New *one-pot* synthesis of 4-arylpyrazolo[3,4-*b*]pyridin-6-ones based on 5-aminopyrazoles and azlactones

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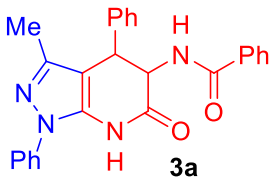
General information

^{1}H and ^{13}C NMR spectra were acquired on a Bruker DRX-400 spectrometer (working frequencies 400 and 100 MHz, respectively) in $CDCl_3$ or DMSO-d_6, with the residual solvent signals ($CDCl_3$: 7.26 ppm for ^{1}H nuclei and 77.0 ppm for ^{13}C nuclei; DMSO-d_6: 2.50 ppm for ^{1}H nuclei and 39.5 ppm for ^{13}C nuclei) serving as internal standards. All chemical shifts (δ) are reported in ppm and coupling constants (*J*) in Hz. Absorption spectra were recorded on a PerkinElmer Lambda 750 diode array spectrophotometer, photoluminescence spectra were recorded on a Cary Eclipse fluorescence spectrophotometer. In both cases, the test compounds were dissolved in EtOH so that the concentration of the resulting solutions was lower than 10^{-5} mol/dm^3. The molar light absorption coefficient was determined according to the described method [1, 2]. The quantum yield was determined relative to quinine sulfate in 0.5 M H_2SO_4 (Φ_f 0.546) using the comparison method [3, 4]. Infra-red spectra were recorded on an Infralum FT-801 spectrometer for others in KBr pellets. The elemental analyses were carried out on a Carlo Erba 1106 CHN analyzer. The melting points were determined on a Reach devices RD-MP. Monitoring of the reaction progress and assessment of the purity of synthesized compounds were done by TLC on Silufol UV-254 plates, eluents $CHCl_3$–EtOAc, 10:1. Visualization of plates was done under UV light. Silica gel 60 (0.063–0.200 mm, Macherey-Nagel) was used for column chromatography.

The starting compounds **1** [5], **2a-i** [6-10] were prepared following the reported methods.

Compounds characterization and analytical data

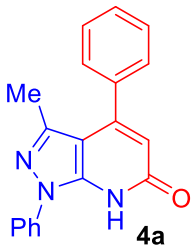
***N*-(3-methyl-6-oxo-1,4-diphenyl-4,5,6,7-tetrahydro-1*H*-pyrazolo[3,4-*b*]pyridin-5-yl)benzamide (3a).** A mixture of 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **1** (346 mg, 2 mmol) and 4-benzylidene-2-phenyloxazol-5(4*H*)-one **2a** (498 mg, 2 mmol) was heated at 150°C for 40 min, after cooling to room temperature, the product was purified by column chromatography on silica gel (eluent, $CHCl_3$–EtOAc, 10:1). Yield: 523 mg (62%) colorless crystals, m.p. >250°C (*i*-PrOH) (m.p. 268–270 (EtOH) [11]). IR (KBr): 3295, 3194, 3062, 3032, 2911, 1698, 1693, 1642, 1601, 1582, 1547, 1496, 1457, 1374, 1357, 1335, 1267, 1255, 1184, 1113, 1075, 1054, 1026, 1002, 916, 819, 819, 800, 754, 694, 660 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) *δ:* 1.46 (s, 3H), 4.40 (d, *J* = 11.9 Hz, 1H), 5.05 (dd, *J* = 11.9, 9.0 Hz, 1H), 7.20-7.26 (m, 1H), 7.31-7.39 (m, 5H), 7.40-7.45 (m, 2H), 7.48-7.53 (m, 3H), 7.55-7.59 (m, 2H), 7.71-7.74 (m, 2H), 8.68 (d, *J* = 9.0 Hz, 1H), 10.79 (s, 1H), ^{13}C NMR (100 MHz, DMSO-d_6) *δ:* 12.5, 41.4, 56.0, 102.3, 122.9, 126.8, 127.1, 127.2, 128.2, 128.3, 128.5, 129.2, 131.3, 134.1, 137.3, 137.9, 140.1, 145.5, 166.4, 168.5. Anal. Calcd for $C_{26}H_{22}N_4O_2$: C 73.92, H 5.25, N 13.26. Found: 73.80, H 5.30, N 13.15.



3a

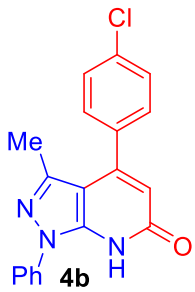
General procedure for the synthesis of 3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4a-i). A mixture of 3-methyl-1-phenyl-1*H*-pyrazol-5-amine **1** (346 mg, 2 mmol) and azlactones **2a-i** (2 mmol) was heated at 150°C for 40 min. Then the mixture was cooled and DMSO (4 mL) and *t*-BuOK (336 mg, 3 mmol) was added, after which the resulting mixture was heated at 150°C for 1.5 h. The reaction mixture was cooled, poured into H_2O (30 mL), and 10% HCl was added on cooling to pH ~ 3. The precipitate formed was filtered off, dried, and purified by column chromatography on silica gel (eluent, $CHCl_3$–EtOAc, 10:1).

3-Methyl-1,4-diphenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4a). Yield: 439 mg (73%), colorless crystals, m.p. 194-195°C (m.p. 193-194°C [12]). IR (KBr): 3295, 3194, 3062, 3032, 2911, 1698, 1693, 1642, 1601, 1582, 1547, 1496, 1457, 1374, 1357, 1335, 1267, 1255, 1184, 1113, 1075, 1054, 1026, 1002, 916, 819, 819, 800, 754, 694, 660 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ:* 1.46 (s, 3H), 4.40 (d, *J* = 11.9 Hz, 1H), 5.05 (dd, *J* = 11.9, 9.0 Hz, 1H), 7.20-7.26 (m, 1H), 7.31-7.39 (m, 5H), 7.40-7.45 (m, 2H), 7.48-7.53 (m, 3H), 7.55-7.59 (m, 2H), 7.71-7.74 (m, 2H), 8.68 (d, *J* = 9.0 Hz, 1H), 10.79 (s, 1H), ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 12.5, 41.4, 56.0, 102.3, 122.9, 126.8, 127.1, 127.2, 128.2, 128.3, 128.5, 129.2, 131.3, 134.1, 137.3, 137.9, 140.1, 145.5, 166.4, 168.5. Anal. Calcd for $C_{19}H_{15}N_3O$: C 75.73, H 5.02, N 13.94. Found: C 75.88, H 5.14, N 13.80.



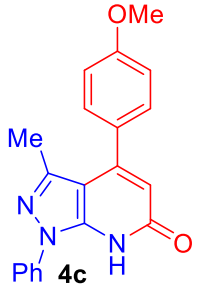
4a

4-(4-Chlorophenyl)-3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4b). Yield: 470 mg (70%), colorless crystals, m.p. 228-229°C. IR (KBr): 3056, 1647, 1642, 1595, 1576, 1503, 1429, 1383, 1348, 1281, 1262, 1159, 1121, 1090, 1015, 988, 887, 862, 830, 760, 731, 714, 691, 675 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ:* 2.10 (s, 3H), 6.30 (s, 1H), 7.16-7.21 (m, 1H), 7.29-7.34 (m, 2H), 7.36-7.41 (m, 2H), 7.46-7.52 (m, 2H), 7.60-7.65 (m, 2H), 10.84 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 14.8, 107.0, 110.3, 122.2, 127.0, 128.7, 129.1, 129.7, 135.2, 135.5, 137.4, 143.8, 143.9, 149.2, 163.4. Anal. Calcd for $C_{19}H_{14}ClN_3O$: C 67.96, H, 4.20, N 12.51. Found: C 67.82, H, 4.11, N 12.34.



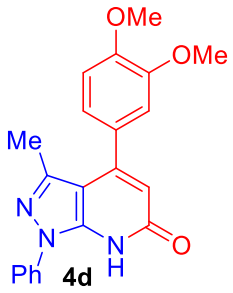
4b

4-(4-Methoxyphenyl)-3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4c). Yield: 384 mg (58%), colorless crystals, m.p. 188-189°C. IR (KBr): 3063, 1632, 1597, 1586, 1574, 1503, 1387, 1356, 1252, 1211, 1159, 1090, 1015, 980, 889, 858, 835, 764, 733, 696 cm^{-1}. ^1H NMR (400 MHz, $CDCl_3$) *δ:* . 2.15 (s, 3H), 3.88 (s, 3H), 6.30 (s, 1H), 6.99-7.04 (m, 2H), 7.11-7.17 (m, 1H), 7.26-



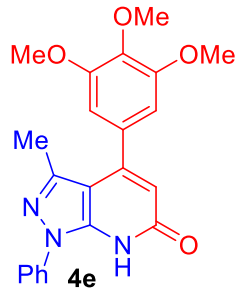
4c

7.31 (m, 2H), 7.37-7.41 (m, 2H), 7.59-7.64 (m, 2H), 10.85 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 15.0, 55.3, 107.3, 110.1, 113.8, 122.2, 126.9, 129.0, 129.4, 129.7, 137.5, 143.8, 144.1, 150.5, 160.3, 163.6. Anal. Calcd for $C_{20}H_{17}N_3O_2$: C 72.49, H 5.17, N 12.68. Found: C 72.34, H 5.13, N 12.79.

4-(3,4-Dimethoxyphenyl)-3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4d). 

4d

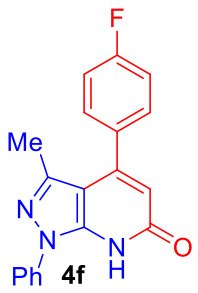
Yield: 397 mg (55%), colorless crystals, m.p. 243-244°C. IR (KBr): 3069, 1634, 1607, 1599, 1582, 1514, 1429, 1356, 1221, 1159, 1115, 1015, 980, 862, 839, 799, 733, 698 cm^{-1}. ^{1}H NMR (400 MHz, DMSO-d_6) *δ:* 2.19 (s, 3H), 3.82 (s, 3H), 3.83 (s, 3H), 6.47 (s, 1H), 7.04-7.11 (m, 2H), 7.13 (s, 1H), 7.25-7.30 (m, 1H), 7.49-7.54 (m, 2H), 8.20-23 (m, 2H), 11.39 (br.s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) *δ:* 15.3, 55.5, 55.6, 106.0, 109.2, 111.4, 112.5, 120.5, 121.3, 125.2, 128.9, 129.4, 139.3, 142.3, 148.3, 148.4, 149.3, 150.0, 163.4. Anal. Calcd for $C_{21}H_{19}N_3O_3$: C 69.79, H 5.30, N 11.63. Found: C 69.60, H 5.19, N 11.48.

3-Methyl-1-phenyl-4-(3,4,5-trimethoxyphenyl)-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4e). 

4e

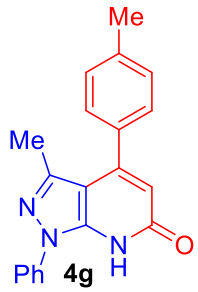
Yield: 438 mg (56%), colorless crystals, m.p. 184-185°C. IR (KBr): 3061, 3001, 2928, 2835, 1644, 1582, 1574, 1509, 1468, 1455, 1410, 1356, 1325, 1237, 1179, 1131, 1003, 828, 760, 731, 693 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 2.19 (s, 3H), 3.89 (s, 6H), 3.92 (s, 3H), 6.34 (s, 1H), 6.66 (s, 2H), 7.18-7.23 (m, 1H), 7.31-7.36 (m, 2H), 7.65-7.68 (m, 2 H), 10.70 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 15.0, 56.2, 61.0, 105.8, 107.2, 110.1, 122.2, 127.0, 129.2, 132.5, 137.5, 138.7, 143.9, 144.0, 150.5, 153.1, 163.4. Anal. Calcd for $C_{22}H_{21}N_3O_4$: C 67.51, H 5.41, N 10.74. Found: C 67.66, H 5.19, N 10.83.

4-(4-Fluorophenyl)-3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4f).



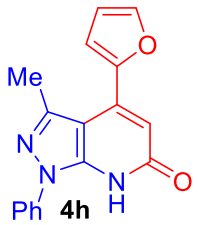
Yield: 427 mg (67%), colorless crystals, m.p. 239-240°C. IR (KBr): 3075, 1632, 1582, 1514, 1429, 1389, 1356, 1266, 1252, 1221, 1157, 1115, 1015, 780, 924, 899, 862, 857, 839, 799, 764, 731, 696, 675, 569 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 2.10 (s, 3H), 6.31 (s, 1H), 7.16-7.24 (m, 3H), 7.31-7.37 (m, 2H), 7.39-7.45 (m, 2H), 7.63-7.67 (m, 2H), 10.50 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 14.8, 107.2, 110.3, 115.5 (d, *J* = 21.6 Hz), 122.3, 127.0, 129.2, 130.2 (d, *J* = 7.8 Hz), 133.1 (d, *J* = 3.5 Hz), 137.5, 143.8, 144.0, 149.5, 163.2 (d, *J* = 248.8 Hz), 163.3. Anal. Calcd for $C_{19}H_{14}FN_3O$: C 71.46, H 4.42, N 13.16. Found: C 71.32, H 4.54, N 12.99.

3-Methyl-1-phenyl-4-(*p*-tolyl)-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4g). Yield:



441 mg (70%), colorless crystals, m.p. 217-218°C. IR (KBr): 3060, 1642, 1584, 1516, 1497, 1428, 1383, 1348, 1266, 1210, 1183, 1159, 1119, 1011, 984, 851, 824, 762, 729, 693 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 2.12 (s, 3H), 2.45 (s, 3H), 6.31 (s, 1H), 7.12-7.17 (m, 1H), 7.26-7.36 (m, 6H), 7.59-7.63 (m, 2H), 10.90 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 14.9, 21.3, 107.2, 110.2, 122.2, 126.9, 128.3, 129.0 (3C), 134.2, 137.4, 139.0, 143.8, 144.1, 150.8, 163.6. Anal. Calcd for $C_{20}H_{17}N_3O$: C 76.17, H 5.43, N 13.32. Found: C 76.54, H 5.53, N 13.12.

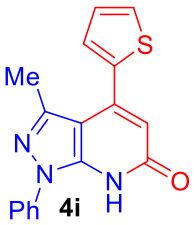
4-(Furan-2-yl)-3-methyl-1-phenyl-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4h).



Yield: 338 mg (58%), colorless crystals, m.p. 188-189°C. IR (KBr): 3048, 1597, 1580, 1557, 1511, 1493, 1418, 1387, 1343, 1277, 1267, 1204, 1175, 1157, 1140, 1038, 1015, 957, 858, 820, 776, 764, 752, 727, 696, 658, 658, 598 cm^{-1}. ^{1}H NMR (400 MHz, $CDCl_3$) *δ:* 2.57 (s, 3H), 6.57 (m, 2H), 6.92 (d, *J* = 3.3 Hz, 1H), 7.09-7.15 (m, 1H), 7.22-7.27 (m, 2H), 7.57-7.61 (m, 2H), 7.65-7.67 (m, 1 H), 10.54 (br.s, 1H). ^{13}C NMR (100 MHz, $CDCl_3$) *δ:* 16.0, 105.2, 106.4, 111.8, 112.2, 122.2,

126.9, 128.9, 137.3, 137.7, 144.0, 144.1, 145.1, 150.4, 163.4. Anal. Calcd for $C_{17}H_{13}N_3O_2$: C 70.09, H 4.50, N 14.42. Found: C 70.19, H 4.41, N 14.28.

3-Methyl-1-phenyl-4-(thiophen-2-yl)-1,7-dihydro-6*H*-pyrazolo[3,4-*b*]pyridin-6-one (4i).



4i

Yield: 368 mg (60%), colorless crystals, m.p. 190-191°C. IR (KBr): 3069, 1642, 1597, 1572, 1511, 1497, 1439, 1385, 1354, 1333, 1219, 1213, 1183, 1138, 1080, 1038, 1026, 1013, 976, 909, 849, 806, 799, 758, 727, 712, 694, 666 cm^{-1}. ^1H NMR (400 MHz, DMSO-d_6) *δ:* 2.32 (s, 3H), 6.54 (s, 1H), 7.23-7.31 (m, 2H), 7.45-7.54 (m, 3H), 7.76-7.79 (m, 1H), 8.15-8.19 (m, 2H), 11.36 (br.s, 1H). ^{13}C NMR (100 MHz, DMSO-d_6) *δ:* 15.3, 106.6, 108.6, 120.7, 125.5, 127.9, 128.2, 128.9, 129.2, 137.2, 139.1, 140.6, 142.1, 150.1, 163.4. Anal. Calcd for $C_{17}H_{13}N_3OS$: C 66.43, H 4.26, N 13.67. Found: C 66.33, H 4.38, N 13.53.

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Copies of NMR spectra

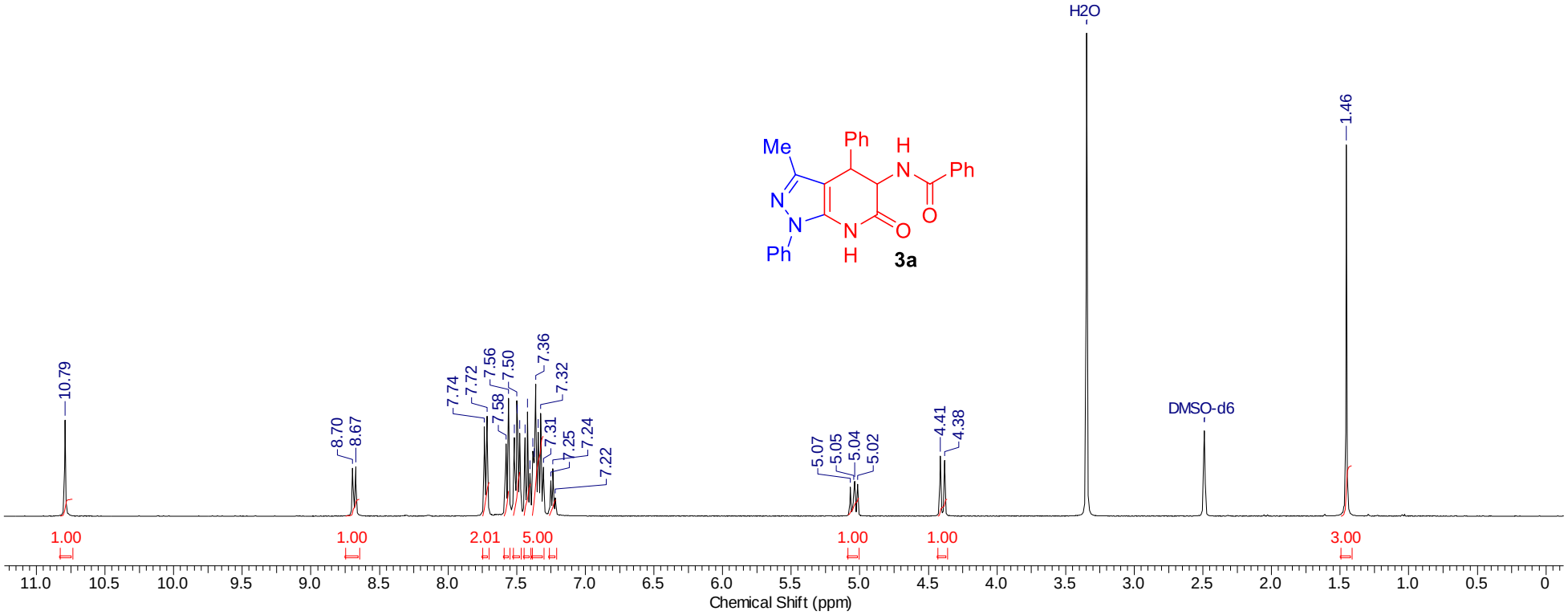

Figure S1: ^{1}H NMR spectrum of compound **3a** (DMSO-d_6).

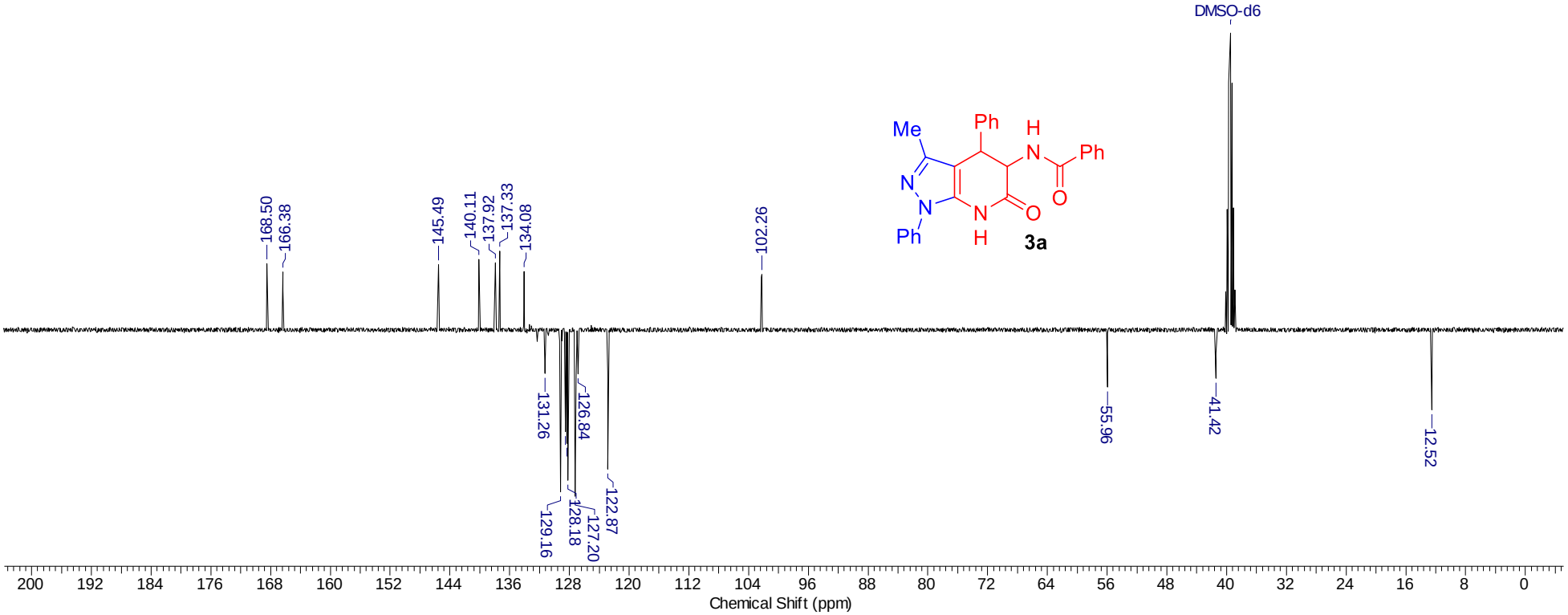

Figure S2: ^{13}C NMR spectrum of compound **3a** (DMSO-d_6).

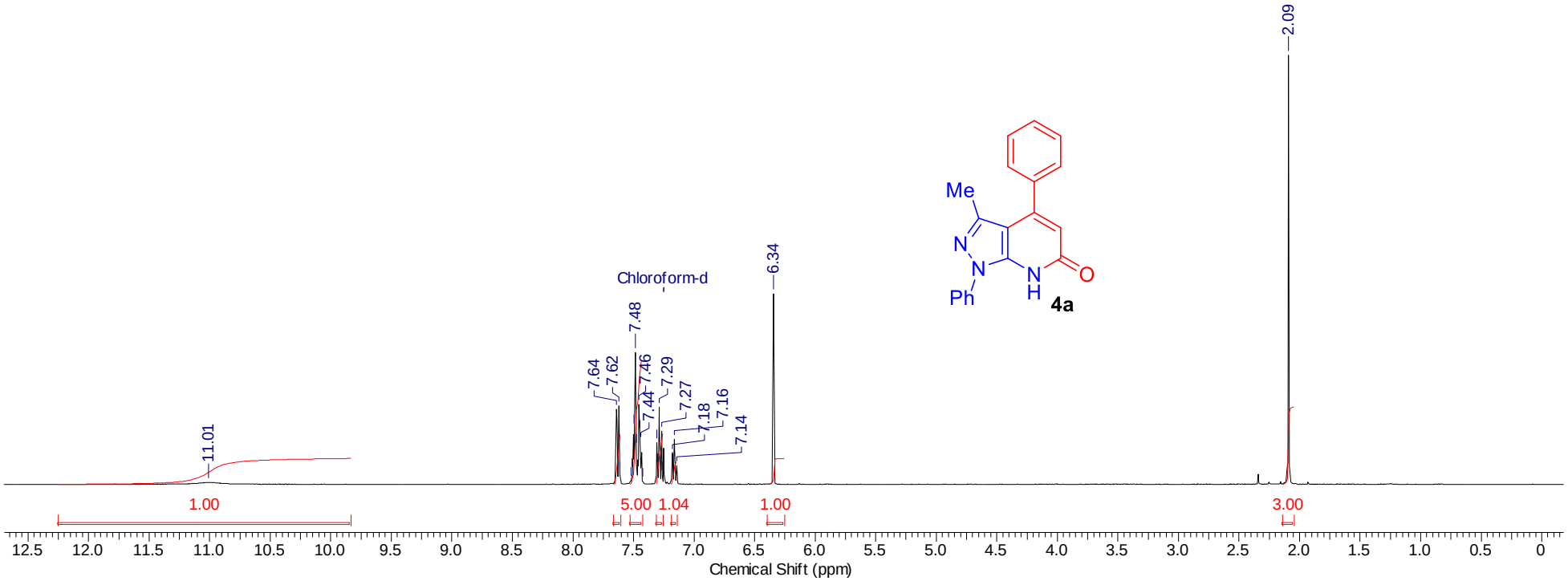

Figure S3: ^{1}H NMR spectrum of compound **4a** ($CDCl_3$).

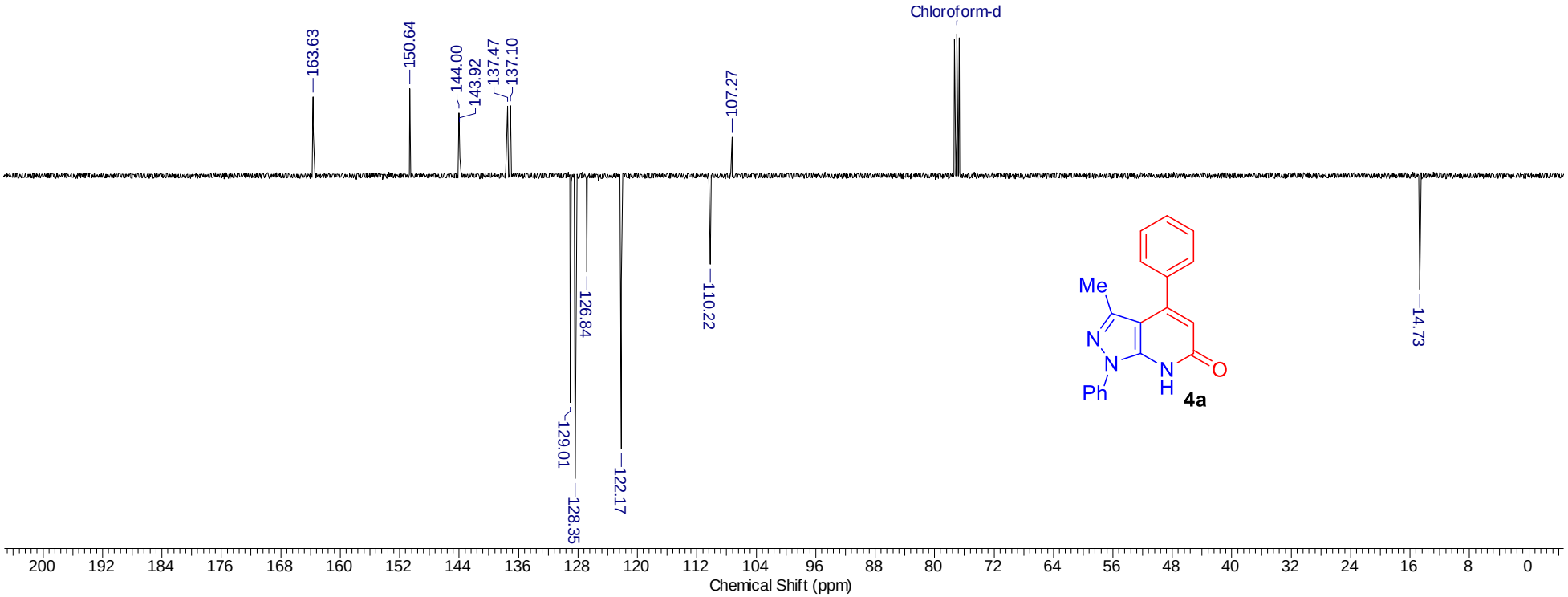

Figure S4: ^{13}C NMR spectrum of compound **4a** ($CDCl_3$).

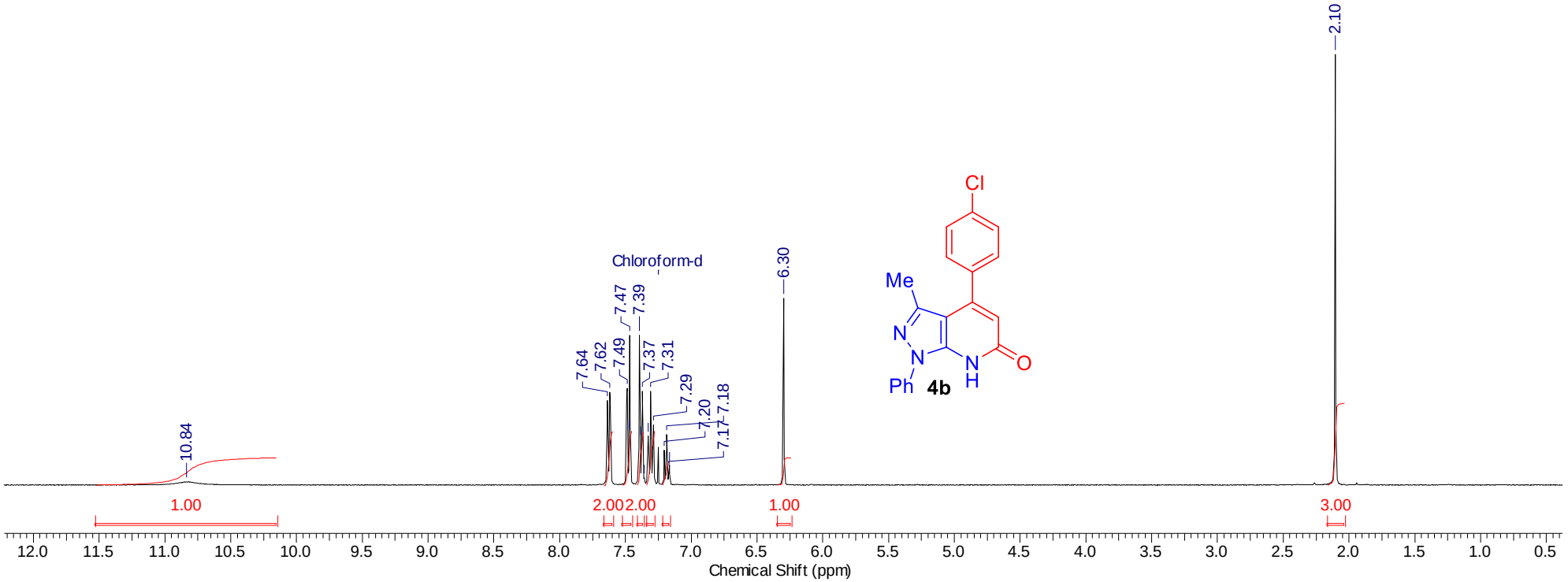

Figure S5: ^{1}H NMR spectrum of compound **4b** ($CDCl_3$).

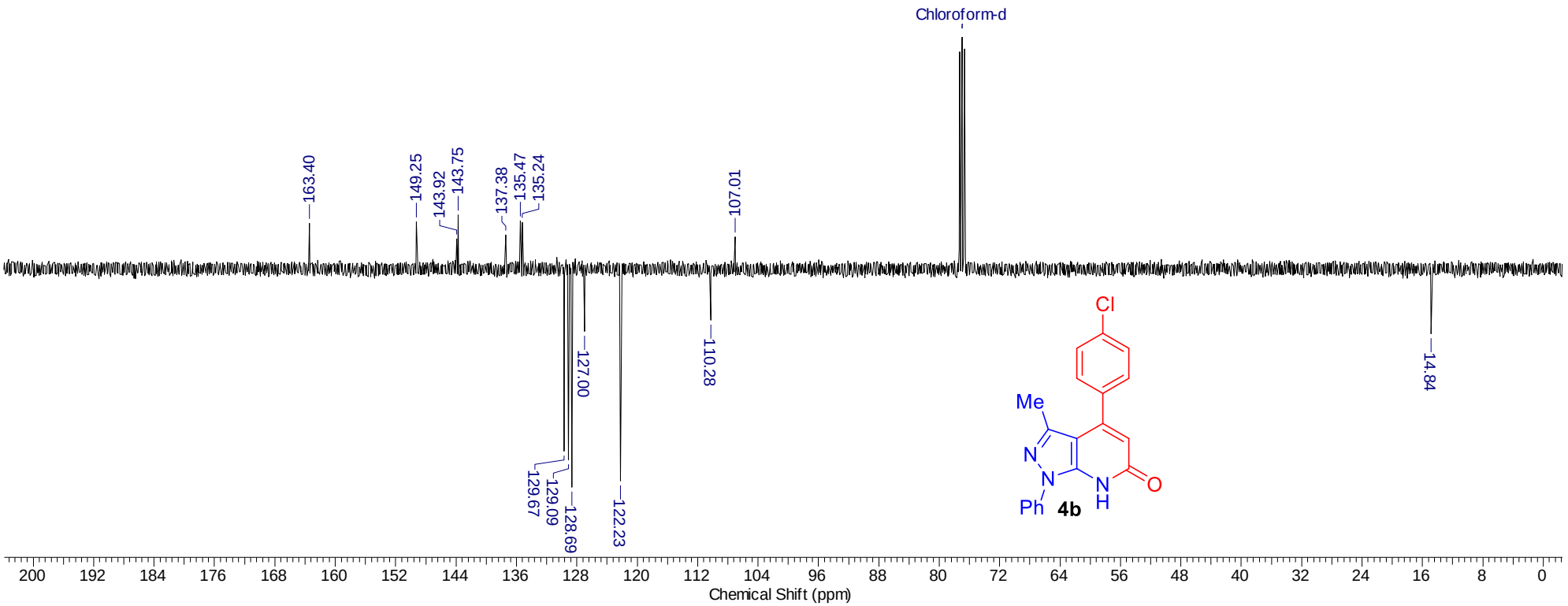

Figure S6: ^{13}C NMR spectrum of compound **4b** ($CDCl_3$).

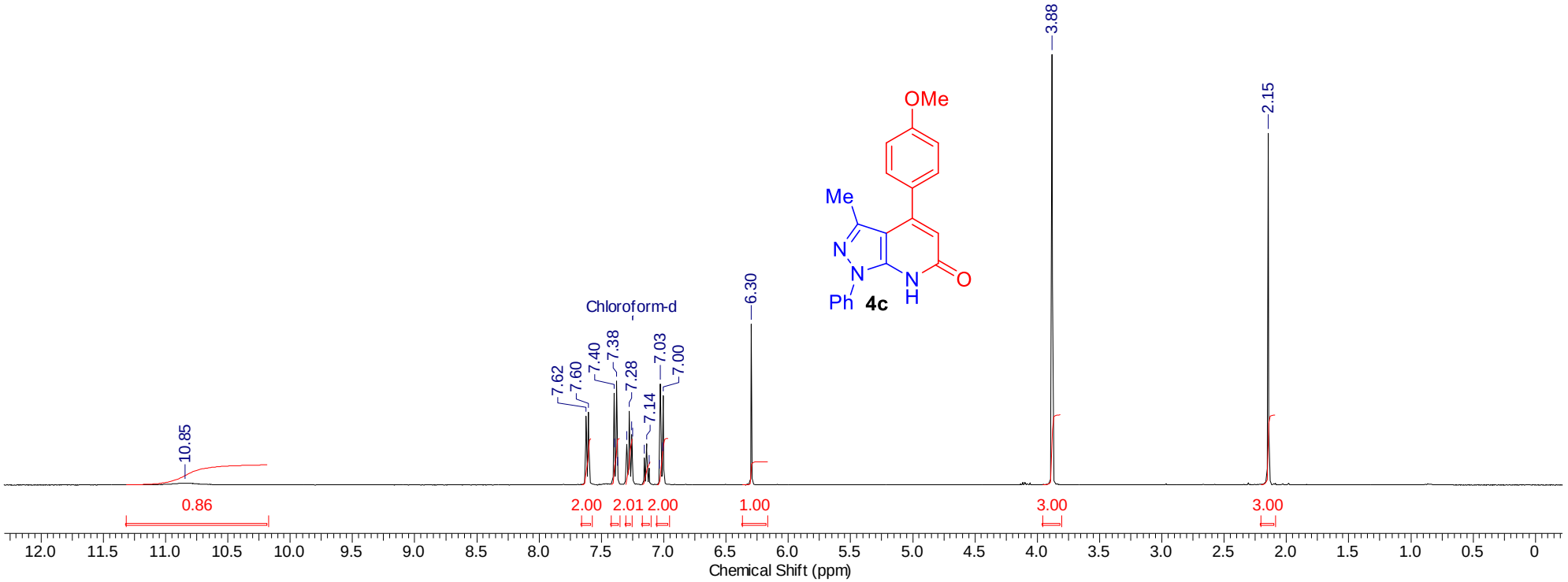

Figure S7: ^{1}H NMR spectrum of compound **4c** ($CDCl_3$).

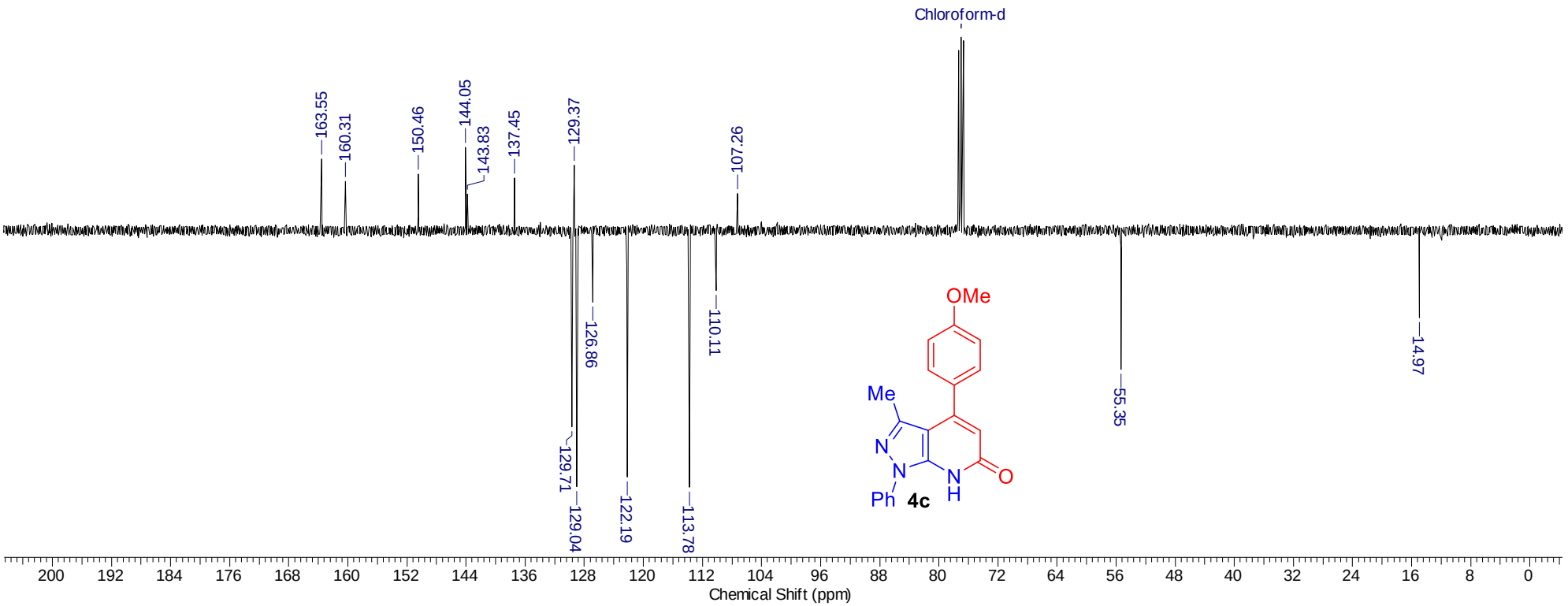

Figure S8: ^{13}C NMR spectrum of compound **4c** ($CDCl_3$).

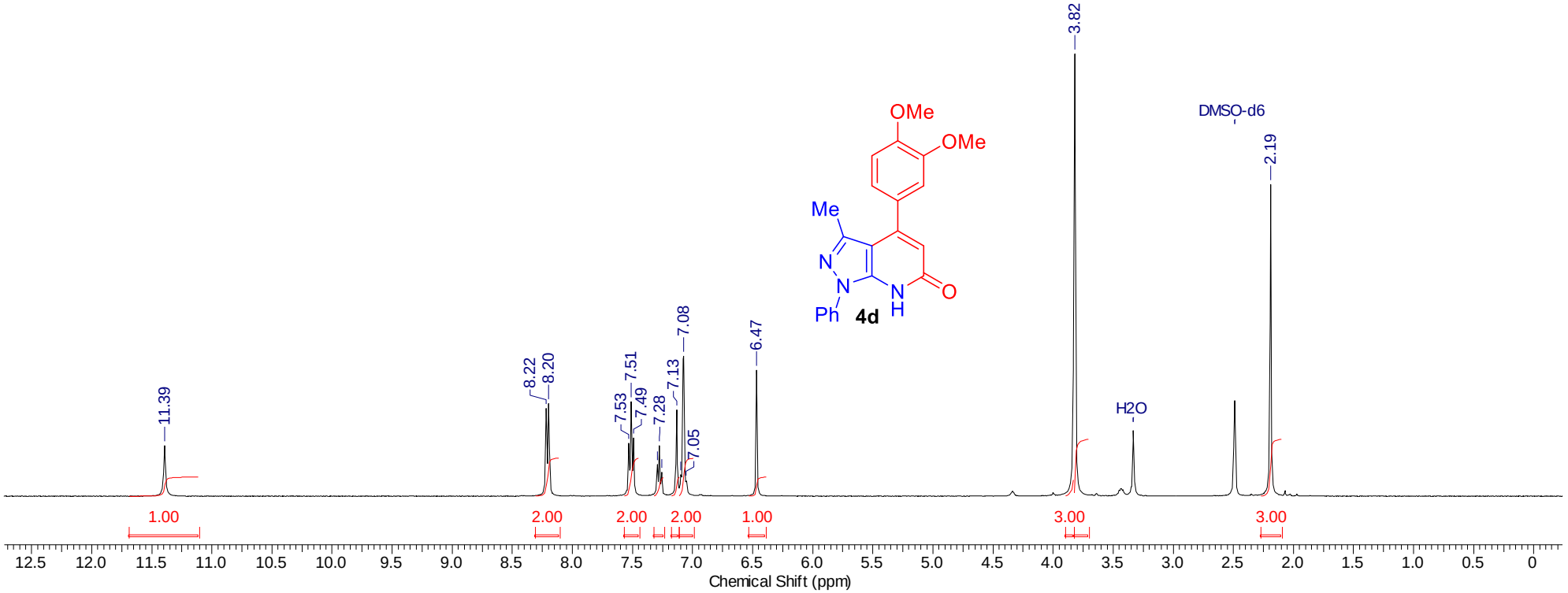

Figure S9: ^{1}H NMR spectrum of compound **4d** (DMSO-d_6).

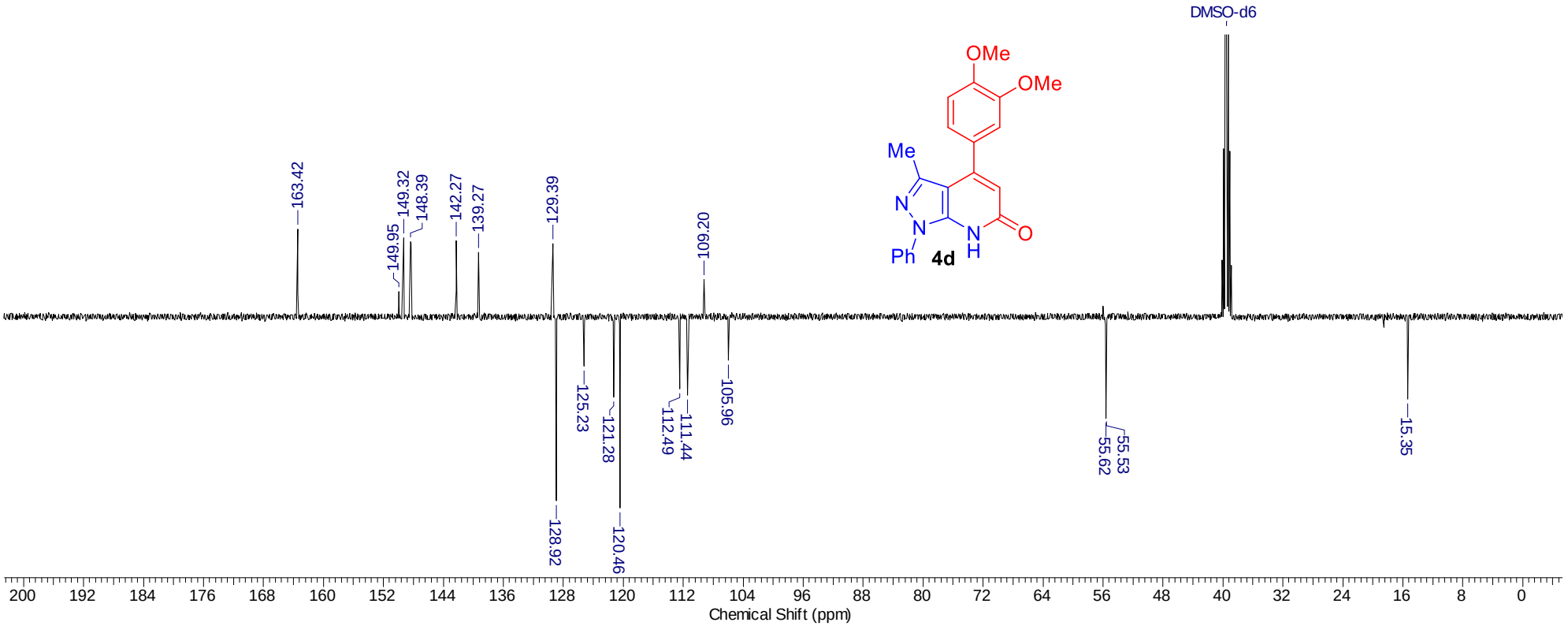

Figure S10: ^{13}C NMR spectrum of compound **4d** (DMSO-d_6).

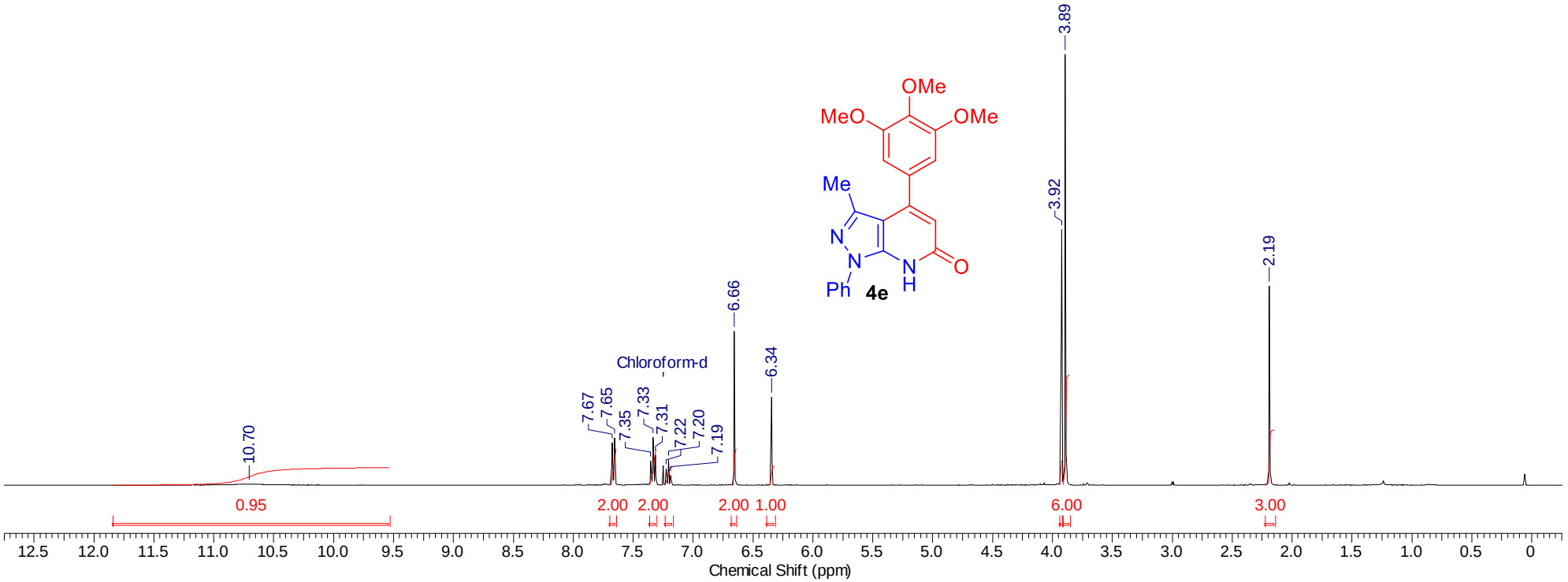

Figure S11: ^{1}H NMR spectrum of compound **4e** ($CDCl_3$).

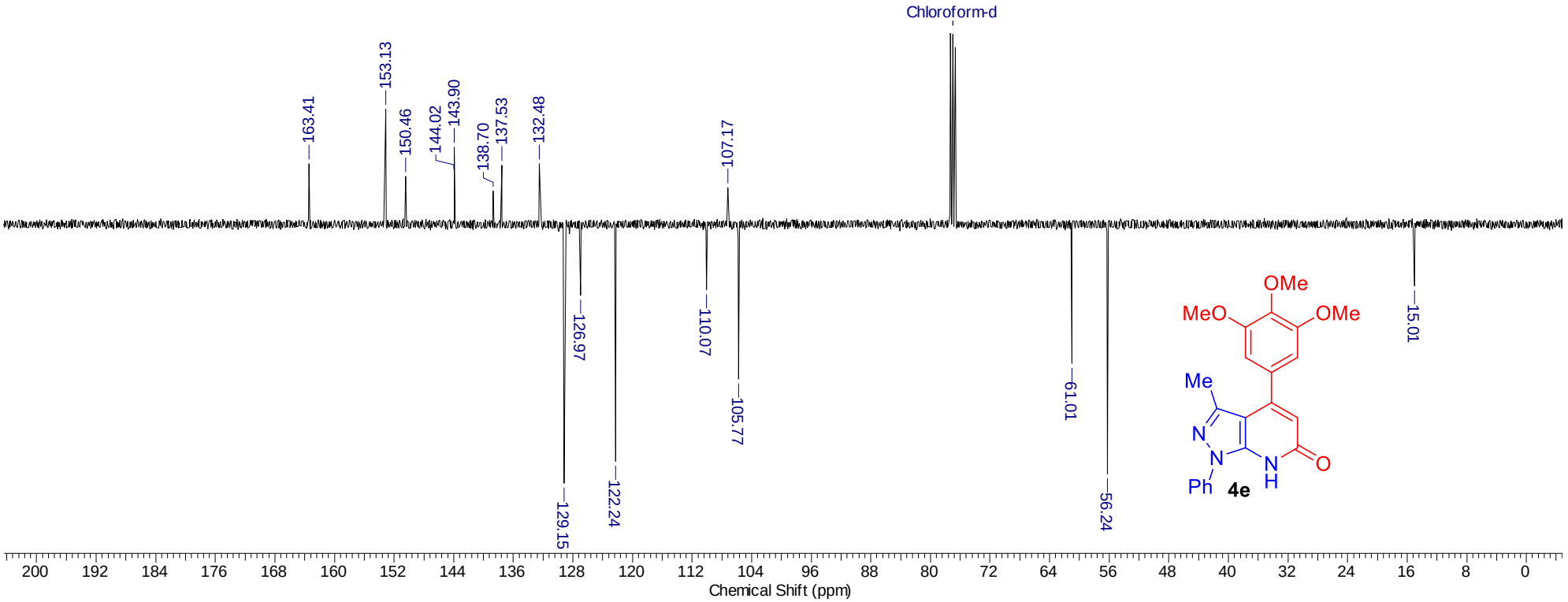

Figure S12: ^{13}C NMR spectrum of compound **4e** ($CDCl_3$).

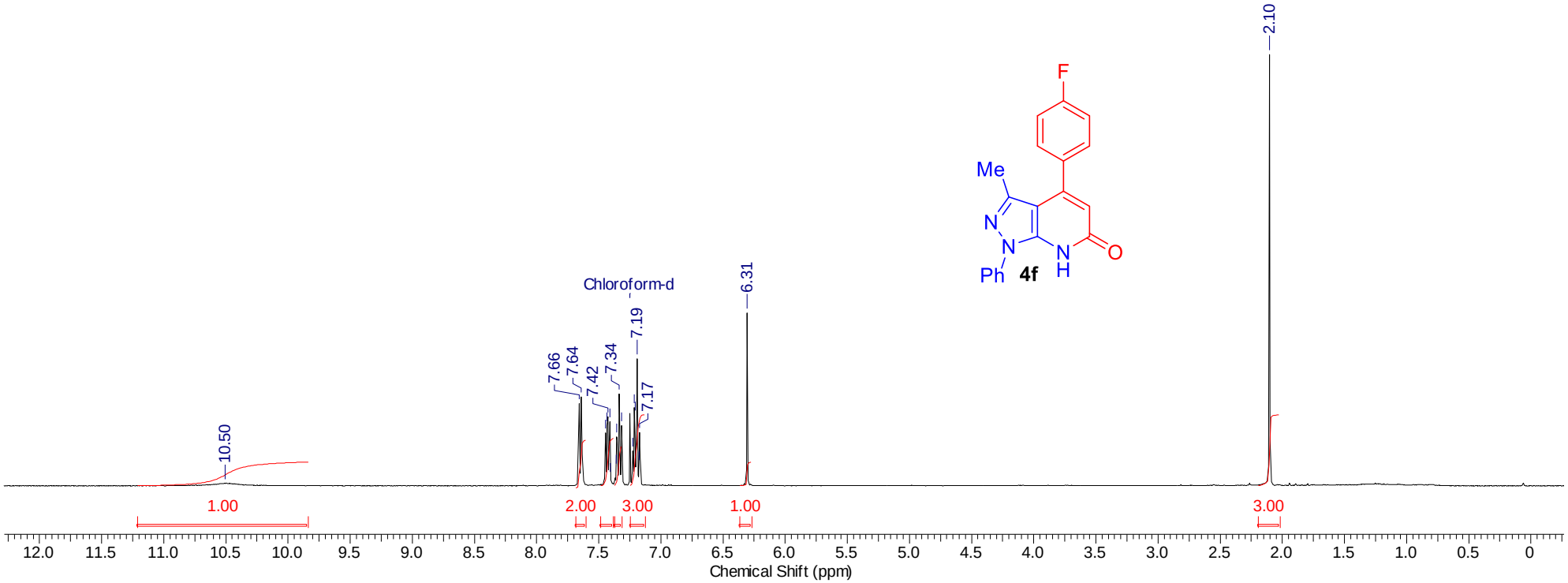

Figure S13: ^{1}H NMR spectrum of compound **4f** ($CDCl_3$).

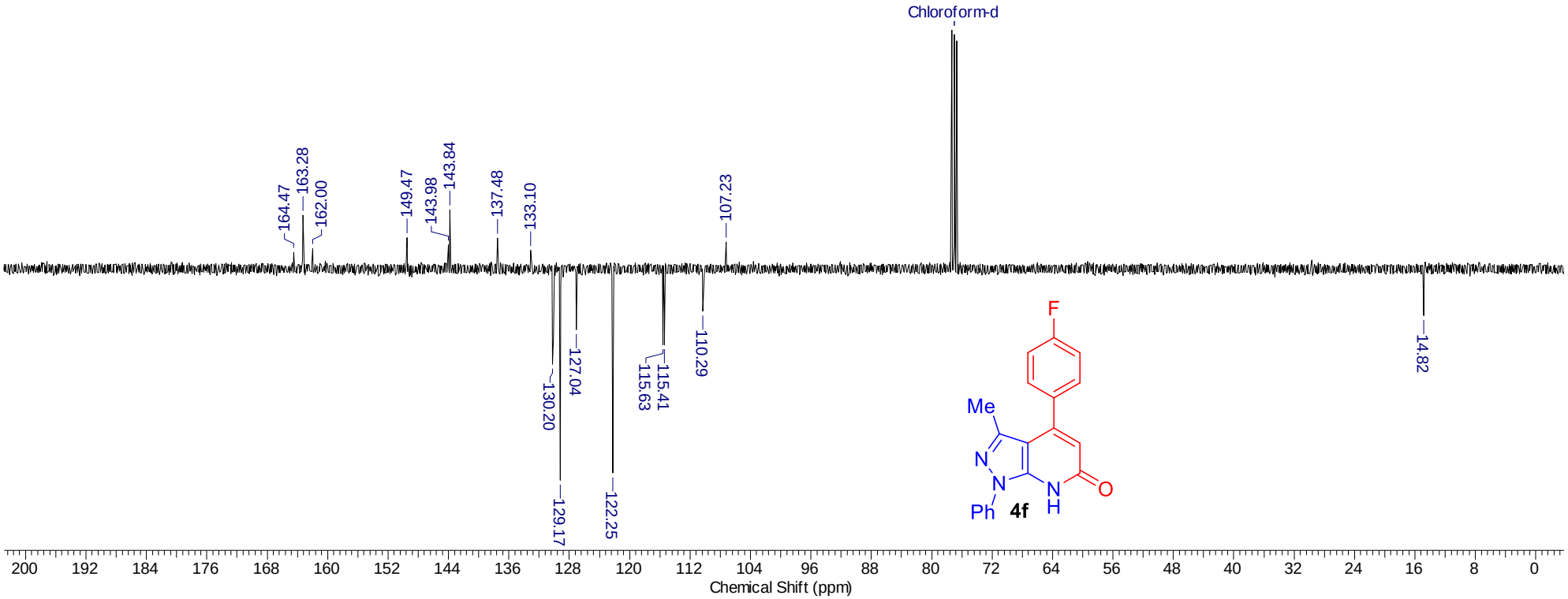

Figure S14: ^{13}C NMR spectrum of compound **4f** ($CDCl_3$).

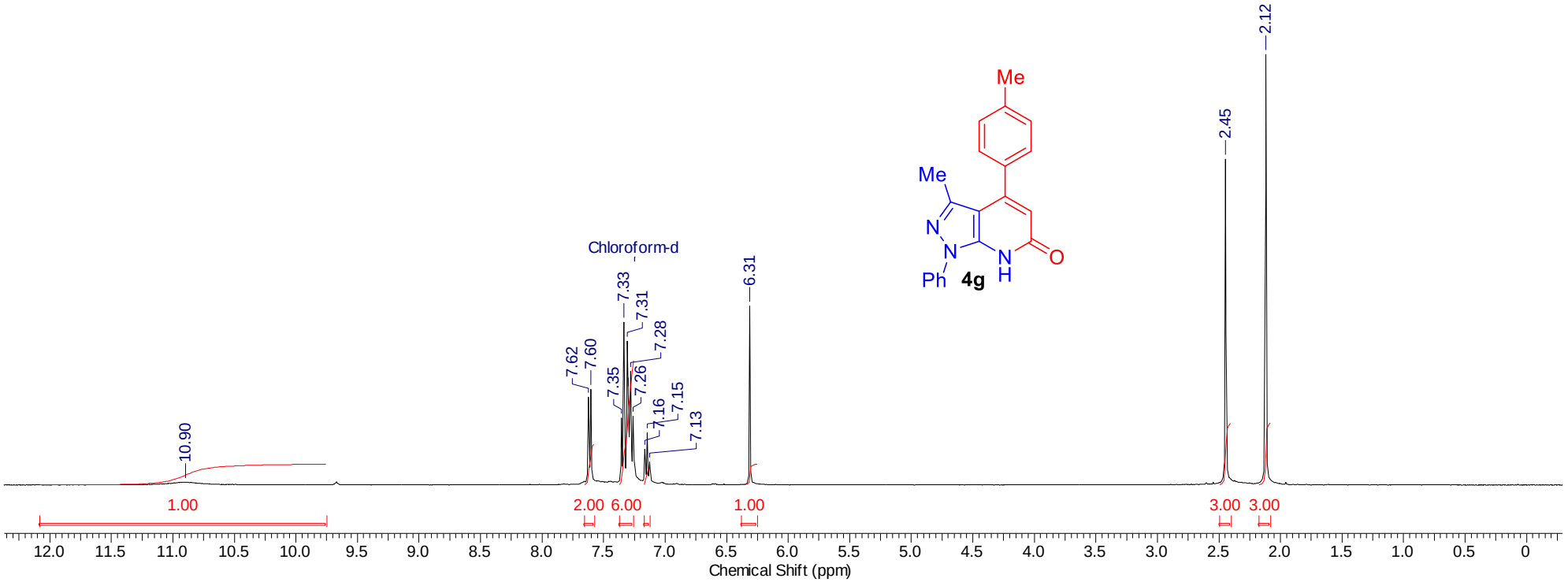

Figure S15: ^{1}H NMR spectrum of compound **4g** ($CDCl_3$).

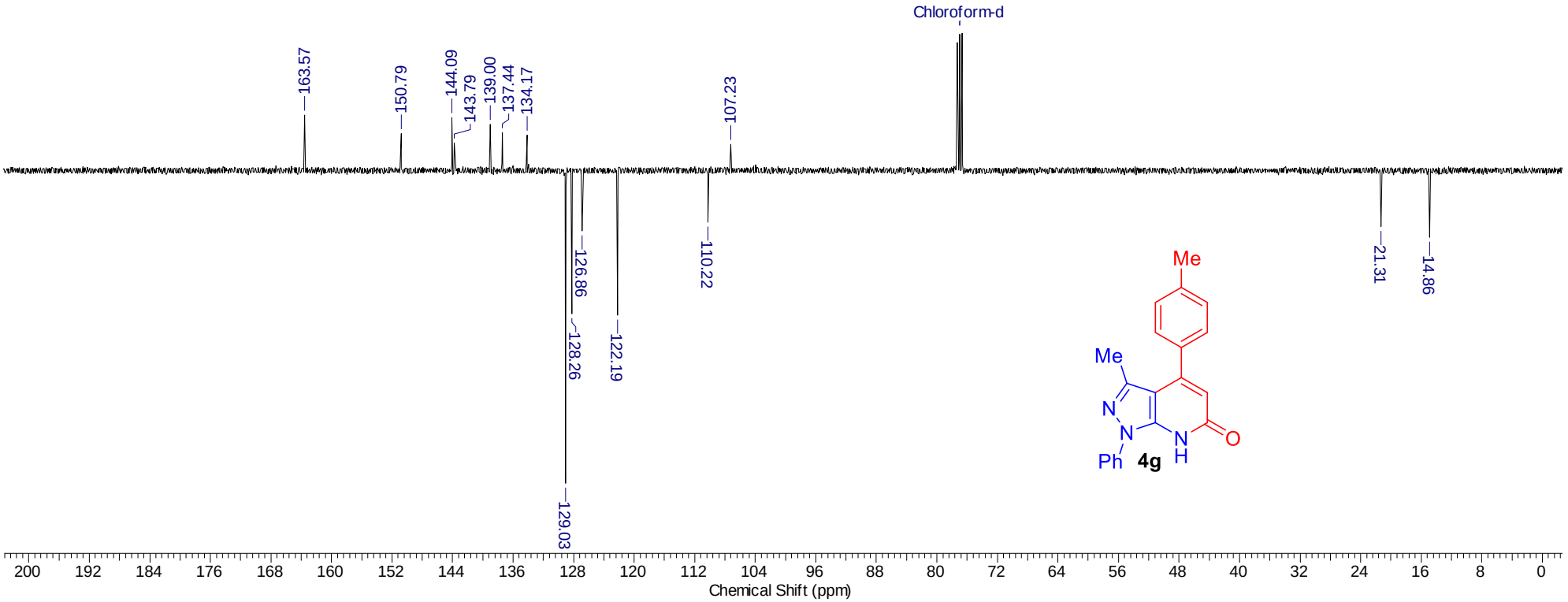

Figure S16: ^{13}C NMR spectrum of compound **4g** ($CDCl_3$).

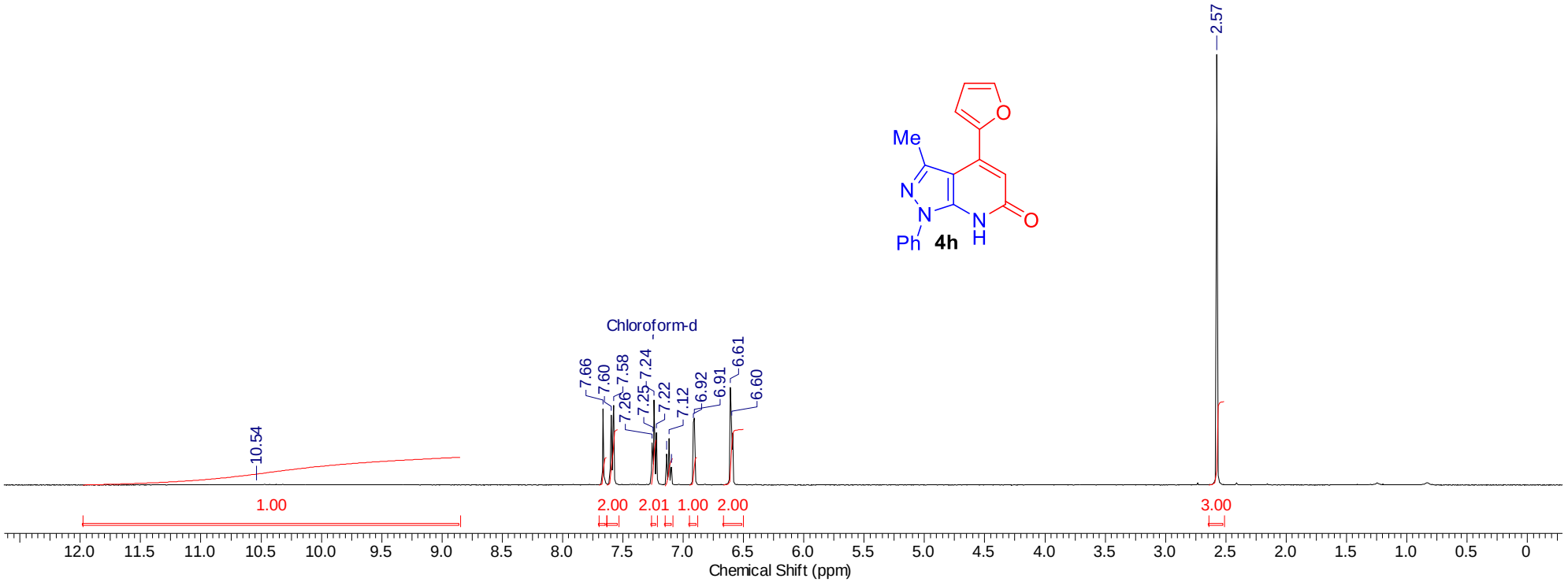

Figure S17: ^{1}H NMR spectrum of compound **4h** ($CDCl_3$).

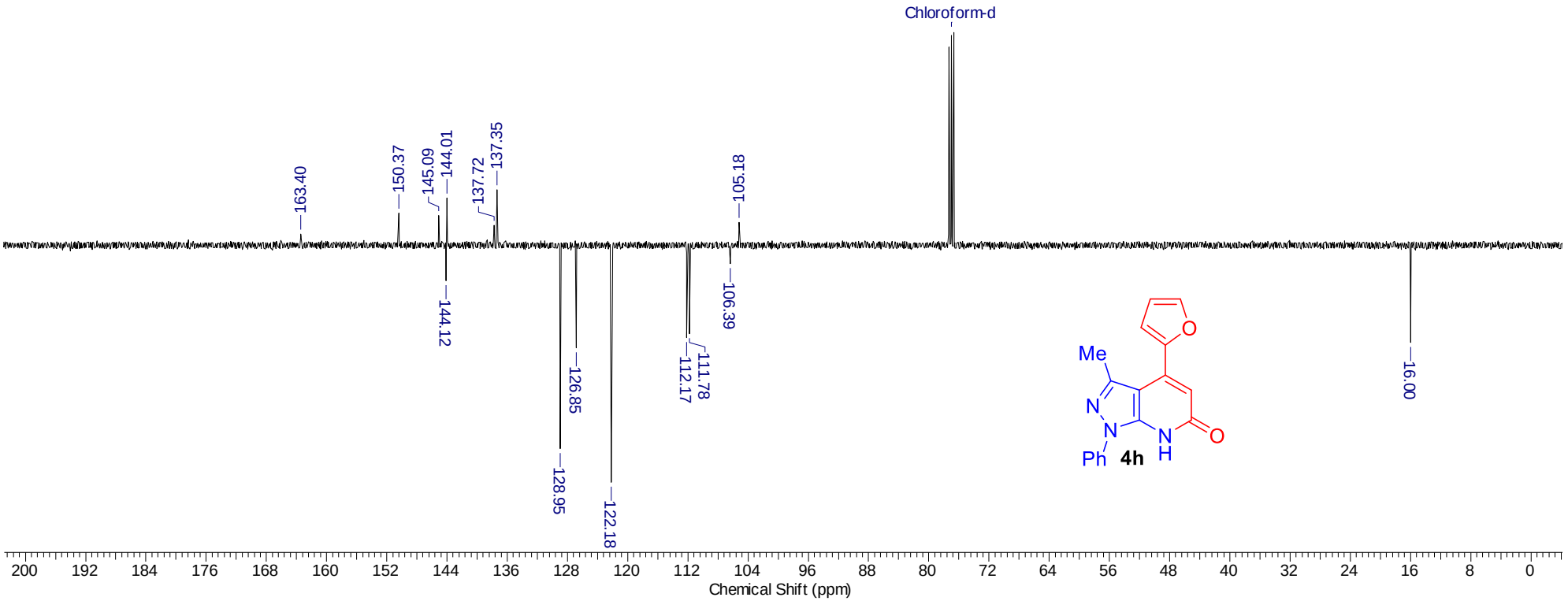

Figure S18: ^{13}C NMR spectrum of compound **4h** ($CDCl_3$).

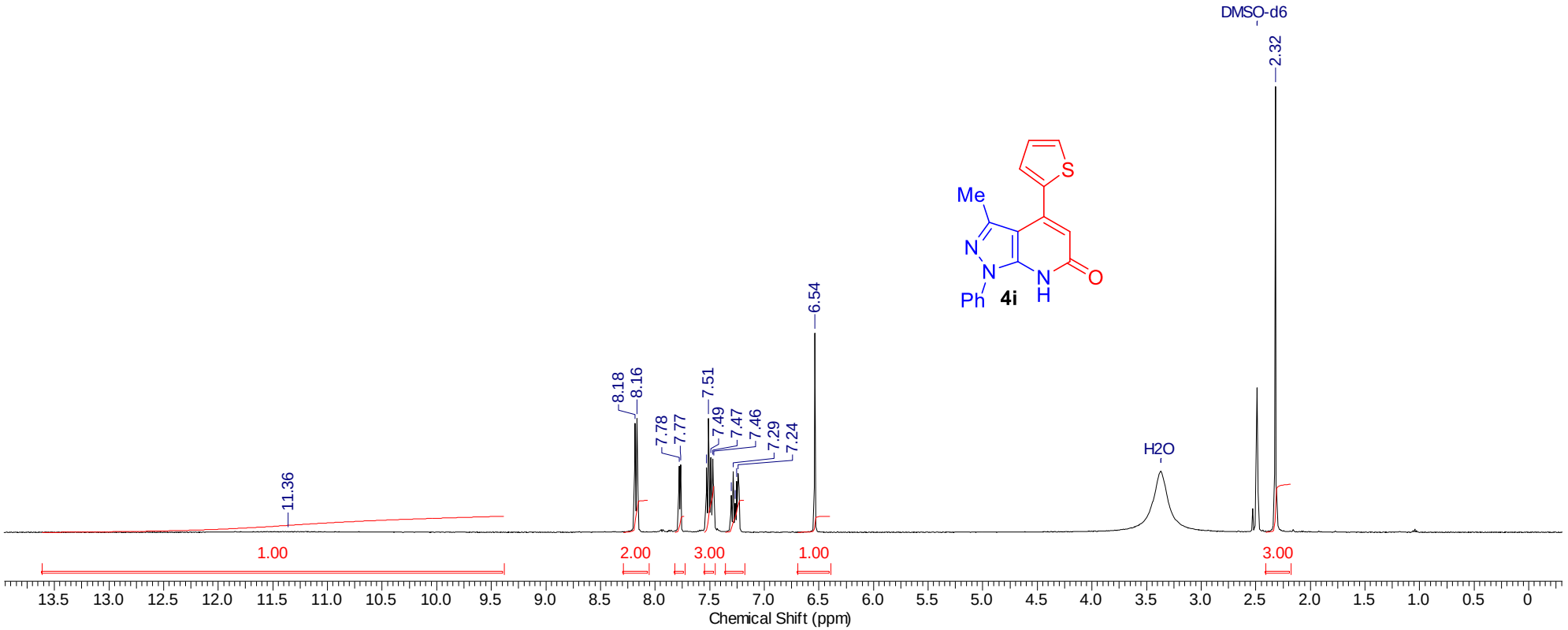

Figure S19: ^{13}C NMR spectrum of compound **4i** (DMSO-d_6).

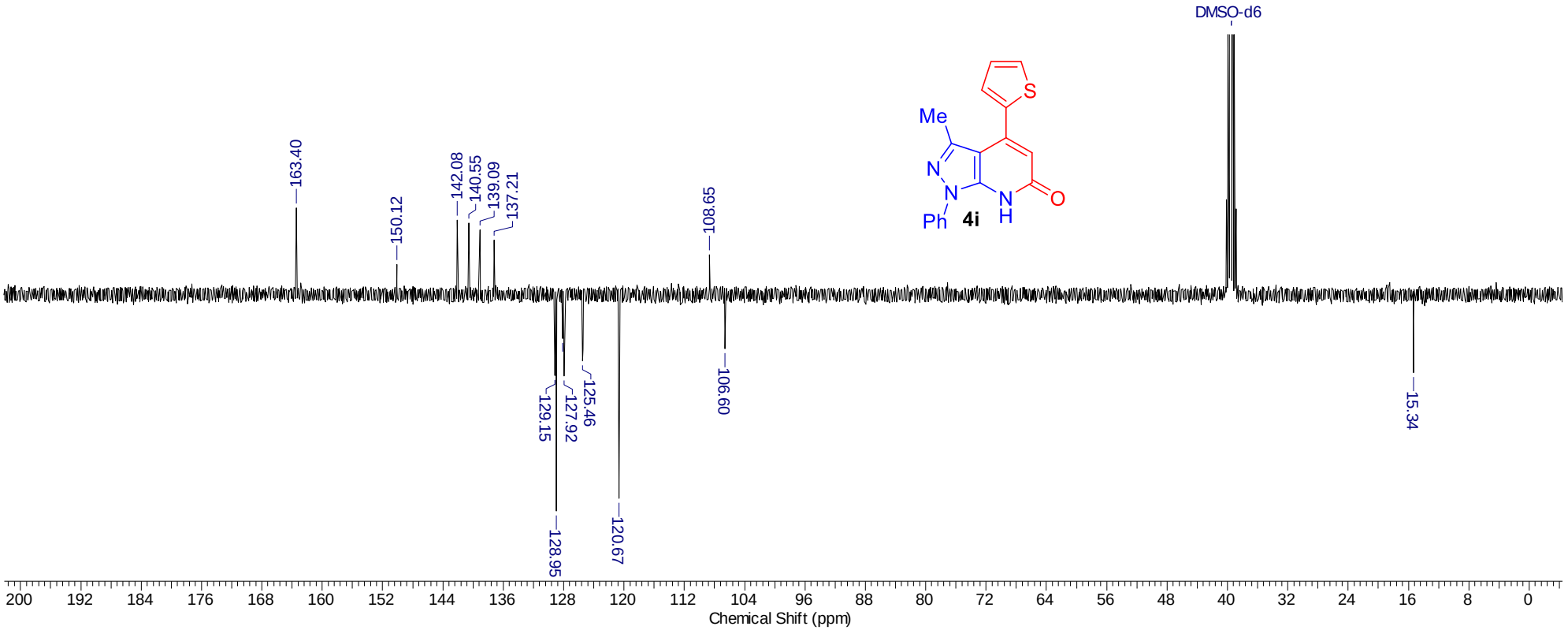

Figure S20: ^{13}C NMR spectrum of compound **4i** (DMSO-d_6).