

Palladium mediated regioselective intramolecular Heck reaction: synthesis of substituted pyrazolo[3,4-*b*]pyridines, 3*H*-pyrazolo[3,4-*c*]isoquinolines and 3*H*-pyrazolo[4,3-*f*][1,7]naphthyridines

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EXPERIMENTAL SECTION

General Experimental: Melting points were measured with a Buchi B-540 melting point apparatus and are uncorrected. IR spectra were recorded on Elmer FT-IR-2000 spectrometer on a thin film using chloroform. NMR spectra were recorded on Avance DPX 300 MHz FT-NMR spectrometer or Bruker Avance III 500 MHz FT-NMR spectrometer using tetramethylsilane (TMS) as an internal standard. Mass spectra were recorded on Trace DSQ GCMS instrument. Elemental analysis was performed on a Perkin Elmer Series II 2400 CHNS/O Micro Elemental Analyzer. All experiments were monitored by thin layer chromatography (TLC). TLC was performed on pre-coated silica gel plates (Merck). Column chromatography was performed on silica gel (100-200 mesh, Merck). All the commercially available reagents were used as received.

General procedure for the synthesis of starting imines 3: A solution of β -bromovinyl aldehyde **1** (1.0 mmol), 5-aminopyrazole **2** (1.0 mmol) and activated molecular sieves (150 mg) in anhydrous DCM (5.0 mL) was stirred at room temperature for 12 hours. After completion of the reaction the molecular sieves were filtered off and the solvent was removed under vacuo. The crude product obtained was purified by column chromatography over silica gel (100-200 mesh, Merck) using EtOAc/Hexane (1:9) as the eluant.

General procedure for the synthesis of pyrazole fused compounds 4a-r: A solution of imine **3** (1.0 mmol), Pd(OAc)₂ (5 mol%), xantphos (10 mol%) and K₂CO₃ (2.0 mmol) was heated at 120 °C in anhydrous DMF (3.0 mL) for 12 hours. After completion of the reaction the reaction mixture was cooled down to room temperature, poured into water and extracted with ethyl acetate. The ethyl acetate layer was then washed with brine and water. Finally, it was dried over anhydrous Na₂SO₄ and the solvent was removed under vacuo. The crude product obtained was

purified by column chromatography over silica gel (100-200 mesh, Merck) using EtOAc/Hexane (1:4) as the eluant. Following this general procedure, compounds **4a-r** were synthesized.

3-Methyl-4-(naphthalen-2-yl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine (4a): Yellow solid (265 mg, 79%), mp: 109 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.63 (s, 3H), 7.29 (t, *J* = 7.3 Hz, 1H), 7.40-7.60 (m, 4H), 7.82-7.97 (m, 4H), 8.14-8.28 (m, 3H), 8.55 (s, 1H), 9.05 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.6, 116.6, 121.3, 125.6, 126.3, 127.1, 127.3, 127.9, 128.6, 128.7, 129.2, 129.4, 131.7, 133.3, 132.4, 134.7, 135.4, 138.9, 144.5, 151.2. IR (CHCl₃, cm⁻¹): 2924, 1607, 1524, 1249, 1031, 773. MS (EI, *m/z*): 335 [M⁺]. Anal. calcd. for C₂₃H₁₇N₃: C, 82.36; H, 5.11; N, 12.53. Found: C, 82.70; H, 5.10; N, 12.26.

3-Methyl-1-phenyl-4-(p-tolyl)-1H-pyrazolo[3,4-b]pyridine (4b): Red gum (249 mg, 83%). ¹H NMR (CDCl₃, 300 MHz) δ 2.48 (s, 3H), 2.69 (s, 3H), 7.19- 7.35 (m, 4H), 7.54 (t, *J* = 7.6 Hz, 1H), 7.76 (d, *J* = 7.8 Hz, 2H), 8.26 (d, *J* = 7.9 Hz, 2H), 8.61 (s, 1H), 9.05 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.5, 21.7, 116.4, 121.2, 126.3, 127.3, 129.2, 129.3, 130.2, 132.3, 134.8, 139.0, 143.8, 144.5, 151.1. IR (CHCl₃, cm⁻¹): 2929, 1601, 1518, 1252, 1025, 770. MS (EI, *m/z*): 299 [M⁺]. Anal. calcd. for C₂₀H₁₇N₃: C, 80.24; H, 5.72; N, 14.04. Found: C, 80.02; H, 5.89; N, 14.10

4-(4-Chlorophenyl)-1,3-dimethyl-1H-pyrazolo[3,4-b]pyridine (4c): Yellow solid (172 mg, 67%), mp: 140 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.60 (s, 3H), 4.14 (s, 3H), 7.51 (d, *J* = 8.4 Hz, 2H), 7.76 (d, *J* = 8.4 Hz, 2H), 8.45 (s, 1H), 8.97 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.5, 33.8, 125.6, 128.7, 128.9, 130.3, 131.2, 132.4, 135.9, 139.1, 142.9, 150.8. IR (CHCl₃, cm⁻¹): 2926, 1597, 1266, 1089, 774. MS (EI, *m/z*): 257 [M⁺]. Anal. calcd. for C₁₄H₁₂ClN₃: C, 65.25; H, 4.69; N, 16.30. Found: C, 65.02; H, 4.41; N, 16.11.

4-(4-Chlorophenyl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine (4d): Yellow solid (229 mg, 72%), mp: 127 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.70 (s, 3H), 7.34 (t, *J* = 7.5 Hz, 1H), 7.47-7.58 (m, 4H), 7.79 (d, *J* = 8.4 Hz, 2H), 8.24 (d, *J* = 7.8 Hz, 2H), 8.52 (d, *J* = 1.5 Hz, 1H), 9.03 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.5, 116.5, 121.2, 126.4, 126.6, 128.9, 129.2, 131.3, 132.3, 135.8, 138.9, 139.3, 144.6, 151.0, 151.5. IR (CHCl₃, cm⁻¹): 2930, 1582, 1266, 1083, 771. MS (EI, *m/z*): 319 [M⁺]. Anal. calcd. for C₁₉H₁₄ClN₃: C, 71.36; H, 4.41; N, 13.14. Found: C, 71.18; H, 4.12; N, 13.03.

3-Methyl-4-(3-nitrophenyl)-1-phenyl-1H-pyrazolo[3,4-b]pyridine (4e): Yellow solid (214 mg, 65%), mp: 127 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.70 (s, 3H), 7.56 (t, *J* = 8.0 Hz, 1H), 7.65- 7.76 (m, 4H), 8.30 (d, *J* = 7.7 Hz, 2H), 8.37 (d, *J* = 8.0 Hz, 2H), 8.78 (s, 2H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.5, 114.1, 120.6, 121.5, 122.3, 123.2, 123.9, 125.6, 127.4, 129.1, 129.9, 130.6, 133.3, 133.8, 148.5. IR (CHCl₃, cm⁻¹): 2925, 1560, 1449, 767. MS (EI, *m/z*): 330 [M⁺]. Anal. calcd. for C₁₉H₁₄N₄O₂: C, 69.08; H, 4.27; N, 16.96. Found: C, 69.31; H, 4.12; N, 16.73.

4-(Furan-2-yl)-3-methyl-1-phenyl-1H-pyrazolo[3,4-b]pyridine (4f): Yellow solid (204 mg, 74%), mp: 112 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.72 (s, 3H), 6.67 (d, *J* = 1.7 Hz, 1H), 7.27-7.57 (m, 4H), 7.76 (s, 1H), 8.25 (d, *J* = 7.8 Hz, 2H), 8.77 (d, *J* = 0.9 Hz, 1H), 9.3 (d, *J* = 0.9 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 12.6, 112.6, 116.6, 120.4, 121.2, 126.3, 126.6, 129.2, 132.0, 144.6, 147.2, 150.6, 152.7. IR (CHCl₃, cm⁻¹): 3401, 2924, 1594, 1283, 690. MS (EI, *m/z*): 275 [M⁺]. Anal. calcd. for C₁₇H₁₃N₃O: C, 74.17; H, 4.76; N, 15.26. Found: C, 74.09; H, 4.58; N, 15.03.

3-Methyl-1-phenyl-4-(thiophen-3-yl)-1H-pyrazolo[3,4-b]pyridine (4g): Red solid (207 mg, 71%), mp: 122 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.65 (s, 3H), 7.24-7.53 (m, 4H), 7.65 (d, *J* = 3.6 Hz, 1H), 7.73 (d, *J* = 4.8 Hz, 1H), 8.18 (d, *J* = 8.1 Hz, 2H), 8.54 (d, *J* = 1.8 Hz, 1H), 9.08 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.0, 116.4, 121.1, 126.2, 128.1, 129.1, 131.4, 134.5, 134.6, 139.5, 140.1, 147.8, 150.1, 151.5. IR (CHCl₃,

cm⁻¹): 3411, 2919, 1637, 771. MS (EI, *m/z*): 291 [M⁺]. Anal. calcd. for C₁₇H₁₃N₃S: C, 70.08; H, 4.50; N, 14.42. Found: C, 69.89; H, 4.21; N, 14.18.

1,3-Dimethyl-6,7-dihydro-3H-benzof[*f*]pyrazolo[3,4-*c*]isoquinoline (4h): Yellow solid (187 mg, 75%), mp: 115 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.65 (s, 3H), 2.84-2.86 (m, 4H), 4.12 (s, 3H), 7.25- 7.42 (m, 3H), 7.75-7.84 (m, 1H), 8.40 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 17.5, 25.9, 29.3, 33.8, 110.9, 125.9, 126.3, 127.9, 129.3, 129.7, 131.6, 138.7, 139.1, 139.9, 147.8, 152.0. IR (CHCl₃, cm⁻¹): 2930, 1607, 1509, 1451, 1233, 1131, 765. MS (EI, *m/z*): 249 [M⁺]. Anal. calcd. for C₁₆H₁₅N₃: C, 77.08; H, 6.06; N, 16.85. Found: C, 77.15; H, 6.09; N, 16.97.

1-Methyl-3-phenyl-6,7-dihydro-3H-benzof[*f*]pyrazolo[3,4-*c*]isoquinoline (4i): Yellow solid (243 mg, 78%), mp: 143 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.73 (s, 3H), 2.79-2.91 (m, 4H), 7.30 (t, *J* = 7.4 Hz, 1H), 7.38- 7.43 (m, 3H), 7.53 (t, *J* = 7.8 Hz, 2H), 7.74-7.78 (m, 1H), 8.21 (d, *J* = 8.0 Hz, 2H), 8.48 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 17.2, 25.4, 28.8, 121.1, 125.3, 125.8, 127.5, 128.6, 128.9, 129.4, 131.0, 138.2, 139.0, 139.5, 140.8, 147.8, 151.5. IR (CHCl₃, cm⁻¹): 2930, 1607, 1509, 1451, 1233, 1131, 765. MS (EI, *m/z*): 311 [M⁺]. Anal. calcd. for C₂₁H₁₇N₃: C, 81.00; H, 5.50; N, 13.49. Found: C, 80.78; H, 5.28; N, 13.20.

1,3-Dimethyl-3H-pyrazolo[3,4-*c*]isoquinoline (4j): Brown solid (148 mg, 75%), mp: 100 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.85 (s, 3H), 4.19 (s, 3H), 7.56 (t, *J* = 7.6 Hz, 1H), 7.83 (t, *J* = 7.3 Hz, 1H), 8.08 (d, *J* = 8.1 Hz, 1H), 8.26 (d, *J* = 8.3 Hz, 1H), 9.02 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 15.4, 33.9, 107.3, 122.1, 124.6, 124.9, 129.5, 131.7, 140.9, 148.2, 153.0. IR (CHCl₃, cm⁻¹): 2921, 2852, 1620, 1563, 1209, 753. MS (EI, *m/z*): 197 [M⁺]. Anal. calcd. for C₁₂H₁₁N₃: C, 73.07; H, 5.62; N, 21.30. Found: C, 73.00; H, 5.43; N, 21.10.

3-Methyl-1-phenyl-3H-pyrazolo[3,4-c]isoquinoline (4k): Brown solid (176 mg, 68%), mp: 98 °C. ¹H NMR (CDCl₃, 300 MHz) δ 4.29 (s, 3H), 7.42-7.60 (m, 4H), 7.64 (t, *J* = 8.1 Hz, 1H), 7.81 (d, *J* = 6.9 Hz, 2H), 8.05 (d, *J* = 8.0 Hz, 1H), 8.21 (d, *J* = 8.3 Hz, 1H), 9.04 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 34.3, 106.6, 122.3, 125.0, 125.1, 128.4, 128.6, 129.3, 129.4, 131.1, 134.7, 144.8, 148.3, 153.3. IR (CHCl₃, cm⁻¹): 2924, 2854, 1622, 1573, 1562, 970, 700. MS (EI, *m/z*): 259 [M⁺]. Anal. calcd. for C₁₇H₁₃N₃: C, 78.74; H, 5.05; N, 16.20. Found: C, 78.45; H, 4.88; N, 16.01.

7,8-Dimethoxy-1-methyl-3-phenyl-3H-pyrazolo[3,4-c]isoquinoline (4l): White solid (220 mg, 69%), mp: 166 °C. ¹H NMR (500 MHz, DMSO-*d*₆): δ 2.91 (s, 3H), 3.95 (s, 3H), 4.08 (s, 3H), 7.33 (tt, *J* = 7.5 Hz, *J* = 1.5 Hz, 1H), 7.45 (s, 1H), 7.57 (t, *J* = 7.5 Hz, 2H), 7.65 (s, 1H), 8.29 (dd, *J* = 7.5 Hz, *J* = 1.0 Hz, 2H), 9.08 (s, 1H). ¹³C NMR (125 MHz, DMSO-*d*₆): δ 15.12, 55.95, 56.0, 102.1, 108.9, 109.1, 120.5, 121.0, 125.9, 127.1, 129.4, 139.7, 142.7, 147.5, 148.5, 151.6, 154.3. IR (CHCl₃, cm⁻¹): 1631, 1596, 1529, 1271, 1169. MS (EI, *m/z*): 319 [M⁺]. Anal. calcd. For C₁₉H₁₇N₃O₂: C, 71.46; H, 5.37; N, 13.16. Found: C, 71.19; H, 5.42; N, 13.28.

3-Ethyl-3H-[1,3]dioxolo[4,5-g]pyrazolo[3,4-c]isoquinoline (4m): Brown solid (174 mg, 72%), mp: 103 °C. ¹H NMR (CDCl₃, 300 MHz) δ 1.57 (t, *J* = 7.2 Hz, 3H), 4.64 (q, *J* = 7.2 Hz, 2H), 6.13 (s, 2H), 7.34 (s, 1H), 7.46 (s, 1H), 8.24 (s, 1H), 8.80 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 15.2, 42.4, 100.1, 101.7, 102.3, 105.6, 110.5, 121.1, 128.6, 130.1, 146.6, 150.5, 151.9. IR (CHCl₃, cm⁻¹): 2923, 2853, 1457, 1248, 772. MS (EI, *m/z*): 241 [M⁺]. Anal. calcd. for C₁₃H₁₁N₃O₂: C, 64.72; H, 4.60; N, 17.42. Found: C, 64.34; H, 4.26; N, 17.61.

1-Methyl-3-phenyl-3H-[1,3]dioxolo[4,5-g]pyrazolo[3,4-c]isoquinoline (4n): Red gum (227 mg, 75%). ¹H NMR (CDCl₃, 300 MHz) δ 2.36 (s, 3H), 6.04 (s, 2H), 6.85-7.52 (m, 5H), 7.73 (d, *J* = 7.8 Hz, 2H), 8.50 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.2, 93.0, 101.8, 106.8, 108.1, 122.0,

124.1, 126.4, 128.5, 130.9, 148.5, 151.1, 158.0. IR (CHCl₃, cm⁻¹): 2923, 2853, 1594, 1448, 666. MS (EI, *m/z*): 303 [M⁺]. Anal. calcd. for C₁₈H₁₃N₃O₂: C, 71.28; H, 4.32; N, 13.85. Found: C, 70.06; H, 4.02; N, 13.67.

7-Fluoro-1,3-dimethyl-3H-pyrazolo[3,4-*c*]isoquinoline (4o): Yellow solid (131 mg, 61%), mp: 111 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.83 (s, 3H), 4.18 (s, 3H), 7.54- 7.62 (m, 1H), 7.70 (d, *J* = 8.9 Hz, 1H), 8.19-8.25 (m, 1H), 8.94 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 15.3, 33.9, 107.1, 113.0, 121.0, 125.4, 128.3, 140.4, 148.1, 151.7, 157.7, 160.9. IR (CHCl₃, cm⁻¹): 2921, 2851, 1582, 1567, 772. MS (EI, *m/z*): 215 [M⁺]. Anal. calcd. for C₁₂H₁₀FN₃: C, 66.97; H, 4.68; N, 19.52. Found: C, 66.88; H, 4.25; N, 19.78.

7-Fluoro-3-methyl-1-phenyl-3H-pyrazolo[3,4-*c*]isoquinoline (4p): Yellow solid (177 mg, 64%), mp: 109 °C. ¹H NMR (CDCl₃, 300 MHz) δ 4.29 (s, 3H), 7.40 (t, *J* = 8.7 Hz, 1H), 7.33- 7.58 (m, 3H), 7.68 (d, *J* = 8.8 Hz, 1H), 7.77 (d, *J* = 7.4 Hz, 2H), 8.16-8.23 (m, 1H), 8.98 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 34.4, 106.6, 112.9, 113.2, 121.0, 124.5, 126.0, 128.8, 129.2, 134.5, 144.4, 148.1, 152.1, 158.0, 161.2. IR (CHCl₃, cm⁻¹): 2924, 2854, 1561, 1447, 1253, 972, 767. MS (EI, *m/z*): 277 [M⁺]. Anal. calcd. for C₁₇H₁₂FN₃: C, 73.63; H, 4.36; N, 15.15. Found: C, 73.29; H, 4.02; N, 14.86.

1,3-Dimethyl-3H-pyrazolo[4,3-*ff*][1,7]naphthyridine (4q): Yellow gum (137 mg, 69%). ¹H NMR (CDCl₃, 300 MHz) δ 2.90 (s, 3H), 4.15 (s, 3H), 7.38-7.45 (m, 1H), 8.3 (d, *J* = 7.7 Hz, 1H), 8.95 (s, 1H), 9.05 (d, *J* = 3.2 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.1, 31.9, 108.3, 114.0, 119.1, 120.0, 136.8, 142.7, 147.8, 152.8, 154.5. IR (CHCl₃, cm⁻¹): 2924, 2853, 1609, 1026, 795. MS (EI, *m/z*): 198 [M⁺]. Anal. calcd. for C₁₁H₁₀N₄: C, 66.65; H, 5.08; N, 28.26. Found: C, 66.58; H, 4.87; N, 28.02.

1-Methyl-3-phenyl-3H-pyrazolo[4,3-f][1,7]naphthyridine (4r): Red gum (177 mg, 68%). ¹H NMR (CDCl₃, 300 MHz) δ 3.01 (s, 3H), 7.29 (t, *J* = 7.4 Hz, 1H), 7.36-7.52 (m, 3H), 8.14 (d, *J* = 7.8 Hz, 2H), 8.35 (d, *J* = 8.4 Hz, 1H), 9.04 (s, 1H), 9.13 (d, *J* = 3.4 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 15.1, 120.1, 120.4, 122.3, 126.6, 129.2, 137.3, 144.7, 153.0, 154.3. IR (CHCl₃, cm⁻¹): 2920, 2853, 1070, 951, 771. MS (EI, *m/z*): 260 [M⁺]. Anal. calcd. for C₁₆H₁₂N₄: C, 73.83; H, 4.65; N, 21.52. Found: C, 73.58; H, 4.63; N, 21.26.

N-(3-Bromo-3-(naphthalen-2-yl)allylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (3a): Yellow solid, mp: 112 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.38 (s, 3H), 6.27 (s, 1H), 7.34 (t, *J* = 7.0 Hz, 2H), 7.45 (t, *J* = 7.5 Hz, 2H), 7.52-7.58 (m, 2H), 7.67 (d, *J* = 8.5 Hz, 2H), 7.75-7.97 (m, 4H), 8.25 (s, 1H), 8.81 (d, *J* = 8.5 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.1, 93.7, 124.0, 124.3, 126.8, 126.9, 127.5, 127.6, 128.3, 128.5, 128.6, 128.7, 128.8, 132.8, 134.0, 135.0, 137.8, 139.0, 149.3, 150.6, 160.4. IR (CHCl₃, cm⁻¹): 2967, 2313, 1593, 1093, 761. MS (EI, *m/z*): 415 [M⁺].

N-(3-Bromo-3-(4-chlorophenyl)allylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (3d): Yellow solid, mp: 109 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.37 (s, 3H), 6.25 (s, 1H), 7.16 (d, *J* = 8.0 Hz, 1H), 7.28-7.34 (m, 1H), 7.37 (d, *J* = 7.0 Hz, 2H), 7.40-7.45 (m, 2H), 7.60-7.69 (m, 4H), 8.70 (d, *J* = 8.0 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.1, 93.7, 124.3, 126.8, 128.4, 128.6, 128.7, 128.8, 128.9, 136.0, 136.4, 136.5, 139.0, 149.2, 150.4, 160.0. IR (CHCl₃, cm⁻¹): 2963, 2311, 1595, 1489, 1092, 760. MS (EI, *m/z*): 399 [M⁺].

N-(3-Bromo-3-(3-nitrophenyl)allylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (3e): Yellow solid, mp: 112 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.70 (s, 3H), 7.20-7.80 (m, 5H), 8.03 (d, *J* = 7.5 Hz, 1H), 8.25-8.35 (m, 2H), 8.42-8.47 (m, 1H), 8.58 (s, 1H), 8.73 (d, *J* = 8.5 Hz, 1H),

8.83 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.0, 93.9, 122.6, 123.1, 124.4, 124.7, 127.0, 127.3, 128.6, 129.7, 129.8, 130.6, 133.1, 133.5, 133.7, 139.0, 139.7, 149.3, 159.1. IR (CHCl₃, cm⁻¹): 2961, 2310, 1594, 1490, 1092, 762. MS (EI, *m/z*): 410 [M⁺].

***N*-(3-Bromo-3-(thiophen-3-yl)allylidene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (3g)**: Red solid, mp: 127 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.36 (s, 3H), 6.22 (s, 1H), 7.05-7.10 (m, 1H), 7.16 (d, *J* = 4.0 Hz, 1H), 7.33 (t, *J* = 4.0 Hz, 1H), 7.40-7.48 (m, 3H), 7.54 (d, *J* = 4.0 Hz, 1H), 7.66 (d, *J* = 8.0 Hz, 2H), 8.67 (d, *J* = 8.5 Hz, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.1, 93.6, 124.3, 125.7, 126.8, 127.9, 128.4, 128.6, 129.2, 130.0, 139.0, 142.1, 149.2, 150.7, 159.8. IR (CHCl₃, cm⁻¹): 2309, 1584, 1416, 1219, 772. MS (EI, *m/z*): 371 [M⁺].

***N*-(1-Bromo-3,4-dihydronaphthalen-2-yl)methylene)-3-methyl-1-phenyl-1H-pyrazol-5-amine (3i)**: Yellow solid, mp: 123 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.37 (s, 3H), 2.75-2.90 (m, 4H), 6.25 (s, 1H), 7.17 (d, *J* = 8.0 Hz, 1H), 7.28-7.38 (m, 3H), 7.43 (t, *J* = 8.0 Hz, 2H), 7.73 (d, *J* = 8.0 Hz, 2H), 7.81 (d, *J* = 8.5 Hz, 1H), 8.97 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.1, 24.5, 27.4, 93.7, 124.0, 126.4, 126.9, 127.3, 128.1, 128.4, 130.0, 133.0, 133.6, 135.4, 138.4, 139.3, 149.3, 150.4, 160.5. IR (CHCl₃, cm⁻¹): 2933, 2309, 1595, 1219, 772. MS (EI, *m/z*): 391 [M⁺].

***N*-(2-Bromobenzylidene)-1-methyl-3-phenyl-1H-pyrazol-5-amine (3k)**: Yellow solid, mp: 98 °C. ¹H NMR (CDCl₃, 300 MHz) δ 3.88 (s, 3H), 6.45 (s, 1H), 7.10-7.38 (m, 5H), 7.46 (d, *J* = 7.0 Hz, 1H), 7.72 (d, *J* = 8.0 Hz, 2H), 8.07 (d, *J* = 7.0 Hz, 1H), 8.86 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 35.0, 89.0, 125.3, 126.3, 127.6, 127.7, 128.4, 128.5, 128.7, 132.8, 133.3, 133.4, 134.1, 150.2, 157.9. IR (CHCl₃, cm⁻¹): 2924, 2301, 1599, 1217, 771. MS (EI, *m/z*): 339 [M⁺].

***N*-(6-Bromobenzo[*d*][1,3]dioxol-5-yl)methylene)-1-ethyl-1H-pyrazol-5-amine (3m)**: Yellow solid, mp: 107 °C. ¹H NMR (CDCl₃, 300 MHz) δ 1.47 (t, *J* = 7.5 Hz, 3H), 4.37 (q, *J* = 7.0 Hz, 2H), 6.07 (s, 2H), 6.25 (d, *J* = 1.5 Hz, 1H), 7.06 (s, 1H), 7.46-7.49 (m, 1H), 7.71 (s, 1H), 8.86 (s,

1H). ¹³C NMR (CDCl₃, 75 MHz) δ 15.5, 42.8, 91.9, 102.3, 107.2, 112.8, 119.2, 128.2, 138.5, 147.9, 148.5, 151.2, 157.5. IR (CHCl₃, cm⁻¹): 2923, 2304, 1592, 1214, 770. MS (EI, *m/z*): 321 [M⁺].

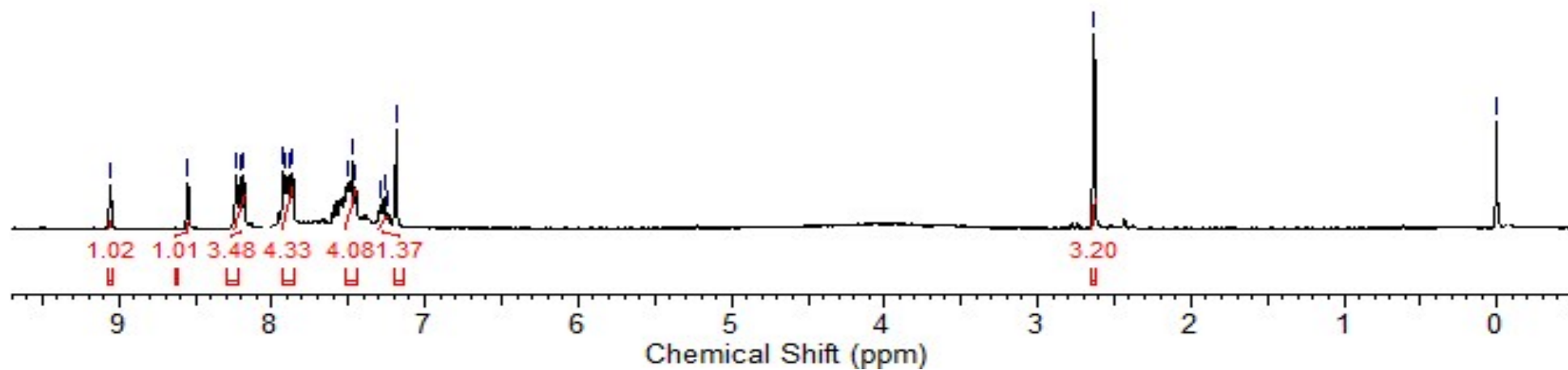
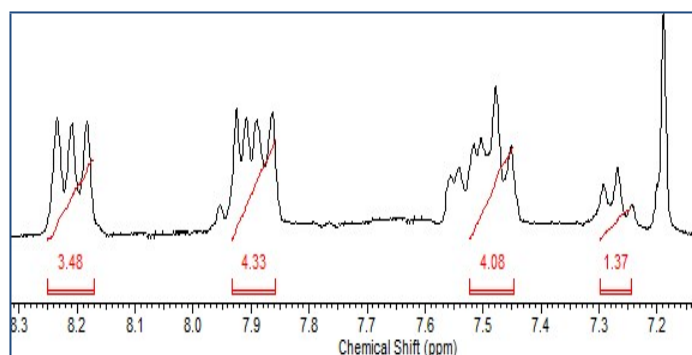
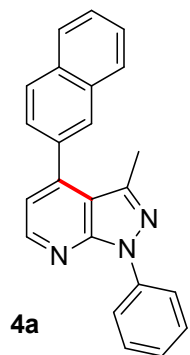
***N*-(2-Bromo-5-fluorobenzylidene)-1,3-dimethyl-1H-pyrazol-5-amine (3o)**: Yellow solid, mp: 116 °C. ¹H NMR (CDCl₃, 300 MHz) δ 2.29 (s, 3H), 3.93 (s, 3H), 6.13 (s, 1H), 7.01-7.18 (m, 1H), 7.50-7.70 (m, 1H), 7.85-8.10 (m, 1H), 8.84 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 14.0, 34.6, 91.8, 114.9, 115.1, 119.8, 120.2, 134.5, 134.6, 156.3, 161.0, 162.9. IR (CHCl₃, cm⁻¹): 2934, 2317, 1592, 1392, 774. MS (EI, *m/z*): 295 [M⁺].

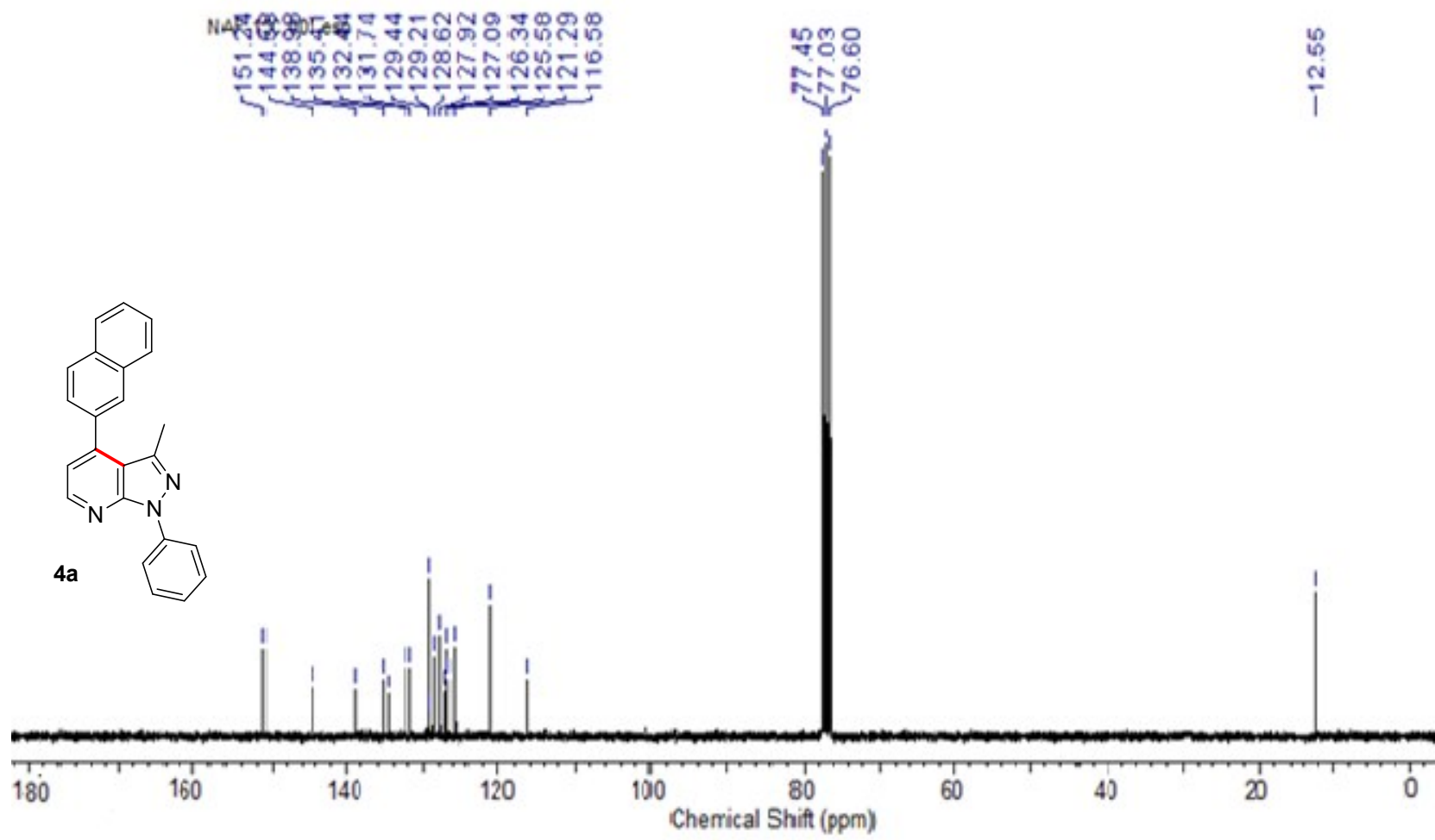
***N*-(3-Bromopyridin-2-yl)methylene)-1-methyl-3-phenyl-1H-pyrazol-5-amine (3r)**: Yellow solid, mp: 129 °C. ¹H NMR (CDCl₃, 300 MHz) δ 4.04 (s, 3H), 6.65 (s, 1H), 7.34 (t, *J* = 6.5 Hz, 1H), 7.38-7.49 (m, 3H), 7.84 (d, *J* = 8.0 Hz, 2H), 8.50 (dd, *J* = 4.5 Hz & 2.0 Hz, 1H), 8.58 (dd, *J* = 7.5 Hz & 2.0 Hz, 1H), 9.00 (s, 1H). ¹³C NMR (CDCl₃, 75 MHz) δ 35.1, 89.3, 122.9, 125.3, 127.8, 128.6, 129.7, 133.1, 136.8, 149.8, 150.4, 151.8, 152.2, 154.1. IR (CHCl₃, cm⁻¹): 2310, 1597, 1398, 1219, 772. MS (EI, *m/z*): 340 [M⁺].

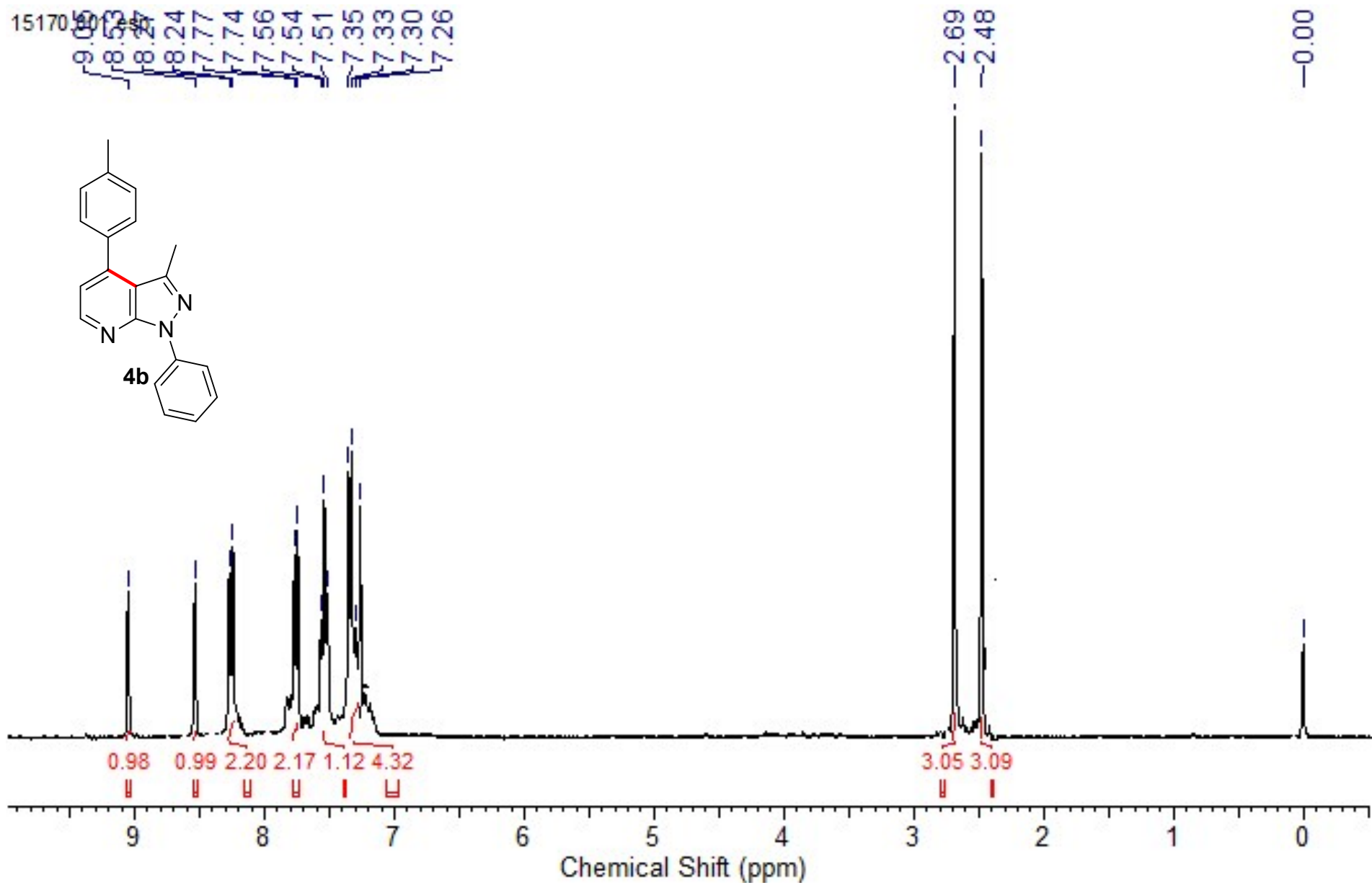
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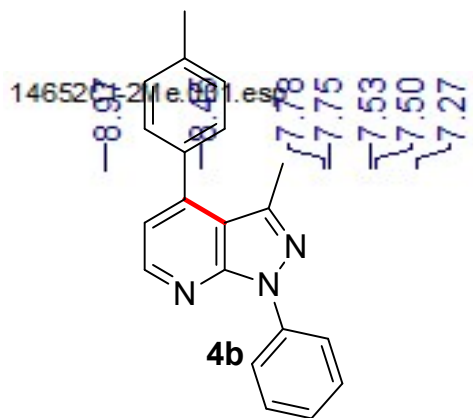
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-4.14

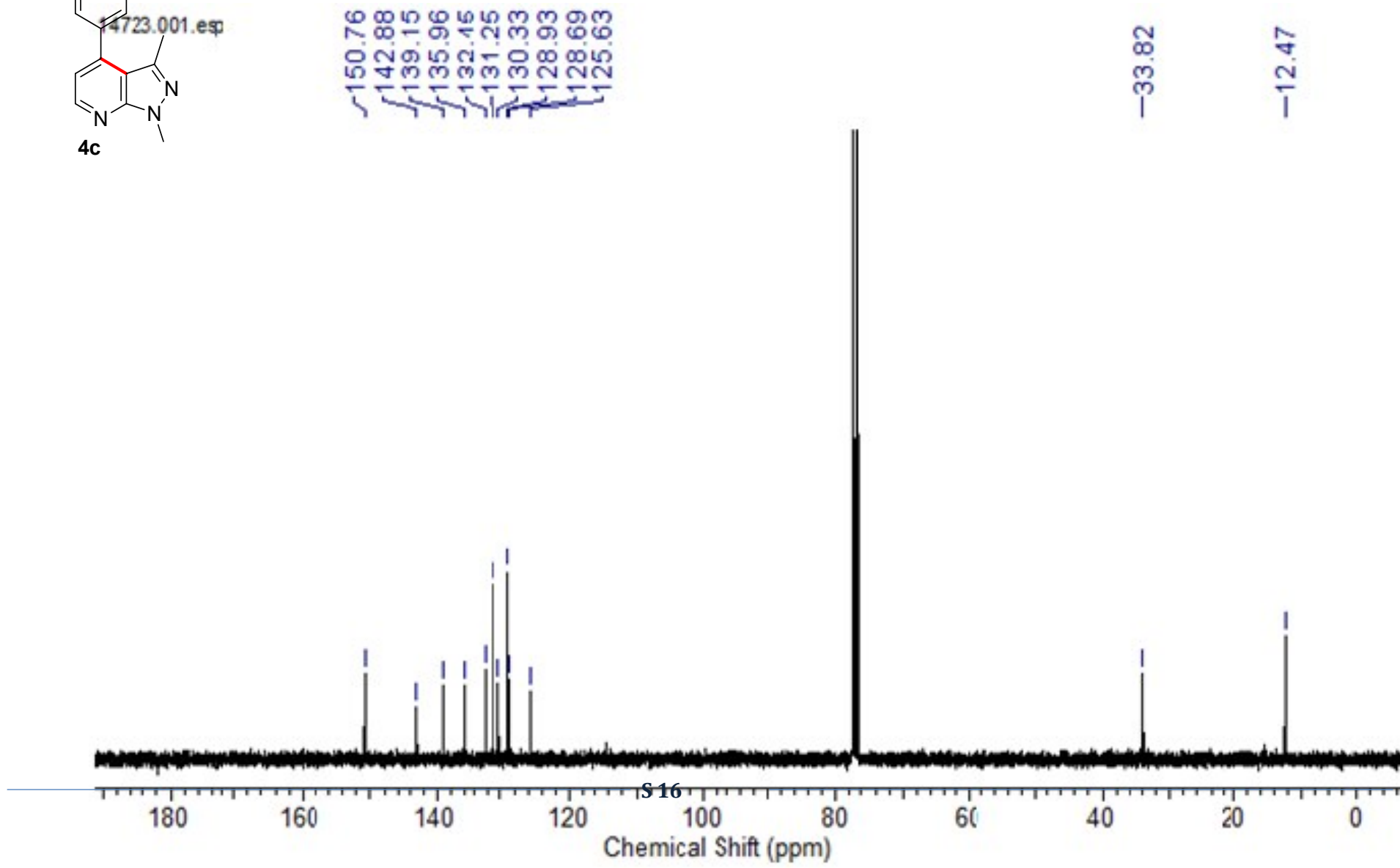
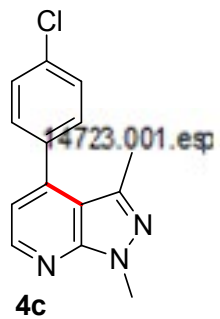
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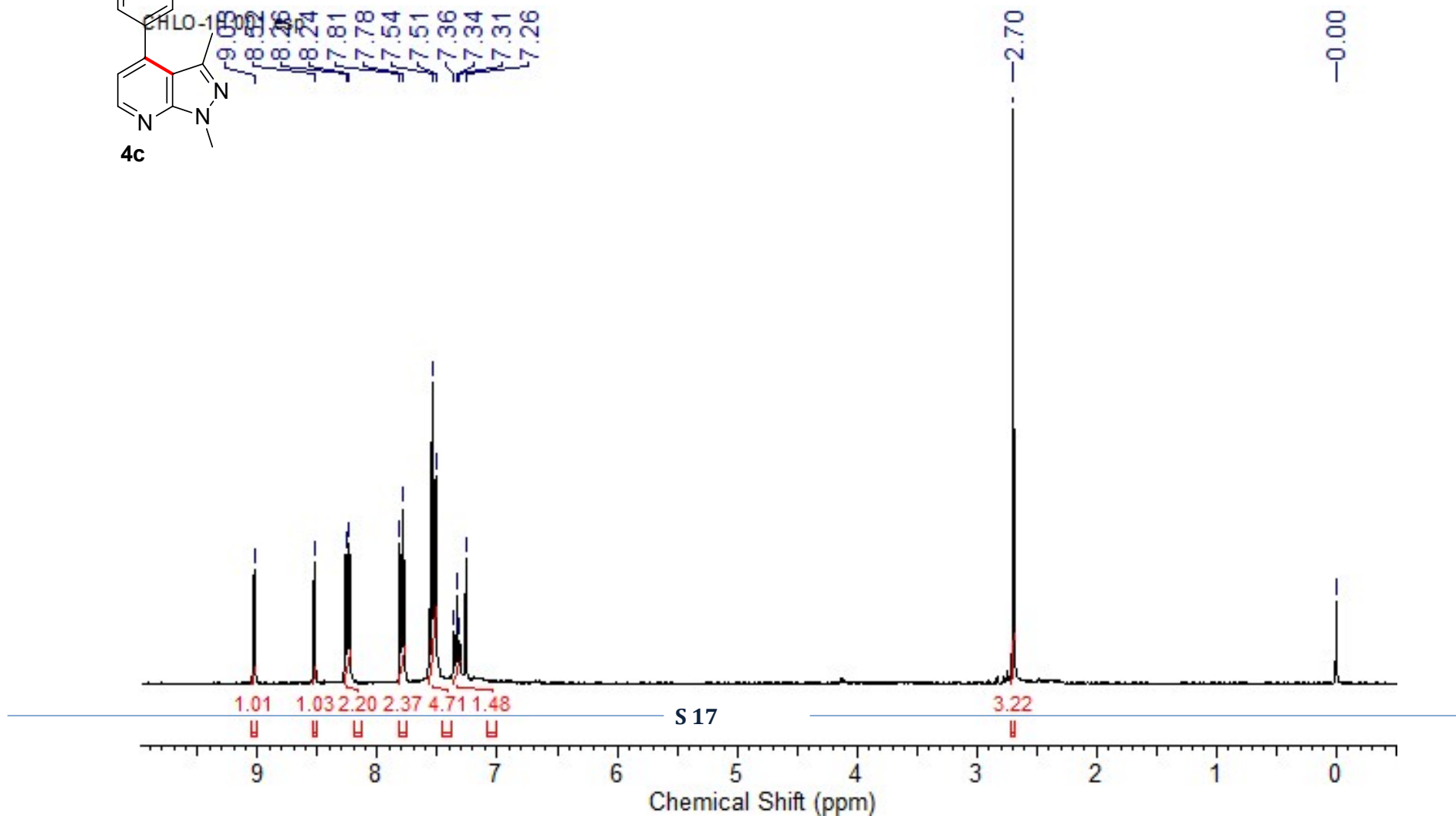
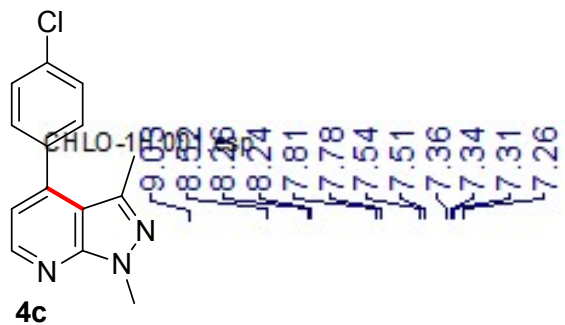
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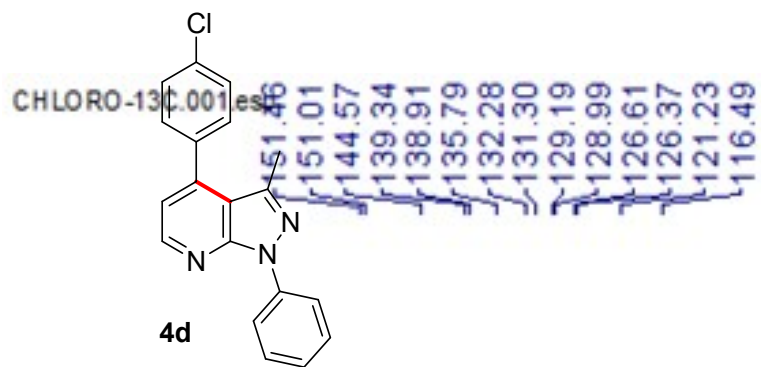
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Chemical Shift (ppm)

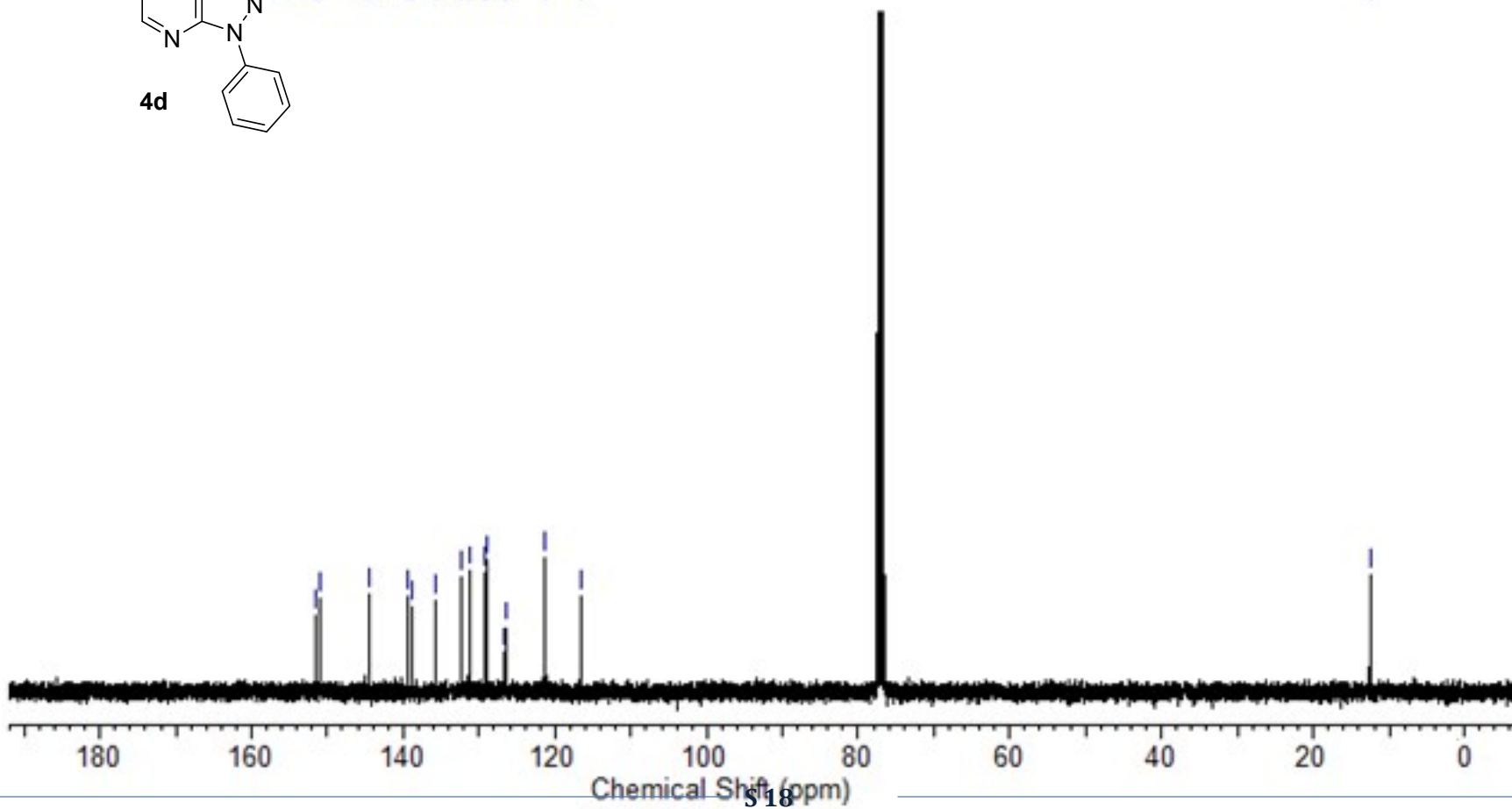


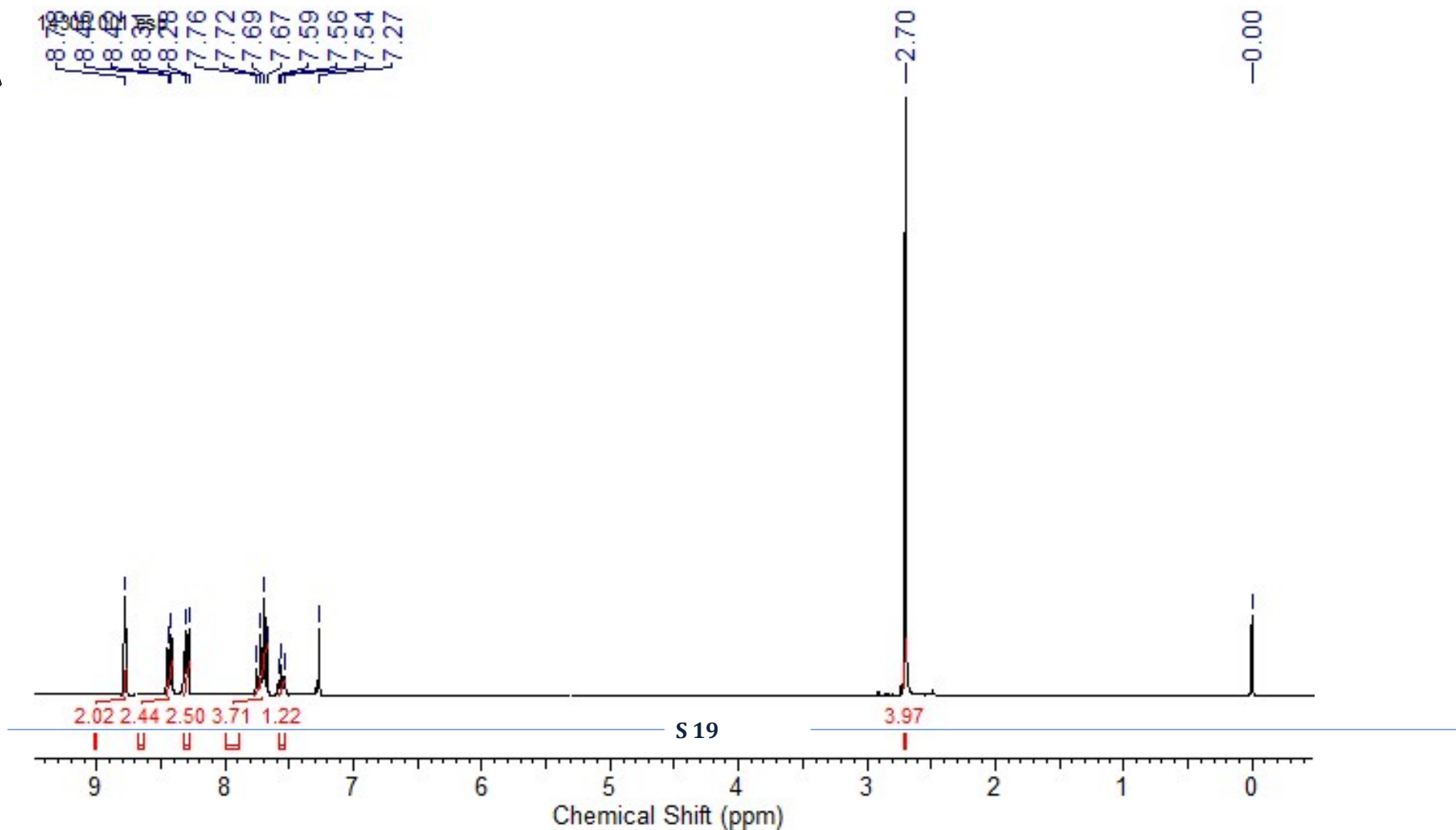
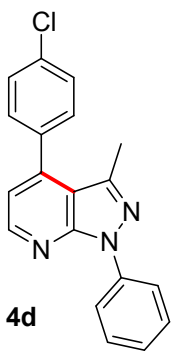


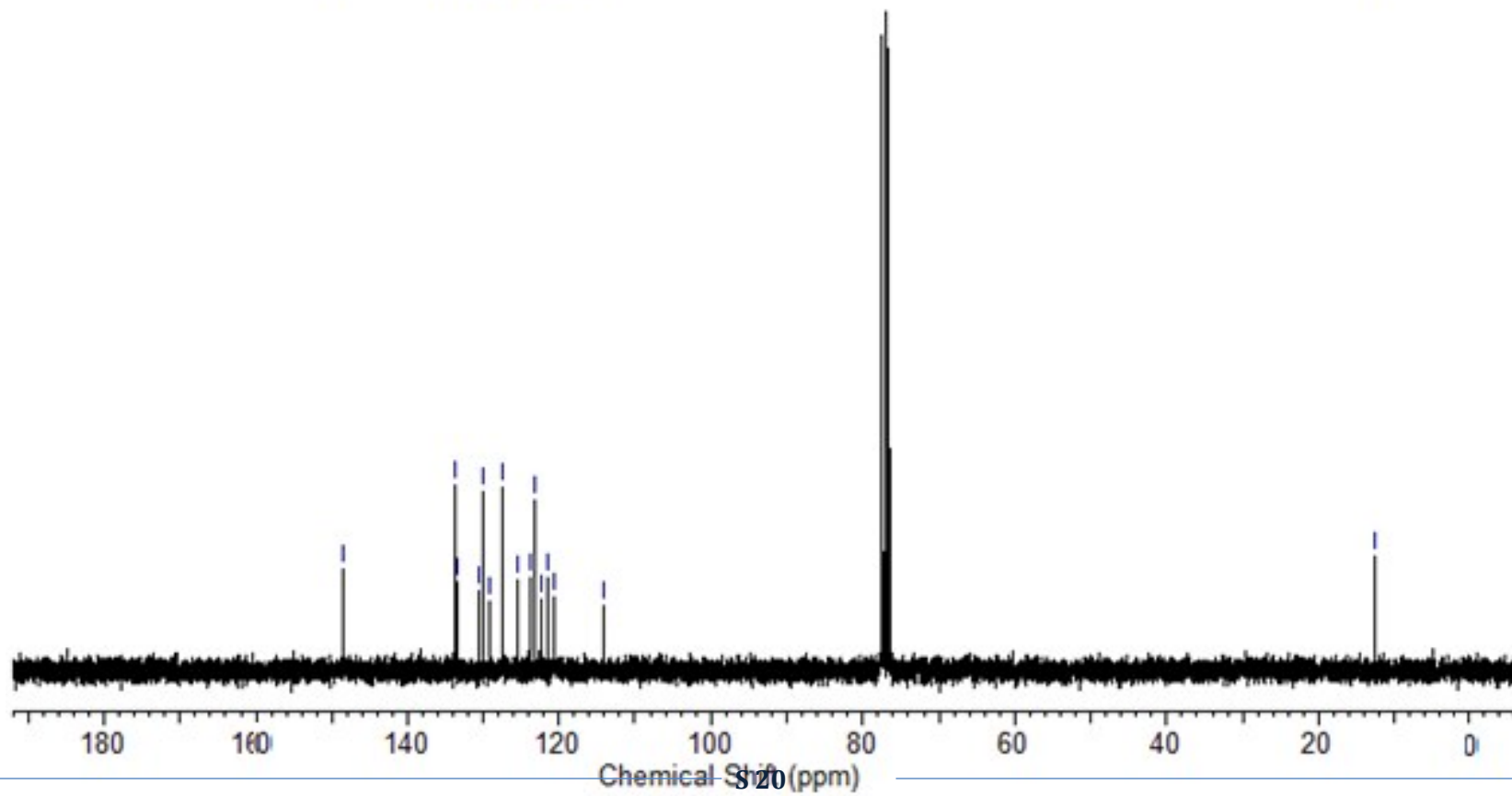
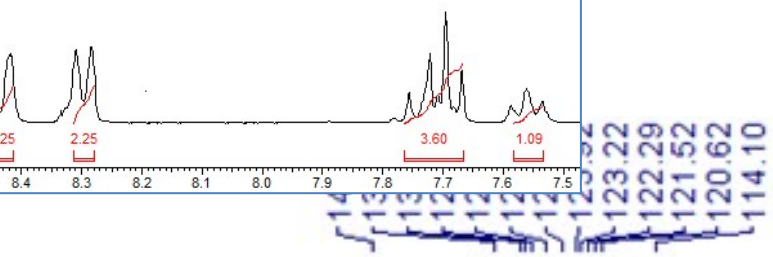
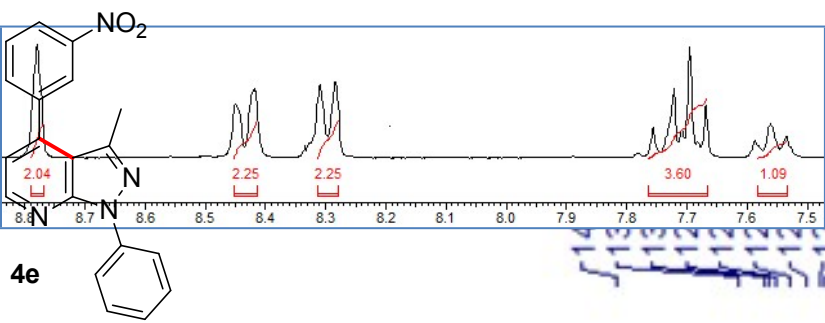


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121.23
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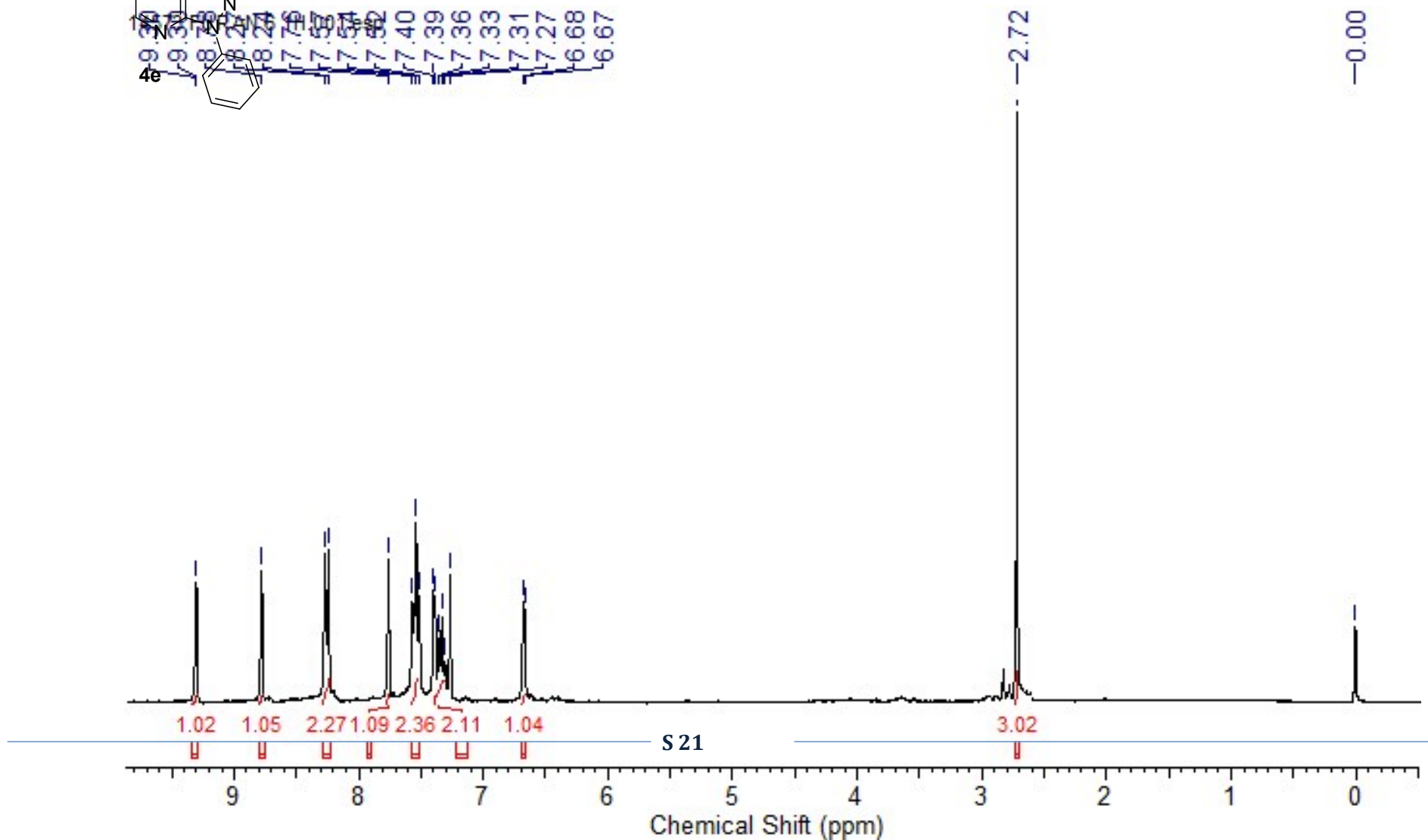
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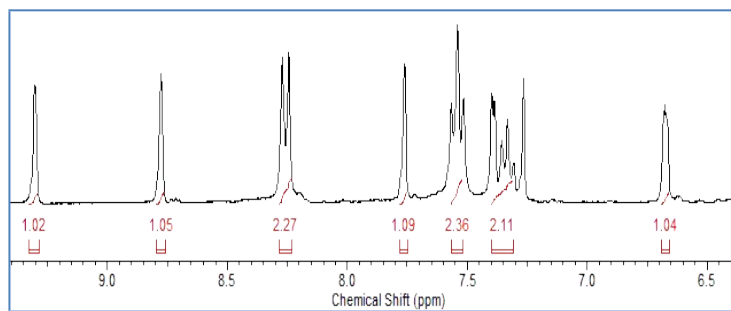
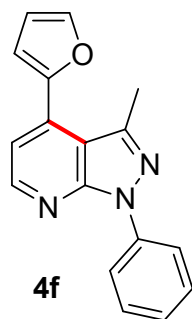




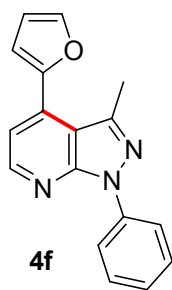


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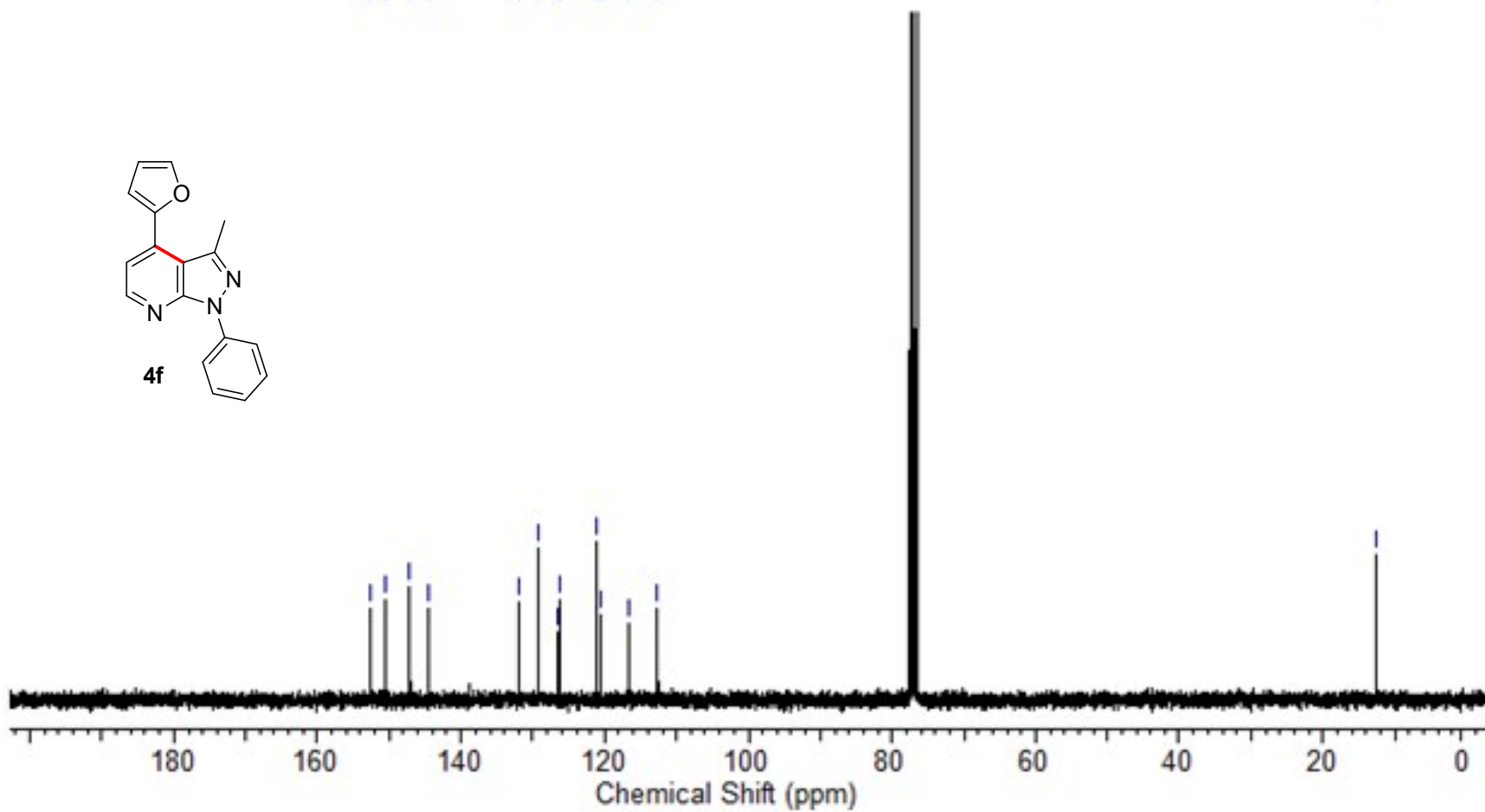


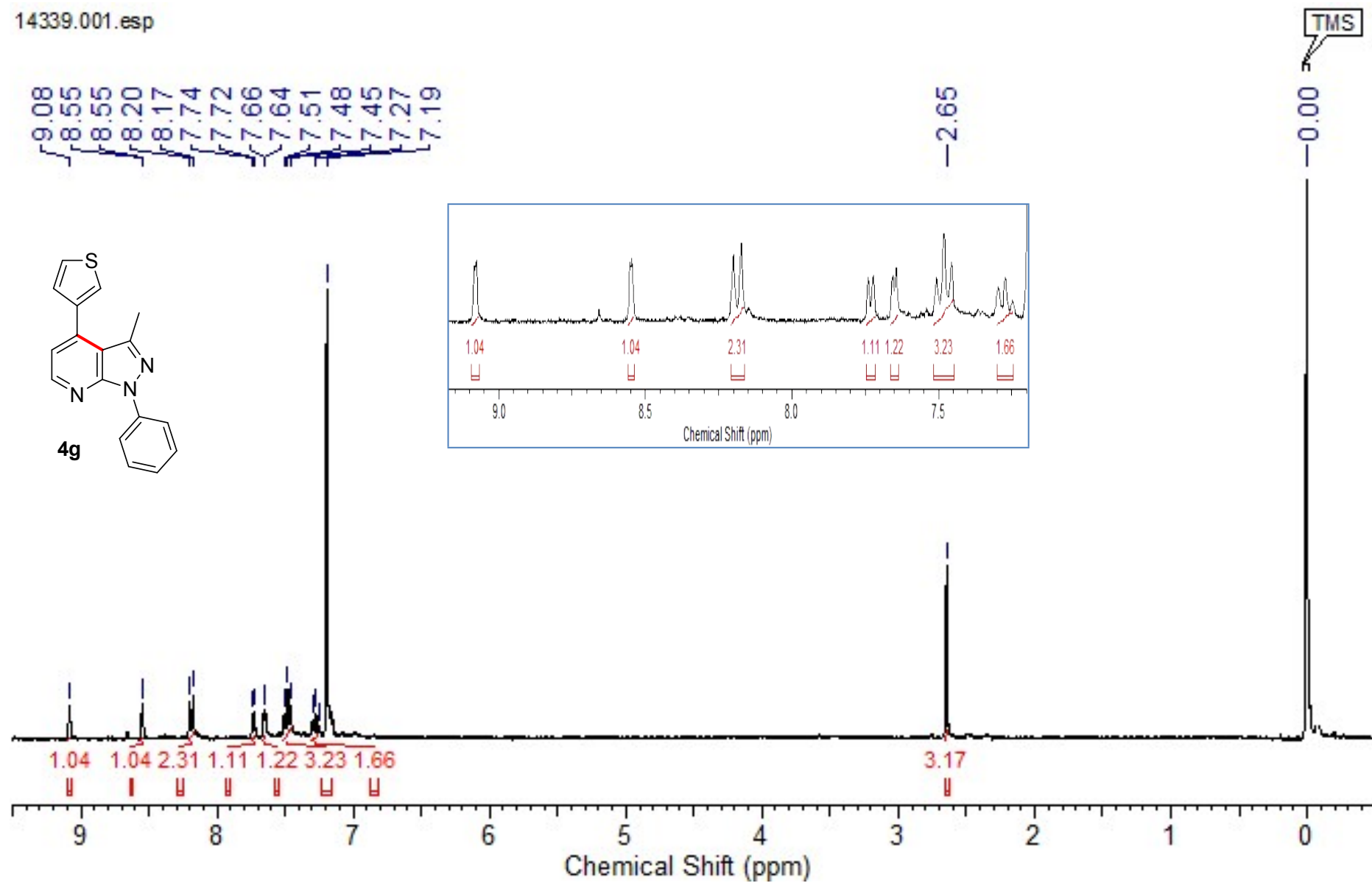
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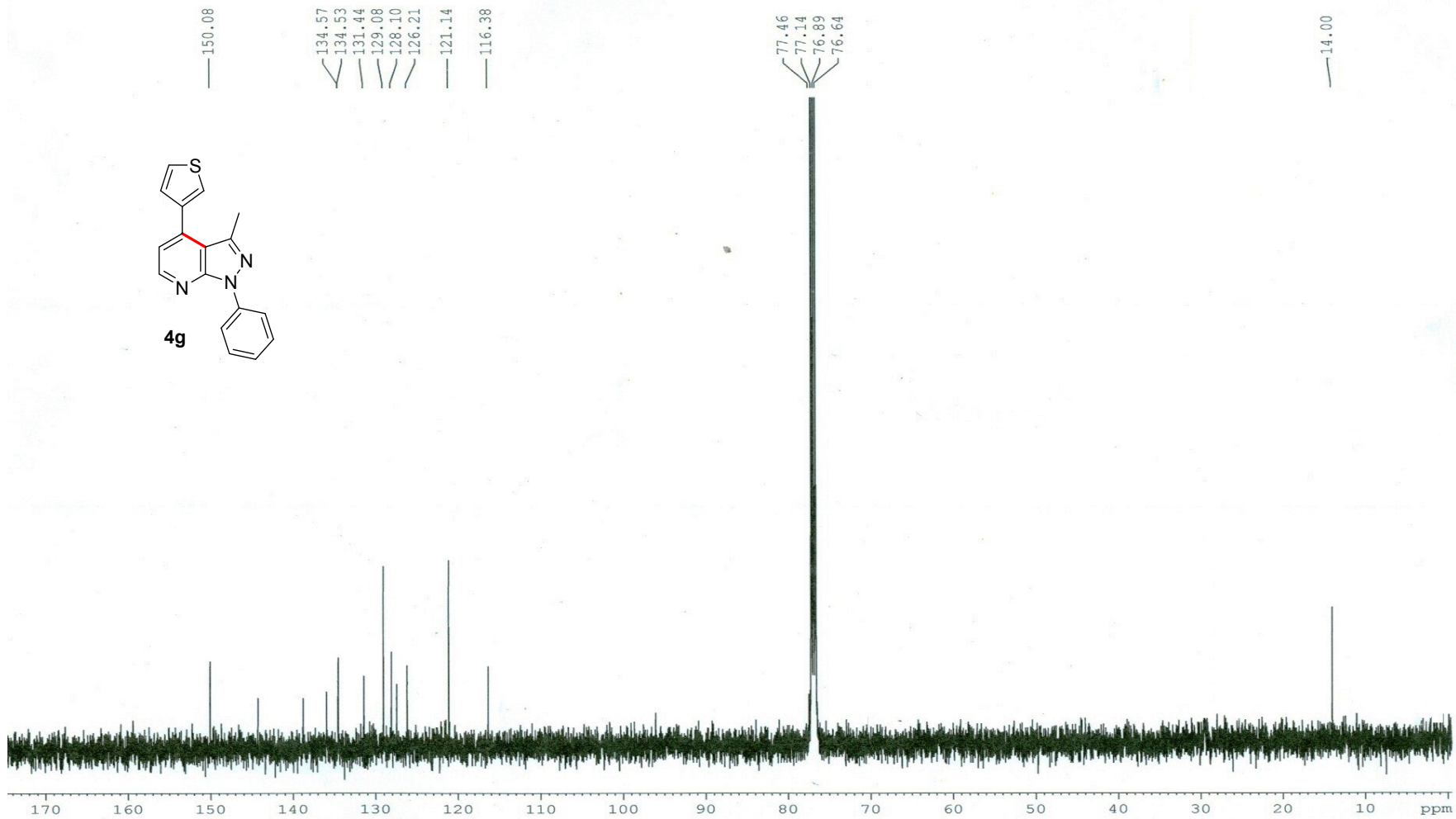
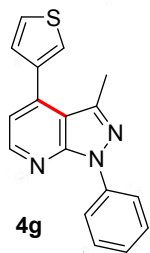


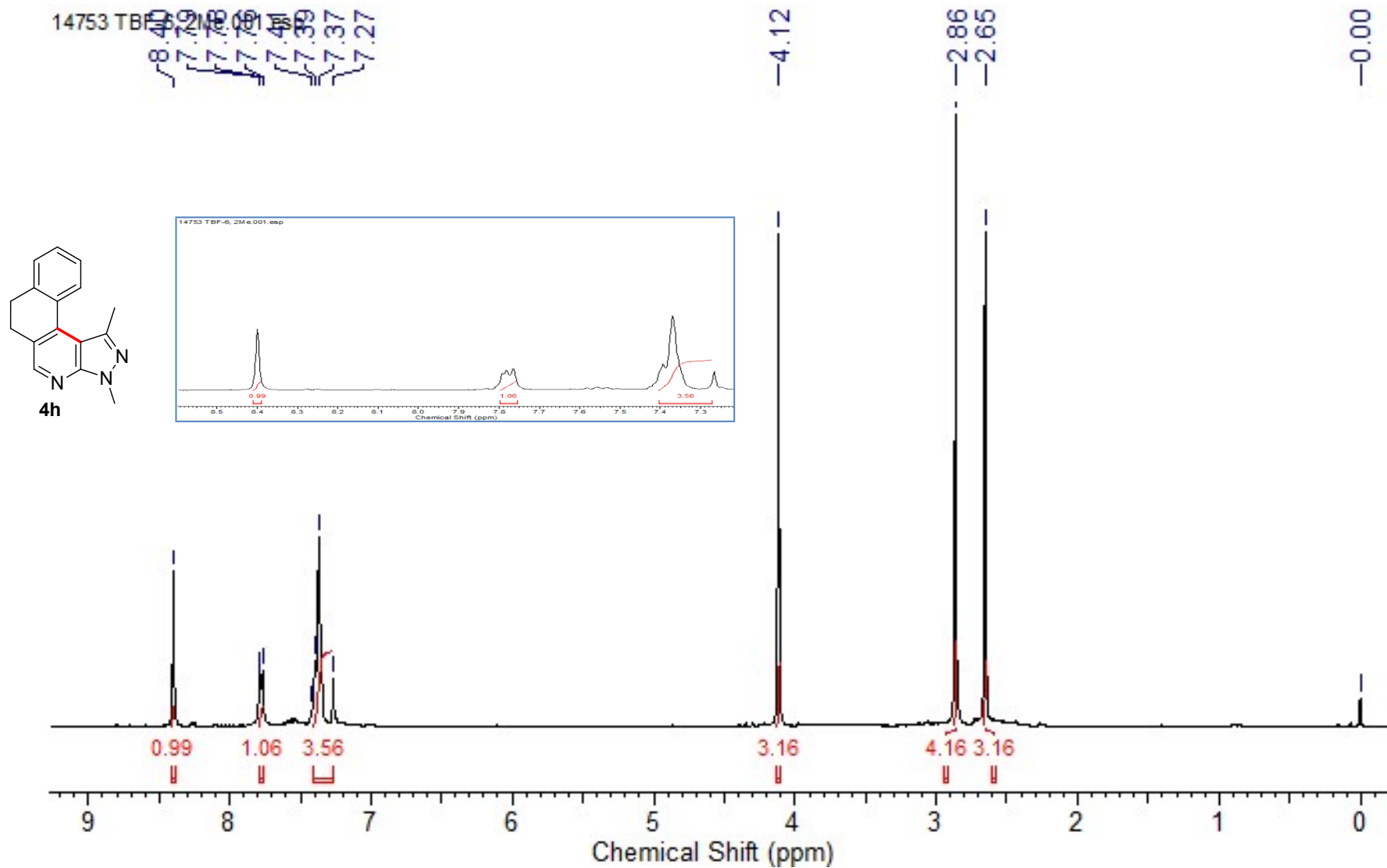
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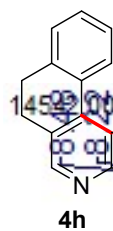








14952.001.esp



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125.91
110.90

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25.88
17.45

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8.48
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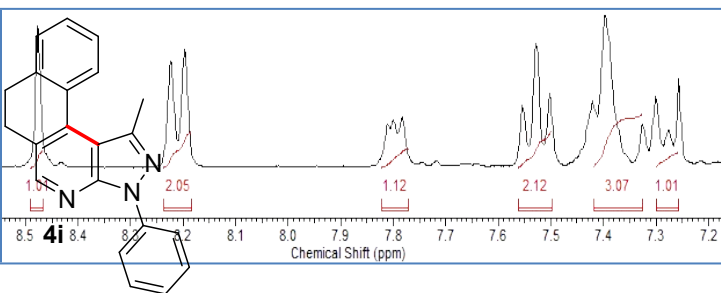
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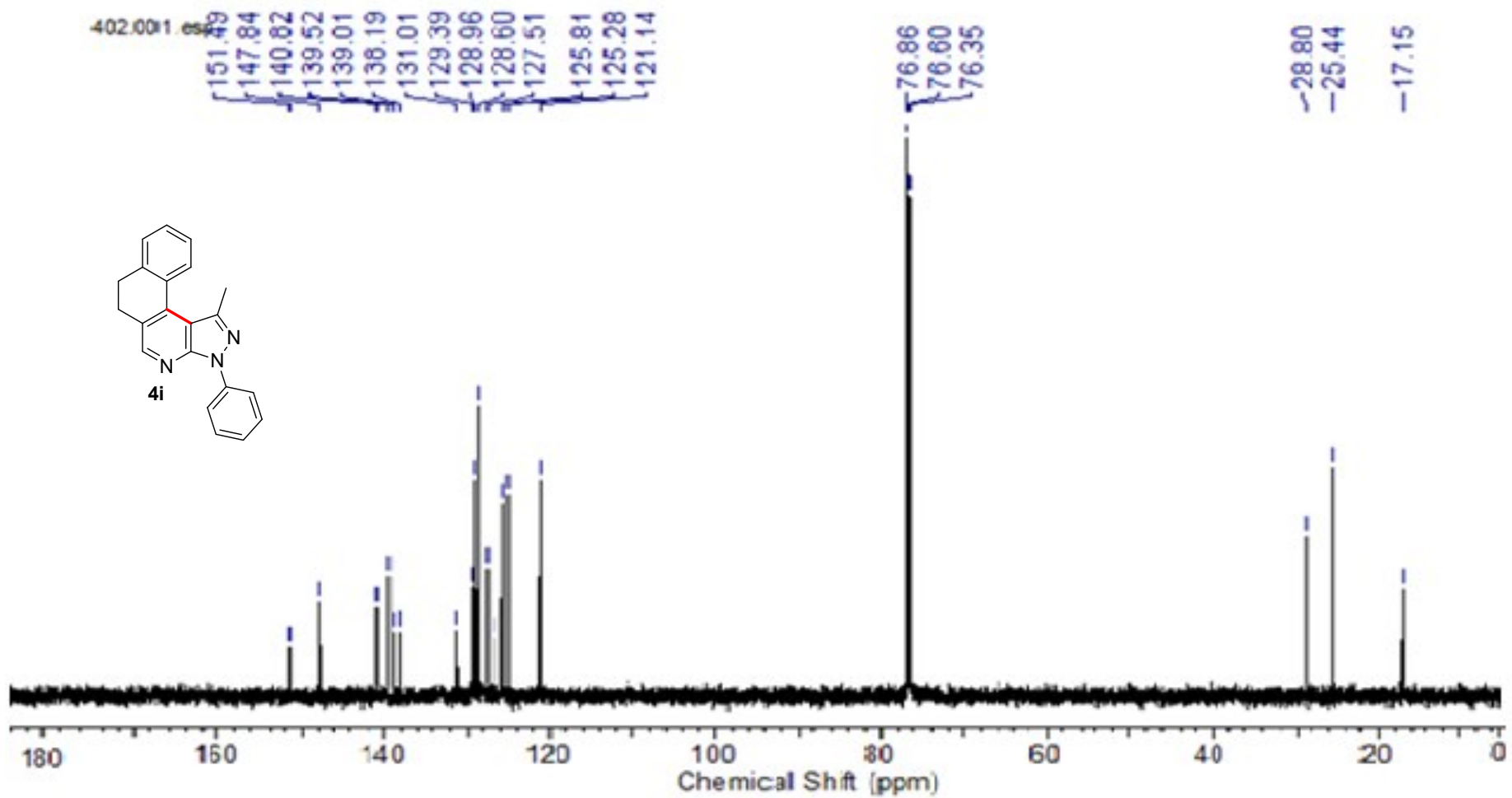
S 27

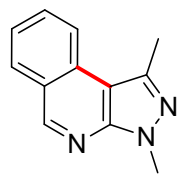
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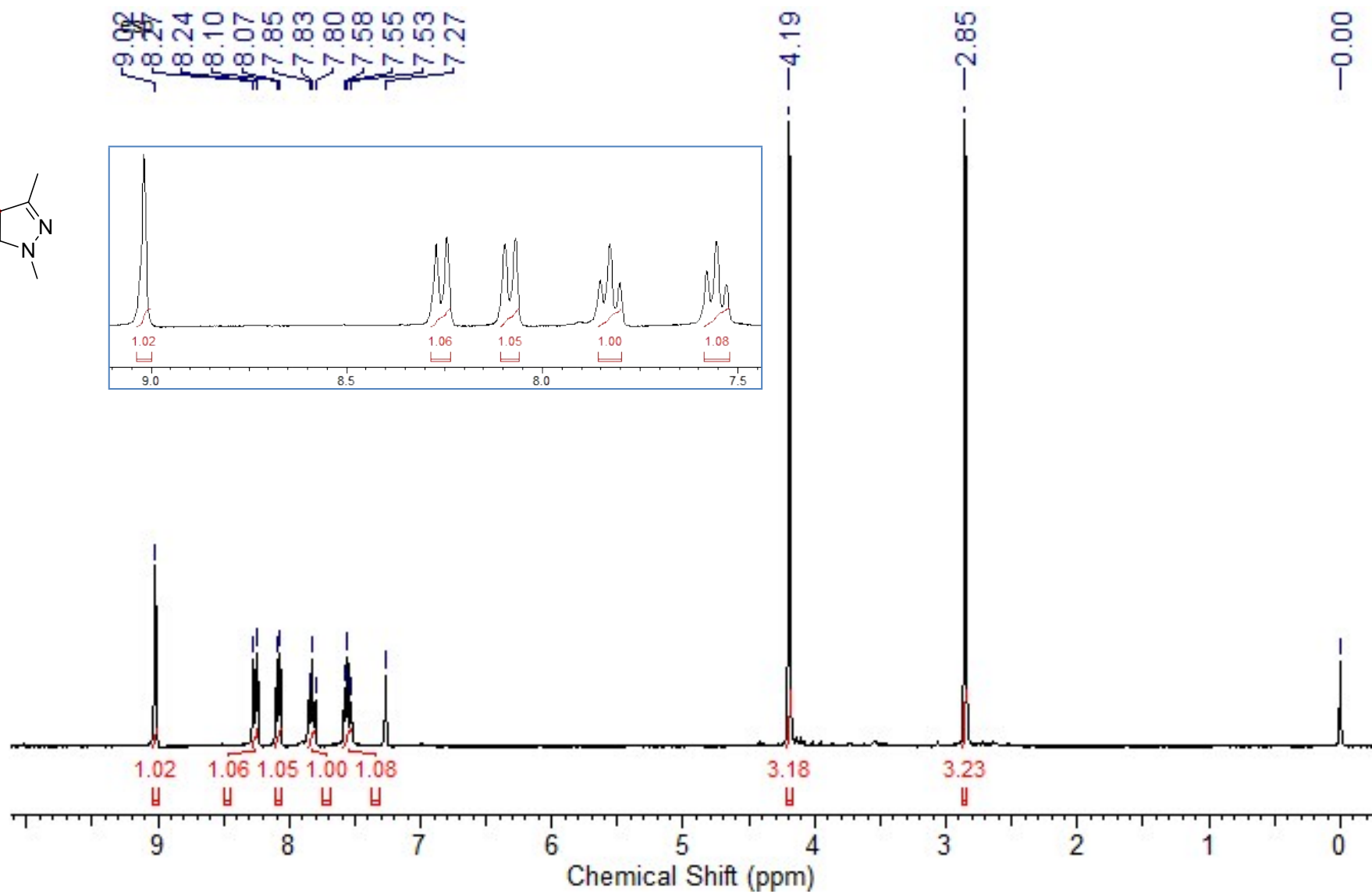
Chemical Shift (ppm)

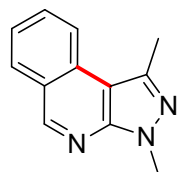






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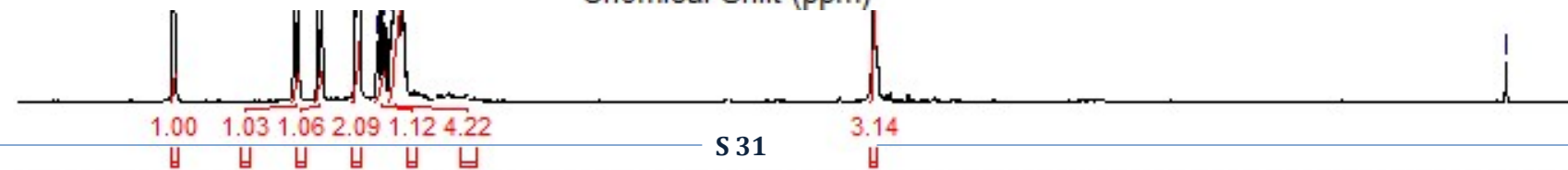
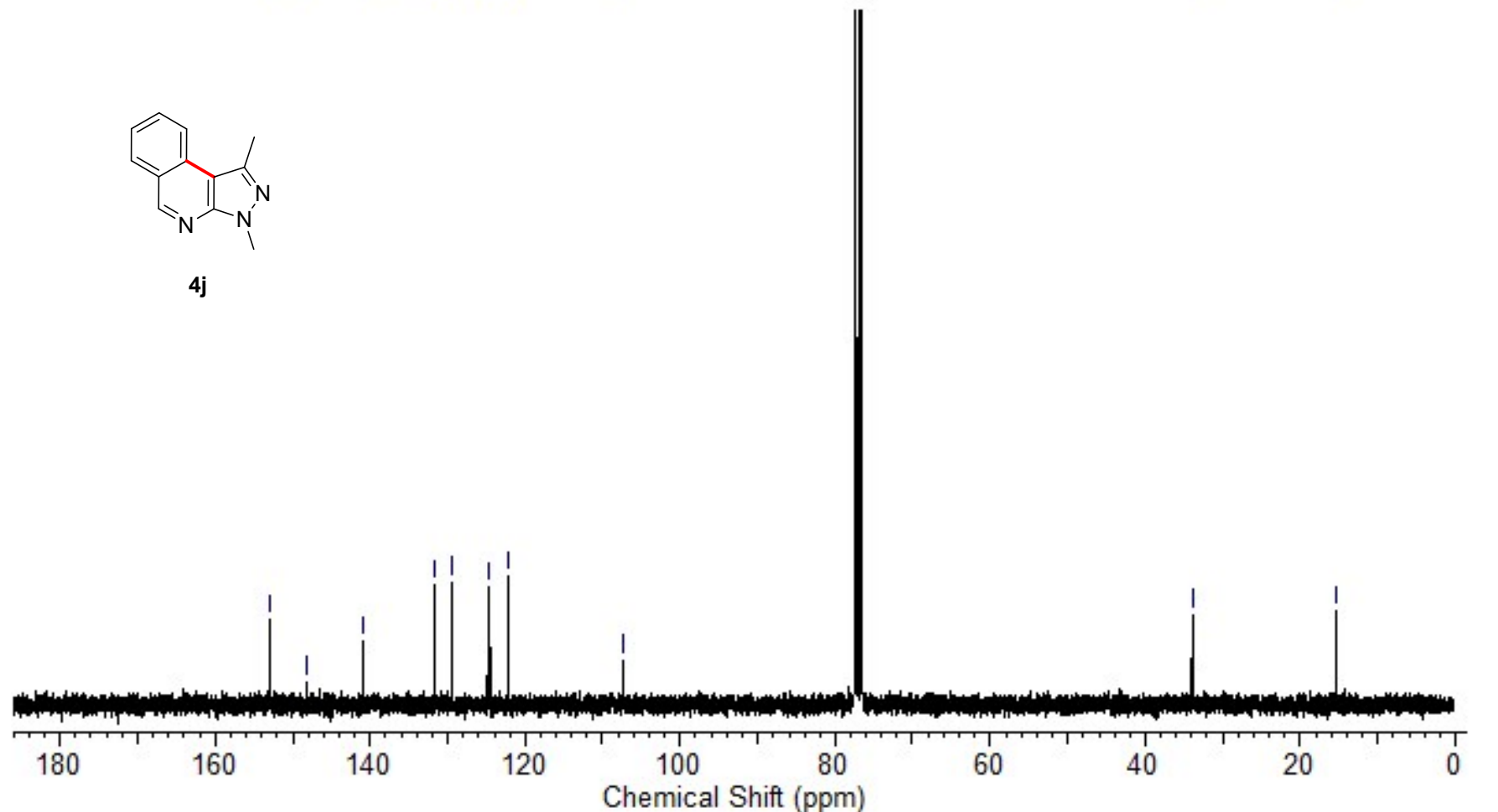




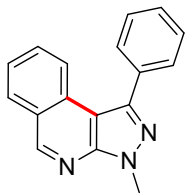
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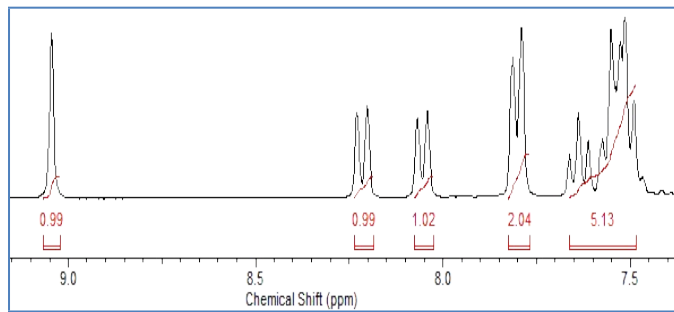
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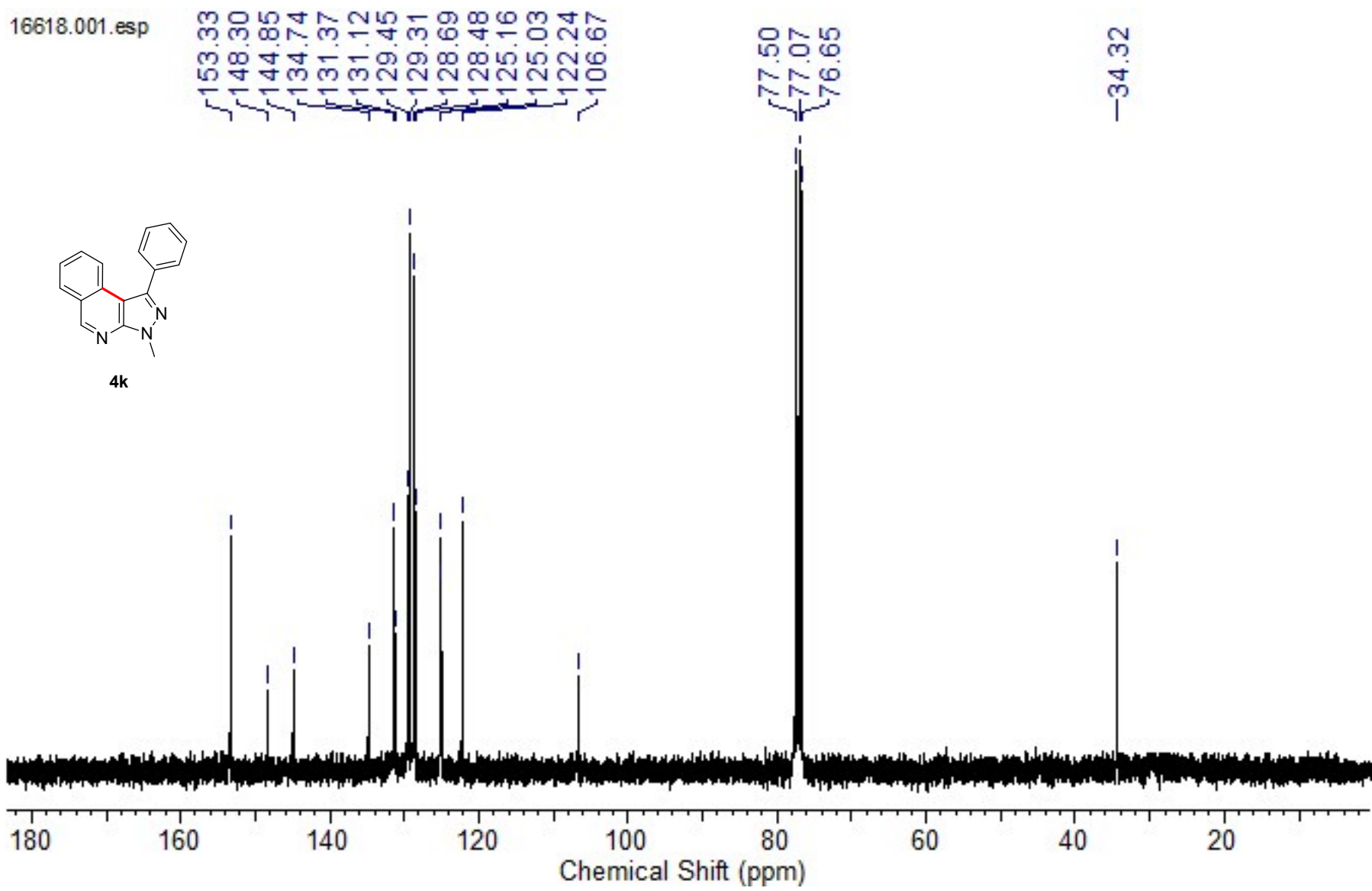
Chemical Shift (ppm)



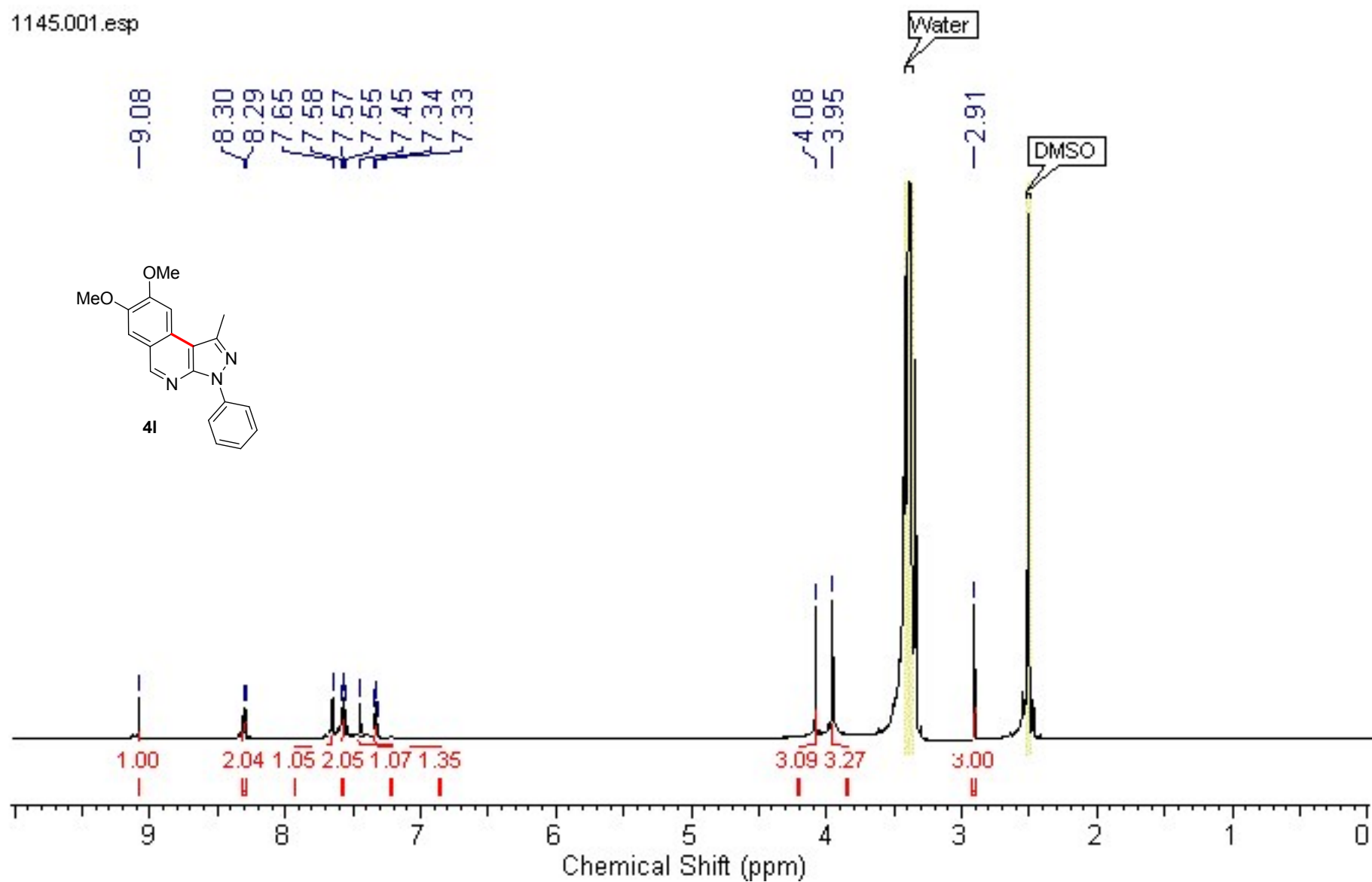
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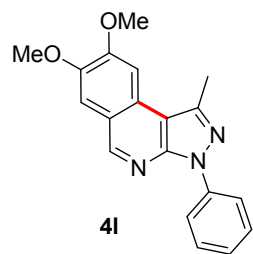
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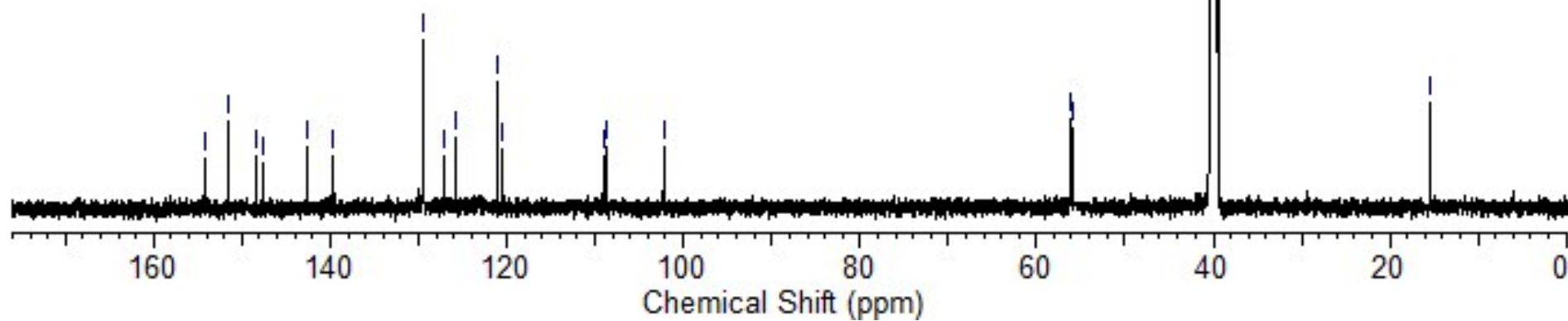
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41



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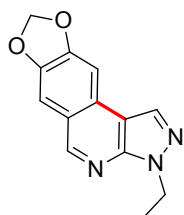
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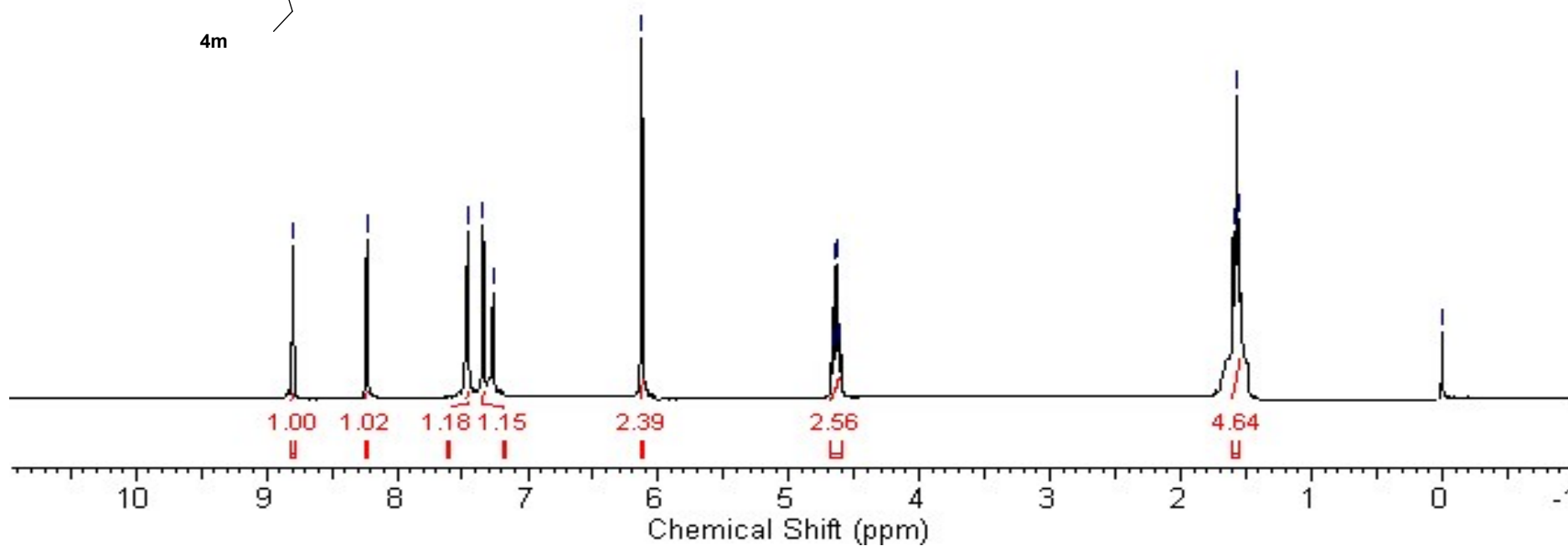
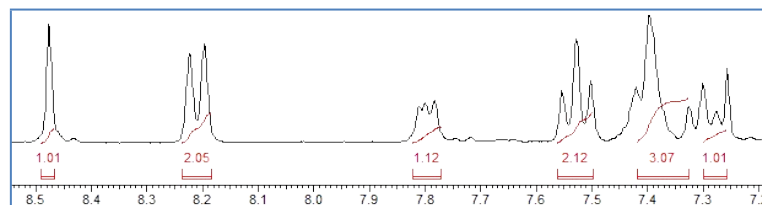
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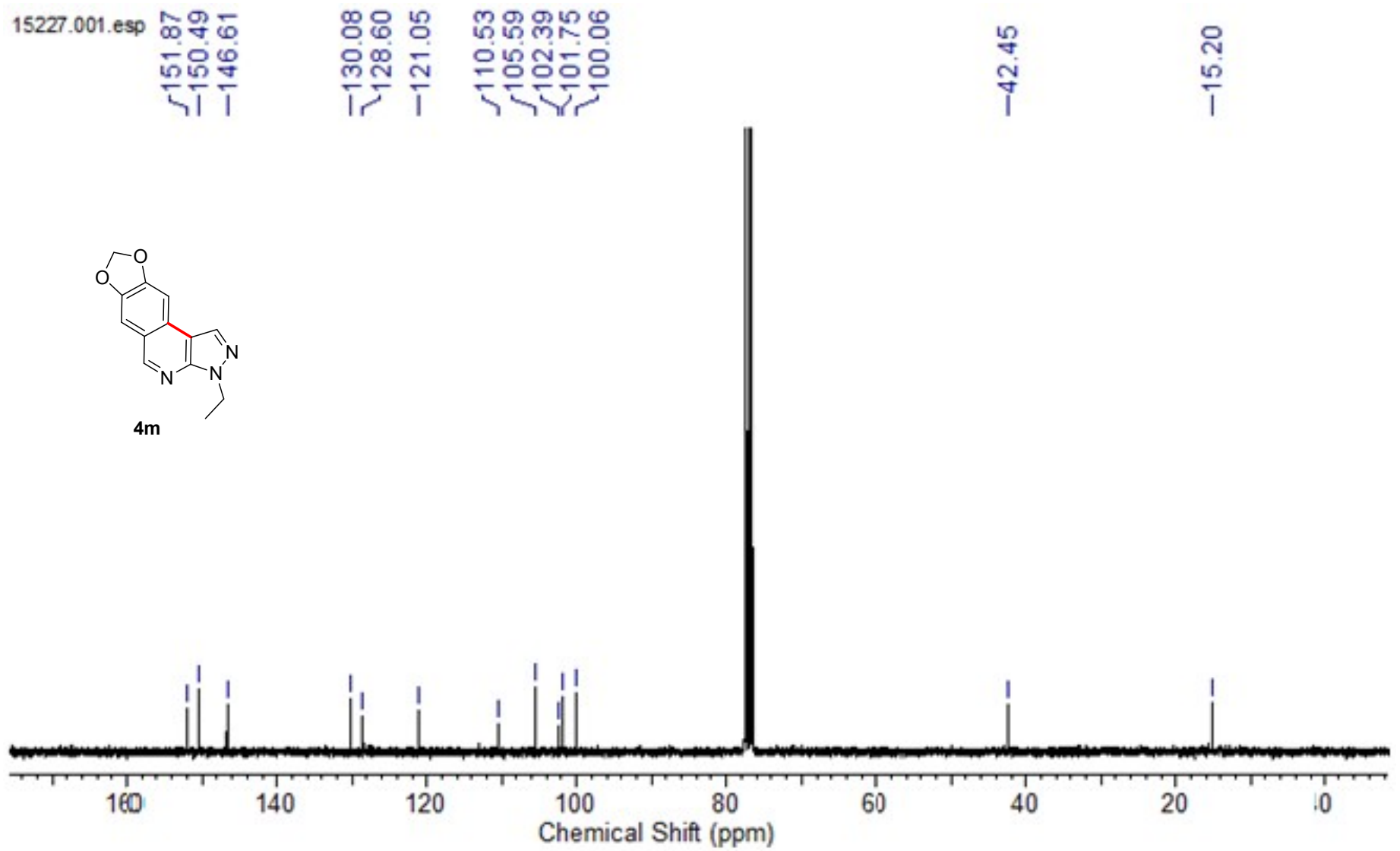
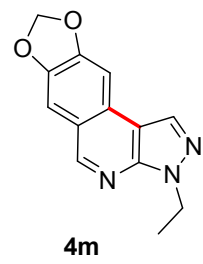
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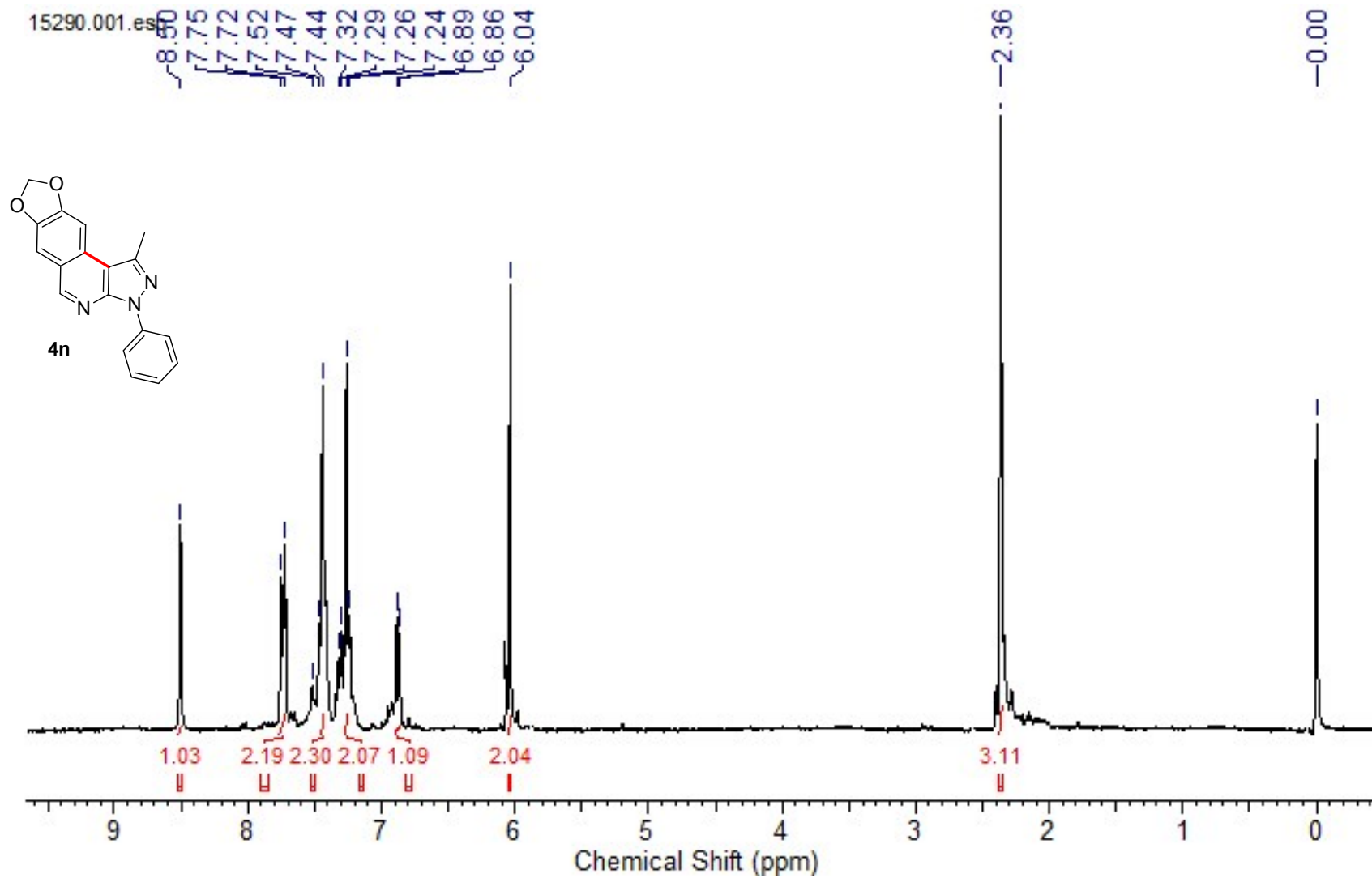


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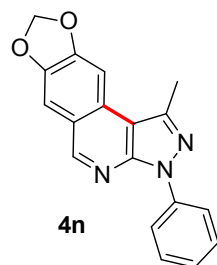


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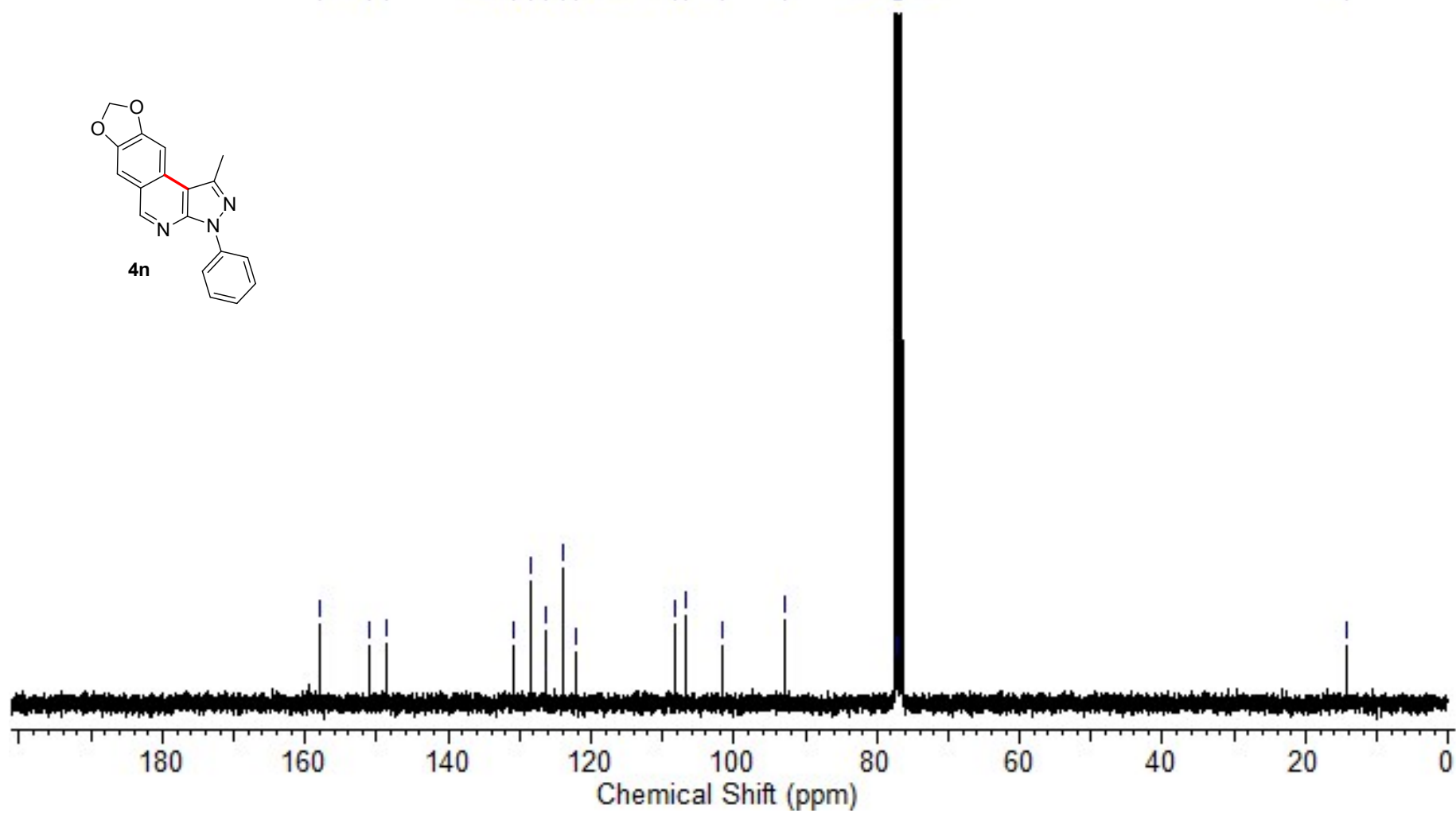


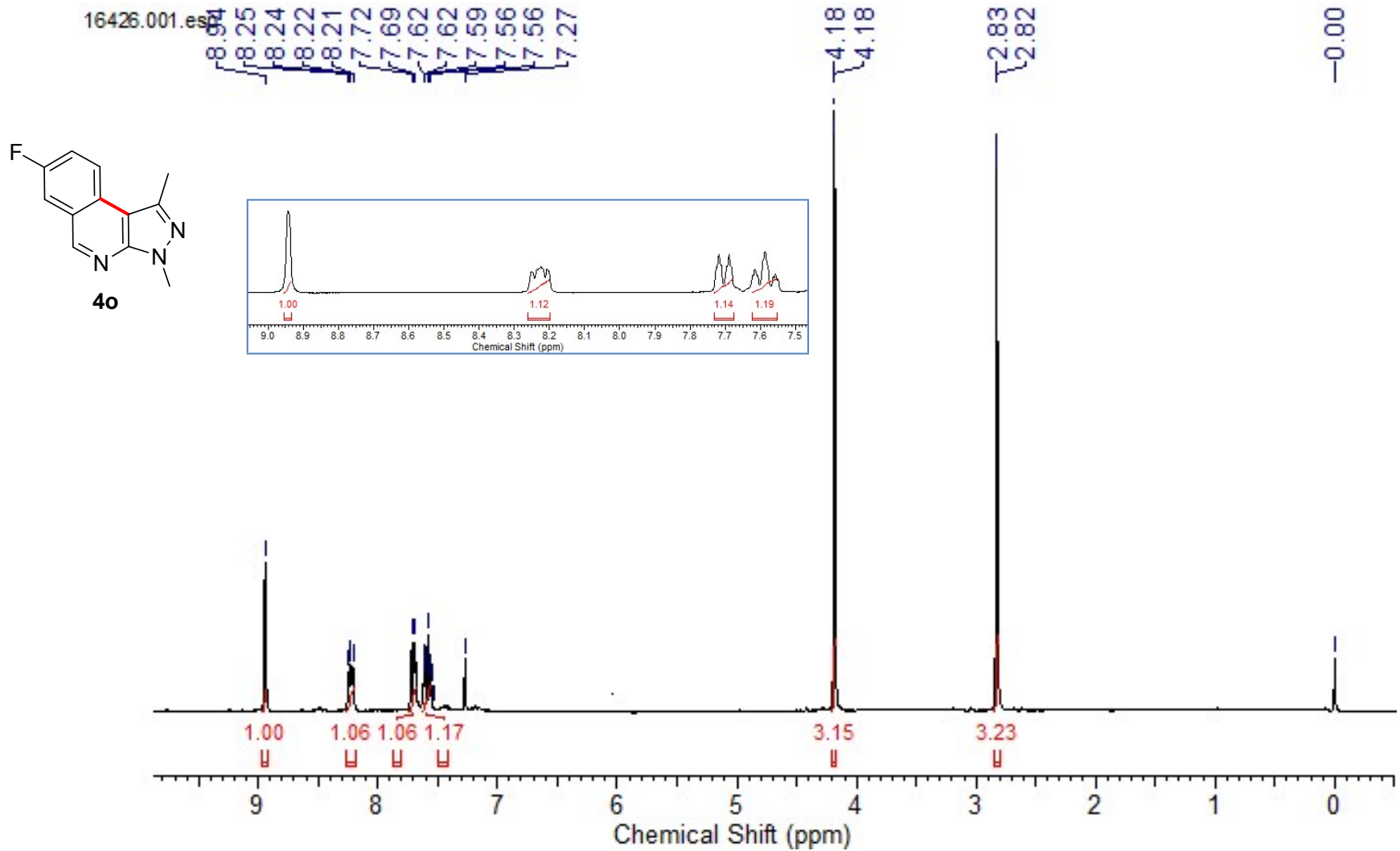


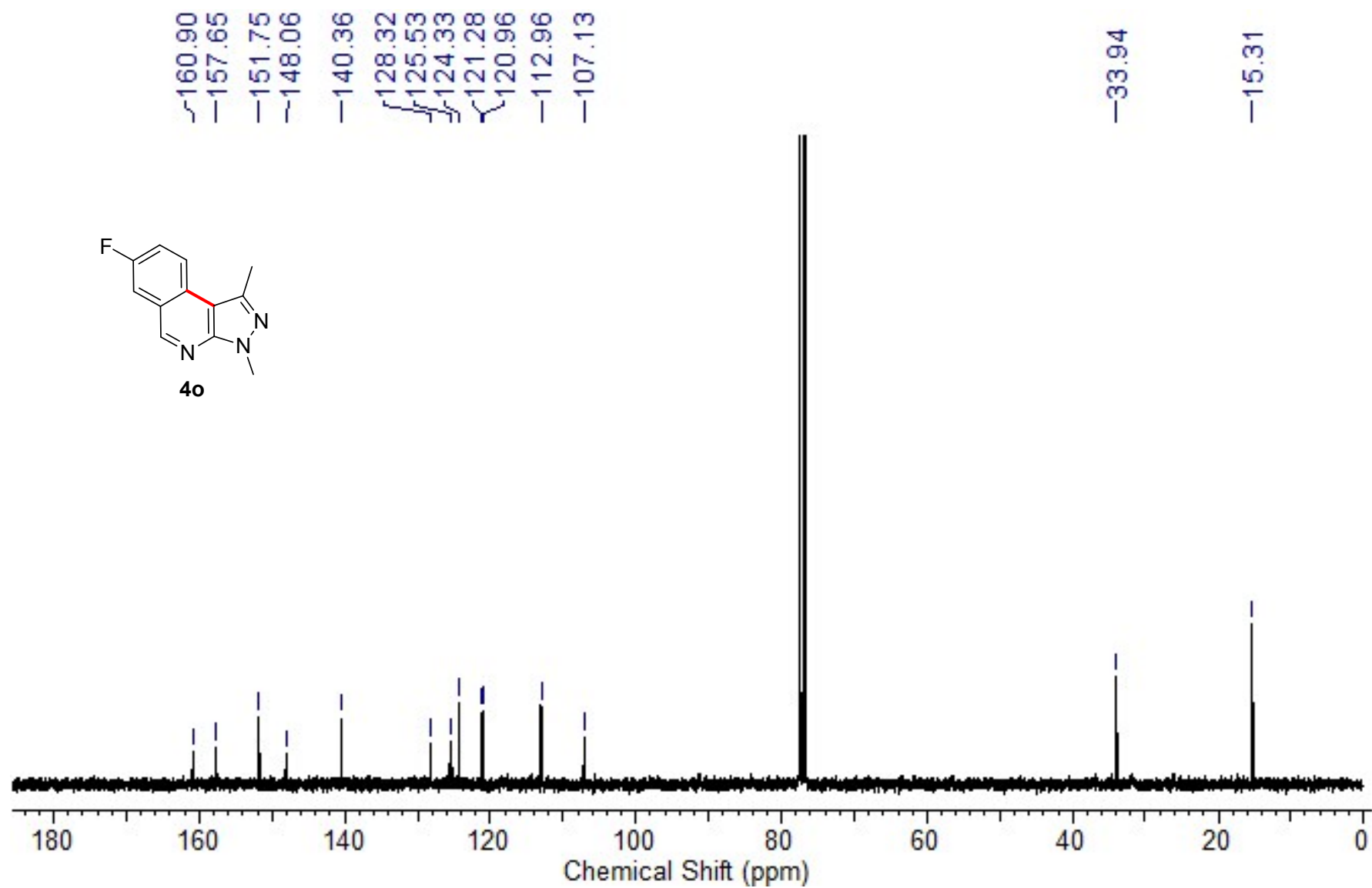
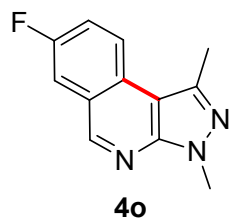
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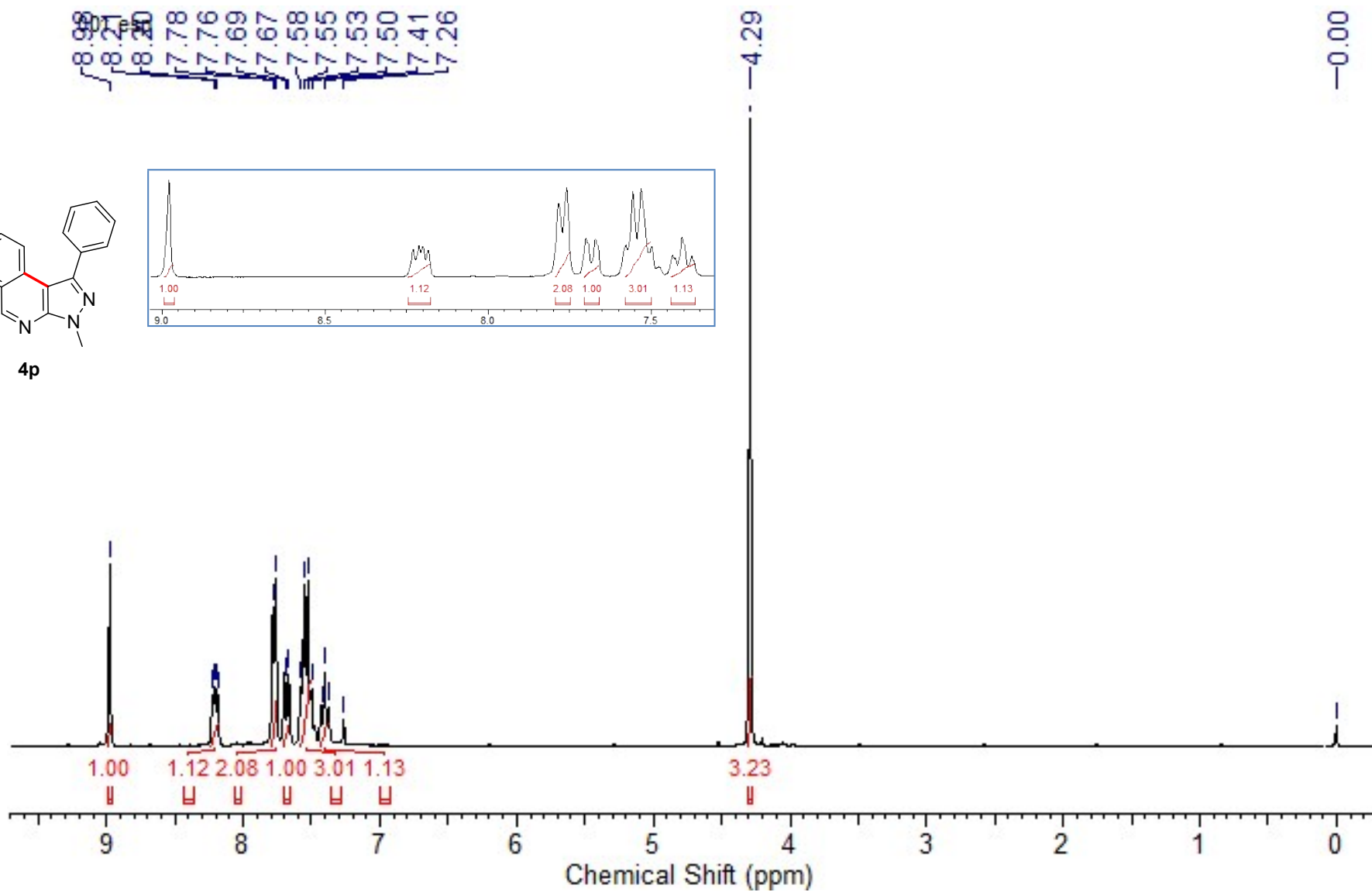
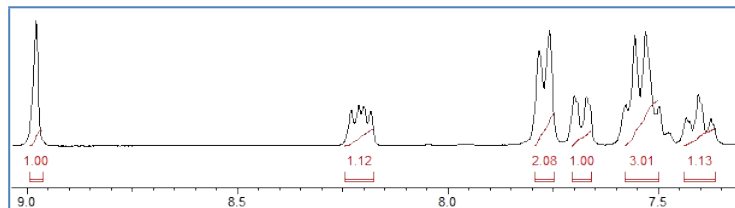
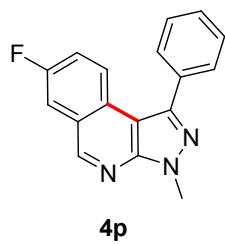


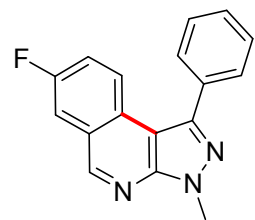
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14.19



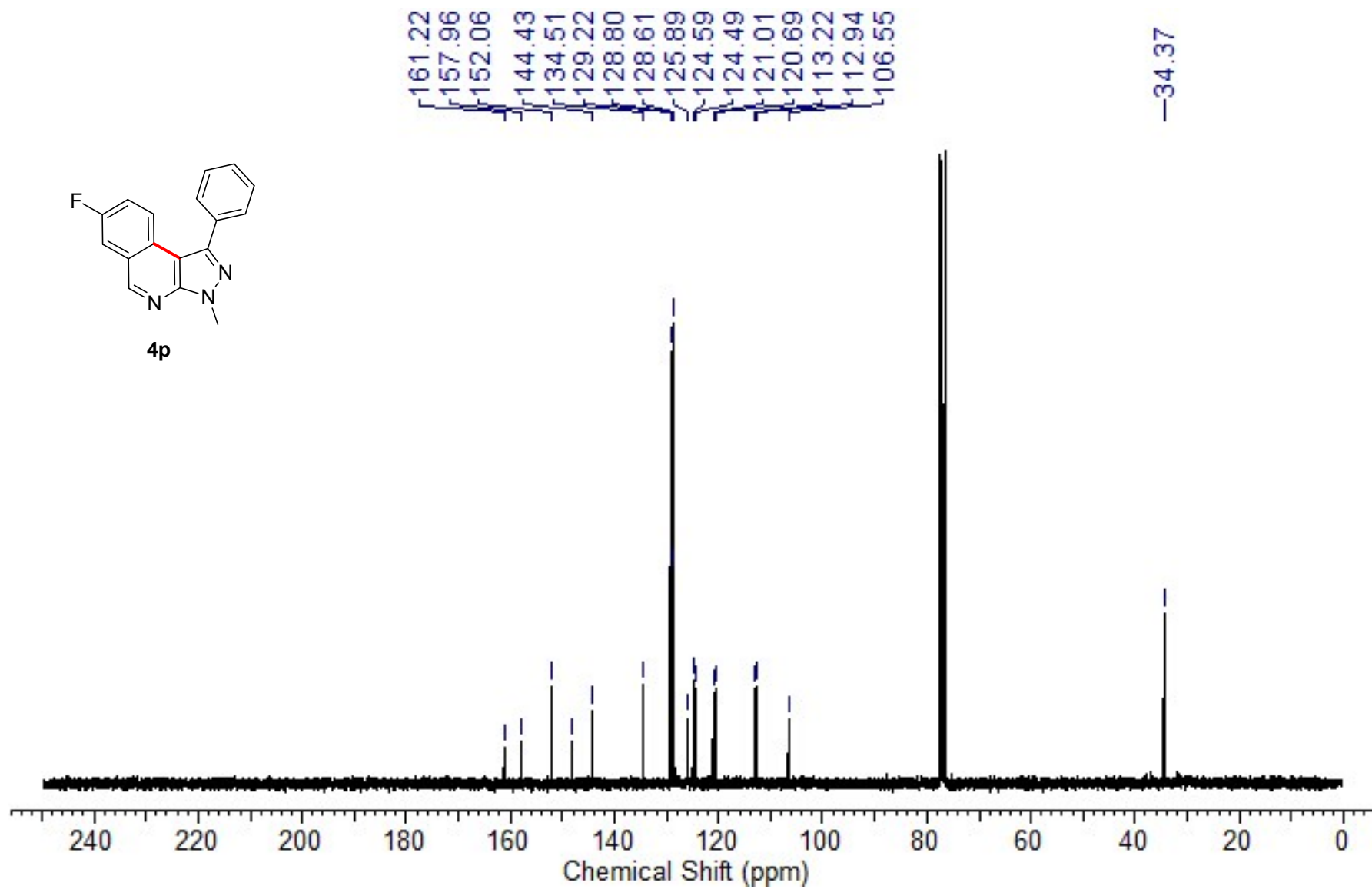








4p



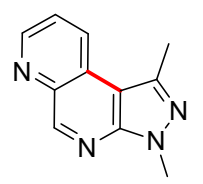
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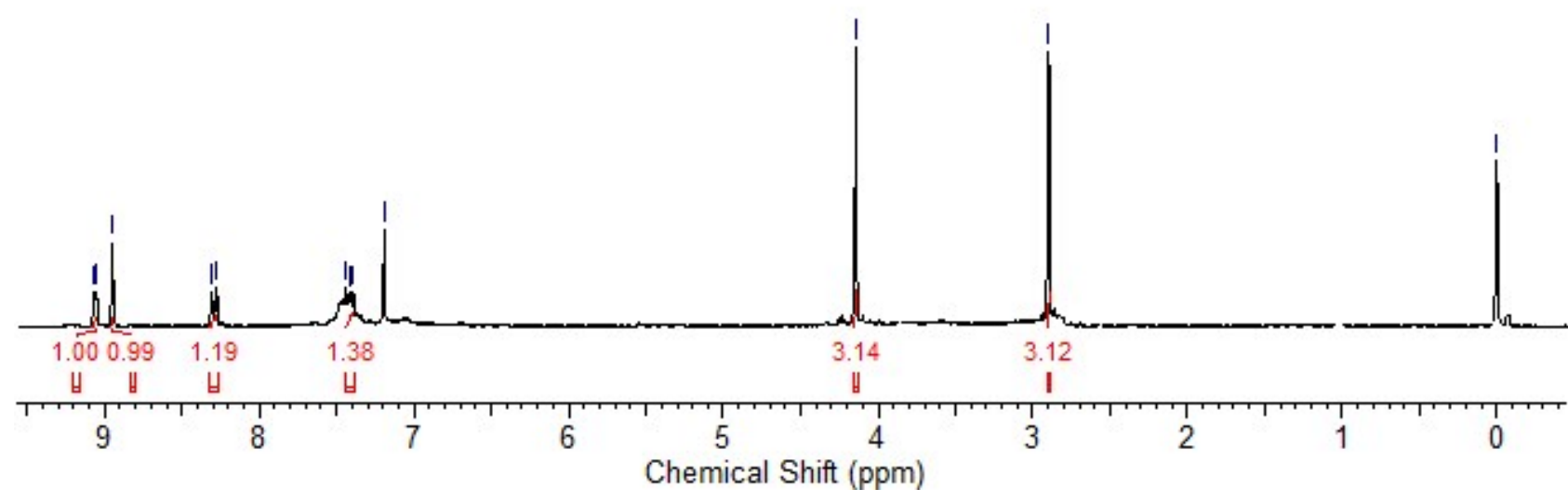
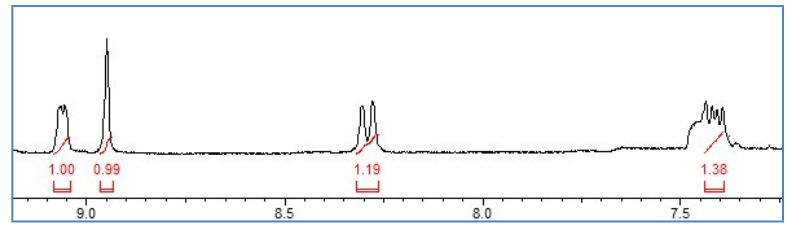
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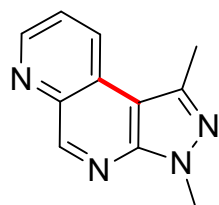
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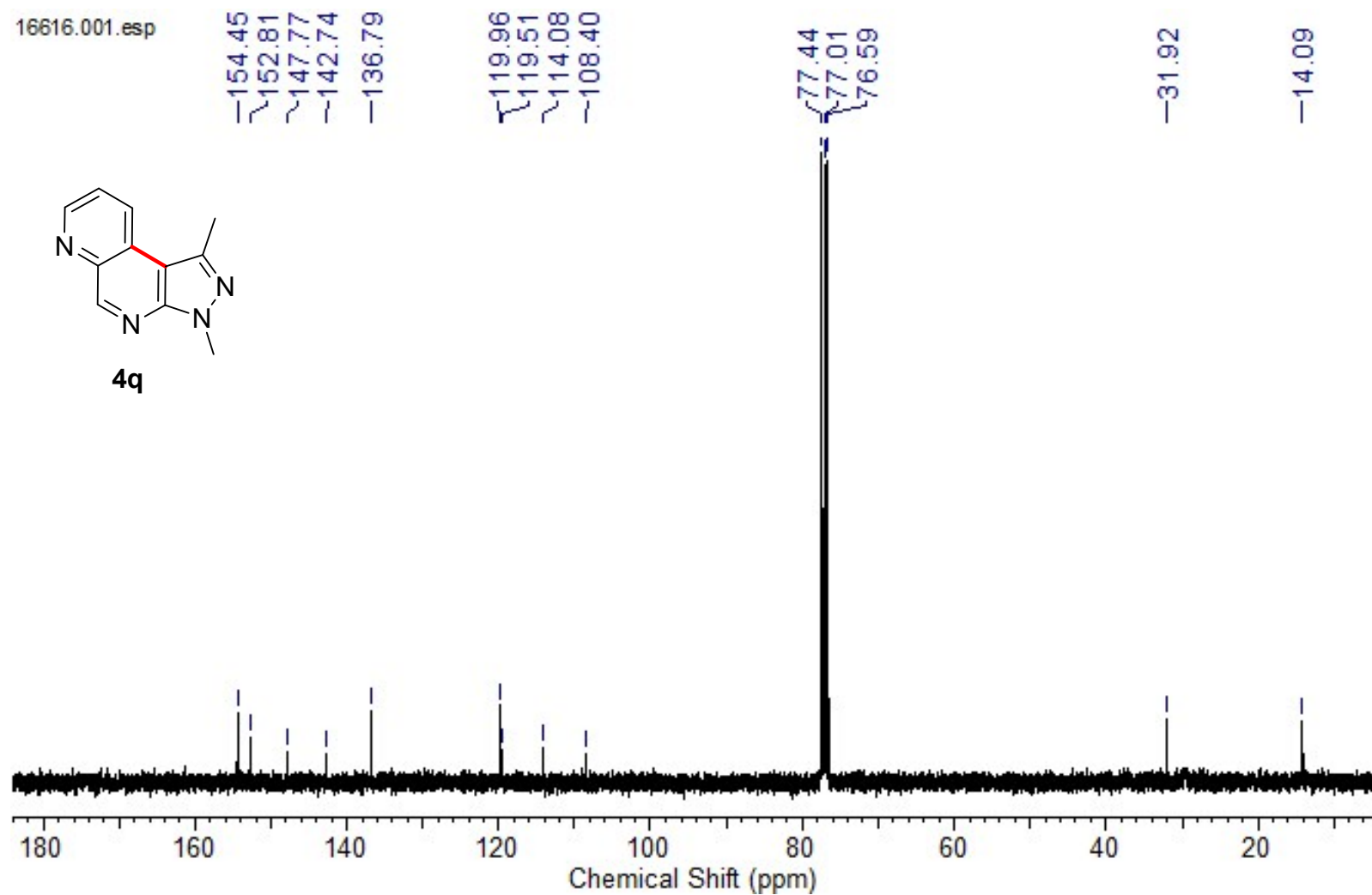
4q



16616.001.esp



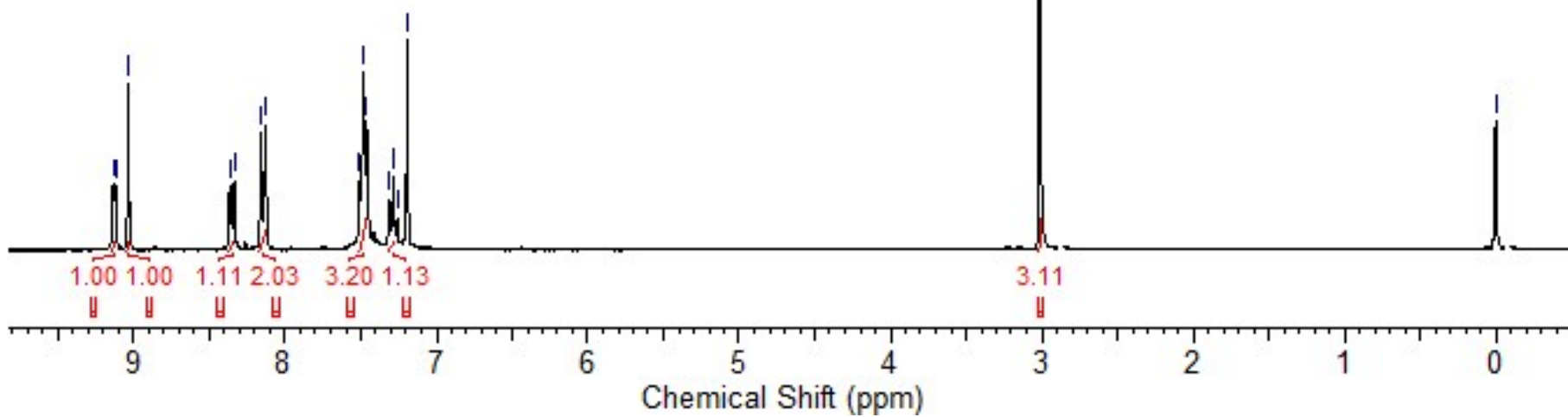
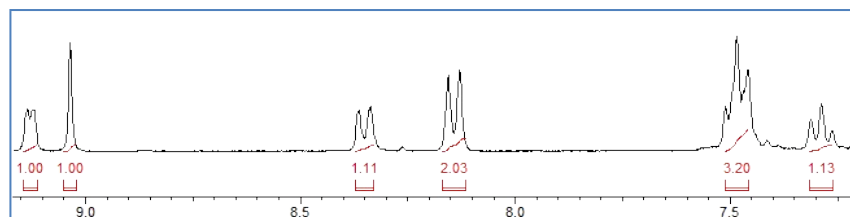
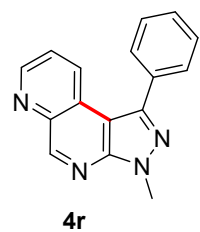
4q



9.19
9.14
9.04
8.36
8.34
8.34
8.16
8.13
7.51
7.48
7.46
7.31
7.29
7.26
7.19

-3.01

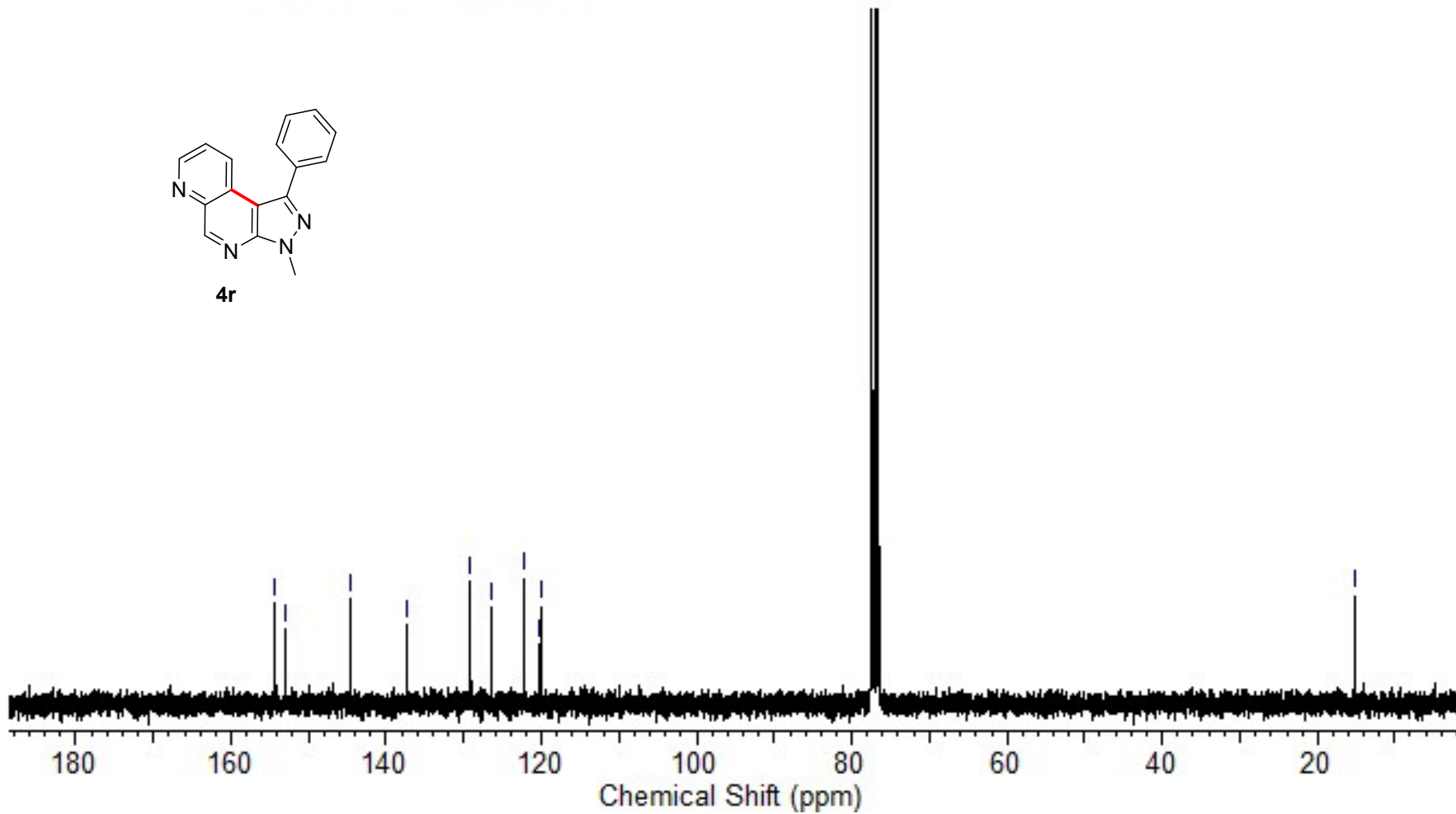
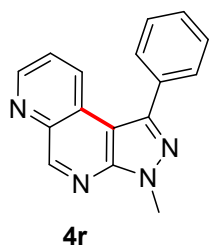
-0.00



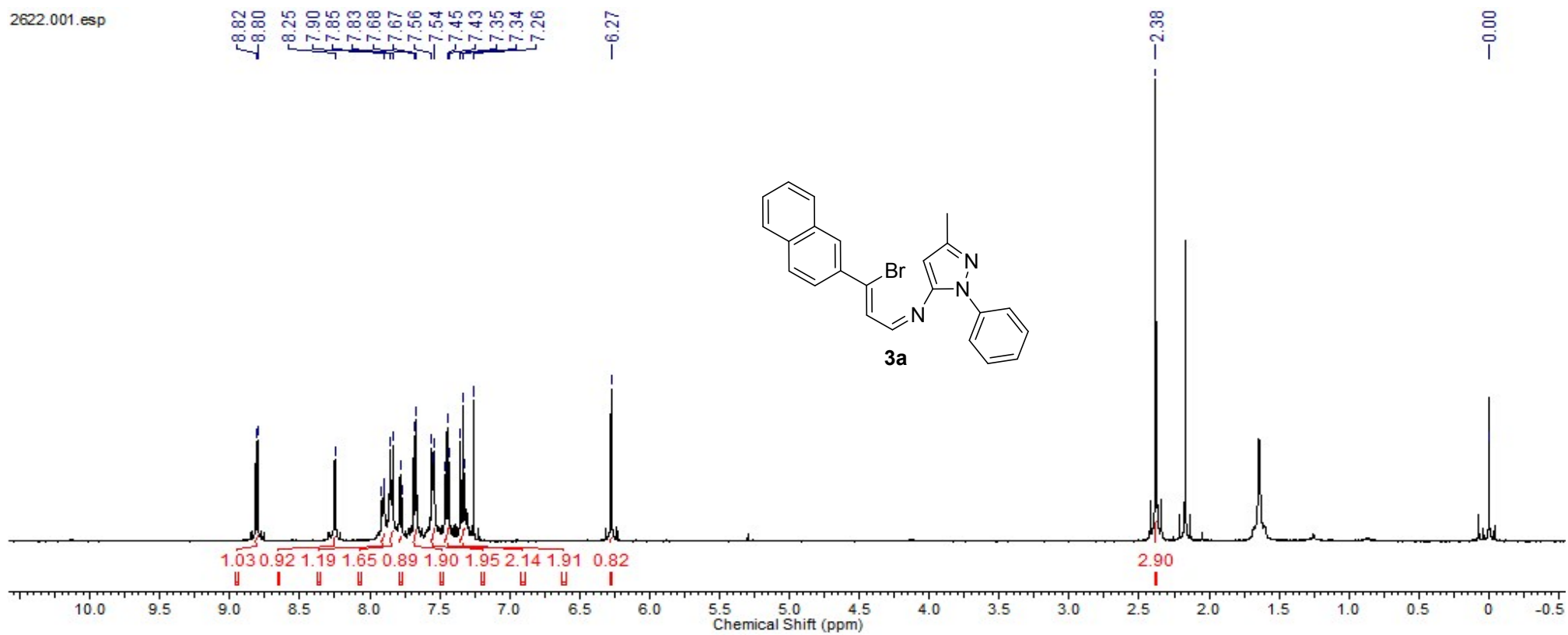
14521.001.esp

154.28
153.04
144.67
137.26
129.15
126.55
122.27
120.39
120.04

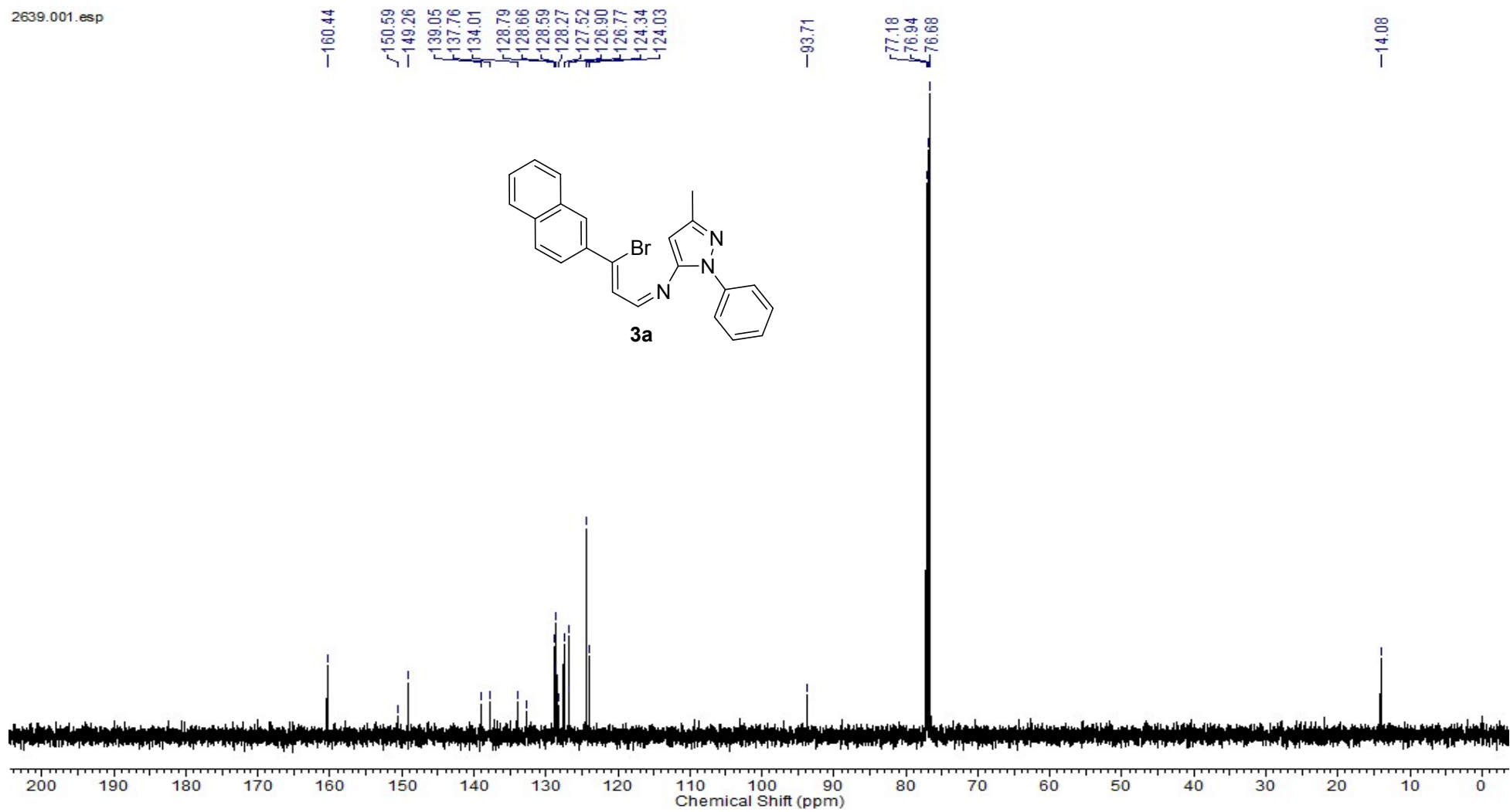
15.11



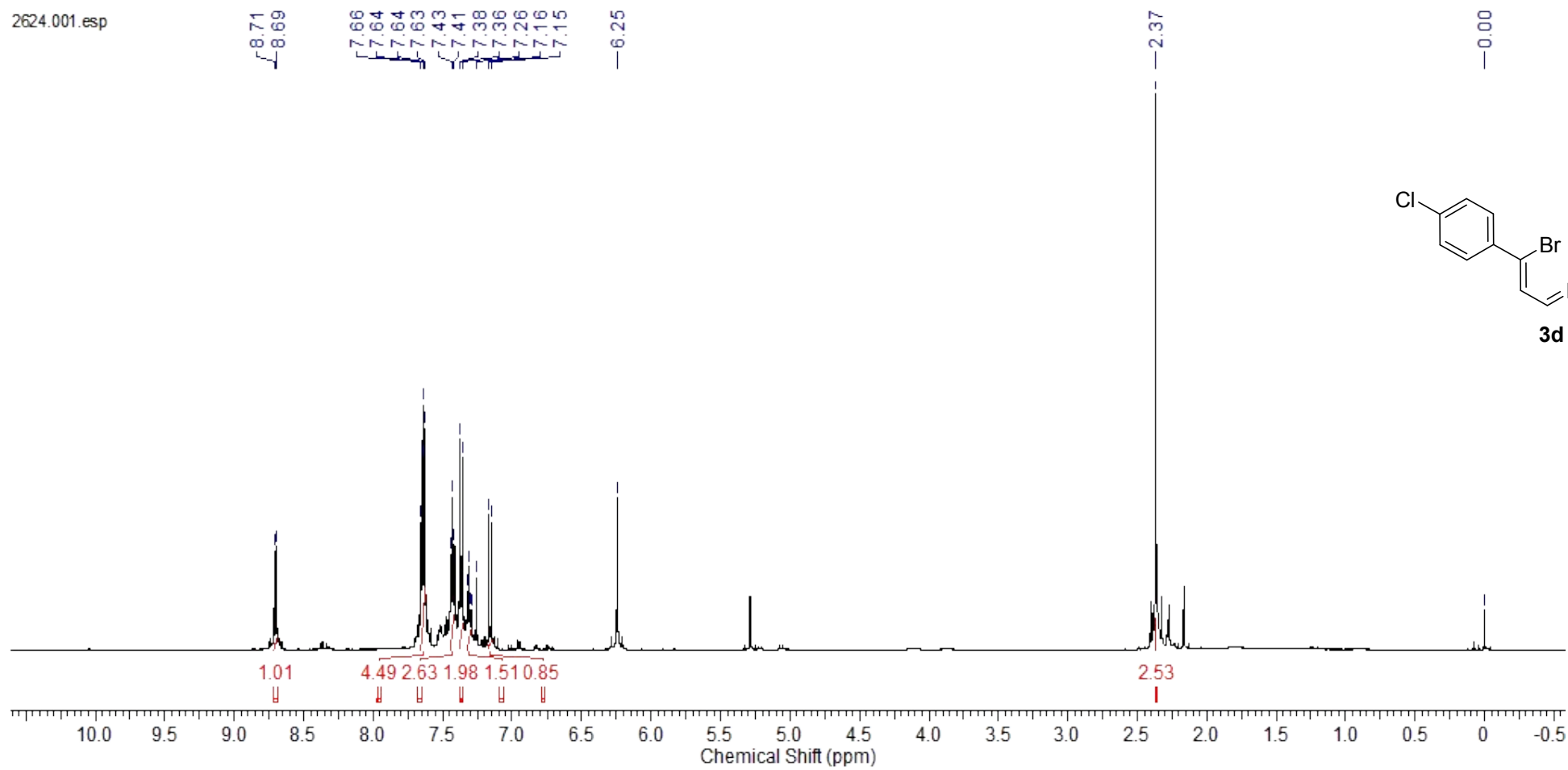
2622.001.esp



2639.001.esp



2624.001.esp



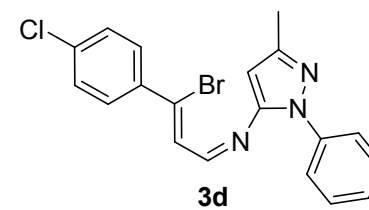
2634.001.esp

159.96
150.39
149.26
139.00
136.53
135.97
128.92
128.78
128.68
128.58
126.80
124.31

93.74

77.23
76.97
76.71

14.08



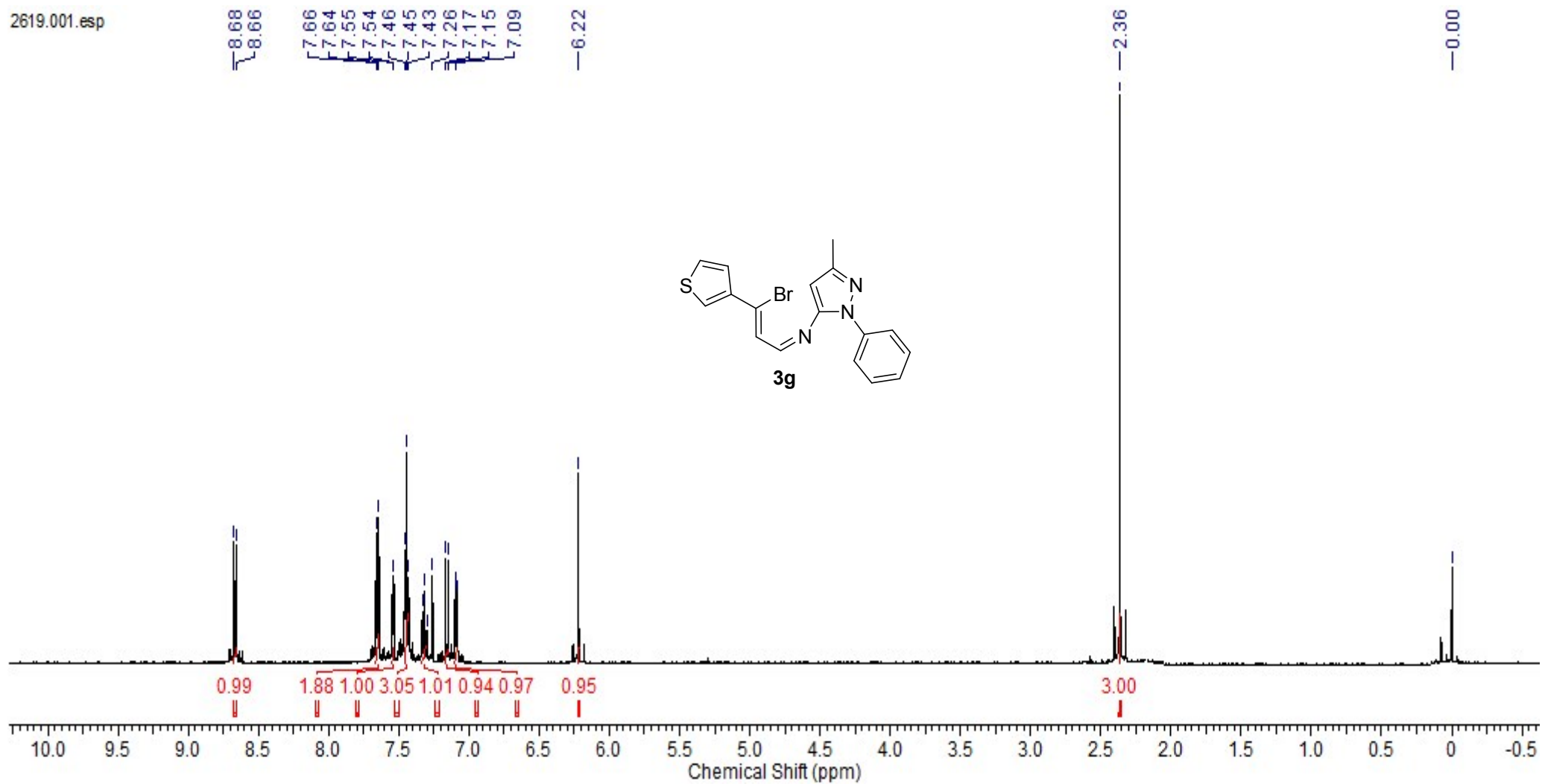
3d



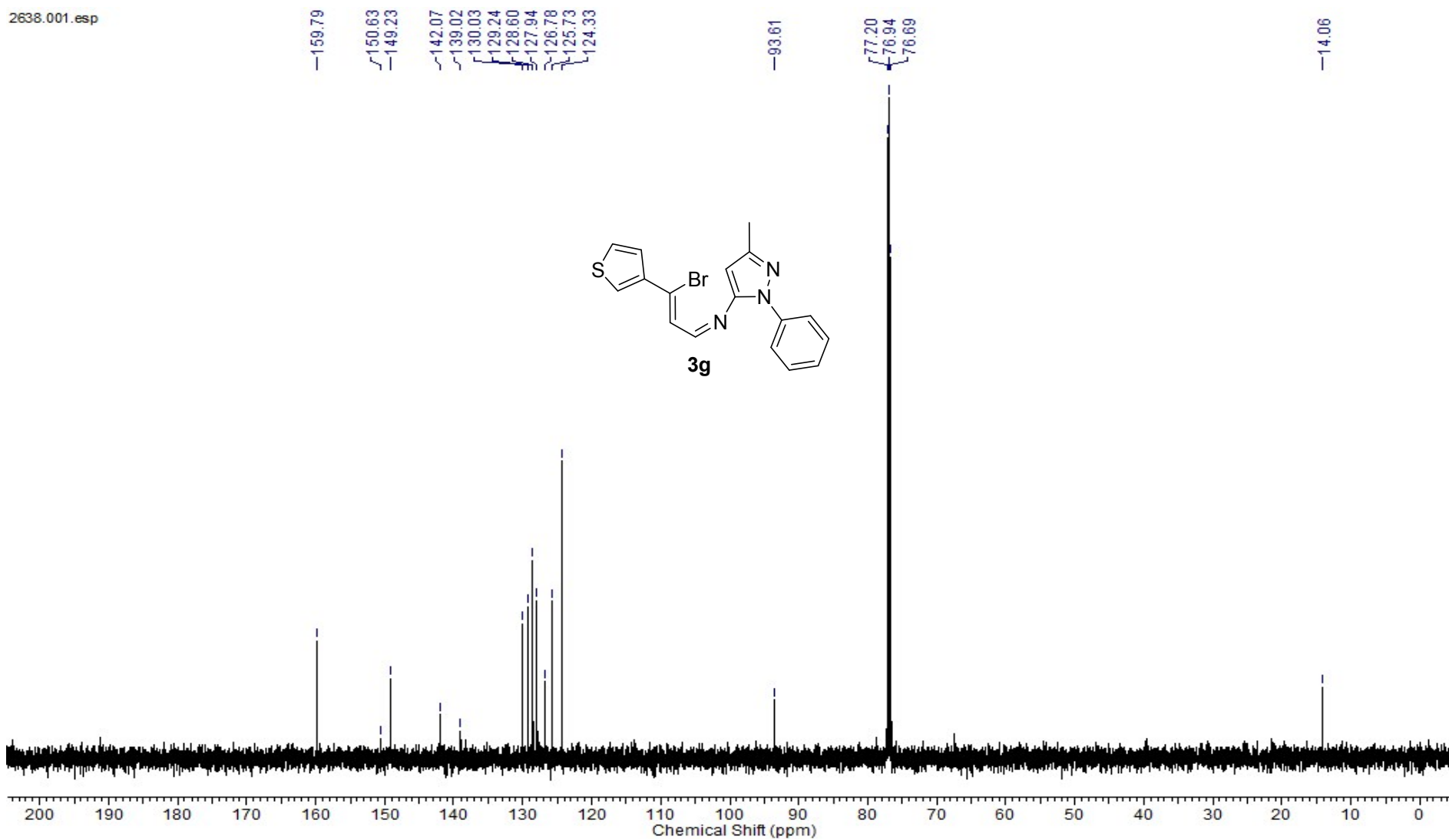
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

Chemical Shift (ppm)

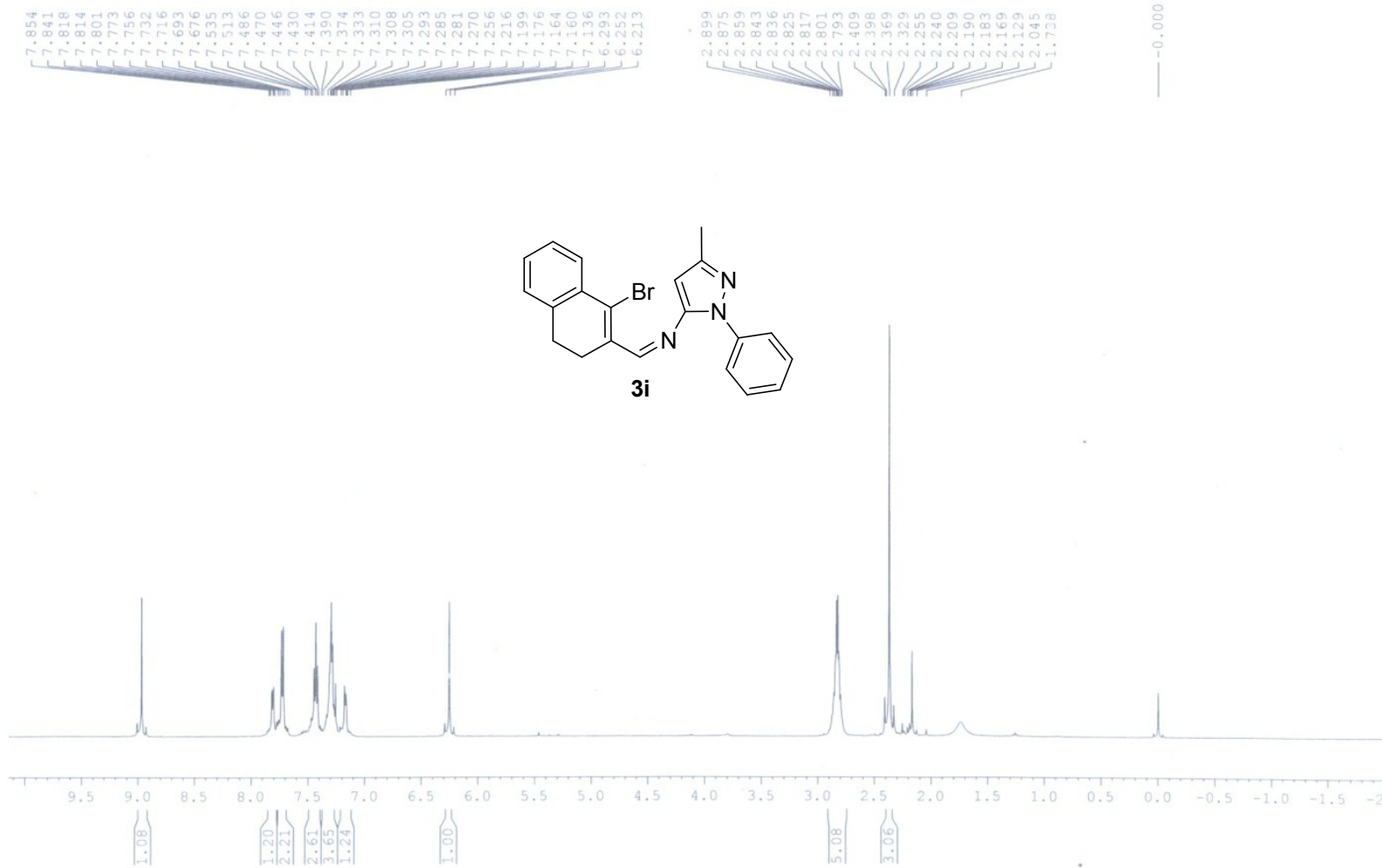
2619.001.esp

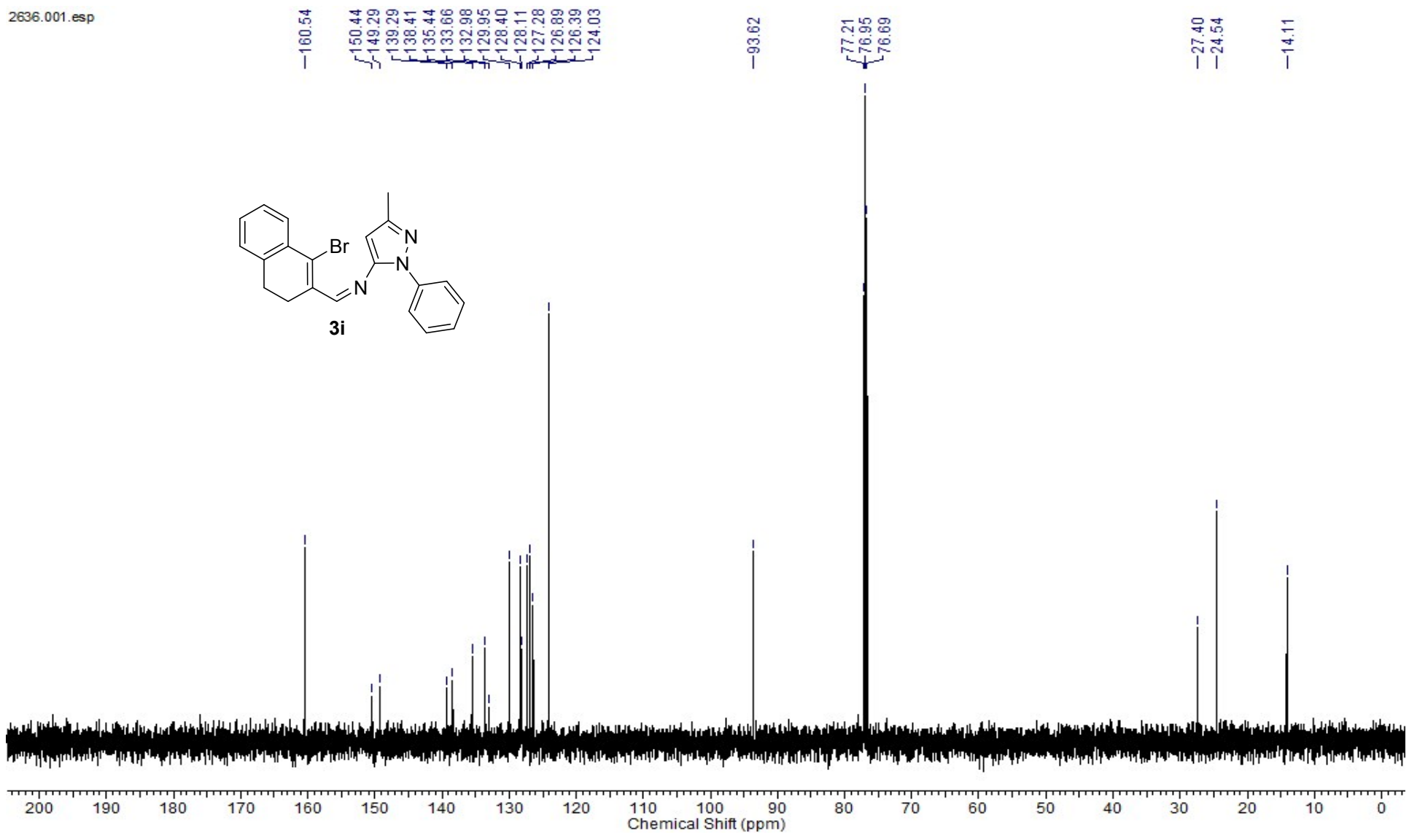
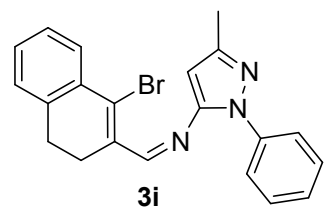


2638.001.esp

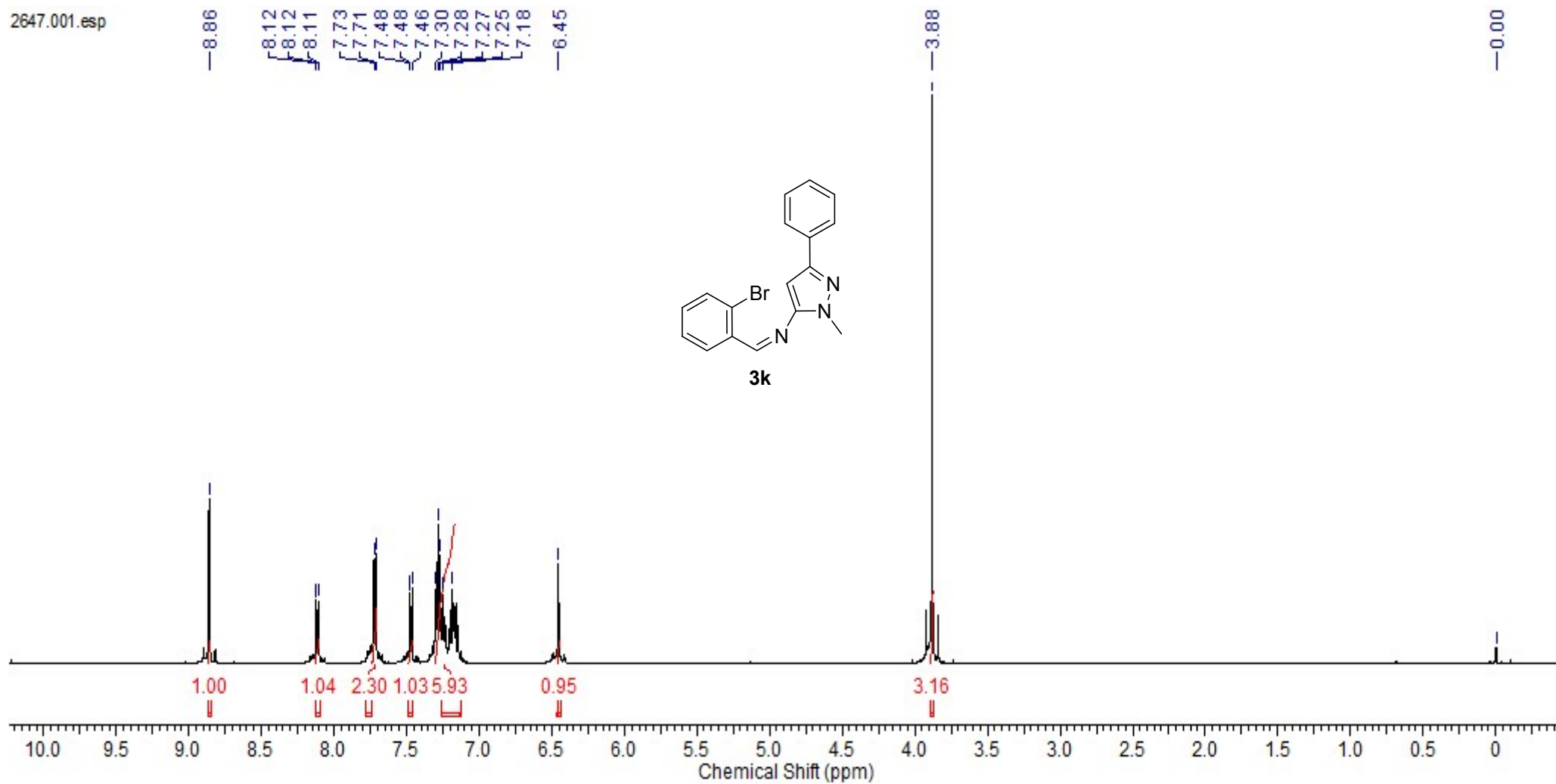


Name of Sample:TBF
Spectrum No.:2621

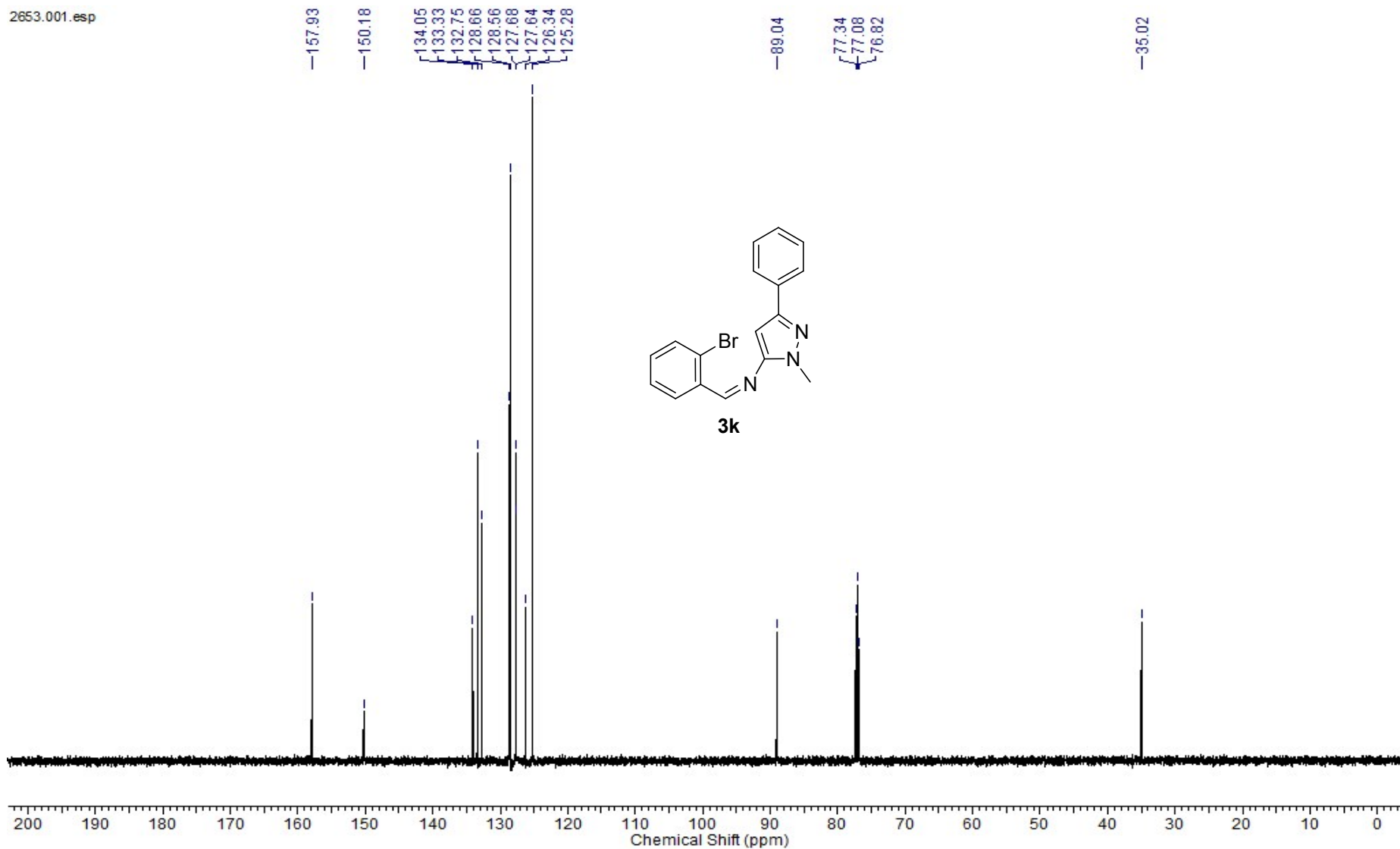




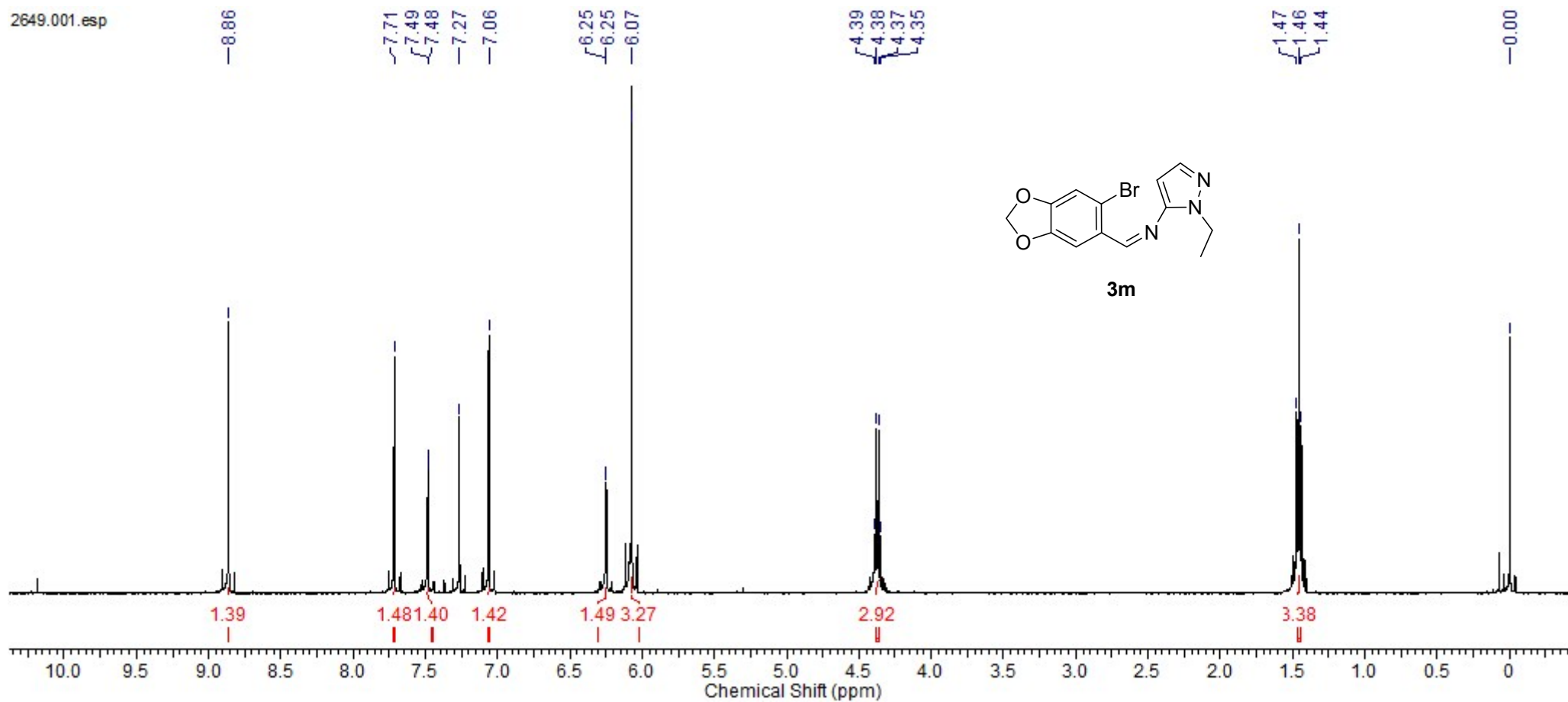
2647.001.esp



2653.001.esp

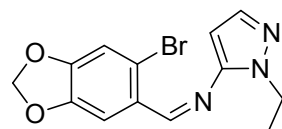


2649.001.esp

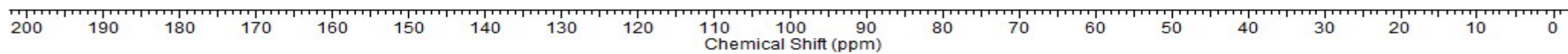


2655.001.esp

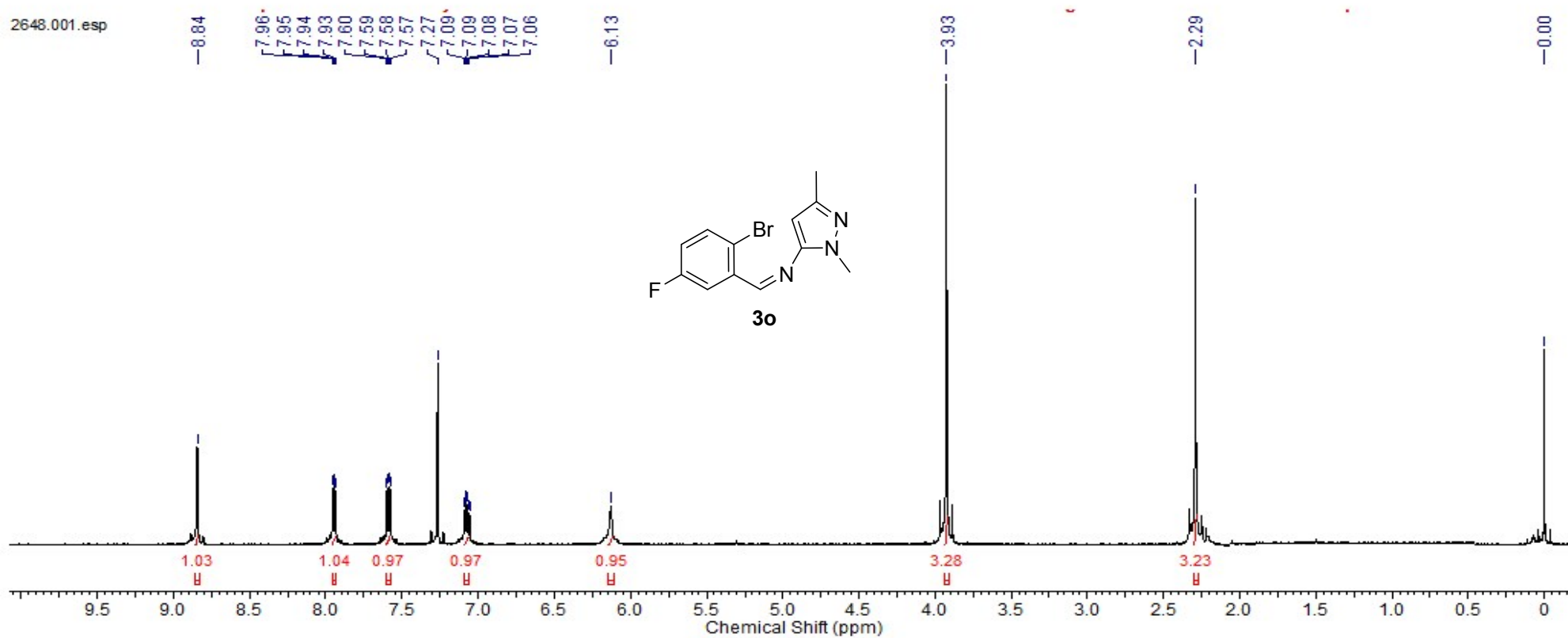
—157.51
—151.25
—148.55
—147.87
—138.51
—128.23
—119.24
—112.85
—107.21
—102.30
—91.86
77.18
76.92
76.68
—42.82
—15.52



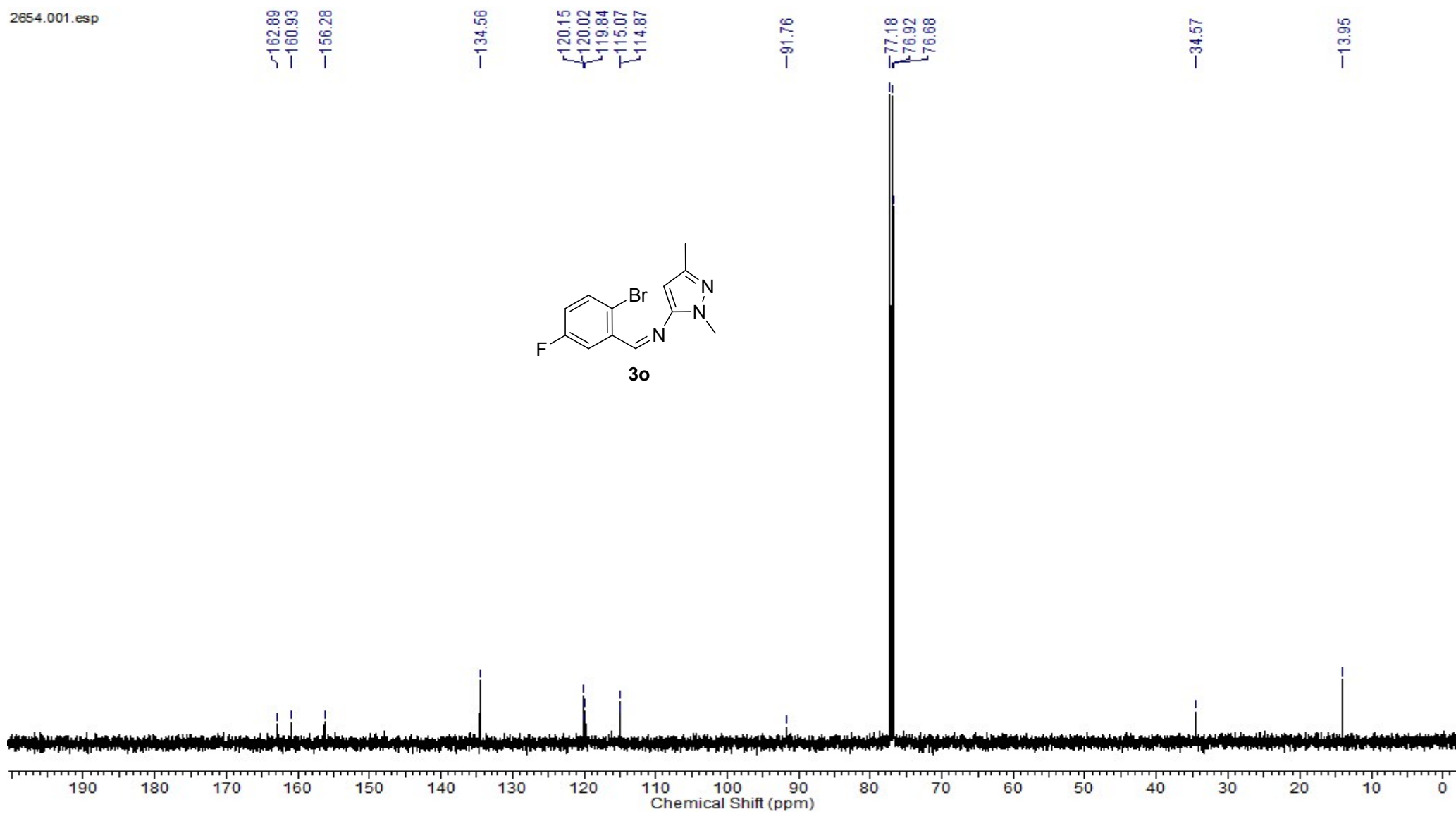
3m



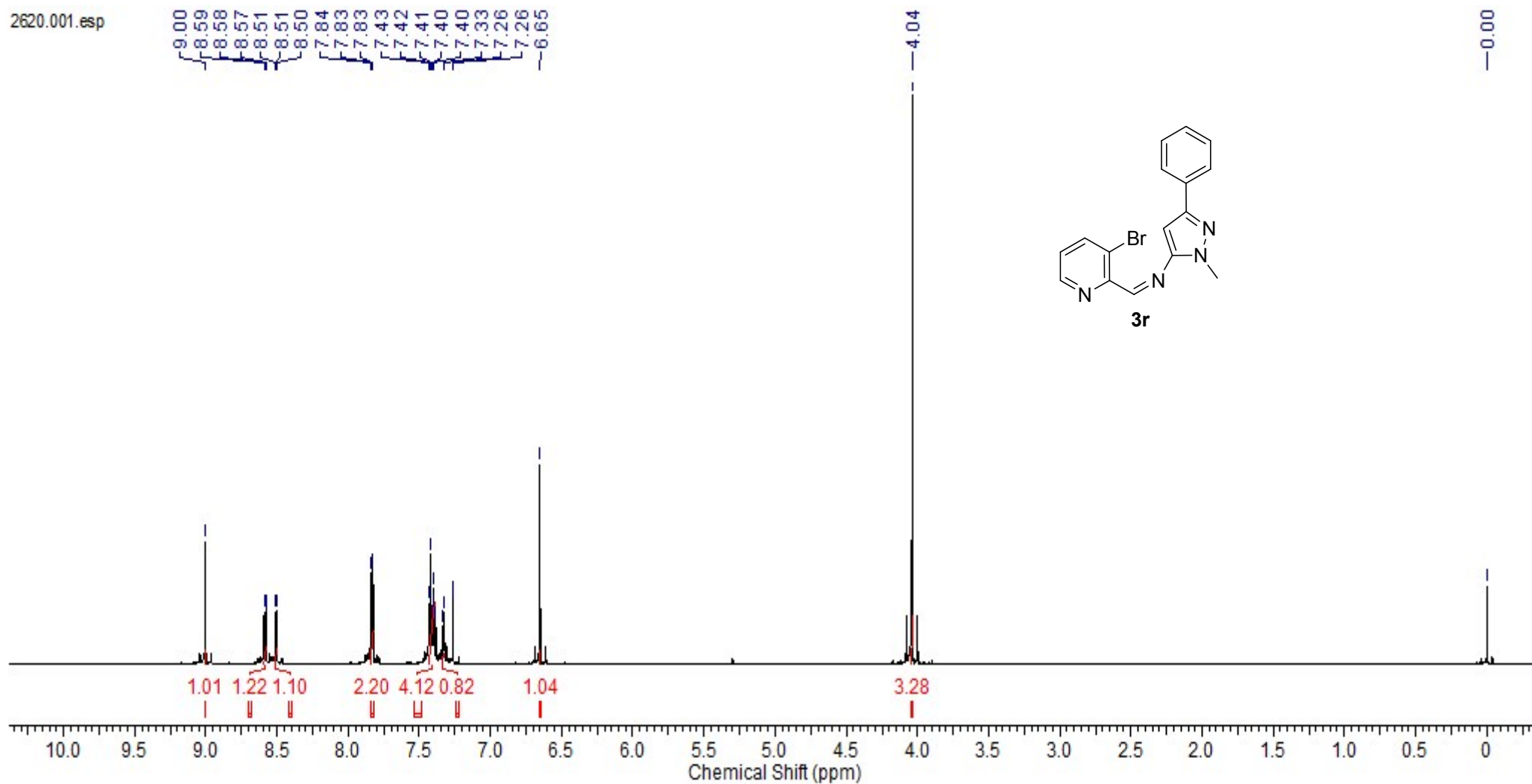
2648.001.esp



2654.001.esp



2620.001.esp



2637.001.esp

154.08
152.22
151.79
150.43
149.84
136.77
133.13
129.73
128.58
127.81
125.27
122.97

89.30

77.20
76.94
76.69

35.08

