Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.
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Copper-Catalyzed Aerobic Annulation of Hydrazones with Dienones: An Efficient Route to Pyrazole-Linked Hybrid Molecules

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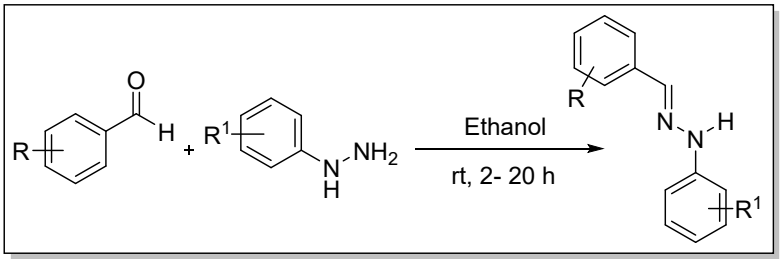
1. General information and procedures

Unless otherwise stated, all the reactions were carried out in a 25 mL round bottom flask. All the reagents were bought from commercial suppliers and used without additional purification. The crude reaction mixture was purified with silica gel (100-200 mesh) column chromatography using a petroleum ether-ethyl acetate solvent mixture as the eluent. The isolated compounds were characterized by ^{1}H and ^{13}C NMR spectroscopy, Infrared spectroscopy, and High-Resolution Mass spectrometry (HRMS). Melting points of the solid samples were determined using the Stuart melting point apparatus. Other characterizations such as ^{1}H NMR (400 MHz) and ^{13}C NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 on Bruker Ascend^{TM} 400 MHz / JEOL JNM-ECZ-400s spectrometer with tetramethyl silane (TMS; δ H=0 ppm) as an internal standard and chemical shifts were reported in ppm relative to TMS. The resonance multiplicity is described as s (singlet), d (doublet), t (triplet), m (multiplate), dd (doublet of doublets), and q (quartet). Fourier transform infrared (FTIR) spectra were recorded using ATR technique on a Bruker Alpha 400 FTIR spectrometer equipped with silicon carbide as an IR source and only intense peaks were reported. HRMS were recorded on a Waters-Xevo G2-XS-QtoF and The ACQUITY^{TM} UPLC^{TM} H-Class PLUS Bio system mass spectrometer using the ESI method with an orbitrap mass analyzer.

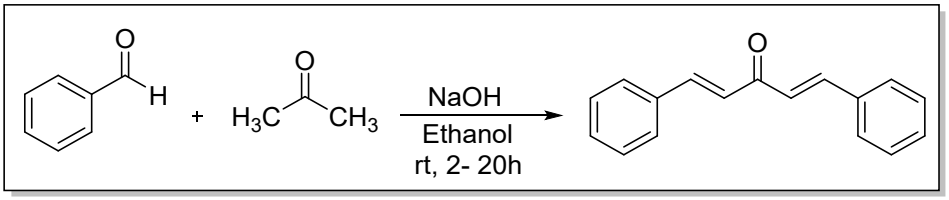
1.1 General procedure for the synthesis of hydrazones[S1]



In ethanol (10 mL), Phenyl hydrazine (1.08 g, 1 equiv) was stirred in a round bottom flask at room temperature. To the stirring solution, the corresponding aldehyde (1.06 g, 10 mmol) was added (solid aldehyde was added portion-wise and liquid aldehyde dropwise) and stirred the mixture for about 8- 20 hours (depending on the electronic nature of aldehydes). The progress of the reaction was monitored by TLC. After the completion of the reaction, the mixture was poured into ice-cold water. The precipitate formed was filtered off and washed with ice-cold water, followed by a pet ether. The solid mass obtained was dissolved in

dichloromethane and dried using Na_2SO_4. The solvent was evaporated under a vacuum, and the obtained product was used for all other reactions.

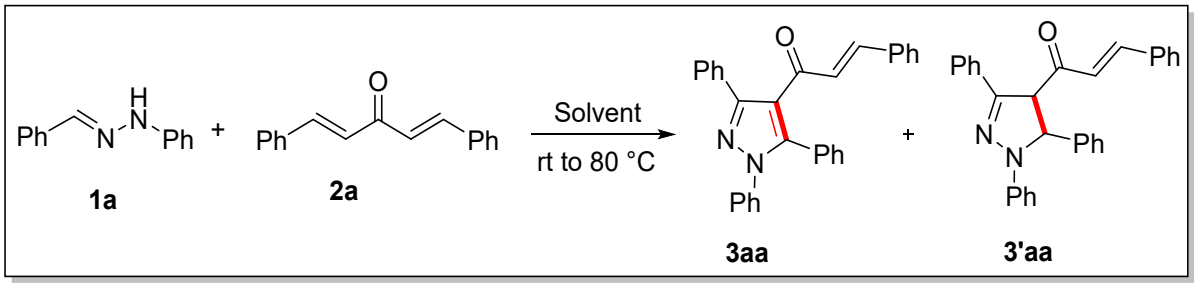
1.2 General procedure for the synthesis of dibenzylidene acetone derivatives [S2]



NaOH (2.0 g, 5 equiv.) in 10 mL water was added dropwise to 20 mL of ethanol in a round bottom flask at 0 - 5 °C followed by the corresponding aldehyde (2.12g, 2 equiv.) (solid aldehyde was added portion-wise and liquid aldehyde dropwise) and stirred for about 15- 20 minutes. Acetone (0.58 g, 10 mmol) was then added, allowing the reaction to reach room temperature slowly. The progress of the reaction was monitored by TLC. After the completion of the reaction, the mixture was poured into ice-cold water. The precipitate formed was filtered off and washed with ice-cold water. The solid mass obtained was dissolved in dichloromethane and dried using Na_2SO_4. The solvent was evaporated under a vacuum, and the obtained product was used for the reaction. The same method is used to prepare other derivatives as well.

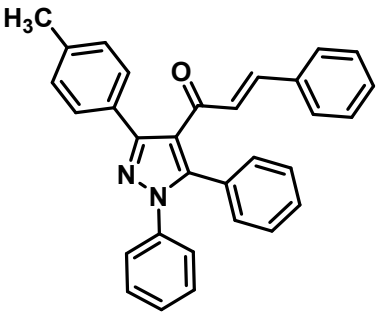
1.3 General procedure for the synthesis of pyrazolyl vinyl ketones derivatives

To an 25 mL round bottom flask equipped with a magnetic stirrer, 1-benzylidene-2-phenylhydrazine, **1a** (0.6 mmol, 1.2 equiv.), 1,5-diphenylpenta-1,4-dien-3-one **2a** (0.5 mmol, 1.0 equiv.) and $CuCl_2 \cdot 2H_2O$ (0.25 mmol, 0.5 equiv.) were weighed and added and followed by 5 mL of 1,2-dichloroethane solvent. The reaction vessel was stirred in an oil bath at 80 °C under oxygen atmosphere. The progress of the reaction was monitored by TLC. After 4h, the reaction predominantly yielded the dihydro pyrazole derivative, **3'aa** as shown below. After 8h, the TLC showed a mixture of both pyrazolyl vinyl ketones, **3aa** and the dihydro derivatives, **3'aa**. After 12 h, the reaction exclusively offered only the pyrazolyl vinyl ketone product, **3aa**. The reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with water. The organic layer was concentrated and the residue was purified by silica gel (100-200 mesh) column chromatography using petroleum ether-ethyl acetate (petroleum ether/ethyl acetate 9:1) as eluent.



1.4 Single Crystal X-ray Data of the Compound 3ca:

Compound 3ca:



CCDC Number: 2326718

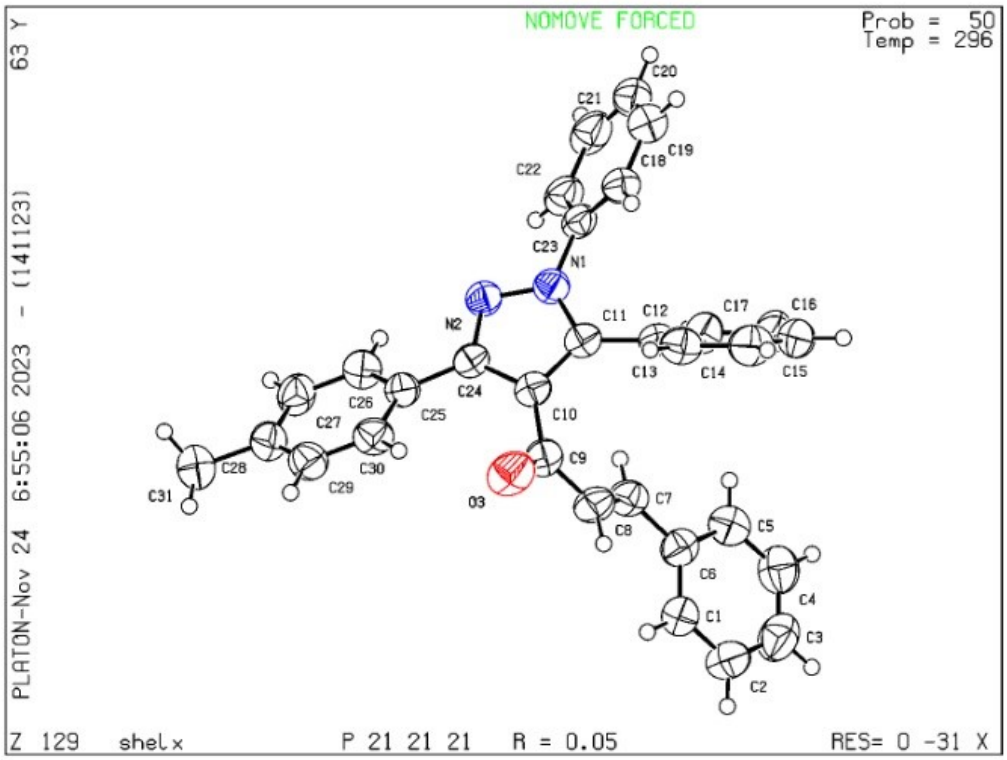


Figure S1

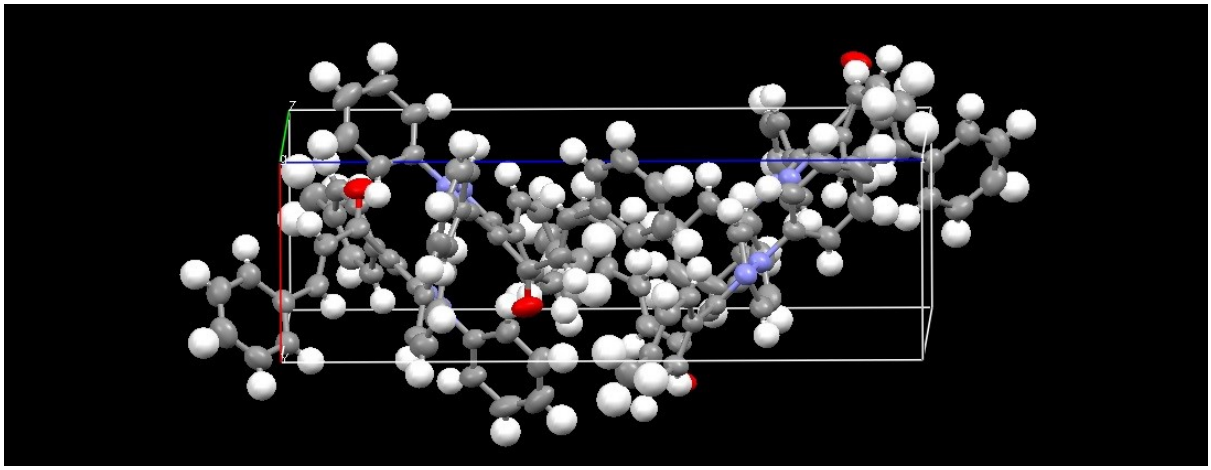


Figure S2

Crystal data and structure refinement for 3ca CCDC Number: 2326718

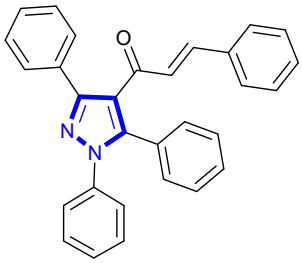
Table 1. Crystal data and structure refinement for 3ca ortho.

Table S1: Crystal Data and Refinement Parameters for **3ca**

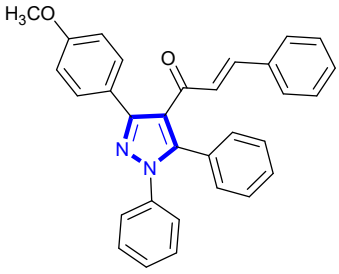
CCDC Deposition Number	**2326718**
Empirical formula	$C_{31}H_{24}N_2O$
Formula weight	440.52
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P 21 21 21
Unit cell dimensions	a = 6.1461(6) A alpha = 90°. b = 19.503(3) A beta = 90°. c = 19.670(2) A gamma = 90°.
Volume	2357.7(5) A^3
Z, Calculated density	4, 1.241 Mg/m^3
Absorption coefficient	0.075 mm^{-1}
F (000)	928
Crystal size	0.500 x 0.300 x 0.200 mm
Theta range for data collection	1.470 to 28.483°.
Limiting indices	-7<=h<=8, -26<=k<=26, -26<=l<=26
Reflections collected / unique	29374 / 5904 [R(int) = 0.0596]
Completeness to theta = 25.242	99.8 %

Absorption correction	Semi-empirical from equivalents
Max. and min. transmission	0.985 and 0.963
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5904 / 0 / 308
Goodness-of-fit on F^2	0.794
Final R indices [I>2sigma(I)]	R_1 = 0.0539, wR_2 = 0.1713
R indices (all data)	R_1 = 0.1232, wR_2 = 0.2488
Extinction coefficient	n/a
Largest diff. peak and hole	0.157 and -0.156 e.A^{-3}

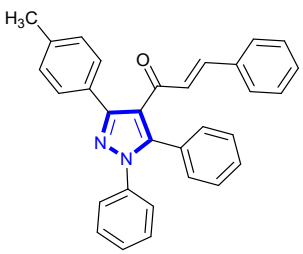
1.5 Characterization data of compounds



3-phenyl-1-(1,3,5-triphenyl-1*H*-pyrazol-4-yl)prop-2-en-1-one (3aa): Yield: 159.8 mg, 75%; white solid; mp: 204-206 °C; FT-IR (ATR) ν_{max} 2923, 1659, 1598, 1490, 1450, 1419, 1067 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.76-7.74 (m, 2H), 7.47 (d, J = 15.9Hz, 1H), 7.44-7.37 (m, 3H), 7.36-7.32 (m, 5H), 7.32-7.30 (m, 4H), 7.29-7.25 (m, 3H), 7.23-7.20 (m, 1H), 7.13-7.10 (m, 2H), 6.60 (d, J = 15.8Hz, 1H); $^{13}C\{1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.2, 152.6, 145.1, 143.2, 139.3, 134.8, 132.8, 130.6, 130.2, 129.5, 129.3, 129.1, 129.0, 128.8, 128.7, 128.6, 128.5, 128.2, 128.0, 127.1, 125.6, 121.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{23}N_2O$ 427.1805; found 427.1825.

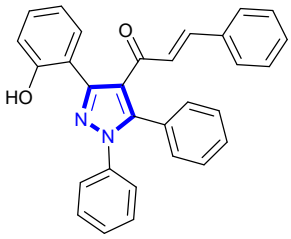


1-(3-(4-methoxyphenyl)-1,5-diphenyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3ba): Yield: 187.2 mg, 82%; white solid; mp: 155-157 °C; FT-IR (ATR) ν_{max} = 2923, 2854, 1737, 1656, 1603, 1494, 1446, 1252 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72-7.68 (m, 2H), 7.48 (d, J = 15.9Hz, 1H), 7.34-7.32 (m, 4H), 7.31-7.28(m, 5H), 7.26-7.23 (m, 4H), 7.14-7.12 (m, 2H), 6.97-6.94 (m, 2H), 6.61 (d, J = 15.8Hz, 1H), 3.82 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.3, 160.1, 152.3, 145.0, 143.0, 139.3, 134.9, 130.5, 130.4, 130.2, 129.6, 129.3, 129.0, 128.8, 128.6, 128.3, 128.0, 127.1, 125.5, 125.2, 121.3, 114.0, 55.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{31}H_{25}N_2O_2$ 457.1911; found 457.1908.

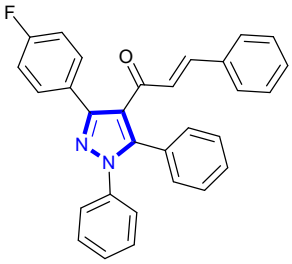


1-(1,5-diphenyl-3-(p-tolyl)-1*H*-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3ca): Yield: 190.8 mg, 86%; white solid; mp: 162-164 °C; FT-IR (ATR) ν_{max} = 2923, 2857, 1658, 1599, 1532, 1491, 1440, 1026 cm^{-1}; ^1H NMR (400

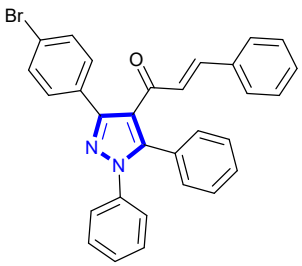
MHz, $CDCl_3$) δ 7.64 (d, J = 8.1Hz, 2H), 7.47 (d, J = 15.8Hz, 1H), 7.34-7.32 (m, 4H), 7.31-7.30 (m, 4H), 7.29-7.27 (m, 2H), 7.26-7.23 (m, 5H), 7.14-7.11 (m, 2H), 6.60 (d, J = 15.7Hz, 1H), 2.37(s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.3, 152.6, 145.0, 143.0, 139.3, 138.5, 135.0, 130.5, 130.2, 129.8, 129.6, 129.3, 129.2, 129.0, 128.9, 128.8, 128.6, 128.3, 128.0, 127.1, 125.6, 121.4, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{31}H_{25}N_2O$ 441.1961; found 441.1962.



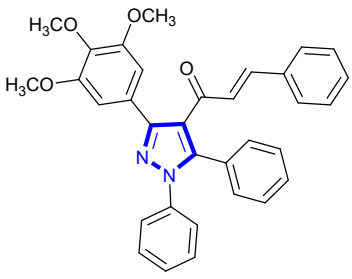
1-(3-(2-hydroxyphenyl)-1,5-diphenyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3da): Yield: 175.2 mg, 79%; white solid; mp: 205-207 °C; FT-IR (ATR) ν_{max} = 3068, 2919, 2853, 1623, 1495, 1288, 978, 759 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 10.32 (s, 1H), 7.57-7.55 (m, 1H), 7.52 (d, J = 16.2Hz, 1H), 7.39-7.36 (m, 7H), 7,34-7.32 (m, 5H), 7.31-7.30 (m, 3H), 7.26-7.25 (m, 1H), 7.11 (d, J = 8.1Hz, 1H), 6.89 (t, J = 7.4Hz, 1H), 6.73 (d, J = 16Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.3, 156.0, 149.7, 145.0, 144.1, 138.6, 134.4, 130.6, 130.2, 129.6, 129.5, 129.1, 128.8, 128.7, 128.4, 128.2, 127.4, 125.1, 121.2, 119.6, 117.5, 116.4, 96.1; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{23}N_2O_2$ 443.1754; found 443.1752.



1-(3-(4-fluorophenyl)-1,5-diphenyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3ea): Yield: 149.1 mg, 67%; white solid; mp: 186-188 °C; FT-IR (ATR) ν_{max} = 2922, 2852, 1659, 1599, 1526, 1442, 1228, 980 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.78-7.52 (m, 2H), 7.47 (d, J = 15.8Hz, 1H), 7.37-7.32 (m, 5H), 7.31-7.28 (m, 5H), 7.27-7.22 (m, 3H), 7.13-7.08 (m,4H), 6.57 (d, J = 15.7Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.0, 163.1 (d, $J_{C\text{-}F}$ = 246.2Hz), 151.7, 145.1, 143.4, 139.2, 134.7, 130.9 (d, $J_{C\text{-}F}$ = 8.2Hz), 130.5, 130.4, 129.4, 128.8, 128.7, 128.2, 128.1, 126.9, 125.5, 121.4, 115.4 (d, $J_{C\text{-}F}$ = 21.5Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{22}FN_2O$ 445.1711; found 445.1713.

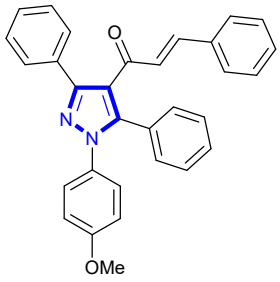


1-(3-(4-bromophenyl)-1,5-diphenyl-1*H*-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3fa): Yield: 176.2 mg, 69%; white solid; mp: 178-180 °C; FT-IR (ATR) ν_{max} = 3058, 2921, 2852, 1737, 1598, 1494, 1010, 696 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.61(s, 4H), 7.41-7.36 (m, 2H), 7.36-7.34 (m, 3H), 7.33-7.28 (m, 7H), 7.27-7.26 (m, 4H), 6.60 (d, J = 15.9Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 188.6, 150.3, 145.4, 144.3, 139.3, 134.7, 132.1, 131.9, 131.1, 130.9, 130.8, 129.9, 129.6, 129.4, 129.1, 128.9, 128.7, 127.4, 126.2, 122.4, 121.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{22}BrN_2O$ 505.0910; found 505.0914.

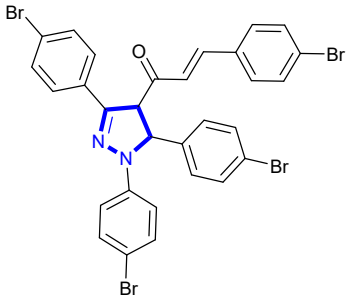


1-(1,5-diphenyl-3-(3,4,5-trimethoxyphenyl)-1H-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3ga): Yield: 196.3 mg, 76%; yellow solid; mp:

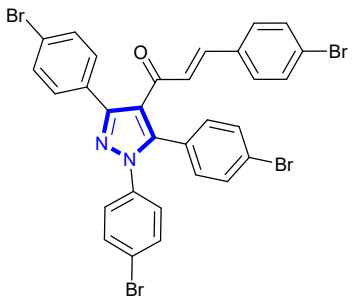
189-191 °C; FT-IR (ATR) ν_{max} = 2938, 2834, 1654, 1593, 1492, 1461, 1333, 1125 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.43 (d, J = 15.7Hz, 1H), 7.31-7.27 (m, 4H), 7.26-7.25 (m, 6H), 7.22-7.20 (m, 3H), 7.18-7.16 (m, 2H), 6.96 (s, 2H), 6.59(d, J = 15.7Hz, 1H), 3.79 (s, 3H), 3.78 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 188.0, 153.2, 152.3, 145.2, 142.8, 139.1, 138.5, 134.7, 130.4, 130.3, 129.3, 129.3, 128.9, 128.8, 128.5, 128.1, 128.0, 127.1, 125.5, 121.4, 106.5, 60.9, 56.29(2C); HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{33}H_{28}NaN_2O_4$ 539.1941; found 539.1965.



1-(1-(4-methoxyphenyl)-3,5-diphenyl-1H-pyrazol-4-yl)-3-phenylprop-2-en-1-one (3ha): Yield: 169.4 mg, 74%; yellow solid; mp: 178-180 °C; FT-IR (ATR) ν_{max} = 3060, 2955, 1659, 1634, 1599, 1511, 1484, 1249 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.67(d, J = 6.1Hz, 2H), 7.46-7.42 (m, 3H), 7.40 (s, 1H), 7.36 (s, 5H), 7.34-7.32 (m, 2H), 7.31-7.29 (m, 5H), 6.94 (d, J = 7.6Hz, 2H) 6.65 (d, J = 16.0Hz, 1H), 3.7(s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 189.6, 160.3, 152.0, 146.2, 144.9, 135.7, 134.0, 133.4, 132.0, 131.8, 130.68, 130.65, 130.4, 130.0, 129.9, 129.7, 128.7, 128.5, 121.9, 115.6, 56.9; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{31}H_{25}N_2O_2$ 457.1911; found 457.1923.

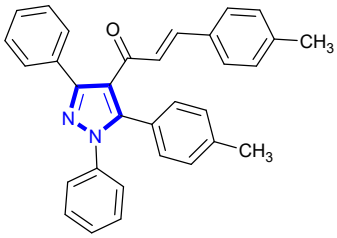


3-(4-bromophenyl)-1-((4S,5S)-1,3,5-tris(4-bromophenyl)-4,5-dihydro-1H-pyrazol-4-yl)prop-2-en-1-one (3'ie): Yield: 84.7 mg, 22%; yellow solid; mp: 216-218 °C; FT-IR (ATR): ν_{max} = 2921, 2856, 1729, 1679, 1594, 1099, 882, 704 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60 (d, J = 15.7Hz, 1H), 7.55-7.53 (m, 2H), 7.49-7.48 (m, 2H), 7.47-7.45 (m, 3H), 7.30-7.24 (m, 5H), 7.10 (d, J = 8.4Hz, 2H), 6.93 (d, J = 9.1Hz, 2H), 6.71 (d, J = 15.8Hz, 1H), 5.36 (d, J = 5.2Hz, 1H), 4.40 (d, J = 5.2Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 193.9, 145.6, 144.0, 142.1, 138.5, 132.8(2C), 132.6(2C), 132.4(2C), 132.1(2C), 130.4, 130.1(2C), 130.0, 129.1, 127.5(2C), 126.0, 123.5, 122.6, 121.9 115.3(2C), 112.6, 68.5, 67.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{21}Br_4N_2O$ 744.8341; found 744.8368.

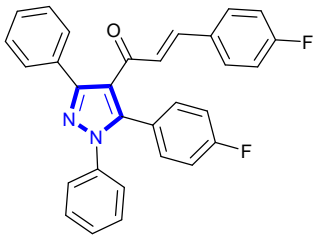


3-(4-bromophenyl)-1-(1,3,5-tris(4-bromophenyl)-1*H*-pyrazol-4-yl) prop-2-en-1-one (3ie): Yield: 237.8 mg, 64%; white solid; mp: 206-208 °C; FT-IR (ATR) ν_{max} = 2921, 2850, 1728, 1659, 1487, 1394, 1099, 823, 738, 701 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.60-7.53 (m, 4H), 7.51-7.46 (m, 4H), 7.42-7.37 (m, 3H), 7.20-7.14 (m, 4H), 7.00-6.97 (m, 2H), 6.50 (d, J = 15.7Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 187.2, 144.0, 142.4, 137.9, 133.4, 132.4, 132.3, 132.1, 132.0, 131.8, 131.3, 131.0, 130.6, 129.5, 127.7, 127.0, 126.8,

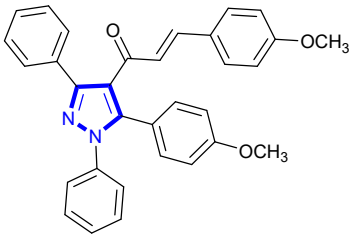
125.0, 124.4, 123.4, 122.4, 121.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{19}Br_4N_2O$ 742.8184; found 742.8202.



1-(1,3-diphenyl-5-(p-tolyl)-1*H*-pyrazol-4-yl)-3-(p-tolyl) prop-2-en-1-one (3ab): Yield: 154.0 mg, 69%; white solid; mp: 233-235 °C; FT-IR (ATR) ν_{max} = 2921, 2858, 1657, 1595, 1492, 1449, 1369, 974 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.66 (d, J = 8.1Hz, 2H), 7.44-7.41 (m, 4H), 7.39-7.35 (m, 5H), 7.23-7.18 (m, 5H), 7.16-7.11 (m, 3H), 6.58 (d, J = 16.0Hz, 1H), 2.27 (s, 6H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 188.7, 151.2, 145.0, 144.0, 141.9, 139.5, 139.4, 133.0, 132.0, 130.7, 130.0, 129.6, 129.5, 128.8, 128.7, 128.6, 126.6, 126.1, 121.2, 21.5, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{32}H_{27}N_2O$ $[M+H]^+$ 455.2118 found 455.2110.

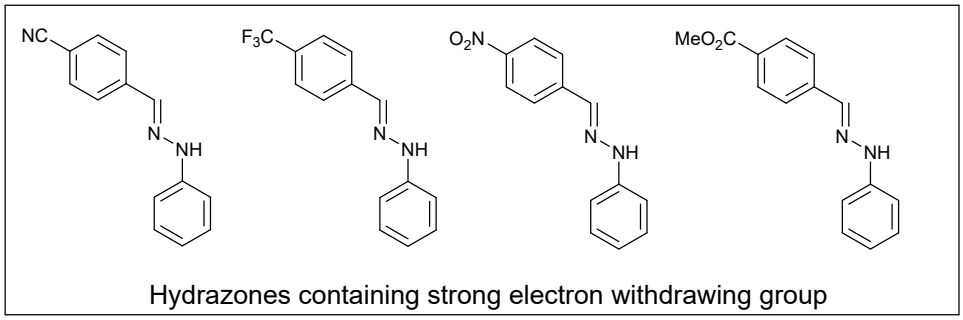


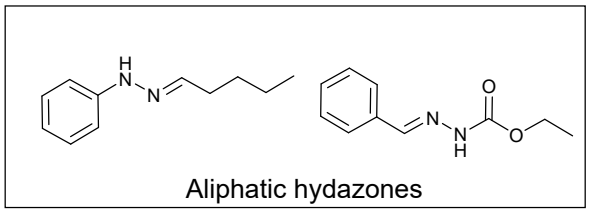
3-(4-fluorophenyl)-1-(5-(4-fluorophenyl)-1,3-diphenyl-1H-pyrazol-4-yl) prop-2-en-1-one (3ac): Yield: 150.1 mg, 65%; White solid; mp: 214-216 °C; FT-IR (ATR) ν_{max} = 2925, 2865, 1684, 1600, 1504, 1456, 1230, 1158, 839 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.65-7.63 (m, 2H), 7.44-7.40 (m, 5H), 7.39-7.37 (m, 5H), 7.36-7.33 (m, 3H), 7.20-7.12 (m, 4H), 6.63 (d, J = 16.0Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 189.0, 163.8 (d, $J_{C\text{-}F}$ = 248.2Hz), 162.9 (d, $J_{C\text{-}F}$ = 245.8Hz), 151.3, 143.3, 139.3, 133.3 (d, $J_{C\text{-}F}$ = 8.6Hz), 132.8, 131.3 (d, $J_{C\text{-}F}$ = 2.2Hz), 131.0 (d, $J_{C\text{-}F}$ = 8.6Hz), 129.6, 129.0, 128.8, 127.5, 126.2, 125.9 (d, $J_{C\text{-}F}$ = 2.7Hz), 121.3, 116.5 (d, $J_{C\text{-}F}$ = 21.5Hz), 116.0 (d, $J_{C\text{-}F}$ = 22.0Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{21}F_2N_2O$ $[M+H]^+$ 463.1616 found 463.1617.

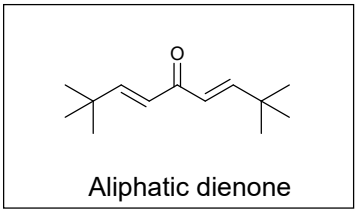


3-(4-methoxyphenyl)-1-(5-(4-methoxyphenyl)-1,3-diphenyl-1H-pyrazol-4-yl)prop-2-en-1-one (3ad): Yield: 174.8 mg, 74%; Yellow liquid; FT-IR (ATR) ν_{max} = 2935, 2837, 1656, 1591, 1509, 1451, 1293, 1172, 1029 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.67 (d, J = 8.2Hz, 2H), 7.45-7.36 (m, 9H), 7.31 (d, J = 8.7Hz, 2H), 7.26 (d, J = 8.2Hz, 2H), 6.92-6.86 (m, 4H), 6.56 (d, J = 15.8Hz, 1H), 3.75 (s, 3H), 3.71 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 189.0, 162.0, 160.1, 151.0, 145.0, 144.0, 139.5, 133.0, 132.1, 130.5, 129.4, 129.0, 128.8, 128.6, 128.5, 127.2, 126.0, 125.4, 121.4, 121.2, 115.0, 114.4, 55.8, 55.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{32}H_{27}N_2O_3$ $[M+H]^+$ 487.2016 found 487.2031.

Following hydrazones and dienones are failed to give the product under the optimized condition.

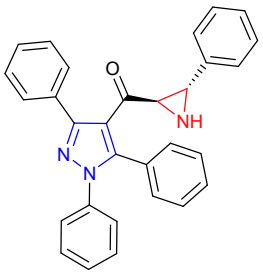




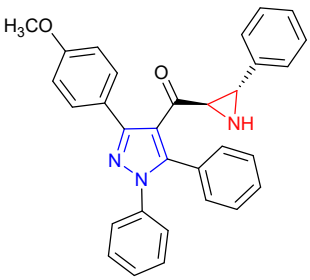


General procedure for the synthesis of pyrazole-linked Aziridines [S3]

To the solution of the appropriate pyrazolyl vinyl ketone (0.1 mmol) in ethanol (2 mL), hydroxylamine hydrochloride (0.2 mmol), and a solution of NaOH in water (0.5 mL, 2N, 10 equiv.) were added and heated up to 80°C for 5-6 h. Progress of the reaction was monitored by the TLC. After completion of the reaction, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with water. The organic layer was concentrated, and the residue was purified by silica gel (100-200 mesh) column chromatography using petroleum ether-ethyl acetate (petroleum ether/ethyl acetate 9:1) as eluent.

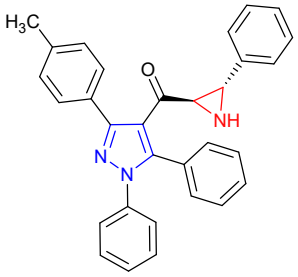


(3-phenylaziridin-2-yl)(1,3,5-triphenyl-1H-pyrazol-4-yl)methanone (4aa): Yield: 32.2 mg, 73%; liquid; FT-IR (ATR) ν_{max} = 3259, 3060, 2928, 1653, 1597, 1492, 1421, 1251, 1177 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) 7.67-7.63 (m, 2H), 7.36-7.34 (m, 3H), 7.32-7.29 (m, 7H), 7.22-7.18 (m, 3H), 7.14-7.08 (m, 3H), 6.98-6.93 (m, 2H), 3.02 (dd, J_1 = 9.3Hz, J_2 = 2.3Hz, 1H), 2.73-2.69 (m, 1H), 2.41 (dd, J_1 = 8.2Hz, J_2= 2.3Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.1, 152.2, 146.6, 139.0, 139.0, 138.9, 132.8, 130.6, 130.4, 129.5, 129.4, 129.0, 128.7, 128.5, 128.3, 127.7, 126.4, 126.2, 119.7, 47.4, 43.7; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{24}N_3O$ 442.1914 found; 442.1915.

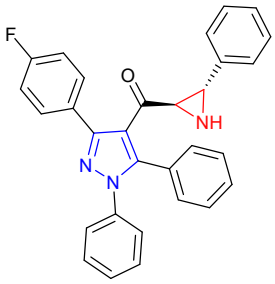


(3-(4-methoxyphenyl)-1,5-diphenyl-1H-pyrazol-4-yl)(3-phenylaziridin-2-yl)methanone (4ba): Yield: 37.2 mg, 75%; white solid; mp: 166-168 °C; FT-IR (ATR) ν_{max} = 3261, 3057, 3031, 1649, 1611, 1497, 1433, 1249, 1178 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.57 (d, J = 8.7Hz, 2H), 7.35-7.31 (m,

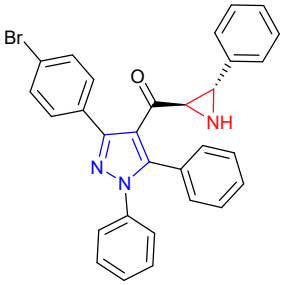
4H), 7.29-7.26 (m, 3H), 7.21-7.18 (m, 3H), 7.15-7.10 (m, 3H), 6.98-6.96 (m, 2H), 6.80 (d, J = 8.8Hz, 2H), 3.71 (s, 3H), 3.01 (dd, J_1 = 9.3Hz, J_2 = 2.2Hz, 1H), 2.69-2.64 (m, 1H), 2.42 (dd, J_1 = 8.2Hz, J_2 = 2.2Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.1, 159.9, 152.0, 146.5, 139.0, 139.0, 130.7, 130.6, 129.4, 129.3, 129.1, 128.7, 128.6, 128.3, 127.6, 126.4, 126.1, 124.9, 119.4, 113.4, 55.5, 47.7, 43.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{31}H_{26}N_3O_2$ 472.2020 found; 472.2036. (Note: D_2O exchange in ^1H NMR confirmed that the peak around 2.67 corresponds to NH and the larger coupling constant is due to CH/NH and the smaller one by CH/CH coupling)



(1,5-diphenyl-3-(p-tolyl)-1H-pyrazol-4-yl)(3-phenylaziridin-2-yl) methanone (4ca): Yield: 33.3 mg, 73%; white solid; mp: 160-162 °C; FT-IR (ATR) ν_{max} = 3260, 3031 2924, 1652, 1494, 1452, 1427, 1249, 978 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.52 (d, J = 8.1Hz, 2H), 7.38-7.33 (m, 4H), 7.32-7.29 (m, 3H), 7.22-7.20 (m, 3H), 7.15-7.13 (m, 3H), 7.06 (d, J = 8.0Hz, 2H), 6.96-6.94 (m 2H), 3.01 (dd, J_1 = 9.3Hz, J_2 = 2.3Hz, 1H), 2.72-2.67 (m, 1H), 2.41 (dd, J_1 = 8.2Hz, J_2 = 2.5Hz, 1H), 2.25 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.1, 152.3, 146.4, 139.0, 138.9, 138.3, 130.6, 129.8, 129.4, 129.3, 129.2, 129.1, 129.0, 128.8, 128.6, 128.3, 127.6, 126.4, 126.2, 119.6, 47.5, 43.6, 21.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{31}H_{26}N_3O$ 456.2070; found 456.2081.

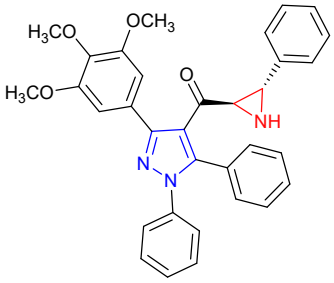


(3-(4-fluorophenyl)-1,5-diphenyl-1H-pyrazol-4-yl)(3-phenylaziridin-2-yl)methanone (4ea): Yield: 31.8 mg, 69%; Liquid; FT-IR (ATR) ν_{max} = 3261, 3057, 2922, 1652, 1599, 1496, 1451, 1433, 1227, 1055 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.71-7.67 (m, 2H), 7.38-7.28 (m, 8H), 7.22-7.19 (m, 2H), 7.10 (t, J = 6.7Hz, 5H), 6.95-6.91 (m, 2H), 3.01 (dd, J_1 = 9.3Hz, J_2 = 2.4Hz, 1H), 2.74-2.69 (m, 1H), 2.37 (dd, J_1 = 8.1Hz, J_2 = 2.3Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.0, 162.7 (d, $J_{C\text{-}F}$ = 243.9Hz), 151.4, 147.0, 139.0, 138.9, 131.6, 131.5, (d, $J_{C\text{-}F}$ = 7.9Hz), 131.0, 129.5, 129.4, 129.2 (d, $J_{C\text{-}F}$ = 3.6Hz), 128.9, 129.8 129.0 , 128.3, 128.0, 126.9 (d, $J_{C\text{-}F}$ = 21.6Hz), 47.4, 44.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{23}FN_3O$ 460.1820; found 460.1821.



(3-(4-bromophenyl)-1,5-diphenyl-1H-pyrazol-4-yl)(3-phenylaziridin-2-yl)methanone (4fa): Yield: 37.2 mg, 71%; white solid; mp: 128-130 °C; FT-IR (ATR) ν_{max} = 3258, 3061, 1655, 1597, 1495, 1449, 1429, 1265, 1072 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.4Hz, 2H), 7.36 (d, J = 8.5Hz, 2H), 7.29-7.25 (m, 4H), 7.22-7.18 (m, 7H), 7.10-7.07 (m, 2H), 6.92 (d, J = 6.1Hz, 2H), 2.97-2.94 (m, 1H), 2.51-2.50 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 190.8, 152.3, 149.0, 146.5, 138.8, 138.0, 131.4, 130.9, 130.2, 129.4, 129.0, 128.8, 128.7, 128.5, 128.3, 127.8,

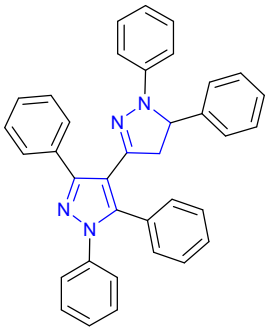
126.0, 125.4, 123.4, 119.6, 47.3, 44.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{30}H_{23}BrN_3O$ 520.1019; found 520.1025.



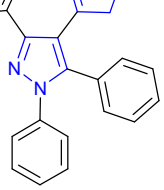
(1,5-diphenyl-3-(3,4,5-trimethoxyphenyl)-1H-pyrazol-4-yl)(3-phenylaziridin-2-yl)methanone (4ga): Yield: 42.1 mg, 79%; Yellow liquid; FT-IR(ATR): ν_{max} = 3259, 3061, 1655, 1597, 1495, 1449, 1429, 1265, 1072 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.39-7.36 (m, 4H), 7.33-7.31 (m, 5H), 7.22-7.20 (m, 2H), 7.16-7.15 (m, 2H), 6.98 (s, 2H), 6.96-6.93 (m, 2H), 3.84 (s, 6H), 3.71 (s, 3H), 3.04 (dd, J_1 = 9.4Hz, J_2 = 2.4Hz, 1H), 2.78-2.74 (m, 1H), 2.53-2.51 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 193.0, 153.3, 153.0, 152.1, 146.2, 139.0, 138.8, 138.3, 131.0, 129.5, 129.4, 128.91, 128.90, 128.7, 128.3, 128.2, 127.7, 126.3, 126.2, 120.0, 107.0, 61.0, 56.3(2C), 47.2, 44.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{33}H_{30}N_3O_4$ 532.2231; found 532.2206.

2. General procedure for the synthesis of pyrazole-linked pyrazolines [S4]

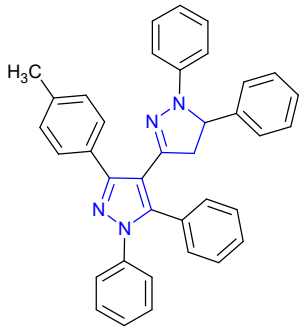
To the solution of the appropriate pyrazolyl vinyl ketone (0.1 mmol) in 2 mL of ethanol, aryl hydrazine (0.1 mmol) was added, and the reaction mixture was refluxed for 8-10h. The progress of the reaction was monitored by TLC. After completion of the reaction, the solid product separated in the reaction mixture was allowed to settle down, and the solvent was drained. The solid product was washed again with small amount of ethanol (2-3 times) and the solvent drained solid product was dried to get the final product. In case if the final product was not separated out as solid, the reaction mixture was poured into ice cold water with vigorous stirring and the precipitated product was filtered, washed with cold water and cold ethanol and dried.



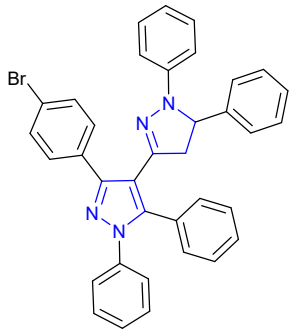
1,1',3',5,5'-pentaphenyl-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5aa): Yield: 36.2 mg, 70%; white solid; mp: 202-204 °C; FT-IR (ATR) ν_{max} = 3061, 2918, 1596, 1450, 1358, 1323, 1265, 1073 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.81-7.78 (m, 2H), 7.40-7.38 (m, 2H), 7.36-7.34 (m, 4H), 7.33-7.30 (m, 7H), 7.26-7.24 (m, 3H), 7.15-7.11 (m, 4H), 6.84 (d, J = 7.6Hz, 2H), 6.75 (t, J = 7.2Hz, 1H), 5.08 (dd, J_1 = 12.0Hz, J_2 = 5.8Hz, 1H), 3.30 (dd, J_1 = 17.5Hz, J_2 = 12.1Hz, 1H), 2.59 (dd, J_1 = 17.3Hz, J_2 = 5.7Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.3, 144.8, 142.6, 142.2, 141.5, 139.7, 133.0, 130.7, 129.7, 128.9, 128.9, 128.82, 128.75, 128.2, 127.4, 127.4, 125.8, 125.1, 118.6, 113.4, 113.0, 63.6, 46.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{36}H_{29}N_4$ 517.2387; found 517.2396.



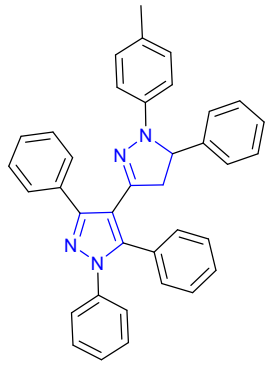
3'-(4-methoxyphenyl)-1,1',5,5'-tetraphenyl-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5ba): Yield: 42.3 mg, 78%; white solid; mp: 207-209 °C; FT-IR (ATR) ν_{max} = 2959, 2928, 1597, 1528, 1498, 1355, 1248, 1177 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.71-7.69 (m, 2H), 7.36-7.33 (m, 2H), 7.31-7.28 (m, 4H), 7.27-7.25 (m, 4H), 7.24-7.21 (m, 3H), 7.12-7.08 (m, 4H), 6.84-7.81 (m, 4H), 6.71 (t, J = 8.4Hz, 1H), 5.05 (dd, J_1 = 11.9Hz, J_2 = 5.8Hz, 1H), 3.80 (s, 3H), 3.26 (dd, J_1 = 17.4Hz, J_2 = 12.0Hz, 1H), 2.56 (dd, J_1 = 17.4Hz, J_2= 5.8Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 159.8, 151.2, 144.9, 142.7, 142.3, 141.8, 139.8, 130.8, 130.1, 129.9, 129.0, 128.9, 128.9, 128.8, 128.3, 127.4, 125.9, 125.6, 125.2, 118.7, 113.7, 113.2, 113.1, 63.6, 55.3, 46.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{37}H_{31}N_4O$ 547.2492; found 547.2491.



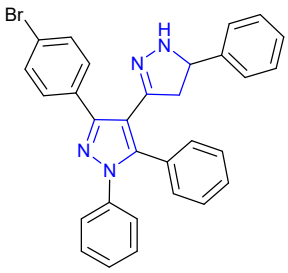
1,1',5,5'-tetraphenyl-3'-(p-tolyl)-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5ca): Yield: 39.2 mg, 74%; white solid; mp: 225-227 °C; FT-IR (ATR) ν_{max} = 3061, 2917, 1597, 1499, 1357, 1266, 1180, 746 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.70 (d, J = 8.0Hz, 2H), 7.41-7.38 (m, 1H), 7.33-7.30 (m, 6H), 7.29-7.25 (m, 6H), 7.17-7.12 (m, 6H), 6.86 (d, J = 8.2Hz, 2H), 6.76 (t, J = 7.2Hz, 1H), 5.08 (dd, J_1 = 12.0Hz, J_2 = 5.8Hz, 1H), 3.32 (dd, J_1 = 17.5Hz, J_2= 12.0Hz, 1H), 2.60 (dd, J_1 = 15.9Hz, J_2 = 5.8Hz, 1H) 2.39 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.4, 144.9, 142.6, 142.2, 141.7, 139.7, 138.0, 130.6, 130.1, 129.7, 128.94, 128.90, 128.85, 128.80, 128.7, 128.6, 128.2, 127.3, 125.9, 125.1, 118.6, 113.3, 113.0, 63.7, 46.3, 21.4; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{37}H_{31}N_4$ 531.2543; found 531.2548.



3'-(4-bromophenyl)-1,1',5,5'-tetraphenyl-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5fa): Yield: 42.1 mg, 71%; white solid; mp: 224-226 °C; FT-IR (ATR) ν_{max} = 3050, 2922, 1597, 1499, 1452, 1356, 743, 697 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.72 (d, J = 8.4Hz, 2H), 7.48 (d, J = 8.5Hz, 2H), 7.36-7.31 (m, 12H), 7.26-7.24 (m, 1H), 7.17-7.12 (m, 4H), 6.84 (d, J = 7.7Hz, 2H), 6.76 (t, J = 7.2Hz, 1H), 5.09 (dd, J_1 = 12.0Hz, J_2 = 5.7Hz, 1H), 3.27 (dd, J_1 = 17.4Hz, J_2 = 12.0Hz, 1H), 2.55 (dd, J_1 = 17.4Hz, J_2 = 5.8Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 150.1, 144.6, 142.9, 142.0, 141.1, 139.5, 132.0, 131.3, 130.6, 130.4, 129.5, 128.97, 128.94, 128.8, 128.3, 127.6, 127.5, 125.8, 125.1, 122.4, 118.8, 113.4, 113.0, 63.5, 46.2; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{36}H_{28}BrN_4$ 595.1492; found 595.1497.



1',3',5,5'-tetraphenyl-1-(p-tolyl)-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5ab): Yield: 36.3 mg, 68%; white solid; mp: 204-206 °C; FT-IR (ATR) ν_{max} = 2924, 2856, 1608, 1528, 1499, 1454, 1250, 1032 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.82-7.80 (m, 2H), 7.40-7.38 (m, 3H), 7.36-7.35 (m, 4H), 7.33-7.32 (m, 4H), 7.30-7.29 (m, 3H), 7.26-7.24 (m, 2H), 7.16-7.14 (m, 2H), 6.95 (d, J = 8.6Hz, 2H),

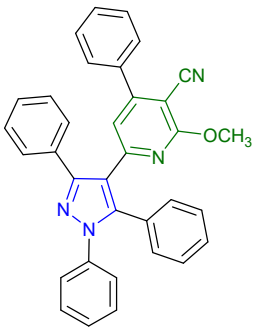


6.76 (d, J = 8.5Hz, 2H), 5.05 (dd, J_1 = 12.0Hz, J_2 = 6.2Hz, 1H), 3.28 (dd, J_1 = 17.3Hz, J_2 = 12.1Hz, 1H), 2.59 (dd, J_1 = 17.3Hz, J_2 = 6.2Hz, 1H), 2.23 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 151.3, 142.8, 142.6, 142.3, 141.0, 139.7, 133.1, 130.7, 129.8, 129.4, 128.9, 128.8, 128.7, 128.7, 128.2, 128.1, 127.9, 127.4, 127.3, 125.9, 125.1, 113.5, 113.1, 64.0, 46.2, 20.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{37}H_{31}N_4$ 531.2543; found 531.2554.

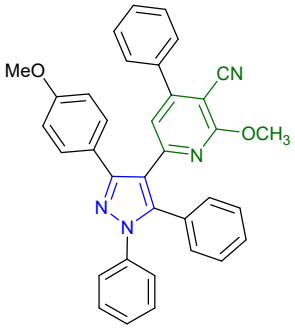
3'-(4-bromophenyl)-1',5,5'-triphenyl-4,5-dihydro-1*H*,1'*H*-3,4'-bipyrazole (5fc): Yield: 34.5 mg, 66%; white solid; mp: 180-182 °C; FT-IR (ATR) ν_{max} = 3384, 3068, 2928, 1667, 1596, 1447, 1122, 737 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.67 (d, J = 8.5Hz, 2H), 7.57 (d, J = 8.4Hz, 2H), 7.43 (s, 1H), 7.39-7.34 (m, 4H), 7.33-7.29 (m, 6H), 7.27-7.24 (m, 3H), 7.18 (d, J = 7.0Hz, 2H), 4.66 (t, J = 8.1Hz, 1H), 2.84-2.78 (m, 1H), 2.20-2.24 (m, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 150.0, 145.1, 142.9, 142.7, 139.5, 132.0, 131.4, 130.4, 130.1, 129.5, 128.9, 128.8, 128.7, 128.4, 127.6, 127.5, 125.9, 125.2, 122.4, 113.5, 63.7, 44.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{37}H_{24}BrN_4$ 519.1179; found 519.1171.

3. General procedure for the synthesis of pyrazole-linked pyridines [S5]

The pyrazolyl vinyl ketone (0.1 mmol) and sodium methoxide (1 equiv.) were taken in methanol (2 mL) in a 10 mL Schlenk tube. To this, malononitrile (1 mmol) was added dropwise with stirring for 3hr. The progress and completion of reaction was checked by TLC. The precipitated product was filtered, washed with cold water, dried and subjected to analysis.



2-methoxy-4-phenyl-6-(1,3,5-triphenyl-1*H*-pyrazol-4-yl)nicotinonitrile (6aa): Yield: 38.6 mg, 78%; yellow solid; mp: 106-108 °C; FT-IR (ATR) ν_{max} = 3072, 2947, 2222, 1671, 1583, 1545, 1360, 764 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.53 (d, J = 5.6Hz, 2H), 7.43-7.41 (m, 3H), 7.40-7.38 (m, 4H), 7.36-7.35 (m, 4H), 7.34-7.29 (m, 5H), 7.21 (d, J = 6.8Hz, 2H), 6.66 (s, 1H), 3.45 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 163.9, 154.6, 153.4, 150.7, 143.6, 138.9, 135.4, 132.8, 130.5, 130.0, 129.5, 128.8, 128.7, 128.6, 128.5, 128.3, 128.2, 128.0, 125.5, 118.4, 117.7, 117.5, 115.1, 91.9, 54.0; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{34}H_{25}N_4O$ 505.2023; found 505.2026.

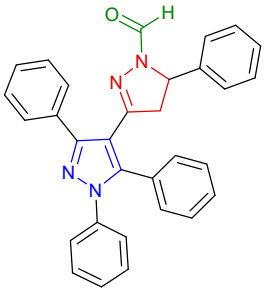


2-methoxy-6-(3-(4-methoxyphenyl)-1,5-diphenyl-1*H*-pyrazol-4-yl)-4 phenyl nicotinenitrile (6ba): Yield: 44.1 mg, 85%; yellow solid; mp: 172-174 °C; FT-IR (ATR) ν_{max} = 2950, 2924, 2222, 1584, 1534, 1498, 1360, 1250 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.53 (d, J = 8.7Hz, 2H), 7.40-7.35 (m, 5H), 7.33 (s, 1H), 7.31-7.30 (m, 4H), 7.29-7.26 (m, 2H), 7.24-7.22 (m, 3H), 6.95

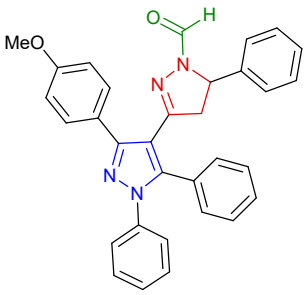
(d, J = 8.7Hz, 2H), 6.69 (s, 1H), 3.85 (s, 3H), 3.55 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 164.8, 159.9, 155.1, 154.0, 151.5, 143.4, 139.4, 136.0, 136.0, 130.6, 130.4, 130.4, 129.8, 128.9, 128.8, 128.7, 128.3, 127.7, 125.5, 125.4, 118.8, 118.2, 115.7, 113.9, 96.2, 91.6, 55.5, 54.3; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{35}H_{27}N_4O_2$ 535.2129; found 535.2126.

4. General procedure for the synthesis of pyrazole-linked pyrazoline carbamides [S6]

A mixture of pyrazolyl vinyl ketone (0.1 mmol), hydrazine hydrate (0.5 mmol), and formic acid (2 mL) were refluxed for 24 hours. The reaction was monitored by TLC continuously using an ethanol-pet ether solvent system. Upon completion of the reaction, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with $NaHCO_3$. The organic layer was concentrated, and the residue was purified by silica gel (100-200 mesh) column chromatography using petroleum ether-ethyl acetate (petroleum ether/ethyl acetate 8.5:1.5) as eluent.



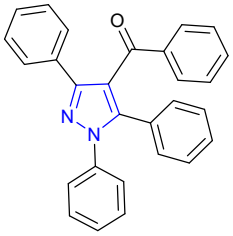
1',3',5,5'-tetraphenyl-4,5-dihydro-1*H*,1'*H*-[3,4'-bipyrazole]-1-carbaldehyde (7aa): Yield: 31.3 mg, 67%; Colourless liquid; FT-IR (ATR) ν_{max} = 2925, 2851, 1678, 1597, 1498, 1358, 1261, 1075 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.82 (s, 1H), 7.73-7.70 (m, 2H), 7.44-7.37 (m, 5H), 7.35-7.32 (m, 4H), 7.32-7.29 (m, 7H), 7.08-7.05 (m, 2H), 5.36 (dd, J_1 = 11.4Hz, J = 4.1Hz, 1H), 3.31-3.24 (m, 1H), 2.61 (dd, J_1 = 18.1Hz, J_2 = 4.1Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.0, 151.5, 150.4, 143.4, 140.2, 139.3, 132.4, 130.4, 129.3, 129.1, 128.92, 128.88, 128.63, 128.60, 128.4, 128.5, 127.9, 127.8, 125.5, 125.6, 111.8, 58.3, 45.6; HRMS (ESI-TOF) m/z: $[M+Na]^+$ calcd for $C_{31}H_{24}N_5NaO$ 491.1842; found 491.1854.



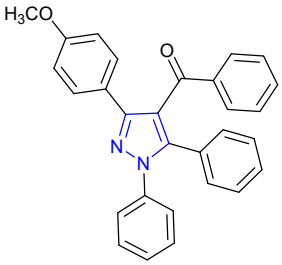
3'-(4-methoxyphenyl) -1',5,5'-triphenyl-4,5-dihydro-1*H*,1'*H*- [3,4'-bipyrazole] -1-carbaldehyde (7ba): Yield: 36.1 mg, 72%; Colourless liquid; FT-IR (ATR) ν_{max} = 2923, 2858, 1675, 1605, 1530, 1498, 1250, 1030 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 8.80 (s, 1H), 7.61 (d, J = 8.8Hz, 2H), 7.37-7.33 (m, 2H), 7.32-7.29 (m, 6H), 7.26-7.25 (m, 5H), 7.24-7.19 (m, 2H), 7.05-7.02 (m, 2H), 6.88-6.84 (m, 2H), 5.33 (dd, J_1 = 10.6Hz, J_2 = 4.1Hz, 1H), 3.81 (s, 3H), 3.27-3.20 (m, 1H), 2.57 (dd, J_1 = 18.0Hz, J_2 = 4.1Hz, 1H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 160.1, 160.0, 151.8, 151.3, 143.4, 140.3, 139.4, 130.5, 130.0, 129.3, 129.2, 129.0, 128.9, 128.5, 127.9, 127.8, 125.6, 125.2, 124.9, 113.9, 111.7, 58.3, 55.4, 45.6; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{32}H_{27}N_4O_2$ 499.2129; found 499.2128.

5. General procedure for the annulation of hydrazones with chalcones.

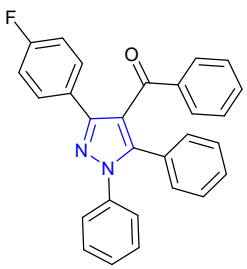
To an 25 mL round bottom flask equipped with a magnetic stirrer, 1-benzylidene-2-phenylhydrazine, **1a** (0.6 mmol, 1.2 equiv.), Chalcone **8a** (0.5 mmol, 1.0 equiv.) and $CuCl_2 \cdot 2H_2O$ (0.25 mmol, 0.5 equiv.) were weighed and added and followed by 5 mL of 1,2-dichloroethane solvent. The reaction vessel was stirred in an oil bath at 80 °C under oxygen atmosphere. The progress of the reaction was monitored by TLC. After the completion of the reaction, the reaction mixture was cooled to room temperature, diluted with ethyl acetate, and washed with water. The organic layer was concentrated and the residue was purified by silica gel (100-200 mesh) column chromatography using petroleum ether-ethyl acetate (petroleum ether/ethyl acetate 9:1) as eluent.



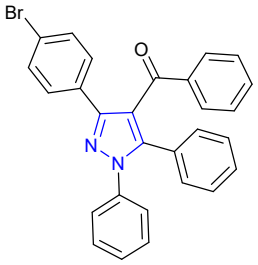
Phenyl(1,3,5-triphenyl-1H-pyrazol-4-yl) methanone (9aa): Yield: 131.9 mg, 66%; yellow liquid; FT-IR (ATR): ν_{max} = 3059, 1652, 1595, 1495, 1449, 1418, 1365, 1026 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$) δ 7.74-7.72 (m, 2H), 7.62-7.59 (m, 2H), 7.35-7.32 (m, 4H), 7.31-7.29 (m, 2H), 7.27-7.26 (m, 1H), 7.25-7.22 (m, 4H), 7.21-7.20 (m, 1H), 7.19-7.18 (m, 2H), 7.17-7.14 (m, 2H); $^{13}C\{^1H\}$ NMR (100 MHz, $CDCl_3$) δ 192.8, 152.0, 144.6, 139.3, 137.9, 132.9, 132.2, 130.1, 129.2, 129.0, 128.9, 128.4, 128.3, 128.1, 127.9, 125.5, 120.0 ppm; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{28}H_{21}N_2O$ 401.1648; found 401.1649.



(3-(4-methoxyphenyl)-1,5-diphenyl-1H-pyrazol-4-yl) (phenyl) methanone (9ba): Yield: 160.3 mg, 74%; yellow liquid; FT-IR (ATR): ν_{max} = 3060, 3036, 1653, 1596, 1493, 1449, 1167, 973 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.70 (d, J = 7.2Hz, 2H), 7.49 -7.44 (m, 3H), 7.41-7.36 (m, 5H), 7.30 (t, J = 7.7Hz, 2H), 7.23-7.16 (m, 5H), 6.89 (d, J = 8.7Hz, 2H), 3.72 (s, 3H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 192.7, 159.7, 150.4, 144.3, 139.4, 137.8, 133.7, 130.3, 129.8, 129.4, 129.3, 129.0, 128.9, 128.7, 128.5, 126.0, 124.8, 119.5, 114.3, 55.5; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{29}H_{23}N_2O_2$ 431.1754; found 431.1753.



(3-(4-fluorophenyl)-1,5-diphenyl-1H-pyrazol-4-yl)(phenyl)methanone (9ea): Yield: 126.0 mg, 60%; yellow liquid; FT-IR (ATR): ν_{max} = 3061, 1654, 1598, 1527, 1448, 1317, 1231, 1161 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 7.68 (d, J = 8.2Hz, 2H), 7.59-7.56 (m, 2H), 7.46-7.35 (m, 6H), 7.29 (t, J = 7.1Hz, 2H), 7.24-7.16 (m, 7H); $^{13}C\{^1H\}$ NMR (100 MHz, DMSO-d_6) δ 197.1, 167.2 (d, $J_{C\text{-}F}$ = 243.6Hz), 154.7, 149.4, 144.0, 142.5, 138.5, 135.1, 135.0 (d, $J_{C\text{-}F}$ = 8.6Hz), 134.6, 134.24, 134.22, 133.7 (d, $J_{C\text{-}F}$ = 3.2Hz), 133.63, 133.61, 133.4, 130.8, 124.4, 120.6 (d, $J_{C\text{-}F}$ = 21.6Hz); HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{28}H_{20}FN_2O$ 419.1554; found 419.1552.



(3-(4-bromophenyl)-1,5-diphenyl-1H-pyrazol-4-yl) (phenyl) methanone (9fa): Yield: 153.1 mg, 63%; yellow liquid; FT-IR (ATR): ν_{max} = 3059, 1654, 1598, 1497, 1363, 1230, 1197, 697 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 7.65 (d, *J* = 6.8Hz, 2H), 7.51-7.44 (m, 4H), 7.42-7.38 (m, 2H), 7.36-7.33 (m, 4H), 7.24 (t, *J* = 8.2Hz, 2H), 7.19-7.10 (m, 5H) ppm; $^{13}C\{^{1}H\}$ NMR (100 MHz, DMSO-d_6) δ 192.4, 149.8, 144.9, 139.3, 137.8, 133.9, 132.0, 131.7, 130.4, 130.1, 129.9, 129.5, 129.1, 128.9, 128.8, 128.8, 126.1, 122.2, 119.8; HRMS (ESI-TOF) m/z: $[M+H]^+$ calcd for $C_{28}H_{20}BrN_2O$ 479.0754; found 479.0748.

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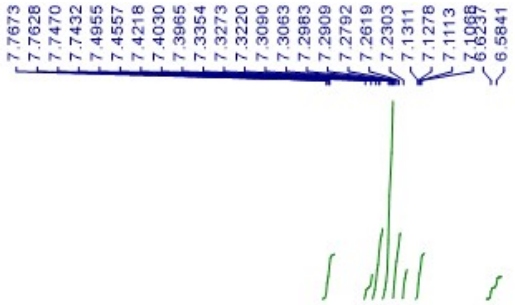
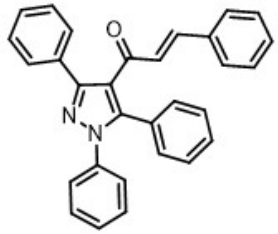
1.6. ^{1}H and ^{13}C $\{^{1}H\}$ NMR spectra of new compounds

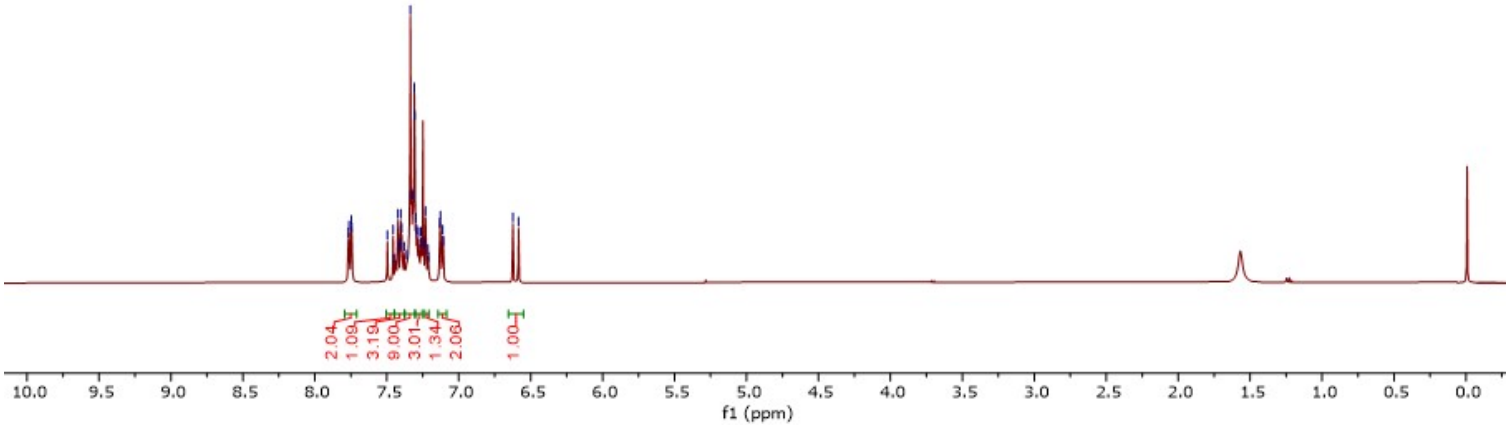
^{1}H NMR of compound 3aa in $CDCl_3$



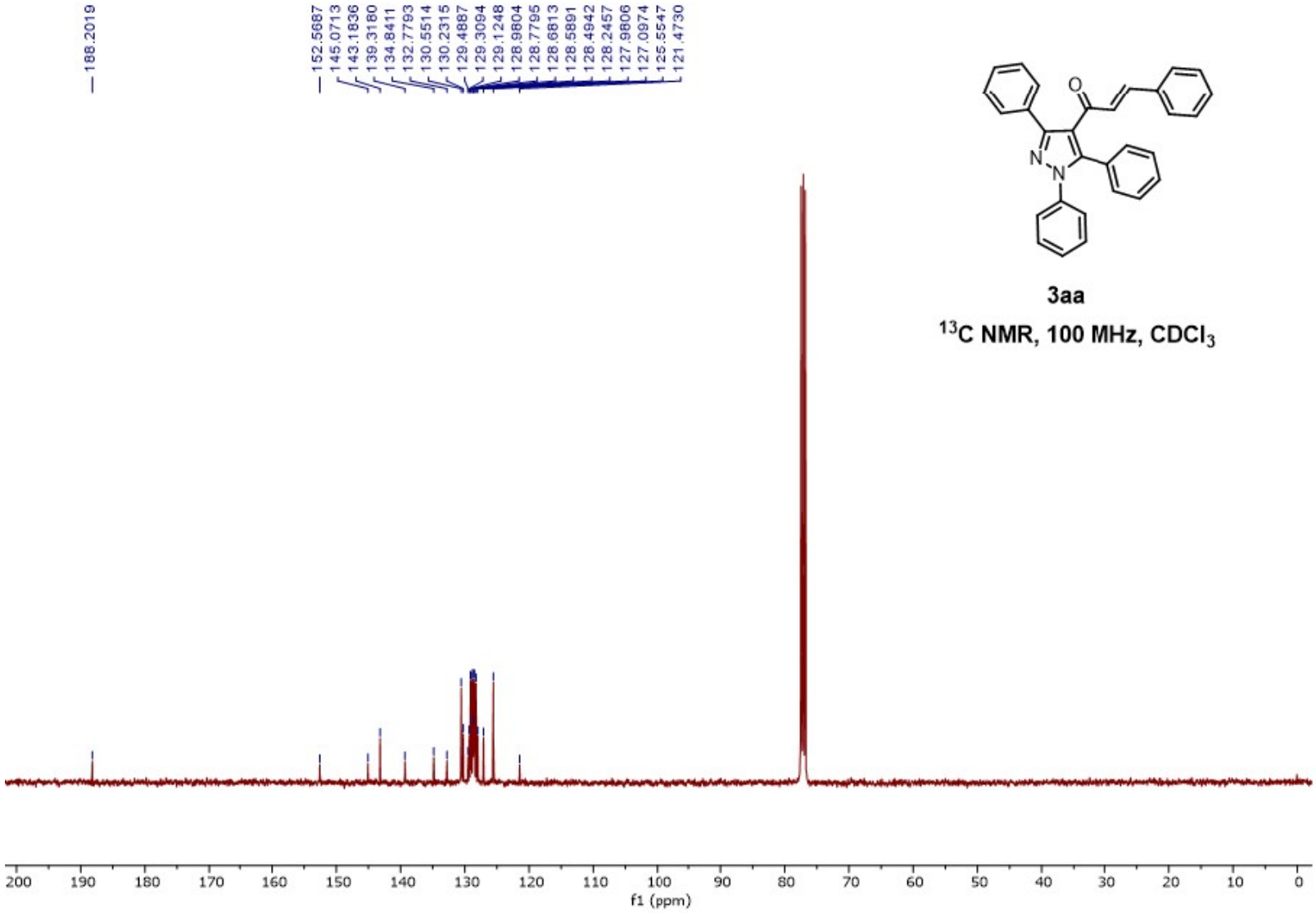


3aa

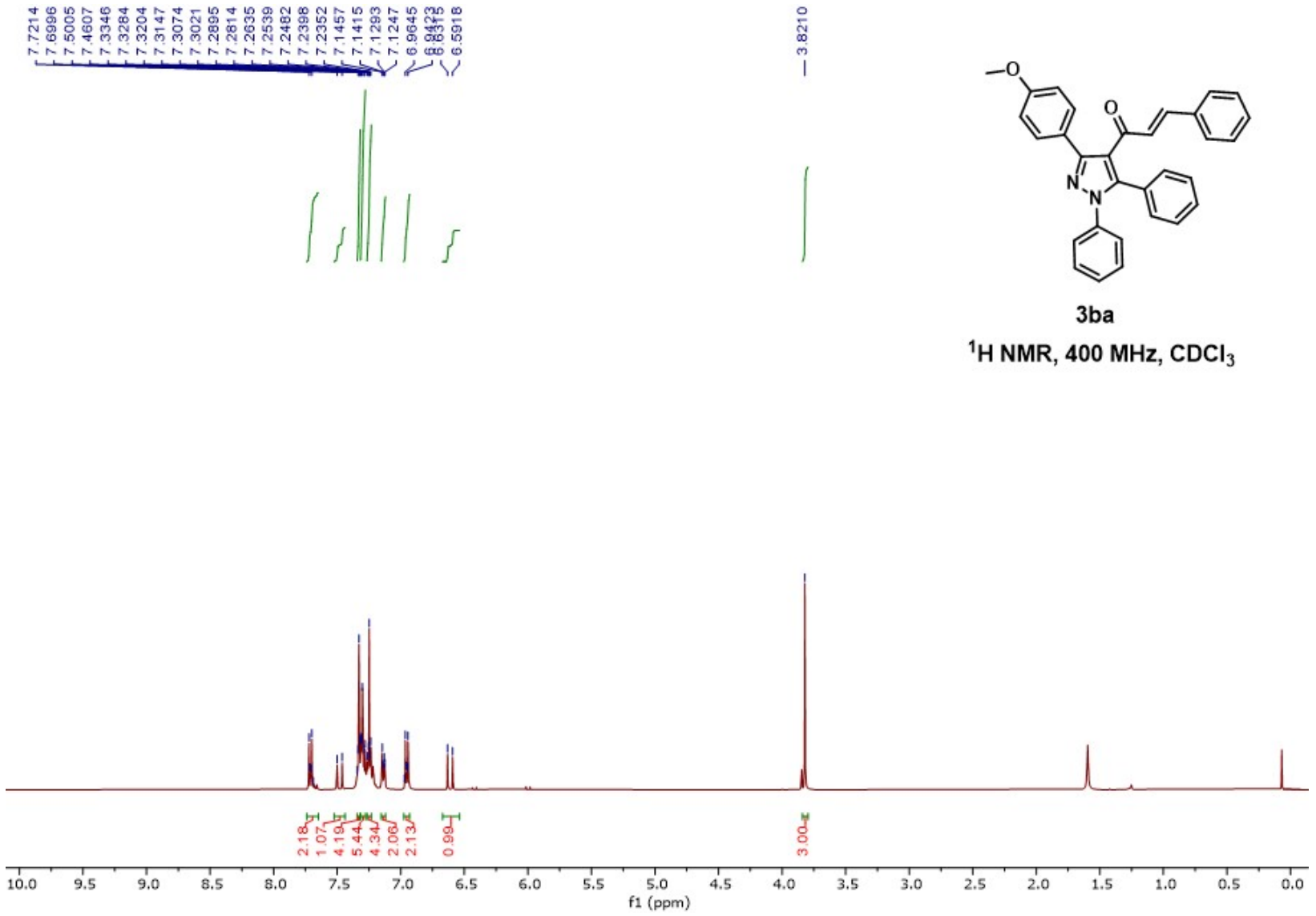
^{1}H NMR, 400 MHz, $CDCl_3$



$^{13}C\{^{1}H\}$ NMR of compound 3aa in $CDCl_3$



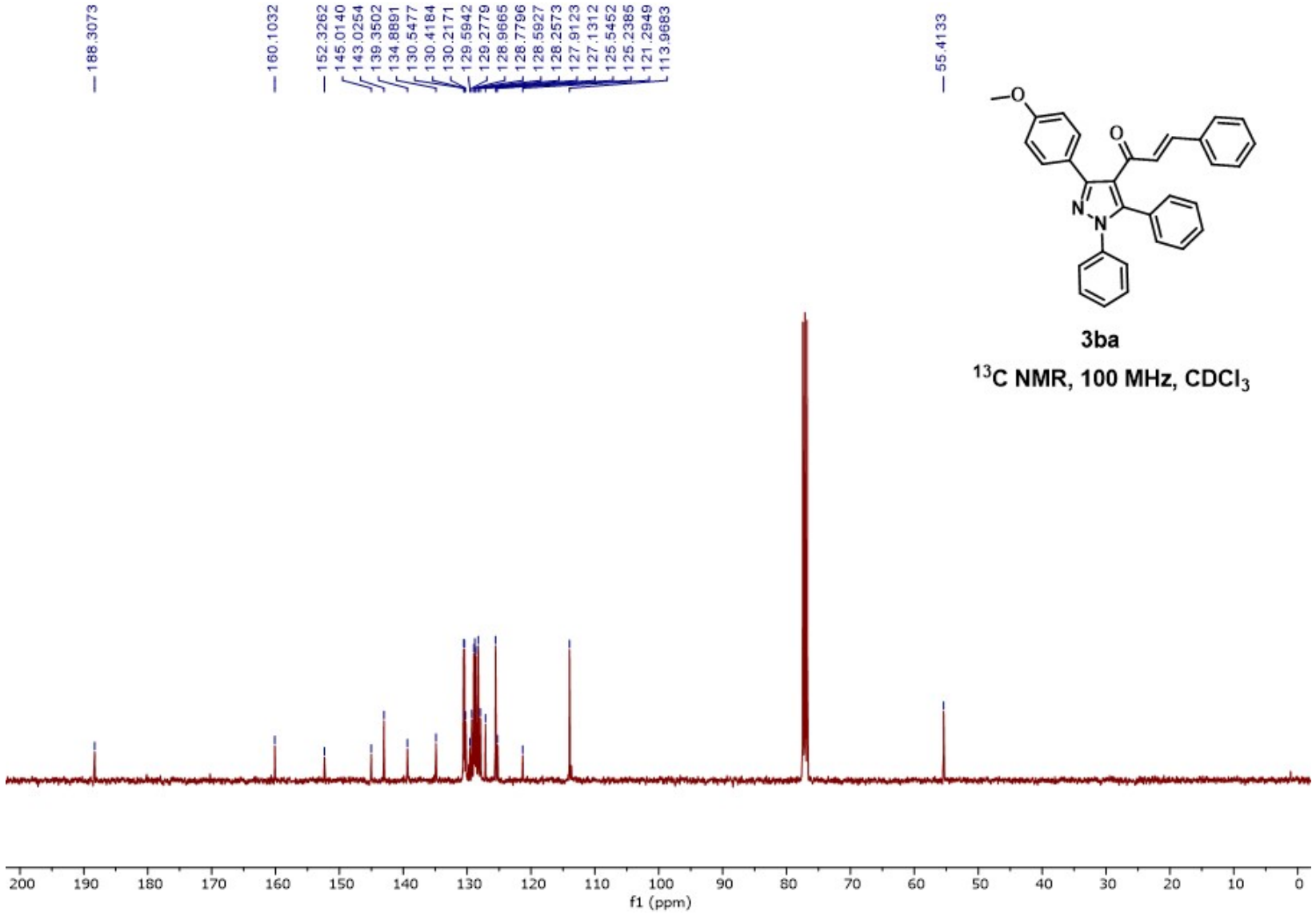
^{1}H NMR of compound 3ba in $CDCl_3$



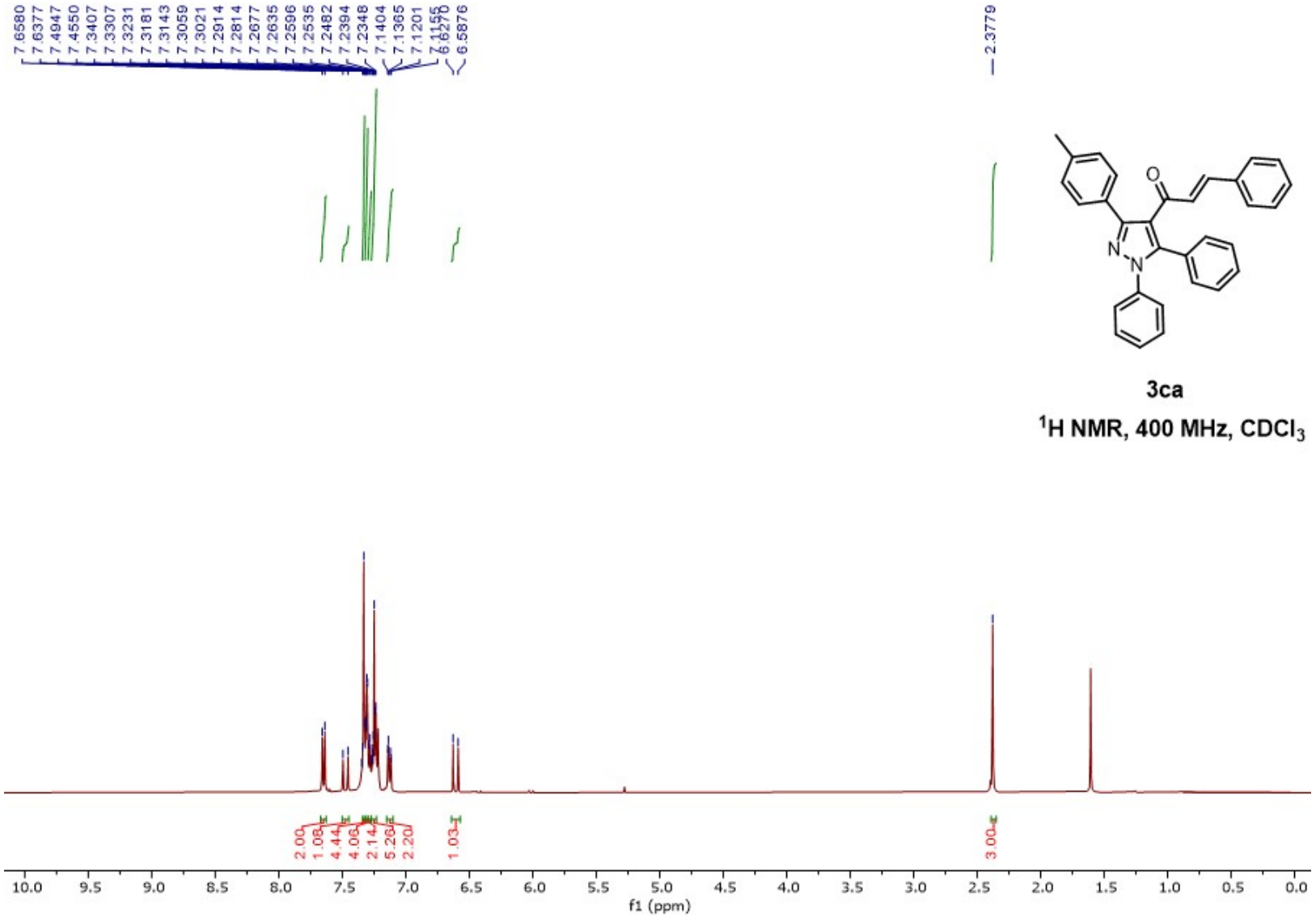
3ba

^{1}H NMR, 400 MHz, $CDCl_3$

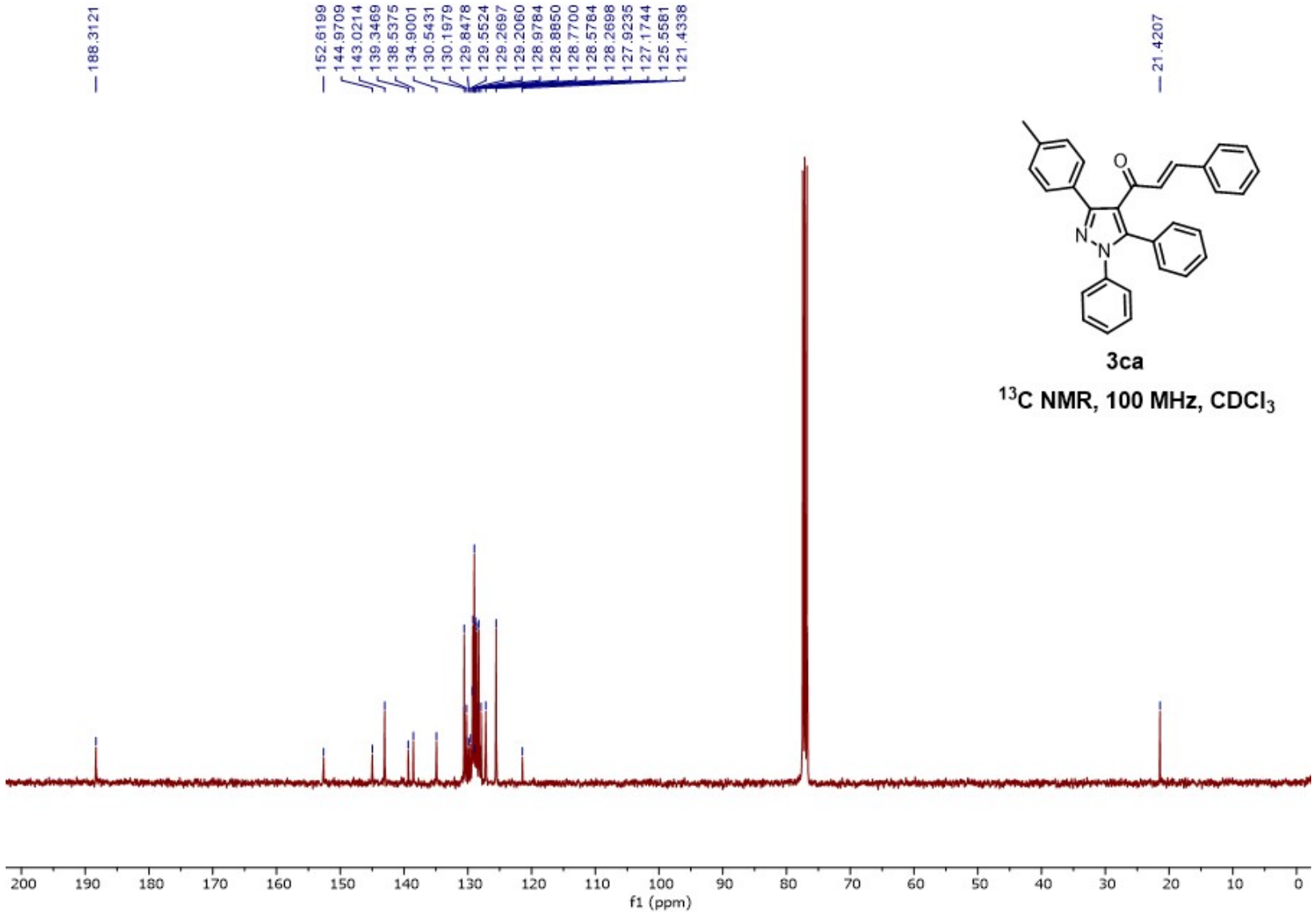
$^{13}C\{^{1}H\}$ NMR of compound 3ba in $CDCl_3$



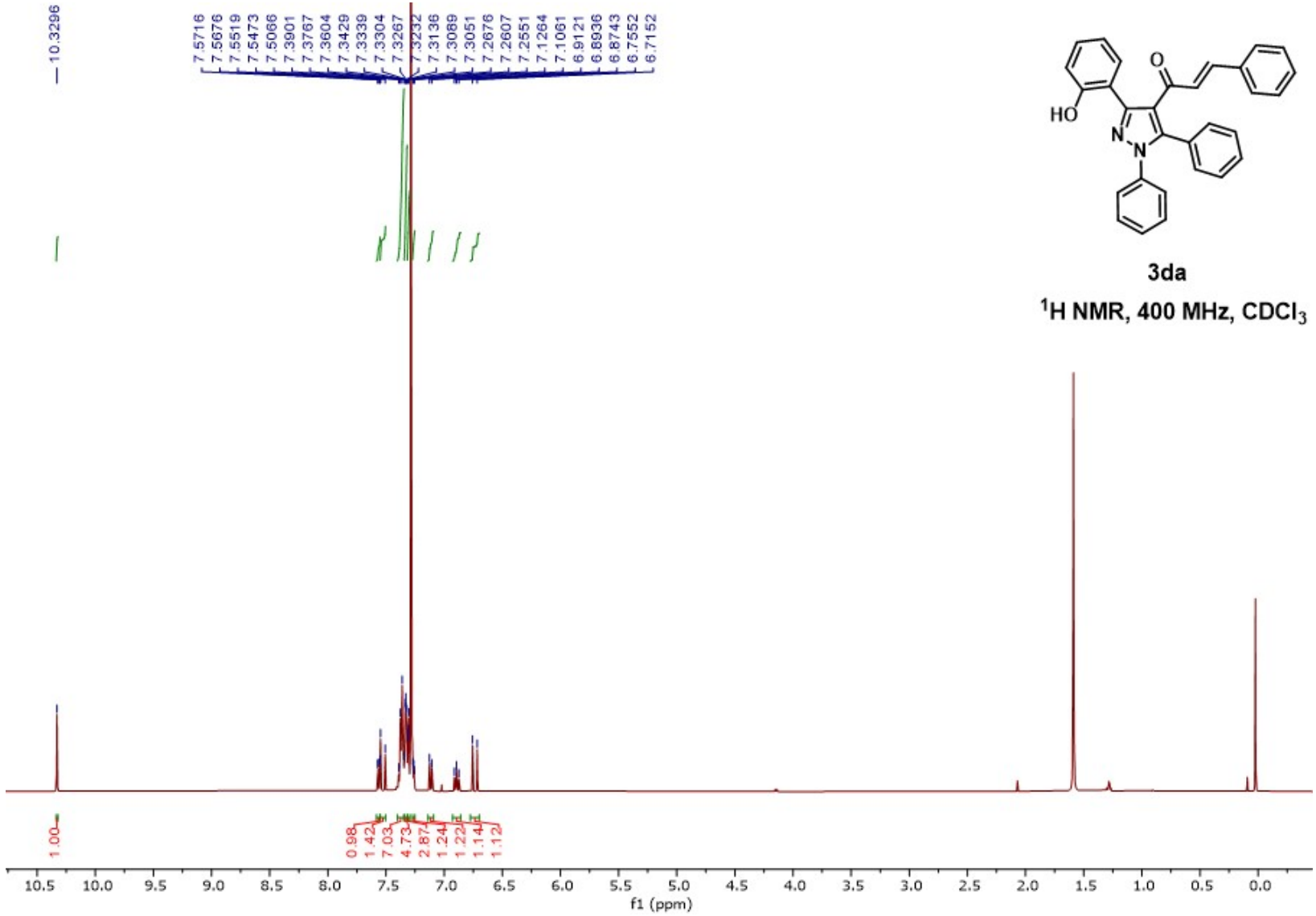
^{1}H NMR of compound 3ca in $CDCl_3$



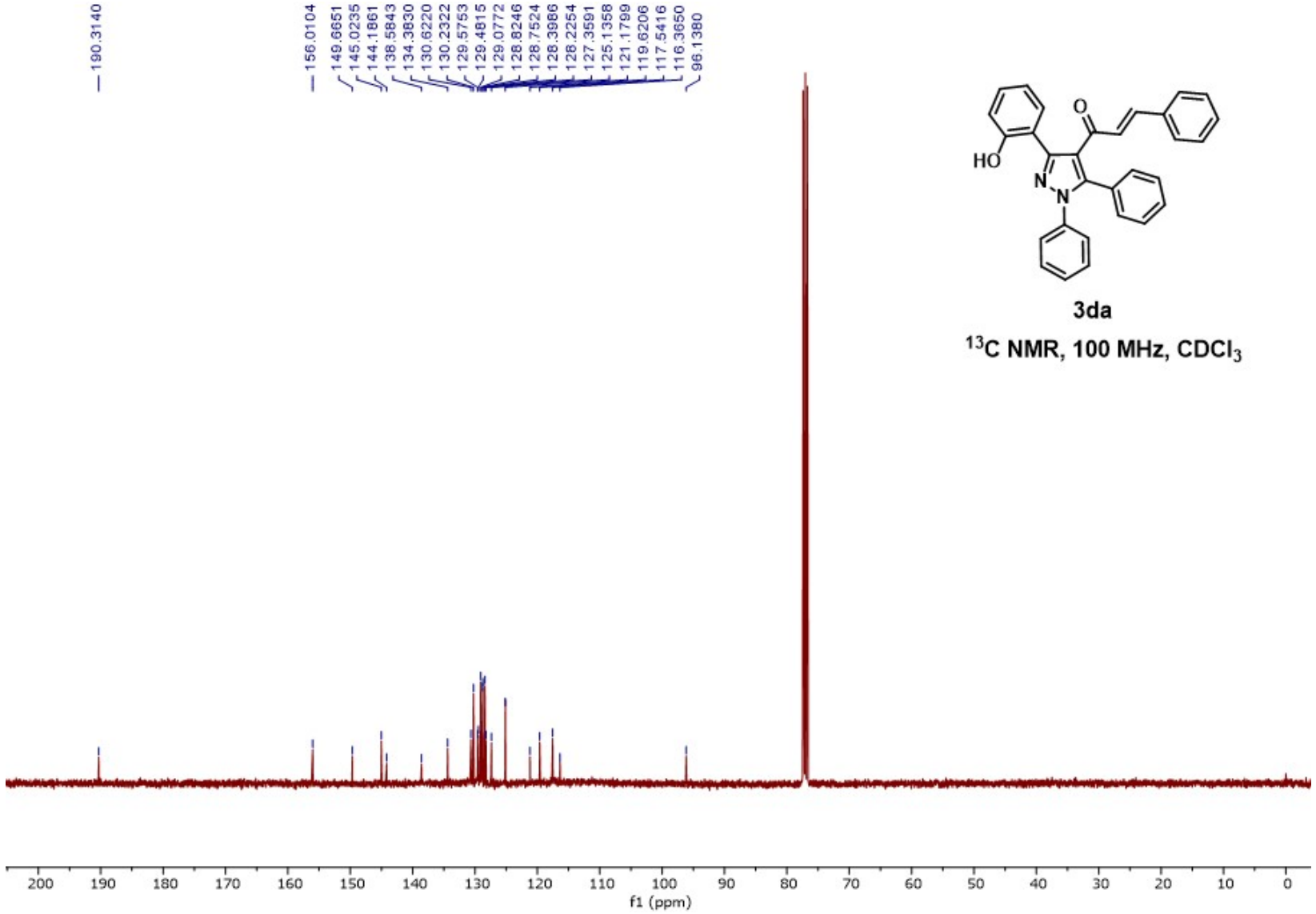
$^{13}C\{^{1}H\}$ NMR of compound 3ca in $CDCl_3$



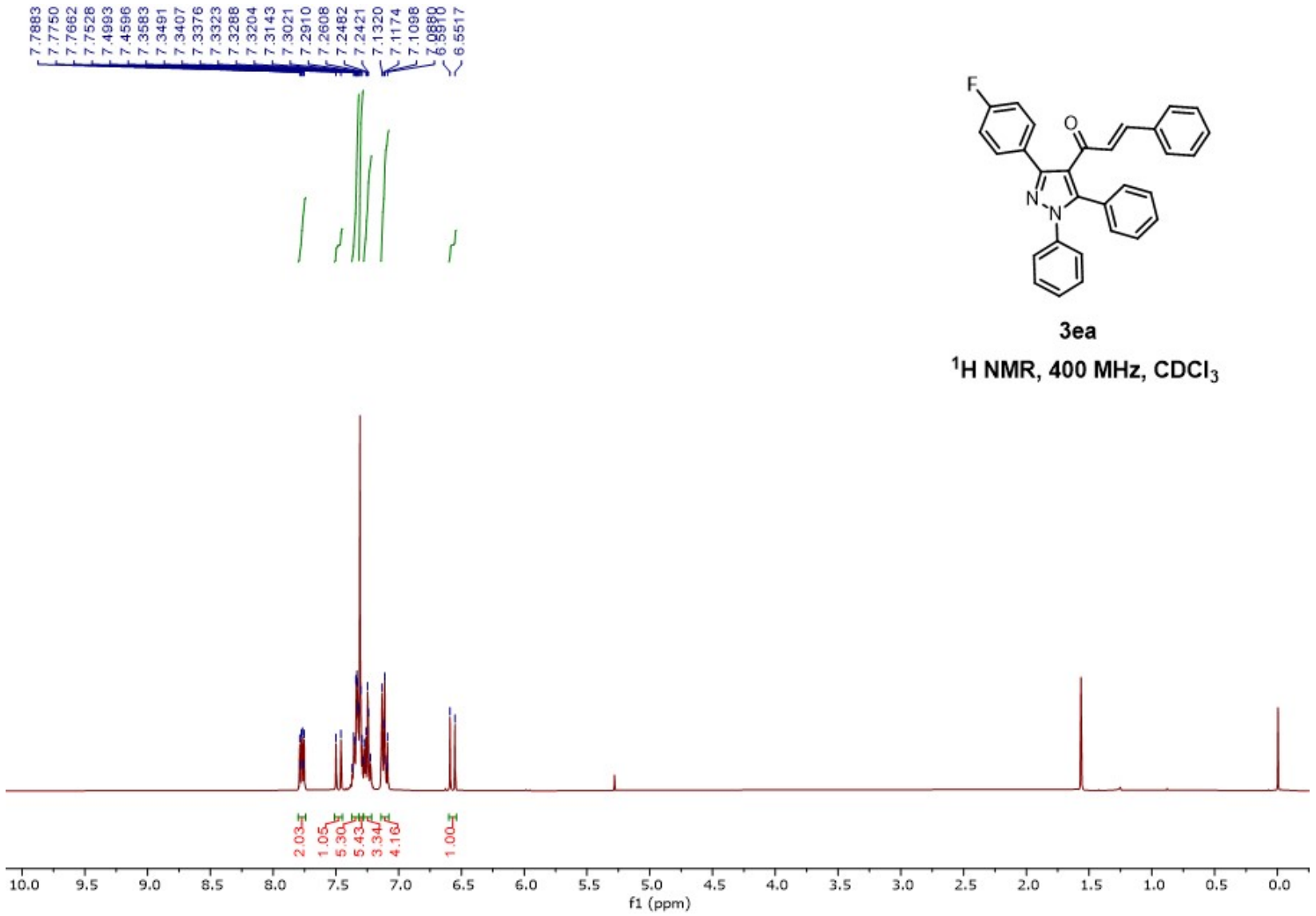
^{1}H NMR of compound 3da in $CDCl_3$



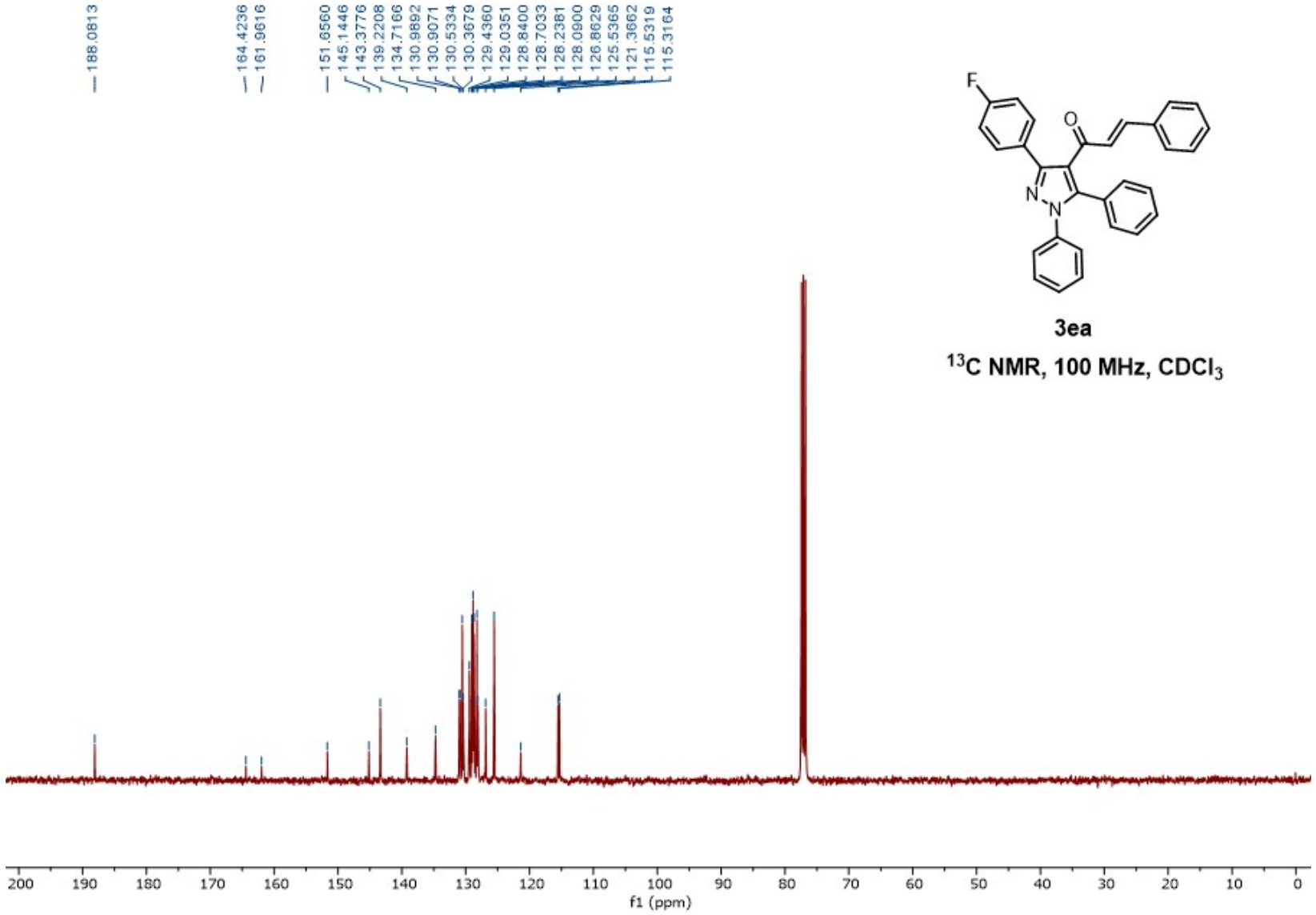
$^{13}C\{^{1}H\}$ NMR of compound 3da in $CDCl_3$



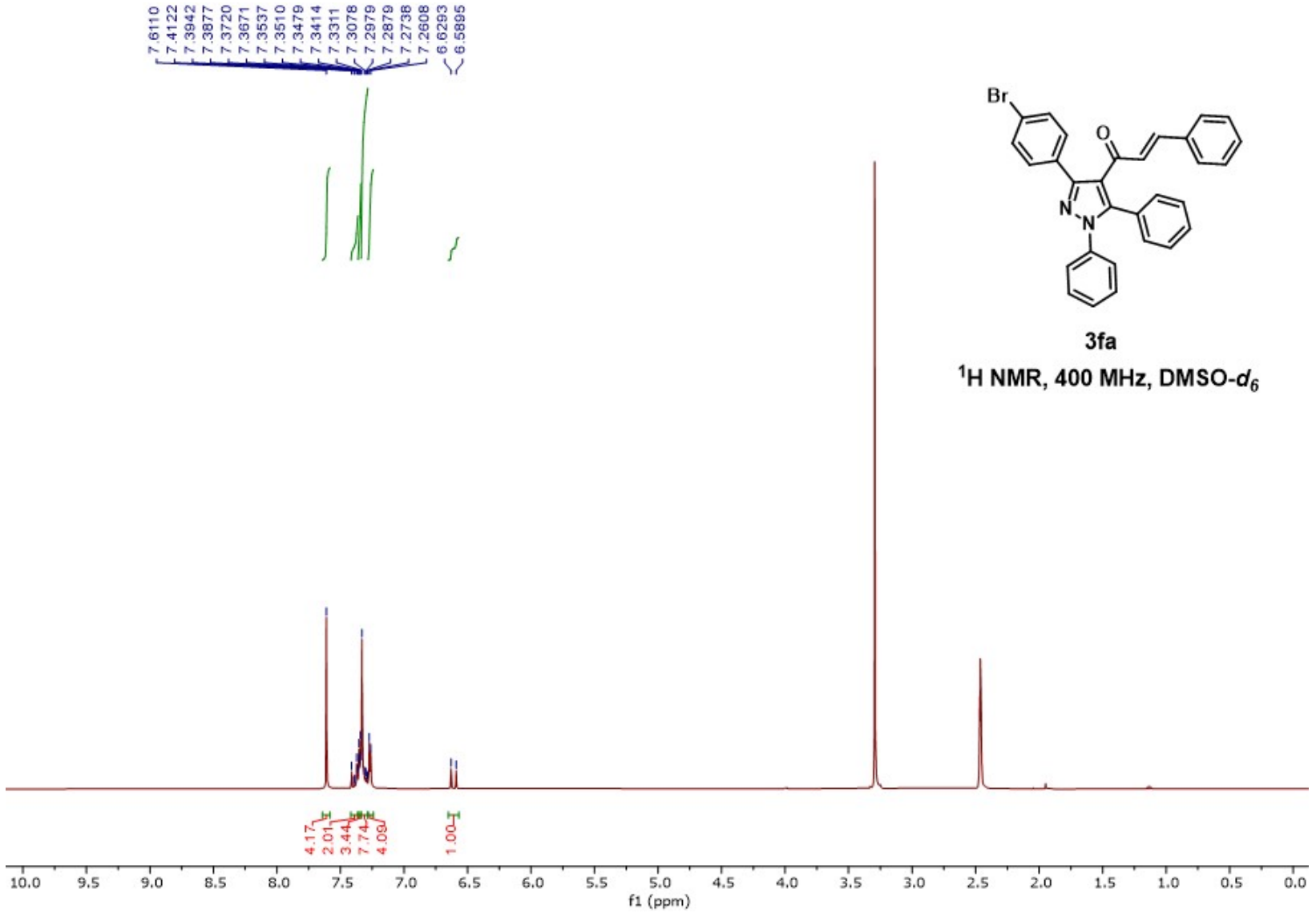
^{1}H NMR of compound 3ea in $CDCl_3$



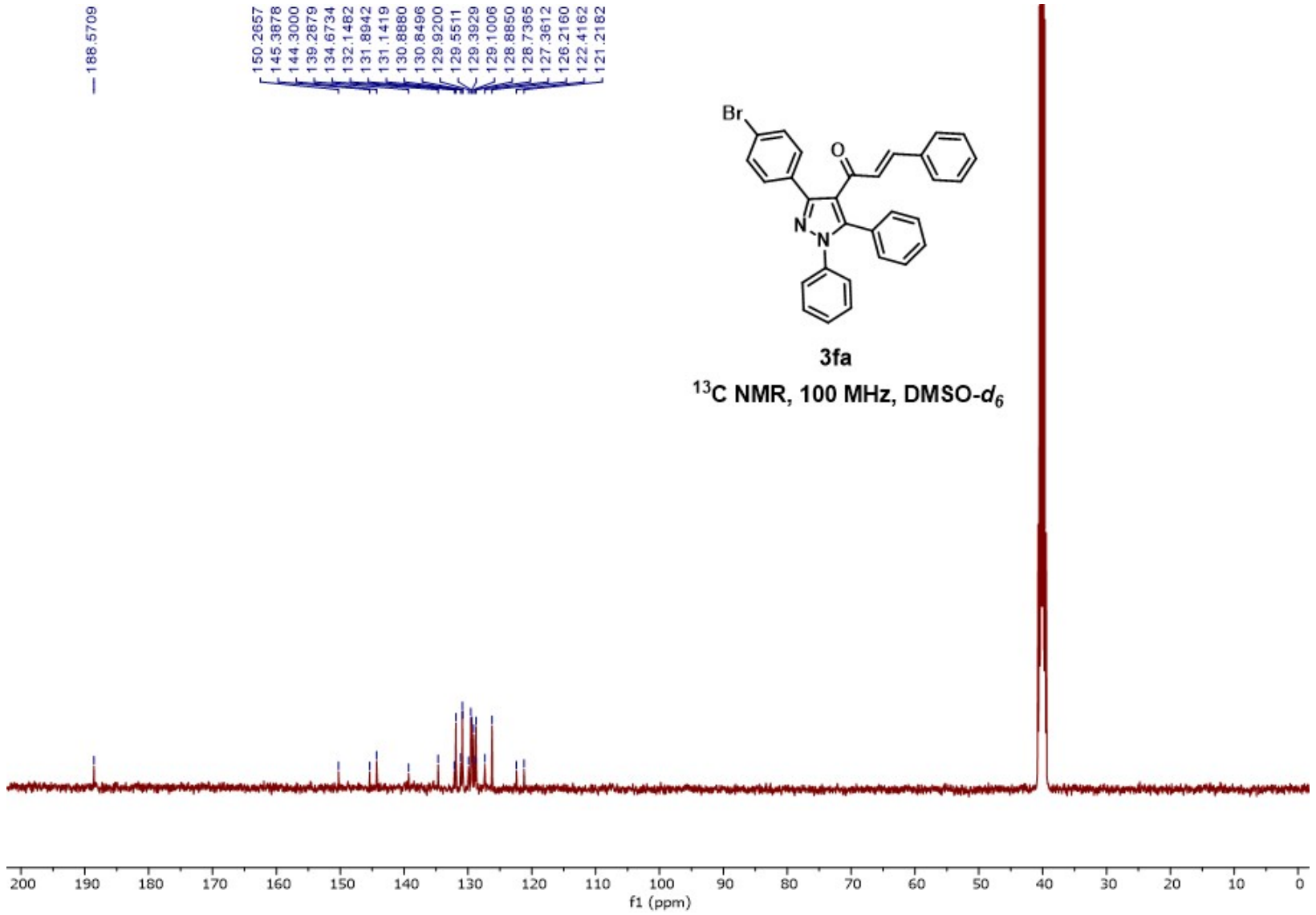
$^{13}C\{^{1}H\}$ NMR of compound 3ea in $CDCl_3$



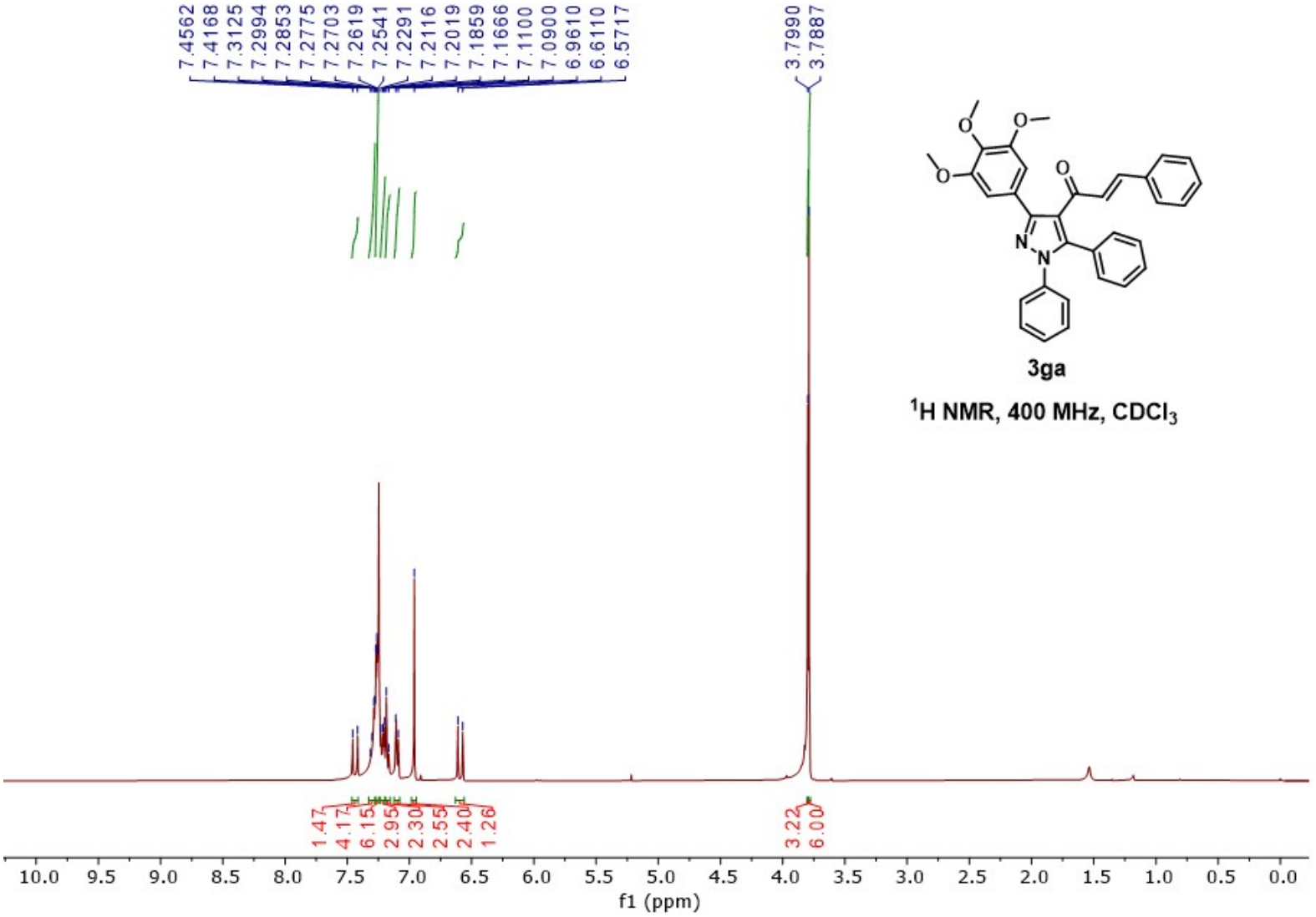
^{1}H NMR of compound 3fa in DMSO-d_6



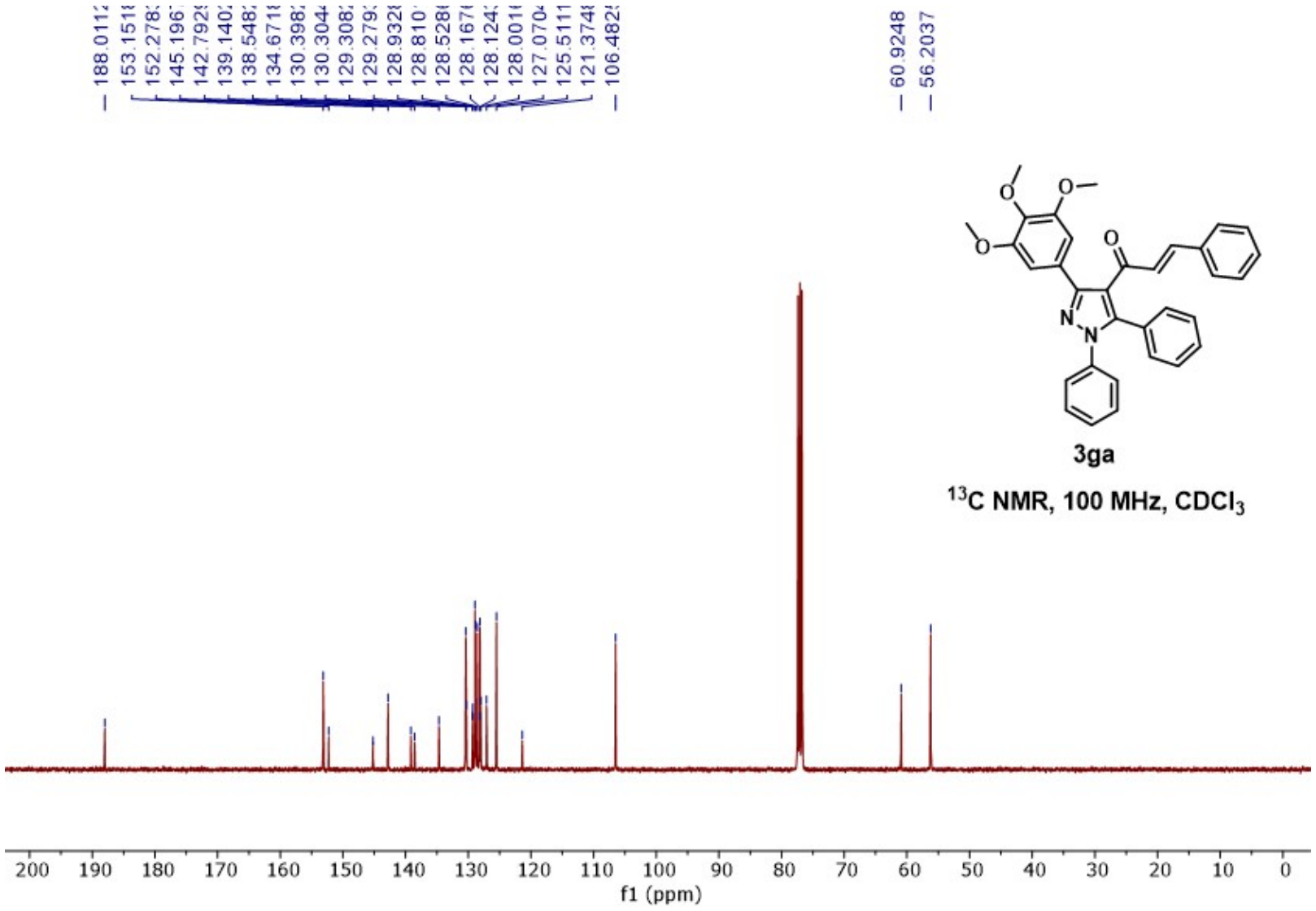
$^{13}C\{^{1}H\}$ NMR of compound 3fa in DMSO-d_6



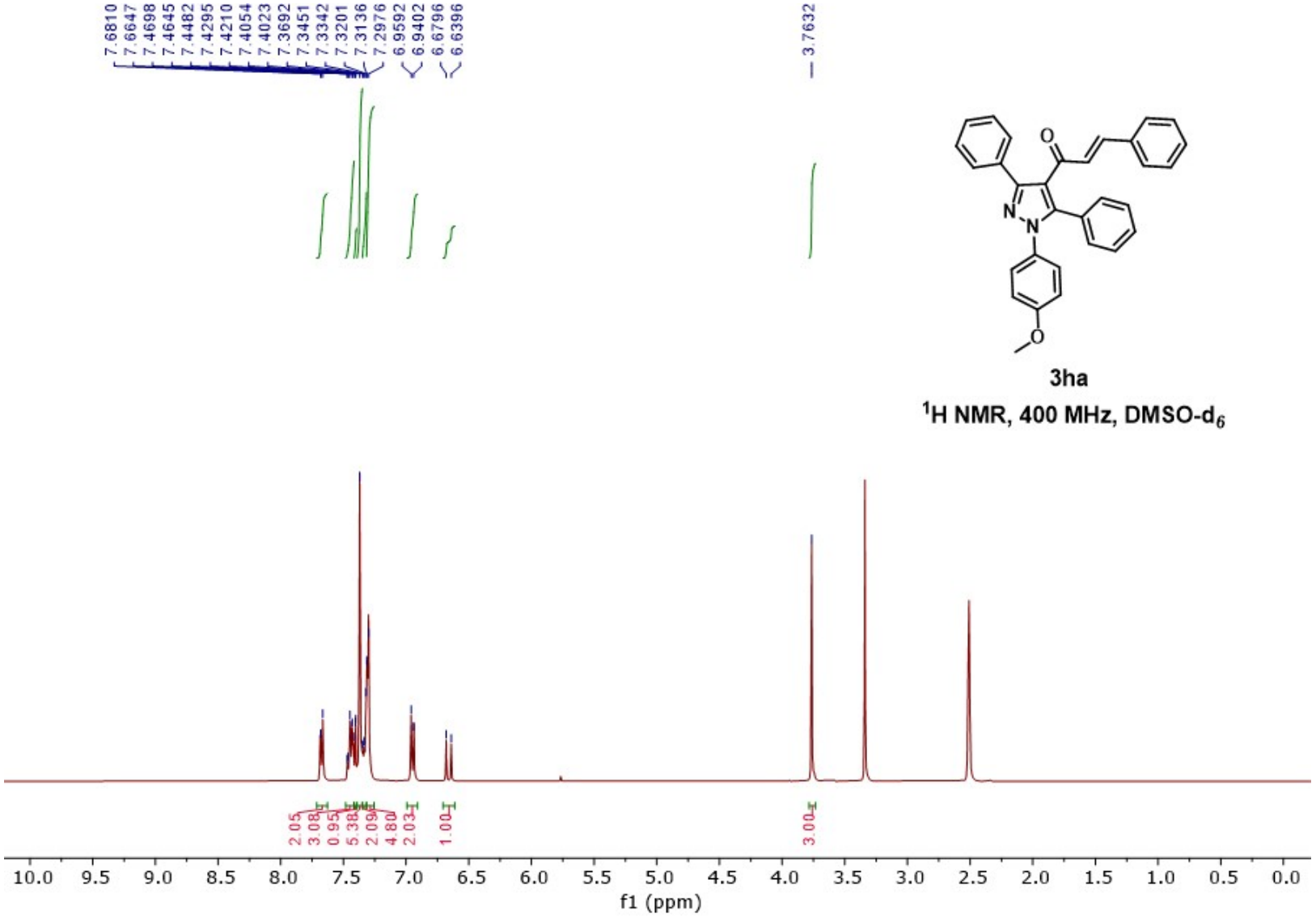
^{1}H NMR of compound 3ga in $CDCl_3$



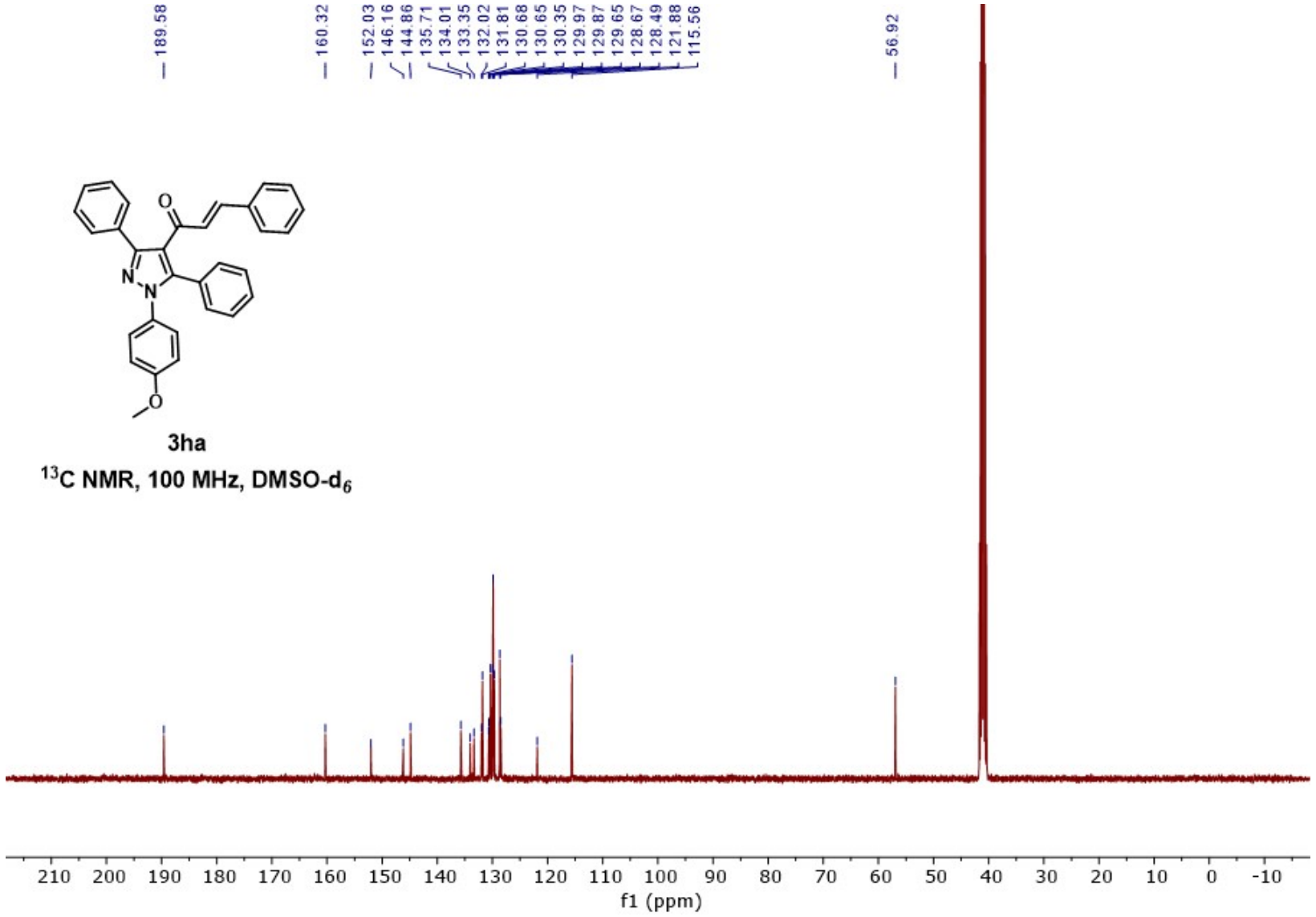
$^{13}C\{^{1}H\}$ NMR of compound 3ga in $CDCl_3$



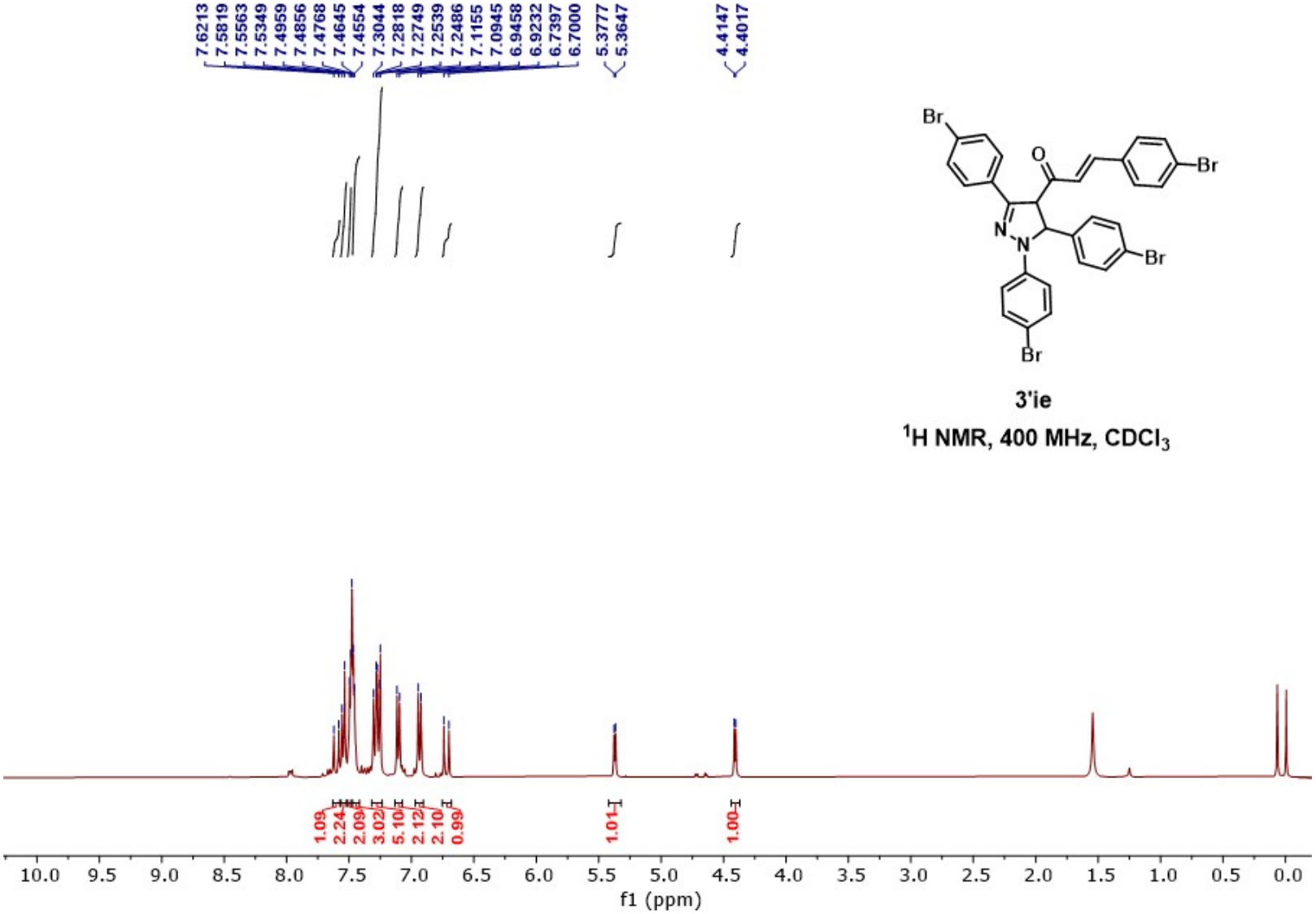
^{1}H NMR of compound 3ha in DMSO-d_6



$^{13}C\{^{1}H\}$ NMR of compound 3ha in DMSO-d_6



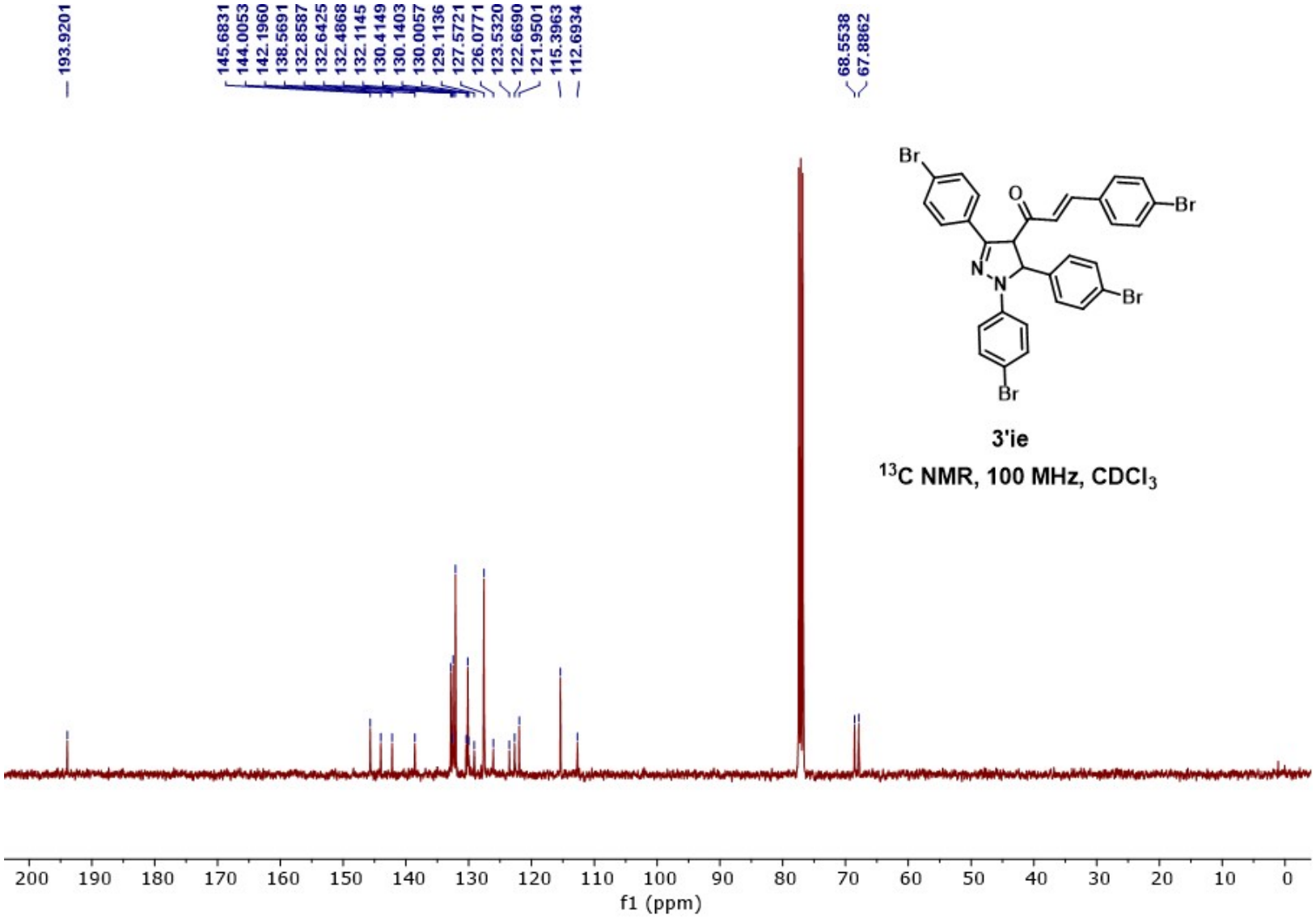
^{1}H NMR of compound 3'ie in $CDCl_3$ (intermediate dihydropyrazole derivative)



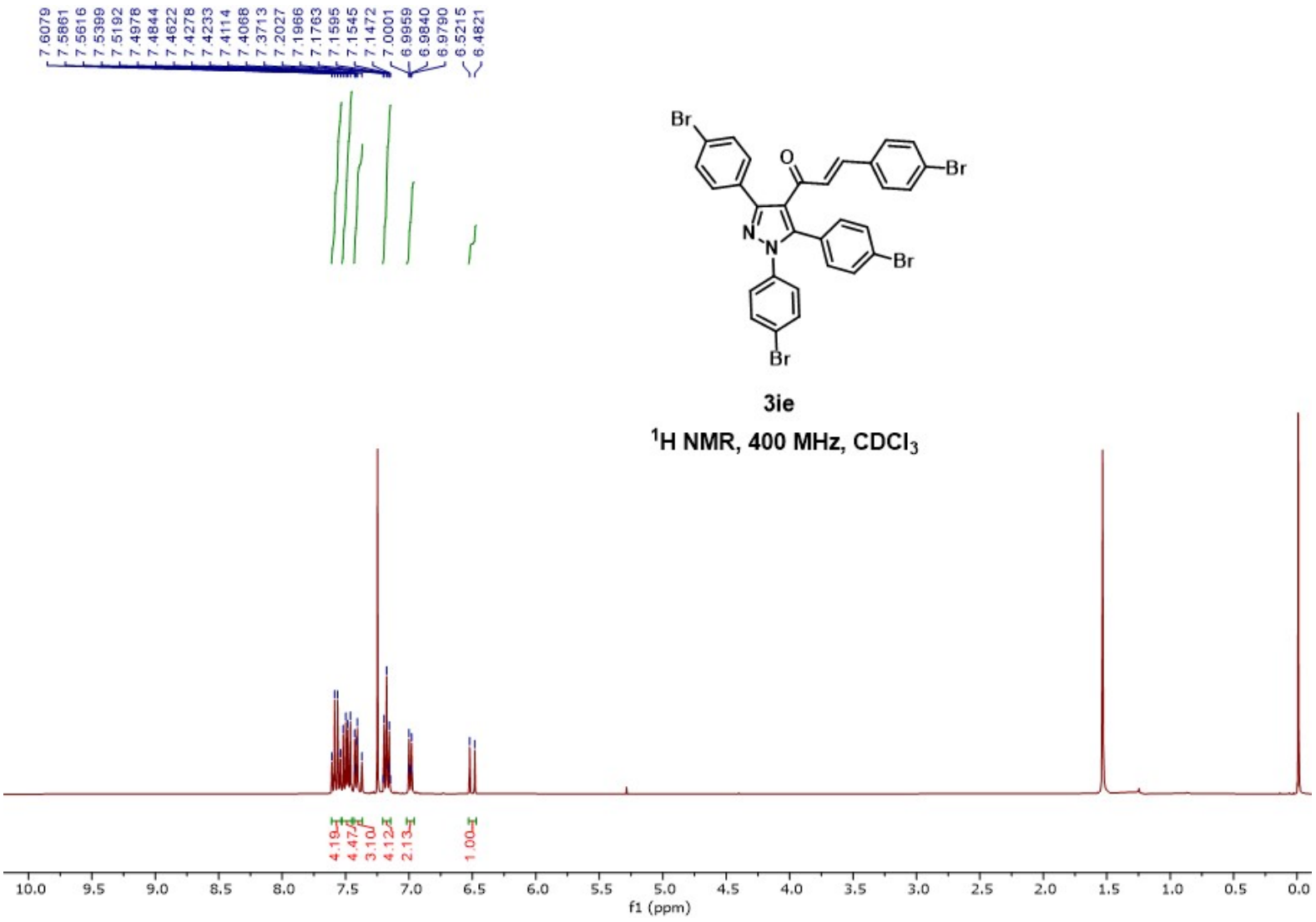
3'ie

^{1}H NMR, 400 MHz, $CDCl_3$

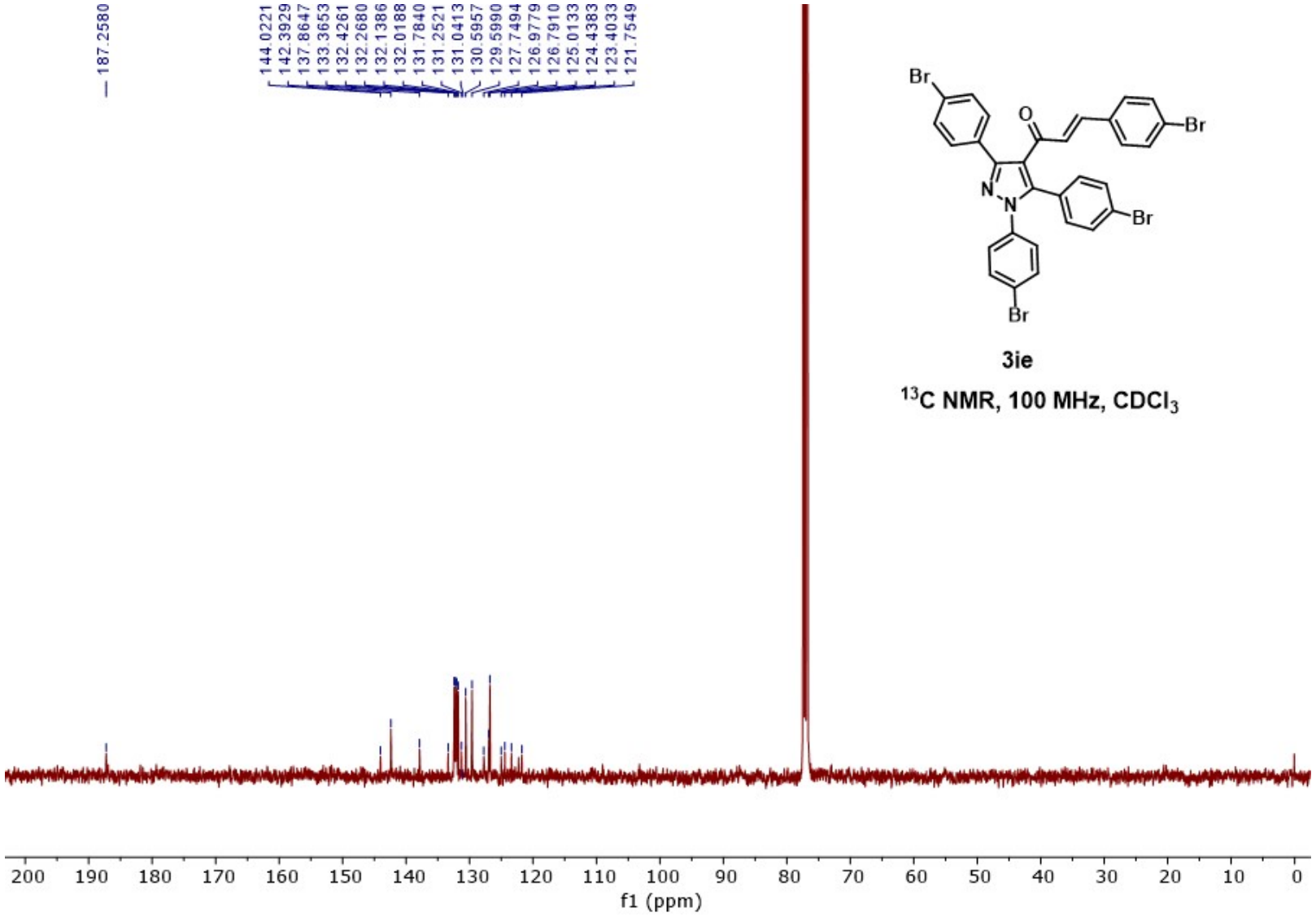
$^{13}C\{^{1}H\}$ NMR of compound 3'ie in $CDCl_3$



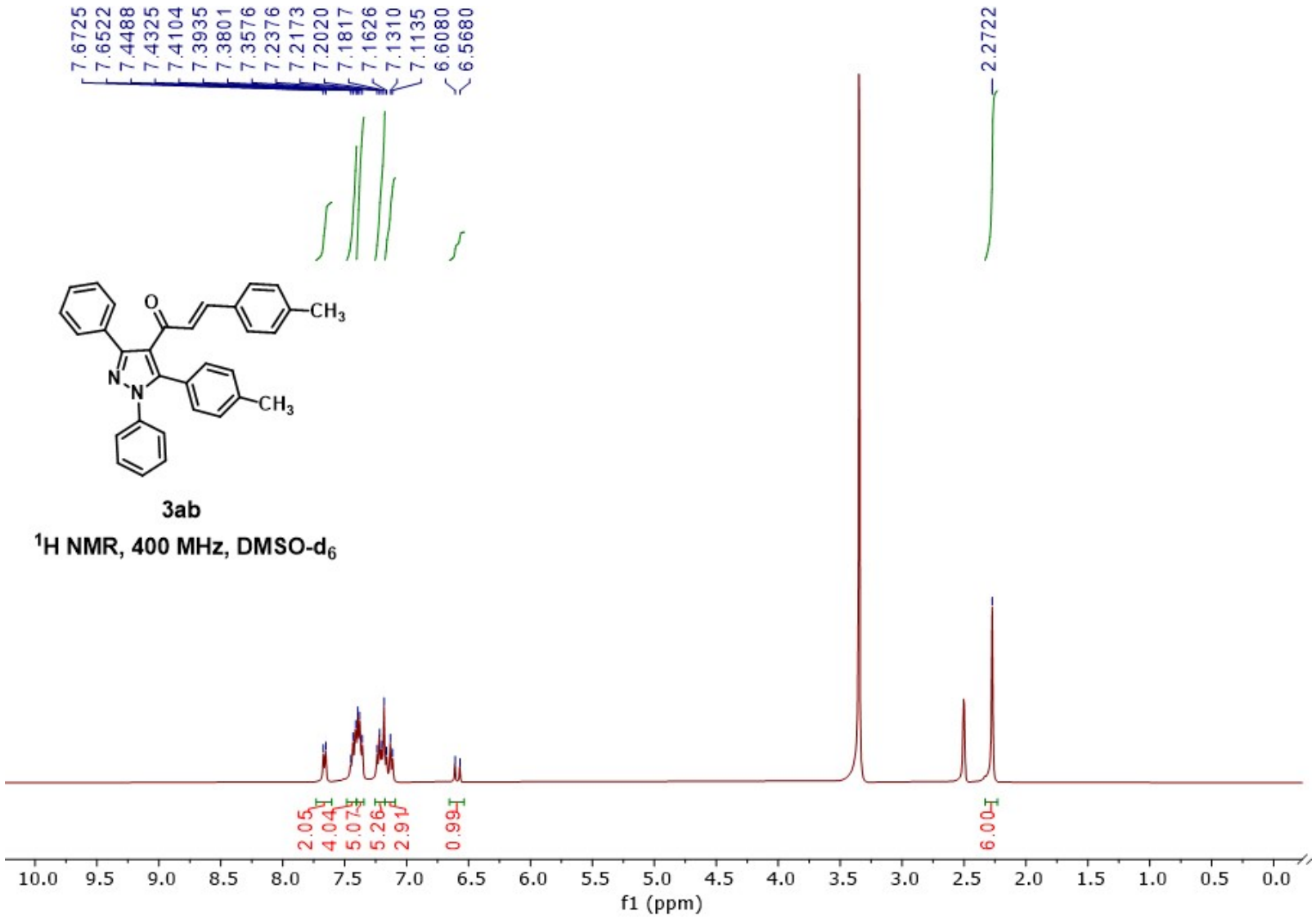
^{1}H NMR of compound 3ie in $CDCl_3$



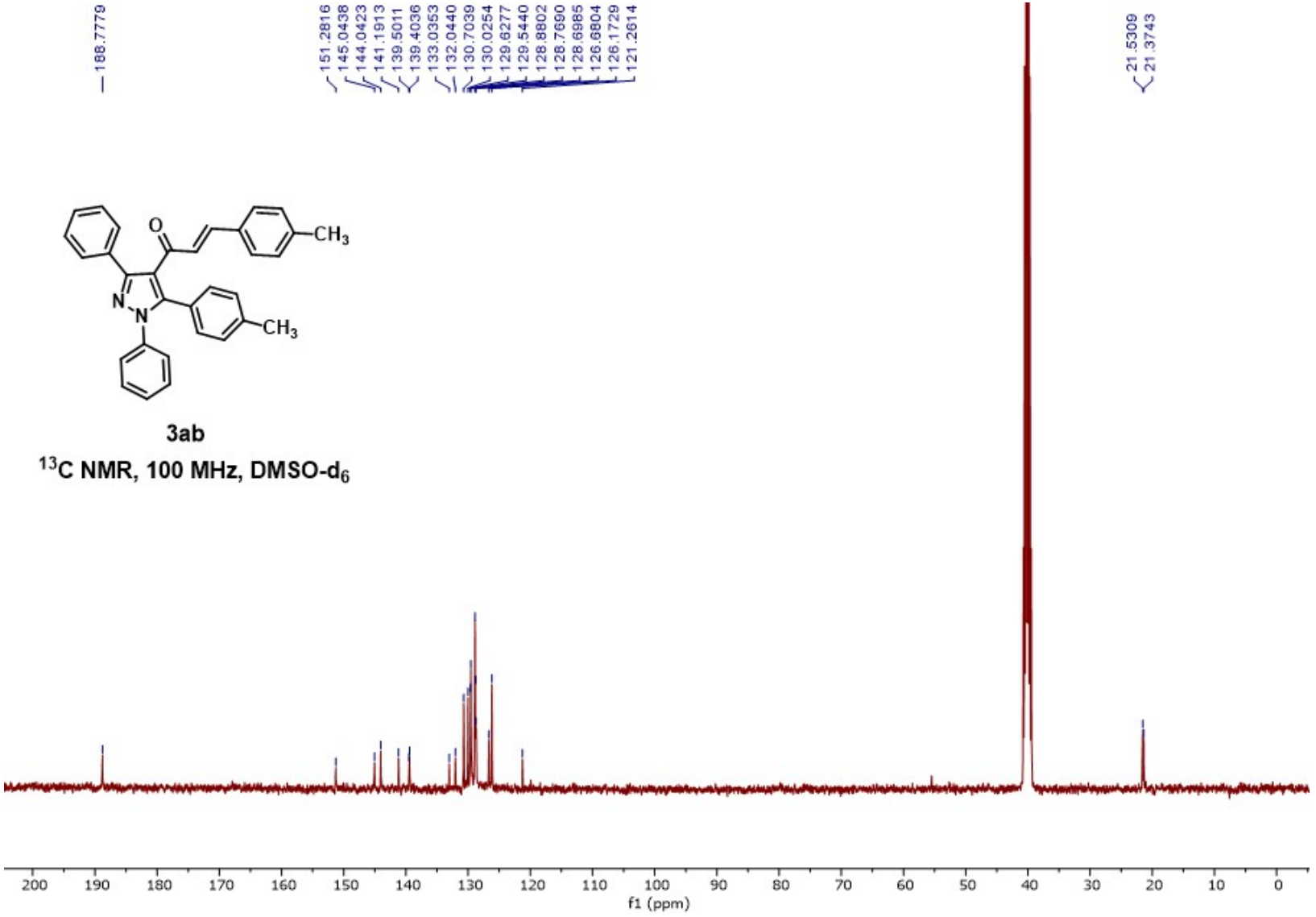
$^{13}C\{^{1}H\}$ NMR of compound 3id in $CDCl_3$



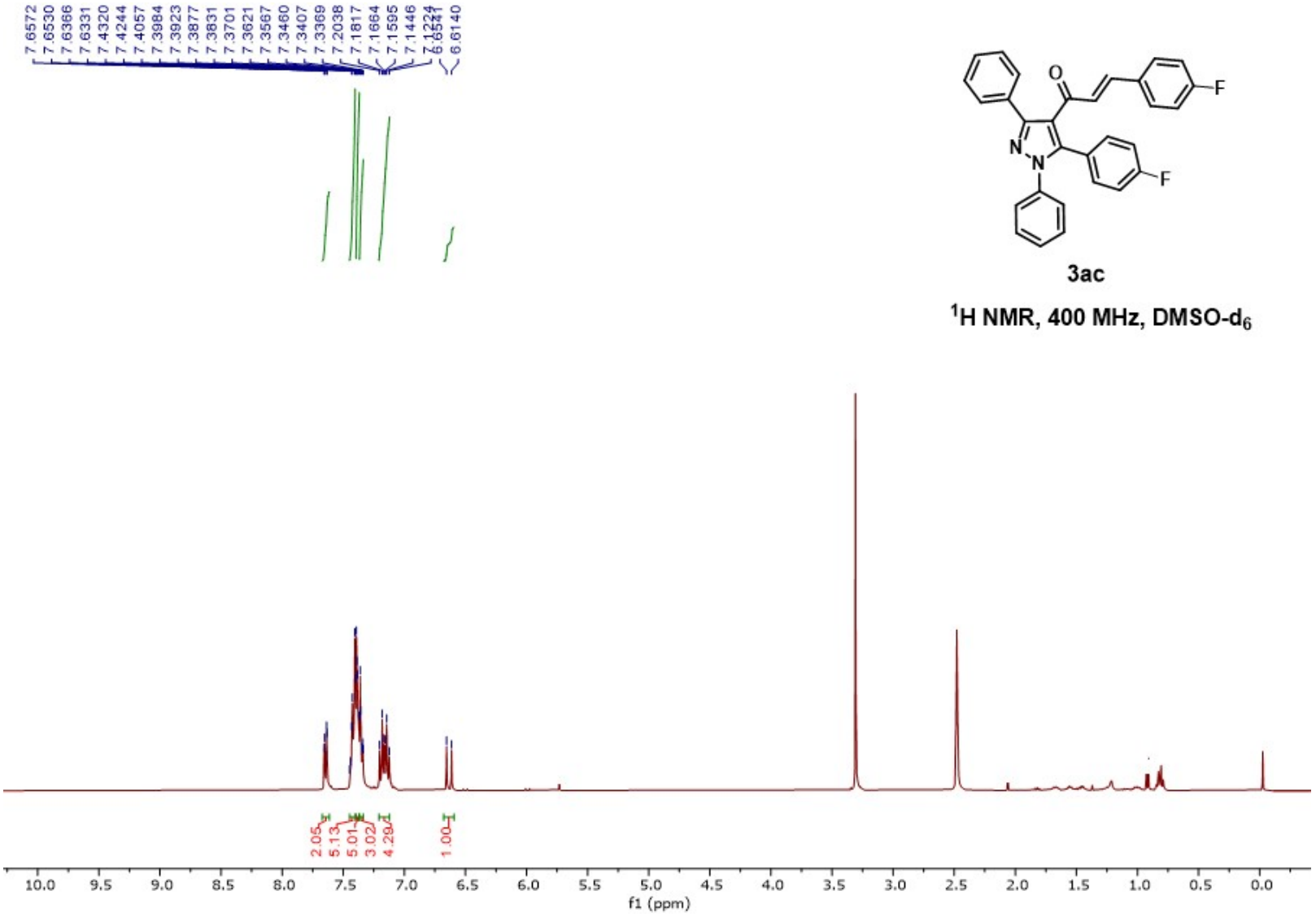
^{1}H NMR of compound 3ab in DMSO-d_6



$^{13}C\{^{1}H\}$ NMR of compound 3ab in $CDCl_3$



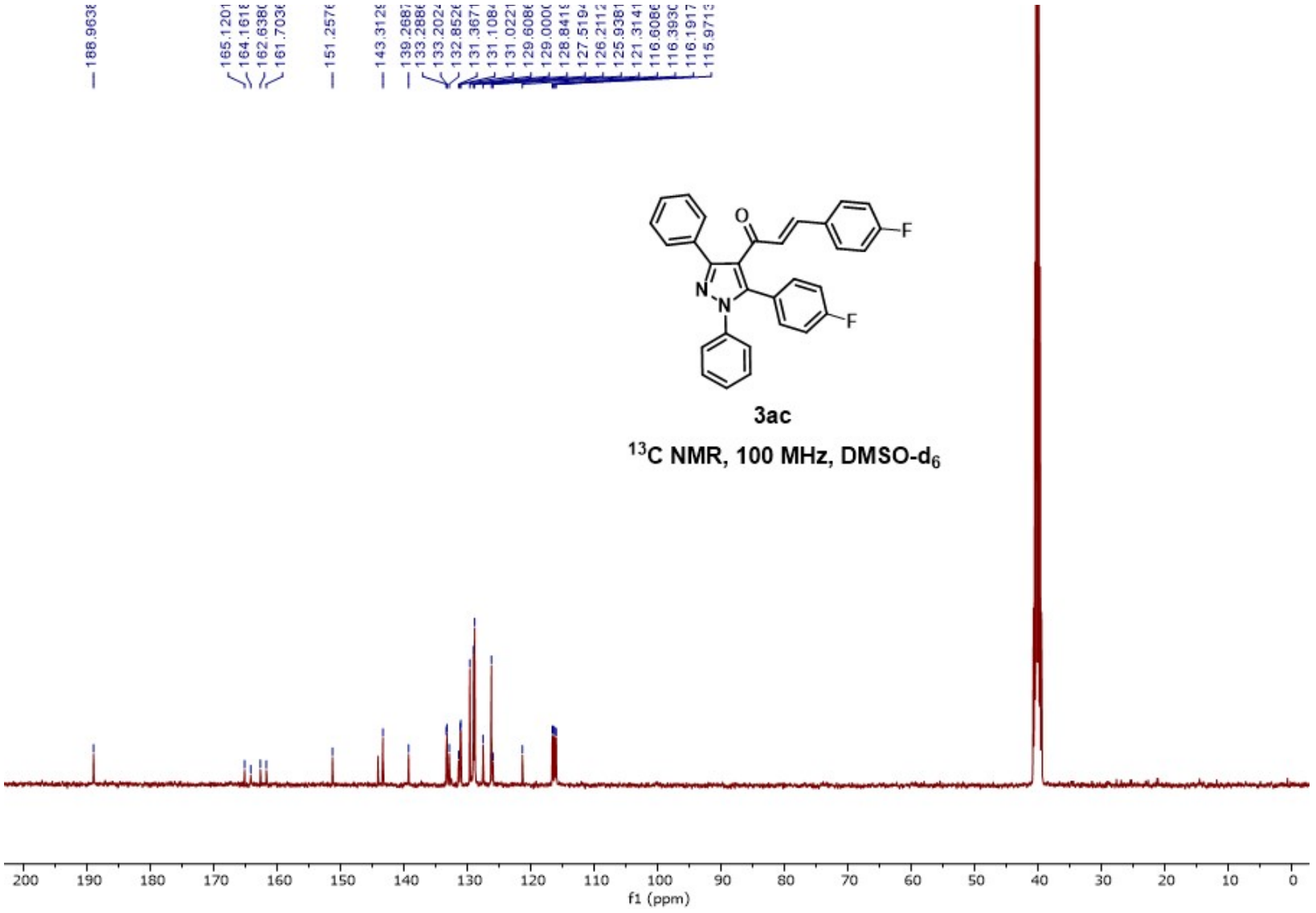
^{1}H NMR of compound 3ac in DMSO-d_6



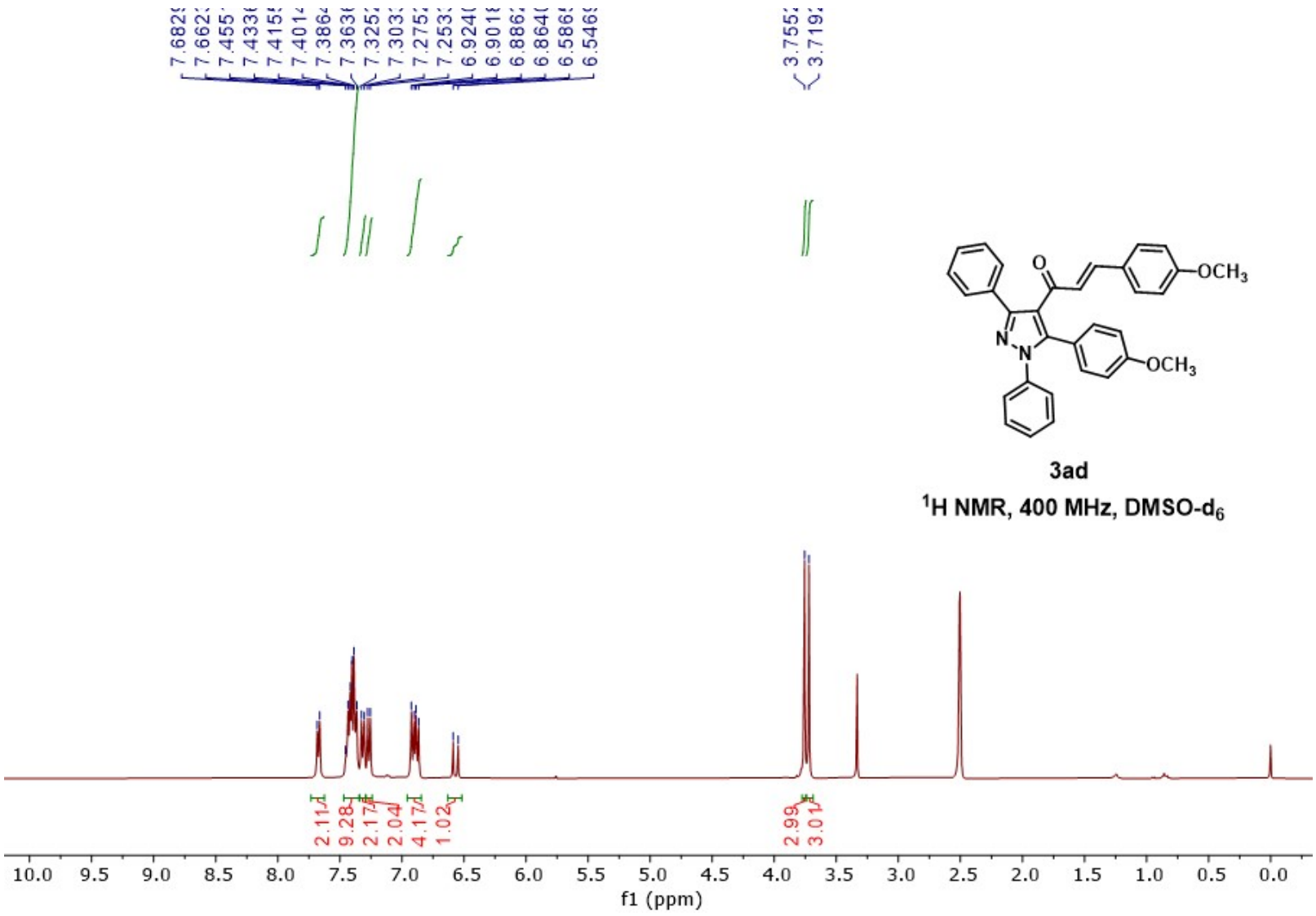
3ac

^{1}H NMR, 400 MHz, DMSO-d_6

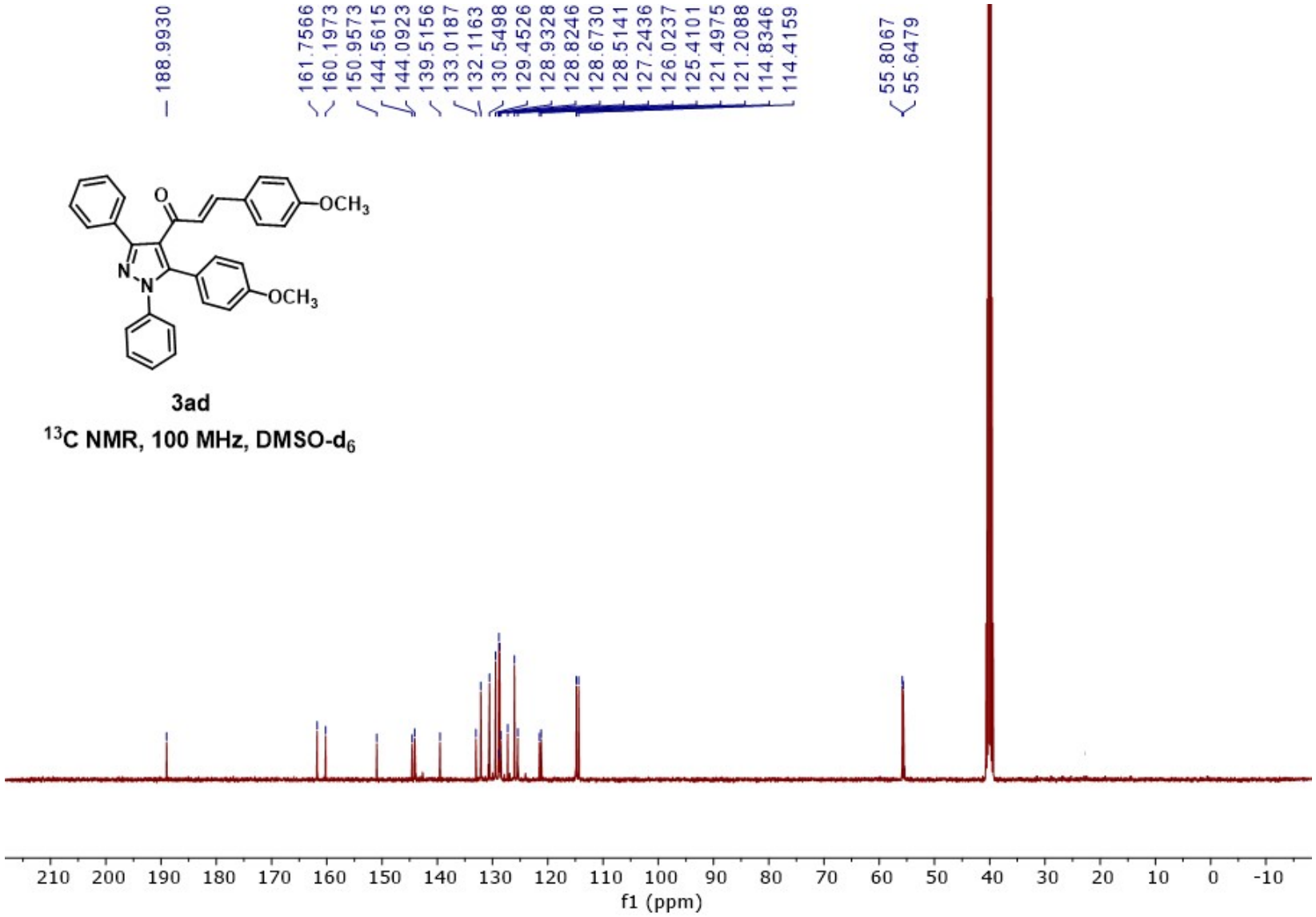
$^{13}C\{^{1}H\}$ NMR of compound 3ac in DMSO-d_6



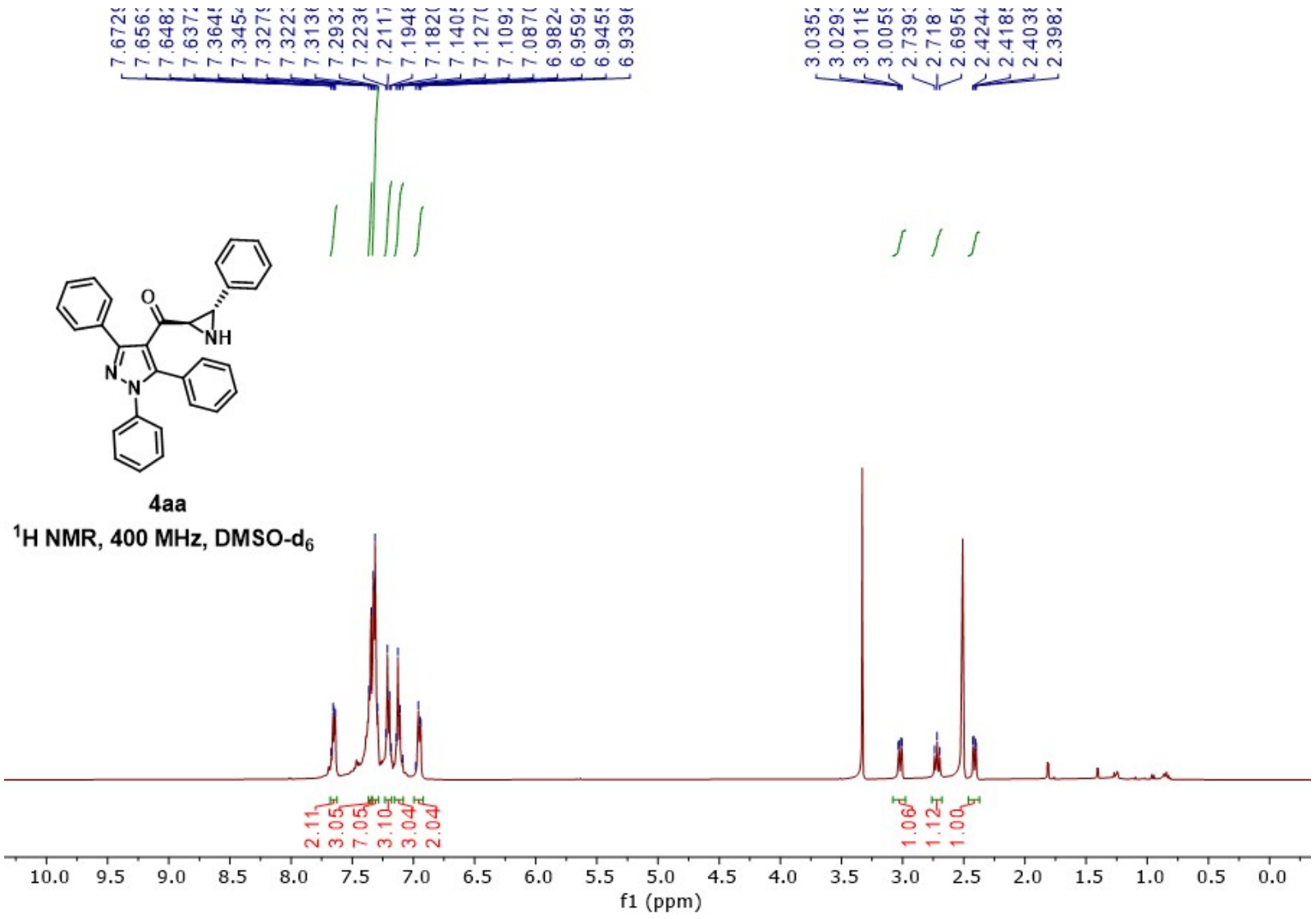
^{1}H NMR of compound 3ad in DMSO-d_6(Re-recorded spectra)



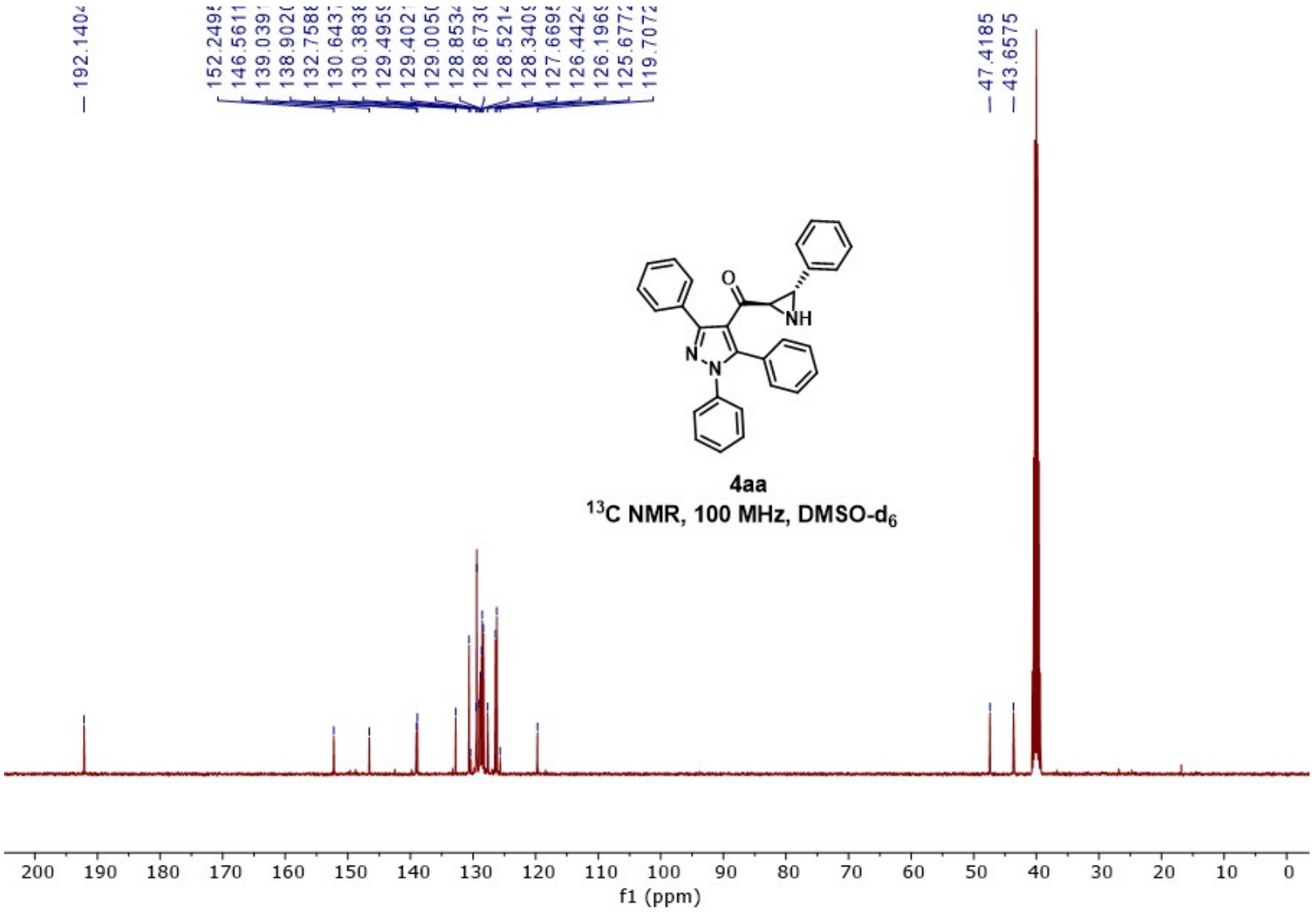
$^{13}C\{^{1}H\}$ NMR of compound 3ad in DMSO-d_6(Re-recorded spectra)



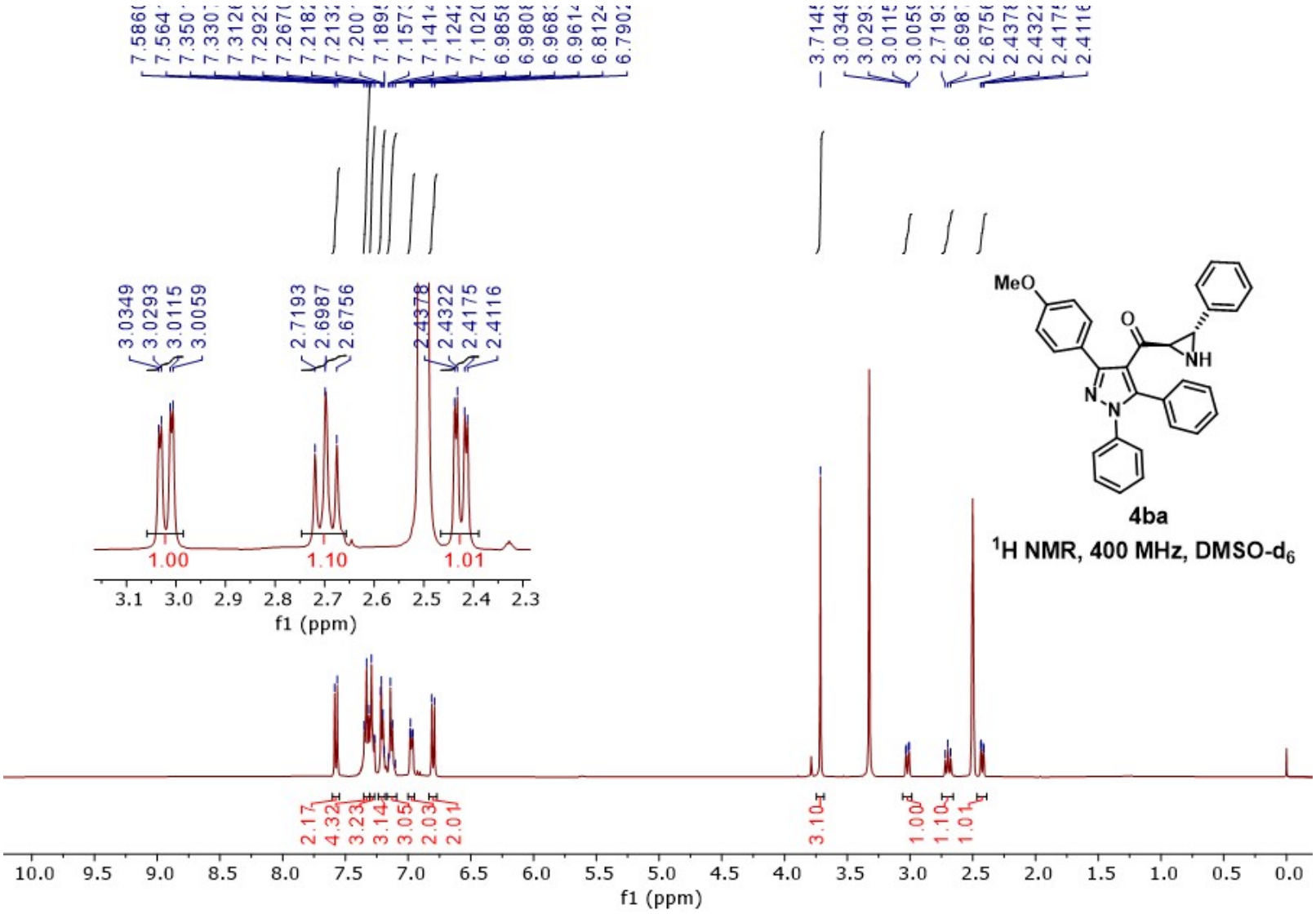
^{1}H NMR of compound 4aa in DMSO-d_6



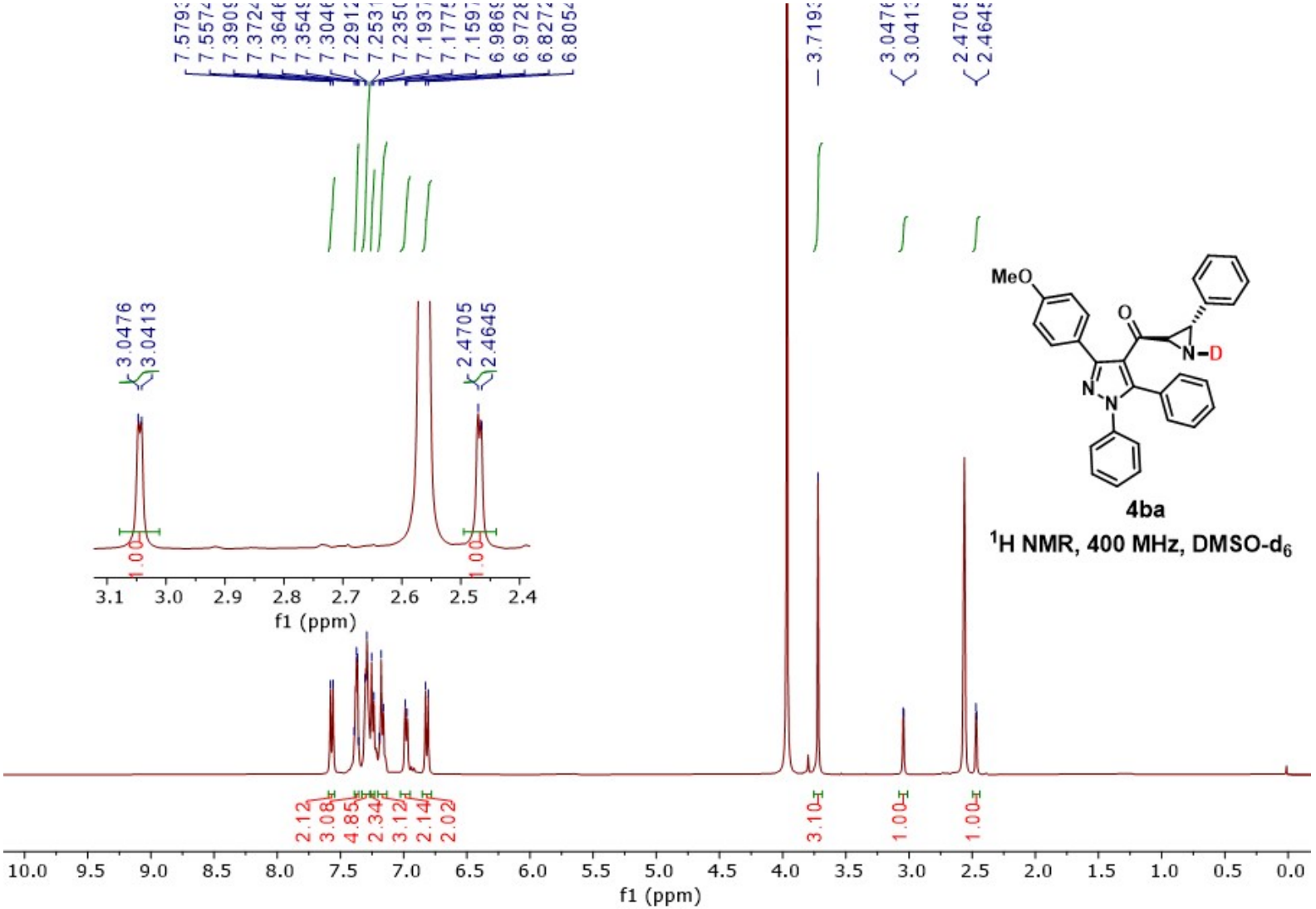
$^{13}C\{^{1}H\}$ of compound 4aa in DMSO-d_6



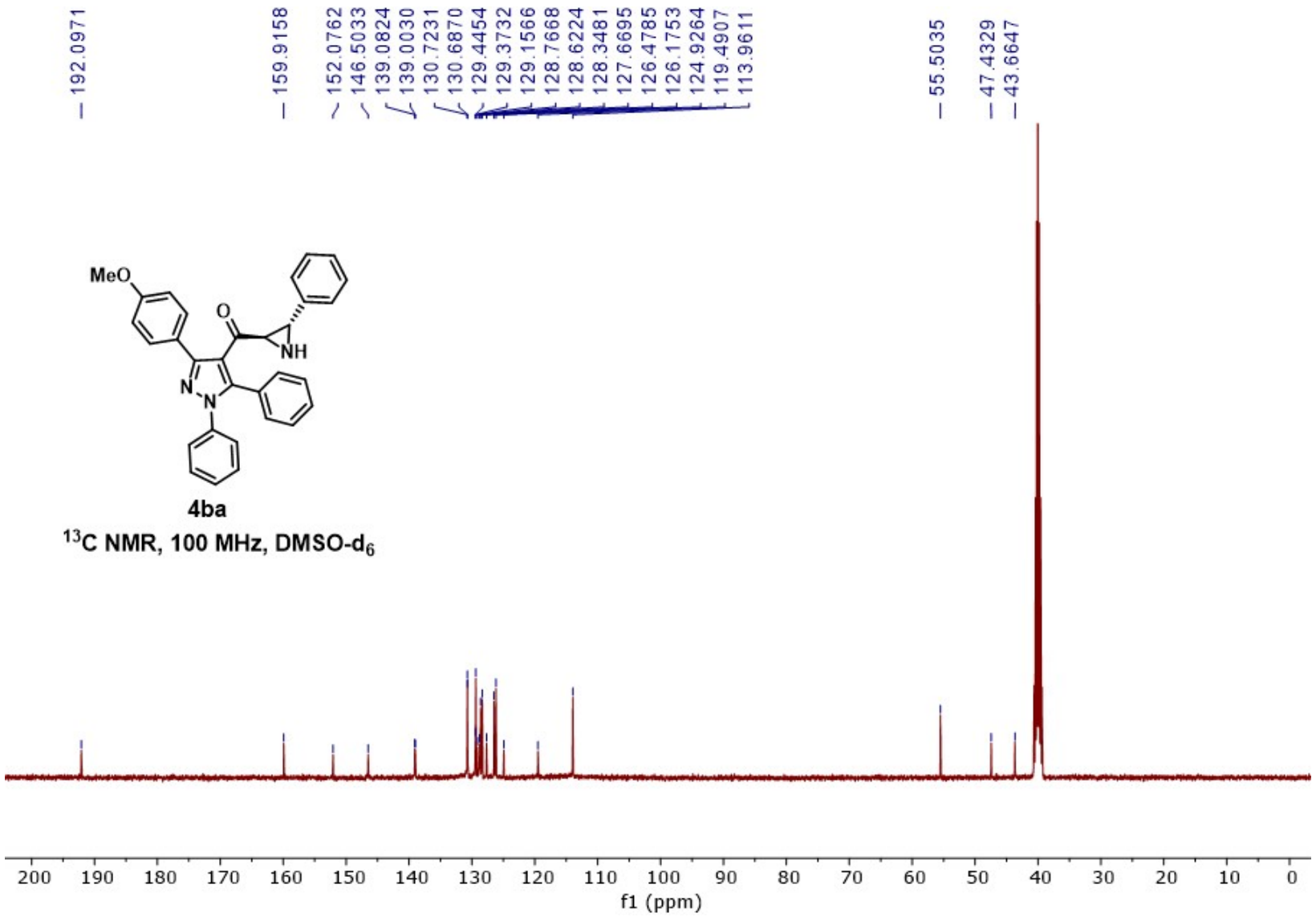
^{1}H NMR of compound 4ba in DMSO-d_6



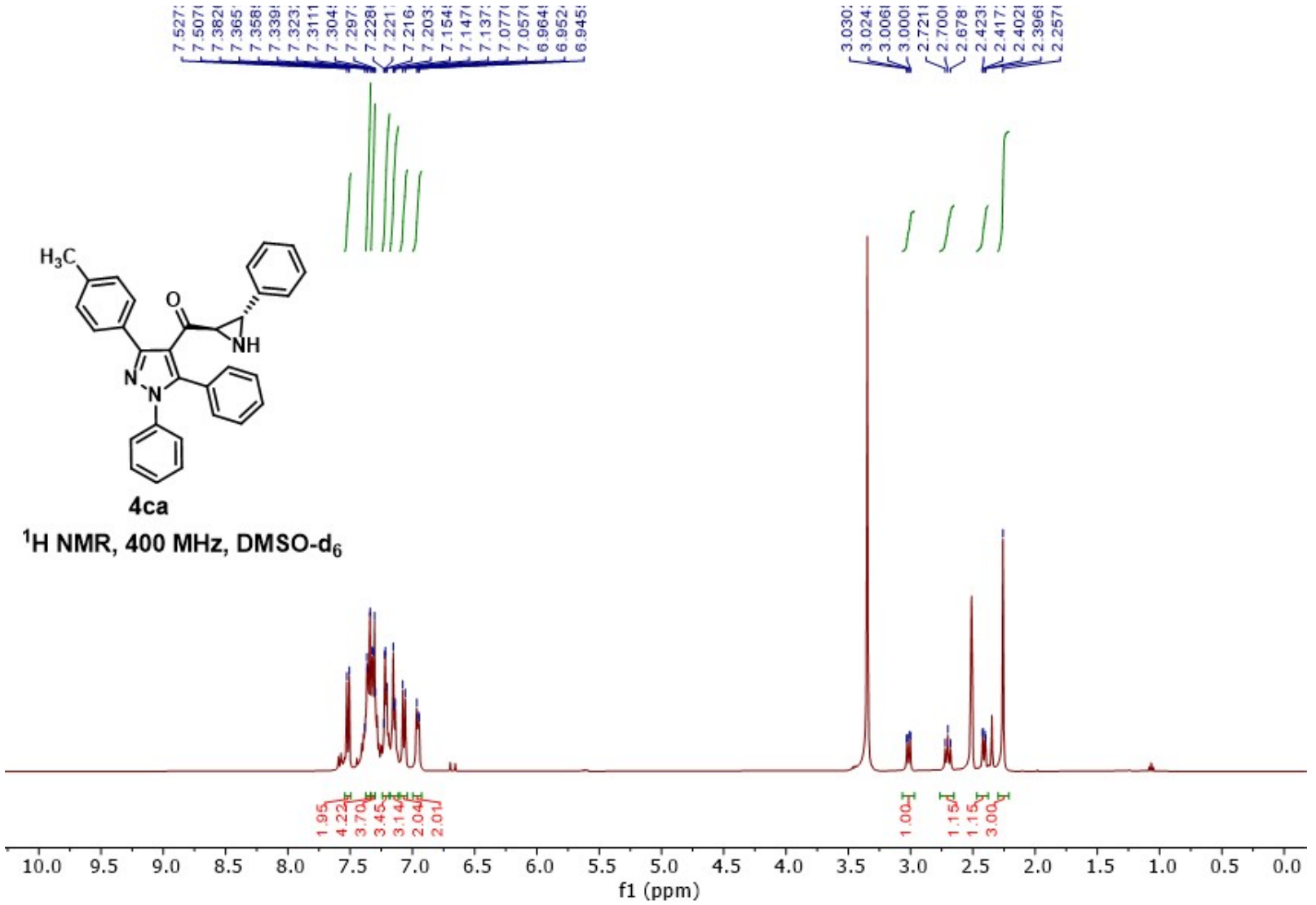
D_2O Exchange of compound 4ba



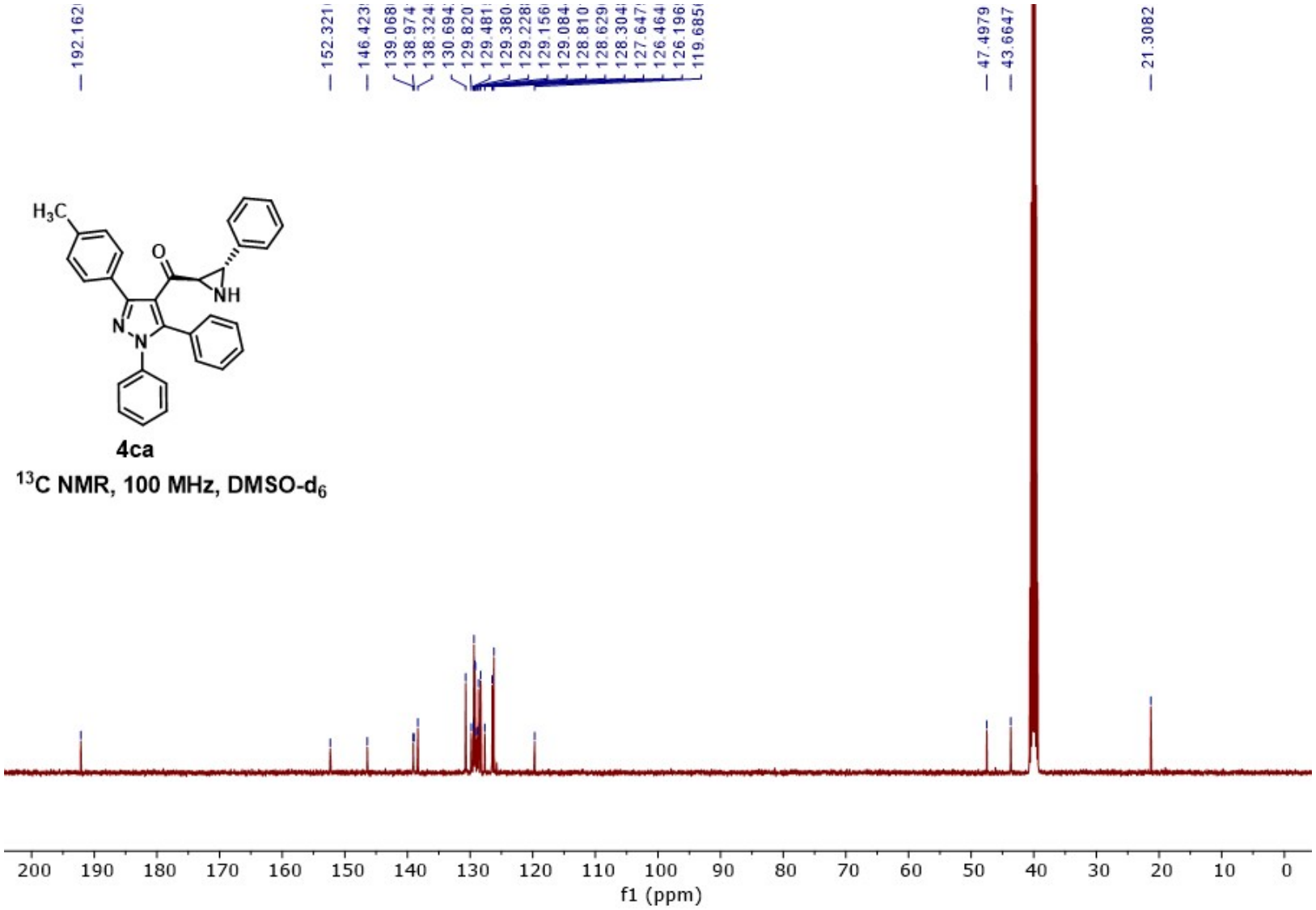
$^{13}C\{^{1}H\}$ of compound 4ba in DMSO-d_6



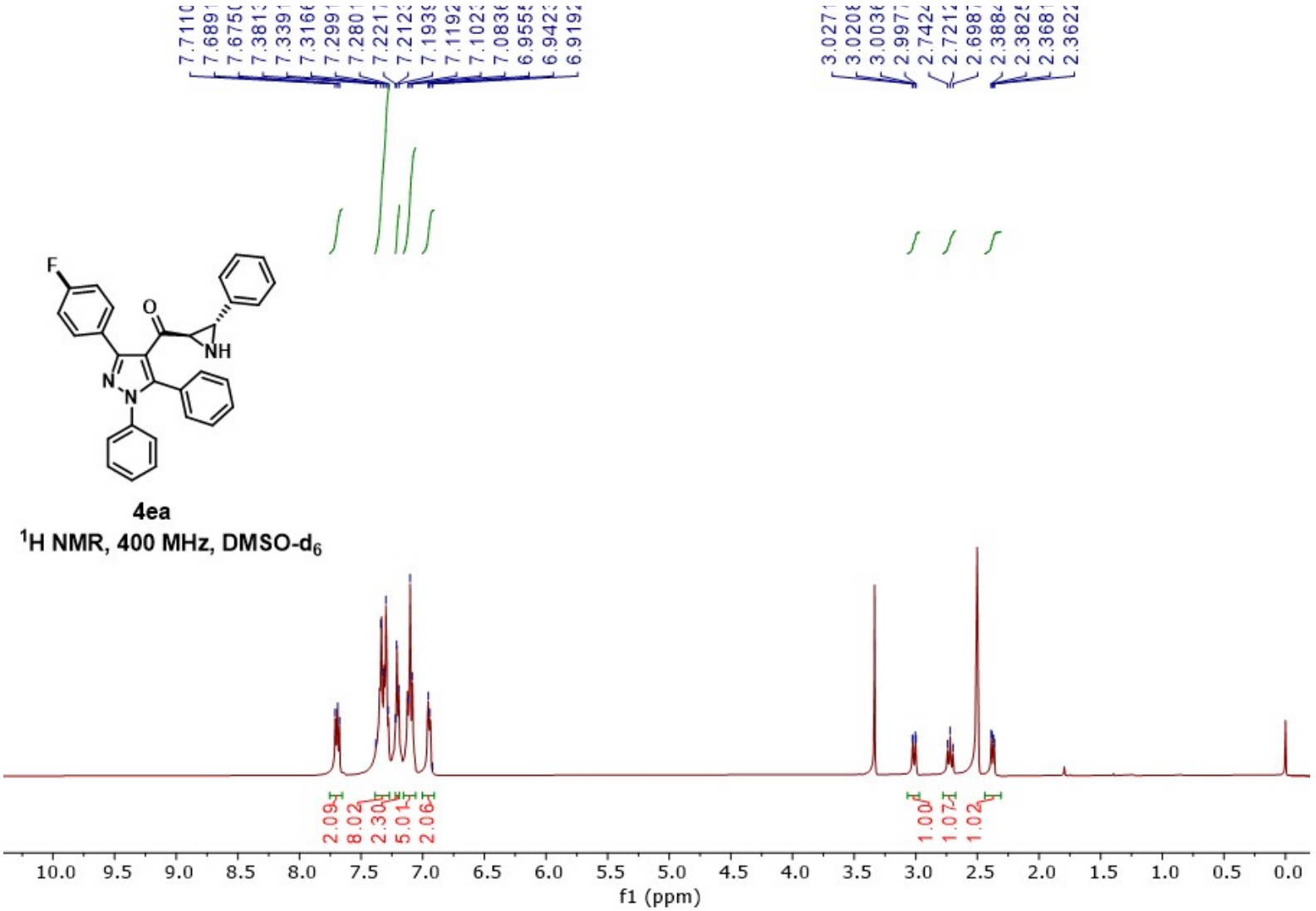
^{1}H NMR of compound 4ca in DMSO-d_6



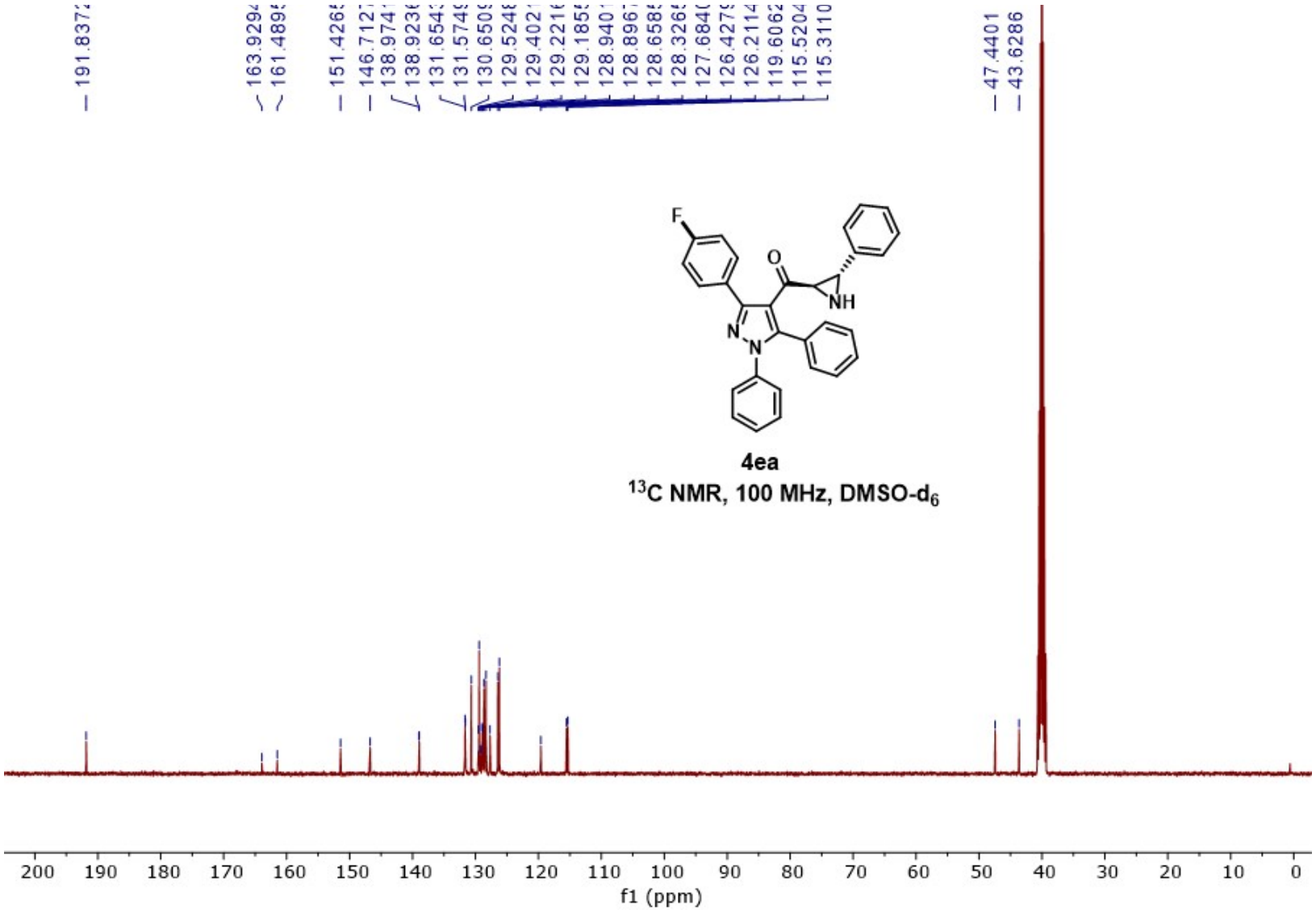
$^{13}C\{^{1}H\}$ of compound 4ca in DMSO-d_6



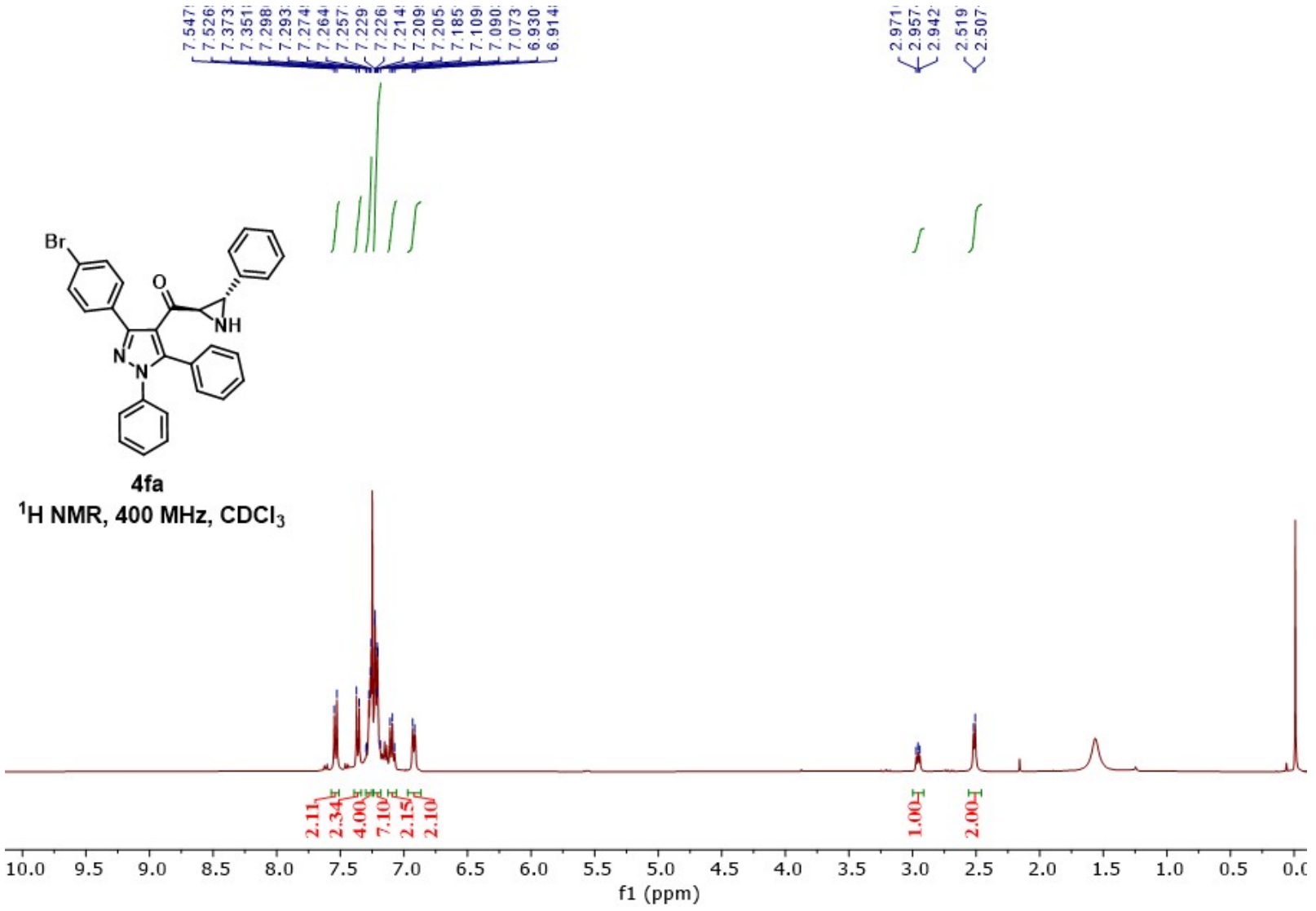
^{1}H NMR of compound 4ea in DMSO-d_6



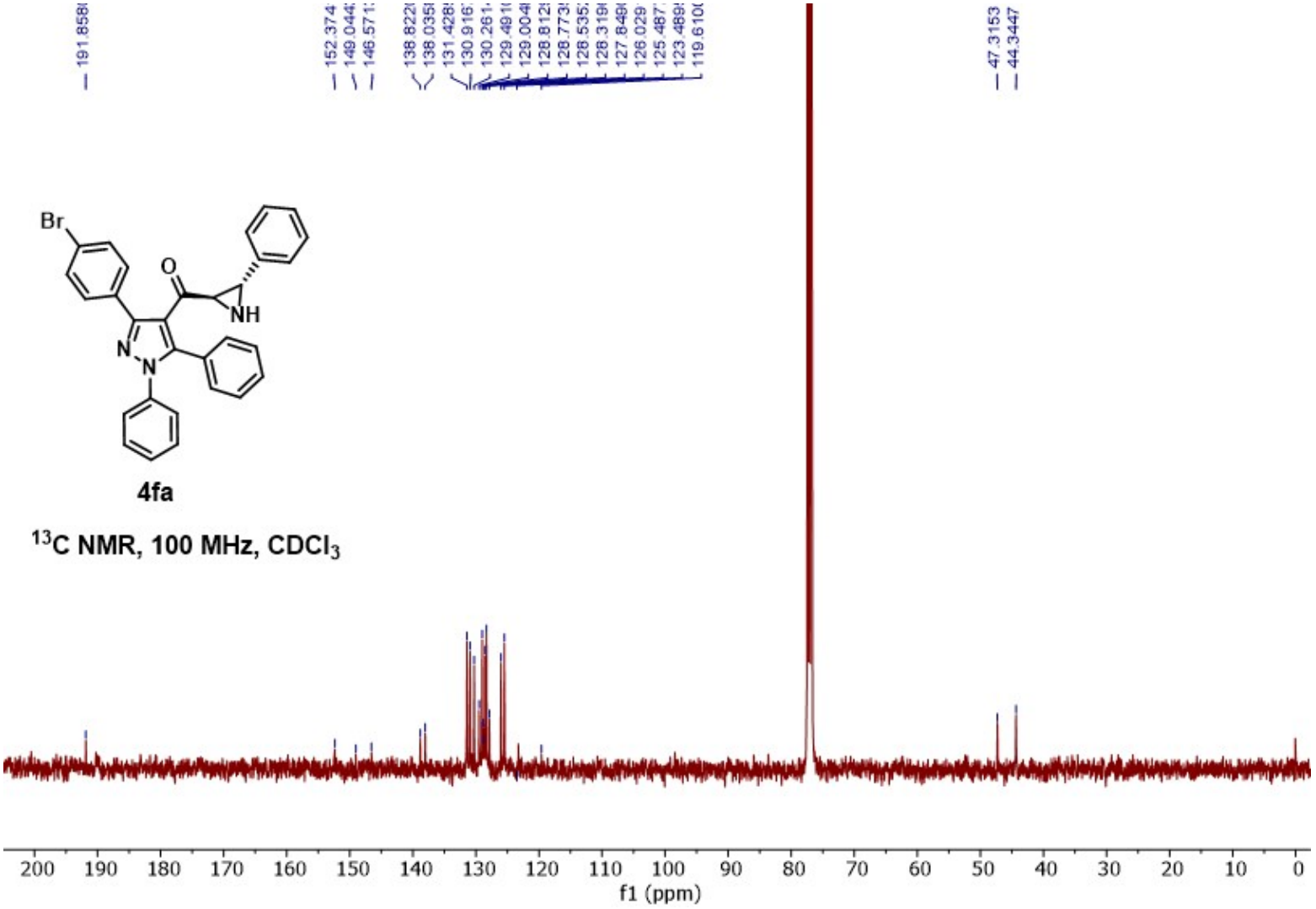
$^{13}C\{^{1}H\}$ of compound 4ea in DMSO-d_6



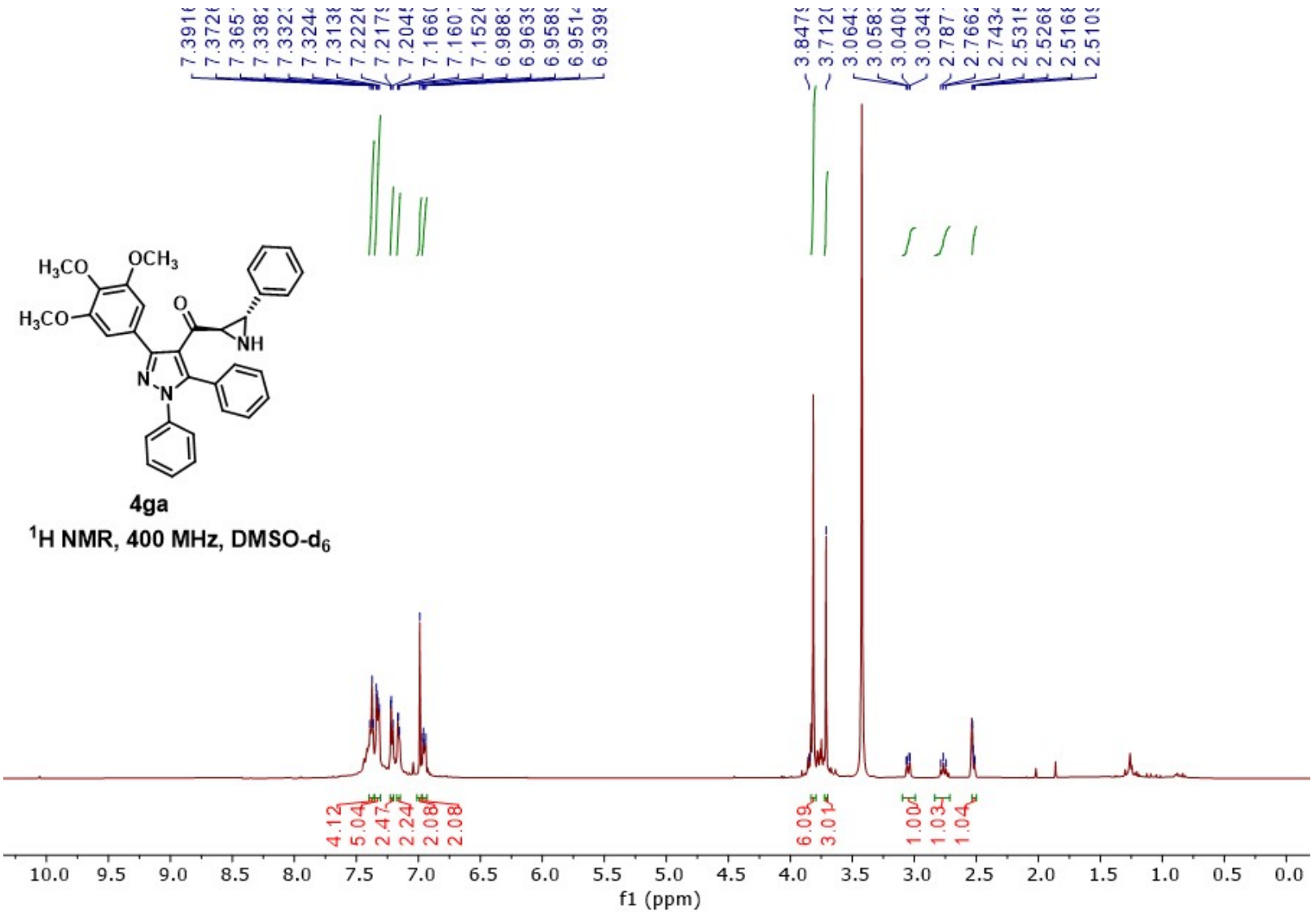
^{1}H NMR of compound 4fa in DMSO-d_6



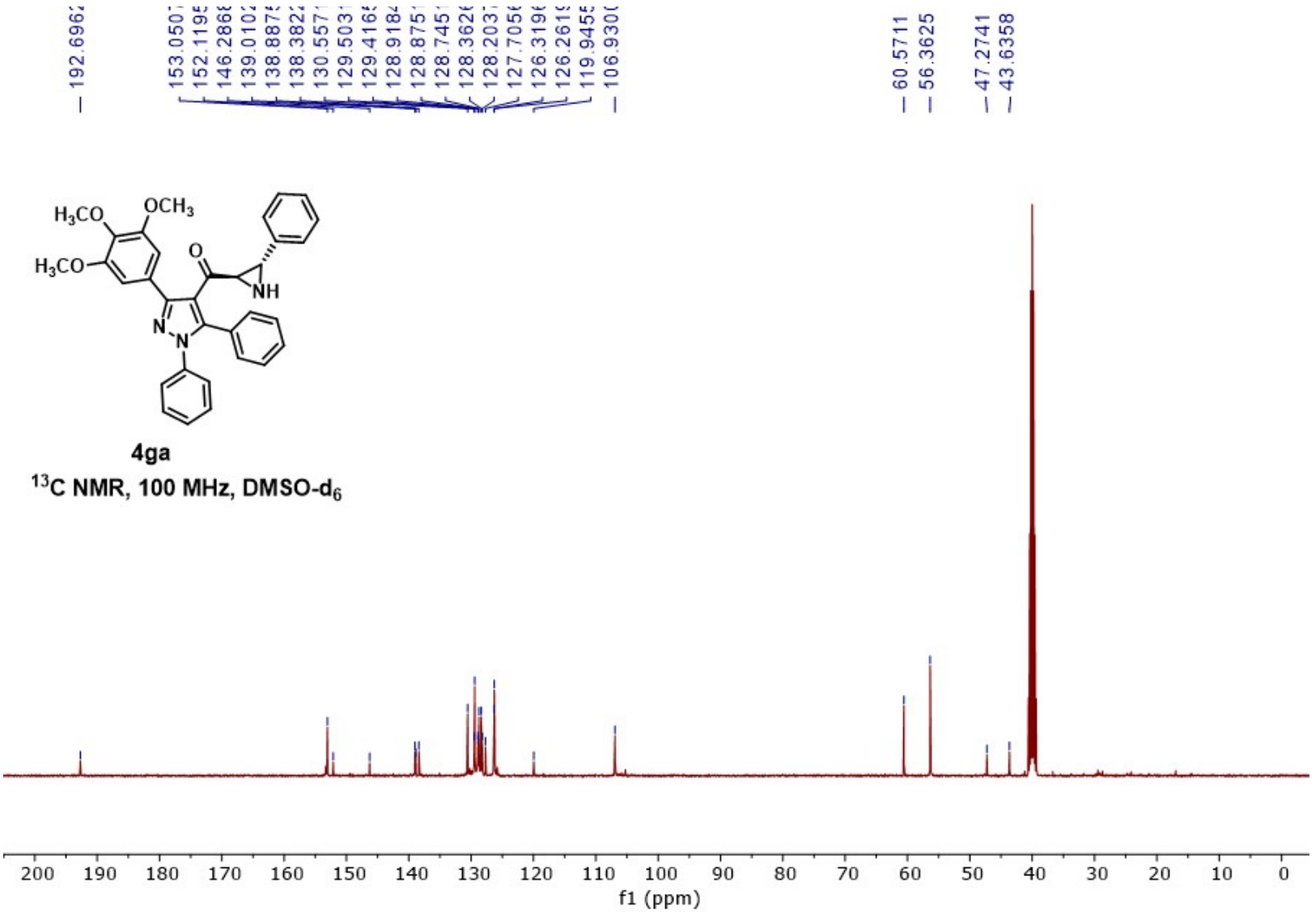
$^{13}C\{^{1}H\}$ of compound 4fa in DMSO-d_6



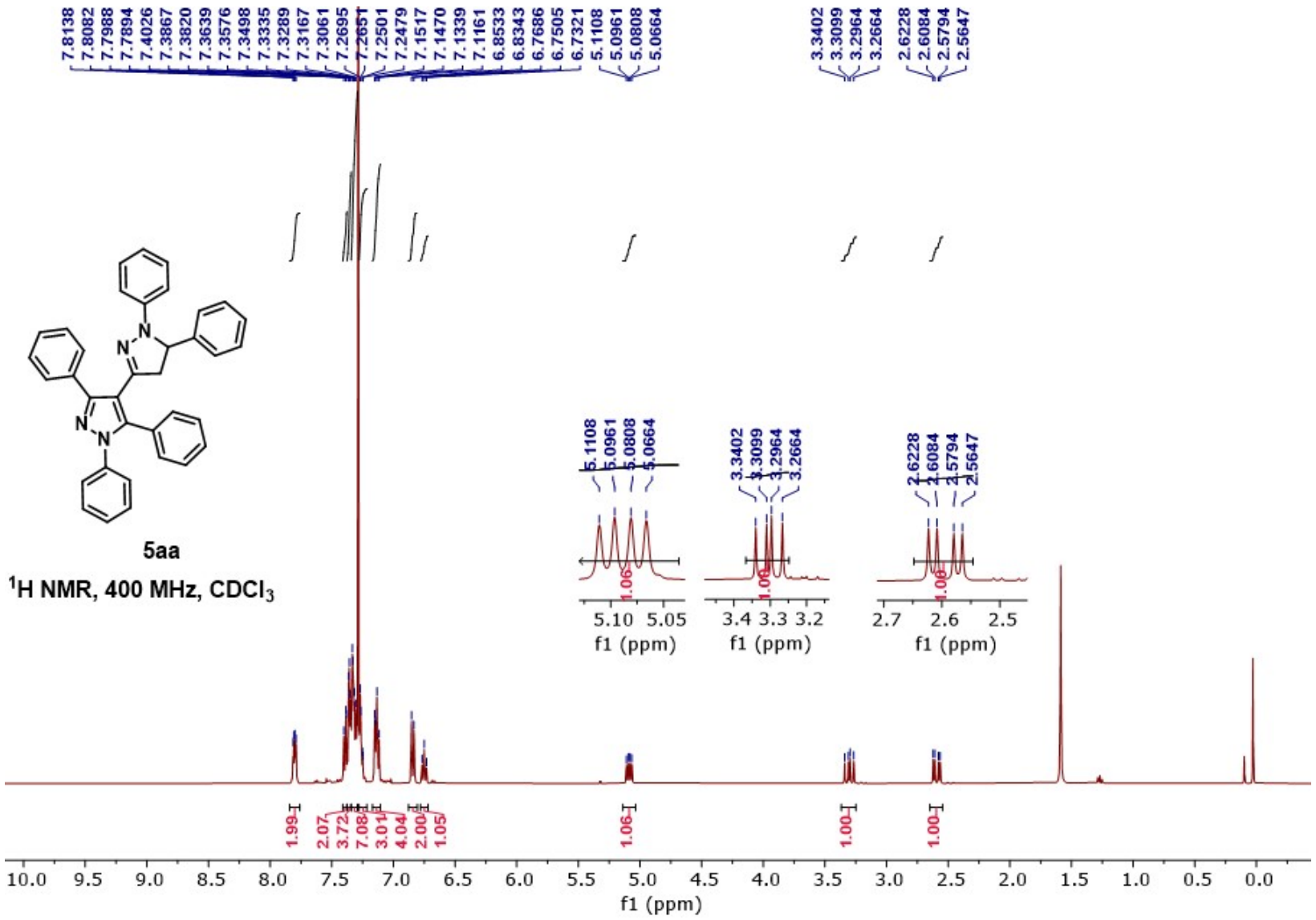
^{1}H NMR of compound 4ga in DMSO-d_6



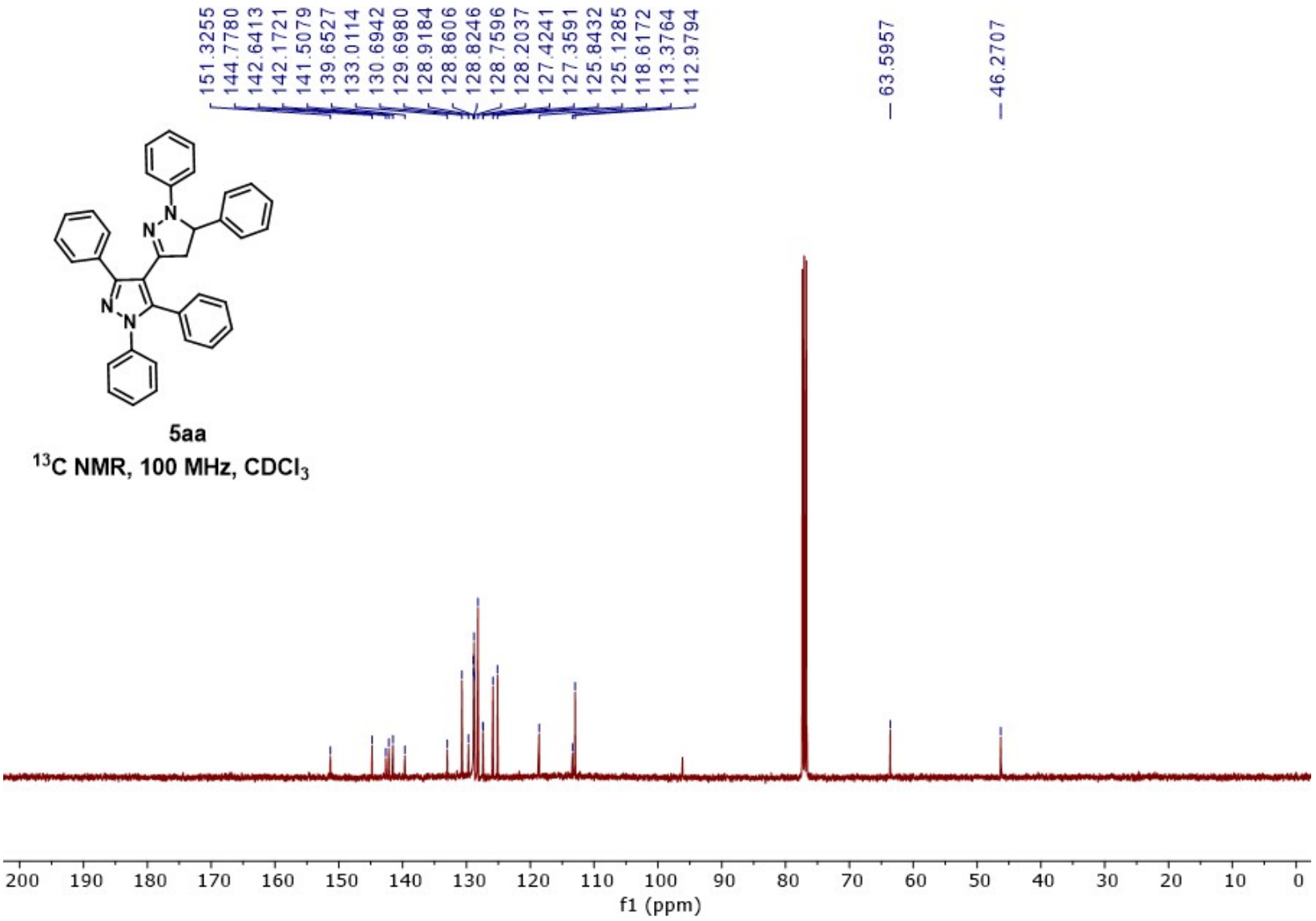
$^{13}C\{^{1}H\}$ of compound 4ga in DMSO-d_6



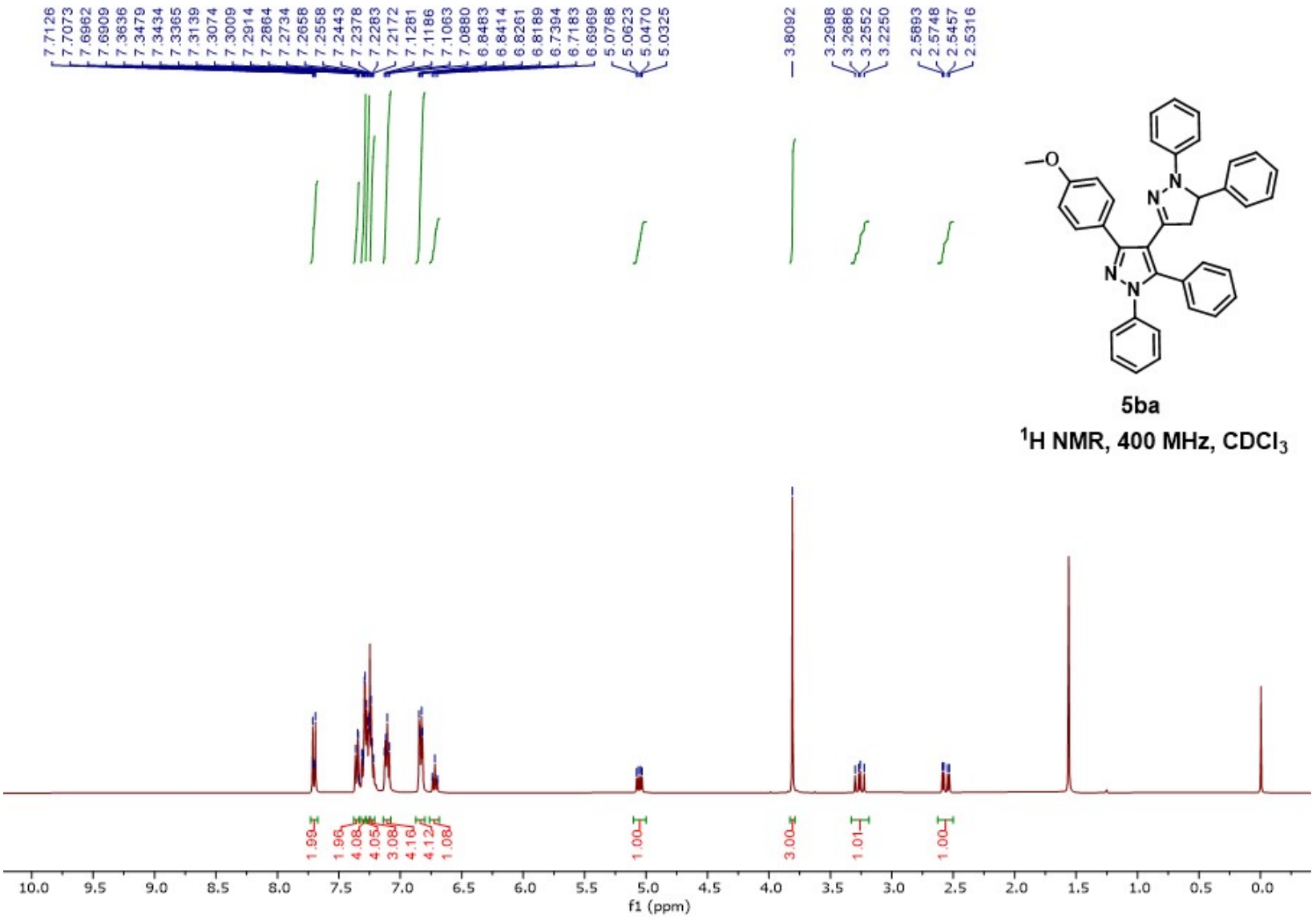
^{1}H NMR of compound 5aa in $CDCl_3$



$^{13}C\{^{1}H\}$ NMR of compound 5aa in $CDCl_3$



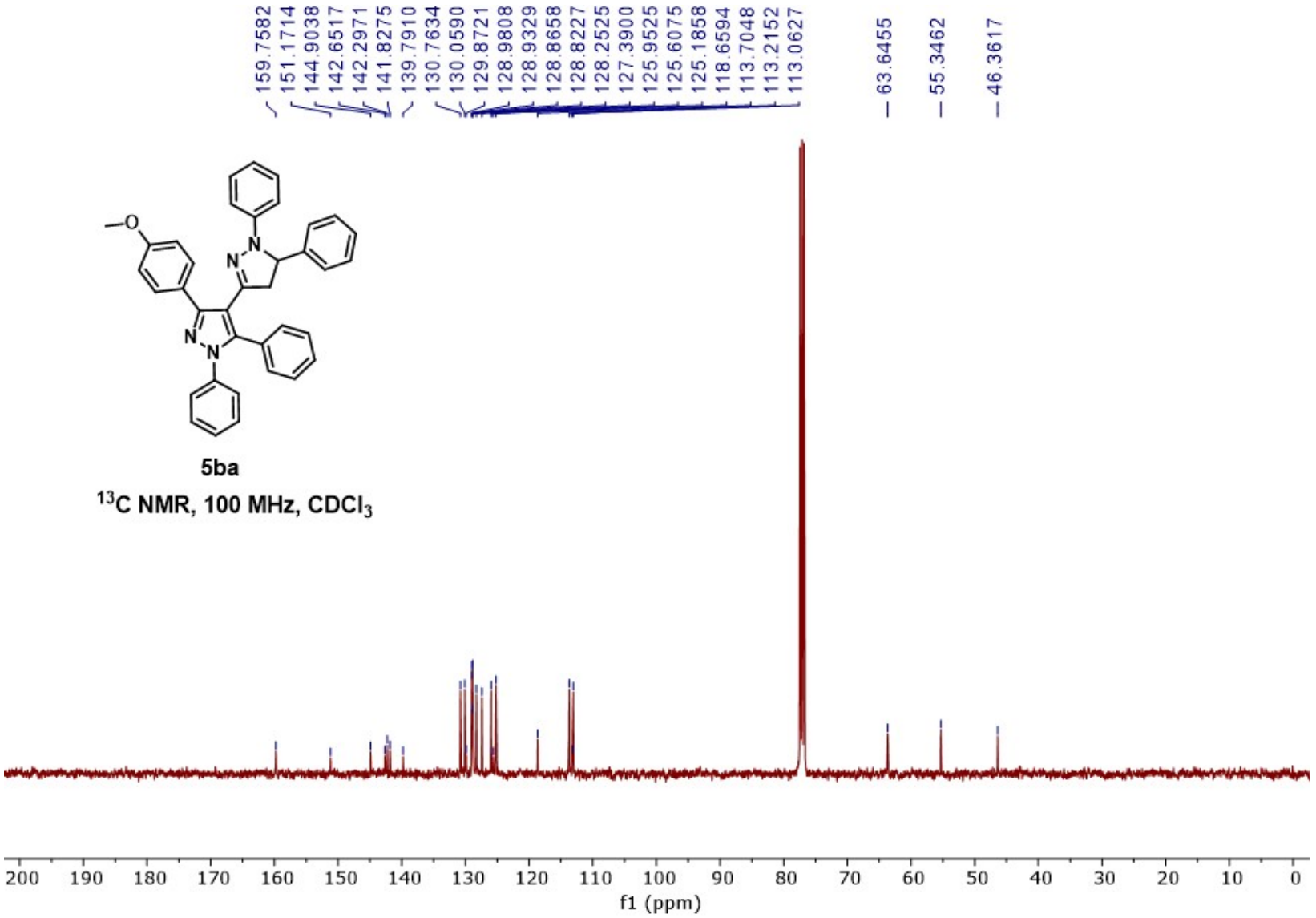
^{1}H NMR of compound 5ba in $CDCl_3$



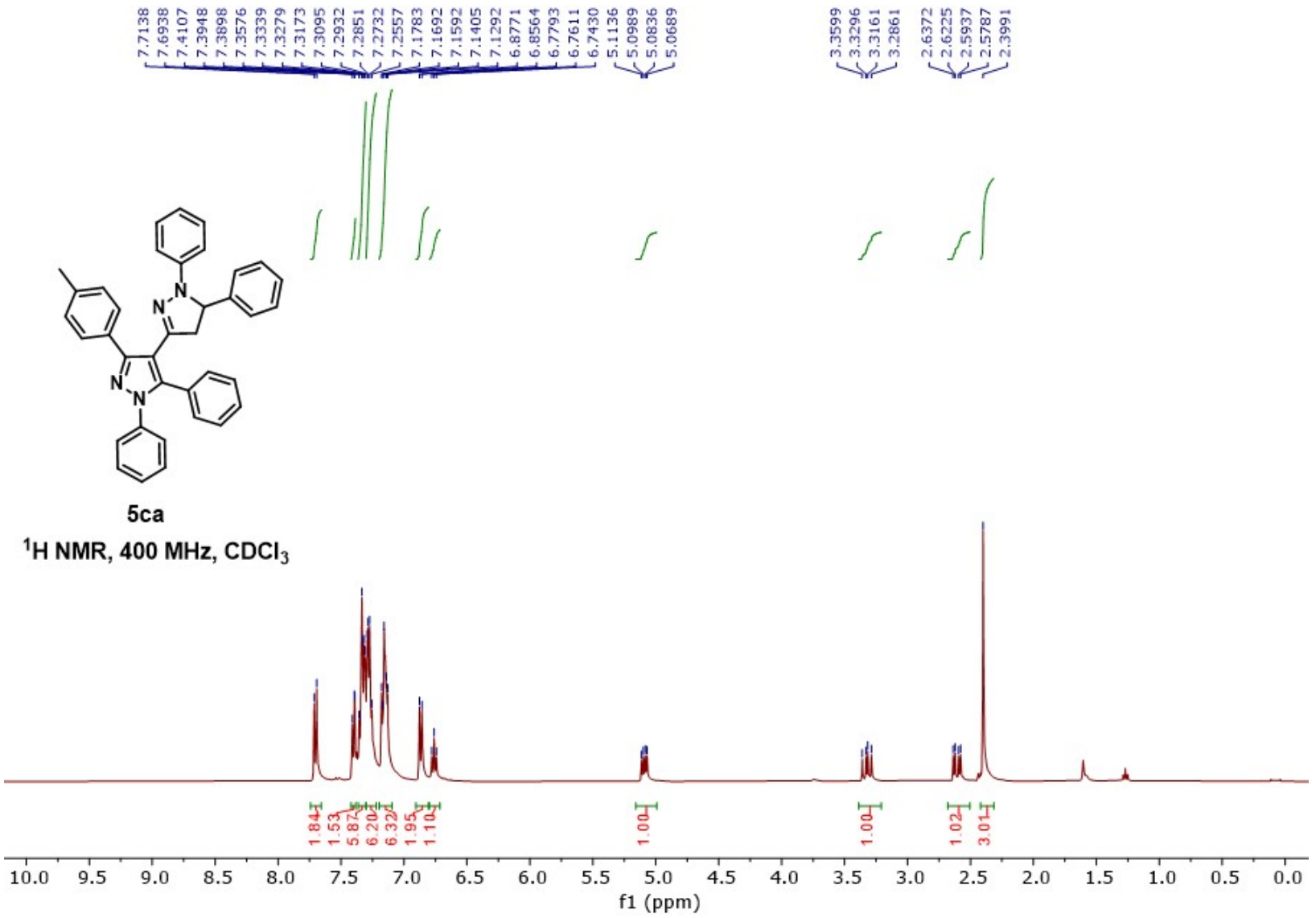
5ba

^{1}H NMR, 400 MHz, $CDCl_3$

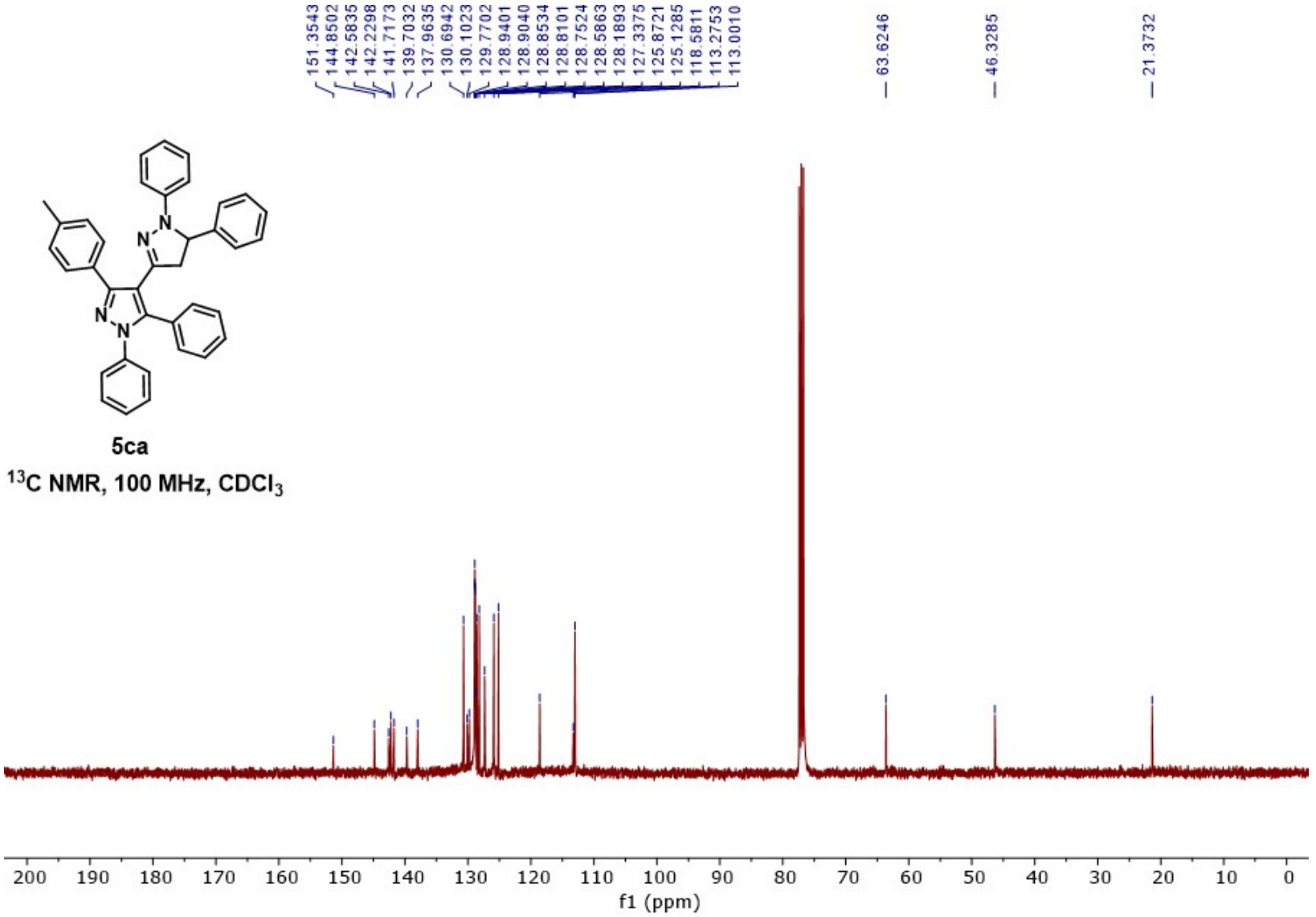
$^{13}C\{^{1}H\}$ of compound 5ba in $CDCl_3$



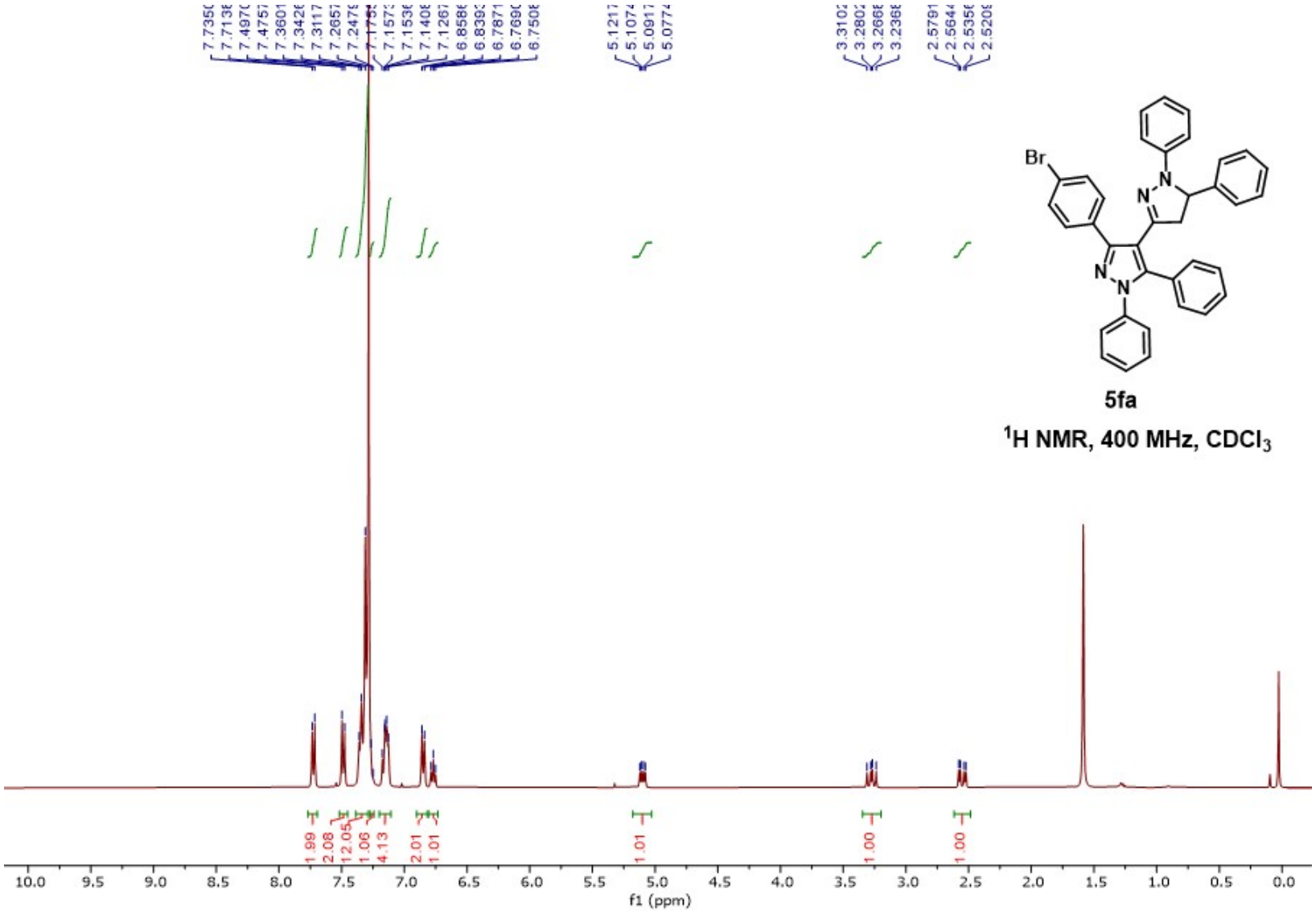
^{1}H NMR of compound 5ca in $CDCl_3$



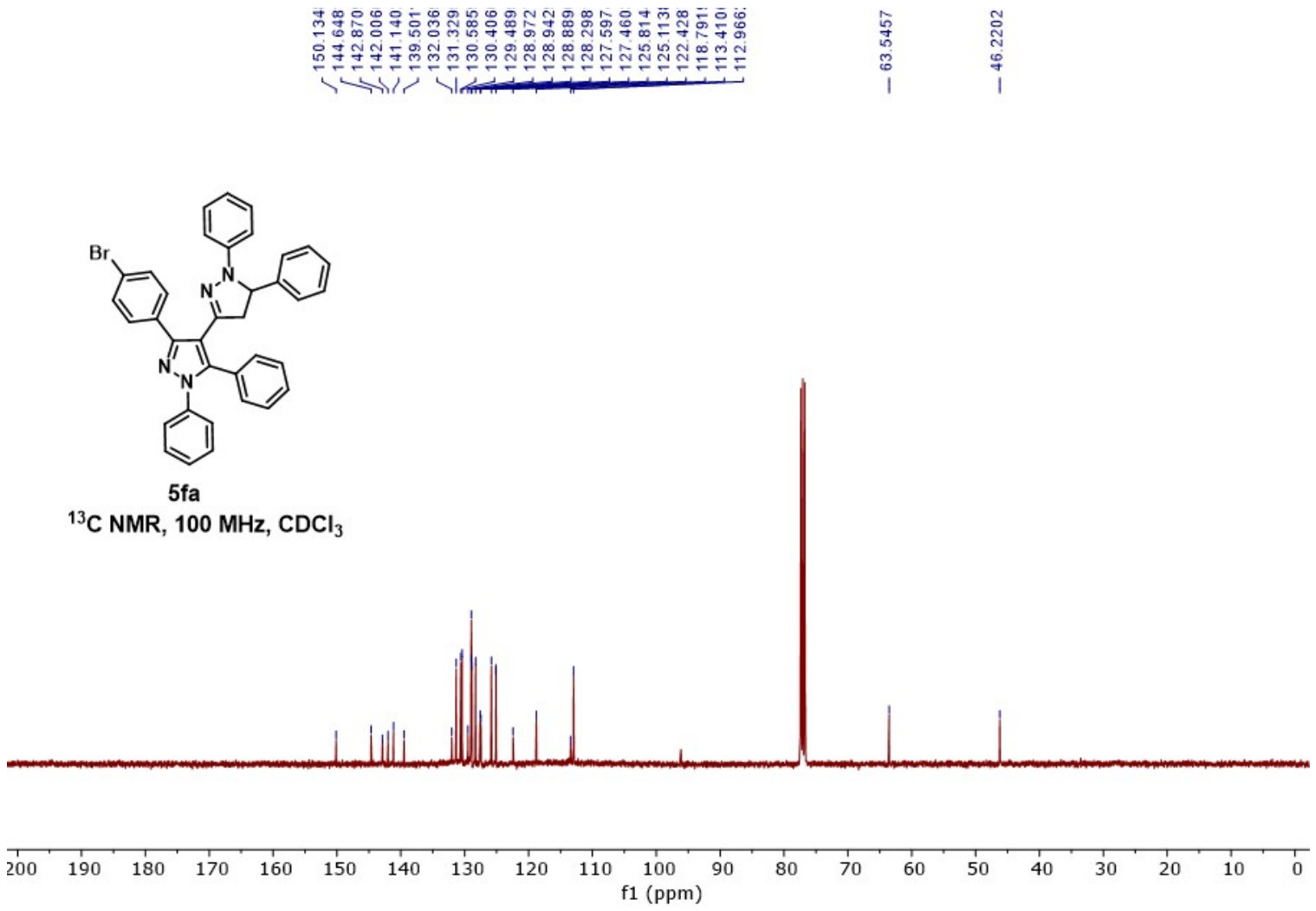
$^{13}C\{^{1}H\}$ of compound 5ca in $CDCl_3$



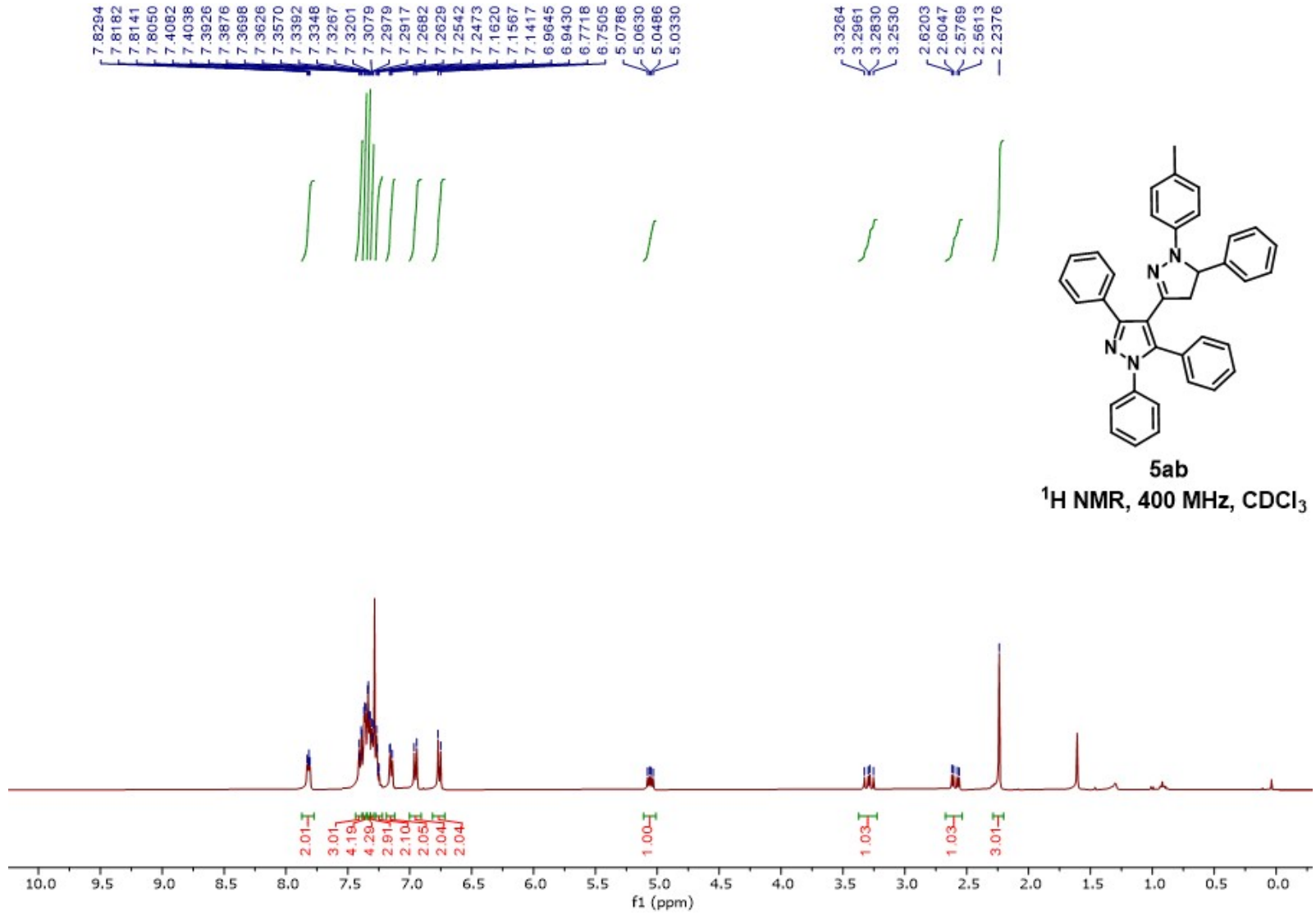
^{1}H NMR of compound 5fa in $CDCl_3$



$^{13}C\{^{1}H\}$ of compound 5fa in $CDCl_3$

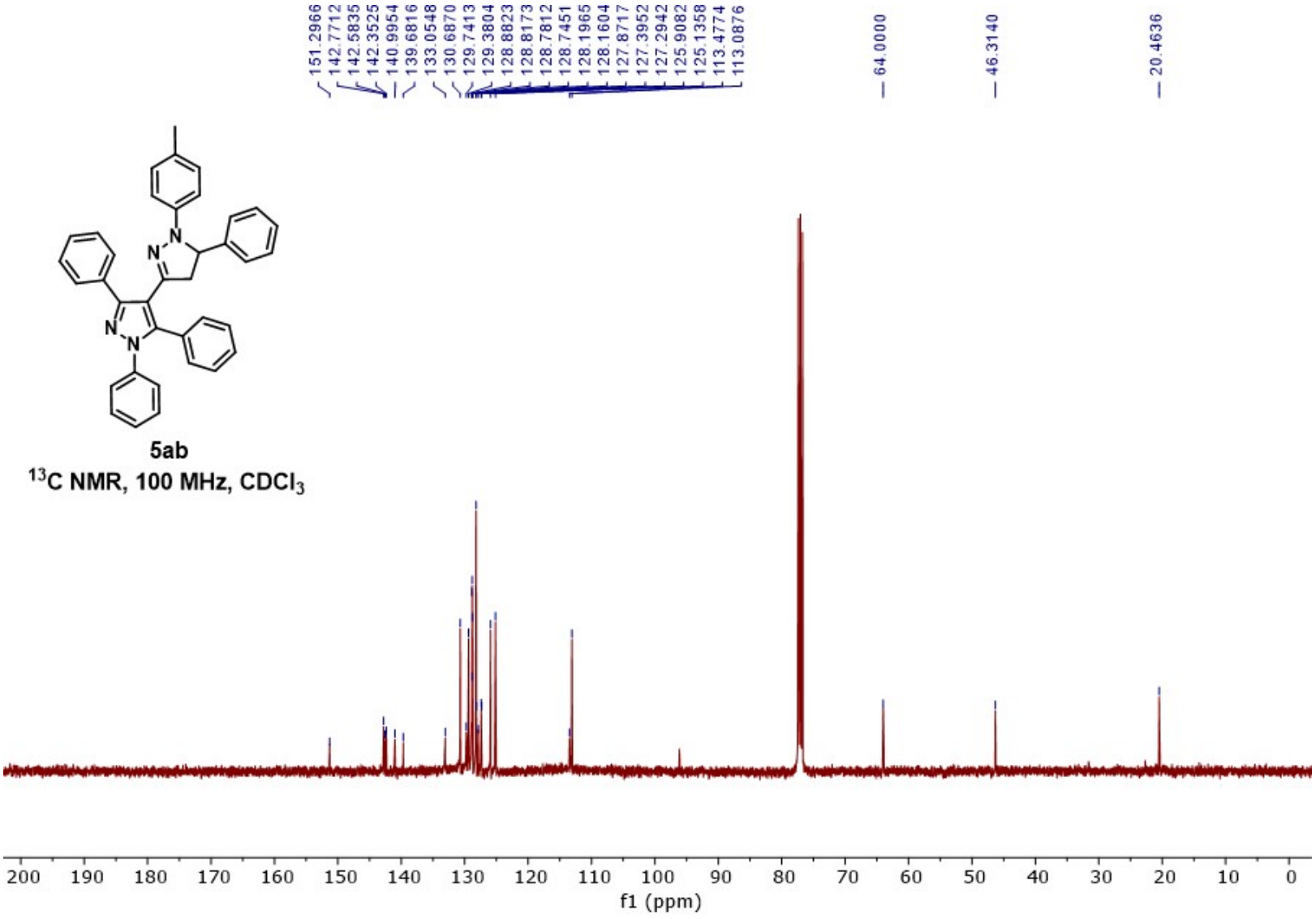


^{1}H NMR of compound 5ab in $CDCl_3$

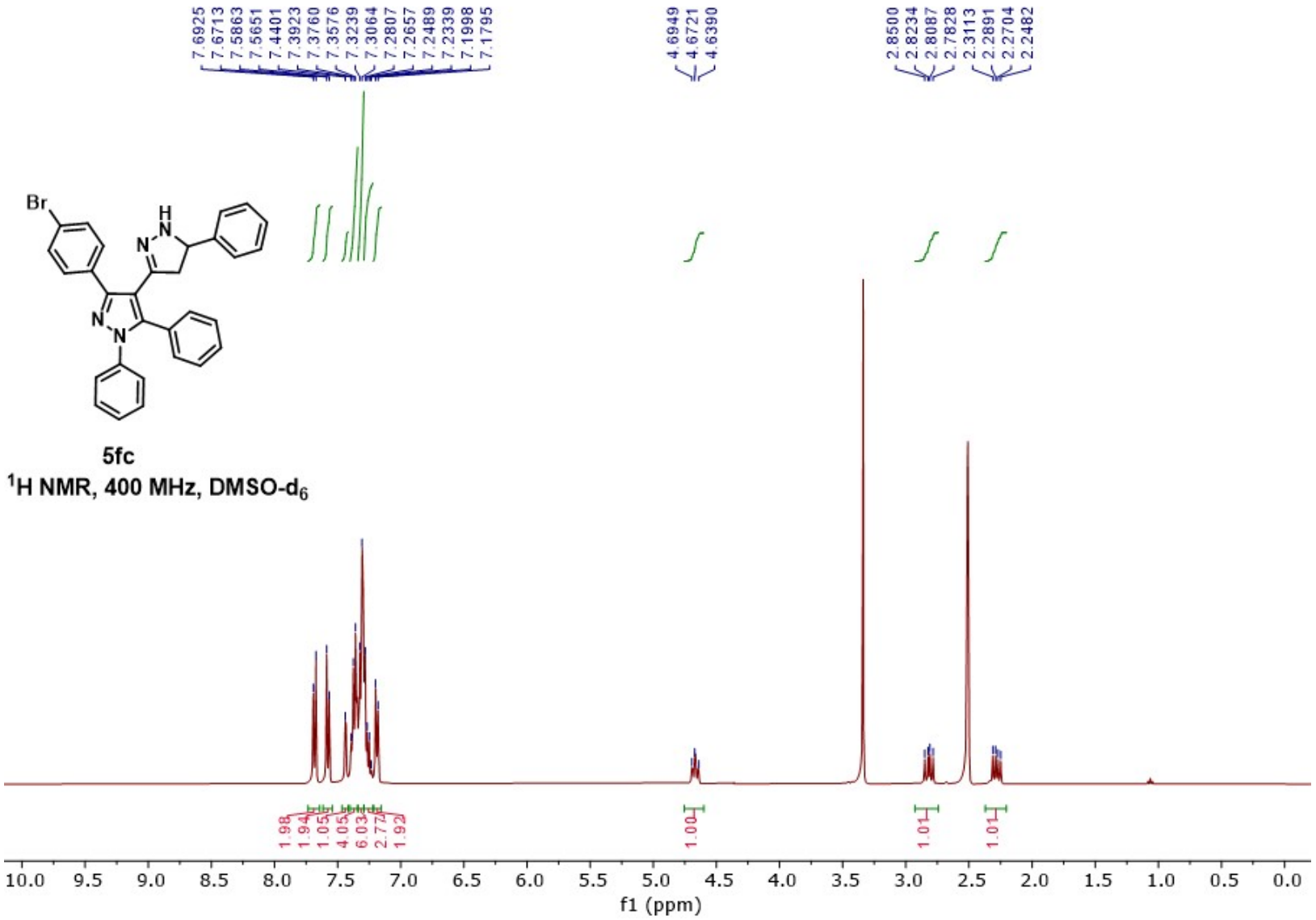


5ab
^{1}H NMR, 400 MHz, $CDCl_3$

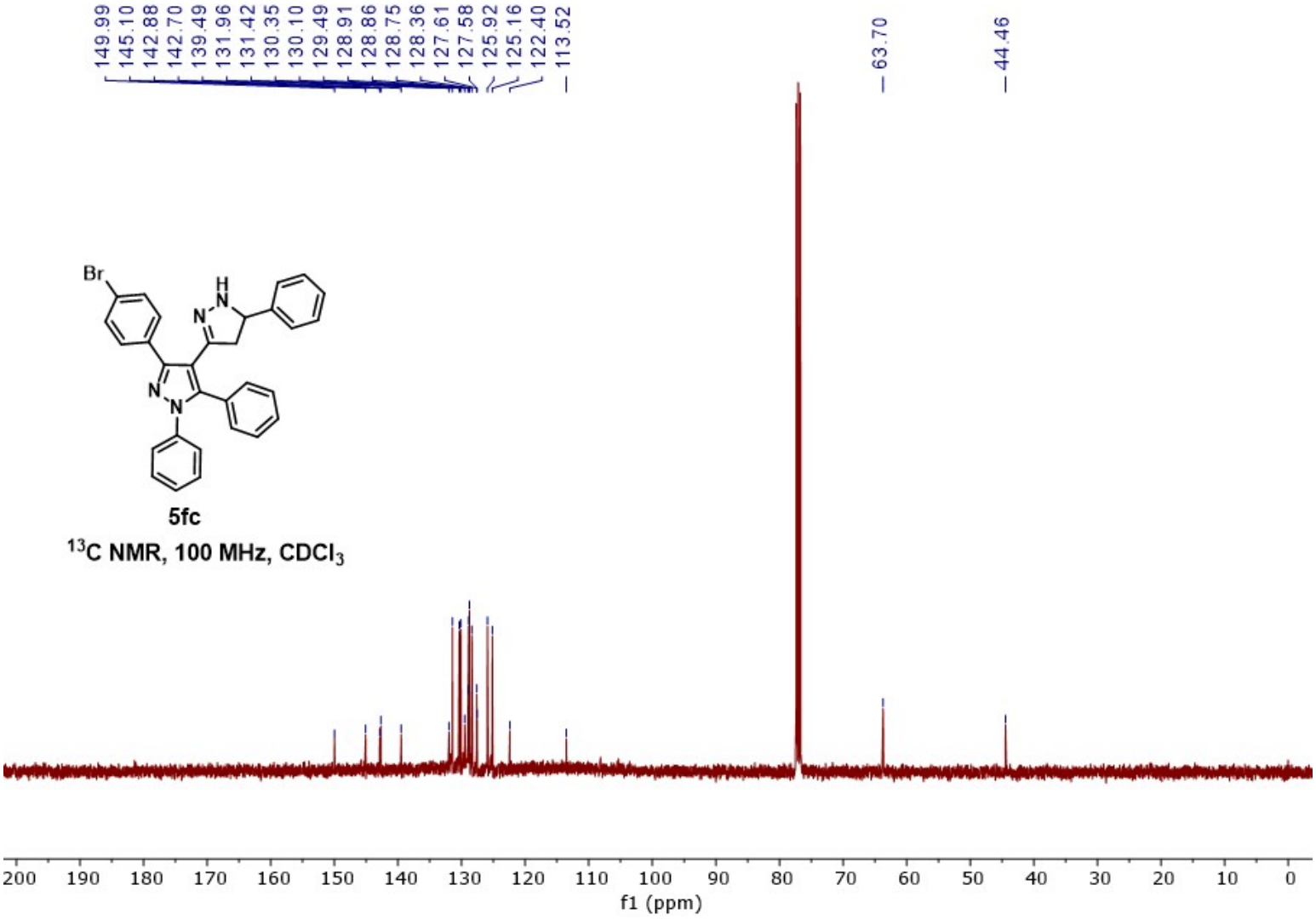
$^{13}C\{^{1}H\}$ of compound 5ab in $CDCl_3$



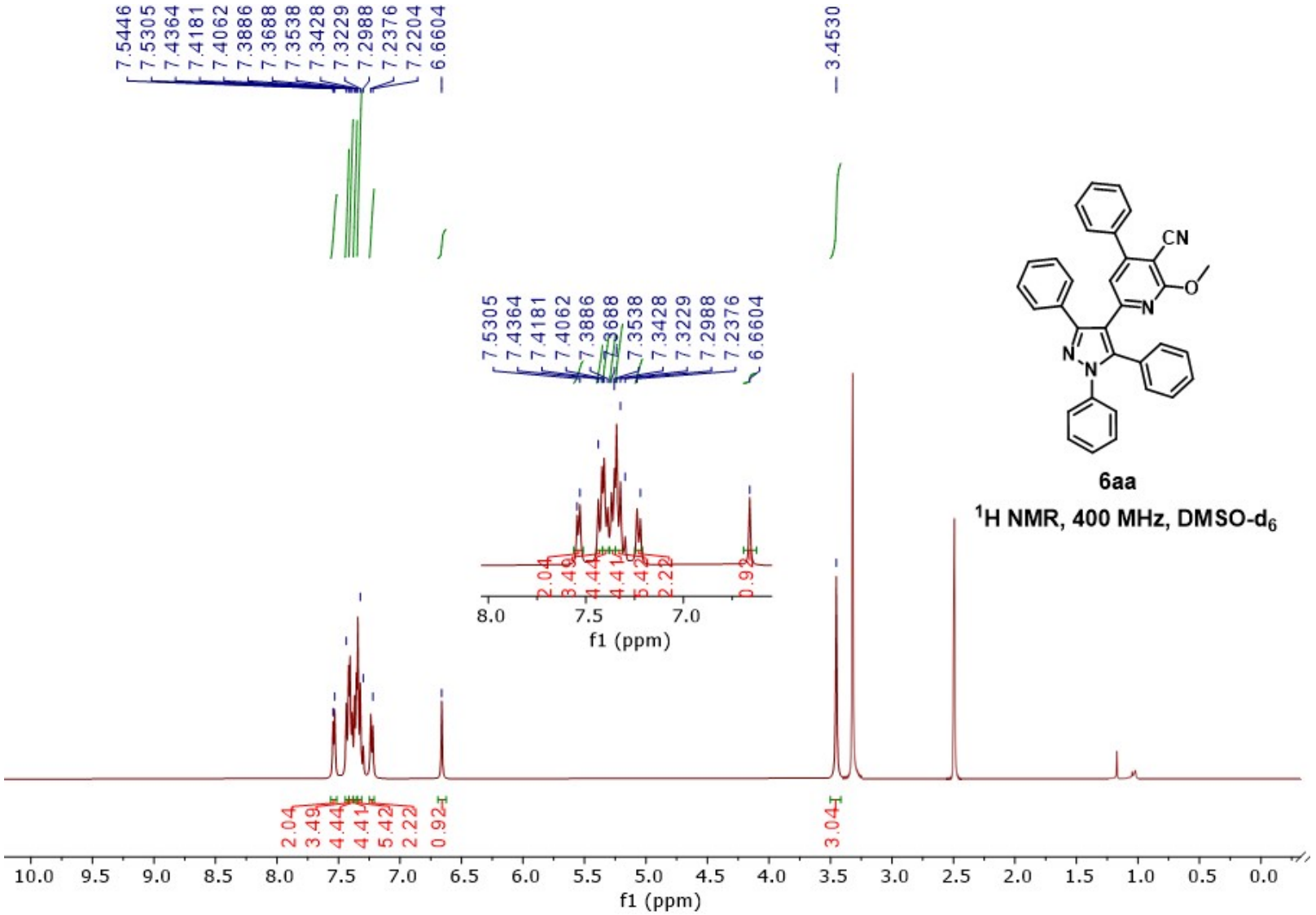
^{1}H NMR of compound 5fc in DMSO-d_6



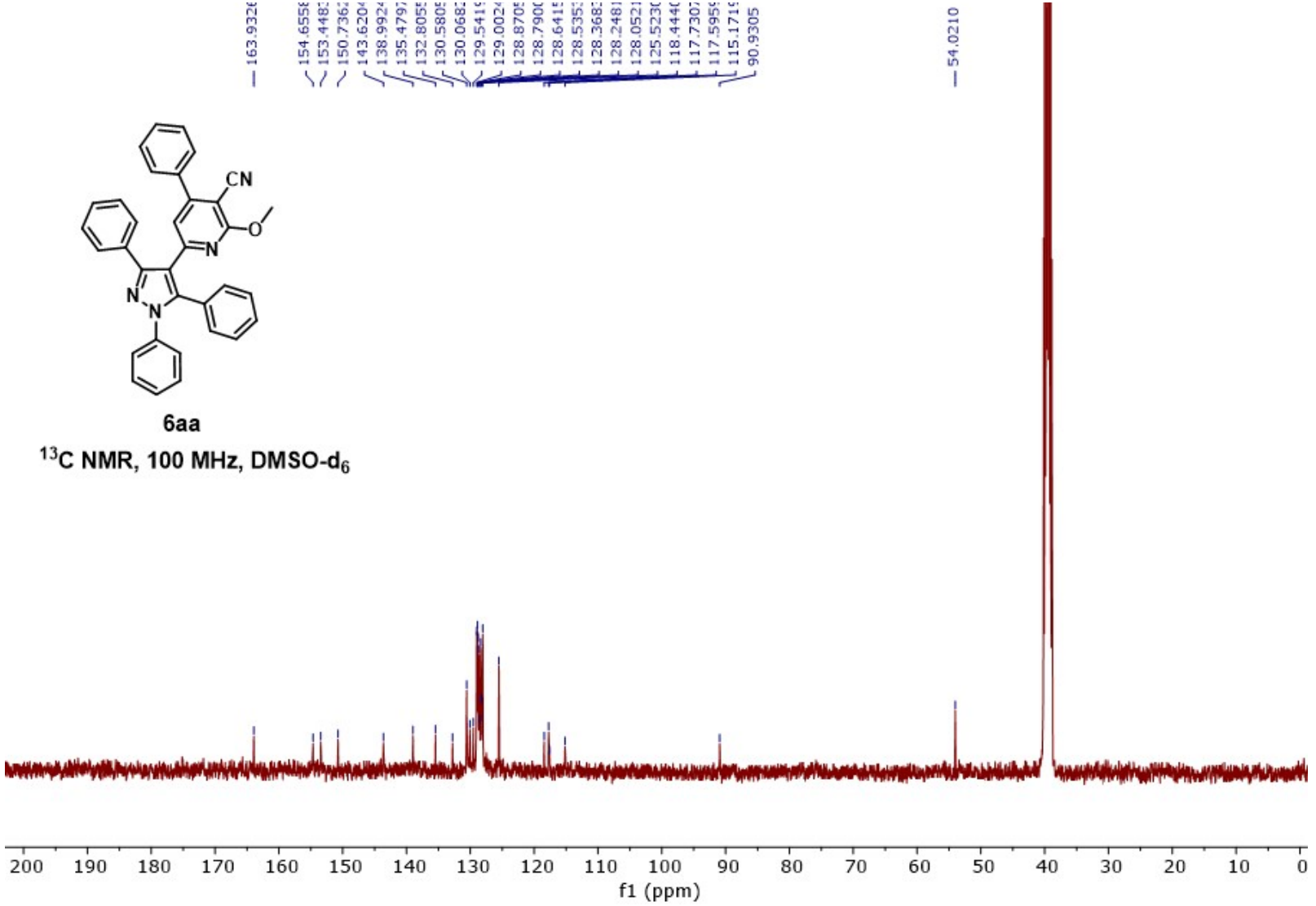
$^{13}C\{^{1}H\}$ NMR of compound 5fc in $CDCl_3$



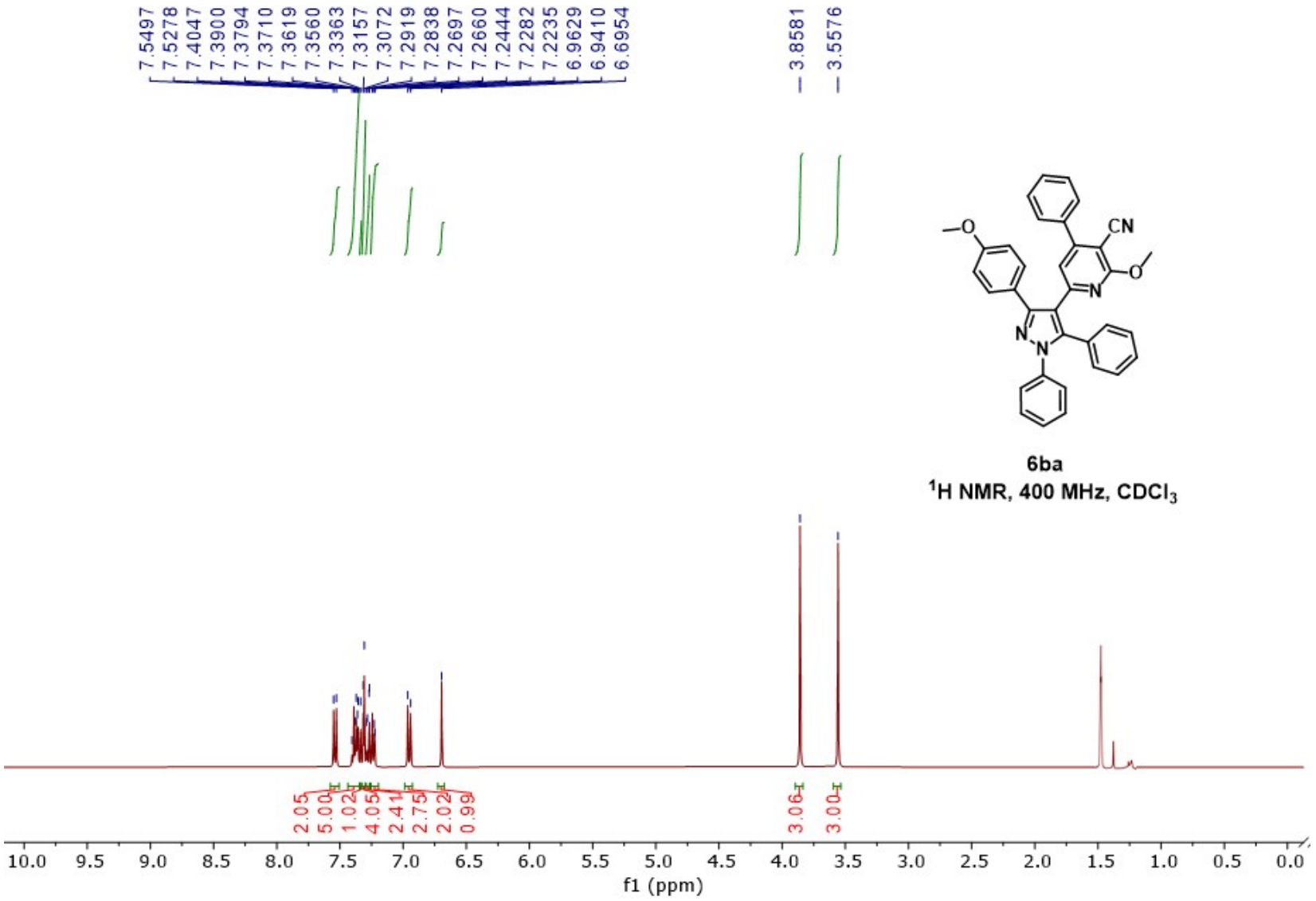
^{1}H NMR of compound 6aa in DMSO-d_6(Re-recorded spectra)



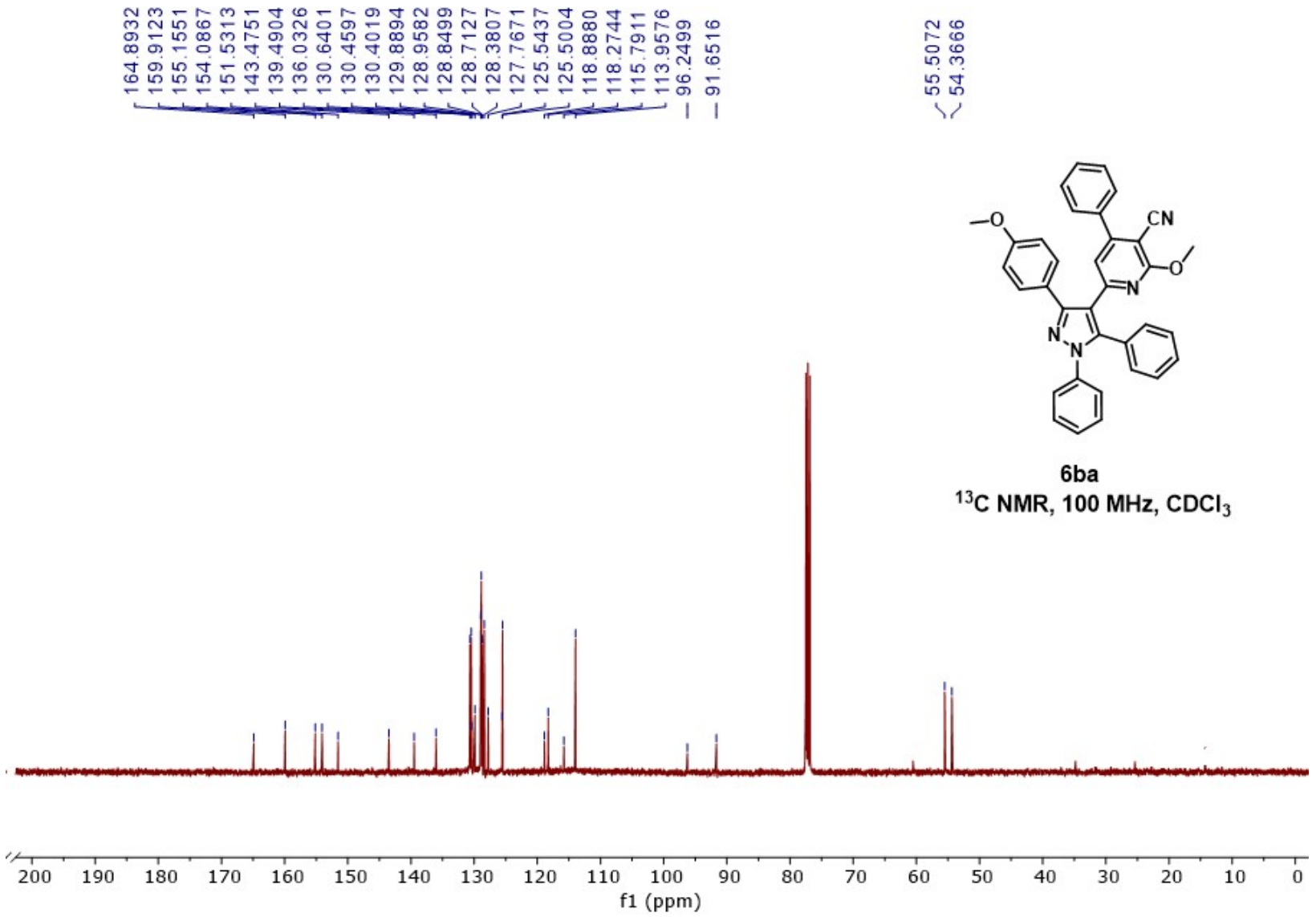
$^{13}C\{^{1}H\}$ of compound 6aa in DMSO-d_6(Re-recorded spectra)



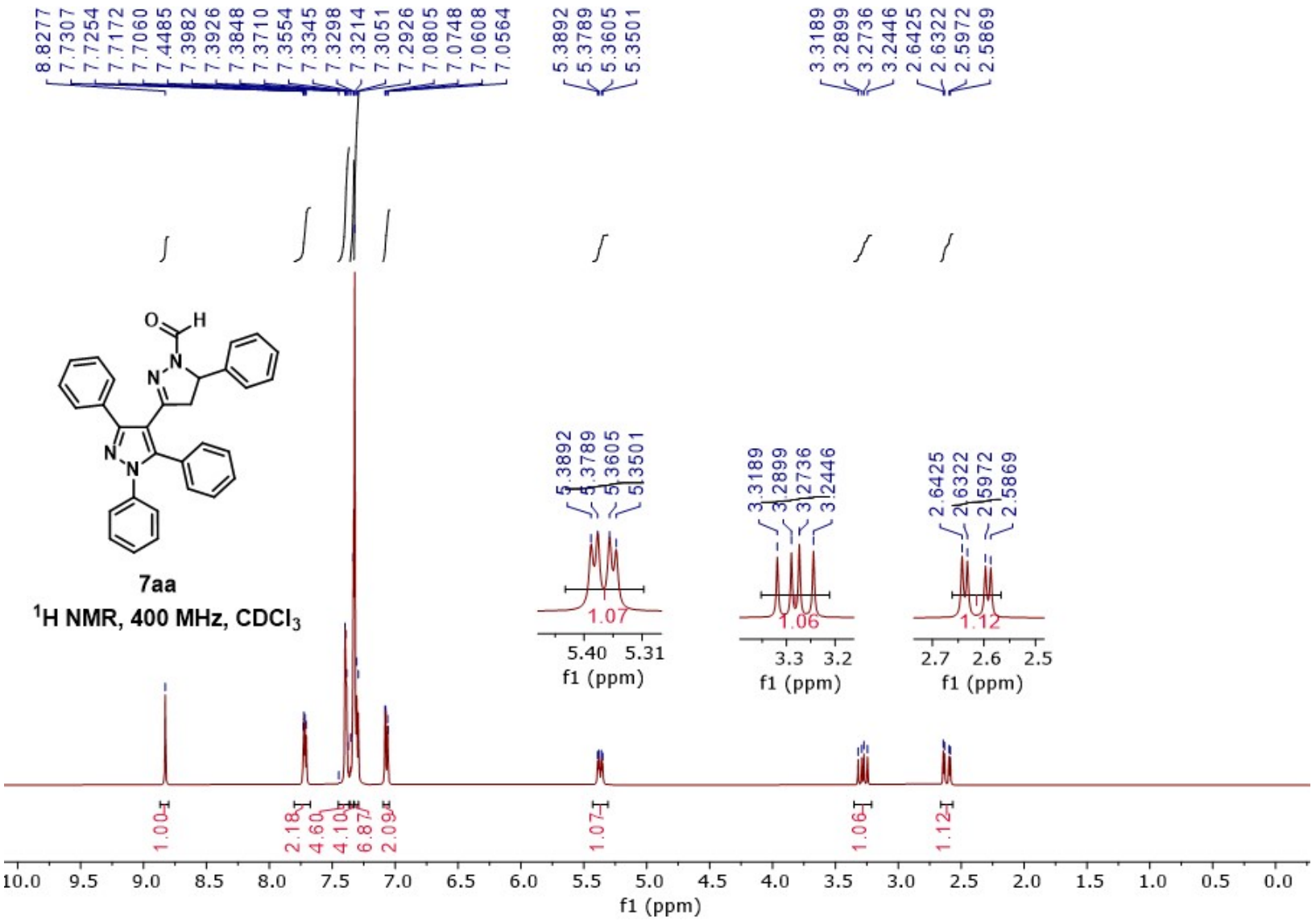
^{1}H NMR of compound 6ba in $CDCl_3$(Re-recorded spectra)



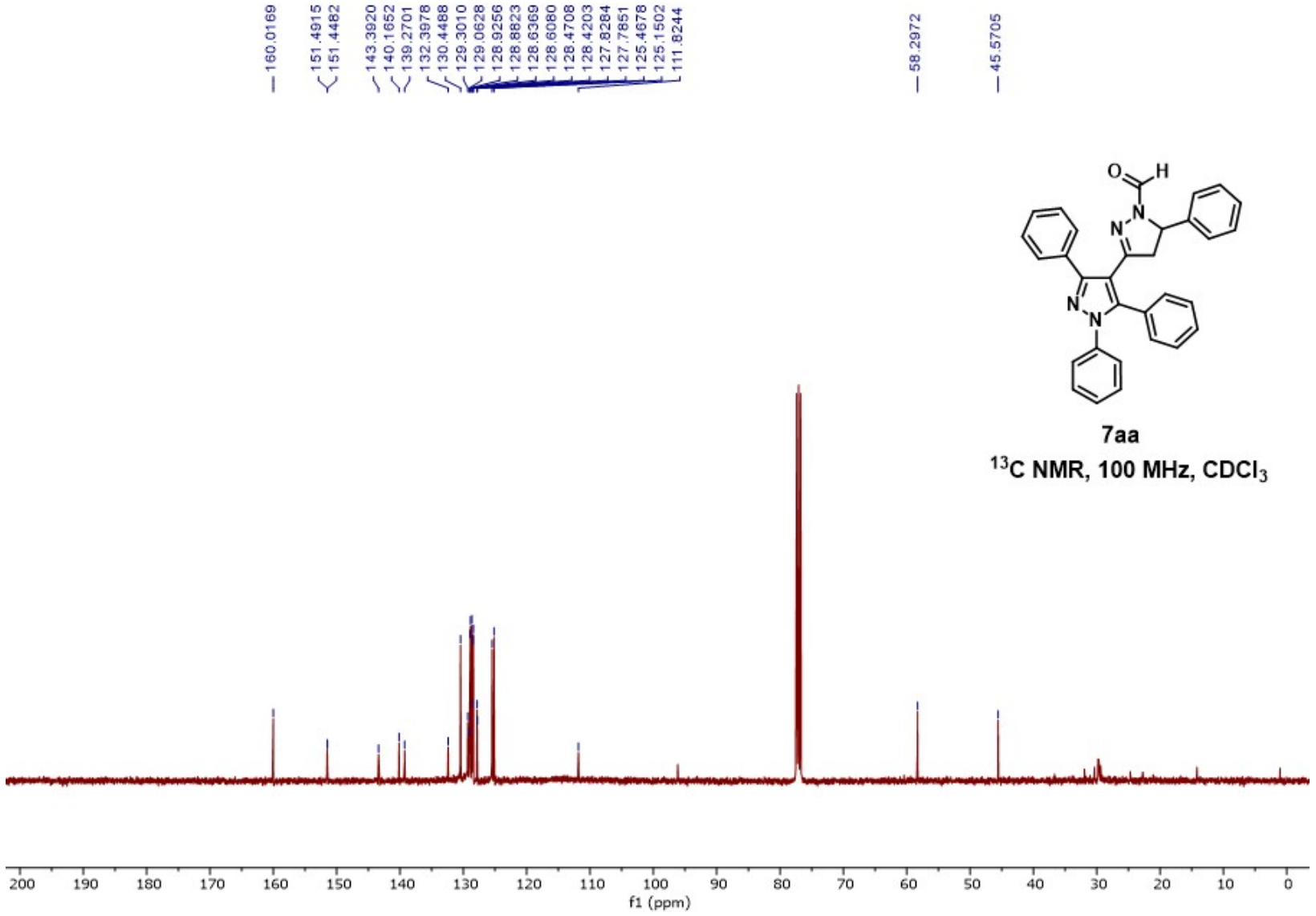
$^{13}C\{^{1}H\}$ NMR of compound 6ba in $CDCl_3$(Re-recorded spectra)



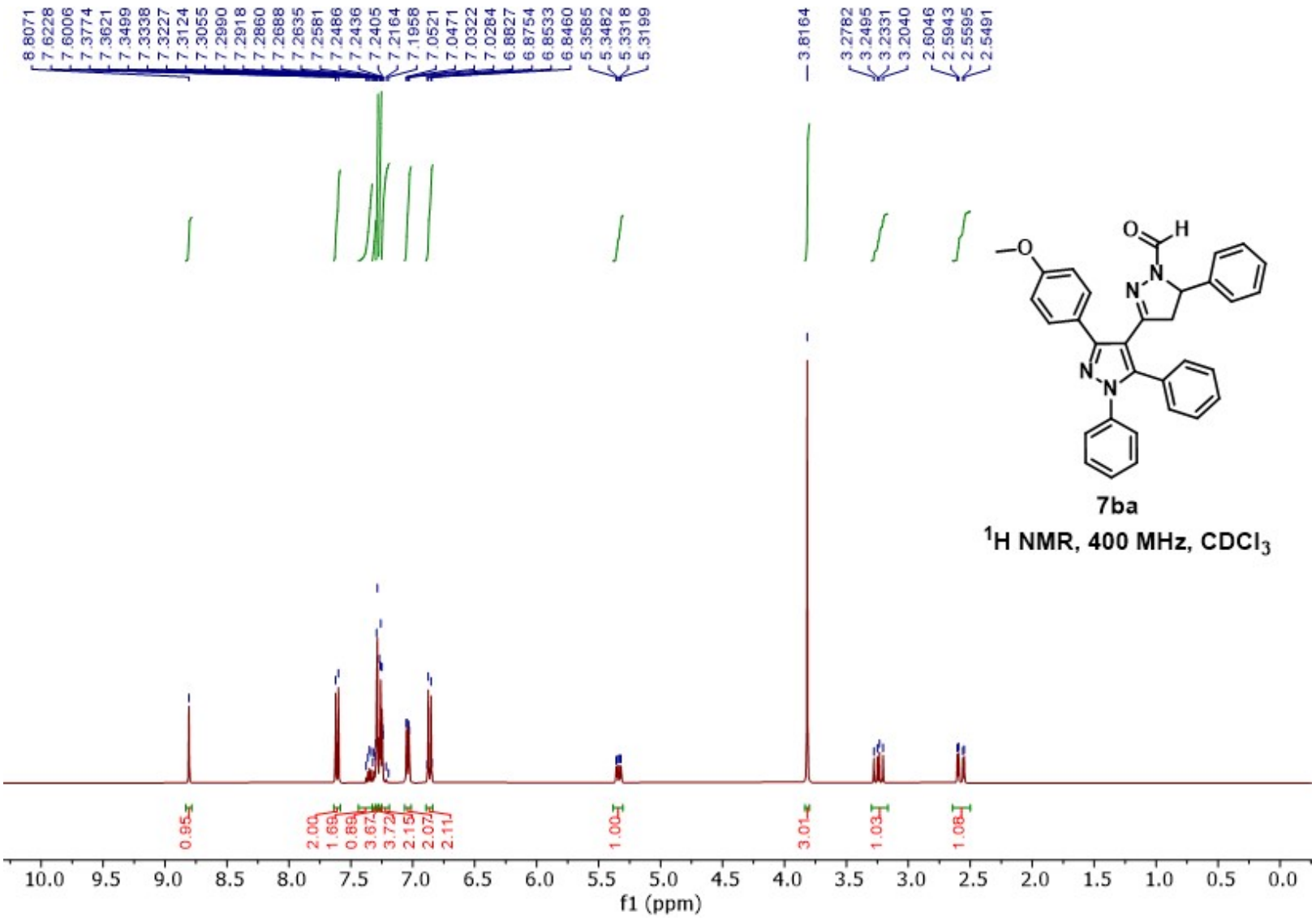
^{1}H NMR of compound 7aa in $CDCl_3$



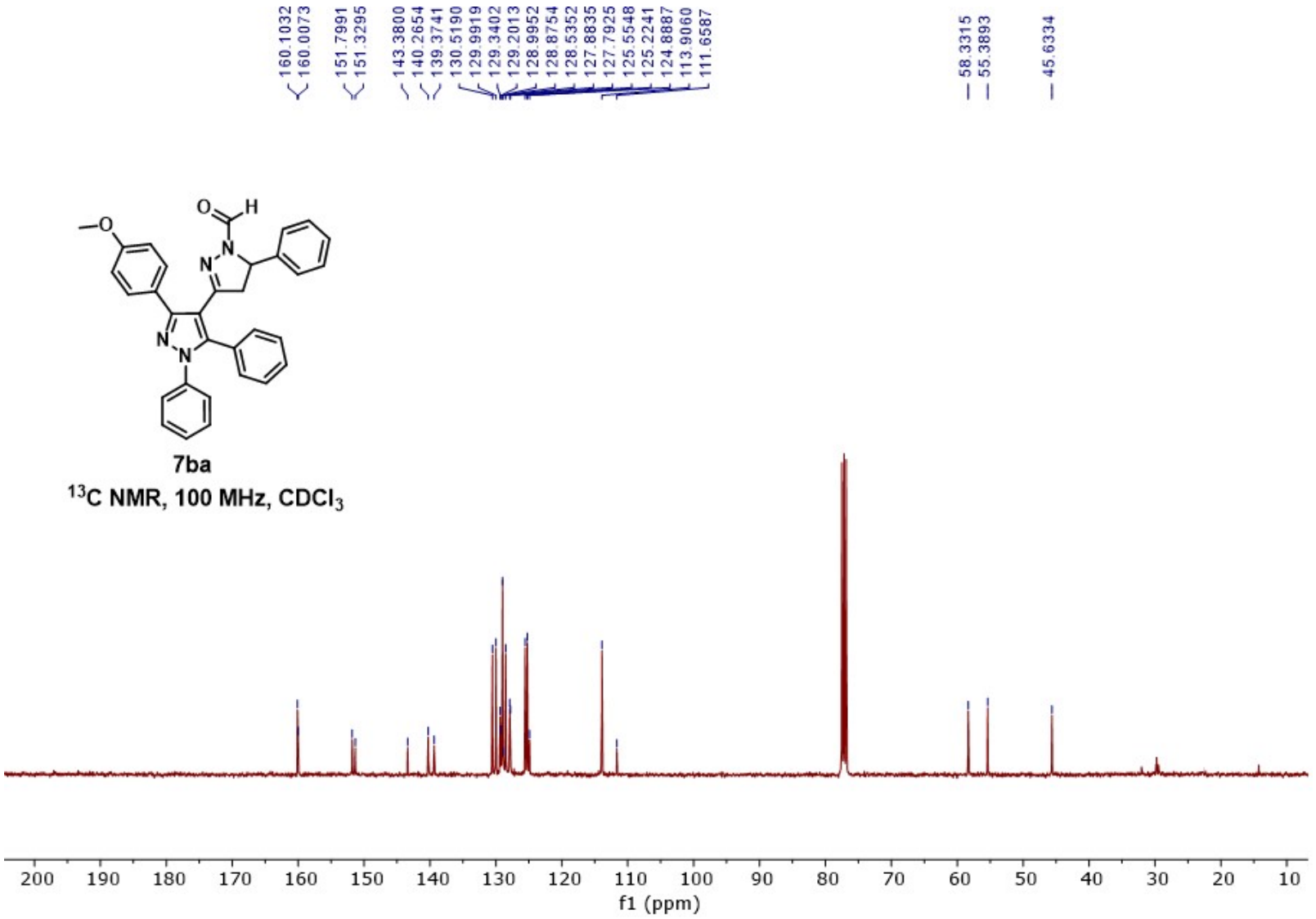
$^{13}C\{^{1}H\}$ NMR of compound 7aa in $CDCl_3$



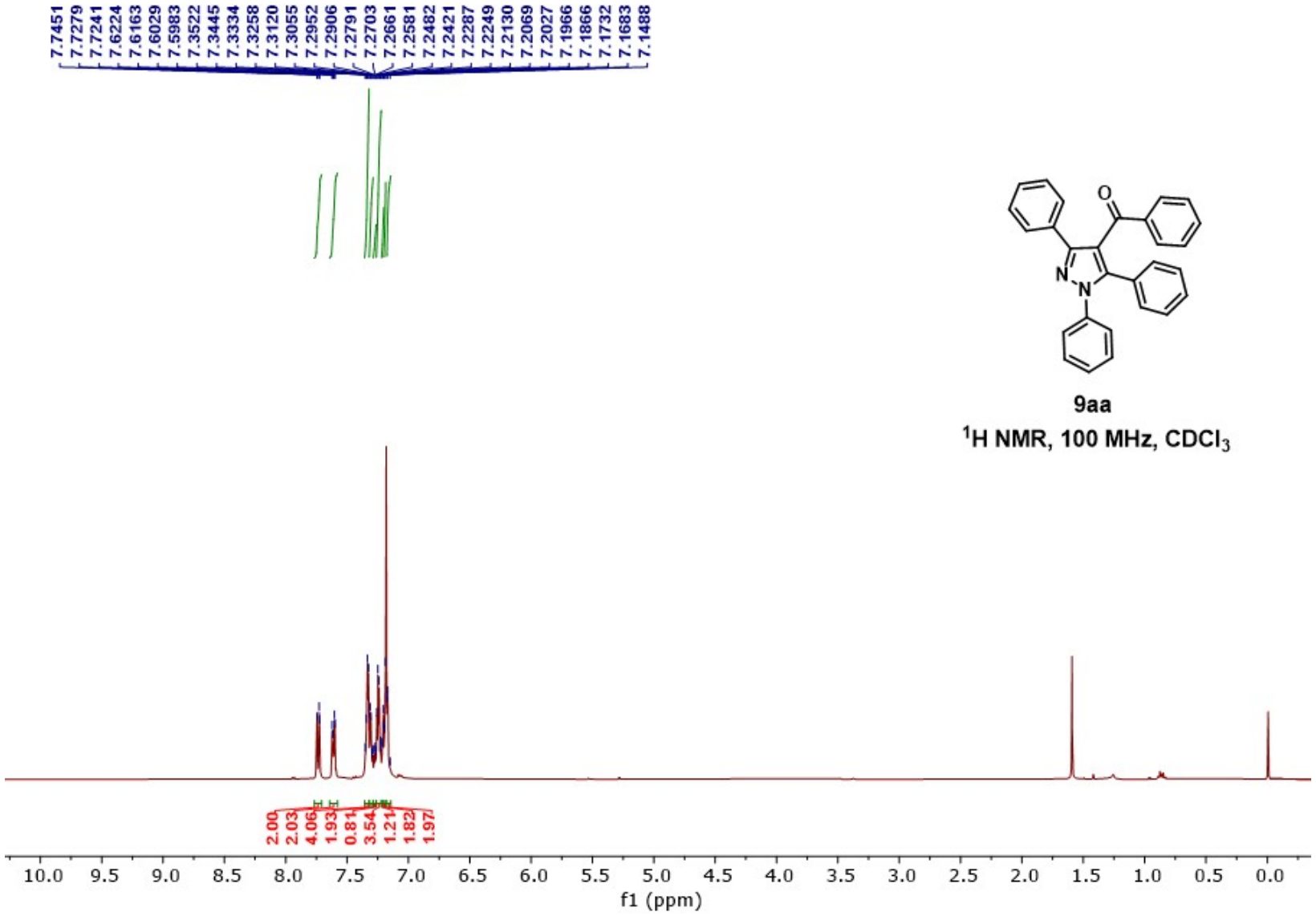
^{1}H NMR of compound 7ba in $CDCl_3$



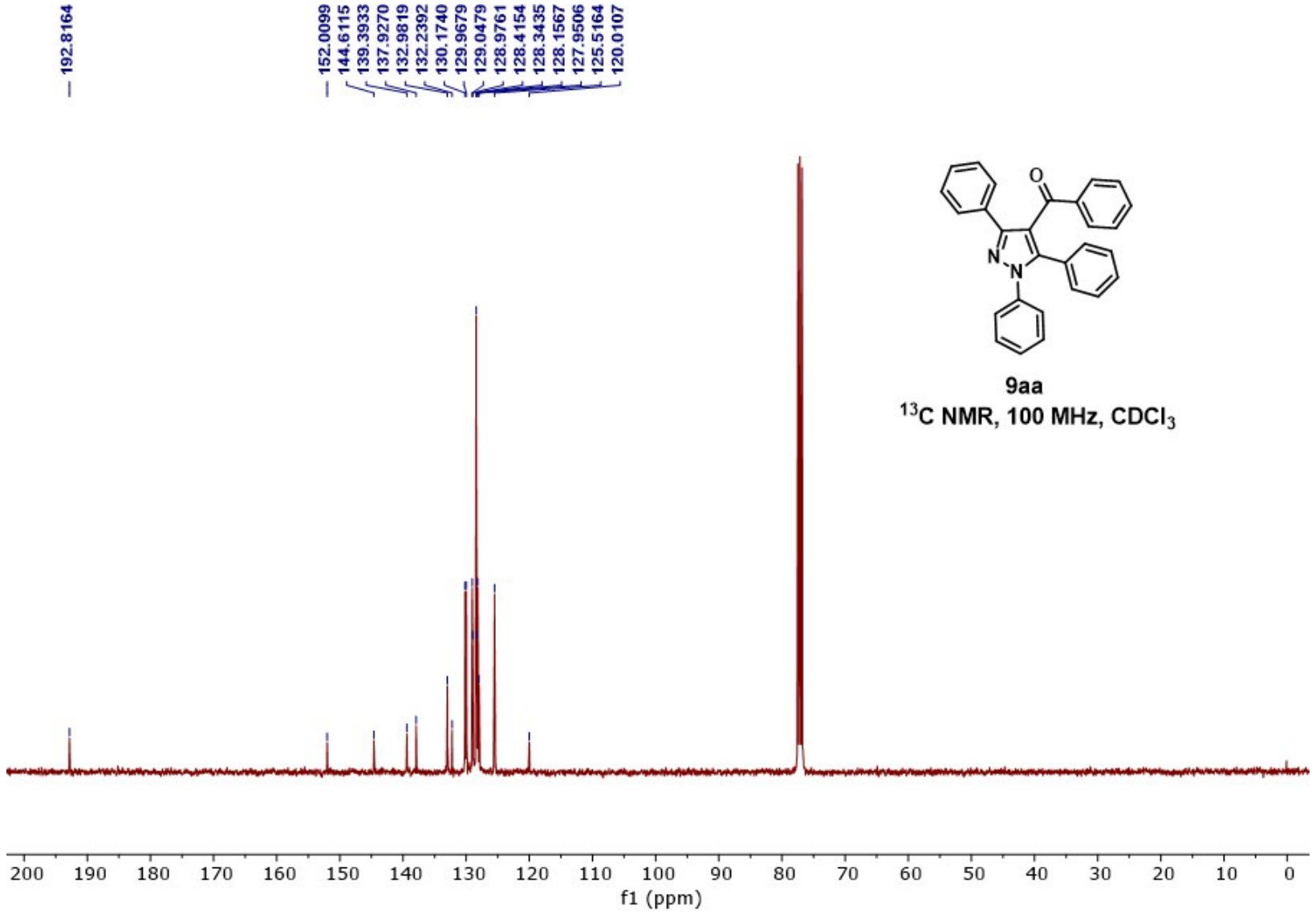
$^{13}C\{^{1}H\}$ NMR of compound 7ba in $CDCl_3$



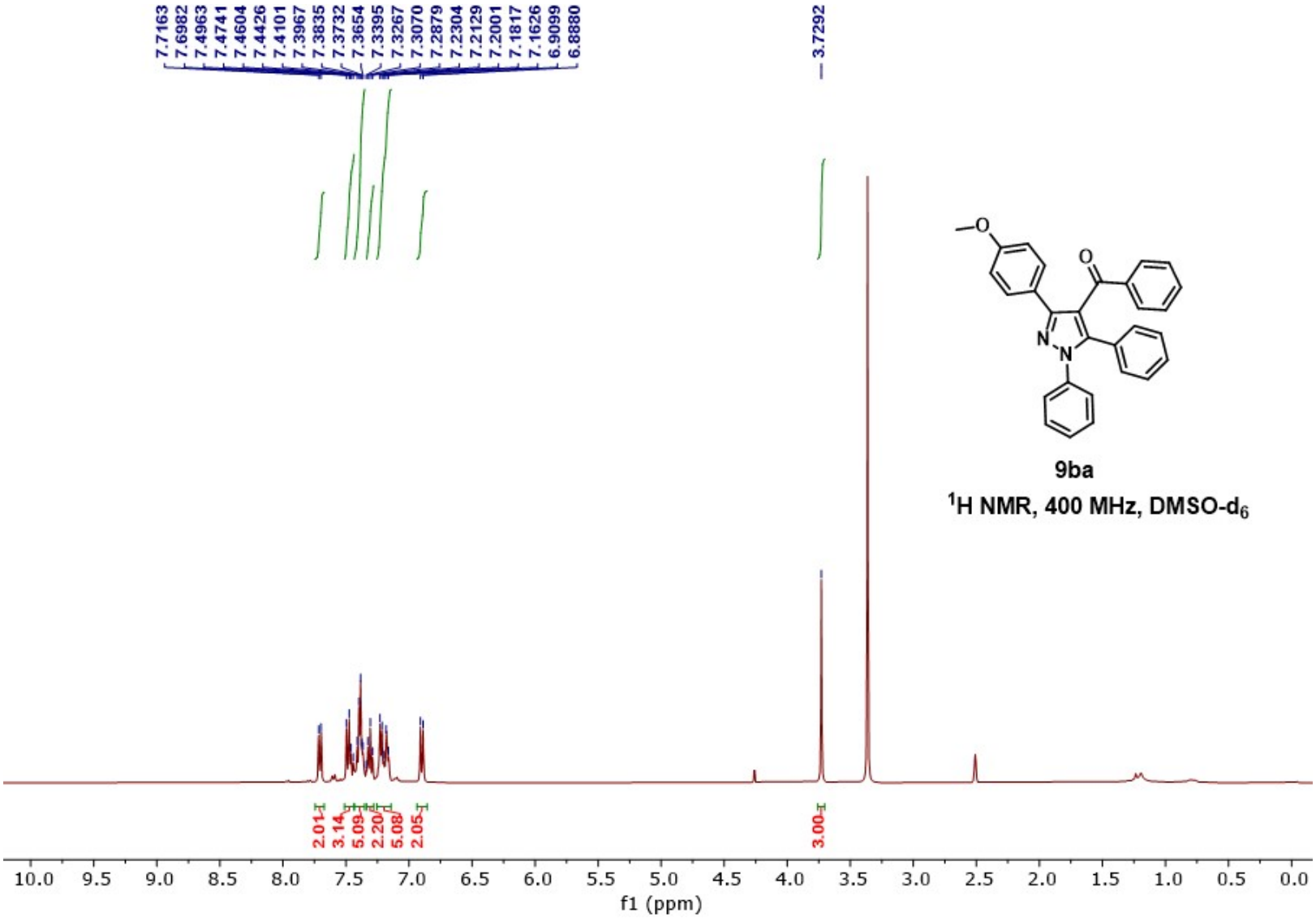
^{1}H NMR of compound 9aa in $CDCl_3$ (Newly added spectra)



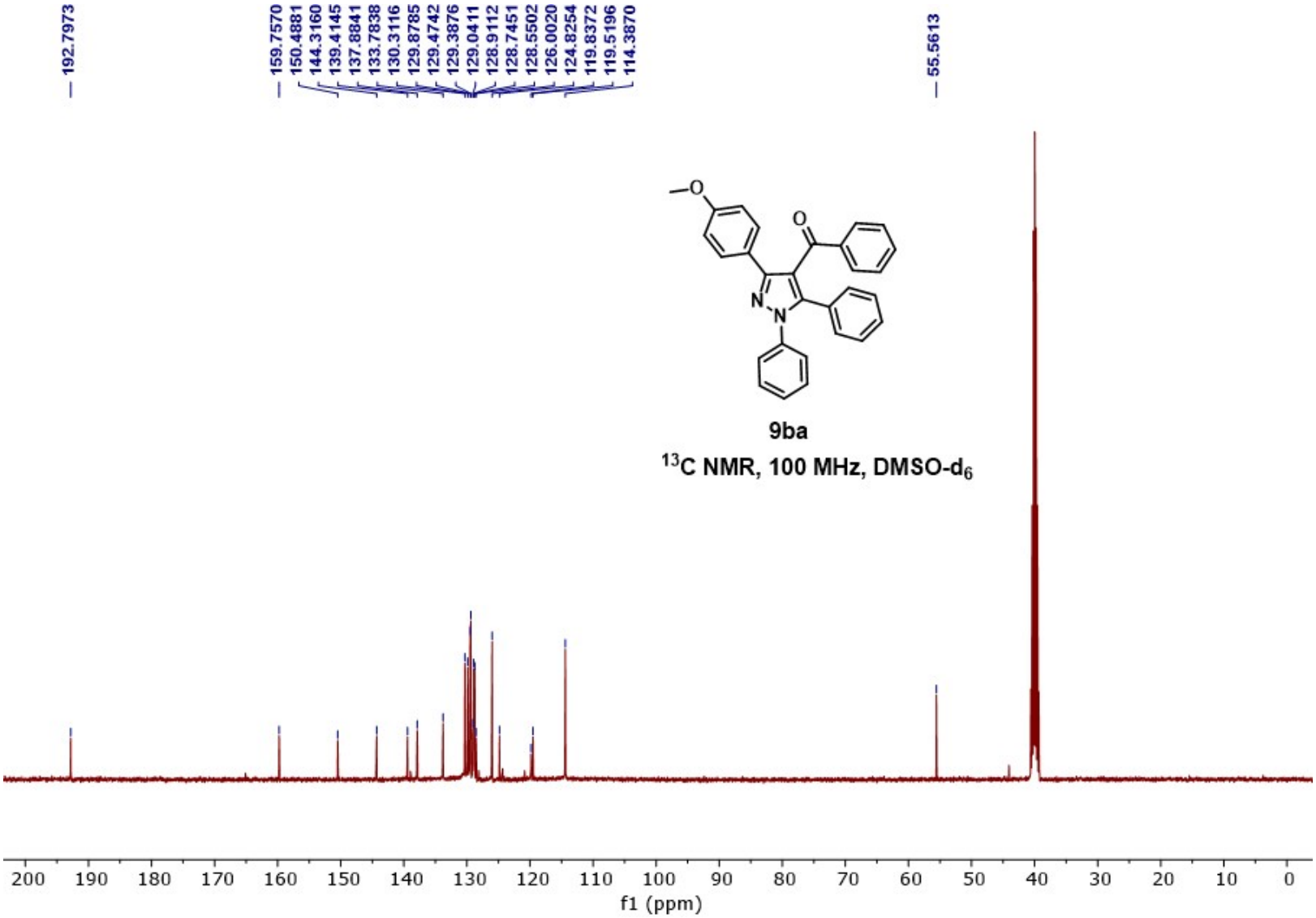
$^{13}C\{^{1}H\}$ NMR of compound 9aa in $CDCl_3$(Newly added spectra)



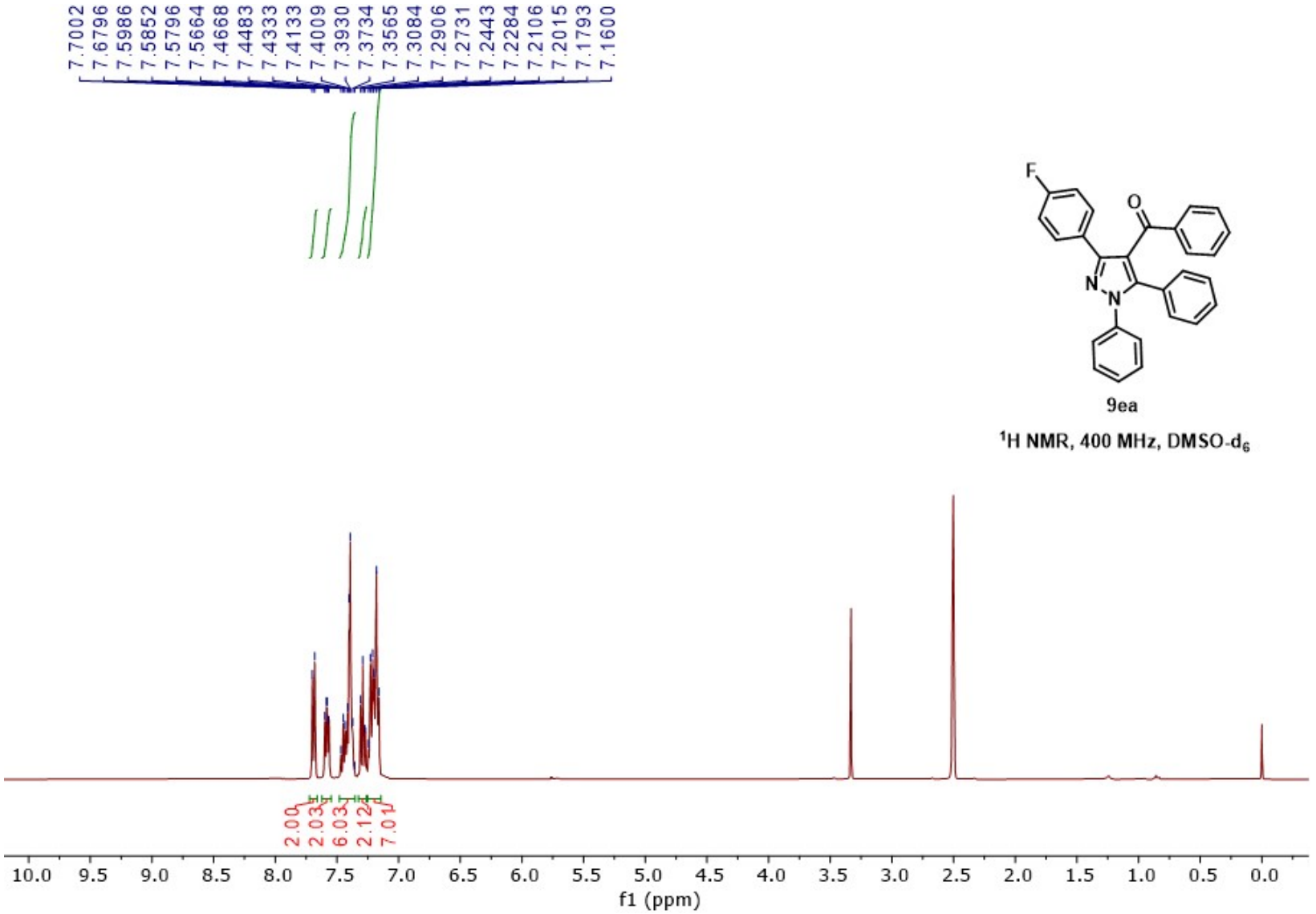
^{1}H NMR of compound 9ba in DMSO-d_6(Newly added spectra)



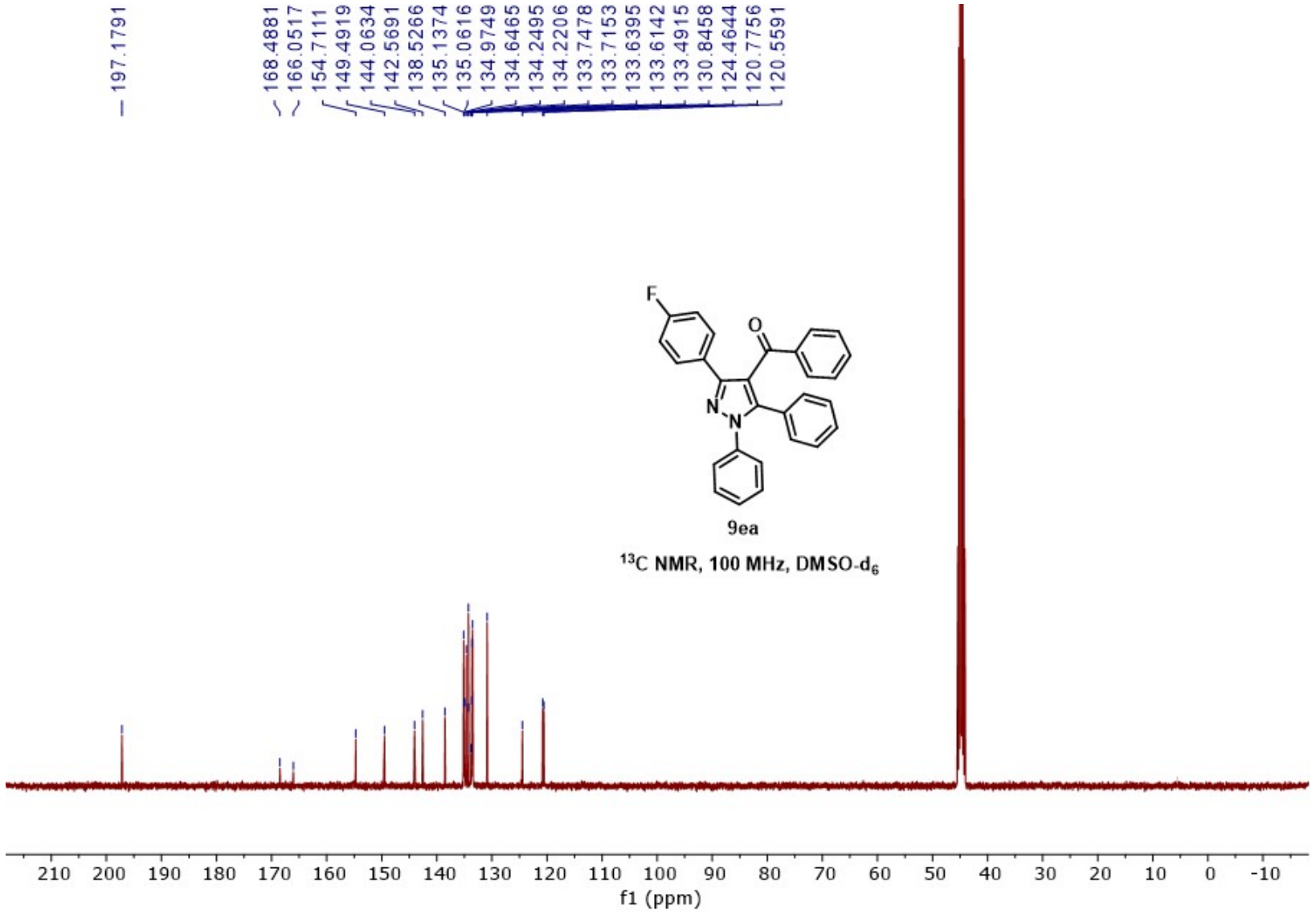
$^{13}C\{^{1}H\}$ NMR of compound 9ba in DMSO-d_6(Newly added spectra)



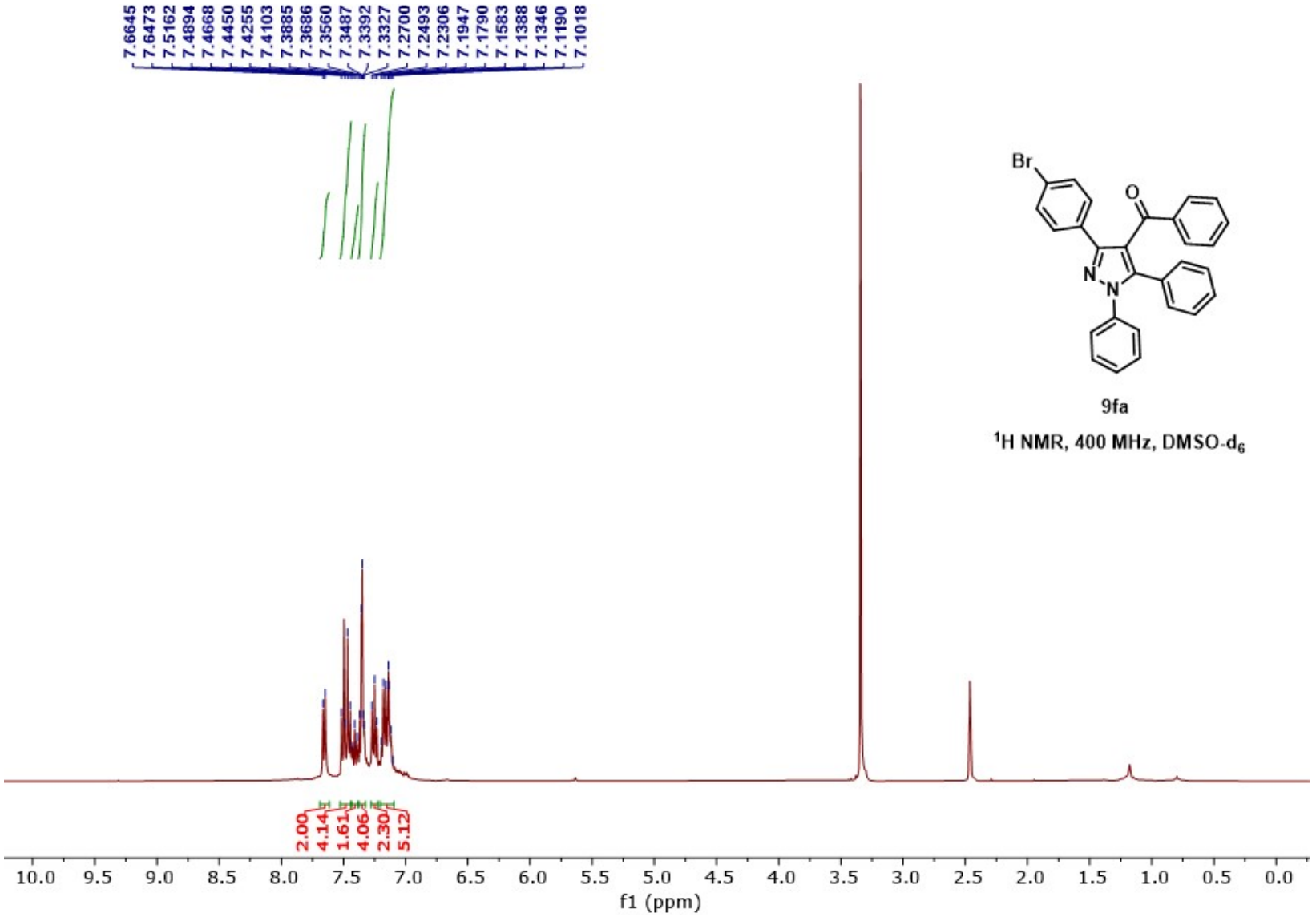
^{1}H NMR of compound 9ea in DMSO-d_6(Newly added spectra)



$^{13}C\{^{1}H\}$ NMR of compound 9ea in DMSO-d_6(Newly added spectra)



^{1}H NMR of compound 9fa in DMSO-d_6(Newly added spectra)



$^{13}C\{^{1}H\}$ NMR of compound 9fa in DMSO-d_6(Newly added spectra)