Synthesis of Benzo[*b*][1,5]diazocin-6(5*H*)-ones via Cu-Catalysed Oxidative Cyclization of 2-Aryl-1H-indoles with 1,1-Enediamines

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Supporting Information

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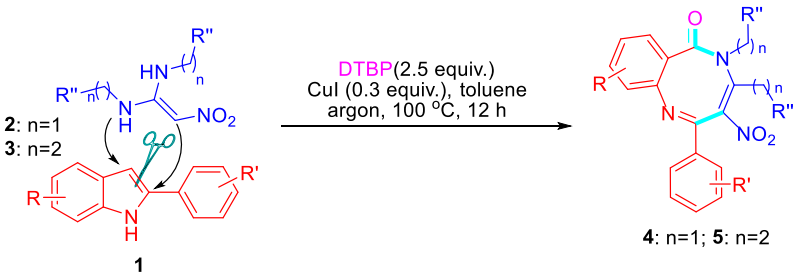
General Information

All compounds were fully characterised by spectroscopic data. The NMR spectra were recorded on a Bruker DRX600 and DRX500. Chemical shifts (δ) are expressed in ppm, J values are given in Hz, DMSO-d_6 or $CDCl_3$ were used as solvent. IR spectra were recorded on a FT-IR Thermo Nicolet Avatar 360 using a KBr pellet. The reactions were monitored by thin layer chromatography (TLC) using silica gel GF_{254}. The melting points were determined on a XT-4A melting point apparatus and are uncorrected. HRMs were performed on an Agilent LC/Msd TOF instrument.

All reactions were carried out under Argon atmosphere. The materials were purchased from Adamas-beta Corporation Limited, compounds **2** were prepared according to the literature.[1] All chemicals and solvents were used as received without further purification unless otherwise stated.

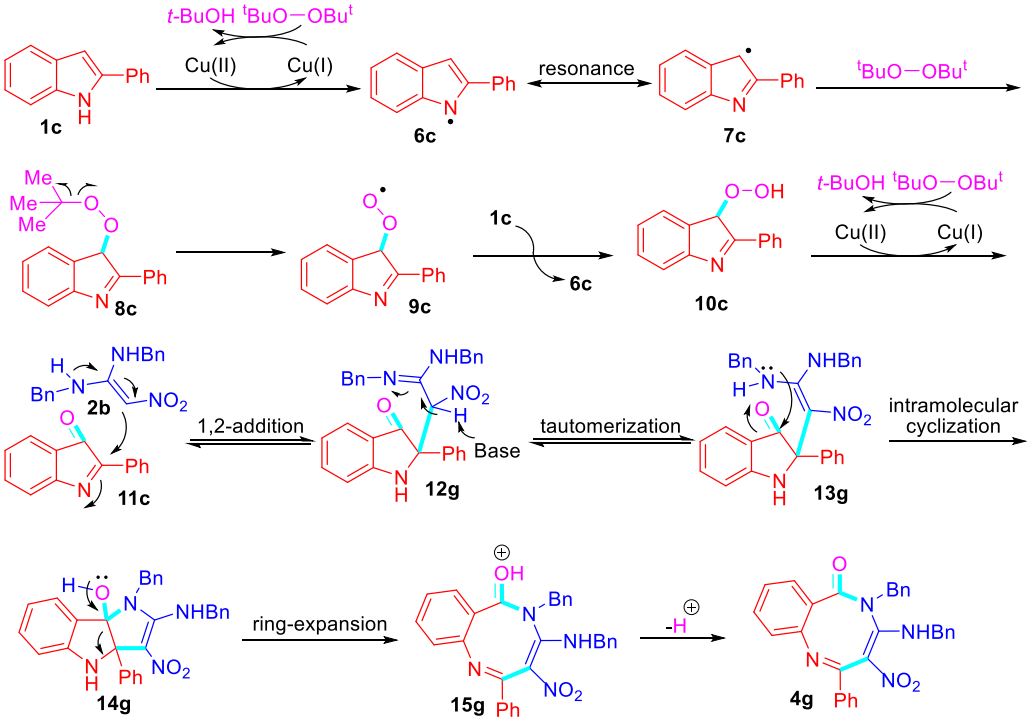
General procedure for the synthesis of benzo[*b*][1,5]diazocin-6(5*H*) -one derivatives 4−5



A round-bottom flask was filled with 2-phenyl-1*H*-indole **1** (0.3 mmol), 1,1-enediamine **2** or **3** (0.36 mmol) and CuI (0.3 equiv). The flask was supplemented with toluene (2 mL) and DTBP (2.5 equiv). The mixture was stirred at 100 °C under argon reflux for 12 hours until the substrates were completely consumed. After cooling the reaction to room temperature, the mixture was extracted with ethyl acetate (3 × 15 mL). The organic layer was washed with water and brine. The combined organic phases were dried over $MgSO_4$, filtered, and concentrated under reduced pressure to afford the crude product. Finally, product **4** or **5** was purified from the crude mixture via flash column chromatography over silica gel using a mixture of petroleum ether/ethyl acetate (8:1-5:1, v/v) as the eluent.

The proposed mechanism of the cascade reaction

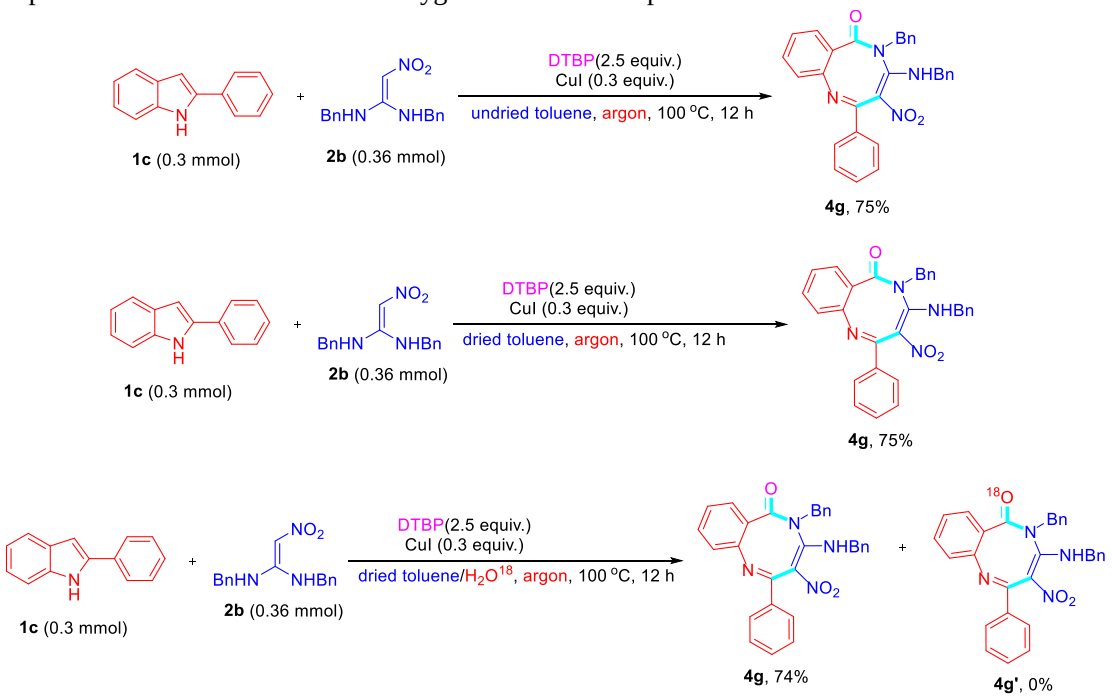
The proposed mechanism of the cascade reaction is shown in Scheme 2 or Scheme S1. First, 2-aryl-1*H*-indole **1c** was oxidized to form a radical intermediate **6c**, and the oxidant DTBP to form the *t*-BuOH. The intermediate **6c** underwent resonance to form intermediate **7c**, which reacted with DTBP to generate the intermediate **8c**. **8c** formed the intermediate **9c** through a SET, which reacted with **1c** to form the intermediate **10c**, and was further oxidized to produce the key intermediate **11c**. The *α*-C of 1,1-enediamine **2b** reacted with the C=N bond *via* a 1,2-addition of imine to yield the intermediate **12g**, which formed the intermediate **13g** via an imine-enamine tautomerization promoted by base. Intermediate **13g** underwent intramolecular cyclization to generate intermediate **14g**. The intermediate **14g** formed the intermediate **15g** via ring expansion reaction. Finally, the intermediate **15g** formed the target compound **4g** via loss of water molecules under heat.



Scheme S1. The proposed mechanism of the cascade reaction.

Control experiments

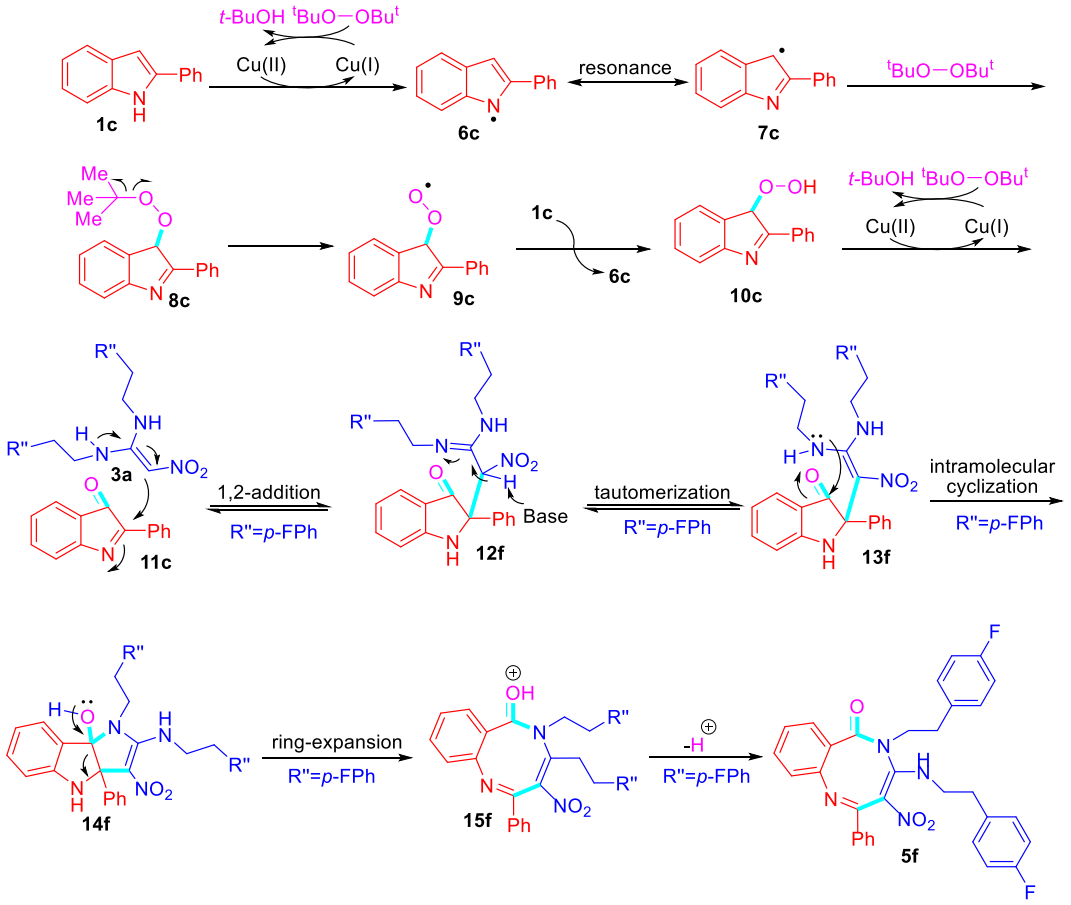
Since the reaction is carried out smoothly in argon (Scheme S2), it indicated that the oxygen element of the product **4g** did not come from the oxygen in the air, and the oxygen of the product may only come from a small amount of water in the solvent (undried toulene) or from the oxidant DTBP. Therefore, we have done the following control experiments (Scheme S2). The experimental results show that the oxygen element in the product comes from the oxidant DTBP.



Scheme S2. Verified the oxygen of the product came from the oxidant DTBP.

Furthermore, we tried to make the mixture of **1c** (0.1 mmol), **3a** (0.2 mmol), DTBP (0.25 mmol) and CuBr (0.03 mmol) in toluene and carried out refluxing for 1 h. Following this, we immediately injected the reaction mixture into the high-pressure liquid chromatography-high-resolution mass spectrometry (HPLC-HRMS) system. Some intermediate molecular ion peaks appeared (ESI, Figures S73–S87). The molecular ion peaks that appeared in the high-resolution mass spectrum were: HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{12}N$ $[M+H]^+$, 194.0964; found, 194.0965, which is the HRMS spectrum of **1c** (SI, Figure S75); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{11}N$ $[M+H]^+$, 193.0886; found, 193.0887. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{11}N^{\cdot}$ $[M+H]^+$, 193.0886; found, 193.0887. There are the HRMS spectra of **6c**/**7c** (SI, Figures S76-S77); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{18}H_{20}NO$ $[M+H]^+$, 282.1489; found, 282.1493, which is the HRMS spectra of intermediate **8c** (SI, Figure S78); HRMS (TOF ES$^+$): HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{11}NO_2^{\cdot}$ $[M+H]^+$, 225.0784; found, 225.0796, which is the HRMS spectra of intermediate **9c** (SI, Figure S79); HRMS (TOF ES$^+$): HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{12}NO_2$ $[M+H]^+$,

226.0863; found, 226.0868, which is the HRMS spectra of intermediate **10c** (SI, Figure S80); HRMS (TOF ES$^+$): HRMS (TOF ES$^+$): *m/z* calcd. for $C_{14}H_{10}NO$ $[M+H]^+$, 208.0757; found, 208.0757, which is the HRMS spectra of intermediate **11c** (SI, Figure S81); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{18}H_{20}F_2N_3O_2$ $[M+H]^+$, 348.1518; found, 348.1519, which is the HRMS spectra of substrate **3a** (ESI, Figure S82); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{32}H_{29}F_2N_4O_3$ $[M+H]^+$, 555.2202; found, 555.2201. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{32}H_{29}F_2N_4O_3$ $[M+H]^+$, 555.2202; found, 555.2201. HRMS (TOF ES$^+$): *m/z* calcd. for $C_{32}H_{29}F_2N_4O_3$ $[M+H]^+$, 555.2202; found, 555.2207. There are the HRMS spectra of intermediates **12f**/**13f**/**14f** (SI, Figures S83-S85); HRMS (TOF ES$^+$): *m/z* calcd. for $C_{33}H_{27}F_2N_4O_3$ $[M+H]^+$, 553.2046; found, 553.2048, which is the HRMS spectrum of intermediate **15f** (SI, Figure S86). HRMS (TOF ES$^+$): *m/z* calcd. for $C_{32}H_{27}F_2N_4O_3$ $[M+H]^+$, 553.2046; found, 553.2053, which is the HRMS spectrum of target compound **5f** (SI, Figure S87).

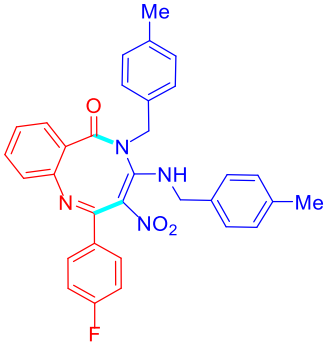


Scheme S3. The mechanism were tested by HPLC-HRMS

Based on control example (Scheme S2) and the molecular ion peaks of intermediates **6c**−**11c** and **12f**−**15f** (ESI, Figures S76–S86). We believe there exist ample evidence in support of the proposed mechanism.

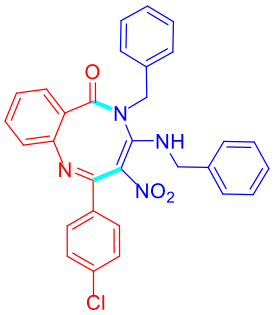
Spectroscopic Data of benzo[*b*][1,5]diazocin-6(5*H*)-ones 4−5.

(1*Z*,3*E*)-2-(4-Fluorophenyl)-5-(4-methylbenzyl)-4-((4-methylbenzyl)amino)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4a)



White solid (73%, 116 mg); Mp: 184.1-184.9 ℃; IR (KBr) 3647, 3356, 3099, 2932, 2874, 1676, 1608, 1512, 1430, 1311, 1234, 1133 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.04 (br, 1H, NH), 7.37-7.43 (m, 3H, ArH), 7.13-7.55 (m, 3H, ArH), 7.09 (s, 1H, ArH), 7.06 (t, *J* = 3.9 Hz, 2H, ArH), 6.98 (t, *J* = 7.6 Hz, 1H, ArH), 6.93 (t, *J* = 8.6 Hz, 2H, ArH), 6.81 (t, *J* = 8.7 Hz, 2H, ArH), 6.67 (t, *J* = 7.8 Hz, 2H, ArH), 5.53 (d, *J* = 14.3 Hz, 1H, CH_2), 4.52 (t, *J* = 5.1 Hz, 2H, CH_2), 3.98 (d, *J* = 14.3 Hz, 1H, CH_2), 2.36 (s, 3H, CH_3), 2.13 (s, 3H, CH_3) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.8, 164.4(*J* = 250.0 Hz), 158.5, 153.9, 148.4, 138.6, 138.5, 132.0, 131.7, 131.5, 131.4, 130.0(*J* = 7.5 Hz), 129.9(*J* = 8.8 Hz), 129.9, 129.9, 129.1, 128.9, 128.9, 128.9, 127.4, 127.0, 127.0, 127.0, 124.6, 124.1, 121.1, 116.0, 115.2(*J* = 22.5 Hz), 50.7, 47.9, 21.1, 21.0 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -109.42. HRMS (TOF ES^+): m/z calcd for $C_{32}H_{28}FN_4O_3$ $[(M+H)^+]$, 535.2140; found, 535.2141.

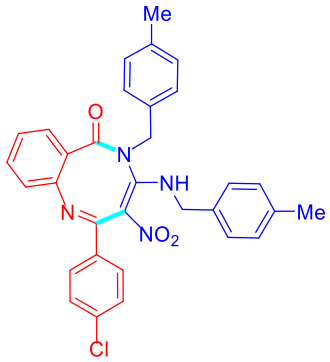
(1*Z*,3*E*)-5-Benzyl-4-(benzylamino)-2-(4-chlorophenyl)-3-nitrobenzo[*b*][1,5]diazocine-6(5*H*)-one (4b)



White solid (73%, 114 mg); Mp: 203.3-204.7 ℃; IR (KBr) 3673, 3340, 3059, 2960, 2882,1677, 1609, 1502, 1480, 1383, 1215, 1120 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.06 (br, 1H, NH), 7.41 (t, *J* = 7.6 Hz, 1H, ArH), 7.34 (t, *J* = 9.2 Hz, 5H, ArH), 7.09-7.12 (m, 8H, ArH), 7.01-7.08 (m, 1H, ArH), 6.99 (t, *J* = 9.6 Hz, 1H, ArH),

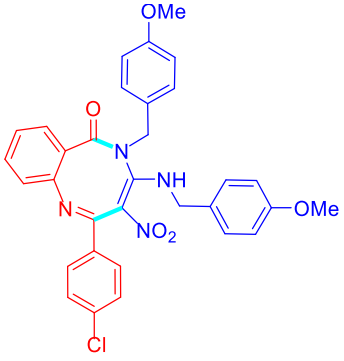
6.88-6.95 (m, 2H, ArH), 5.69 (d, *J* = 14.3 Hz, 1H, CH_2), 4.54 (d, *J* = 6.2 Hz, 2H, CH_2), 4.06 (d, *J* = 14.3 Hz, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.8, 158.6, 154.0, 148.4, 137.1, 135.1, 134.3, 134.1, 131.6, 129.4, 128.9, 128.9, 128.7, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.5, 128.5, 127.5, 127.0, 127.0, 124.7, 124.0, 121.0, 116.0, 51.1, 48.1 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{30}H_{24}ClN_4O_3$ [(M+H)$^+$], 523.1531; found, 523.1534

(1*Z*,3*E*)-2-(4-Chlorophenyl)-5-(4-methylbenzyl)-4-((4-methylbenzyl)amino)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4c)



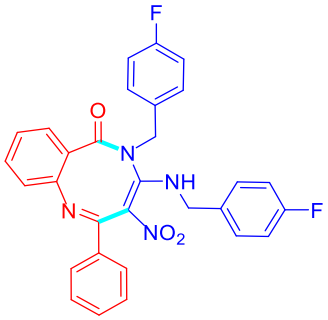
White solid (71%, 117 mg); Mp: 223.4-224.5 ℃; IR (KBr) 3683, 3408, 3096, 1698, 1617, 1540, 1458, 1374, 1292, 1100 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.07 (br, 1H, NH), 7.45 (t, *J* = 7.7 Hz, 1H, ArH), 7.34 (d, *J* = 8.5 Hz, 2H, ArH), 7.10-7.19 (m, 6H, ArH), 6.94-7.03 (m, 3H, ArH), 6.07 (d, *J* = 7.6 Hz, 2H, ArH), 5.78 (d, *J* = 14.3 Hz, 1H, CH_2), 4.56 (t, *J* = 7.4 Hz, 2H, CH_2), 3.99 (d, *J* = 14.3 Hz, 1H, CH_2), 2.40 (s, 3H, CH_3), 2.19 (s, 3H, CH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.7, 158.7, 153.9, 148.3, 138.8, 138.6, 136.8, 134.0, 132.0, 131.6, 131.4, 130.0, 130.0, 130.0, 129.1, 128.9, 128.9, 128.9, 128.8, 128.4, 127.4, 127.4, 127.4, 127.0, 124.7, 124.0, 121.0, 115.8, 50.6, 47.9, 21.2, 21.1 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{23}H_{28}ClN_4O_3$ [(M+H)$^+$], 551.1844; found, 551.1844.

(1*Z*,3*E*)-2-(4-Chlorophenyl)-5-(4-methoxybenzyl)-4-((4-methoxybenzyl)amino)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4d)



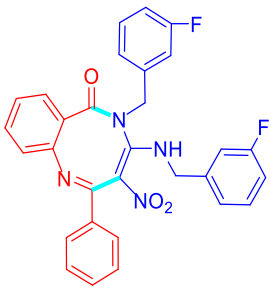
White solid (70%, 122 mg); Mp: 226.4-227.8 ℃; IR (KBr) 3683, 3409, 3062, 2960, 2889, 1685, 1605, 1504, 1457, 1379, 1262, 1188 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.01 (br, 1H, NH), 7.41 (d, *J* = 7.5 Hz, 1H, ArH), 7.31 (d, *J* = 7.9 Hz, 2H, ArH), 7.18 (d, *J* = 7.6 Hz, 1H, ArH), 7.11 (t, *J* = 7.6 Hz, 3H, ArH), 7.03 (d, *J* = 7.9 Hz, 2H, ArH), 6.96 (d, *J* = 7.1 Hz, 3H, ArH), 6.86 (d, *J* = 7.9 Hz, 2H, ArH), 6.39 (d, *J* = 7.8 Hz, 2H, ArH), 5.74 (d, *J* = 14.3 Hz, 1H, CH_2), 4.51 (t, *J* = 6.9 Hz, 2H, CH_2), 3.94 (d, *J* = 14.2 Hz, 1H, CH_2), 3.82 (s, 3H, OCH_3), 3.66 (s, 3H, OCH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.7, 160.0, 159.8, 128.6, 153.8, 148.4, 136.9, 134.0, 131.5, 130.2, 130.2, 130.2, 129.0, 128.5, 128.5, 128.4, 128.4, 128.4, 127.4, 126.9, 126.6, 124.6, 124.1, 121.1, 114.8, 114.8, 113.7, 113.7, 55.4, 54.9, 50.3, 47.7 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{28}ClN_4O_5$ $[(M+H)^+]$, 583.1743; found, 583.1741.

(1*Z*,3*E*)-5-(4-Fluorobenzyl)-4-((4-fluorobenzyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (4e)



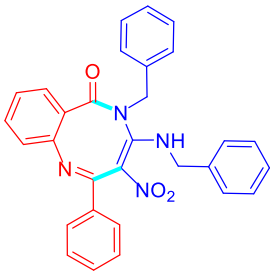
White solid (77%, 121 mg); Mp: 178.3.4-1709.7 ℃; IR (KBr) 3688, 3403, 3014, 2956, 2831, 1682, 1621, 1576, 1482, 1355, 1263, 1190 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.22 (br, 1H, NH), 7.64-7.71 (m, 4H, ArH), 7.46-7.53 (m, 2H, ArH), 7.25-7.36 (m, 9H, ArH), 6.77 (t, *J* = 8.6 Hz, 2H, ArH), 5.93 (d, *J* = 14.3 Hz, 1H, CH_2), 4.77 (t, *J* = 5.9 Hz, 2H, CH_2), 4.28 (d, *J* = 14.4 Hz, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.9, 162.8(*J* = 246.0 Hz), 162.6(*J* = 246.0 Hz), 159.4, 153.5, 148.6, 135.2, 131.7, 131.2, 131.0, 130.7(*J* = 7.5 Hz), 130.1, 130.1, 128.7(*J* = 9.0 Hz), 128.7, 128.4, 128.4, 128.4, 127.7, 127.7, 127.7, 127.3, 124.5, 123.8, 121.2, 116.7, 116.4(*J* = 21.0 Hz), 115.4(*J* = 20.0 Hz), 50.4, 47.3 ppm. ^{19}F NMR (564 MHz, $CDCl_3$): δ = -112.7, δ = -112.9. HRMS (TOF ES^+): *m/z* calcd for $C_{30}H_{23}F_2N_4O_3$ $[(M+H)^+]$, 525.1733; found, 525.1728.

(1*Z*,3*E*)-5-(3-Fluorobenzyl)-4-((3-fluorobenzyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (4f)



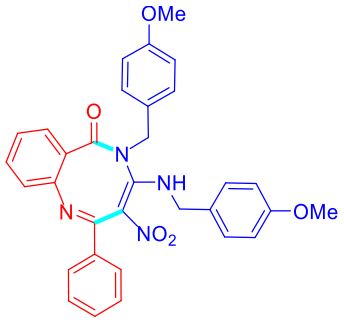
White solid (77%, 121 mg); Mp: 183.4-184.7 ℃; IR (KBr) 3647, 3462, 3071, 2963, 2804, 1678, 1611, 1490, 1431, 1307, 1236, 1137 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.01 (br, 1H, NH), 7.51 (d, *J* = 7.6 Hz, 2H, ArH), 7.32-7.47 (m, 3H, ArH), 7.18-7.27 (m, 4H, ArH), 7.05-7.13 (m, 4H, ArH), 6.96 (d, *J* = 8.0 Hz, 1H, ArH), 6.86-6.90 (m, 1H, ArH), 6.57-6.64 (m, 2H, ArH), 5.59 (d, *J* = 14.5 Hz, 1H, CH_2), 4.54-4.67 (m, 2H, CH_2), 4.48 (d, *J* = 14.5 Hz, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 168.1, 160.6(*J* = 246.3 Hz), 160.4(*J* = 245.0 Hz), 153.5, 148.6, 135.3, 131.6, 131.3, 131.0, 131.7(*J* = 8.8 Hz), 130.5(*J* = 8.8 Hz), 129.6, 129.1, 128.4, 127.7, 127.6, 125.0(*J* = 3.75 Hz), 124.6, 124.2(*J* = 2.5 Hz), 123.8, 122.4, 122.3, 121.4, 121.3, 121.1, 116.2(*J* = 25.0 Hz), 116.0(*J* = 20.0 Hz), 115.0(*J* = 22.5 Hz), 43.5(*J* = 5.0 Hz), 42.1(*J* = 3.8 Hz) ppm. ^{19}F NMR (MHz, $CDCl_3$): δ = -117.3, δ = -118.4. HRMS (TOF ES^+): *m/z* calcd for $C_{30}H_{24}F_2N_4NaO_3$ $[(M+Na)^+]$, 547.1558; found, 547.1550.

(1*Z*,3*E*)-5-Benzyl-4-(benzylamino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (4g)



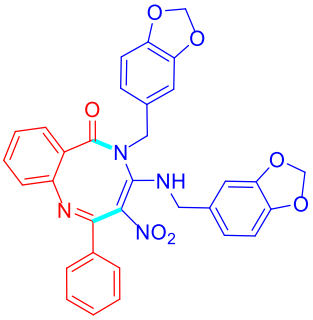
White solid (75%, 110 mg); Mp: 188.6-189.8 ℃; IR (KBr) 3691, 3386, 3086, 1943, 2854, 1678, 1610, 1493, 1377, 1310, 1210, 1133 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 10.05 (br, 1H, NH), 7.47 (d, *J* = 7.7 Hz, 2H, ArH), 7.34-7.42 (m, 1H, ArH), 7.30-7.32 (m, 4H, ArH), 7.16-7.25 (m, 2H, ArH), 7.03-7.10 (m, 6H, ArH), 6.97 (t, *J* = 10.4 Hz, 1H, ArH), 6.93 (d, *J* = 7.4 Hz, 1H, ArH), 6.87 (t, *J* = 7.4 Hz, 2H, ArH), 5.56 (d, *J* = 14.3 Hz, 1H, CH_2), 4.46-4.93 (m, 2H, CH_2), 4.17 (d, *J* = 14.3 Hz, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.0, 159.7, 154.0, 148.6, 135.5, 135.2, 134.1, 131.6, 131.0, 129.3, 128.9, 128.6, 128.6, 128.4, 128.4, 128.4, 128.4, 128.0, 127.7, 127.5, 127.0, 127.0, 127.0, 126.7, 124.5, 124.1, 121.1, 116.4, 51.4, 48.1 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{30}H_{25}N_4O_3$ $[(M+H)^+]$, 489.1921; found, 489.1920.

(1*Z*,3*E*)-5-(4-Methoxybenzyl)-4-((4-methoxybenzyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (4h)



White solid (73%, 120 mg); Mp: 185.3-186.7 ℃; IR (KBr) 3631, 3358, 3077, 2933, 2796, 1641, 1605, 1516, 1475, 1330, 1295, 1174 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.91 (br, 1H, NH), 7.33-7.38 (m, 3H, ArH), 7.19-7.26 (m, 1H, ArH), 7.11 (t, *J* = 7.0 Hz, 3H, ArH), 7.01 (t, *J* = 7.7 Hz, 1H, ArH), 6.90-6.94 (m, 5H, ArH), 6.78 (d, *J* = 8.3 Hz, 2H, ArH), 6.30 (d, *J* = 8.1 Hz, 2H, ArH), 5.53 (d, *J* = 14.3 Hz, 1H, CH_2), 4.39 (d, *J* = 5.9 Hz, 2H, CH_2), 3.99 (d, *J* = 14.3 Hz, 1H, CH_2), 3.74 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.9, 159.9, 159.7, 159.5, 153.8, 148.6, 135.4, 131.5, 130.8, 130.3, 128.5, 128.5, 128.2, 128.2, 128.2, 127.8, 127.4, 127.1, 126.5, 124.5, 124.2, 121.1, 116.3, 114.7, 114.7, 114.7, 113.7, 113.7, 55.4, 54.8, 50.6, 47.7 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{29}N_4O_5$ $[(M+H)^+]$, 549.2132; found, 549.2131.

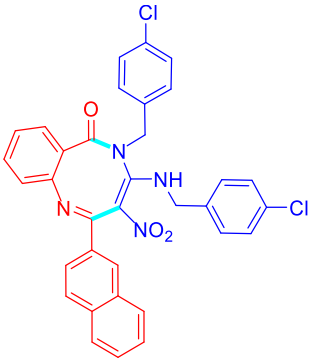
(1*Z*,3*E*)-5-(Benzo[*d*][1,3]dioxol-5-ylmethyl)-4-((benzo[*d*][1,3]dioxol-5-ylmethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (4i)



White solid (70%, 120 mg); Mp: 177.9-178.7 ℃; IR (KBr) 3597, 3355, 3074, 2969, 2880, 1673, 1608, 1496, 1445, 1371, 1251, 1135 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.94 (br, 1H, NH), 7.49 (d, *J* = 7.9 Hz, 2H, ArH), 7.43 (t, *J* = 7.7 Hz, 1H, ArH), 7.36 (t, *J* = 7.3 Hz, 1H, ArH), 7.20-7.26 (m, 3H, ArH), 7.12 (t, *J* = 7.5 Hz, 1H, ArH), 6.98 (d, *J* = 8.0 Hz, 1H, ArH), 6.75 (d, *J* = 7.9 Hz, 1H, ArH), 6.59 (d, *J* = 7.9 Hz, 1H, ArH), 6.51-6.55 (m, 3H, ArH), 6.32 (d, *J* = 7.6 Hz, 1H, ArH), 5.99 (t, *J* = 6.3 Hz, 2H, OCH_2), 5.80 (s, 1H, CH_2), 5.63-5.58 (m, 2H, OCH_2), 4.44-4.46 (m, 2H, CH_2), 3.93 (d, *J* = 14.3 Hz, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.9, 156.5, 153.5,

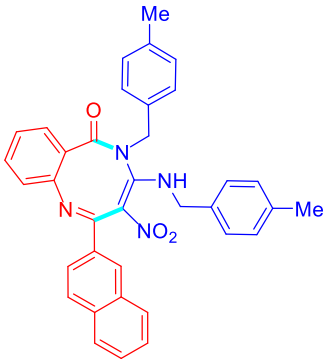
148.7, 148.5, 148.0, 147.8, 147.7, 135.3, 131.6, 130.7, 128.7, 128.3, 128.2, 127.7, 127.7, 127.3, 127.3, 124.5, 124.0, 122.5, 121.1, 120.7, 116.4, 109.3, 108.8, 107.9, 107.5, 101.5, 101.0, 50.8, 47.9 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{25}N_4O_7$ [(M+H)$^+$], 577.1718; found, 577.1719.

(1*Z*,3*E*)-5-(4-Chlorobenzyl)-4-((4-chlorobenzyl)amino)-2-(naphthalen-2-yl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4j)



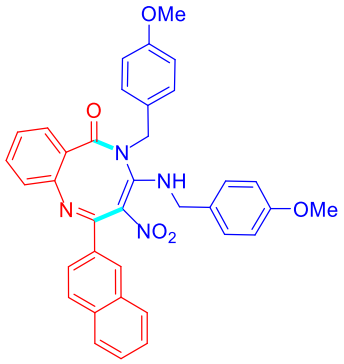
White solid (67%, 120 mg); Mp: 120.4-121.9 ℃; IR (KBr) 3729, 3350, 3002, 2932, 2807, 1649, 1603, 1532, 1451, 1307, 1276, 1001 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 10.55 (br, 1H, NH), 7.94 (d, *J* = 9.2 Hz, 1H, ArH), 7.78-7.86 (m, 4H, ArH), 7.59 (t, *J* = 8.9 Hz, 2H, ArH), 7.46 (t, *J* = 10.5 Hz, 3H, ArH), 7.27 (d, *J* = 9.7 Hz, 2H, ArH), 7.03 (t, *J* = 11.6 Hz, 3H, ArH), 6.93 (d, *J* = 9.5 Hz, 1H, ArH), 6.71 (d, *J* = 8.7 Hz, 1H, ArH), 6.47 (d, *J* = 9.7 Hz, 2H, ArH), 5.53 (d, *J* = 17.6 Hz, 1H, CH_2), 4.80 (d, *J* = 18.1 Hz, 1H, CH_2), 4.63-4.68 (m, 1H, CH_2), 4.30 (d, *J* = 17.6 Hz, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.5, 160.6, 153.9, 148.3, 136.6, 134.8, 134.4, 133.3, 133.0, 132.7, 131.7, 130.7, 130.7, 129.8, 129.8, 129.7, 129.7, 129.4, 129.4, 129.3, 129.3, 128.4, 128.2, 128.1, 127.7, 127.7, 127.7, 127.7, 127.1, 123.7, 120.6, 114.8, 50.3, 47.0 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{34}H_{25}Cl_2N_4O_3$ [(M+H)$^+$], 607.1298; found, 607.1297.

(1*Z*,3*E*)-5-(4-Methylbenzyl)-4-((4-methylbenzyl)amino)-2-(naphthalen-2-yl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4k)



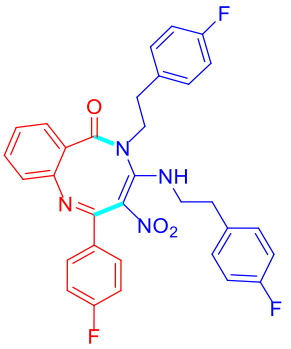
White solid (63%, 110 mg); Mp: 116.3-117.7 ℃; IR (KBr) 3693, 3403, 3010, 1649, 1606, 1509, 1470, 1384, 1213, 1179 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 10.07 (br, 1H, NH), 7.92 (t, *J* = 4.3 Hz, 1H, ArH), 7.80 (d, *J* = 8.0 Hz, 1H, ArH), 7.69 (d, *J* = 8.8 Hz, 1H, ArH), 7.62 (d, *J* = 7.8 Hz, 1H, ArH), 7.41-7.50 (m, 4H, ArH), 7.15 (t, *J* = 8.8 Hz, 3H, ArH), 7.02-7.09 (m, 1H, ArH), 7.01 (t, *J* = 3.9 Hz, 3H, ArH), 6.89 (d, *J* = 7.9 Hz, 2H, ArH), 6.34 (d, *J* = 7.7 Hz, 2H, ArH), 5.74 (d, *J* = 14.3 Hz, 1H, CH_2), 4.54 (t, *J* = 6.4 Hz, 2H, CH_2), 3.98 (d, *J* = 14.3 Hz, 1H, CH_2), 2.37 (s, 3H, CH_3), 1.37 (s, 3H, CH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.6, 160.3, 154.5, 149.4, 139.2, 138.9, 135.4, 133.7, 133.4, 132.8, 132.0, 131.8, 130.6, 130.6, 130.0, 129.9, 129.6, 129.6, 129.3, 129.3, 128.4, 128.2, 128.1, 127.9, 127.9, 126.7, 126.7, 125.0, 124.8, 124.5, 121.7, 117.1, 51.4, 48.5, 21.7, 20.7 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{36}H_{31}N_4O_3$ $[(M+H)^+]$, 567.2391; found, 567.2390.

(1*Z*,3*E*)-5-(4-Methoxybenzyl)-4-((4-methoxybenzyl)amino)-2-(naphthalen-2-yl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (4l)



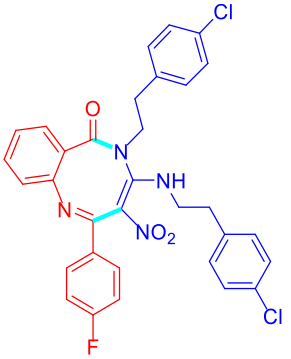
White solid (65%, 113 mg); Mp: 130.4-131.8 ℃; IR (KBr) 3675, 3362, 3053, 2963, 2845, 1669, 1623, 1472, 1421, 1358, 1245, 1124 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 10.55 (br, 1H, NH), 7.81(d, *J* = 8.5 Hz, 1H, ArH), 7.80(d, *J* = 8.4 Hz, 1H, ArH), 7.65-7.69 (m, 2H, ArH), 7.57 (s, 1H, ArH), 7.51 (d, *J* = 7.1 Hz, 1H, ArH), 7.42-7.49 (m, 2H, ArH), 7.19 (d, *J* = 7.6 Hz, 1H, ArH), 7.10 (t, *J* = 7.5 Hz, 1H, ArH), 7.01-7.05 (m, 3H, ArH), 6.94 (d, *J* = 8.3 Hz, 2H, ArH), 6.86 (d, *J* = 8.5 Hz, 2H, ArH), 6.06 (d, *J* = 8.3 Hz, 2H, ArH), 5.69 (d, *J* = 14.3 Hz, 1H, CH_2), 4.51 (t, *J* = 5.3 Hz, 2H, CH_2), 3.99 (d, *J* = 14.3 Hz, 1H, CH_2), 3.81 (s, 3H, OCH_3), 3.00 (s, 3H, OCH_3) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.9, 159.9, 159.7, 159.1, 153.8, 148.8, 134.7, 133.0, 132.7, 131.5, 130.1, 130.1, 129.3, 129.3, 128.5, 127.9, 127.9, 127.9, 127.6, 127.4, 127.0, 126.3, 126.2, 124.5, 124.2, 123.9, 121.2, 116.4, 114.7, 114.7, 113.5, 113.5, 55.4, 54.3, 50.5, 47.7 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{36}H_{31}N_4O_5$ $[(M+H)^+]$, 599.2289; found, 599.2291.

(1*Z*,3*E*)-5-(4-Fluorophenethyl)-4-((4-fluorophenethyl)amino)-2-(4-fluorophenyl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (5a)



White solid (81%, 139 mg); Mp: 167.6-168.5 ℃; IR (KBr) 3682, 3490, 2956, 2842, 1684, 1606, 1509, 1449, 1365, 1237, 1124 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.73 (br, 1H, NH), 7.96-7.98 (m, 2H, ArH), 7.47 (t, *J* = 7.6 Hz, 1H, ArH), 7.32 (d, *J* = 7.5 Hz, 1H, ArH), 7.13-7.18 (m, 3H, ArH), 7.02 (t, *J* = 3.6 Hz, 3H, ArH), 6.91-6.97 (m, 6H, ArH), 4.23-4.30 (m, 1H, CH_2), 3.45-3.51 (m, 2H, CH_2), 2.83-2.91 (m, 2H, CH_2), 2.74 -2.80 (m, 2H, CH_2), 2.05-2.10 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.4, 160.1(*J* = 252.0 Hz), 162.1(*J* = 244.5 Hz), 161.8(*J* = 243.0 Hz), 158.2, 154.1, 148.6, 132.8, 132.2, 132.1, 131.8, 130.2(*J* = 7.5 Hz), 130.2(*J* = 22.5 Hz), 130.2(*J* = 7.5 Hz), 130.0(*J* = 22.5 Hz), 130.0, 129.9(*J* = 7.5 Hz), 129.9, 127.4, 124.9, 124.0, 121.2, 116.1, 116.1(*J* = 6.0 Hz), 116.0(*J* = 7.5 Hz), 115.6(*J* = 22.5 Hz), 115.6, 115.2, 50.3, 45.8, 35.3, 33.7 ppm. ^{19}F NMR (564 MHz, $CDCl_3$): δ = -107.09, δ = -114.55, δ = -115.61. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{26}F_3N_4O_3$ $[(M+H)^+]$, 571.1952; found, 571.1950.

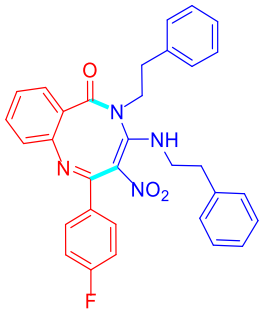
(1*Z*,3*E*)-5-(4-Chlorophenethyl)-4-((4-chlorophenethyl)amino)-2-(4-fluorophenyl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (5b)



White solid (80%, 145 mg); Mp: 183.0-184.3 ℃; IR (KBr) 3644, 3350, 3027, 2973, 2867, 1675, 1610, 1490, 1397, 1313, 1239, 1134 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.70 (br, 1H, NH), 7.95-7.98 (m, 2H, ArH), 7.46 (t, *J* = 7.6 Hz, 1H, ArH), 7.12-7.30

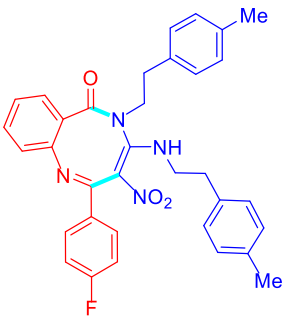
(m, 8H, ArH), 6.98-7.06 (m, 3H, ArH), 6.88 (d, *J* = 8.1 Hz, 2H, ArH), 4.25-4.31 (m, 1H, CH_2), 3.42-3.52 (m, 2H, CH_2), 2.73-2.94 (m, 4H, CH_2), 2.04 -2.12 (m, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, $CDCl_3$): δ = 167.4, 165.1(*J* = 252.5 Hz), 158.2, 154.1, 148.6, 135.6, 134.9, 133.5, 132.8, 132.2, 132.2, 131.8, 130.3(*J* = 8.8 Hz), 130.3, 129.9, 129.9, 129.8, 129.8, 129.3, 129.3, 128.9, 128.9, 127.3, 125.0, 123.9, 121.2, 116.1(*J* = 22.5 Hz), 115.2, 50.0, 45.7, 35.4, 33.8 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -106.98. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{26}Cl_2FN_4O_3$ [(M+H)$^+$], 603.1361; found, 603.1353.

(1*Z*,3*E*)-2-(4-Fluorophenyl)-3-nitro-5-phenethyl-4-(phenethylamino)benzo[*b*][1,5] diazocin-6(5*H*)-one (5c)



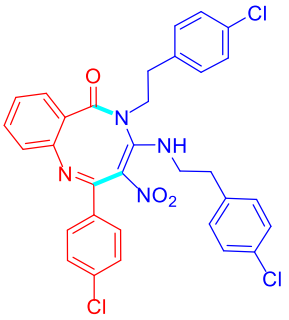
White solid (77%, 123 mg); Mp: 175.7-176.3 ℃; IR (KBr) 3672, 3388, 3013, 2972, 2831, 1674, 1608, 1512, 1430, 1311, 1234, 1133 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$): δ = 9.76 (br, 1H, NH), 7.97-8.00 (m, 2H, ArH), 7.47 (t, *J* = 7.7 Hz, 1H, ArH), 7.38 (d, *J* = 7.6 Hz, 1H, ArH), 7.23-7.30 (m, 5H, ArH), 7.13-7.19 (m, 4H, ArH), 7.07 (d, *J* = 7.2 Hz, 2H, ArH), 7.03 (d, *J* = 8.0 Hz, 1H, ArH), 6.96 (d, *J* = 7.3 Hz, 2H, ArH), 4.23-4.36 (m, 1H, CH_2), 3.49-3.53 (m, 2H, CH_2), 2.75-2.97 (m, 4H, CH_2), 2.07-2.13 (m, 1H, CH_2) ppm; ^{13}C NMR (125 MHz,$CDCl_3$): δ = 167.4, 165.1(*J* = 252.5 Hz), 158.3, 154.2, 148.7, 137.3, 136.4, 132.3, 132.2, 131.8, 130.4(*J* = 8.8 Hz), 129.2, 128.7, 128.7, 128.7, 128.6, 128.6, 128.6, 128.5, 128.5, 128.5, 127.5, 127.4, 126.9, 124.2, 121.2, 116.0(*J* = 22.5 Hz), 115.0, 50.3, 45.8, 36.1, 34.5 ppm. ^{19}F NMR (470 MHz, $CDCl_3$): δ = -107.29. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{28}FN_4O_3$ [(M+H)$^+$], 535.2140; found, 535.2134.

(1*Z*,3*E*)-2-(4-Fluorophenyl)-5-(4-methylphenethyl)-4-((4-methylphenethyl)amino -3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (5d)



White solid (76%, 127 mg); Mp: 156.8-157.6 ℃; IR (KBr) 3683, 3356, 3021, 2928, 2837, 1675, 1609, 1511, 1483, 1313, 1236, 1133 cm^{-1}; ^{1}H NMR (600 MHz, $CDCl_3$): δ = 9.77 (br, 1H, NH), 7.96-7.99 (m, 2H, ArH), 7.44-7.47 (m, 1H, ArH), 7.36-7.37 (m, 1H, ArH), 7.09-7.17 (m, 5H, ArH), 7.01-7.05 (m, 3H, ArH), 6.96 (d, *J* = 8.0 Hz, 2H, ArH), 6.86 (d, *J* = 7.9 Hz, 2H, ArH), 4.28-4.33 (m, 1H, CH_2), 3.56-3.50 (m, 2H, CH_2), 2.92-2.97 (m, 1H, CH_2), 2.70-2.85 (m, 3H, CH_2), 2.30 (d, *J* = 13.0 Hz, 6H, CH_3), 2.05 -2.10 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.4, 165.1(*J* = 250.5 Hz), 158.4, 154.2, 148.7, 137.1, 136.5, 134.2, 133.3, 132.3, 131.7, 130.4(*J* = 9.0 Hz), 129.8, 129.8, 129.8, 129.4, 129.4, 129.4, 128.5, 128.5, 128.5, 128.4, 127.4, 124.8, 124.2, 121.1, 116.0(*J* = 22.5 Hz), 115.0, 50.4, 45.9, 35.6, 34.1, 21.0, 21.0 ppm. ^{19}F NMR (564 MHz, $CDCl_3$): δ = -107.36. HRMS (TOF ES^+): *m/z* calcd for $C_{34}H_{32}FN_4O_3$ [$(M+H)^+$], 563.2453; found, 563.2454.

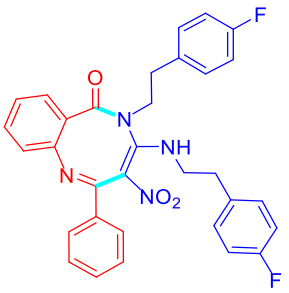
(1*Z*,3*E*)-5-(4-Chlorophenethyl)-4-((4-chlorophenethyl)amino)-2-(4-chlorophenyl)-3-nitrobenzo[*b*][1,5]diazocin-6(5*H*)-one (5e)



White solid (76%, 140 mg); Mp: 204.2-205.6 ℃; IR (KBr) 3672, 3352, 3095, 2927, 2857, 1676, 1613, 1523, 1489, 1312, 1206, 1135 cm-1; 1H NMR (600 MHz, $CDCl_3$): δ = 9.71 (br, 1H, NH), 7.89 (d, J = 8.4 Hz, 2H, ArH), 7.43-7.49 (m, 3H, ArH), 7.16-7.30 (m, 6H, ArH), 6.99-7.02 (m, 3H, ArH), 6.89 (d, J = 8.1 Hz, 2H, ArH), 4.26-4.31 (m, 1H, CH_2), 3.44-3.52 (m, 2H, CH_2), 2.74-2.94 (m, 4H, CH_2), 2.08-2.13 (m, 1H, CH_2) ppm; 13C NMR (150 MHz, $CDCl_3$): δ = 167.4, 158.3, 154.1, 148.5, 138.3, 135.5, 134.8, 134.4, 133.6, 132.9, 131.8, 131.8, 129.9,

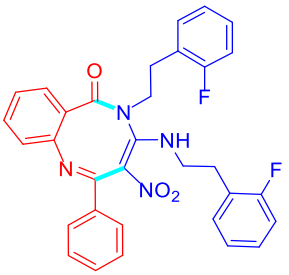
129.9, 129.8, 129.8, 129.4, 129.4, 129.2, 129.2, 129.2, 128.9, 128.9, 127.4, 125.1, 123.8, 121.1, 115.1, 50.0, 45.7, 35.4, 33.9 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{26}Cl_3N_4O_3$ $[(M+H)^+]$, 619.1065; found, 619.1058.

(1*Z*,3*E*)-5-(4-Fluorophenethyl)-4-((4-fluorophenethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5f)



White solid (79%, 131 mg); Mp: 176.3-176.9 ℃; IR (KBr) 3693, 3379, 3064, 2973, 2867, 1675, 1614, 1511, 1449, 1350, 1226, 1133 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.69 (br, 1H, NH), 7.97 (d, *J* = 7.4 Hz, 2H, ArH), 7.45-7.55 (m, 4H, ArH), 7.33 (d, *J* = 7.6 Hz, 1H, ArH), 7.08-7.17 (m, 1H, ArH), 7.01-7.03 (m, 3H, ArH), 6.96 (t, *J* = 8.5 Hz, 2H, ArH), 6.88-6.92 (m, 4H, ArH), 4.24-4.29 (m, 1H, CH_2), 3.45-3.51 (m, 2H, CH_2), 2.74-2.92 (m, 4H, CH_2), 2.04-2.10 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 168.0, 162.7(*J* = 246.0 Hz), 162.4(*J* = 244.5 Hz), 160.1, 154.7, 149.5, 136.5, 133.7, 133.7, 132.8, 132.8, 132.7, 132.4, 130.7(*J* = 9.0 Hz), 130.6(*J* = 21.0 Hz), 130.6(*J* = 7.5 Hz), 129.5, 128.7, 128.7, 128.7, 128.0, 128.0, 128.0, 125.4, 124.6, 121.8, 116.7(*J* = 21.0 Hz), 116.1(*J* = 21.0 Hz), 51.0, 46.4, 35.9, 34.1 ppm. ^{19}F NMR (564 MHz, $CDCl_3$): δ = -119.4, δ = -120.6. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{27}F_2N_4O_3$ $[(M+H)^+]$, 553.2046; found, 553.2042.

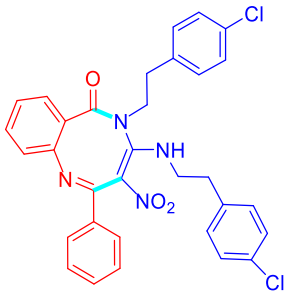
(1*Z*,3*E*)-5-(2-Fluorophenethyl)-4-((2-fluorophenethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5g)



White solid (79%, 130 mg); Mp: 154.7-158.1 ℃; IR (KBr) 3659, 3317, 3026, 2951, 2864, 1674, 1617, 1495, 1448, 1371, 1217, 1138 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.70 (br, 1H, NH), 7.91 (d, *J* = 7.7 Hz, 2H, ArH), 7.30-7.40 (m, 4H, ArH), 7.05-7.16 (m, 2H, ArH), 6.84-6.99 (m, 8H, ArH), 4.17-4.22 (m, 1H, CH_2), 3.39-3.46

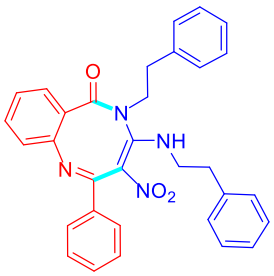
(m, 2H, CH_2), 2.89-2.94 (m, 1H, CH_2), 2.80-2.85 (m, 1H, CH_2), 2.70-2.75 (m, 1H, CH_2), 2.63-2.68 (m, 1H, CH_2), 2.23-2.28 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 166.5, 160.1(J = 244.5 Hz), 160.0(J = 244.5 Hz), 158.7, 153.1, 147.8, 134.8, 130.9, 130.6, 130.0, 130.0(J = 9.0 Hz), 129.2(J = 4.5 Hz), 128.4(J = 9.0 Hz), 127.8(J = 24.0 Hz), 127.7(J = 7.5 Hz), 127.1, 127.1, 126.4, 123.8, 123.6(J = 4.5 Hz), 123.3(J = 3.0 Hz), 123.2(J = 9.0 Hz), 123.2(J = 3.0 Hz), 122.5, 122.4, 120.0, 114.7(J = 21.5 Hz), 114.3(J = 21.0 Hz), 47.6, 43.3, 29.1, 27.0 ppm. ^{19}F NMR (564 MHz, $CDCl_3$): δ = -118.2, δ = -118.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{27}F_2N_4O_3$ [(M+H)$^+$], 553.2046; found, 553.2050.

(1*Z*,3*E*)-5-(4-Chlorophenethyl)-4-((4-chlorophenethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5h)



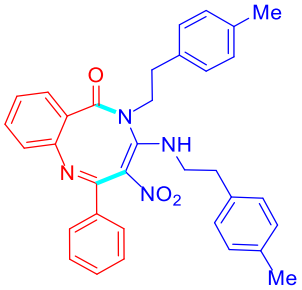
White solid (79%, 139 mg); Mp: 185.2-186.4 ℃; IR (KBr) 3698, 3353, 3045, 2935, 2856, 1671, 1615, 1490, 1441, 1314, 1210, 1133 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.14 (br, 1H, NH), 8.05 (d, J = 7.1 Hz, 2H, ArH), 7.50-7.58 (m, 4H, ArH), 7.20-7.35 (m, 8H, ArH), 6.93-7.03 (m, 3H, ArH), 4.10-4.15 (m, 1H, CH_2), 3.62-3.66 (m, 1H, CH_2), 3.53 (t, J = 6.5 Hz, 1H, CH_2), 3.30-3.39 (m, 1H, CH_2), 2.87 (t, J = 6.9 Hz, 2H, CH_2), 2.51-2.58 (m, 1H, CH_2), 2.08-2.13 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 167.1, 161.0, 154.2, 148.5, 137.3, 137.0, 136.4, 132.4, 131.9, 131.7, 131.7, 131.0, 130.8, 129.3, 129.0, 129.0, 129.0, 128.8, 128.8, 128.8, 128.6, 128.6, 128.6, 127.9, 125.3, 125.1, 120.5, 114.0, 49.4, 45.9, 34.8, 33.5 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{32}H_{27}Cl_2N_4O_3$ [(M+H)$^+$], 585.1455; found, 585.1457.

(1*Z*,3*E*)-3-Nitro-5-phenethyl-4-(phenethylamino)-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5i)



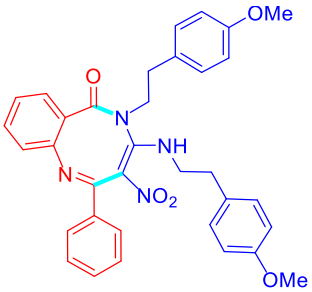
White solid (78%, 120 mg); Mp: 157.9-158.4 ℃; IR (KBr) 3667, 3472, 3081, 2932, 2814, 1676, 1610, 1533, 1481, 1348, 1200, 1129 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.74 (br, 1H, NH), 7.99 (d, *J* = 8.2 Hz, 2H, ArH), 7.49-7.51 (m, 3H, ArH), 7.47 (t, *J* = 7.1 Hz, 1H, ArH), 7.37 (d, *J* = 7.7 Hz, 2H, ArH), 7.25-7.30 (m, 4H, ArH), 7.19-7.24 (m, 2H, ArH), 7.16 (t, *J* = 8.0 Hz, 2H, ArH), 7.04-7.08 (m, 1H, ArH), 6.94 (d, *J* = 7.4 Hz, 2H, ArH), 4.29-4.34 (m, 1H, CH_2), 3.49-3.52 (m, 2H, CH_2), 2.76-2.96 (m, 4H, CH_2), 2.07-2.12 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.5, 159.6, 154.1, 148.9, 137.5, 136.5, 135.9, 132.0, 131.7, 129.1, 128.9, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.6, 128.2, 128.2, 127.5, 127.4, 126.8, 124.9, 124.2, 121.2, 115.3, 50.4, 45.8, 36.2, 34.4 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{29}N_4O_3$ $[(M+H)^+]$, 517.2234; found, 517.2232.

(1*Z*,3*E*)-5-(4-Methylphenethyl)-4-((4-methylphenethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5j)



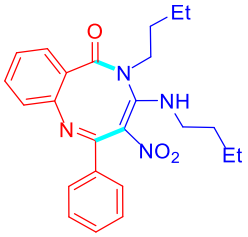
White solid (73%, 119 mg); Mp: 177.9-178.4 ℃; IR (KBr) 3690, 3347, 3039, 2972, 2834, 1675, 1615, 1514, 1446, 1313, 1205, 1132 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.75 (br, 1H, NH), 7.97 (t, *J* =4.0 Hz, 2H, ArH), 7.44-7.50 (m, 4H, ArH), 7.37 (d, *J* = 7.6 Hz, 1H, ArH), 7.14-7.26 (m, 1H, ArH), 7.10 (d, *J* = 7.6 Hz, 2H, ArH), 7.03-7.05 (m, 3H, ArH), 6.96 (d, *J* = 7.8 Hz, 2H, ArH), 6.84 (d, *J* = 7.8 Hz, 2H, ArH), 4.27-4.32 (m, 1H, CH_2), 3.46-3.49 (m, 2H, CH_2), 2.91-2.96 (m, 1H, CH_2), 2.72-2.85 (m, 3H, CH_2), 2.29 (d, *J* = 18.1 Hz, 6H, OCH_3), 2.04-2.09 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.5, 159.6, 154.2, 148.9, 137.1, 136.4, 136.0, 134.4, 133.4, 132.0, 131.6, 129.8, 129.8, 129.8, 129.3, 128.8, 128.5, 128.5, 128.4, 128.4, 128.2, 128.2, 128.2, 127.4, 124.8, 124.3, 121.1, 115.3, 50.5, 45.9, 35.7, 33.9, 21.1, 21.0 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{34}H_{33}N_4O_3$ $[(M+H)^+]$, 545.2547; found, 545.2538.

(1*Z*,3*E*)-5-(4-Methoxyphenethyl)-4-((4-methoxyphenethyl)amino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5k)



White solid (75%, 130 mg); Mp: 157.9-158.4 ℃; IR (KBr) 3629, 3477, 3066, 2958, 2840, 1676, 1611, 1513, 1450, 1357, 1248, 1135 cm^{-1}; ^1H NMR (600 MHz, $CDCl_3$): δ = 9.69 (br, 1H, NH), 7.90 (d, J = 7.5 Hz, 2H, ArH), 7.36-7.42 (m, 4H, ArH), 7.23 (d, J = 7.6 Hz, 1H, ArH), 7.18 (s, 1H, ArH), 7.06-7.10 (m, 3H, ArH), 6.96-6.97 (m, 2H, ArH), 6.33-6.79 (m, 2H, ArH), 6.68 (d, J = 8.4 Hz, 2H, ArH), 4.17-4.22 (m, 1H, CH_2), 3.70 (d, J = 6.5 Hz, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 3.37-3.41 (m, 2H, CH_2), 2.63-2.86 (m, 4H, CH_2), 1.95-1.99 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, $CDCl_3$): δ = 167.5, 159.6, 158.9, 158.5, 154.2, 148.8, 136.0, 132.0, 131.6, 129.7, 129.6, 129.6, 129.5, 129.5, 128.8, 128.5, 128.4, 128.4, 128.2, 127.4, 124.8, 124.2, 121.1, 115.2, 114.5, 114.5, 114.1, 113.9, 55.3, 55.3, 50.6, 46.0, 35.2, 33.5 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{34}H_{33}N_4O_5$ $[(M+H)^+]$, 577.2445; found, 577.2439.

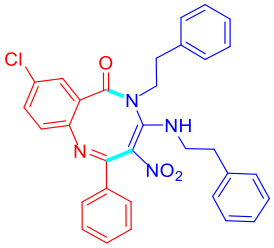
(1*Z*,3*E*)-5-Butyl-4-(butylamino)-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5l)



Yellow solid (82%, 103 mg); Mp: 180.9-181.4 ℃; IR (KBr) 3667, 3472, 3081, 2932, 2814, 1676, 1610, 1533, 1481, 1348, 1200, 1129 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.10 (br, 1H, NH), 7.93 (d, J = 7.3 Hz, 2H, ArH), 7.43-7.58 (m, 5H, ArH), 7.24 (t, J = 7.5 Hz, 1H, ArH), 6.96 (d, J = 7.9 Hz, 1H, ArH), 4.03-4.09 (m, 1H, CH_2), 3.36-3.44 (m, 1H, CH_2), 3.26 (t, J = 6.2 Hz, 1H, CH_2), 3.07-3.12 (m, 1H, CH_2), 1.44-1.55 (m, 2H, CH_2), 1.13-1.25 (m, 3H, CH_2), 0.84-1.03 (m, 6H, CH_3), 0.42-0.83 (m, 3H, CH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 167.1, 160.9, 154.6, 148.6, 136.2, 132.2, 131.8, 129.2, 128.5, 128.5, 128.1, 128.1, 125.3, 125.1, 120.6, 113.8, 48.0, 44.4, 31.8, 30.7, 20.0, 19.8, 14.0, 13.7 ppm. HRMS (TOF ES^+): *m/z* calcd for

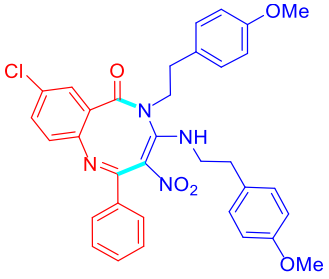
$C_{24}H_{29}N_4O_3$ [$(M+H)^+$], 421.2234; found, 421.2234.

(1*Z*,3*E*)-8-Chloro-3-nitro-5-phenethyl-4-(phenethylamino)-2-phenylbenzo[*b*][1,5] diazocin-6(5*H*)-one (5m)



White solid (76%, 116 mg); Mp: 167.9-168.4 ℃; IR (KBr) 3632, 3366, 3065, 2935, 2853, 1680, 1613, 1463, 1380, 1315, 1199, 1128 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.14 (br, 1H, NH), 8.05 (d, J = 4.2 Hz, 2H, ArH), 7.52-7.59 (m, 5H, ArH), 7.16-7.30 (m, 8H, ArH), 7.04 (d, J = 8.7 Hz, 1H, ArH), 7.00 (d, J = 7.2 Hz, 2H, ArH), 4.08-4.14 (m, 1H, CH_2), 3.61-3.66 (m, 2H, CH_2), 3.30-3.36 (m, 1H, CH_2), 2.89 (t, J = 7.0 Hz, 2H, CH_2), 2.51-2.58 (m, 1H, CH_2), 2.06-2.12 (m, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 165.5, 161.6, 153.9, 147.4, 138.1, 137.9, 136.3, 132.6, 131.9, 129.5, 129.4, 129.2, 129.0, 129.0, 129.0, 128.9, 128.9, 128.9, 128.9, 128.9, 128.7, 127.6, 127.2, 127.0, 126.9, 122.8, 113.5, 49.8, 46.0, 35.4, 34.0 ppm. HRMS (TOF ES^+): *m/z* calcd for $C_{32}H_{28}ClN_4O_3$ [$(M+H)^+$], 551.1844; found, 551.1843.

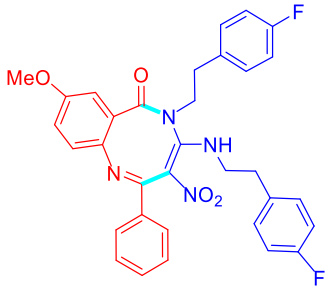
(1*Z*,3*E*)-8-Chloro-5-(4-methoxyphenethyl)-4-((3-methoxyphenethyl)amino)-3-nitr o-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one (5n)



White solid (73%, 134 mg); Mp: 154.9-155.4 ℃; IR (KBr) 3652, 3385, 3066, 2930, 2853, 1679, 1613, 1491, 1464, 1357, 1258, 1126 cm^{-1}; ^1H NMR (500 MHz, DMSO-d_6): δ = 10.10 (br, 1H, NH), 8.03 (t, J = 4.2 Hz, 2H, ArH), 7.51-7.60 (m, 5H, ArH), 7.14 (d, J = 8.6 Hz, 2H, ArH), 7.03 (d, J = 8.6 Hz, 1H, ArH), 6.79-6.92 (m, 6H, ArH), 4.02-4.08 (m, 1H, CH_2), 3.70 (d, J = 11.5 Hz, 6H, OCH_3), 3.61 (t, J = 6.7 Hz, 2H, CH_2), 3.25-3.30 (m, 1H, CH_2), 2.82 (t, J = 7.4 Hz, 2H, CH_2), 2.45-2.52 (m, 1H, CH_2), 2.01-2.07 (m, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 165.5, 161.7, 158.6, 158.5, 154.0, 147.4, 136.2, 132.6, 131.8, 130.2, 129.9, 129.9, 129.8,

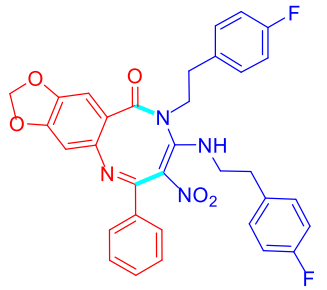
129.7, 129.7, 129.7, 129.5, 129.5, 129.5, 129.3, 128.7, 127.6, 127.6, 122.8, 114.4, 114.4, 114.4, 114.4, 113.5, 55.5, 50.0, 46.1, 34.5, 33.2 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{34}H_{32}ClN_4O_5$ [(M+H)$^+$], 611.2056; found, 611.2051.

(1*Z*,3*E*)-5-(4-Fluorophenethyl)-4-((4-fluorophenethyl)amino)-8-methoxy-3-nitro-2-phenylbenzo[*b*][1,5]diazocin-6(5*H*)-one(5o)



White solid (69%, 145 mg); Mp: 177.9-178.4 ℃; IR (KBr) 3647, 3334, 3101, 2919, 2823, 1670, 1601, 1525, 1467, 1378, 1211, 1100 cm^{-1}; ^{1}H NMR (500 MHz, DMSO-d_6): δ = 10.11 (br, 1H, NH), 8.01 (t, *J* = 4.0 Hz, 2H, ArH), 7.50-7.56 (m, 3H, ArH), 7.24-7.26 (m, 2H, ArH), 7.01-7.12 (m, 8H, ArH), 6.93 (d, *J* = 8.8 Hz,1H, ArH), 4.05-4.11 (m, 1H, CH_2), 3.77 (s, 3H, OCH_3), 3.57-3.64 (m, 2H, CH_2), 3.24-3.31 (m, 1H, CH_2), 2.88 (t, *J* = 7.1 Hz, 2H, CH_2), 2.51-2.56 (m, 1H, CH_2), 2.08-2.14 (m, 1H, CH_2) ppm; ^{13}C NMR (125 MHz, DMSO-d_6): δ = 166.7, 161.6(*J* = 241.3 Hz), 161.5(*J* = 241.3 Hz), 160.8, 156.7, 154.2, 141.7, 136.6, 134.3, 134.1, 132.1, 131.1, 131.1(*J* = 7.5 Hz), 131.0, 130.7(*J* = 7.5 Hz), 129.3, 129.3, 128.4, 128.4, 126.1, 122.3, 117.9, 115.8, 115.7(*J* = 21.3 Hz), 115.7, 115.6(*J* = 21.3 Hz), 113.9, 112.5, 56.0, 49.6, 45.9, 34.7, 33.3 ppm. ^{19}F NMR (470MHz, DMSO-d_6): δ = -116.1, δ =-116.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{28}F_2N_4O_4$ [(M+H)$^+$], 583.2151; found, 583.2146

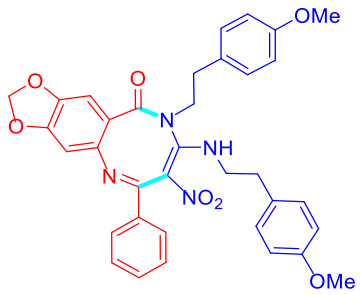
(5*Z*,7*E*)-9-(4-Fluorophenethyl)-8-((3-fluorophenethyl)amino)-7-nitro-6-phenyl-[1,3]dioxolo[4',5':4,5]benzo[1,2-*b*][1,5]diazocin-10(9*H*)-one (5p)



White solid (73%, 130 mg); Mp: 187.9-188.4 ℃; IR (KBr) 3627, 3434, 3007, 2902, 2864, 1696, 1616, 1523, 1456, 1398, 1200, 1109 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.16 (br, 1H, NH), 8.01 (d, *J* = 7.0 Hz, 2H, ArH), 7.51-7.56 (m, 3H,

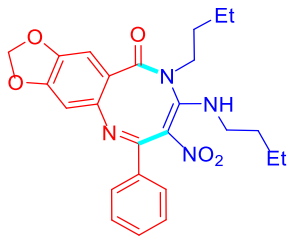
ArH), 7.25-7.27 (m, 2H, ArH), 7.00-7.12 (m, 6H, ArH), 6.89 (s, 1H, ArH), 6.55 (s, 1H, ArH), 6.15 (s, 1H, OCH_2), 6.07 (s, 1H, OCH_2), 4.02-4.07 (m, 1H, CH_2), 3.61-3.65 (m, 1H, CH_2), 3.49-3.54 (m, 1H, CH_2), 3.23-3.28 (m, 1H, CH_2), 2.89 (t, *J* = 6.9 Hz, 2H, CH_2), 2.49-2.53 (m, 1H, CH_2), 2.03-2.08 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 166.6, 161.6(*J* = 241.5 Hz), 161.5(*J* = 240.0 Hz), 154.3, 150.3, 145.0, 144.2, 136.5, 134.4, 134.1, 132.2, 131.2, 131.2, 131.1, 131.1, 130.7(*J* = 7.5 Hz), 129.3, 129.3, 128.5, 128.5, 117.4, 115.7(*J* = 7.5 Hz), 115.7(*J* = 21.0 Hz), 115.6(*J* = 21.0 Hz), 115.6(*J* = 7.5 Hz), 113.8, 107.2, 102.5, 101.6, 49.6, 46.1, 34.5, 33.3 ppm. ^{19}F NMR (564MHz, DMSO-d_6): δ = -116.2, δ =-116.3. HRMS (TOF ES$^+$): *m/z* calcd for $C_{33}H_{27}F_2N_4O_5$ [(M+H)$^+$], 597.1944; found, 597.1942.

(5*Z*,7*E*)-9-(4-Methoxyphenethyl)-8-((3-methoxyphenethyl)amino)-7-nitro-6-phenyl-[1,3]dioxolo[4',5':4,5]benzo[1,2-*b*][1,5]diazocin-10(9*H*)-one (5q)



White solid (70%, 130 mg); Mp: 165.9-166.4 ℃; IR (KBr) 3636, 3379, 3089, 2928, 2876, 1676, 1616, 1509, 1438, 1370, 1250, 1131 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.16 (br, 1H, NH), 8.02 (d, *J* = 6.8 Hz, 2H, ArH), 7.53 (t, *J* = 8.3 Hz, 3H, ArH), 7.14 (d, *J* = 7.8 Hz, 2H, ArH), 6.96 (s, 1H, ArH), 6.79-6.91 (m, 6H, ArH), 6.57 (s, 1H, ArH), 6.14 (s, 1H, OCH_2), 6.08 (s, 1H, OCH_2), 4.01-4.04 (m, 1H, CH_2), 3.70 (d, *J* = 17.1 Hz, 6H, OCH_3), 3.60 (t, *J* = 6.2 Hz, 1H, CH_2), 3.25 (s, 1H, CH_2), 3.20-3.23 (m, 1H, CH_2), 2.83 (d, *J* = 5.9 Hz, 2H, CH_2), 2.46-2.49 (m, 1H, CH_2), 2.00-2.04 (m, 1H, CH_2) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 166.5, 160.8, 158.6, 158.5, 154.4, 150.4, 145.0, 144.2, 136.6, 132.2, 130.2, 130.2, 129.9, 129.9, 129.9, 129.9, 129.2, 129.2, 128.6, 117.5, 114.4, 114.4, 114.4, 114.4, 113.8, 113.8, 107.3, 102.6, 101.6, 55.5, 55.5, 49.9, 46.2, 34.6, 33.3 ppm. HRMS (TOF ES$^+$): *m/z* calcd for $C_{35}H_{33}N_4O_7$ [(M+H)$^+$], 621.2344; found, 621.2349.

(5*Z*,7*E*)-9-Butyl-8-(butylamino)-7-nitro-6-phenyl-[1,3]dioxolo[4',5':4,5]benzo[1,2-*b*][1,5]diazocin-10(9*H*)-one (5r)



Yellow solid (80%, 111 mg); Mp: 158.9-159.4 ℃; IR (KBr) 3634, 3423, 3009, 2912, 2876, 1689, 1613, 1523, 1456, 1321, 1200, 1100 cm^{-1}; ^{1}H NMR (600 MHz, DMSO-d_6): δ = 10.13 (br, 1H, NH), 7.91 (d, J = 7.3 Hz, 2H, ArH), 7.48-7.56 (m, 3H, ArH), 6.97 (s, 1H, ArH), 6.55 (s, 1H, ArH), 6.12 (s, 1H, OCH_2), 6.09 (s, 1H, OCH_2), 3.99-4.02 (m, 1H, CH_2), 3.39-3.42 (m, 1H, CH_2), 3.26-3.35 (m, 1H, CH_2), 3.05-3.09 (m, 1H, CH_2), 1.51-1.57 (m, 2H, CH_2), 1.25-1.28 (m, 2H, CH_2), 1.14-1.17 (m, 1H, CH_2), 0.87-0.99 (m, 6H, CH_3), 0.42-0.86 (m, 3H, CH_2) ppm; ^{13}C NMR (150 MHz, DMSO-d_6): δ = 166.6, 160.8, 154.7, 150.3, 145.0, 144.2, 136.3, 123.0, 129.1, 129.1, 128.5, 128.5, 117.7, 113.8, 107.2, 102.5, 101.6, 48.0, 44.4, 31.8, 30.6, 19.9, 19.9, 14.0, 13.6 ppm. HRMS (TOF ES^+): m/z calcd for $C_{25}H_{29}N_4O_5$ $[(M+H)^+]$, 465.2132; found, 465.2127.

X-ray Structure and Data of 4h[2]

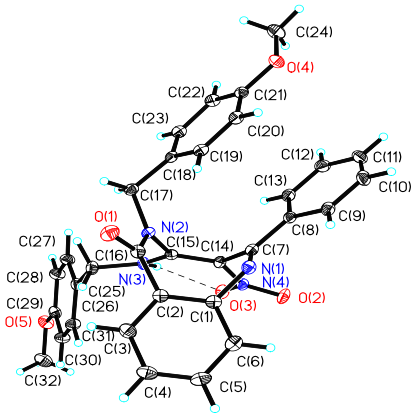


Figure S1. X-Ray crystal structure of **4h**, ellipsoid is drawn at the 30% probability level.

Table S1. Crystal data and structure refinement for **4h**

Identification code	1
Empirical formula	$C_{32}H_{28}N_4O_5$
Formula weight	548.58
Temperature	150.00 K
Crystal system	Orthorhombic
Space group	P2(1)2(1)2(1)
Unit cell dimensions	a = 7.8871(7) Å = 90 °. b = 10.9414(9) Å = 90 °. c = 30.867(3) Å = 90 °.
Volume	2663.7(4) $Å^3$
Z	4
Density (calculated)	1.368 mg/m^3
Absorption coefficient	0.094 mm^{-1}
F(000)	1152
Theta range for data collection	1.975 to 28.363 °.
Index ranges	-9<=h<=10, -14<=k<=12, -36<=l<=41
Reflections collected	31745
Independent reflections	6628 [R(int) = 0.0787]
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	6628 / 0 / 372
Goodness-of-fit on F^2	1.024
Final R indexes [I>=2sigma(I)]	R_1 = 0.0461, wR_2 = 0.1034
Final R indexes (all data)	R_1 = 0.0703, wR_2 = 0.1169
Extinction coefficient	n/a
Largest diff. peak and hole	0.220 /-0.296e.$Å^{-3}$

Table S2. Bond Lengths for **4h**

Atom	Atom	Length/Å	Atom	Atom	Length/Å
O(1)	C(16)	1.222(3)	C(12)	H(12)	0.9500
O(2)	N(4)	1.242(3)	C(12)	C(13)	1.385(4)
O(3)	N(4)	1.250(3)	C(13)	H(13)	0.9500
O(4)	C(21)	1.371(3)	C(14)	C(15)	1.373(4)
O(4)	C(24)	1.433(3)	C(17)	H(17A)	0.9900
O(5)	C(29)	1.372(3)	C(17)	H(17B)	0.9900
O(5)	C(32)	1.425(4)	C(17)	C(18)	1.510(4)
N(1)	C(1)	1.418(3)	C(18)	C(19)	1.398(4)
N(1)	C(7)	1.284(3)	C(18)	C(23)	1.383(4)
N(2)	C(15)	1.422(3)	C(19)	H(19)	0.9500
N(2)	C(16)	1.374(3)	C(19)	C(20)	1.378(4)
N(2)	C(17)	1.487(3)	C(20)	H(20)	0.9500
N(3)	H(3)	0.8800	C(20)	C(21)	1.393(4)
N(3)	C(15)	1.334(3)	C(21)	C(22)	1.385(4)
N(3)	C(25)	1.473(3)	C(22)	H(22)	0.9500
N(4)	C(14)	1.401(3)	C(22)	C(23)	1.387(4)
C(1)	C(2)	1.403(4)	C(23)	H(23)	0.9500
C(1)	C(6)	1.401(4)	C(24)	H(24A)	0.9800
C(2)	C(3)	1.392(4)	C(24)	H(24B)	0.9800
C(2)	C(16)	1.494(4)	C(24)	H(24C)	0.9800
C(3)	H(3A)	0.9500	C(25)	H(25A)	0.9900
C(3)	C(4)	1.379(4)	C(25)	H(25B)	0.9900
C(4)	H(4)	0.9500	C(25)	C(26)	1.515(4)
C(4)	C(5)	1.389(5)	C(26)	C(27)	1.388(4)
C(5)	H(5)	0.9500	C(26)	C(31)	1.383(4)
C(5)	C(6)	1.378(4)	C(27)	H(27)	0.9500
C(6)	H(6)	0.9500	C(27)	C(28)	1.381(4)
C(7)	C(8)	1.482(4)	C(28)	H(28)	0.9500
C(7)	C(14)	1.492(3)	C(28)	C(29)	1.391(4)
C(8)	C(9)	1.397(4)	C(29)	C(30)	1.377(4)
C(8)	C(13)	1.390(4)	C(30)	H(30)	0.9500
C(9)	H(9)	0.9500	C(30)	C(31)	1.389(4)
C(9)	C(10)	1.382(4)	C(31)	H(31)	0.9500
C(10)	H(10)	0.9500	C(32)	H(32A)	0.9800
C(10)	C(11)	1.383(5)	C(32)	H(32B)	0.9800
C(11)	H(11)	0.9500	C(32)	H(32C)	0.9800
C(11)	C(12)	1.379(4)			

Table S3. Bond Angles for **4h**

Atom	Atom	Atom	Angle/°	Atom	Atom	Atom	Angle/°
C(21)	O(4)	C(24)	117.5(2)	N(2)	C(17)	H(17A)	108.9
C(29)	O(5)	C(32)	116.7(2)	N(2)	C(17)	H(17B)	108.9
C(7)	N(1)	C(1)	120.9(2)	N(2)	C(17)	C(18)	113.2(2)
C(15)	N(2)	C(17)	116.9(2)	H(17A)	C(17)	H(17B)	107.8
C(16)	N(2)	C(15)	122.8(2)	C(18)	C(17)	H(17A)	108.9
C(16)	N(2)	C(17)	120.1(2)	C(18)	C(17)	H(17B)	108.9
C(15)	N(3)	H(3)	117.9	C(19)	C(18)	C(17)	121.7(2)
C(15)	N(3)	C(25)	124.2(2)	C(23)	C(18)	C(17)	120.1(2)
C(25)	N(3)	H(3)	117.9	C(23)	C(18)	C(19)	118.1(2)
O(2)	N(4)	O(3)	121.3(2)	C(18)	C(19)	H(19)	119.7
O(2)	N(4)	C(14)	117.7(2)	C(20)	C(19)	C(18)	120.6(2)
O(3)	N(4)	C(14)	121.0(2)	C(20)	C(19)	H(19)	119.7
C(2)	C(1)	N(1)	123.3(2)	C(19)	C(20)	H(20)	119.8
C(6)	C(1)	N(1)	116.8(3)	C(19)	C(20)	C(21)	120.4(2)
C(6)	C(1)	C(2)	119.5(2)	C(21)	C(20)	H(20)	119.8
C(1)	C(2)	C(16)	121.7(2)	O(4)	C(21)	C(20)	115.4(2)
C(3)	C(2)	C(1)	119.2(3)	O(4)	C(21)	C(22)	124.8(2)
C(3)	C(2)	C(16)	118.4(3)	C(22)	C(21)	C(20)	119.8(2)
C(2)	C(3)	H(3A)	119.5	C(21)	C(22)	H(22)	120.5
C(4)	C(3)	C(2)	121.0(3)	C(21)	C(22)	C(23)	119.0(2)
C(4)	C(3)	H(3A)	119.5	C(23)	C(22)	H(22)	120.5
C(3)	C(4)	H(4)	120.2	C(18)	C(23)	C(22)	122.1(2)
C(3)	C(4)	C(5)	119.7(3)	C(18)	C(23)	H(23)	119.0
C(5)	C(4)	H(4)	120.2	C(22)	C(23)	H(23)	119.0
C(4)	C(5)	H(5)	119.7	O(4)	C(24)	H(24A)	109.5
C(6)	C(5)	C(4)	120.6(3)	O(4)	C(24)	H(24B)	109.5
C(6)	C(5)	H(5)	119.7	O(4)	C(24)	H(24C)	109.5
C(1)	C(6)	H(6)	120.0	H(24A)	C(24)	H(24B)	109.5
C(5)	C(6)	C(1)	120.0(3)	H(24A)	C(24)	H(24C)	109.5
C(5)	C(6)	H(6)	120.0	H(24B)	C(24)	H(24C)	109.5
N(1)	C(7)	C(8)	119.2(2)	N(3)	C(25)	H(25A)	109.9
N(1)	C(7)	C(14)	122.5(2)	N(3)	C(25)	H(25B)	109.9
C(8)	C(7)	C(14)	118.3(2)	N(3)	C(25)	C(26)	109.1(2)
C(9)	C(8)	C(7)	119.9(2)	H(25A)	C(25)	H(25B)	108.3
C(13)	C(8)	C(7)	121.1(2)	C(26)	C(25)	H(25A)	109.9
C(13)	C(8)	C(9)	119.0(2)	C(26)	C(25)	H(25B)	109.9
C(8)	C(9)	H(9)	120.1	C(27)	C(26)	C(25)	120.5(2)
C(10)	C(9)	C(8)	119.8(3)	C(31)	C(26)	C(25)	120.8(2)
C(10)	C(9)	H(9)	120.1	C(31)	C(26)	C(27)	118.6(2)
C(9)	C(10)	H(10)	119.7	C(26)	C(27)	H(27)	119.6
C(9)	C(10)	C(11)	120.6(3)	C(28)	C(27)	C(26)	120.8(3)
C(11)	C(10)	H(10)	119.7	C(28)	C(27)	H(27)	119.6

C(10)	C(11)	H(11)	119.9	C(27)	C(28)	H(28)	120.1
C(12)	C(11)	C(10)	120.2(3)	C(27)	C(28)	C(29)	119.8(3)
C(12)	C(11)	H(11)	119.9	C(29)	C(28)	H(28)	120.1
C(11)	C(12)	H(12)	120.2	O(5)	C(29)	C(28)	115.5(2)
C(11)	C(12)	C(13)	119.6(3)	O(5)	C(29)	C(30)	124.4(2)
C(13)	C(12)	H(12)	120.2	C(30)	C(29)	C(28)	120.1(2)
C(8)	C(13)	H(13)	119.5	C(29)	C(30)	H(30)	120.3
C(12)	C(13)	C(8)	120.9(3)	C(29)	C(30)	C(31)	119.4(2)
C(12)	C(13)	H(13)	119.5	C(31)	C(30)	H(30)	120.3
N(4)	C(14)	C(7)	114.6(2)	C(26)	C(31)	C(30)	121.2(3)
C(15)	C(14)	N(4)	121.6(2)	C(26)	C(31)	H(31)	119.4
C(15)	C(14)	C(7)	123.6(2)	C(30)	C(31)	H(31)	119.4
N(3)	C(15)	N(2)	115.4(2)	O(5)	C(32)	H(32A)	109.5
N(3)	C(15)	C(14)	126.7(2)	O(5)	C(32)	H(32B)	109.5
C(14)	C(15)	N(2)	117.8(2)	O(5)	C(32)	H(32C)	109.5
O(1)	C(16)	N(2)	121.2(3)	H(32A)	C(32)	H(32B)	109.5
O(1)	C(16)	C(2)	121.0(2)	H(32A)	C(32)	H(32C)	109.5
N(2)	C(16)	C(2)	117.8(2)	H(32B)	C(32)	H(32C)	109.5

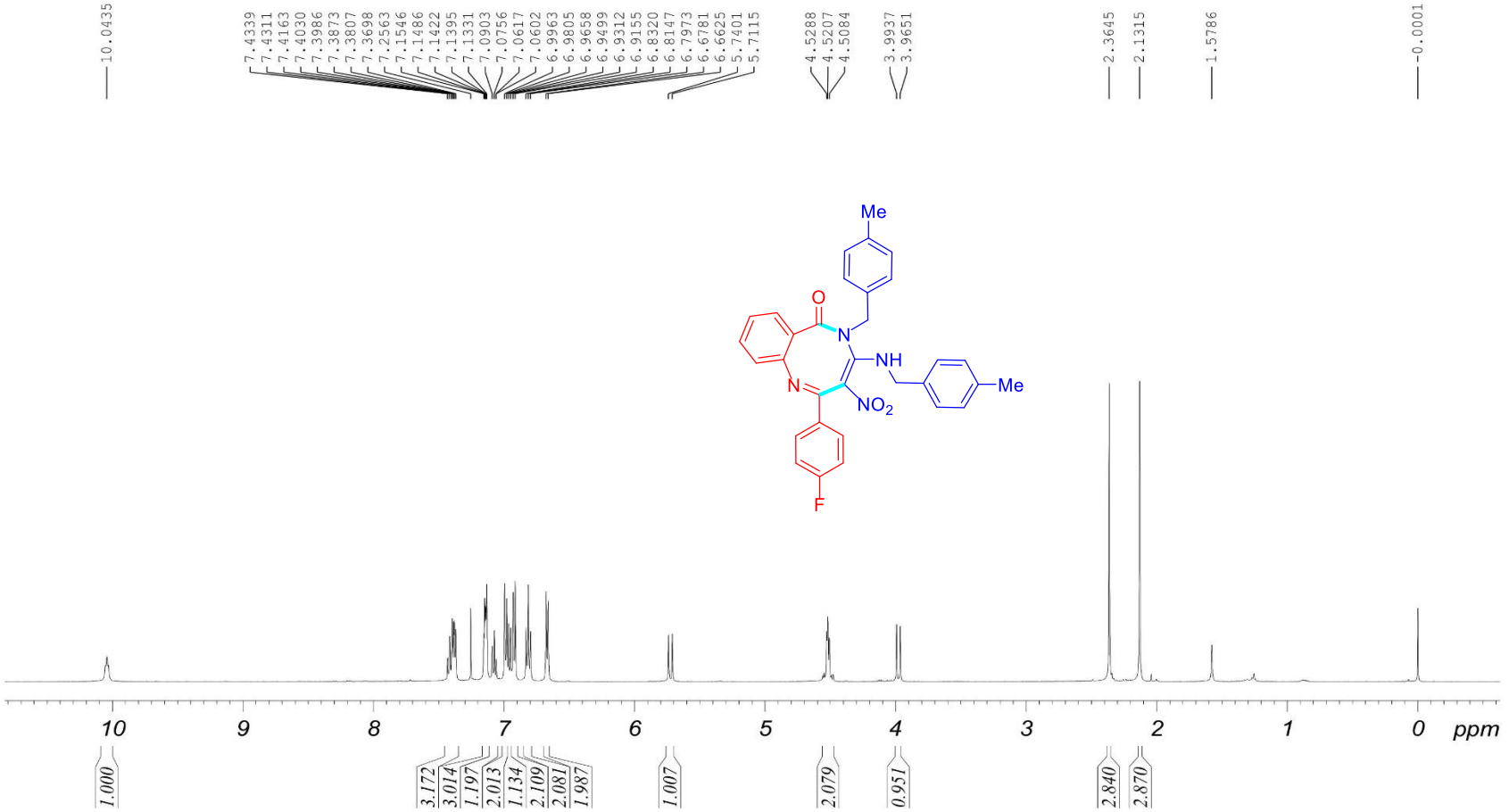


Figure S2. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **4a**

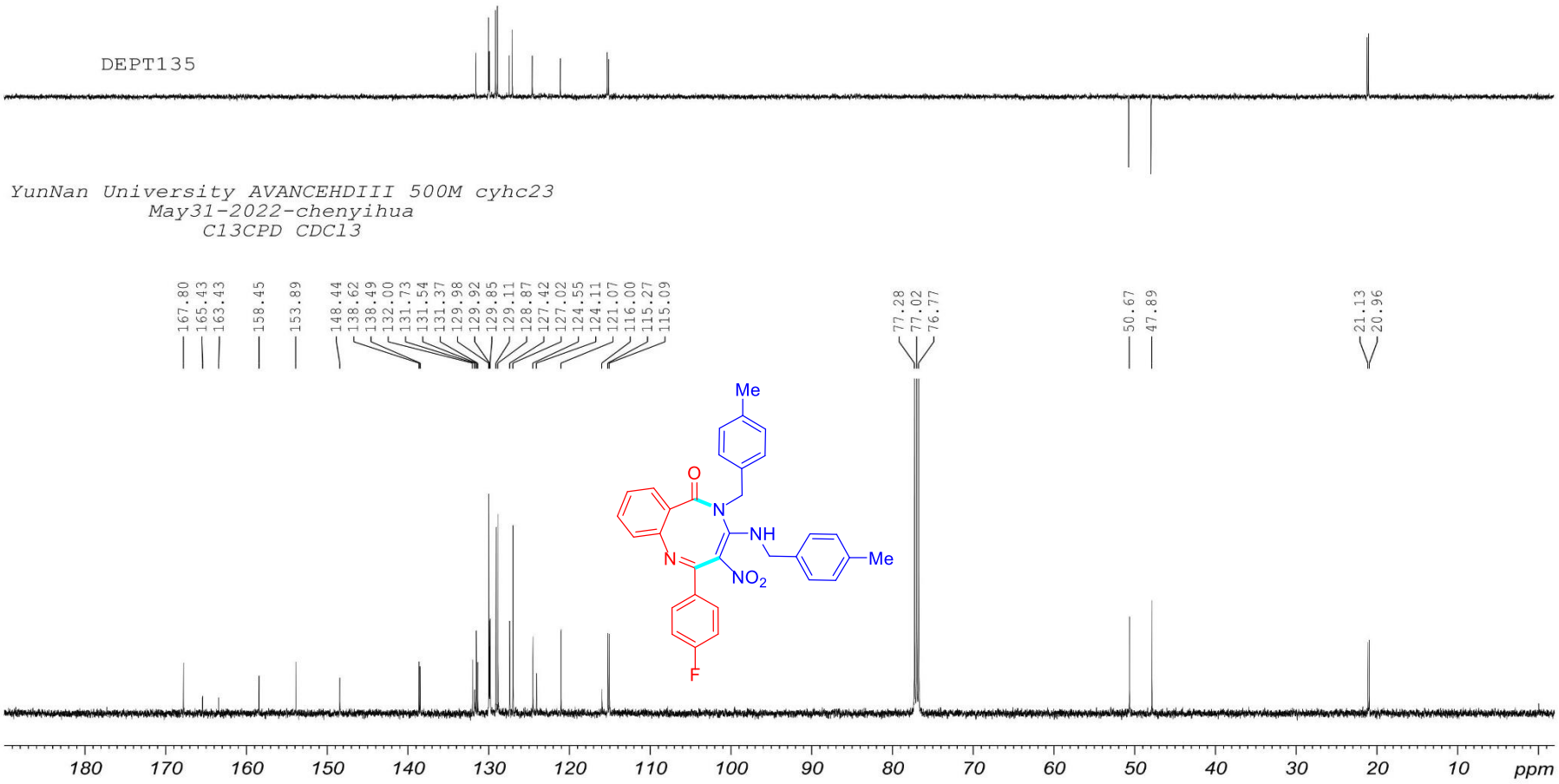


Figure S3. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **4a**

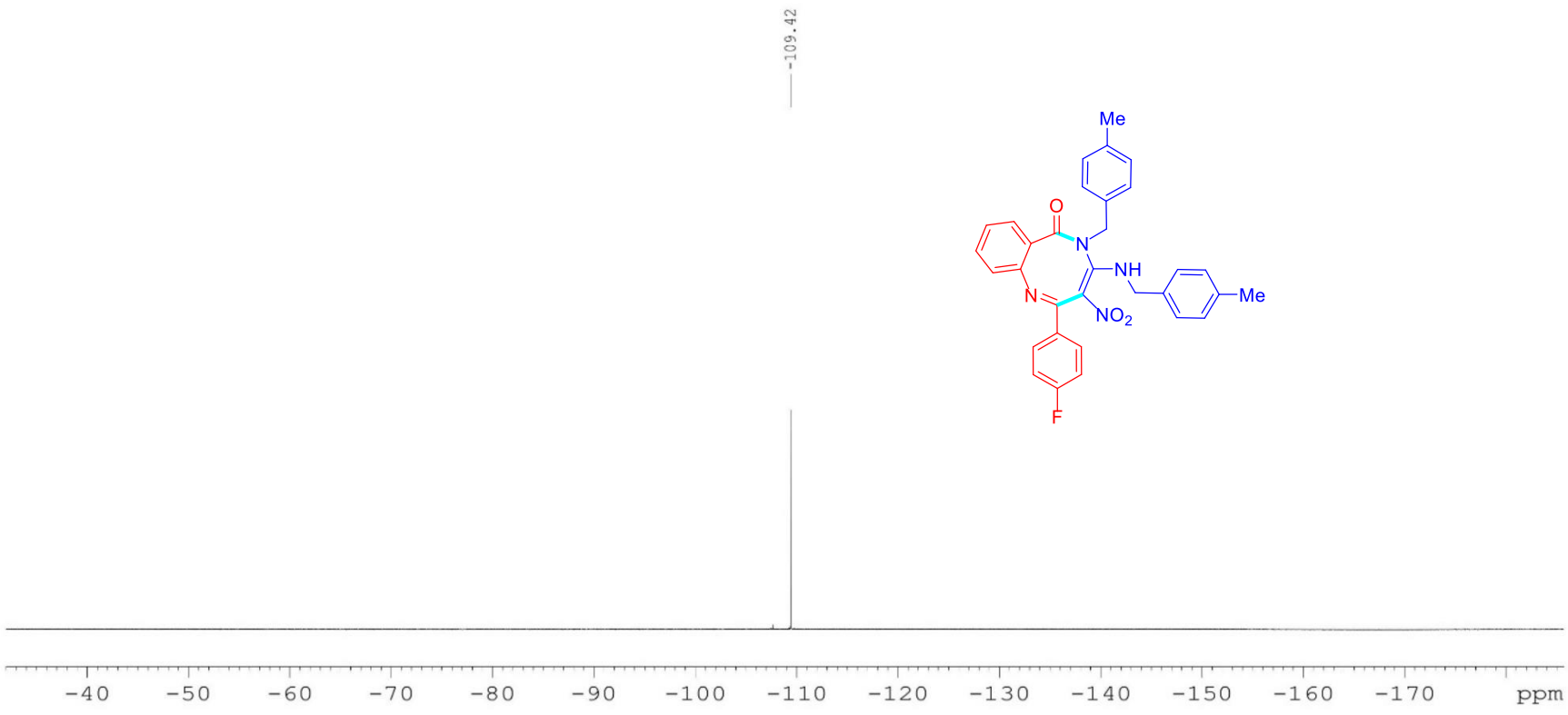


Figure S4. ^{19}F NMR (470 MHz, $CDCl_3$) spectra of compound **4a**

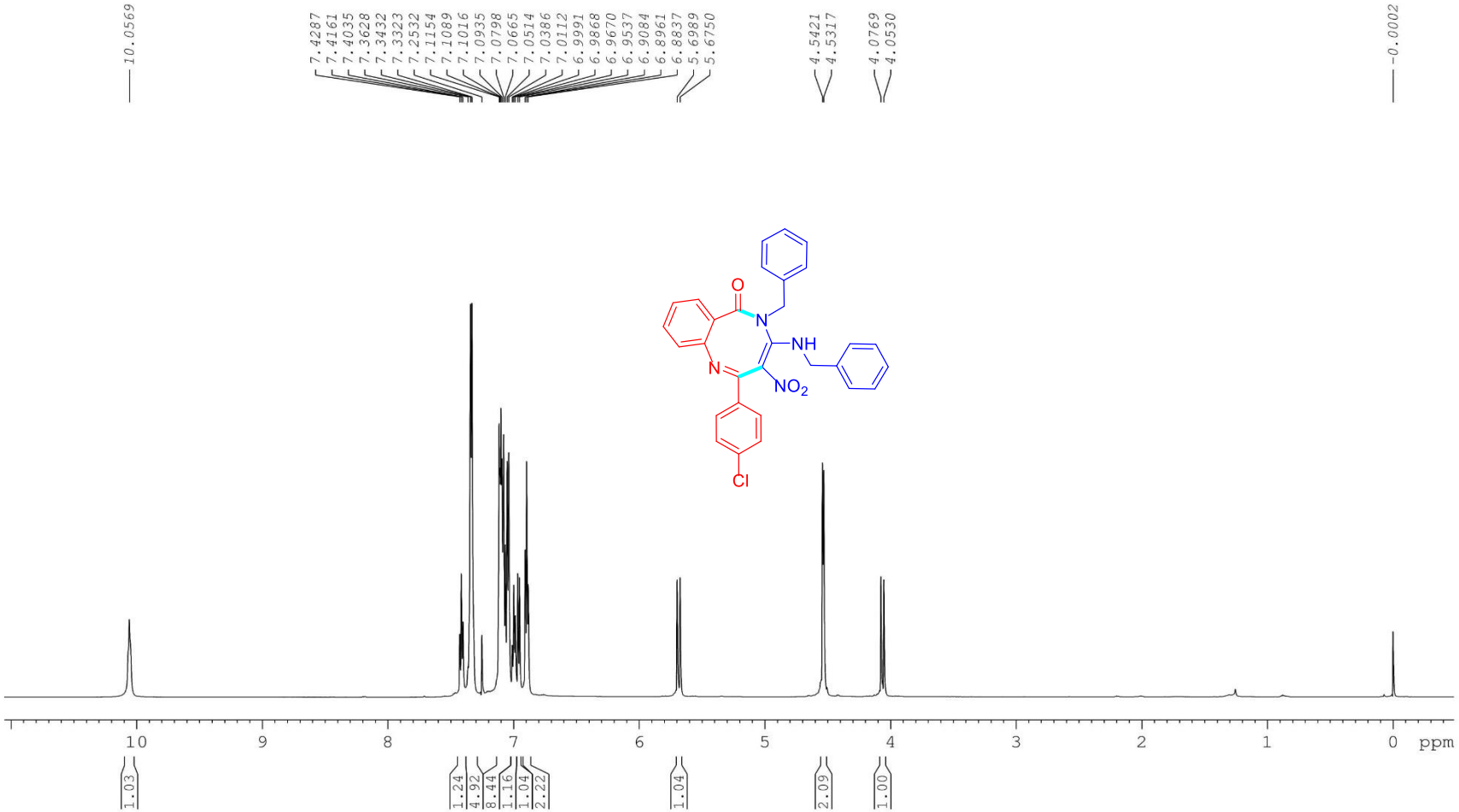


Figure S5. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4b**

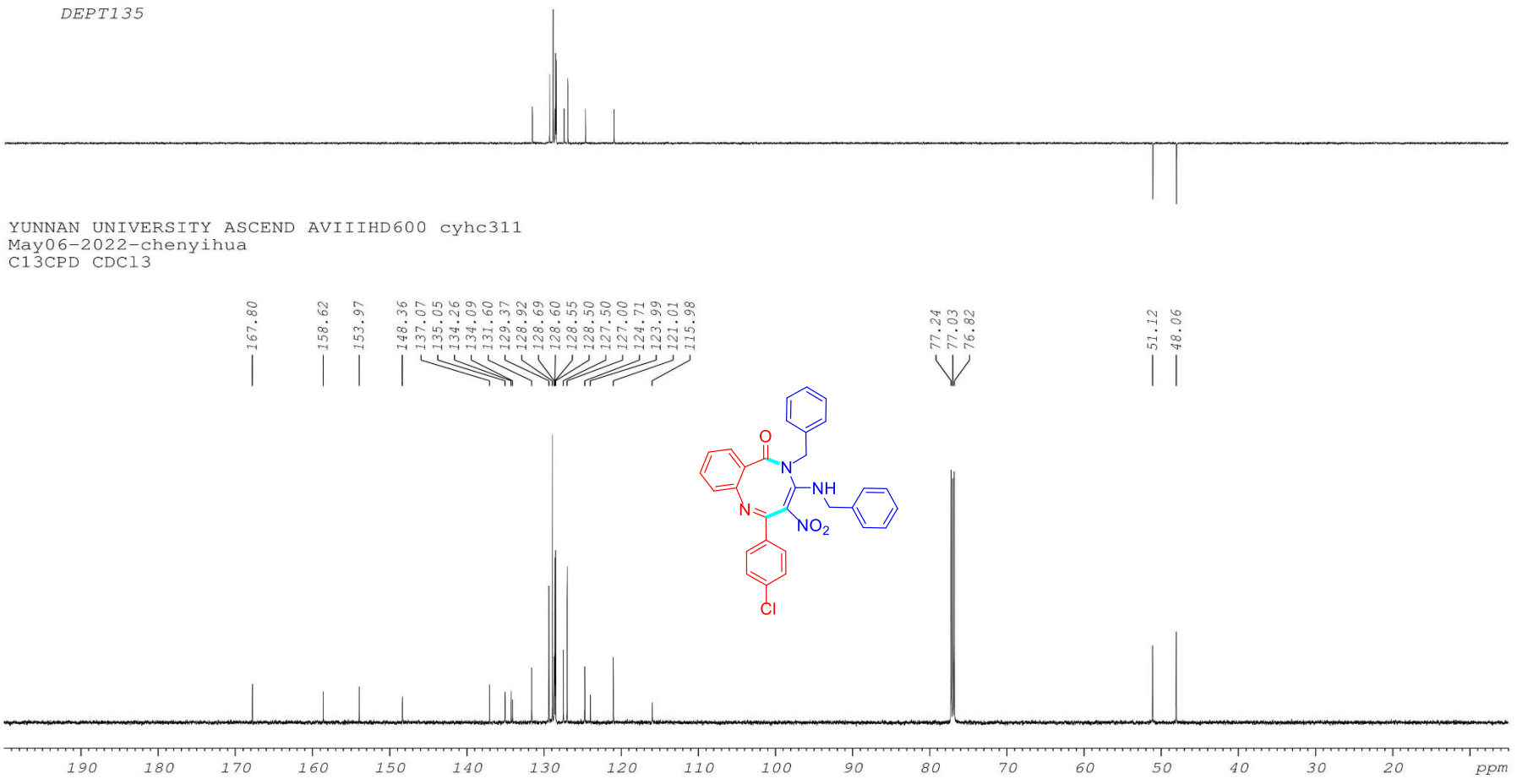


Figure S6. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4b**

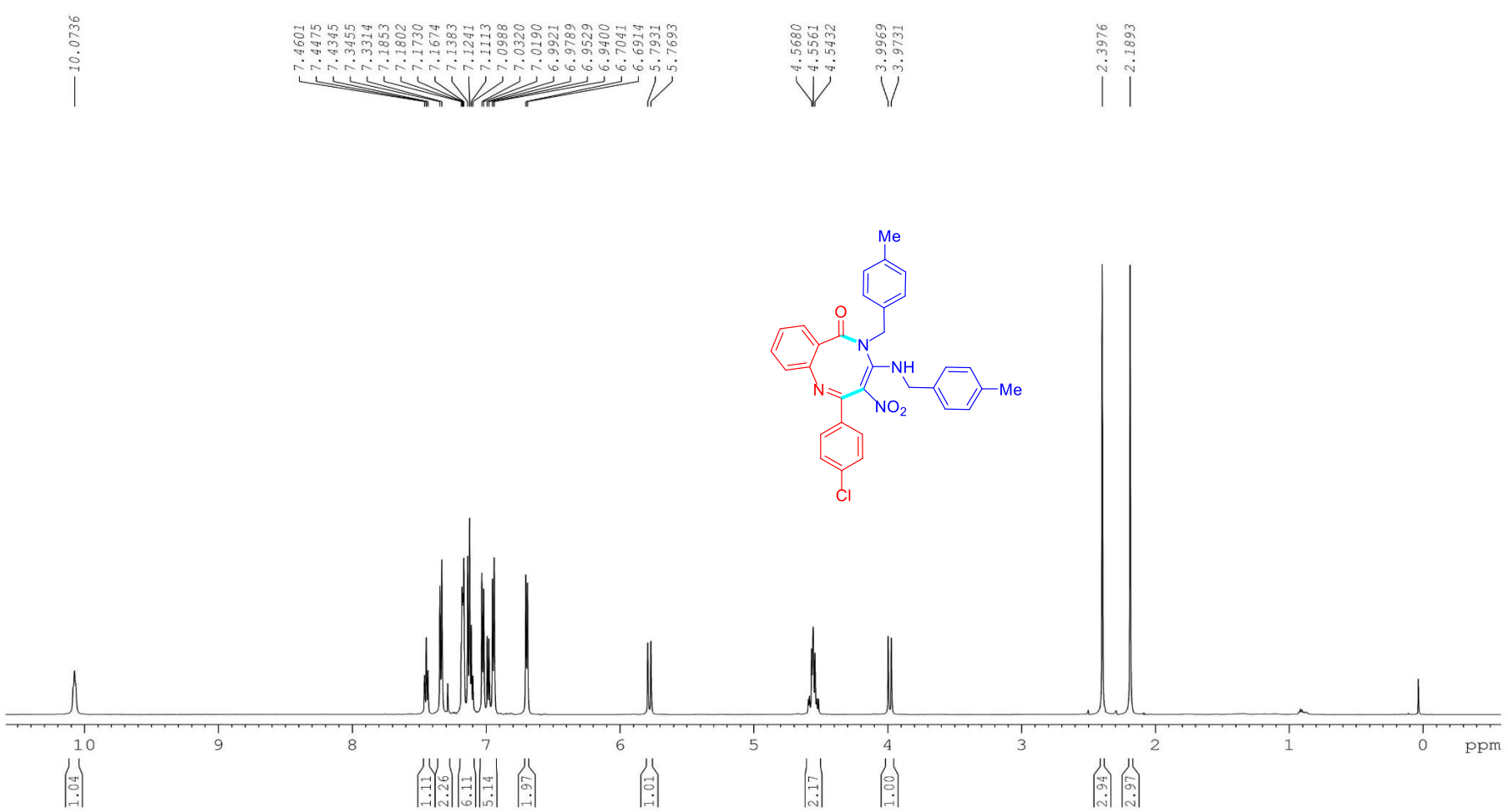


Figure S7. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4c**

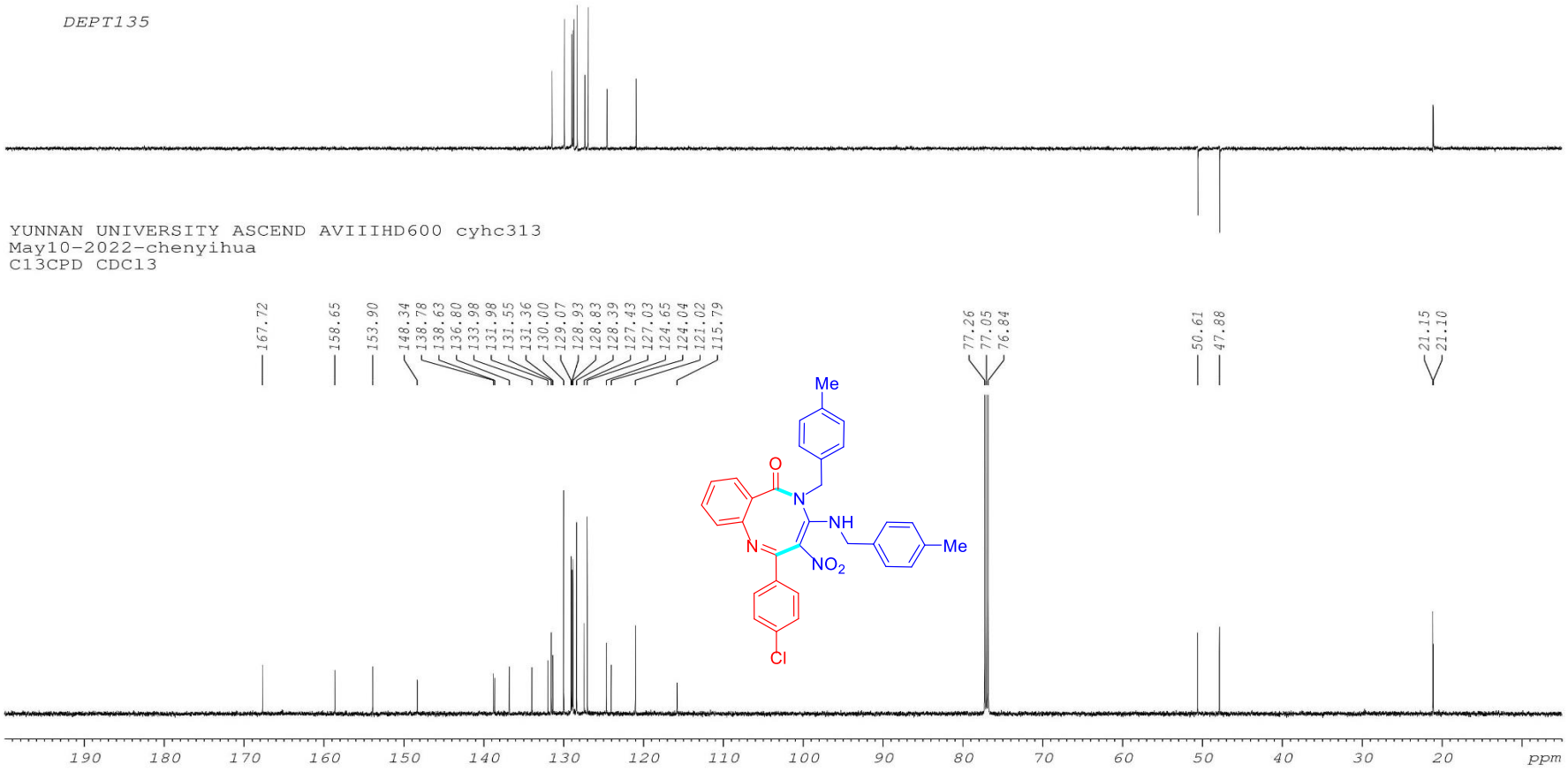


Figure S8. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4c**

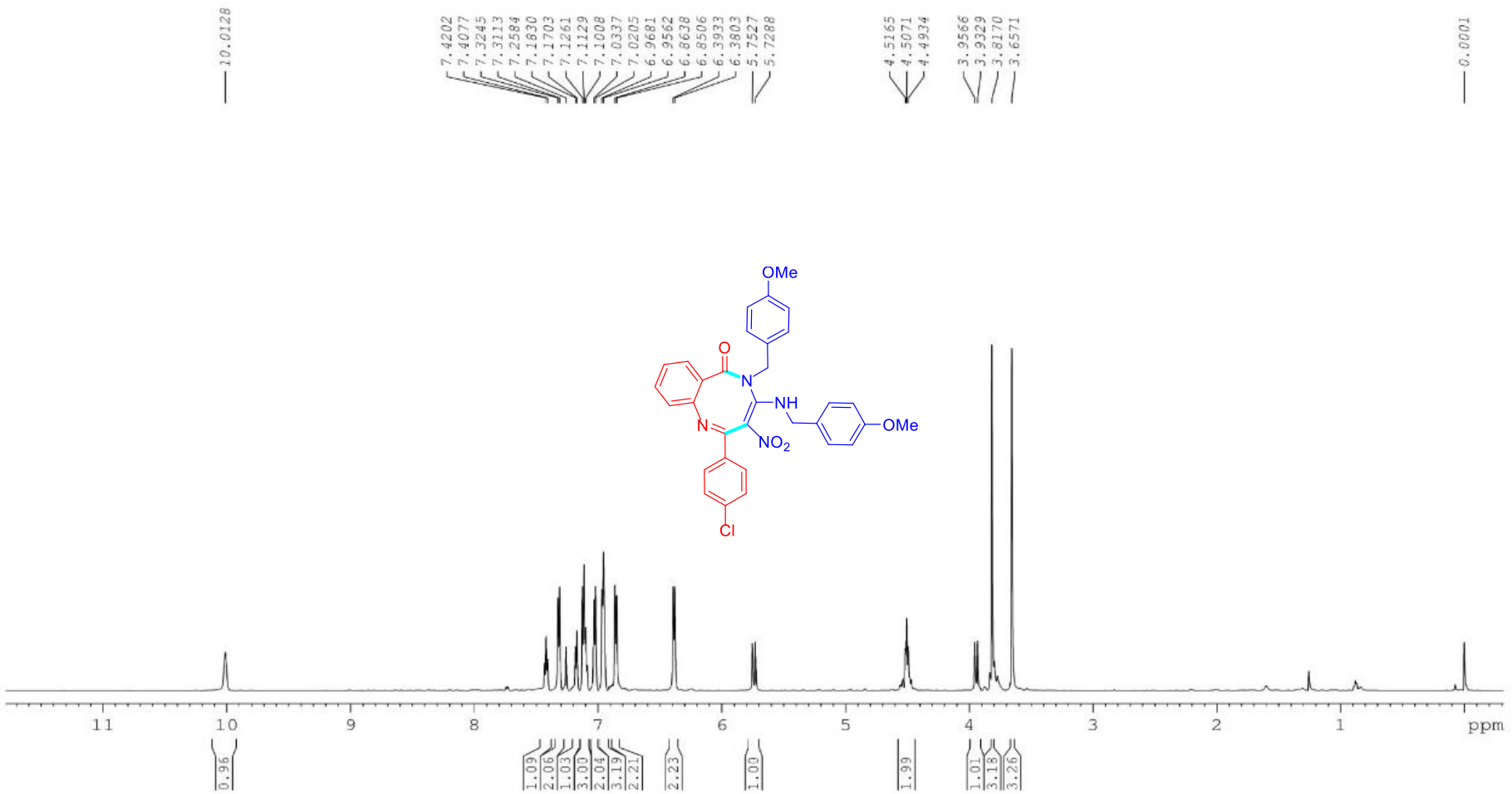


Figure S9. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4d**

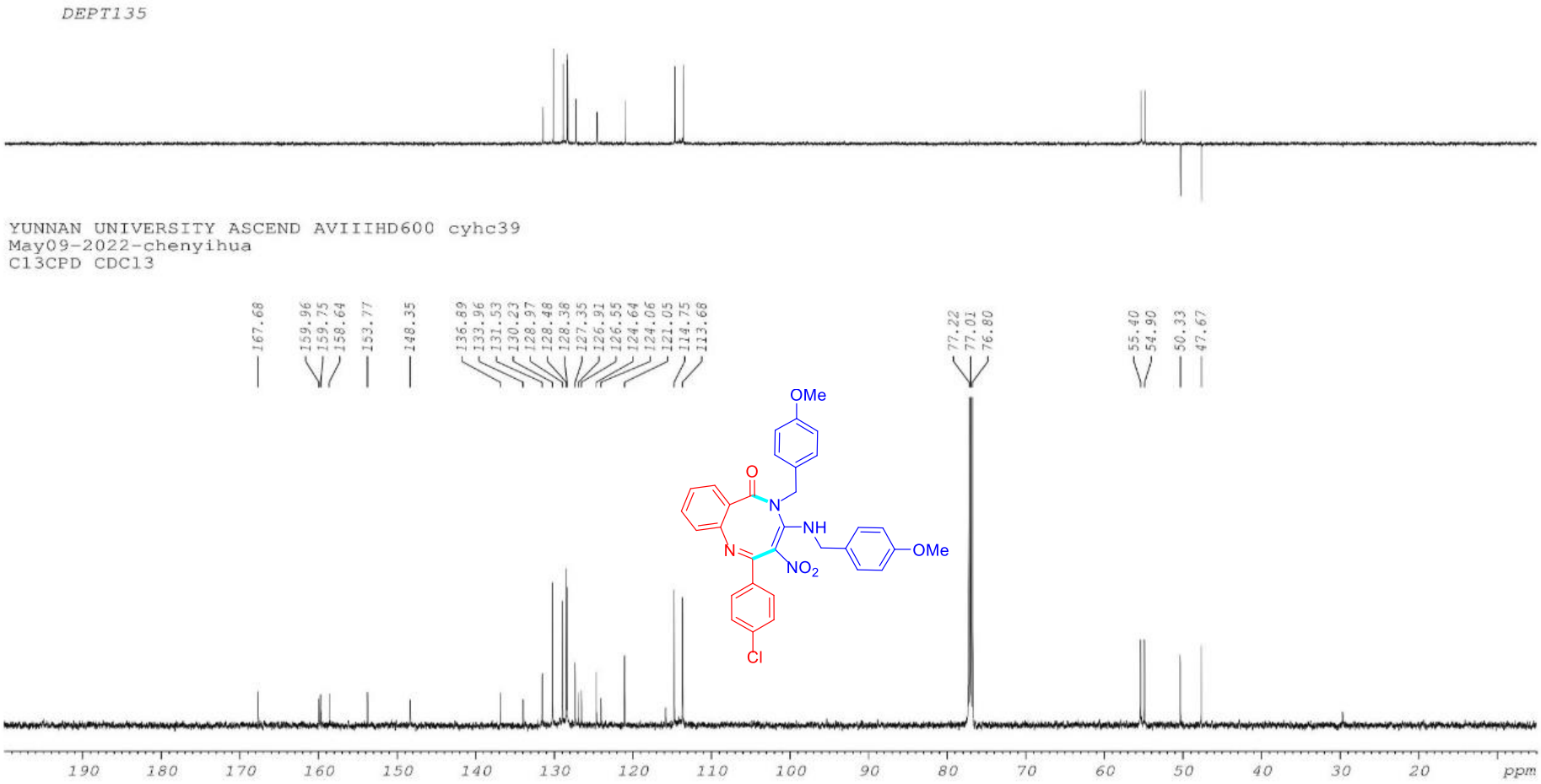


Figure S10. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4d**

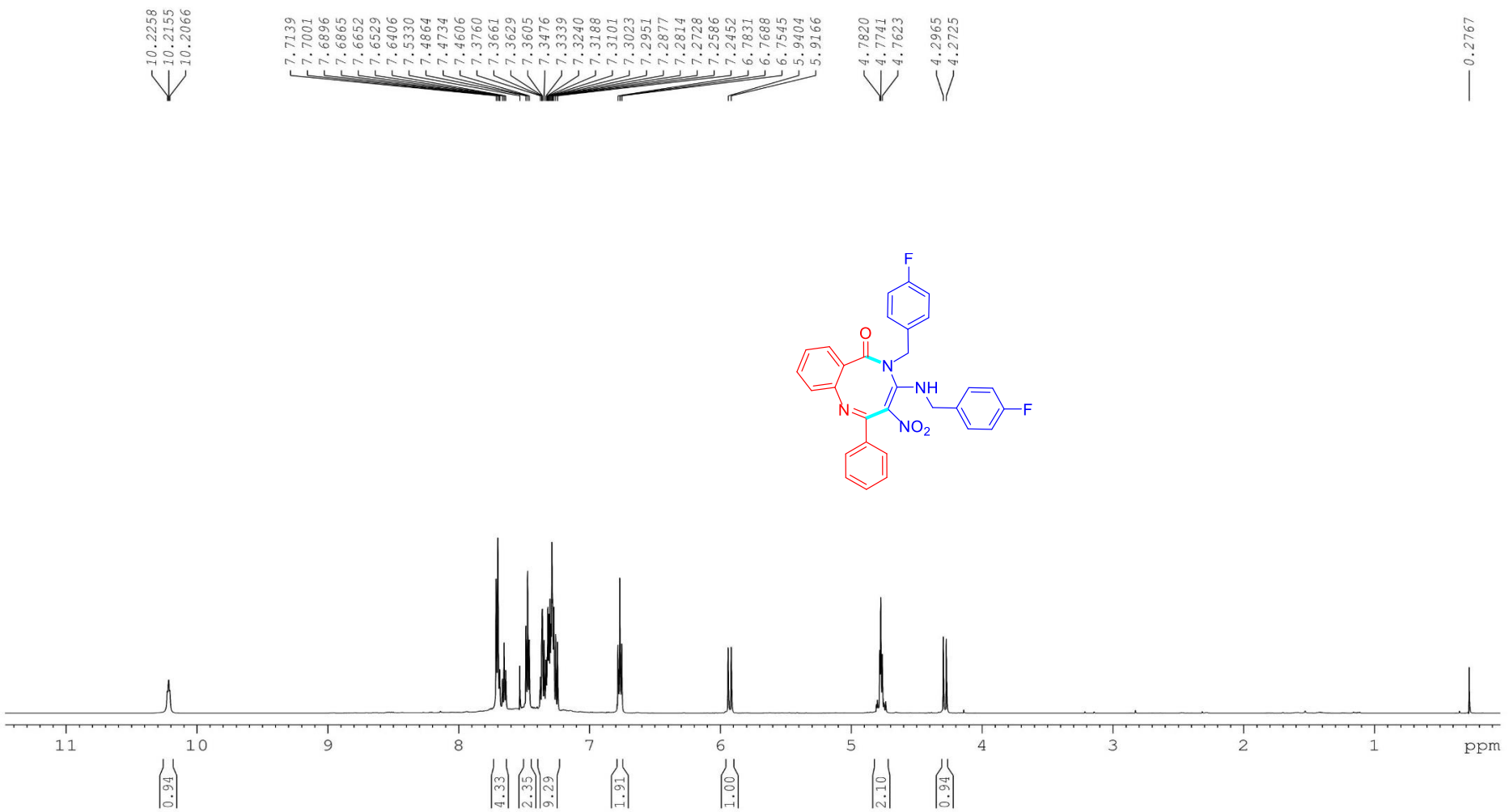


Figure S11. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4e**

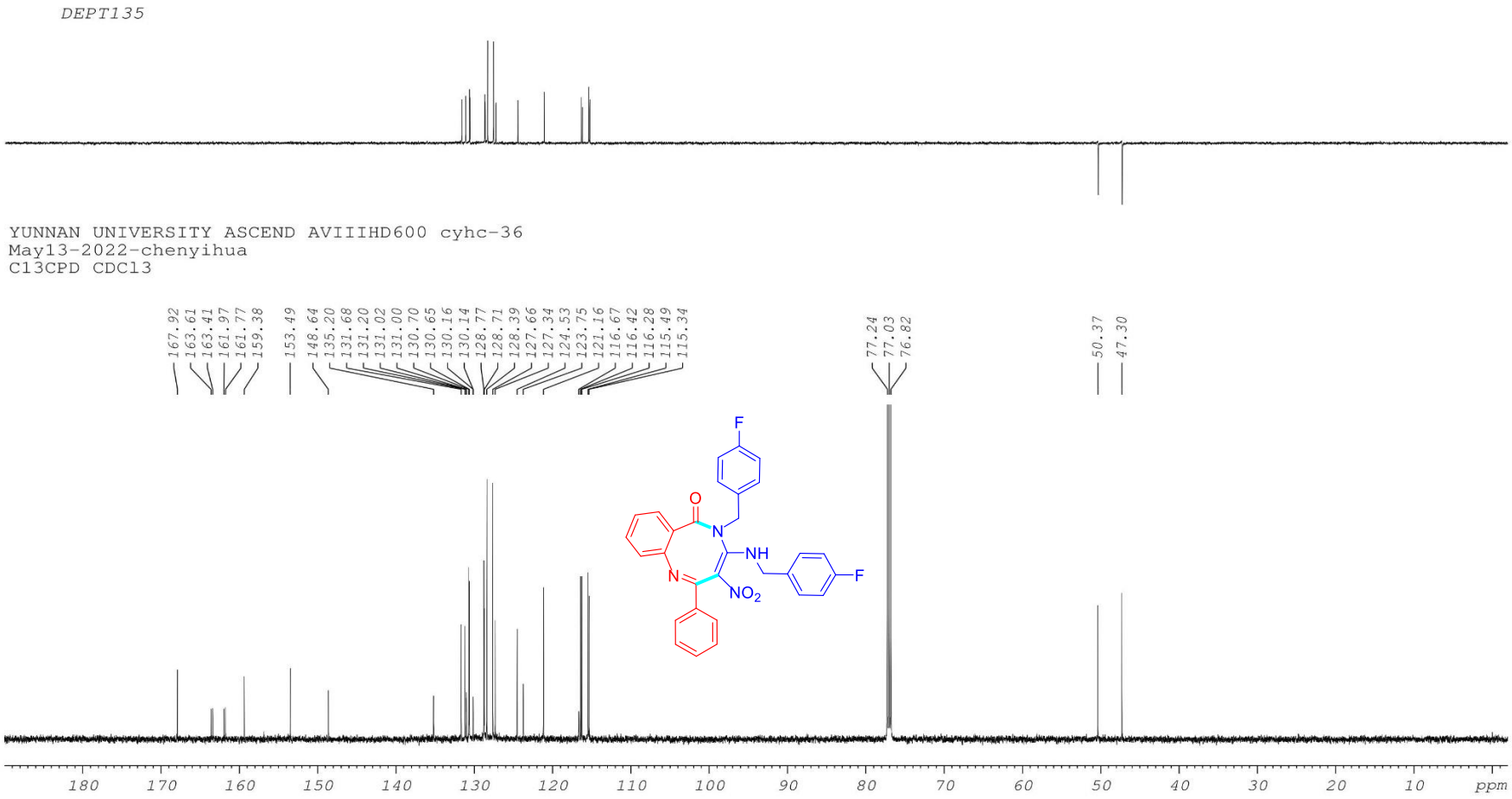


Figure S12. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4e**

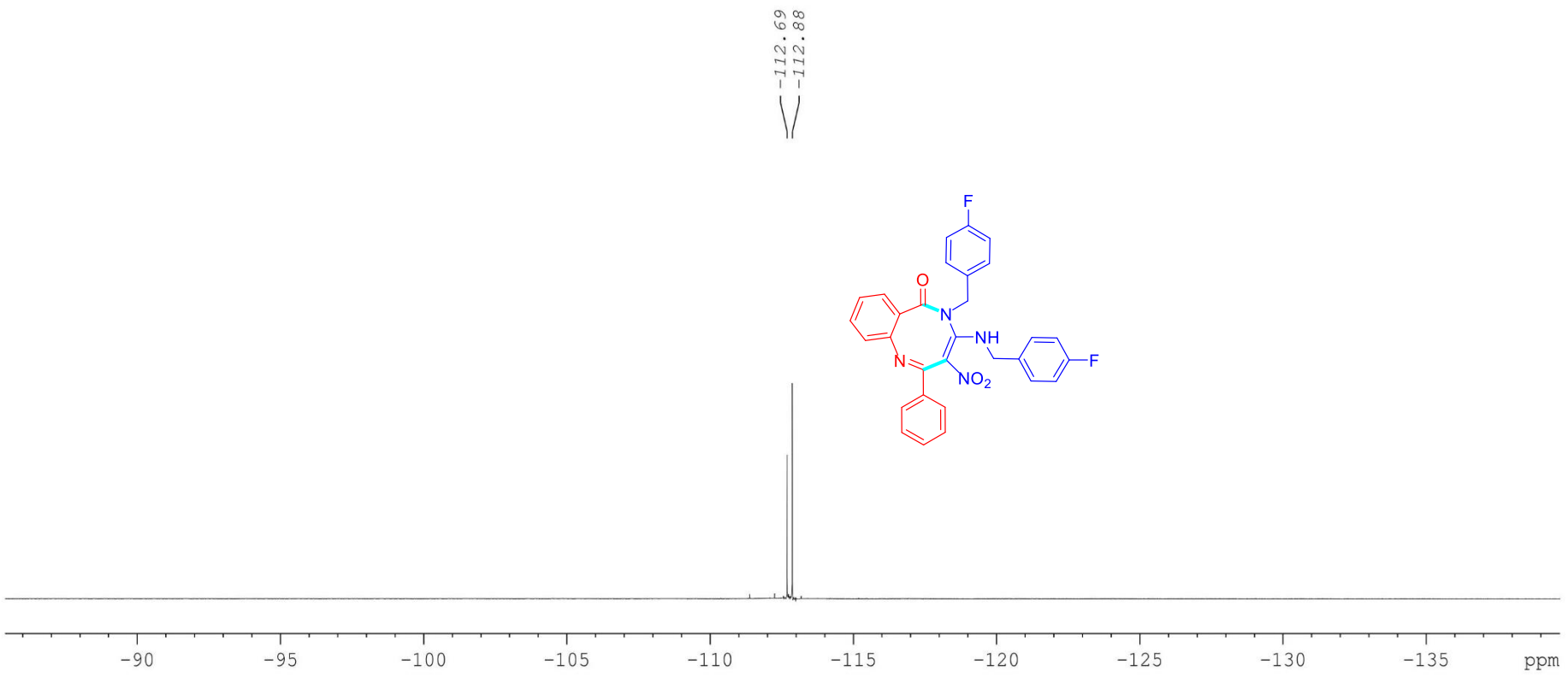


Figure S13. ^{19}F NMR (564 MHz, $CDCl_3$) spectra of compound **4e**

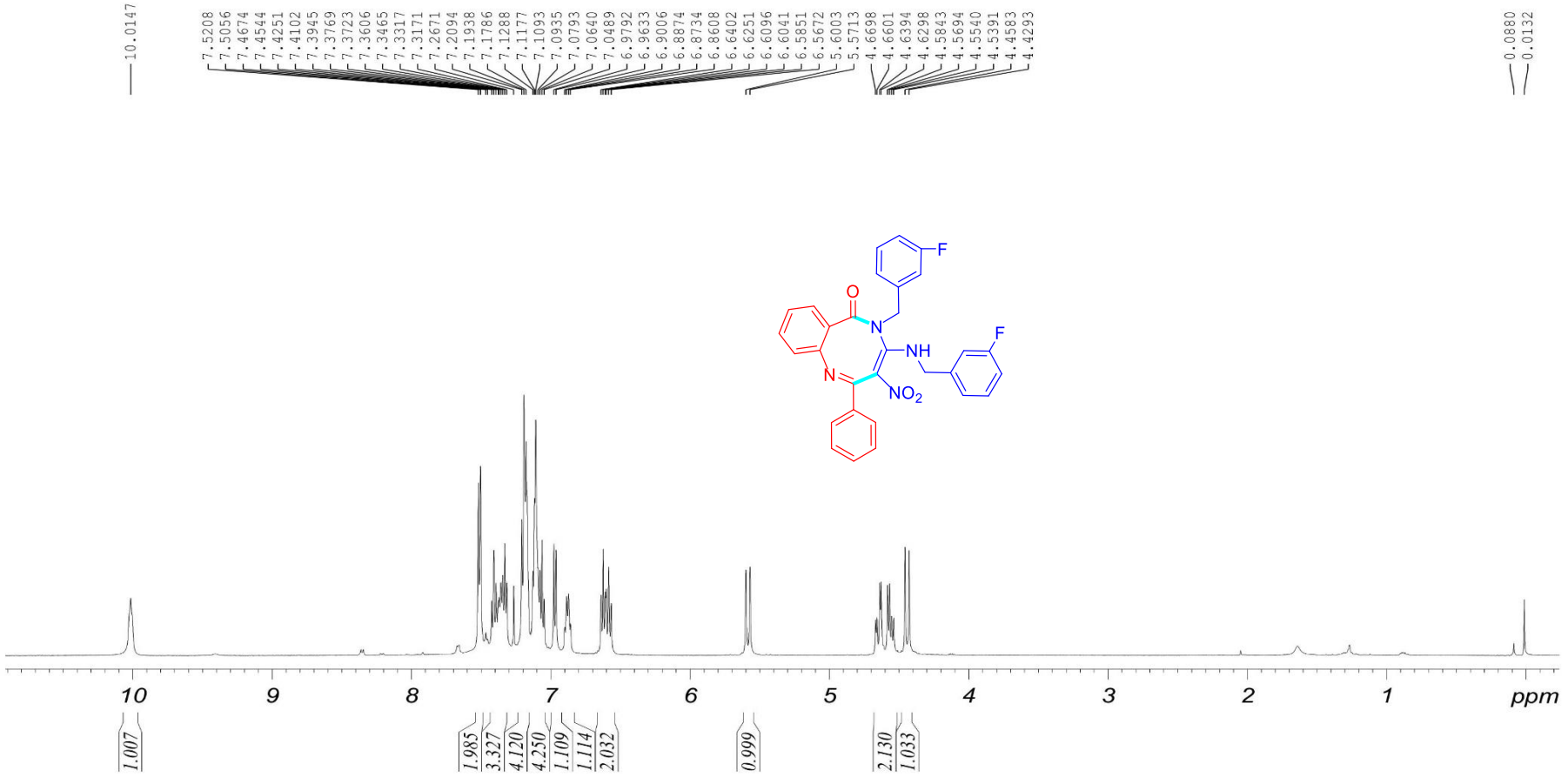


Figure S14. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **4f**

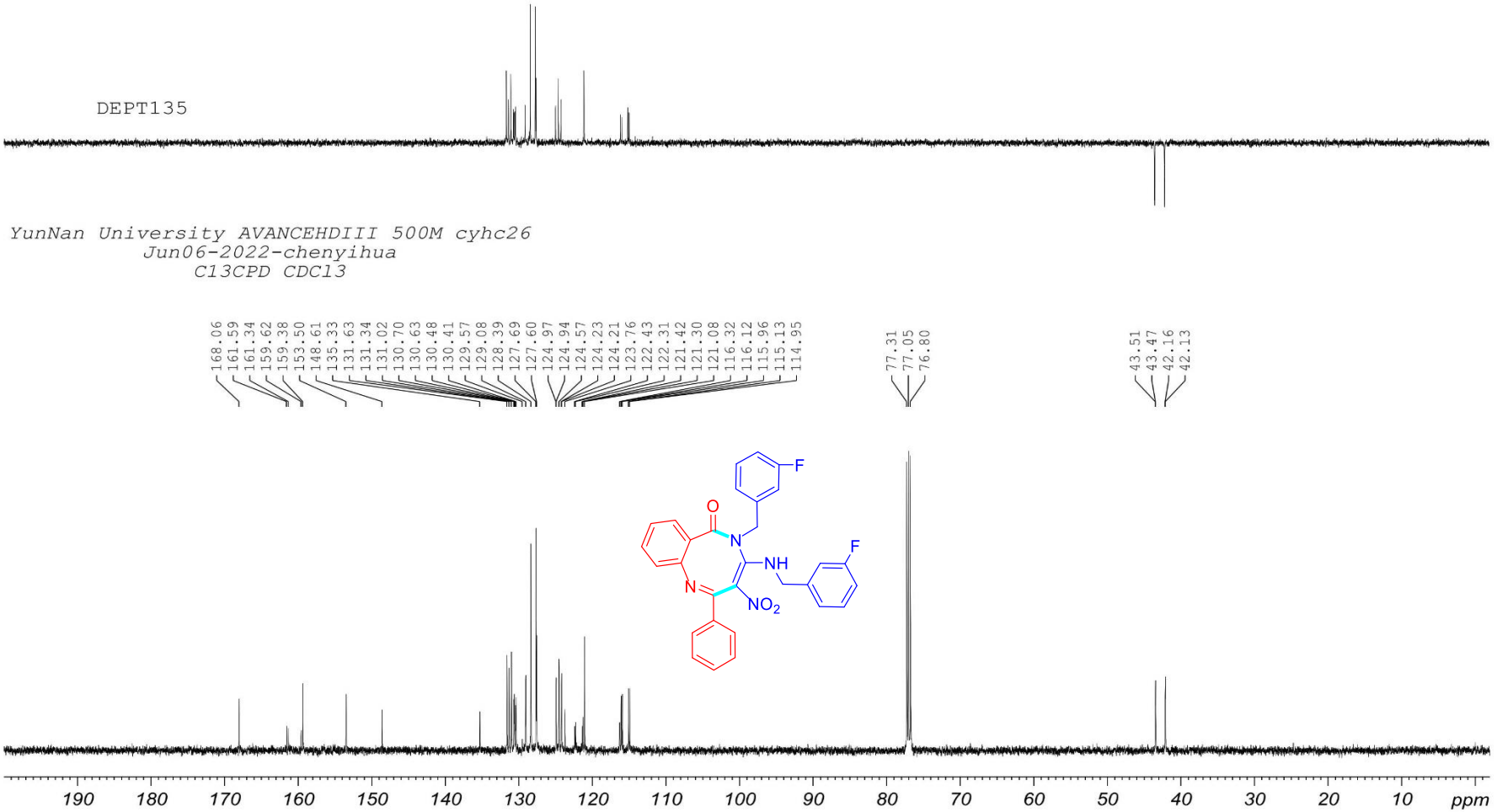


Figure S15. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **4f**

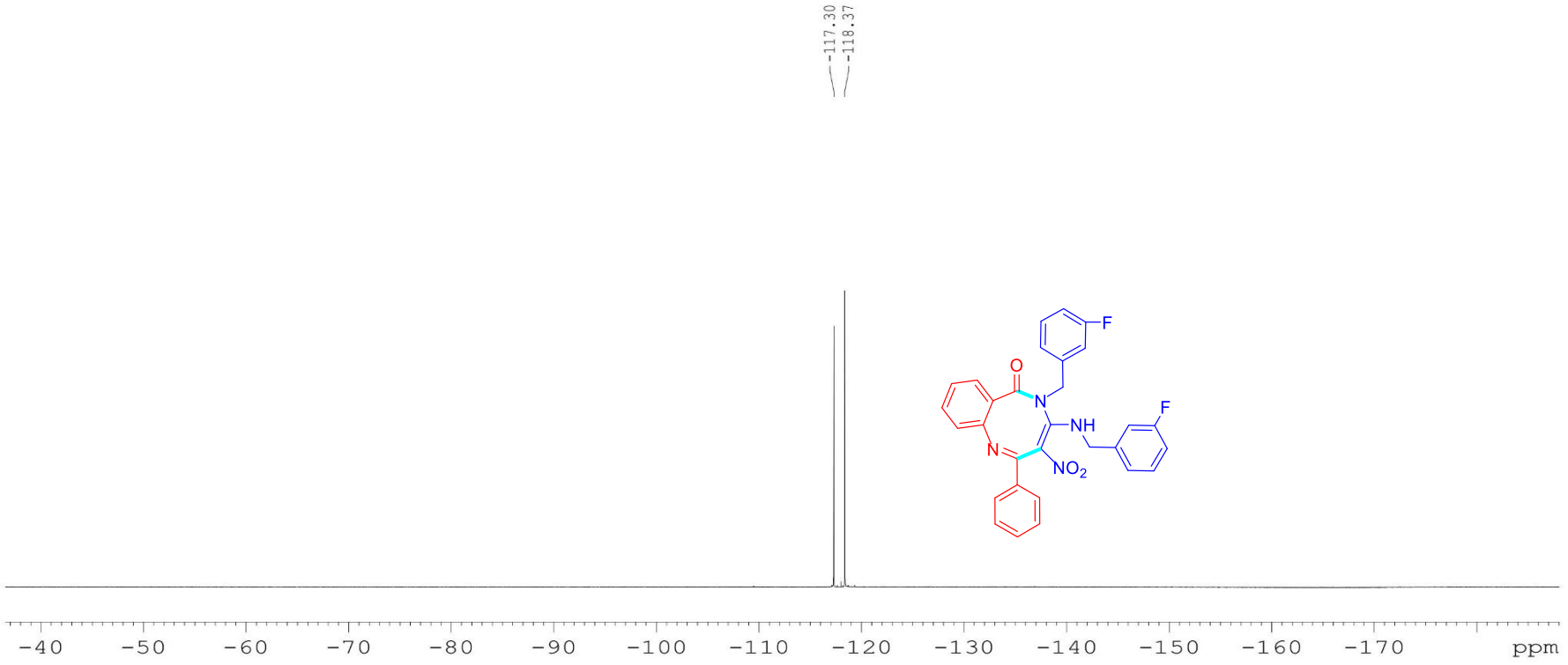


Figure S16. ^{19}F NMR (470 MHz, $CDCl_3$) spectra of compound **4f**

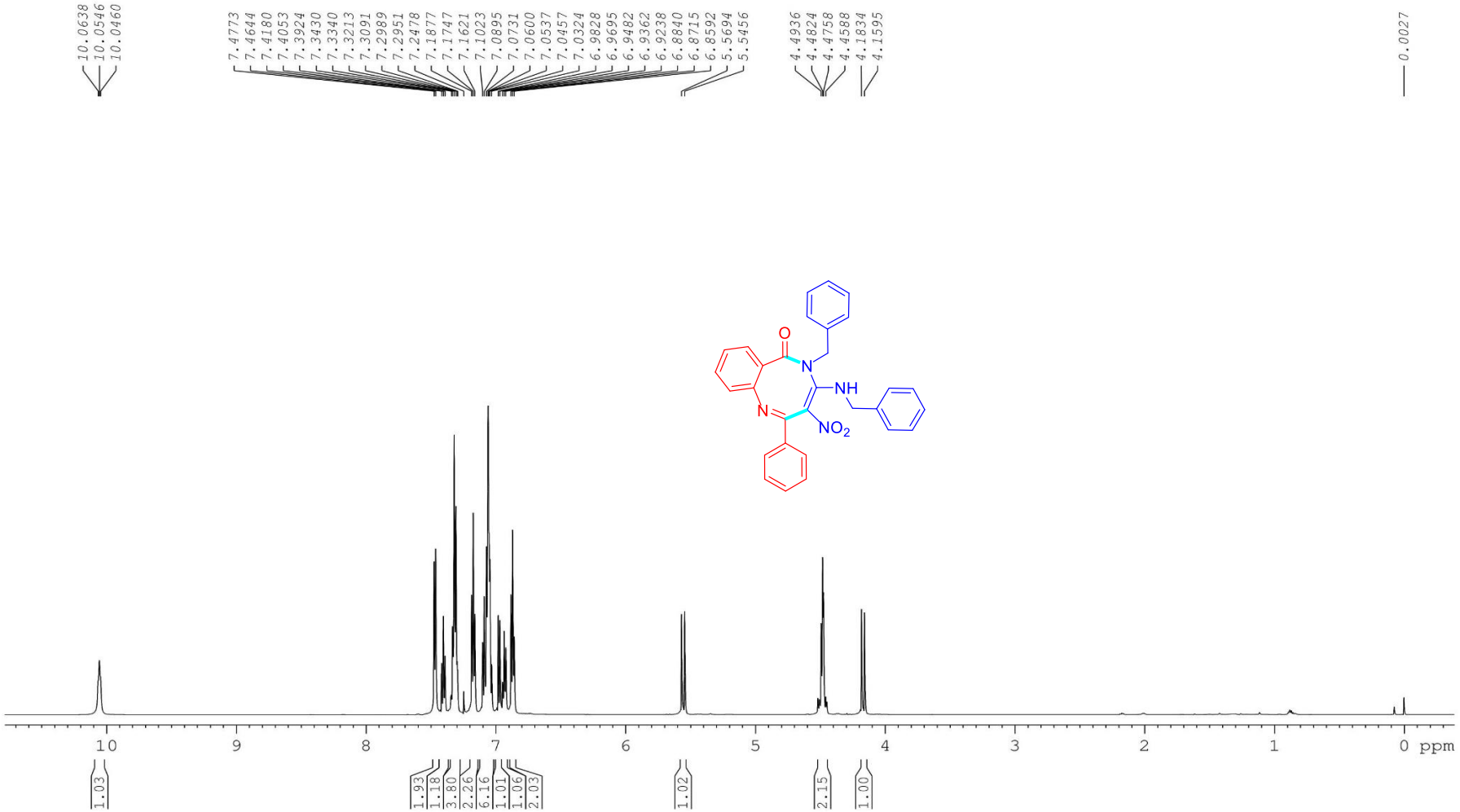


Figure S17. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4g**

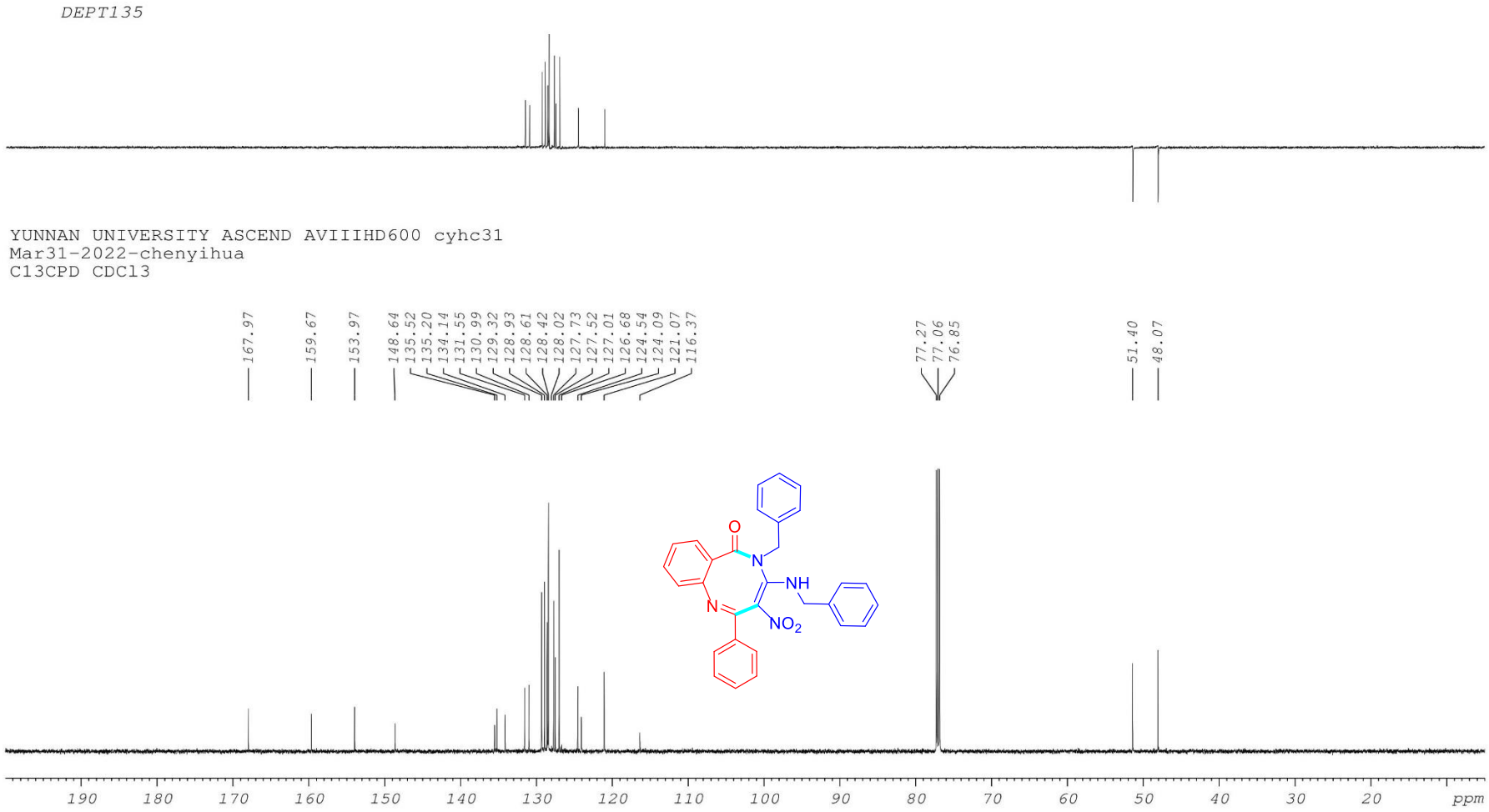


Figure S18. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4g**

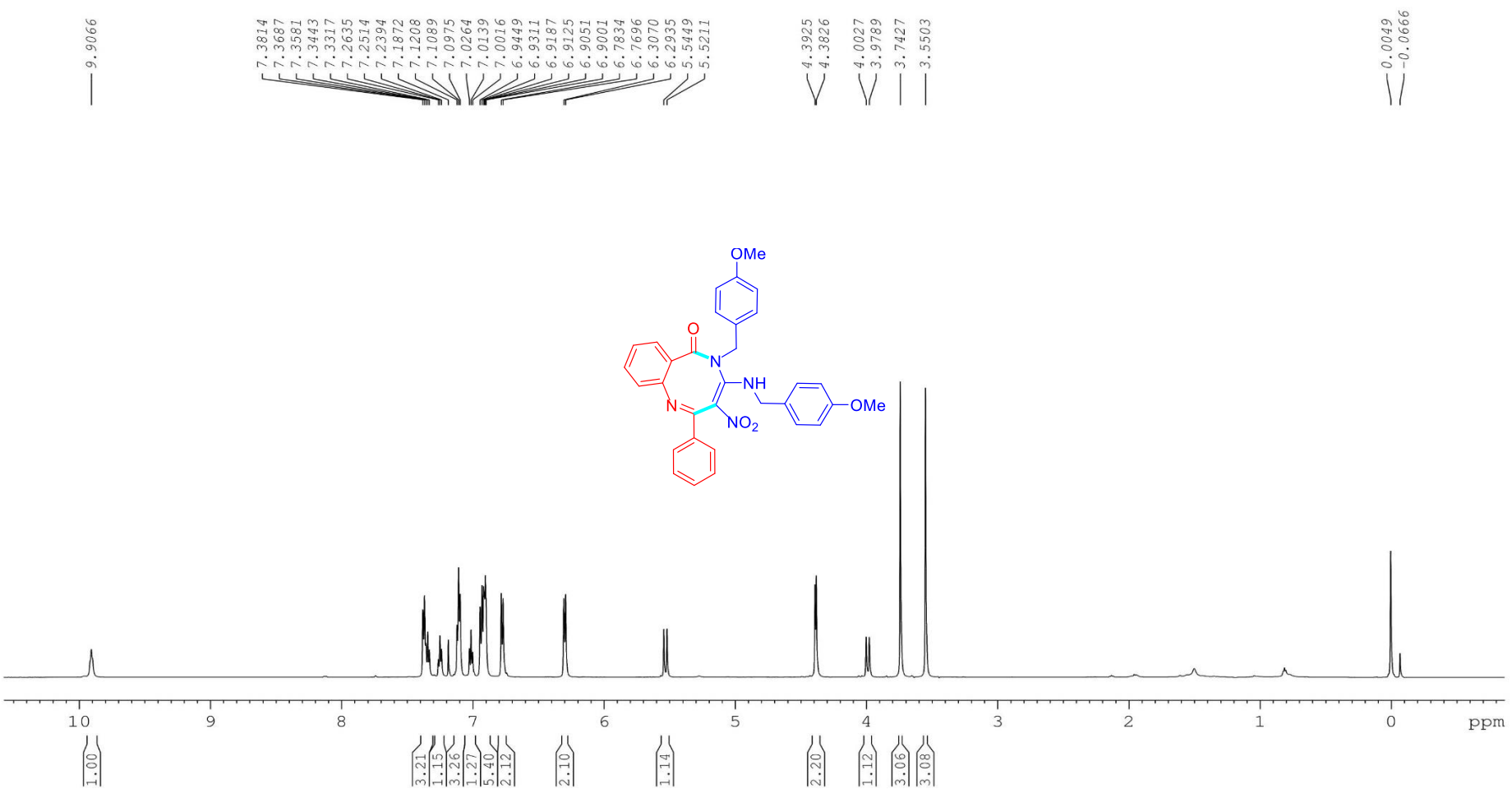


Figure S19. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4h**

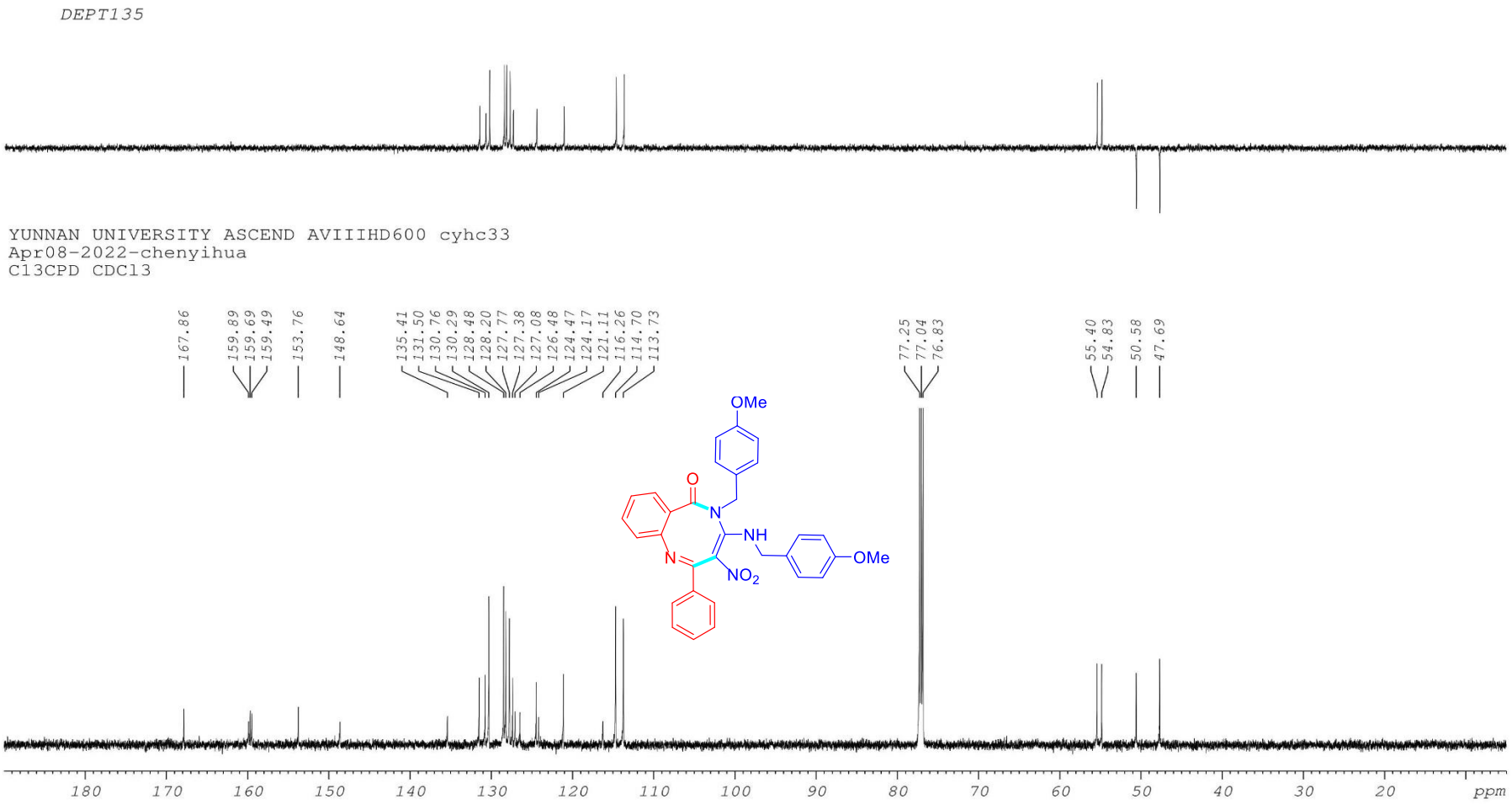


Figure S20. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4h**

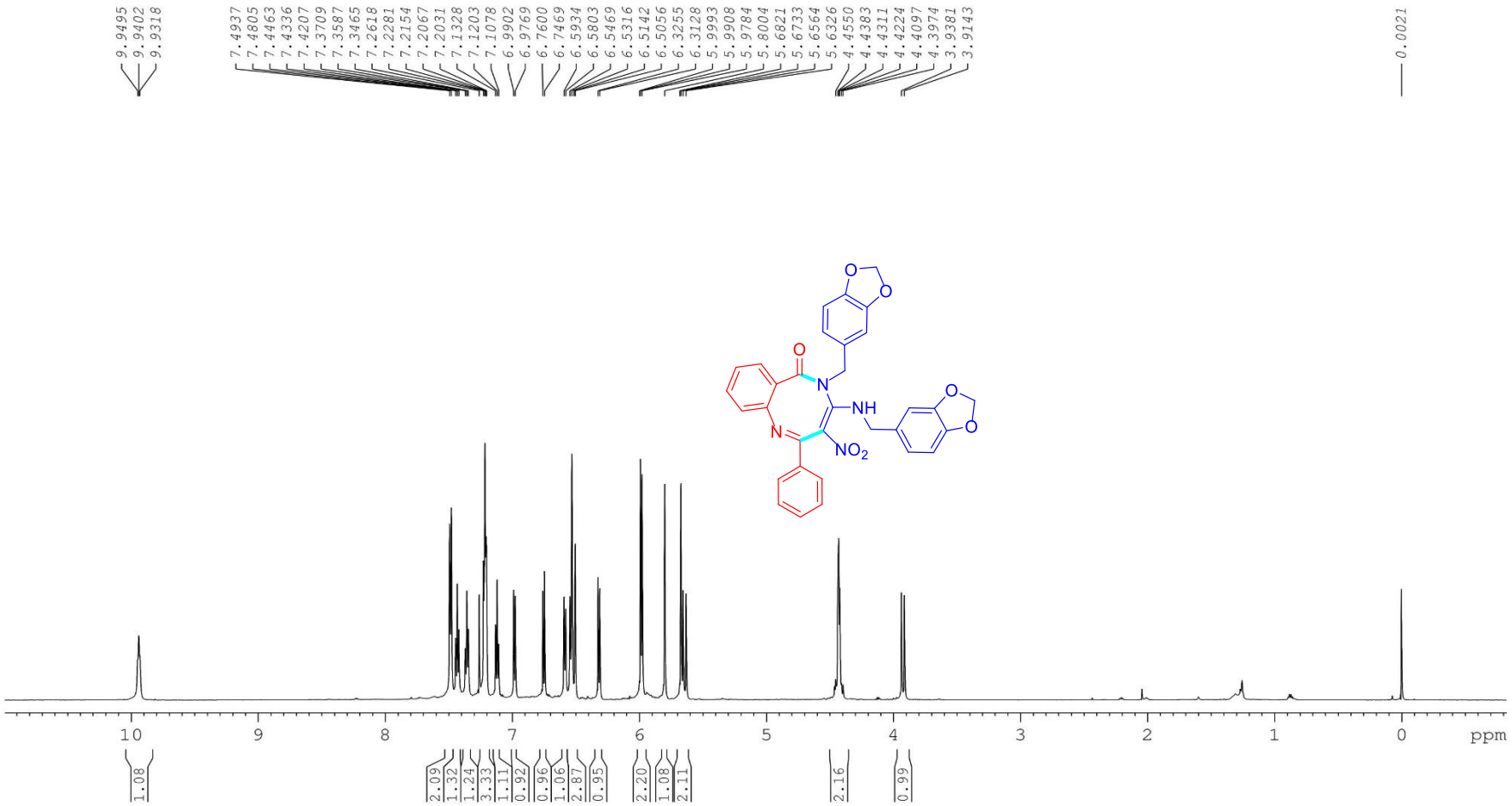


Figure S21. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4i**

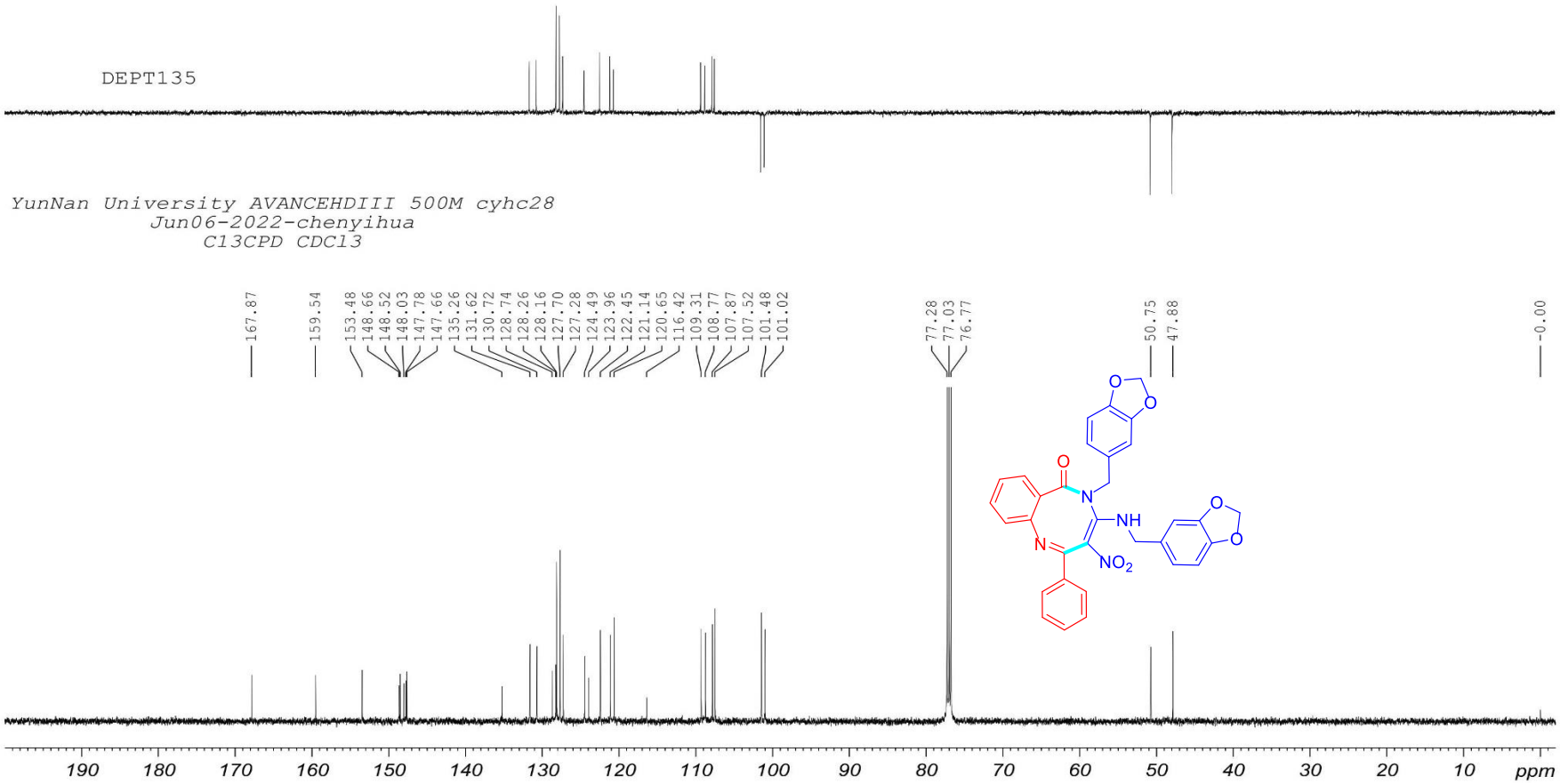


Figure S22. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **4i**

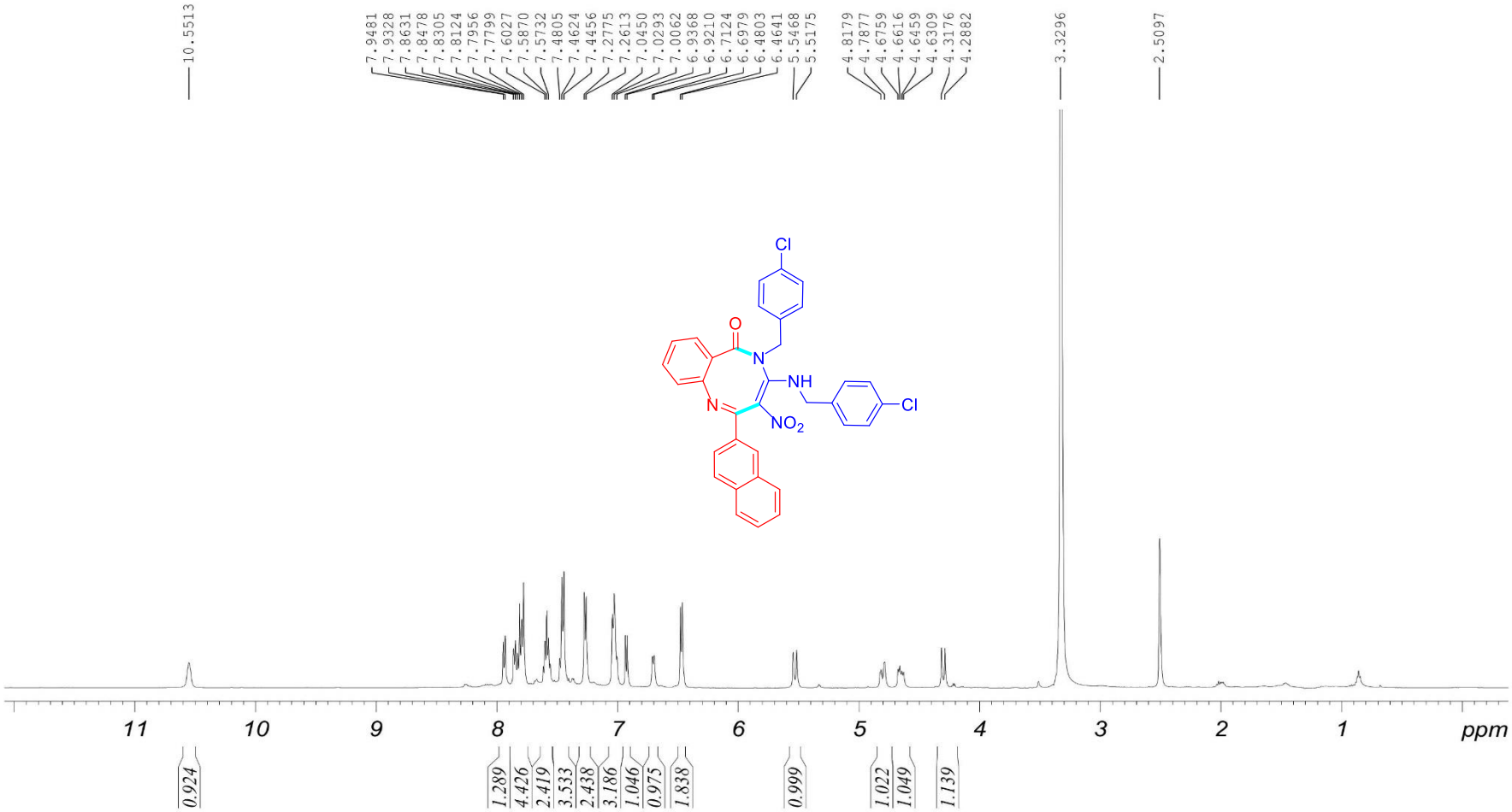


Figure S23. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **4j**

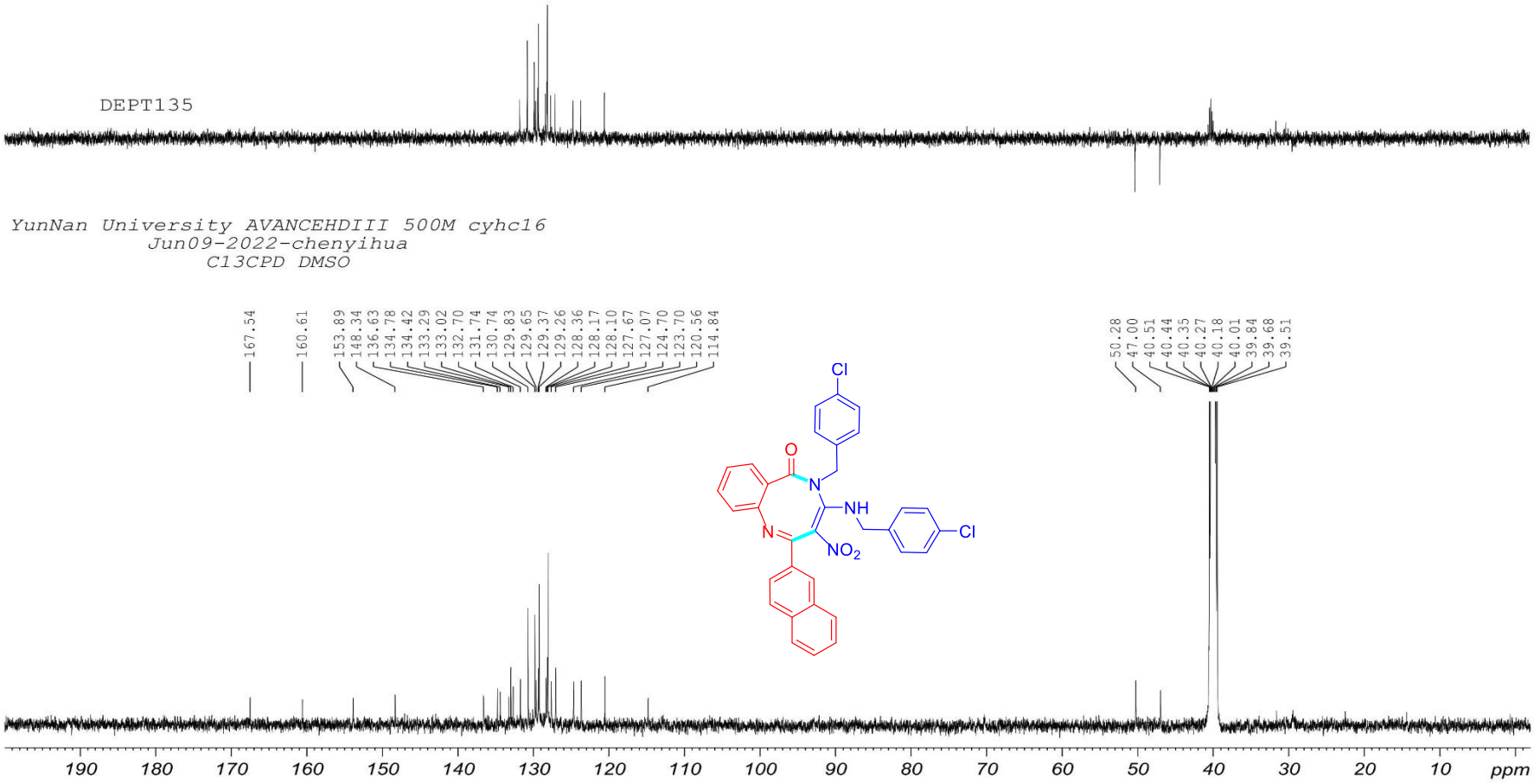


Figure S24. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **4j**

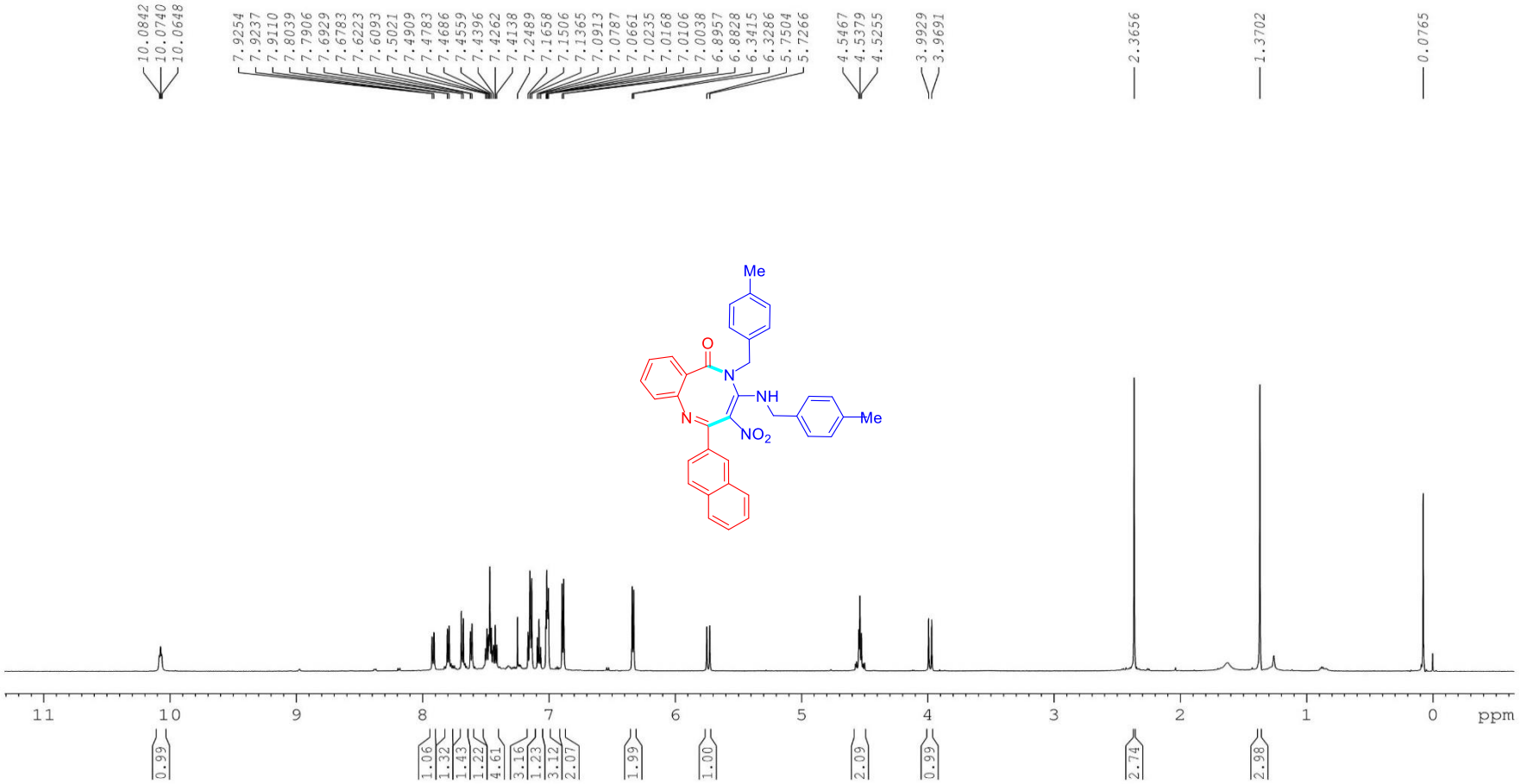


Figure S25. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4k**

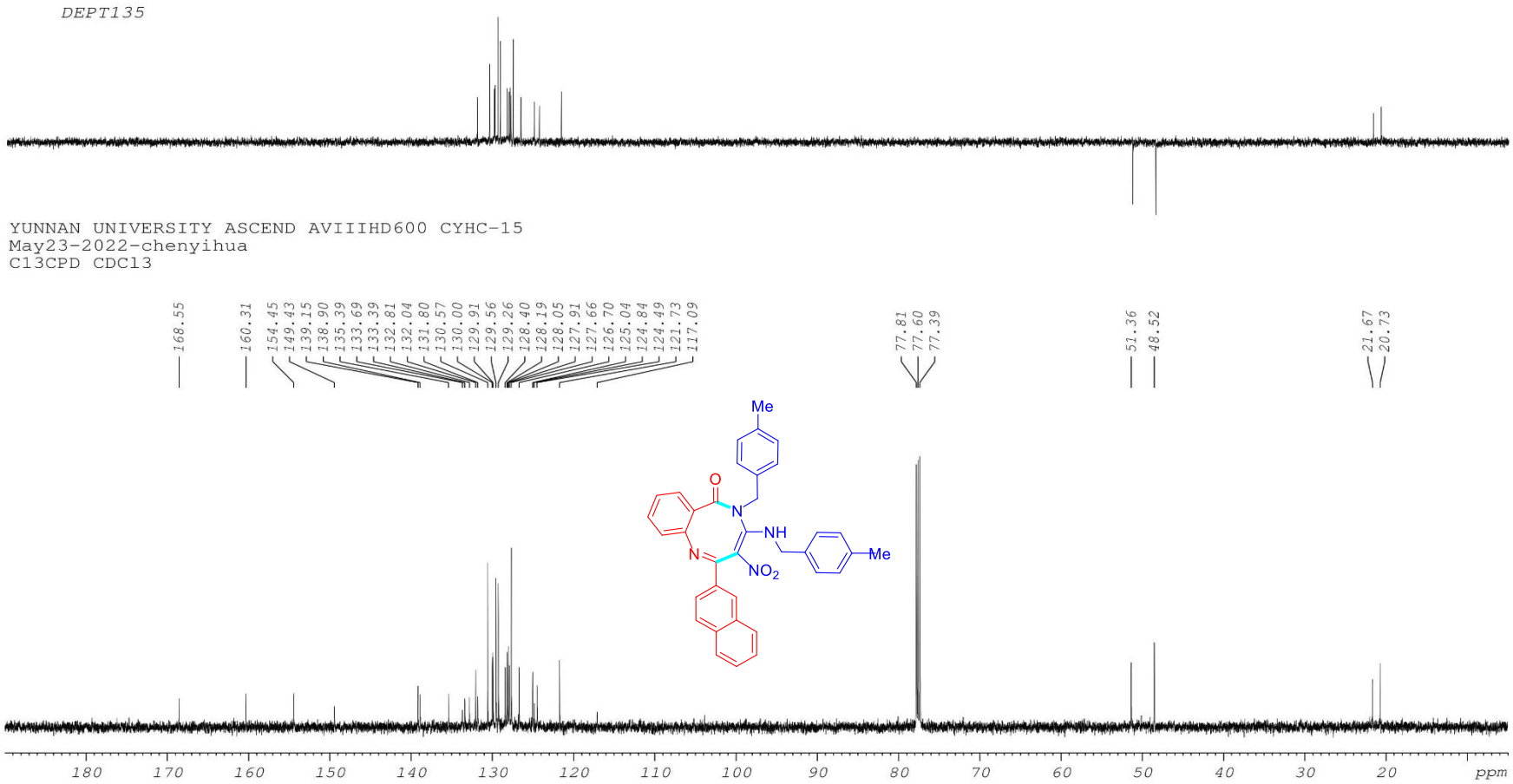


Figure S26. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4k**

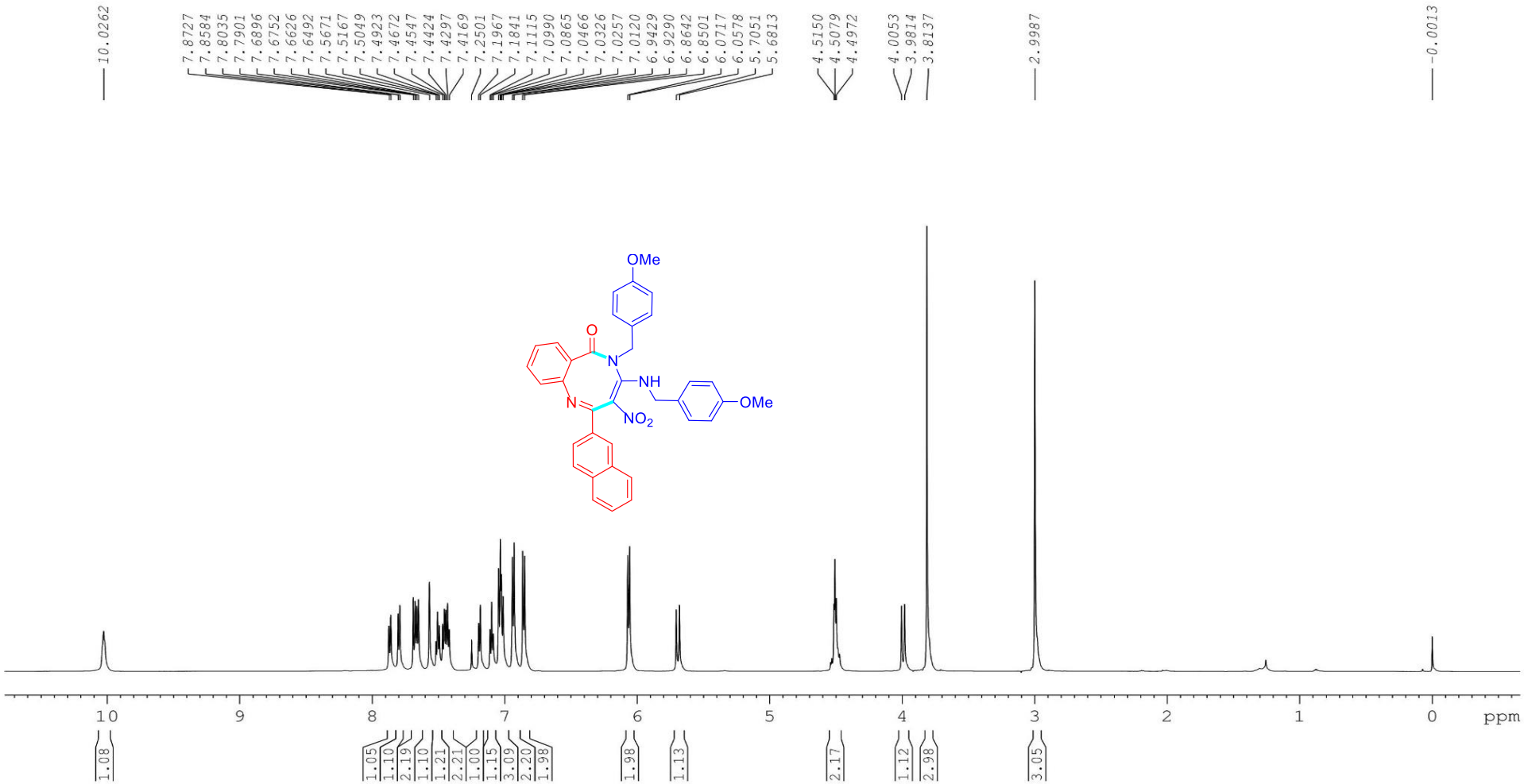


Figure S27. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **4l**

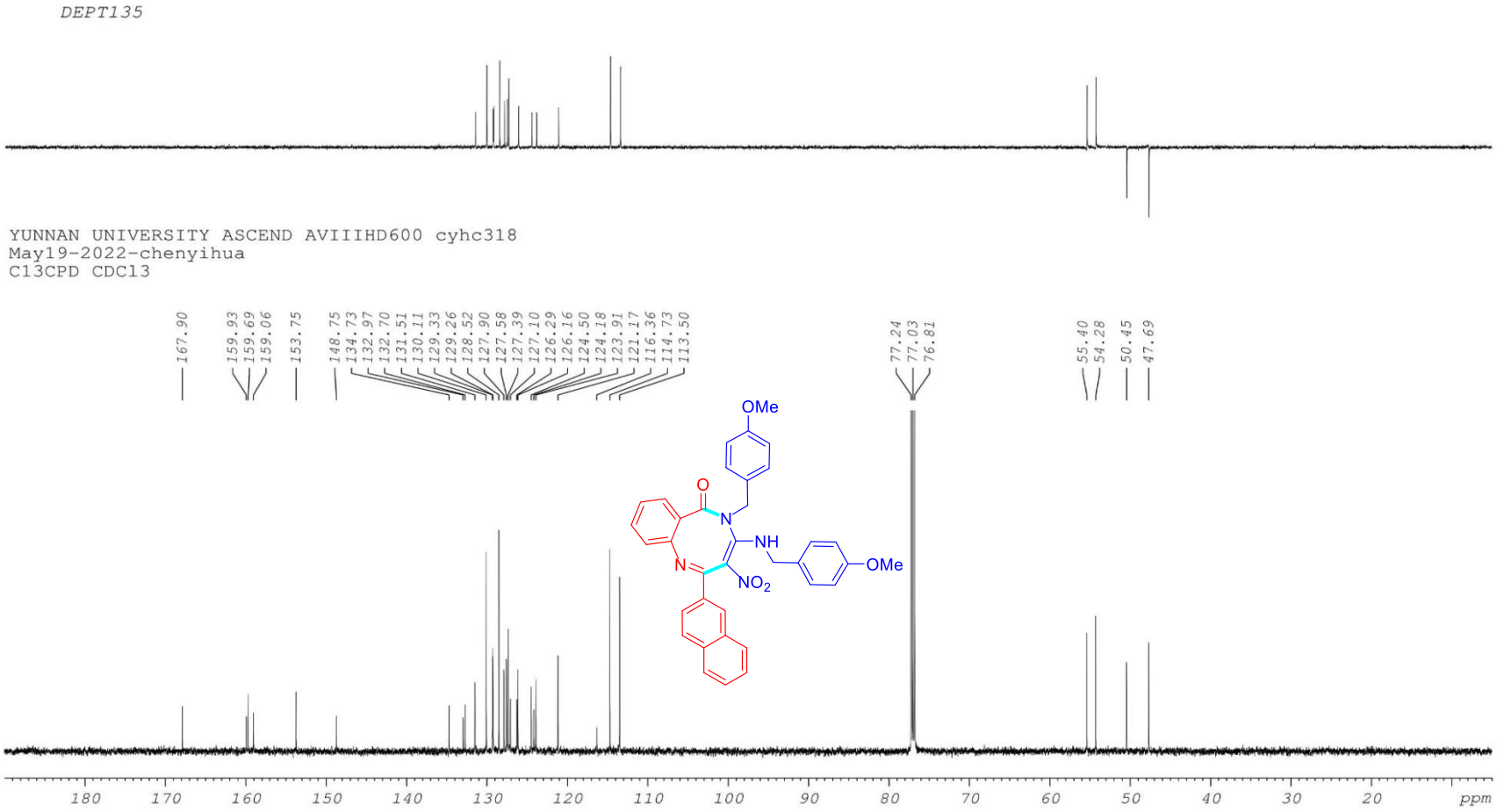


Figure S28. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **4l**

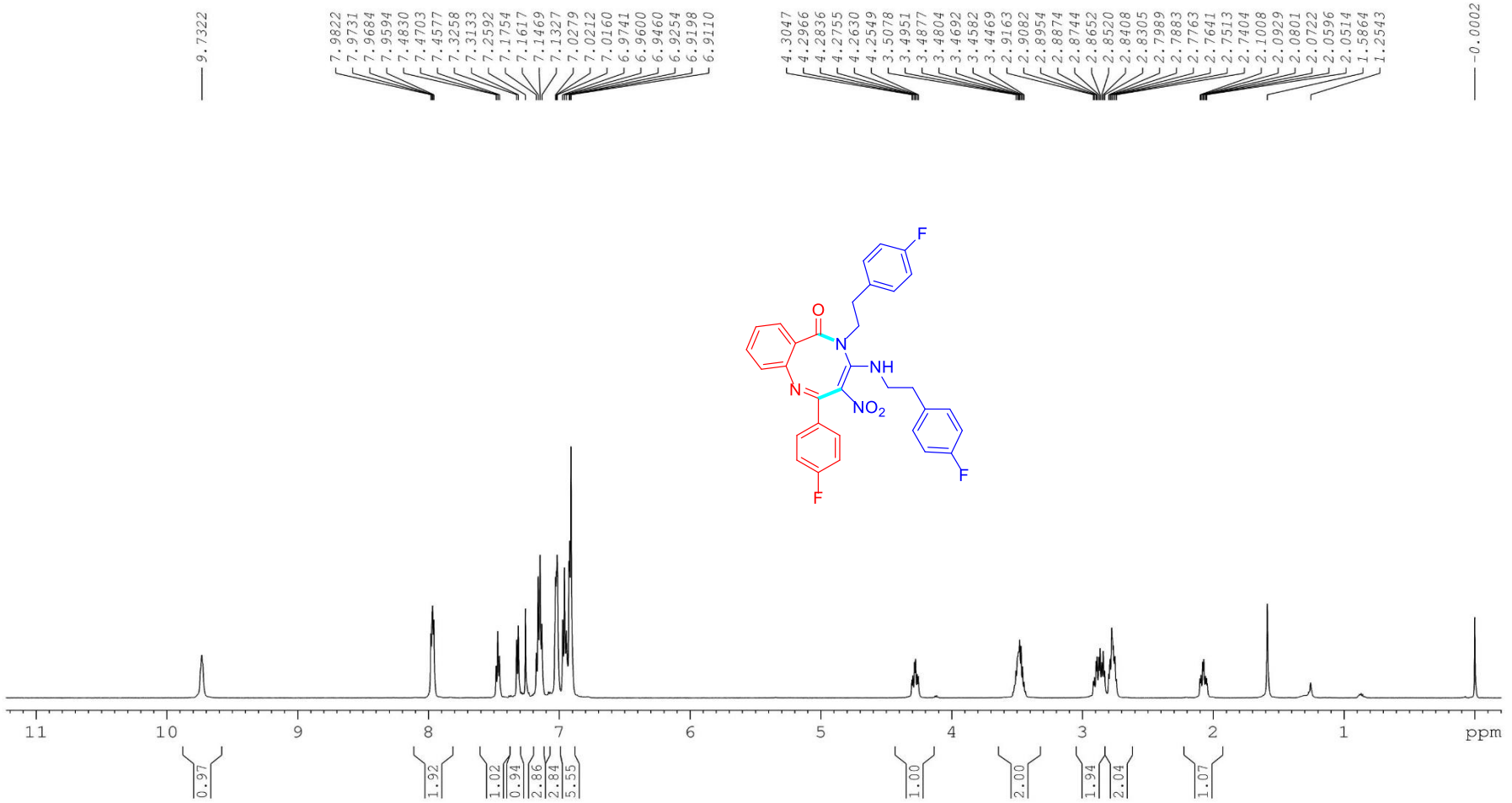


Figure S29. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5a**

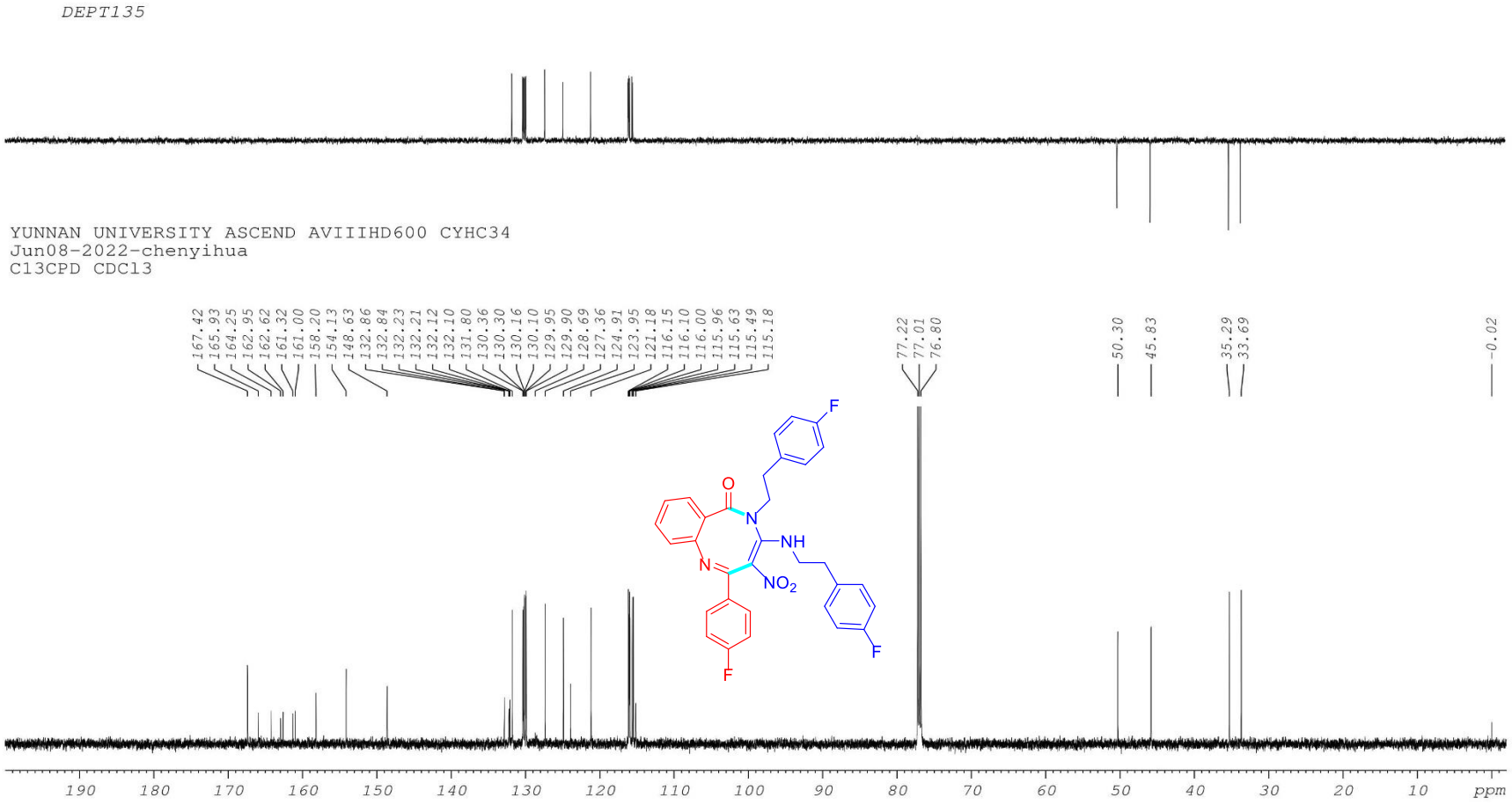


Figure S30. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5a**

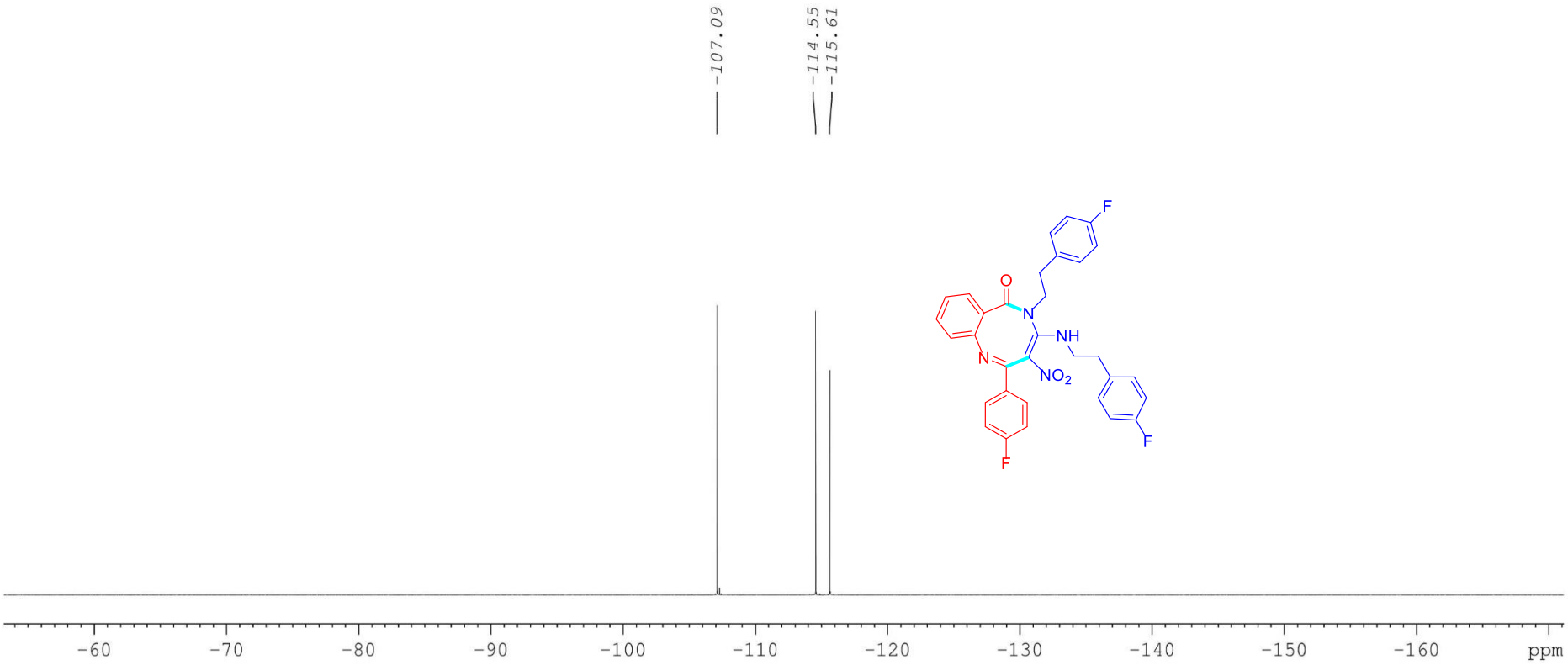


Figure S31. ^{19}F NMR (564 MHz, $CDCl_3$) spectra of compound **5a**

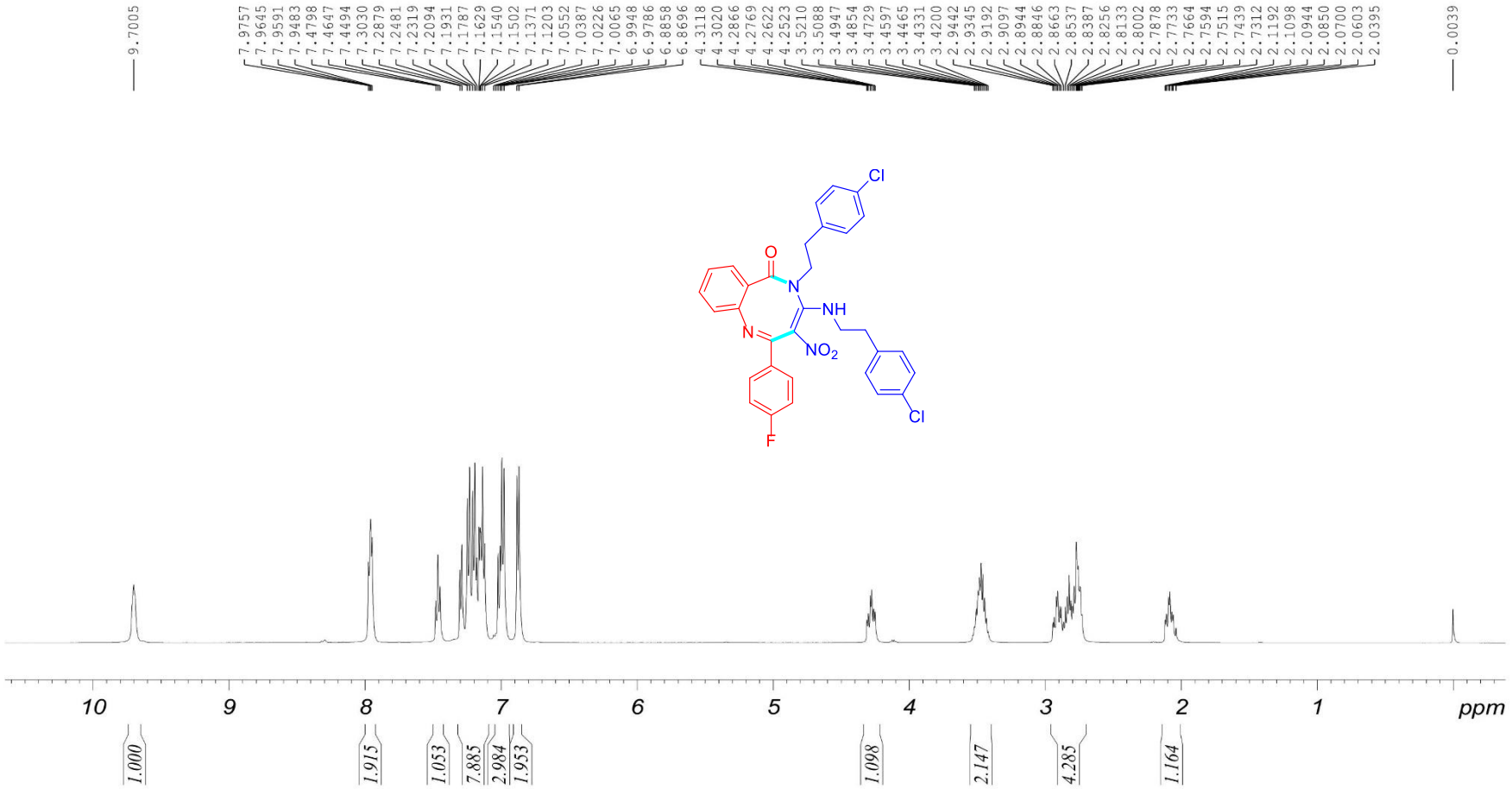


Figure S32. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **5b**

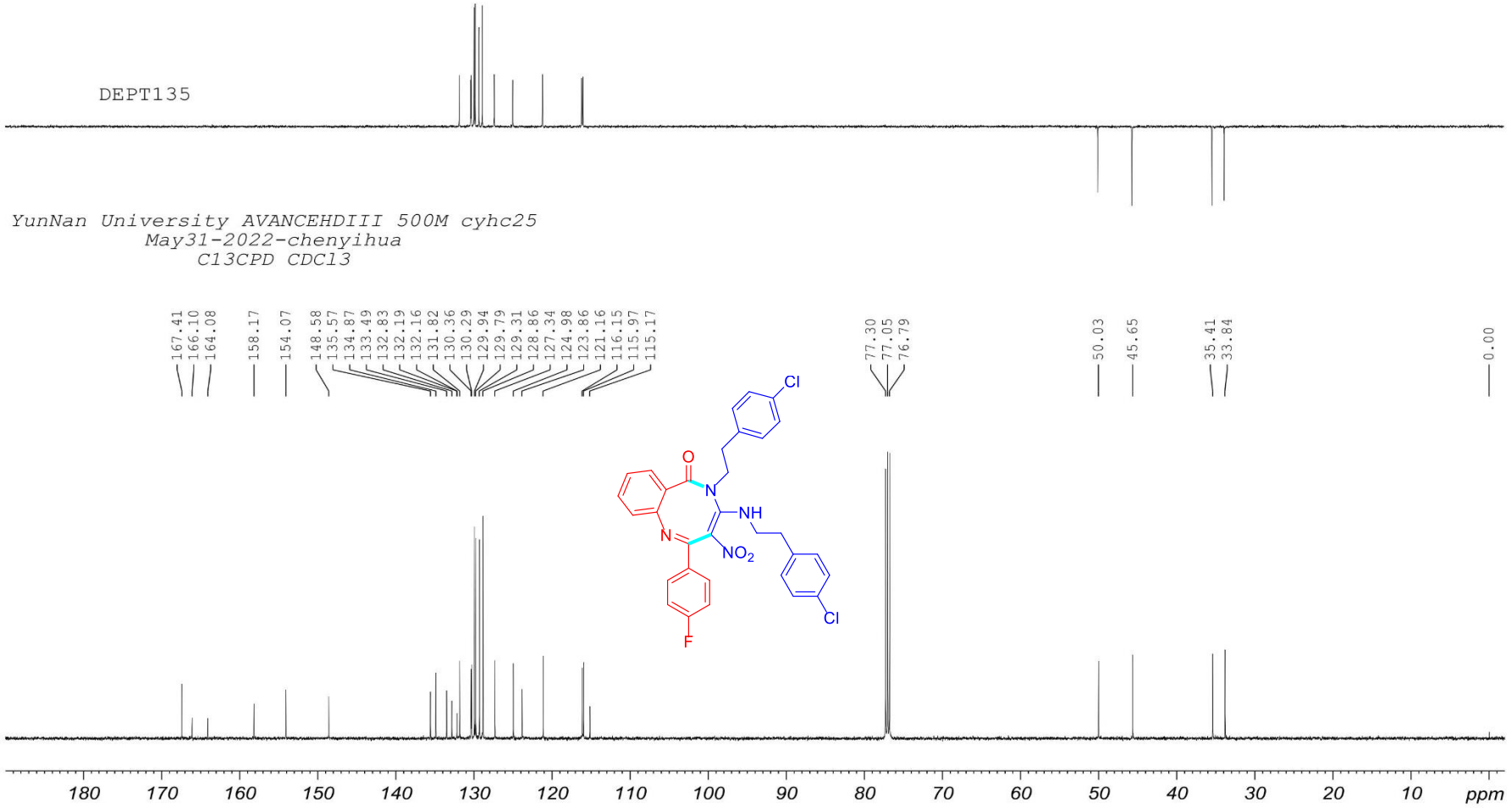


Figure S33. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **5b**

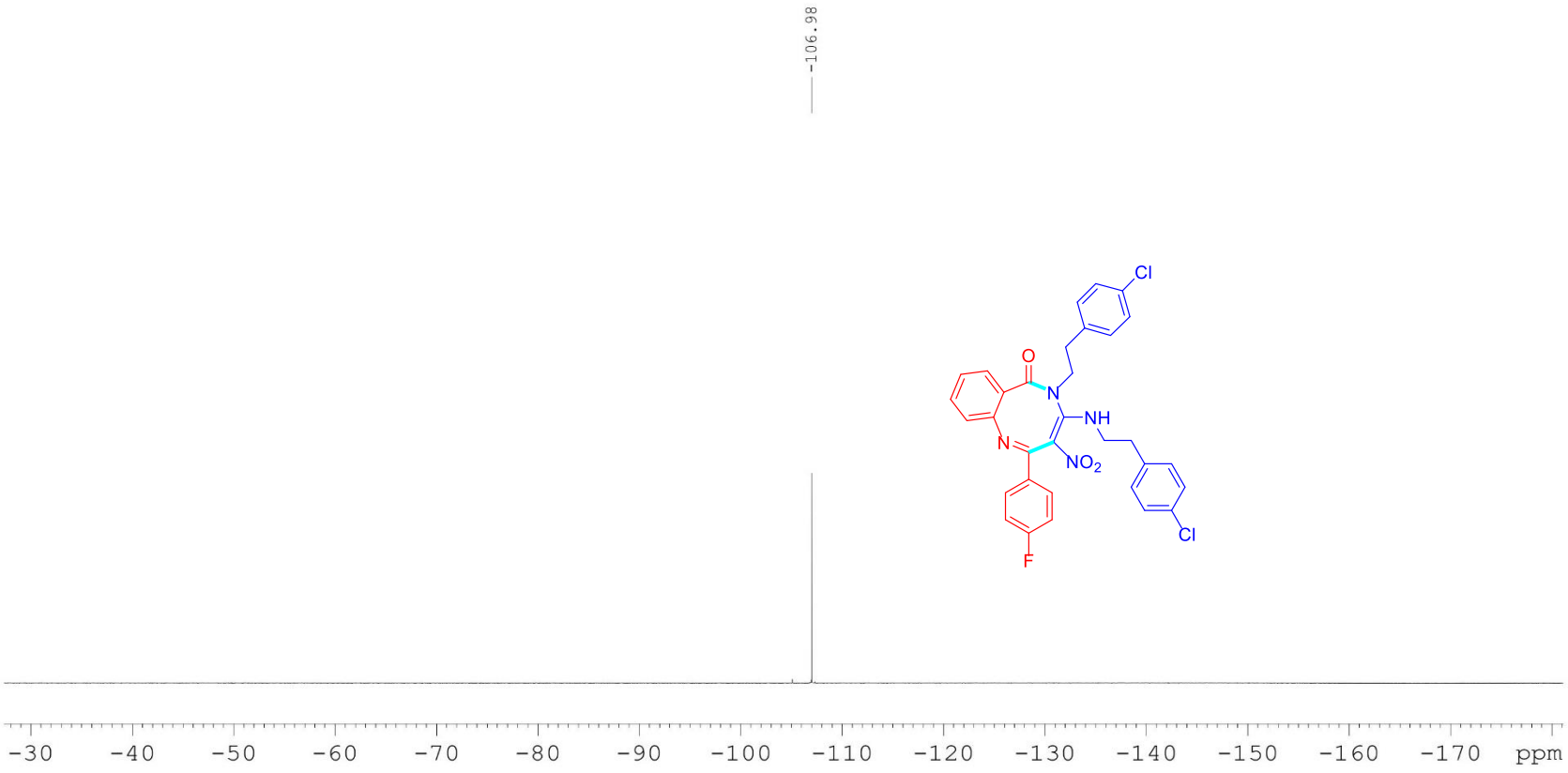


Figure S34. ^{19}F NMR (470 MHz, $CDCl_3$) spectra of compound **5b**

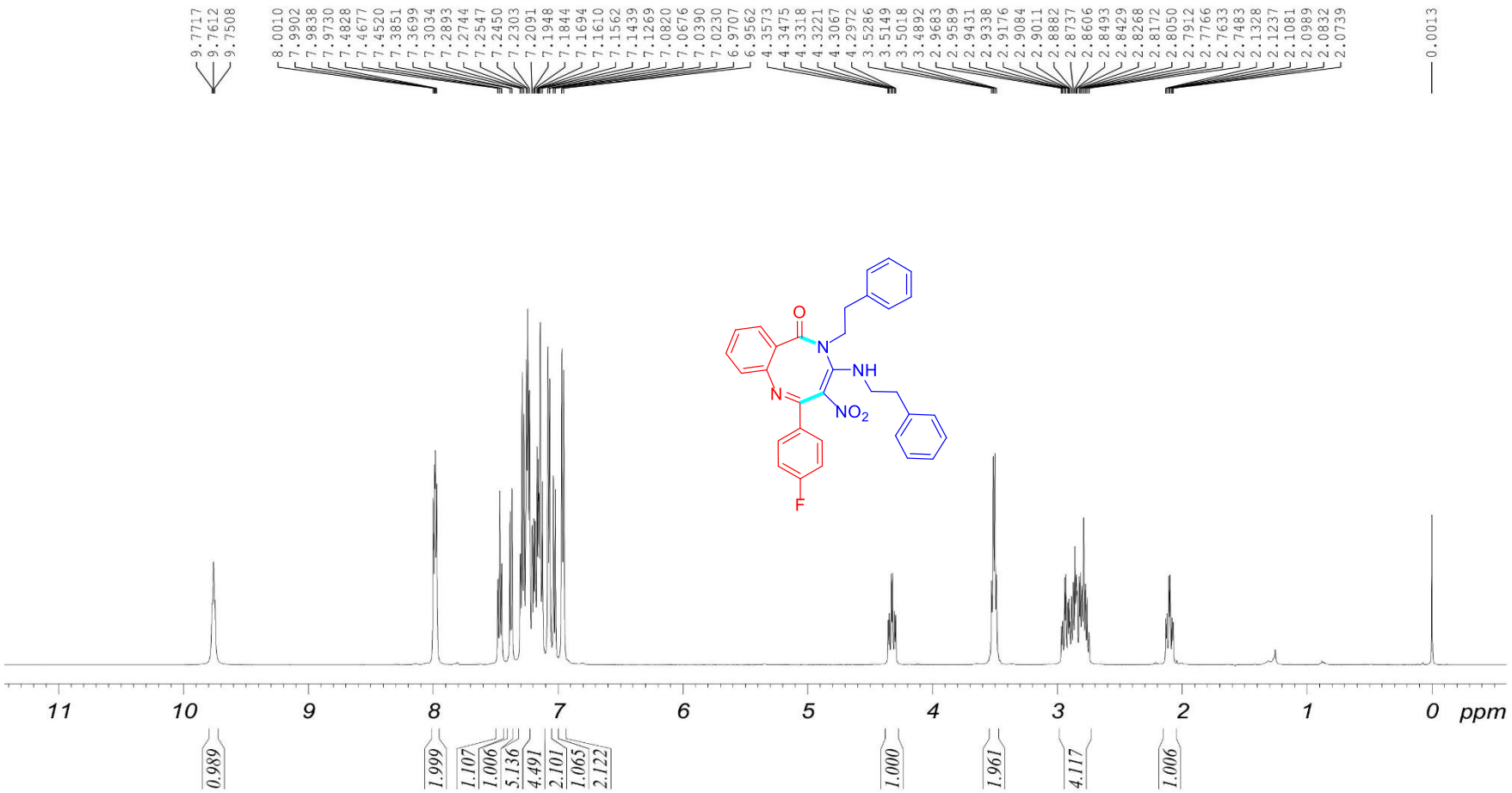


Figure S35. ^{1}H NMR (500 MHz, $CDCl_3$) spectra of compound **5c**

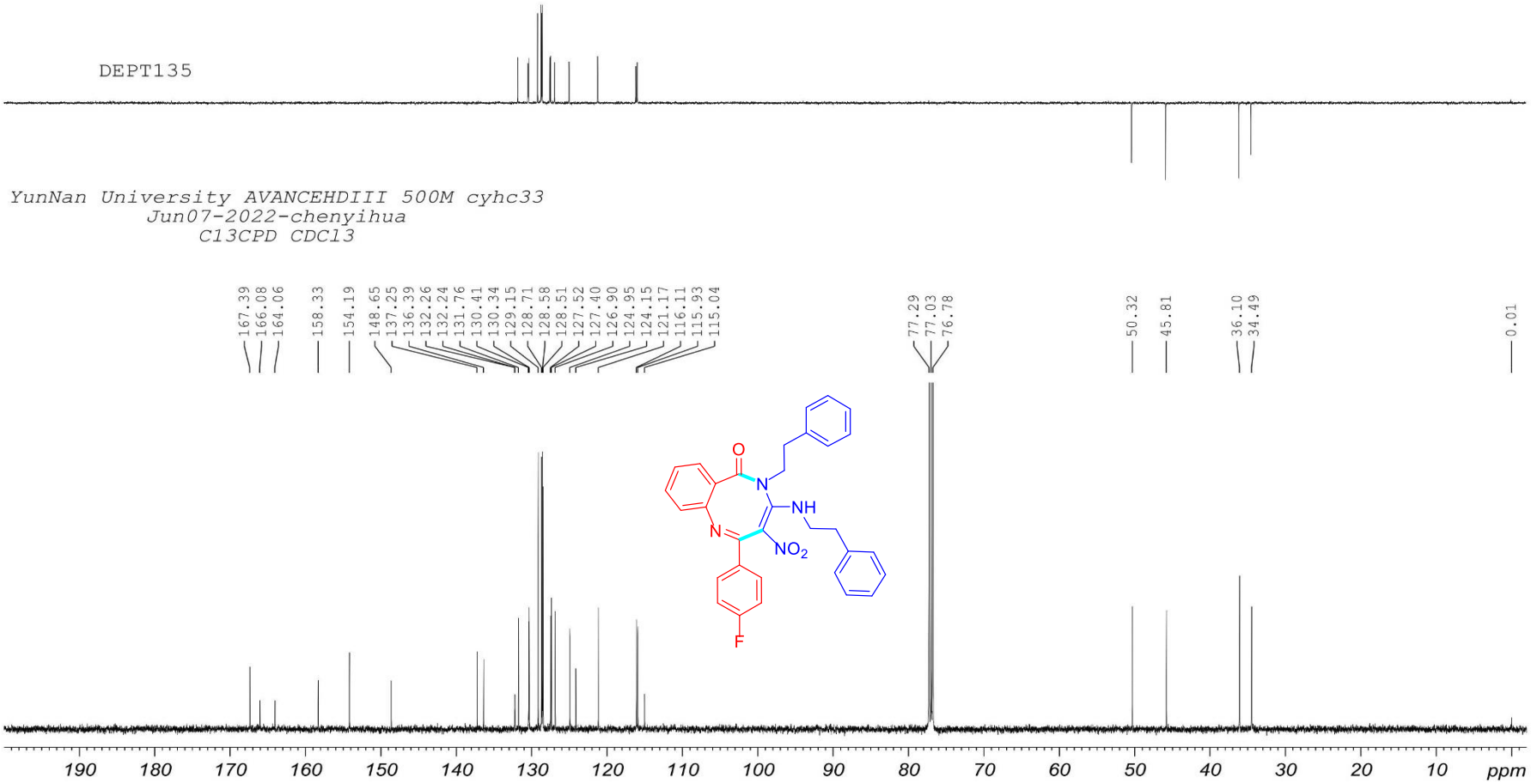


Figure S36. ^{13}C NMR (125 MHz, $CDCl_3$) spectra of compound **5c**

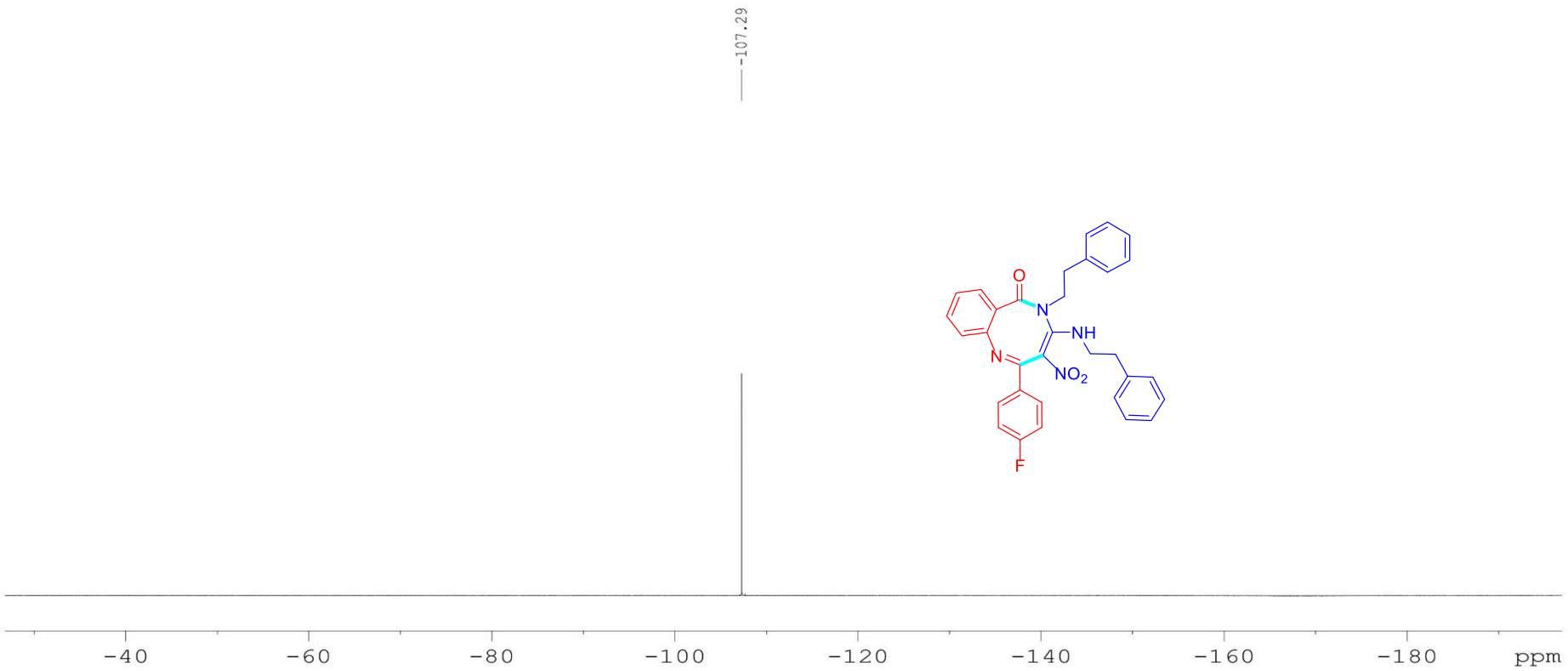


Figure S37. ^{19}F NMR (470 MHz, $CDCl_3$) spectra of compound **5c**

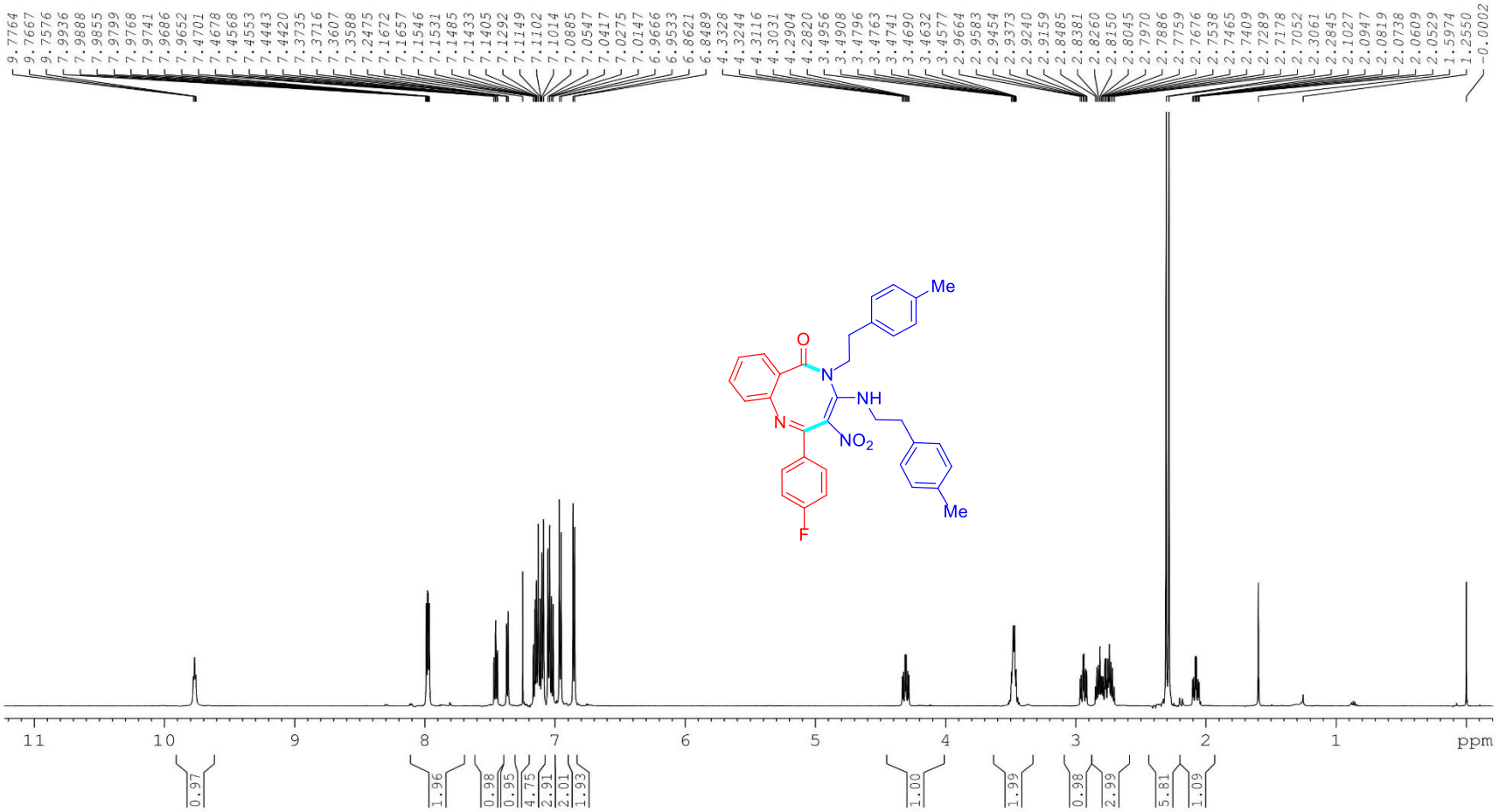


Figure S38. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5d**

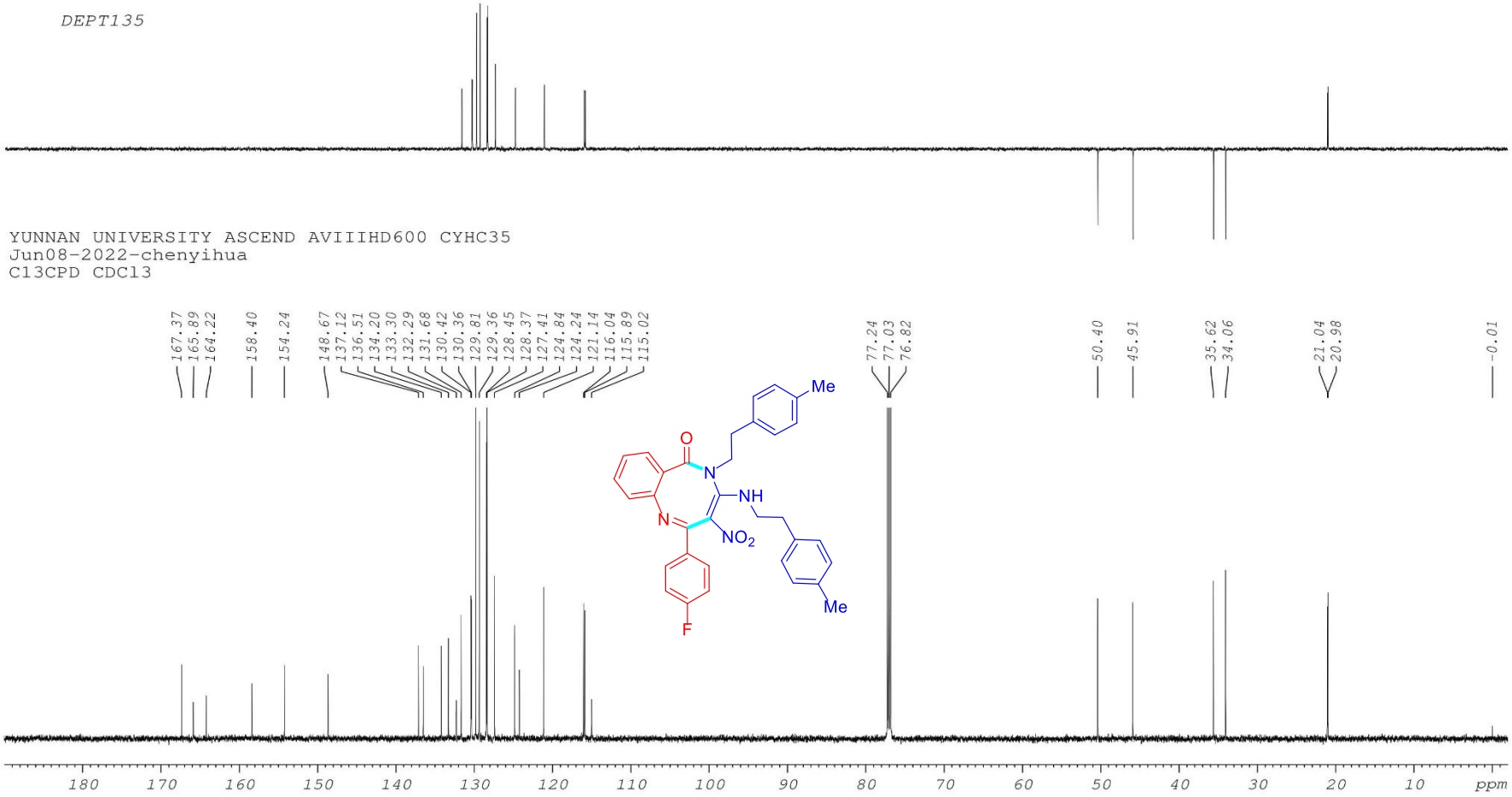


Figure S39. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5d**

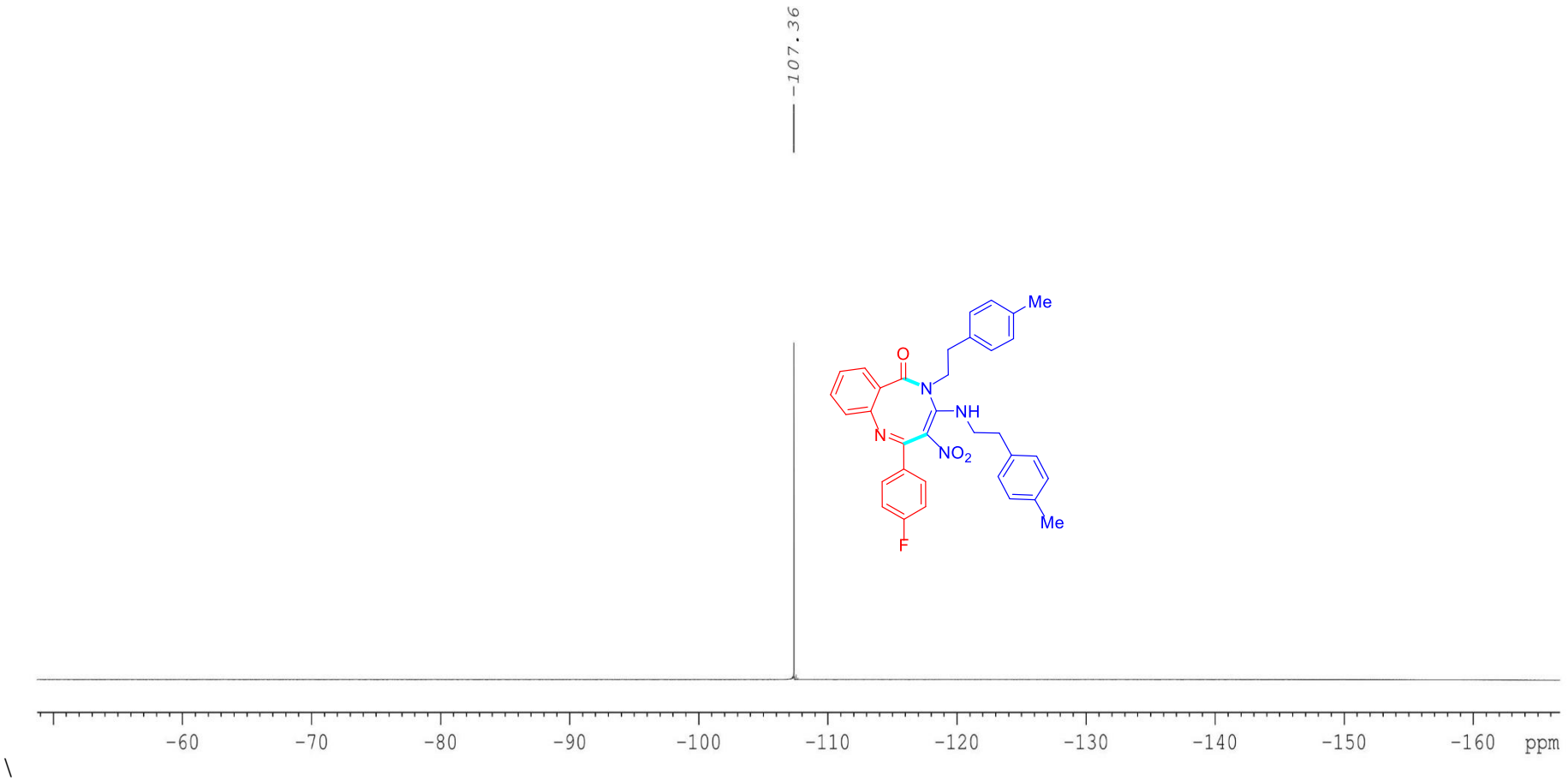


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Figure S40. ^{19}F NMR (564 MHz, $CDCl_3$) spectra of compound **5d**

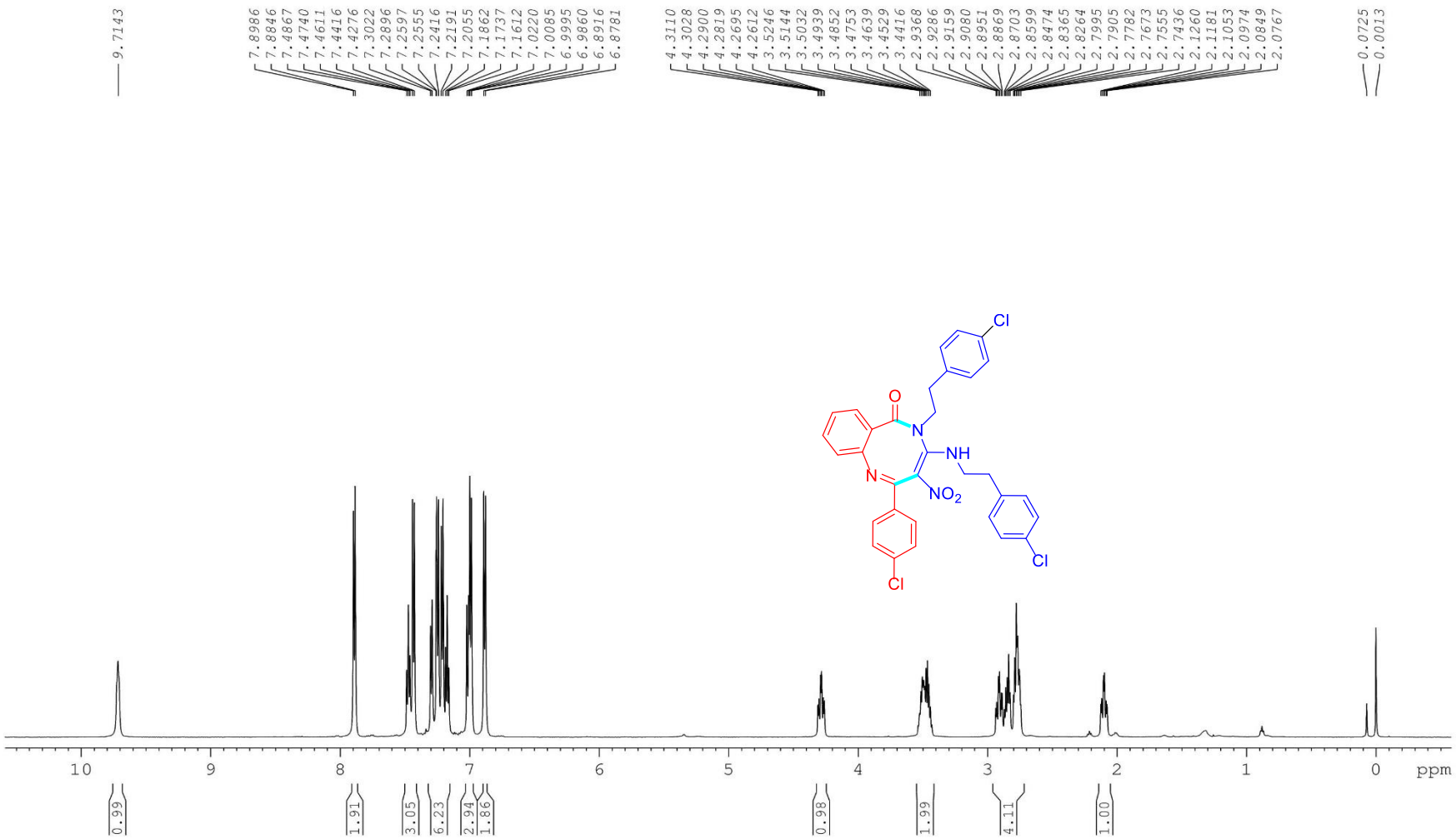

Figure S41. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5e**

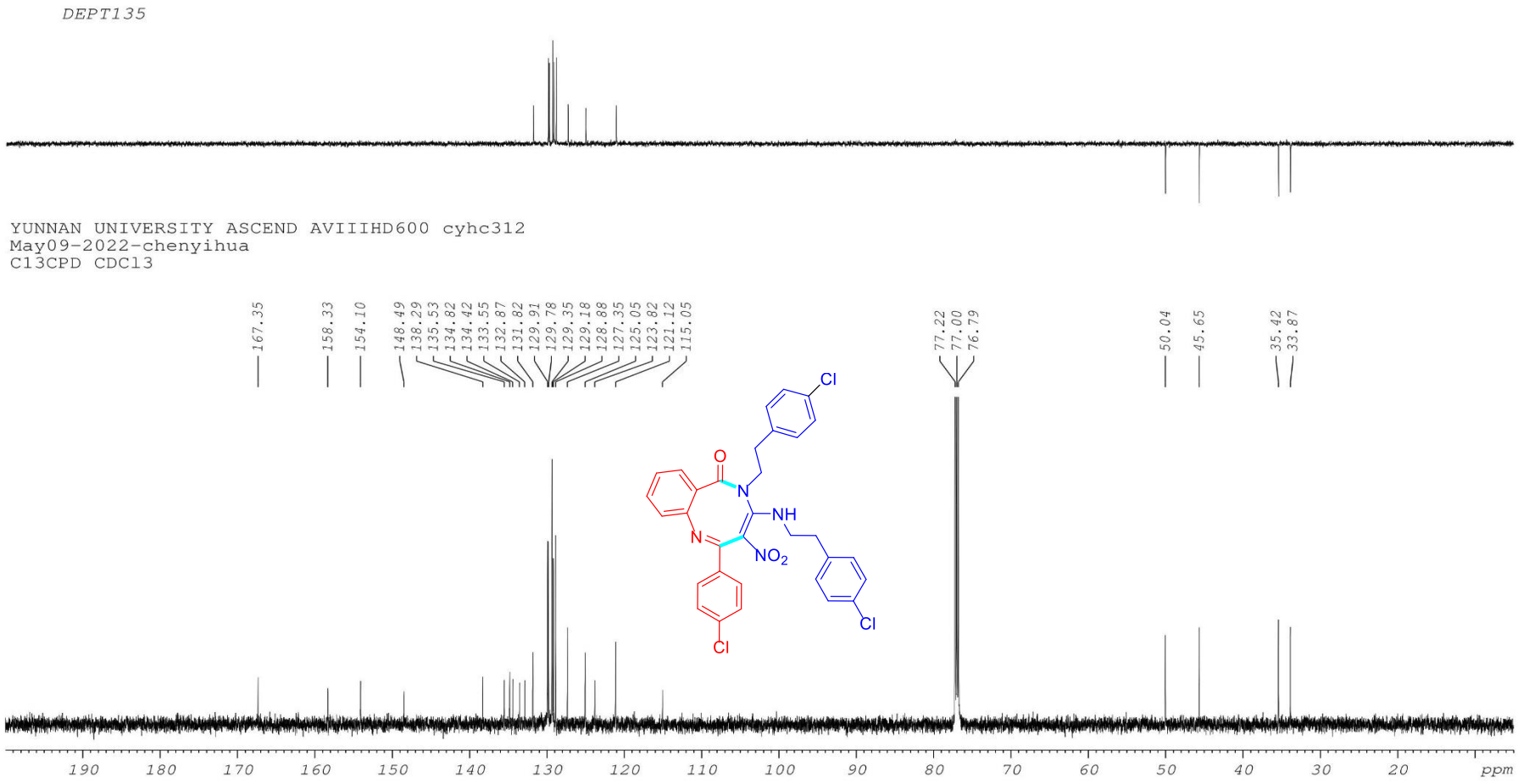

Figure S42. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5e**

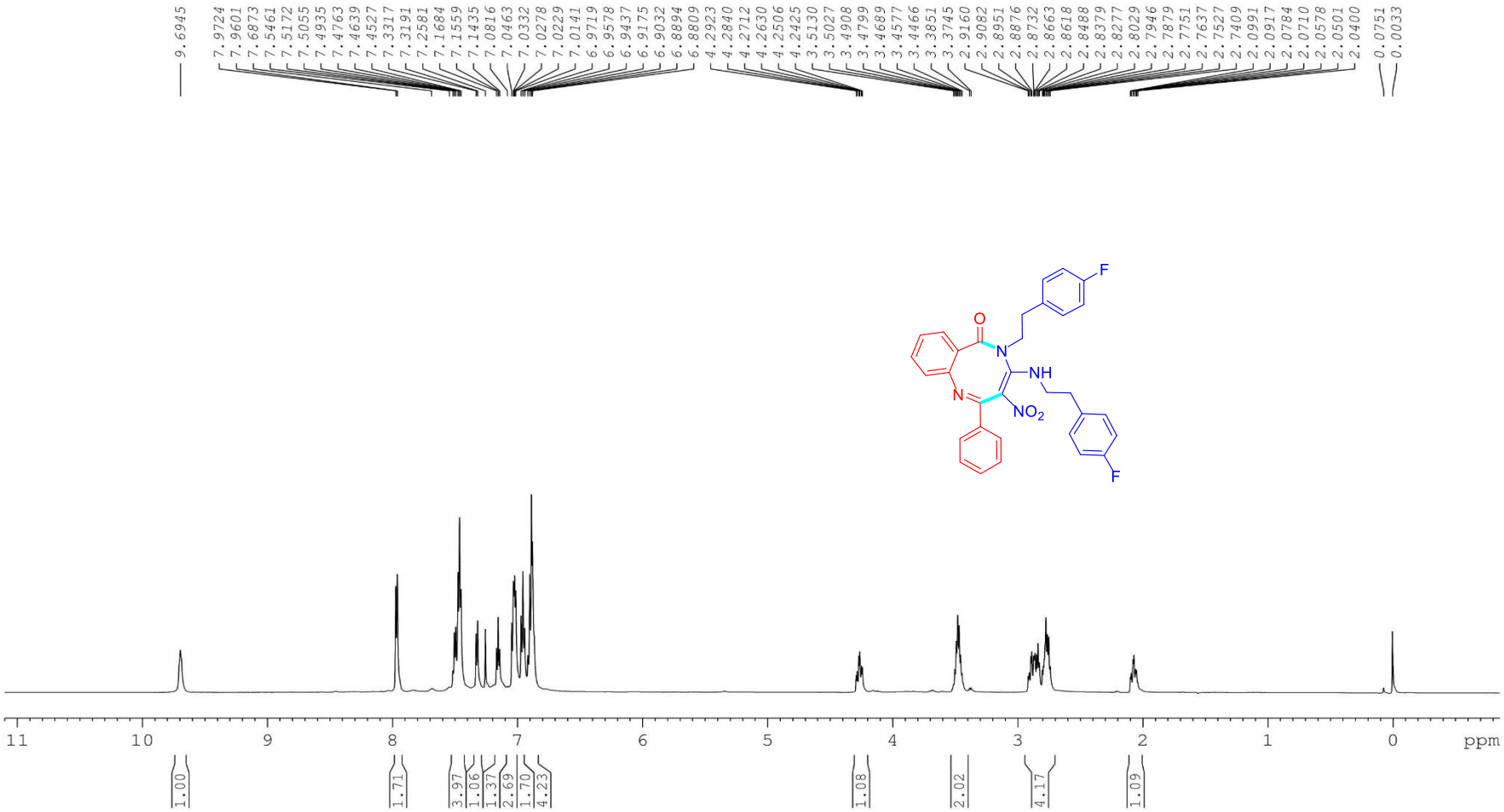

Figure S43. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5f**

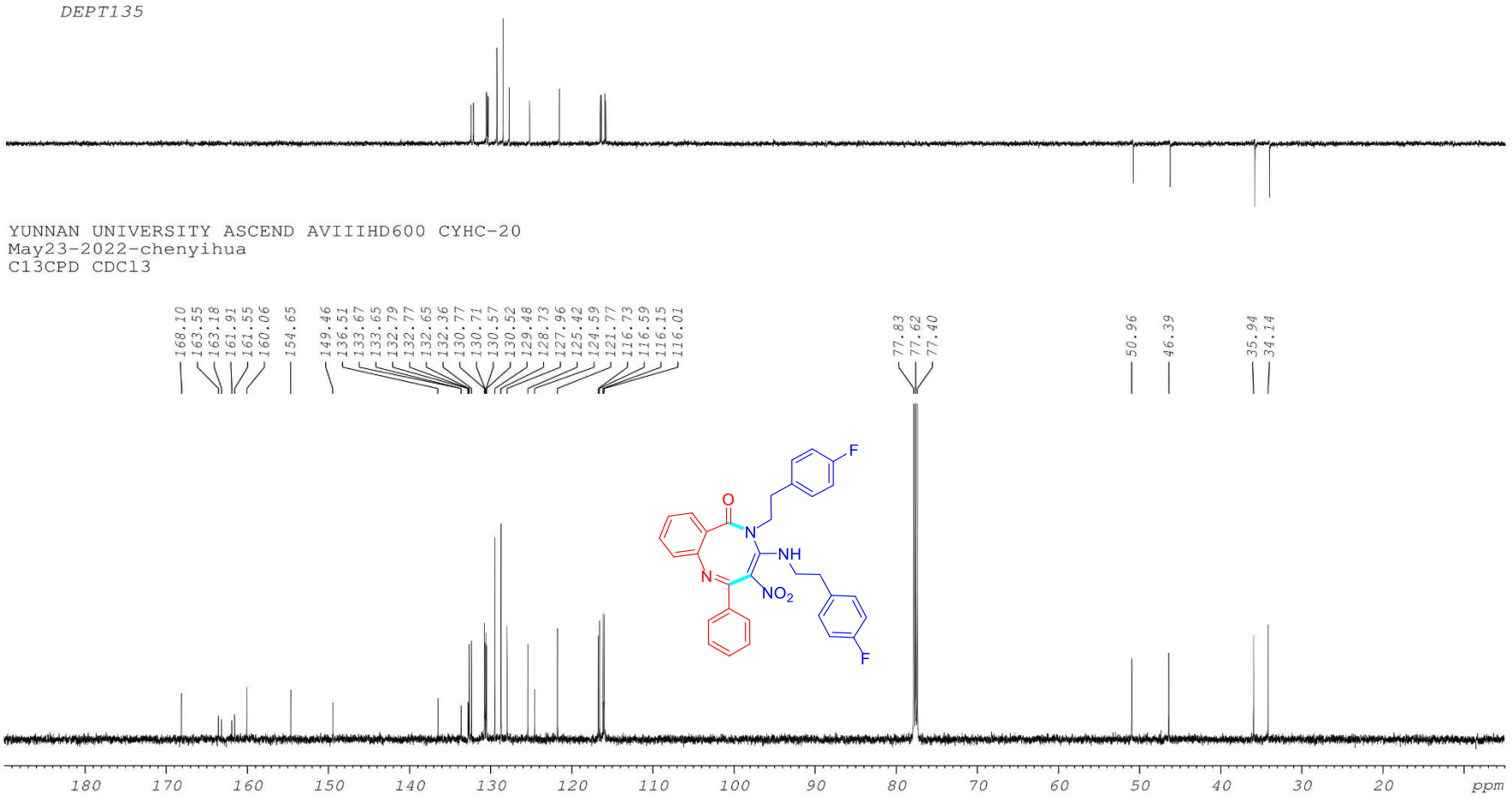

Figure S44. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5f**

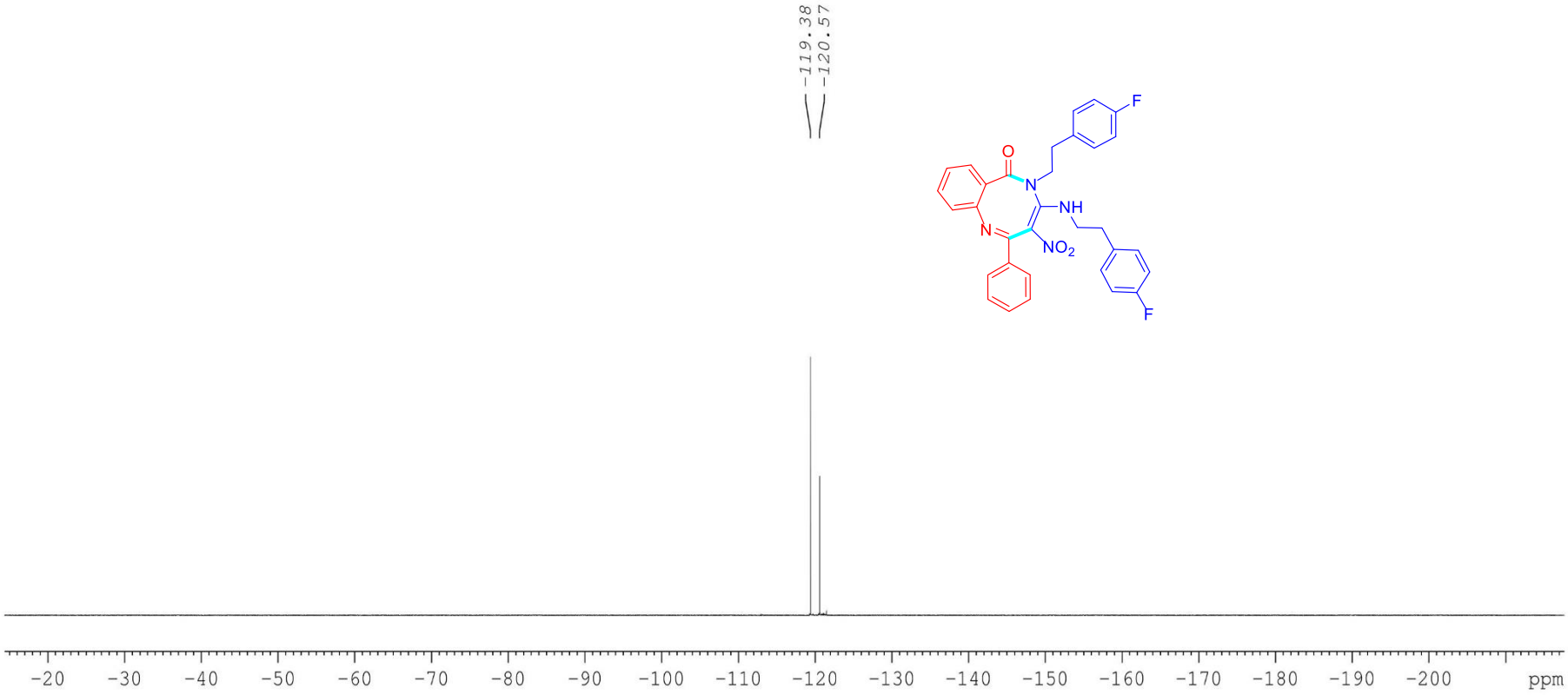

Figure S45. ^{19}F NMR (564 MHz, $CDCl_3$) spectra of compound **5f**

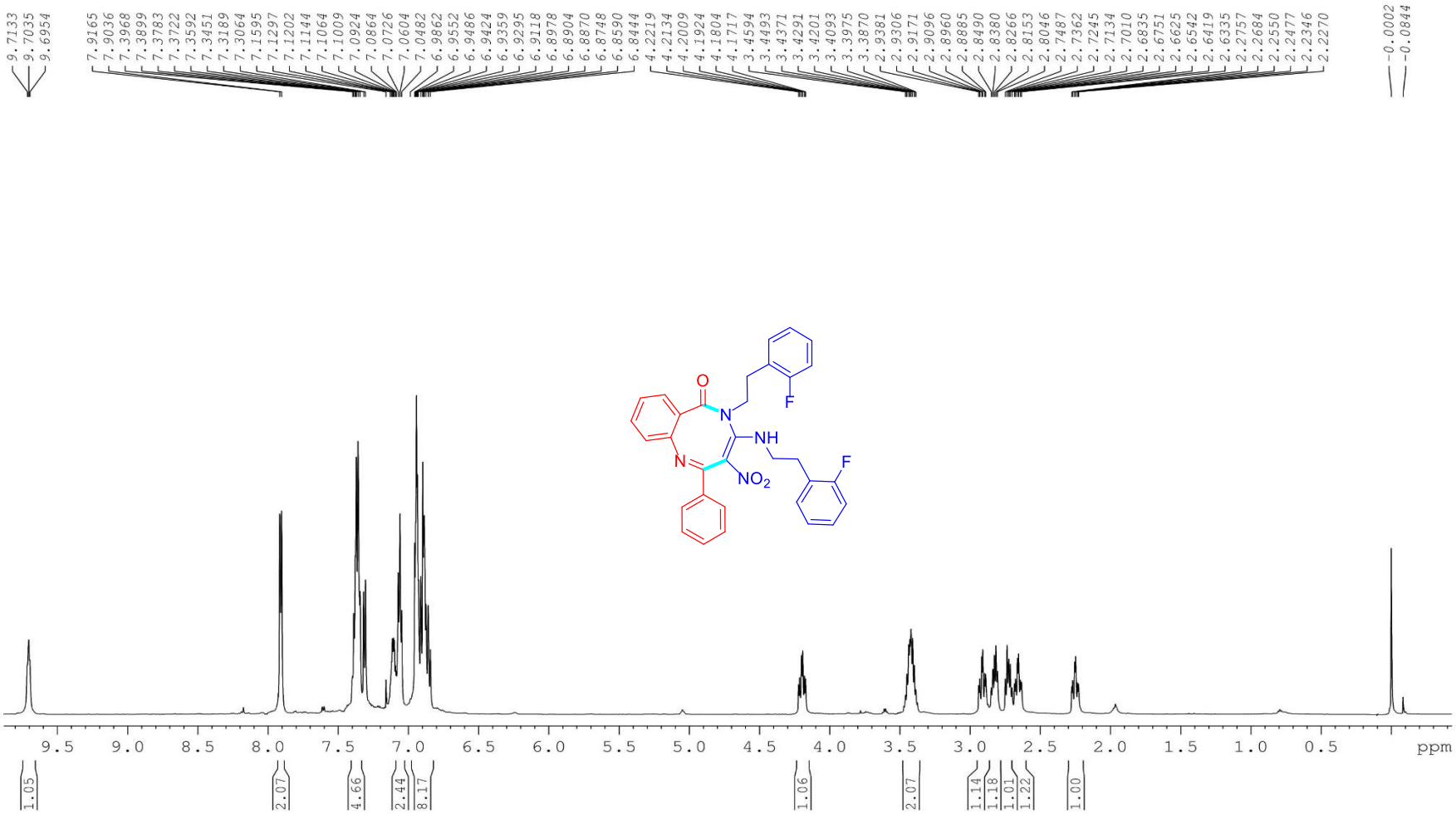

Figure S46. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5g**

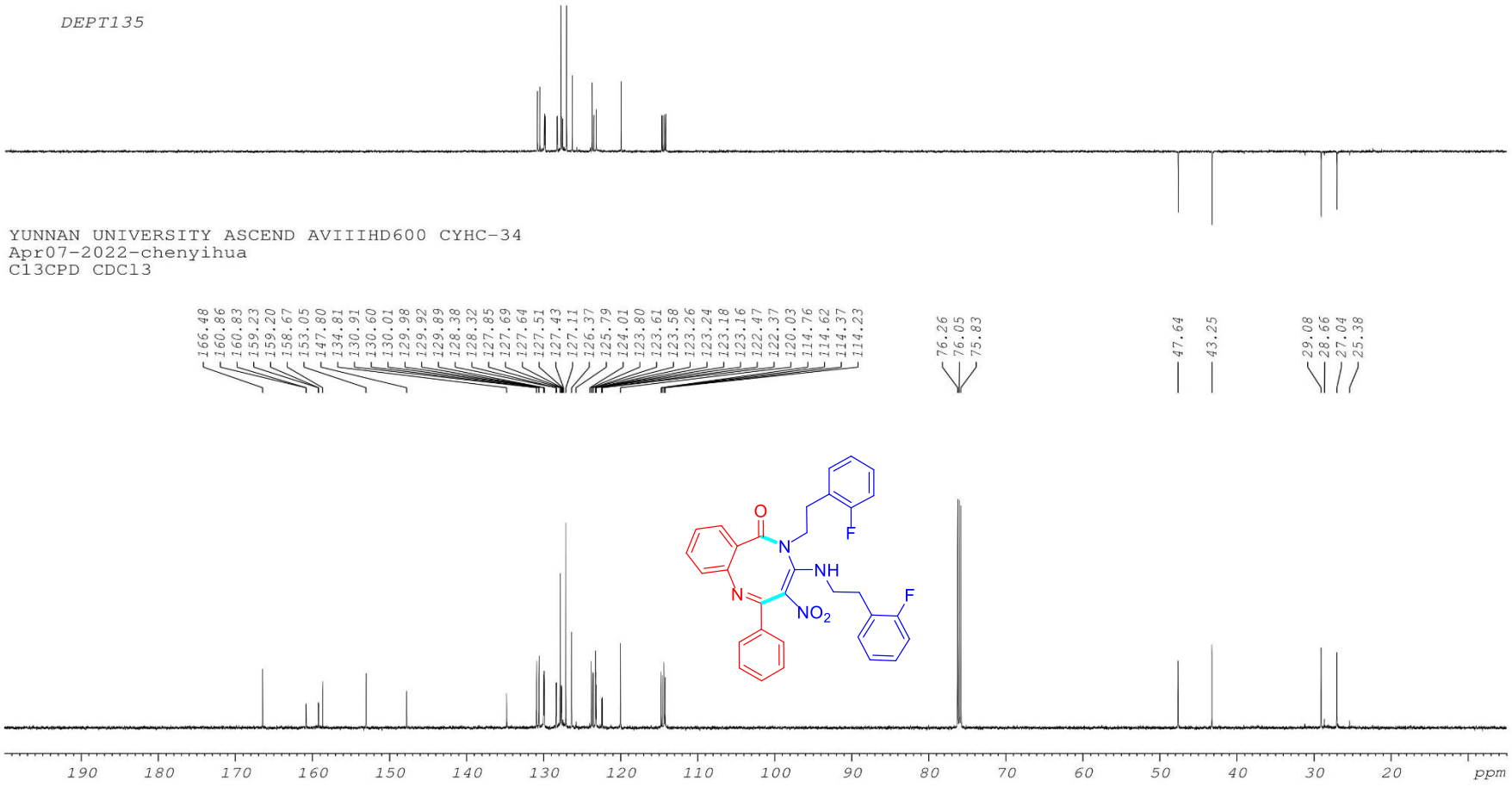

Figure S47. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5g**

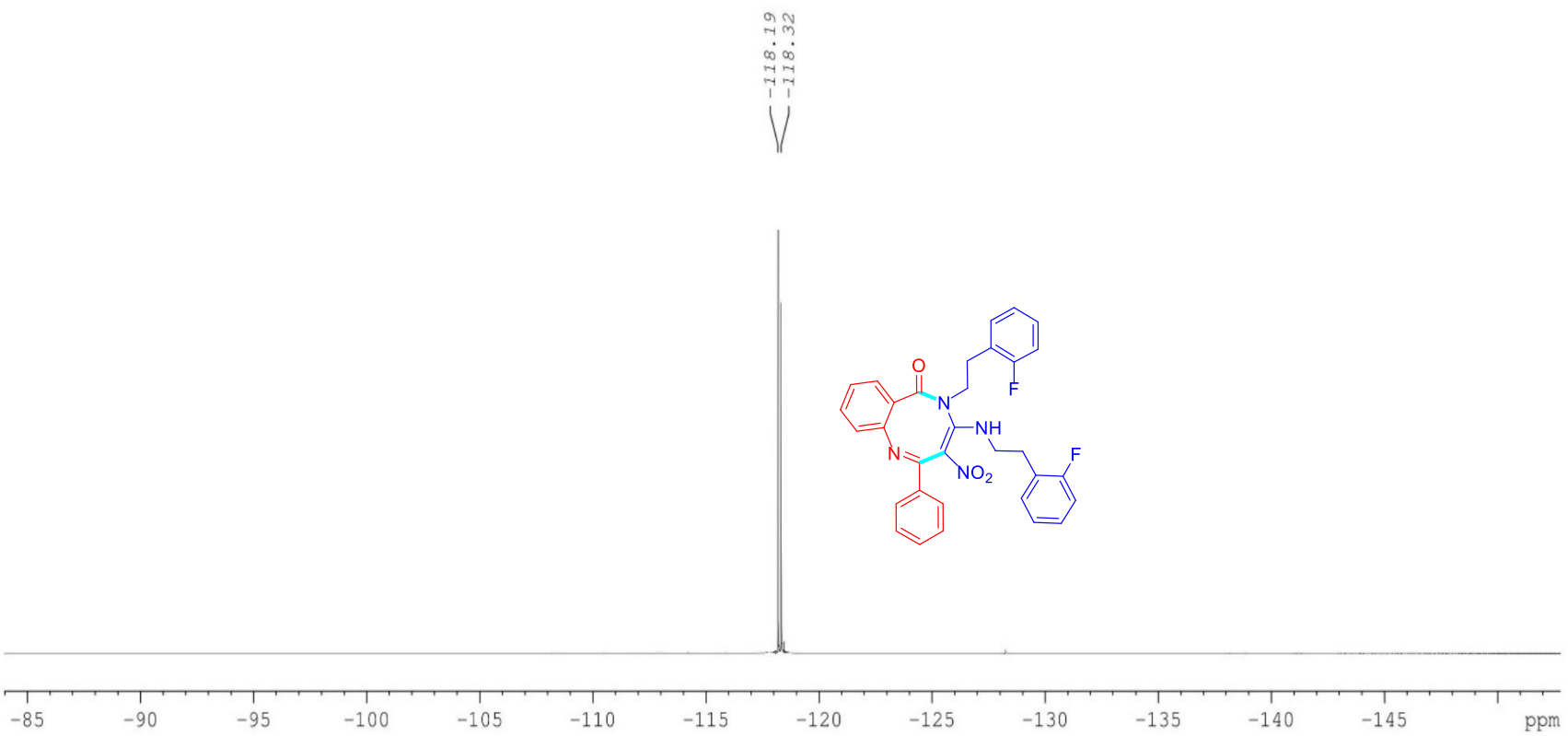

Figure S48. ^{19}F NMR (564 MHz, $CDCl_3$) spectra of compound **5g**

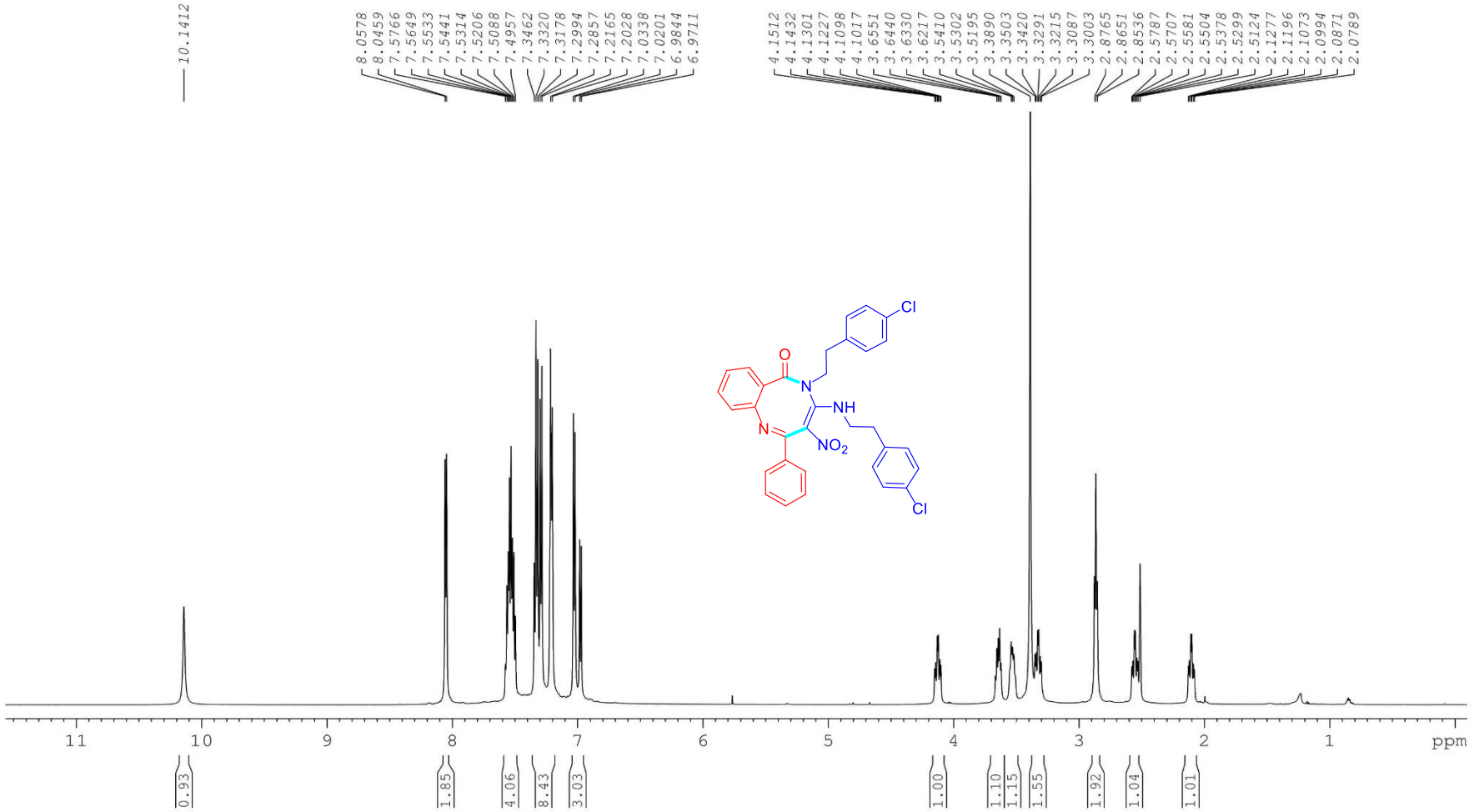

Figure S49. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5h**

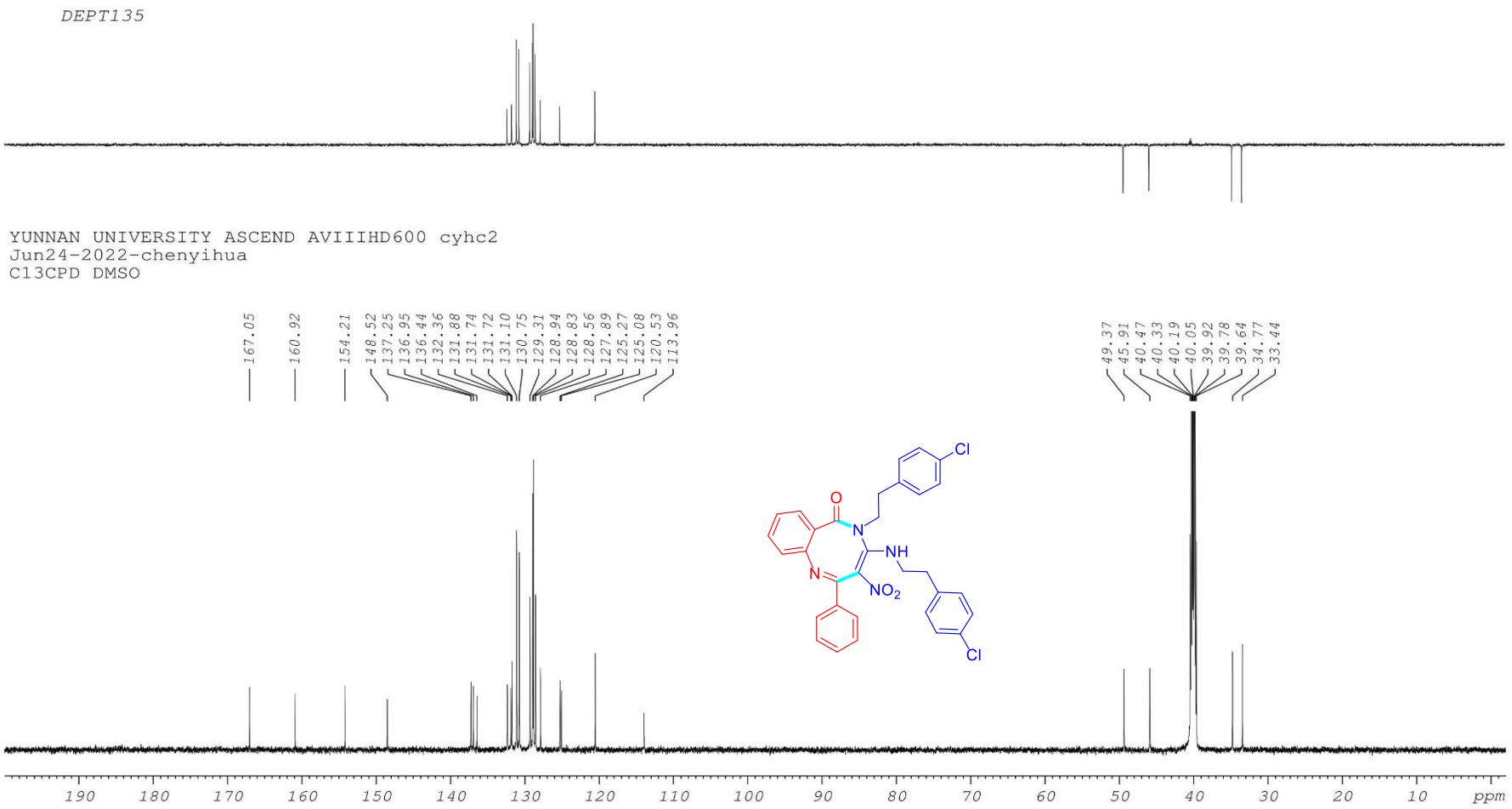

Figure S50. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5h**

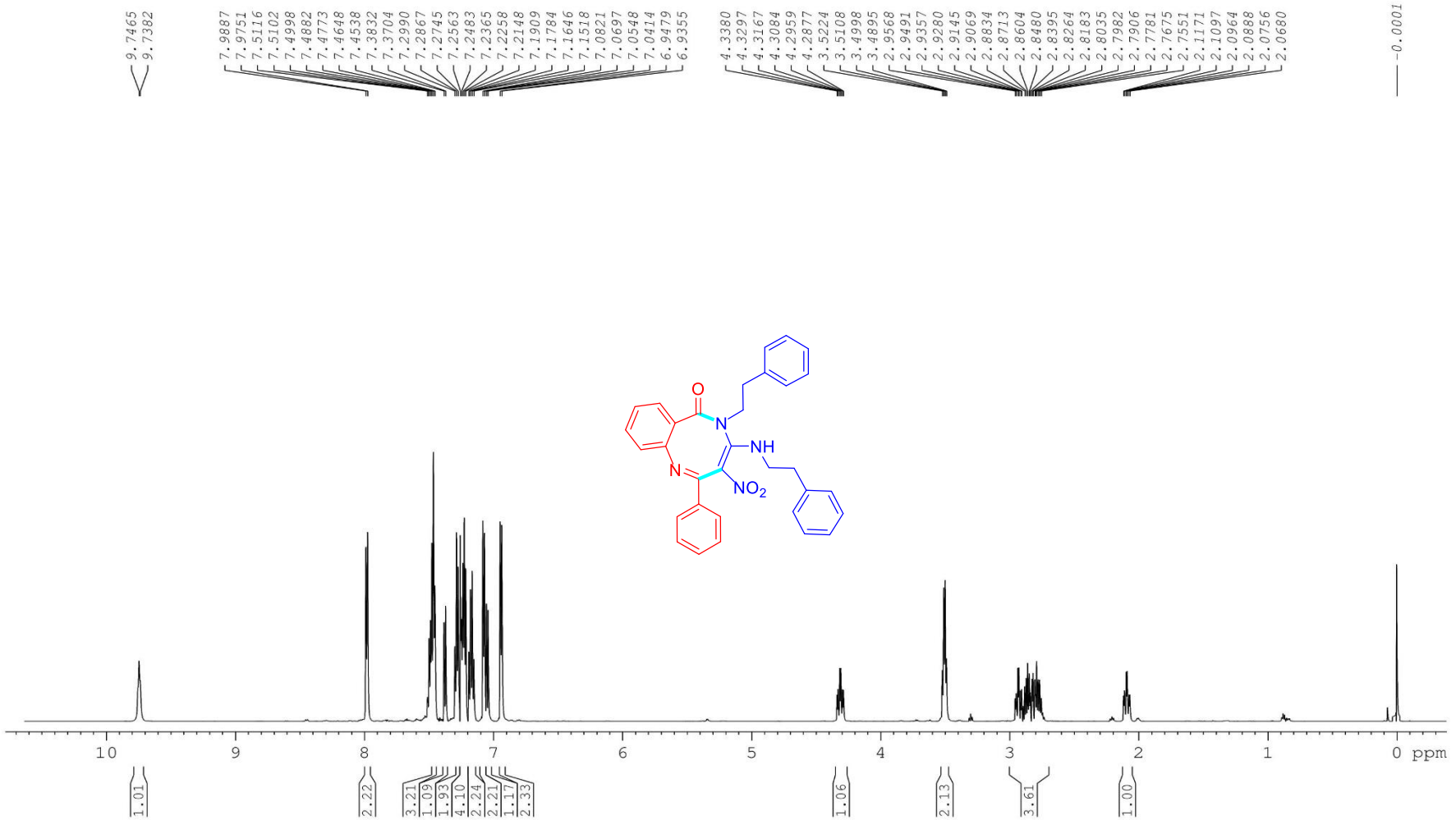

Figure S51. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5i**

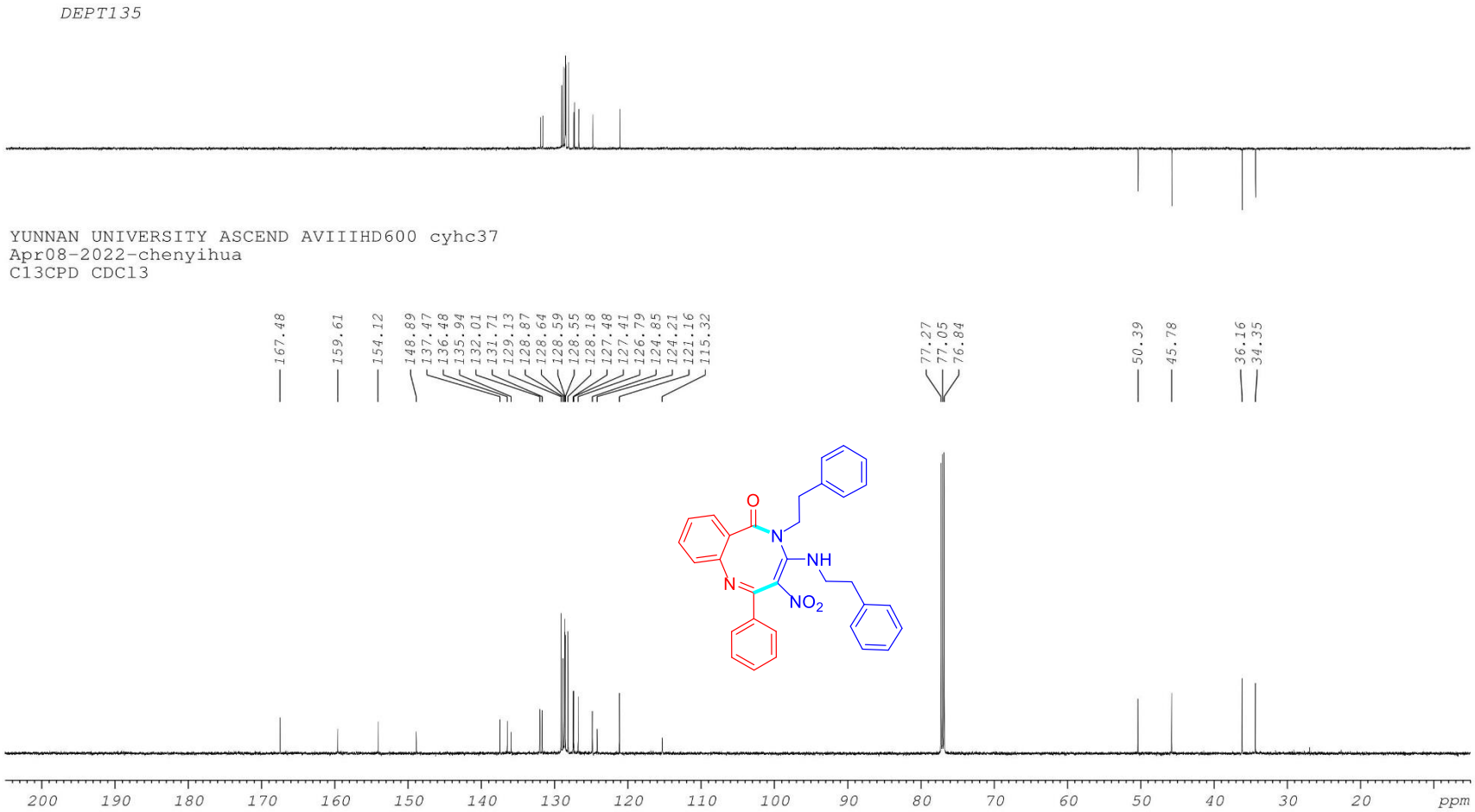

Figure S52. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5i**

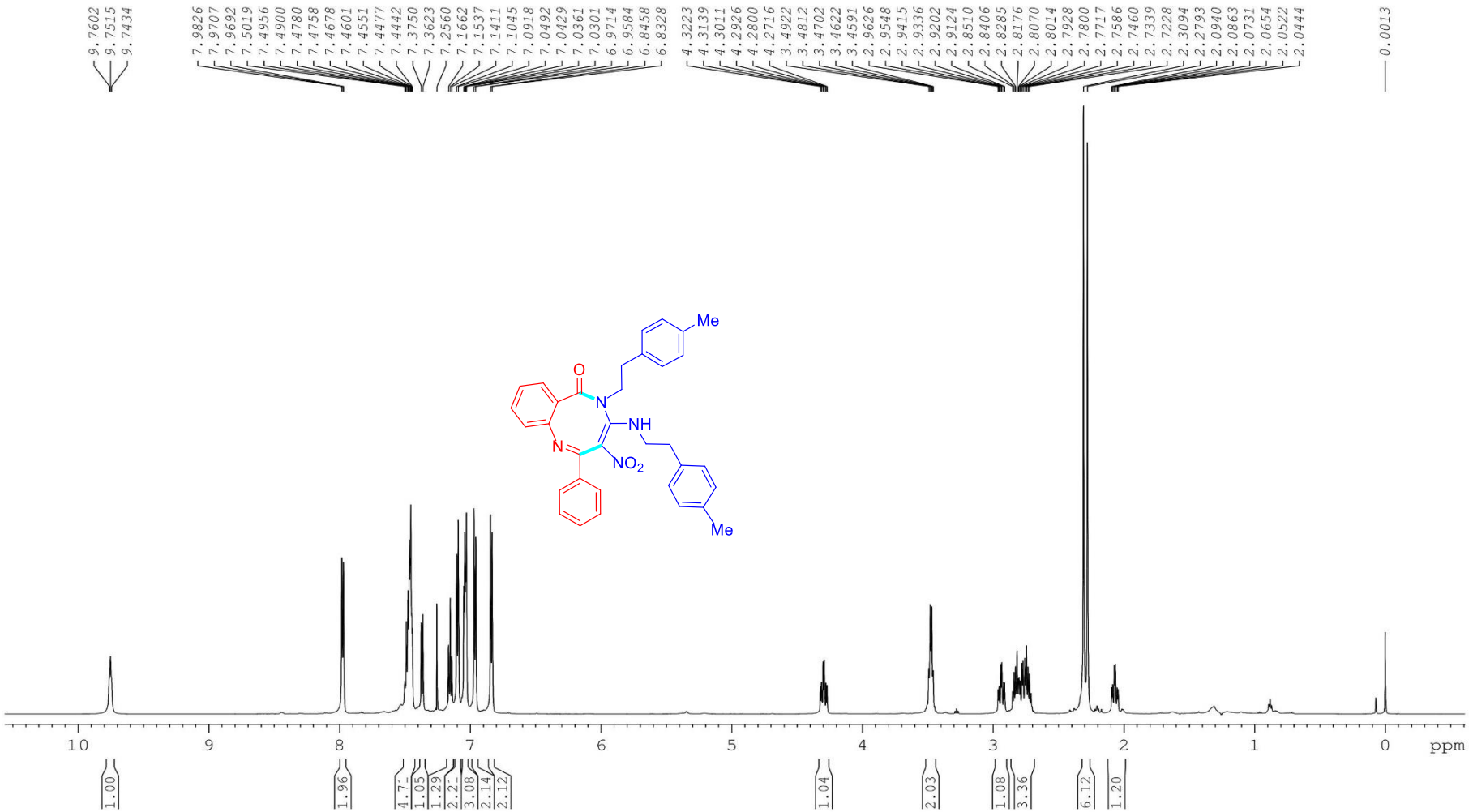

Figure S53. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5j**

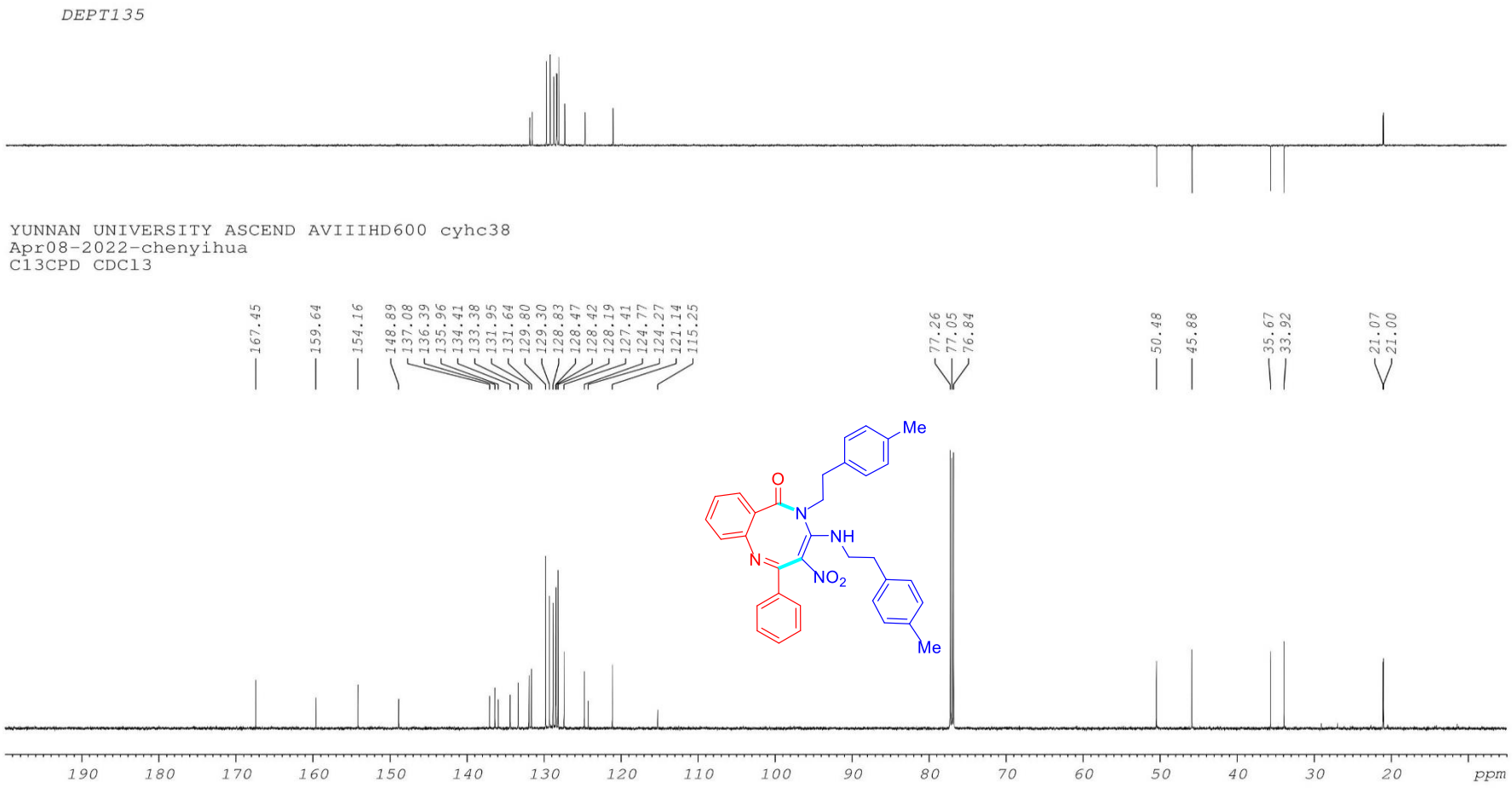

Figure S54. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5j**

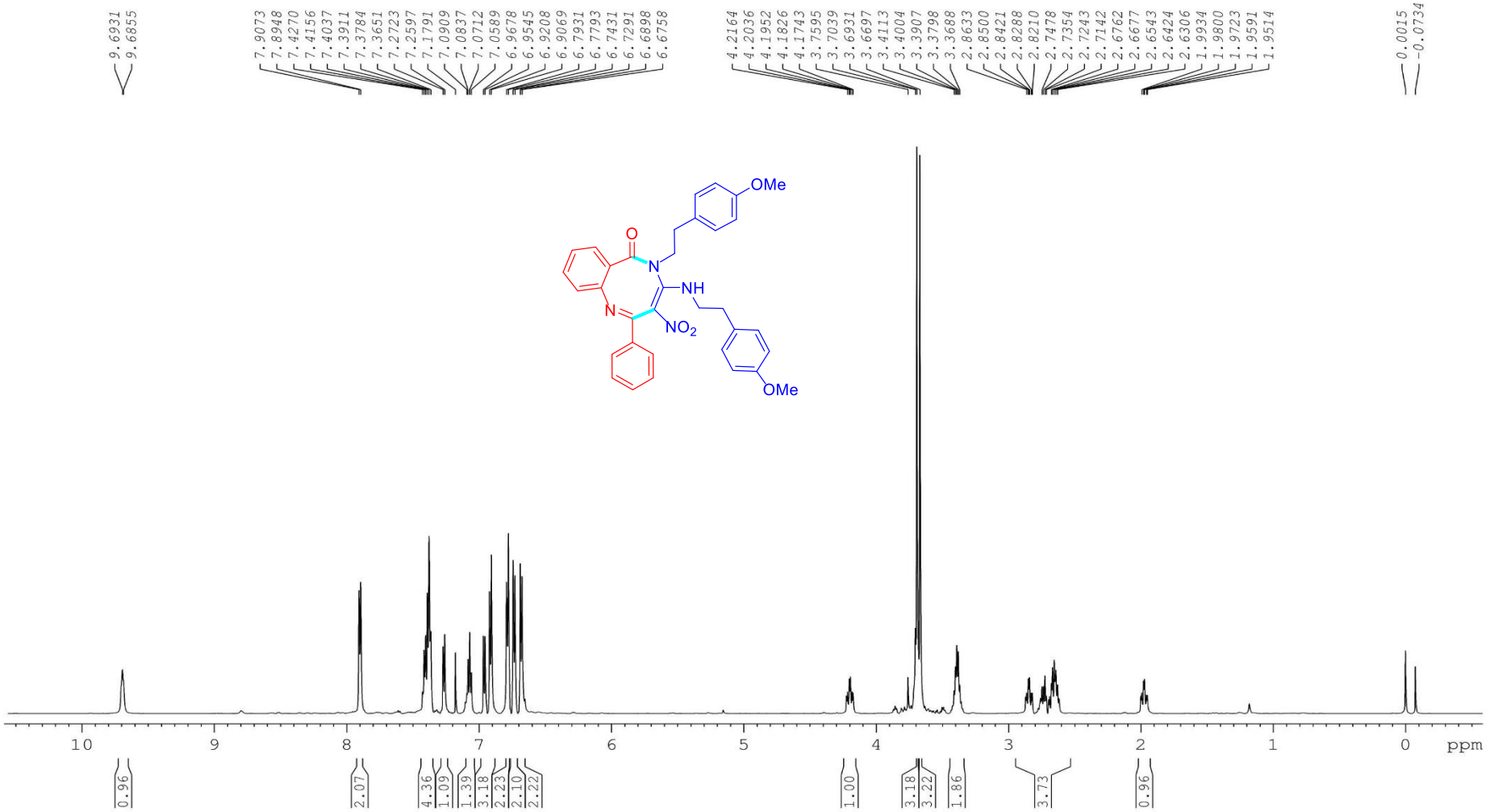

Figure S55. ^{1}H NMR (600 MHz, $CDCl_3$) spectra of compound **5k**

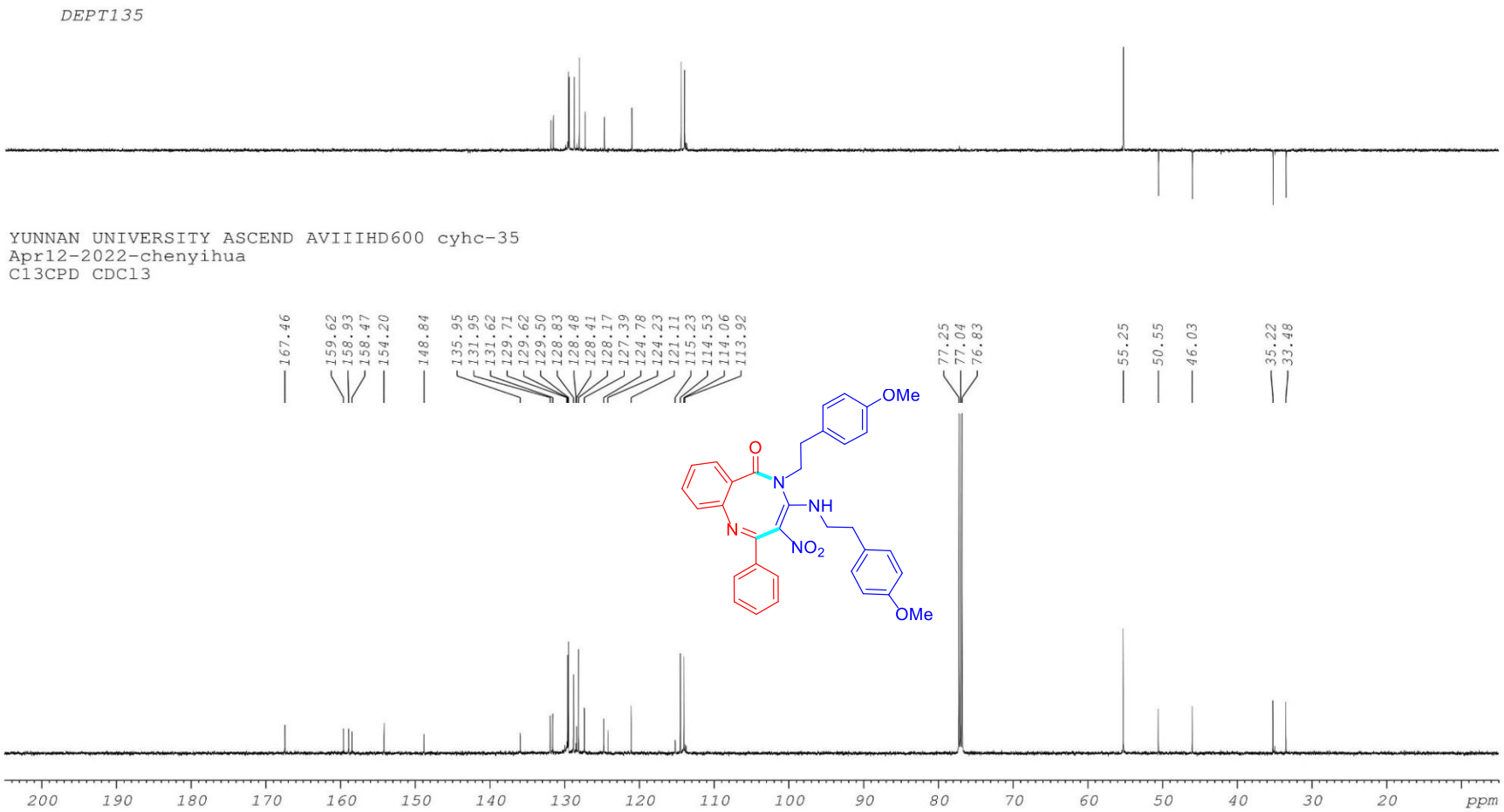

Figure S56. ^{13}C NMR (150 MHz, $CDCl_3$) spectra of compound **5k**

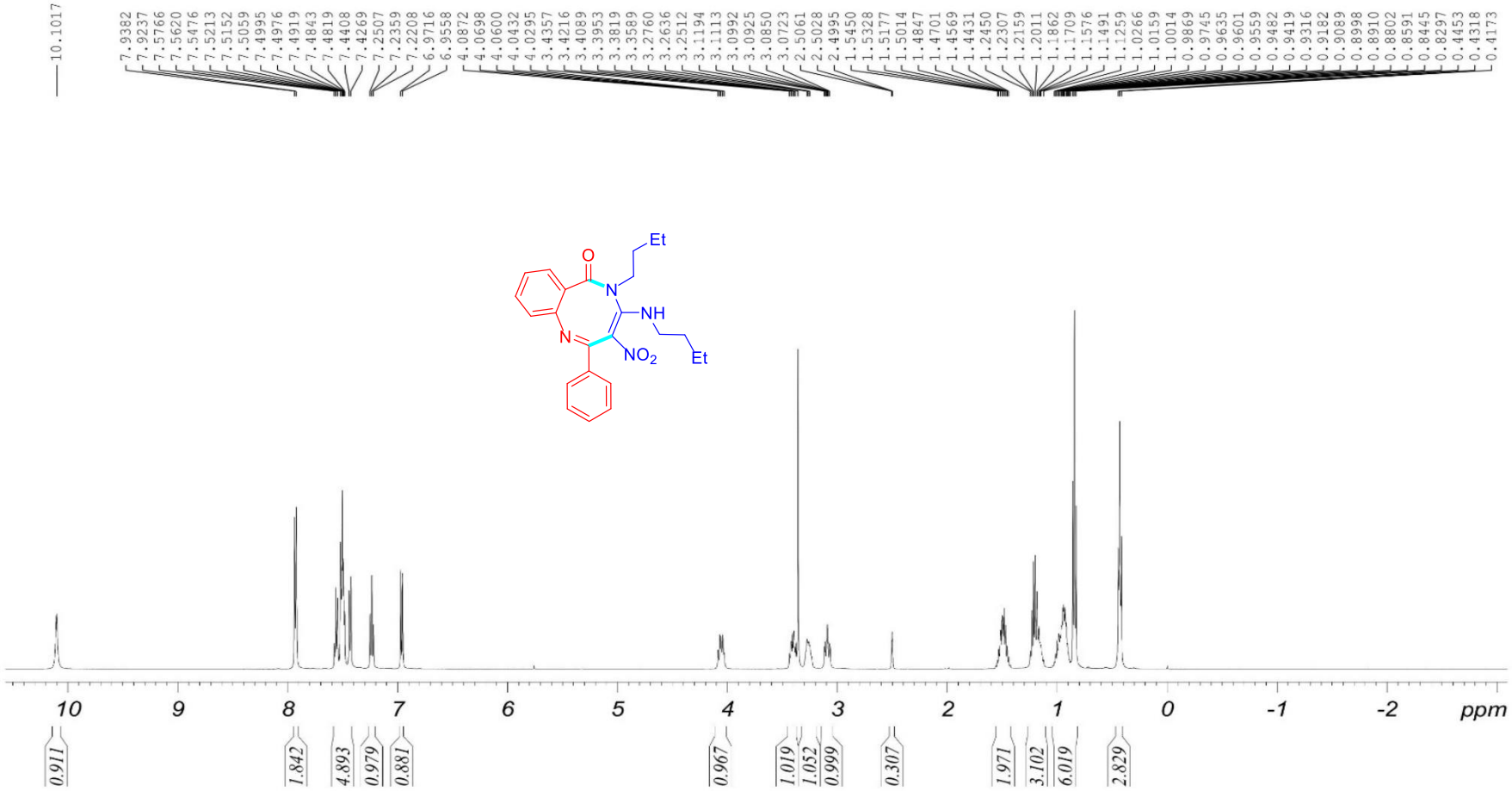

Figure S57. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5l**

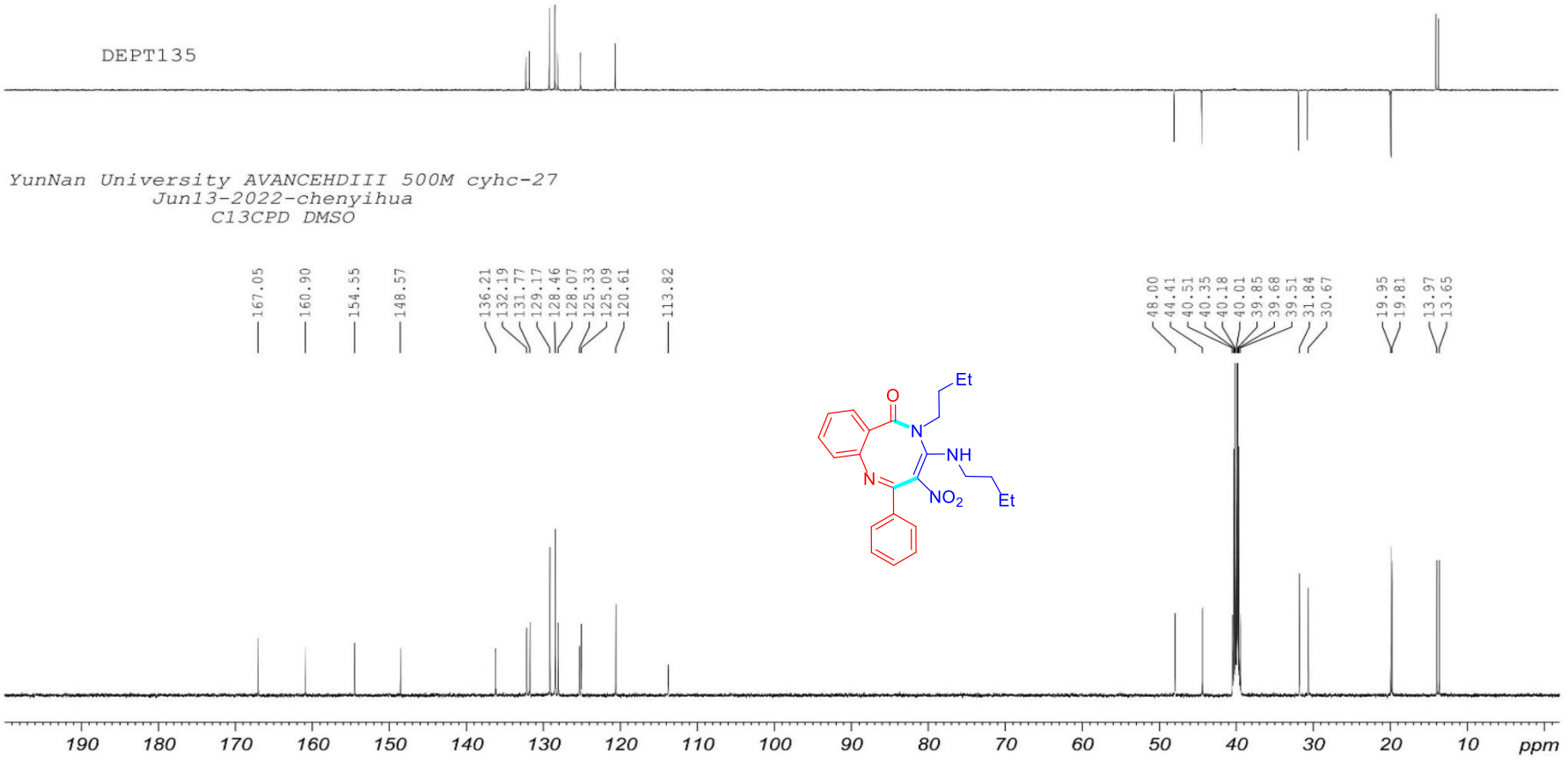

Figure S58. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5l**

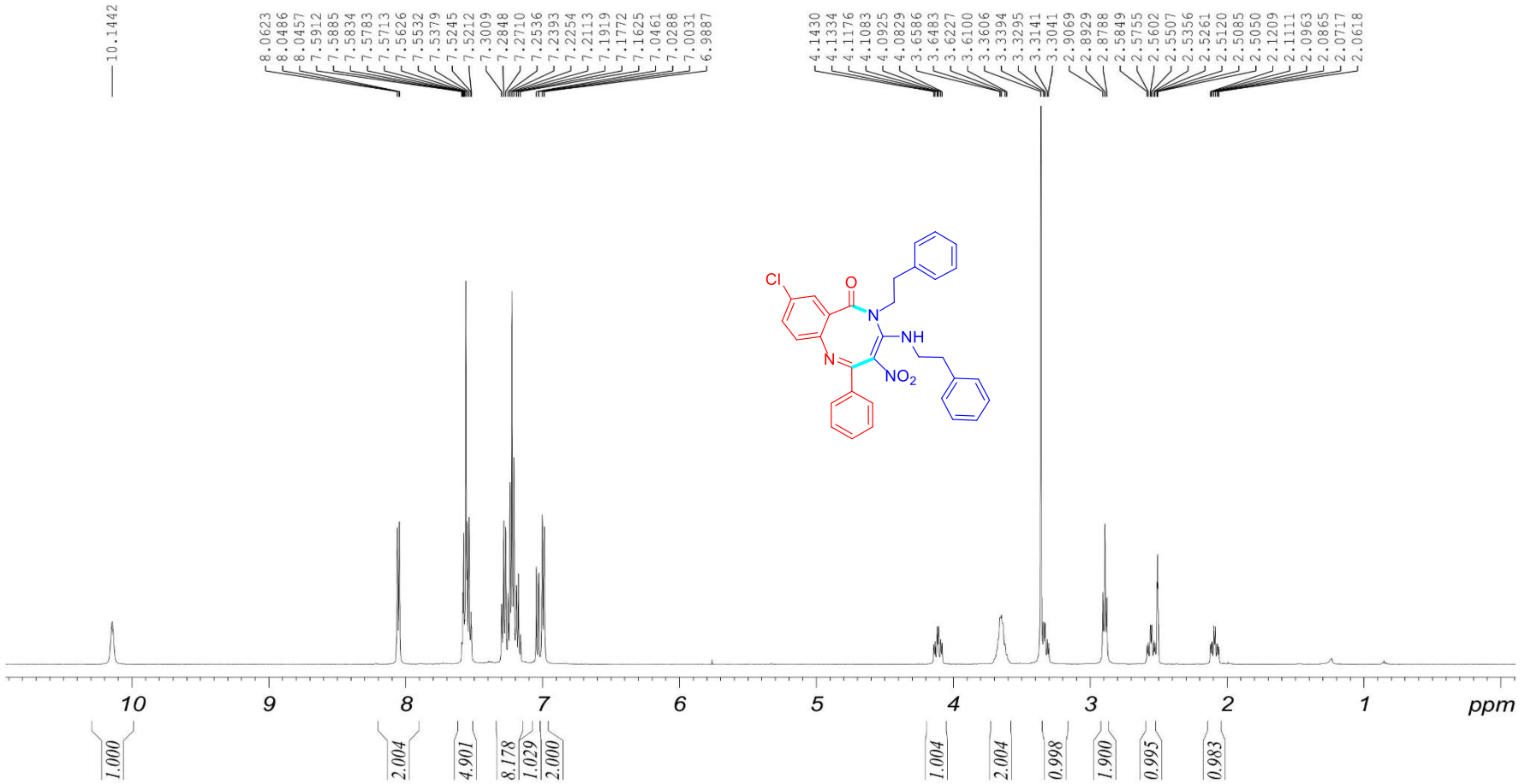

Figure S59. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5m**

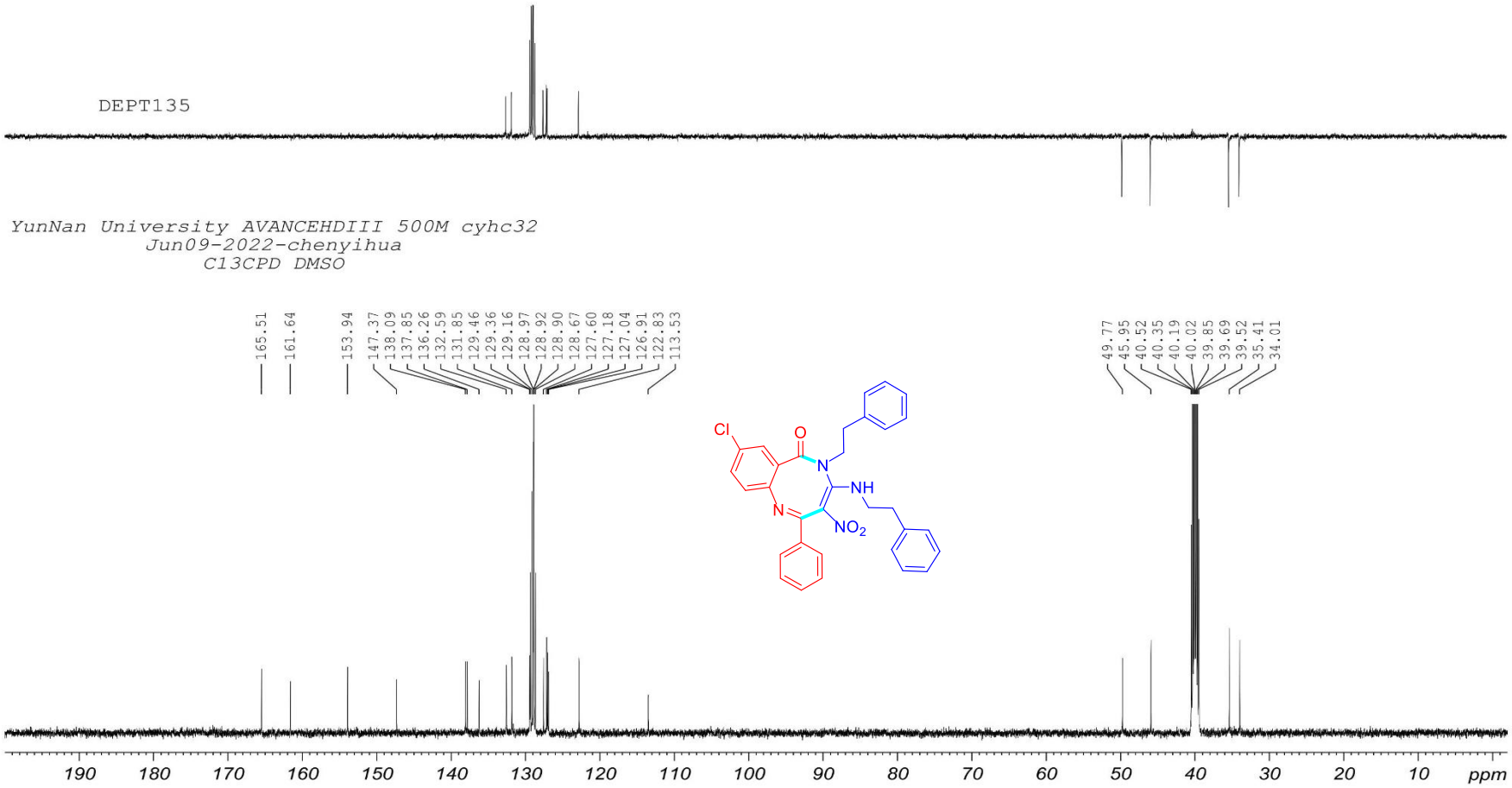

Figure S60. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5m**

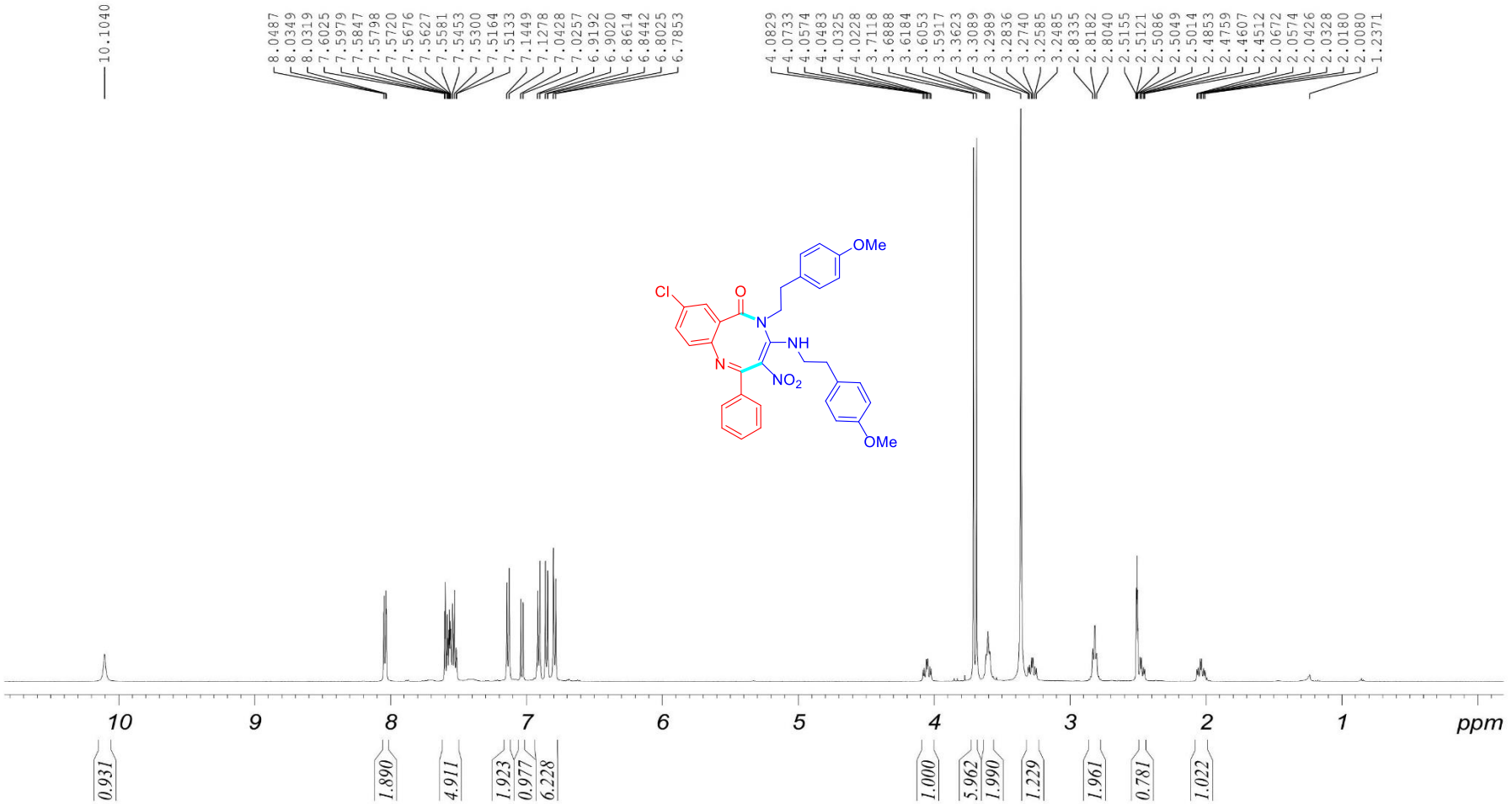

Figure S61. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5n**

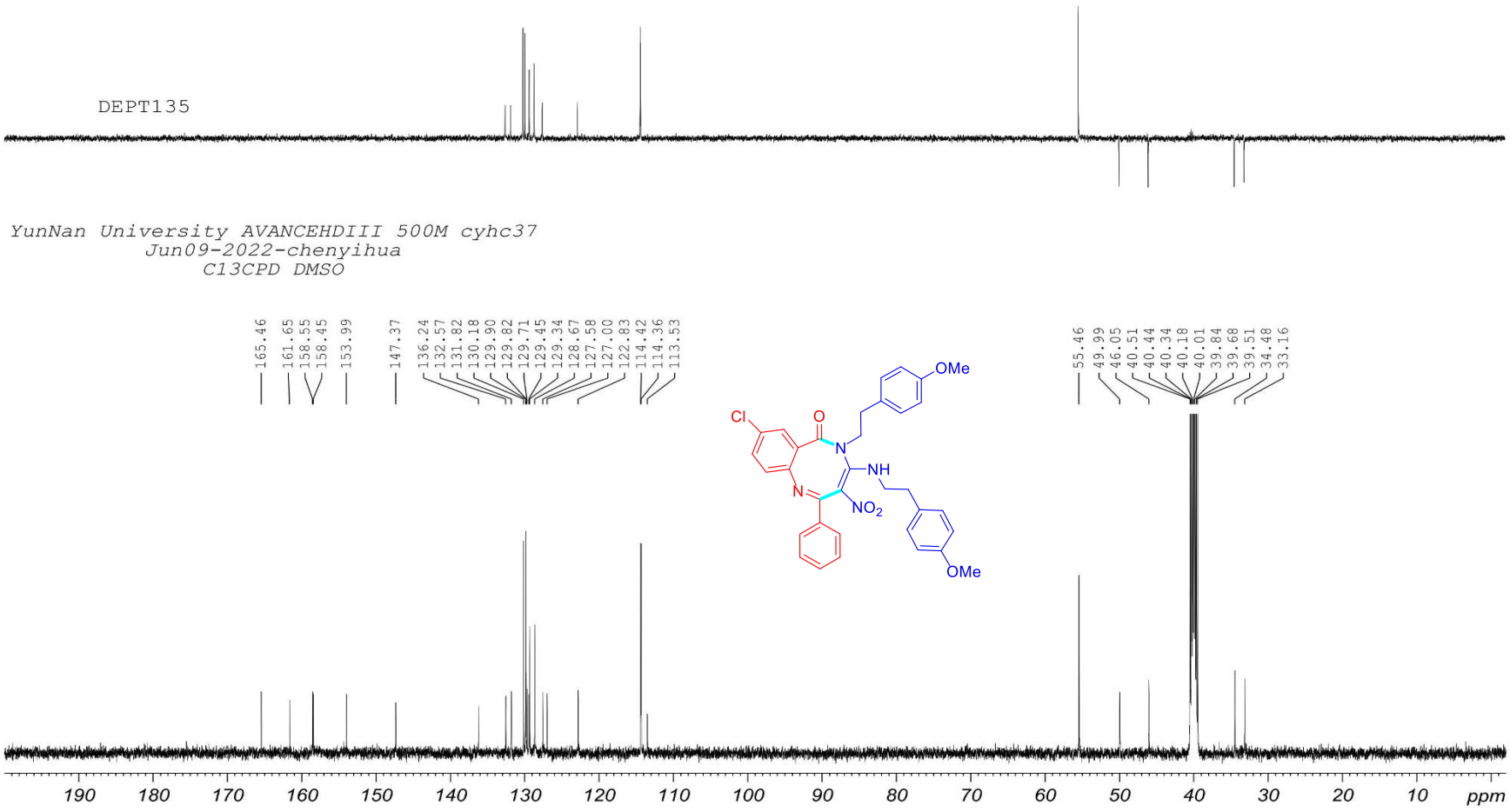

Figure S62. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5n**

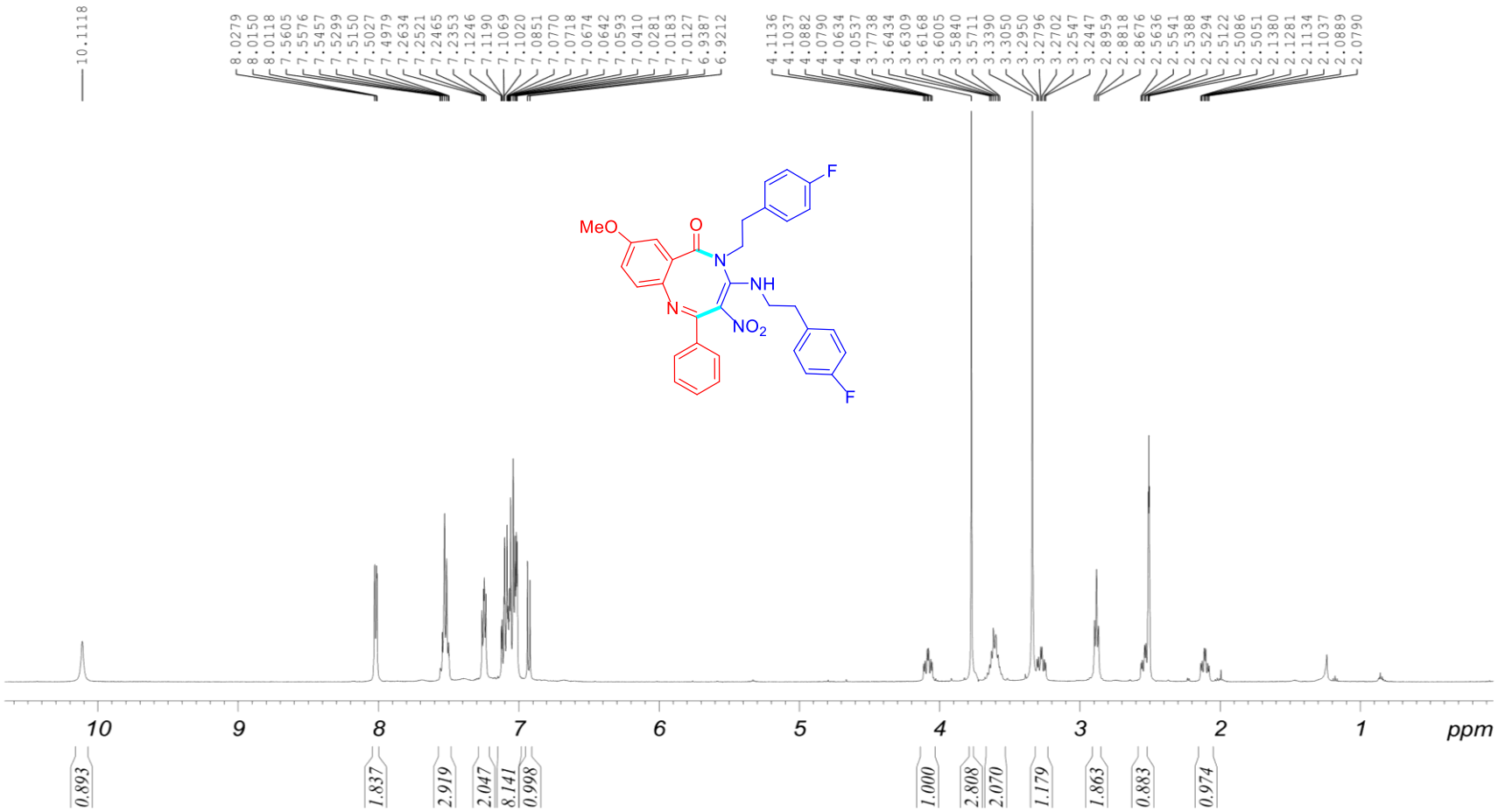

Figure S63. ^{1}H NMR (500 MHz, DMSO-d_6) spectra of compound **5o**

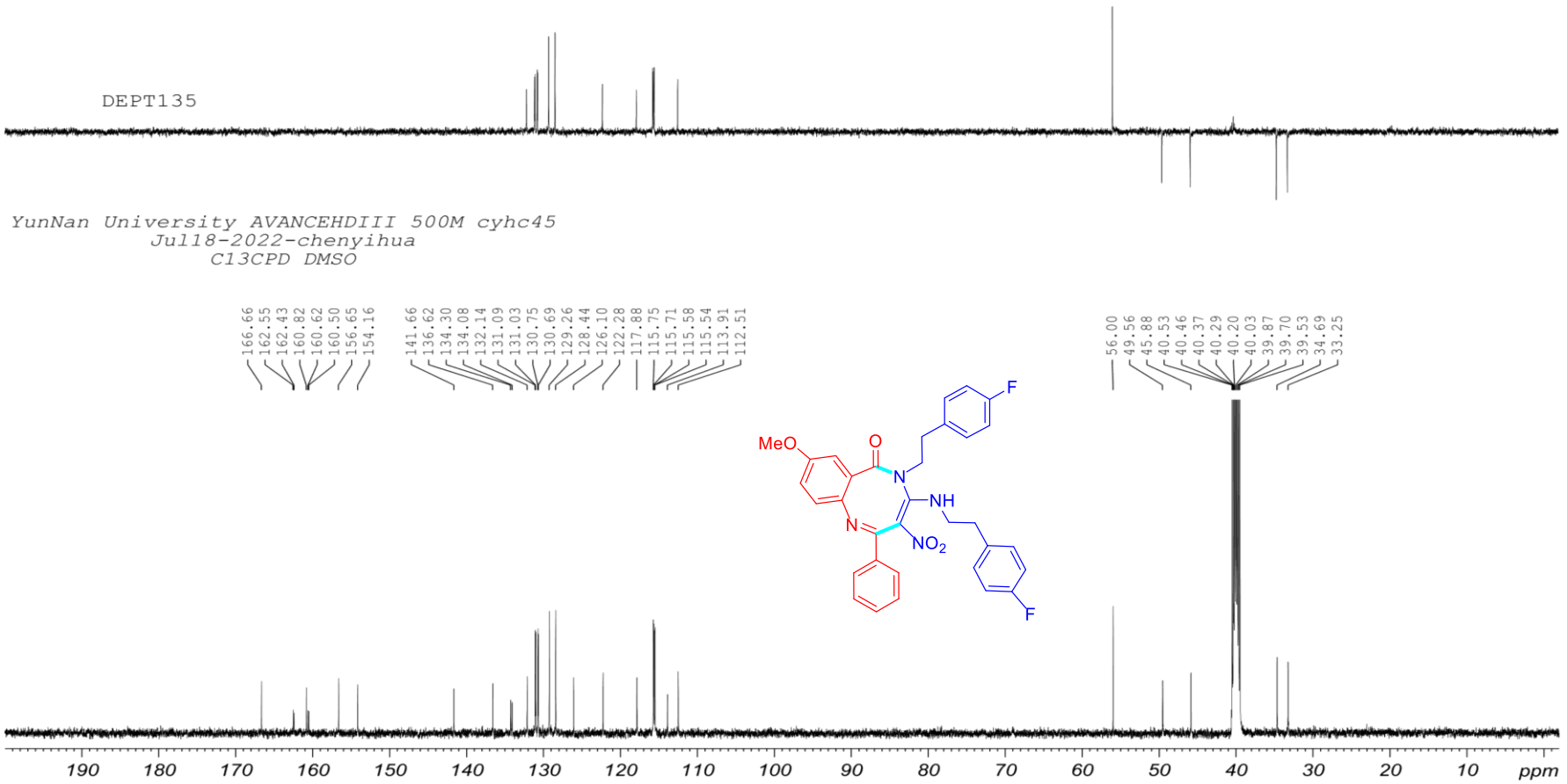

Figure S64. ^{13}C NMR (125 MHz, DMSO-d_6) spectra of compound **5o**

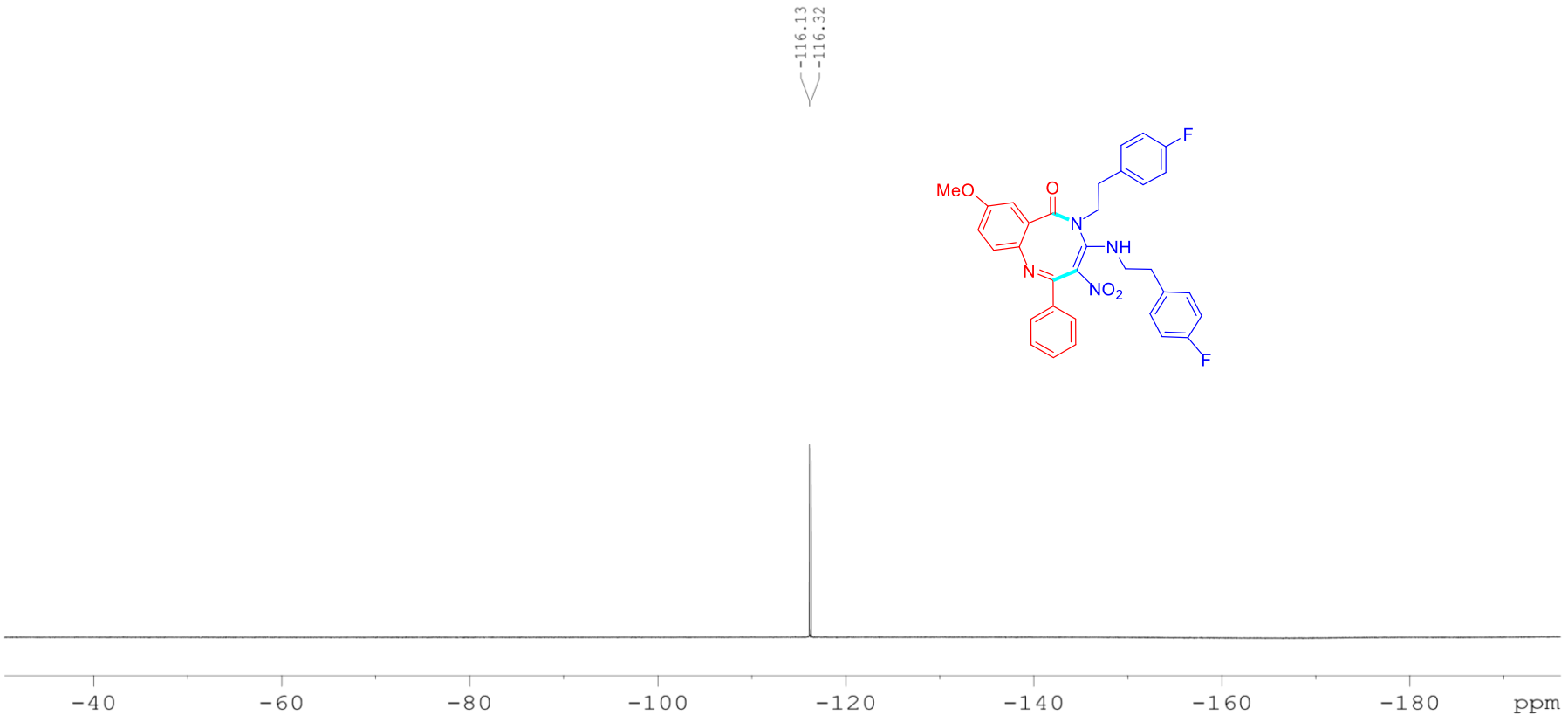

Figure S65. ^{19}F NMR (470 MHz, DMSO-d_6) spectra of compound **5o**

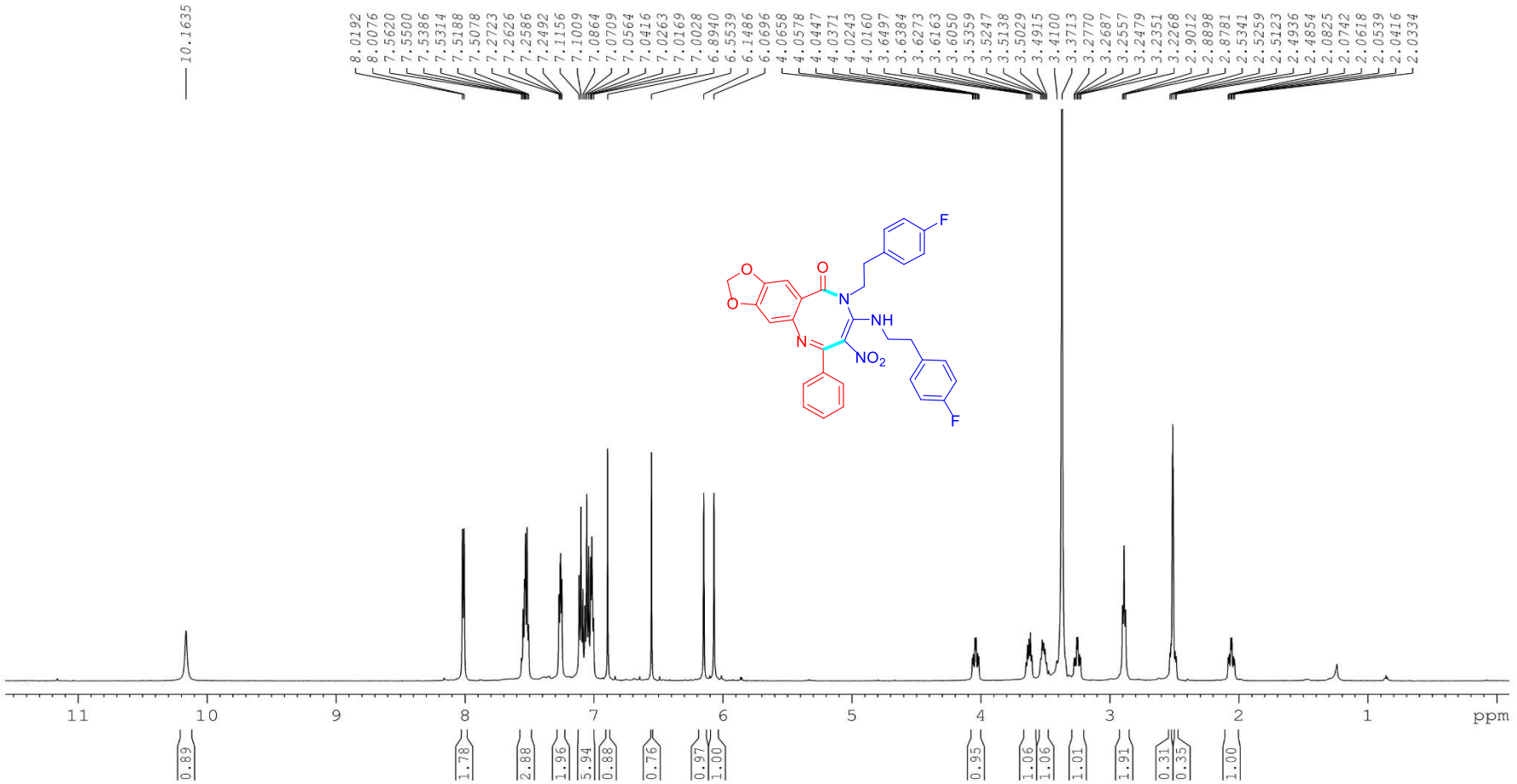

Figure S66. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5p**

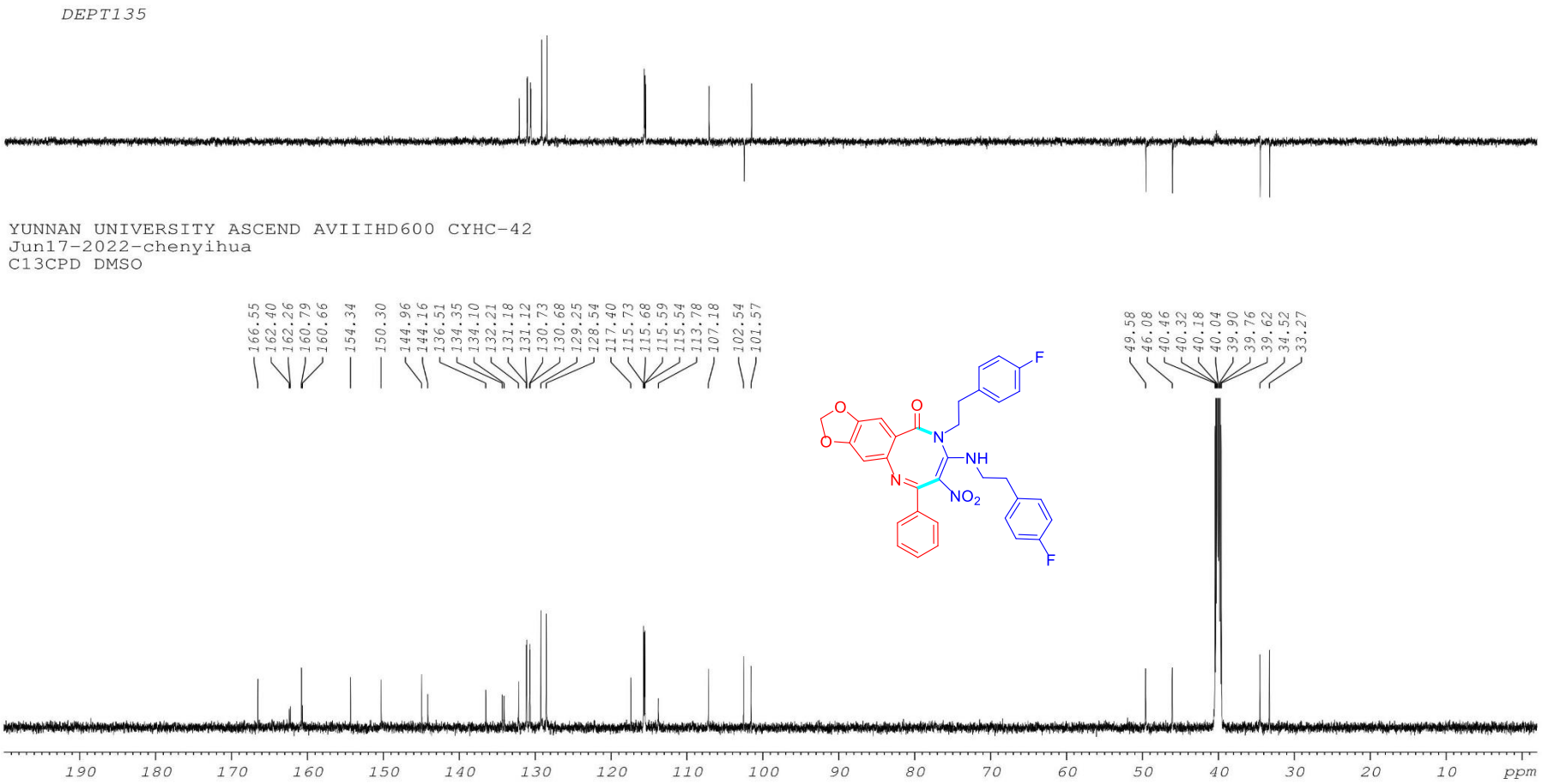

Figure S67. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5p**

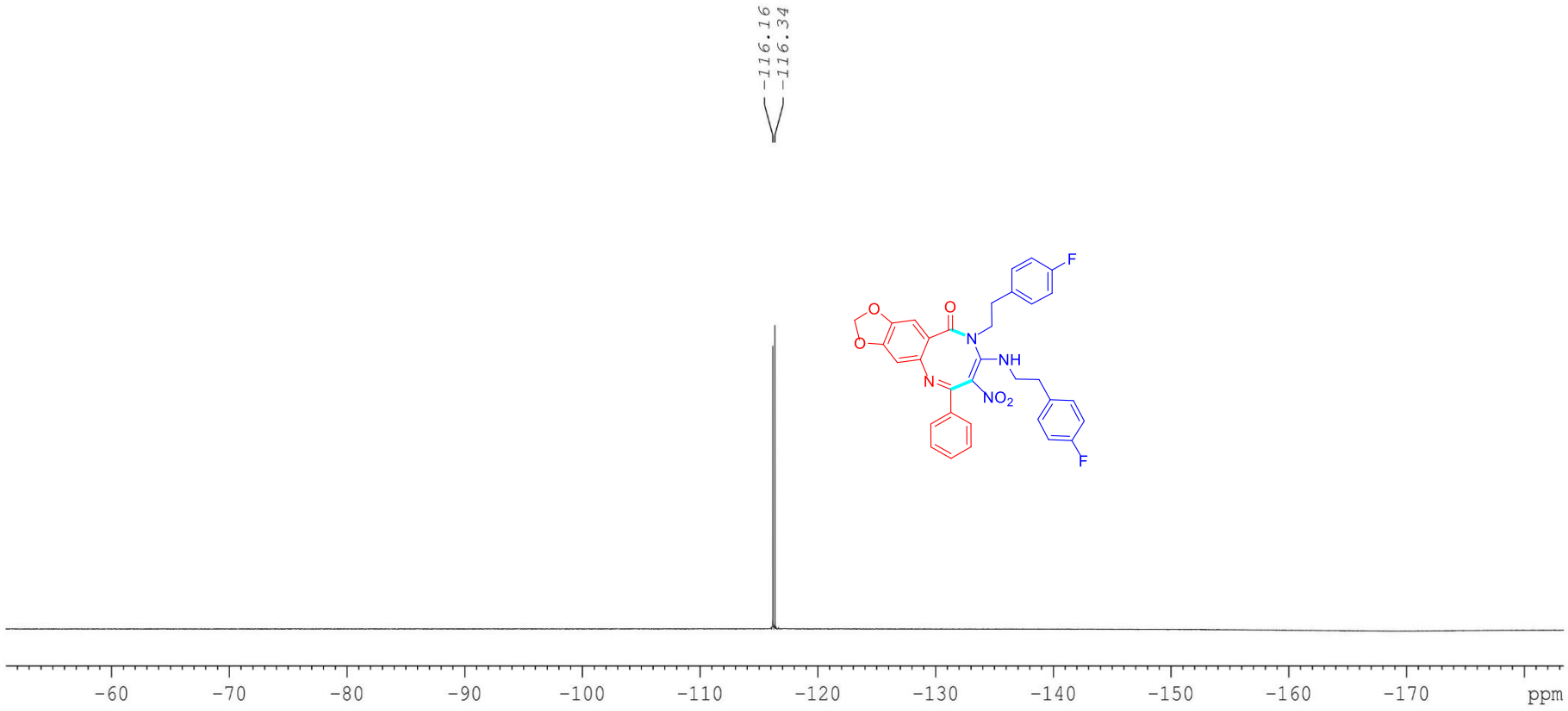

Figure S68. ^{19}F NMR (564 MHz, DMSO-d_6) spectra of compound **5p**

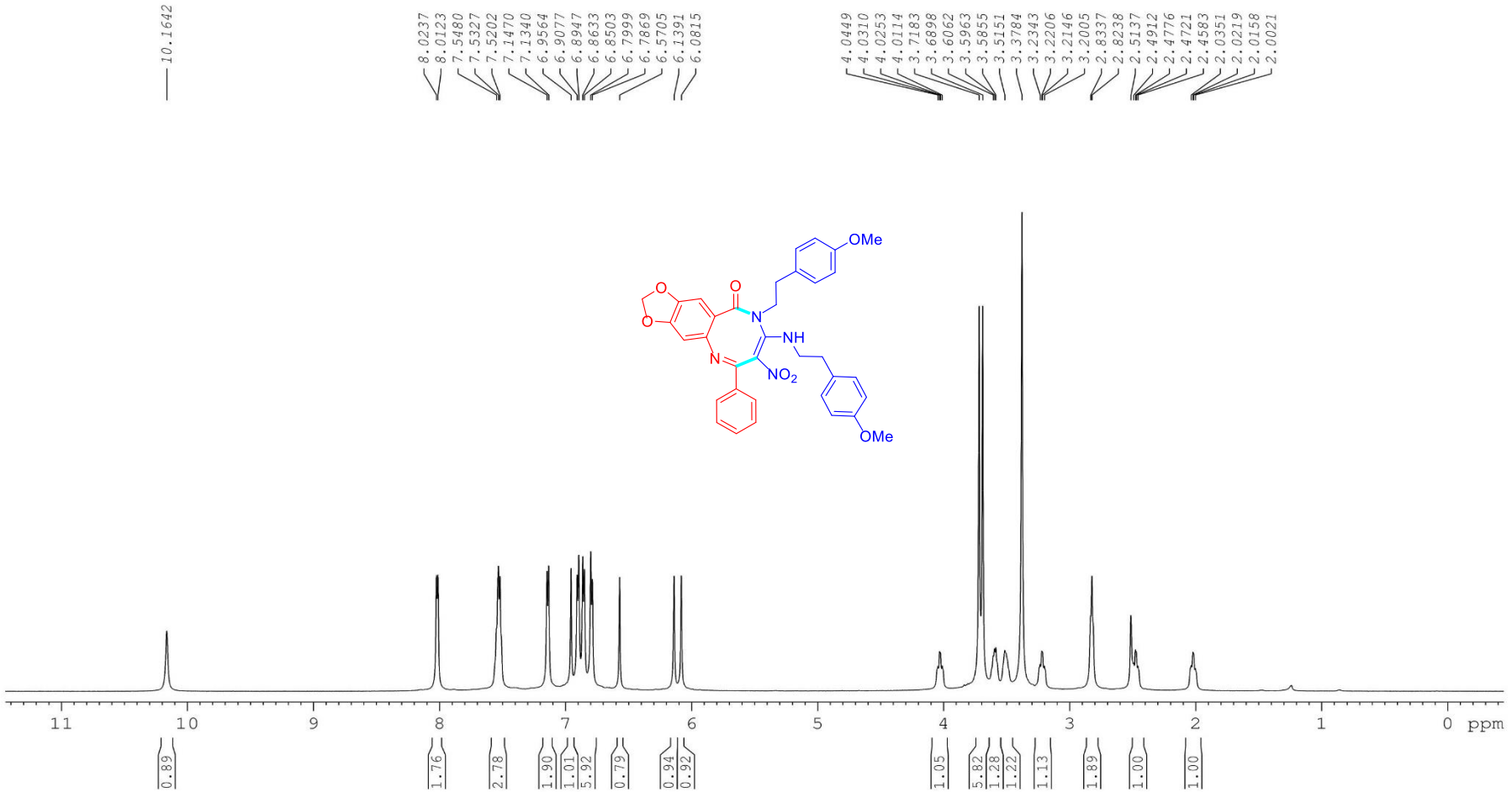

Figure S69. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5q**

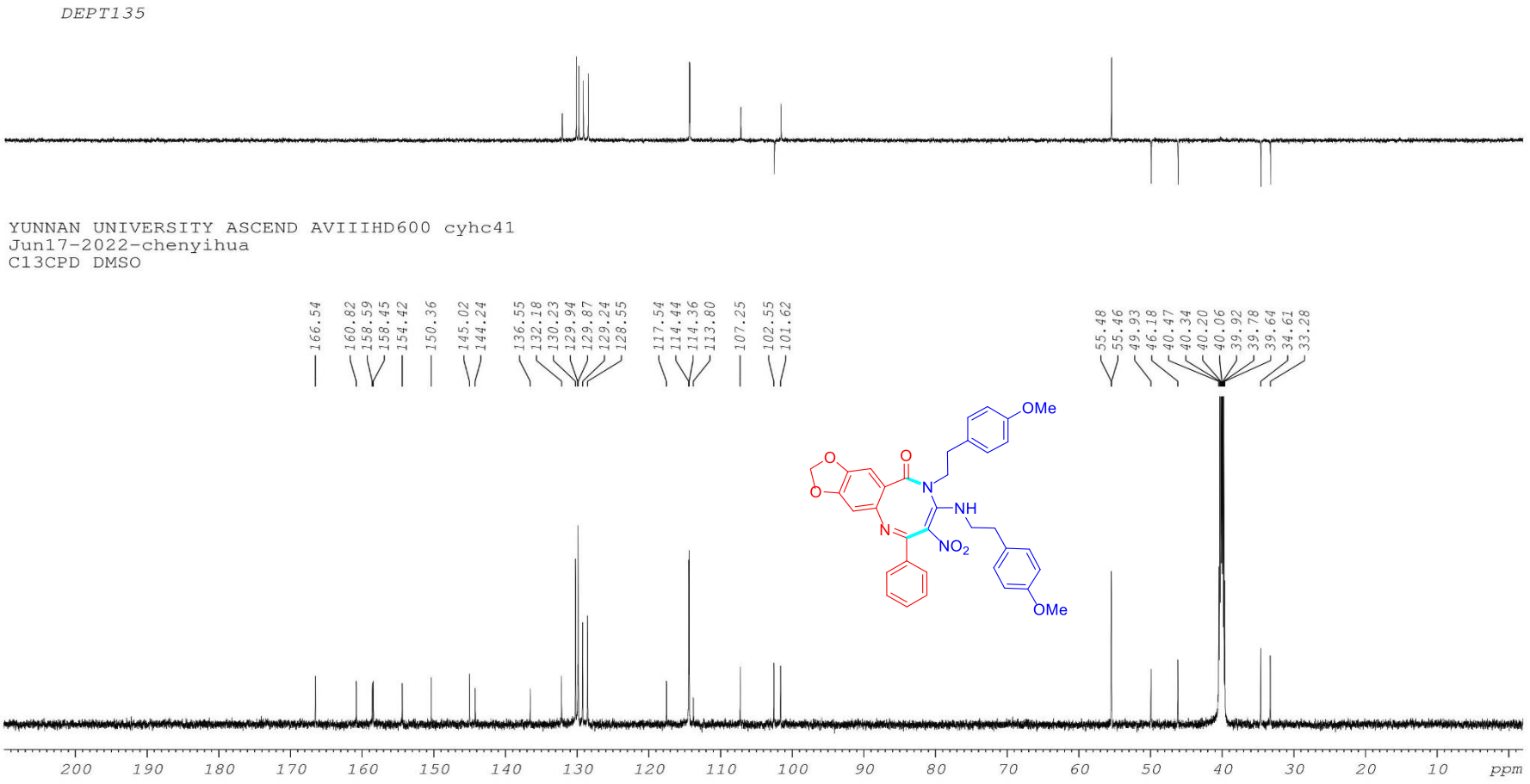

Figure S70. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5q**

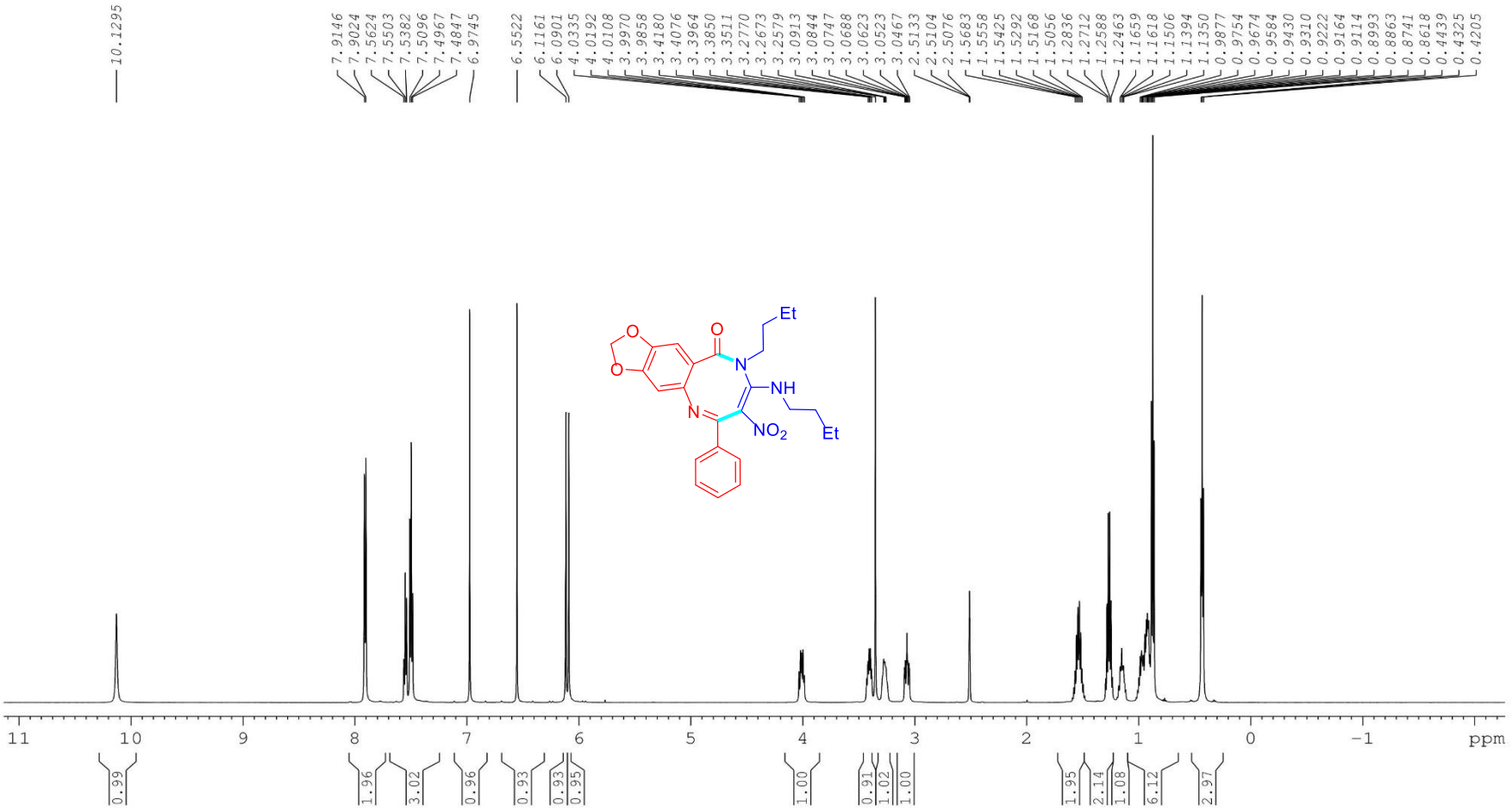

Figure S71. ^{1}H NMR (600 MHz, DMSO-d_6) spectra of compound **5r**

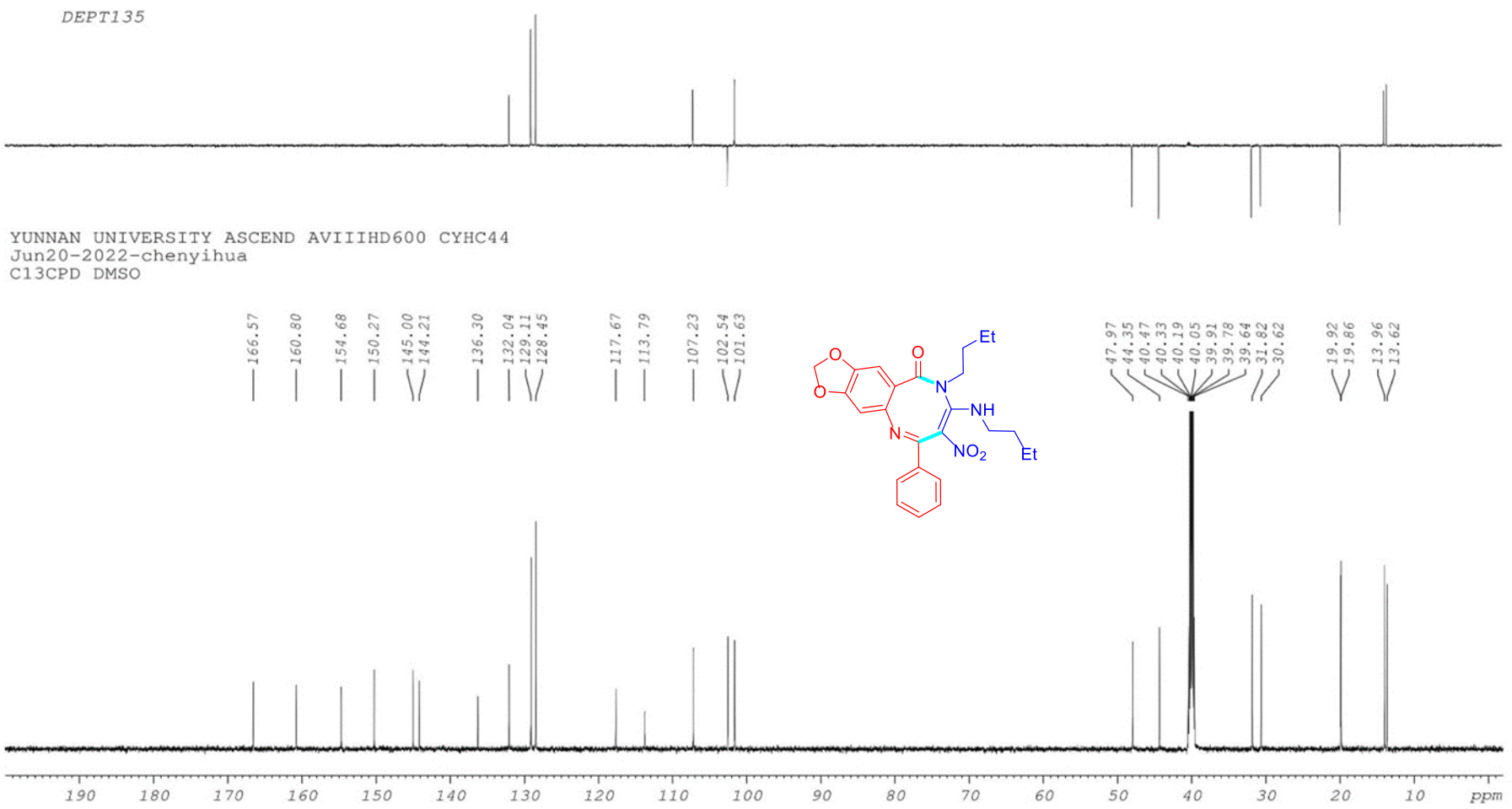

Figure S72. ^{13}C NMR (150 MHz, DMSO-d_6) spectra of compound **5r**

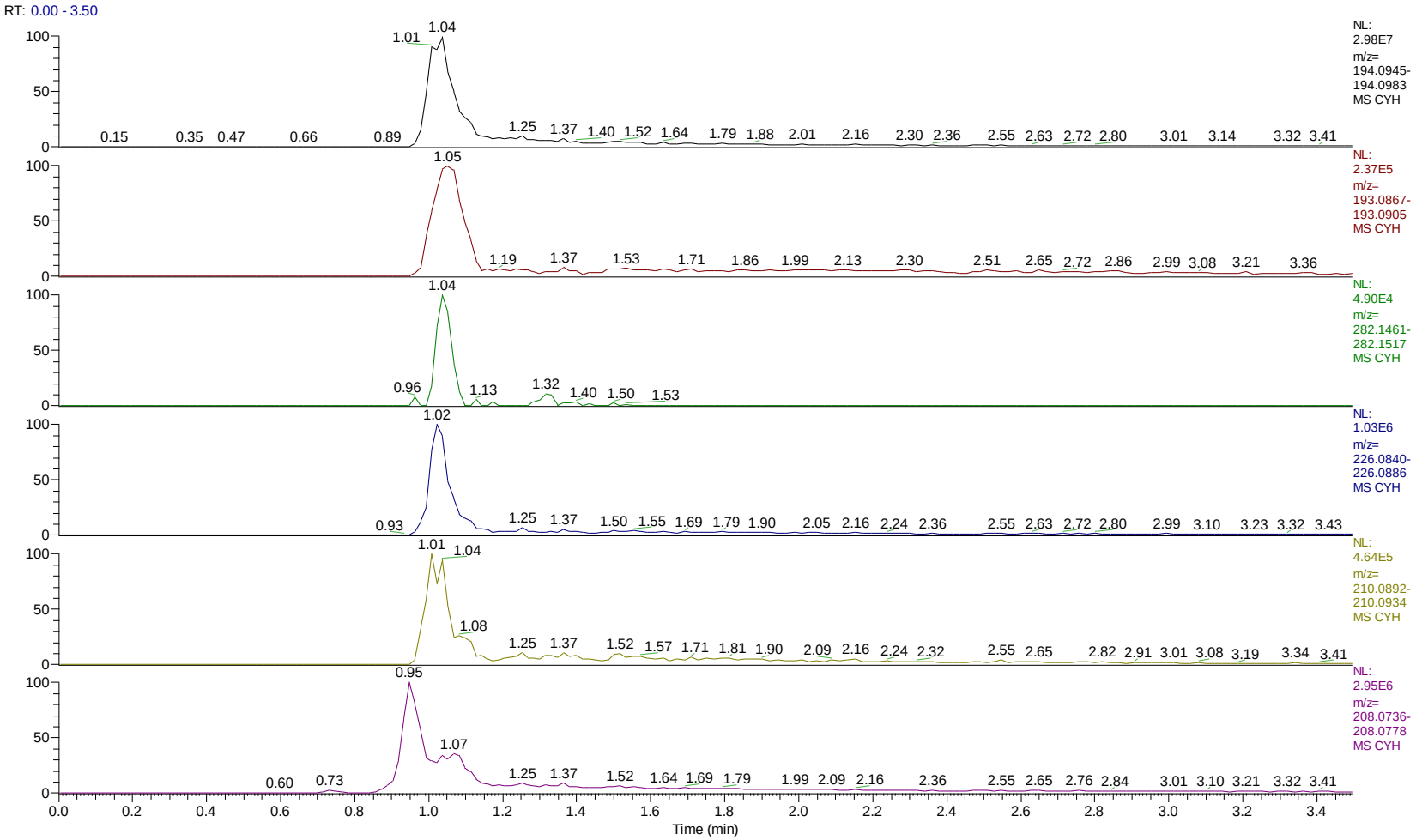

Figure S73. HPLC of the reaction mixture

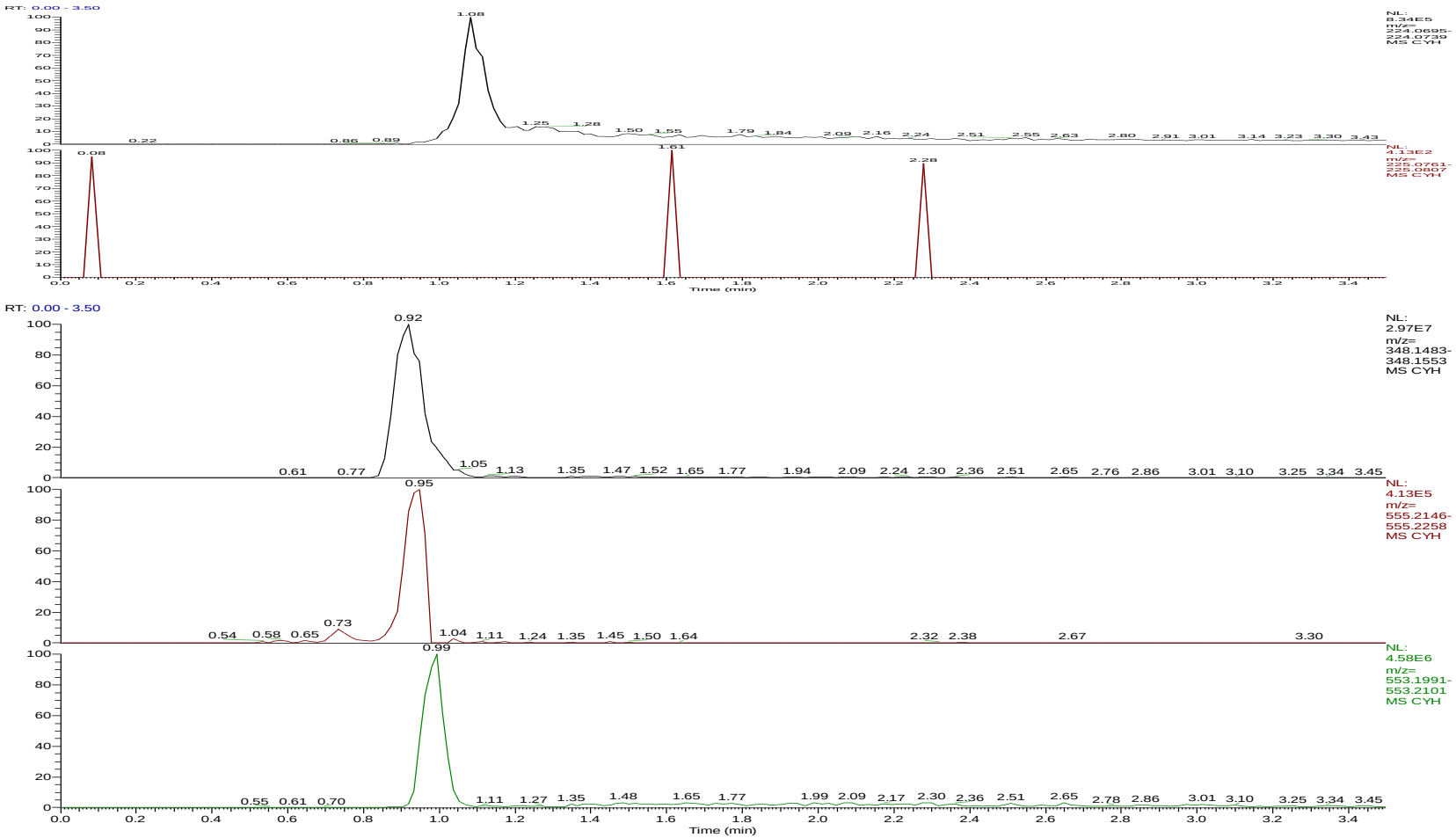

Figure S74. HPLC of the reaction mixture

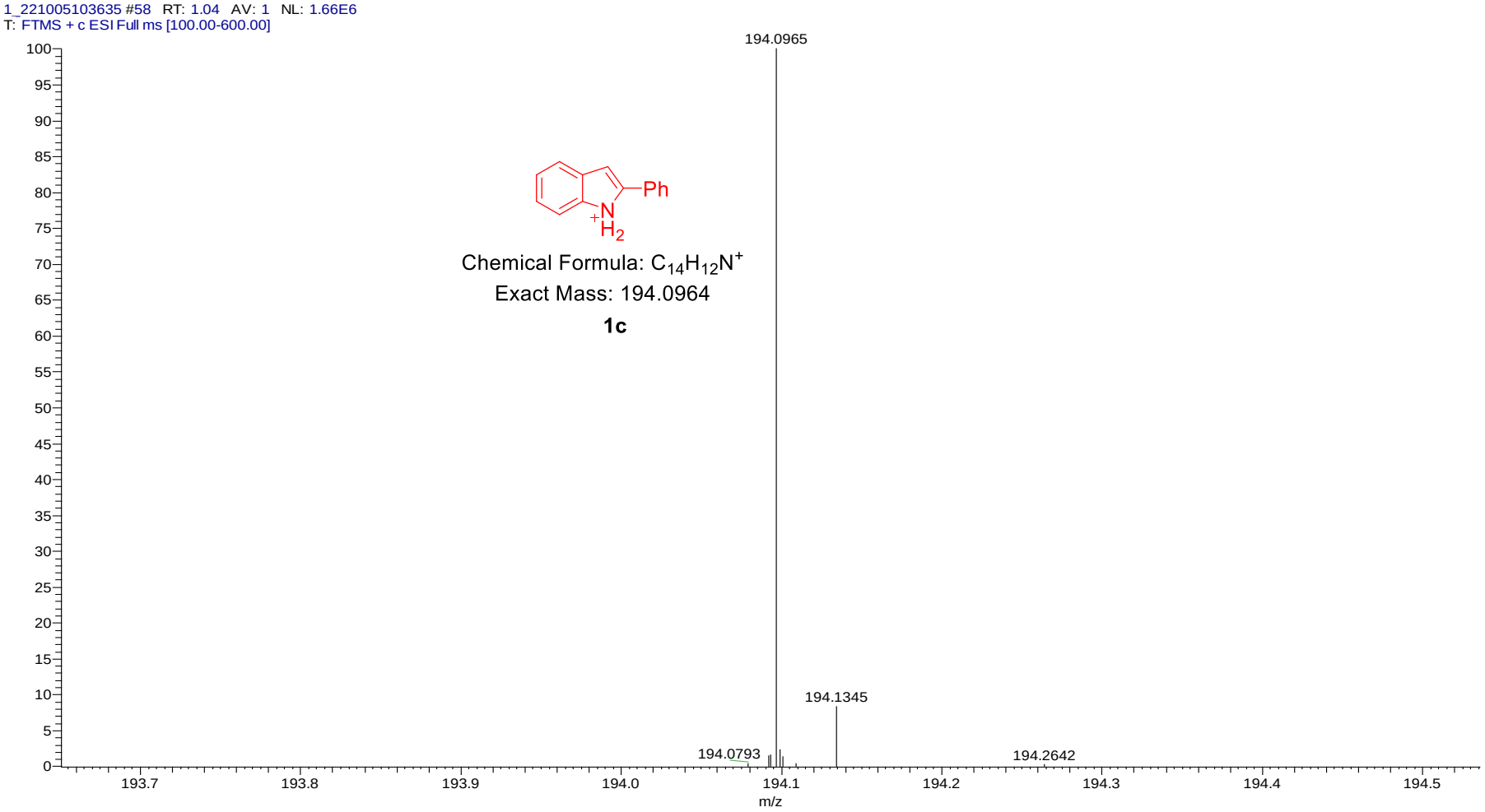

Figure S75. HRMS of intermediate **1c**

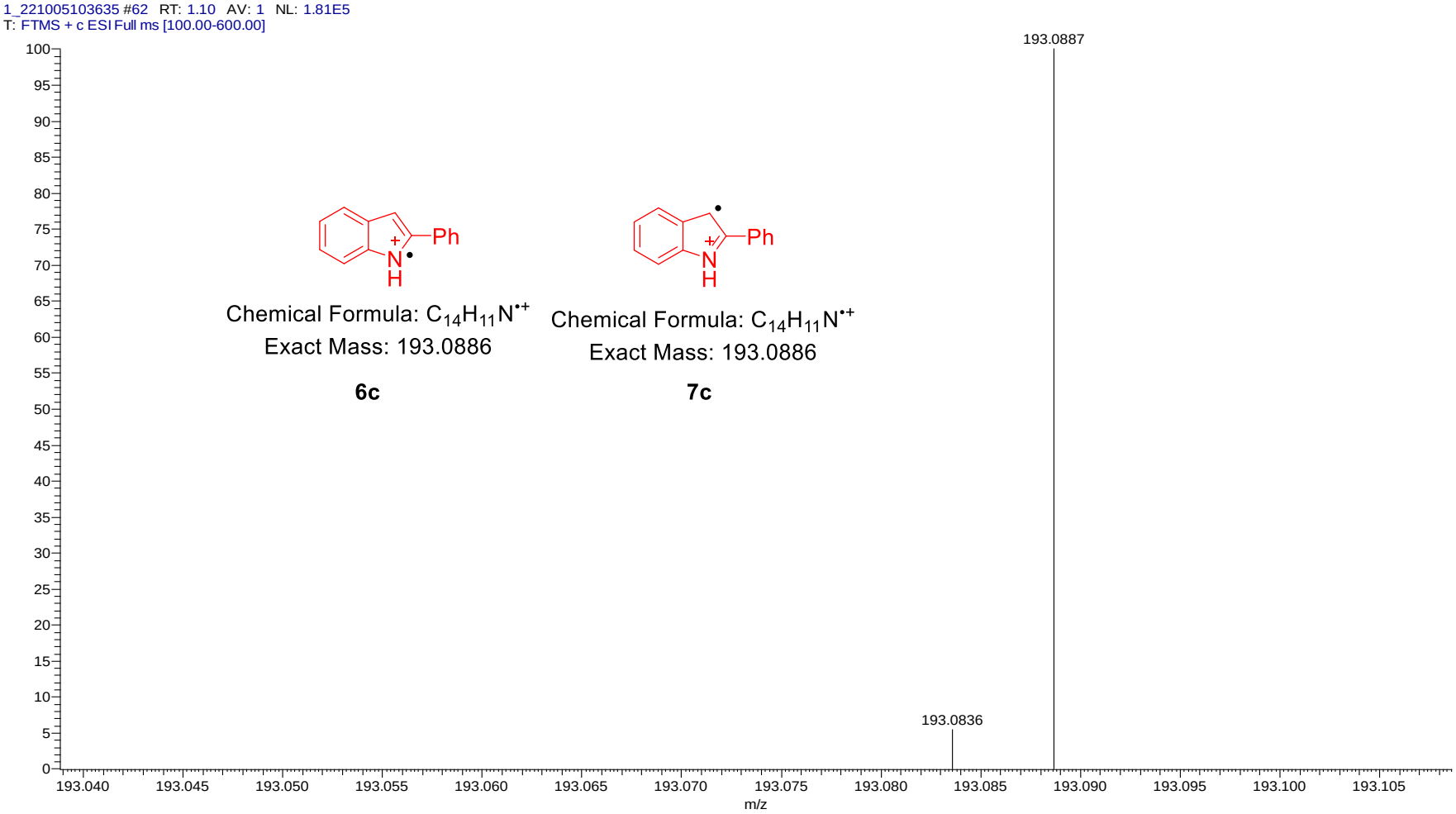

Figure S76. HRMS of intermediate **6c/7c**

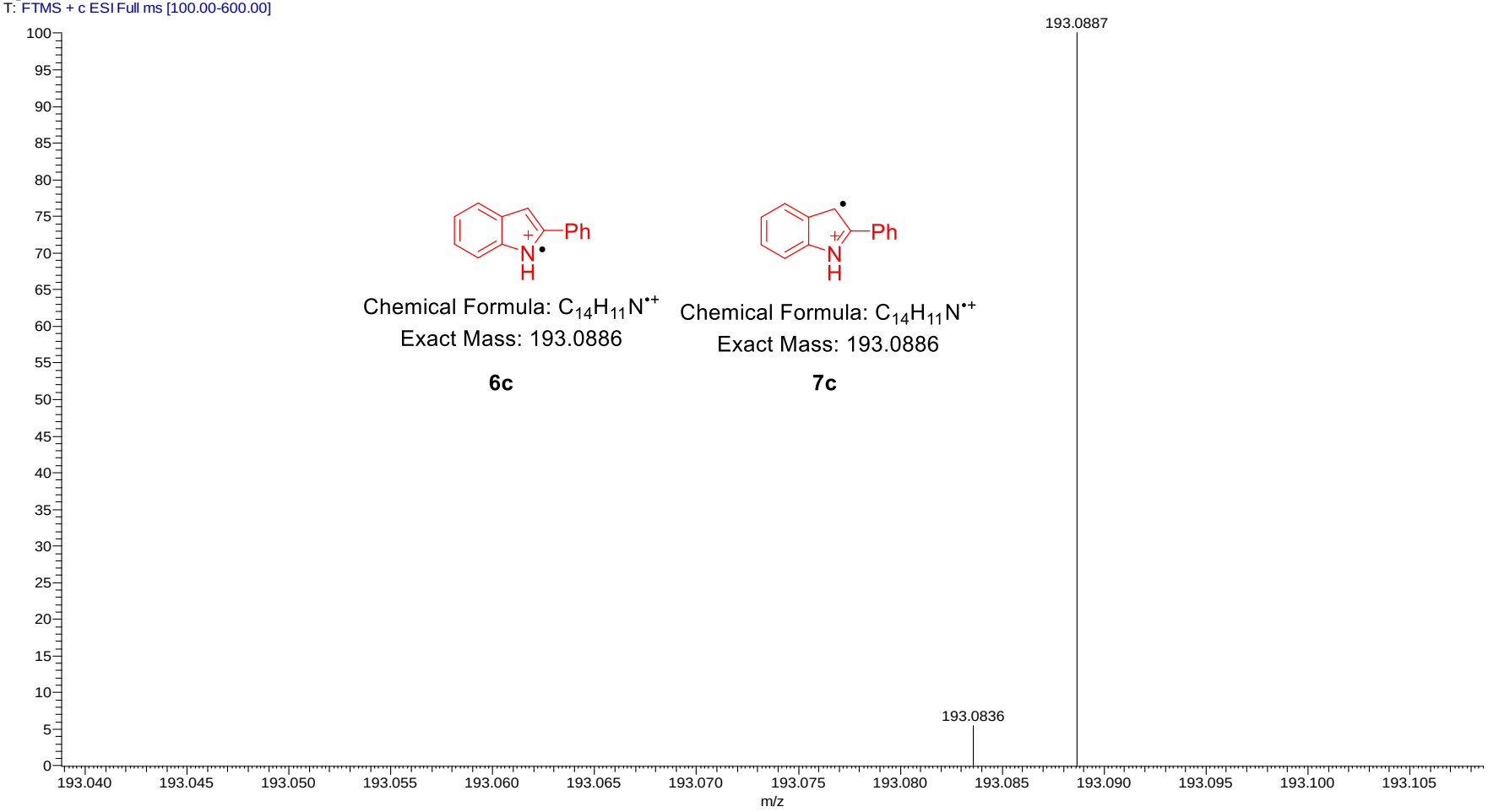

Figure S77. HRMS of intermediate **6c/7c**

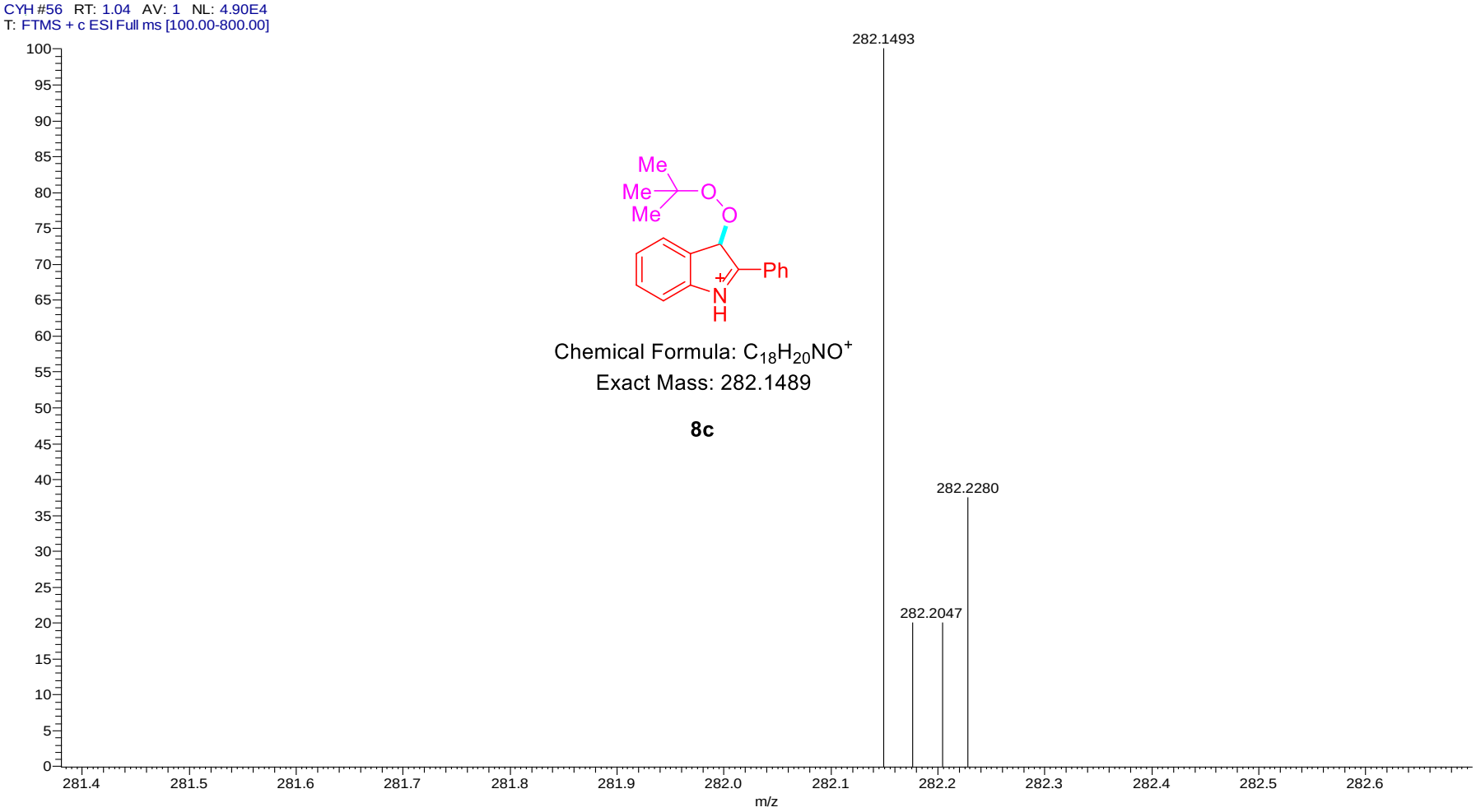

Figure S78. HRMS of intermediate **8c**

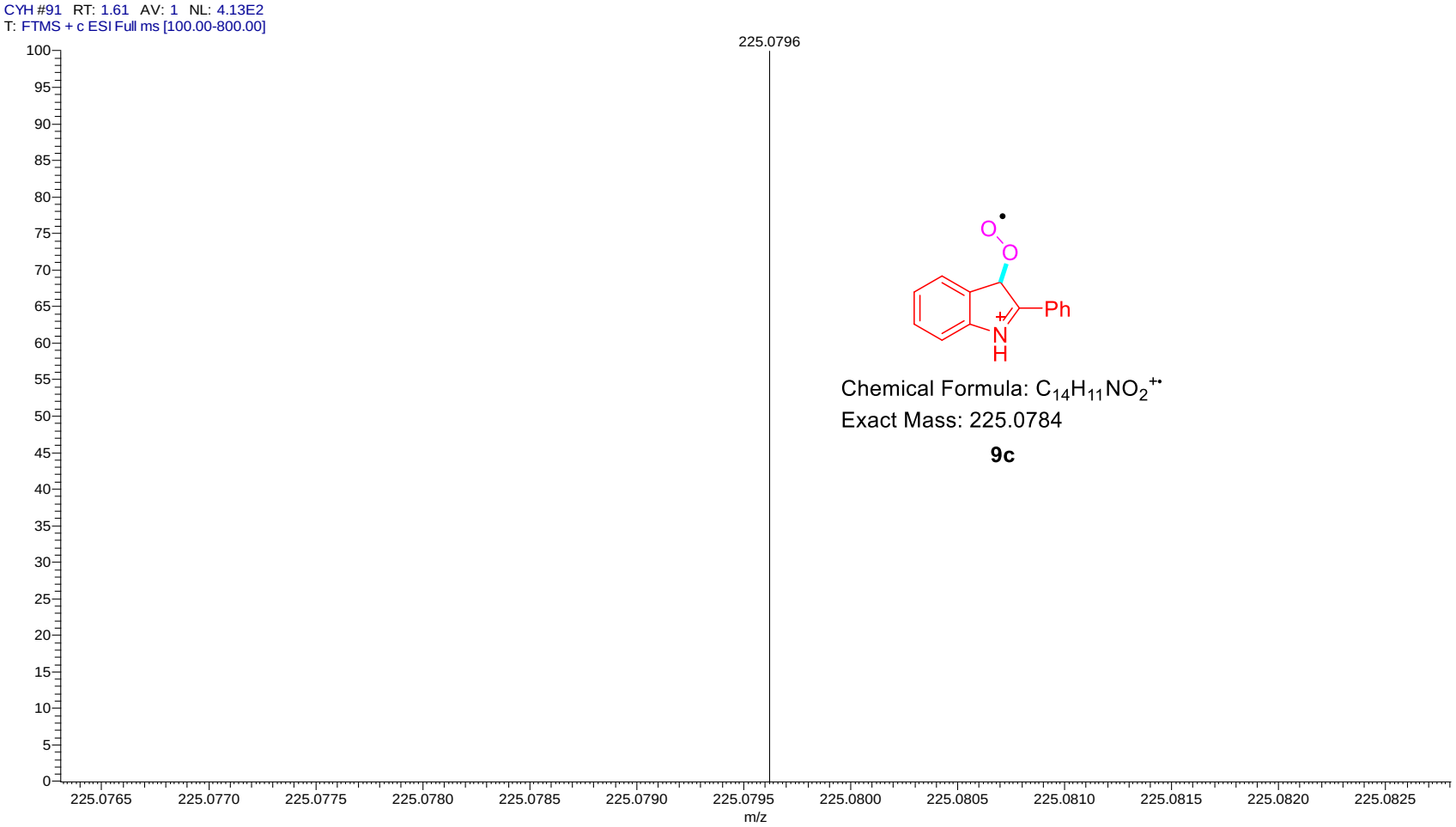

Figure S79. HRMS of intermediate **9c**

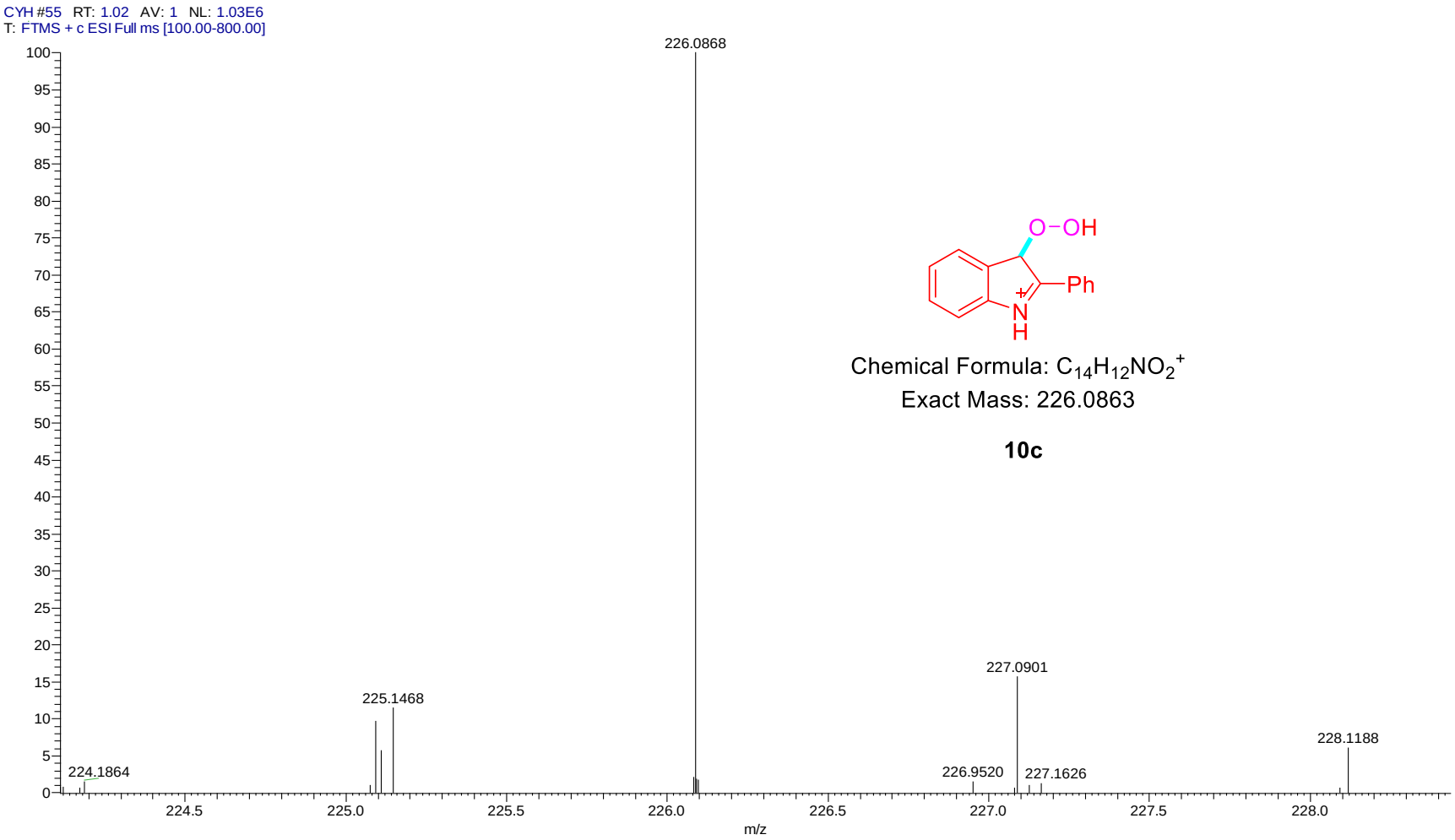

Figure S80. HRMS of intermediate **10c**

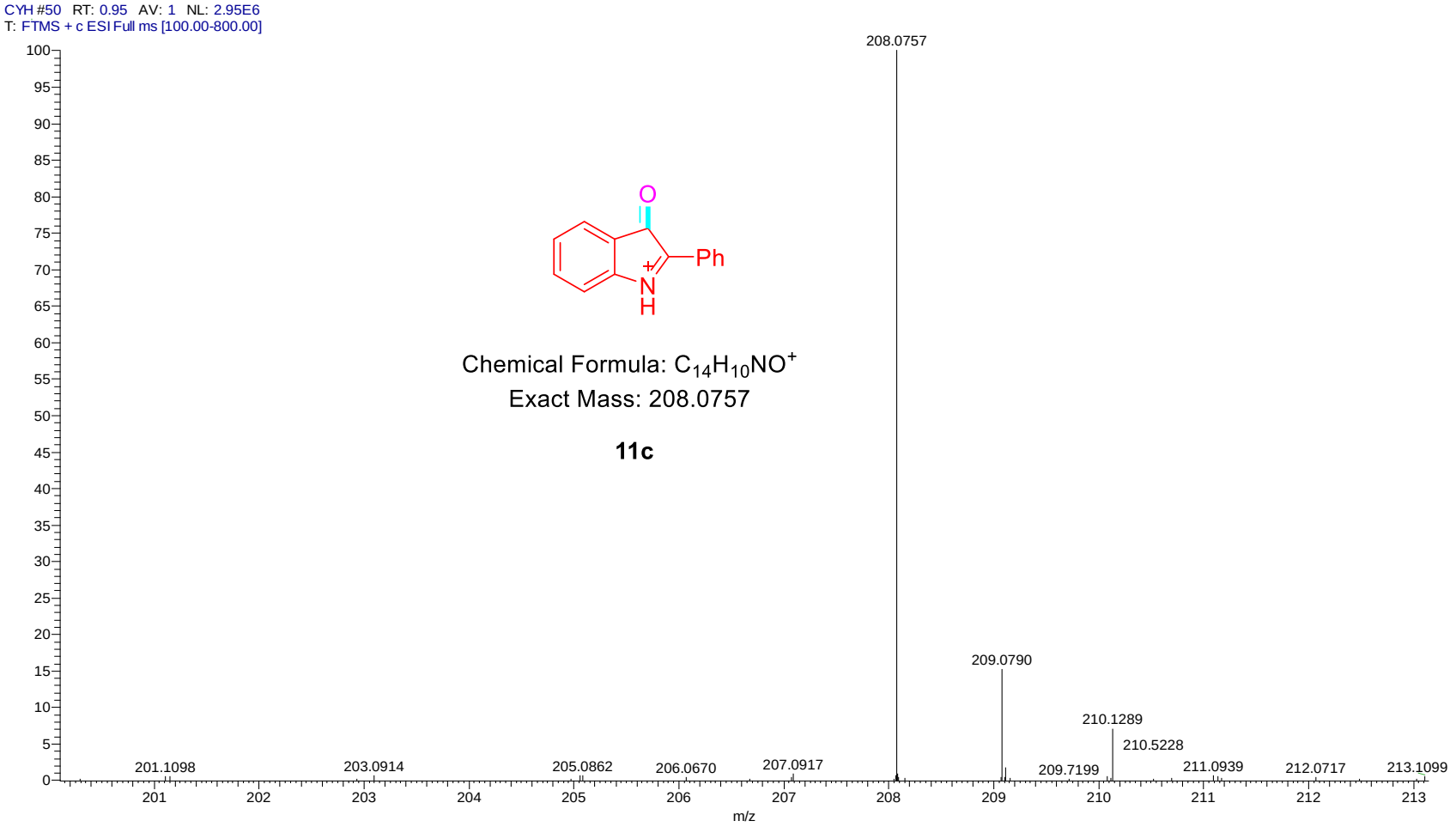

Figure S81. HRMS of intermediate **11c**

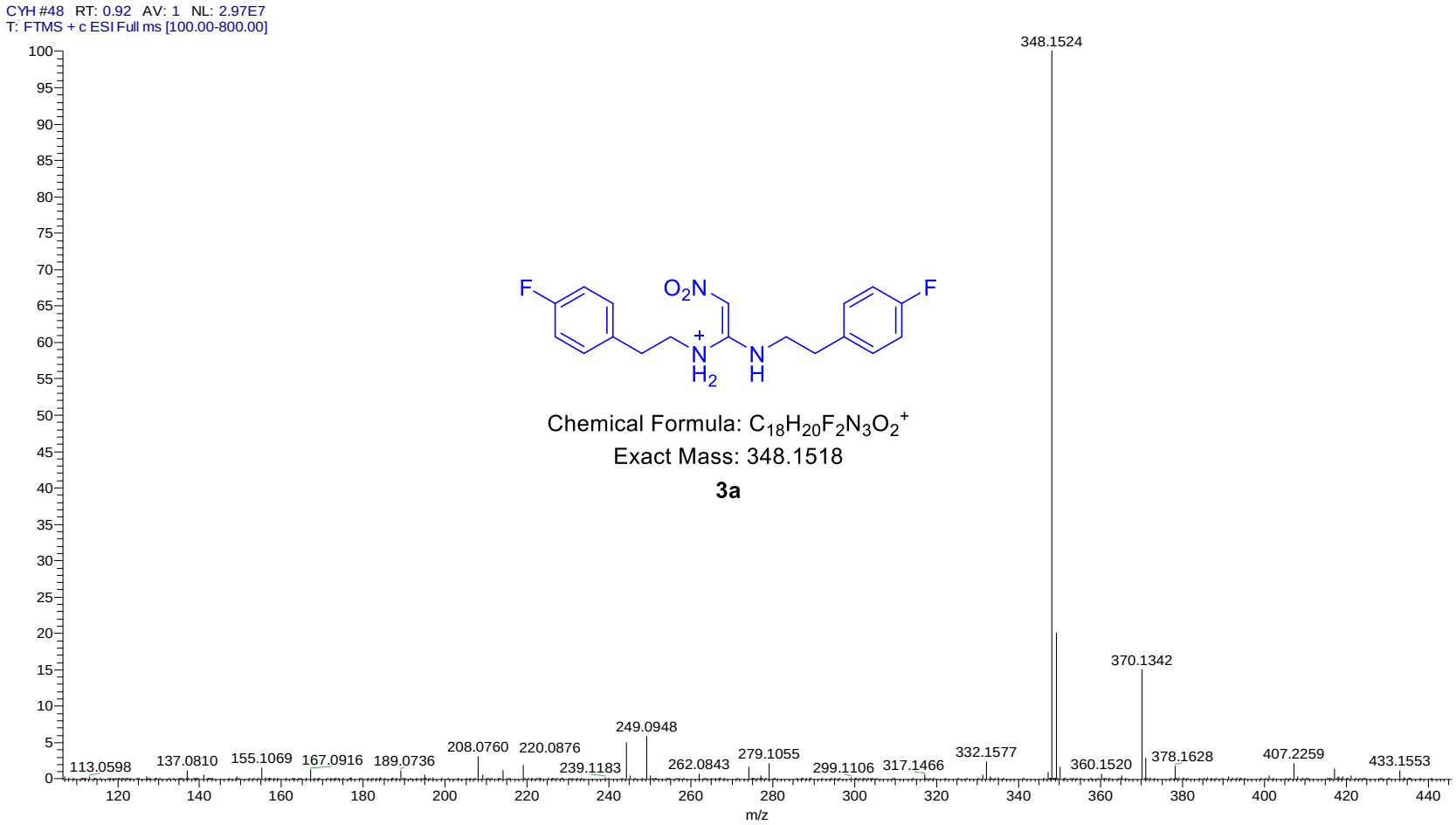

Figure S82. HRMS of intermediate **3a**

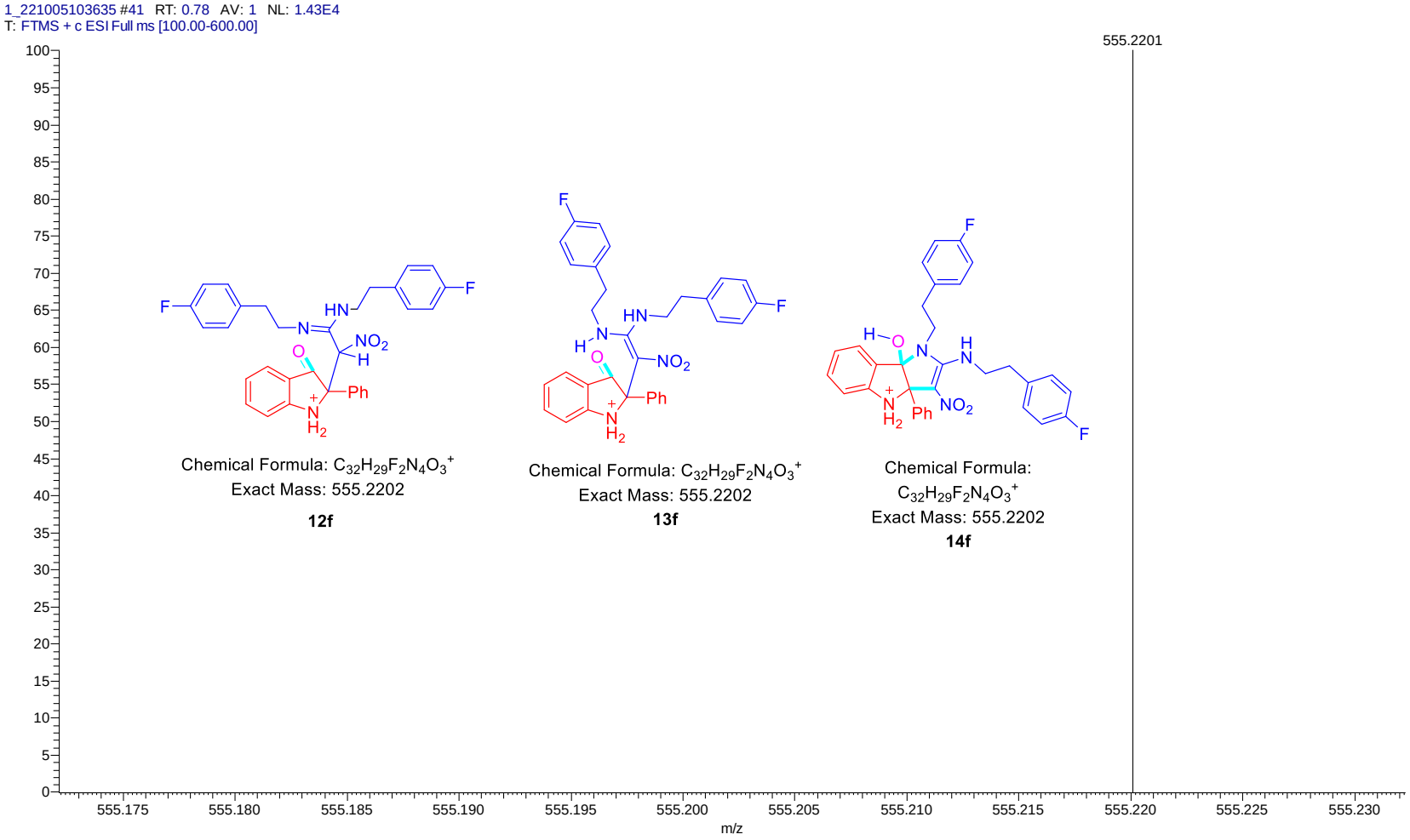

Figure S83. HRMS of intermediate **12f/13f/14f**

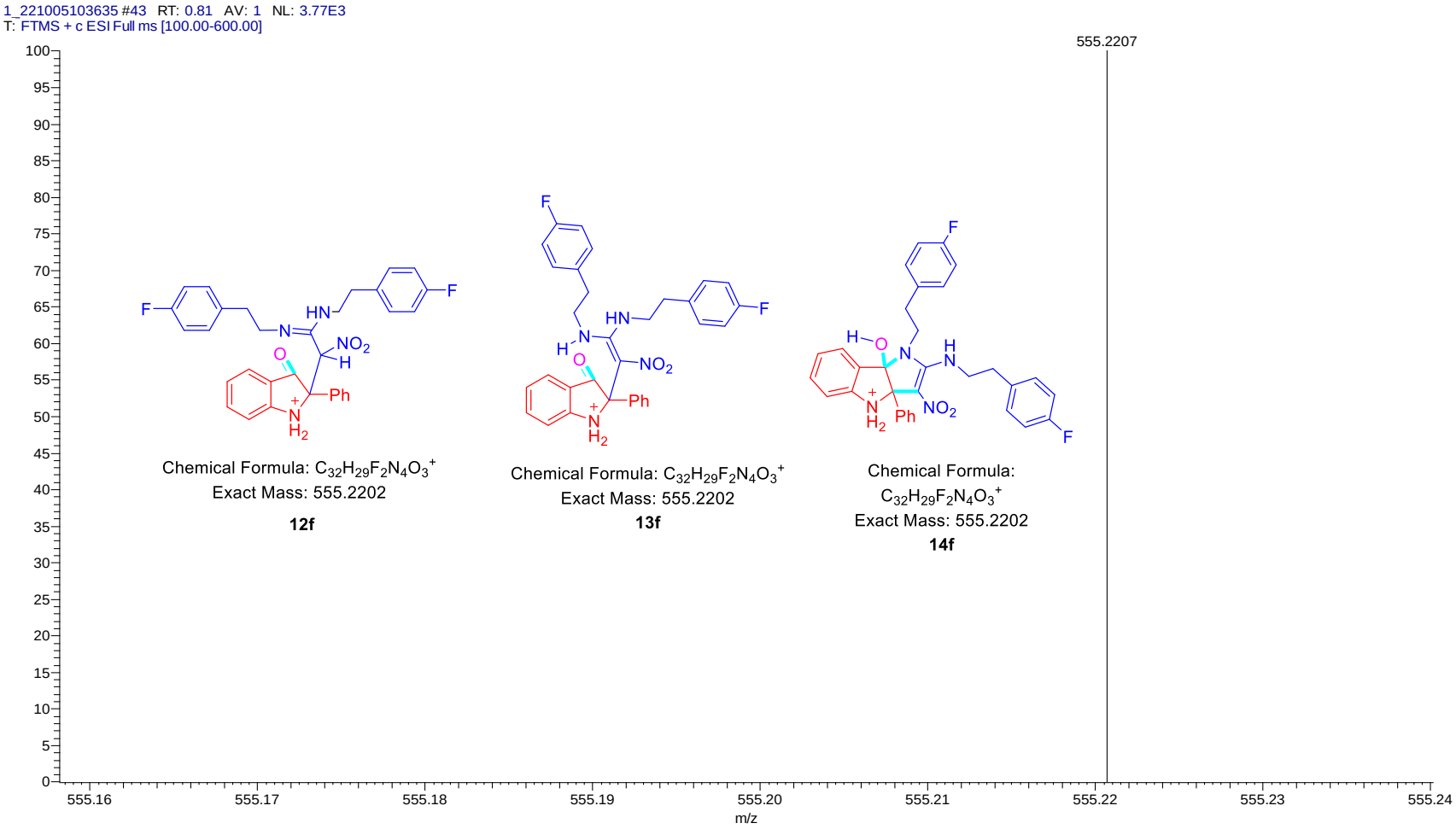

Figure S84. HRMS of intermediate **12f/13f/14f**

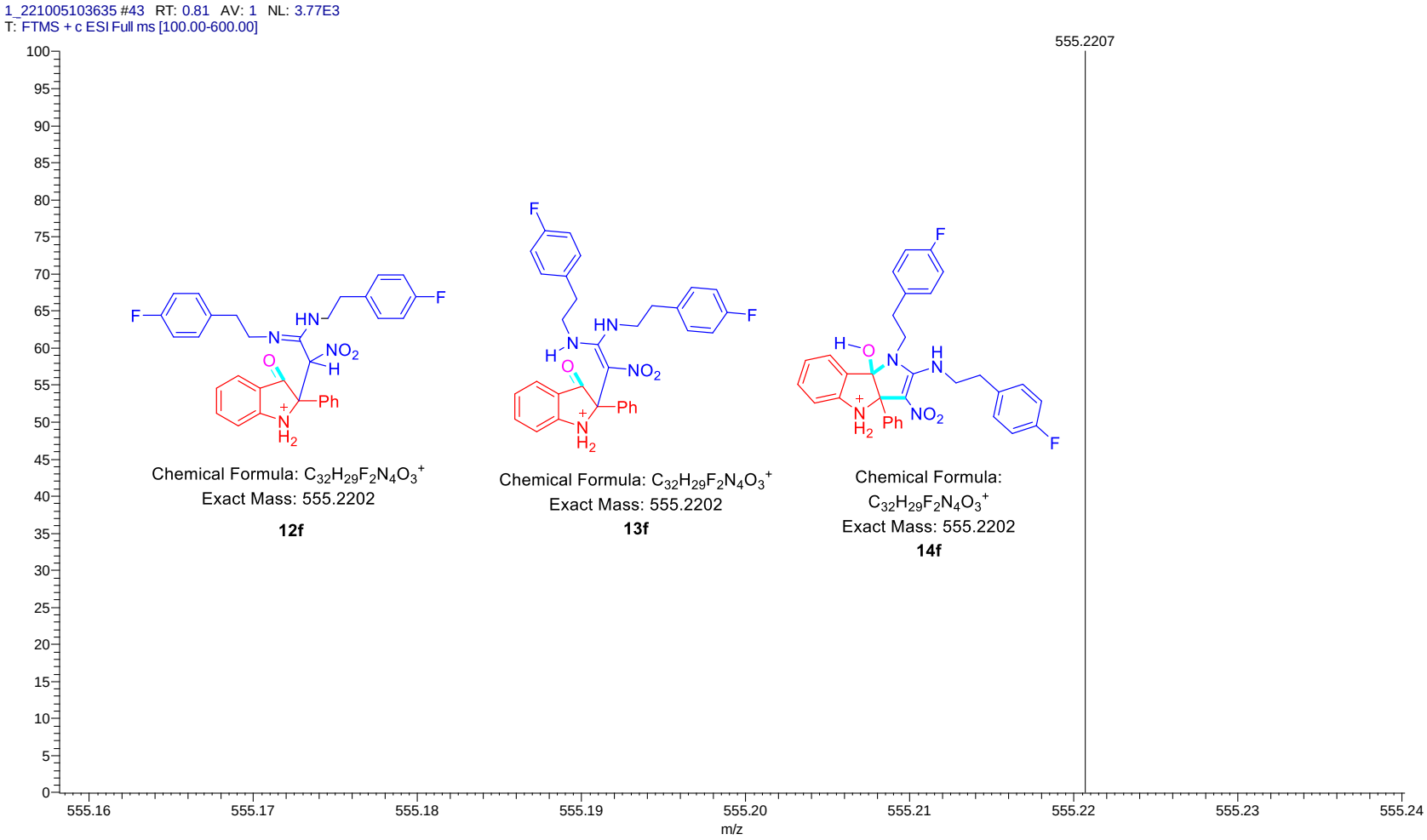

Figure S85. HRMS of intermediate **12f/13f/14f**

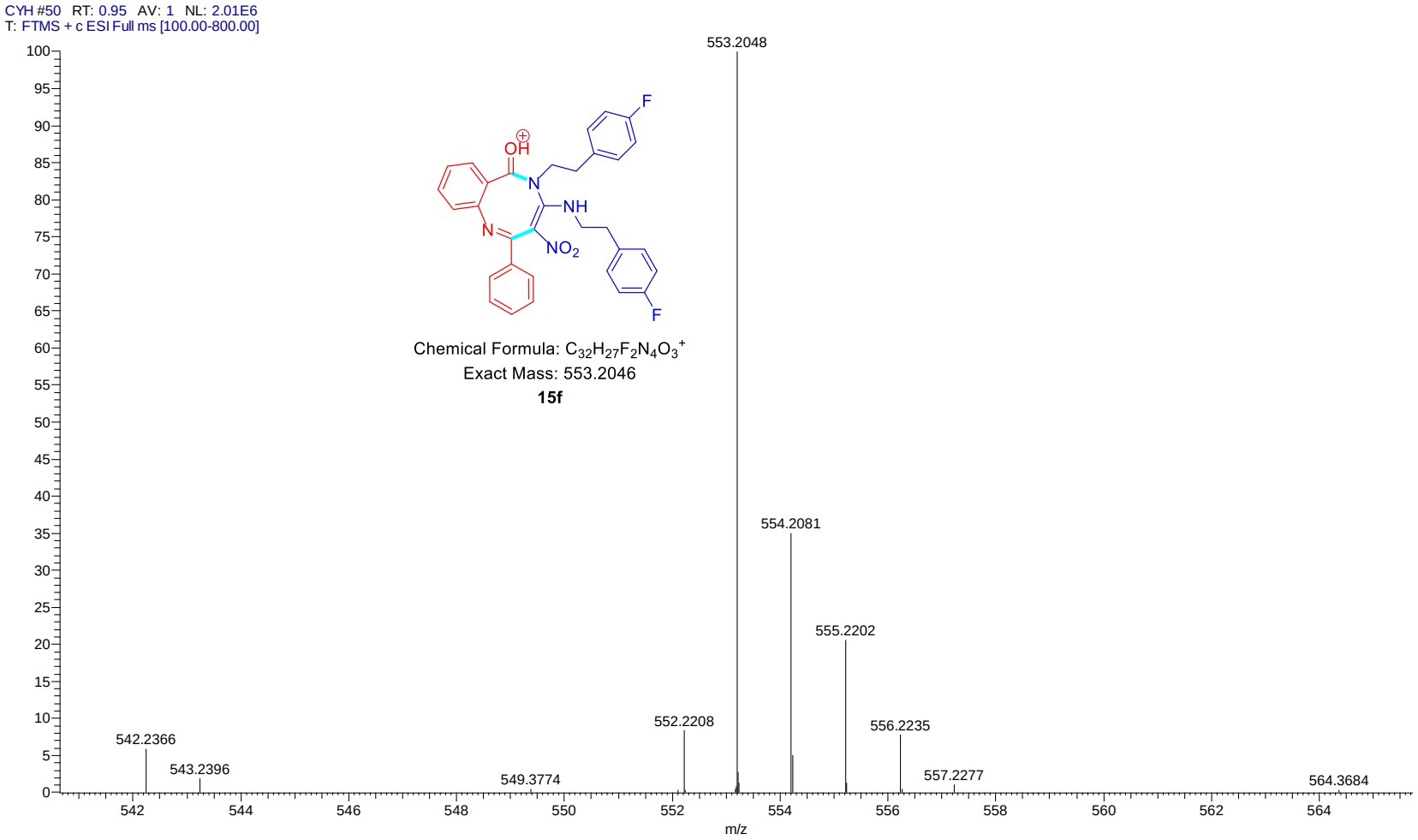

Figure S86. HRMS of intermediate **15f**

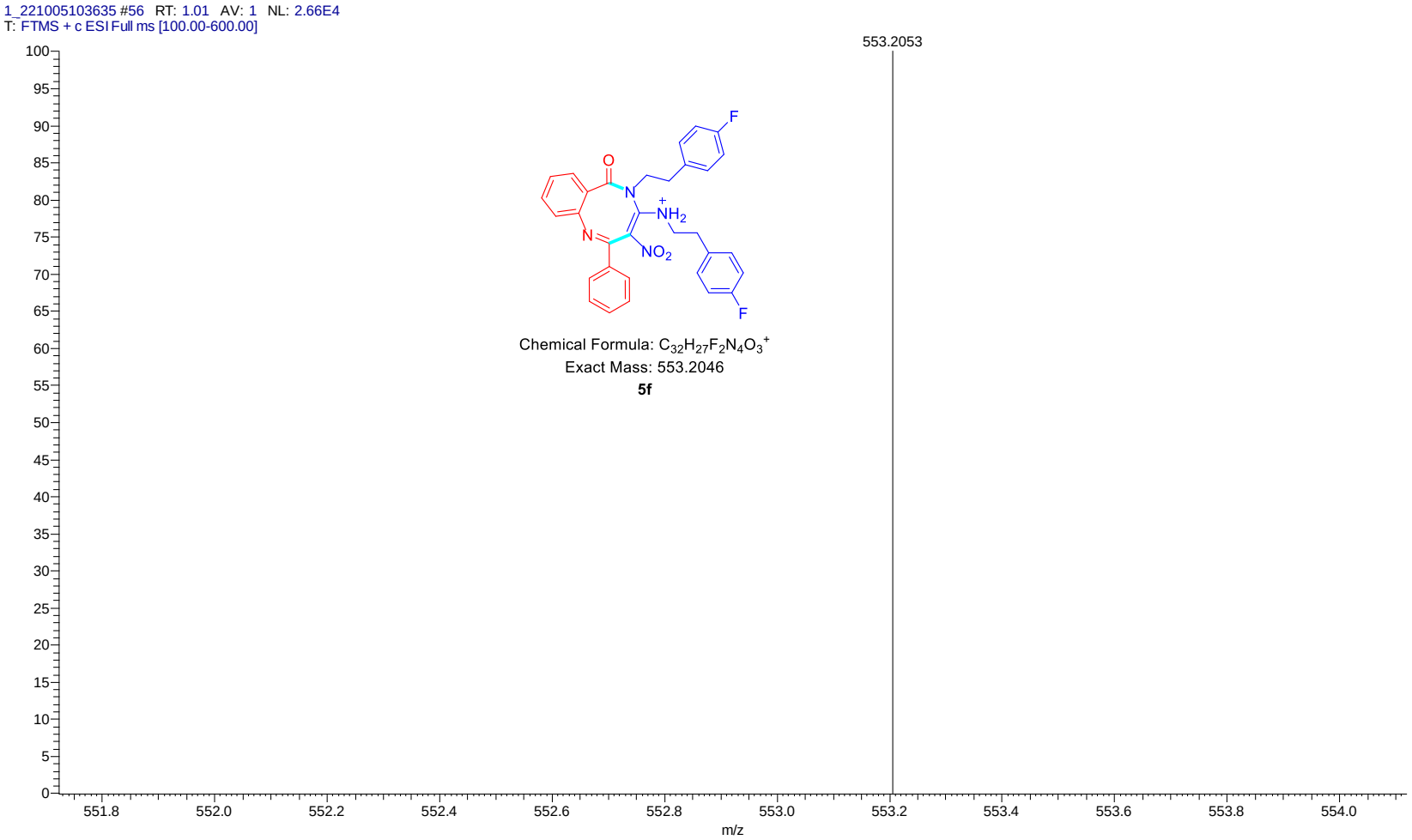

Figure S87. HRMS of the target compound **5f**

References and Notes

1. (*a*) B.-Q. Wang, Q. Luo, Q. Xiao, J. Lin, S.-J. Yan, *ACS Omega*, 2017, **5**, 8382−8389; (*b*) Mertens, H.; Troschuetz, R.; Roth, H. J.; *Arch. Pharm.* (Weinheim, Germany), **1986**, *319*, 161−167. (*c*) Kenda, B.; Quesnel, Y.; Ates, A.; Michel, P.; Turet, L.; Mercier. J.; WO 2006128693 A2.
2. CCDC 2213202 contains 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