

A new general synthesis of functionally substituted pyrazolo[1,5-*a*]pyrimidines

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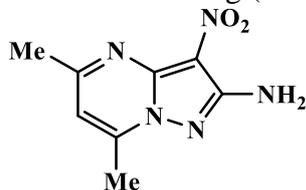
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General Experimental

IR spectra were recorded on a Bruker ALPHA instrument in KBr pellets. ^1H , ^{13}C NMR spectra were acquired on a Bruker AM-300 instrument (300.13, 75.47 MHz, respectively), 2D spectra HMBC ^1H – ^{13}C were acquired on a Bruker AV600 instrument (600.13 and 150.90 MHz, respectively), in DMSO- d_6 at 299 K. Chemical shifts (δ , ppm) are reported relative to TMS. The electron-impact mass spectra were obtained at 70 eV using a direct inlet system on a Finnigan MAT INCOS 50 instrument. High-resolution mass spectra with electrospray ionization were recorded on a Bruker MicroOTOF II instrument. Elemental analysis was performed on a PerkinElmer 2400 Series II instrument. Melting points were determined by Kofler method on a Boetius bench (heating rate 4° min^{-1}) and were not corrected. The reaction progress and purity of the obtained compounds were controlled by TLC on Merck Silicagel 60 F₂₅₄ plates. Visualization of spots on TLC plate was accomplished with UV light (254 nm).

Most of the reagents and starting materials were purchased from commercial sources and used as such. The starting 5,7-dimethyl-2,3-dinitropyrazolo[1,5-*a*]pyrimidine (**1**)^[S1] and 3,5-diamino-4-nitro-1*H*-pyrazol (**5**)^[S2] were obtained according a published procedure.

*Preparation of 2-amino-5,7-dimethyl-3-nitropyrazolo[1,5-*a*]pyrimidine 2a from diamine 5.* To the suspension of diaminopyrazole **5**^[S2] (0.20 g, 1.4 mmol) in 2 N HCl (2 ml) acetylacetone (0.14 g, 1.4 mmol) was added and the reaction mixture was left for 10 h at ambient temperature. The precipitate formed was filtered off, washed cold H₂O and dried *in vacuo* over P₂O₅. Yield 0.23 g (79%), light-yellow solid, mp 256 °C (lit.^[S3] mp 244-246 °C).



^1H NMR, δ : 7.16 (br.s, 3 H, NH₂, H-6); 2.59 (s, 3 H, Me); 2.55 (s, 3 H, Me).

^{13}C NMR, δ : 162.2, 155.3, 146.0, 143.1, 112.1 (C⁶(H)), 108.6 (br.s, C³(NO₂)), 24.0 (Me), 16.4 (Me).

*Preparation of 2-NRR'-5,7-dimethyl-3-nitropyrazolo[1,5-*a*]pyrimidines 2a-s (general procedure).* To a solution of pyrazolopyrimidine **1**^[S1] (0.24 g, 1 mmol) in MeOH (6 ml), an appropriated amine (10 equiv. in case **2a,b** and 3 equiv. in case **2c-s**) was added. The mixture was stirred for 18 h (in case **2a,b**) and 6-12 h (in case **2c-s**) at ambient temperature. The precipitate was filtered off, washed cold MeOH, dried and crystallized from H₂O–EtOH (1:1).

2-Amino-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine 2a:

Yield 77%, mp 256 °C (H₂O) (lit.^[S3] mp 244-246 °C).

¹H NMR, δ : 7.18 (s, 2 H, NH₂); 7.16 (s, 1 H, H-6); 2.59 (s, 3 H, Me); 2.55 (s, 3 H, Me).

¹³C NMR, δ : 162.8, 155.9, 146.7, 143.8, 112.8 (C⁶(H)), 108.6 (br.s, C³(NO₂)), 24.7 (Me), 17.0 (Me).

IR (ν /cm⁻¹): 3438, 3298, 3223, 3179, 1635, 1573, 1542, 1508, 1472, 1445, 1365, 1351, 1248, 1217, 1181, 1164, 1095, 1025, 776, 668, 480.

MS (EI), m/z : 207 [M]⁺.

Elemental analysis: found (%): C, 45.46; H, 4.35; N, 32.64; calculated for C₈H₉N₅O₂ 0.2H₂O; (%): C, 45.58; H, 4.49; N, 33.22.

5,7-Dimethyl-2-methylamino-3-nitropyrazolo[1,5-a]pyrimidine 2b:



Yield 75 %, mp 254 °C.

¹H NMR, δ : 7.42 (q, 1 H, NH, J 4.5 Hz); 7.17 (s, 1 H, H-6); 2.99 (d, 3 H, NHCH₃, J 4.7 Hz); 2.63 (s, 3 H, Me); 2.56 (s, 3 H, Me).

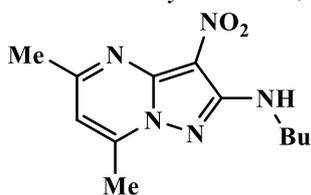
¹³C NMR, δ : 162.3, 155.0, 146.2, 143.5, 111.9 (C⁶(H)), 108.4 (br.s, C³(NO₂)), 28.5 (NHMe), 24.0 (Me), 16.2 (Me).

IR (ν /cm⁻¹): 3417, 3060, 1627, 1604, 1557, 1532, 1486, 1472, 1459, 1447, 1412, 1375, 1345, 1321, 1251, 1211, 1166, 1150, 1131, 1031, 882, 772, 614, 548, 516, 491.

MS (EI), m/z : 221 [M]⁺.

Elemental analysis: found (%): C, 48.02; H, 5.04; N, 31.25; calculated for C₉H₁₁N₅O₂ 0.2H₂O (%): C, 48.08; H, 5.11; N, 31.15.

2-Butylamino-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine 2c:



Yield 65%, white solid, mp 161 °C.

¹H NMR, δ : 7.32 (br.s, 1 H, NH); 7.18 (s, 1 H, H-6); 3.43 (t, 2 H, NHCH₂, J 6.8 Hz); 2.62 (s, 3 H, Me); 2.56 (s, 3 H, Me); 1.66 (qv, 2 H, CH₂, J 7.1 Hz); 1.37 (sk, 2 H, CH₂, J 7.3 Hz); 0.93 (t, 3 H, CH₂CH₃, J 7.3 Hz).

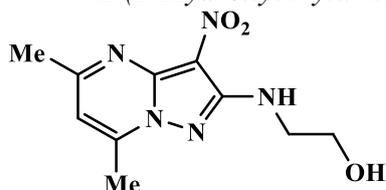
¹³C NMR, δ : 162.4, 154.5, 146.3, 143.6, 112.2 (C⁶(H)), 108.4 (br.s, C³(NO₂)), 41.3 (NHCH₂), 30.8 (CH₂), 24.1 (Me), 19.6 (CH₂), 16.3 (Me), 13.6 (CH₂CH₃).

IR (ν /cm⁻¹): 3365, 2963, 2929, 1622, 1606, 1557, 1527, 1520, 1481, 1438, 1376, 1364, 1352, 1245, 1226, 1187, 1167, 1132, 1034, 886, 773, 614.

MS (EI), m/z : 263 [M]⁺, 207 [M-Bu]⁺.

Elemental analysis: found (%): C, 54.59; H, 6.42; N, 26.50; calculated for C₁₂H₁₇N₅O₂ (%): C, 54.74; H, 6.51; N, 26.60.

2-(2-Hydroxyethylamino)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2d**:



Yield 89%, mp 228 °C.

¹H NMR, δ : 7.32 (t, 1 H, NH, *J* 5.3 Hz); 7.20 (s, 1 H, H-6); 4.93 (t, 1 H, OH, *J* 5.0 Hz); 3.67 (t, 2 H, OHCH₂, *J* 5.2 Hz); 3.50 (t, 2 H, NHCH₂, *J* 5.6 Hz); 2.64 (s, 3 H, Me); 2.58 (s, 3 H, Me).

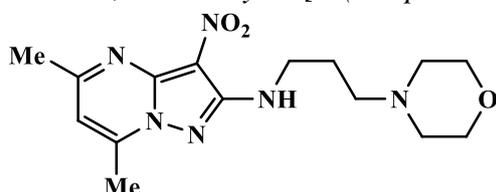
¹³C NMR, δ : 162.6, 154.5, 146.4, 143.5, 112.2 (C⁶(H)), 108.4 (br.s, C(NO₂)), 59.1 (OHCH₂), 44.1 (NHCH₂), 24.2 (Me), 16.4 (Me).

IR (ν /cm⁻¹): 3421, 3390, 3080, 1627, 1558, 1533, 1469, 1447, 1376, 1348, 1248, 1215, 1167, 1145, 1064, 861, 774, 565, 524.

HRMS, *m/z*: 252.1100 [M + H]⁺ (calc., *m/z*: 252.1091).

Elemental analysis: found (%): C, 47.94; H, 5.19; N, 28.14; calculated for C₁₀H₁₃N₅O₃ (%): C, 47.81; H, 5.22; N, 27.87.

5,7-Dimethyl-2-[3-(morpholine-4-yl)propylamino]-3-nitropyrazolo[1,5-a]pyrimidine **2e**:



Yield 75%, mp 198 °C.

¹H NMR, δ : 7.75 (t, 1 H, NH, *J* 5.4 Hz); 7.20 (s, 1 H, H-6); 3.65 (t, 4 H, OCH₂, *J* 4.3 Hz); 3.52 (q, 2 H, NHCH₂, *J* 6.2 Hz); 2.63 (s, 3 H, Me); 2.58 (s, 3 H, Me); 2.45–2.39 (m, 6 H, NCH₂); 1.83 (qv, 2 H, CH₂, *J* 6.4 Hz).

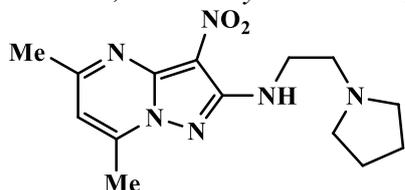
¹³C NMR, δ : 162.4, 154.4, 146.3, 143.6, 112.1 (C⁶(H)), 108.4 (br.s, C(NO₂)), 65.9 (OCH₂), 56.7 (NHCH₂), 53.4 (NCH₂), 41.1 (CH₂), 24.6 (CH₂), 24.0 (Me), 16.3 (Me).

MS (EI), *m/z*: 334 [M]⁺.

IR (ν /cm⁻¹): 3243, 3061, 2943, 2869, 2813, 1624, 1598, 1552, 1446, 1387, 1356, 1300, 1252, 1213, 1177, 1148, 1117, 1093, 1035, 990, 861, 773.

Elemental analysis: found (%): C, 53.69; H, 6.70; N, 25.13; calculated for C₁₅H₂₂N₆O₃ (%): C, 53.88; H, 6.63; N, 25.13.

5,7-Dimethyl-3-nitro-2-[2-(pyrrolidin-1-yl)ethylamino]pyrazolo[1,5-a]pyrimidine **2f**:



Yield 45 %, mp 155–157 °C.

¹H NMR, δ : 7.38 (br.s, 1 H, NH); 7.20 (s, 1 H, H-6); 3.54 (br.s, 2 H, NHCH₂); 2.73 (s, 3 H, Me); 2.64 (s, 3 H, Me); 2.55 (br.s, 6 H, CH₂); 1.72 (br.s, 4 H, CH₂).

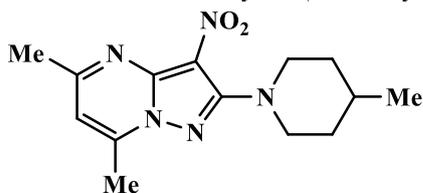
¹³C NMR, δ : 162.5, 154.4, 146.4, 143.5, 112.2 (C⁶(H)), 108.5 (br.s, C³(NO₂)), 54.2 (NCH₂), 53.4 (NCH₂), 40.5 (NHCH₂), 24.1 (Me), 23.1 (CH₂), 16.3 (Me).

IR (ν /cm⁻¹): 3400, 2939, 2928, 2869, 2808, 1622, 1596, 1554, 1458, 1439, 1377, 1346, 1251, 1215, 1171, 1136, 1065, 835, 772, 552.

HRMS, *m/z*: 305.1719 [M + H]⁺ (calc., *m/z*: 305.1721).

Elemental analysis: found (%): C, 55.09; H, 6.77; N, 27.47; calculated for C₁₄H₂₀N₆O₂ (%): C, 55.25; H, 6.62; N, 27.61.

5,7-Dimethyl-2-(4-methylpiperidin-1-yl)-3-nitropyrazolo[1,5-a]pyrimidine **2g**:



Yield 84%, mp 191–192 °C.

¹H NMR, δ : 7.21 (s, 1 H, H-6); 3.83 (d, 2 H, NCH₂, *J* 12.4 Hz); 2.91 (t, 2 H, NCH₂, *J* 12.0 Hz); 2.64 (s, 3 H, Me); 2.57 (s, 3 H, Me); 1.72 (d, 2 H, CH₂, *J* 12.7 Hz); 1.56–1.63 (m, 1 H, CH); 1.33 (q, 2 H, CH₂, *J* 10.7 Hz); 0.96 (d, 3 H, CHCH₃, *J* 6.0 Hz).

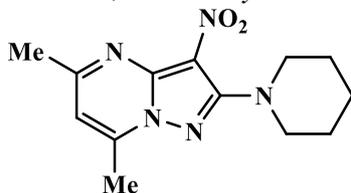
IR (ν /cm⁻¹): 2949, 2936, 2919, 2910, 2833, 1619, 1568, 1533, 1506, 1474, 1460, 1442, 1418, 1377, 1350, 1311, 1250, 1219, 1184, 1167, 1037, 930, 834, 826, 779.

MS (EI), *m/z*: 289 [M]⁺.

HRMS, *m/z*: 290.1620 [M + H]⁺ (calc., *m/z*: 290.1612).

Elemental analysis: found (%): C, 57.58; H, 6.62; N, 23.97; calculated for C₁₄H₁₉N₅O₂*0.2H₂O (%): C, 57.40; H, 6.68; N, 23.91.

5,7-Dimethyl-3-nitro-2-(piperidin-1-yl)pyrazolo[1,5-a]pyrimidine **2h**:



Yield 97%, mp 156 °C.

¹H NMR, δ : 7.20 (s, 1 H, H-6); 3.33 (m, 4 H, N(CH₂)₂); 2.63 (s, 3 H, Me); 2.57 (s, 3 H, Me); 1.65 (br.s, 6 H, (CH₂)₃).

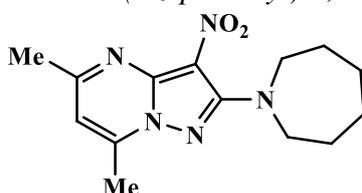
¹³C NMR, δ : 163.3, 156.6, 146.4, 144.7, 112.1 (C⁶(H)), 111.6 (br.s, C³(NO₂)), 49.6 (NCH₂), 24.9 (CH₂), 24.3 (CH₂), 23.7 (Me), 16.2 (Me).

IR (ν /cm⁻¹): 3424, 2924, 2859, 1616, 1564, 1526, 1491, 1459, 1446, 1412, 1373, 1360, 1333, 1296, 1261, 1249, 1226, 1185, 1161, 1126, 1045, 931, 862, 847, 774.

MS (EI), *m/z*: 275 [M]⁺.

Elemental analysis: found (%): C, 51.26; H, 6.92; N, 22.84; calculated for C₁₃H₁₇N₅O₂*1.67H₂O (%): C, 51.14; H, 6.71; N, 22.94.

2-(Azepan-1-yl)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2i**:



Yield 96%, mp 117 °C.

¹H NMR, δ : 7.14 (s, 1 H, H-6); 3.58 (t, 4 H, N(CH₂)₂, *J* 5.8 Hz); 2.62 (s, 3 H, Me); 2.55 (s, 3 H, Me); 1.81 (br.s, 4 H, (CH₂)₂); 1.56 (t, 4 H, (CH₂)₂, *J* 2.9 Hz).

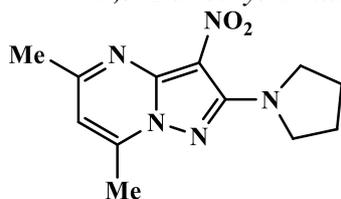
¹³C NMR, δ : 162.2, 155.4, 145.7, 144.7, 111.7 (C⁶(H)), 110.8 (br.s, C³(NO₂)), 50.6 (NCH₂), 27.5 (CH₂), 26.8 (CH₂), 24.2 (Me), 16.1 (Me).

IR (ν /cm⁻¹): 3425, 2948, 2926, 2857, 1616, 1573, 1533, 1468, 1447, 1409, 1367, 1338, 1281, 1257, 1229, 1218, 1189, 1167, 1135, 1000, 864, 769, 678.

HRMS, *m/z*: 290.1623 [M + H]⁺ (calc., *m/z*: 290.1612).

Elemental analysis: found (%): C, 58.06; H, 6.58; N, 24.41; calculated for C₁₄H₁₉N₅O₂ (%): C, 58.12; H, 6.62; N, 24.20.

5,7-Dimethyl-3-nitro-2-(pyrrolidin-1-yl)pyrazolo[1,5-a]pyrimidine **2j**:



Yield 95%, mp 191 °C.

$^1\text{H NMR}$, δ : 7.13 (s, 1 H, H-6); 3.50 (t, 4 H, $\text{N}(\text{CH}_2)_2$, J 6.5 Hz); 2.62 (s, 3 H, Me); 2.55 (s, 3 H, Me); 1.93 (d.t, 4 H, $(\text{CH}_2)_2$, J 6.6 Hz, $J = 2.8$ Hz).

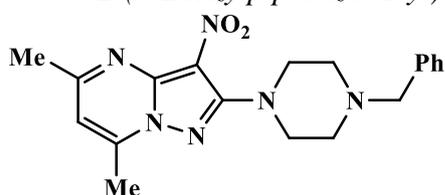
$^{13}\text{C NMR}$, δ : 162.1, 153.9, 145.6, 144.4, 111.6 ($\text{C}^6(\text{H})$), 110.5 (br.s, $\text{C}^3(\text{NO}_2)$), 49.6 (CH_2), 25.0 (CH_2), 24.1 (Me), 16.2 (Me).

IR (ν/cm^{-1}): 2968, 2875, 1613, 1573, 1539, 1501, 1448, 1412, 1373, 1362, 1352, 1330, 1253, 1223, 1209, 1176, 1158, 1046, 851, 826, 772, 700.

MS (EI), m/z : 261 $[\text{M}]^+$.

Elemental analysis: found (%): C, 55.10; H, 6.01; N, 26.74; calculated for $\text{C}_{12}\text{H}_{15}\text{N}_5\text{O}_2$ (%): C, 55.16; H, 5.79; N, 26.80.

2-(4-Benzylpiperazin-1-yl)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2k**:



Yield 93%, mp 158 °C.

$^1\text{H NMR}$, δ : 7.34 (d, 2 H, H_{Ph} , J 4.0 Hz); 7.28 (t, 3 H, H_{Ph} , J 4.1 Hz); 7.22 (s, 1 H, H-6); 3.55 (s, 2 H, NCH_2); 3.41 (br.s, 4 H, NCH_2); 3.32 (br.s, 4 H, NCH_2); 2.64 (s, 3 H, Me); 2.57 (s, 3 H, Me).

$^{13}\text{C NMR}$, δ : 163.6, 156.1, 146.5, 144.7, 137.8 (C_{Ph}), 128.8 (CH_{Ph}), 128.1 (CH_{Ph}), 126.9 (CH_{Ph}), 112.2 ($\text{C}^6(\text{H})$), 111.7 (br.s, $\text{C}^3(\text{NO}_2)$), 62.0 (NCH_2), 51.9 (NCH_2), 48.4 (NCH_2), 24.3 (Me), 16.2 (Me).

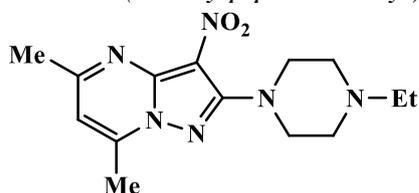
IR (ν/cm^{-1}): 3077, 2811, 2768, 1628, 1569, 1527, 1493, 1464, 1435, 1414, 1384, 1371, 1352, 1335, 1277, 1268, 1250, 1186, 1165, 1150, 1035, 1009, 987, 827, 768, 738, 697, 649.

MS (EI), m/z : 366 $[\text{M}]^+$.

HRMS, m/z : 367.1886 $[\text{M} + \text{H}]^+$ (calc., m/z : 367.1877).

Elemental analysis: found (%): C, 62.39; H, 6.02; N, 23.17; calculated for $\text{C}_{19}\text{H}_{22}\text{N}_6\text{O}_2$ (%): C, 62.28; H, 6.05; N, 22.94.

2-(4-Ethylpiperazin-1-yl)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2l**:



Yield 62%, mp 197 °C.

$^1\text{H NMR}$, δ : 7.22 (s, 1 H, H-6); 3.40 (br.s, 4 H, NCH_2); 3.33 (br.s, 4 H, NCH_2); 2.64 (s, 3 H, Me); 2.57 (s, 3 H, Me); 2.39 (br.s, 2 H, NCH_2); 1.03 (br.s, 3 H, CH_2CH_3).

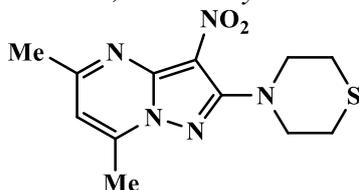
$^{13}\text{C NMR}$, δ : 163.6, 156.1, 146.6, 144.8, 112.3 ($\text{C}^6(\text{H})$), 111.7 (br.s, $\text{C}^3(\text{NO}_2)$), 51.7 (NCH_2), 51.6 (NCH_2), 48.4 (NCH_2), 24.4 (Me), 16.2 (Me), 11.8 (CH_2CH_3).

IR (ν/cm^{-1}): 2981, 2959, 2928, 2893, 2874, 2848, 2818, 1619, 1568, 1532, 1504, 1472, 1449, 1431, 1418, 1378, 1350, 1342, 1313, 1299, 1267, 1252, 1223, 1189, 1167, 1149, 1124, 1046, 1023, 951, 839, 826, 778, 767, 647.

MS (EI), m/z : 304 $[M]^+$.

Elemental analysis: found (%): C, 54.95; H, 6.49; N, 27.50; calculated for $C_{14}H_{20}N_6O_2$ (%): C, 55.25; H, 6.62; N, 27.61.

5,7-Dimethyl-3-nitro-2-(thiomorpholin-4-yl)pyrazolo[1,5-a]pyrimidine 2m:



Yield 87%, mp 180 °C.

1H NMR, δ : 7.20 (s, 1 H, H-6); 3.68 (br.s, 4 H, CH_2); 2.79 (br.s, 4 H, CH_2); 2.63 (s, 3 H, Me); 2.57 (s, 3 H, Me).

^{13}C NMR, δ : 163.8, 156.3, 146.6, 144.7, 112.4 ($C^6(H)$), 111.8 (br.s, $C^3(NO_2)$), 51.3 (NCH_2), 26.1 (SCH_2), 24.4 (Me), 16.2 (Me).

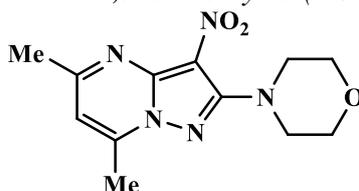
IR (ν/cm^{-1}): 3072, 2959, 2915, 1625, 1566, 1529, 1499, 1462, 1447, 1415, 1376, 1353, 1332, 1253, 1184, 1162, 1123, 1034, 1006, 948, 867, 812, 774, 655.

MS (EI), m/z : 293 $[M]^+$.

HRMS, m/z : 294.1022 $[M + H]^+$ (calc., m/z : 294.1019).

Elemental analysis: found (%): C, 49.20; H, 5.24; N, 24.03; calculated for $C_{12}H_{15}N_5O_2S$ (%): C, 49.13; H, 5.15; N, 23.87.

5,7-Dimethyl-2-(morpholin-4-yl)-3-nitropyrazolo[1,5-a]pyrimidine 2n:



Yield 86%, mp 212–213 °C.

1H NMR, δ : 7.23 (s, 1 H, H-6); 3.77 (t, 4 H, CH_2 , J 4.4 Hz); 3.40 (t, 4 H, CH_2 , J 4.4 Hz); 2.65 (s, 3 H, Me); 2.54 (s, 3 H, Me).

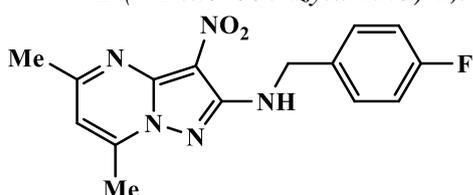
^{13}C NMR, δ : 163.8, 156.1, 146.6, 144.7, 112.4 ($C^6(H)$), 111.8 (br.s, $C^3(NO_2)$), 69.6 (OCH_2), 48.9 (NCH_2), 24.4 (Me), 16.2 (Me).

IR (ν/cm^{-1}): 3051, 2970, 2865, 1618, 1568, 1527, 1496, 1465, 1439, 1417, 1376, 1364, 1346, 1310, 1282, 1268, 1255, 1230, 1191, 1162, 1115, 1065, 1040, 942, 925, 860, 827, 777, 647.

MS (EI), m/z : 277 $[M]^+$.

Elemental analysis: found (%): C, 52.02; H, 5.41; N, 25.39; calculated for $C_{12}H_{15}N_5O_3$ (%): C, 51.98; H, 5.45; N, 25.26.

2-(4-Fluorobenzylamino)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine 2o:



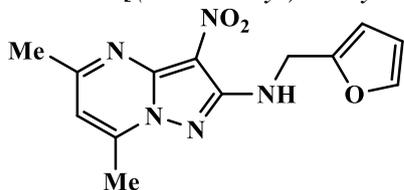
Yield 80%, mp 162°C.

1H NMR, δ : 7.99 (t, 1 H, NH, J 6.2 Hz); 7.48 (t, 2 H, H_{Ph} , J 6.9); 7.17 (s, 1 H, H-6); 7.12 (t, 2 H, H_{Ph} , J 7.2 Hz); 4.59 (d, 2 H, $NHCH_2$, J = 6.2 Hz); 2.60 (s, 3 H, Me); 2.54 (s, 3 H, Me).

^{13}C NMR, δ : 162.6, 161.2 (d, CF_{Ph} , $^1J_{CF}$ 242.4 Hz), 154.2, 146.4, 143.6, 135.4 (C^1_{Ph}), 129.8 (d, $C^{3',5'}$ (H) $_{Ph}$, $^3J_{CF}$ 8.1 Hz), 114.8 (d, $C^{2',6'}$ (H) $_{Ph}$, $^2J_{CF}$ 21.2 Hz), 112.2 ($C^6(H)$), 108.5 (br.s, $C^3(NO_2)$), 44.5 (CH_2), 24.1 (Me), 16.3 (Me).

IR (ν/cm^{-1}): 3415, 3072, 1626, 1598, 1559, 1509, 1458, 1434, 1368, 1351, 1333, 1251, 1217, 1166, 1139, 1098, 1028, 829, 771, 578.
 MS (EI), m/z : 315 $[\text{M}]^+$, 297 $[\text{M}-\text{F}]^+$.
 HRMS, m/z : 316.1200 $[\text{M} + \text{H}]^+$ (calc., m/z : 316.1204).
 Elemental analysis: found (%): C, 57.06; H, 4.50; N, 22.44; calculated for $\text{C}_{15}\text{H}_{14}\text{FN}_5\text{O}_2$ (%): C, 57.14; H, 4.48; N, 22.21.

2-[(Furan-2-yl)methylamino]-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2p**:



Yield 74%, Mp 154–155°C.

^1H NMR, δ : 7.76 (t, 1 H, NH, J 6.0 Hz); 7.60 (s, 1 H); 7.20 (s, 1 H, H-6); 6.41 (s, 1 H); 6.39 (s, 1 H); 4.63 (d, 2 H, CH_2 , J 6.1 Hz); 2.64 (s, 3 H, Me); 2.57 (s, 3 H, Me).

^{13}C NMR, δ : 162.8, 154.0, 152.0, 146.5, 143.5, 142.1 (CH_{Ar}), 112.2 ($\text{C}^6(\text{H})$), 110.5 (CH_{Ar}), 108.5 (br.s, $\text{C}^3(\text{NO}_2)$), 107.5 (CH_{Ar}), 38.4 (CH_2), 24.1 (Me), 16.3 (Me).

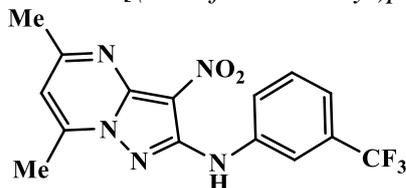
IR (ν/cm^{-1}): 3386, 1625, 1608, 1553, 1508, 1462, 1379, 1348, 1266, 1249, 1212, 1170, 1138, 1074, 1012, 921, 820, 774, 765, 742.

MS (EI), m/z : 287 $[\text{M}]^+$.

HRMS, m/z : 288.1101 $[\text{M} + \text{H}]^+$ (calc., m/z : 289.1091).

Elemental analysis: found (%): C, 54.45; H, 4.61; N, 24.49; calculated for $\text{C}_{13}\text{H}_{13}\text{N}_5\text{O}_3$ (%) C, 54.35; H, 4.56; N, 24.38.

2-[(3-Trifluoromethyl)phenylamino]-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **2q**:



Yield 65%, Mp 212–213°C (EtOH– H_2O , 1:1).

^1H NMR, δ : 9.60 (s, 1 H, NH); 8.45 (s, 1 H, H_{Ph}); 8.16 (d, 1 H, H_{Ph} , J 8.1 Hz); 7.61 (t, 1 H, H_{Ph} , J 7.9 Hz); 7.40 (d, 1 H, H_{Ph} , J 7.6 Hz); 7.33 (s, 1 H, H-6); 2.73 (s, 3 H, Me); 2.63 (s, 3 H, Me).

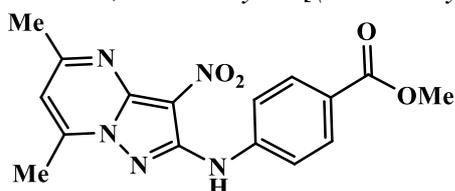
^{13}C NMR, δ : 164.3, 150.0, 146.8, 142.5, 139.7, 129.4 (q, CCF_3 , $^2J_{\text{CF}}$ 28.9 Hz), 129.6 ($\text{C}(\text{H})_{\text{Ph}}$), 124.1 (q, CF_3 , $^1J_{\text{CF}}$ 265.9 Hz), 122.4 ($\text{C}(\text{H})_{\text{Ph}}$), 118.4 (d, $\text{C}(\text{H})_{\text{Ph}}$, $^3J_{\text{CF}}$ 3.9 Hz), 115.1 (d, $\text{C}(\text{H})_{\text{Ph}}$, $^3J_{\text{CF}}$ 3.5 Hz), 112.7 ($\text{C}^6(\text{H})$), 108.8 (br.s, $\text{C}^3(\text{NO}_2)$), 24.2 (Me), 16.0 (Me).

IR (ν/cm^{-1}): 3442, 3304, 1628, 1602, 1582, 1527, 1499, 1483, 1467, 1446, 1418, 1374, 1341, 1325, 1280, 1256, 1236, 1193, 1160, 1122, 1071, 889, 794, 698.

MS (EI), m/z : 351 $[\text{M}]^+$.

Elemental analysis: found (%): C, 49.43; H, 3.52; N, 19.24; calculated for $\text{C}_{15}\text{H}_{12}\text{F}_3\text{N}_5\text{O}_2 \cdot 0.67\text{H}_2\text{O}$ (%): C, 49.59; H, 3.70; N, 19.28.

5,7-Dimethyl-2-[(4-methoxycarbonyl)phenylamino]-3-nitropyrazolo[1,5-a]pyrimidine **2r**:



Yield 65%, mp 131°C.

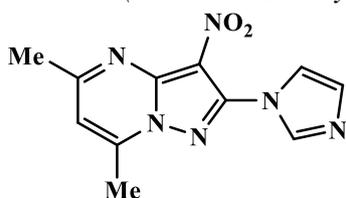
^1H NMR, δ : 7.62 (d, 2 H, H_{Ph} , J 8.5 Hz); 7.60 (s, 1 H, H-6); 6.55 (d, 2 H, H_{Ph} , J 8.4 Hz); 5.94 (br.s, 1 H, NH); 3.73 (s, 3 H, OCH_3); 2.74 (s, 3 H, Me); 2.71 (s, 3 H, Me).

^{13}C NMR, δ : 168.5 (COOMe), 166.3, 153.3, 148.6, 142.2, 131.0 ($\text{C}(\text{H})_{\text{Ph}}$), 130.2, 118.4, 115.3 ($\text{C}^6(\text{H})$), 112.6 ($\text{C}(\text{H})_{\text{Ph}}$), 108.1 (br.s, $\text{C}^3(\text{NO}_2)$), 51.1 (OMe), 24.4 (Me), 16.0 (Me).

IR (ν/cm^{-1}): 3470, 3378, 1698, 1633, 1601, 1558, 1509, 1483, 1454, 1435, 1388, 1377, 1344, 1323, 1309, 1278, 1224, 1185, 1171, 1111, 886, 846, 781, 770, 700, 516.

Elemental analysis: found (%): C, 56.35; H, 4.40; N, 20.69; calculated for $\text{C}_{16}\text{H}_{15}\text{N}_5\text{O}_4$ (%): C, 56.30; H, 4.43; N, 20.52.

2-(1*H*-Imidazol-1-yl)-5,7-dimethyl-3-nitropyrazolo[1,5-*a*]pyrimidine **2s**:



Yield 51%, mp 203°C.

^1H NMR, δ : 8.26 (s, 1 H, H_{Ar}); 7.72 (s, 1 H, H_{Ar}); 7.47 (s, 1 H, H_{Ar}); 7.18 (s, 1 H, H_{Ar}); 2.76 (s, 3 H, Me); 2.69 (s, 3 H, Me).

^{13}C NMR, δ : 166.4, 147.7, 144.2, 143.4, 138.1 (br.s), 129.2, 120.3 (br.s), 113.8 ($\text{C}^6(\text{H})$), 113.6 (br.s, $\text{C}^3(\text{NO}_2)$), 24.7 (Me), 16.0 (Me).

IR (ν/cm^{-1}): 34436, 1625, 1568, 1537, 1523, 1475, 1440, 1381, 1359, 1331, 1266, 1223, 1179, 1042, 816, 772, 736, 655.

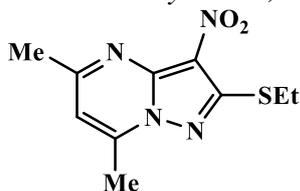
MS (EI), m/z : 258 [M] $^+$.

HRMS, m/z : 259.0941 [$\text{M} + \text{H}$] $^+$ (calc., m/z : 259.0938).

Elemental analysis: found (%): C, 50.97; H, 3.84; N, 32.73; calculated for $\text{C}_{11}\text{H}_{10}\text{N}_6\text{O}_2$ (%): C, 51.16; H, 3.90; N, 32.54.

*Preparation of 2-SR-5,7-dimethyl-3-nitropyrazolo[1,5-*a*]pyrimidines 3a-d (general procedure).* To a solutions of K_2CO_3 (0.30 g, 2.2 mmol) and appropriate thiol (2.2 mmol) in MeCN (5 ml), pyrazolopyrimidine **1**^[S1] (0.47 g, 2 mmol) was added, and the reaction mixture was stirred for 7 h at ambient temperature. The precipitate formed was filtered off, washed cold MeCN, cold H_2O , dried and crystallized from H_2O -EtOH (1:1).

2-Ethylthio-5,7-dimethyl-3-nitropyrazolo[1,5-*a*]pyrimidine **3a**:



Yield 79%, mp 215 °C.

^1H NMR, δ : 7.29 (s, 1 H, H-6); 3.23 (q, 2 H, CH_2 , J 7.3 Hz); 2.61 (s, 3 H, Me); 2.45 (s, 3 H, Me); 1.42 (t, 3 H, CH_2CH_3 , J 7.3 Hz).

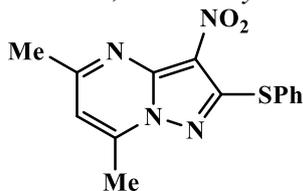
^{13}C NMR, δ : 164.8, 153.8, 146.8, 143.6, 112.3 ($\text{C}^6(\text{H})$), 108.1 (br.s, $\text{C}^3(\text{NO}_2)$), 24.3 (Me), 23.7 (CH_2), 18.9 (Me), 13.6 (CH_2CH_3).

IR (ν/cm^{-1}): 3073, 2970, 1620, 1557, 1476, 1450, 1408, 1369, 1351, 1324, 1259, 1215, 1172, 1044, 1022, 868, 838, 771, 759, 654.

MS (EI), m/z : 252 [M] $^+$.

Elemental analysis: found (%): C, 47.83; H, 4.70; N, 22.45; calculated for $\text{C}_{10}\text{H}_{12}\text{N}_4\text{O}_2\text{S}$ (%): C, 47.61; H, 4.79; N, 22.21.

5,7-Dimethyl-3-nitro-2-(phenylthio)pyrazolo[1,5-a]pyrimidine 3b:



Yield 88%, mp 232°C.

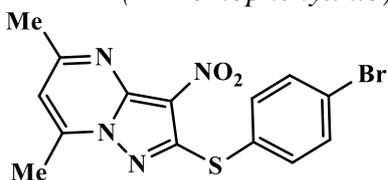
¹H NMR, δ : 7.72 (br.s, 2 H, H_{Ph}); 7.50 (br.s, 3 H, H_{Ph}); 7.26 (s, 1 H, H-6); 2.61 (s, 3 H, Me); 2.45 (s, 3 H, Me).

IR (ν /cm⁻¹): 3057, 1620, 1555, 1515, 1470, 1445, 1437, 1401, 1370, 1351, 1324, 1257, 1214, 1173, 1023, 859, 838, 771, 748, 691, 662.

MS (EI), m/z : 300 [M]⁺.

Elemental analysis: found (%): C, 56.12; H, 4.06; N, 18.57; calculated for C₁₄H₁₂N₄O₂S (%): C, 55.99; H, 4.03; N, 18.65.

2-(4-Bromophenylthio)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine 3c:



Yield 97%, mp 240°C.

¹H NMR, δ : 7.59 (d, 2 H, H_{Ph}, J 6.7 Hz); 7.46 (d, 2 H, H_{Ph}, J 7.2 Hz); 7.30 (s, 1 H, H-6); 2.62 (s, 3 H, Me); 2.48 (s, 3 H, Me).

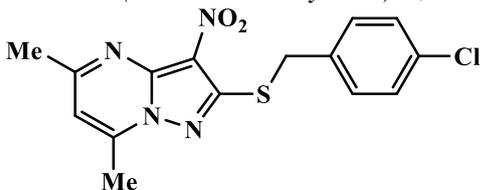
IR (ν /cm⁻¹): 1625, 1556, 1474, 1445, 1409, 1383, 1374, 1350, 1321, 1261, 1176, 1068, 1009, 837, 825, 813, 655, 481.

MS (EI), m/z : 378, 380 (1:1) [M]⁺.

HRMS, m/z : 378.9853 [M⁷⁹ + H]⁺, 380.9835 [M⁸¹ + H]⁺ (calc., m/z : 378.9859, 380.9839).

Elemental analysis: found (%): C, 44.40; H, 2.85; N, 14.90; calculated for C₁₄H₁₁BrN₄O₂S (%): C, 44.34; H, 2.92; N, 14.77.

2-(4-Chlorobenzylthio)-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine 3d:



Yield 89%, mp 213°C.

¹H NMR, δ : 7.54 (d, 2 H, H_{Ph}, J 8.1 Hz); 7.37 (d, 2 H, H_{Ph}, J 8.2 Hz); 7.29 (s, 1 H, H-6); 4.42 (s, 2 H, SCH₂); 2.73 (s, 3 H, Me); 2.60 (s, 3 H, Me).

¹³C NMR, δ : 165.3, 153.4, 147.1, 143.7, 136.5, 131.8, 131.2 (C(H)_{Ph}), 128.3 (C(H)_{Ph}), 112.7 (C⁶(H)), 109.2 (br.s, C³(NO₂)), 32.9 (CH₂), 24.6 (Me), 16.3 (Me).

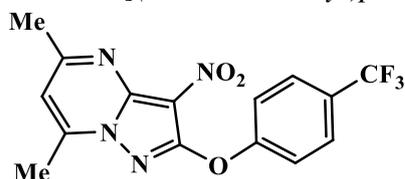
IR (ν /cm⁻¹): 3434, 1621, 1554, 1482, 1445, 1428, 1407, 1371, 1352, 1322, 1257, 1175, 1088, 1016, 842, 771, 505.

MS (EI), m/z : 349, 351 (3:1) [M]⁺.

Elemental analysis: found (%): C, 51.46; H, 3.69; N, 16.04; Cl, 10.09; S, 9.05; calculated for C₁₅H₁₃ClN₄O₂S (%): C, 51.65; H, 3.76; N, 16.06; Cl, 10.16; S, 9.19.

Preparation of 2-OR-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidines **4a,b,d** (general procedure). To the solutions of K₂CO₃ (0.28 g, 2 mmol) and appropriated phenol (2 mmol) or 2,2,2-trifluoroethanol (2 mmol) in CH₃CN (5 ml) pyrazolopyrimidine **1**¹ (0.47 g, 2 mmol) was added. The reaction mixture was stirred for 10-12 h at ambient temperature in case phenols and was refluxed for 8 h in case 2,2,2-trifluoroethanol. The precipitate formed was filtered off, washed cold CH₃CN, cold H₂O, dried and crystallized from H₂O–EtOH (1:1).

2-[(4-Fluoromethyl)phenoxy]-5,7-dimethyl-3-nitropyrazolo[1,5-a]pyrimidine **4a**:



Yield 44%, mp 221°C.

¹H NMR, δ : 7.77 (br.s, 1 H, H_{Ph}); 7.68 (br.s, 2 H, H_{Ph}); 7.64 (br.s, 1 H, H_{Ph}); 7.35 (s, 1 H, H-6); 2.64 (s, 3 H, Me); 2.56 (s, 3 H, Me).

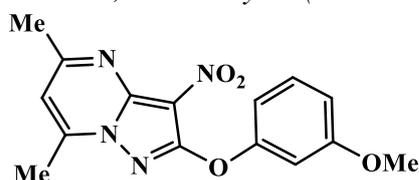
¹³C NMR, δ : 165.6, 157.7, 154.6, 147.8, 143.4, 131.3 (C(H)_{Ph}), 130.6 (q, CCF₃, ²J_{CF} 32.2 Hz), 123.7 (q, CF₃, ¹J_{CF} 272.4 Hz), 123.3 (C(H)_{Ph}), 121.8 (d, C(H)_{Ph}, ³J_{CF} 3.4 Hz), 116.1 (C(H)_{Ph}), 113.2 (C⁶(H)), 109.6 (br.s, C³(NO₂)), 24.6 (Me), 16.2 (Me).

IR (ν /cm⁻¹): 3074, 1626, 1564, 1527, 1508, 1494, 1463, 1441, 1379, 1356, 1326, 1263, 1204, 1180, 1162, 1116, 1092, 1070, 914, 904, 784, 772, 697.

MS (EI), m/z : 352 [M]⁺.

Elemental analysis: found (%): C, 50.84; H, 3.13; N, 15.78; calculated for C₁₅H₁₁F₃N₄O₃ (%): C, 51.14; H, 3.15; N, 15.90.

5,7-Dimethyl-2-(3-methoxyphenoxy)-3-nitropyrazolo[1,5-a]pyrimidine **4b**:



Yield 98%, mp 194°C.

¹H NMR, δ : 7.34 (s, 1 H, H-6); 6.93–6.85 (m, 4 H, H_{Ph}); 3.77 (s, 3 H, OMe); 2.63 (s, 3 H, Me); 2.57 (s, 3 H, Me).

¹³C NMR, δ : 165.4, 160.4, 158.1, 155.3, 147.8, 143.4, 130.3 (C(H)_{Ph}), 113.0 (C⁶(H)), 111.1 (C(H)_{Ph}), 110.9 (C(H)_{Ph}), 110.0 (br.s, C³(NO₂)), 105.2 (C(H)_{Ph}), 55.5 (OMe), 24.6 (Me), 16.3 (Me).

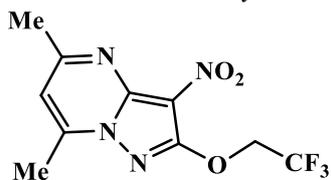
IR (ν /cm⁻¹): 2968, 1627, 1614, 1593, 1565, 1527, 1490, 1469, 1446, 1374, 1356, 1330, 1286, 1262, 1223, 1198, 1183, 1172, 1152, 1076, 1039, 940, 861, 785, 770, 686.

MS (EI), m/z : 314 [M]⁺.

HRMS, m/z : 315.1092 [M + H]⁺ (calc., m/z : 315.1088).

Elemental analysis: found (%): C, 57.41; H, 4.54; N, 18.05; calculated for C₁₅H₁₄N₄O₄ (%) C, 57.32; H, 4.49; N, 17.83.

5,7-Dimethyl-3-nitro-2-(2,2,2-trifluoroethoxy)pyrazolo[1,5-a]pyrimidine 4d:



Yield 51%, mp 155°C.

$^1\text{H NMR}$, δ : 7.34 (s, 1 H, H-6); 5.22 (q, 2 H, CH_2CF_3 , J 5.8 Hz); 2.68 (s, 3 H, Me); 2.62 (s, 3 H, Me).

$^{13}\text{C NMR}$, δ : 165.5, 158.2, 147.6, 143.4, 123.2 (q, CF_3 , $^1J_{\text{CF}}$ 277.8 Hz), 112.8 ($\text{C}^6(\text{H})$), 108.5 (br.s, $\text{C}^3(\text{NO}_2)$), 64.8 (q, CH_2CF_3 , $^2J_{\text{CF}}$ 35.6 Hz), 24.5 (Me), 16.0 (Me).

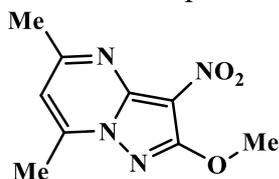
IR (ν/cm^{-1}): 1630, 1570, 1537, 1510, 1474, 1464, 1446, 1376, 1359, 1271, 1193, 1178, 1141, 1033, 961, 829, 773, 659.

MS (EI), m/z : 290 $[\text{M}]^+$.

HRMS, m/z : 291.0709 $[\text{M} + \text{H}]^+$ (calc., m/z : 291.0700).

Elemental analysis: found (%): C, 41.28; H, 3.09; N, 19.46; calculated for $\text{C}_{10}\text{H}_9\text{F}_3\text{N}_4\text{O}_3$ (%): C, 41.39; H, 3.13; N, 19.31.

5,7-Dimethyl-2-methoxy-3-nitropyrazolo[1,5-a]pyrimidine 4c. To a solution of NaOH (0.04 g, 1.1 mmol) in MeOH (4 ml), pyrazolopyrimidine **1**^[S1] (0.24 g, 1 mmol) was added. The reaction mixture was stirred for 5 h at ambient temperature. The precipitate formed was filtered off, washed cold MeOH, dried and crystallized from H_2O –EtOH (1:1). Yield 0.12 g (52%), white solid, mp 271 °C.



$^1\text{H NMR}$, δ : 7.27 (s, 1 H, H-6); 4.15 (s, 3 H, OMe); 2.70 (s, 3 H, Me); 2.62 (s, 3 H, Me).

IR (ν/cm^{-1}): 3063, 1628, 1577, 1536, 1508, 1475, 1450, 1441, 1405, 1385, 1366, 1356, 1259, 1223, 1193, 1174, 1136, 1030, 999, 958, 885, 774, 611.

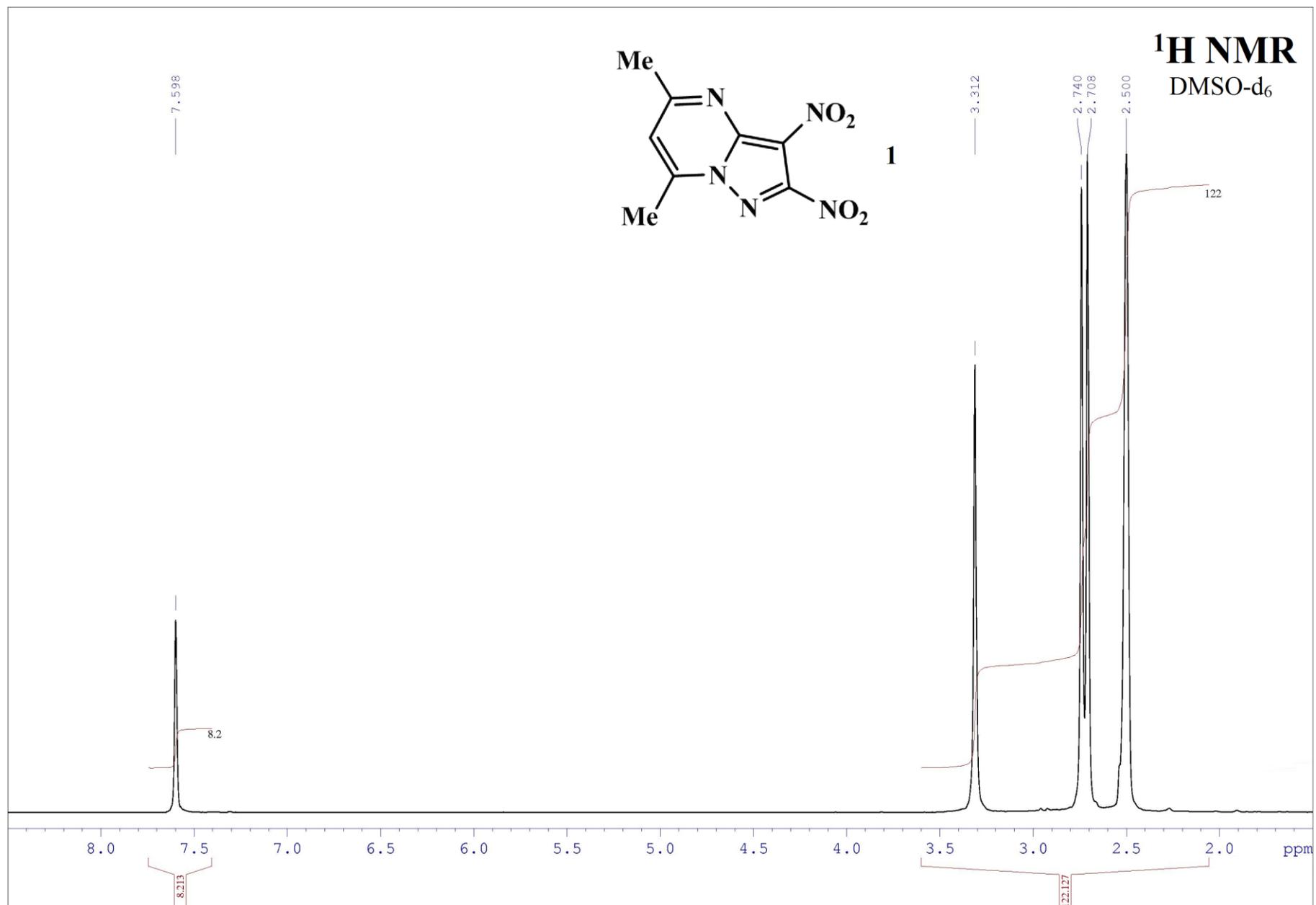
MS (EI), m/z : 222 $[\text{M}]^+$, 192 $[\text{M}-\text{OMe}]^+$.

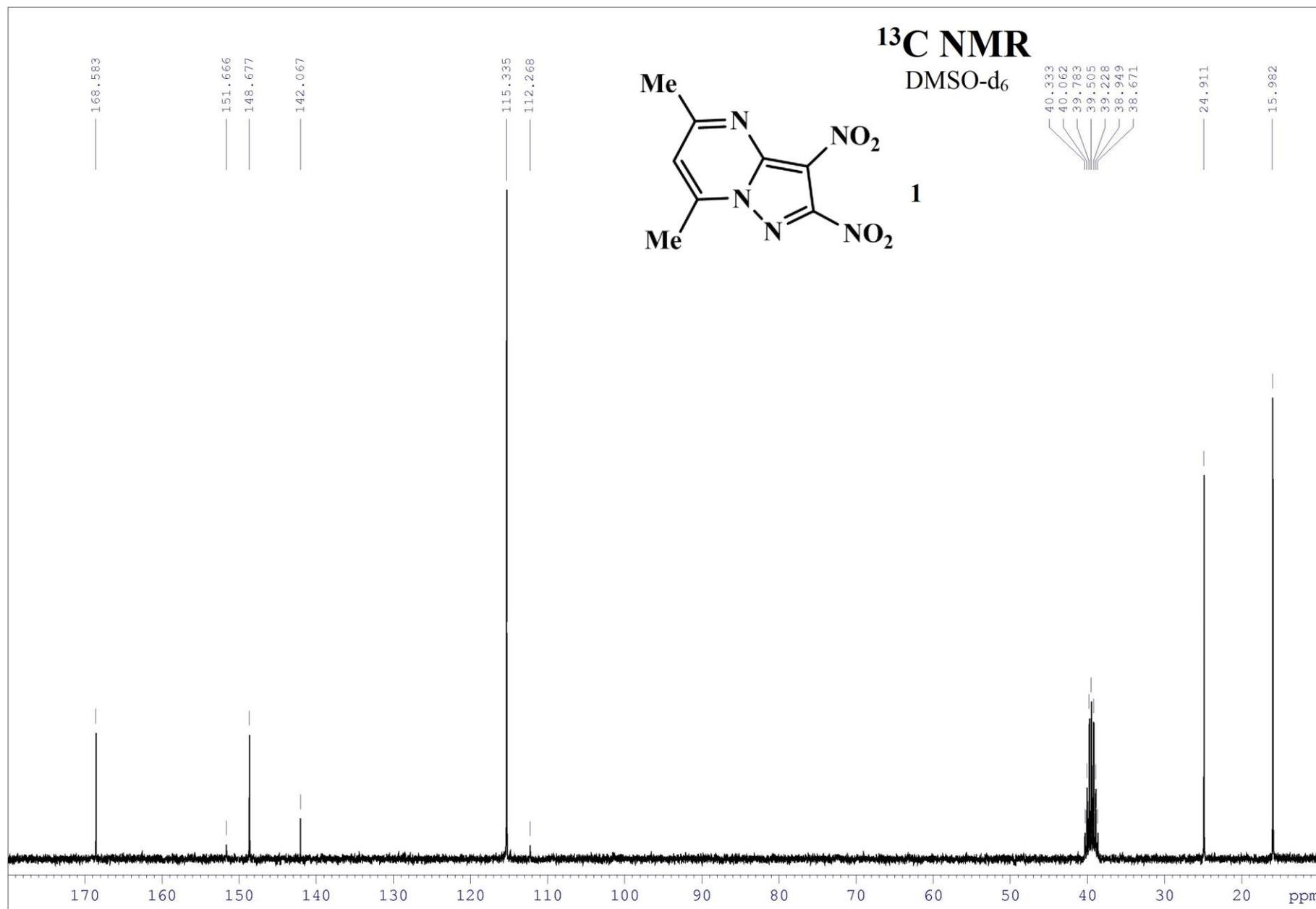
HRMS, m/z : 223.0832 $[\text{M} + \text{H}]^+$ (calc., m/z : 223.0826).

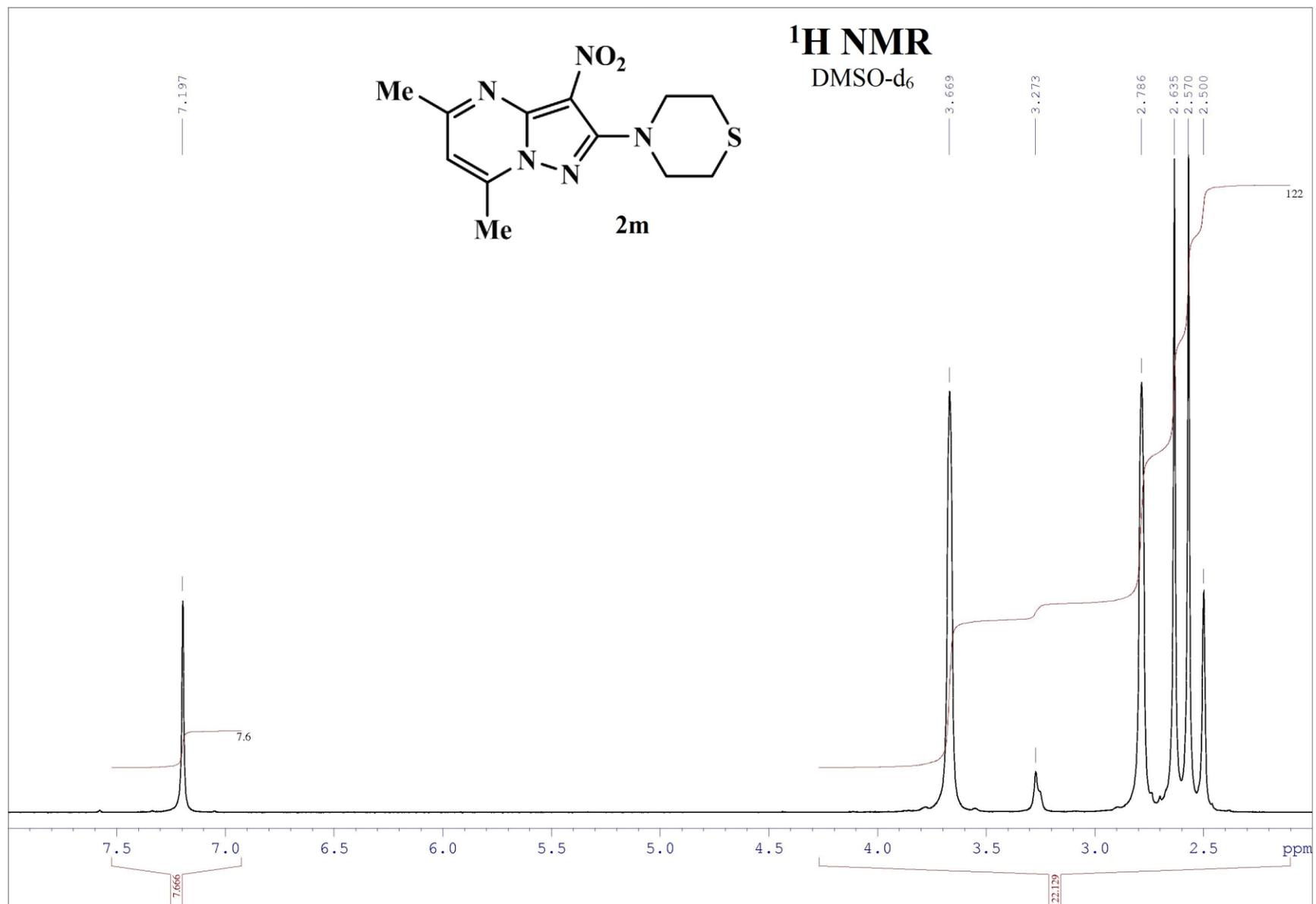
Elemental analysis: found (%): C, 48.71; H, 4.50; N, 25.40; calculated for $\text{C}_9\text{H}_{10}\text{N}_4\text{O}_3$ (%): C, 48.65; H, 4.54; N, 25.21.

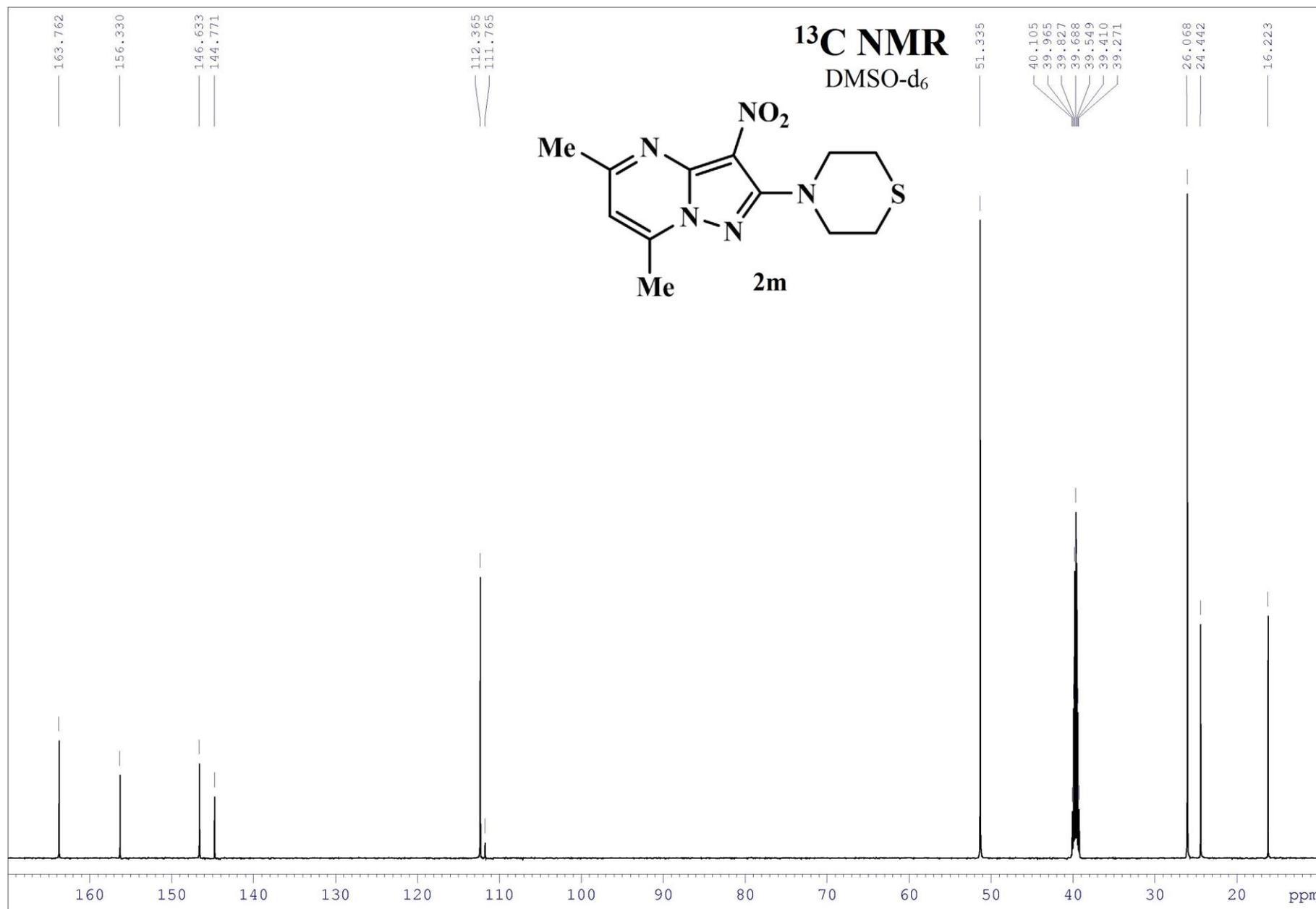
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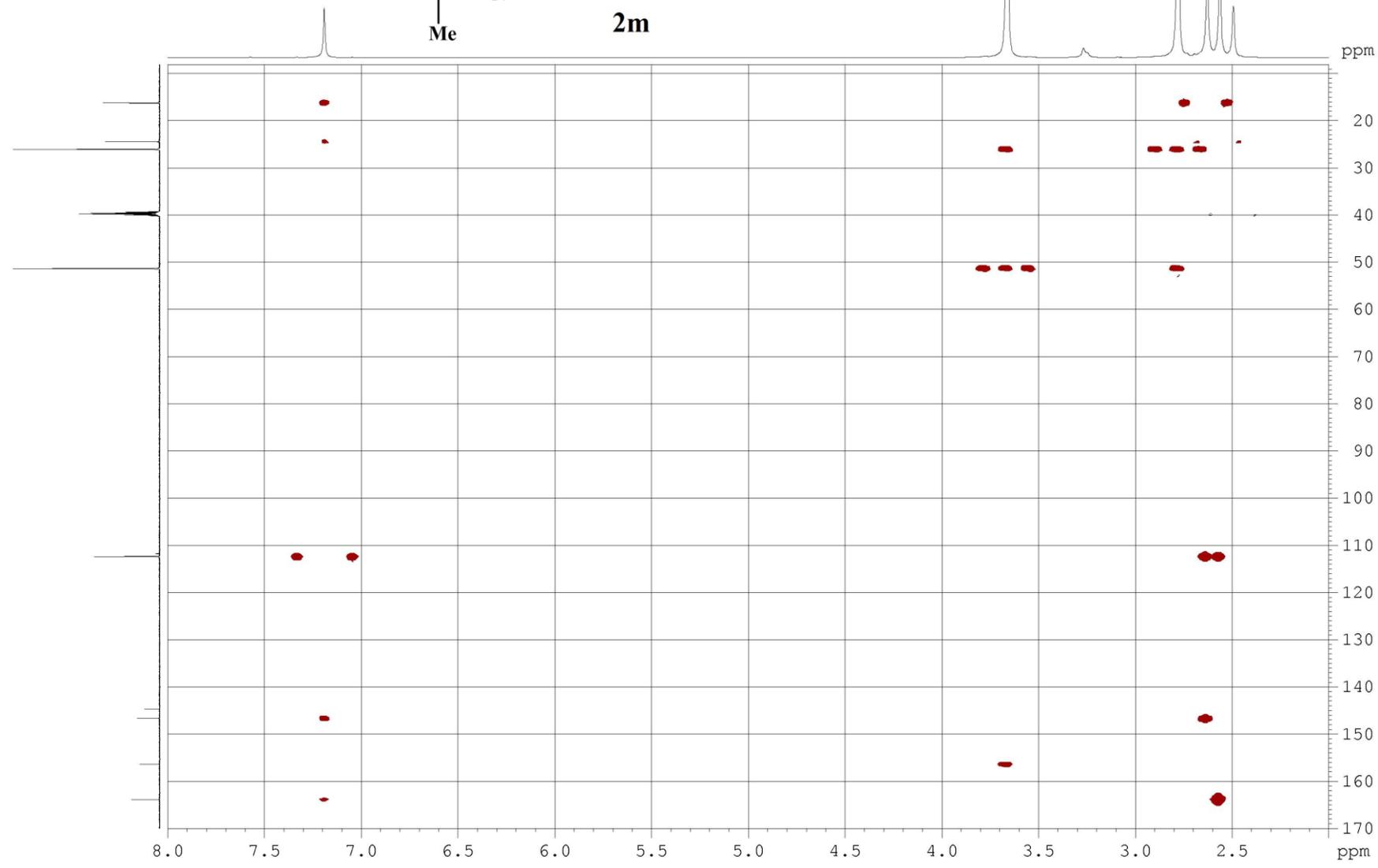
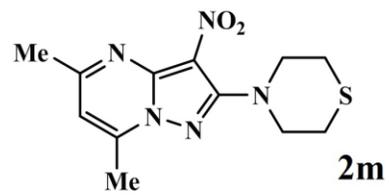




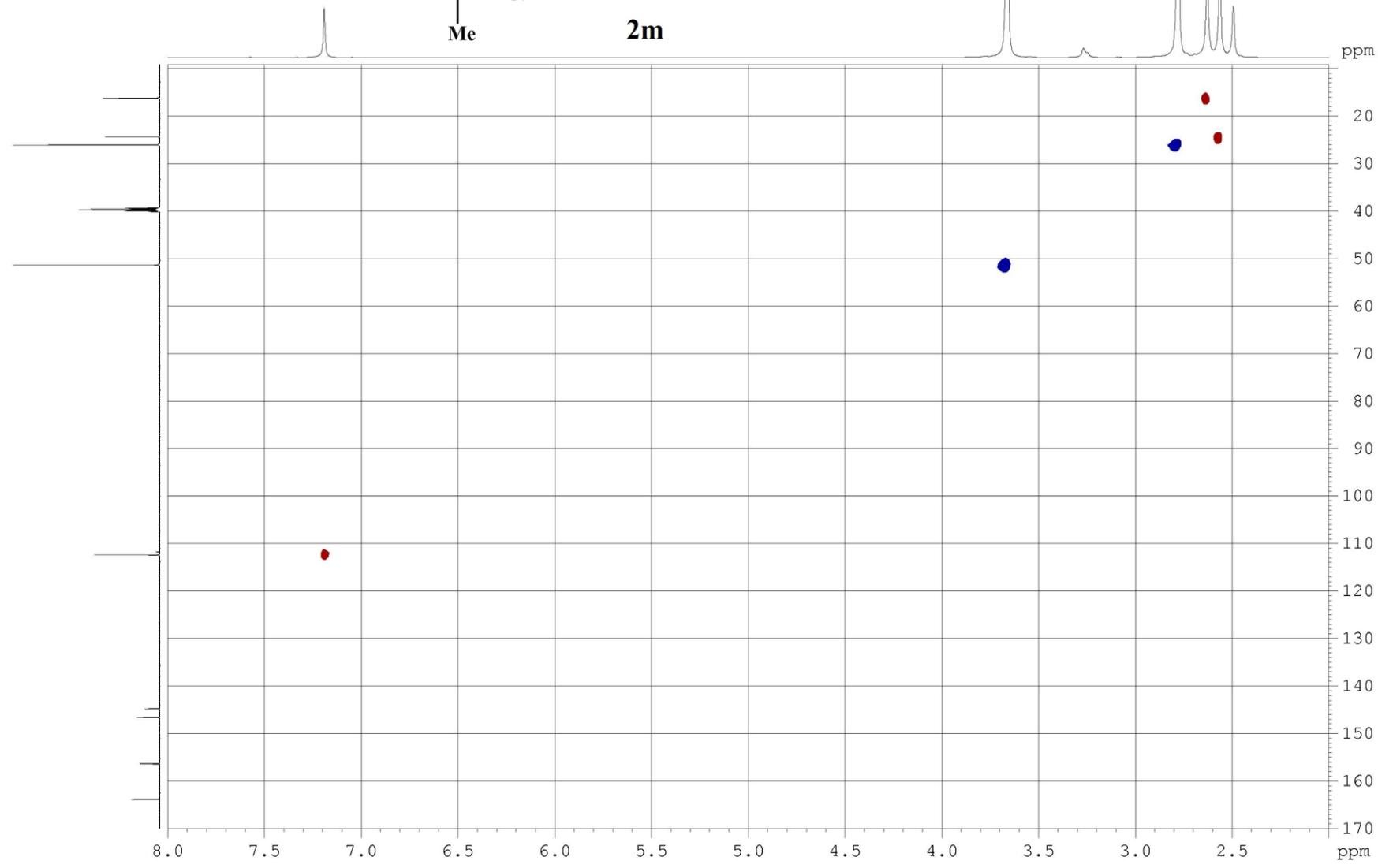
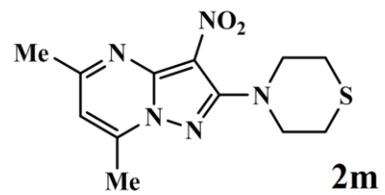


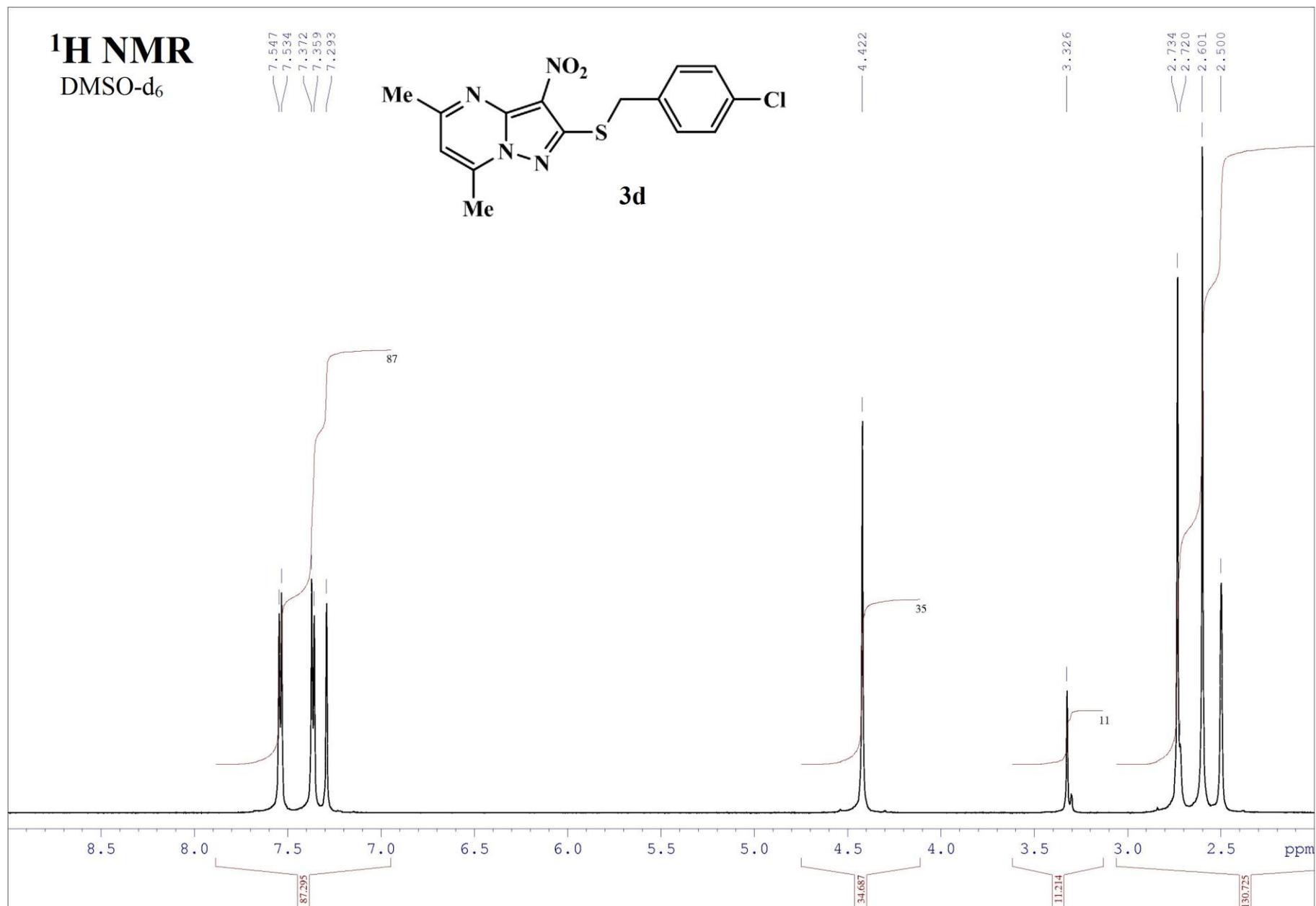


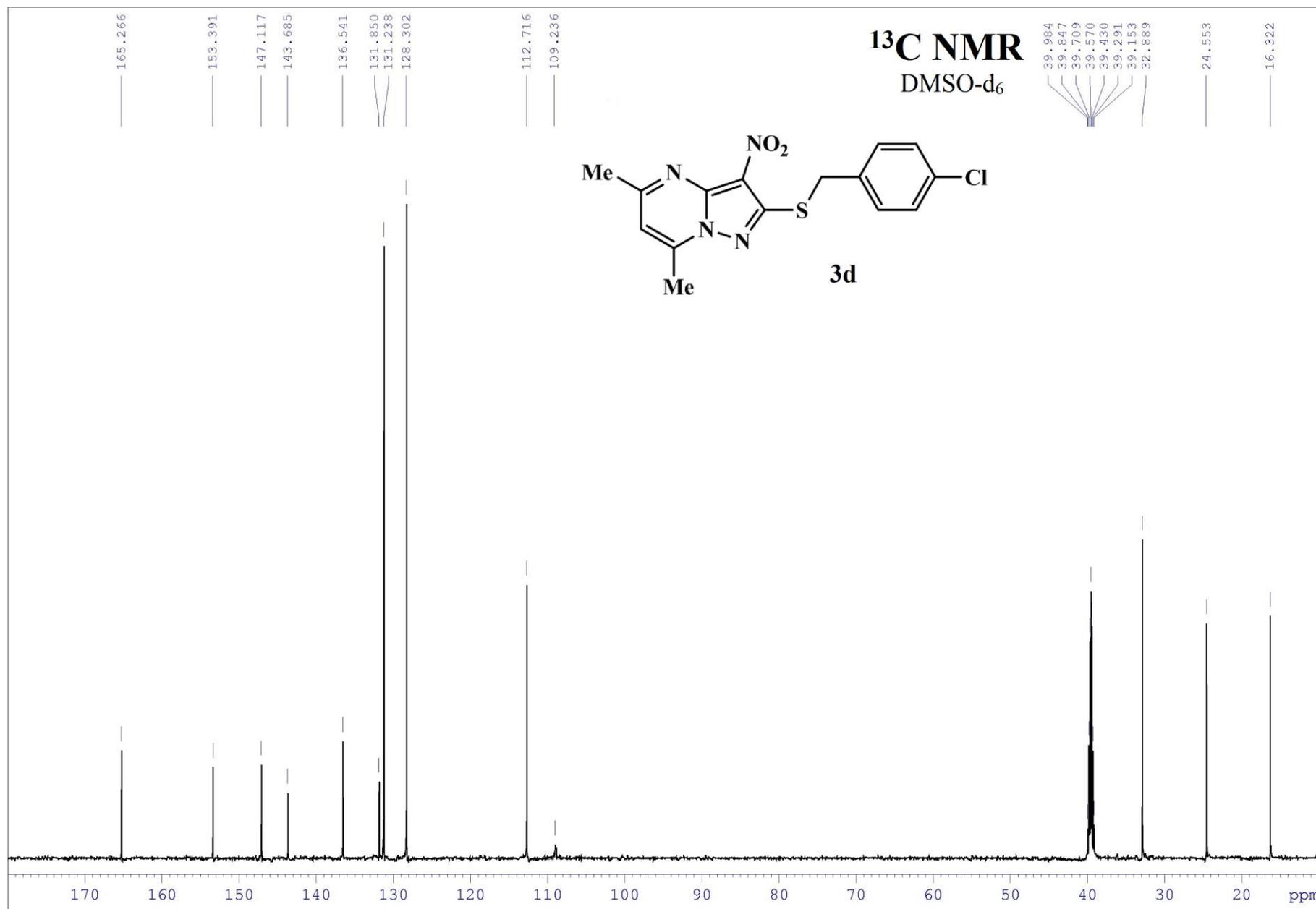
^1H - ^{13}C HMBC
DMSO- d_6



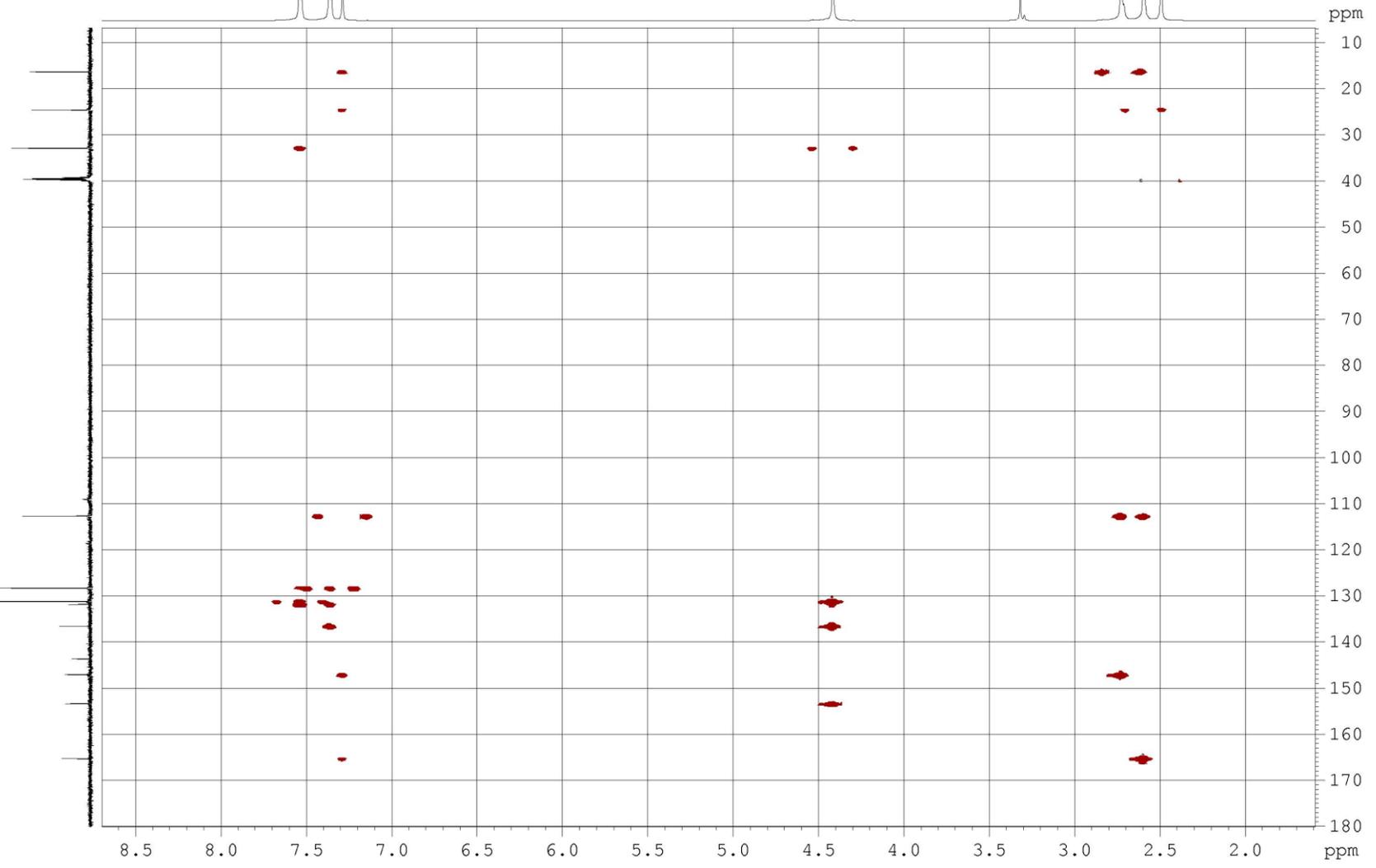
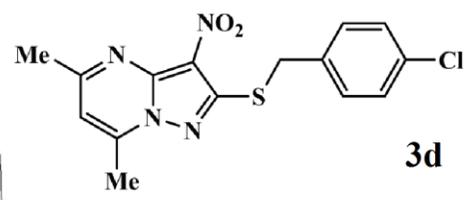
¹H-¹³C HSQC
DMSO-d₆



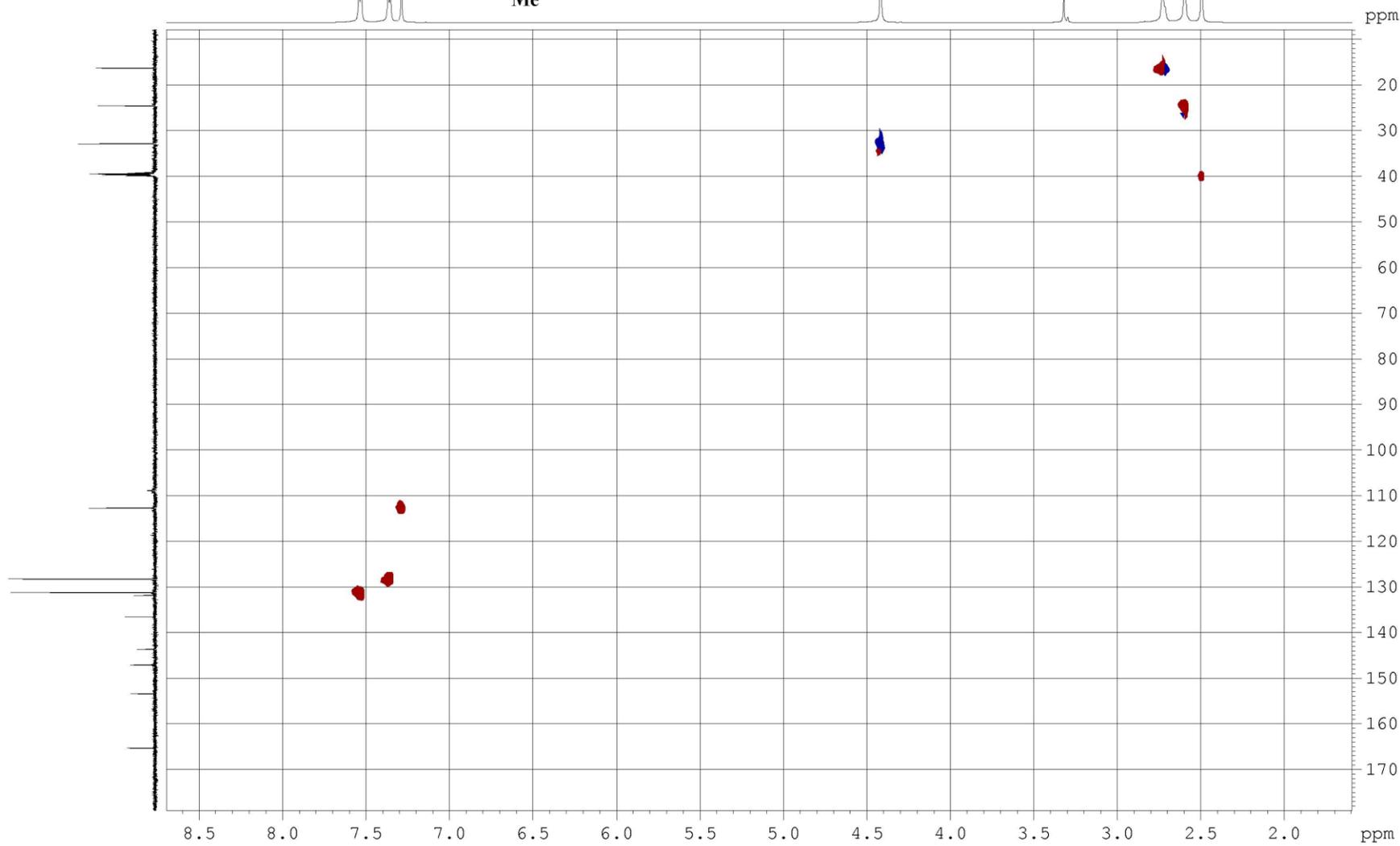
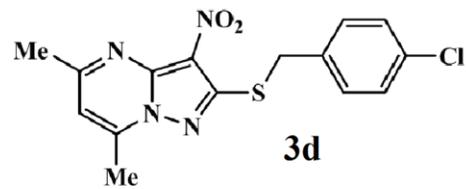


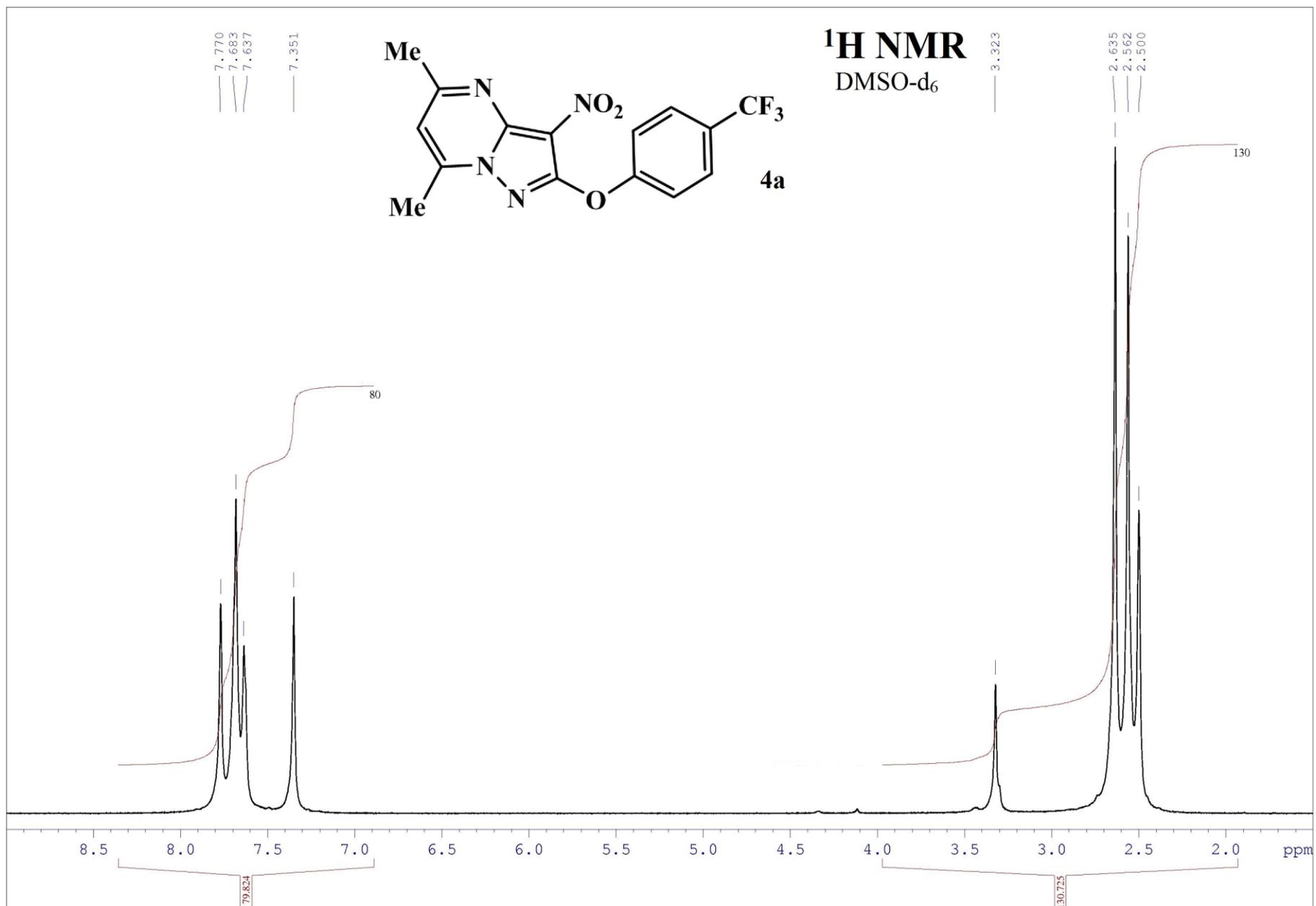


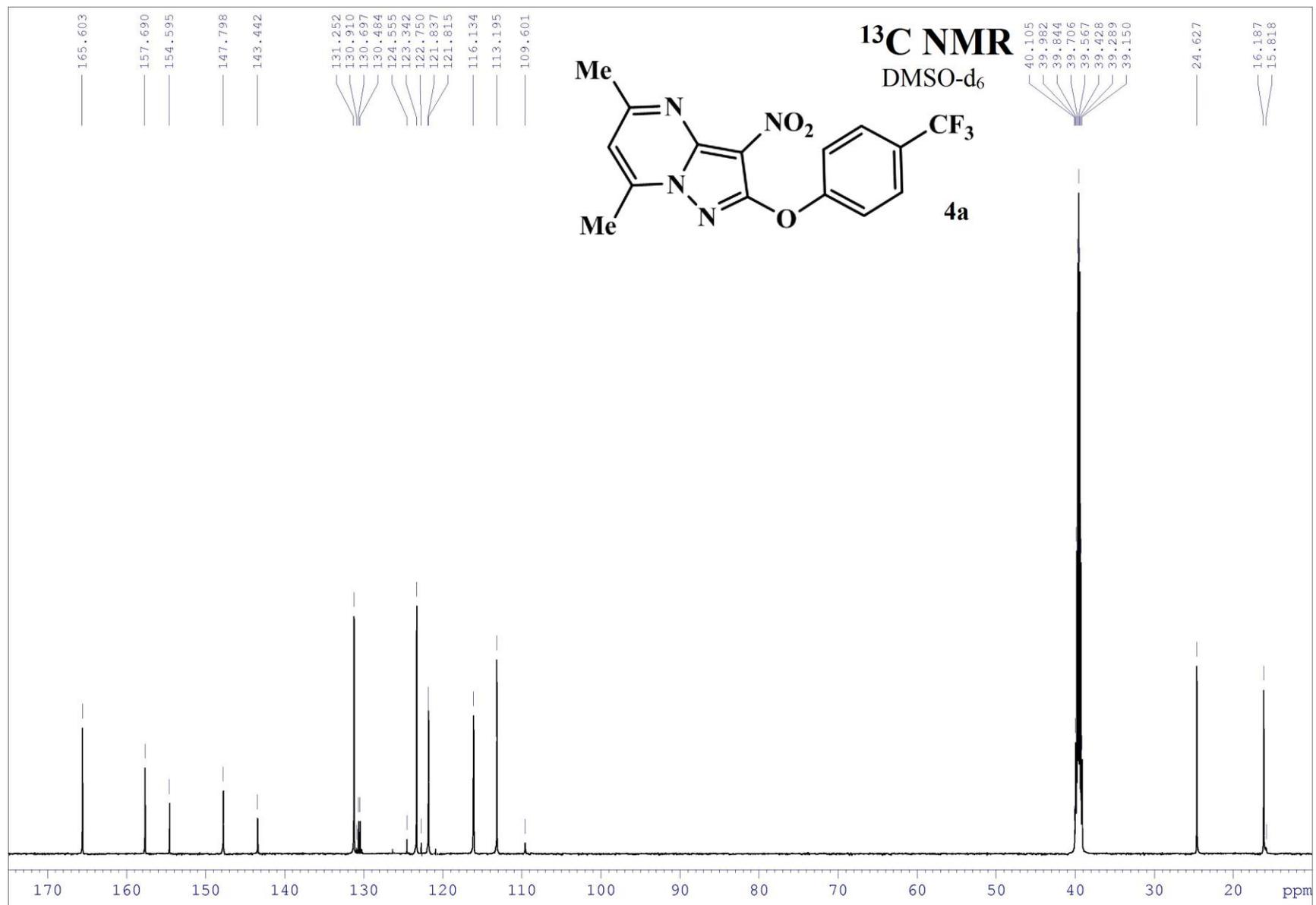
^1H - ^{13}C HMBC
DMSO- d_6



^1H - ^{13}C HSQC
DMSO- d_6

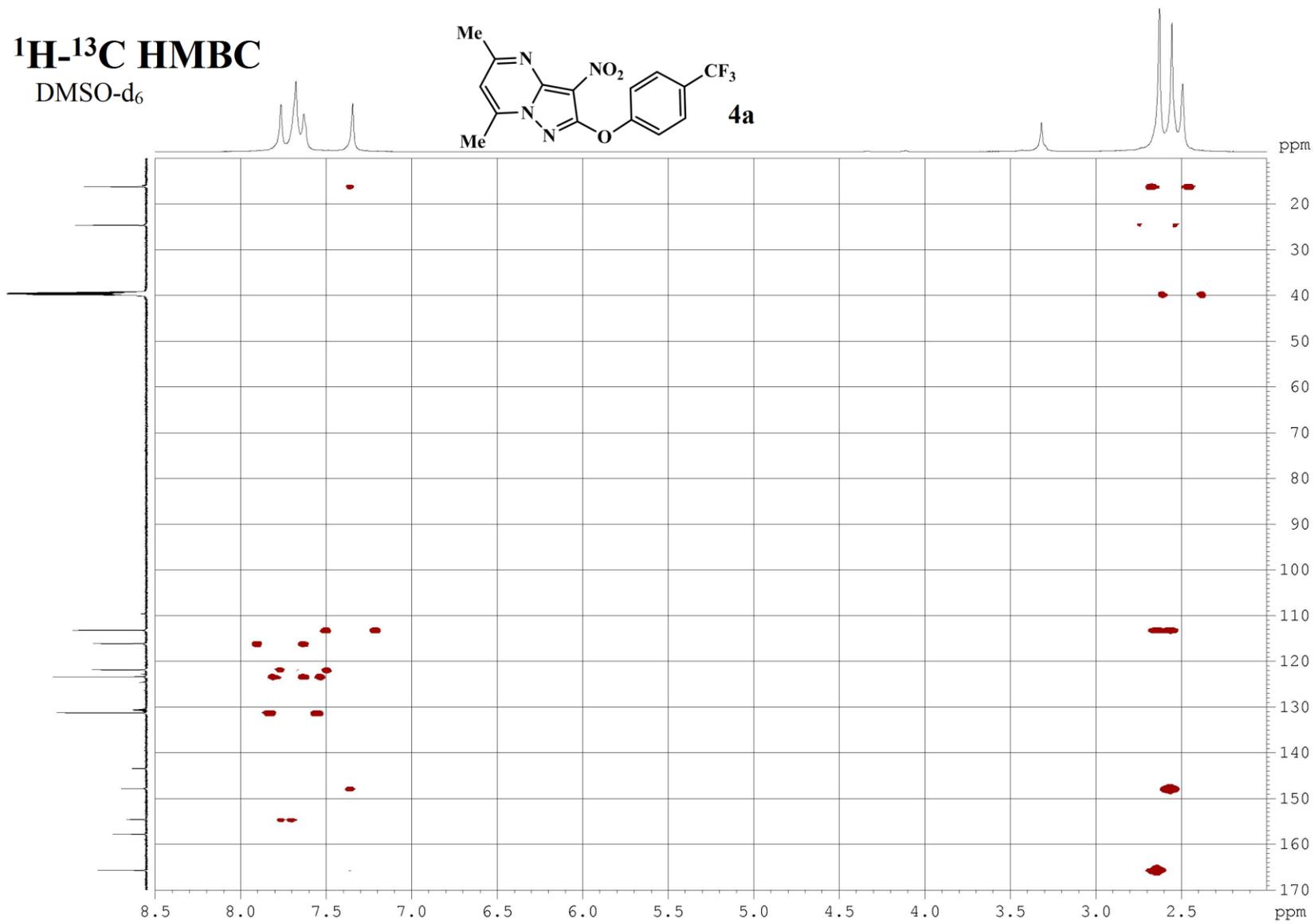
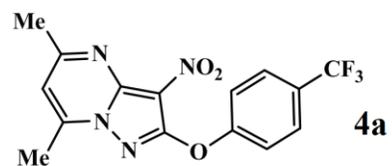






^1H - ^{13}C HMBC

DMSO- d_6



^1H - ^{13}C HSQC
DMSO- d_6

