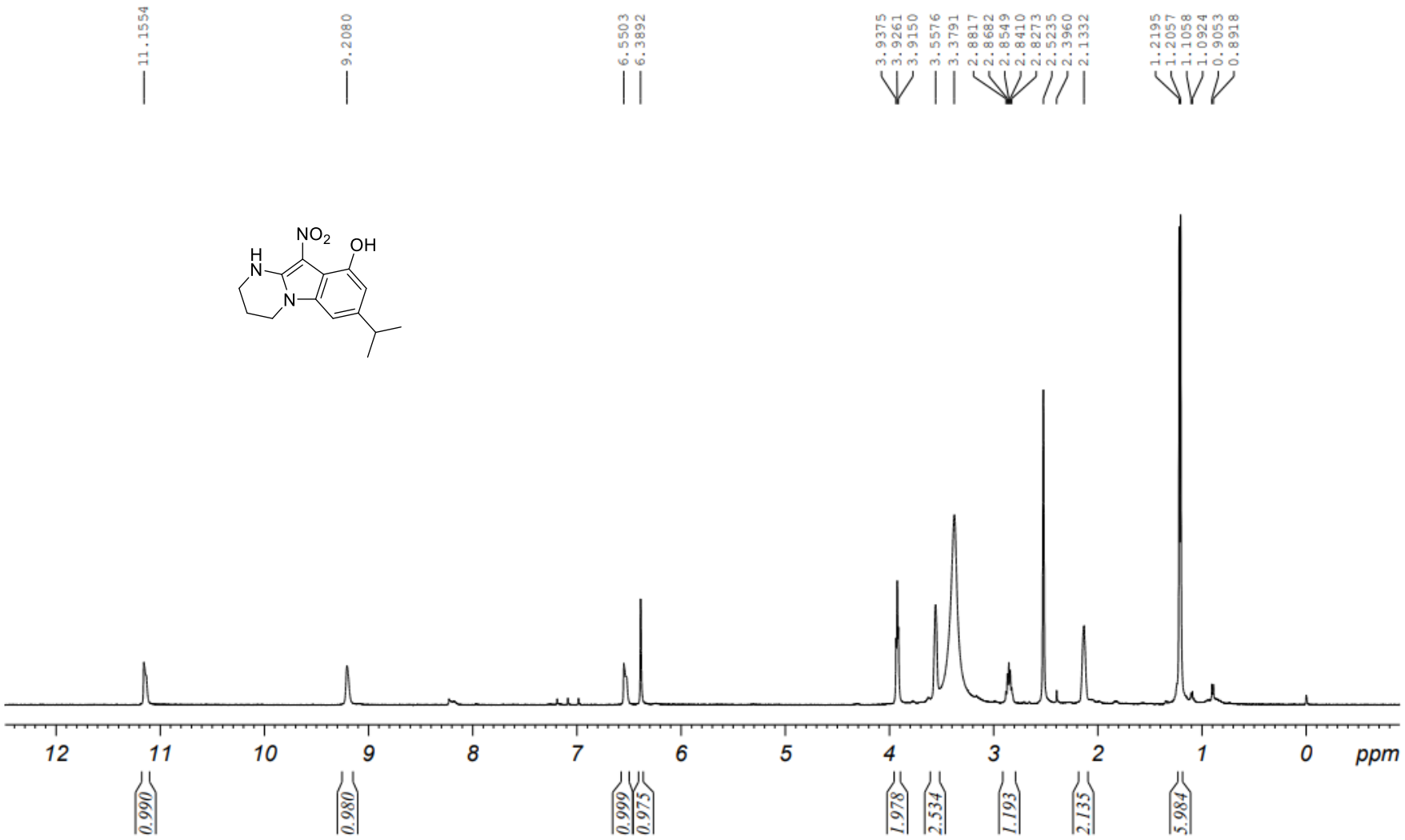


Figure S71. ^{1}H NMR (500 MHz,DMSO-d_6) spectra of compound **5d**

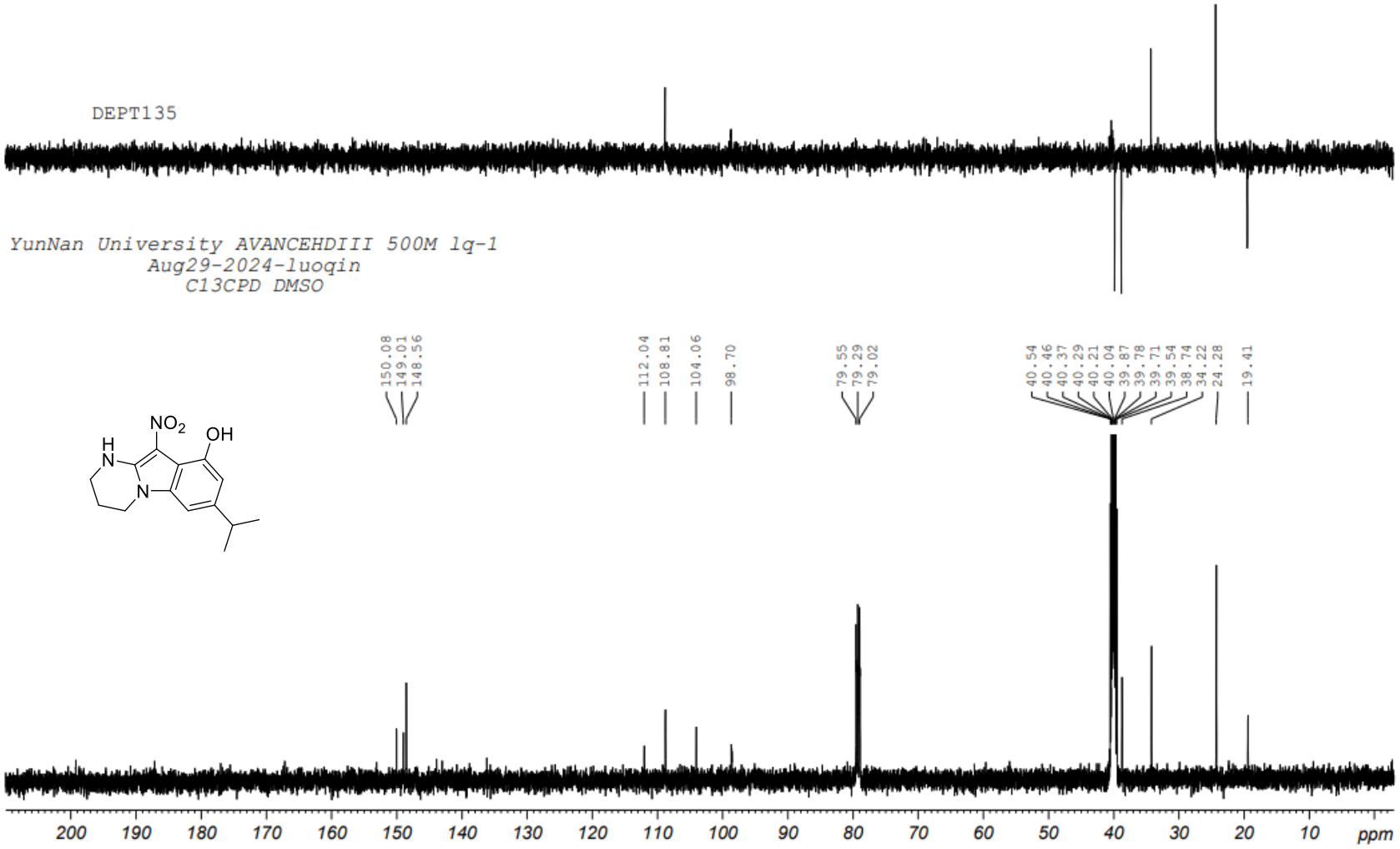


Figure S72. ^{13}C NMR (125 MHz,DMSO-d_6) spectra of compound **5d**

References

1. (a) Q.-X. Zi, C.-L. Yang, K. Li, Q. Luo, J. Lin, S.-J. Yan, J. Org. Chem., 2020, 85, 327. (b) Z.-T. Huang, Z.-R. Liu, Synthesis, 1987, 357. (c) C.-Y. Yu, P.-H. Yang, M.-X. Zhao, Z.-T. Huang, Synthesis, 2006, 12, 1835. (d) K. Luo, Y. Zhao, J. Zhang, J. He, R. Huang, S. Yan, J. Lin, Y. Jin, Org. Lett., 2019, 21, 423. (e) Z.-T. Huang, Z.-R. Liu, Synth. Commun., 1989, 19, 943.
2. (a) Mayakrishnan, S.; Tamizmani, M.; Maheswari, N. U. Chem. Commun., 2020, 56, 15462. (b) Yang, L.; Pi, C.; Wu, Y.; Cui, X. Org. Lett., 2022, 24, 7502.
3. CCDC 2373953 contain the supplementary crystallographic data for compound **3d**. CCDC 2373954 contain the supplementary crystallographic data for compound **4h**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif