Facile Route to the Synthesis of 1,3-Diazaheterocycle-Fused [1,2-*a*]Quinoline Derivatives via Cascade Reactions

Liang Chen,[†] Rong Huang,[†] Ling-Bin Kong,[†] Jun Lin*,[†] and Sheng-Jiao Yan*,[†]

[†]Key Laboratory of Medicinal Chemistry for Natural Resources (Yunnan University), Ministry of Education, School of Chemical Science and Technology, Yunnan University, Kunming, 650091, P. R. China

Supporting Information

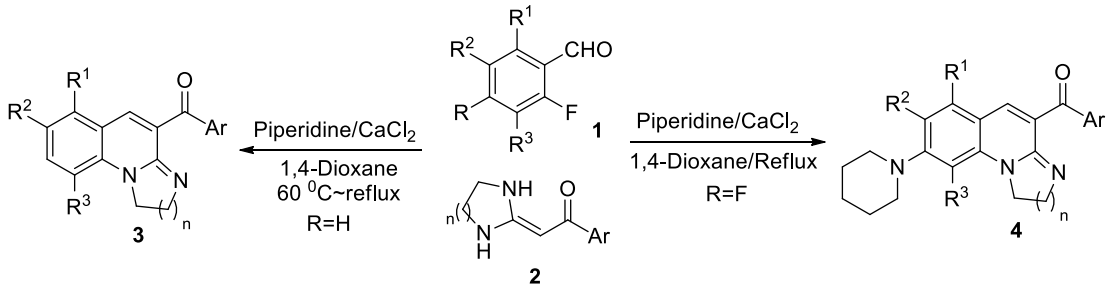
Table of Contents

General Information

All compounds were fully characterized by spectroscopic data. The NMR spectra were recorded on a Bruker DRX300 (^{1}H: 300 MHz, ^{13}C: 75 MHz), a Bruker DRX400 (^{1}H: 400 MHz, ^{13}C: 100 MHz), a Bruker DRX500 (^{1}H: 500 MHz, ^{13}C: 125 MHz) and a Bruker DRX600 (^{1}H: 600 MHz, ^{13}C: 150 MHz) with DMSO-d_6 and $CDCl_3$ as the solvents. The chemical shifts (δ) are expressed in parts per million relative to the residual deuterated solvent signal, and coupling constants (J) are given in Hertz. 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 an Agilent LC/Ms TOF instrument. All chemicals and solvents were used as received without further purification unless otherwise stated. X-ray diffraction was obtained by APEX DUO.

The materials **1a-d** were purchased from Aldrich Corporation Limited. HKAs **2** were prepared according to a procedure described in the literature. [1-3]

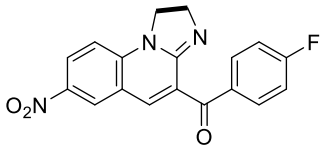
General Procedure for the Preparation of 3 and 4



A mixture of 2-fluorobenzaldehyde **1** (1.1 mmol), HKAs 2 (1.0 mmol), and piperidine (1.5 mmol) are mixed by stirring at different temperatures (**1a** as starting material, the temperature of the reaction was 60 ℃; **1b** was 75 ℃; **1c** and **1d** (at reflux) in 1,4-dioxane (15 mL). When the solution of the reaction was clear, the $CaCl_2$ (0.5 mmol) was added. After completion of the reaction, as indicated by TLC (CH_2Cl_2─EtOAc, 1:10 v/v), the mixture was cooled to room temperature and filtered. The solid was then washed with small amount of ethanol (*ca*. 5 mL), and dissolved in $CHCl_3$ (20 mL). Then, the organic phase was washed with saturated salt water (25 mL) and $NaHCO_3$ (25 mL), dried over anhydrous Na_2SO_4, concentrated, and petroleum ether was added for recrystallization to obtain the pure products **3** or **4**.

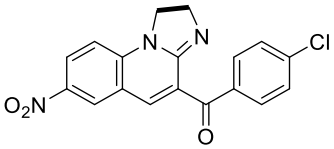
Spectroscopic Data of 3 and 4

4-(4'-Fluorophenyl)methanoneyl-7-nitro-1,2-dihydroimi-dazo[1,2-*a*]quinoline (3aa).



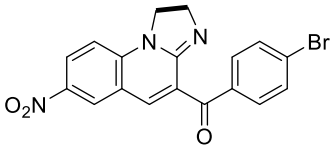
Yellow solid, m.p. 229–230 °C; IR (KBr): 3438, 1636, 1613, 1517, 1330, 1263, 1154, 853 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.88–3.95 (m, 2H, CH_2N), 4.01–4.08 (m, 2H, NCH_2), 6.98 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.35 (t, *J* = 8.9 Hz, 2H, Ar*H*), 7.80 (s, 1H, C*H*), 7.97–8.02 (m, 2H, Ar*H*), 8.24–8.28 (m, 1H, Ar*H*), 8.45(d, *J* = 2.4 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.5, 53.5, 112.4, 115.8 (d, *J* = 21.8 Hz), 119.1, 124.9, 127.2 129.4, 132.4, 132.6 (d, *J* = 9.8 Hz), 136.2, 139.5, 143.9, 152.8, 165.4 (d, *J* = 251.3 Hz), 190.9; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{13}FN_3O_3$[M+H], 338.0935; found, 338.0935.

4-(4'-Chlorophenyl)methanoneyl-7-nitro-1,2-dihydroimi-dazo[1,2-*a*]quinoline (3ab).



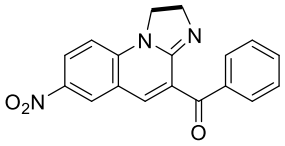
Yellow solid, m.p. 273–274 °C; IR (KBr): 2938, 1635, 1610, 1330, 1265, 1093, 871 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.92–3.95 (m, 2H, CH_2N), 4.02–4.05 (m, 2H, NCH_2), 7.00(d, *J* = 9.0 Hz, 1H, Ar*H*), 7.59 (d, *J* = 8.4 Hz, 2H, Ar*H*), 7.84 (s, 1H, C*H*), 7.91 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.26–8.29 (m, 1H, Ar*H*), 8.48 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.5, 53.4, 112.5, 119.1, 125.1, 127.3, 128.8, 129.1, 131.4, 134.4, 136.8, 138.8, 139.6, 143.9, 152.8, 191.3; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{13}N_3O_3Cl$ [M+H], 354.0640; found, 354.0638.

4-(4'-Bromophenyl)methanoneyl-7-nitro-1,2-dihydroimi-dazo[1,2-*a*]quinoline (3ac).



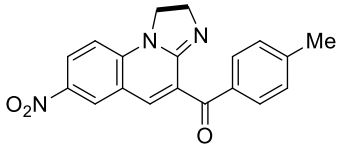
Yellow solid, m.p. 281–282 °C; IR (KBr): 3439, 2938, 1636, 1613, 1325, 1264, 1091, 868 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.89–3.95 (m, 2H, CH_2N), 4.02–4.09 (m, 2H, NCH_2), 7.01(d, J = 9.0 Hz, 1H, ArH), 7.74 (d, J = 8.7 Hz, 2H, ArH), 7.83 (d, J = 6.9 Hz, 2H, ArH), 7.84 (s, 1H, CH), 8.27–8.31 (m, 1H, ArH), 8.49 (d, J = 2.4 Hz, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.5, 53.5, 112.5, 119.1, 125.1, 127.3, 128.1, 129.1, 131.4, 131.8, 134.8, 136.7, 139.6, 144.0, 152.8, 191.6; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{13}N_3O_3Br$[M+H], 398.0134; found, 398.0137.

4-(Phenyl)methanoneyl-7-nitro-1,2-dihydroimidazo[1,2-*a*]quinoline (3ad).



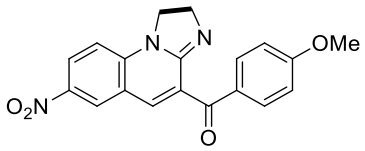
Yellow solid, m.p. 284–285 °C; IR (KBr): 3439, 2927, 1635, 1592, 1325, 1262, 1094, 729 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.90–3.96 (m, 2H, CH_2N), 4.03–4.09 (m, 2H, NCH_2), 7.01(d, J = 9.3 Hz, 1H, ArH), 7.54 (t, J = 7.5 Hz, 2H, ArH), 7.69 (t, J = 7.4 Hz, 1H, ArH), 7.80 (s, 1H, CH), 7.91 (d, J = 7.5 Hz, ArH), 8.27–8.30 (m, 1H, ArH), 8.48 (d, J = 2.4 Hz, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 50.8, 58.8, 117.7, 124.4, 130.2, 132.4, 134.0, 134.8, 135.0, 139.2, 140.9, 141.1, 144.8, 149.2, 158.1, 197.7; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{14}N_3O_3$[M+H], 320.1029; found, 320.1029.

4-(*p*-Tolyl)methanoneyl-7-nitro-1,2-dihydroimidazo[1,2-*a*]quinoline (3ae).



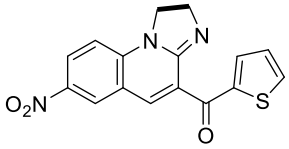
Yellow solid, m.p. 283–284 °C; IR (KBr): 3439, 2935, 1657, 1635, 1610, 1517, 1325, 1288, 1264, 1090, 870 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 2.39 (s, 3H, CH_3), 3.92–3.95 (m, 2H, CH_2N), 4.02–4.05 (m, 2H, NCH_2), 7.00 (d, J = 9.0 Hz, 1H, ArH), 7.34 (d, J = 7.8 Hz, 2H, ArH), 7.75 (s, 1H, CH), 7.80 (d, J = 7.8 Hz, 2H, ArH), 8.27 (d, J = 8.7 Hz, 1H, ArH), 8.47 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 21.2, 45.5, 53.5, 112.3, 119.1, 124.8, 127.0, 129.3, 129.7, 129.9, 133.1, 135.5, 139.5, 143.8, 144.6, 152.8, 191.9; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{16}N_3O_3$[M+H], 334.1186; found, 334.1186.

4-(4'-Methoxyphenyl)methanoneyl-7-nitro-1,2-dihydroimidazo[1,2-*a*]quinolin e (3af).



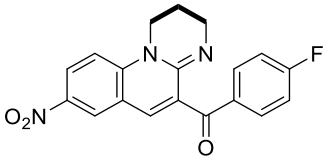
Yellow solid, m.p. 260–261 °C; IR (KBr): 1651, 1613, 1592, 1330, 1260, 1172, 585 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.85 (s, 3H, OCH_3), 3.89–3.96 (m, 2H, CH_2N), 4.03–4.09 (m, 2H, NCH_2), 7.00 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.05 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.72 (s, 1H, C*H*), 7.88 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.25–8.29 (m, 1H, Ar*H*), 8.46 (d, *J* = 2.4 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.5, 53.5, 55.6, 112.3, 114.0, 119.2, 124.7, 126.9, 128.4, 130.1, 132.0, 135.0, 139.5, 143.7, 152.9, 163.8, 190.7; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{16}N_3O_4$[M+H], 350.1135; found, 350.1132.

4-(Thiophen-2'-yl)methanoneyl-7-nitro-1,2-dihydroimidazo[1,2-*a*]quinoline (3ag).



Orange solid, m.p. 274–275 °C; IR (KBr): 3076, 2975, 1641, 1589, 1410, 1324, 1262, 1054, 742 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.97–4.00 (m, 2H, CH_2N), 4.04–4.06 (m, 2H, NCH_2), 7.00(d, *J* = 9.0 Hz, 1H, Ar*H*), 7.25–7.28 (m, 1H, C*H*), 7.86 (s, 1H, C*H*), 7.89–7.90 (m,1H, C*H*), 8.14–8.16 (m, 1H, C*H*), 8.26-8.30 (m, 1H, Ar*H*), 8.48 (d, *J* = 2.4 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.6, 53.5, 112.4, 119.0, 125.0, 127.3, 129.0, 135.7, 136.6, 136.9, 139.5, 142.5, 143.9, 152.5, 184.1; HRMS (TOF ES^+): *m/z* calcd for $C_{16}H_{12}N_3O_3S$[M+H], 326.0593; found, 326.0595.

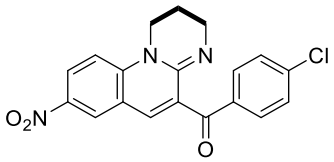
5-(4'-Fluorophenyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quin oline (3ah).



Yellow solid, m.p. 224–225 °C; IR (KBr): 2934, 1634, 1596, 1508, 1327, 1277, 907, 585 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.90–1.92 (m, 2H, CH_2),

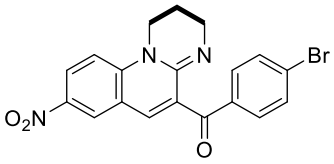
3.27–3.31 (m, 2H, CH_2N), 3.97–3.99 (m, 2H, NCH_2), 7.30–7.42 (m, 3H, Ar*H*), 7.63 (s, 1H, C*H*), 7.95–8.00 (m, 2H, Ar*H*), 8.25–8.29 (m, 1H, Ar*H*), 8.44(d, *J* = 2.4 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.3, 42.9, 44.4, 112.4, 115.8 (d, *J* = 22.5), 119.5, 124.2, 125.8 130.8, 132.2 (d, *J* = 9.8 Hz), 132.7, 136.2, 140.4, 145.1, 146.7, 165.2 (d, *J* = 250.5 Hz), 192.5; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{15}N_3O_3F$[M+H], 352.1091; found, 352.1088.

5-(4'-Chlorophenyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3ai).



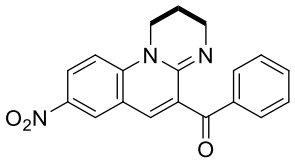
Yellow solid, m.p. 272–273 °C; IR (KBr): 2928, 1662, 1640, 1324, 1277, 1094, 899, 834 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.86–1.90 (m, 2H, CH_2), 3.25–3.28 (m, 2H, CH_2N), 3.92–3.96 (m, 2H, NCH_2), 7.36 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.59 (s, 1H, C*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.89 (d, *J* = 8.4 Hz, 2H, Ar*H*), 8.24–8.28 (m, 1H, Ar*H*), 8.42 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 43.1, 44.3, 112.1, 119.4, 124.2, 125.8, 128.8 130.3, 130.9, 134.7, 136.7, 138.4, 140.2, 145.3, 146.5, 193.0; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{15}N_3O_3Cl$[M+H], 368.0796; found, 368.0795.

5-(4'-Bromophenyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3aj).



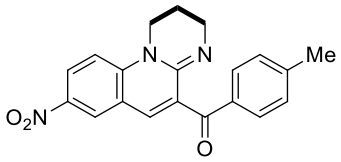
Yellow solid, m.p. 264–265 °C; IR (KBr): 2966, 1653, 1613, 1326, 1273, 743 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.86–1.90 (m, 2H, CH_2), 3.25–3.28 (m, 2H, CH_2N), 3.92–3.96 (m, 2H, NCH_2), 7.36 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.59 (s, 1H, C*H*), 7.70 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.81 (d, *J* = 8.4 Hz, 2H, Ar*H*), 8.24–8.28 (m, 1H, Ar*H*), 8.42 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 43.1, 44.3, 112.1, 119.5, 124.2, 125.8, 127.6 130.3, 131.0, 131.8, 135.1, 136.7, 140.3, 145.3, 146.5, 193.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{15}N_3O_3Br$[M+H], 412.0291; found, 412.0291.

5-(Phenyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3ak).



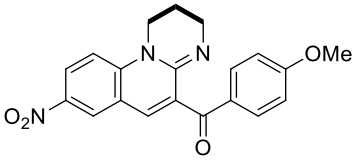
Yellow solid, m.p. 285–286 °C; IR (KBr): 2954, 2849, 1640, 1595, 1324, 1277, 1095, 904, 718 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.88 (m, 2H, CH_2), 3.27 (m, 2H, CH_2N), 3.95 (m, 2H, NCH_2), 7.37 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.51 (t, *J* = 7.5 Hz, 2H, Ar*H*), 7.56 (s, 1H, C*H*), 7.64 (t, *J* = 7.1 Hz, 1H, Ar*H*), 7.90 (d, *J* = 7.5 Hz, Ar*H*), 8.27–8.25 (m, 1H, Ar*H*), 8.42 (s, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 43.1, 44.3, 112.1, 119.5, 124.1, 125.6, 128.7, 129.1, 129.8, 133.6, 135.9, 137.2, 140.3, 145.2, 146.5, 194.0; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{16}N_3O_3$[M+H], 334.1186; found, 334.1186.

5-(*p*-Tolyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3al).



Yellow solid, m.p. 282–283 °C; IR (KBr): 2959, 1642, 1595, 1323, 1277, 1093, 904 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.86–1.89 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 3.26–3.29 (m, 2H, CH_2N), 3.92–3.96 (m, 2H, NCH_2), 7.30 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.35 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.51 (s, 1H, C*H*), 7.78 (d, *J* = 8.1 Hz, 2H, Ar*H*), 8.22–8.26 (m, 1H, Ar*H*), 8.40 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 21.2, 43.1, 44.3, 112.0, 119.5, 124.0, 125.6, 129.2 129.2, 129.5, 133.5, 137.4, 140.2, 144.1, 145.2, 146.4, 193.5; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{18}N_3O_3$[M+H], 348.1342; found, 348.1341.

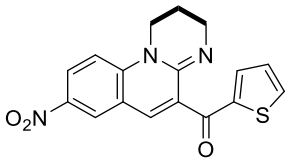
5-(4'-Methoxyphenyl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3am).



Yellow solid, m.p. 221–222 °C; IR (KBr): 2934, 1641, 1595, 1328, 1277, 1162, 986 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.87–1.90 (m, 2H, CH_2),

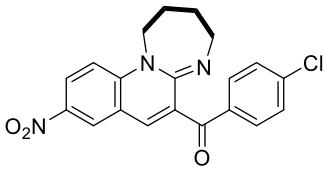
3.27–3.30 (m, 2H, CH_2N), 2.83 (s, 3H, OCH_3), 3.92–3.96 (m, 2H, NCH_2), 7.02 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.35 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.49 (s, 1H, C*H*), 7.85 (d, *J* = 8.7 Hz, 2H, Ar*H*), 8.22–8.26 (m, 1H, Ar*H*), 8.40 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 43.1, 44.3, 55.6, 112.0, 113.9, 119.6, 123.9, 125.5, 128.9, 129.2, 131.6, 137.5, 140.2, 145.2, 146.4, 163.4, 192.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{18}N_3O_4$[M+H], 364.1291; found, 364.1293.

5-(Thiophen-2'-yl)methanoneyl-8-nitro-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3an).



Yellow solid, m.p. 224–225 °C; IR (KBr): 2960, 1645, 1594, 1511, 1329, 1279, 1054, 737 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.89–1.92 (m, 2H, CH_2), 3.31–3.35 (m, 2H, CH_2N), 3.92–3.96 (m, 2H, NCH_2), 7.20–7.23 (m, 1H, C*H*), 7.34(d, *J* = 9.3 Hz, 1H, Ar*H*), 7.58 (s, 1H, C*H*), 7.77–7.79 (m,1H, C*H*), 8.05–8.07 (m, 1H, C*H*), 8.22–8.40 (m, 1H, Ar*H*), 8.40 (d, *J* = 2.7Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.4, 43.1, 44.4, 112.0 119.4, 124.2, 125.8, 128.9, 129.7, 135.5, 135.8, 136.6, 140.2, 143.1, 145.3, 146.1, 186.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{17}H_{14}N_3O_3S$[M+H], 340.0750; found, 340.0752.

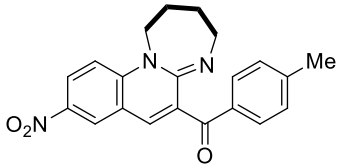
6-(4'-Chlorophenyl)methanoneyl-9-nitro-1,2,3,4-tetrahydro-[1,3]diazepino [1,2-*a*]quinoline (3ao).



Yellow solid, m.p. 232–233 °C; IR (KBr): 2930, 1657, 1626, 1597, 1340, 1285, 1087, 840 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.78 (m, 2H, CH_2), 2.04–2.07 (m, 2H, CH_2), 3.62–3.66 (m, 2H, CH_2N), 4.11–4.15 (m, 2H, NCH_2), 7.38 (d, *J* = 9.3 Hz, 1H, Ar*H*), 7.56 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.62 (s, 1H, C*H*), 7.90 (d, *J* = 8.4 Hz, 2H, Ar*H*), 8.22–8.26 (m, 1H, Ar*H*), 8.45 (d, *J* = 2.7 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 23.6, 25.0, 47.2, 49.2,112.8, 120.0, 124.1, 125.6, 128.8, 130.6, 130.8, 134.8, 137.0, 138.2, 140.1, 146.9, 148.5, 192.9; HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{17}ClN_3O_3$[M+H], 382.0953; found,

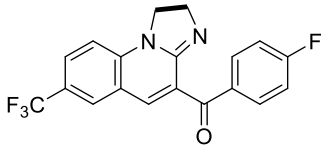
382.0952.

6-(*p*-Tolyl)methanoneyl-9-nitro-1,2,3,4-tetrahydro-[1,3]diazepino[1,2-*a*]quinoline (3ap).



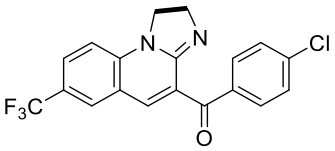
Yellow solid, m.p. 236–237 °C; IR (KBr): 1663, 1636, 1594, 1500, 1486, 1327, 1265, 1206, 1090, 861, 819 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.79 (m, 2H, CH_2), 2.04–2.08 (m, 2H, CH_2), 3.63–3.66 (m, 2H, CH_2N), 4.11–4.15 (m, 2H, NCH_2), 7.31 (d, J = 8.1 Hz, 1H, ArH), 7.37 (d, J = 9.3 Hz, 2H, ArH), 7.54 (s, 1H, CH), 7.79 (d, J = 8.1 Hz, 2H, ArH), 8.21–8.25 (m, 1H, ArH), 8.43 (d, J = 2.7 Hz, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 21.2, 23.6, 25.1, 47.2, 49.2,112.8, 120.2, 123.9, 125.3, 129.1, 129.2, 129.7, 133.5, 137.8, 140.0, 143.9, 146.8, 148.5, 193.5; HRMS (TOF ES^+): *m/z* calcd for $C_{21}H_{20}N_3O_3$[M+H], 362.1499; found, 362.1500.

4-(4'-Fluorophenyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo [1,2-*a*]quinoline (3ba).



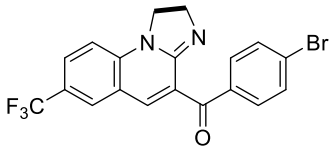
Yellow solid, m.p. 198–199 °C; IR (KBr): 3438, 1663, 1636, 1599, 1386, 1336, 1207, 1155, 1115, 1077, 998, 859, 610 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.85–3.93 (m, 2H, CH_2N), 3.98–4.04 (m, 2H, NCH_2), 7.01 (d, J = 8.7 Hz, 1H, ArH), 7.30–7.38 (m, 2H, ArH), 7.72 (s, 1H, CH), 7.72–7.76 (dd, J_1= 9.0 Hz, J_2= 1.8 Hz, 1H, ArH), 7.92 (d, J = 1.5 Hz, 1H, ArH), 7.94–8.01 (m, 2H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.3, 53.3, 112.5, 115.8 (d, J_2= 21.8 Hz), 119.3, 119.8–120.7 (m), 124.4 (d, J_1= 269.3 Hz), 126.4, 128.2, 129.0, 132.5 (d, J_3= 9.8 Hz), 136.3, 142.1, 153.2, 165.3 (d, J_1= 251.3 Hz), 191.2; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{13}N_2OF_4$[M+H], 361.0958; found, 361.0958.

4-(4'-Chlorophenyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo [1,2-*a*]quinoline (3bb).



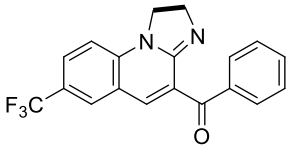
Yellow solid, m.p. 232–233 °C; IR (KBr): 3442, 1661, 1635, 1580, 1334, 1206, 1159, 1112, 1076, 997, 840, 519 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) (δ, ppm): 3.87–3.91 (m, 2H, CH_2N), 3.98–4.02 (m, 2H, NCH_2), 7.02 (d, J = 8.6 Hz, 1H, ArH), 7.59 (d, J = 8.3 Hz, 2H, ArH), 7.75 (s, 1H, ArH), 7.76 (s, 1H, ArH), 7.90 (d, J = 8.5 Hz, 2H, ArH), 7.94 (s, 1H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 45.7, 53.7, 112.9, 119.6, 120.5 (d, J_2= 32.5 Hz), 124.8 (d, J_1= 270.0 Hz), 126.9, 128.8, 129.1, 129.2, 131.7, 135.1, 137.2, 139.1, 142.6, 153.6, 192.0; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{13}N_2OF_3Cl$[M+H], 377.0663; found, 377.0664.

4-(4'-Bromophenyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo [1,2-*a*]quinoline (3bc).



Yellow solid, m.p. 237–238 °C; IR (KBr): 1662, 1635, 1582, 1399, 1334, 1206, 1159, 1111, 1075, 996, 837, 765 cm^{-1}; ^1H NMR (400 MHz, $DCCl_3$) (δ, ppm): 4.22–4.27 (t, J = 12.2 Hz, 2H, CH_2N), 4.35–4.42 (t, J = 12.4 Hz, 2H, NCH_2), 7.04 (d, J = 11.2 Hz, 1H, ArH), 7.66 (s, 1H, CH), 7.82 (m, 2H, ArH), 7.85–7.88 (m, 2H, ArH), 8.02 (d, J = 10.0 Hz, 2H, ArH); ^{13}C NMR (125 MHz, $DCCl_3$) (δ, ppm): 45.8, 53.9, 111.9, 119.2, 122.5 (m), 125.3, 126.7, 128.6, 129.0, 129.2, 131.4, 131.9, 134.9, 138.1, 142.0, 154.0, 191.5; HRMS (TOF ES^+): *m/z* calcd for $C_{19}H_{13}N_2OF_3Br$[M+H], 421.0157; found, 421.0158.

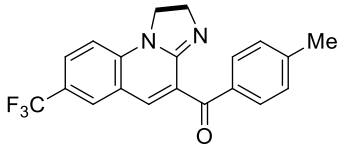
4-(Phenyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo[1,2-*a*]quinoli ne (3bd).



Yellow solid, m.p. 212–213 °C; IR (KBr): 1666, 1635, 1578, 1387, 1333, 1204, 1160, 1117, 1073, 996, 817, 519 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 3.85–3.92 (m, 2H, CH_2N), 3.98–4.05 (m, 2H, NCH_2), 7.02 (d, J = 8.7 Hz, 1H, ArH), 7.51–7.56 (m, 2H, ArH), 7.67 (d, J = 7.2 Hz, 1H, ArH), 7.71 (s, 1H, CH),

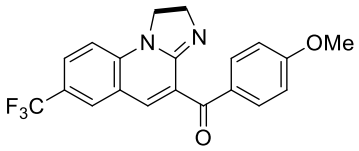
7.73–7.76 (dd, J_1= 8.7 Hz, J_2= 1.5 Hz, 1H, Ar*H*), 7.89 (s, 1H, Ar*H*), 7.92 (d, *J* = 5.4 Hz, 2H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 45.3, 53.3, 112.5, 119.3, 120.0 (d, *J* = 32.3 Hz), 124.4 (d, *J* = 277.5 Hz), 126.3, 128.2, 128.7, 129.3, 129.5, 133.8, 135.8, 135.9, 142.1, 153.2, 192.6; HRMS (TOF ES$^+$): *m/z* calcd for $C_{19}H_{14}N_2OF_3$[M+H], 343.1052; found, 343.1050.

4-(*p*-Tolyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo[1,2-*a*]quinoline (3be).



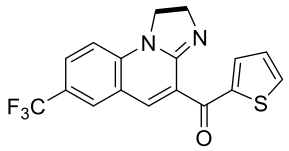
Yellow solid, m.p. 249–250 °C; IR (KBr): 1660, 1637, 1333, 1206, 1157, 1110, 1075, 997, 828, 762 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 2.38 (s, 3H, C*H*$_3$), 3.85–3.91 (m, 2H, C*H*$_2$N), 3.97–4.04 (m, 2H, NC*H*$_2$), 7.00 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.32 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.66 (s, 1H, C*H*), 7.73 (d, *J* = 8.4 Hz, 1H, Ar*H*), 7.78 (d, J_1= 8.1 Hz, 2H, Ar*H*), 7.92 (s, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 21.2, 45.3, 53.3, 112.4, 119.3, 119.7, 124.4 (d, *J* = 269.3 Hz), 126.2, 128.1, 129.3, 129.5, 129.6, 133.3, 135.5, 142.0, 144.4, 153.2, 192.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{16}N_2OF_3$[M+H], 357.1209; found, 357.1210.

4-(4'-Methoxyphenyl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo [1,2-*a*]quinoline (3bf).



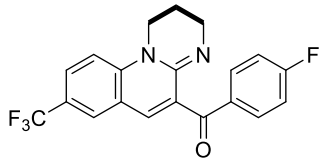
Yellow solid, m.p. 228–229 °C; IR (KBr): 2945, 1658, 1635, 1596, 1387, 1334, 1265, 1205, 1155, 1109, 856 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 3.85 (s, 3H, C*H*$_3$), 3.88–3.92 (m, 2H, C*H*$_2$N), 4.00–4.04 (m, 2H, NC*H*$_2$), 7.03 (d, *J* = 9.0 Hz, 1H, Ar*H*), 7.05 (d, *J* = 8.6 Hz, 2H, Ar*H*), 7.65 (s, 1H, C*H*), 7.75 (d, *J* = 8.5 Hz, 1H, Ar*H*), 7.88 (d, J_1= 8.5 Hz, 2H, Ar*H*), 7.92 (s, 1H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 45.7, 53.6, 56.0, 112.8, 114.4, 119.8, 120.2, 125.9, 126.5, 128.4, 129.0, 130.1, 132.4, 135.5, 142.3, 153.7, 164.2, 192.4; HRMS (TOF ES$^+$): *m/z* calcd for $C_{20}H_{16}N_2O_2F_3$[M+H], 373.1158; found, 373.1160.

4-(Thiophen-2'-yl)methanoneyl-7-(trifluoromethyl)-1,2-dihydroimidazo [1,2-*a*]quinoline (3bg).



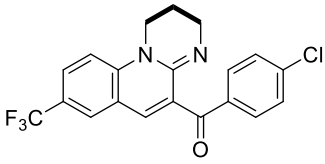
Orange solid, m.p. 208–209 °C; IR (KBr): 3069, 1650, 1633, 1413, 1334, 1204, 1159, 1118, 1073, 821, 743 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) (δ, ppm): 3.92–3.96 (m, 2H, CH_2N), 4.00–4.04 (m, 2H, NCH_2), 7.00 (d, J = 8.7 Hz, 1H, C*H*), 7.26 (t, J = 4.3 Hz, 1H, C*H*), 7.73–7.75 (m, 1H, C*H*), 7.78 (s, 1H, C*H*), 7.88 (d, J = 3.7 Hz, 1H, Ar*H*), 7.93 (s, 1H, Ar*H*), 8.13 (d, J = 4.8 Hz, 1H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 45.8, 53.6, 56.0, 112.8, 119.6, 120.4 (d, J = 32.5 Hz), 124.8 (d, J = 270.0 Hz), 126.8, 128.7, 129.0, 129.3, 136.2, 136.6, 136.9, 142.4, 143.0, 153.4, 184.7; HRMS (TOF ES^+): *m/z* calcd for $C_{17}H_{12}N_2OF_3S$[M+H], 349.0616; found, 349.0614.

5-(4'-Fluorophenyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimid o[1,2-*a*]quinoline (3bh).



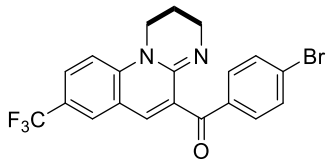
Yellowy solid, m.p. 172–173 °C; IR (KBr): 1668, 1642, 1596, 1319, 1210, 1154, 1116, 846, 814 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.87–1.89 (m, 2H, CH_2), 3.25–3.27 (m, 2H, CH_2N), 3.90-3.92 (m, 2H, NCH_2), 7.32 (t, J = 8.6 Hz, 2H, Ar*H*), 7.37 (d, J = 8.9 Hz 1H, Ar*H*), 7.49 (s, 1H, C*H*), 7.75 (d, J_1= 8.7 Hz, 1H, Ar*H*), 7.89 (s, 1H, Ar*H*), 7.95–7.98 (m, 2H, Ar*H*); ^{13}C NMR (123 MHz, DMSO-d_6) (δ, ppm): 19.9, 43.5, 44.3, 112.4, 116.1 (d, J = 22.5 Hz), 119.9, 121.3 (d, J = 33.8 Hz), 124.7 (d, J = 268.8 Hz), 126.1 (d, J = 3.8 Hz), 127.4 (d, J = 2.5 Hz), 130.4, 132.4 (d, J = 10.0 Hz), 133.3, 137.0, 143.8, 147.2, 165.5 (d, J = 252.5 Hz), 193.2; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{15}N_2OF_4$[M+H], 375.1115; found, 375.1113.

5-(4'-Chlorophenyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimid o[1,2-*a*]quinoline (3bi).



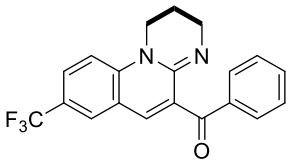
Yellowy solid, m.p. 181–182 °C; IR (KBr): 2931, 1670, 1640, 1592, 1319, 1208, 1161, 1115, 815 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.85–1.88 (m, 2H, CH_2), 3.22–3.26 (m, 2H, CH_2N), 3.89–3.92 (m, 2H, NCH_2), 7.37 (d, J = 8.7 Hz, 1H, ArH), 7.51 (s, 1H, CH), 7.55 (d, J = 8.4 Hz, 2H, ArH), 7.75 (d, J = 9.0 Hz, 1H, ArH), 7.87–7.90 (m, 3H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.5, 43.0, 43.9, 112.1, 119.5, 121.0 (d, J = 33.0 Hz), 124.3 (d, J = 270.0 Hz), 125.8, 127.0, 128.8, 130.4, 130.8, 134.9, 136.2, 138.2, 143.4, 146.8, 193.2; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{15}N_2OF_3Cl$[M+H], 391.0819; found, 391.0816.

5-(4'-Bromophenyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3bj).



Yellowy solid, m.p. 195–196 °C; IR (KBr): 2951, 1671, 1641, 1590, 1318, 1277, 1112, 814 cm^{-1}; ^1H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.86 (m, 2H, CH_2), 3.23 (m, 2H, CH_2N), 3.88–3.92 (m, 2H, NCH_2), 7.37 (d, J = 9.0 Hz, 1H, ArH), 7.51 (s, 1H, CH), 7.70 (d, J = 8.4 Hz, 2H, ArH), 7.76 (d, J = 9.3 Hz, 1H, ArH), 7.80 (d, J = 8.4 Hz, 2H, ArH), 7.90 (s, 1H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.5, 43.0, 43.8, 112.1, 119.5, 120.5 (d, J_2= 32.3), 124.3 (d, J_1= 269.3 Hz), 125.8, 127.1, 127.5, 130.4, 130.9, 131.8, 135.2, 136.2, 143.4, 146.8, 193.5; HRMS (TOF ES^+): *m/z* calcd for $C_{20}H_{15}N_2OF_3Br$[M+H], 435.0314; found, 435.0317.

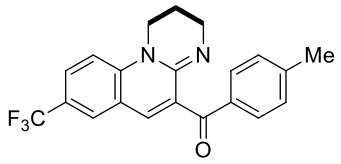
5-(Phenyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3bk).



Yellowy solid, m.p. 187–188 °C; IR (KBr): 1667, 1640, 1589, 1343, 1320, 1213, 1160, 1099, 814 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.87–1.89 (m, 2H, CH_2), 3.24–3.26 (m, 2H, CH_2N), 3.90–3.93 (m, 2H, NCH_2), 7.37 (d, J = 8.9 Hz, 1H, ArH), 7.48–7.52 (m, 3H, CH), 7.63 (t, J = 7.4 Hz, 1H, ArH), 7.75 (d, J = 8.8 Hz, 1H, ArH), 7.88–7.90 (m, 3H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 19.9, 43.4, 44.3, 112.4, 120.0, 121.4 (d, J = 32.5 Hz), 124.8 (d, J = 267.5 Hz), 126.0, 127.3, 129.0, 129.4, 130.3, 133.8, 136.5, 137.2, 143.7, 147.3, 194.6; HRMS

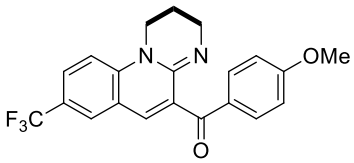
(TOF ES$^+$): *m/z* calcd for $C_{20}H_{16}N_2OF_3$[M+H], 357.1209; found, 357.1205.

5-(*p*-Tolyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimido[1,2-*a*] quinoline (3bl).



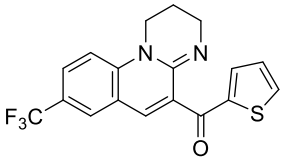
Yellowy solid, m.p. 226–227 °C; IR (KBr): 1663, 1642, 1319, 1209, 1160, 1112, 1083, 828 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.86–1.88 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 3.24–3.26 (m, 2H, CH_2N), 3.89–3.92 (m, 2H, NCH_2), 7.30 (d, *J* = 8.0 Hz, 2H, Ar*H*), 7.36 (d, *J* = 8.9 Hz, 1H, Ar*H*), 7.43 (s, 1H, C*H*), 7.74 (d, *J* = 8.7 Hz, 1H, Ar*H*), 7.78 (d, *J* = 8.1 Hz, 2H, Ar*H*), 7.88 (s, 1H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 19.9, 21.6, 43.4, 44.3, 112.4, 120.0, 121.3 (d, *J* = 32.5), 124.8 (d, *J* = 270.0 Hz), 125.9, 127.1, 127.2, 129.6, 129.9, 134.1, 137.4, 143.7, 144.4, 147.2, 194.2; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{18}N_2OF_3$[M+H], 371.1365; found, 371.1363.

5-(4'-Methoxyphenyl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimi do[1,2-*a*]quinoline (3bm).



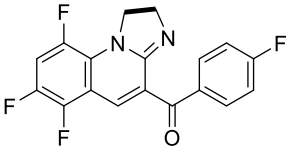
White solid, m.p. 192–193 °C; IR (KBr): 1662, 1641, 1593, 1319, 1264, 1157, 1029, 839 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.87–1.88 (m, 2H, CH_2), 3.26 (m, 2H, CH_2N), 3.84 (s, 3H, CH_3), 3.90–3.91 (m, 2H, NCH_2), 7.01–7.03 (m, 2H, Ar*H*), 7.36 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.41 (s, 1H, C*H*), 7.74 (d, *J* = 8.8 Hz, 1H, Ar*H*), 7.84–7.88 (m, 3H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 19.9, 43.4, 44.3, 55.9, 112.3, 114.3, 120.0, 121.3 (d, *J* = 32.5), 124.8 (d, *J* = 270.0 Hz), 125.9, 127.2, 127.2, 129.5, 129.7, 137.5, 143.7, 147.2, 163.8, 193.1; HRMS (TOF ES$^+$): *m/z* calcd for $C_{21}H_{18}N_2O_2F_3$ [M+H], 387.1314; found, 387.1317.

5-(Thiophen-2'-yl)methanoneyl-8-(trifluoromethyl)-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3bn).



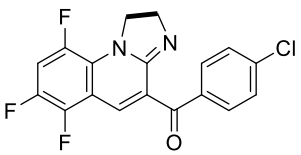
Light red solid, m.p. 209–210 °C; IR (KBr): 1645, 1586, 1343, 1319, 1209, 1156, 1102, 821, 732 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.87–1.91 (m, 2H, CH_2), 3.29–3.32 (m, 2H, CH_2N), 3.88–3.92 (m, 2H, NCH_2), 7.19–7.22 (m, 1H, C*H*), 7.35 (d, *J* = 8.7 Hz, 1H, C*H*), 7.50 (s, 1H, C*H*), 7.72–7.76 (m, 2H, C*H*), 7.88 (d, *J* = 1.8 Hz, 1H, Ar*H*), 8.04 (dd, J_1= 4.8 Hz, J_2= 1.2 Hz, 1H, Ar*H*); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.5, 43.0, 43.9, 112.0, 119.4, 120.9 (q, J_2= 32.3 Hz), 124.3 (d, J_1= 269.3 Hz), 125.7, 126.1, 127.0, 128.7, 129.8, 135.2, 135.5, 136.2, 143.3 (d, J_3= 9.8 Hz), 146.5, 186.3; HRMS (TOF ES^+): *m/z* calcd for $C_{18}H_{14}N_2OF_3S$[M+H], 363.0773; found, 363.0777.

6,7,9-Trifluoro-4-(4'-fluorophenyl)methanoneyl-1,2-dihydroimidazo[1,2-a] quinoline (3ca).



Red solid, m.p. 177–178 °C; IR (KBr): 1668, 1636, 1598, 1496, 1393, 1267, 1157, 858, 603 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 3.84 (t, *J* = 10.3 Hz, 2H, CH_2N), 4.20–4.25 (m, 2H, NCH_2), 7.35 (t, *J* = 8.7 Hz, 2H, Ar*H*), 7.61 (s, 1H, C*H*), 7.70–7.76 (m, 1H, Ar*H*), 7.97–8.00 (m, 2H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 48.6, 54.1, 108.8 (t, *J* = 25.0 Hz), 111.5 (d, *J* = 15.0 Hz), 116.2 (d, *J* = 22.5 Hz), 126.4 (d, *J* = 13.8 Hz), 127.3, 131.2, 132.7, 132.9 (d, *J* = 10.0 Hz), 140.9 (t, *J* = 11.9 Hz), 141.9 (m), 142.7 (d, *J* = 12.5 Hz), 143.9 (t, *J* = 18.8 Hz), 153.7, 165.8 (d, *J* = 251.3 Hz), 191.1; ^{19}F NMR (565 MHz, DMSO-d_6) (δ, ppm): -148.4 (t, *J* = 16.9 Hz), -147.0 (d, *J* = 22.6 Hz), -132.8 (d, *J* = 11.3 Hz), -104.5; HRMS (TOF ES^+): m/z calcd for $C_{18}H_{11}N_2OF_4$[M+H], 347.0802; found, 347.0801.

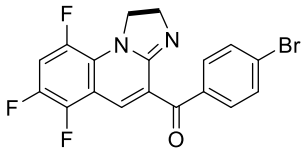
6,7,9-Trifluoro-4-(4'-chlorophenyl)methanoneyl-1,2-dihydroimidazo[1,2-a]qui noline (3cb).



Red solid, m.p. 186–187 °C; IR (KBr): 1664, 1638, 1595, 1499, 1393, 1269, 1090,

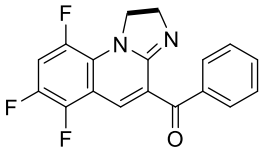
776 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) (δ, ppm): 3.81–3.85 (m, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.60 (d, J = 8.5 Hz, 2H, ArH), 7.65 (s, 1H, CH), 7.73–7.78 (m, 1H, ArH), 7.91 (d, J = 8.5 Hz, 2H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6) (δ, ppm): 48.7 (d, J = 9.0 Hz), 54.2, 109.0 (t, J = 25.5 Hz), 111.6 (d, J = 10.5 Hz), 126.6 (d, J = 10.0 Hz), 127.8, 129.3, 131.0, 131.8, 134.8, 139.4, 141.1, 142.5 (d, J = 60.0 Hz), 144.0 (d, J = 8.8 Hz), 153.8, 191.7; HRMS (TOF ES^+): m/z calcd for $C_{18}H_{11}N_2OF_3Cl$ [M+H], 363.0506; found, 363.0503.

6,7,9-Trifluoro-4-(4'-bromophenyl)methanoneyl-1,2-dihydroimidazo[1,2-a]quinoline (3cc).



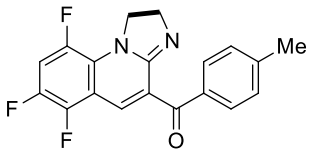
Orange solid, m.p. 203–204 °C; IR (KBr): 1663, 1635, 1586, 1496, 1269, 1124, 774, 609 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6 + $DCCl_3$) (δ, ppm): 3.83 (t, J = 10.3 Hz, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.64 (s, 1H, CH), 7.73–7.74 (m, 3H, ArH), 7.82 (d, J = 8.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6 + $DCCl_3$) (δ, ppm): 48.7 (d, J = 9.0 Hz), 54.2, 109.0 (t, J = 25.5 Hz), 111.6 (d, J = 10.5 Hz), 126.6, 127.9, 128.6, 131.0, 131.8, 132.3, 135.1, 141.1, 142.7, 143.9 (d, J = 51.0 Hz), 153.8, 191.8; HRMS (TOF ES^+): m/z calcd for $C_{18}H_{11}N_2OF_3Br$ [M+H], 407.0001; found, 407.0000.

6,7,9-Trifluoro-4-(phenyl)methanoneyl-1,2-dihydroimidazo[1,2-a]quinoline (3cd).



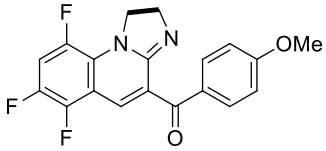
Orange solid, m.p. 195–196 °C; IR (KBr): 1667, 1636, 1498, 1392, 1270, 803, 609 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 3.84 (t, J = 10.3 Hz, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.54 (d, J = 7.7 Hz, 2H, ArH), 7.59 (s, 1H, CH), 7.67–7.76 (m, 2H, ArH), 7.90 (d, J = 7.5 Hz, 2H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 48.6 (d, J = 8.8 Hz), 54.1, 108.7 (t, J = 24.4 Hz), 111.5 (d, J = 11.3 Hz), 126.4 (d, J = 12.5 Hz), 127.1, 129.1, 129.8, 131.4, 134.3, 135.9, 140.9, 141.9, 142.8, 143.9 (d, J = 33.8 Hz), 153.7, 192.6; HRMS (TOF ES^+): m/z calcd for $C_{18}H_{12}N_2OF_3$ [M+H], 329.0896; found, 329.0894.

6,7,9-Trifluoro-4-(*p*-tolyl)methanoneyl-1,2-dihydroimidazo[1,2-a]quinoline (3ce).



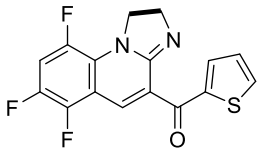
Red-orange solid, m.p. 185–186 °C; IR (KBr): 1662, 1635, 1496, 1392, 1272, 1193, 603 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 2.39 (s, 3H, CH_3), 3.83 (t, J = 10.3 Hz, 2H, CH_2N), 4.19–4.25 (m, 2H, NCH_2), 7.33 (d, J = 8.0 Hz, 2H, ArH), 7.53 (s, 1H, CH), 7.69–7.75 (m, 1H, ArH), 7.79 (d, J = 8.1 Hz, 2H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 21.6, 48.6 (d, J = 8.8 Hz), 54.1, 108.6 (t, J = 25.0 Hz), 111.6, 126.4, 126.7, 129.7, 130.0, 131.7, 133.5, 140.9, 141.9 (d, J = 30.0 Hz), 142.8, 143.9, 145.0, 153.7, 192.0; HRMS (TOF ES$^+$): m/z calcd for $C_{19}H_{14}N_2OF_3$ [M+H], 343.1052; found, 343.1050.

6,7,9-Trifluoro-4-(4'-methoxyphenyl)methanoneyl-1,2-dihydroimidazo [1,2-a]quinoline (3cf).



Orange solid, m.p. 191–192 °C; IR (KBr): 1633, 1598, 1497, 1260, 1162, 1026, 603 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6 + $DCCl_3$) (δ, ppm): 3.82–3.89 (m, 2H, CH_2N), 3.85 (s, 3H, CH_3), 4.19–4.27 (m, 2H, NCH_2), 7.02 (d, J = 9.0 Hz, 2H, ArH), 7.46 (d, J = 1.5 Hz, 1H, CH), 7.57–7.67 (m, 1H, ArH), 7.83–7.88 (m, 2H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 48.2 (d, J = 8.3 Hz), 5.71, 55.5, 108.0 (t, J = 24.8 Hz), 111.1 (d, J = 10.5 Hz), 113.9, 126.0, 128.3, 131.3, 131.9, 139.8, 140.8, 143.1 (d, J = 18.8 Hz), 144.0, 153.4, 163.8, 190.3; HRMS (TOF ES$^+$): m/z calcd for $C_{19}H_{14}N_2O_2F_3$ [M+H], 359.1001; found, 359.0999.

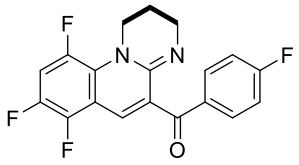
6,7,9-Trifluoro-4-(thiophen-2-yl)methanoneyl-1,2-dihydroimidazo[1,2-a] quinoline (3cg).



Orange solid, m.p. 170–171 °C; IR (KBr): 1640, 1496, 1413, 1280, 1127, 733 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) (δ, ppm): 3.86–3.89 (m, 2H, CH_2N), 4.22–4.25 (m,

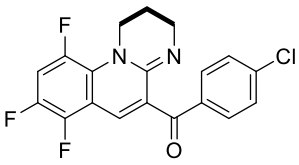
2H, NCH_2), 7.25–7.26 (m, 1H, C*H*), 7.63 (s, 1H, C*H*), 7.66–7.72 (m, 1H, Ar*H*), 7.86–7.87 (m, 1H, C*H*), 8.13–8.14 (m, 1H, C*H*); ^{13}C NMR (150 MHz, DMSO-d_6) (δ, ppm): 48.8, 54.2, 108.9 (m), 111.5 (m), 126.5 (d, *J* = 12.0 Hz), 127.1, 129.4, 130.8, 136.9, 137.2, 141.1–142.7 (m), 142.0–142.4 (m), 142.9, 143.6–144.0 (m), 153.5, 184.4; HRMS (TOF ES$^+$): m/z calcd for $C_{16}H_{10}N_2OF_3S$ [M+H], 335.0460; found, 335.0464.

7,8,10-Trifluoro-5-(4'-fluorophenyl)methanoneyl-2,3-dihydro-1*H*-pyrimido [1,2-*a*]quinoline (3ch).



Yellow solid, m.p. 179–180 °C; IR (KBr): 2845, 1665, 1639, 1599, 1492, 1265, 1151, 992, 844 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.75 (m, 2H, CH_2), 3.22 (m, 2H, CH_2N), 4.14 (m, 2H, NCH_2), 7.32 (t, *J* = 8.7 Hz, 2H, Ar*H*), 7.43 (s, 1H, C*H*), 7.66–7.72 (m, 1H, Ar*H*), 7.94–7.97 (m, 2H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 20.1, 43.5, 48.5 (d, *J* = 17.5 Hz), 108.2 (m), 112.4 (d, *J* = 18.8 Hz), 116.0 (t, *J* = 25.6 Hz), 121.3, 127.4, 132.4 (d, *J* = 10.0 Hz), 133.2 (d, *J* = 10.0 Hz), 138.5, 141.5 (d, *J* = 21.3 Hz), 143.5 (d, *J* = 6.3 Hz), 145.6, 146.8, 165.5 (d, *J* = 251.3 Hz), 192.5; ^{19}F NMR (470 MHz, DMSO-d_6) (δ, ppm): -149.6, -145.5 (t, *J* = 9.4 Hz), -123.2, -105.3; HRMS (TOF ES$^+$): m/z calcd for $C_{19}H_{13}N_2OF_4$ [M+H], 361.0958; found, 361.0959.

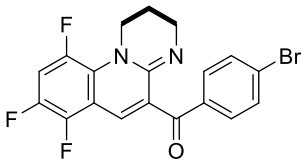
7,8,10-Trifluoro-5-(4'-chlorophenyl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1, 2-*a*]quinoline (3ci).



Yellow solid, m.p. 199–200 °C; IR (KBr): 2924, 1663, 1638, 1600, 1492, 1264, 1088, 991, 842 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6 + $HClO_4$) (δ, ppm): 2.16 (m, 2H, CH_2), 3.54 (m, 2H, CH_2N), 4.67 (m, 2H, NCH_2), 7.71 (d, *J* = 8.2 Hz, 2H, Ar*H*), 7.99 (d, *J* = 8.3 Hz, 2H, Ar*H*), 8.26–8.31 (m, 1H, Ar*H*), 8.48 (s, 1H, C*H*); ^{13}C NMR (150 MHz, DMSO-d_6 + $HClO_4$) (δ, ppm): 18.3, 39.1, 50.8 (d, *J* = 19.5 Hz), 112.7 (m), 113.6 (d, *J* = 16.5 Hz), 124.8, 125.1, 129.6, 132.7, 134.9, 135.1, 140.3, 143.5 (d, *J* = 6.3 Hz), 145.6, 146.8, 150.7, 190.9; ^{19}F NMR (565 MHz, DMSO-d_6 +

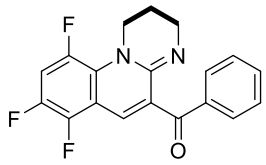
$HClO_4$) (δ, ppm): -145.3 (m), -138.3 (m), -115.8; HRMS (TOF ES^+): m/z calcd for $C_{19}H_{13}N_2OF_3Cl$ [M+H], 377.0663; found, 377.0665.

7,8,10-Trifluoro-5-(4'-bromophenyl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1, 2-*a*]quinoline (3cj).



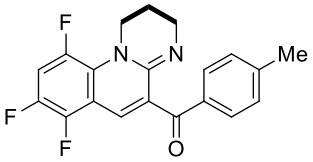
Yellow solid, m.p. 193–194 °C; IR (KBr): 2948, 1669, 1638, 1587, 1493, 1263, 1163, 1070, 906, 844 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) (δ, ppm): 1.74 (m, 2H, CH_2), 3.21 (m, 2H, CH_2N), 4.14 (m, 2H, NCH_2), 7.47 (s, 1H, Ar*H*), 7.71–7.72 (m, 3H, Ar*H*), 7.79–7.81 (m, 2H, Ar*H*); ^{13}C NMR (150 MHz, DMSO-d_6 + $HClO_4$) (δ, ppm): 20.2, 43.6, 48.6 (d, *J* = 16.5 Hz), 108.4 (m), 112.5 (d, *J* = 18.0 Hz), 121.8, 127.5, 128.0, 131.5, 132.2, 135.6, 138.3, 141.9 (d, *J* = 12.0 Hz), 143.5, 144.0, 147.0, 193.3;HRMS (TOF ES^+): m/z calcd for $C_{19}H_{13}N_2OF_3Br$ [M+H], 421.0158; found, 421.0159.

7,8,10-Trifluoro-5-(phenyl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1,2-*a*] quinoline (3ck).



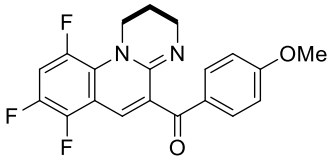
Yellow solid, m.p. 191–192 °C; IR (KBr): 2958, 1669, 1638, 1597, 1492, 1267, 1198, 1165, 990, 665 cm^{-1}; ^1H NMR (600 MHz, DMSO-d_6) (δ, ppm): 1.72–1.76 (m, 2H, CH_2), 3.21 (m, 2H, CH_2N), 4.13–4.16 (m, 2H, NCH_2), 7.42 (s, 1H, C*H*), 7.48–7.52 (m, 2H, Ar*H*), 7.64 (t, *J* = 7.4 Hz, 1H, Ar*H*), 7.67–7.72 (m, 1H, Ar*H*), 7.85–7.88 (m, 2H, Ar*H*); ^{13}C NMR (150 MHz, DMSO-d_6) (δ, ppm): 20.2, 43.6, 48.6, 108.2 (m), 112.5 (t, *J* = 10.5 Hz), 121.2, 127.4, 129.1, 129.5, 134.0, 136.4, 138.9, 141.8 (m), 143.4 (m), 145.6 (m), 147.0, 194.0; HRMS (TOF ES^+): m/z calcd for $C_{19}H_{14}N_2OF_3$ [M+H], 343.1052; found, 343.1054.

7,8,10-Trifluoro-5-(*p*-tolyl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1,2-*a*] quinoline (3cl).



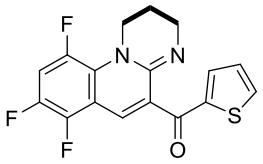
Yellow solid, m.p. 196–197 °C; IR (KBr): 1663, 1602, 1492, 1268, 1163, 990, 836 cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6) (δ, ppm): 1.69–1.76 (m, 2H, CH_2), 2.37 (s, 3H, CH_3), 3.19–3.22 (m, 2H, CH_2N), 4.10–4.16 (m, 2H, NCH_2), 7.30 (d, J = 7.8 Hz, 2H, ArH), 7.35 (s, 1H, CH), 7.62–7.73 (m, 1H, ArH), 7.75 (d, J = 8.4 Hz, 2H, ArH); ^{13}C NMR (75 MHz, DMSO-d_6) (δ, ppm): 19.7, 21.2, 43.0, 48.2, 107.6 (m), 112.0 (d, J = 20.3 Hz), 120.4, 127.0, 129.2, 129.2, 133.5, 138.6, 140.6 (m), 143.7 (m), 142.6–145.8 (m), 144.0, 146.4, 193.1; HRMS (TOF ES^+): m/z calcd for $C_{20}H_{16}N_2OF_3$ [M+H], 357.1209; found, 357.1208.

7,8,10-Trifluoro-5-(4'-methoxyphenyl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3cm).



Yellow solid, m.p. 174–175 °C; IR (KBr): 1659, 1597, 1493, 1257, 1162, 1019, 849 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6) (δ, ppm): 1.74–1.76 (m, 2H, CH_2), 3.23–3.24 (m, 2H, CH_2N), 3.85 (s, 3H, CH_3), 4.14–4.15 (m, 2H, NCH_2), 7.03 (d, J = 8.8 Hz, 2H, ArH), 7.34 (s, 1H, CH), 7.63–7.73 (m, 1H, ArH), 7.84 (d, J = 8.7 Hz, 2H, ArH); ^{13}C NMR (125 MHz, DMSO-d_6) (δ, ppm): 20.1, 43.4, 48.5, 56.0, 108.0 (m), 112.4, 114.3, 120.7, 127.3, 129.3, 131.9, 139.0, 141.6 (m), 143.3 (m), 143.7–145.5 (m), 146.8, 163.9, 192.3; HRMS (TOF ES^+): m/z calcd for $C_{20}H_{16}N_2O_2F_3$ [M+H], 373.1158; found, 373.1158.

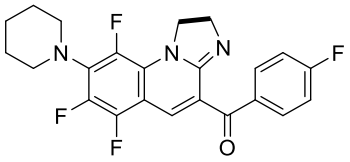
7,8,10-Trifluoro-5-(thiophen-2'-yl)methanoneyl-2,3-dihydro-1*H*-pyrimido[1,2-*a*]quinoline (3cn).



Yellow solid, m.p. 178–179 °C; IR (KBr): 2959, 1641, 1599, 1492, 1409, 1256, 1197, 983, 857 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) (δ, ppm): 1.75–1.78 (m, 2H, CH_2), 3.26–3.28 (m, 2H, CH_2N), 4.12–4.15 (m, 2H, NCH_2), 7.20–7.22 (m, 1H, CH), 7.42 (s, 1H, CH), 7.66–7.72 (m, 1H, ArH), 7.75–7.76 (m, 1H, CH), 8.04–8.05

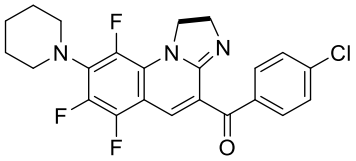
(m, 1H, C*H*); ^{13}C NMR (150 MHz, DMSO-d_6) (δ, ppm): 20.2, 43.5, 48.6, 108.4 (m), 112.3 (t, *J* = 7.5 Hz), 121.2, 127.5 (d, *J* = 7.5 Hz), 129.2, 135.8, 136.0, 138.3, 141.7–142.0 (m), 143.4–143.5 (m), 143.5, 143.8–145.5 (m), 146.6, 186.2; HRMS (TOF ES$^+$): m/z calcd for $C_{17}H_{12}N_2OF_3S$ [M+H], 349.0616; found, 349.0618.

6,7,9-Trifluoro-4-(4'-fluorophenyl)methanoneyl-8-(piperidin-1-yl)-1,2-dihydro imidazo[1,2-*a*]quinoline (4da).



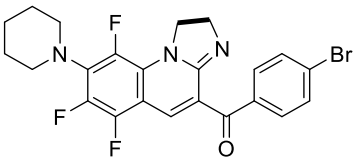
Red solid, m.p. 170–171 °C; IR (KBr): 2935, 2851, 1653, 1628, 1482, 1271, 1232, 1156, 1119, 1001, 848, 768, 602cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6+ $CDCl_3$) (δ, ppm): 1.62–1.68 (m, 6H, CH_2), 3.23 (m, 4H, CH_2), 3.84 (t, *J* = 10.2 Hz, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.28 (t, *J* = 8.7 Hz, 2H, Ar*H*), 7.48 (s, 1H, C*H*), 7.90–7.93 (m, 2H, Ar*H*); ^{13}C NMR (125 MHz, DMSO-d_6 + $CDCl_3$) (δ, ppm): 24.0, 26.5, 48.8, 52.2, 53.9, 115.9 (d, J_2= 22.5 Hz), 127.3, 128.7, 132.7 (d, J_3= 10.0 Hz), 133.1, 133.6, 154.0, 165.7 (d, J_1 = 252.5 Hz), 191.1; ^{19}F NMR (471 MHz, DMSO-d_6+ $DCCl_3$) (δ, ppm): -105.0, -145.9, -148.5, -156.9 (d, *J* = 18.8 Hz); HRMS (TOF ES$^+$): m/z calcd for $C_{23}H_{20}N_3OF_4$ [M+H], 430.1537; found, 430.1533.

6,7,9-Trifluoro-4-(4'-chlorophenyl)methanoneyl-8-(piperidin-1-yl)-1,2-dihydr oimidazo[1,2-*a*]quinoline (4db).



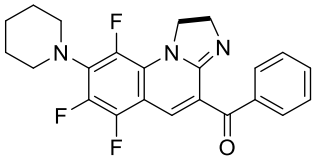
Red solid, m.p. 160–161 °C; IR (KBr): 2932, 2854, 1628, 1483, 1269, 1120, 1090, 1000, 844, 766cm^{-1}; ^{1}H NMR (300 MHz, DMSO-d_6+ $CDCl_3$) (δ, ppm): 1.61 (m, 6H, CH_2), 3.22 (m, 4H, CH_2), 3.84 (t, *J* = 10.2 Hz, 2H, CH_2N), 4.17–4.26 (m, 2H, NCH_2), 7.47 (s, 1H, C*H*), 7.49 (d, *J* = 8.7 Hz, 2H, Ar*H*), 7.82 (d, *J* = 8.4 Hz, 2H, Ar*H*); ^{13}CNMR (75 MHz, DMSO-d_6 + $CDCl_3$) (δ, ppm): 23.6, 26.1, 48.3, 51.8, 53.6, 103.2, 126.0, 126.5, 128.5, 128.8, 131.0, 134.7, 138.6, 153.6, 191.0; HRMS (TOF ES$^+$): m/z calcd for $C_{23}H_{20}ClN_3OF_3$ [M+H], 446.1242; found, 446.1239.

6,7,9-Trifluoro-4-(4'-bromophenyl)methanoneyl-8-(piperidin-1-yl)-1,2-dihydroimidazo[1,2-*a*]quinoline (4dc).



Orange solid, m.p. 181–181 °C; IR (KBr): 2933, 2855, 1654, 1633, 1478, 1386, 1270, 1156, 1121, 997, 832, 761cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6+ $CDCl_3$) (δ, ppm): 1.62 (m, 6H, CH_2), 3.24 (m, 4H, CH_2), 3.83 (t, J = 10.2 Hz, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.52 (s, 1H, CH), 7.69 (d, J = 8.4 Hz, 2H, ArH), 7.76 (d, J = 8.4 Hz, 2H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6 + $CDCl_3$) (δ, ppm): 23.80, 26.6, 44.7, 50.8, 52.4, 104.9, 114.7, 124.0, 126.6, 127.0, 128.1, 131.9, 132.4, 135.6, 137.4, 138.1, 139.7, 140.2, 140.5, 141.6, 146.7, 155.2, 190.9; ^{19}F NMR (565 MHz, DMSO-d_6 + $DCCl_3$) (δ, ppm): -143.9, -144.0, -148.7 (d, J = 16.9 Hz); HRMS (TOF ES$^+$): m/z calcd for $C_{23}H_{20}N_3OF_3Br$ [M+H], 490.0735; found, 490.0737.

6,7,9-Trifluoro-4-(phenyl)methanoneyl-8-(piperidin-1-yl)-1,2-dihydroimidazo[1,2-*a*]quinoline (4dd).



Orange-red solid, m.p. 186–187 °C; IR (KBr): 2938, 2853, 1633, 1480, 1456, 1268, 1119, 1000, 656cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6) (δ, ppm): 1.62 (m, 6H, CH_2), 3.23 (m, 4H, CH_2), 3.86 (t, J = 10.3 Hz, 2H, CH_2N), 4.21–4.26 (m, 2H, NCH_2), 7.43 (s, 1H, CH), 7.46–7.49 (m, 2H, ArH), 7.60–7.62 (m, 1H, ArH), 7.83 (d, J = 7.5 Hz, 2H, ArH); ^{13}C NMR (150 MHz, DMSO-d_6) (δ, ppm): 23.7, 26.5, 44.7, 50.7, 52.3, 104.8 (d, J_3= 19.5 Hz), 114.8, 124.0, 129.3, 129.9, 133.9, 136.5, 137.2, 137.9, 139.8, 140.4, 155.2, 191.7; ^{19}F NMR (471 MHz, DMSO-d_6 + $DCCl_3$) (δ, ppm): -143.9, -144.6, -149.0 (d, J = 22.6 Hz); HRMS (TOF ES$^+$): m/z calcd for $C_{23}H_{21}N_3OF_3$ [M+H], 412.1631; found, 412.1633.

X-ray Structure and Data[4] of 3bf

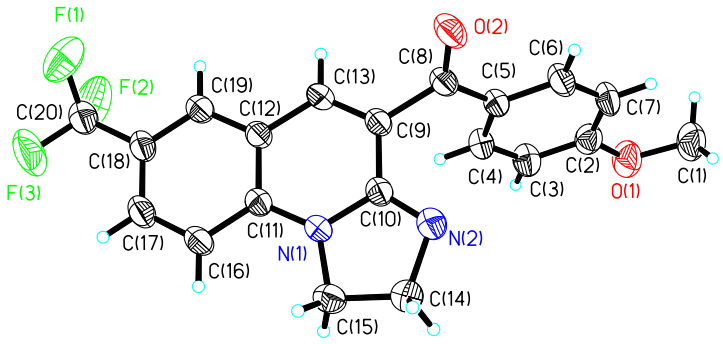


Figure S1. X-Ray crystal structure of **3bf**

Table S1 Crystal data and structure refinement for **3bf**

Identification code	1
Empirical formula	C_{20} H_{15} F_3 N_2 O_2
Formula weight	372.34
Temperature	293(2) K
Wavelength	0.71073 Å
Crystal system, space group	Monoclinic, P2(1)/n
Unit cell dimensions	a = 13.0354(17) A alpha = 90 deg b = 8.9711(12) A beta = 103.316(2) deg. c = 15.209(2) A gamma = 90 deg.
Volume	1730.8(4) A^3
Z, Calculated density	4, 1.429 Mg/m^3
Absorption coefficient	0.115 mm^-1
F(000)	768
Crystal size	0.40 x 0.36 x 0.32 mm
Theta range for data collection	1.86 to 25.14 deg.
Limiting indices	-15<=h<=15, -10<=k<=10, -18<=l<=18
Reflection collected/unique	13129 / 3092 [R(int) = 0.0456]
Completeness to theta = 30.07	99.9 %
Max. and min. transmission	0.9641 and 0.9554
Refinement method	Full-matrix least-squares on F^2
Data/restraints/parameters	3092 / 0 / 246
Goodness-of-fit on F^2	1.022
Final R indices [I>2sigma(I)]	R1 = 0.0563, wR2 = 0.1471
R indices (all data)	R1 = 0.1038, wR2 = 0.1812
Extinction coefficient	0.0047(16)
Largest diff. peak and hole	0.387 and -0.330 e.A^-3

Table S2 Bond lengths [A] and angles [deg] for **3bf**

F(1)-C(20)	1.341(4)
F(2)-C(20)	1.295(5)
F(3)-C(20)	1.297(4)
N(1)-C(11)	1.376(4)
N(1)-C(10)	1.394(3)
N(1)-C(15)	1.459(4)
N(2)-C(10)	1.288(4)
N(2)-C(14)	1.487(4)
O(1)-C(2)	1.371(4)
O(1)-C(1)	1.423(4)
O(2)-C(8)	1.228(3)
C(1)-H(1A)	0.9600
C(1)-H(1B)	0.9600
C(1)-H(1C)	0.9600
C(2)-C(7)	1.380(5)
C(2)-C(3)	1.383(5)
C(3)-C(4)	1.374(4)
C(3)-H(3)	0.9300
C(4)-C(5)	1.391(4)
C(4)-H(4)	0.9300
C(5)-C(6)	1.390(4)
C(5)-C(8)	1.477(4)
C(6)-C(7)	1.389(4)
C(6)-H(6)	0.9300
C(7)-H(7)	0.9300
C(8)-C(9)	1.517(4)
C(9)-C(13)	1.352(4)
C(9)-C(10)	1.457(4)
C(11)-C(16)	1.403(4)
C(11)-C(12)	1.417(4)
C(12)-C(19)	1.392(4)
C(12)-C(13)	1.452(4)
C(13)-H(13)	0.9300
C(14)-C(15)	1.535(4)
C(14)-H(14A)	0.9700
C(14)-H(14B)	0.9700
C(15)-H(15A)	0.9700
C(15)-H(15B)	0.9700
C(16)-C(17)	1.381(4)
C(16)-H(16)	0.9300
C(17)-C(18)	1.390(4)
C(17)-H(17)	0.9300
C(18)-C(19)	1.381(4)
C(18)-C(20)	1.479(5)

C(19)-H(19)	0.9300
C(11)-N(1)-C(10)	124.6(2)
C(11)-N(1)-C(15)	127.0(2)
C(10)-N(1)-C(15)	108.3(2)
C(10)-N(2)-C(14)	106.5(2)
C(2)-O(1)-C(1)	118.2(3)
O(1)-C(1)-H(1A)	109.5
O(1)-C(1)-H(1B)	109.5
H(1A)-C(1)-H(1B)	109.5
O(1)-C(1)-H(1C)	109.5
H(1A)-C(1)-H(1C)	109.5
H(1B)-C(1)-H(1C)	109.5
O(1)-C(2)-C(7)	124.7(3)
O(1)-C(2)-C(3)	115.9(3)
C(7)-C(2)-C(3)	119.4(3)
C(4)-C(3)-C(2)	120.8(3)
C(4)-C(3)-H(3)	119.6
C(2)-C(3)-H(3)	119.6
C(3)-C(4)-C(5)	120.9(3)
C(3)-C(4)-H(4)	119.5
C(5)-C(4)-H(4)	119.5
C(6)-C(5)-C(4)	117.8(3)
C(6)-C(5)-C(8)	121.0(3)
C(4)-C(5)-C(8)	121.2(3)
C(7)-C(6)-C(5)	121.5(3)
C(7)-C(6)-H(6)	119.2
C(5)-C(6)-H(6)	119.2
C(2)-C(7)-C(6)	119.6(3)
C(2)-C(7)-H(7)	120.2
C(6)-C(7)-H(7)	120.2
O(2)-C(8)-C(5)	122.5(3)
O(2)-C(8)-C(9)	119.3(3)
C(5)-C(8)-C(9)	118.2(2)
C(13)-C(9)-C(10)	119.5(3)
C(13)-C(9)-C(8)	122.3(3)
C(10)-C(9)-C(8)	118.1(3)
N(2)-C(10)-N(1)	116.1(3)
N(2)-C(10)-C(9)	126.7(3)
N(1)-C(10)-C(9)	117.2(3)
N(1)-C(11)-C(16)	121.9(3)
N(1)-C(11)-C(12)	118.2(2)
C(16)-C(11)-C(12)	119.9(3)
C(19)-C(12)-C(11)	118.5(3)
C(19)-C(12)-C(13)	123.0(3)
C(11)-C(12)-C(13)	118.5(3)

C(9)-C(13)-C(12)	121.9(3)
C(9)-C(13)-H(13)	119.0
C(12)-C(13)-H(13)	119.0
N(2)-C(14)-C(15)	107.0(3)
N(2)-C(14)-H(14A)	110.3
C(15)-C(14)-H(14A)	110.3
N(2)-C(14)-H(14B)	110.3
C(15)-C(14)-H(14B)	110.3
H(14A)-C(14)-H(14B)	108.6
N(1)-C(15)-C(14)	102.1(2)
N(1)-C(15)-H(15A)	111.3
C(14)-C(15)-H(15A)	111.3
N(1)-C(15)-H(15B)	111.3
C(14)-C(15)-H(15B)	111.3
H(15A)-C(15)-H(15B)	109.2
C(17)-C(16)-C(11)	119.9(3)
C(17)-C(16)-H(16)	120.1
C(11)-C(16)-H(16)	120.1
C(16)-C(17)-C(18)	120.7(3)
C(16)-C(17)-H(17)	119.7
C(18)-C(17)-H(17)	119.7
C(19)-C(18)-C(17)	119.7(3)
C(19)-C(18)-C(20)	120.1(3)
C(17)-C(18)-C(20)	120.1(3)
C(18)-C(19)-C(12)	121.4(3)
C(18)-C(19)-H(19)	119.3
C(12)-C(19)-H(19)	119.3
F(2)-C(20)-F(3)	108.5(4)
F(2)-C(20)-F(1)	102.7(3)
F(3)-C(20)-F(1)	102.1(4)
F(2)-C(20)-C(18)	114.8(3)
F(3)-C(20)-C(18)	114.4(3)
F(1)-C(20)-C(18)	113.0(3)

Symmetry transformations used to generate equivalent atoms:

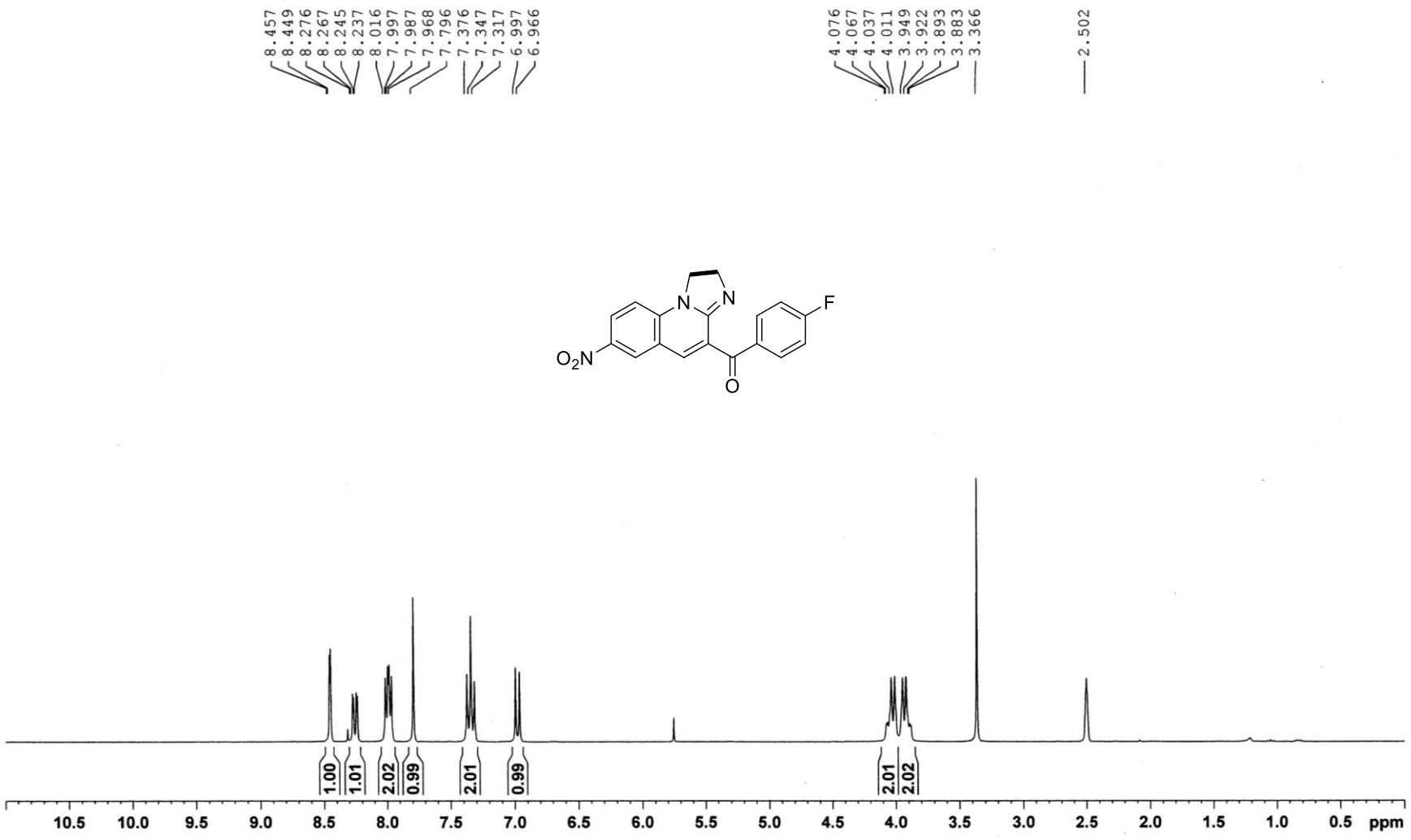


Figure S2. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3aa**

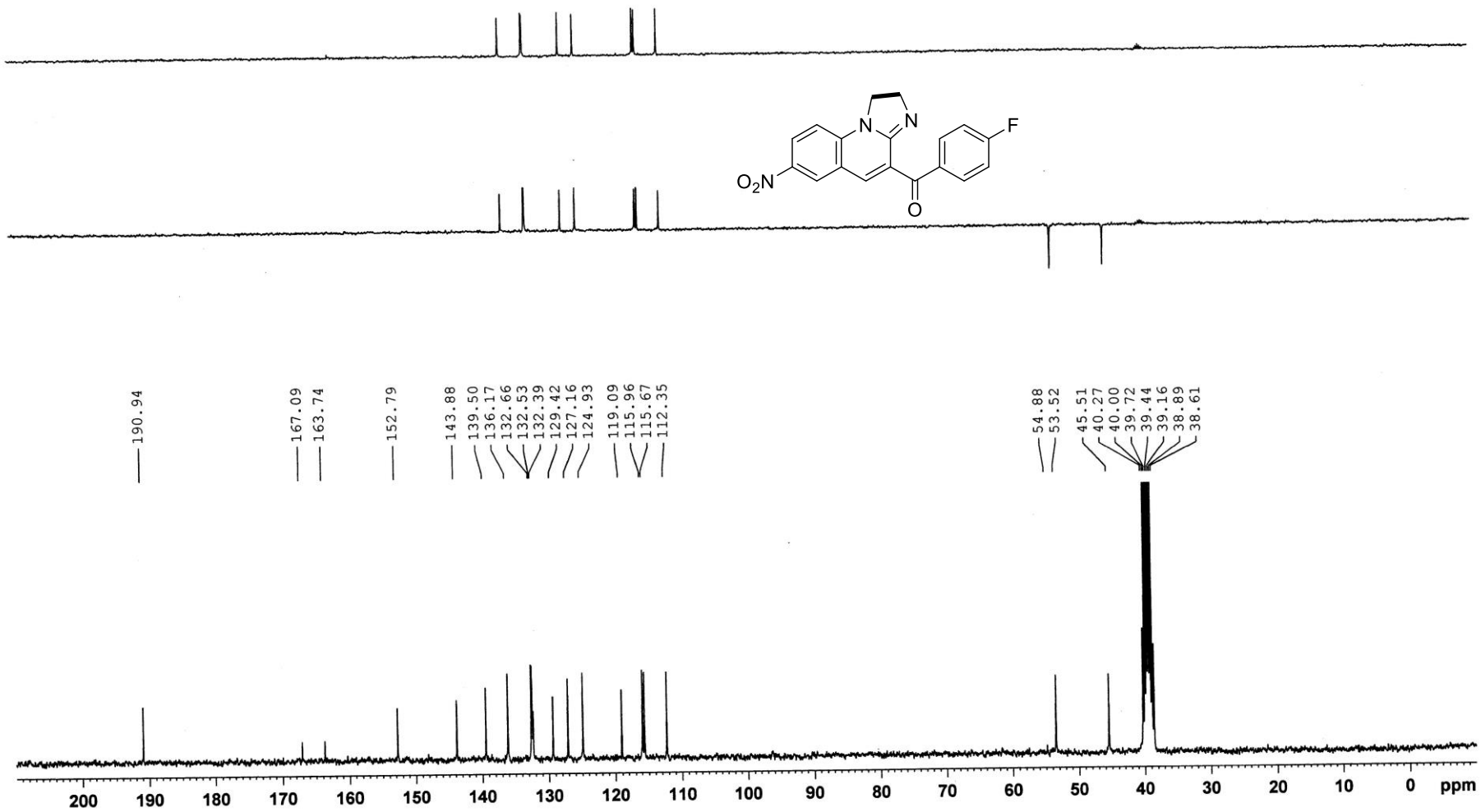


Figure S3. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3aa**

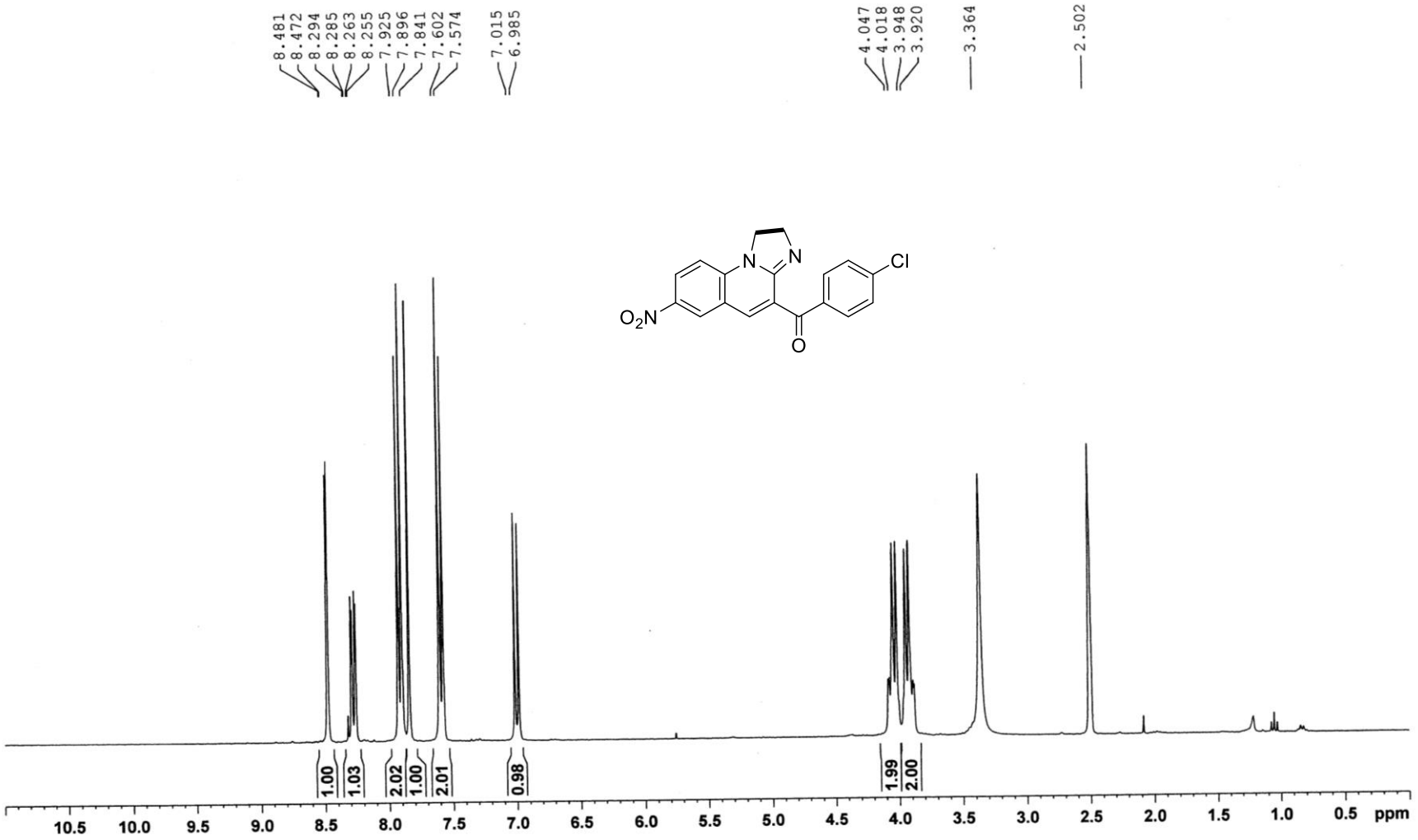


Figure S4. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ab**

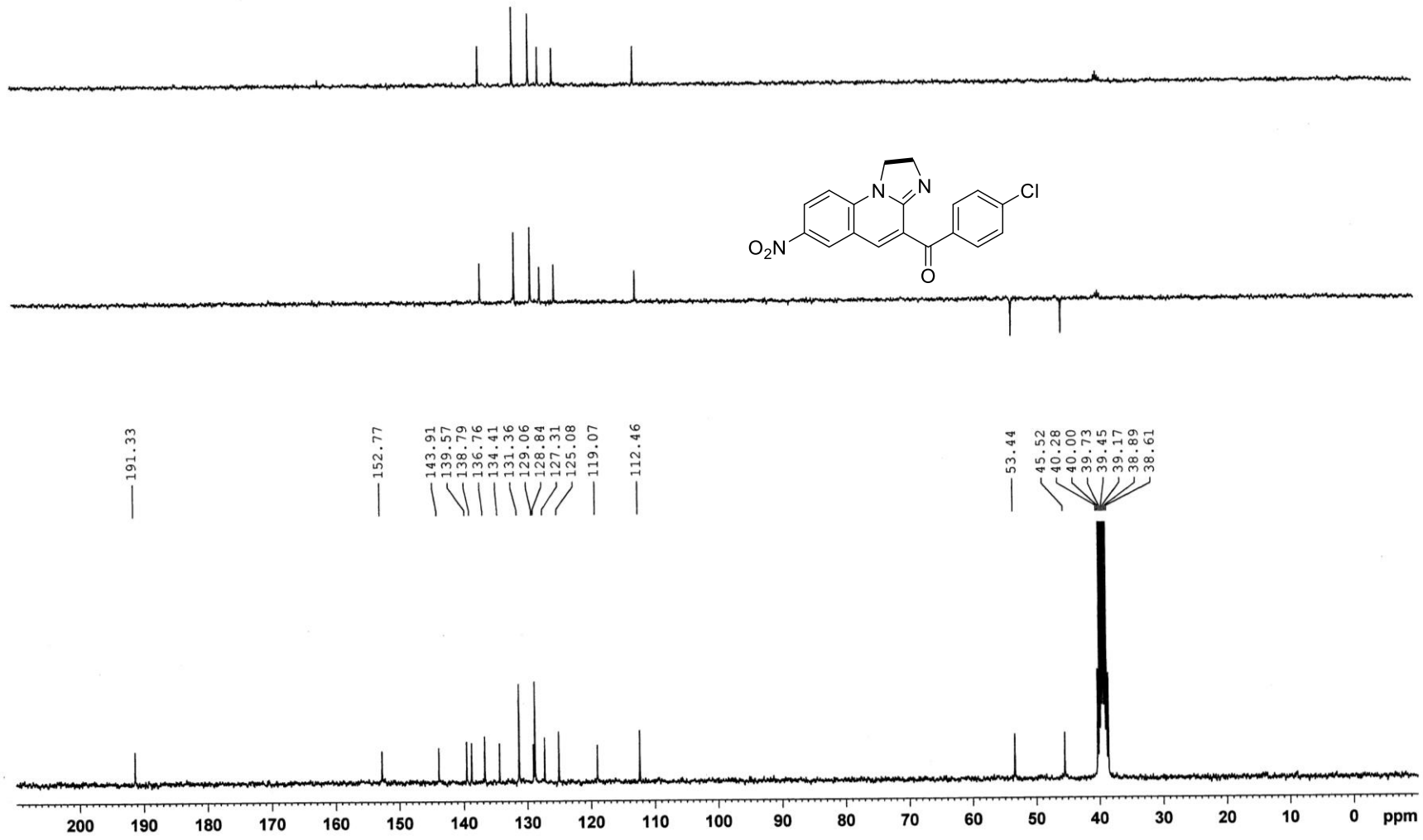


Figure S5. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ab**

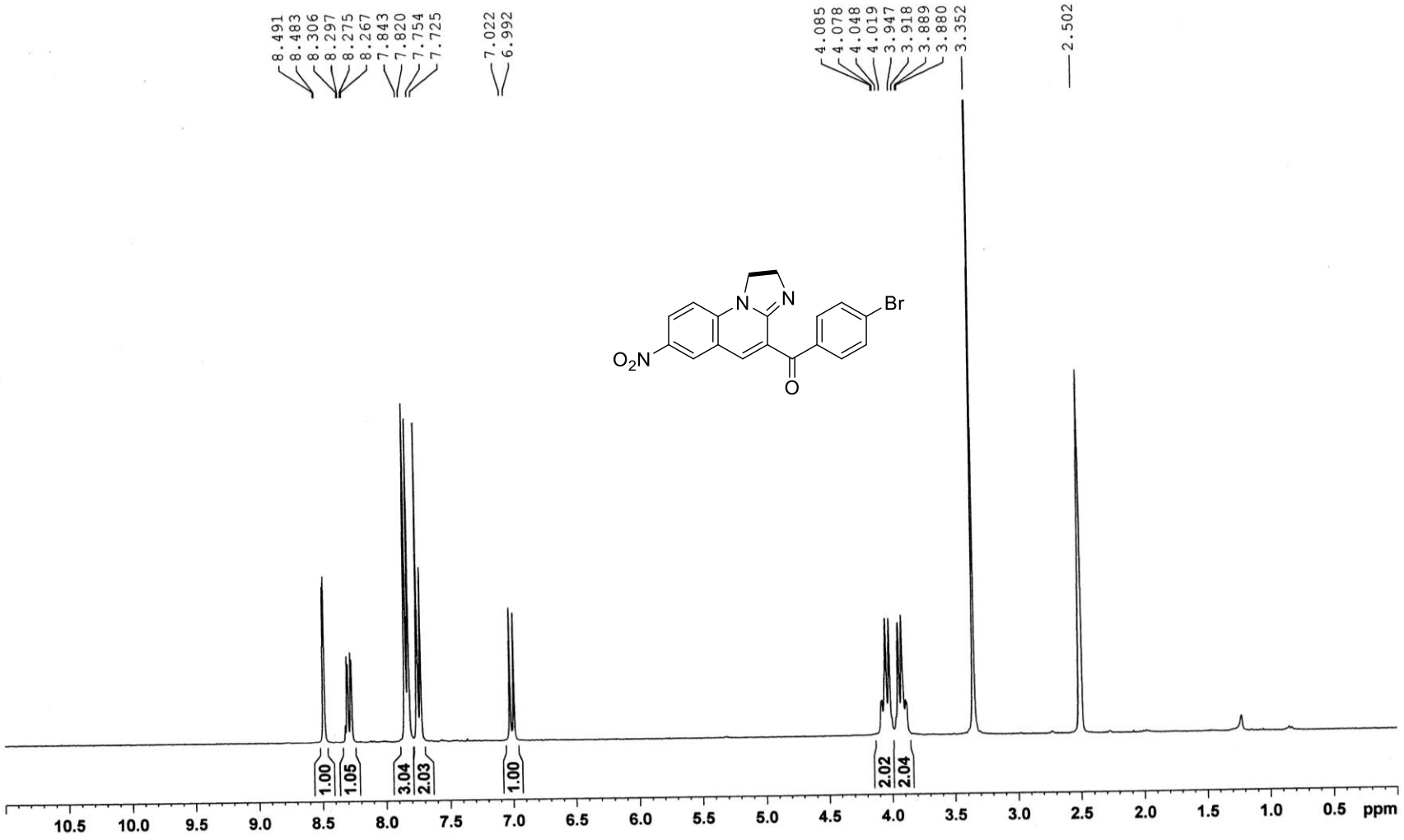


Figure S6. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ac**

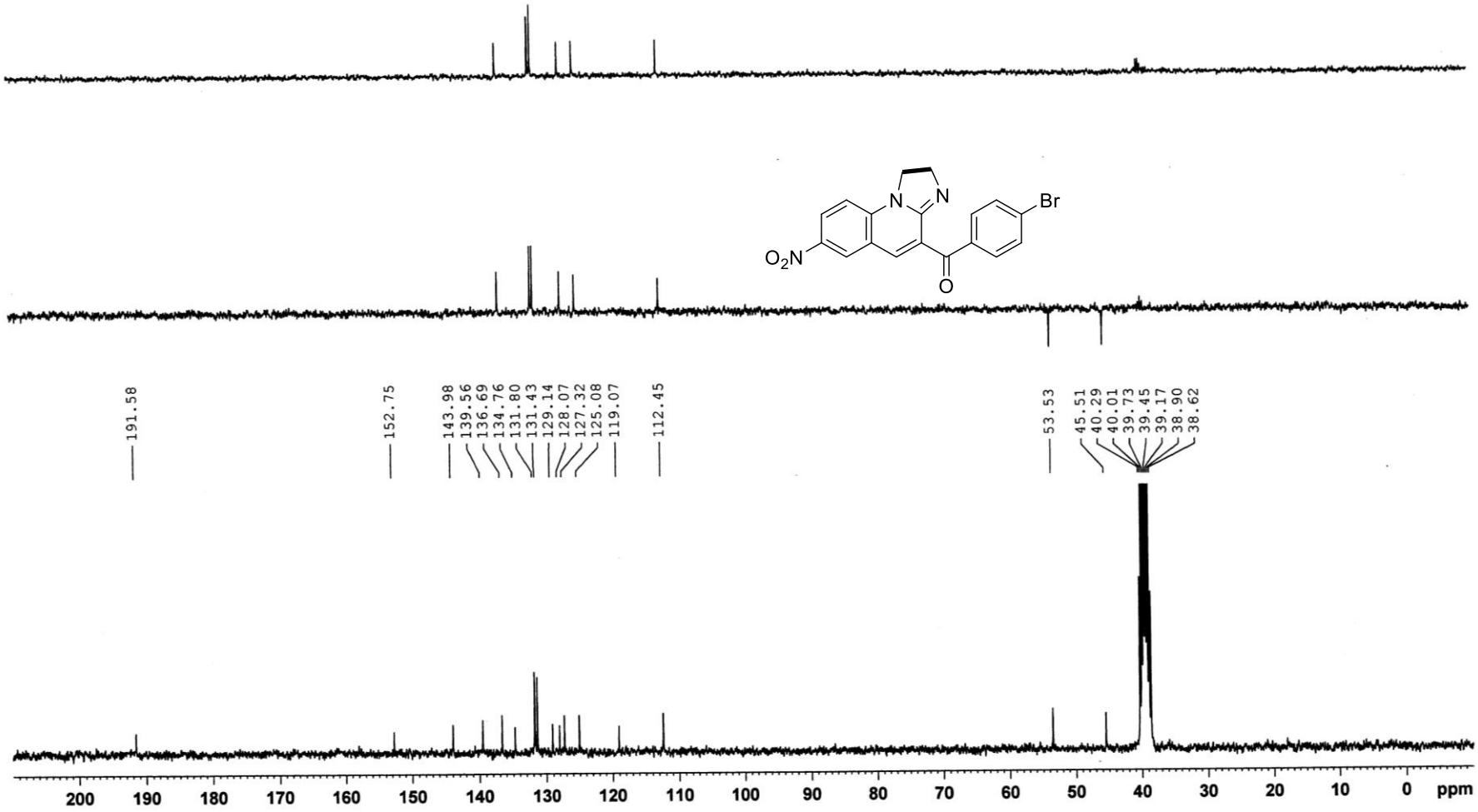


Figure S7 ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ac**

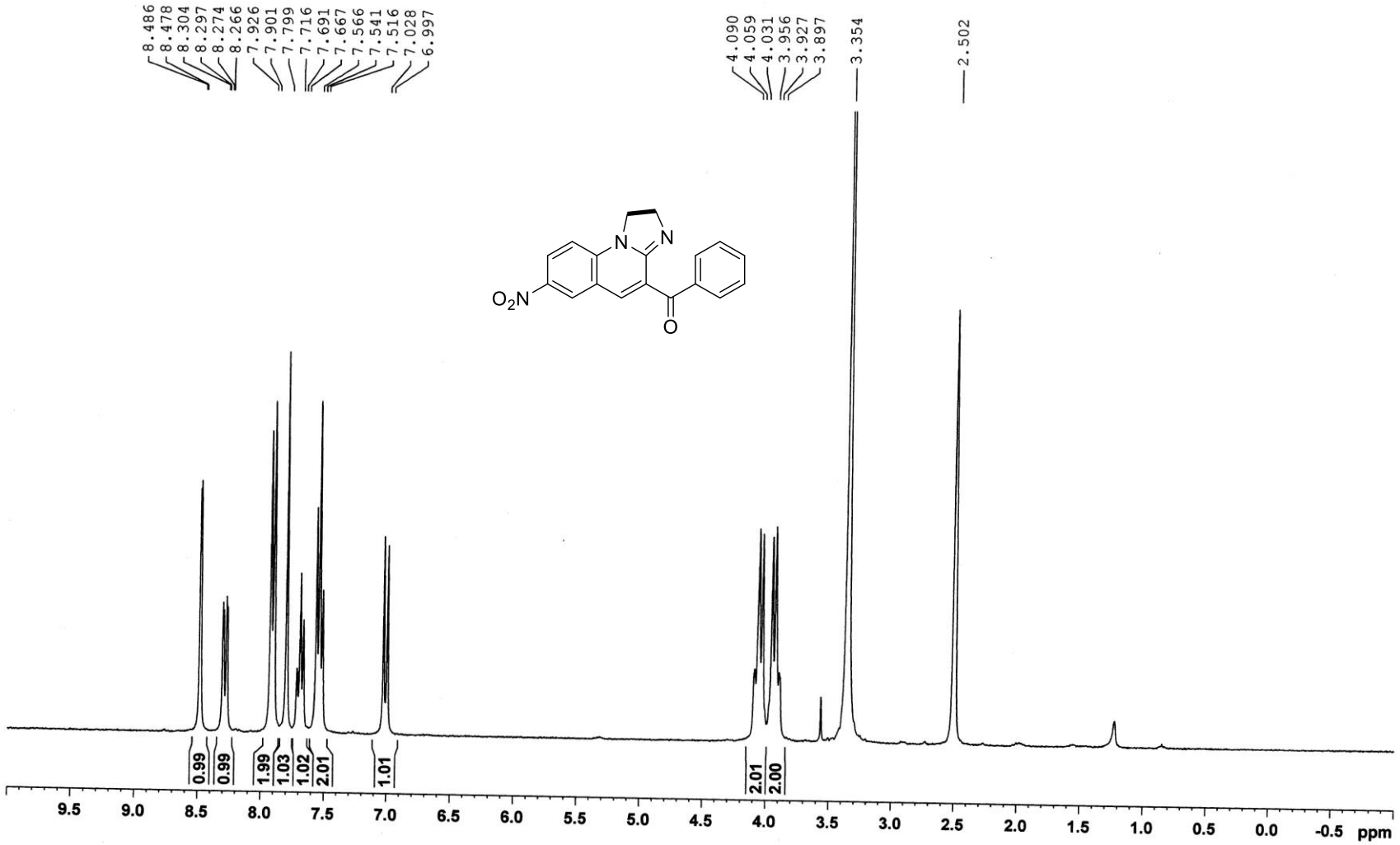


Figure S8. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ad**

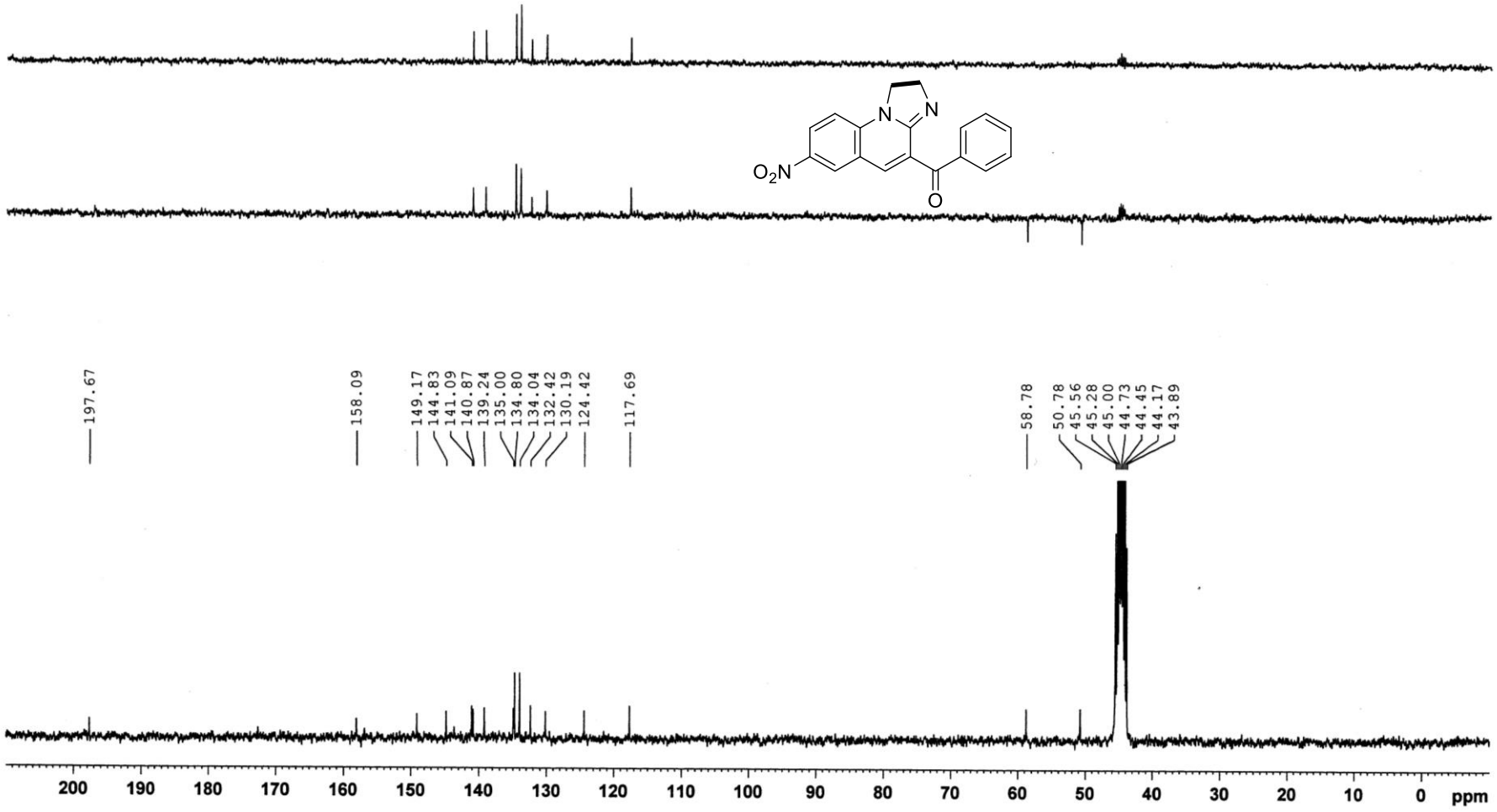


Figure S9. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ad**

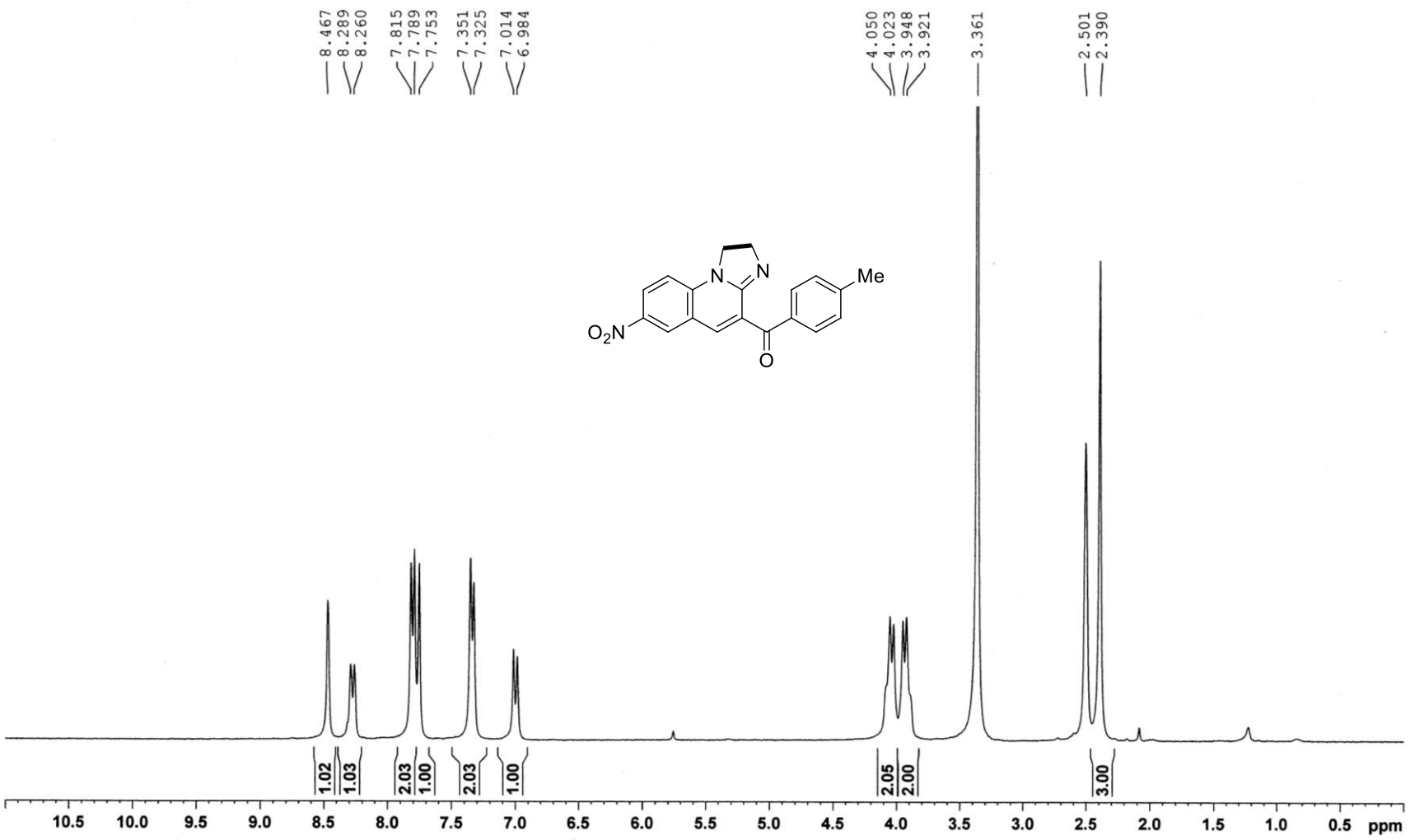


Figure S10. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ae**

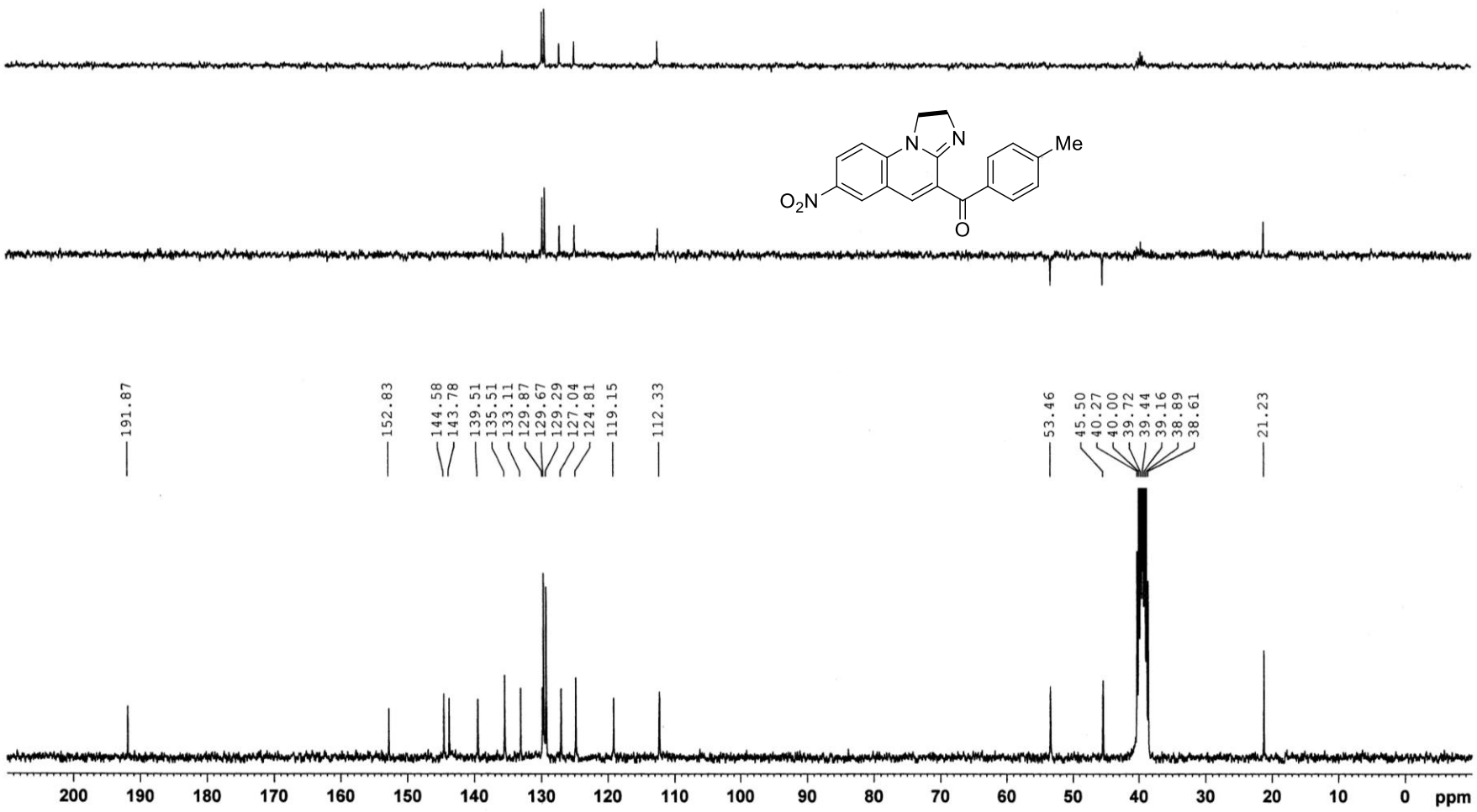


Figure S11. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ae**

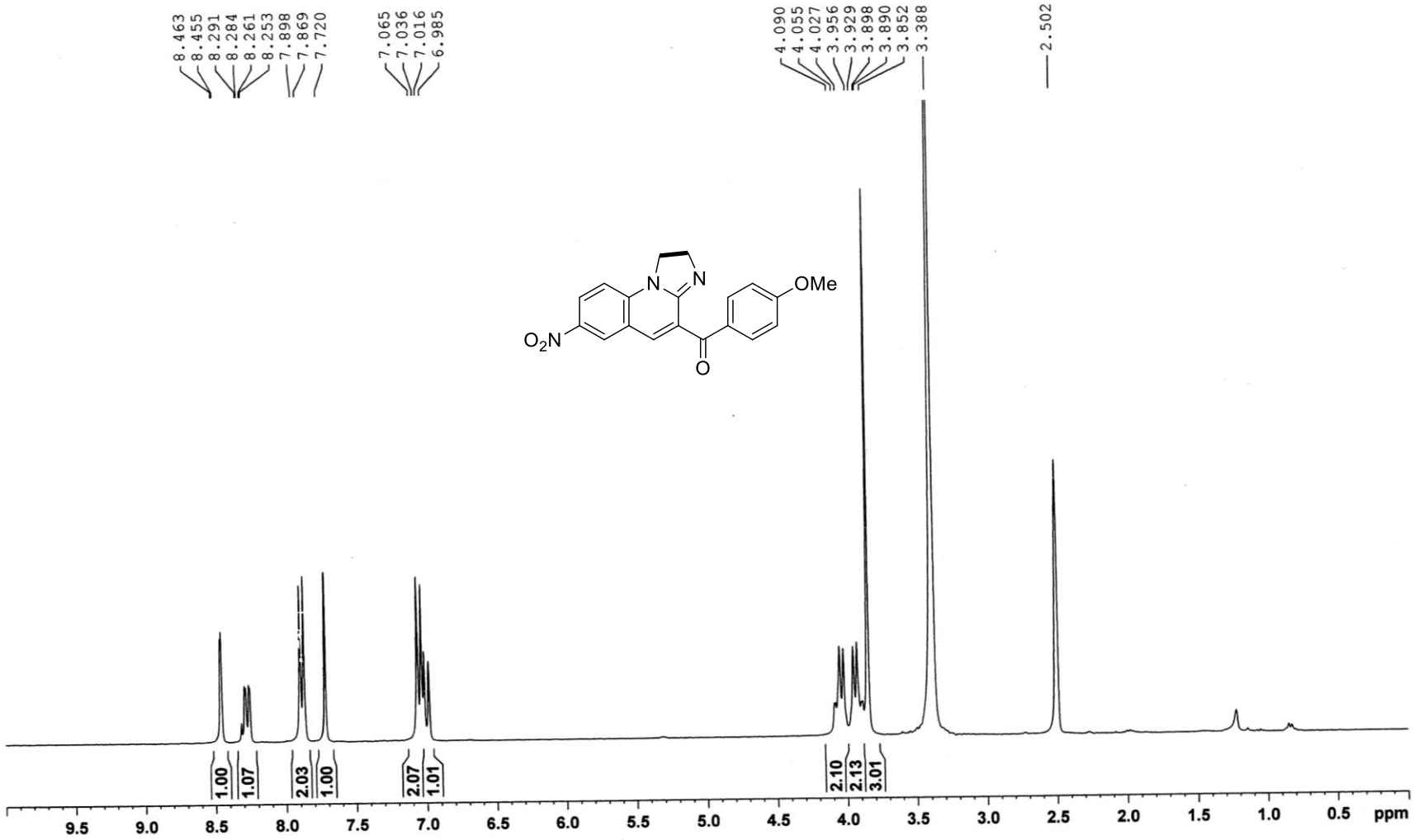


Figure S12. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3af**

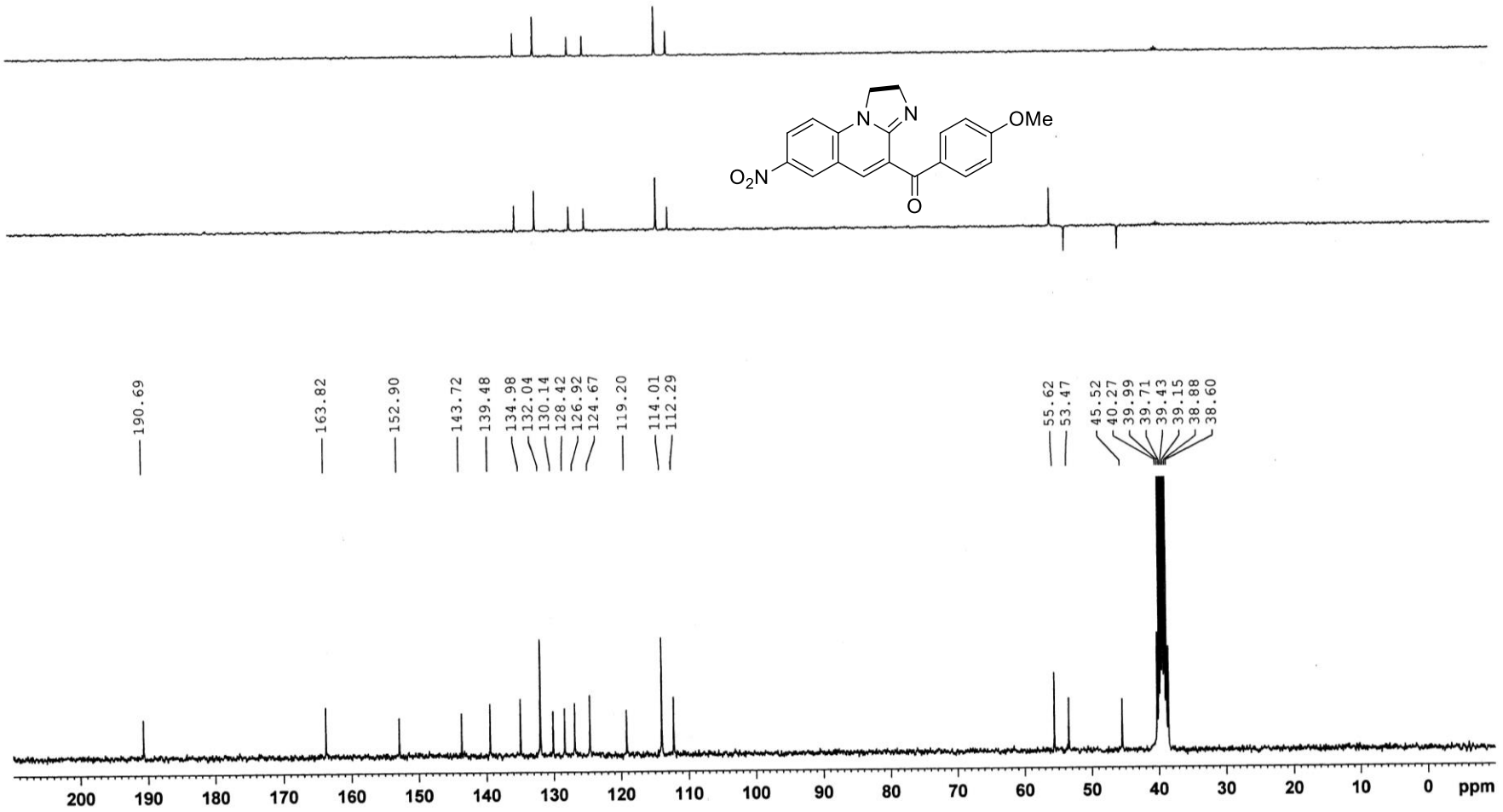


Figure S13. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3af**

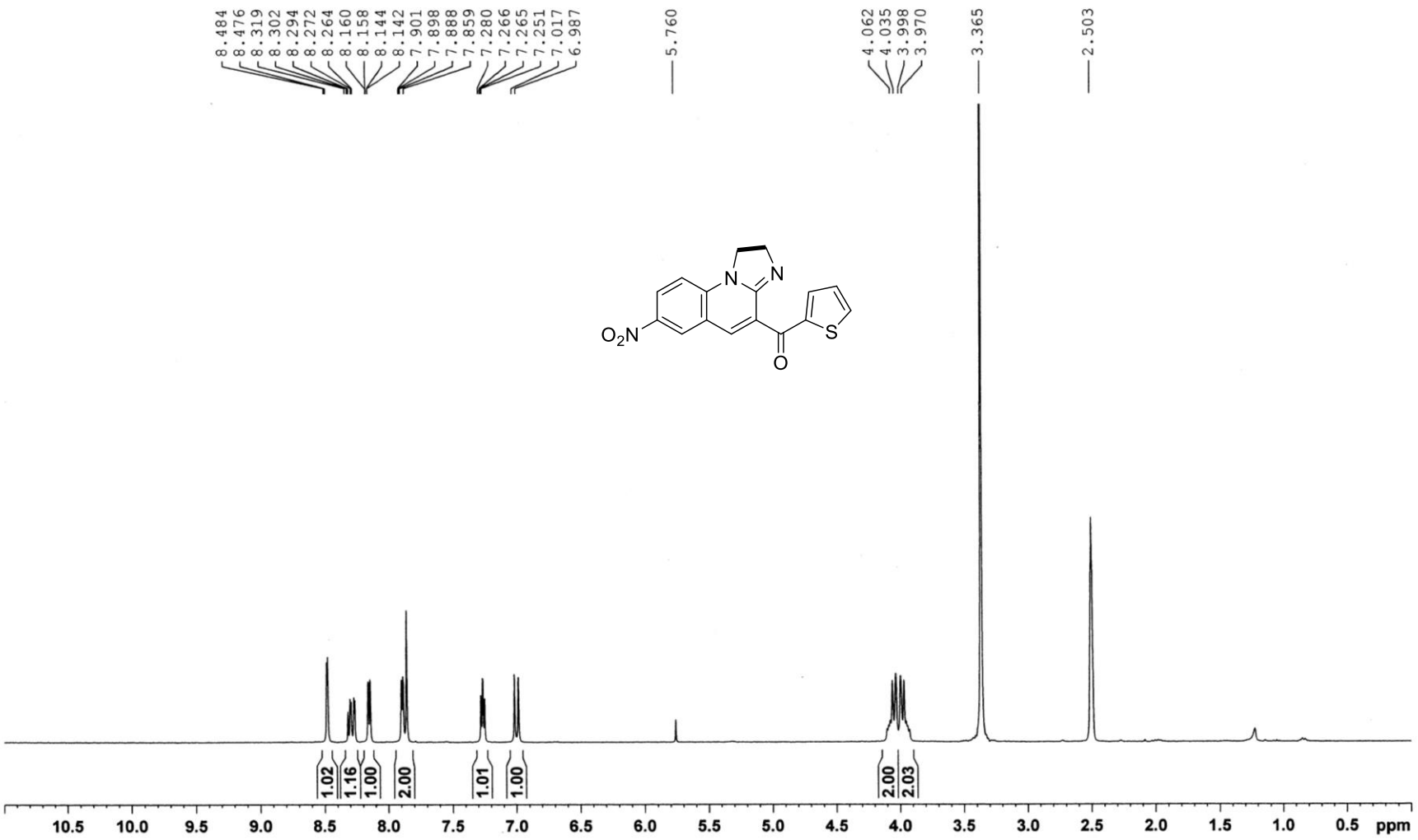


Figure S14. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ag**

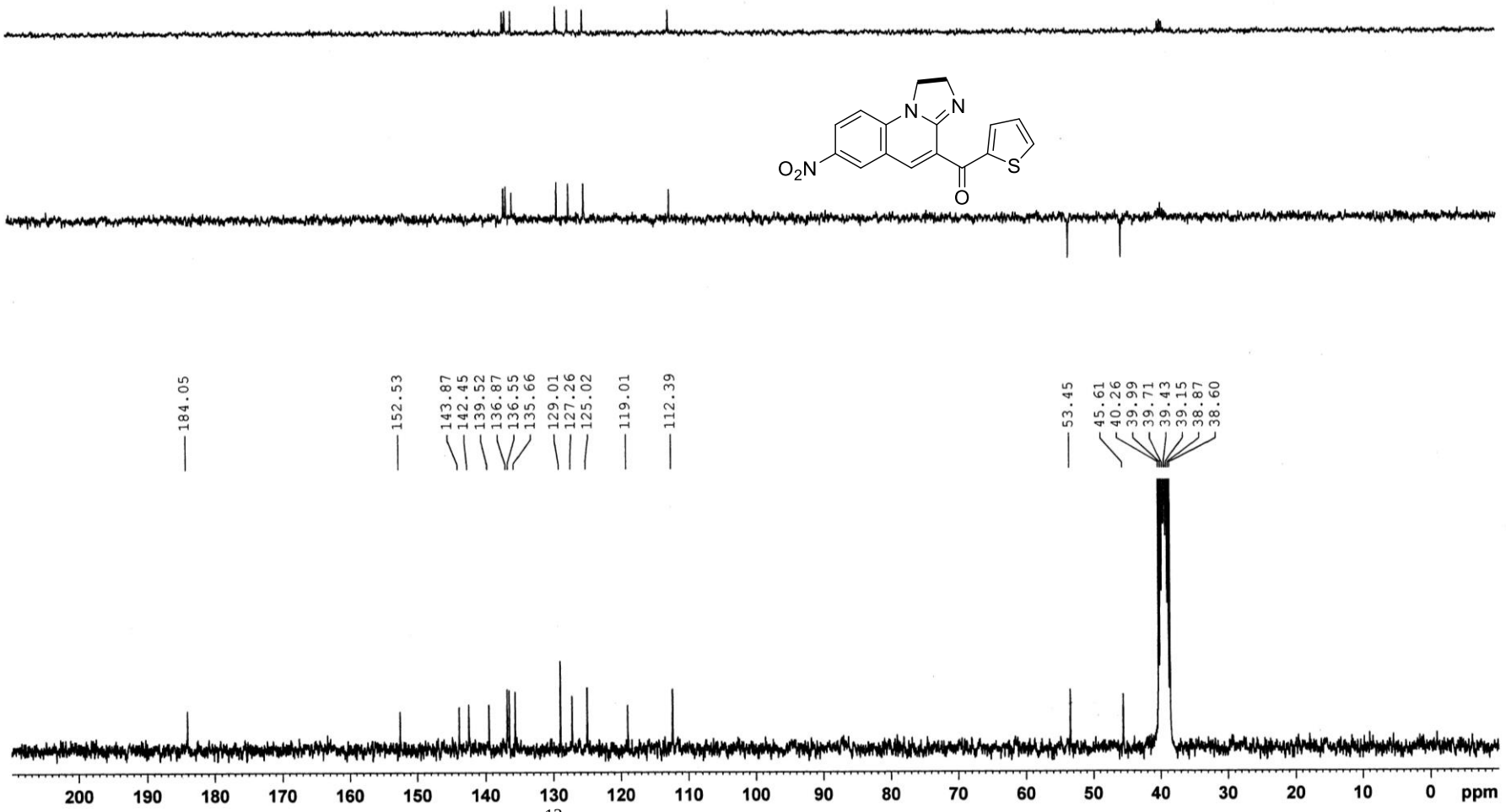


Figure S15. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ag**

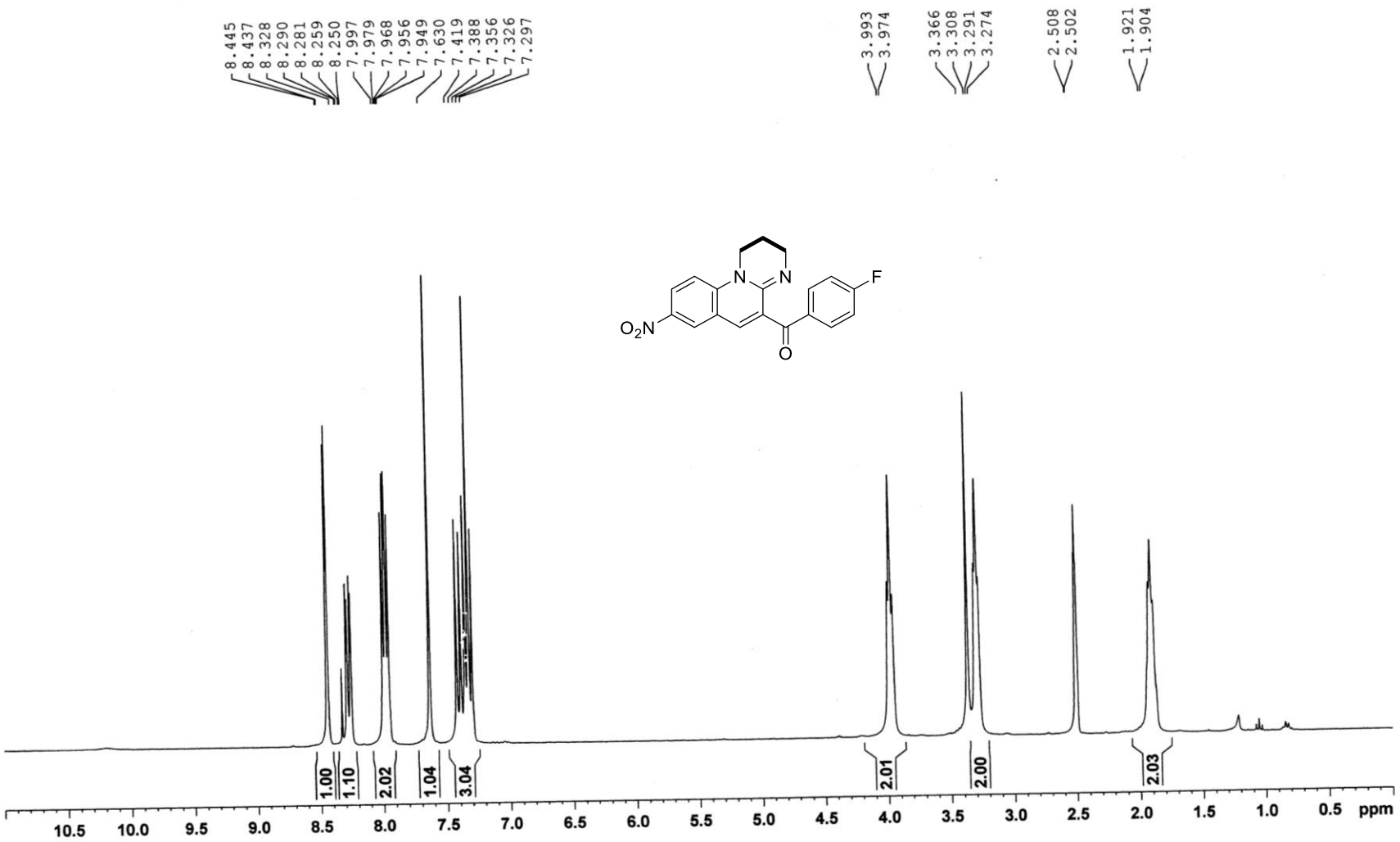


Figure S16. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ah**

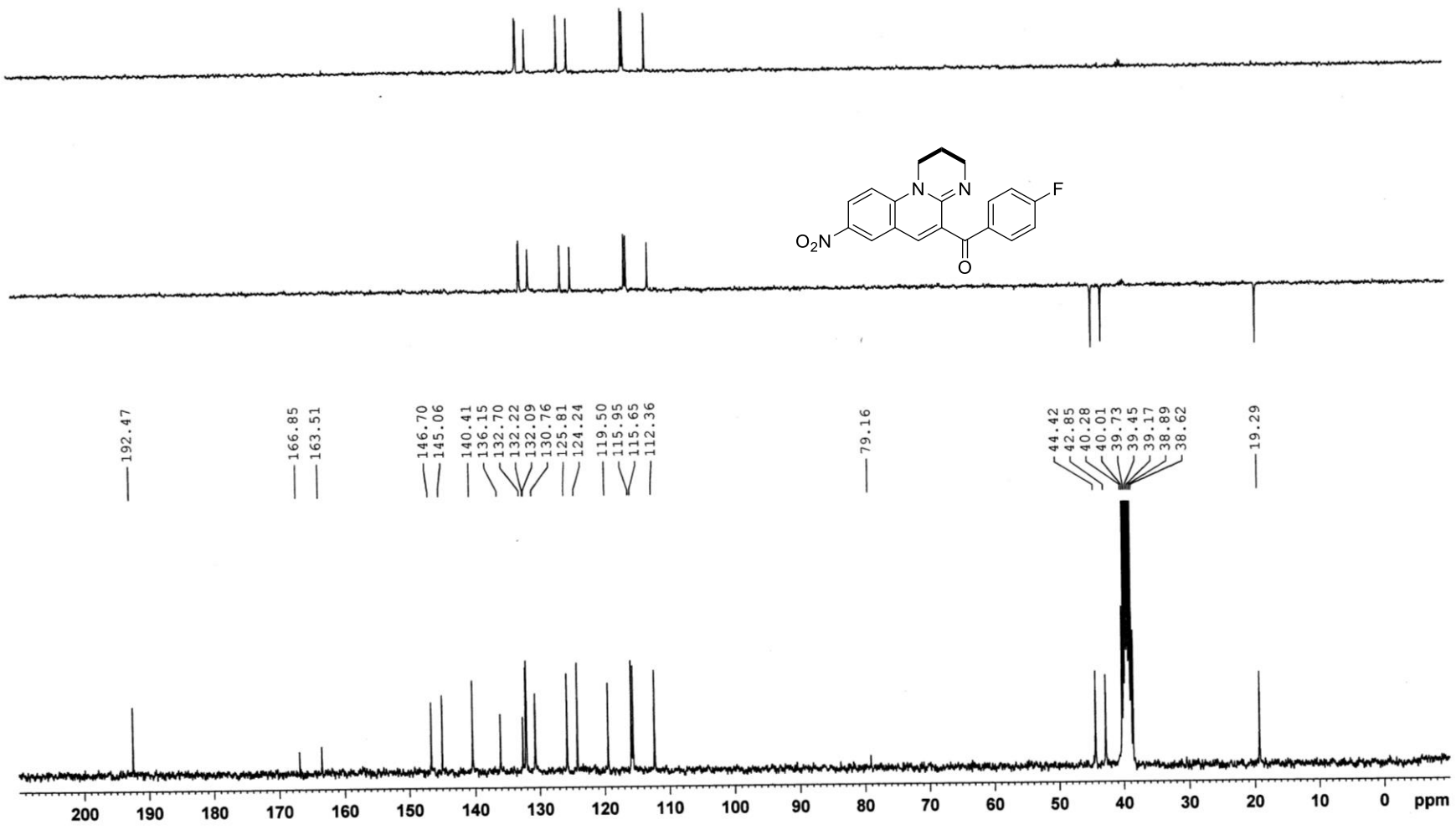


Figure S17. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ah**

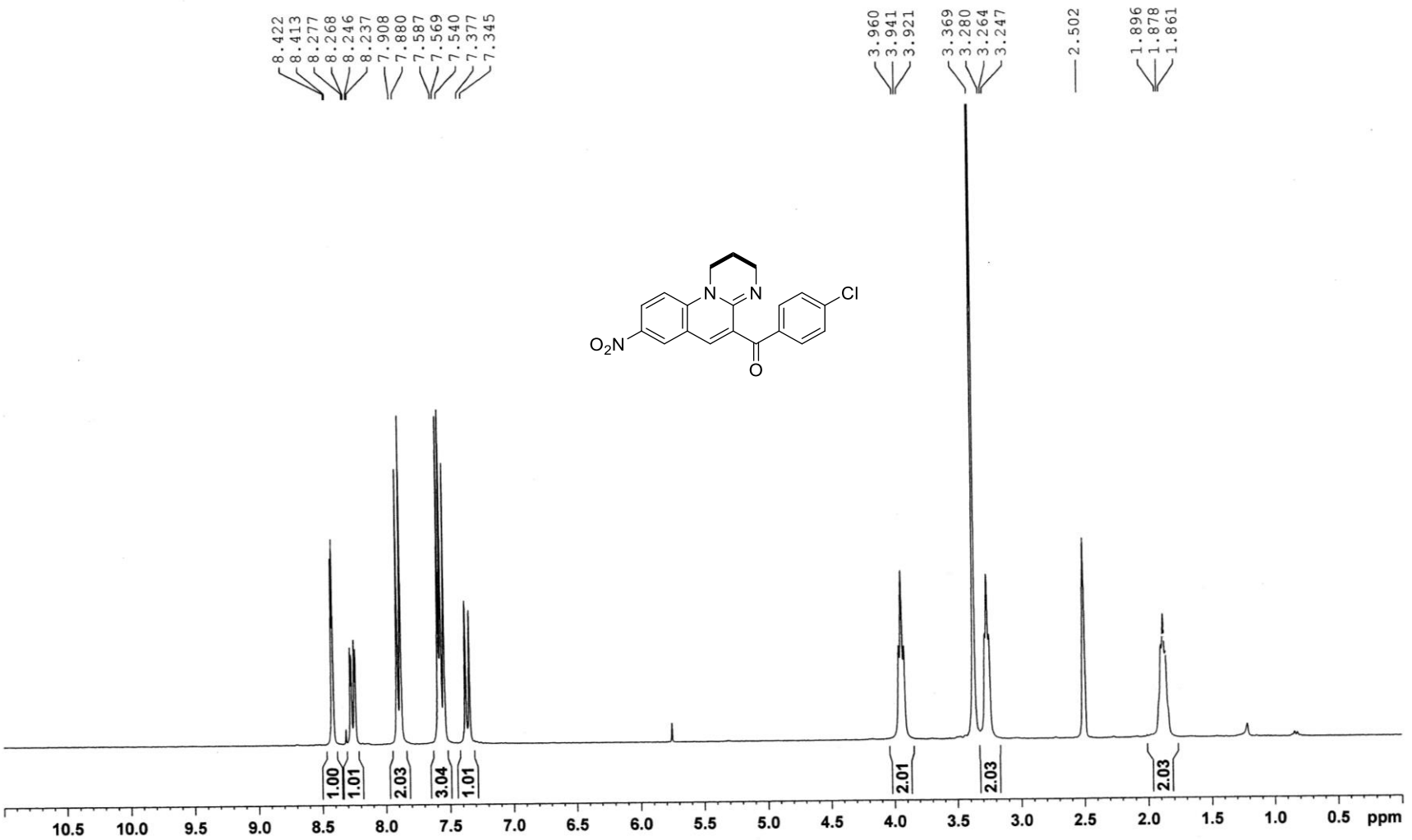


Figure S18. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ai**

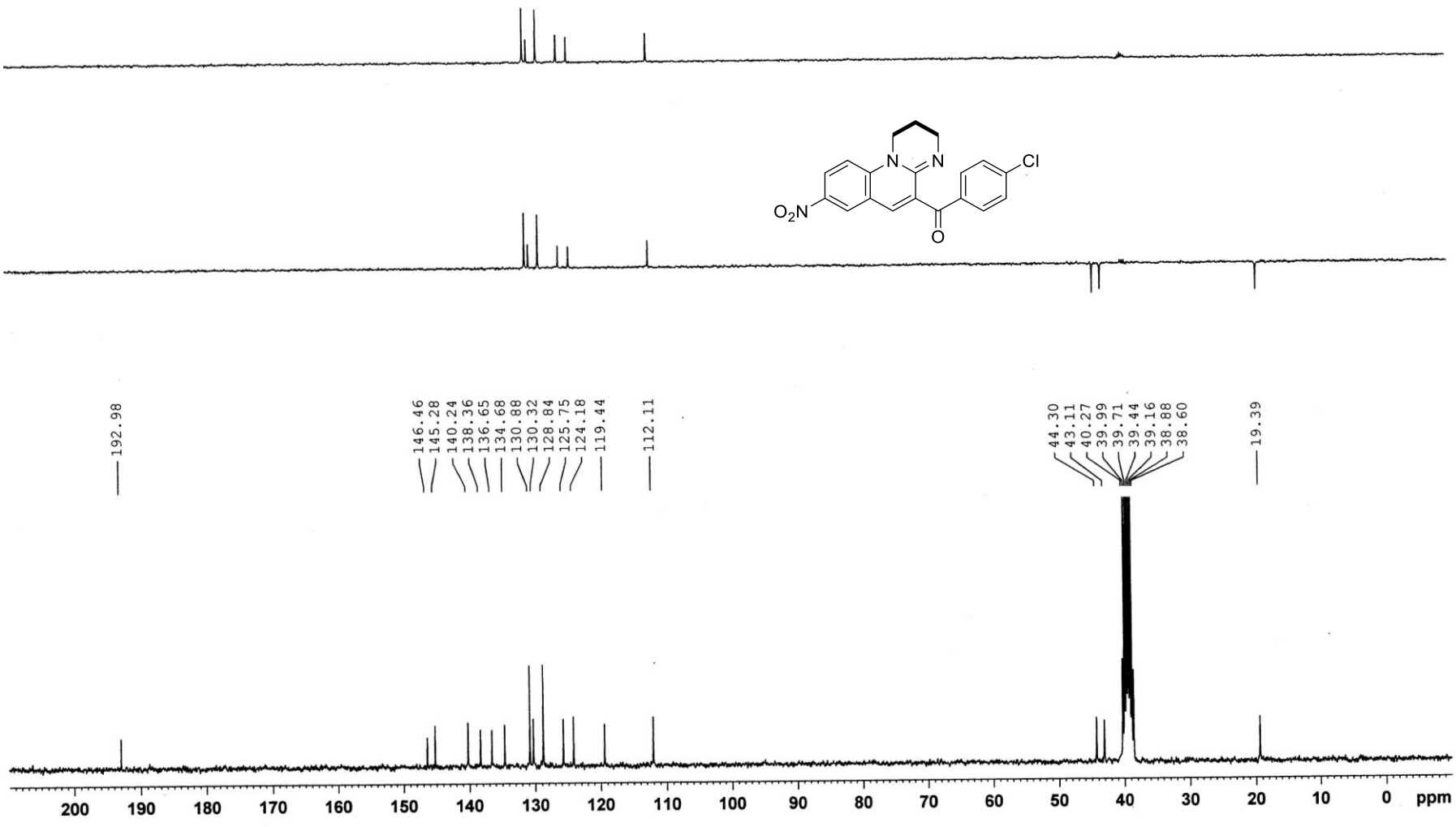


Figure S19. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ai**

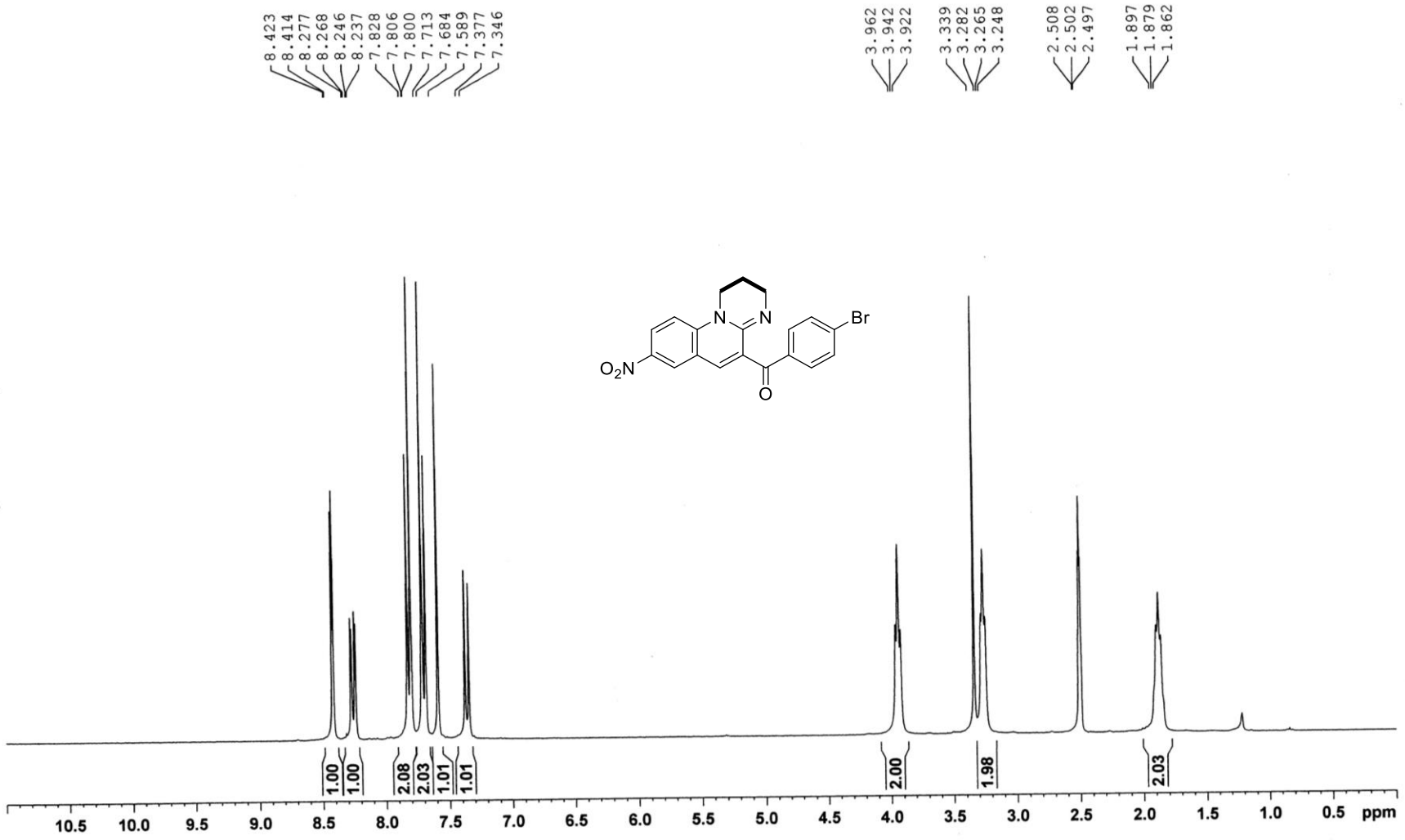


Figure S20. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3aj**

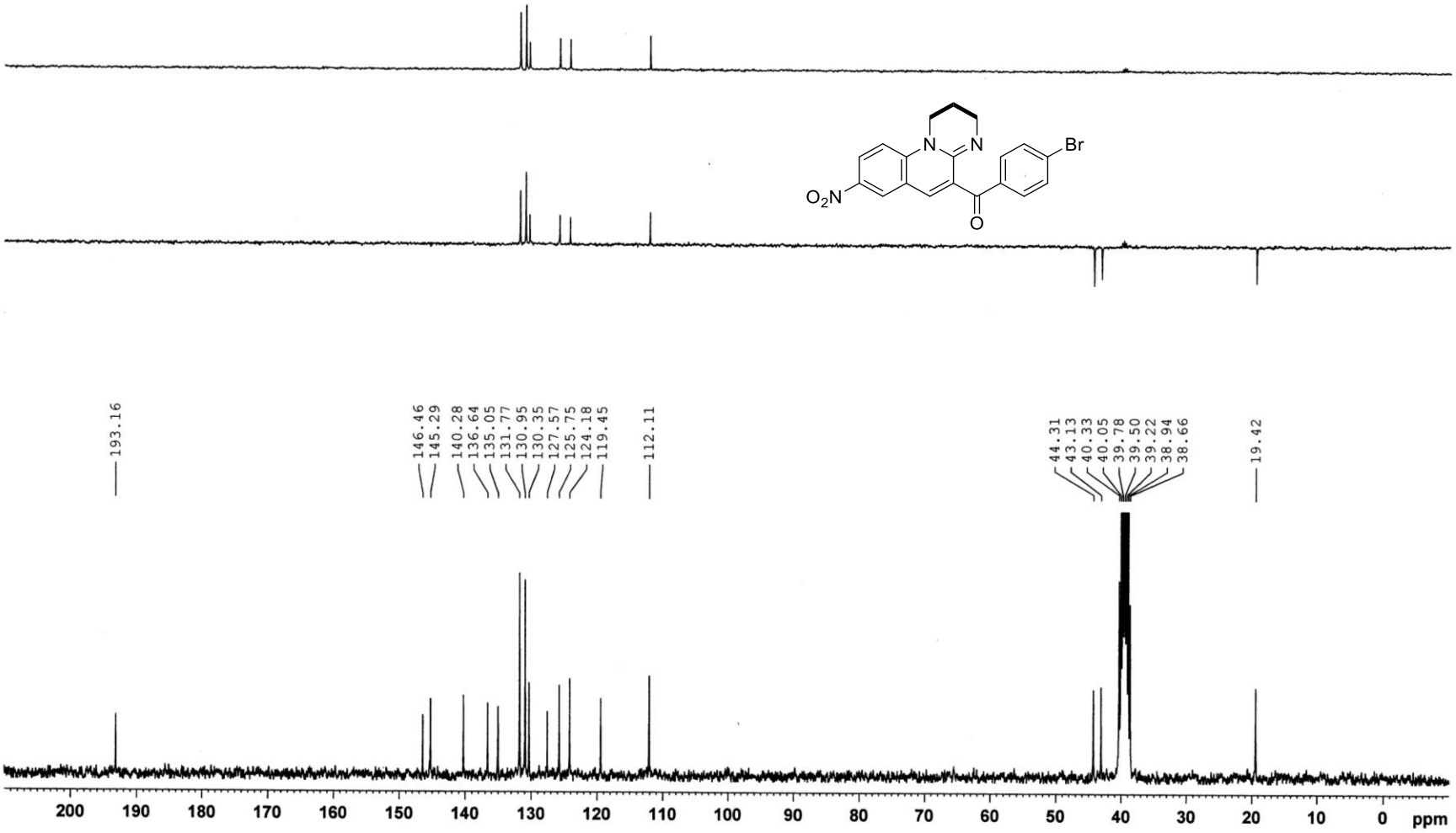


Figure S21. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3aj**

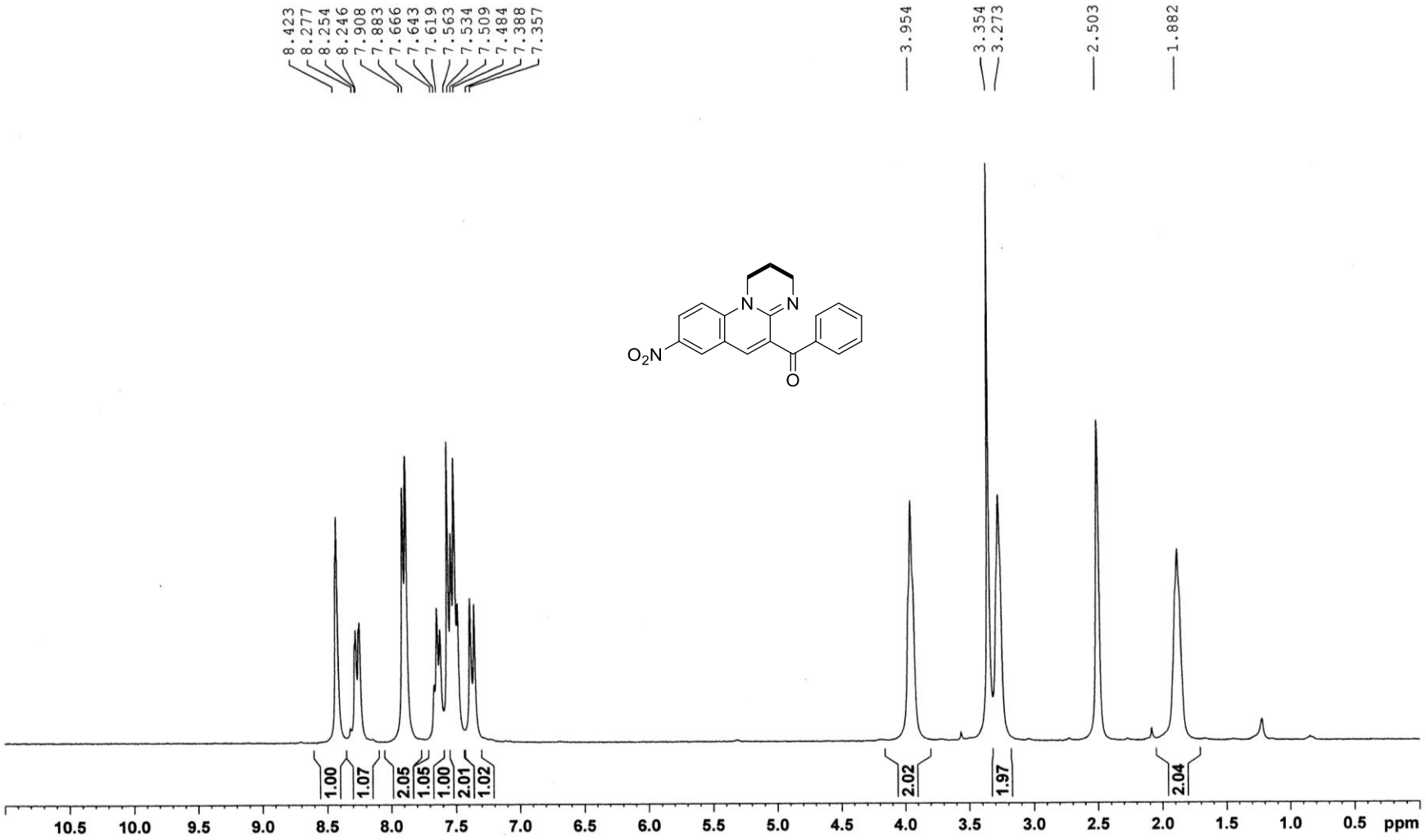


Figure S22. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ak**

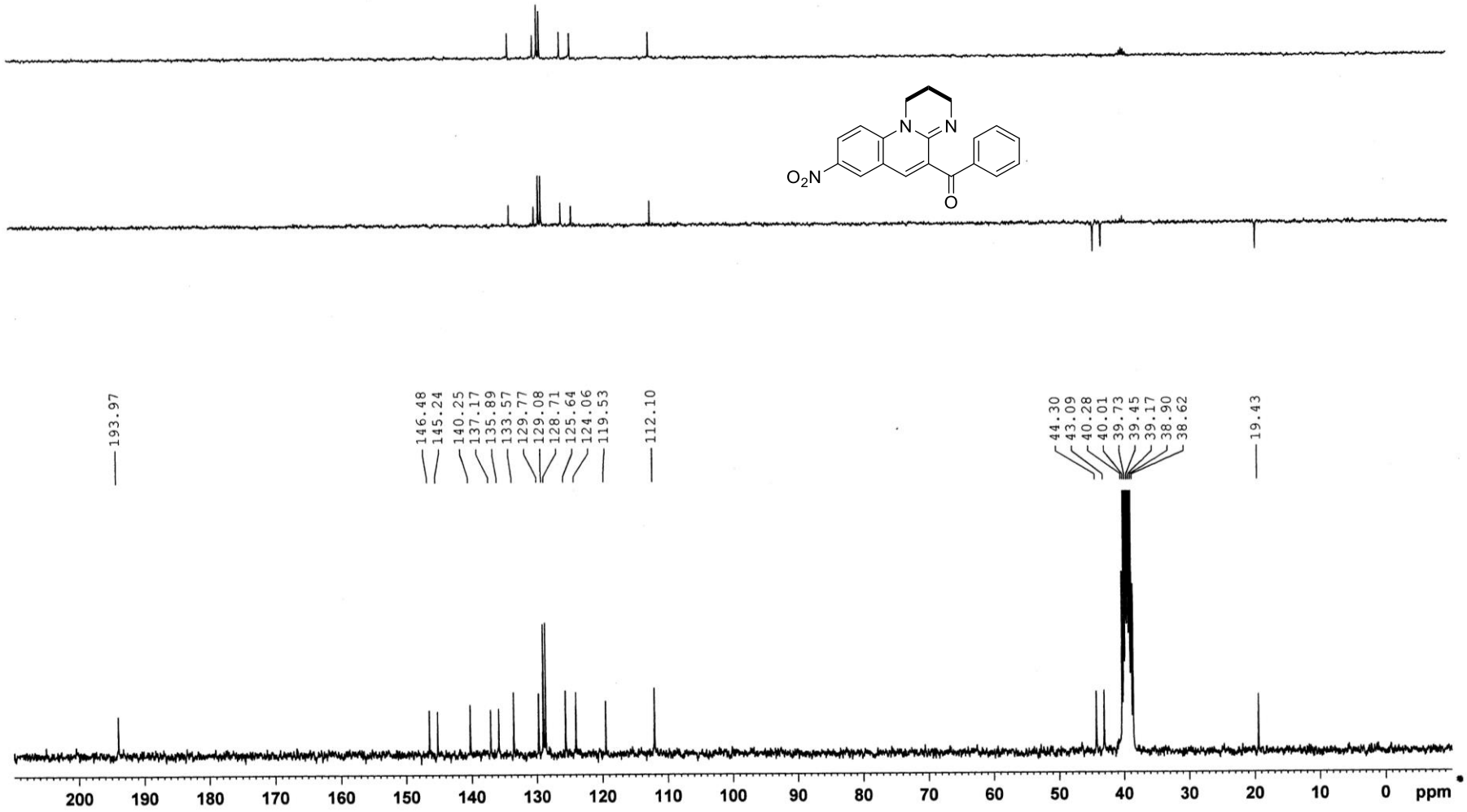


Figure S23. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ak**

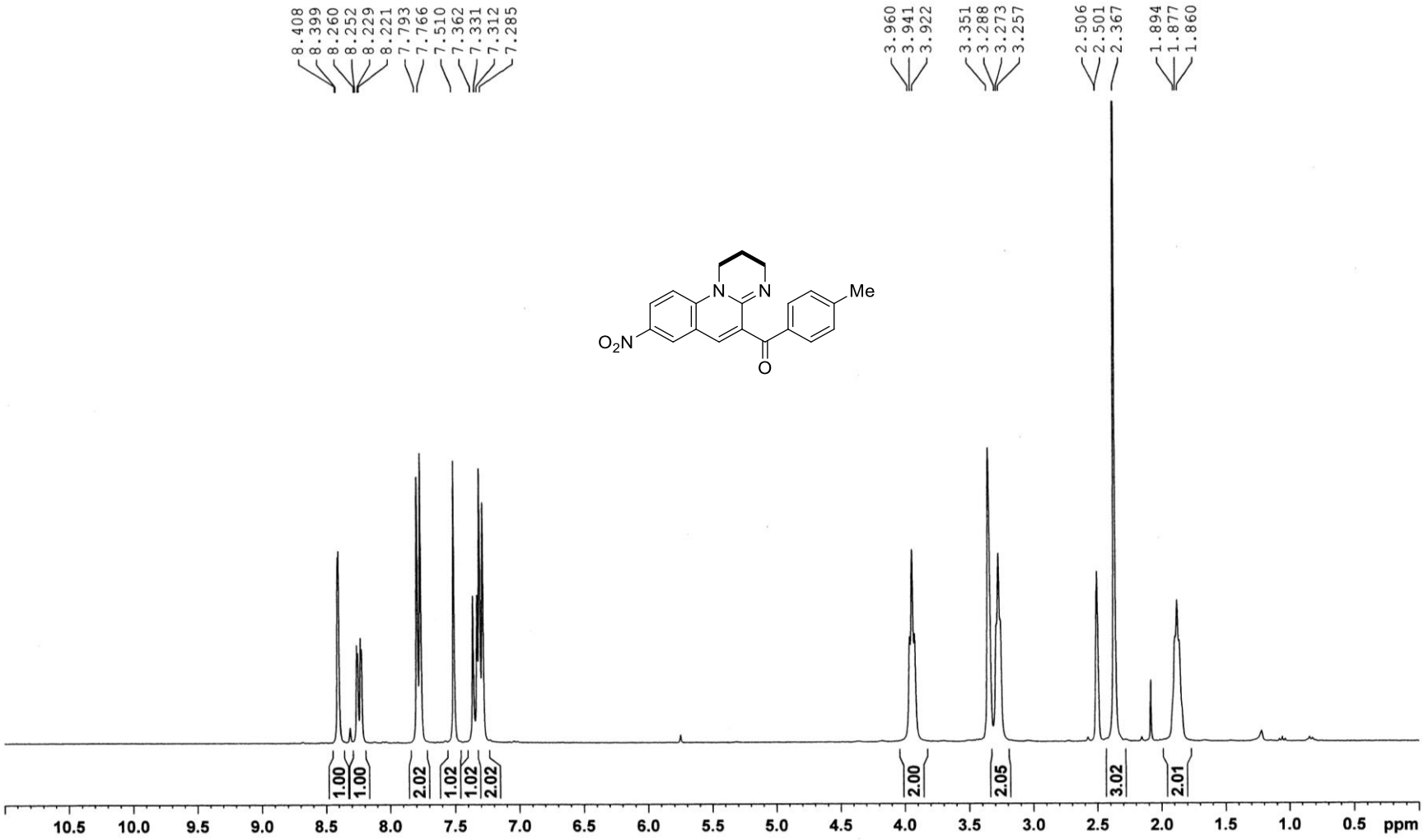


Figure S24. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3al**

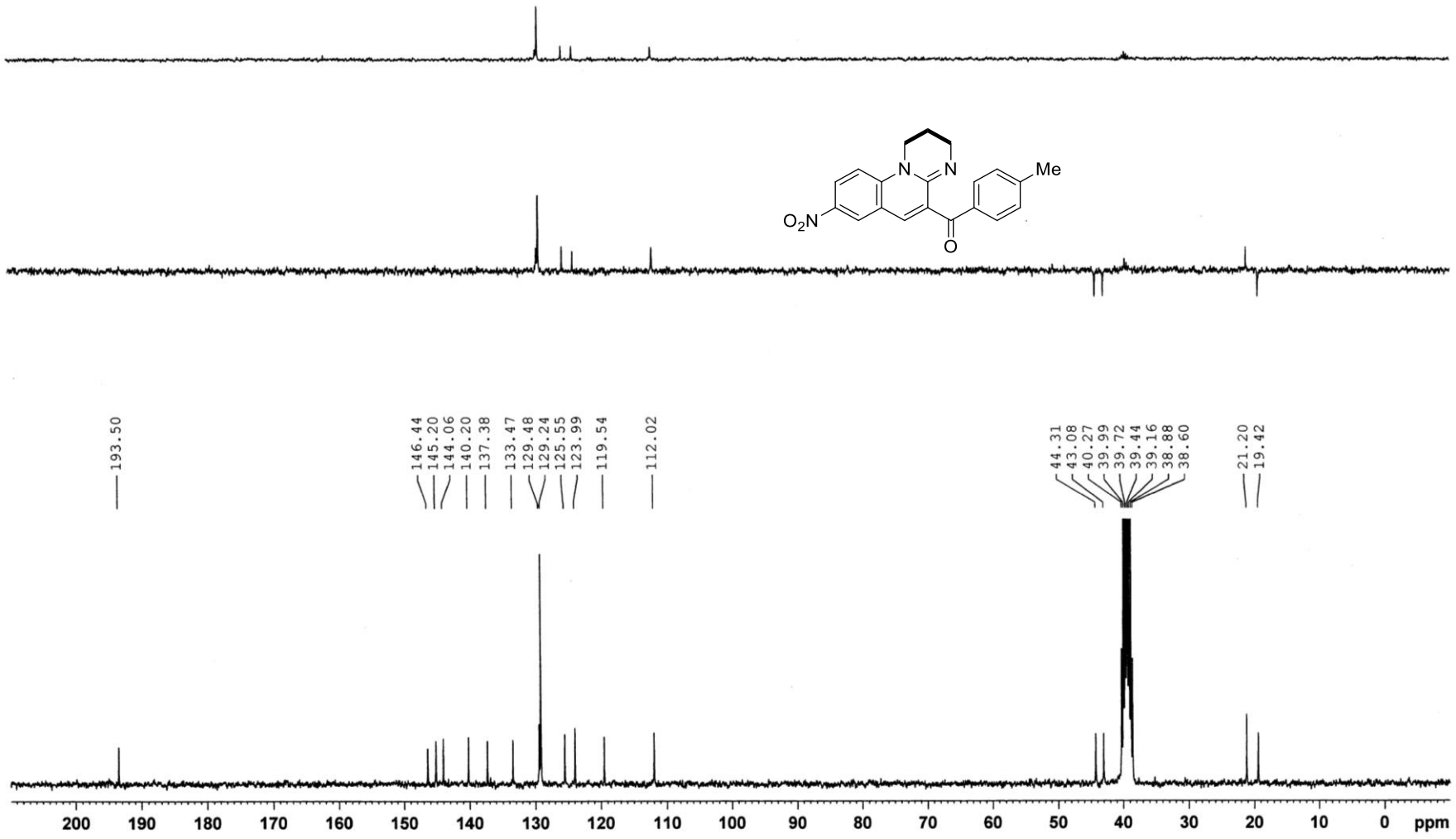


Figure S25. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3al**

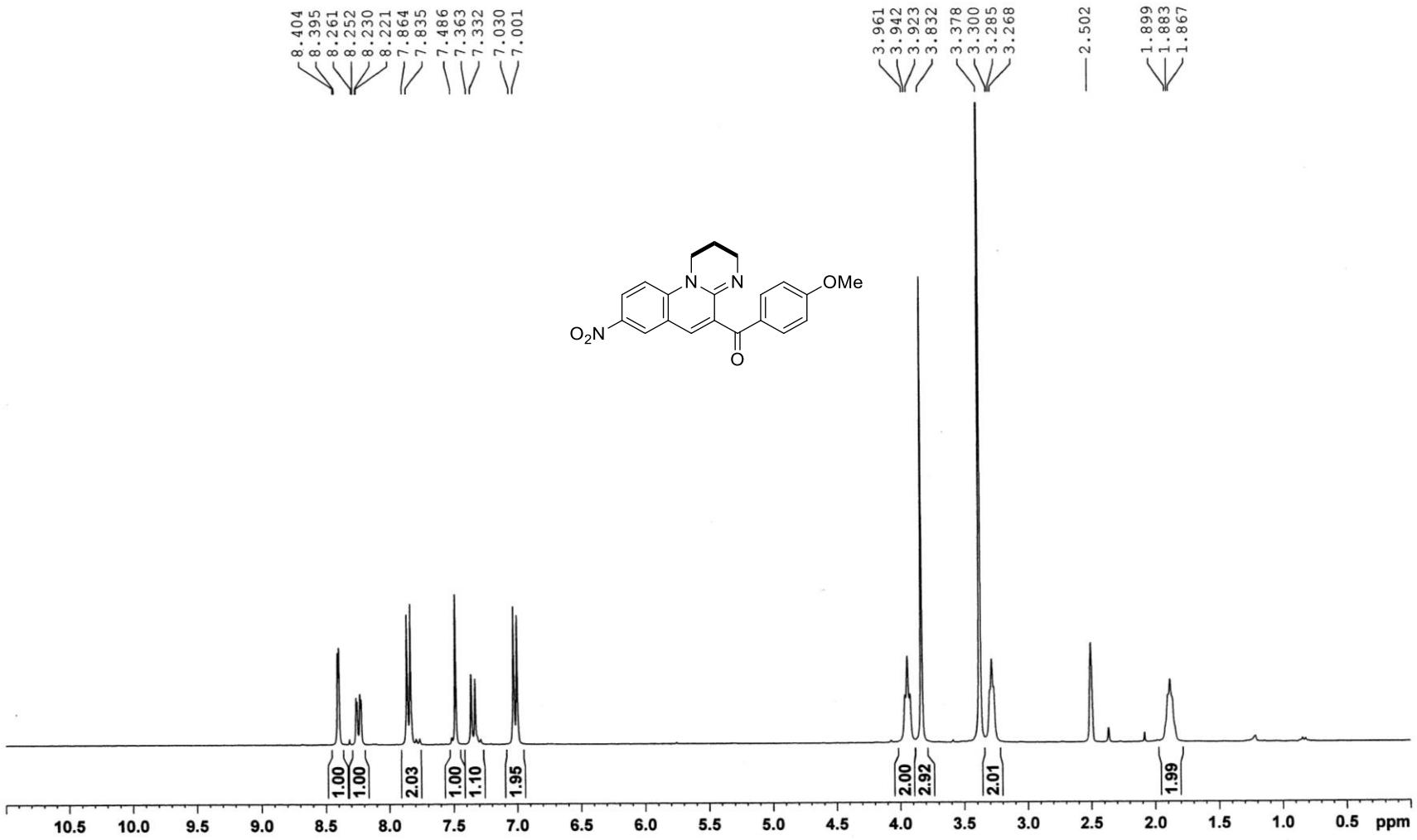


Figure S26. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3am**

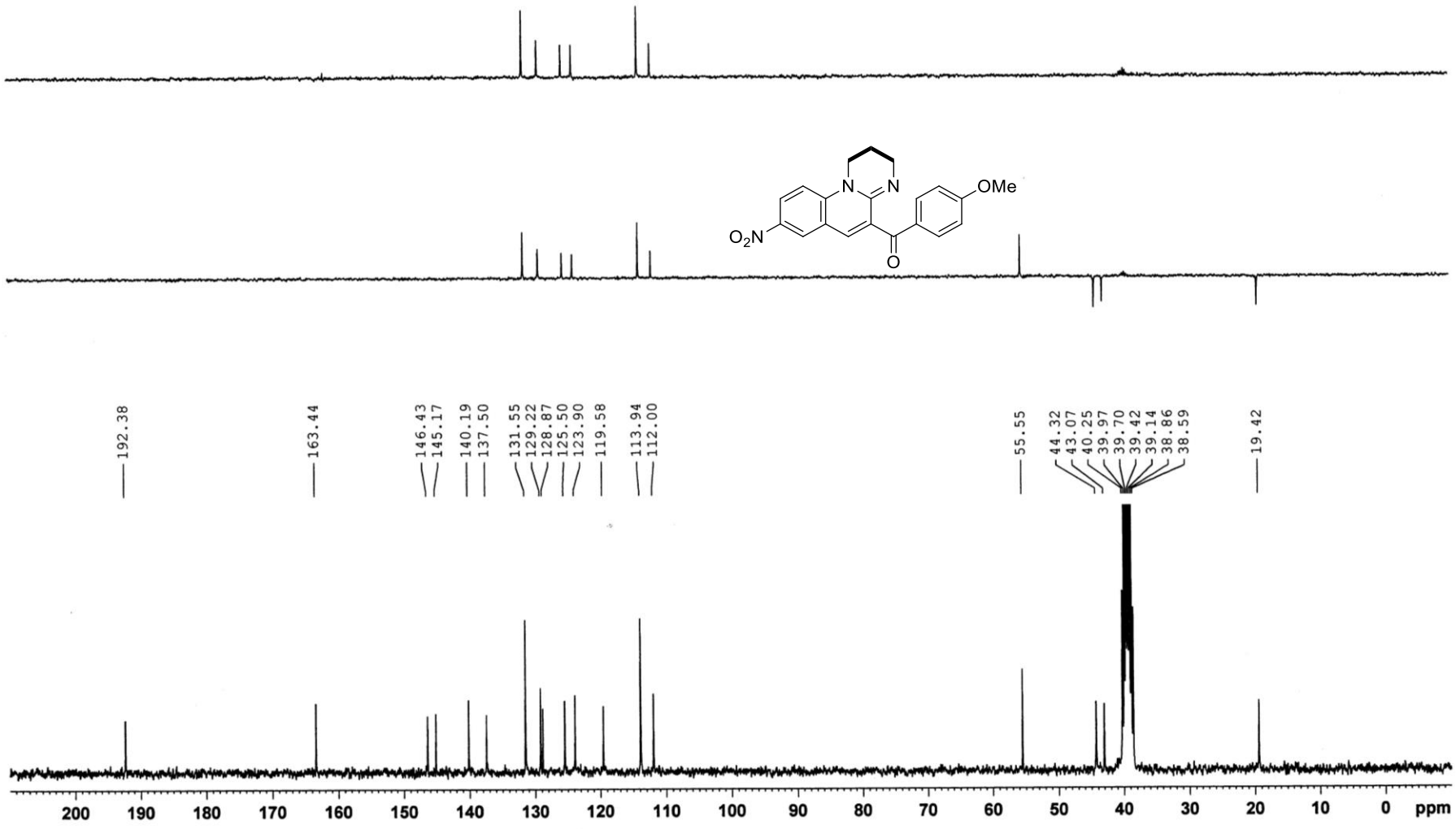


Figure S27. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3am**

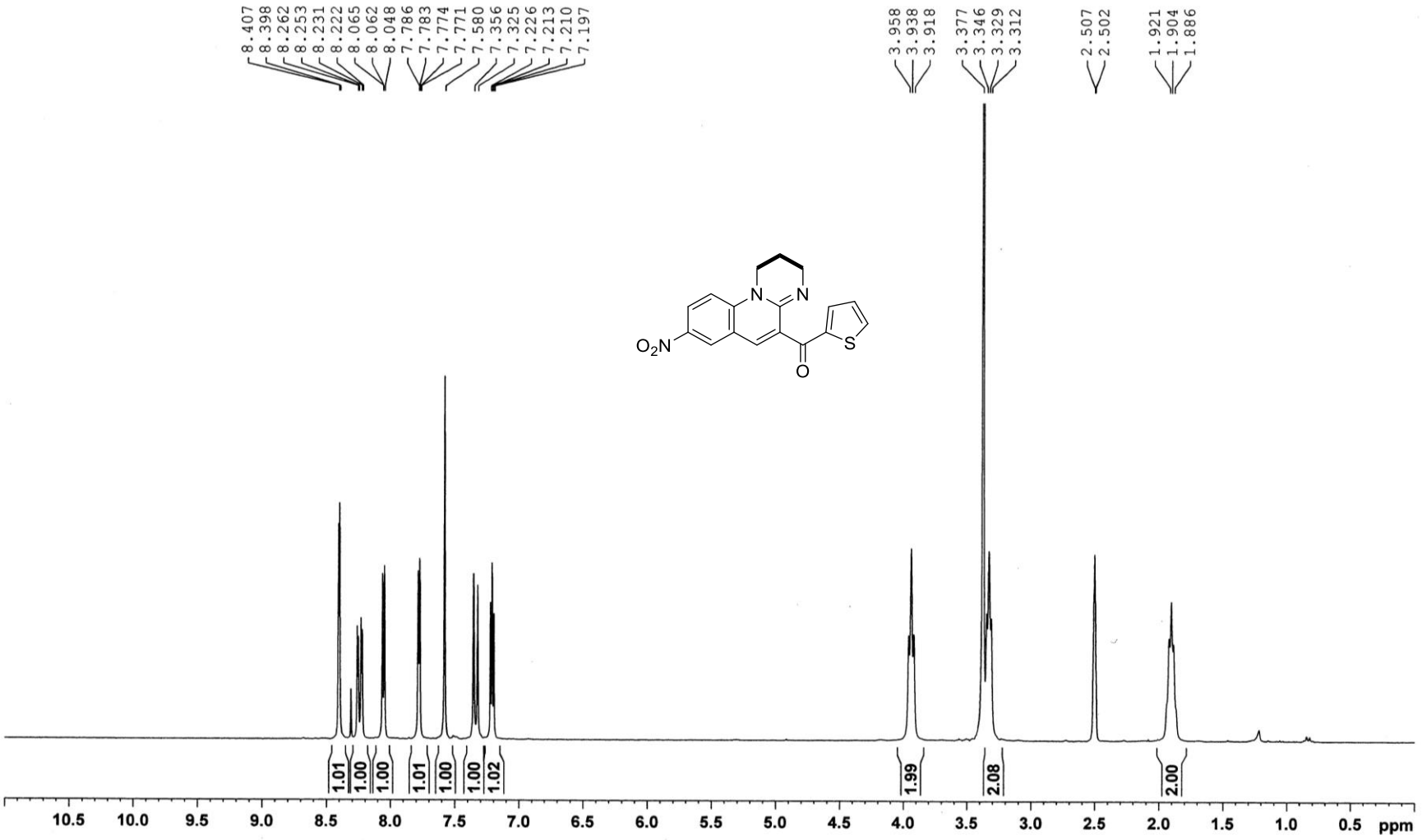


Figure S28. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3an**

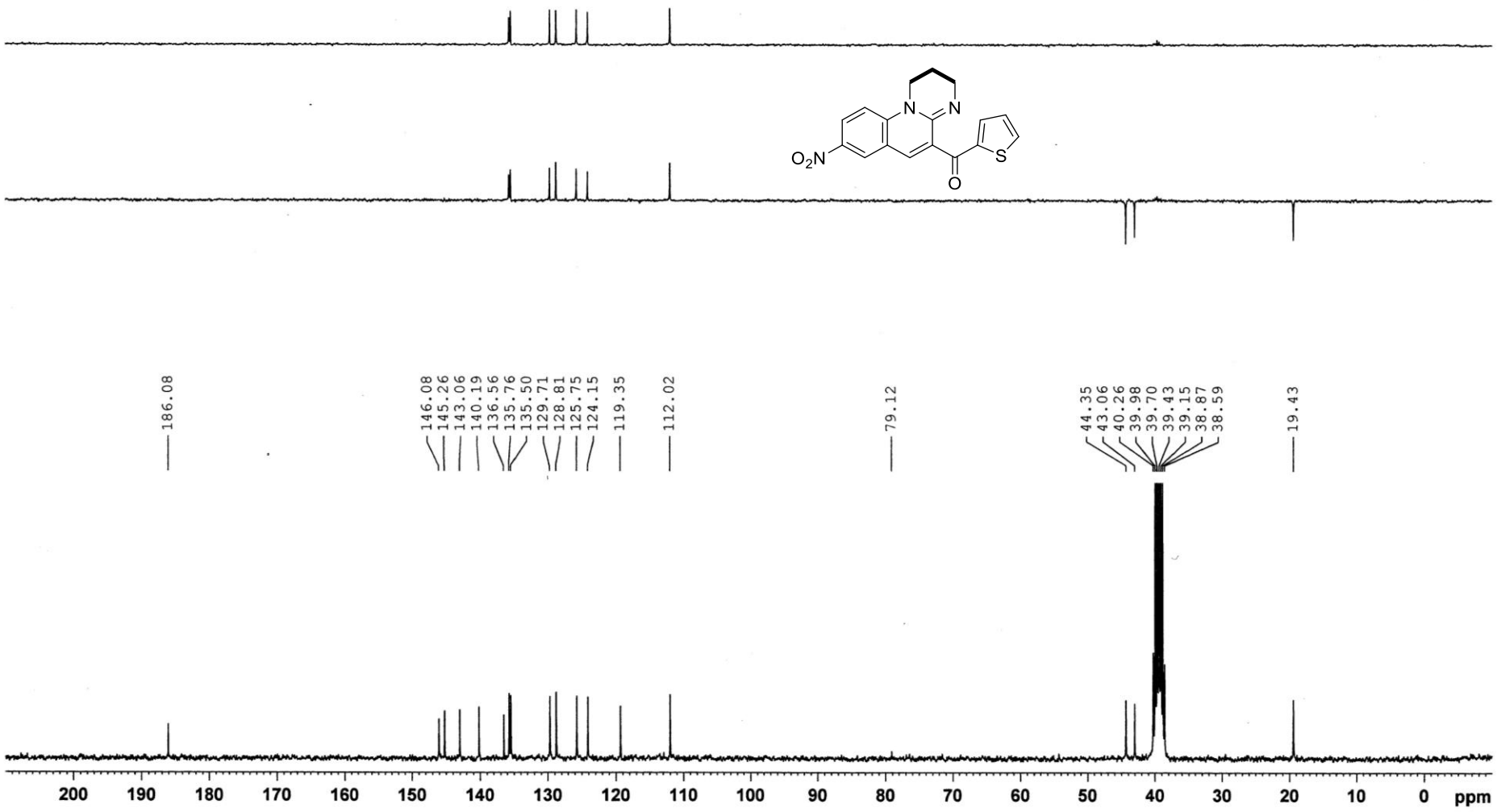


Figure S29. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3an**

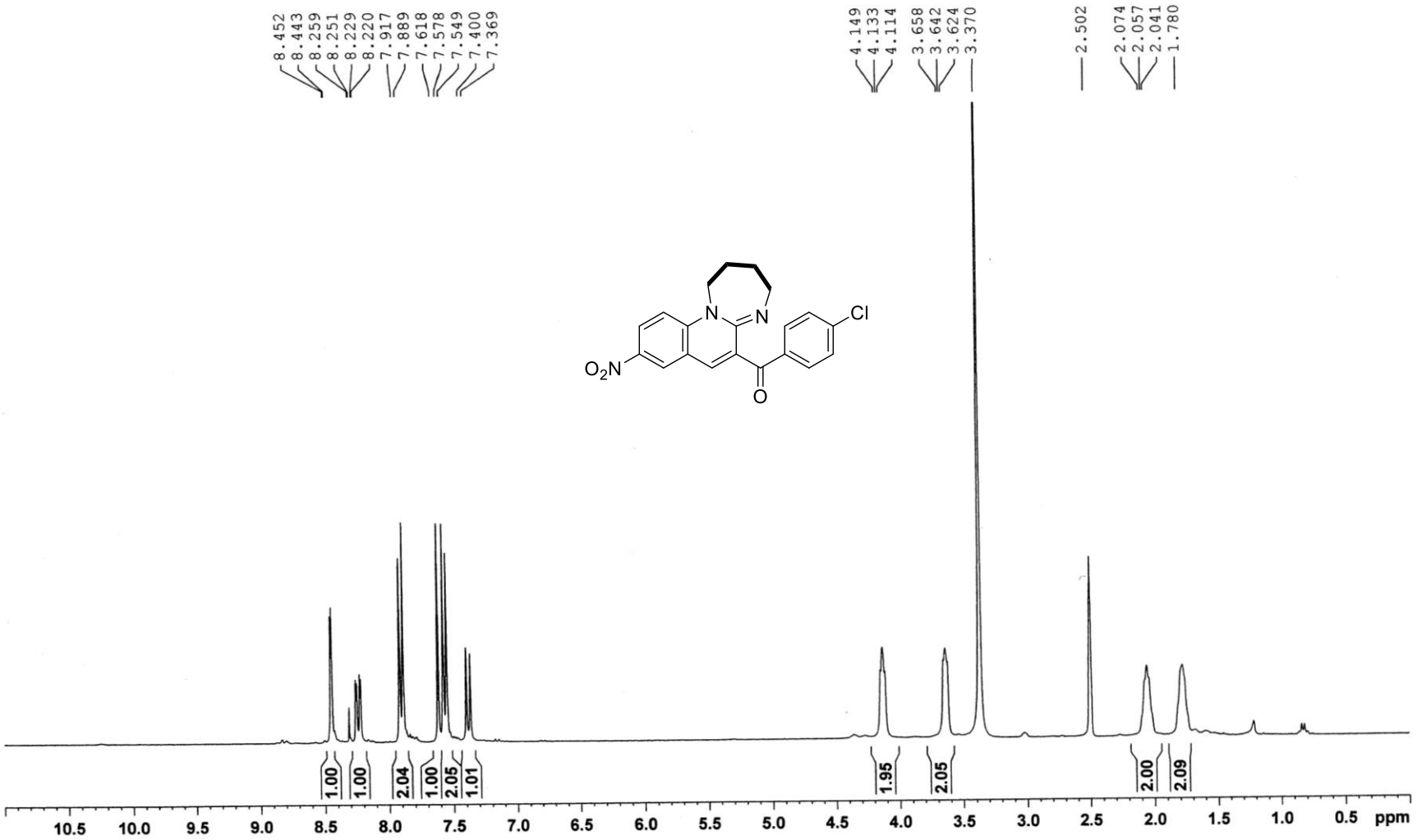


Figure S30. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ao**

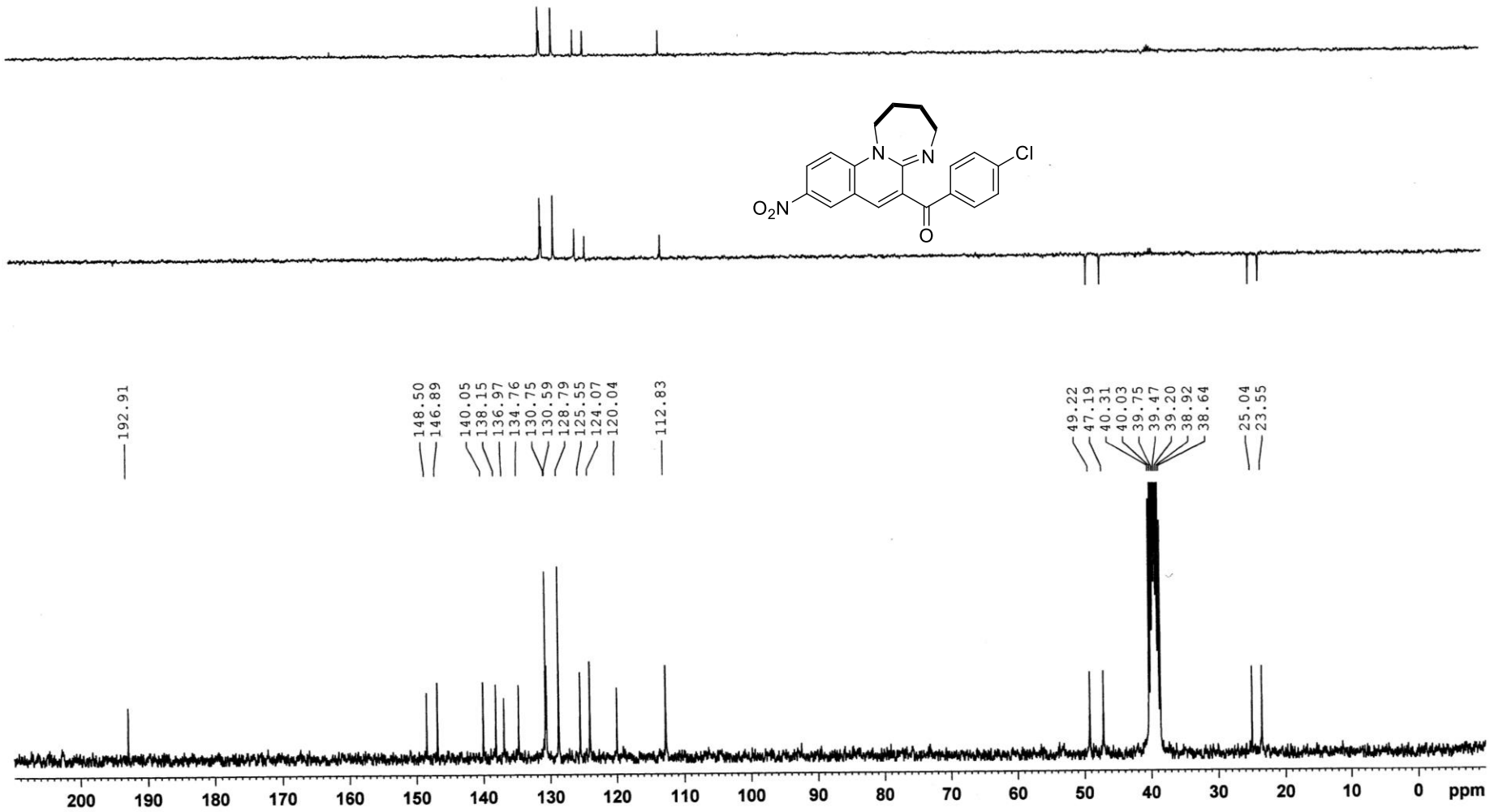


Figure S31. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ao**

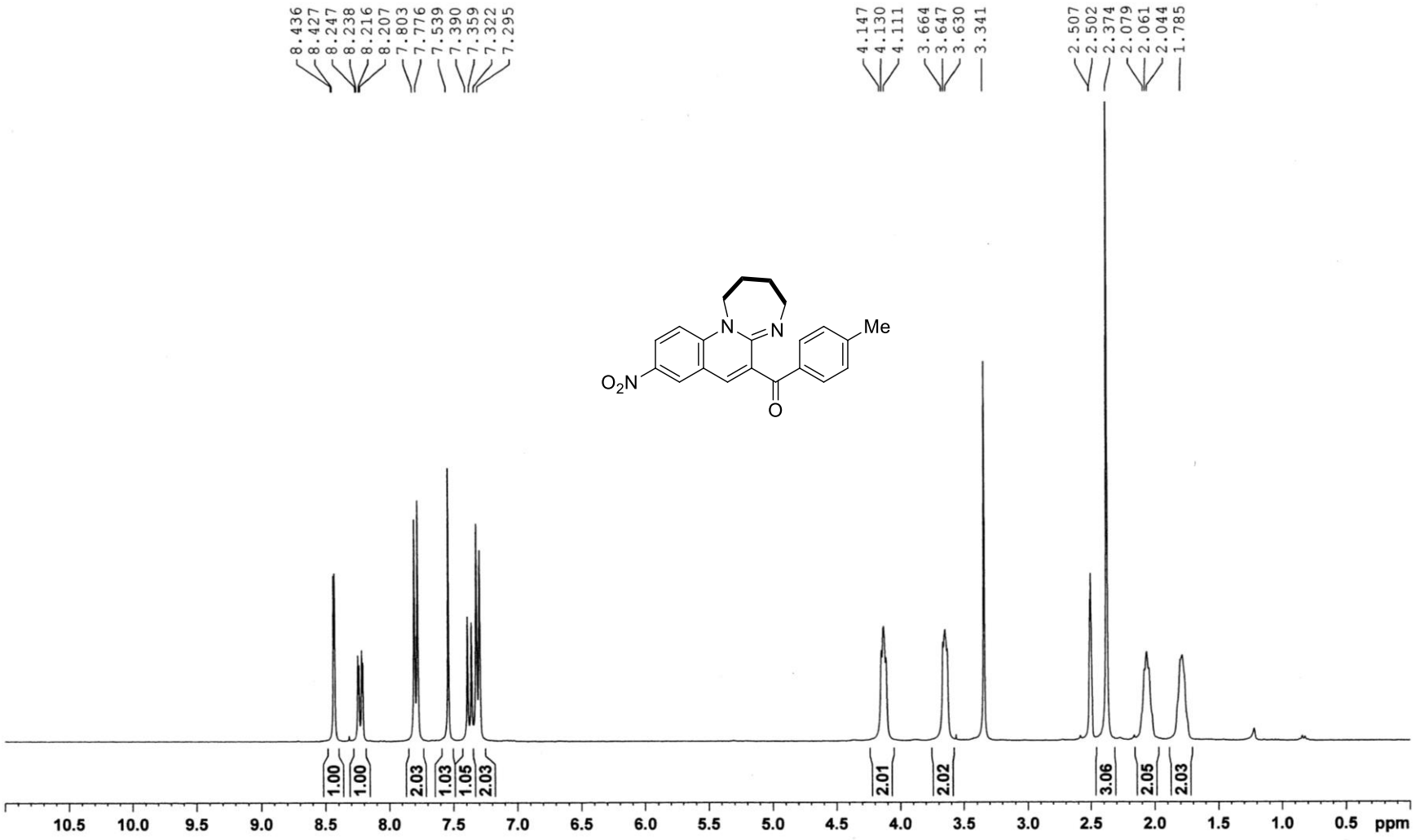


Figure S32. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ap**

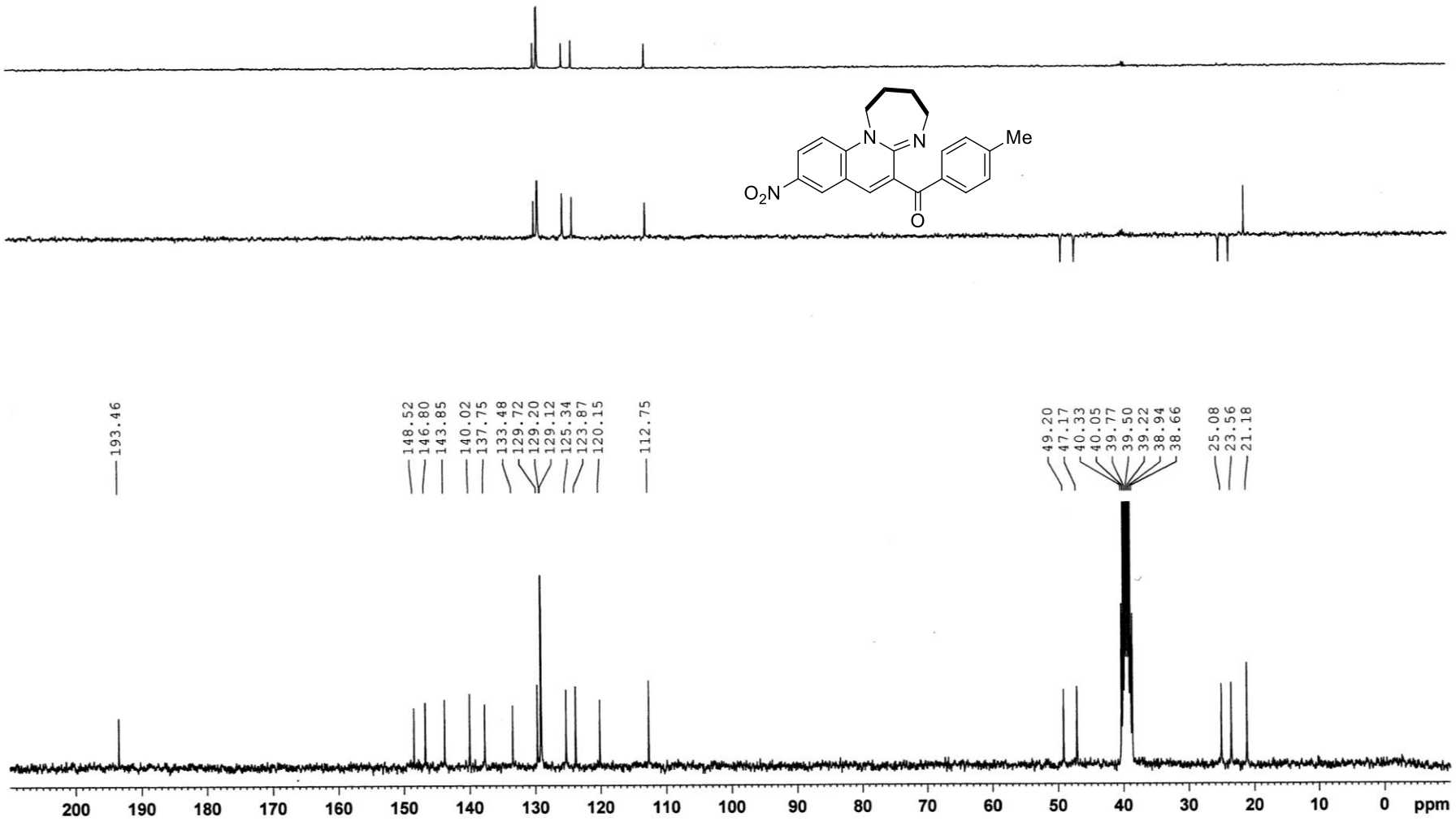


Figure S33. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ap**

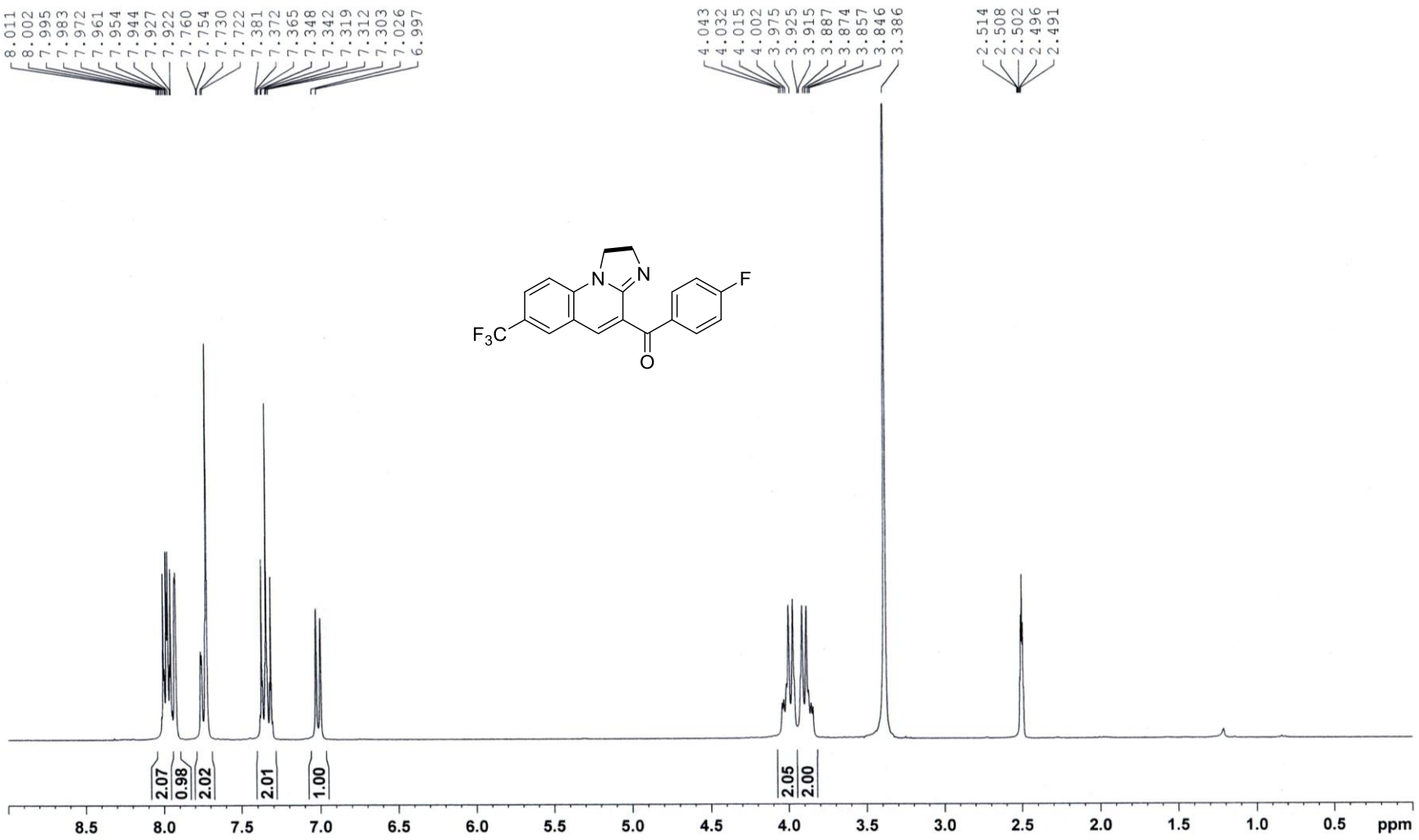


Figure S34. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3ba**

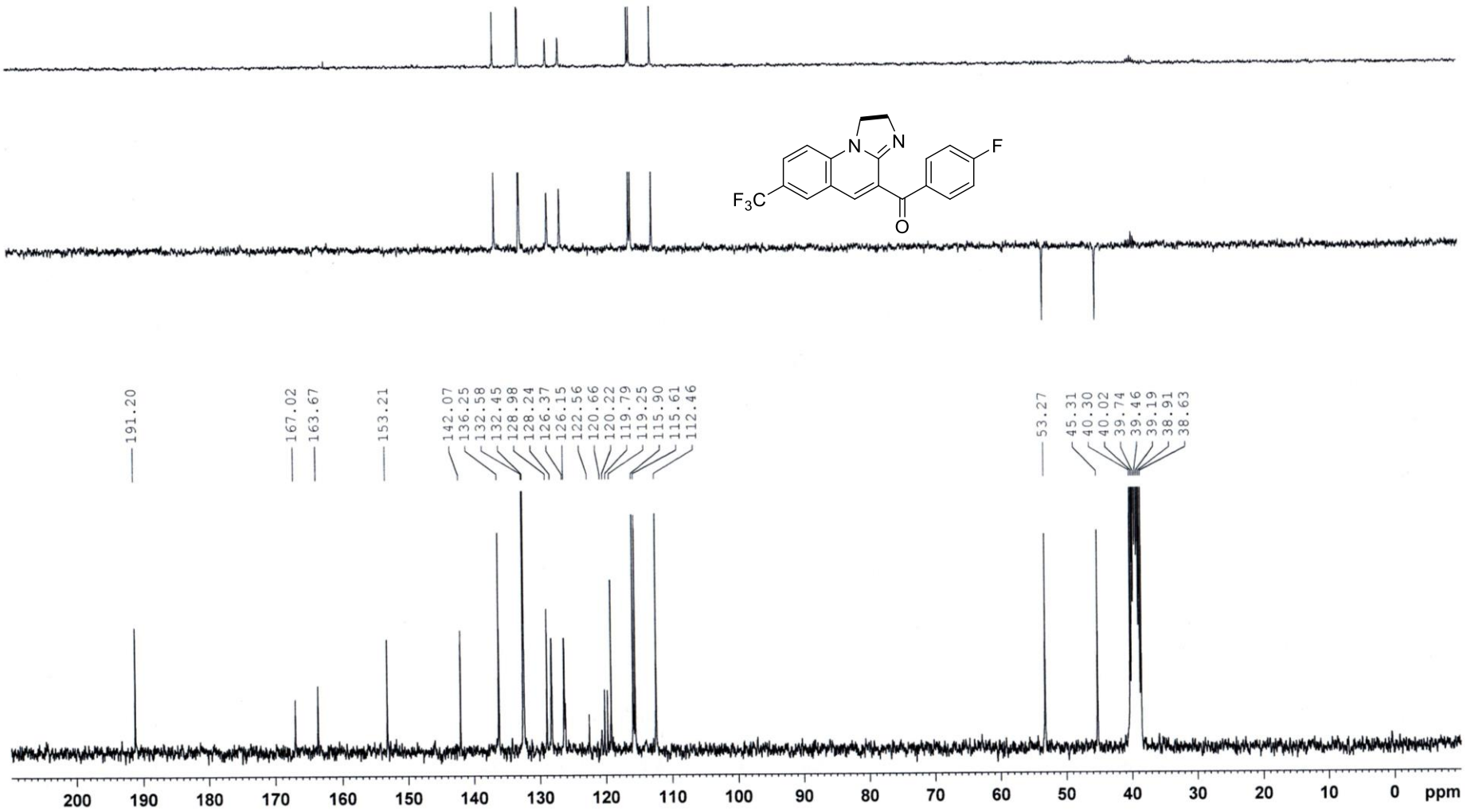


Figure S35. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3ba**

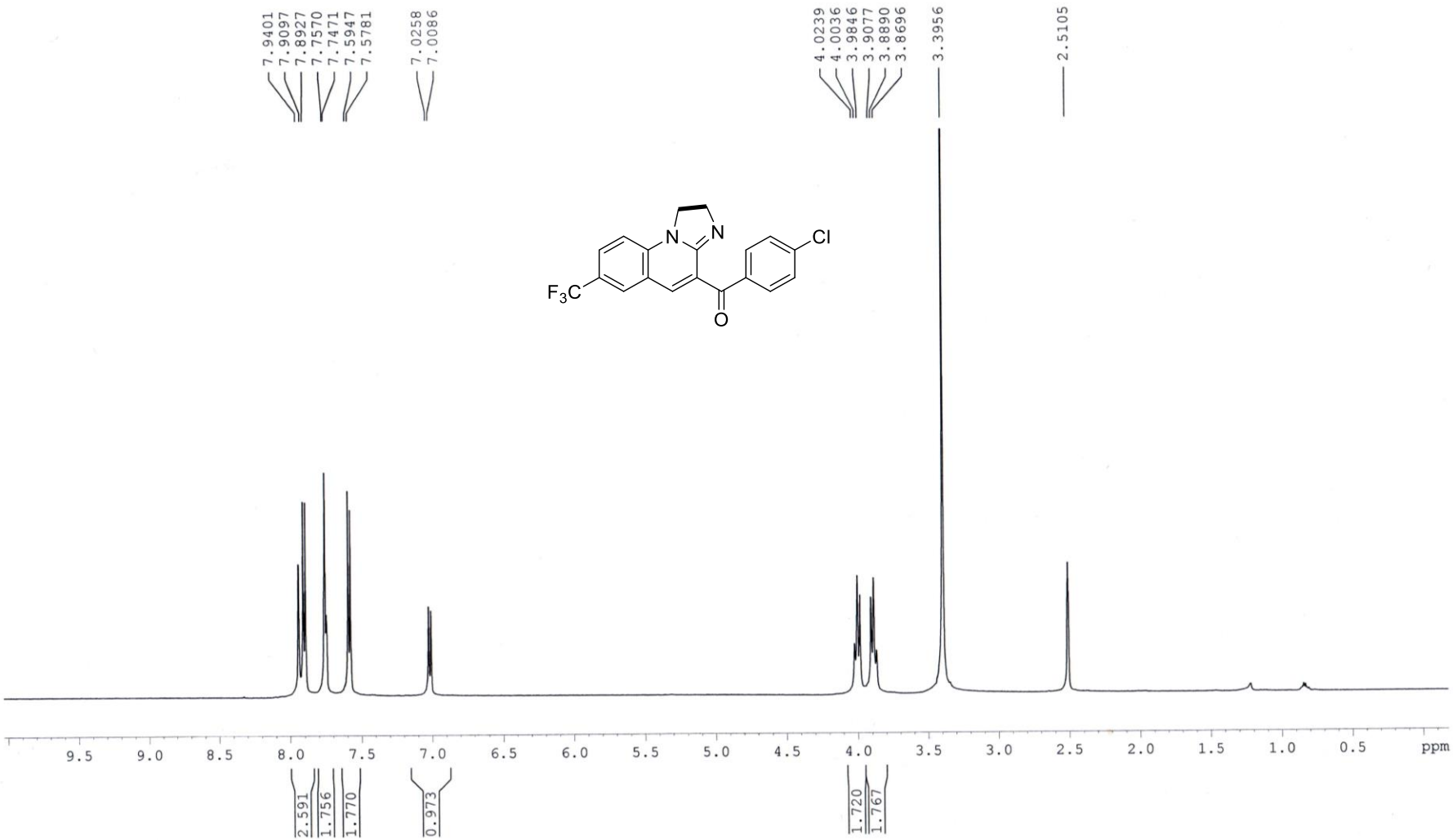


Figure S36. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bb**

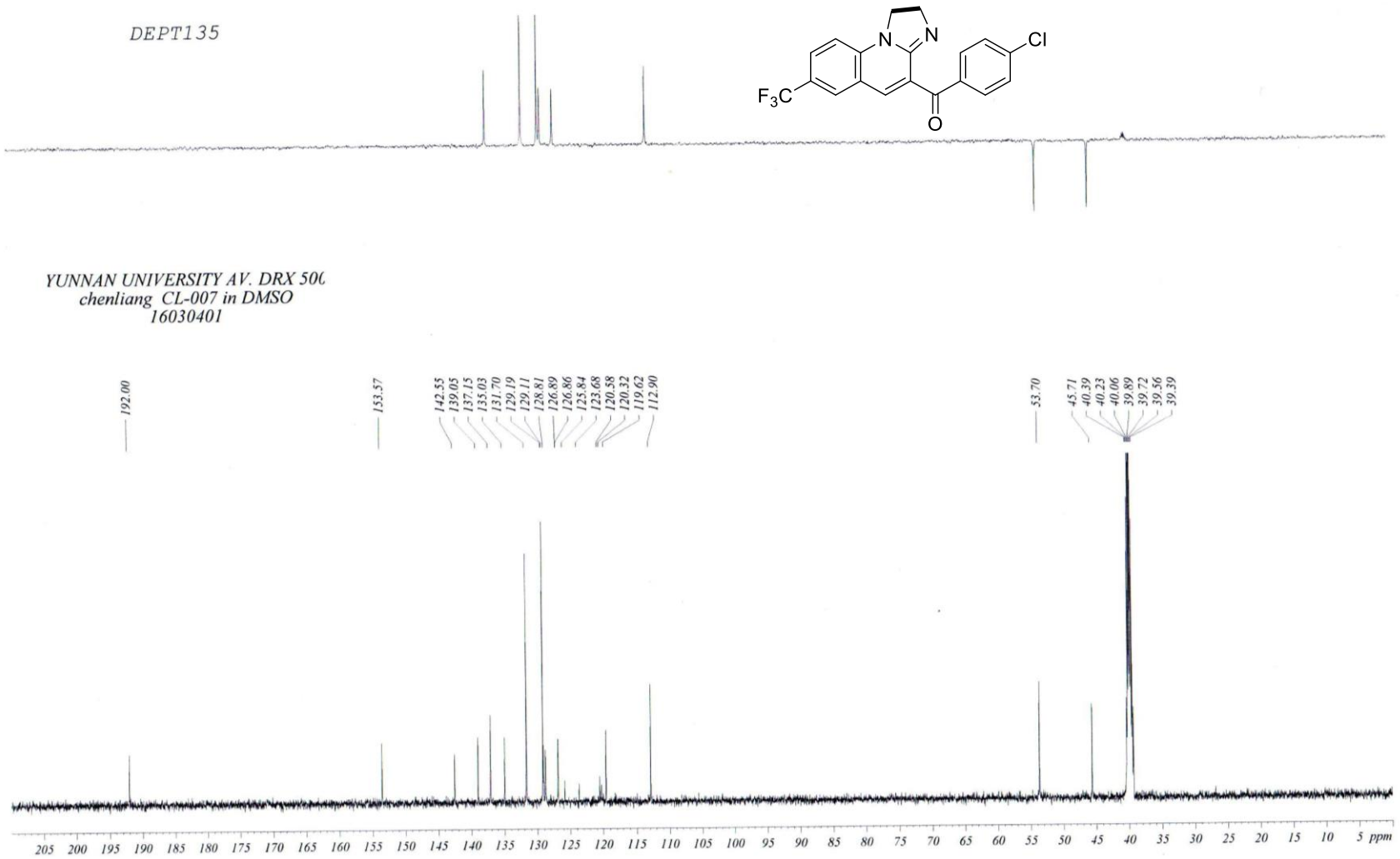


Figure S37. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bb**

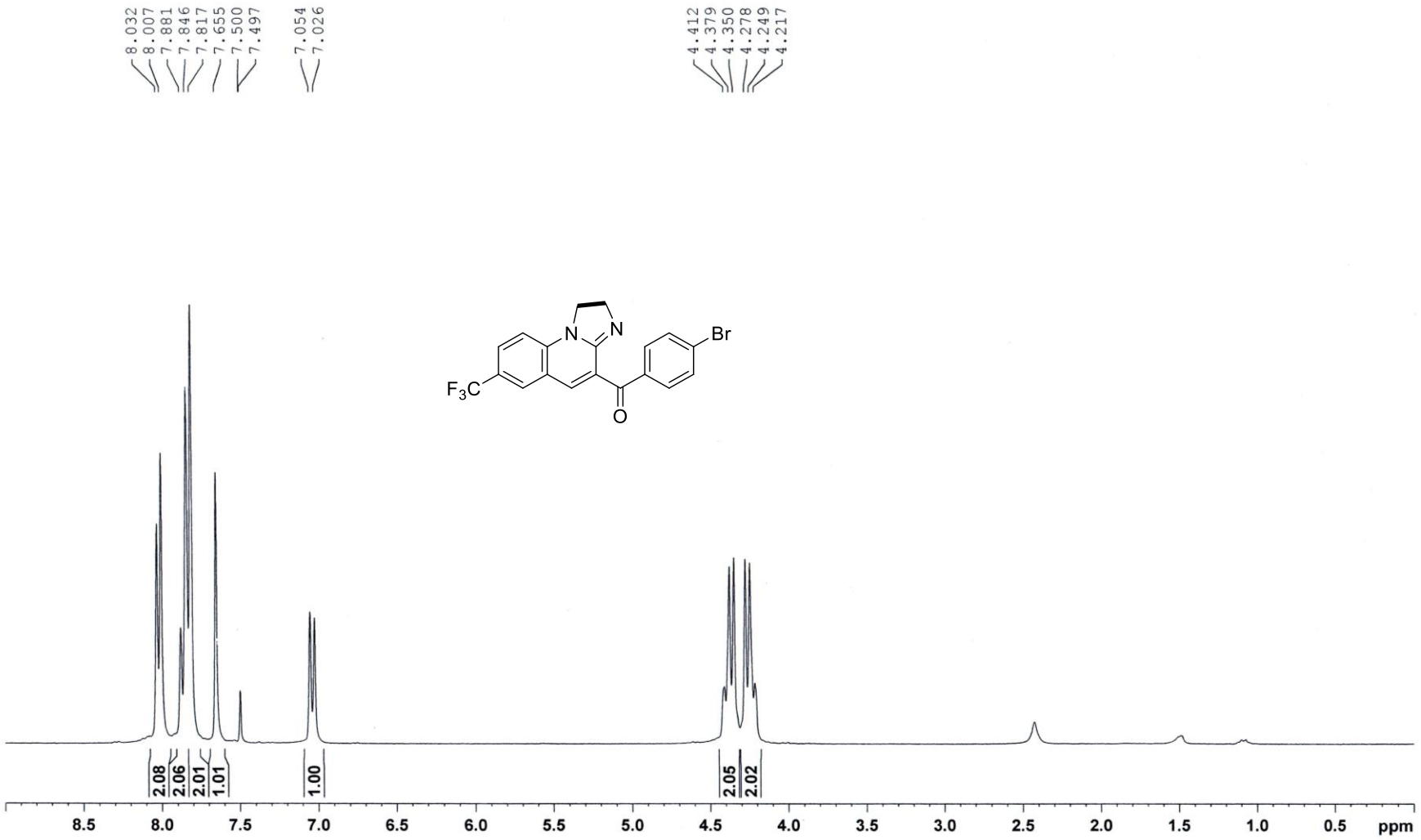


Figure S38. ^{1}H NMR (400 MHz, $DCCl_3$) spectra of compound **3bc**

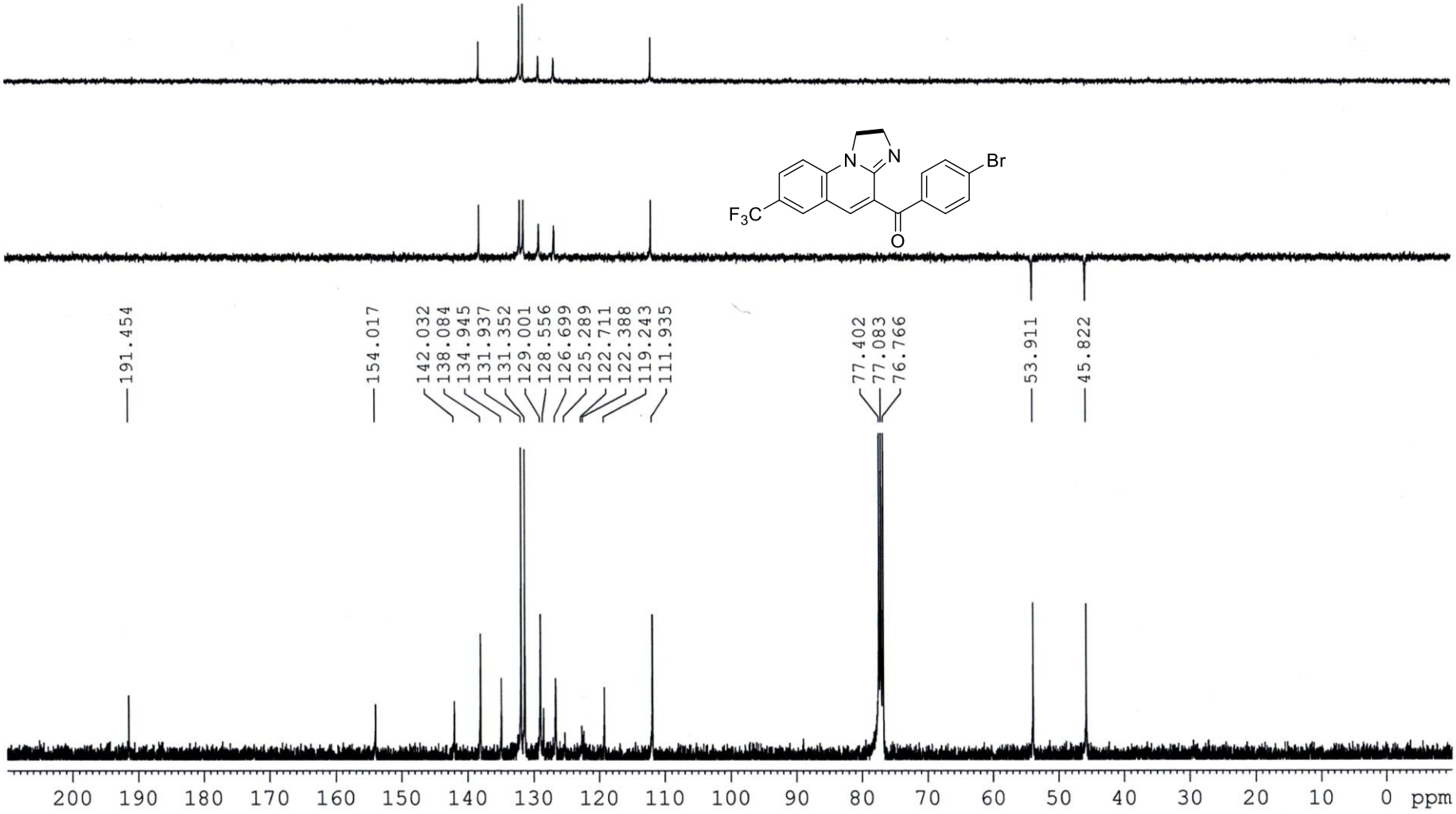


Figure S39. ^{13}C NMR (100 MHz, $DCCl_3$) spectra of compound **3bc**

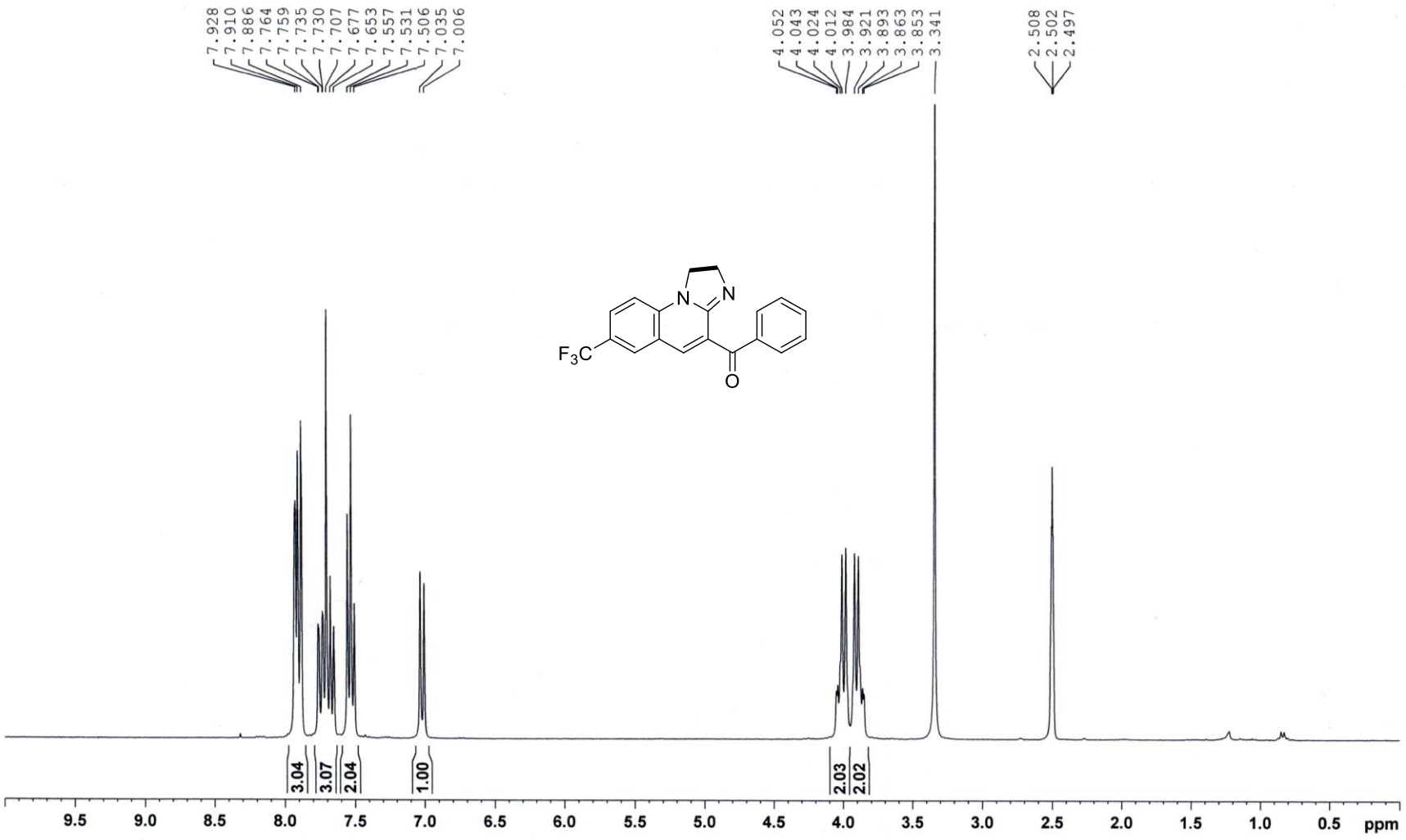


Figure S40. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3bd**

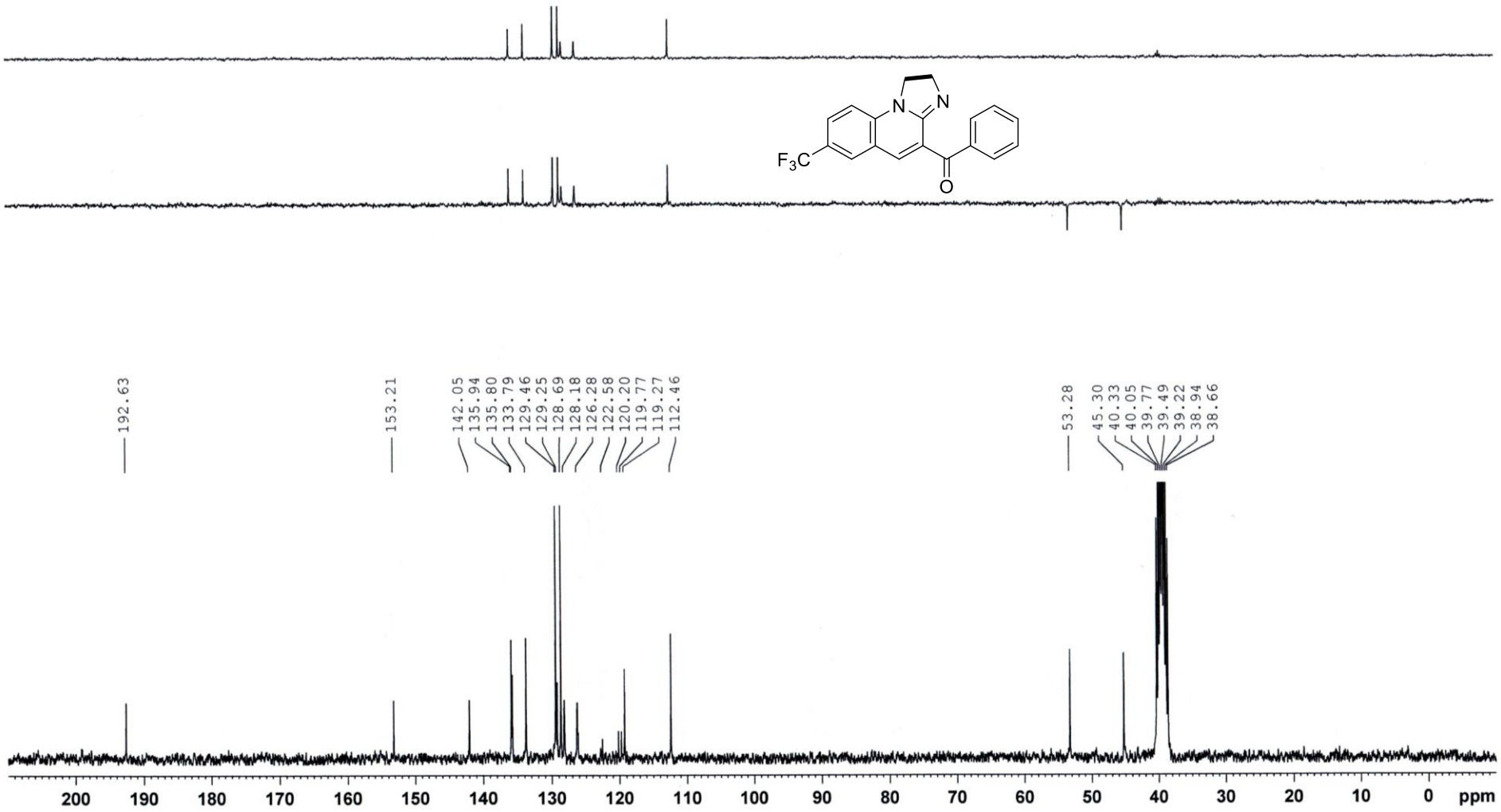


Figure S41. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3bd**

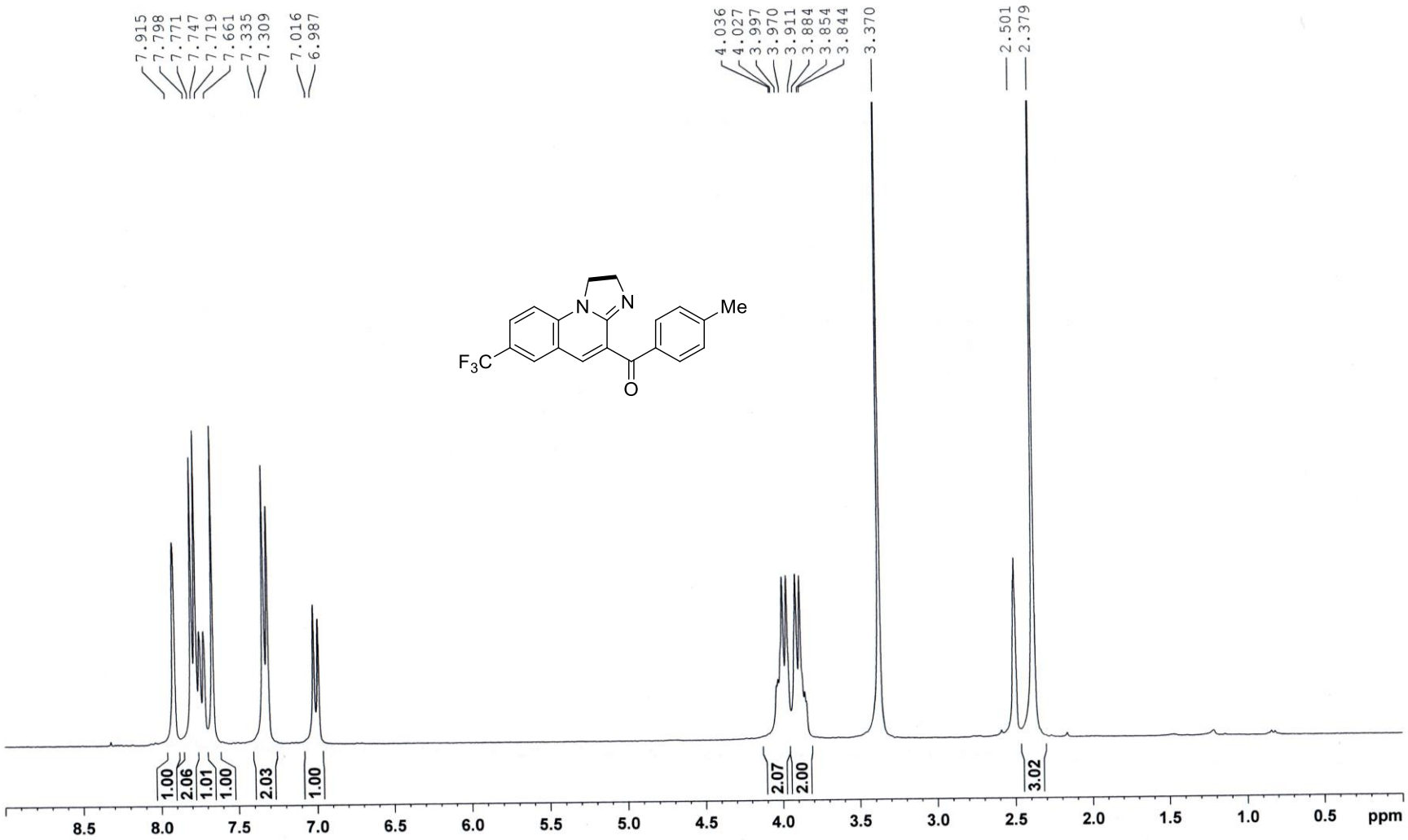


Figure S42. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3be**

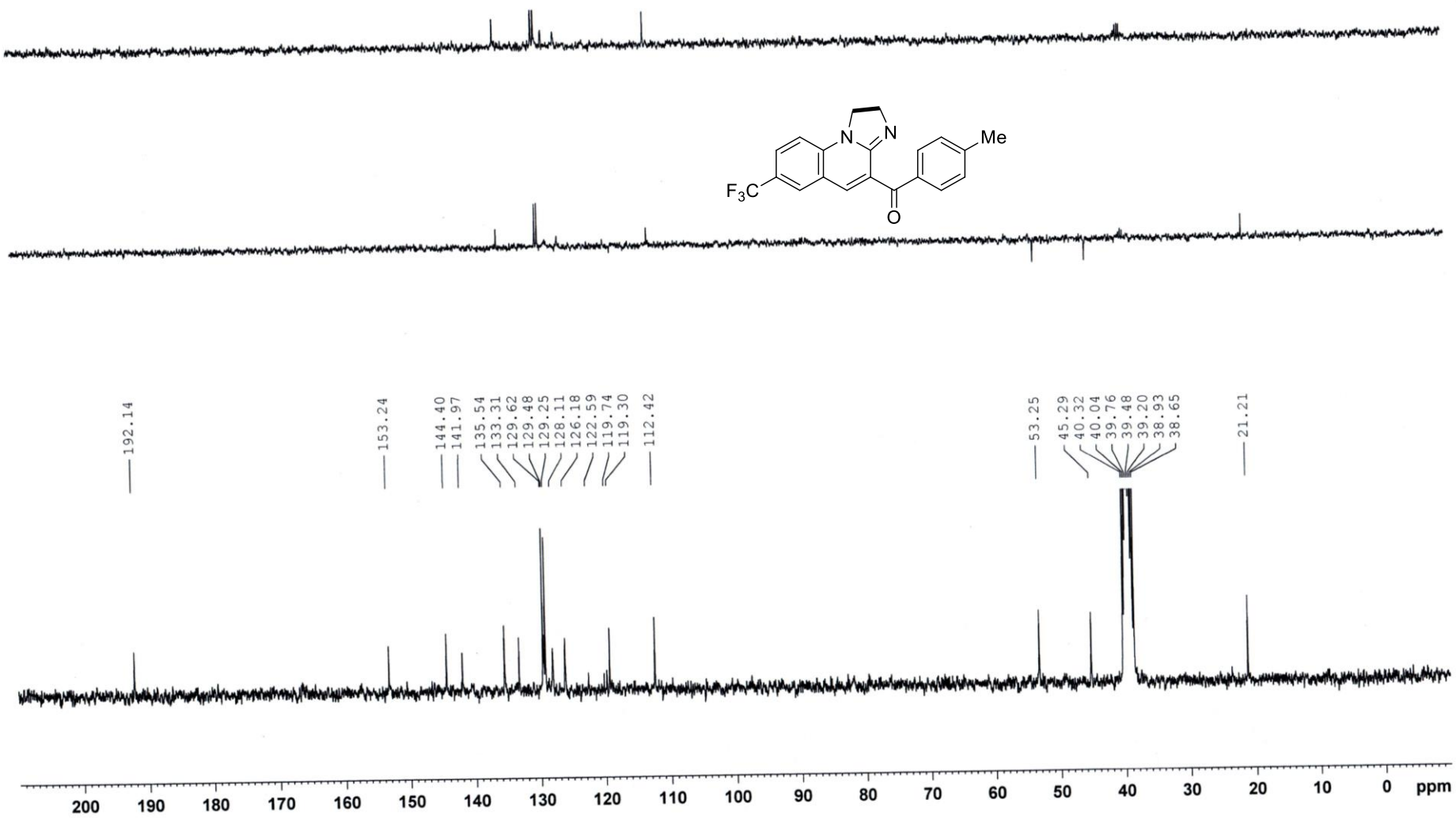


Figure S43. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3be**

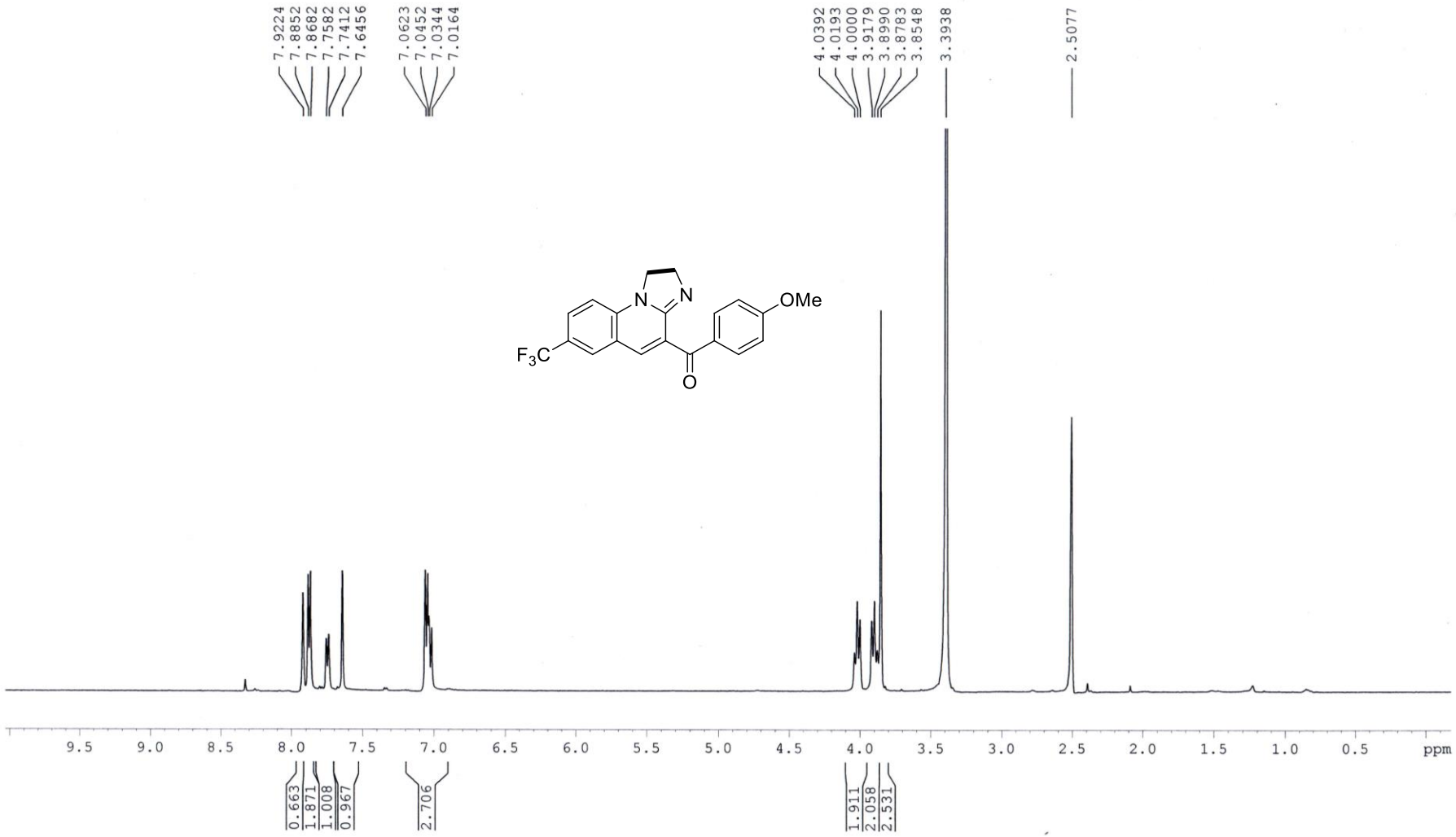


Figure S44. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bf**

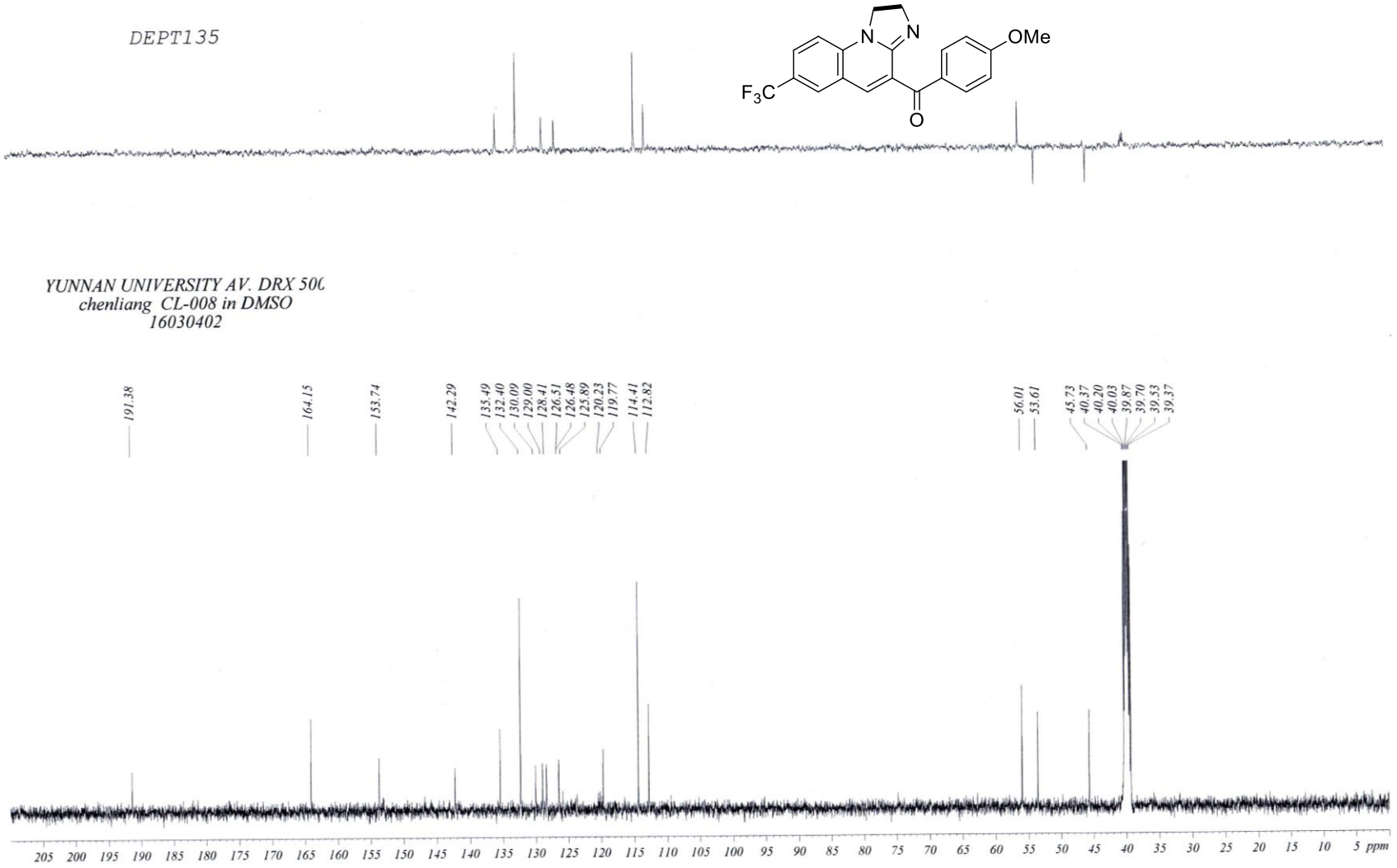


Figure S45. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bf**

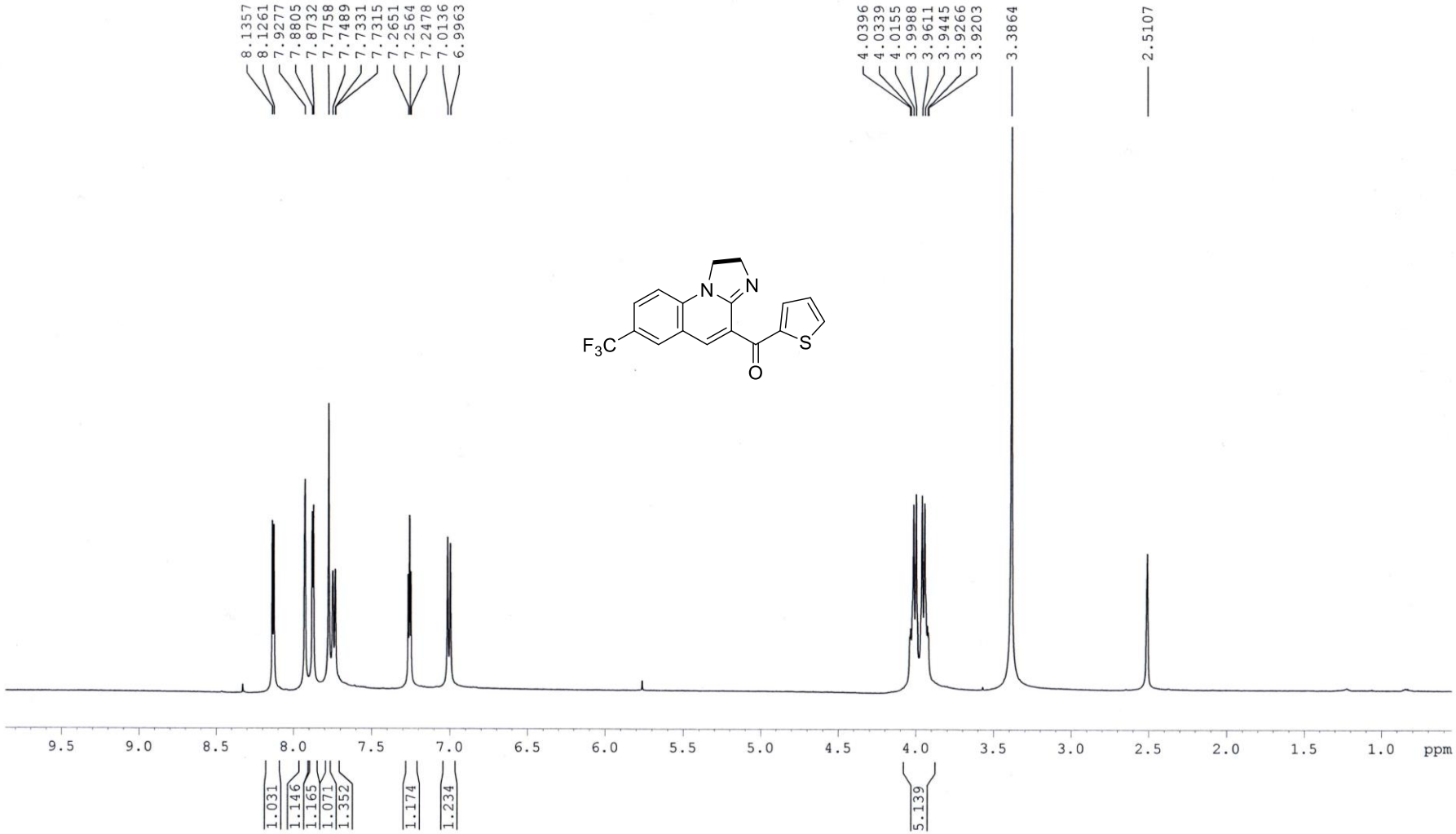


Figure S46. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bg**

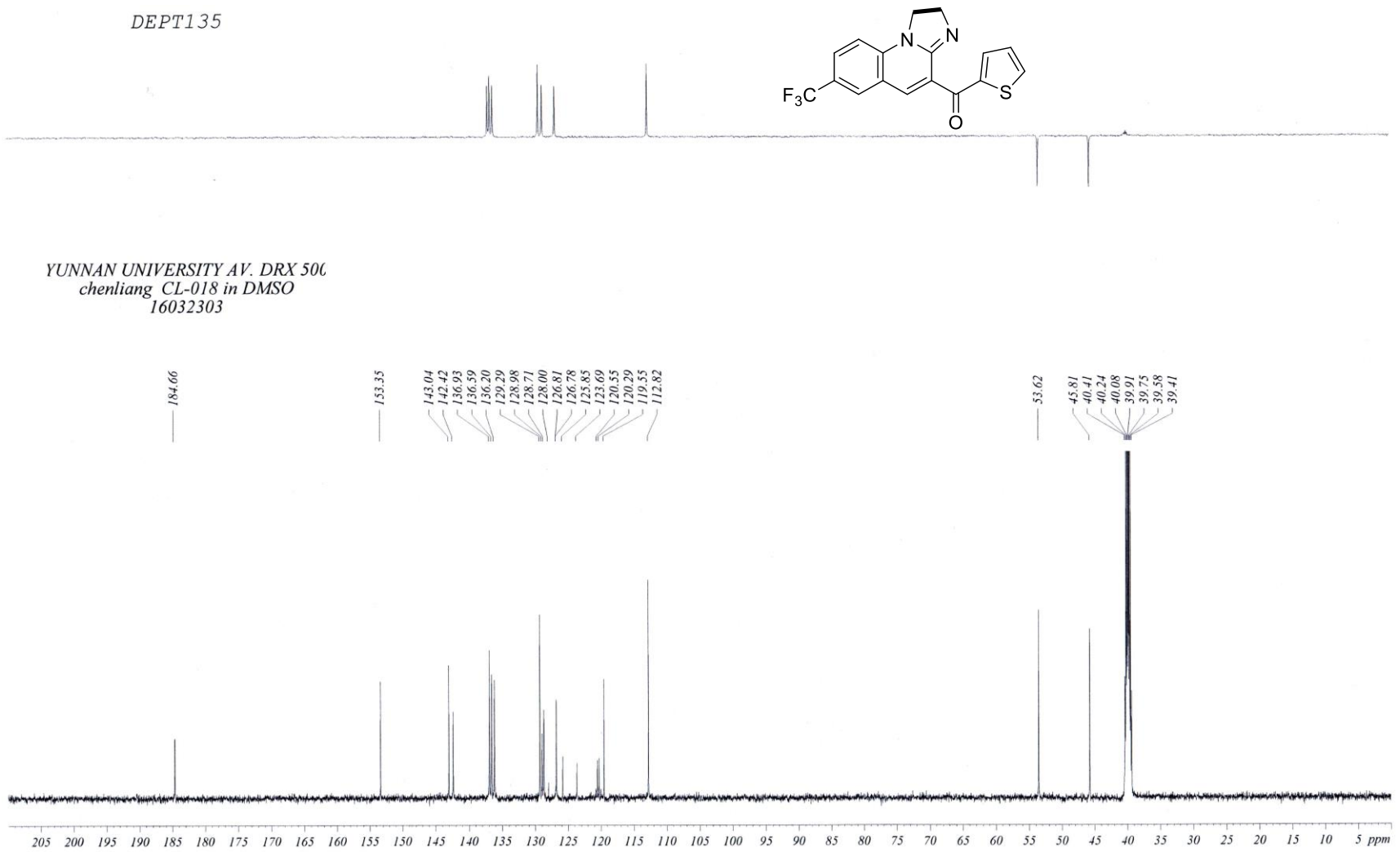


Figure S47. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bg**

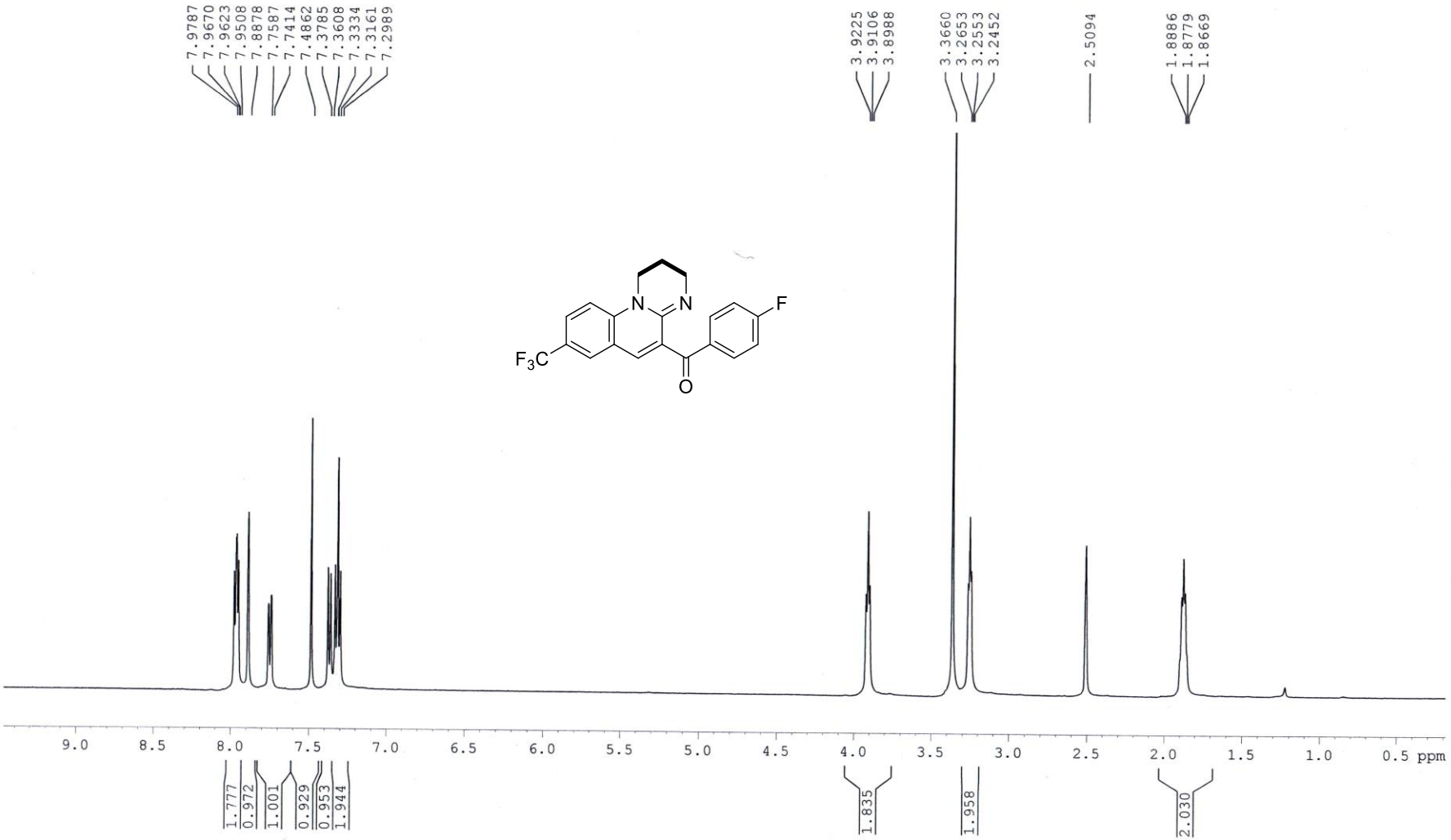


Figure S48. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bh**

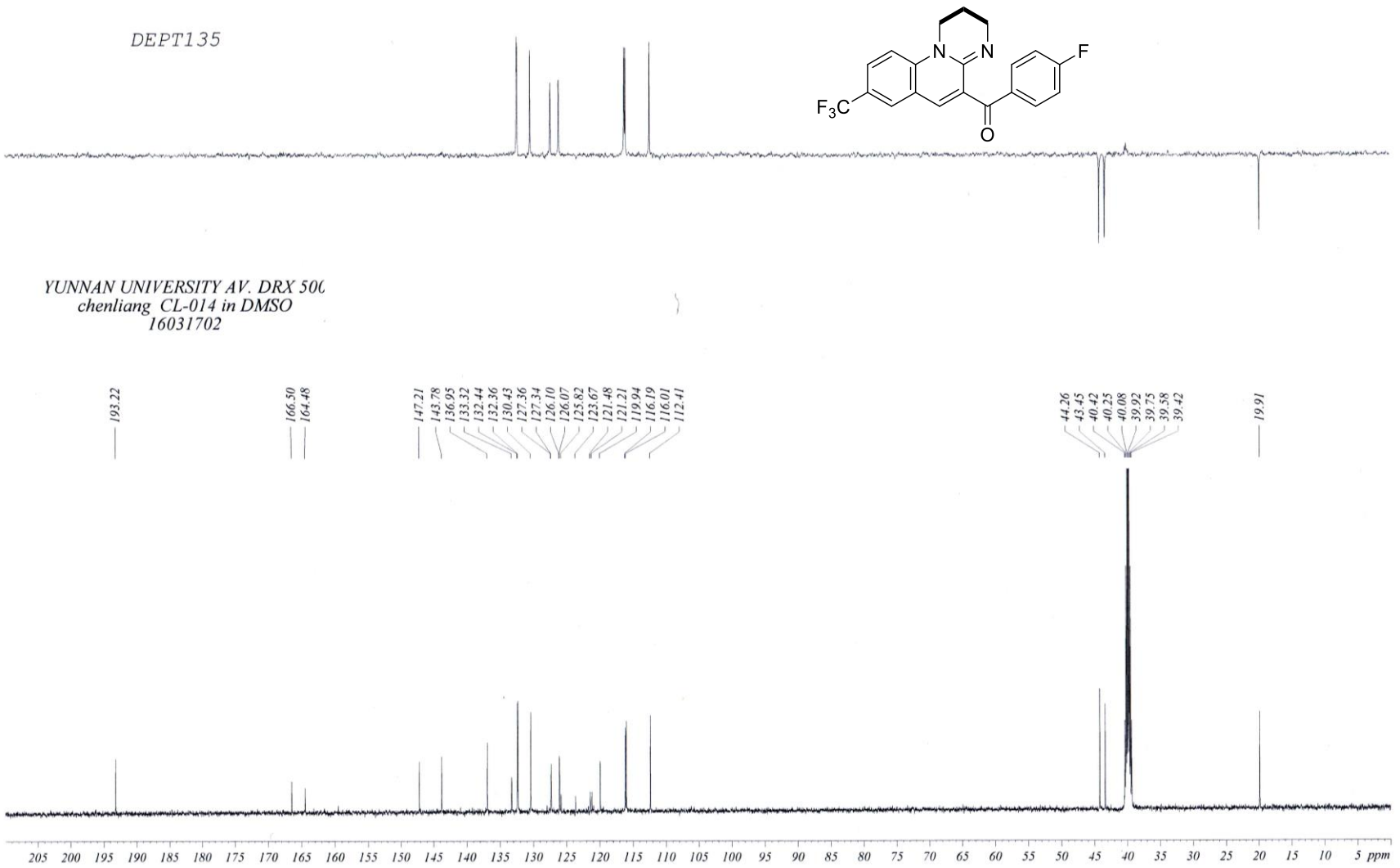


Figure S49. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bh**

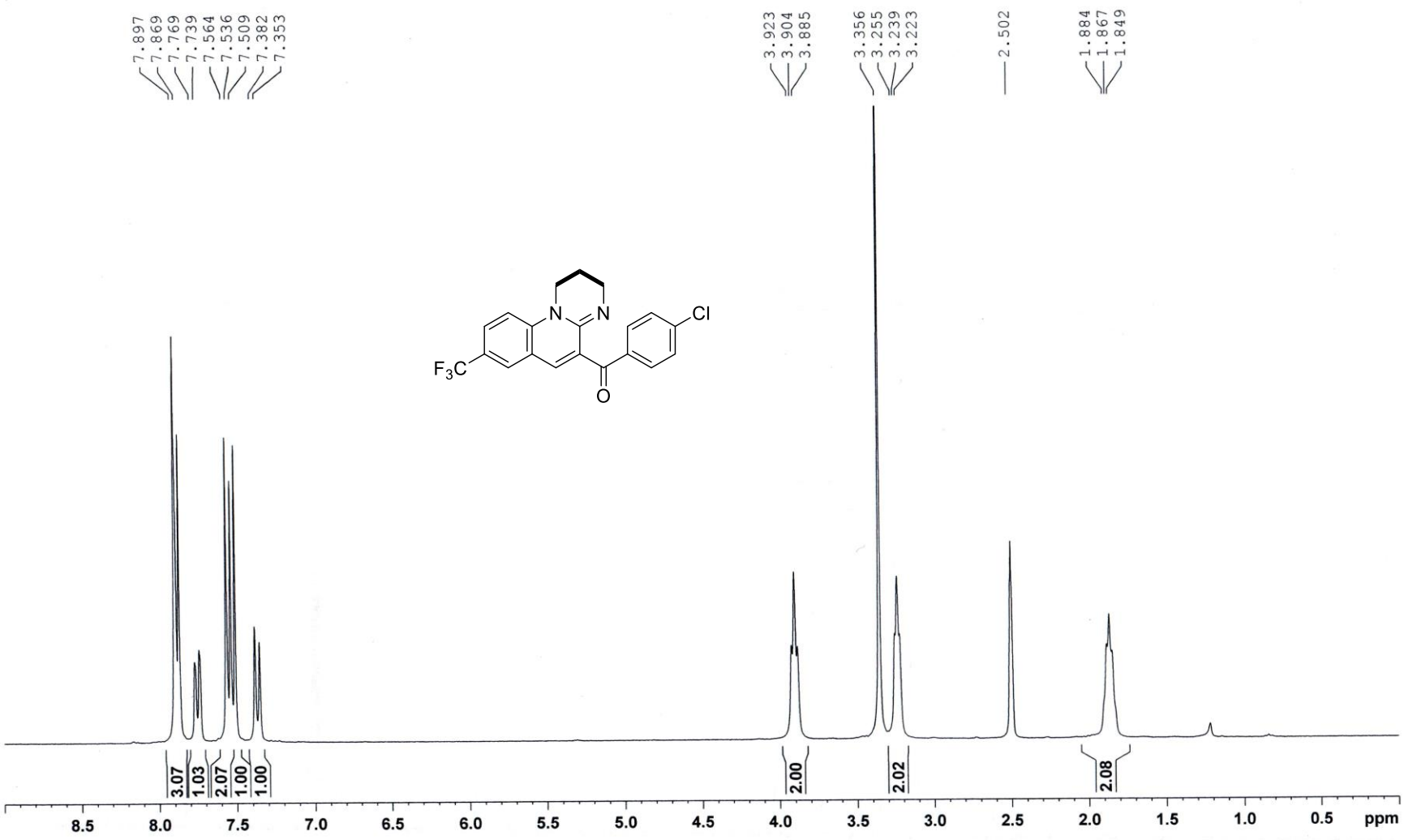


Figure S50. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3bi**

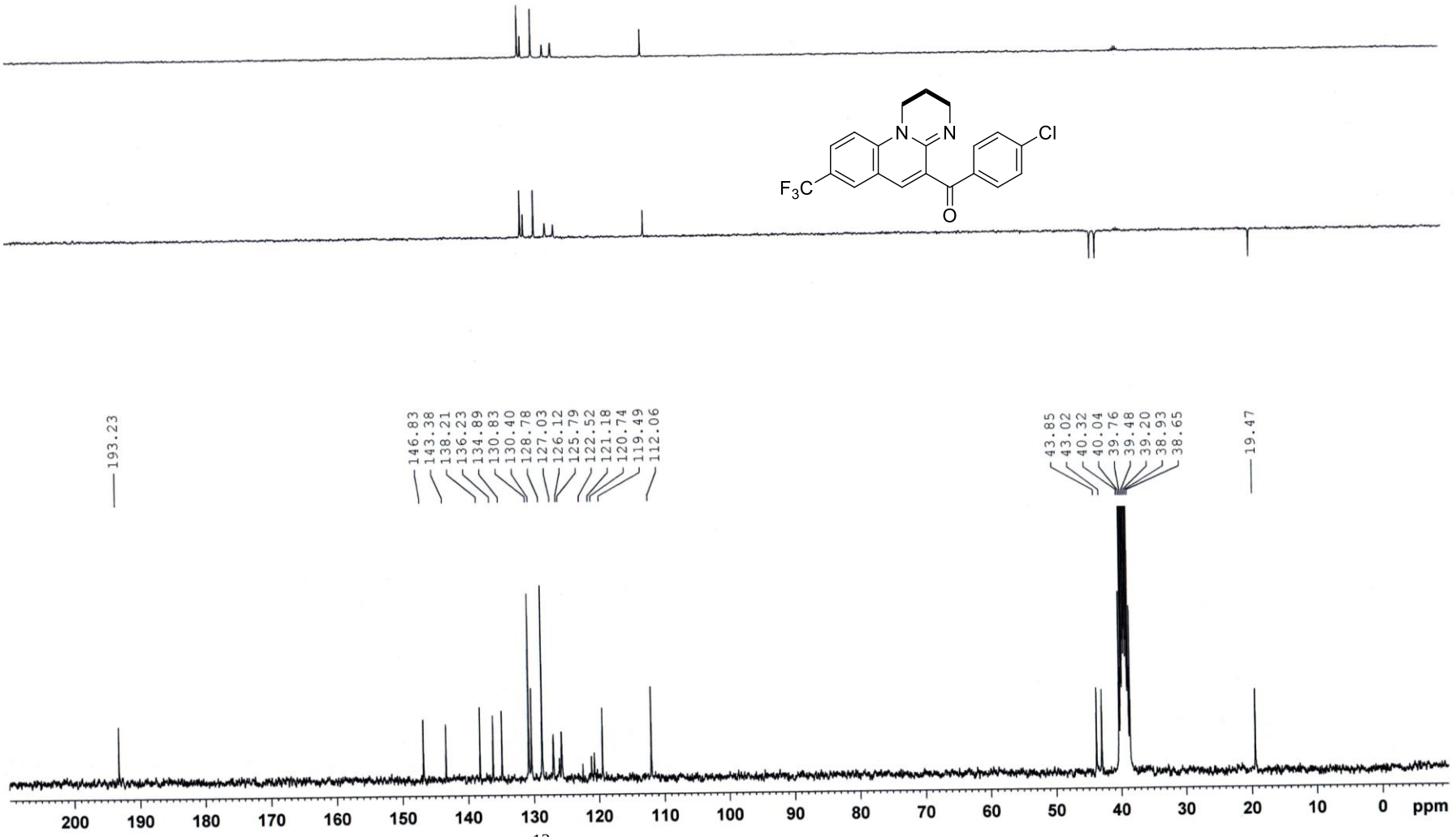


Figure S51. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3bi**

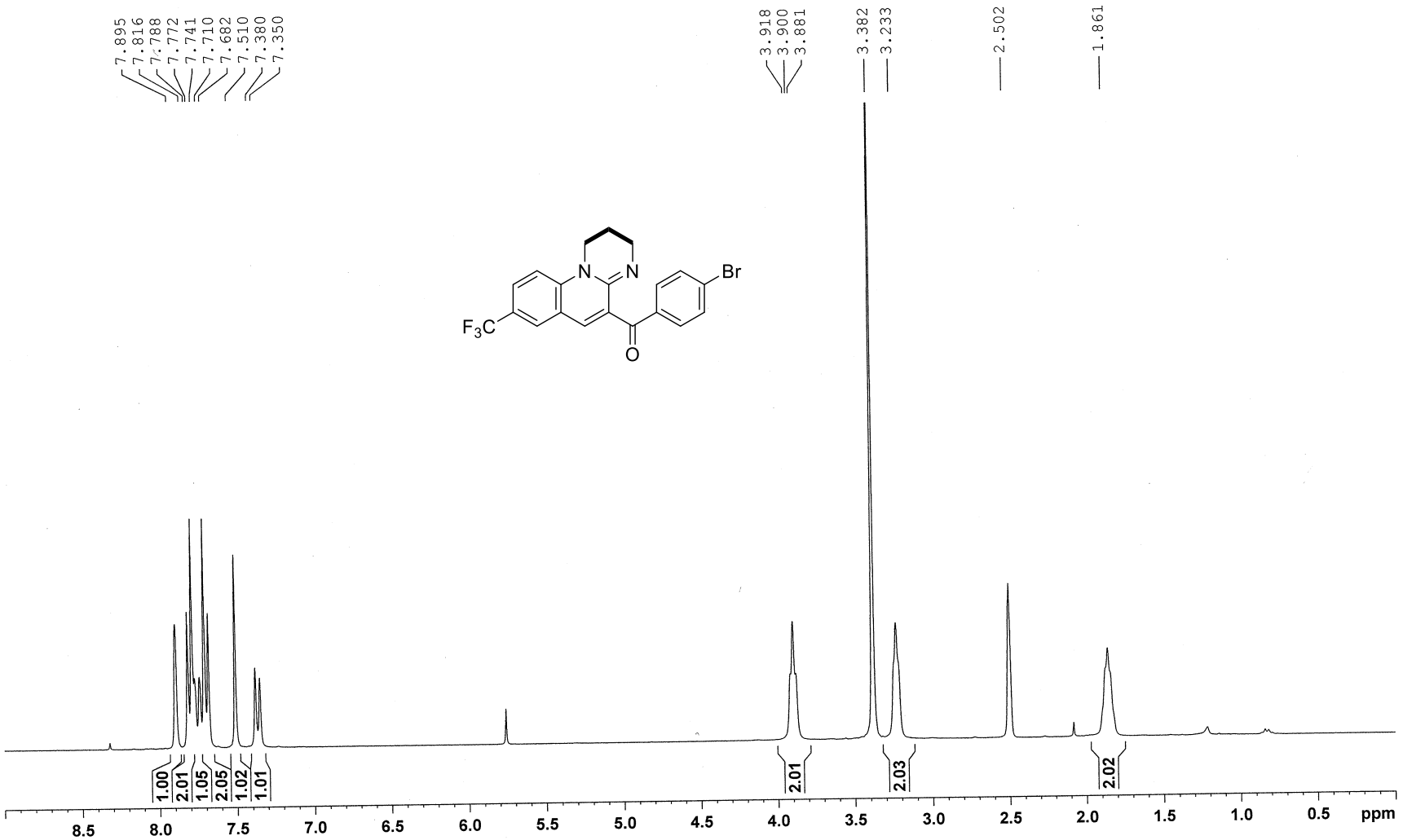


Figure S52. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3bj**

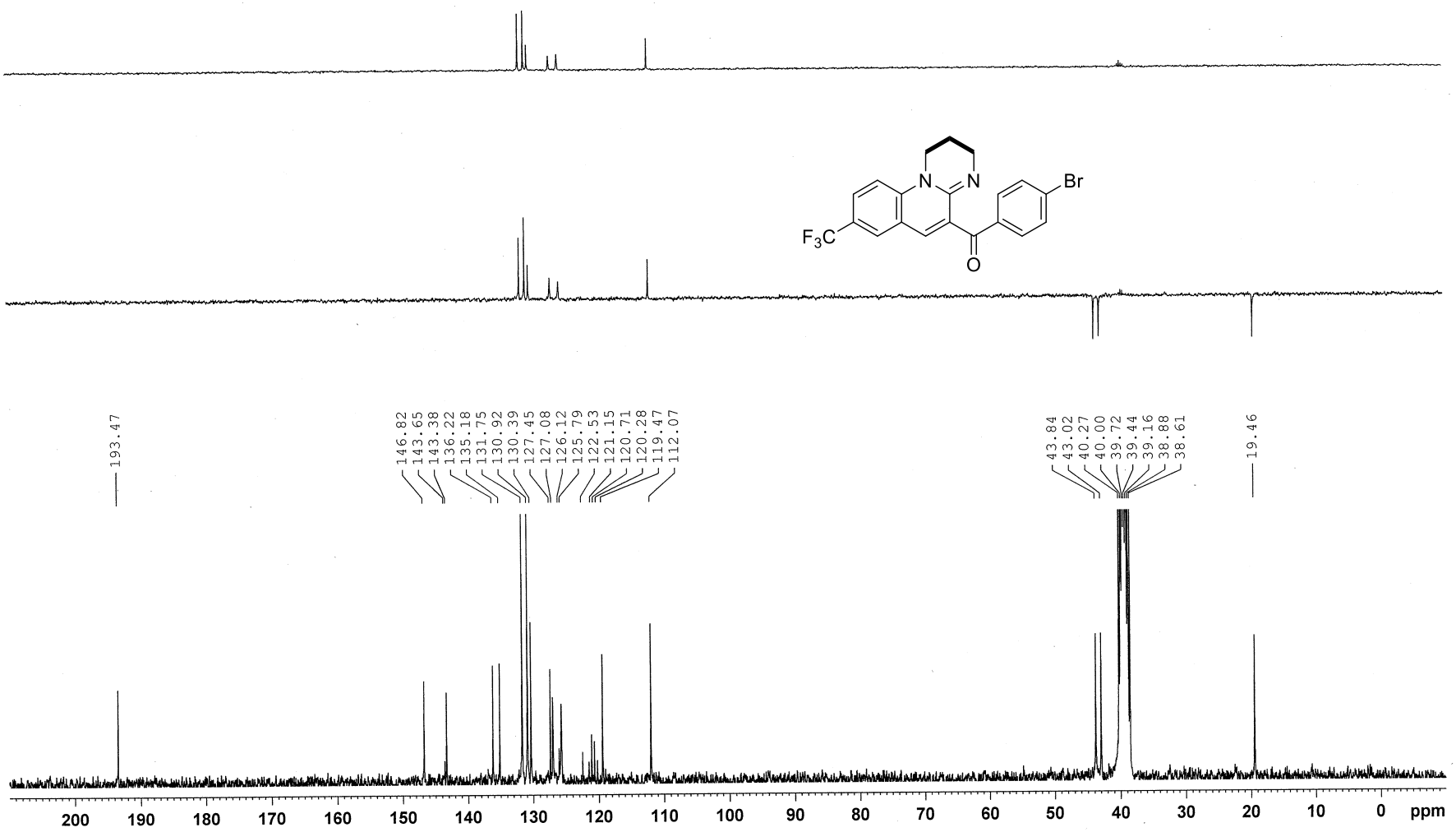


Figure S53. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3bj**

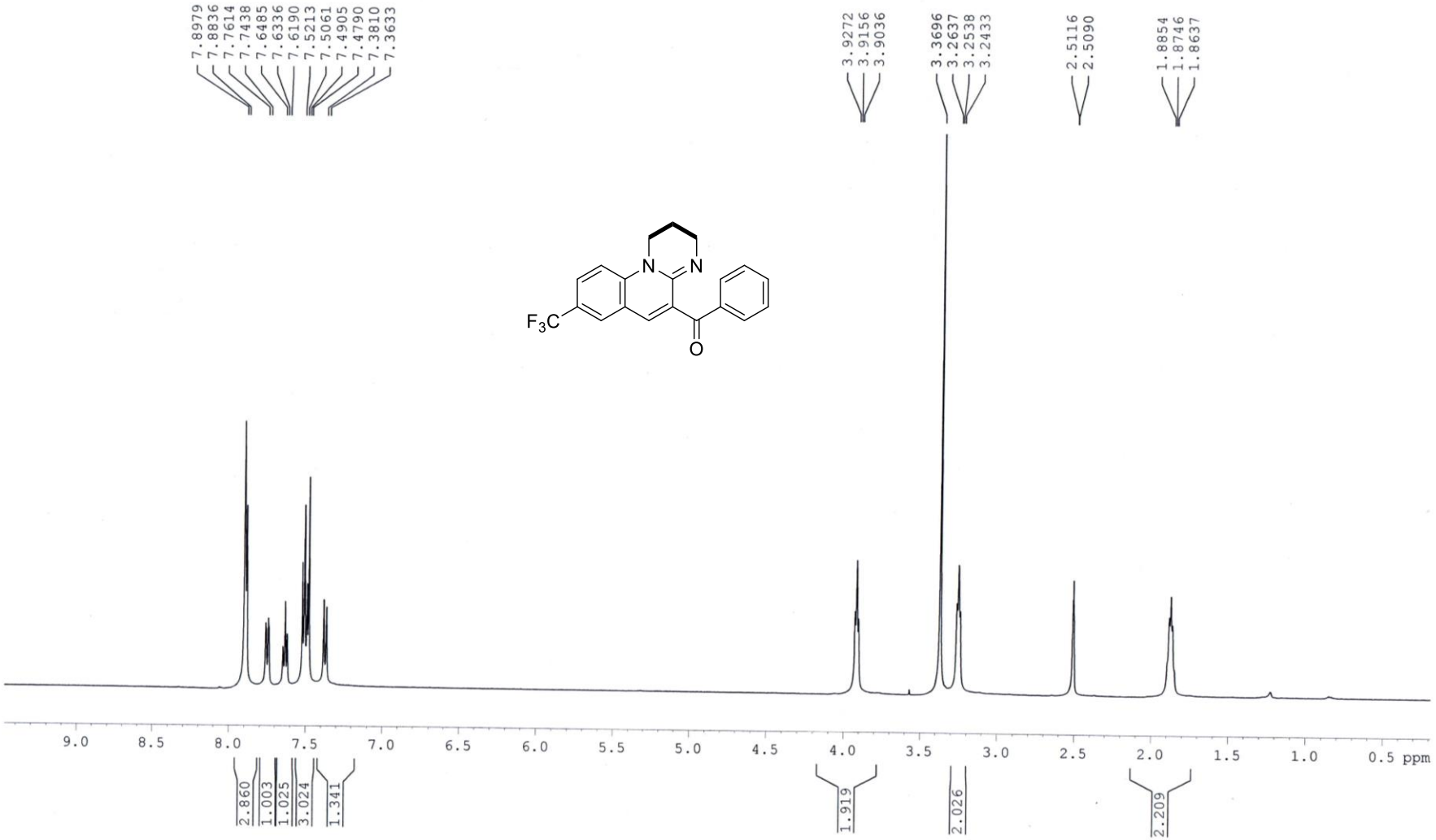


Figure S54. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bk**

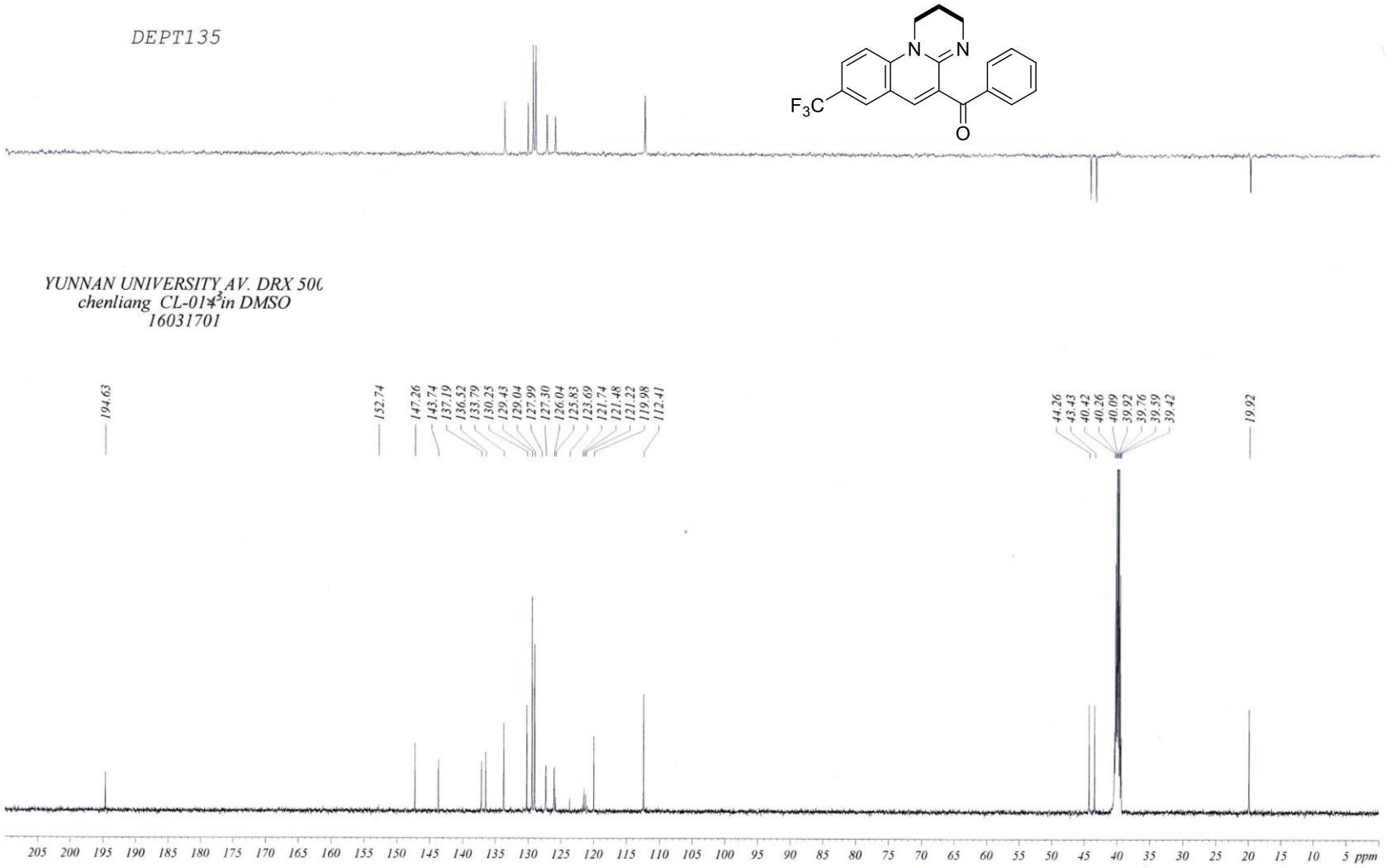


Figure S55. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bk**

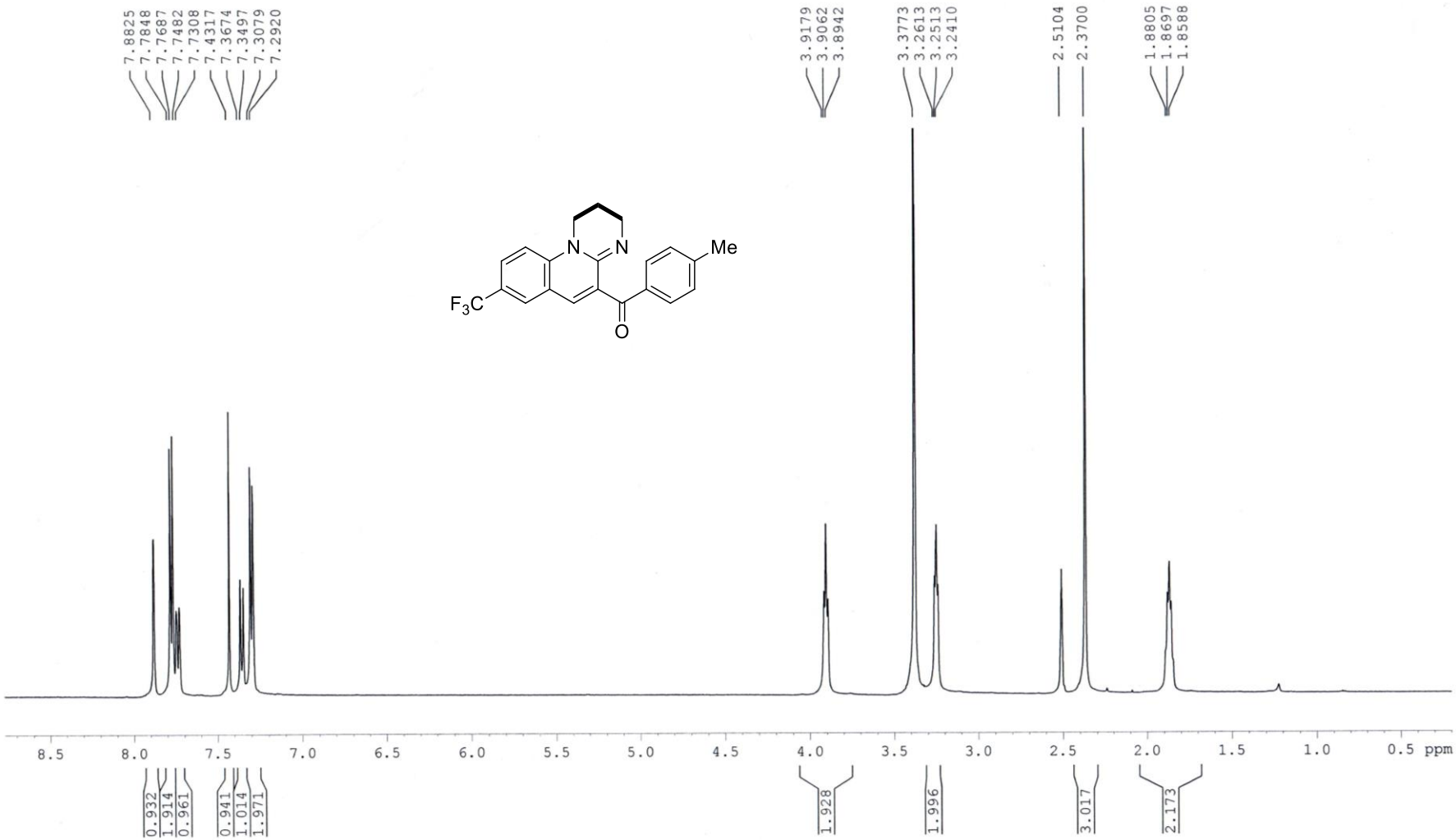


Figure S56. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bl**

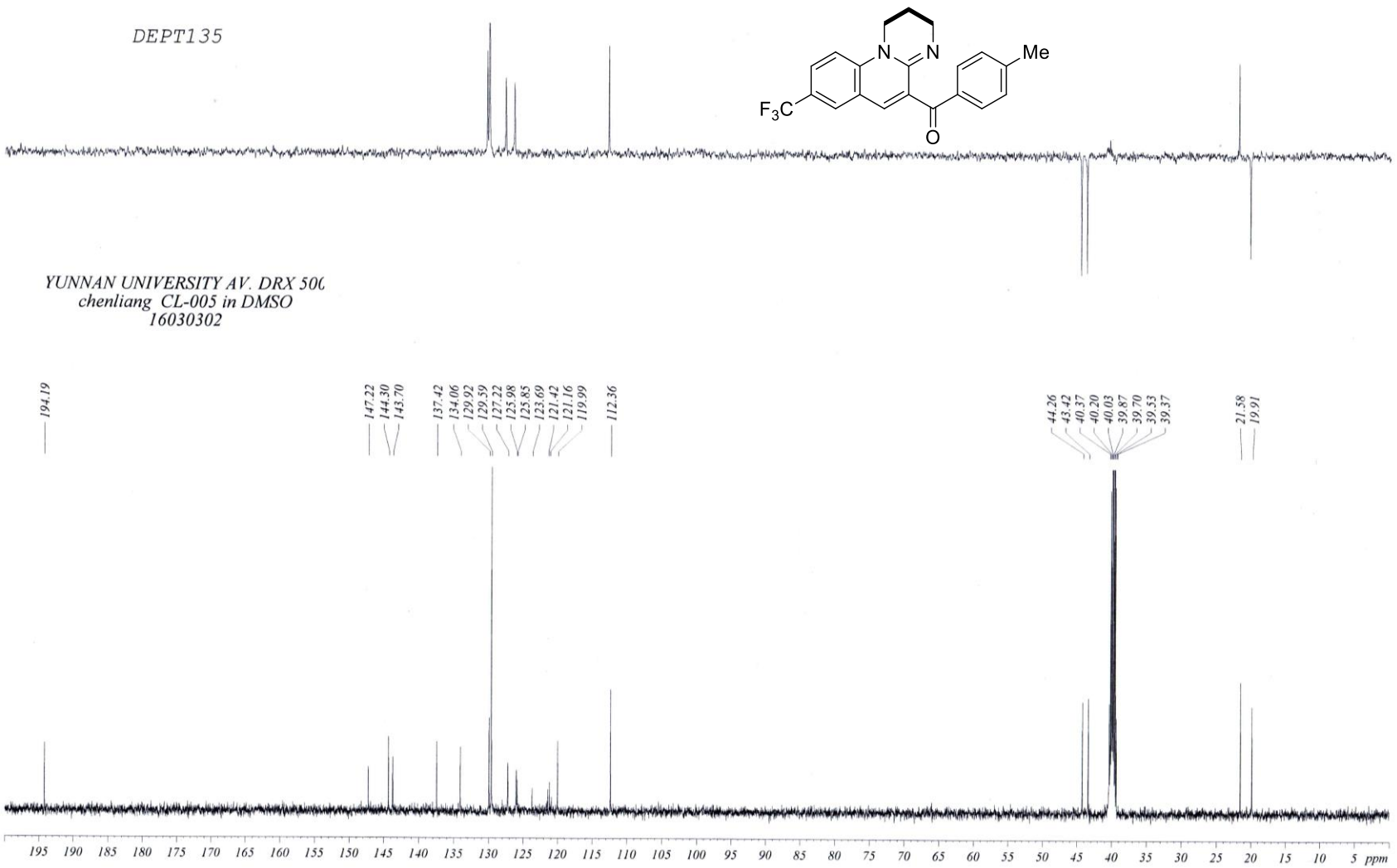


Figure S57. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bl**

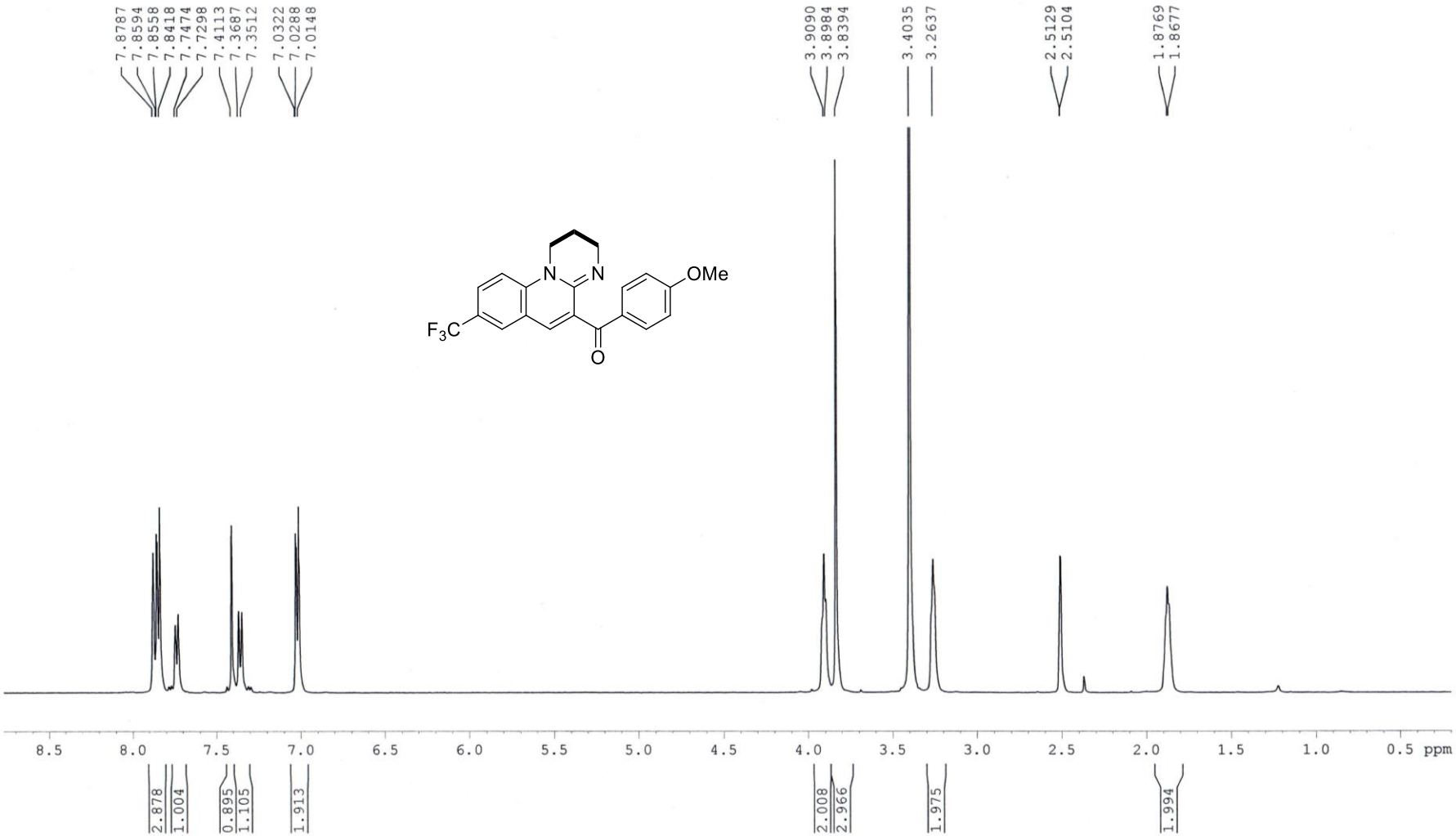


Figure S58. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3bm**

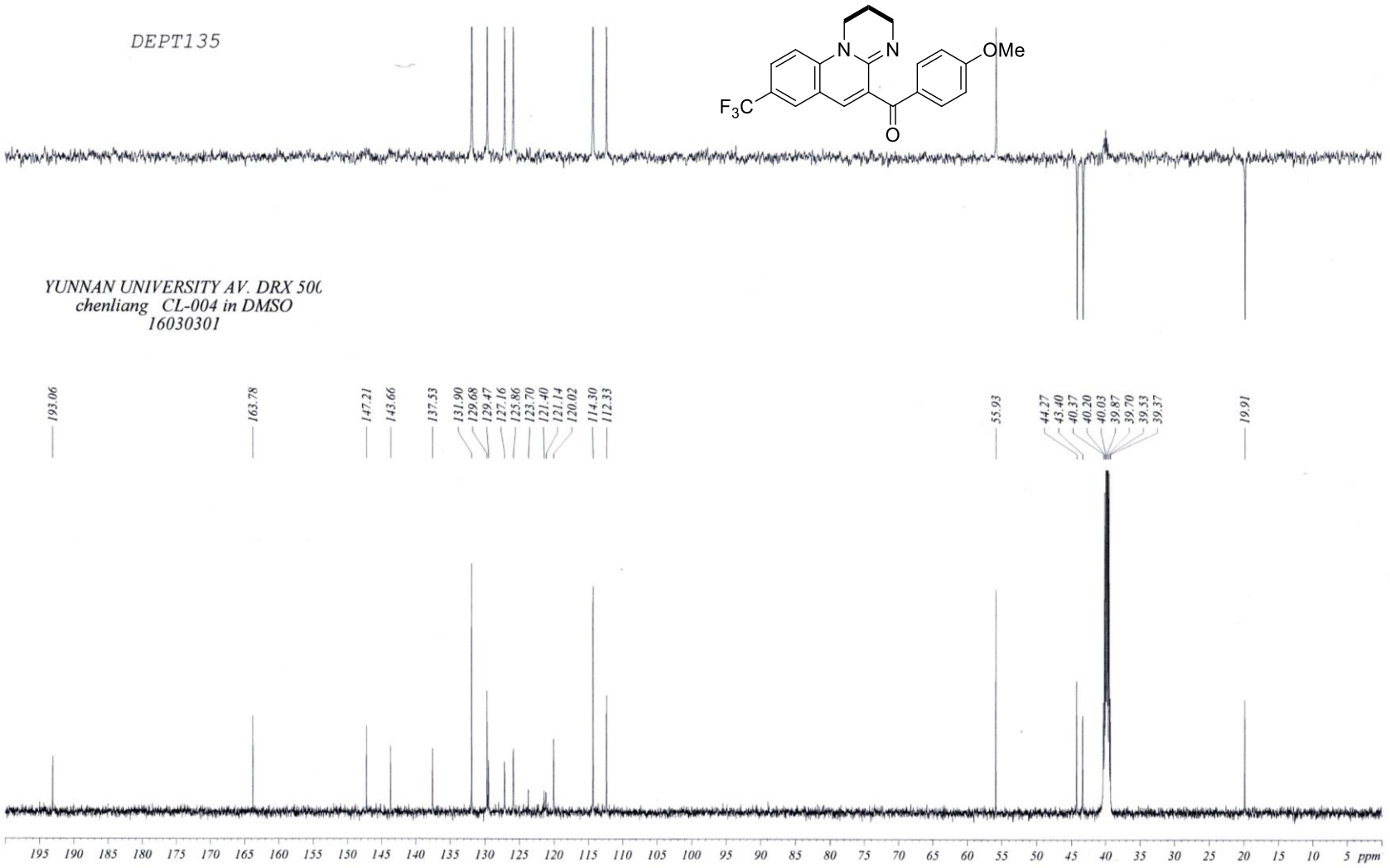


Figure S59. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3bm**

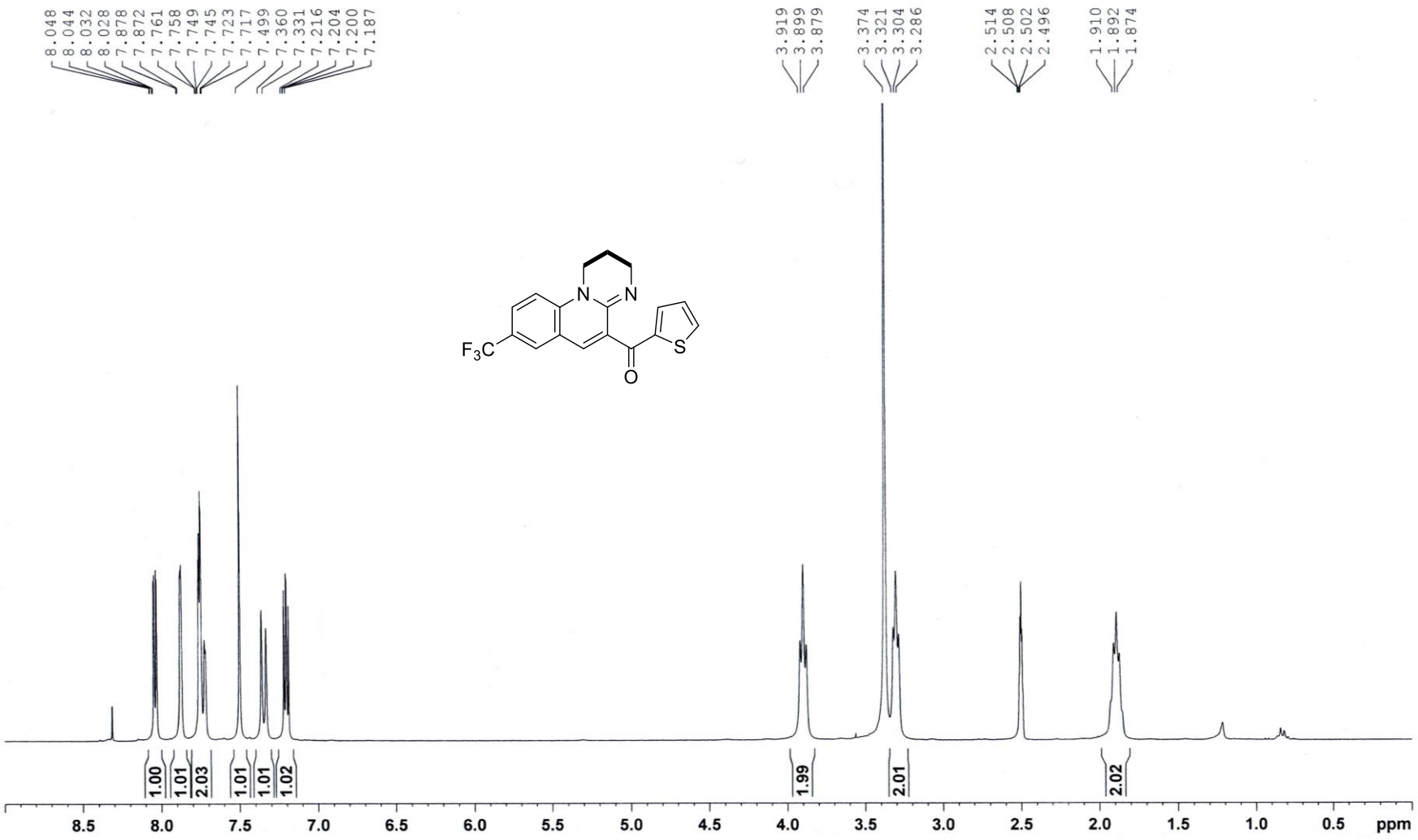


Figure S60. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3bn**

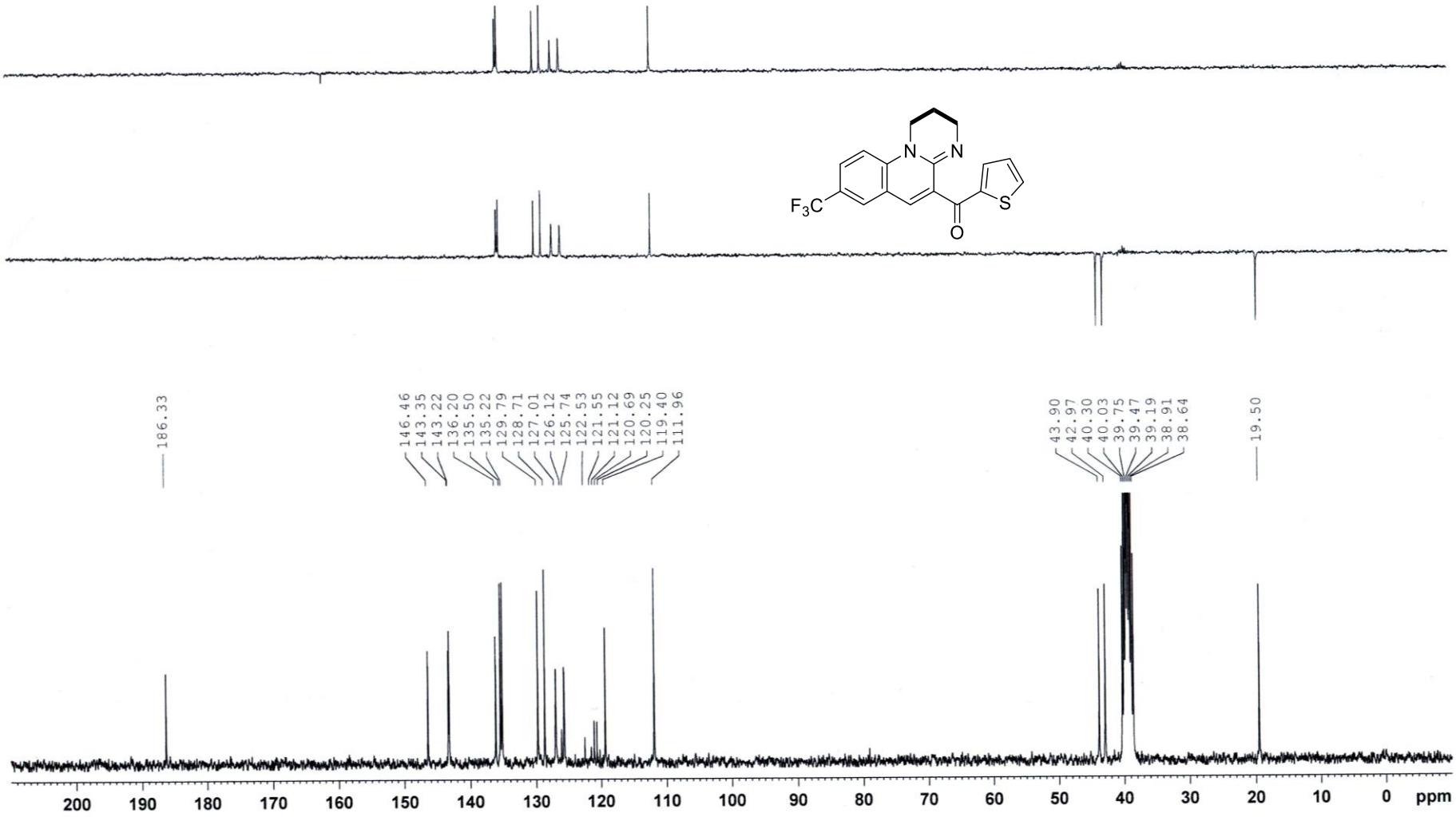


Figure S61. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3bn**

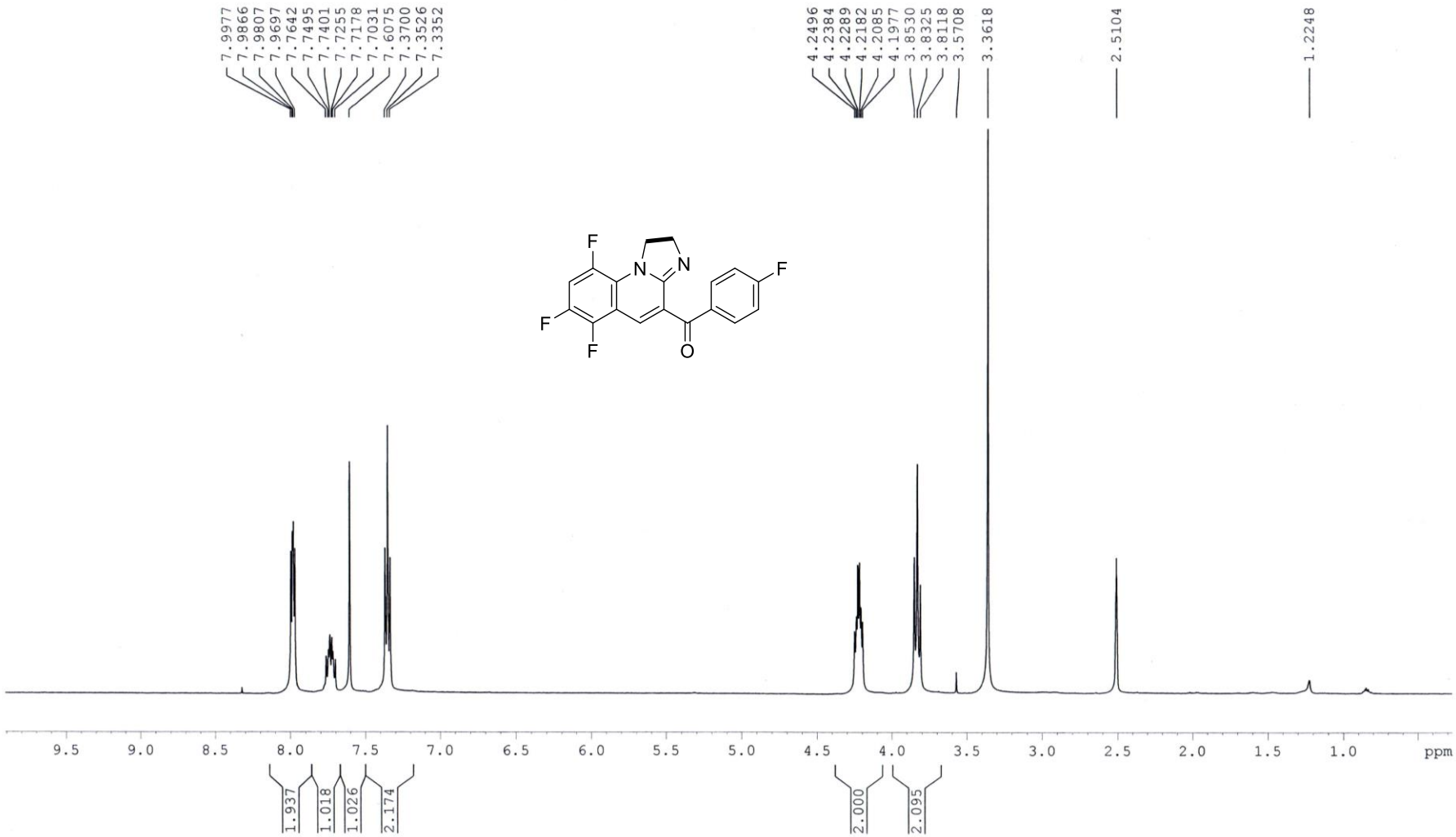


Figure S62. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3ca**

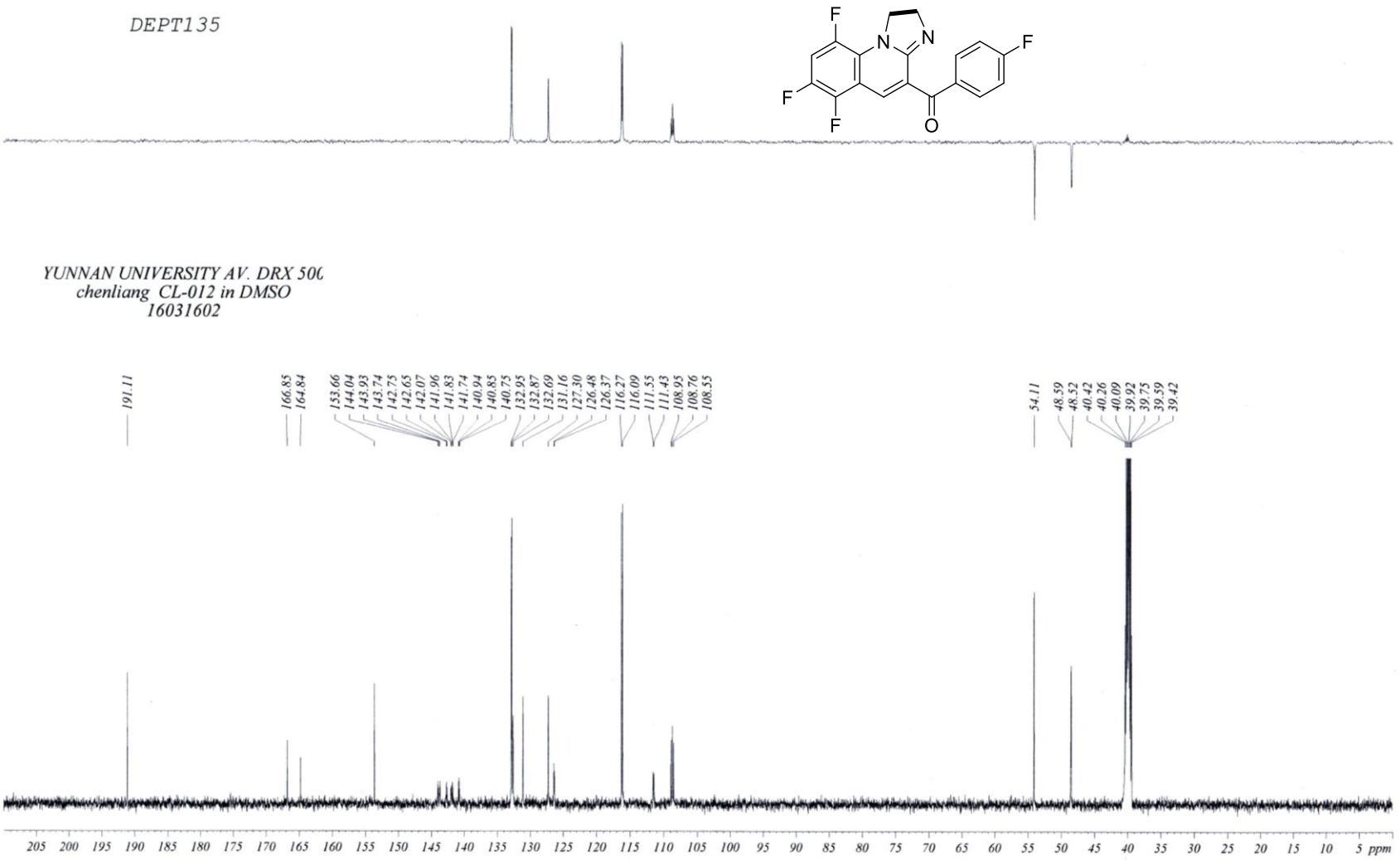


Figure S63. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3ca**

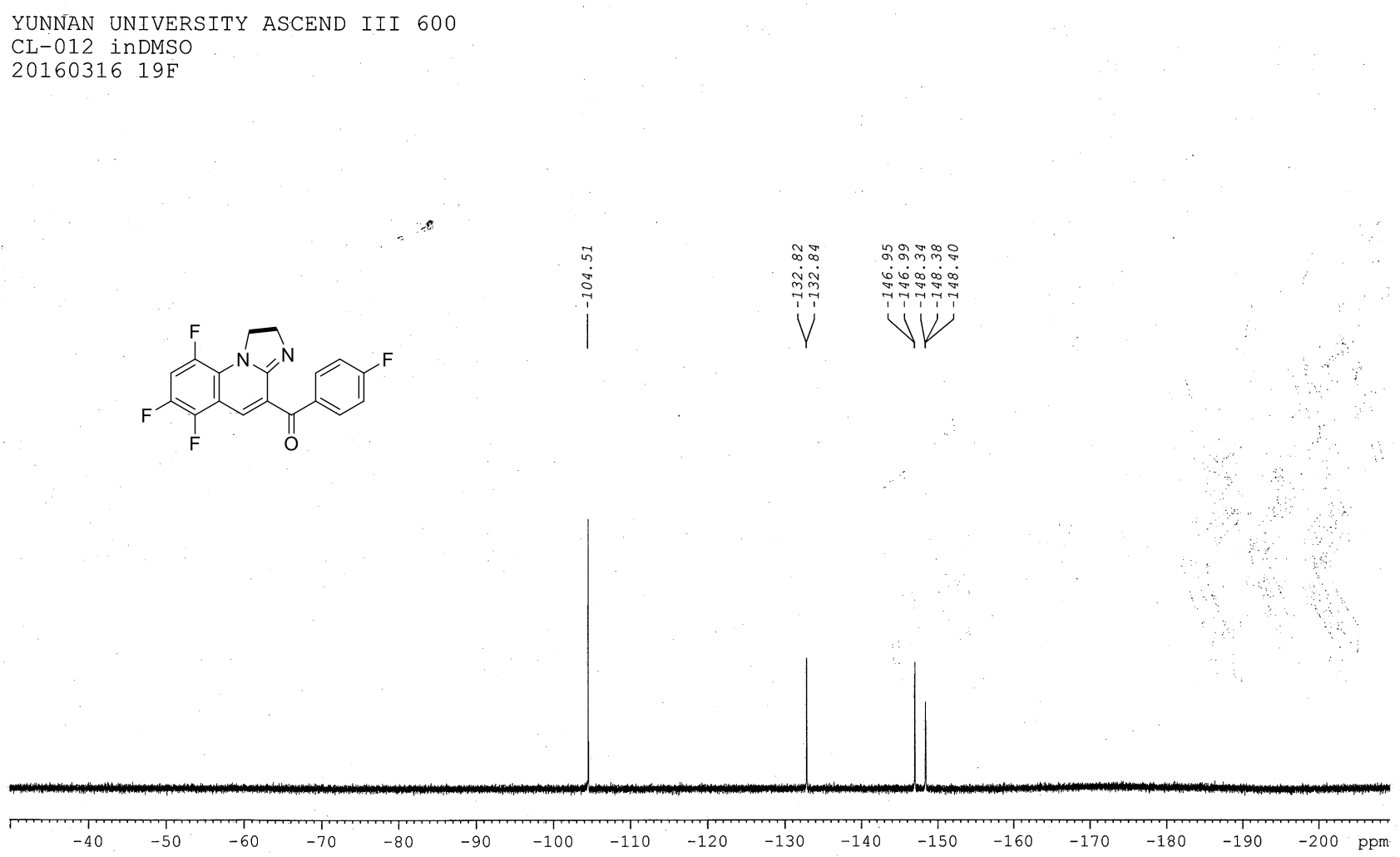


Figure S64. ^{19}F NMR (565 MHz, DMSO-d_6) spectra of compound **3ca**

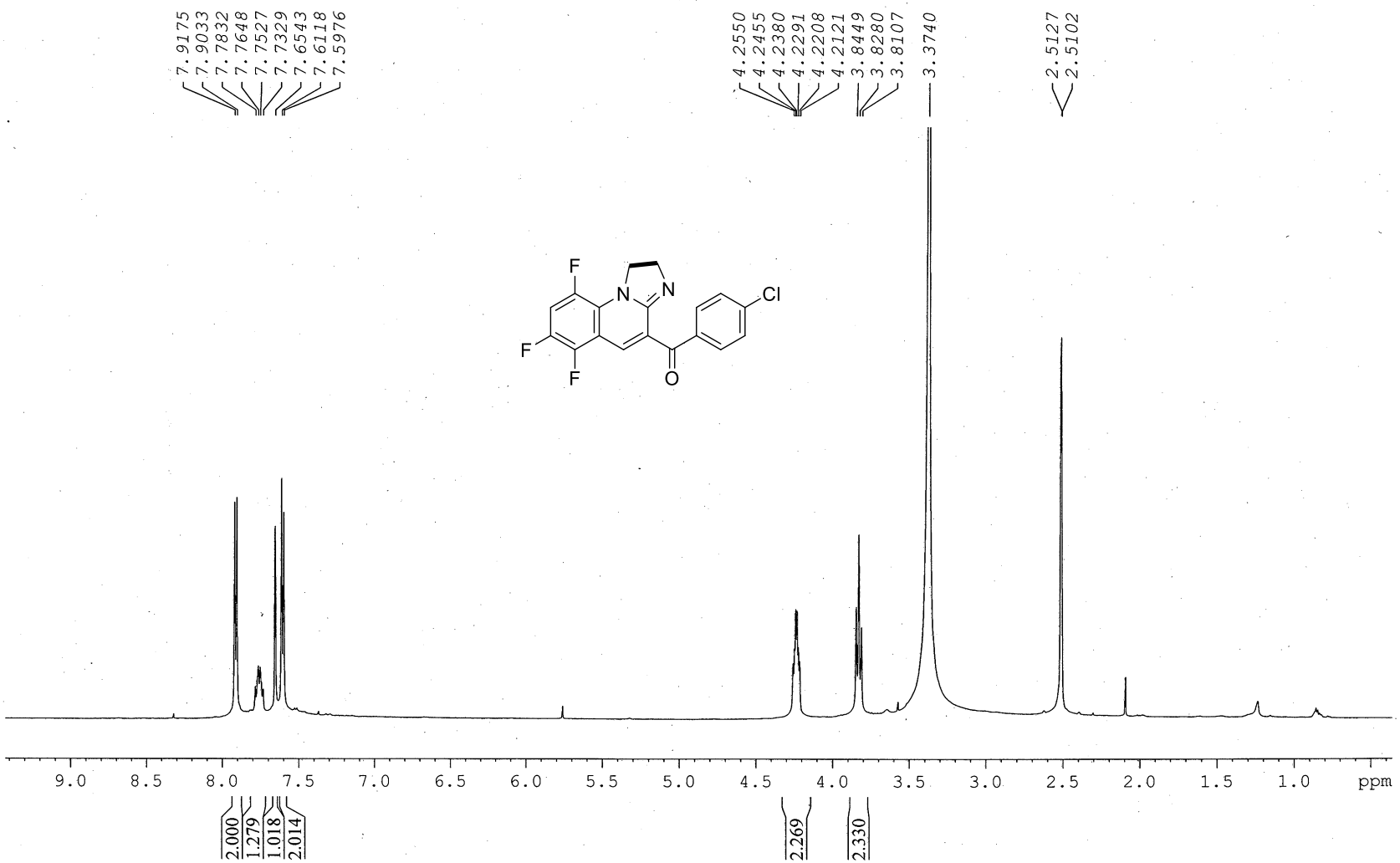


Figure S65. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3cb**

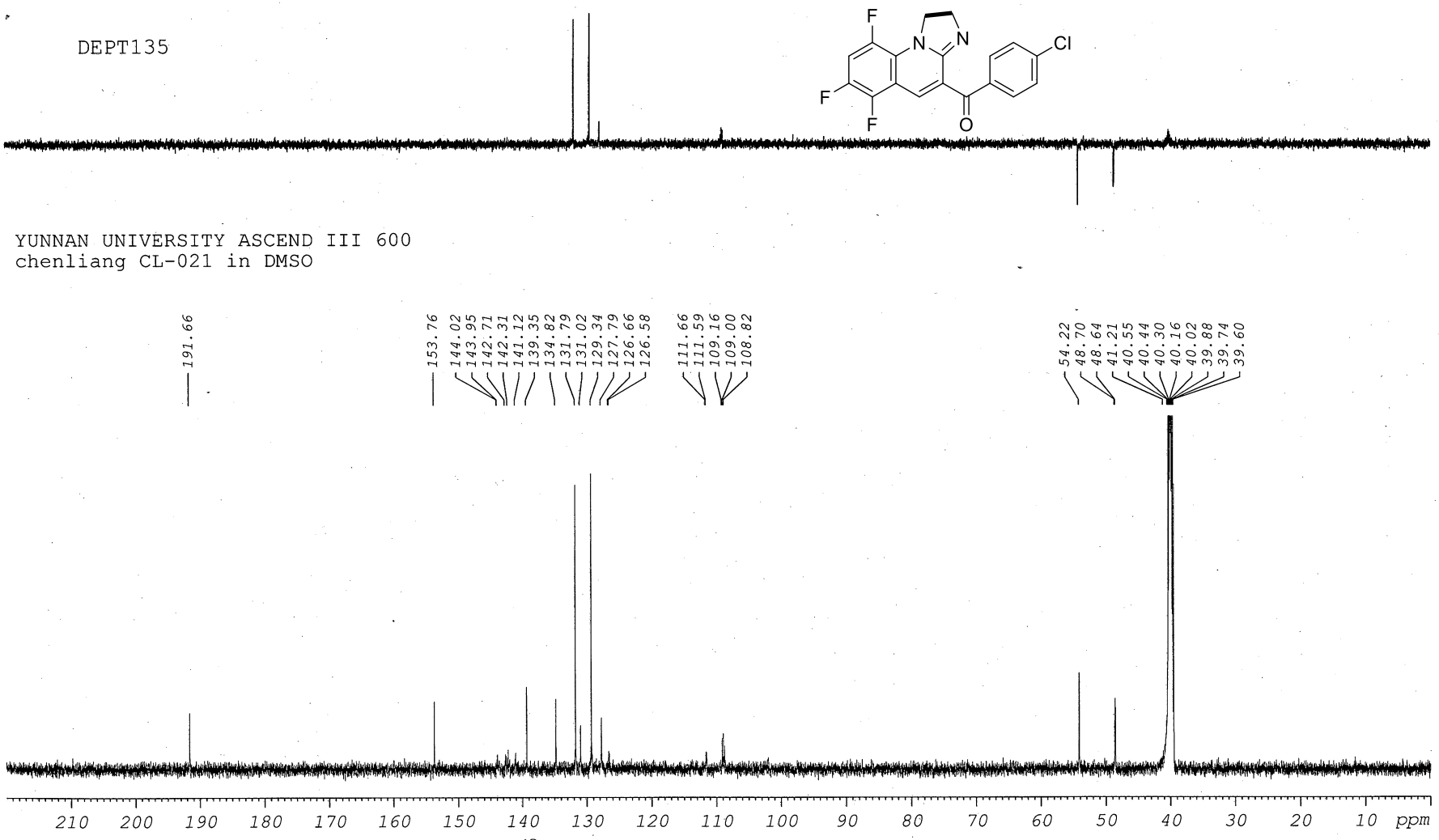


Figure S66. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3cb**

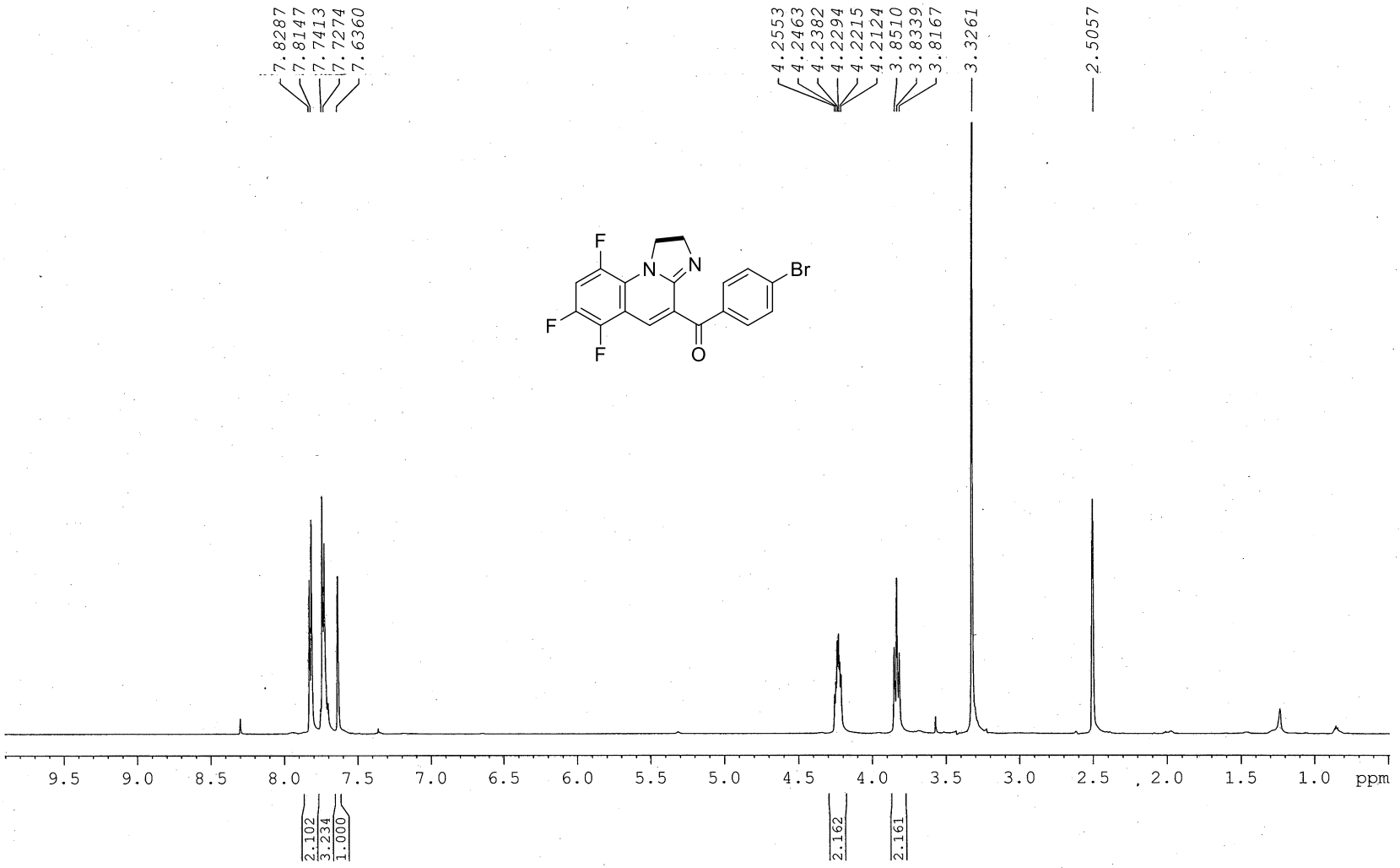


Figure S67. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3cc**

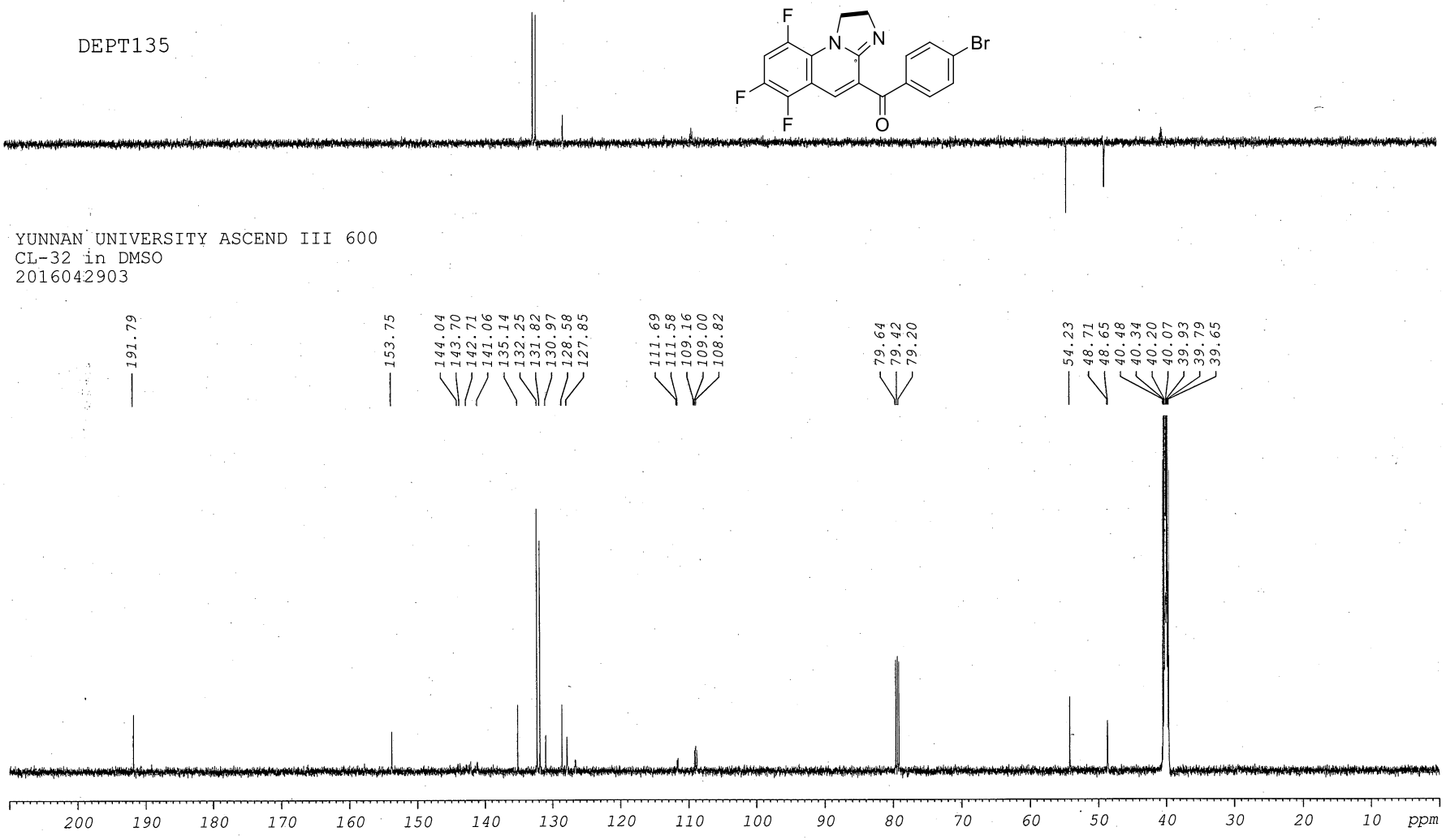


Figure S68. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3cc**

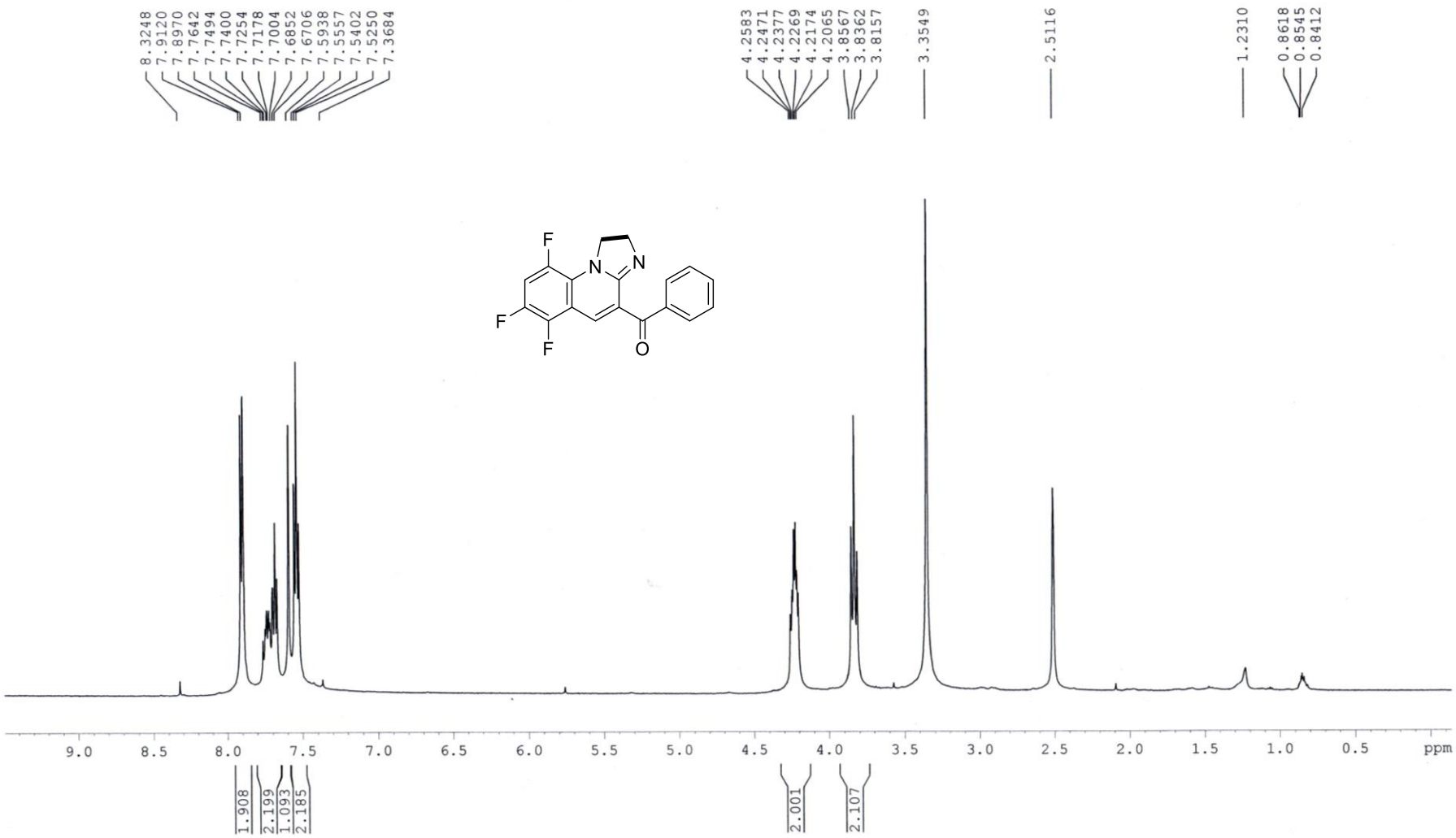


Figure S69. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3cd**

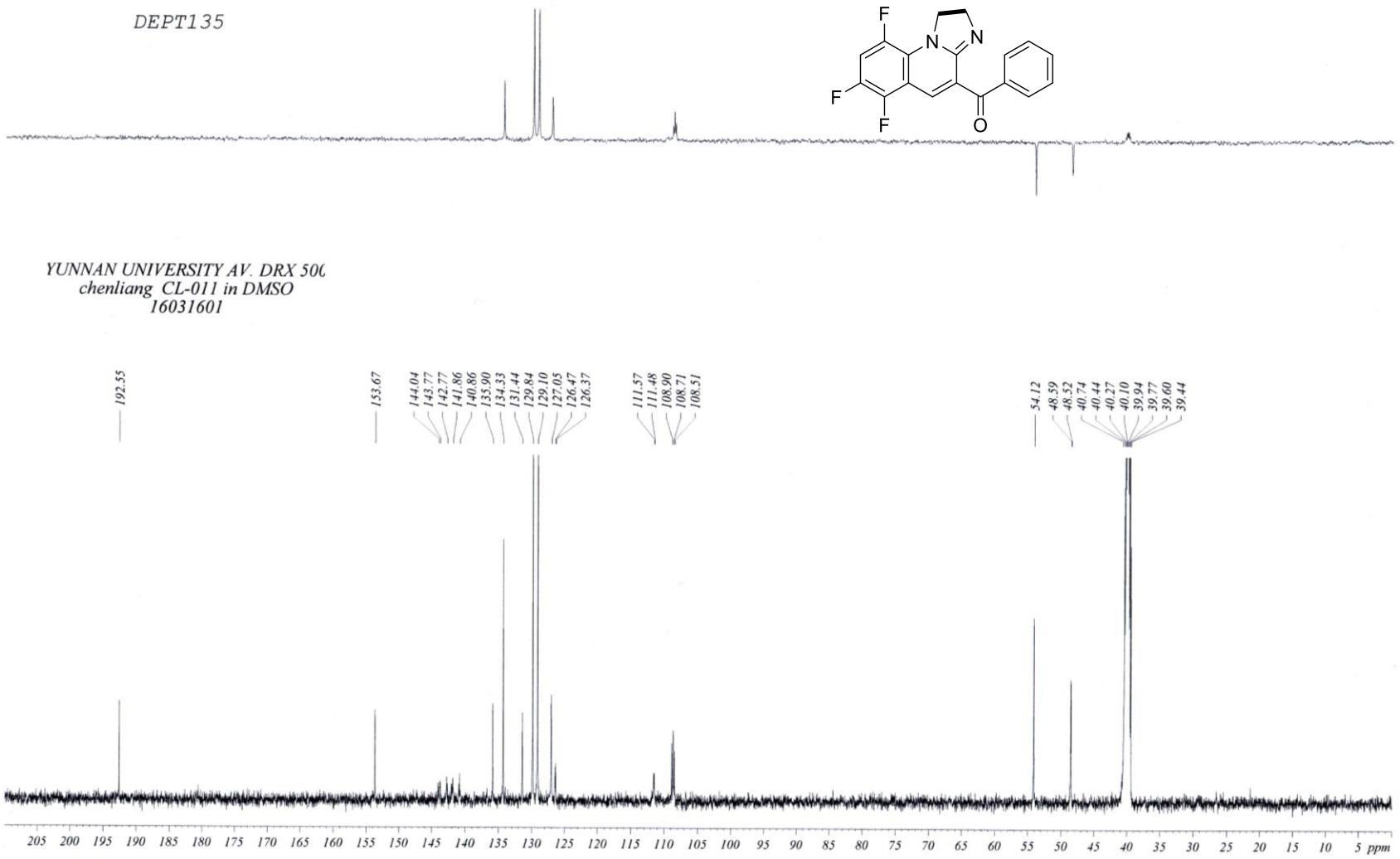


Figure S70. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3cd**

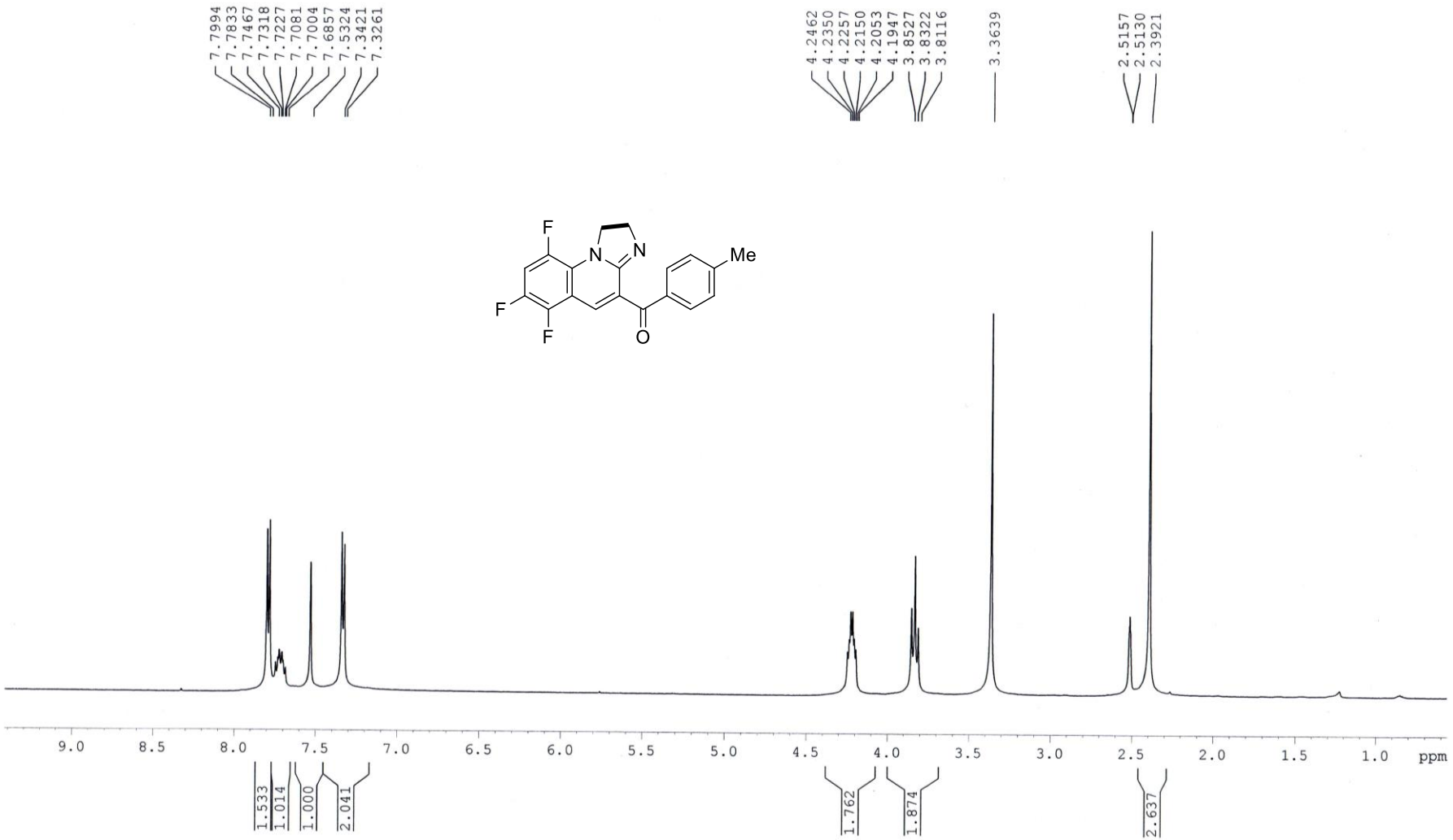


Figure S71. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3ce**

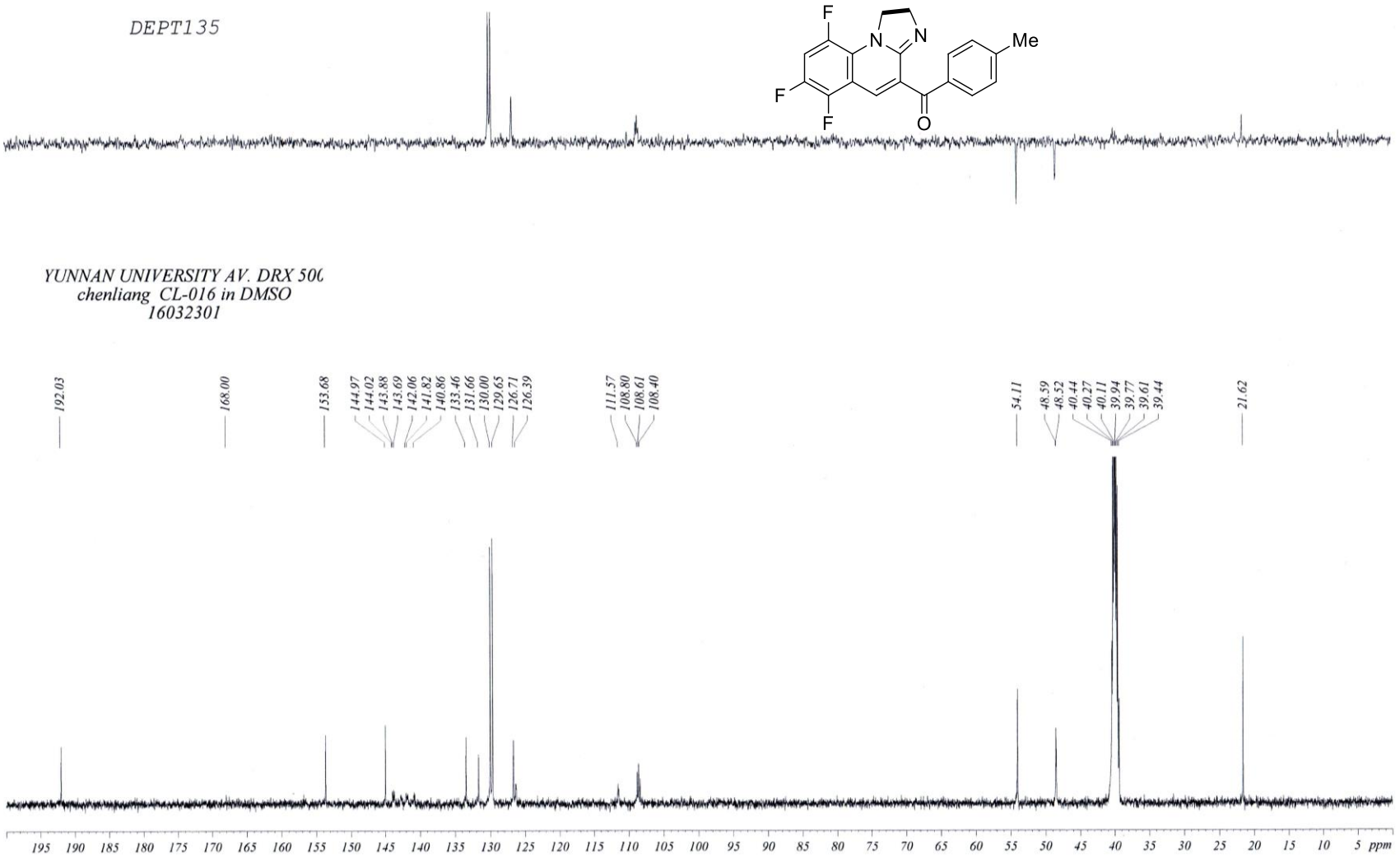


Figure S72. ^{13}C NMR (125MHz, DMSO-d_6) spectra of compound **3ce**

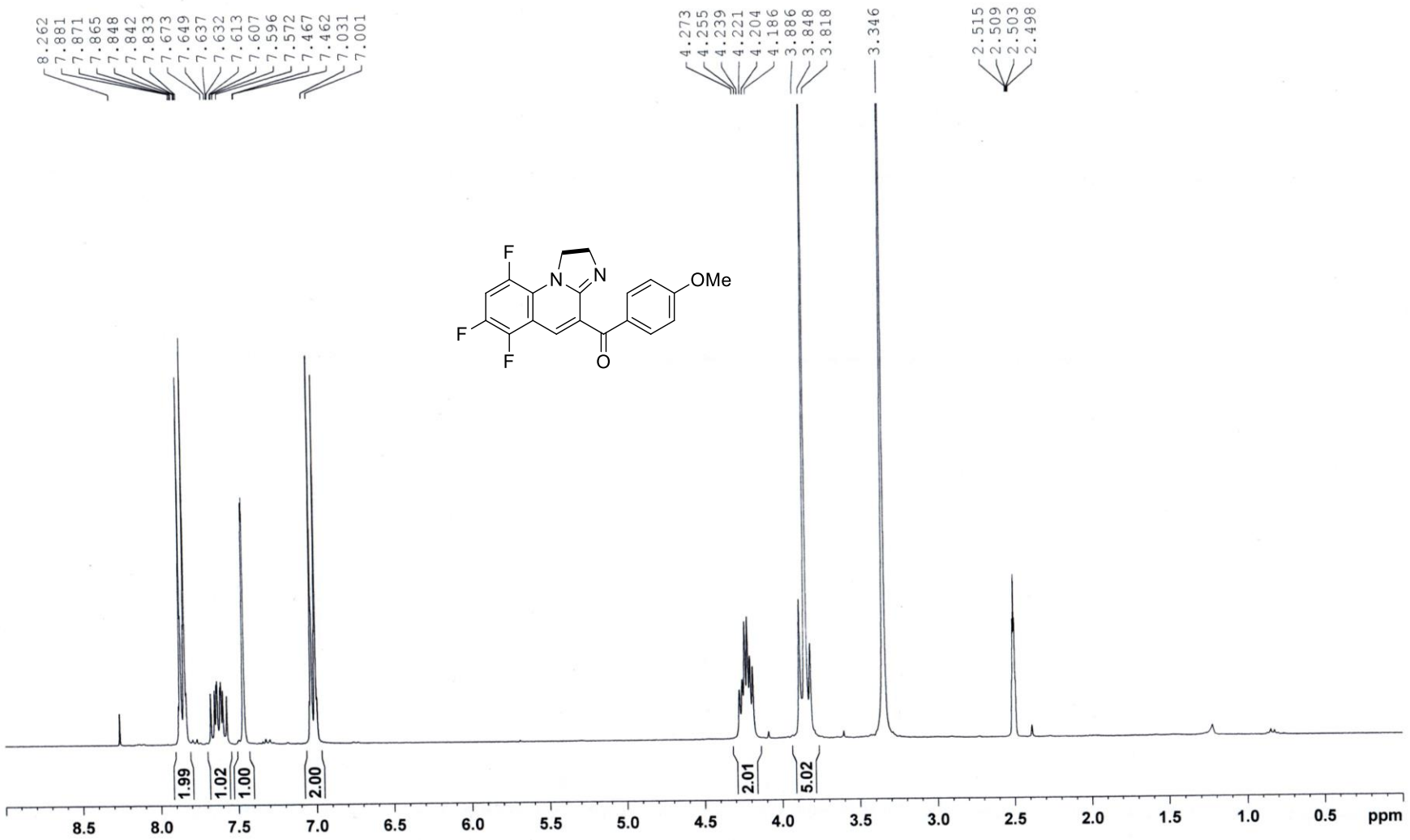


Figure S73. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3cf**

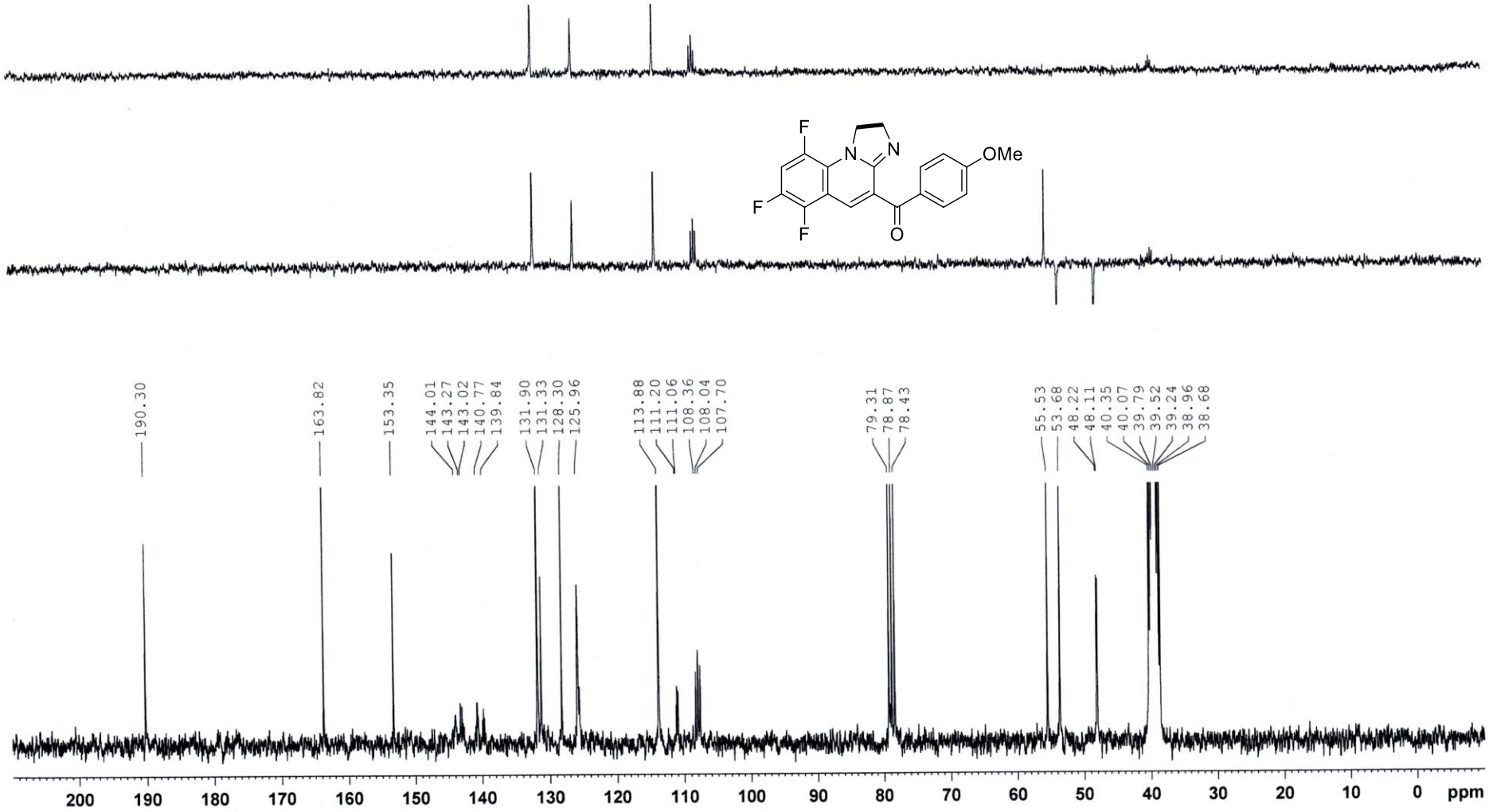


Figure S74. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3cf**

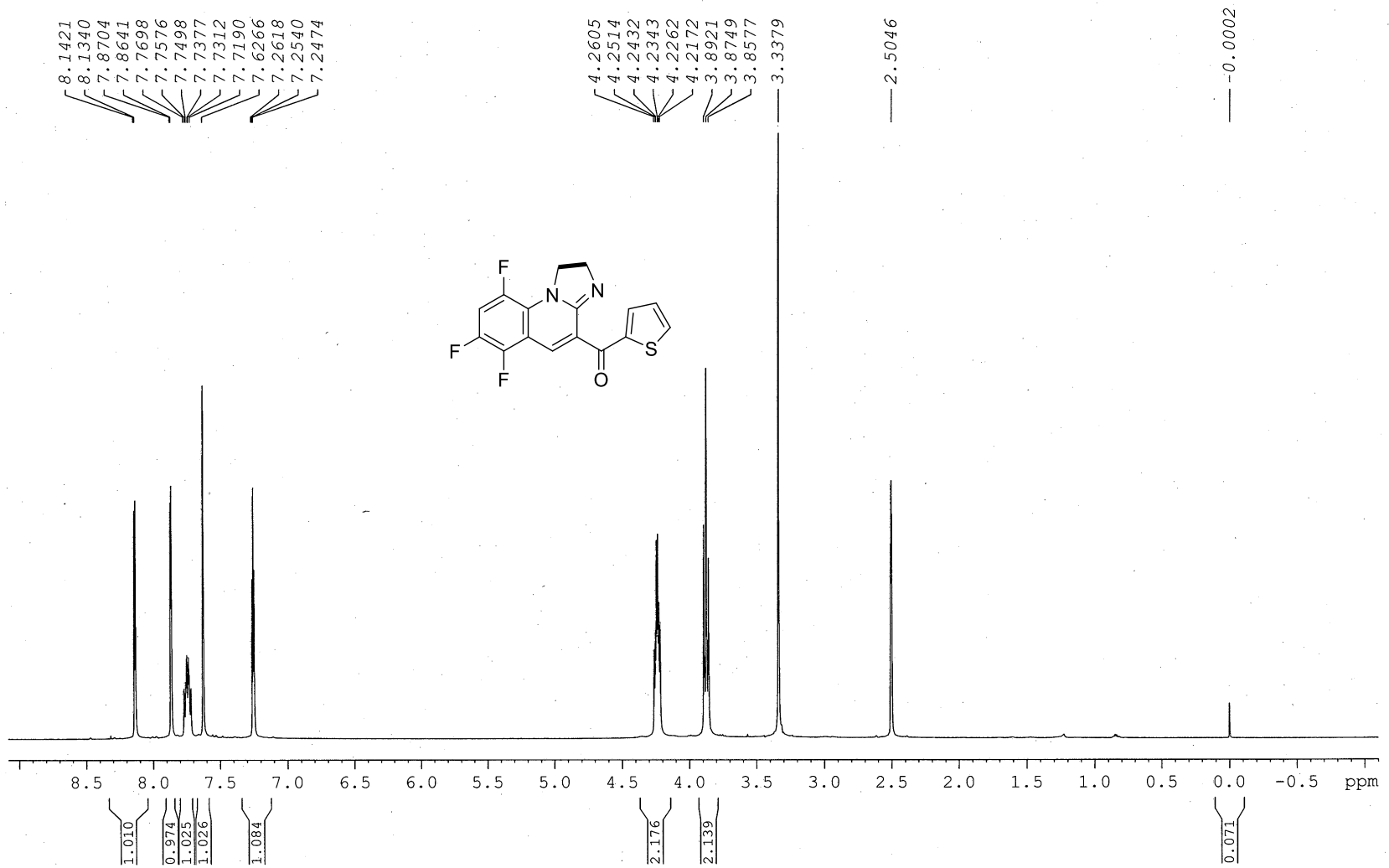


Figure S75. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3cg**

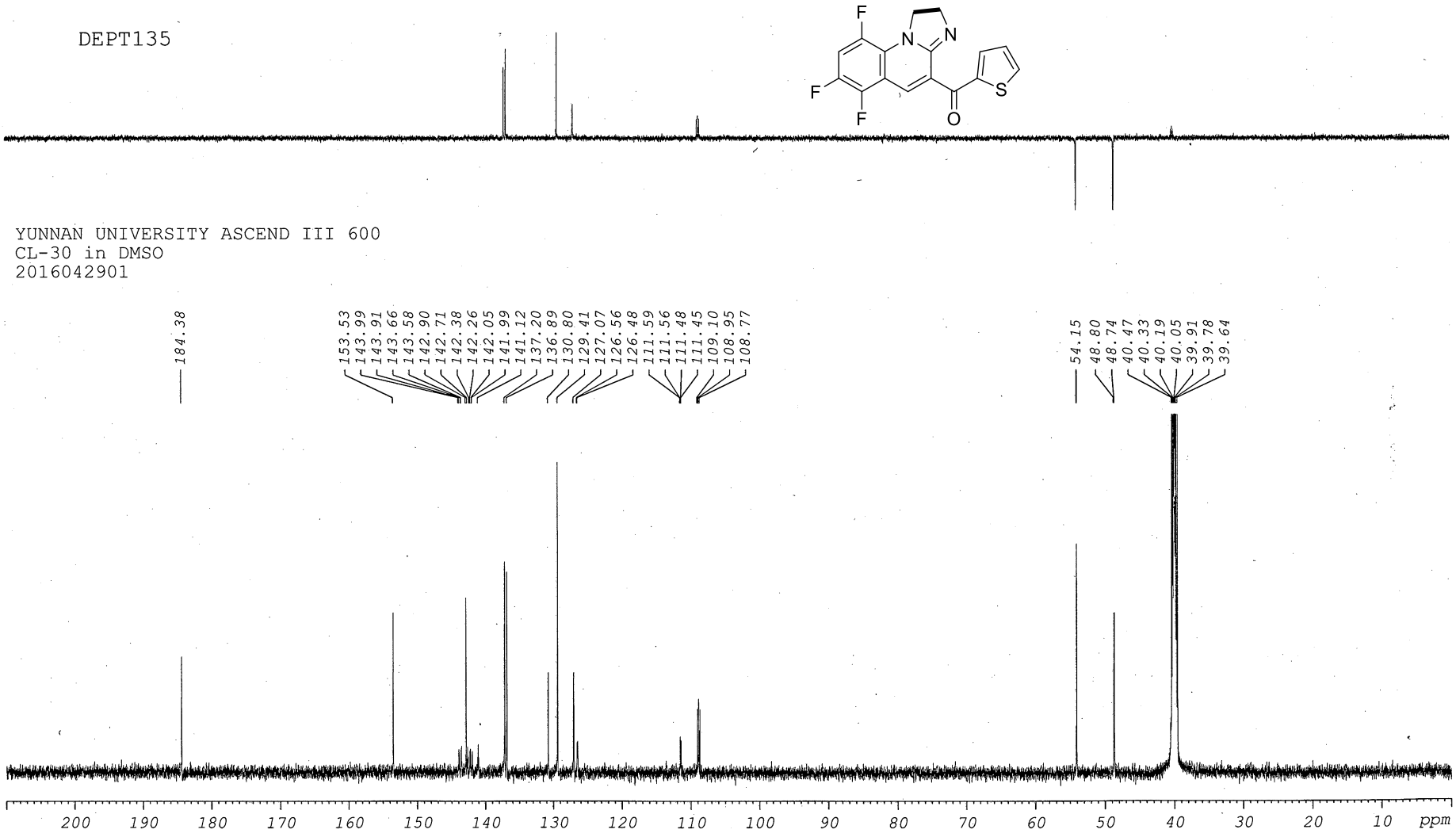


Figure S76. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3cg**

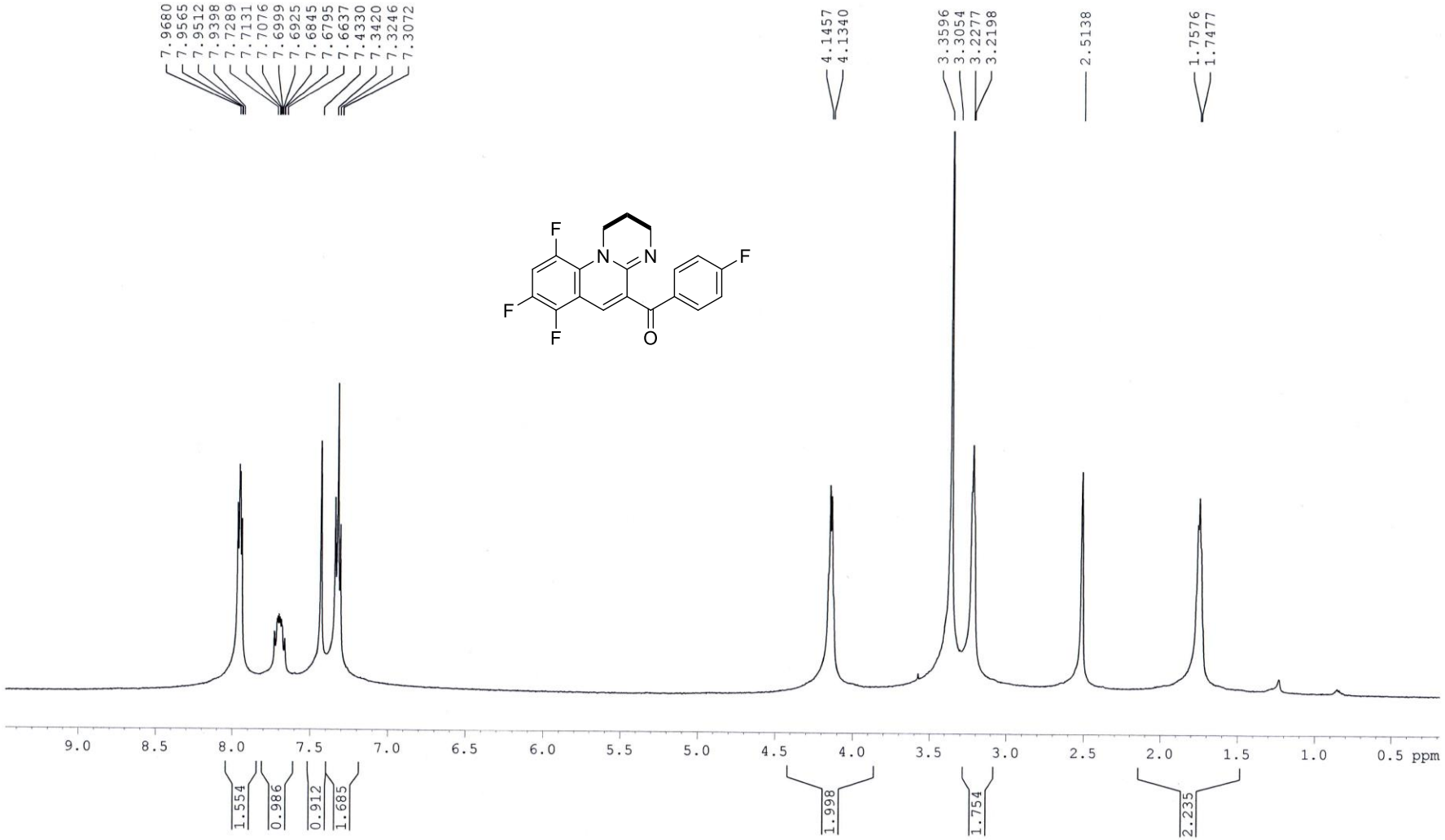


Figure S77. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3ch**

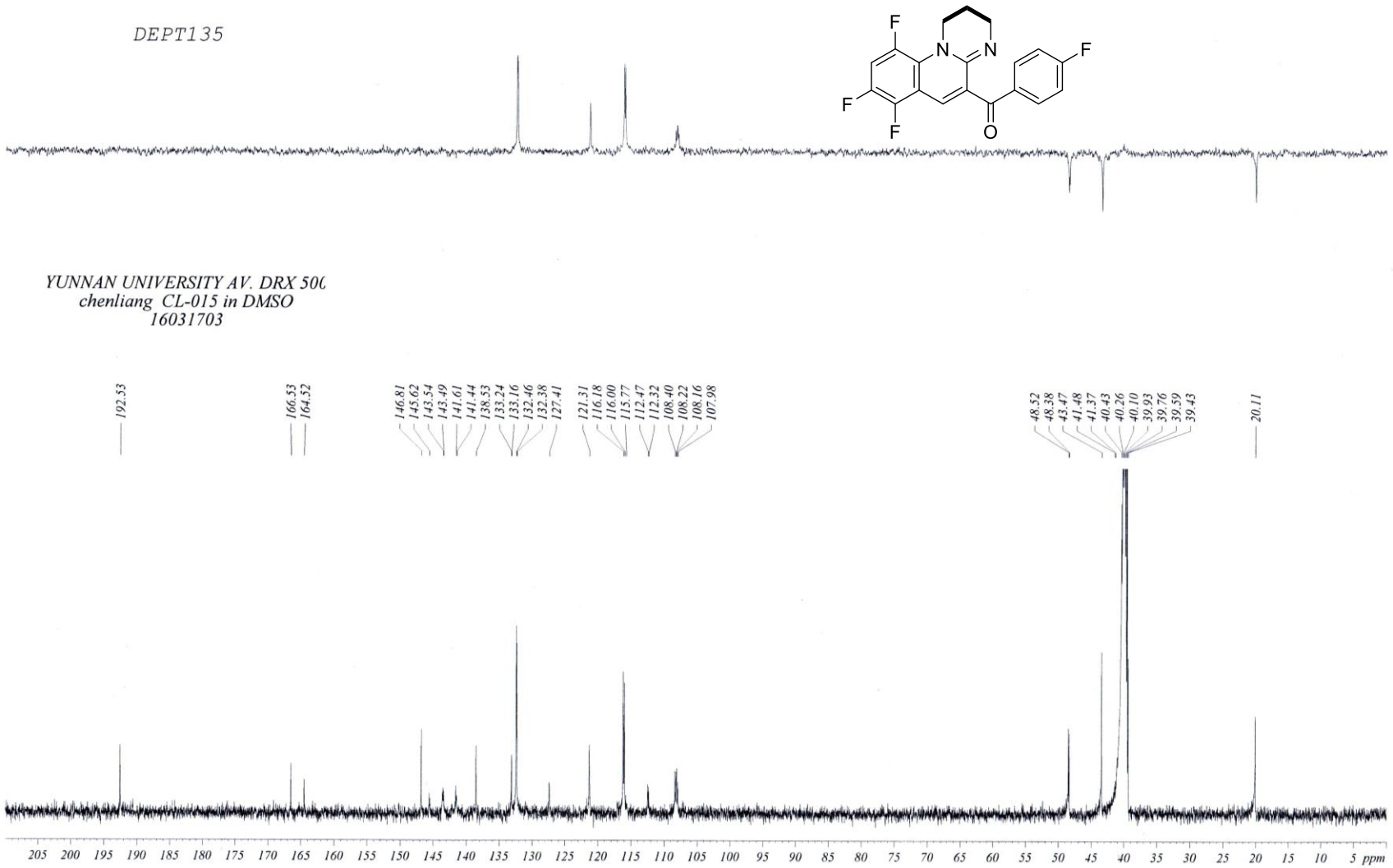


Figure S78. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3ch**

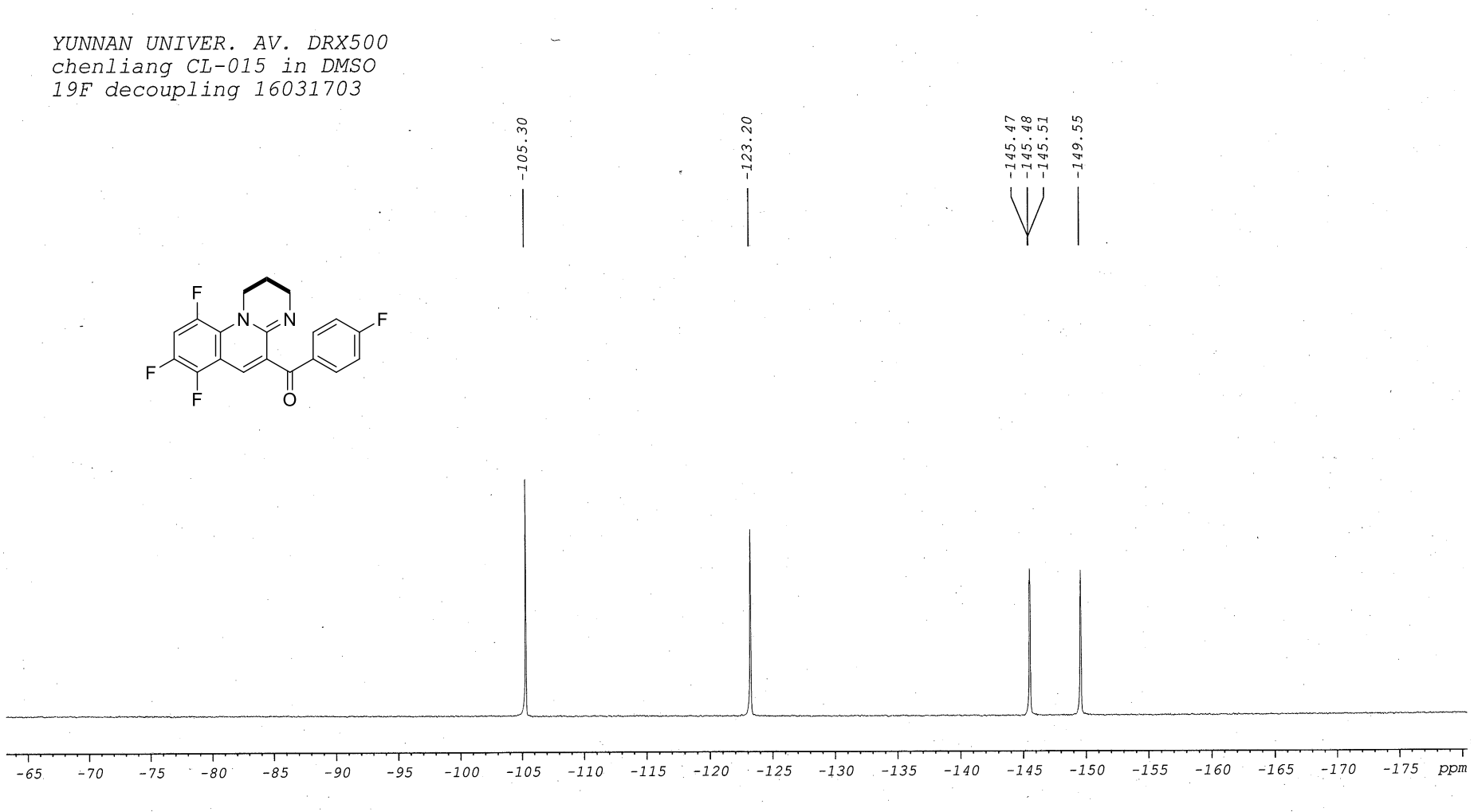


Figure S79. ^{19}F NMR (470 MHz, DMSO-d_6) spectra of compound **3ch**

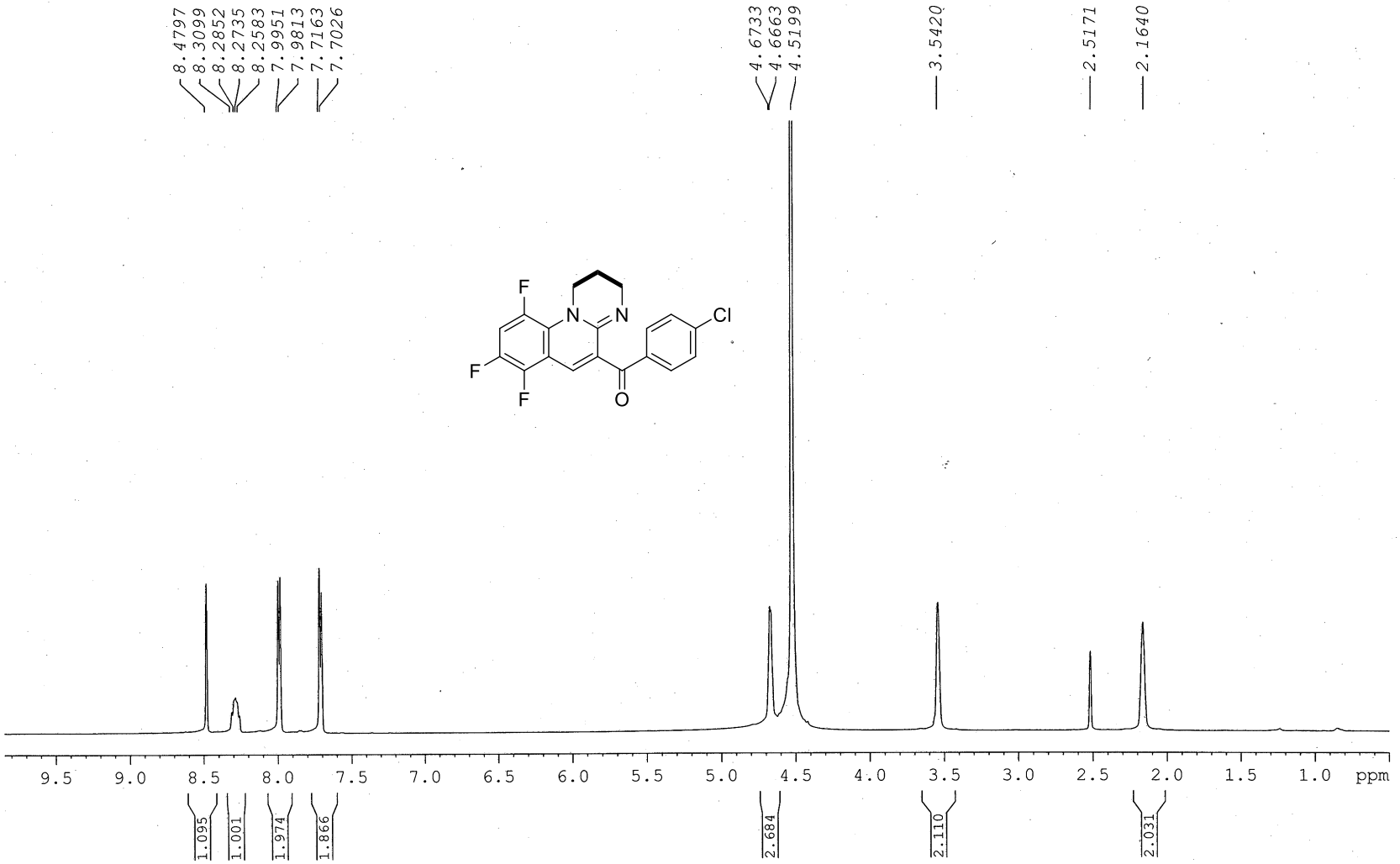


Figure S80. ^{1}H NMR (600 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **3ci**

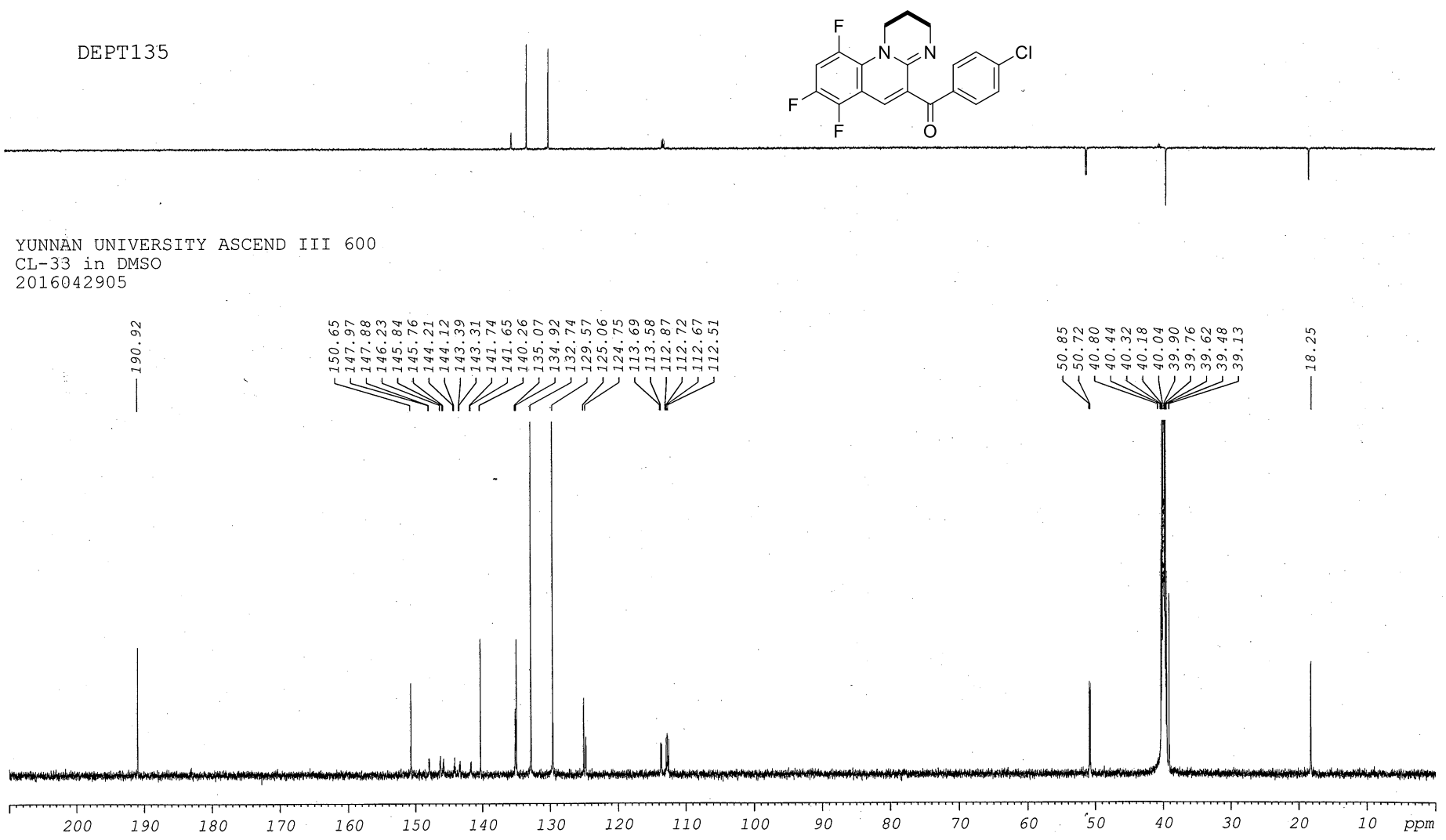


Figure S81. ^{13}C NMR (150 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **3ci**

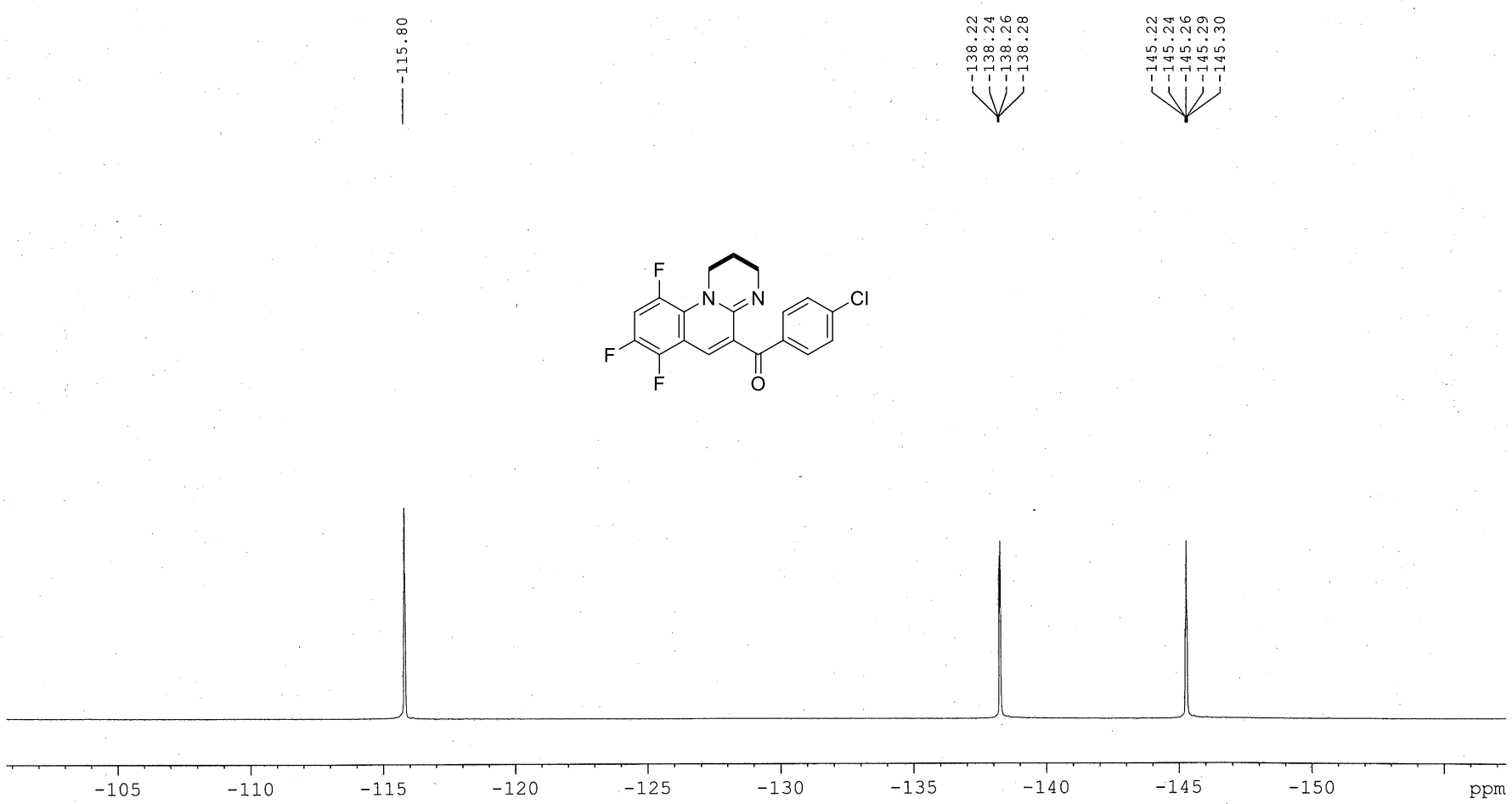


Figure S82. ^{19}F NMR (565 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **3ci**

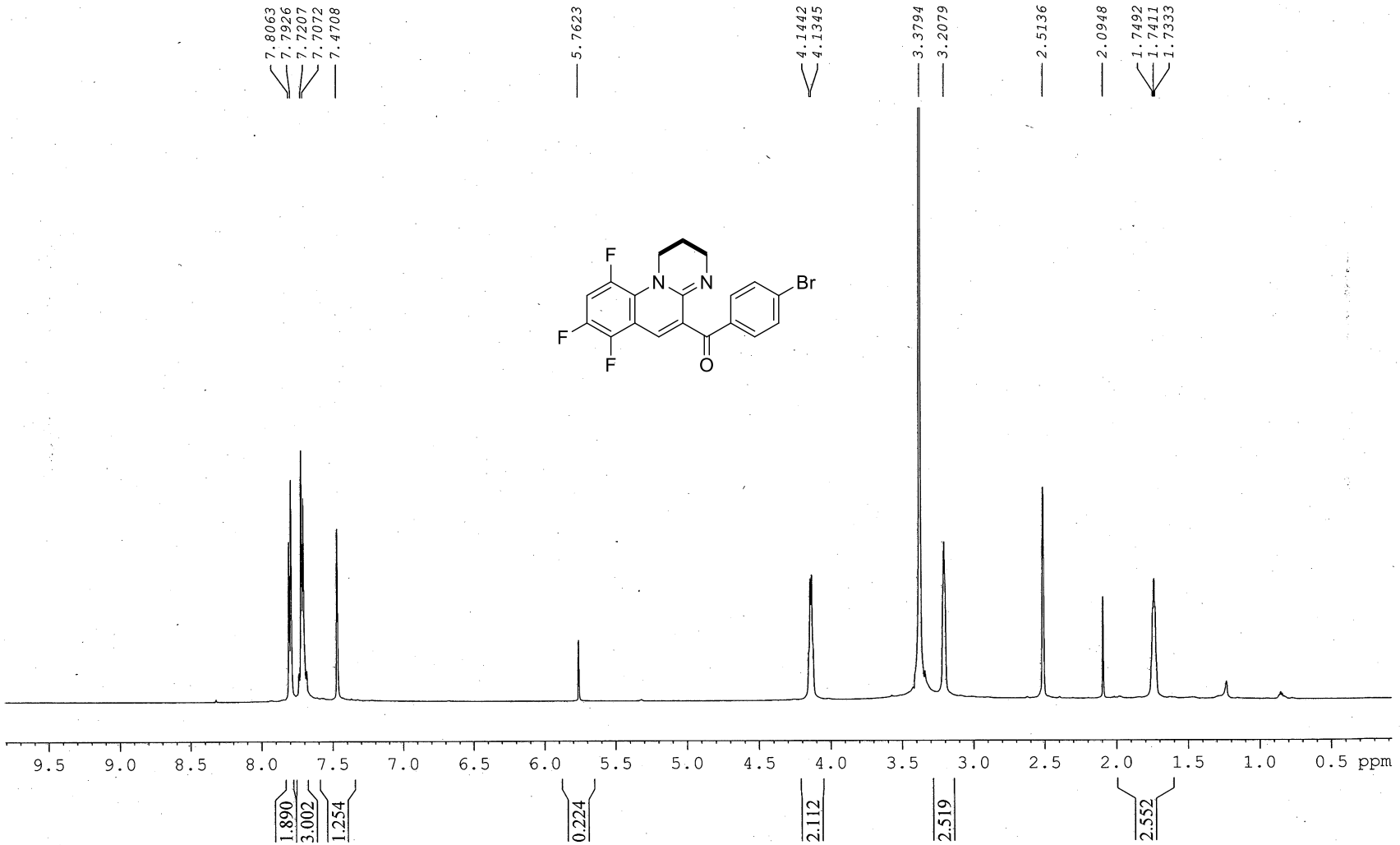


Figure S83. ^{1}H NMR (600 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **3cj**

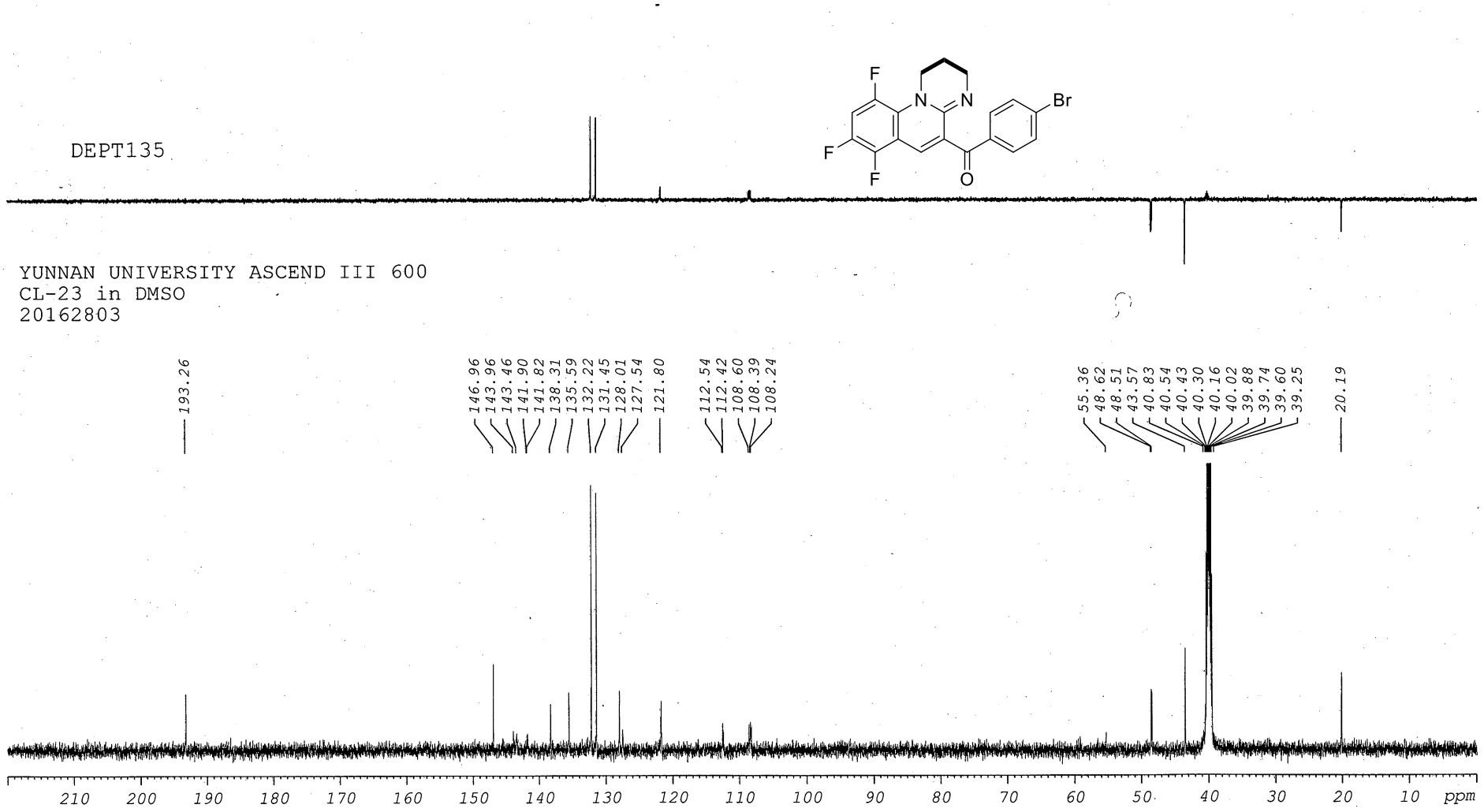


Figure S84. ^{13}C NMR (150 MHz, DMSO-d_6 + $HClO_4$) spectra of compound **3cj**

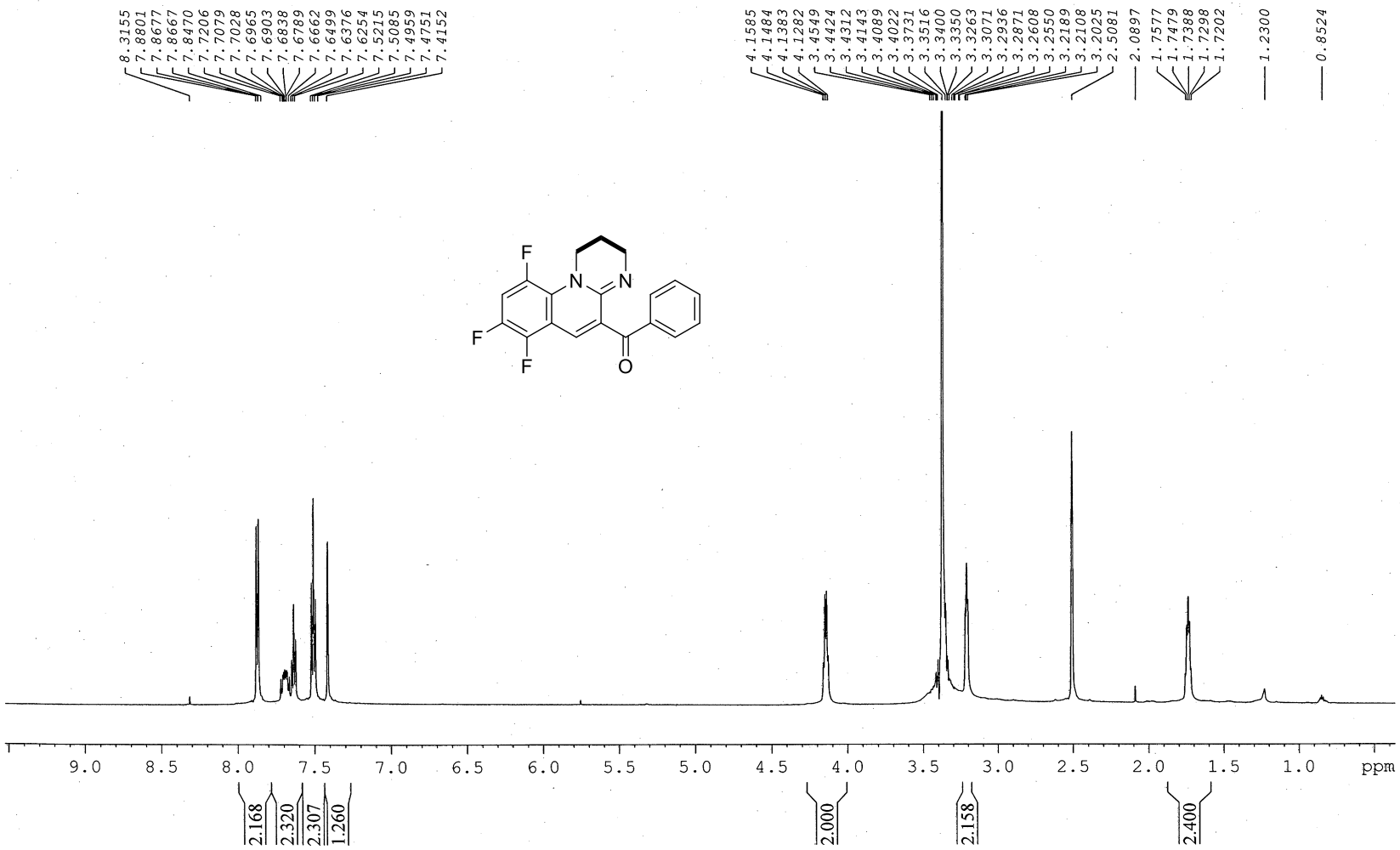


Figure S85. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3ck**

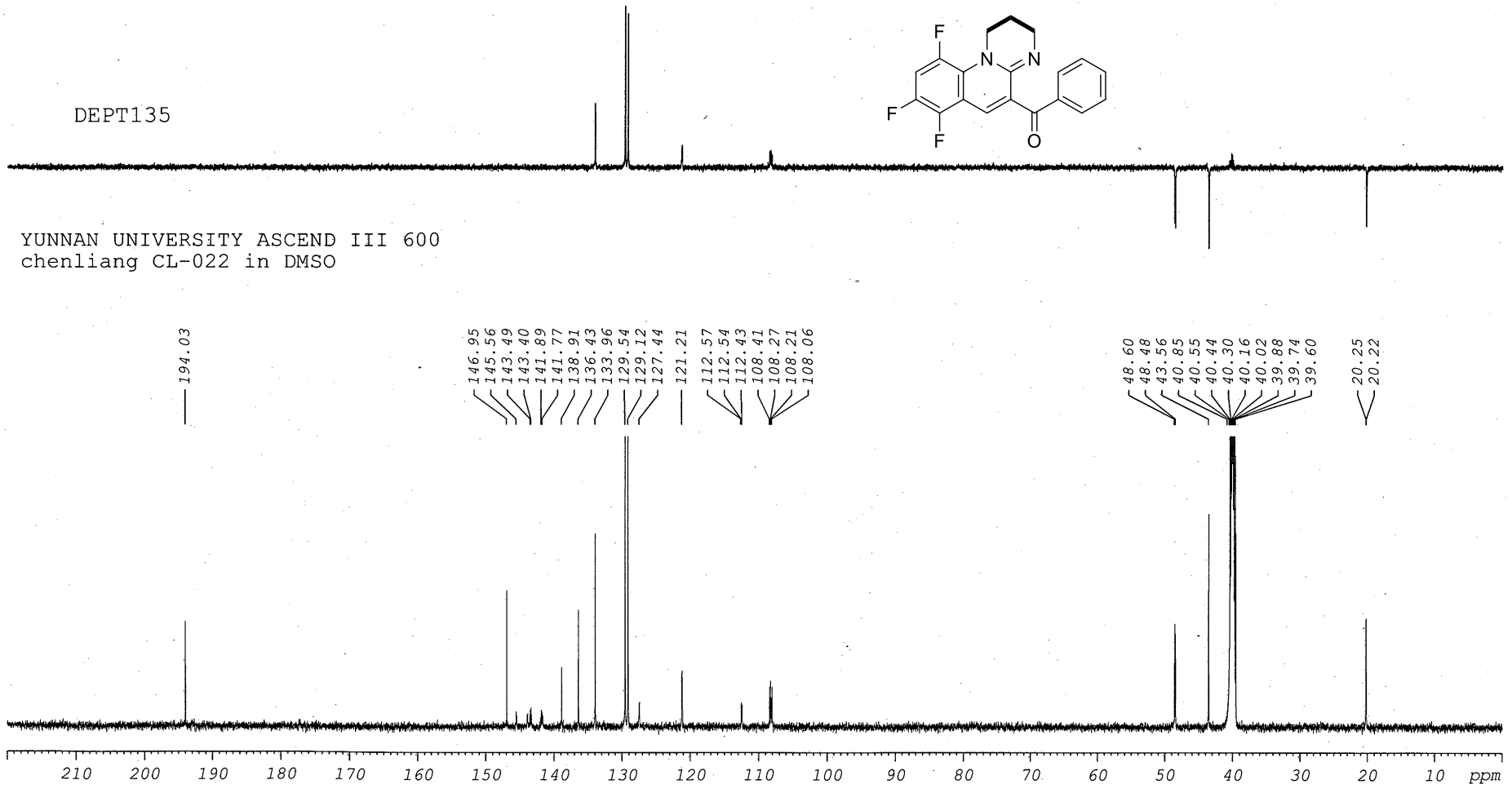


Figure S86. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3ck**

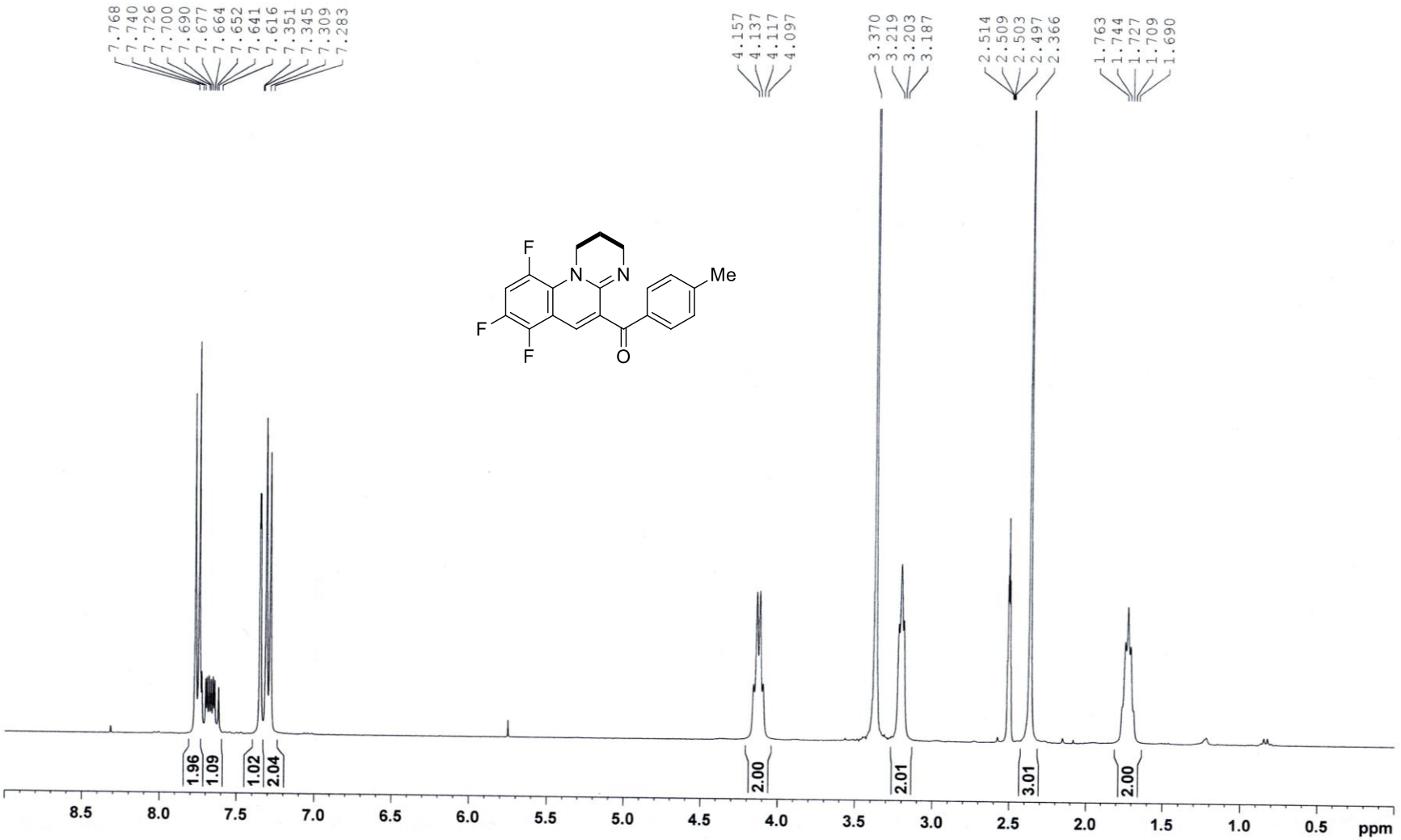


Figure S87. ^{1}H NMR (300 MHz, DMSO-d_6) spectra of compound **3cl**

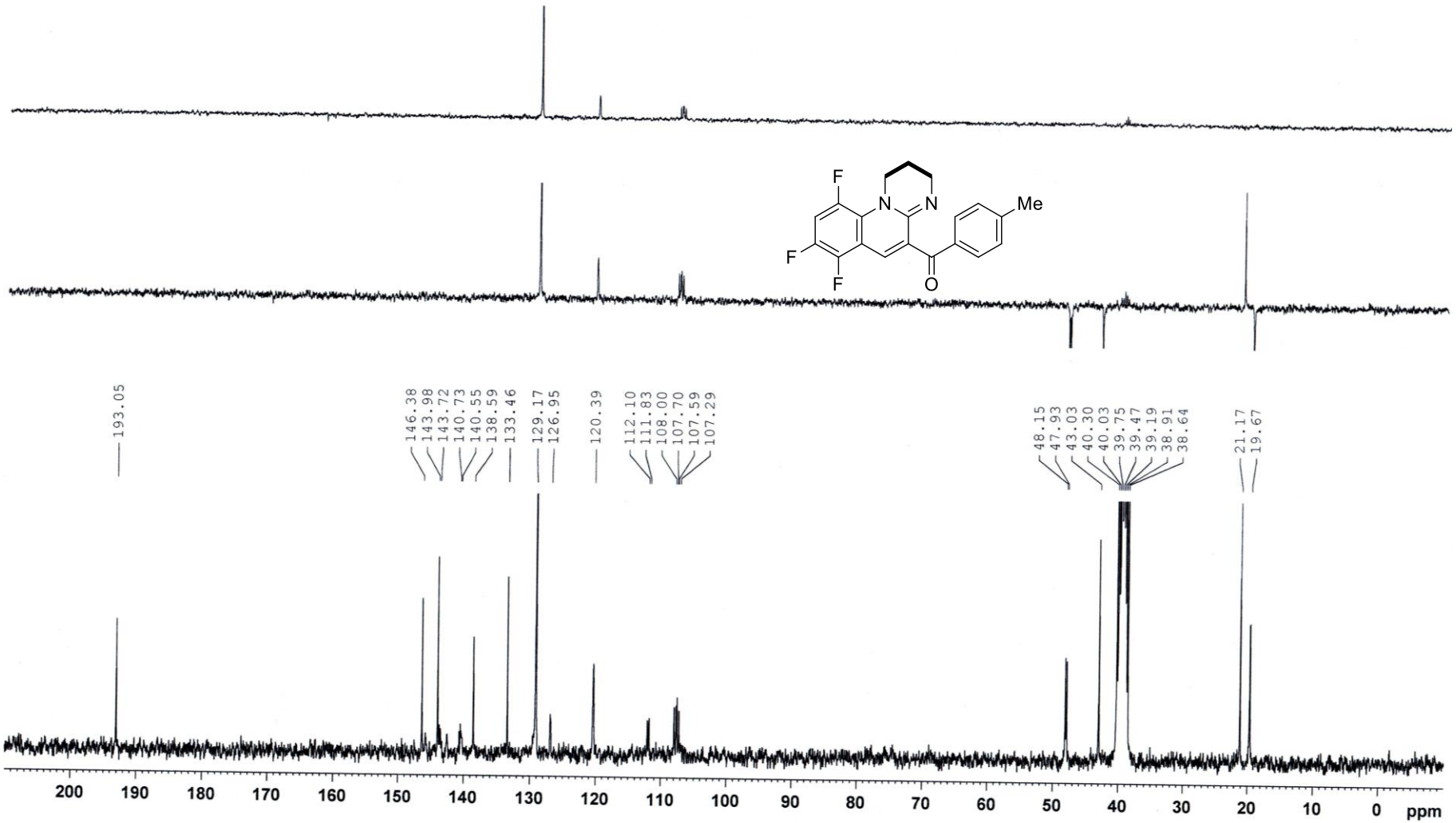


Figure S88. ^{13}C NMR (75 MHz, DMSO-d_6) spectra of compound **3cl**

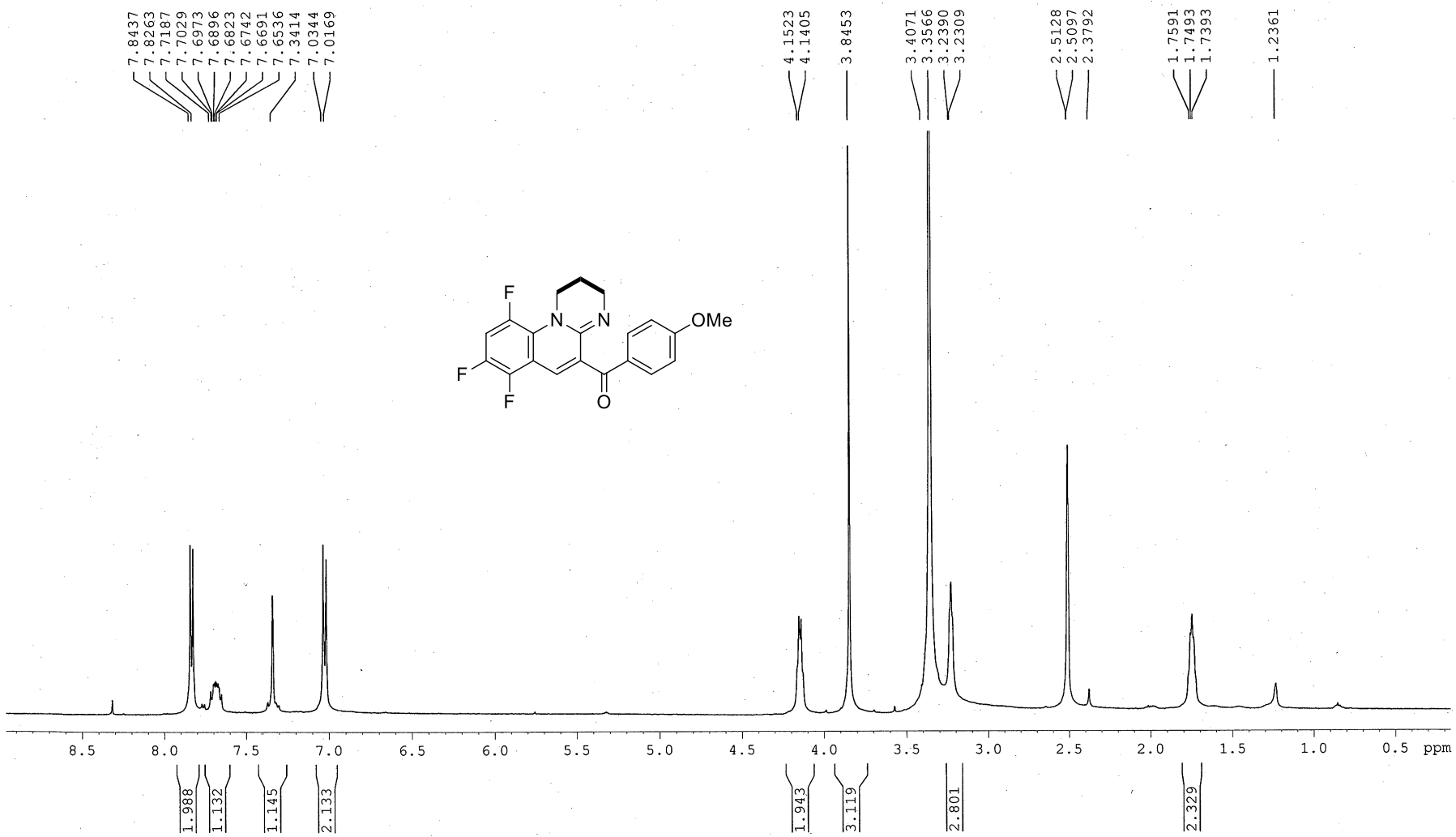


Figure S89. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **3cm**

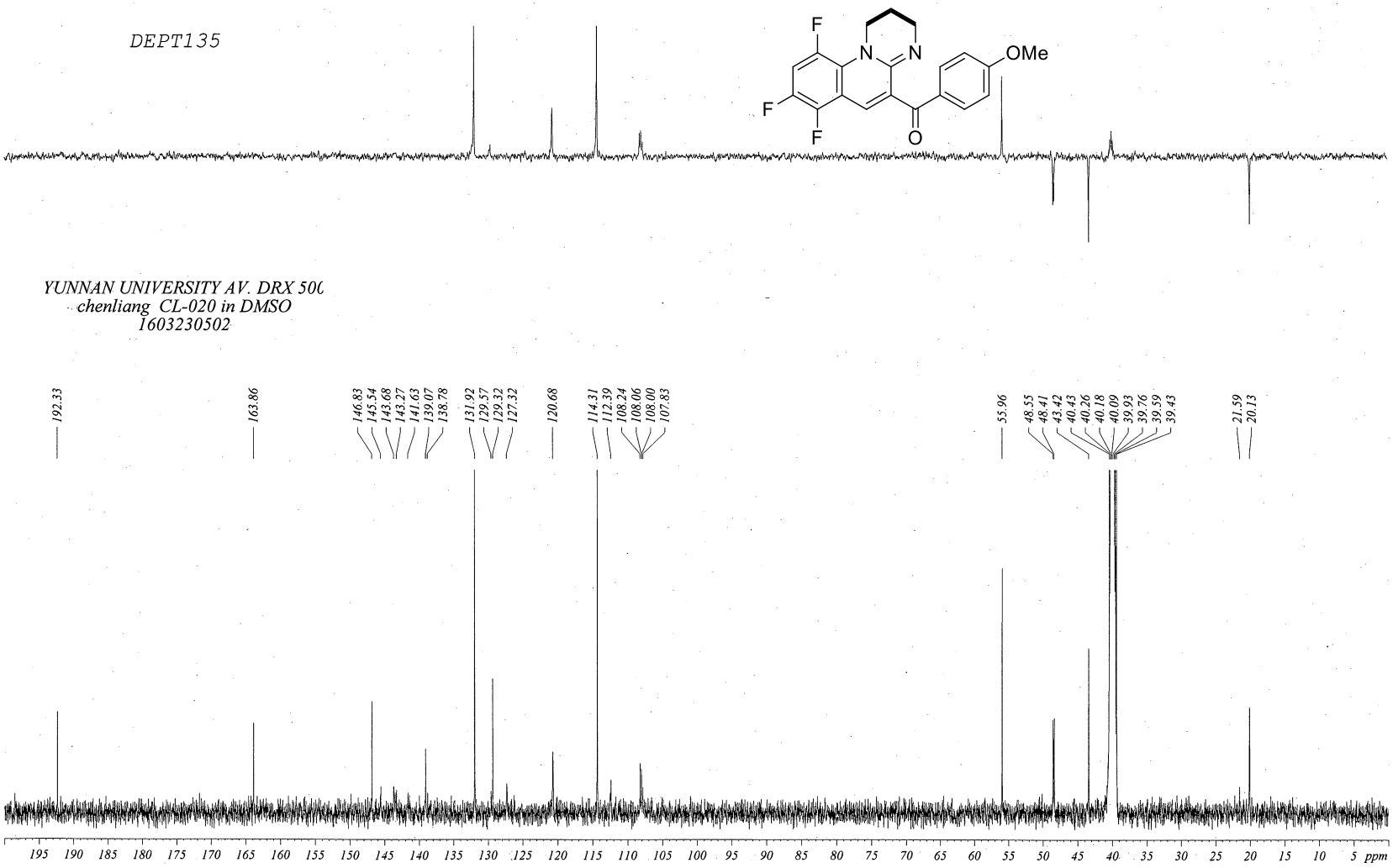


Figure S90. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **3cm**

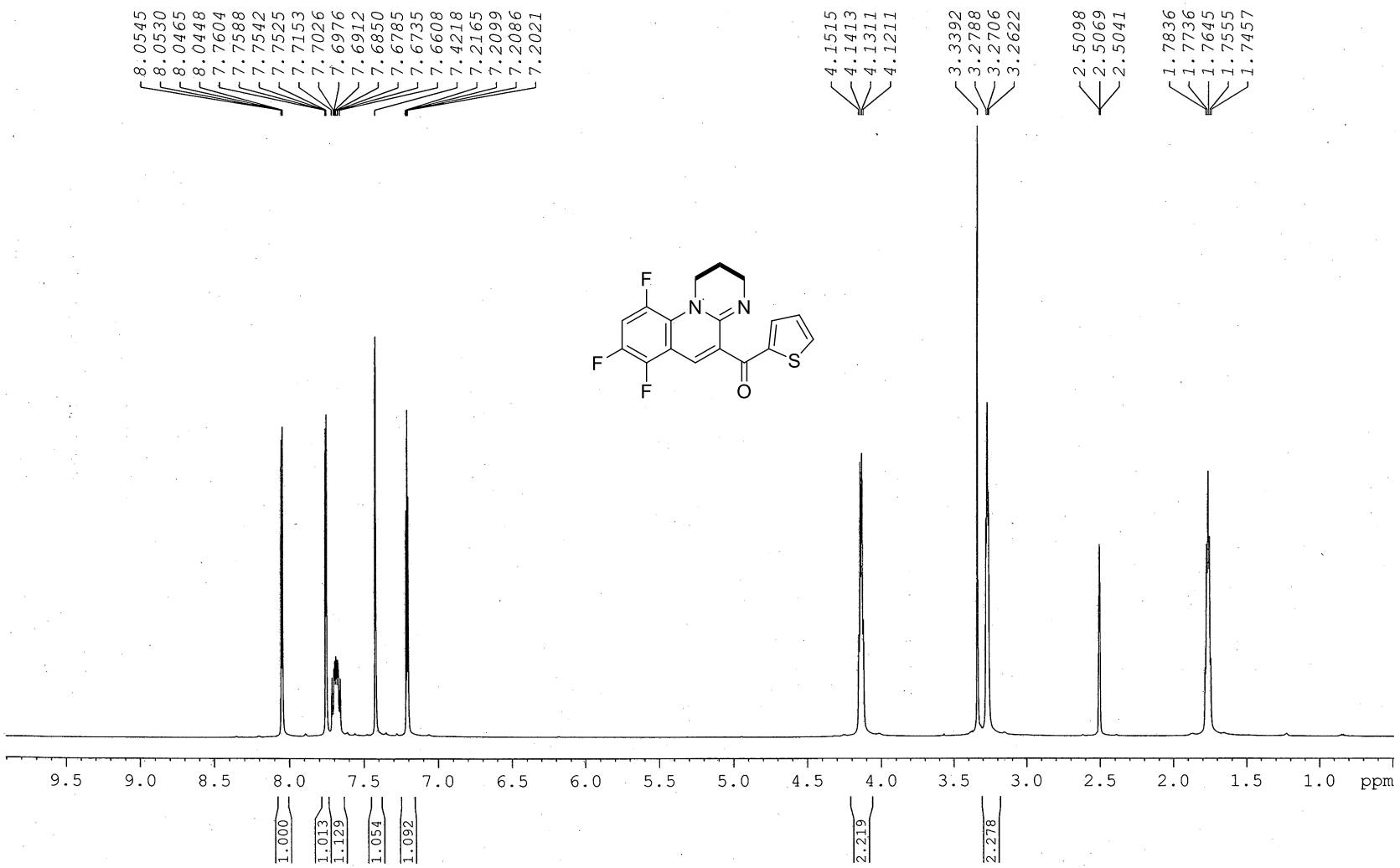


Figure S91. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **3cn**

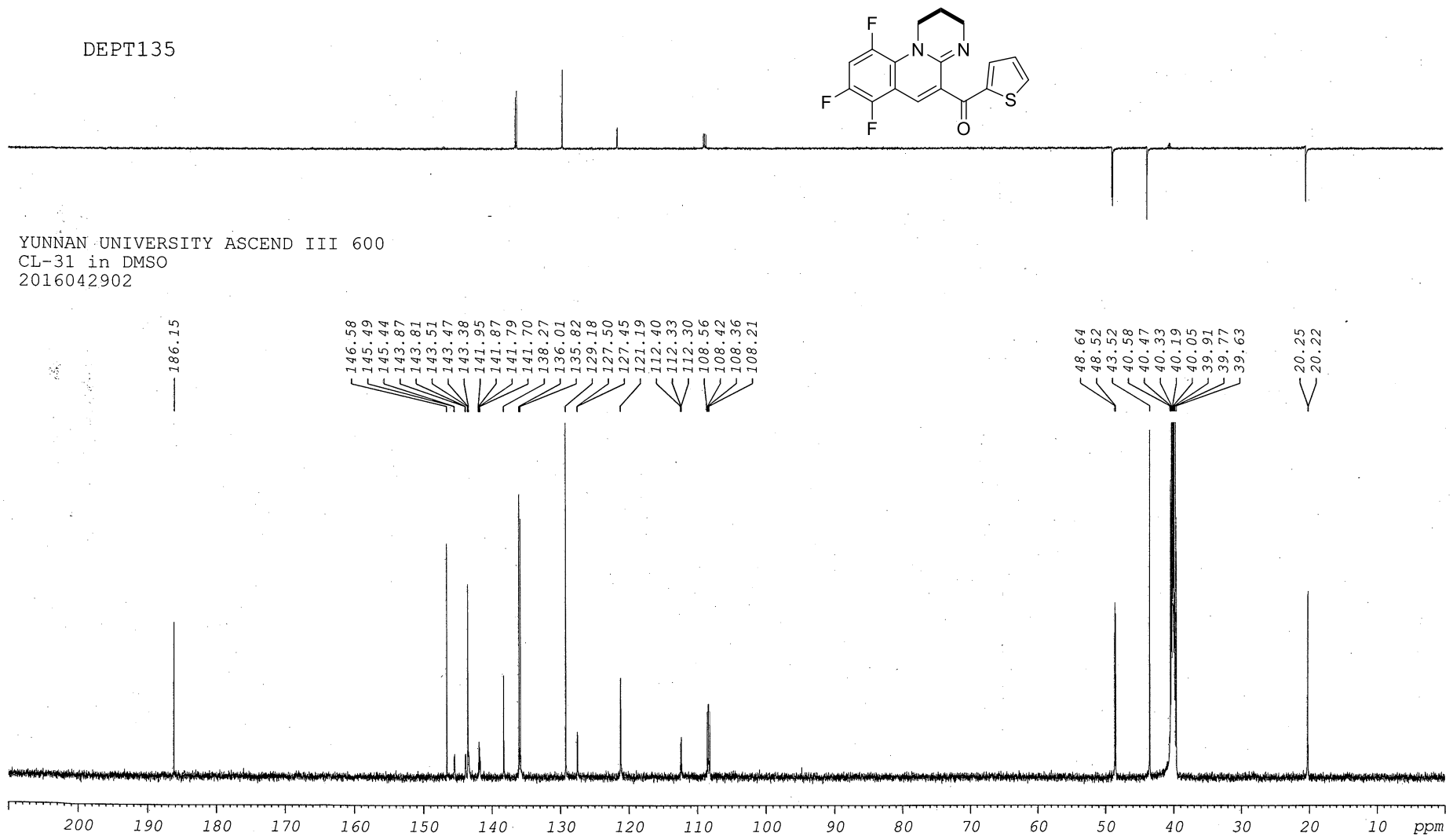


Figure S92. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **3cn**

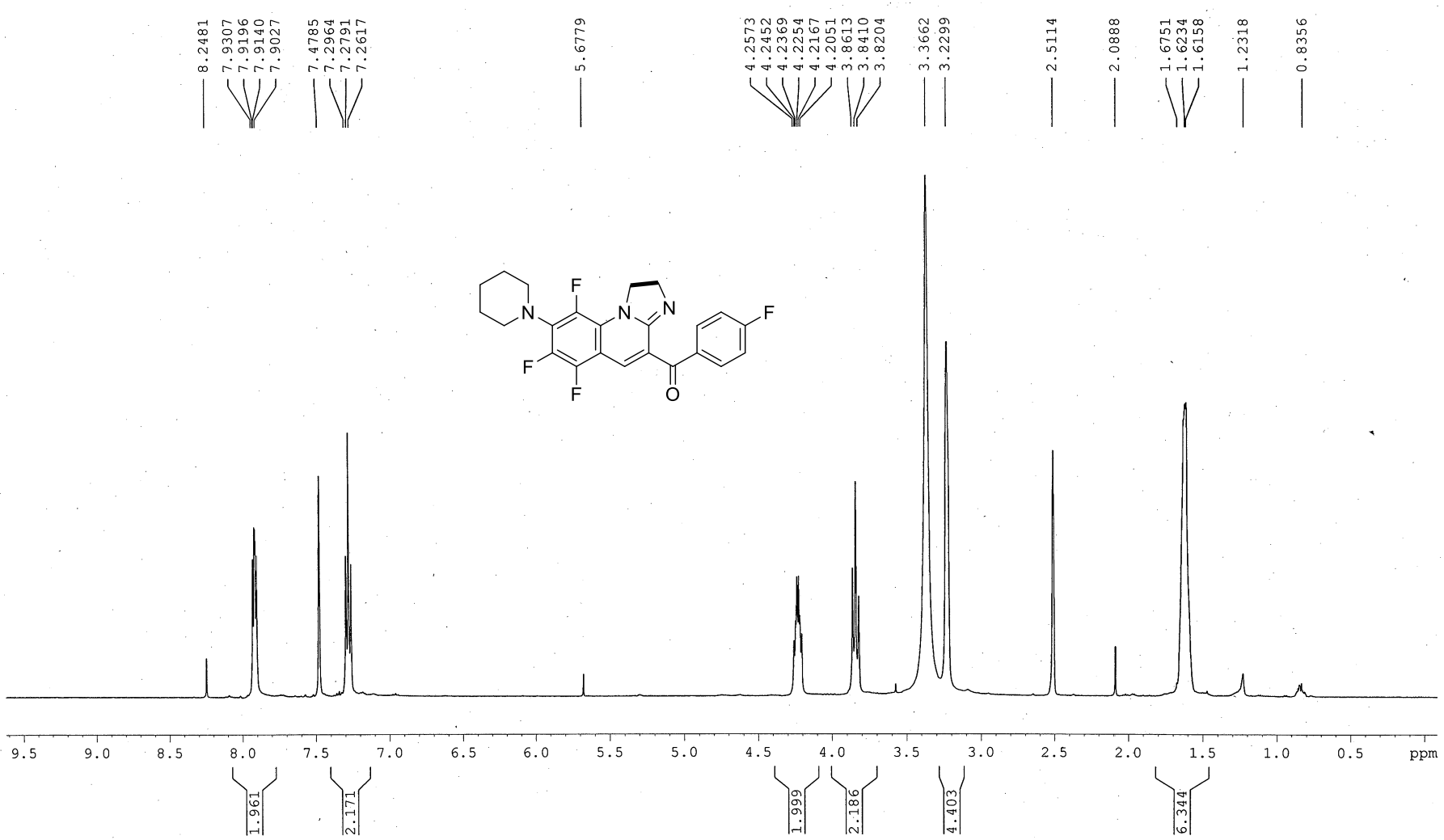


Figure S93. ^{1}H NMR (500 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4da**

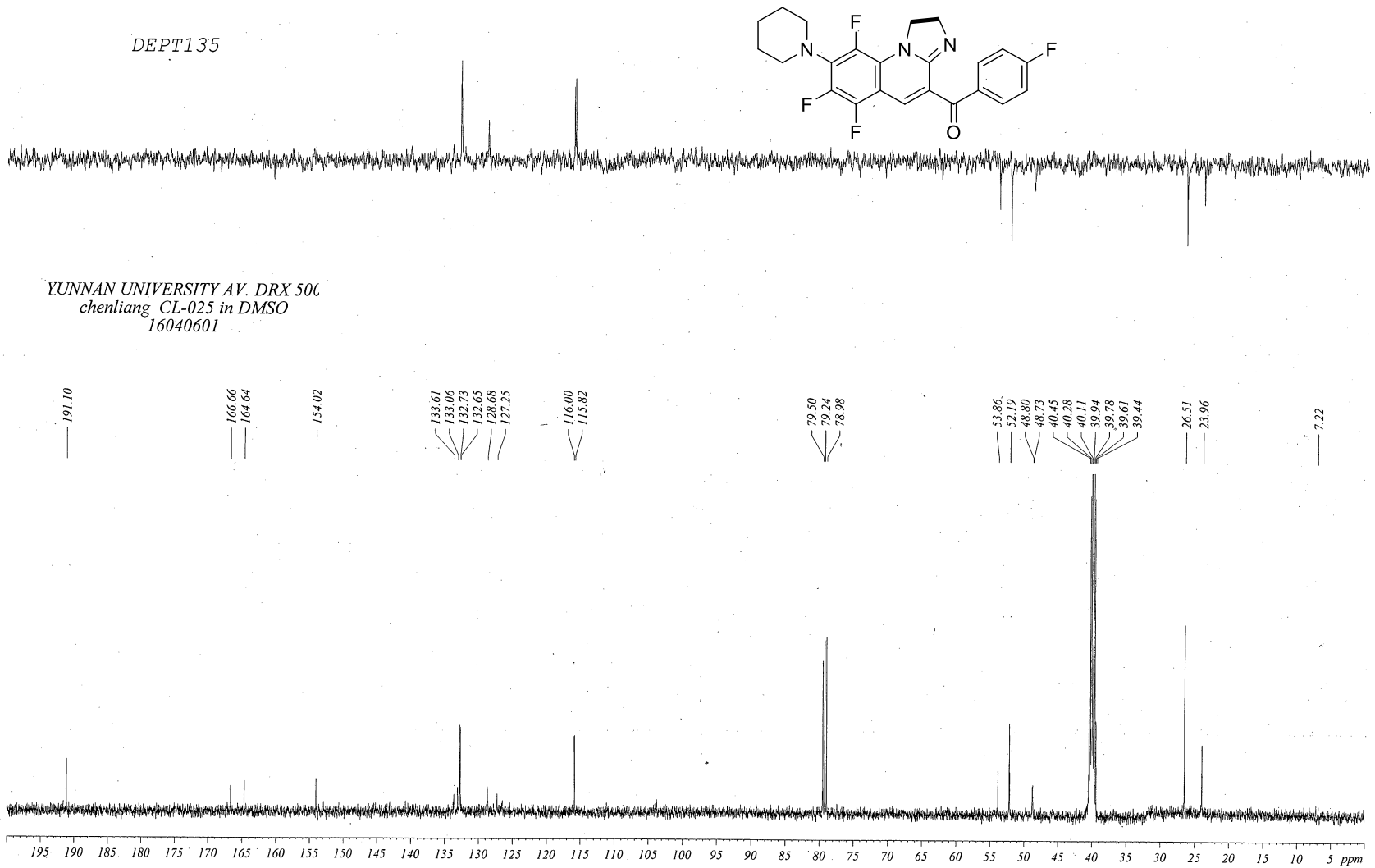


Figure S94. ^{13}C NMR (125 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4da**

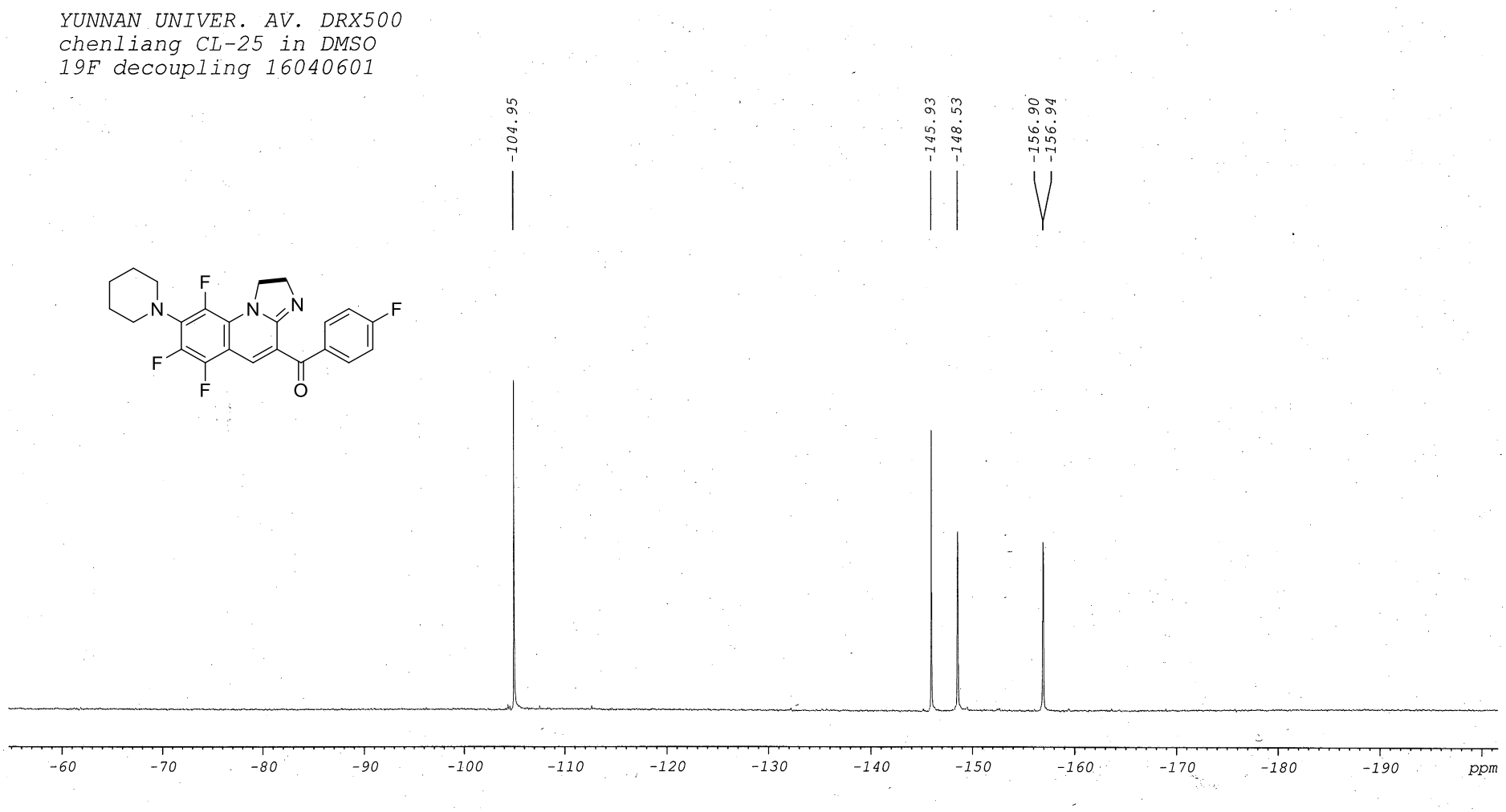


Figure S95. ^{19}F NMR (471 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4da**

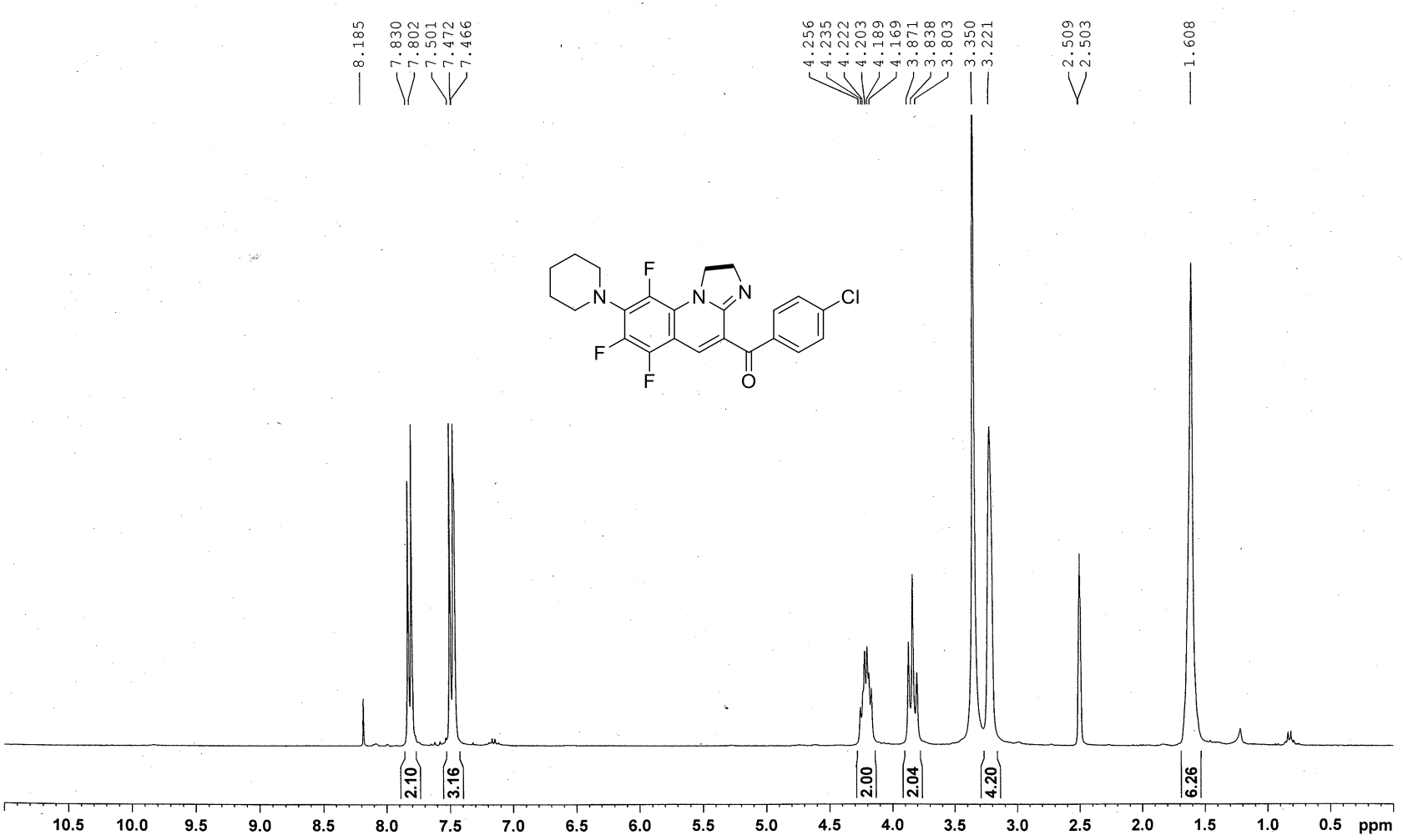


Figure S96. ^{1}H NMR (300 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4db**

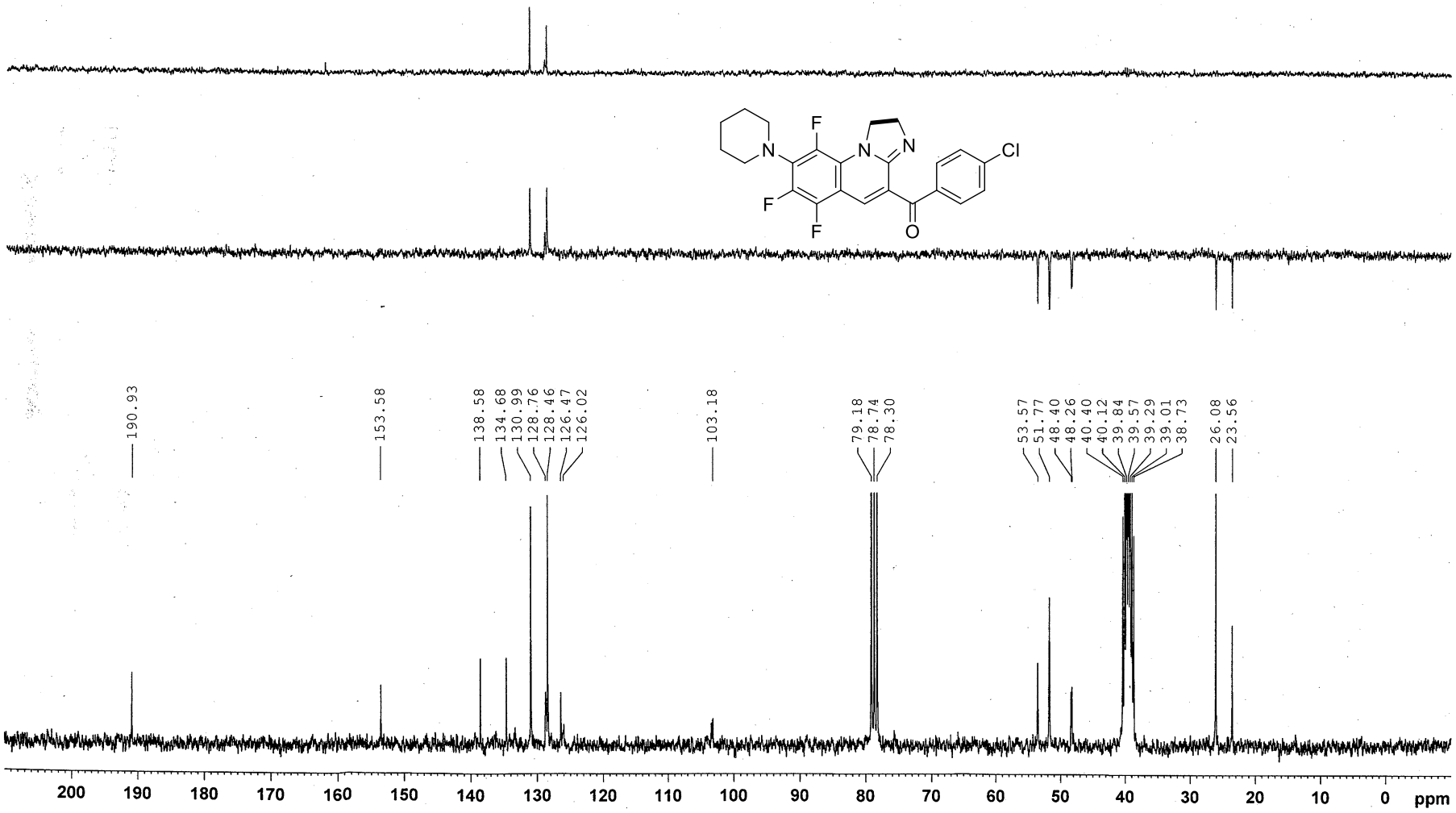


Figure S97. ^{13}C NMR (75 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4db**

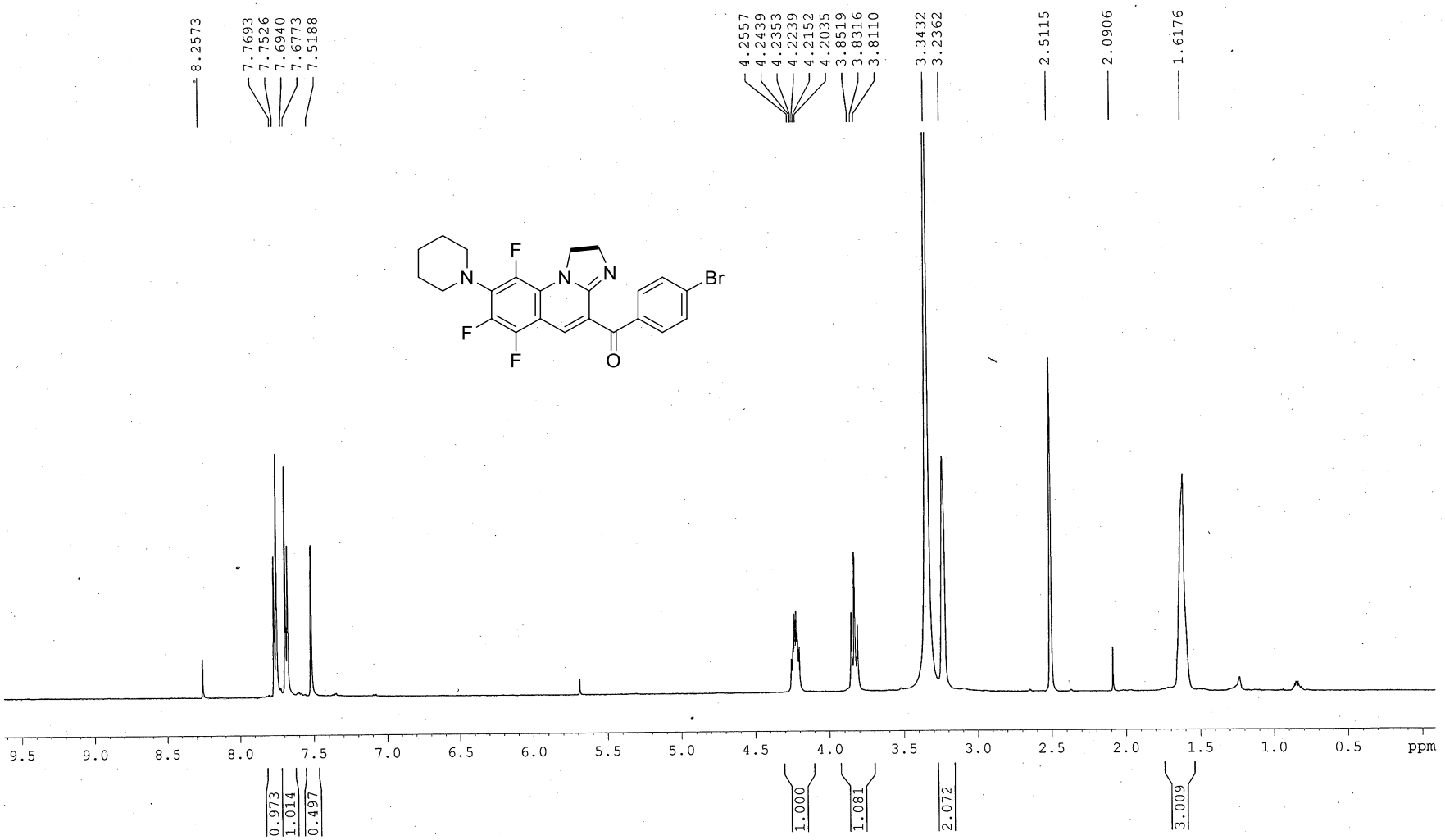


Figure S98. ^{1}H NMR (500 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4dc**

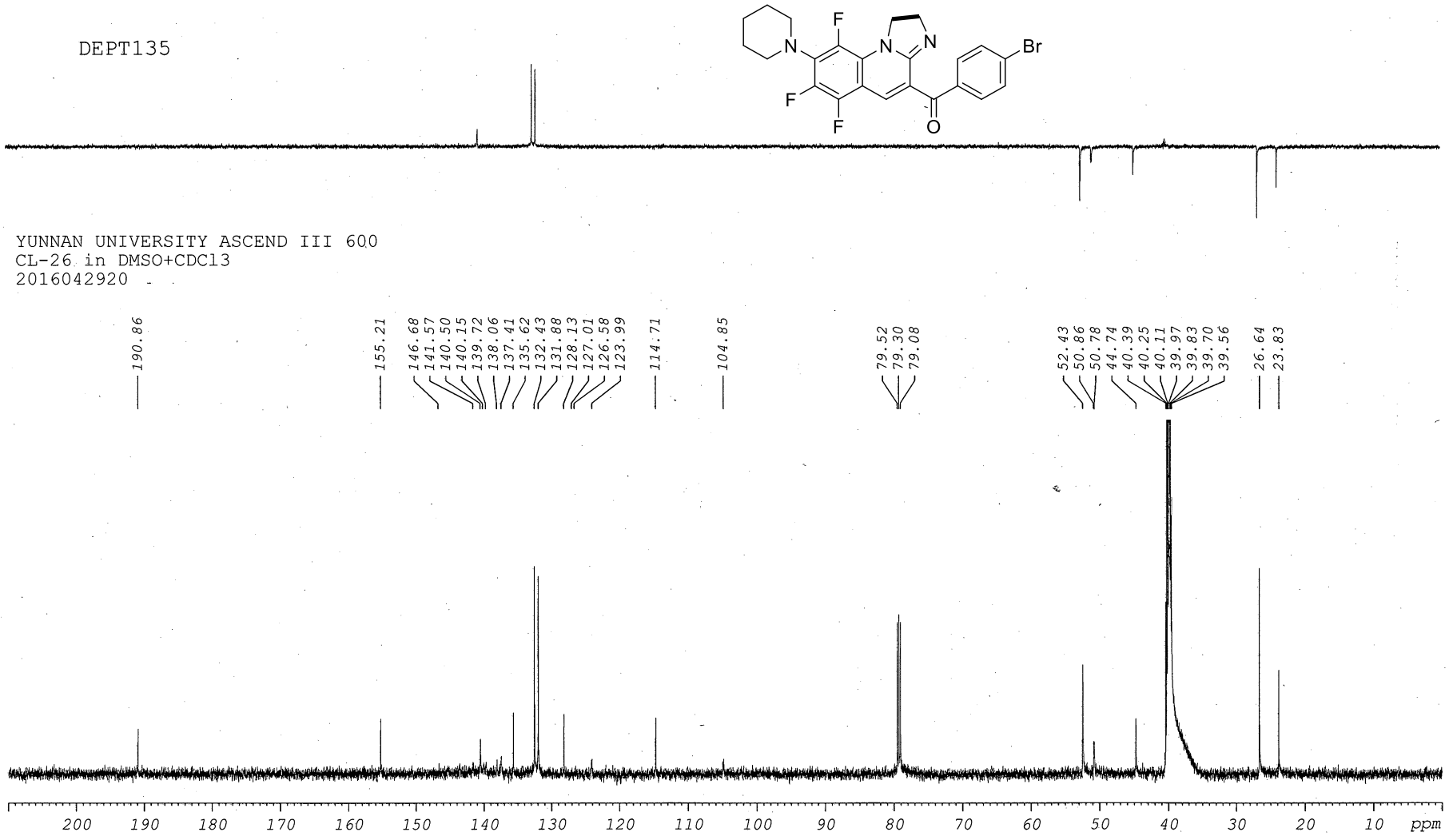


Figure S99. ^{13}C NMR (150 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4dc**

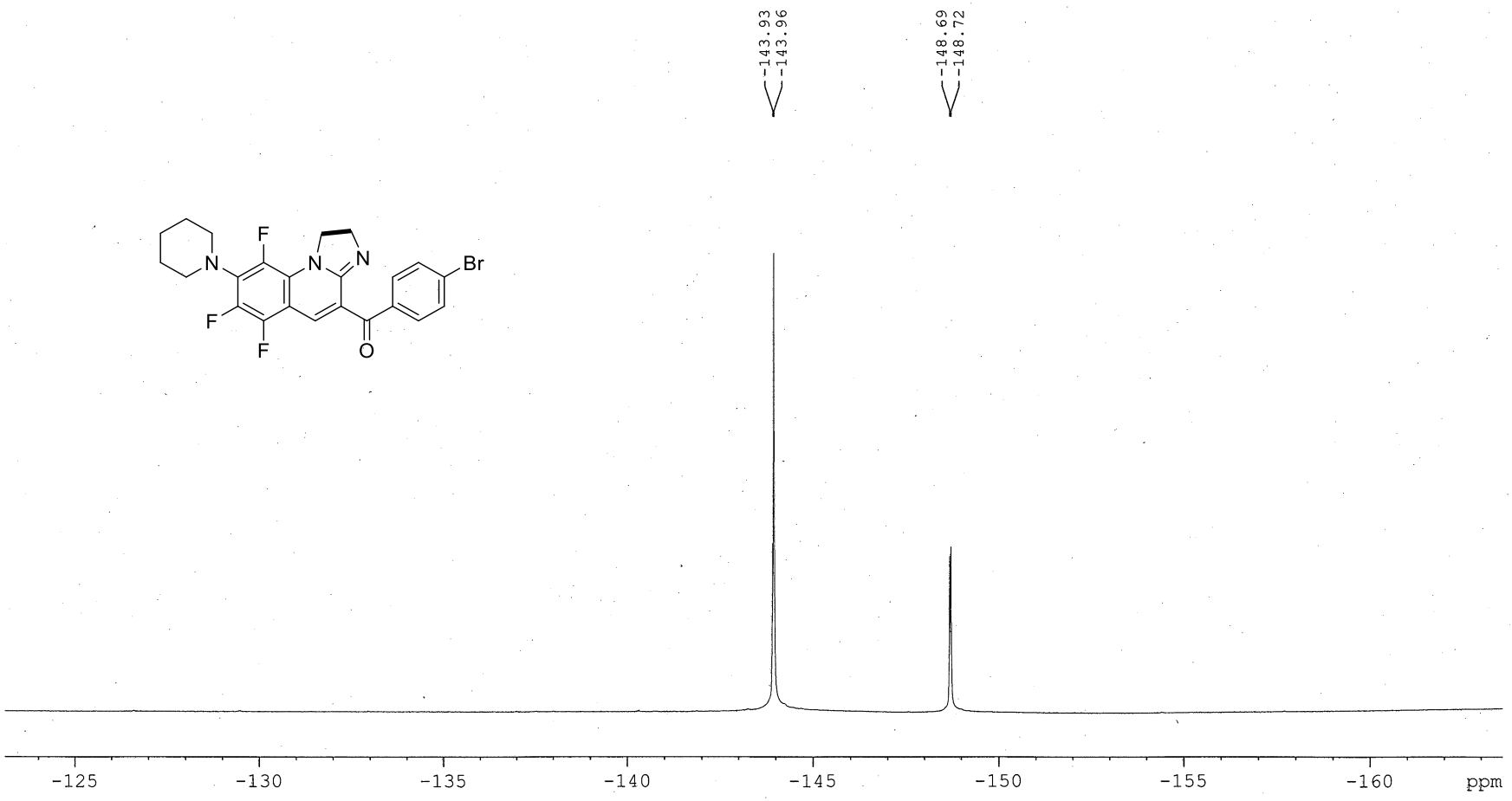


Figure S100. ^{19}F NMR (565 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4dc**

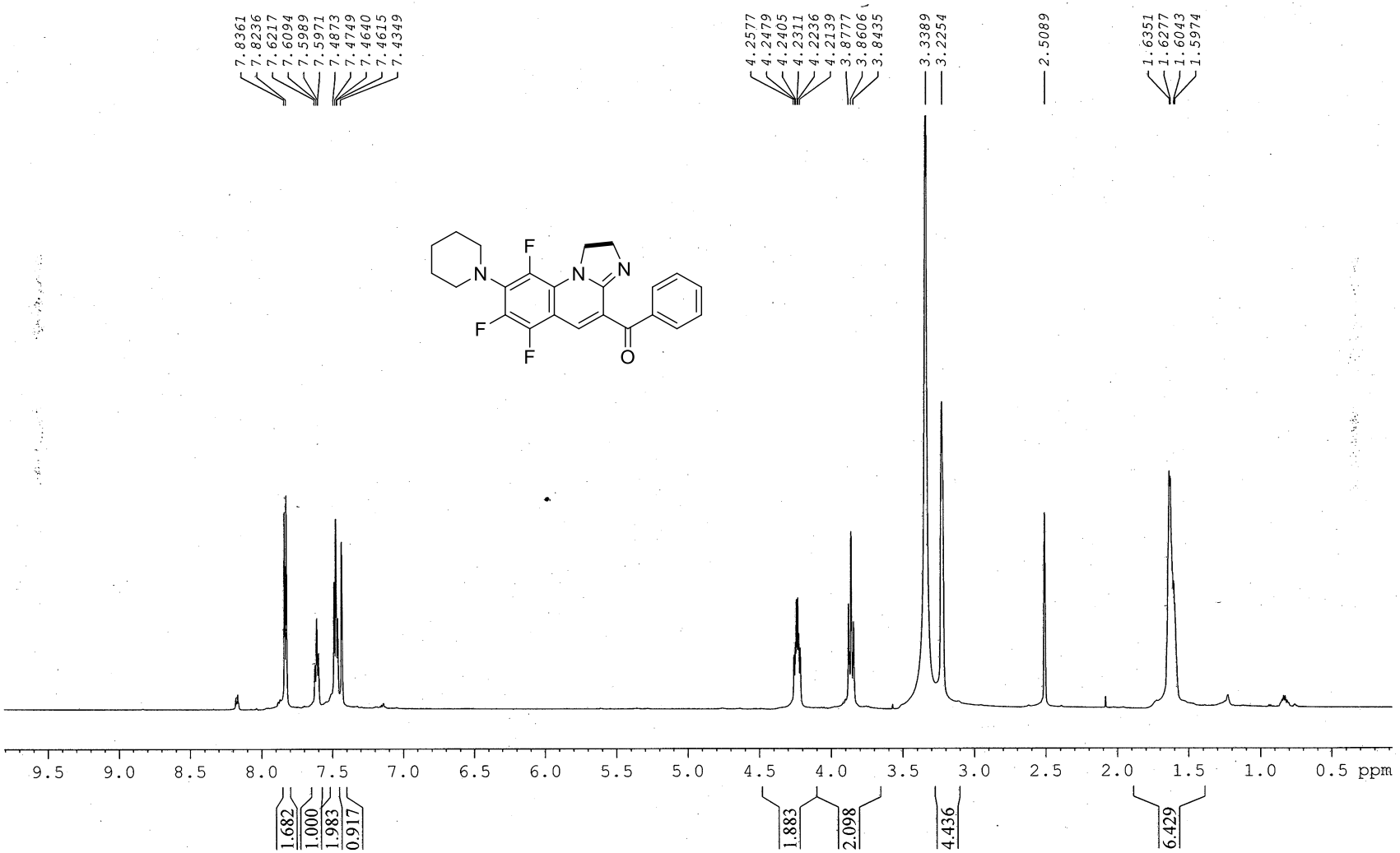


Figure S101. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **4dd**

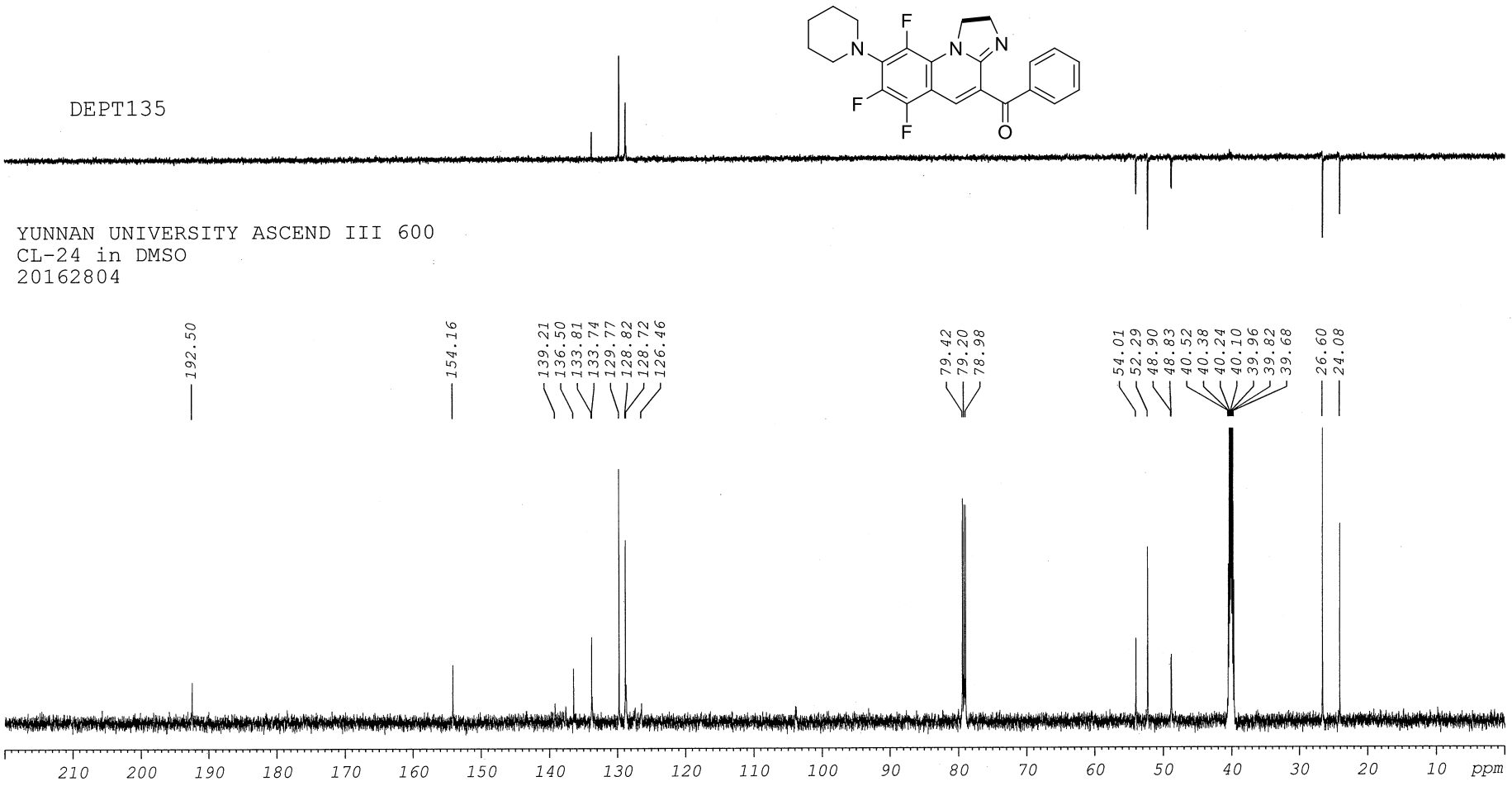


Figure S102. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **4dd**

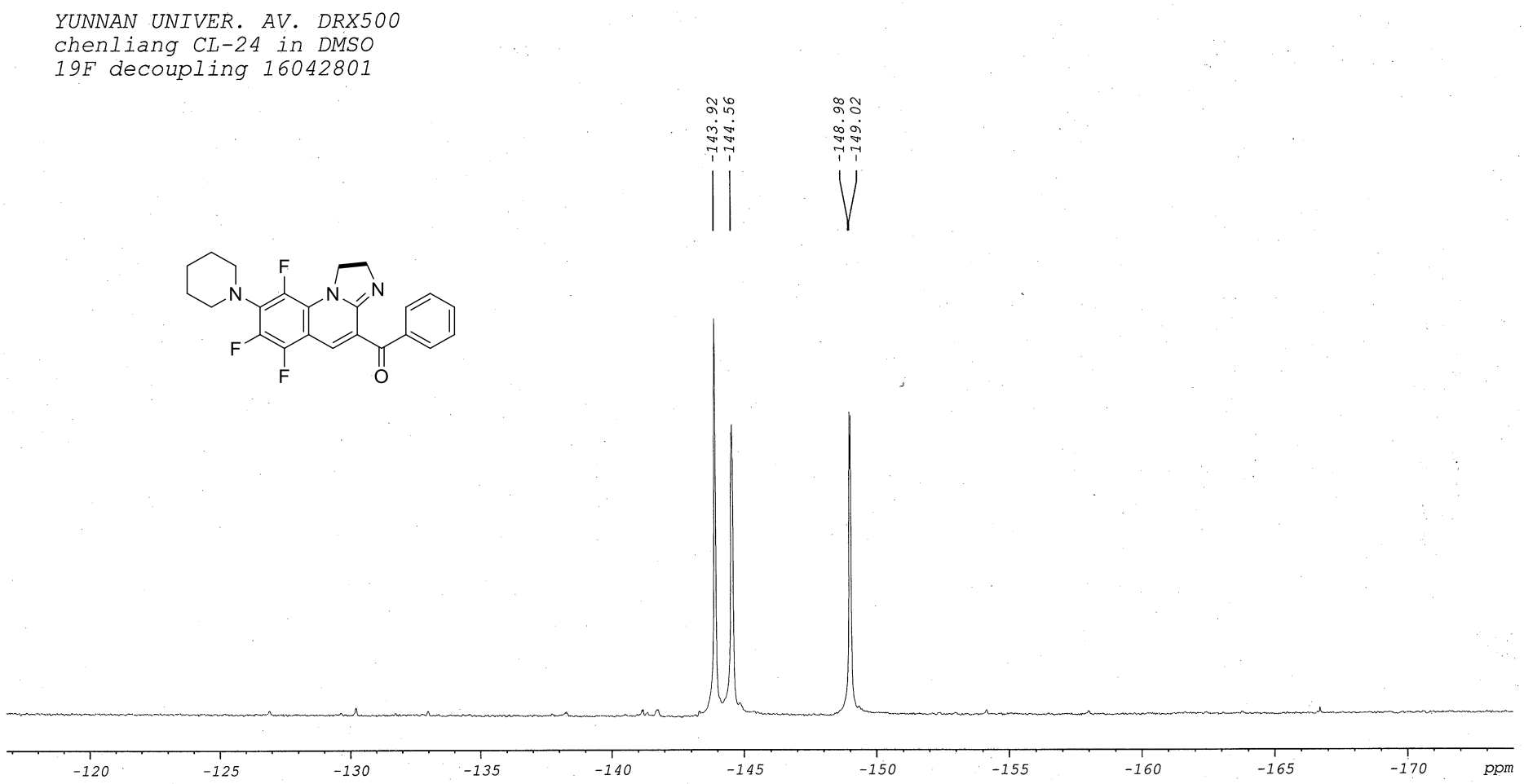


Figure S103. ^{19}F NMR (471 MHz, DMSO-d_6 + $DCCl_3$) spectra of compound **4dd**

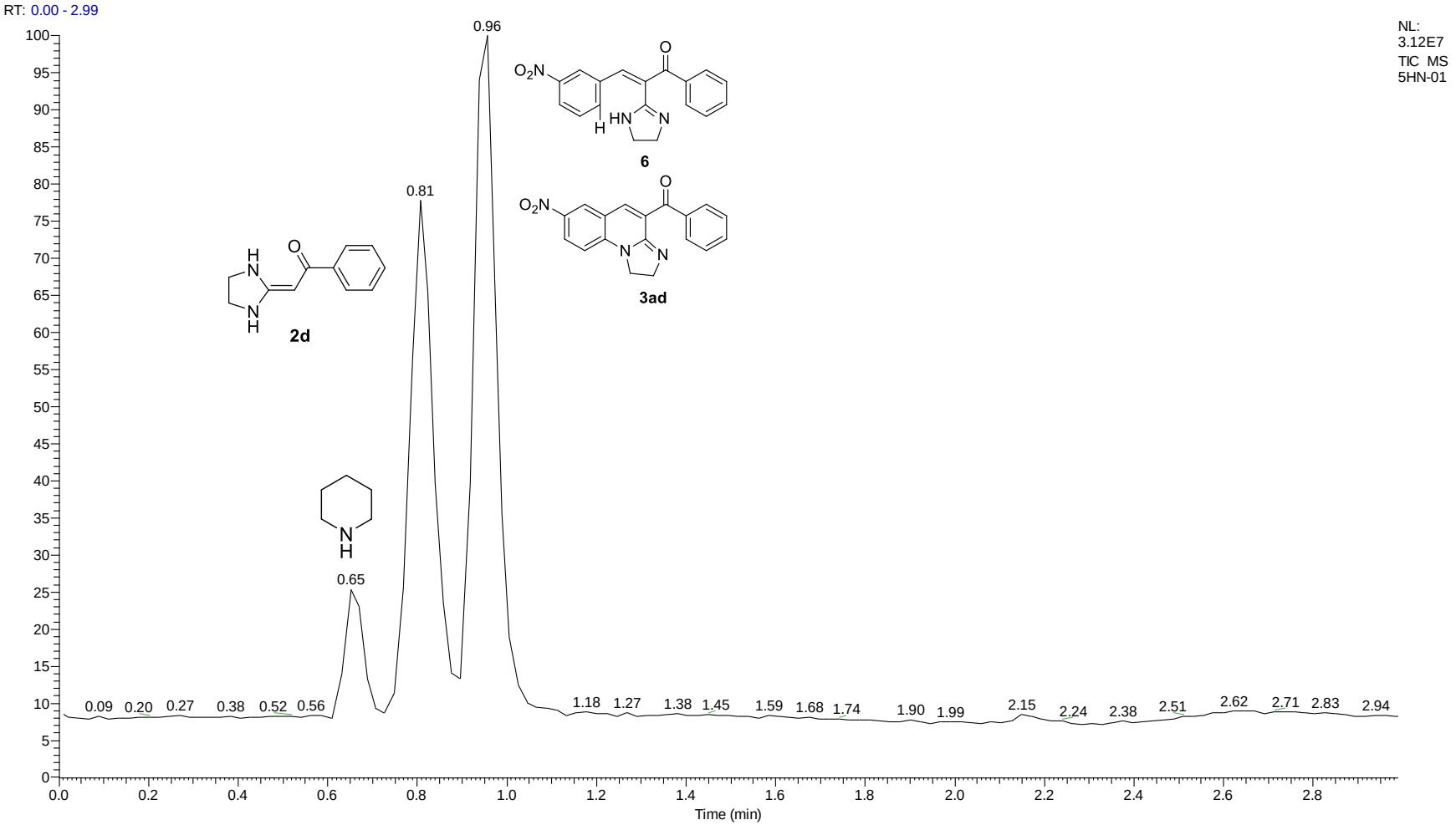


Figure S104. HPLC of intermediate **6**

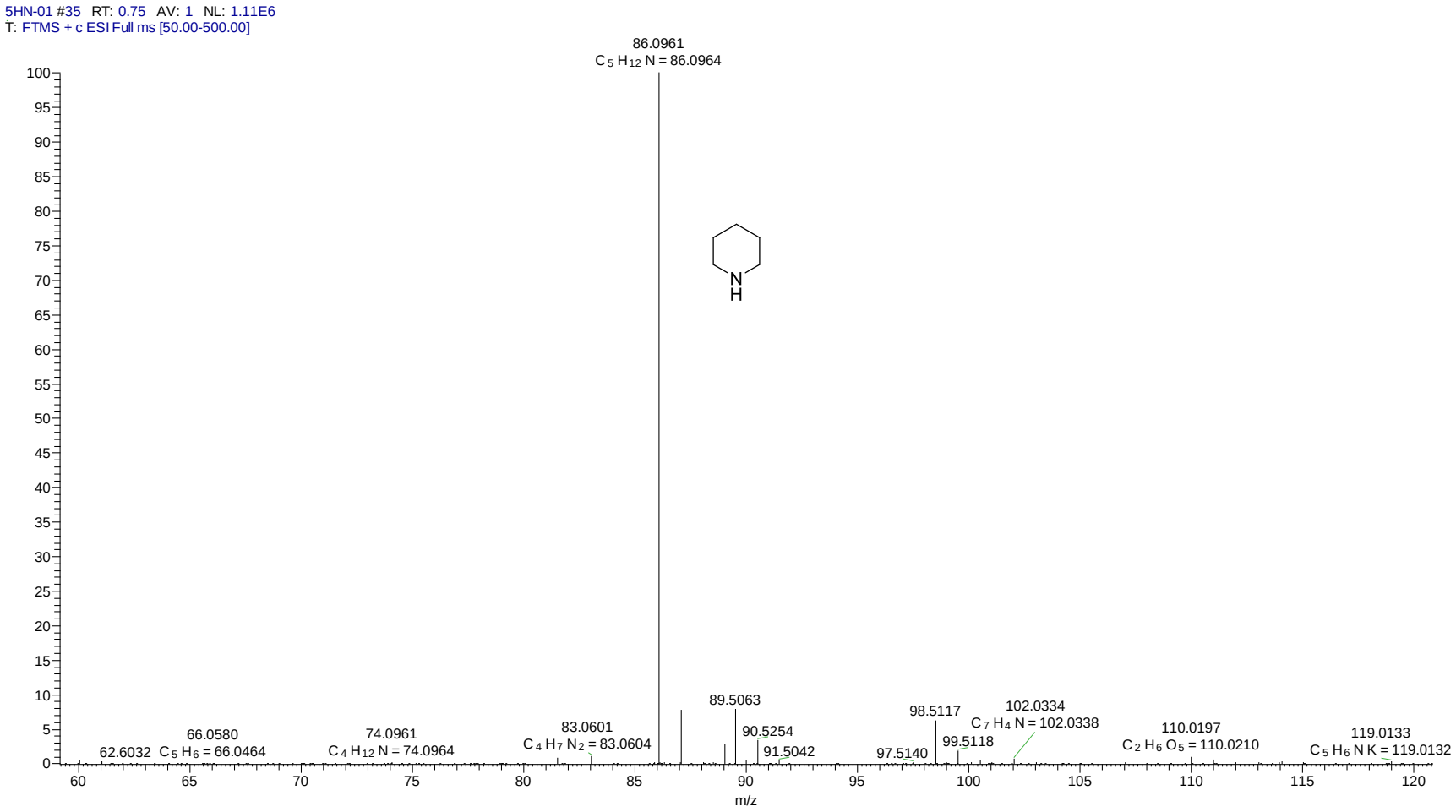


Figure S105. HRMS of piperidine

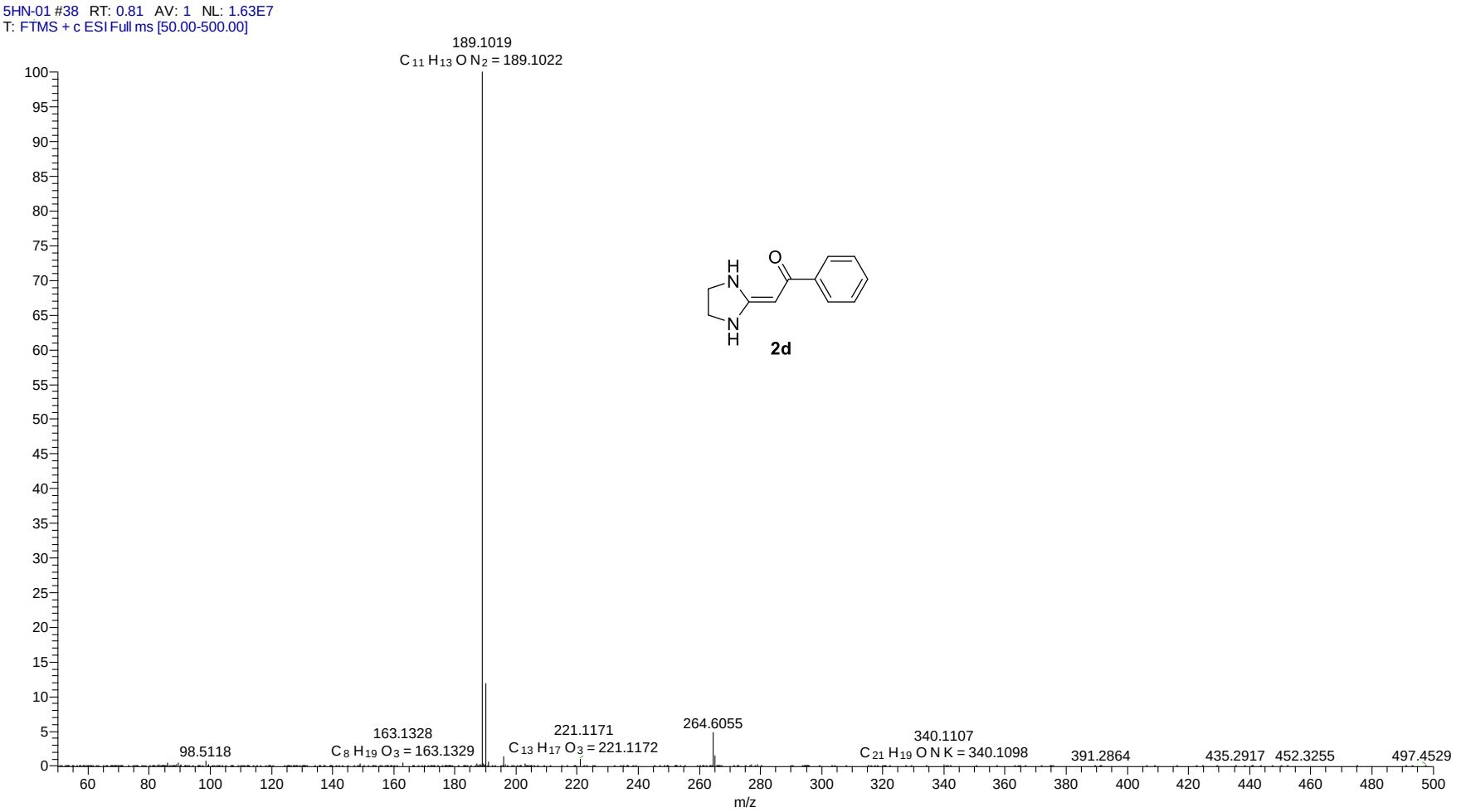


Figure S106. HRMS of compound **2d**

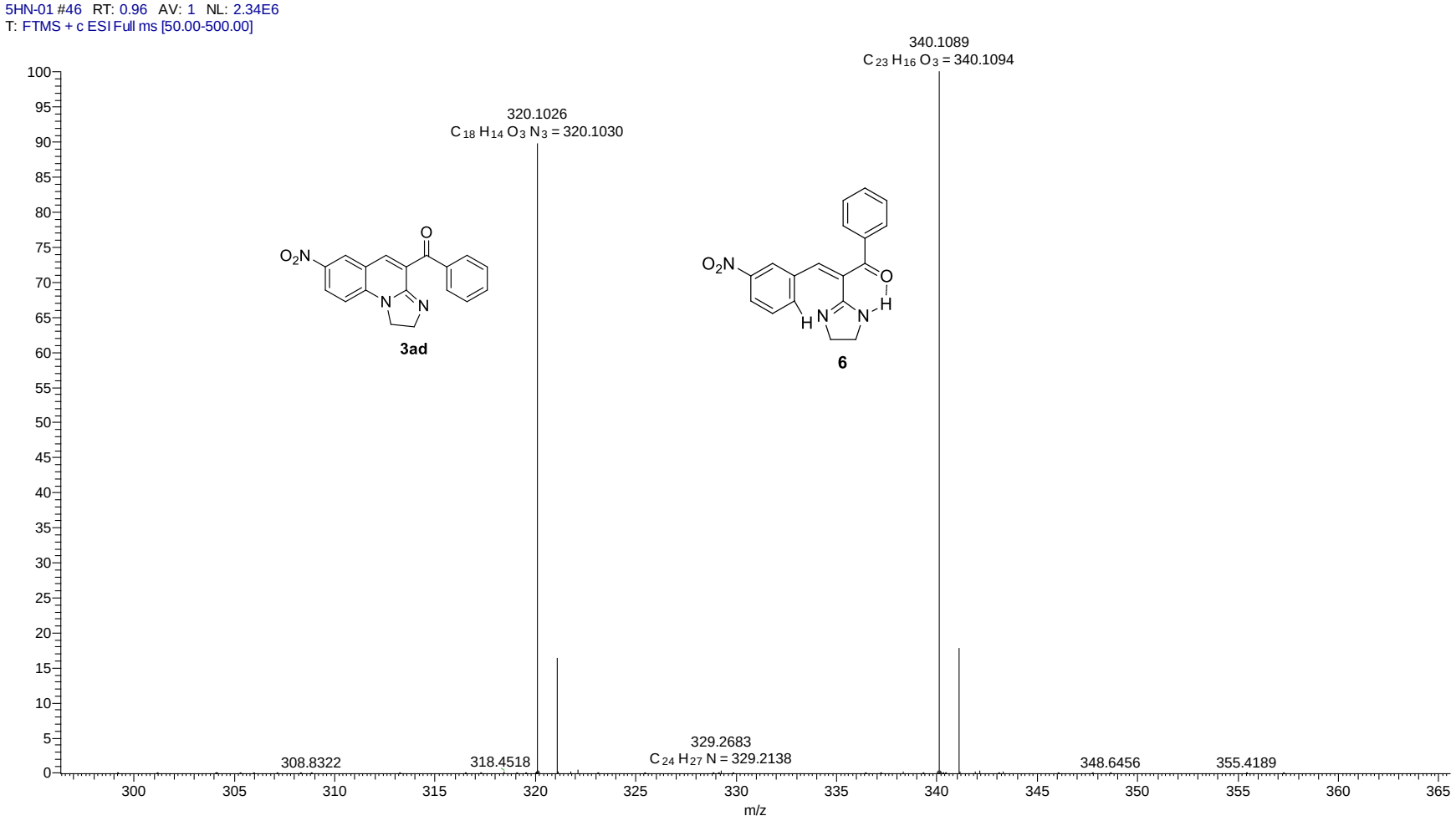


Figure S107. HRMS of intermediate **6**

References and Notes

1. X.-B. Chen, X.-M. Liu, R. Huang, S.-J. Yan and J. Lin, *Eur. J. Org. Chem.*, 2013, **2013**, 4607-4613.
2. F. Yu, R. Huang, H. Ni, J. Fan, S. Yan and J. Lin, *Green Chem.*, 2013, **15**, 453-462.
3. S.-J. Yan, Y.-J. Liu, Y.-L. Chen, L. Liu and J. Lin, *Bioorg. Med. Chem. Lett.*, 2010, **20**, 5225-5228
4. CCDC 1587141 contains the supplementary crystallographic data for compound **3bf**. These data can be obtained free of charge from The Cambridge Crystallographic Data Center *via* www.ccdc.cam.ac.uk/data_request/cif.