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Synthesis of hybrid molecules based on thioglycolurils and 1,2,5-oxadiazoles *via* the Eschenmoser sulfide contraction

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Experimental

Melting points were determined in open glass capillaries on a Gallenkamp (Sanyo) melting point apparatus. The ^{1}H and ^{13}C NMR spectra were recorded on Bruker AM300 (300.13 and 75.47 MHz, respectively), Bruker AV300 (300.13 and 75.47 MHz, respectively), Bruker DRX500 (125.76 MHz (^{13}C)) spectrometers using DMSO-d_6 as solvent. Chemical shifts (δ) are given in ppm from TMS as an internal standard. IR spectra were recorded on a Bruker ALPHA instrument in KBr pellets. High resolution mass spectra (HRMS) were measured on a Bruker micrOTOF II instrument using electrospray ionization (ESI). The measurements were done in a positive ion mode (interface capillary voltage–4500 V) or in a negative ion mode (3200 V); mass range from *m/z* 50 to *m/z* 3000 Da; external or internal calibration was done with electrospray calibrant solution (Fluka). A syringe injection was used for solutions in acetonitrile or methanol (flow rate 3 mL min^{-1}). Nitrogen was applied as a dry gas; the interface temperature was set at 180 °C. All the reagents were purchased from Acros Organics and used without further purification. Column chromatography was carried out with silica gel (Acros Silica gel, for column chromatography, 60 Angstrom pore size, 0.060–0.200 mm). Thin-layer chromatography was carried out using silica gel 60 F_{254} aluminium backed plates. The plates were viewed under UV light.

Compounds **1a–f**[S1-S4] and **2a,b**[S5,S6]**, 4a**[S7] were prepared according to known procedures.

General Procedure for the synthesis of compounds 3a-q

To a thioglycoluril **1** (0.25 mmol, 1 eq.) and $NaHCO_3$ (0.75 mmol, 3 eq.) in MeCN (10 ml), corresponding 1,2,5-oxadiazole **2a,b** or **4a** (0.5 mmol, 2 eq.) was added portionwise. The reaction mixture was stirred under reflux for 4 hours. After completion of the reaction, the inorganic precipitate was filtered off and the solvent was evaporated. Methanol was added to the residue, and the resulting precipitate was filtered off and recrystallized from methanol (for compounds **3a-f,l-q**) or the residue was purified using column chromatography (for compounds **3g-k**, eluent CH_2Cl_2/acetone=5:1).

4-Amino-3-((*E*)-2-(1-(((*E*)-benzylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3a). Yield 64 mg (65%); brown solid; mp: 202–204 °C (decomp.). IR (KBr): ν 3404 (NH_2), 3270 (NH), 3058 (CH_{Ar}), 2925, 2854 (CH_{Alk}), 1723 (C-C=O), 1615 (N-C=O), 1541 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.84 (s, 3H, NMe), 2.98 (s, 3H, NMe), 5.65 (d, *J* = 8.1 Hz, 1H, CH), 6.25 (d, *J* = 8.1 Hz, 1H, CH), 6.46 (s, 1H, C=CH), 6.65 (br.s, 2H, NH_2), 7.43–7.57 (m, 3H, Ph), 7.73–7.84 (m, 2H, Ph), 8.42 (s, 1H, N=CH), 10.09 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.45 (NMe), 31.13 (NMe), 70.12, 70.60 (CH, =CH), 75.80 (CH), 107.24 (C-NH_2), 126.96, 128.98 (Ph-2,6, Ph-3,5), 130.35, 133.87, 143.00 (Ph-1, Ph-4, HN-C=), 157.61, 157.67, 160.12 (C=N$^+$, N=CH, N-C=O), 171.75 (C=O). HRMS (ESI): Calculated for $C_{17}H_{18}N_8O_4$ $[M + H]^+$: 399.1524; found: 399.1530.

4-Amino-3-((*E*)-2-(1-(((*E*)-4-methoxybenzylidene)amino)-4,6-dimethyl-5-oxohexahydro-imidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3b). Yield 45 mg (42%); beige solid; mp: 197–199 °C (decomp.). IR (KBr): ν 3413 (NH_2), 3281 (NH), 3077 (CH_{Ar}), 2937, 2838 (CH_{Alk}), 1730 (C-C=O), 1603 (N-C=O), 1528 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.84 (s, 3H, NMe), 2.96 (s, 3H, NMe), 3.82 (s, 3H, OMe), 5.63 (d, *J* = 8.1 Hz, 1H, CH), 6.22 (d, *J* = 8.1 Hz, 1H, CH), 6.42 (s, 1H, C=CH), 6.65 (br.s, 2H, NH_2), 7.08 (d, *J* = 8.6 Hz, 2H, Ar), 7.72 (d, *J* = 8.6 Hz, 2H, Ar), 8.37 (s, 1H, N=CH), 10.03 (br.s, 1H, NH). ^{13}C NMR (75

MHz, DMSO-d_6): δ 28.40 (NMe), 31.11 (NMe), 55.33 (OMe), 70.19, 70.49 (CH, =CH), 75.76 (CH), 107.20 (C-NH_2), 114.50, 126.37, 128.59, 143.41, 157.59, 157.67, 160.06, 161.09, 171.52 (C=O). HRMS (ESI): Calculated for $C_{18}H_{20}N_8O_5$ $[M + H]^+$: 429.1629; found: 429.1623.

4-Amino-3-((*E*)-2-(1-(((*E*)-4-fluorobenzylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3c). Yield 42 mg (40%); brown solid; mp: 190–192 °C (decomp.). IR (KBr): ν 3405 (NH_2), 3283 (NH), 3072 (CH_{Ar}), 2933, 2885 (CH_{Alk}), 1728 (C-C=O), 1602 (N-C=O), 1526, 1507 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.84 (s, 3H, NMe), 2.97 (s, 3H, NMe), 5.64 (d, *J* = 8.1 Hz, 1H, CH), 6.21 (d, *J* = 8.1 Hz, 1H, CH), 6.44 (s, 1H, C=CH), 6.65 (br.s, 2H, NH_2), 7.37 (t, *J* = 8.8 Hz, 2H, Ar), 7.83 (dd, *J* = 8.6, 5.6 Hz, 2H, Ar), 8.42 (s, 1H, N=CH), 10.09 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.44 (NMe), 31.10 (NMe), 70.18, 70.59 (CH, =CH), 75.77 (CH), 107.22 (C-NH_2), 116.12 (d, J_{CF} = 22.1 Hz, Ar), 129.09 (d, J_{CF} = 8.5 Hz, Ar), 130.49 (d, J_{CF} = 2.6 Hz, Ar), 141.91, 157.59, 157.65, 160.10 (HN-C=, C=N^+, N=CH, N-C=O), 163.24 (d, J_{CF} = 248.3 Hz, Ar), 171.75 (C=O). HRMS (ESI): Calculated for $C_{17}H_{17}N_8O_4F$ $[M + H]^+$: 417.1430; found: 417.1422.

4-Amino-3-((*E*)-2-(1-(((*E*)-benzylidene)amino)-4,6-diethyl-5-oxohexahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3d). Yield 45 mg (42%); yellowish solid; mp: 158–160 °C. IR (KBr): ν 3430 (NH_2), 3312 (NH), 3063, 3024 (CH_{Ar}), 2959, 2931, 2873 (CH_{Alk}), 1727 (C-C=O), 1615 (N-C=O), 1519 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.00 (t, *J* = 6.9 Hz, 3H, Me), 1.11 (t, *J* = 7.0 Hz, 3H, Me), 3.35–3.59 (m, 4H, $2NCH_2$), 5.76 (d, *J* = 8.1 Hz, 1H, CH), 6.30 (d, *J* = 8.1 Hz, 1H, CH), 6.44 (s, 1H, C=CH), 6.65 (br.s, 2H, NH_2), 7.44–7.57 (m, 3H, Ph), 7.77 (d, *J* = 6.6 Hz, 2H, Ph), 8.29 (s, 1H, N=CH), 10.09 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.43 (Me), 14.00 (Me), 36.06 (NCH_2), 38.41 (NCH_2), 69.03, 69.13 (CH, =CH), 75.82 (CH), 107.33 (C-NH_2), 127.00, 129.13, 130.56, 133.75 (Ph), 143.22, 157.09, 157.65, 159.99 (HN-C=, C=N^+, N=CH, N-C=O), 171.88 (C=O). HRMS (ESI): Calculated for $C_{19}H_{22}N_8O_4$ $[M + H]^+$: 427.1837; found: 427.1831.

4-Amino-3-((*E*)-2-(1-(((*E*)-benzylidene)amino)-6-methyl-5-oxo-4-phenylhexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3e). Yield 63 mg (55%); light beige solid; mp: 205–207 °C. IR (KBr): ν 3410 (NH_2), 3271 (NH), 3062 (CH_{Ar}), 2922, 2892 (CH_{Alk}), 1716 (C-C=O), 1621 (N-C=O), 1520 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 3.09 (s, 3H, NMe), 6.44–6.53 (m, 3H, 2CH, C=CH), 6.58 (br.s, 2H, NH_2), 7.18 (t, *J* = 7.4 Hz, 1H, Ph), 7.39–7.48 (m, 2H, Ph), 7.49–7.58 (m, 3H, Ph), 7.69 (d, *J* = 8.2 Hz, 2H, Ph), 7.78–7.85 (m, 2H, Ph), 8.53 (s, 1H, N=CH), 10.01 (br.s, 1H, NH). ^{13}C NMR (126 MHz, DMSO-d_6): δ 31.01 (NMe), 68.61, 69.52 (CH, =CH), 76.04 (CH), 107.34 (C-NH_2), 119.26, 123.88, 127.08, 129.00, 129.17, 130.53, 133.69, 137.37, 144.02, 154.87, 157.42, 160.65, 172.42 (C=O). HRMS (ESI): Calculated for $C_{22}H_{20}N_8O_4$ $[M + H]^+$: 461.1680; found: 461.1669.

4-Amino-3-((*E*)-2-(1-(((1*E*,2*E*)-3-(2-methoxyphenyl)allylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-1,2,5-oxadiazole 2-oxide (3f). Yield 66 mg (58%); white solid; mp: 192–194 (decomp.) °C. IR (KBr): ν 3427 (NH_2), 3293 (NH), 3078 (CH_{Ar}), 2944, 2886, 2838 (CH_{Alk}), 1705 (C-C=O), 1616 (N-C=O), 1523 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.83 (s, 3H, NMe), 2.94 (s, 3H, NMe), 3.87 (s, 3H, OMe), 5.62 (d, *J* = 8.0 Hz, 1H, CH), 6.22 (d, *J* = 8.1 Hz, 1H, CH), 6.27 (s, 1H, C=CH), 6.64 (br.s, 2H, NH_2), 6.94–7.10 (m, 3H, =CH, Ar), 7.34 (t, *J* = 7.8 Hz, 1H, Ar), 7.44 (d, *J* = 16.1 Hz, 1H, =CH), 7.74 (d, *J* = 7.6 Hz, 1H, Ar), 8.32 (d, *J* = 9.0 Hz, 1H, N=CH), 10.08 (br.s, 1H, NH). ^{13}C NMR (75 MHz,

DMSO-d_6): δ 28.36 (NMe), 31.02 (NMe), 55.53 (OMe), 69.89, 70.28 (CH, =CH), 75.73 (CH), 107.16 (C-NH_2), 111.55, 120.74, 123.96, 125.07, 127.26, 130.52, 134.72 (Ar, =CH-), 147.04, 156.83, 157.59, 159.80 (HN-C=, C=N^+, N=CH, N-C=O), 171.64 (C=O). HRMS (ESI): Calculated for $C_{20}H_{22}N_8O_5$ $[M + H]^+$: 455.1786; found: 455.1792.

4-((*E*)-2-(1-(((*E*)-Benzylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-3-phenyl-1,2,5-oxadiazole 2-oxide (3g). Yield 80 mg (70%); R_f=0.62 (CH_2Cl_2/acetone, 2:1); light brown solid; mp: 220–222 °C. IR (KBr): ν 3272 (NH), 3063, 3030 (CH_{Ar}), 2926, 2854 (CH_{Alk}), 1712 (C-C=O), 1585 (N-C=O), 1539 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.83 (s, 3H, NMe), 2.97 (s, 3H, NMe), 5.62 (d, *J* = 8.1 Hz, 1H, CH), 5.92 (s, 1H, C=CH), 6.24 (d, *J* = 8.1 Hz, 1H, CH), 7.45–7.56 (m, 6H, Ph), 7.69–7.82 (m, 4H, Ph), 8.41 (s, 1H, N=CH), 10.08 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.51 (NMe), 31.15 (NMe), 70.10, 70.59 (CH, =CH), 76.58 (CH), 114.17, 122.86, 127.04, 128.41, 128.93, 130.28, 133.78, 143.01, 156.72, 157.70, 159.62, 173.37 (C=O). HRMS (ESI): Calculated for $C_{23}H_{21}N_7O_4$ $[M + H]^+$: 460.1728; found: 460.1723.

4-((*E*)-2-(1-(((*E*)-4-Methoxybenzylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-3-phenyl-1,2,5-oxadiazole 2-oxide (3h). Yield 65 mg (53%); R_f=0.55 (CH_2Cl_2/acetone, 2:1); brown solid; mp: 230–232 °C. IR (KBr): ν 3432 (NH), 3064, 2996 (CH_{Ar}), 2926, 2840 (CH_{Alk}), 1718 (C-C=O), 1585 (N-C=O), 1551 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.82 (s, 3H, NMe), 2.95 (s, 3H, NMe), 3.81 (s, 3H, OMe), 5.61 (d, *J* = 8.0 Hz, 1H, CH), 5.88 (s, 1H, C=CH), 6.21 (d, *J* = 8.1 Hz, 1H, CH), 7.05 (d, *J* = 8.7 Hz, 2H, Ar), 7.50–7.56 (m, 3H, Ar), 7.69 (d, *J* = 8.7 Hz, 2H, Ar), 7.72–7.80 (m, 2H, Ar), 8.35 (s, 1H, N=CH), 10.01 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.51 (NMe), 31.18 (NMe), 55.36 (OMe), 70.20, 70.54 (CH, =CH), 76.59 (CH), 114.25, 114.47, 122.88, 126.34, 128.45, 128.75, 128.96, 130.31, 143.44, 156.81, 157.77, 159.61, 161.10, 173.21 (C=O). HRMS (ESI): Calculated for $C_{24}H_{23}N_7O_5$ $[M + H]^+$: 490.1883; found: 490.1818.

4-((*E*)-2-(1-(((*E*)-4-Fluorobenzylidene)amino)-4,6-dimethyl-5-oxohexahydroimidazo[4,5-*d*]-imidazol-2(1*H*)-ylidene)acetyl)-3-phenyl-1,2,5-oxadiazole 2-oxide (3i). Yield 59 mg (50%); R_f=0.57 (CH_2Cl_2/acetone, 2:1); brown solid; mp: 237–239 °C. IR (KBr): ν 3260 (NH), 3065 (CH_{Ar}), 2926, 2854 (CH_{Alk}), 1716 (C-C=O), 1584 (N-C=O), 1540 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.83 (s, 3H, NMe), 2.97 (s, 3H, NMe), 5.62 (d, *J* = 8.0 Hz, 1H, CH), 5.91 (s, 1H, C=CH), 6.21 (d, *J* = 8.1 Hz, 1H, CH), 7.34 (t, *J* = 8.8 Hz, 2H, Ar), 7.50–7.58 (m, 3H, Ar), 7.70–7.86 (m, 4H, Ar), 8.40 (s, 1H, N=CH), 10.08 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.52 (NMe), 31.14 (NMe), 70.18, 70.61 (CH, =CH), 76.61 (CH), 114.19, 116.05 (d, J_{CF} = 22.0 Hz), 122.86, 128.44, 128.96, 129.25 (d, J_{CF} = 8.6 Hz), 130.31, 130.42 (d, J_{CF} = 2.7 Hz), 141.94, 156.72, 157.72, 159.64, 163.24 (d, J_{CF} = 246.9 Hz), 173.40 (C=O). HRMS (ESI): Calculated for $C_{23}H_{20}N_7O_4F$ $[M + H]^+$: 478.1634; found: 478.1614.

4-((*E*)-2-(1-(((1*E*,2*E*)-3-(2-Methoxyphenyl)allylidene)amino)-4,6-dimethyl-5-oxohexahydro-imidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-3-phenyl-1,2,5-oxadiazole 2-oxide (**3j)**. Yield 57 mg (44%); R_f=0.60 (CH_2Cl_2/acetone, 2:1); brown solid; mp: 208–210 °C. IR (KBr): ν 3250 (NH), 3060 (CH_{Ar}), 2923, 2847 (CH_{Alk}), 1714 (C-C=O), 1586 (N-C=O), 1538 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.82 (s, 3H, NMe), 2.95 (s, 3H, NMe), 3.87 (s, 3H, OMe), 5.59 (d, *J* = 8.0 Hz, 1H, CH), 5.85 (s, 1H, C=CH), 6.19 (d, *J* = 8.1 Hz, 1H, CH), 6.95–7.03 (m, 1H, Ar), 7.05–7.11 (m, 2H, =CH, Ar), 7.31–7.37 (m, 1H, Ar), 7.43 (d, *J* = 16.1 Hz, 1H, =CH), 7.50–7.54

(m, 3H, Ar), 7.70–7.77 (m, 3H, Ar), 8.31 (d, *J* = 9.0 Hz, 1H, N=CH), 9.99 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 28.53 (NMe), 31.13 (NMe), 55.60 (OMe), 69.95, 70.51 (CH, =CH), 76.38 (CH), 111.66, 120.85, 122.90, 124.04, 125.35, 127.30, 128.46, 129.03, 130.32, 130.63, 134.68, 146.86, 156.94, 157.76, 157.92, 159.31, 173.33 (C=O). HRMS (ESI): Calculated for $C_{26}H_{25}N_7O_5$ $[M + H]^+$: 516.1990; found: 516.1970.

4-((*E*)-2-(1-(((*E*)-Benzylidene)amino)-4,6-diethyl-5-oxohexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-ylidene)acetyl)-3-phenyl-1,2,5-oxadiazole 2-oxide (3k). Yield 55 mg (45%); R_f=0.62 (CH_2Cl_2/acetone, 2:1); yellow solid; mp: 215–217 °C. IR (KBr): ν 3245 (NH), 3065, 3025 (CH_{Ar}), 2975, 2935 (CH_{Alk}), 1720 (C-C=O), 1578 (N-C=O), 1535 (C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.00 (t, *J* = 7.0 Hz, 3H, Me), 1.08 (t, *J* = 7.0 Hz, 3H, Me), 3.26–3.56 (m, 4H, $2NCH_2$), 5.74 (d, *J* = 8.0 Hz, 1H, CH), 5.90 (s, 1H, C=CH), 6.30 (d, *J* = 8.0 Hz, 1H, CH), 7.43-7.61 (m, 6H, Ph), 7.68–7.83 (m, 4H, Ph), 8.28 (s, 1H, N=CH), 10.10 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 13.35 (Me), 13.98 (Me), 35.94 (NCH_2), 38.38 (NCH_2), 69.02 (CH, =CH), 76.66 (CH), 114.20, 122.86, 127.05, 128.45, 128.95, 129.04, 130.34, 130.46, 133.64, 143.16, 156.76, 157.05, 159.47, 173.49 (C=O). HRMS (ESI): Calculated for $C_{25}H_{25}N_7O_4$ $[M + H]^+$: 488.2041; found: 488.2028.

(*E*)-4-(((*E*)-Benzylidene)amino)-1,3-dimethyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3l). Yield 55 mg (58%); light brown solid; mp: 235–237 °C. IR (KBr): ν 3268 (NH), 3054 (CH_{Ar}), 2933 (CH_{Alk}), 1717 (C-C=O), 1629, 1542 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.55 (s, 3H, Me), 2.86 (s, 3H, NMe), 2.98 (s, 3H, NMe), 5.64 (d, *J* = 8.0 Hz, 1H, CH), 6.05 (s, 1H, C=CH), 6.25 (d, *J* = 8.1 Hz, 1H, CH), 7.43–7.54 (m, 3H, Ar), 7.75–7.82 (m, 2H, Ar), 8.42 (s, 1H, N=CH), 10.13 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.18 (Me), 28.49 (NMe), 31.22 (NMe), 70.12, 70.53 (CH, =CH), 76.55 (CH), 127.06, 129.04 (Ph-2,6, Ph-3,5), 130.34, 133.90, 142.96 (Ph-1, Ph-4, HN-C=), 151.48, 152.98, 157.80, 159.51 (C-Me, $C=N^+$, N=CH, N-C=O), 174.32 (C=O). HRMS (ESI): Calculated for $C_{18}H_{19}N_7O_3$ $[M + H]^+$: 382.1622; found: 382.1619.

(*E*)-4-(((*E*)-4-Methoxybenzylidene)amino)-1,3-dimethyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3m). Yield 57 mg (56%); yellow solid; mp: 217–219 °C. IR (KBr): ν 3274 (NH), 3080, 3037, 3006 (CH_{Ar}), 2938 (CH_{Alk}), 1701 (C-C=O), 1609, 1532 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.55 (s, 3H, Me), 2.85 (s, 3H, NMe), 2.96 (s, 3H, NMe), 3.81 (s, 3H, OMe), 5.63 (d, *J* = 8.0 Hz, 1H, CH), 6.01 (s, 1H, C=CH), 6.22 (d, *J* = 8.2 Hz, 1H, CH), 7.07 (d, *J* = 8.8 Hz, 2H, Ar), 7.73 (d, *J* = 8.8 Hz, 2H, Ar), 8.37 (s, 1H, N=CH), 10.08 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.13 (Me), 28.42 (NMe), 31.13 (NMe), 55.32 (OMe), 70.14, 70.41 (CH, =CH), 76.42 (CH), 114.49, 126.41, 128.65, 143.20, 151.39, 152.95, 157.73, 159.42, 161.02, 174.02 (C=O). HRMS (ESI): Calculated for $C_{19}H_{21}N_7O_4$ $[M + H]^+$: 412.1728; found: 412.1724.

(*E*)-4-(((*E*)-4-Fluorobenzylidene)amino)-1,3-dimethyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3n). Yield 50 mg (50%); beige solid; mp: 227–229 °C. IR (KBr): ν 3269 (NH), 3070, 3047 (CH_{Ar}), 2935, 2886 (CH_{Alk}), 1724 (C-C=O), 1617, 1535 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.55 (s, 3H, Me), 2.86 (s, 3H, NMe), 2.97 (s, 3H, NMe), 5.64 (d, *J* = 8.0 Hz, 1H, CH), 6.03 (s, 1H, C=CH), 6.21 (d, *J* = 8.1 Hz, 1H, CH), 7.35 (t, *J* = 8.8 Hz, 2H, Ar), 7.84 (dd, *J* = 8.6, 5.6 Hz, 2H, Ar), 8.42 (s, 1H, N=CH), 10.14 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.11 (Me), 28.43 (NMe), 31.11

(NMe), 70.11, 70.48 (CH, =CH), 76.44 (CH), 116.07 (d, J_{CF} = 22.0 Hz, Ar), 129.21 (d, J_{CF} = 8.5 Hz, Ar), 130.50 (d, J_{CF} = 2.7 Hz, Ar), 141.71, 151.39, 152.89, 157.69, 159.43, 163.18 (d, J_{CF} = 248.2 Hz, Ar), 174.24 (C=O). HRMS (ESI): Calculated for $C_{18}H_{18}N_7O_3F$ $[M + H]^+$: 400.1528; found: 400.1523.

(*E*)-4-(((*E*)-Benzylidene)amino)-1,3-diethyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3o). Yield 44 mg (43%); light brown solid; mp: 199–201 °C. IR (KBr): ν 3257 (NH), 3081, 3066, 3040 (CH_{Ar}), 2982, 2957, 2934 (CH_{Alk}), 1718 (C-C=O), 1618, 1567 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 1.01 (t, *J* = 7.0 Hz, 3H, Me), 1.12 (t, *J* = 7.0 Hz, 3H, Me), 2.55 (s, 3H, Me), 3.32–3.60 (m, 4H, $2CH_2$), 5.75 (d, *J* = 8.0 Hz, 1H, CH), 6.03 (s, 1H, C=CH), 6.31 (d, *J* = 8.1 Hz, 1H, CH), 7.41–7.57 (m, 3H, Ph), 7.72–7.86 (m, 2H, Ph), 8.30 (s, 1H, N=CH), 10.14 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.11 (Me), 13.37 (Me), 13.93 (Me), 35.92 (NCH_2), 38.29 (NCH_2), 68.85, 68.91 (CH, =CH), 76.43 (CH), 126.94, 129.03 (Ph-2,6, Ph-3,5), 130.34, 133.71, 142.89 (Ph-1, Ph-4, HN-C=), 151.38, 152.90, 156.99, 159.25 (C-Me, $C=N^+$, N=CH, N-C=O), 174.28 (C=O). HRMS (ESI): Calculated for $C_{20}H_{23}N_7O_3$ $[M + H]^+$: 410.1935; found: 410.1929.

(*E*)-4-(((*E*)-Benzylidene)amino)-3-methyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)-1-phenylhexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3p). Yield 41 mg (37%); beige solid; mp: 248–250 °C. IR (KBr): ν 3257 (NH), 3105, 3049 (CH_{Ar}), 2977, 2933 (CH_{Alk}), 1708 (C-C=O), 1630, 1537 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.50 (s, 3H, Me), 3.01 (s, 3H, NMe), 6.10 (s, 1H, C=CH), 6.49 (s, 2H, 2CH), 7.19 (t, *J* = 7.3 Hz, 1H, Ph), 7.42–7.58 (m, 5H, Ph), 7.72 (d, *J* = 7.8 Hz, 2H, Ph), 7.84 (d, *J* = 7.8 Hz, 2H, Ph), 8.54 (s, 1H, N=CH), 10.07 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.09 (Me), 31.04 (NMe), 68.53, 69.52 (CH, =CH), 76.82 (CH), 119.26, 123.85, 127.15, 129.00, 129.16, 130.46, 133.70, 137.42, 143.92, 151.38, 152.74, 154.92, 160.03, 174.94 (C=O). HRMS (ESI): Calculated for $C_{23}H_{21}N_7O_3$ $[M + H]^+$: 444.1779; found: 444.1770.

(*E*)-4-(((1*E*,2*E*)-3-(2-Methoxyphenyl)allylidene)amino)-1,3-dimethyl-5-(2-(4-methyl-1,2,5-oxadiazol-3-yl)-2-oxoethylidene)hexahydroimidazo[4,5-*d*]imidazol-2(1*H*)-one (3q). Yield 57 mg (52%); light brown solid; mp: 220–222 °C. IR (KBr): ν 3235 (NH), 3077, 3050, 3016 (CH_{Ar}), 2967, 2936 (CH_{Alk}), 1715 (C-C=O), 1616, 1533 (N-C=O, C=N) cm^{-1}. ^{1}H NMR (300 MHz, DMSO-d_6): δ 2.54 (s, 3H, Me), 2.85 (s, 3H, NMe), 2.95 (s, 3H, NMe), 3.87 (s, 3H, OMe), 5.61 (d, *J* = 7.8 Hz, 1H, CH), 5.94 (s, 1H, C=CH), 6.19 (d, *J* = 7.9 Hz, 1H, CH), 6.97 (t, *J* = 7.3 Hz, 1H, Ar), 7.04–7.15 (m, 2H, =CH, Ar), 7.34 (t, *J* = 7.5 Hz, 1H, Ar), 7.42 (d, *J* = 16.2 Hz, 1H, =CH), 7.74 (d, *J* = 7.6 Hz, 1H, Ar), 8.30 (d, *J* = 8.8 Hz, 1H, N=CH), 10.06 (br.s, 1H, NH). ^{13}C NMR (75 MHz, DMSO-d_6): δ 9.12 (Me), 28.39 (NMe), 31.04 (NMe), 55.51 (OMe), 69.80, 70.31 (CH, =CH), 76.39 (CH), 111.54, 120.72, 124.02, 125.32, 127.15, 130.45, 134.30, 146.49, 151.40, 152.86, 156.80, 157.64, 159.06, 174.00 (C=O). HRMS (ESI): Calculated for $C_{21}H_{23}N_7O_4$ $[M + H]^+$: 438.1884; found: 438.1879.

Crystallographic data

Single crystals of **3e** were obtained from DMSO solution. X-ray diffraction data were collected at 100 K on a four-circle Rigaku Synergy S diffractometer equipped with a HyPix6000HE area-detector (kappa geometry, shutterless ω-scan technique), using monochromatized Cu K_α-radiation. The intensity data were integrated and corrected for absorption and decay by the CrysAlisPro program.[S8] The structure was solved by direct methods using SHELXT[S9] and refined on F^2 using SHELXL-2018[S10] in the OLEX2 program.[S11] All non-hydrogen atoms were refined with individual anisotropic displacement parameters. Locations of hydrogen atoms H7, H25, H33A, H33B were found from the electron density-difference map. All other hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. Full crystallographic data have been deposited at the Cambridge Crystallographic Data Center (deposit CCDC 2298361).

Single crystals of **3n** were obtained from acetonitrile solution. X-ray diffraction data were collected at 100K on a four-circle Rigaku Synergy S diffractometer equipped with a HyPix6000HE area-detector (kappa geometry, shutterless ω-scan technique), using monochromatized Cu K_α-radiation. The intensity data were integrated and corrected for absorption and decay by the CrysAlisPro program.[S8] The structure was solved by direct methods using SHELXT[S9] and refined on F^2 using SHELXL-2018[S10] in the OLEX2 program.[S11] All non-hydrogen atoms were refined with individual anisotropic displacement parameters. Locations of amino hydrogen atom (H7) and bridged hydrogen atoms (H4, H8) were found from the electron density-difference map; these hydrogen atoms were refined with individual isotropic displacement parameters. All other hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. A non-coordinating disordered MeOH molecule was removed by the SQUEEZE method[S12] implemented in the OLEX2 program.[S11] Full crystallographic data have been deposited at the Cambridge Crystallographic Data Center (deposit CCDC 2298362).

References

S1. G. A. Gazieva, P. A. Poluboyarov, L. D. Popov, N. G. Kolotyrkina, A. N. Kravchenko and N. N. Makhova, *Synthesis*, 2012, **44**, 3366.

S2. G. A. Gazieva, L. V. Anikina, S. A. Pukhov, T. B. Karpova, Yu. V. Nelyubina, and A. N. Kravchenko, *Mol. Diversity*, 2016, **20**, 837.

S3. G. A. Gazieva, L. V. Anikina, T. V. Nechaeva, S. A. Pukhov, T. B. Karpova, S. V. Popkov, Yu. V. Nelyubina, N. G. Kolotyrkina and A. N. Kravchenko, *Eur. J. Med. Chem.*, 2017, **140**, 141.

S4. E. E. Vinogradova, G. A. Gazieva, A. N. Izmest'ev, V. A. Karnoukhova and A. N. Kravchenko, *RSC Adv.*, 2021, **11**, 28395.

S5. A. S. Kulikov and N. N. Makhova, *Russ. Chem. Bull.*, 1998, **47**, 139 (*Izv. Akad. Nauk, Ser. Khim.*, 1998, 137).

S6. M. A. Epishina, A. S. Kulikov, L. L. Fershtat, I. V. Ananyev and N. N. Makhova, *Mendeleev Commun.*, 2019, **29**, 288.

S7. A. B. Sheremetev, A. S. Kulikov and L. I. Khmel'nitskii, *Russ. Chem. Bull.*, 1993, **42**, 708 (*Izv. Akad. Nauk, Ser. Khim.*, 1993, 744).

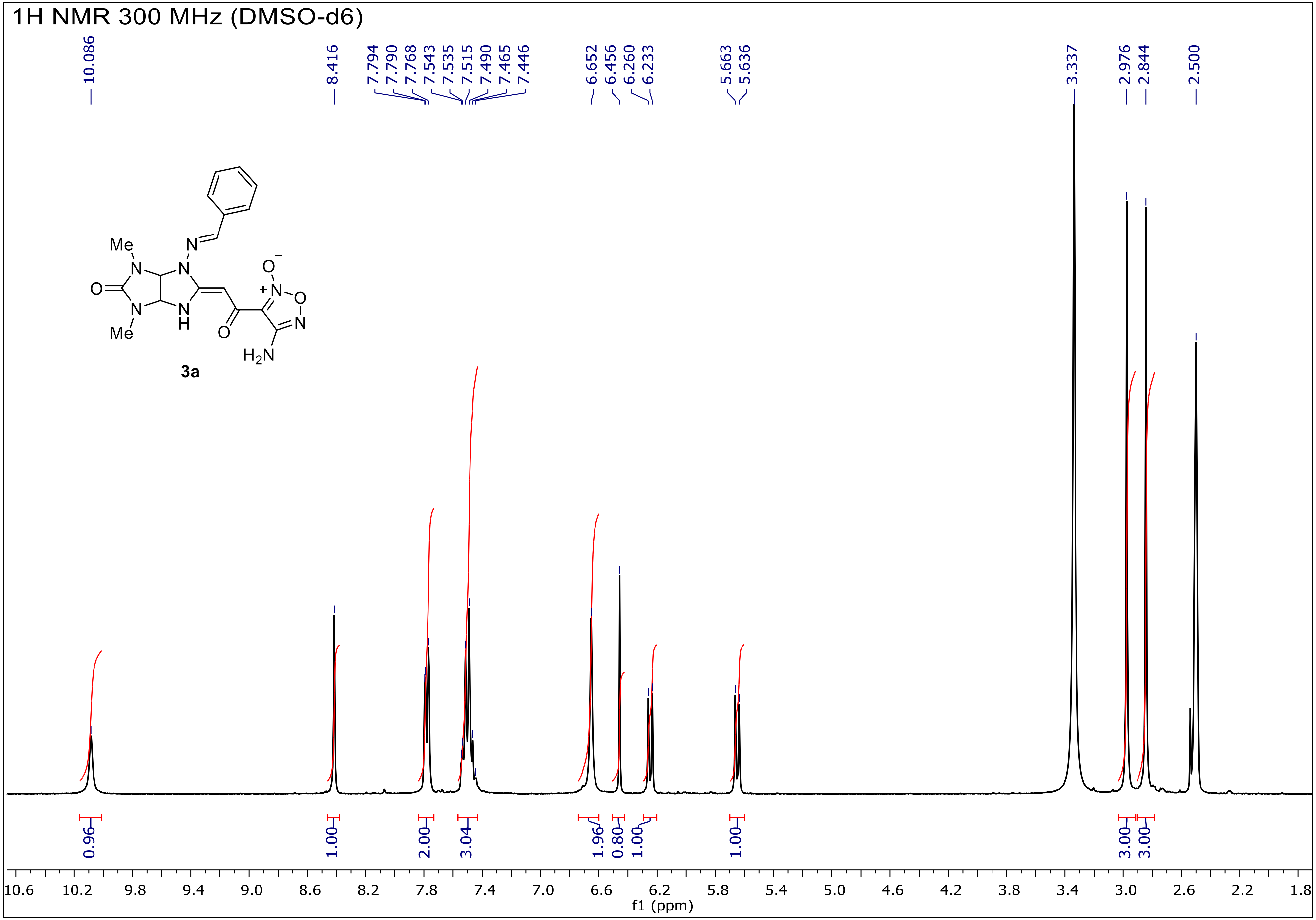
S8. *CrysAlisPro, version 1.171.42*, Rigaku Oxford Diffraction, 2022.

S9. G. M. Sheldrick, *Acta Crystallogr.*, 2015, **A71**, 3.

S10. G. M. Sheldrick, *Acta Crystallogr.*, 2015, **C71**, 3.

S11. O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Crystallogr.*, 2009, **42**, 339.

S12. A. L. Spek, *Acta Crystallogr.*, 2015, **C71**, 9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3.337
2.976 2.844
2.500
Me
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N
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N
N
H
N
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H2N
3a
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1.00
2.00
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1.00
3.00
3.00
10.6 10.2 9.8 9.4 9.0 8.6 8.2 7.8 7.4 7.0 6.6 6.2 5.8 5.4 5.0 4.6 4.2 3.8 3.4 3.0 2.6 2.2 1.8
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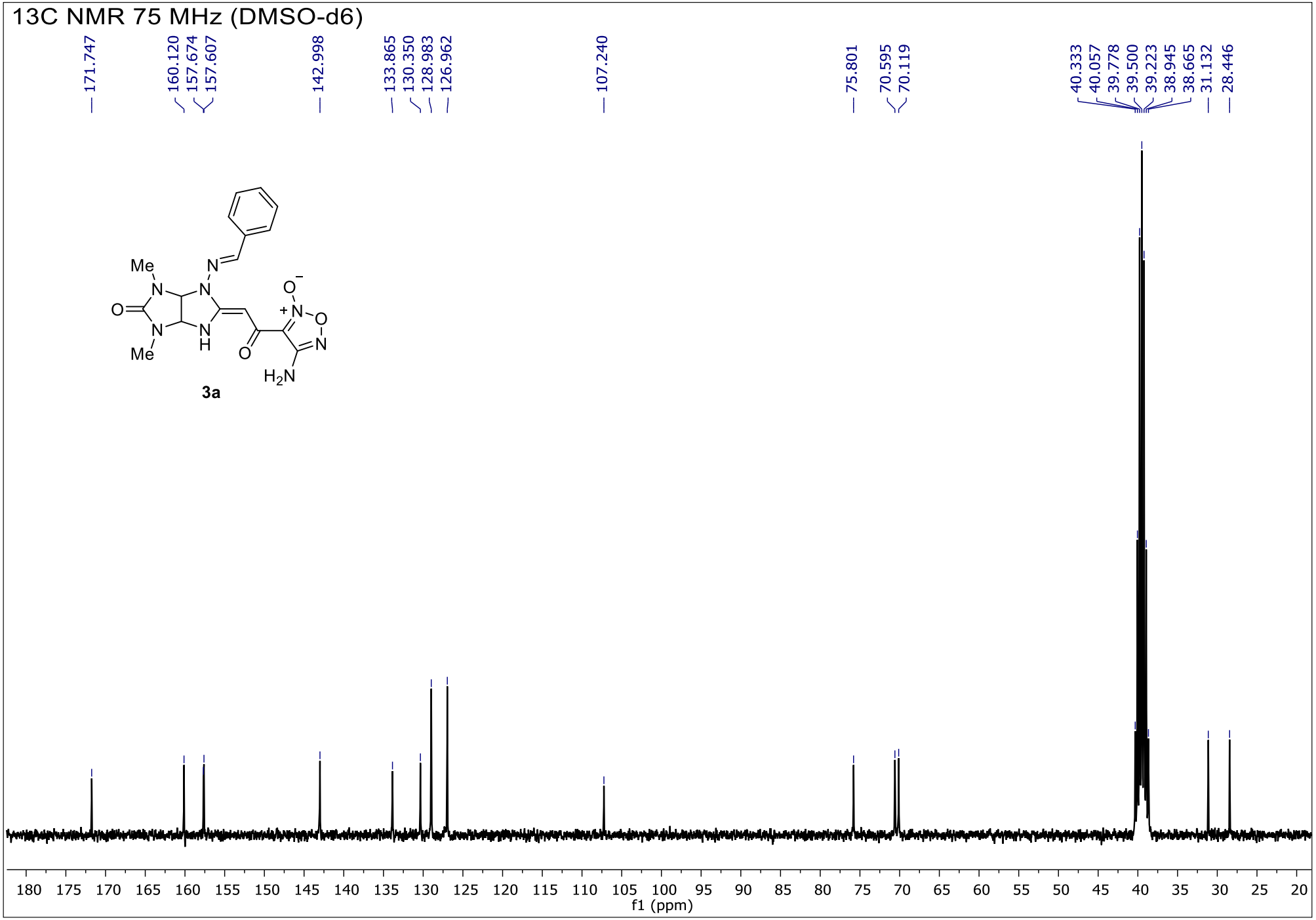
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N
N
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O
+N
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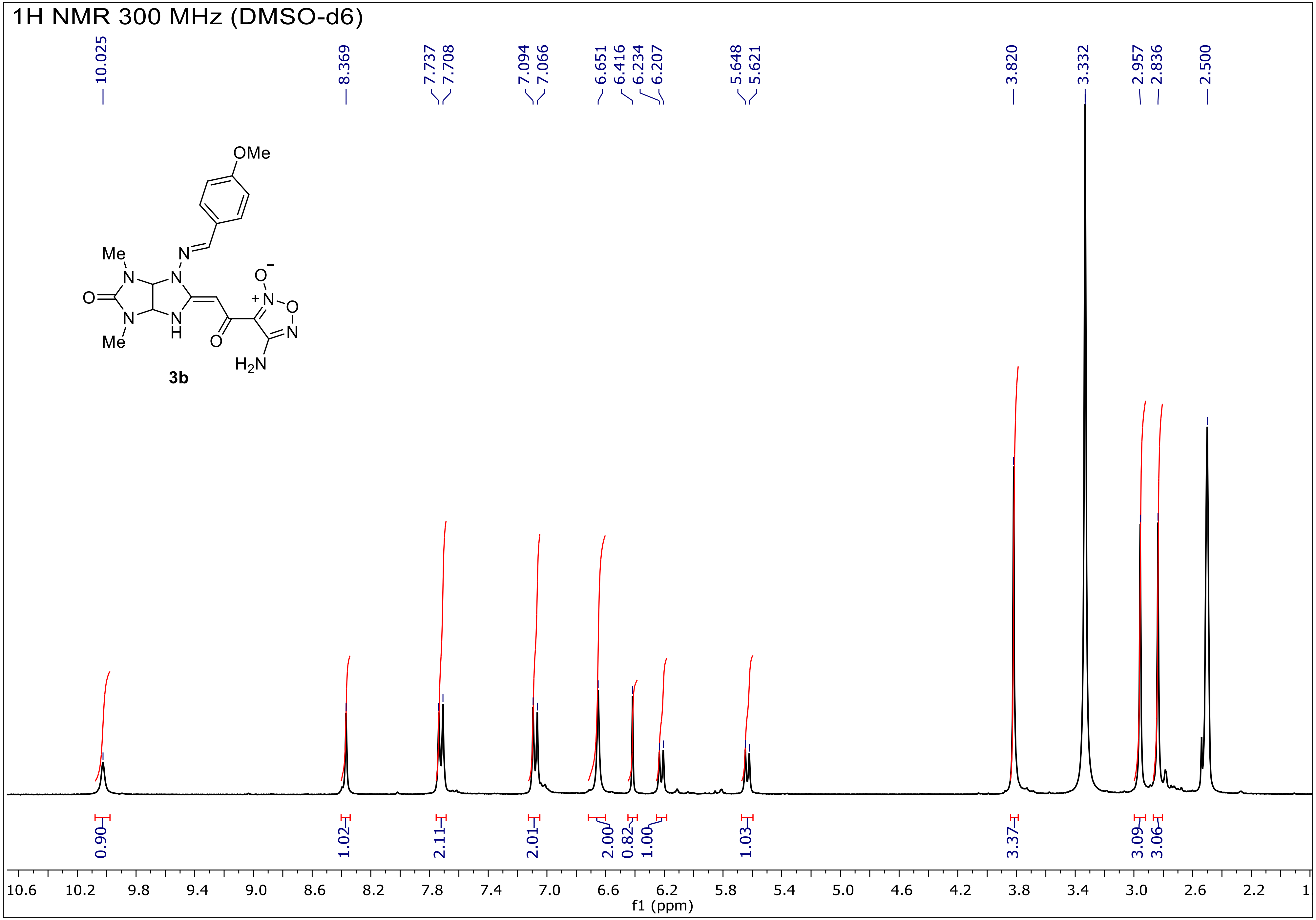
f1 (ppm)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N
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O
+N
O
N
H2N
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2.01
2.00
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1.03
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9.4
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8.2
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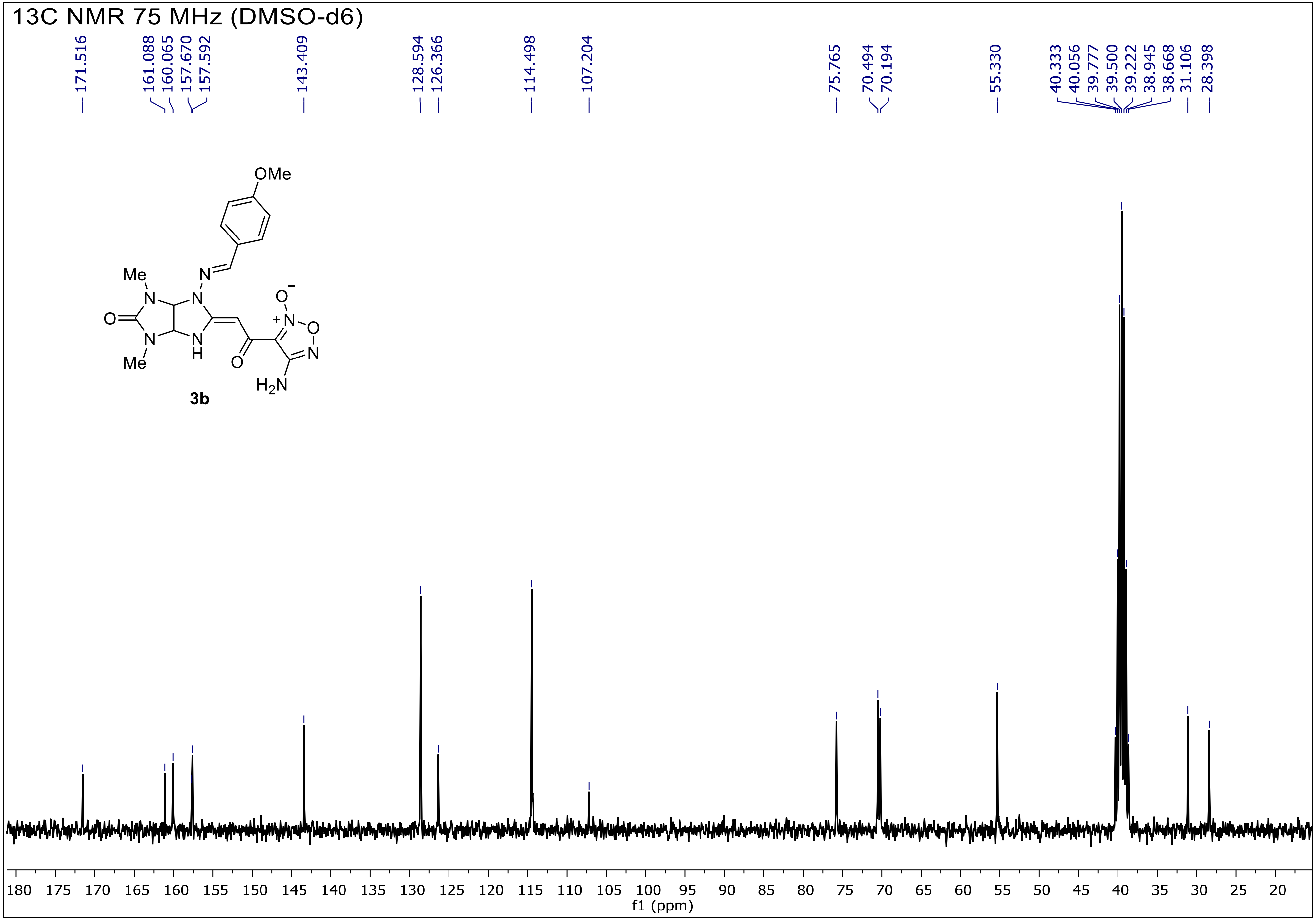
f1 (ppm)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N
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+N
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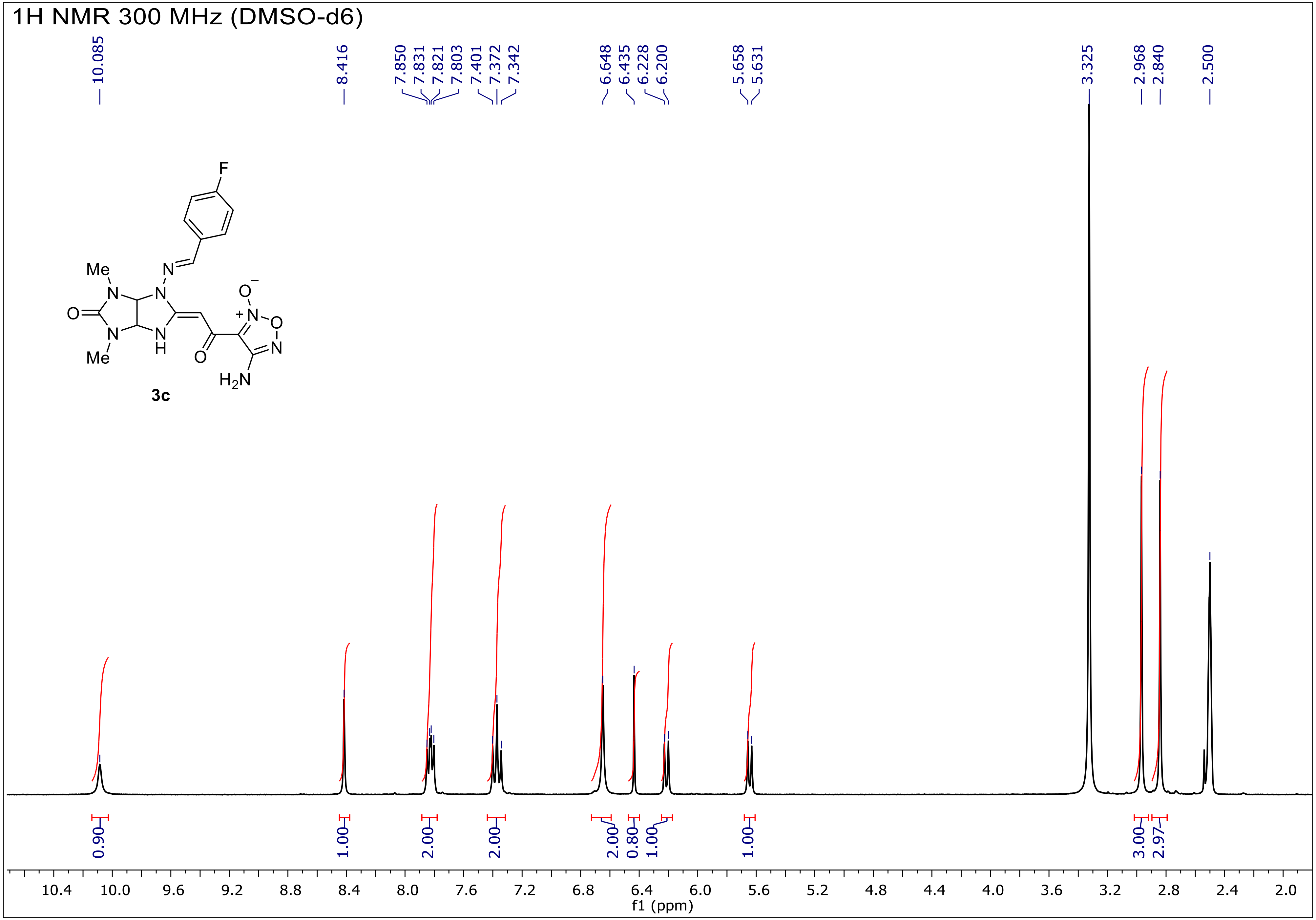
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5.658 5.631
3.325
2.968 2.840
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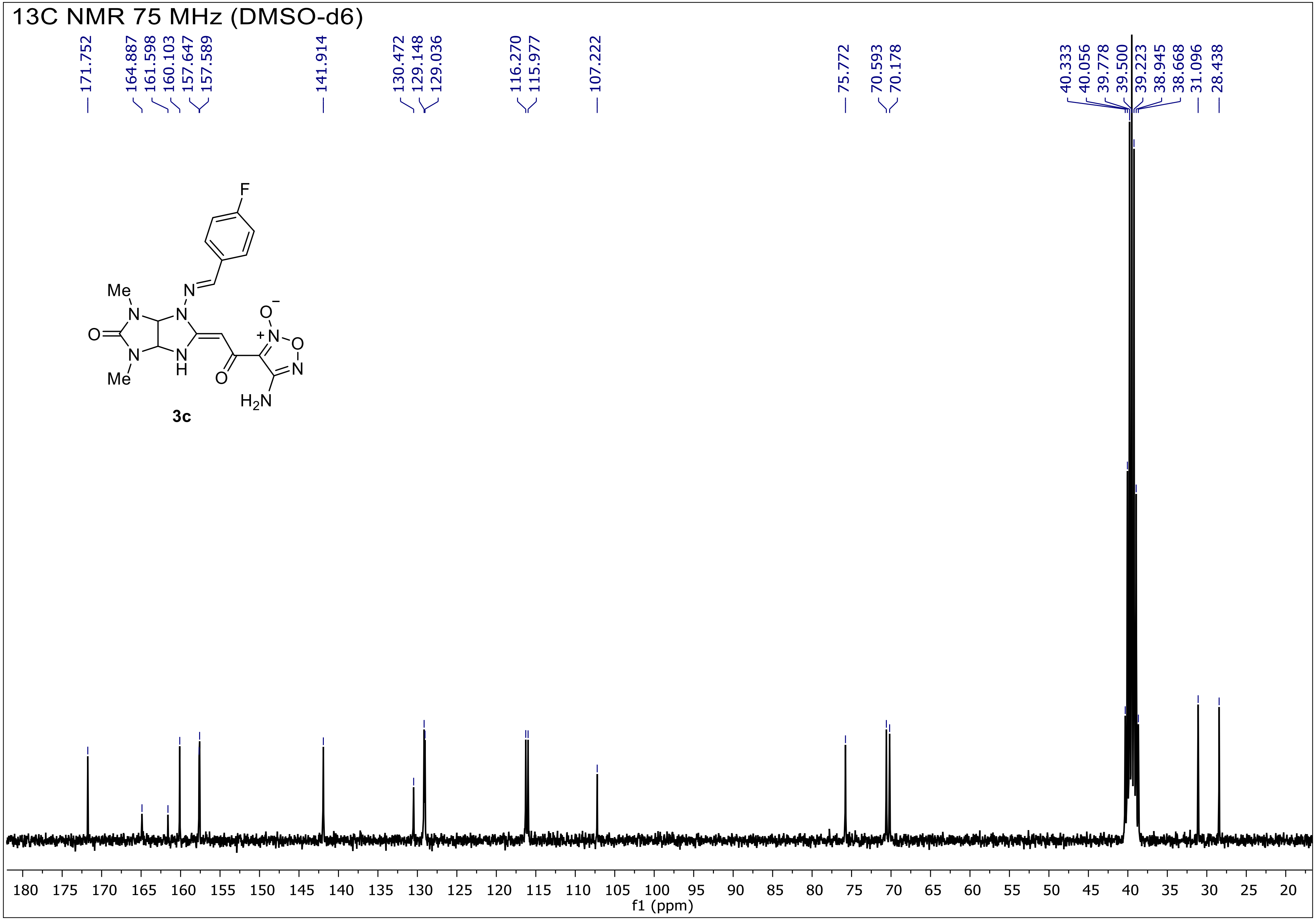
f1 (ppm)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Me
N
H
O
O
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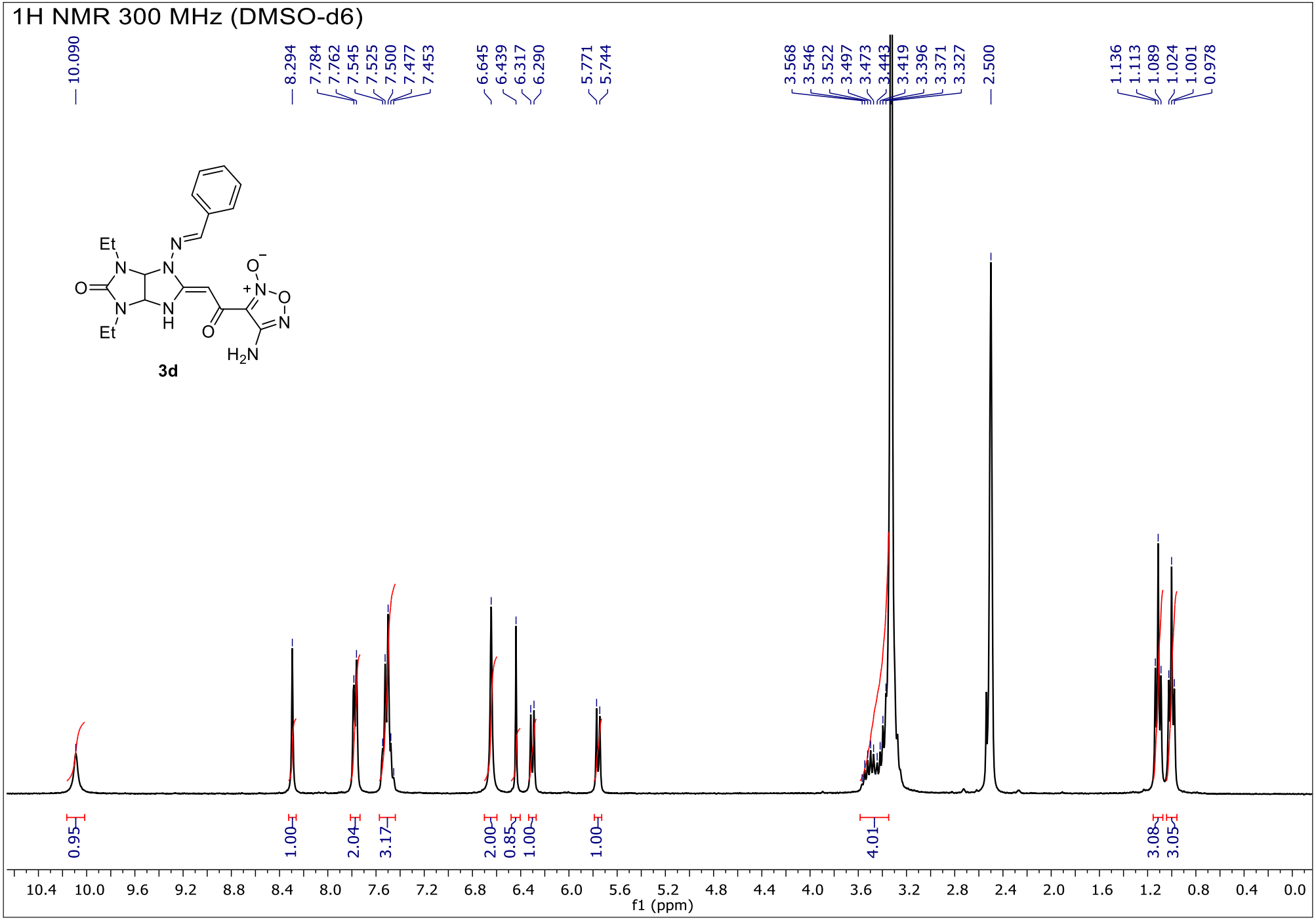
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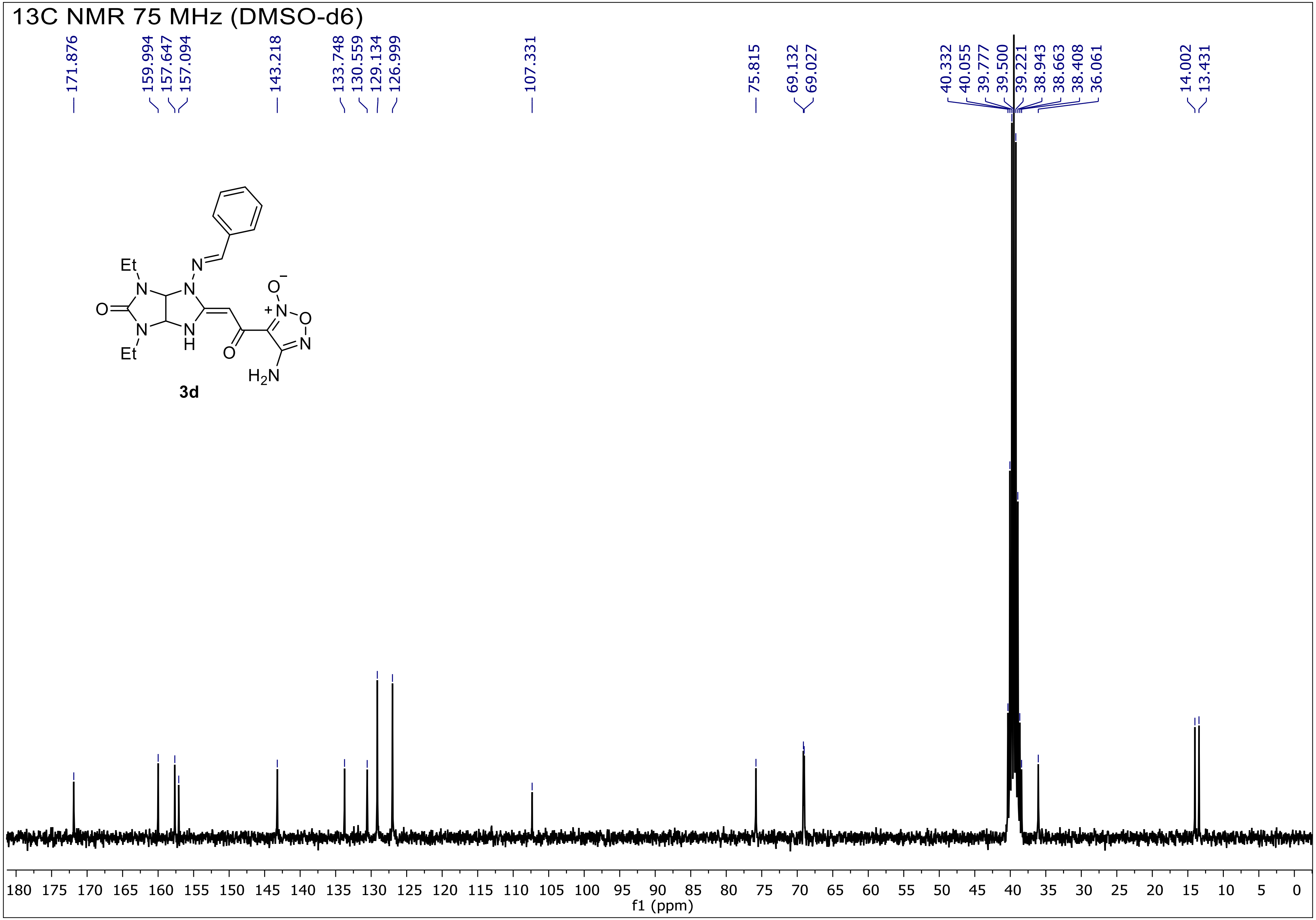

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40.055
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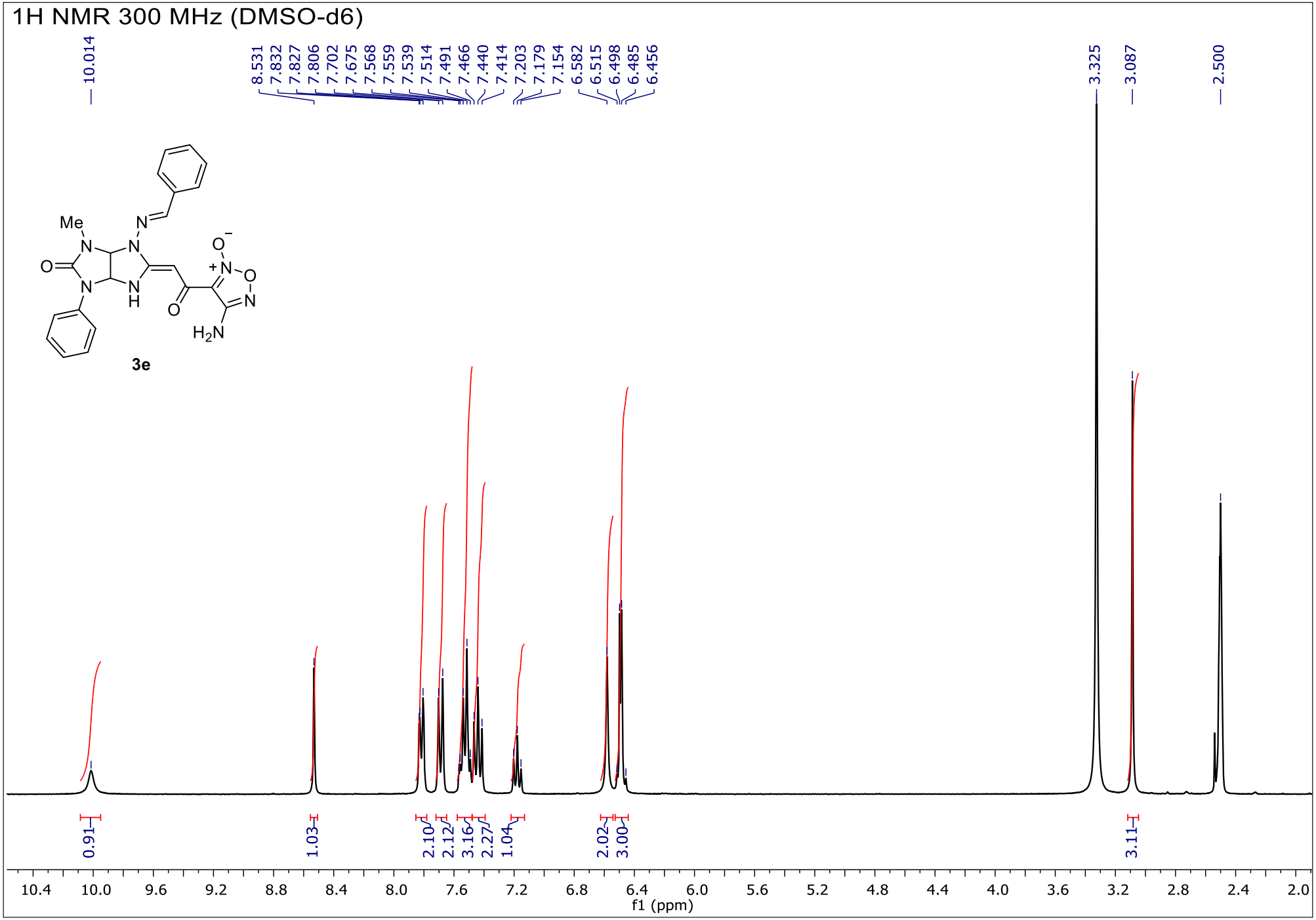
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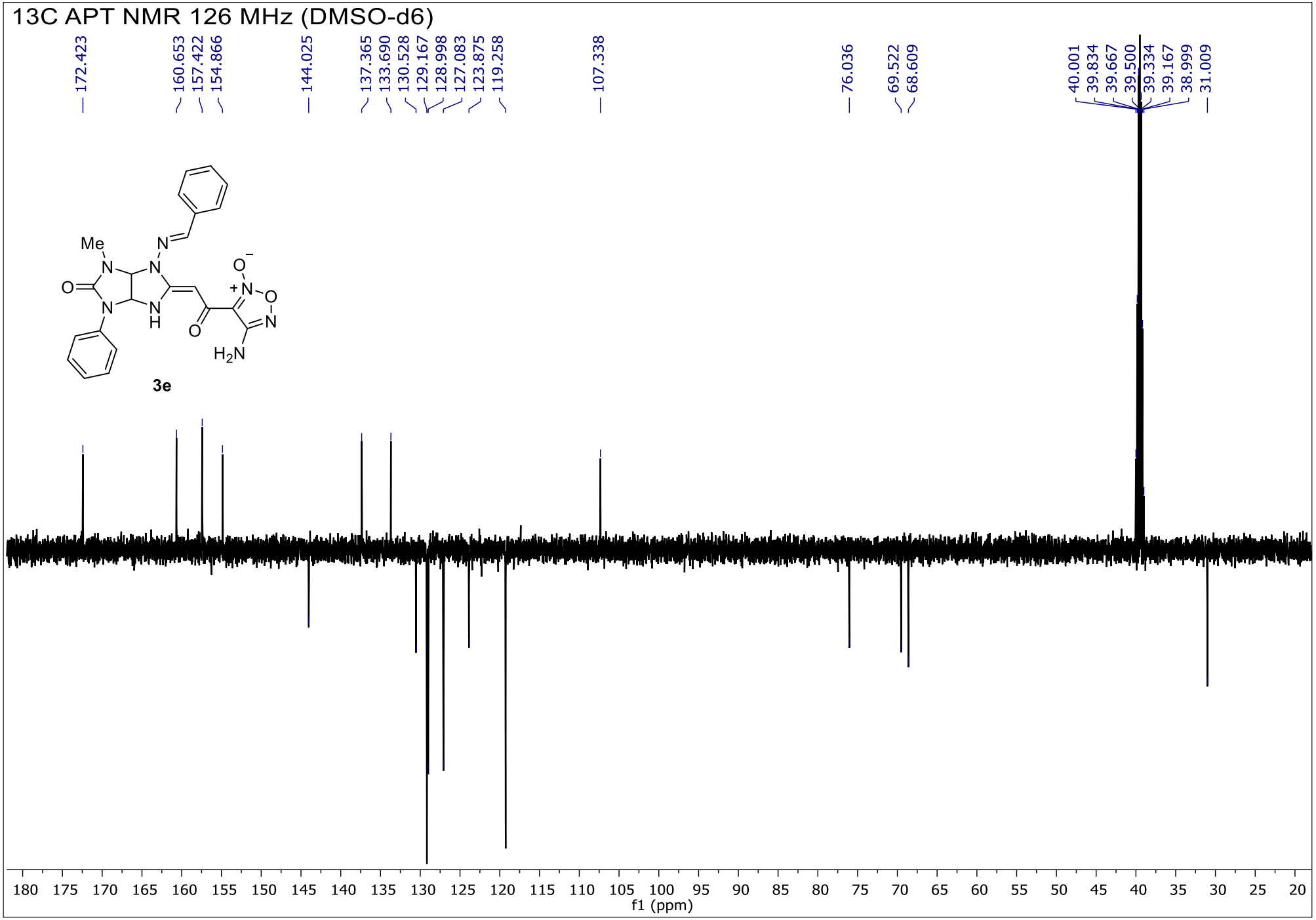
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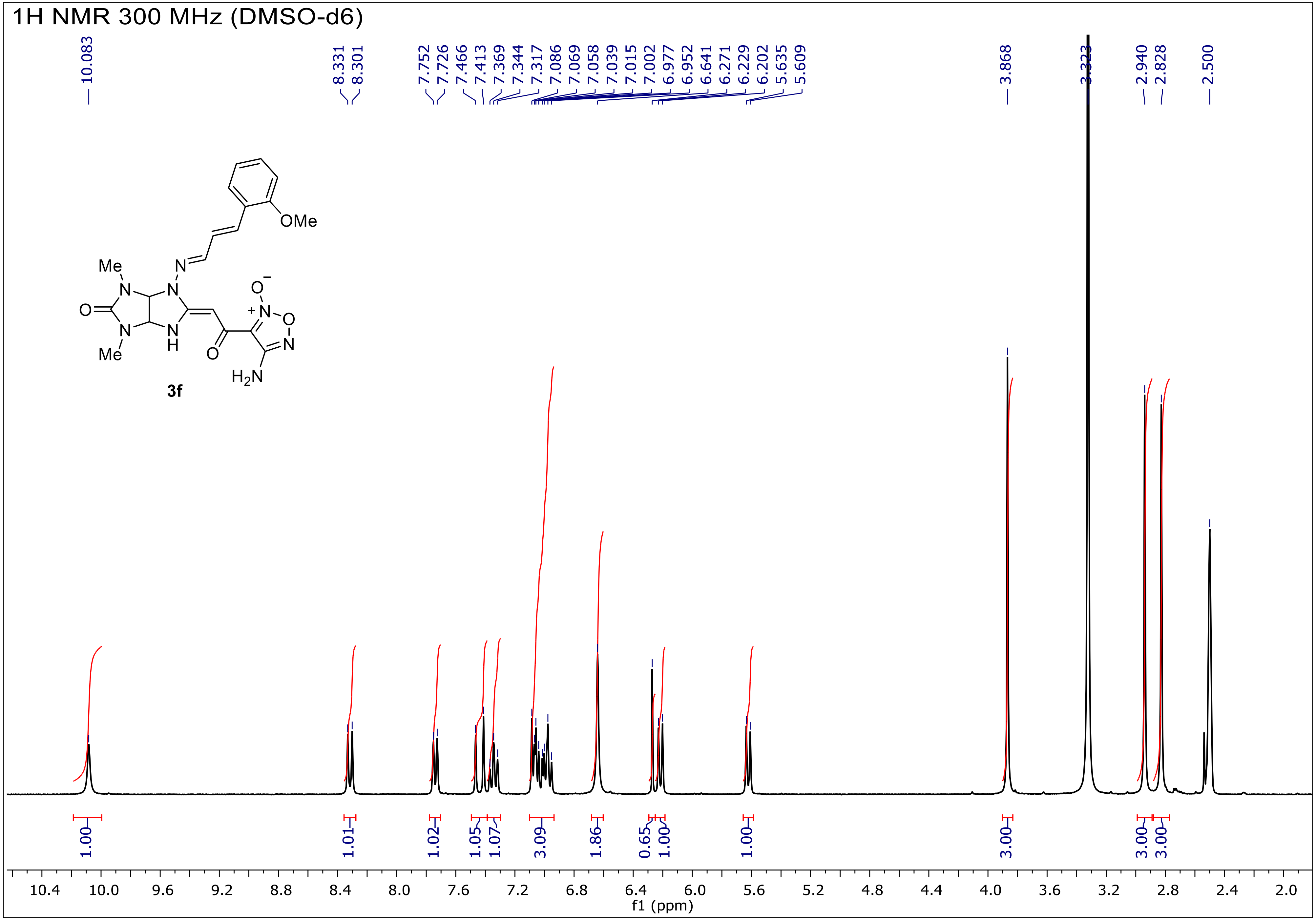
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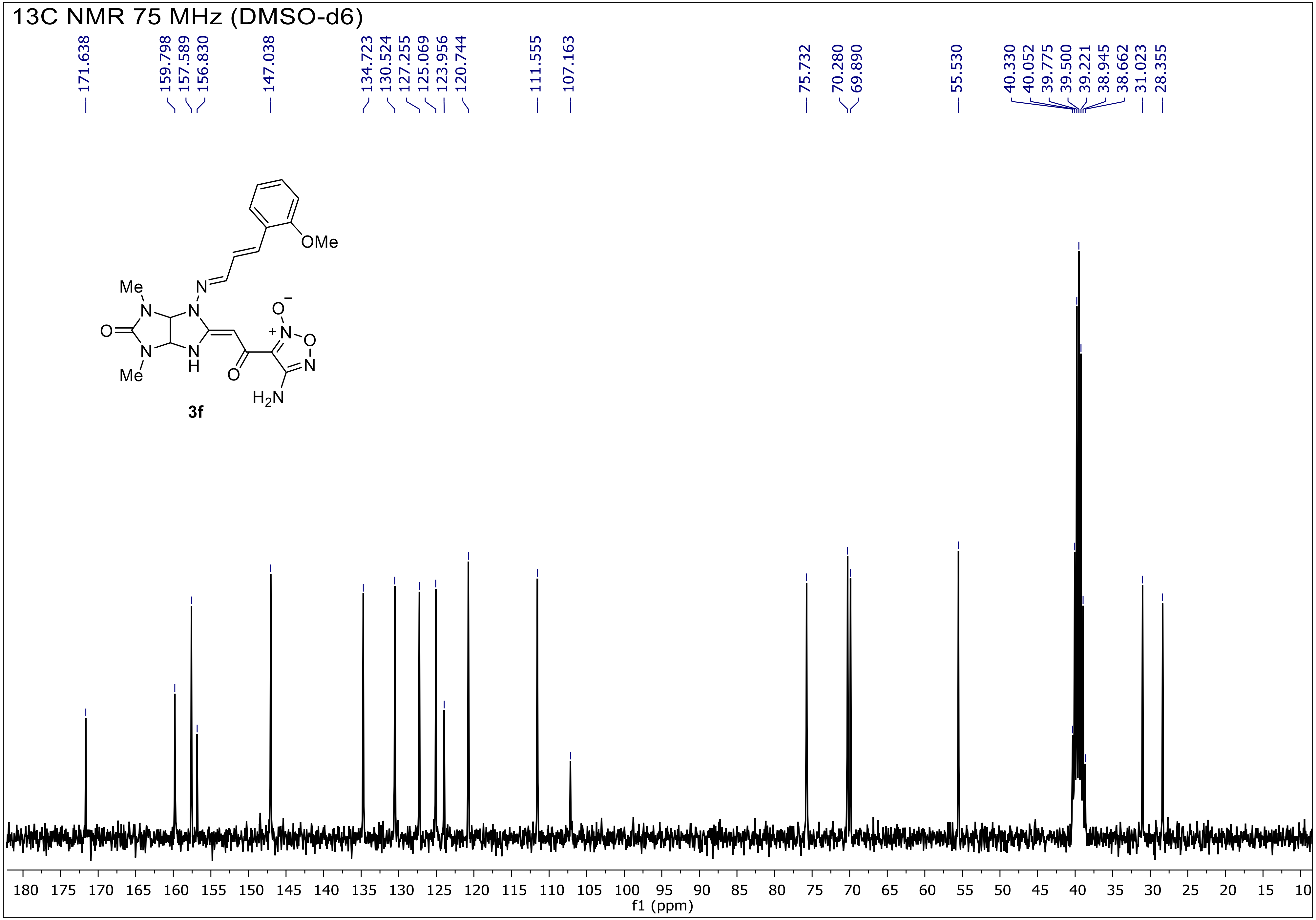
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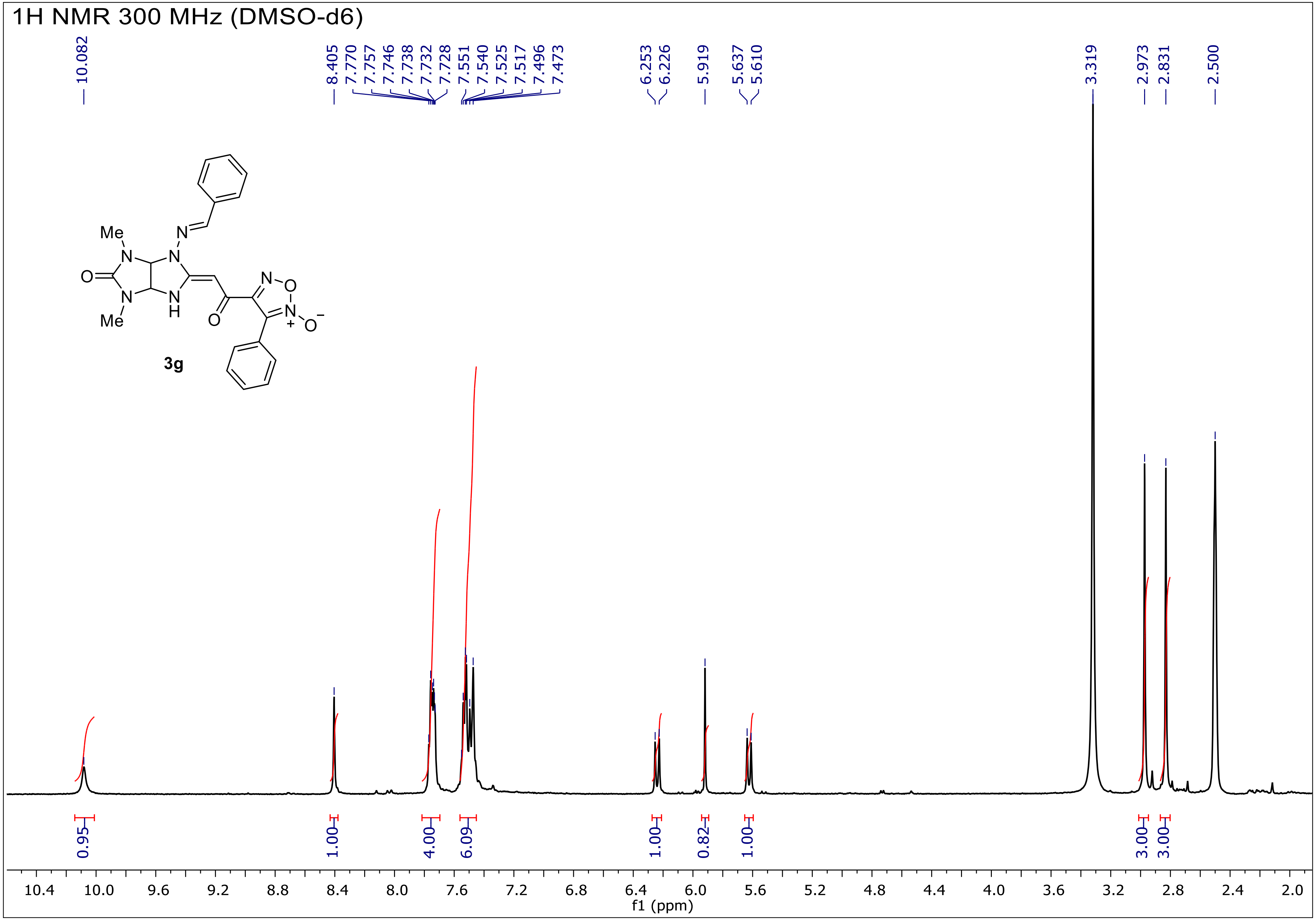
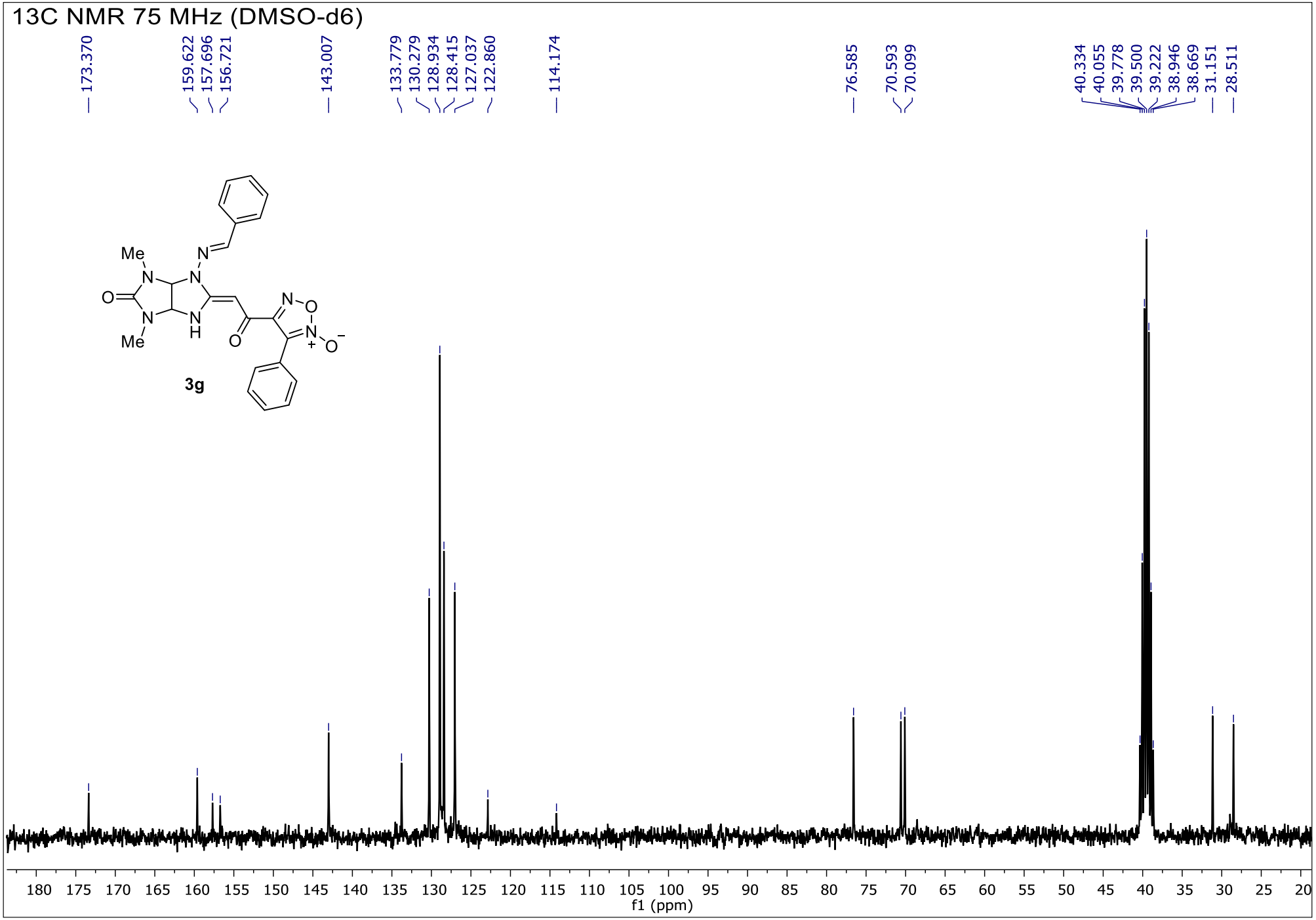
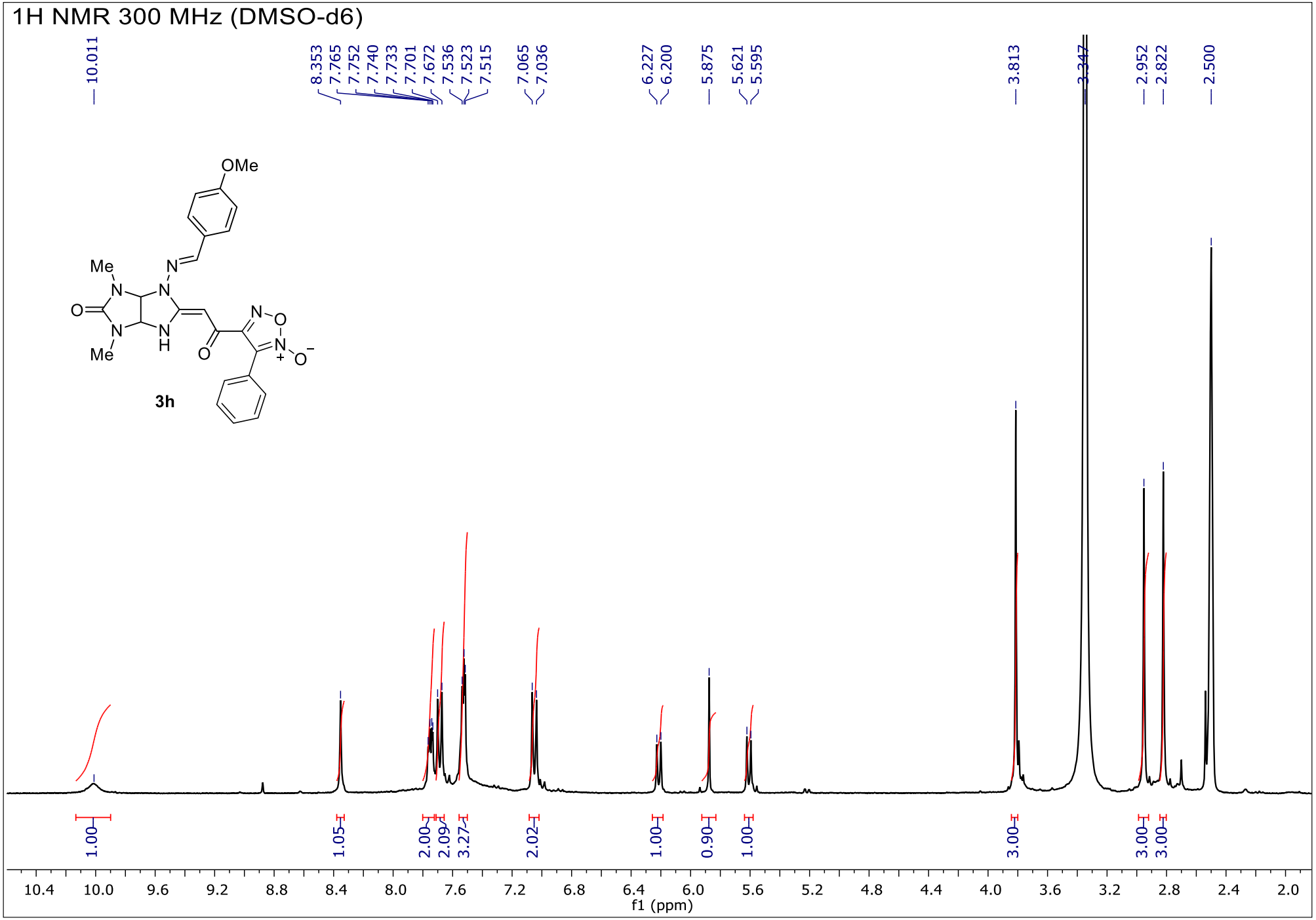
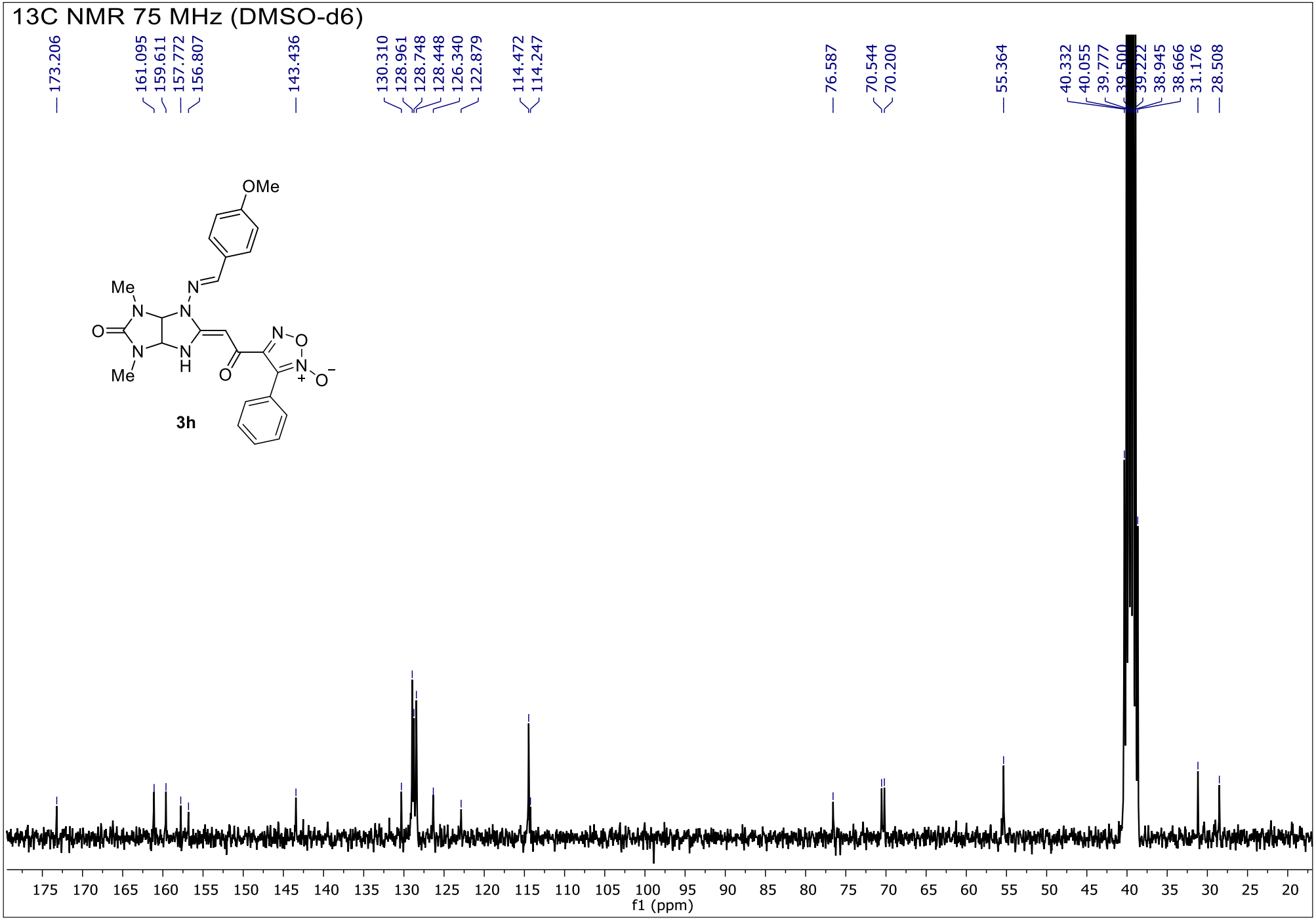
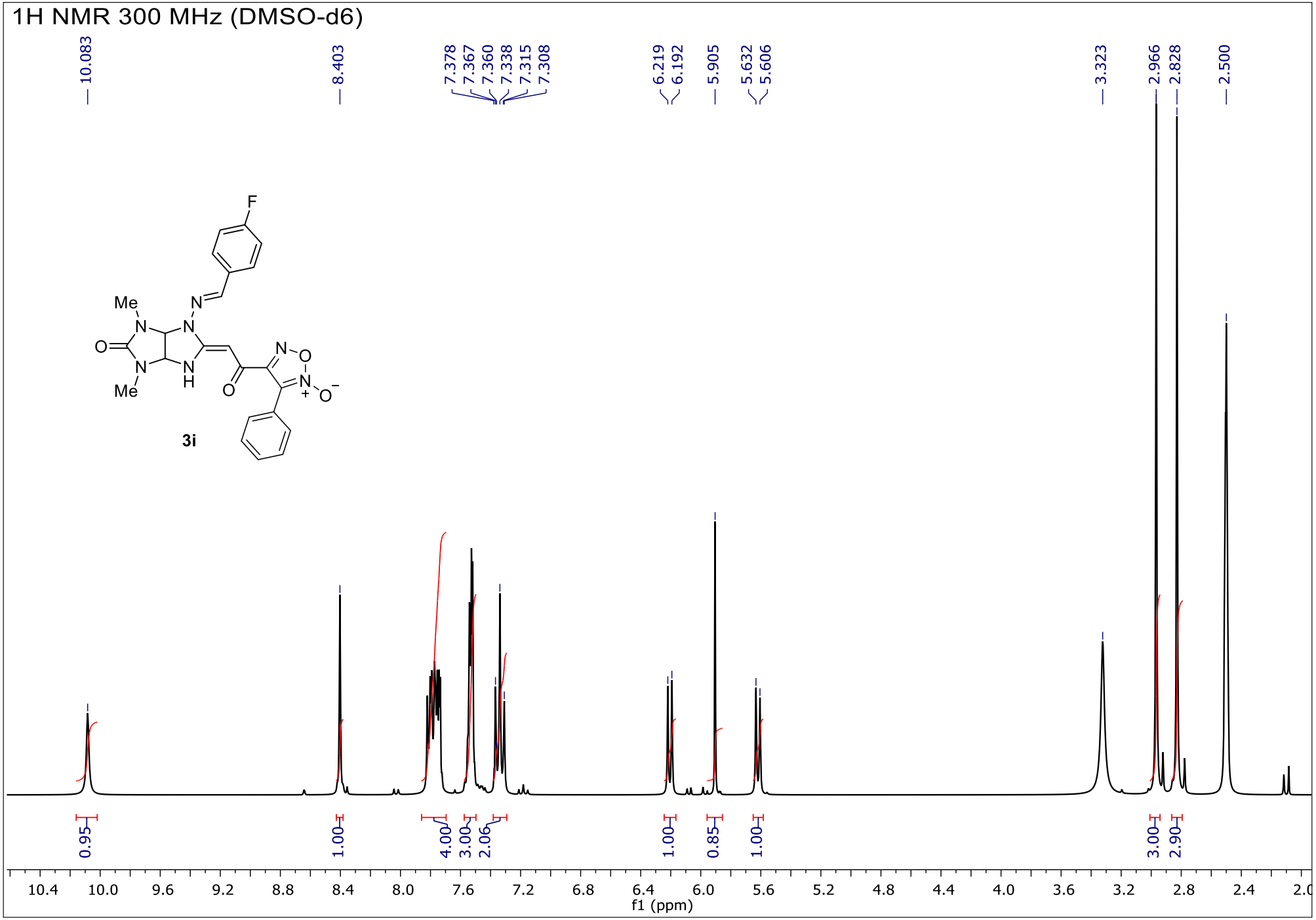
120.744
111.555
107.163
75.732
70.280
69.890
55.530
40.330
40.052
39.775
39.500
39.221
38.945
38.662
31.023
28.355
OMe
Me
N
O
H
H2N
3f
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10
f1 (ppm)

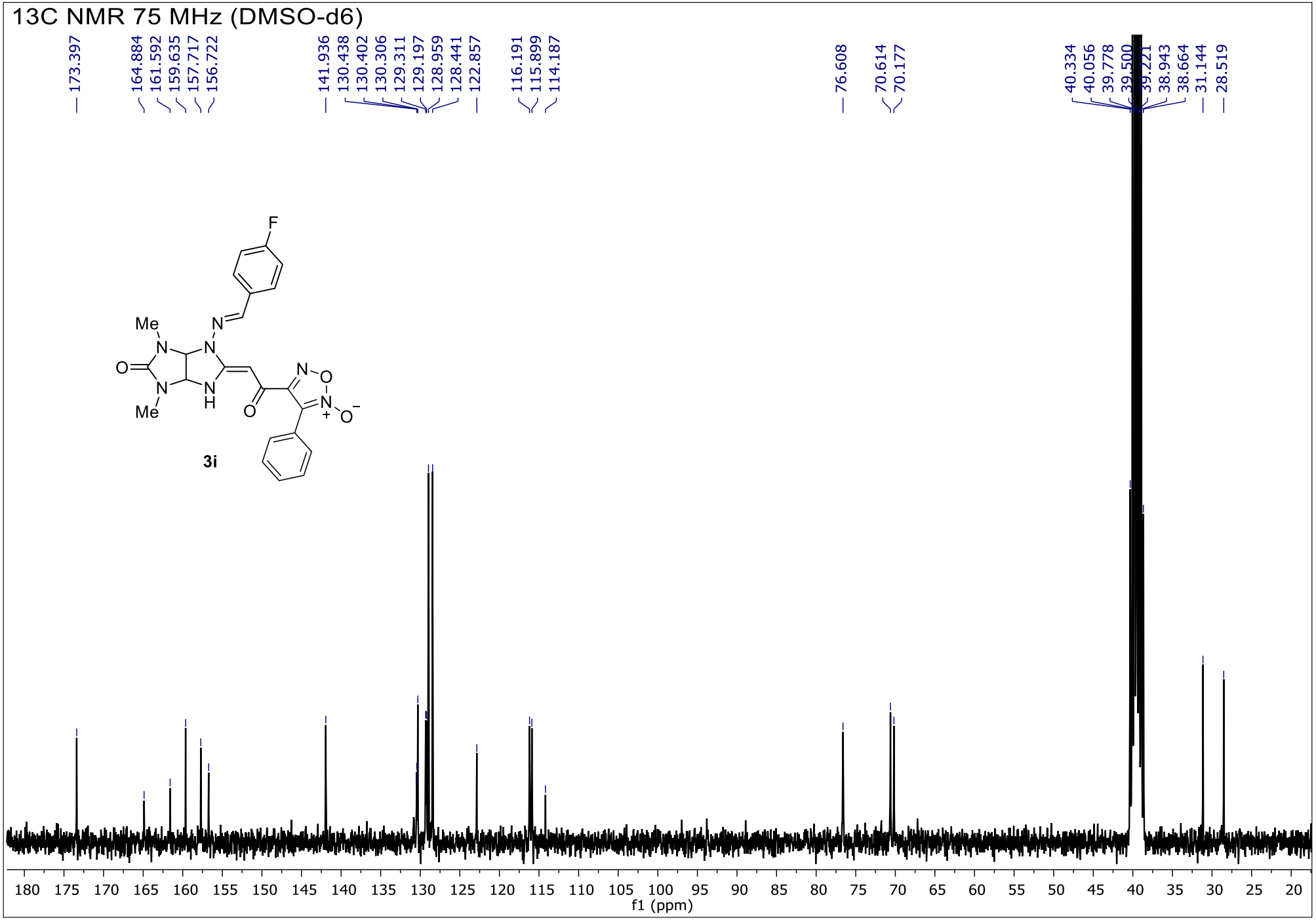

1H NMR 300 MHz (DMSO-d6)
10.082
8.405
7.770
7.757
7.746
7.738
7.732
7.728
7.551
7.540
7.525
7.517
7.496
7.473
6.253
6.226
5.919
5.637
5.610
3.319
2.973
2.831
2.500
Me
N
N
O
Me
H
3g
O
O
+
0.95
1.00
4.00
6.09
1.00
0.82
1.00
3.00
3.00
f1 (ppm)

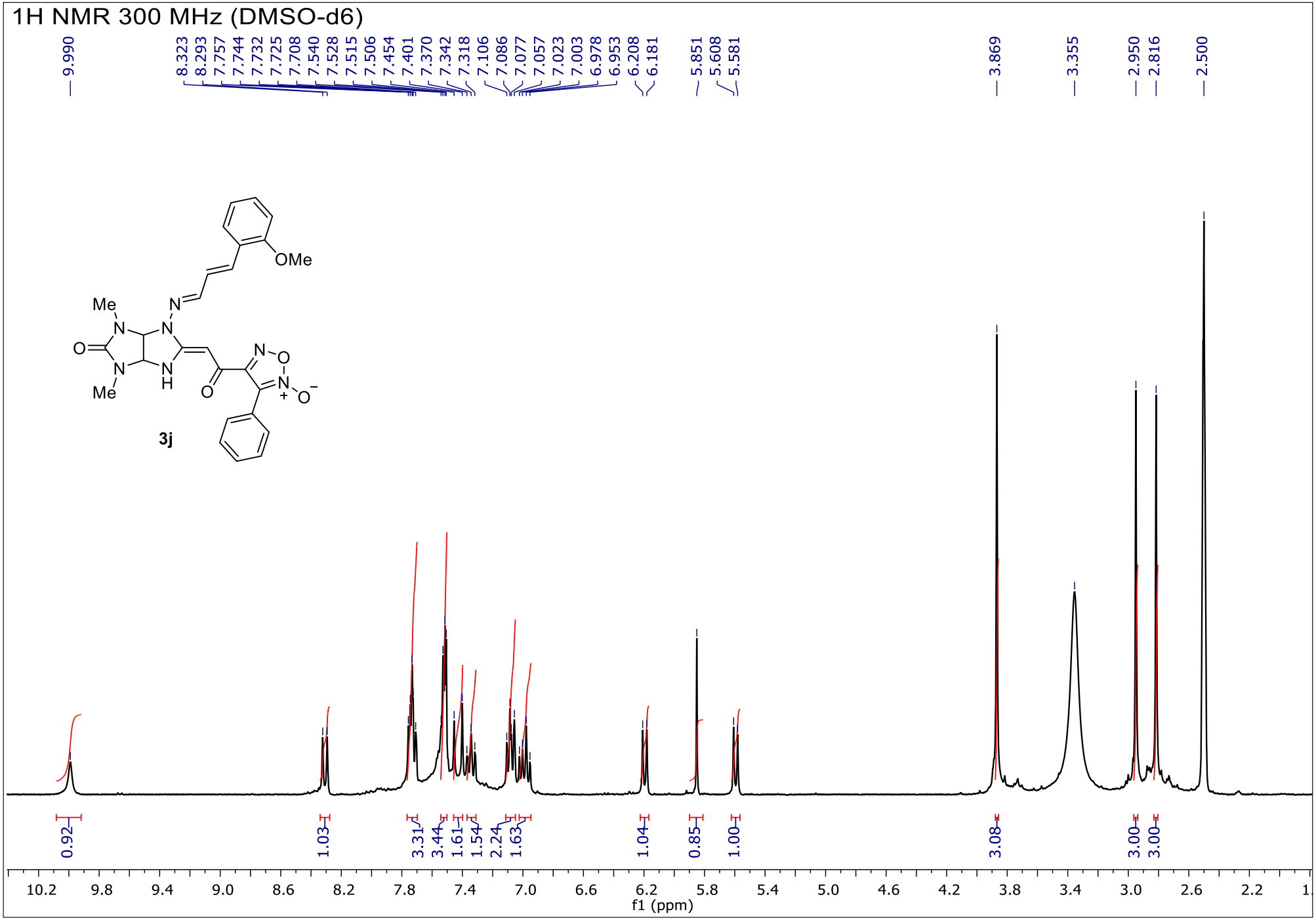

13C NMR 75 MHz (DMSO-d6)
173.370
159.622
157.696
156.721
143.007
133.779
130.279
128.934
128.415
127.037
122.860
114.174
76.585
70.593
70.099
40.334
40.055
39.778
39.500
39.222
38.946
38.669
31.151
28.511
Me
N
N
O
N
N
H
Me
O
N
O
N+
O−
3g
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

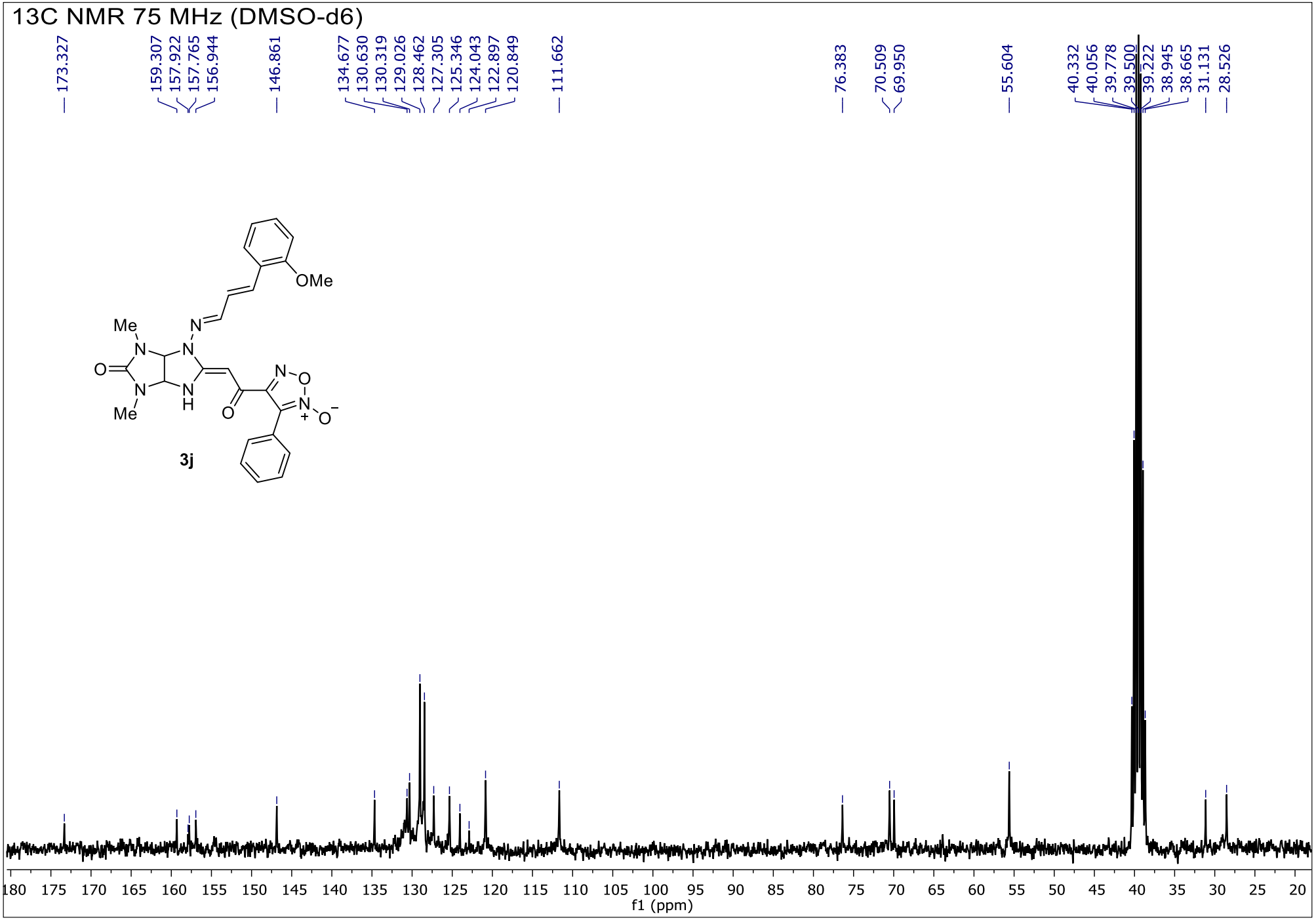

1H NMR 300 MHz (DMSO-d6)
10.011
8.353
7.765
7.752
7.740
7.733
7.701
7.672
7.536
7.523
7.515
7.065
7.036
6.227
6.200
5.875
5.621
5.595
3.813
3.347
2.952
2.822
2.500
OMe
Me
N
N
O
N
N
H
Me
N
O
N
O
O
3h
1.00
1.05
2.00
2.09
3.27
2.02
1.00
0.90
1.00
3.00
3.00
3.00
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)

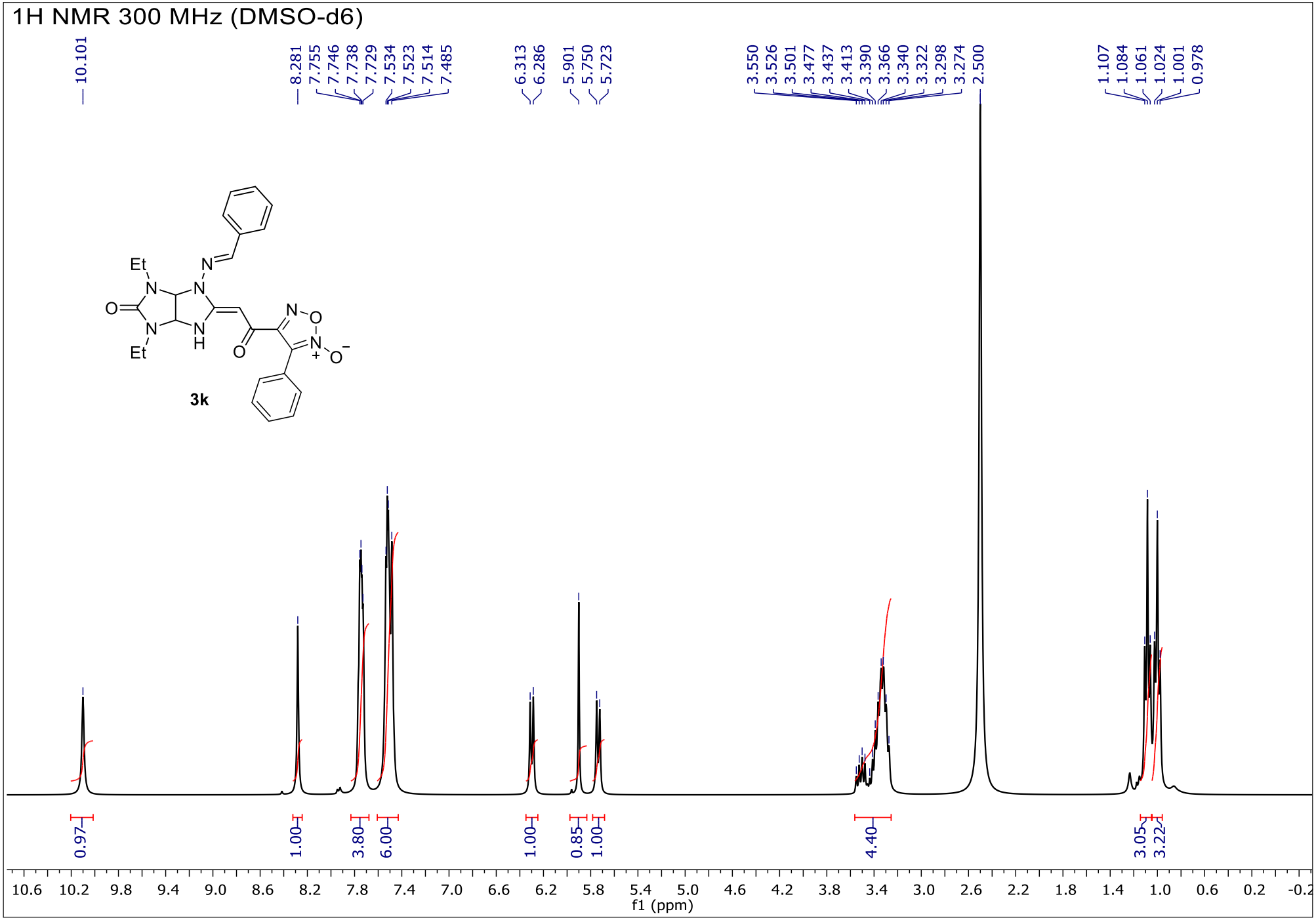

13C NMR 75 MHz (DMSO-d6)
173.206
161.095
159.611
157.772
156.807
143.436
130.310
128.961
128.748
128.448
126.340
122.879
114.472
114.247
76.587
70.544
70.200
55.364
40.332
40.055
39.777
39.500
39.222
38.945
38.666
31.176
28.508
OMe
Me
N
N
O
N
N
H
Me
O
N
O
N
+
O
−
3h
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

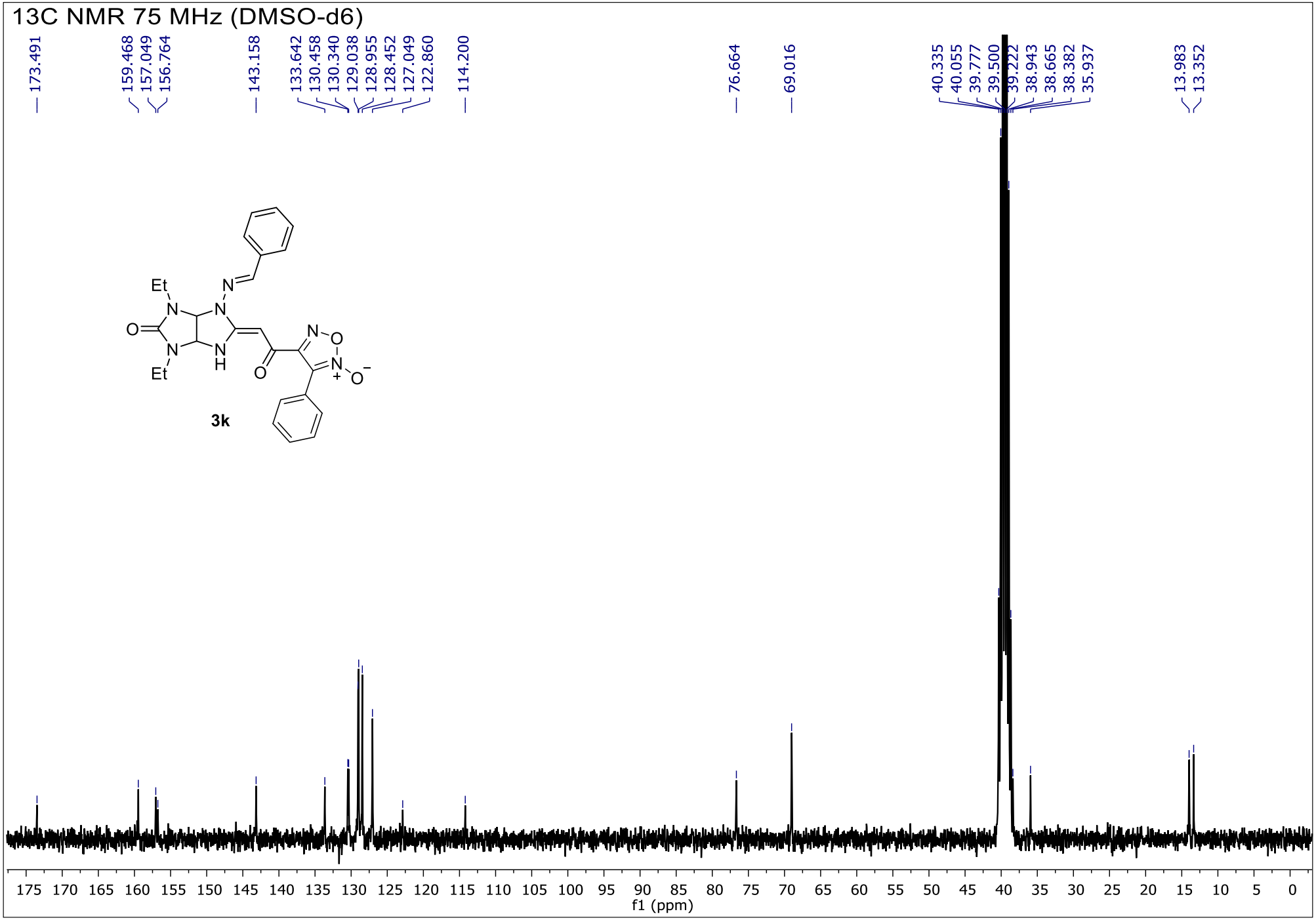

1H NMR 300 MHz (DMSO-d6)
10.083
8.403
7.378
7.367
7.360
7.338
7.315
7.308
6.219
6.192
5.905
5.632
5.606
3.323
2.966
2.828
2.500
F
Me
N
N
O
N
N
H
Me
O
N
O
N
+
O
−
3i
0.95
1.00
4.00
3.00
2.06
1.00
0.85
1.00
3.00
2.90
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
f1 (ppm)


13C NMR 75 MHz (DMSO-d6)
173.397
164.884
161.592
159.635
157.717
156.722
141.936
130.438
130.402
130.306
129.311
129.197
128.959
128.441
122.857
116.191
115.899
114.187
76.608
70.614
70.177
40.334
40.056
39.778
39.500
39.221
38.943
38.664
31.144
28.519
F
Me
N
N
O
N
N
H
Me
O
N
O
N
+
O
−
3i
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

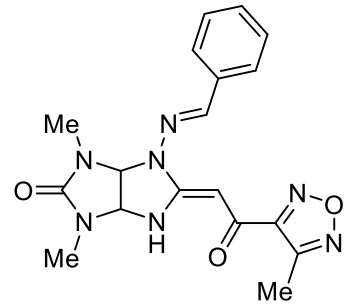

1H NMR 300 MHz (DMSO-d6)
9.990
8.323
8.293
7.757
7.744
7.732
7.725
7.708
7.540
7.528
7.515
7.506
7.454
7.401
7.370
7.342
7.318
7.106
7.086
7.077
7.057
7.023
7.003
6.978
6.953
6.208
6.181
5.851
5.608
5.581
3.869
3.355
2.950
2.816
2.500
OMe
Me
N
N
O
N
N
H
Me
O
N
O
N
O
3j
0.92
1.03
3.31
3.44
1.61
1.54
2.24
1.63
1.04
0.85
1.00
3.08
3.00
3.00
10.2
9.8
9.4
9.0
8.6
8.2
7.8
7.4
7.0
6.6
6.2
5.8
5.4
5.0
4.6
4.2
3.8
3.4
3.0
2.6
2.2
f1 (ppm)


13C NMR 75 MHz (DMSO-d6)
173.327
159.307
157.922
157.765
156.944
146.861
134.677
130.630
130.319
129.026
128.462
127.305
125.346
124.043
122.897
120.849
111.662
76.383
70.509
69.950
55.604
40.332
40.056
39.778
39.500
39.222
38.945
38.665
31.131
28.526
OMe
Me
N
N
O
N
N
H
Me
N
O
O
N
+
O
−
3j
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20
f1 (ppm)

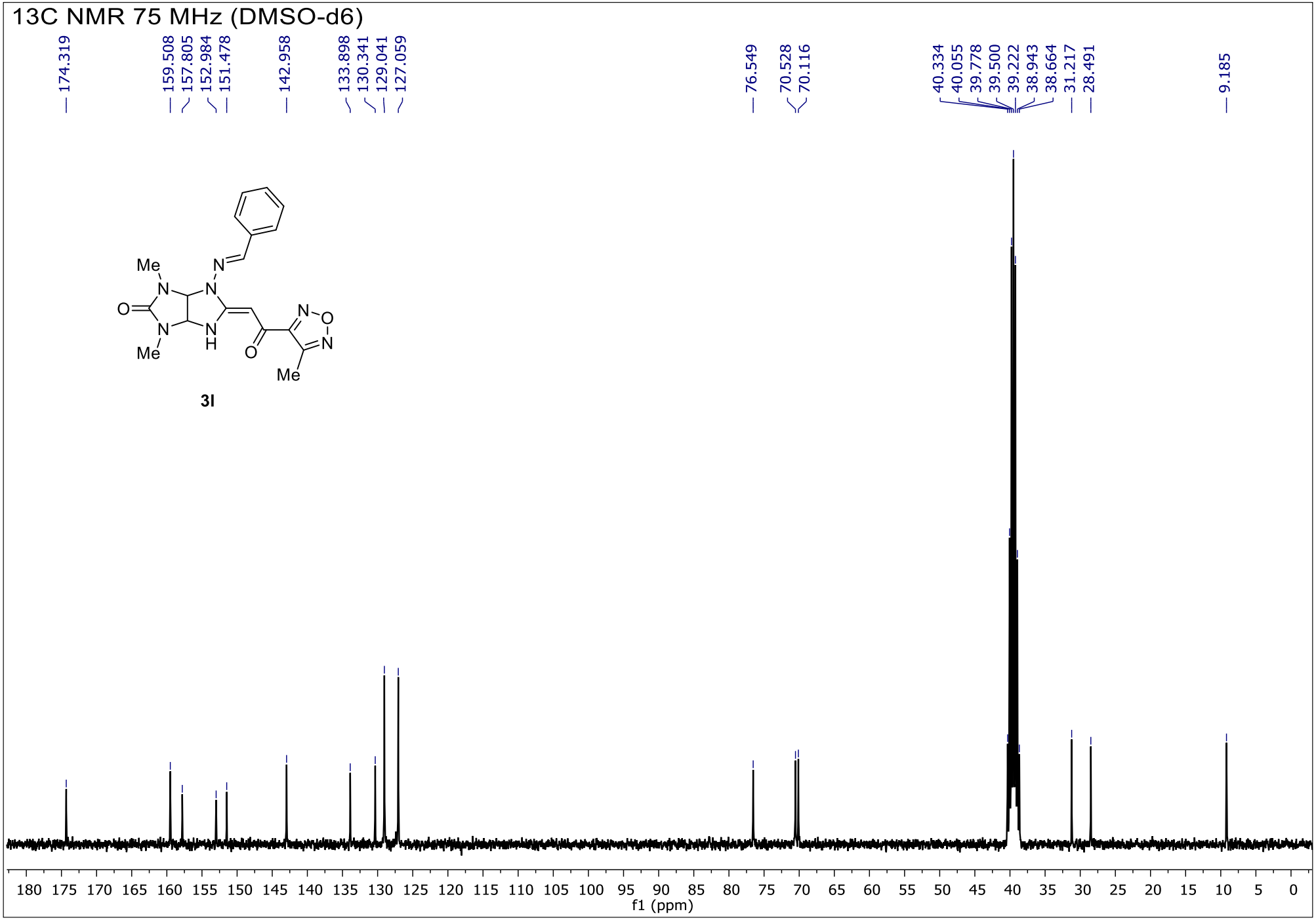

1H NMR 300 MHz (DMSO-d6)
10.101
8.281
7.755
7.746
7.738
7.729
7.534
7.523
7.514
7.485
6.313
6.286
5.901
5.750
5.723
3.550
3.526
3.501
3.477
3.437
3.413
3.390
3.366
3.340
3.322
3.298
3.274
2.500
1.107
1.084
1.061
1.024
1.001
0.978
3k
0.97
1.00
3.80
6.00
1.00
0.85
1.00
4.40
3.05
3.22
f1 (ppm)

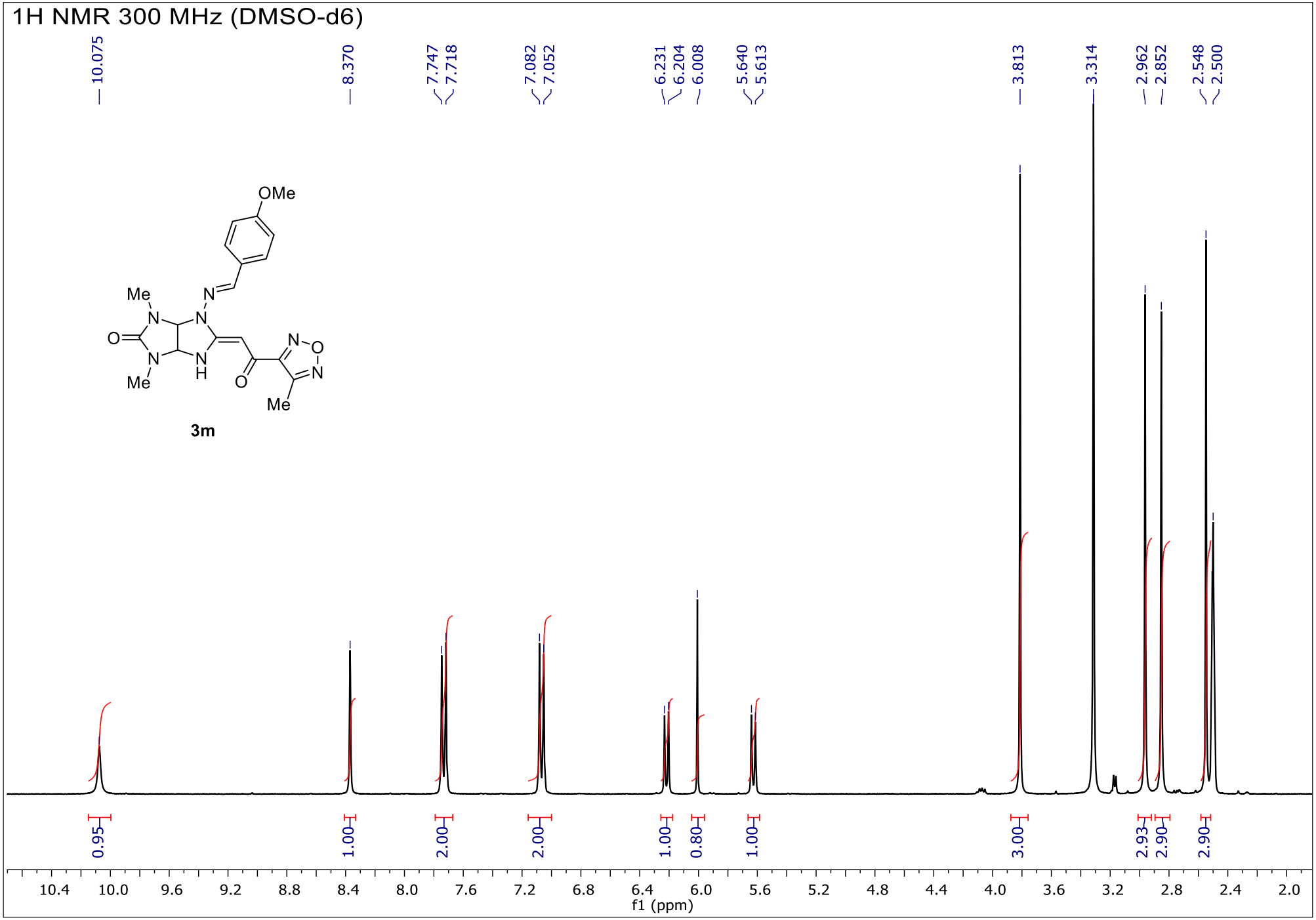

13C NMR 75 MHz (DMSO-d6)
173.491
159.468
157.049
156.764
143.158
133.642
130.458
130.340
129.038
128.955
128.452
127.049
122.860
114.200
76.664
69.016
40.335
40.055
39.777
39.500
39.222
38.943
38.665
38.382
35.937
13.983
13.352
Et
N
N
O
N
N
H
Et
O
N
O
N
O
3k
175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

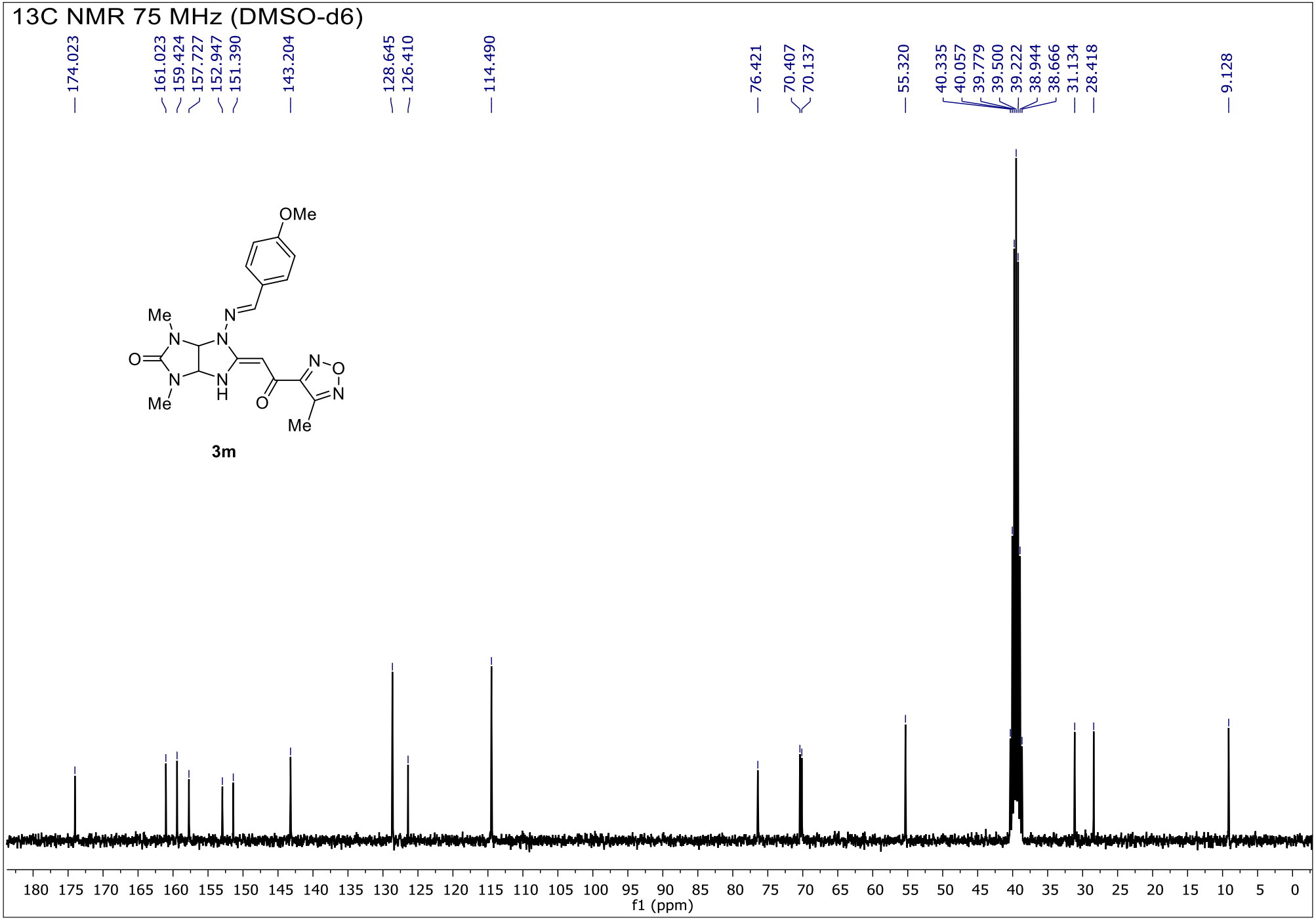
1H NMR 300 MHz (DMSO-d6)

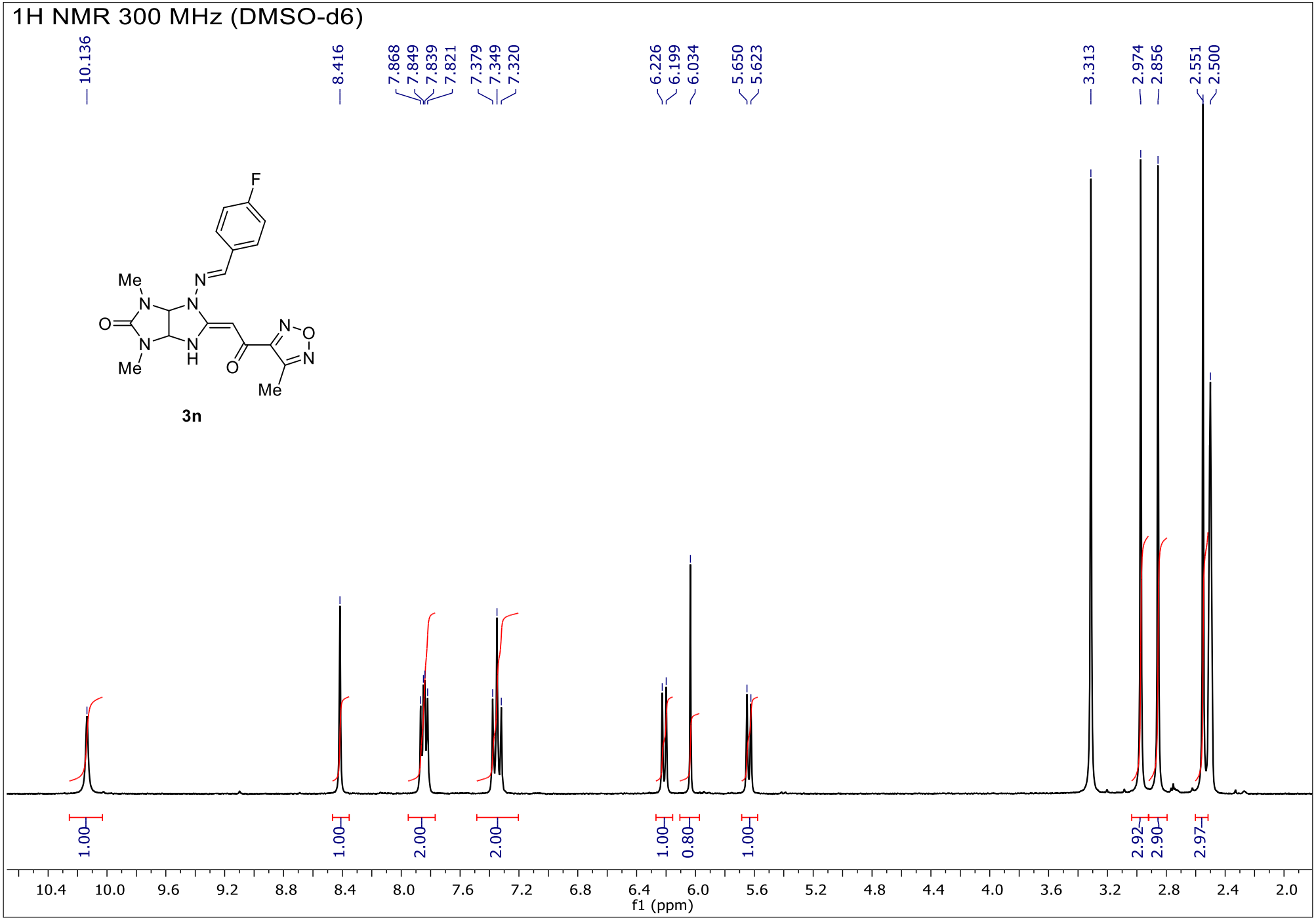


3l


13C NMR 75 MHz (DMSO-d6)
174.319
159.508
157.805
152.984
151.478
142.958
133.898
130.341
129.041
127.059
76.549
70.528
70.116
40.334
40.055
39.778
39.500
39.222
38.943
38.664
31.217
28.491
9.185
Me
N
N
O
N
N
H
Me
O
N
O
N
Me
3l
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)


1H NMR 300 MHz (DMSO-d6)
10.075
8.370
7.747
7.718
7.082
7.052
6.231
6.204
6.008
5.640
5.613
3.813
3.314
2.962
2.852
2.548
2.500
OMe
Me
N
N
N
N
O
N
H
O
N
O
N
Me
Me
3m
0.95
1.00
2.00
2.00
1.00
0.80
1.00
3.00
2.93
2.90
2.90
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)


13C NMR 75 MHz (DMSO-d6)
174.023
161.023
159.424
157.727
152.947
151.390
143.204
128.645
126.410
114.490
76.421
70.407
70.137
55.320
40.335
40.057
39.779
39.500
39.222
38.944
38.666
31.134
28.418
9.128
OMe
Me
N
N
O
N
N
H
N
O
N
O
Me
Me
3m
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)


1H NMR 300 MHz (DMSO-d6)
10.136
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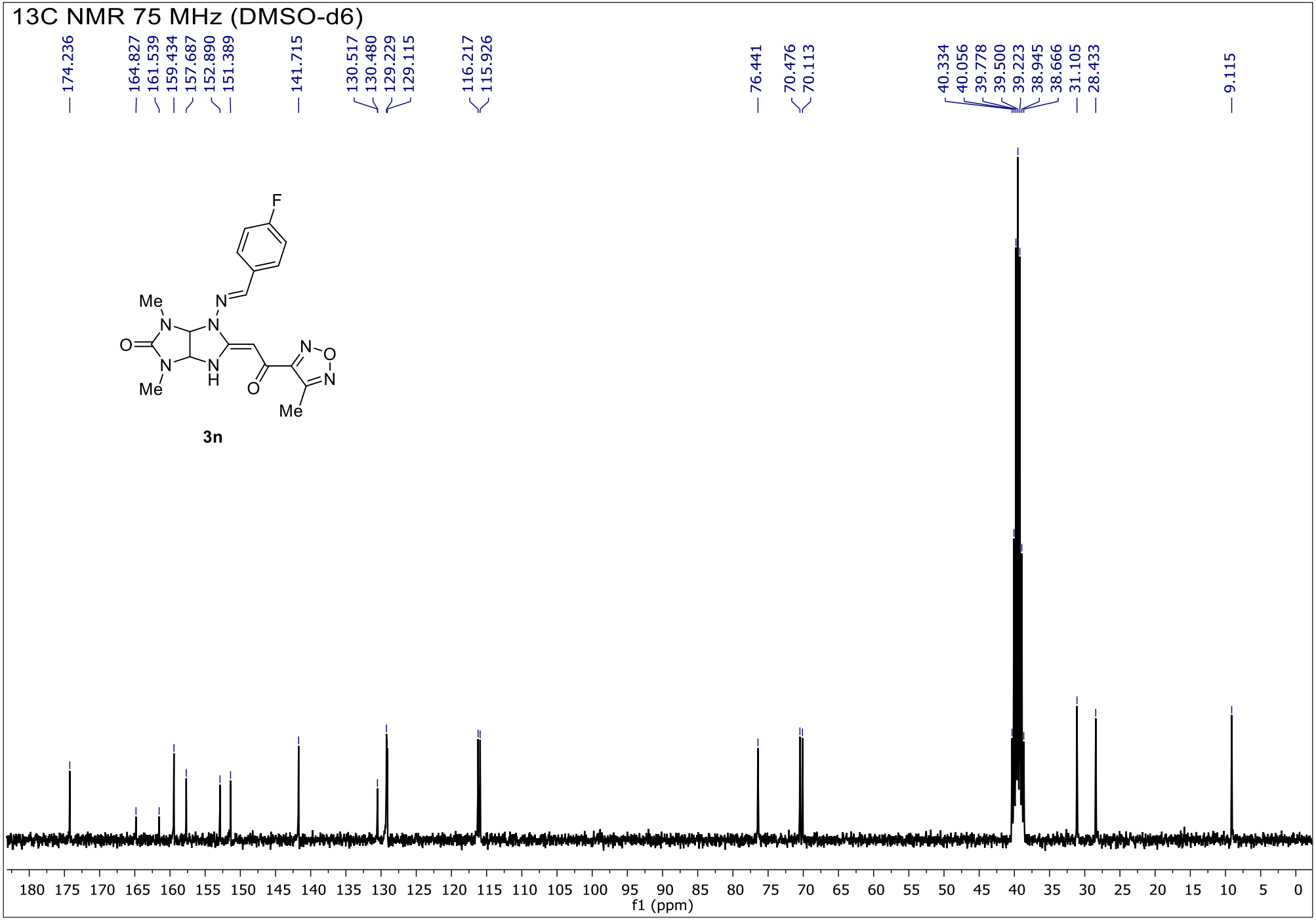
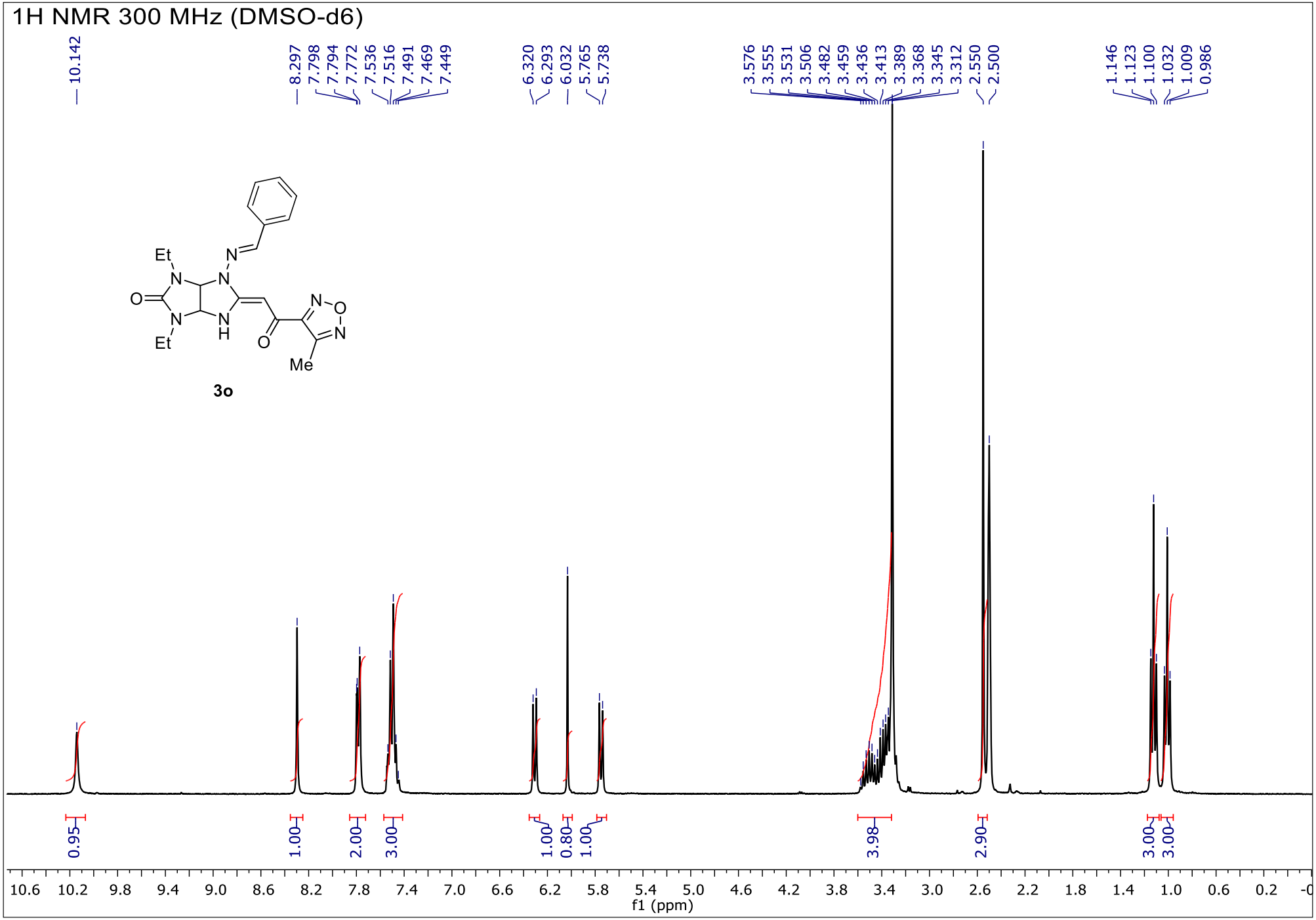
7.849
7.839
7.821
7.379
7.349
7.320
6.226
6.199
6.034
5.650
5.623
3.313
2.974
2.856
2.551
2.500
F
Me
N
N
O
N
N
H
O
N
O
N
Me
Me
3n
1.00
1.00
2.00
2.00
1.00
0.80
1.00
2.92
2.90
2.97
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)


13C NMR 75 MHz (DMSO-d6)
174.236
164.827
161.539
159.434
157.687
152.890
151.389
141.715
130.517
130.480
129.229
129.115
116.217
115.926
76.441
70.476
70.113
40.334
40.056
39.778
39.500
39.223
38.945
38.666
31.105
28.433
9.115
F
Me
N
N
N
O
N
H
O
N
O
N
Me
Me
3n
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)


1H NMR 300 MHz (DMSO-d6)
10.142
8.297
7.798
7.794
7.772
7.536
7.516
7.491
7.469
7.449
6.320
6.293
6.032
5.765
5.738
3.576
3.555
3.531
3.506
3.482
3.459
3.436
3.413
3.389
3.368
3.345
3.312
2.550
2.500
1.146
1.123
1.100
1.032
1.009
0.986
Et
N
N
O
N
N
H
Et
O
N
O
N
Me
0.95
1.00
2.00
3.00
1.00
0.80
1.00
3.98
2.90
3.00
3.00
10.6
10.2
9.8
9.4
9.0
8.6
8.2
7.8
7.4
7.0
6.6
6.2
5.8
5.4
5.0
4.6
4.2
3.8
3.4
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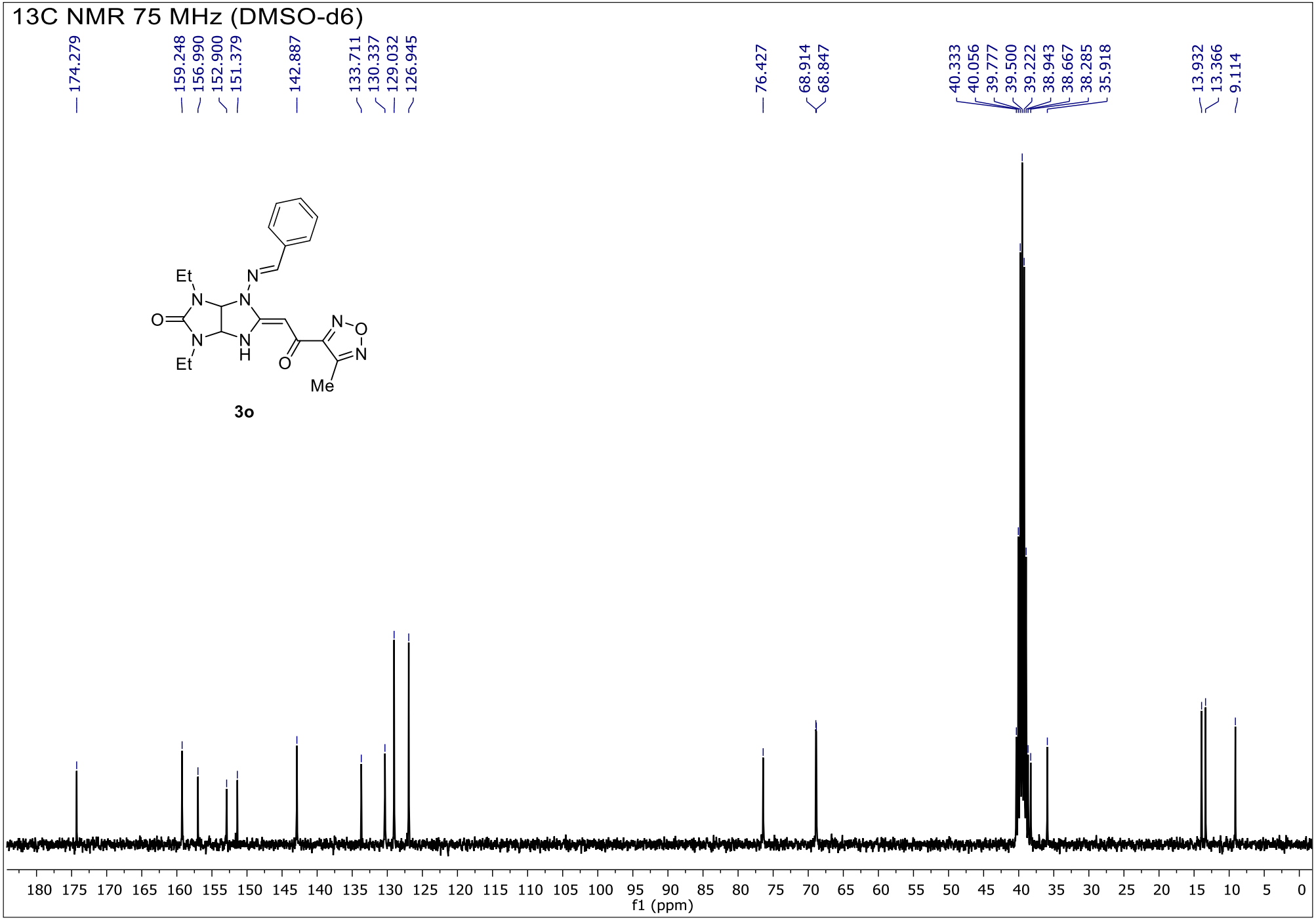
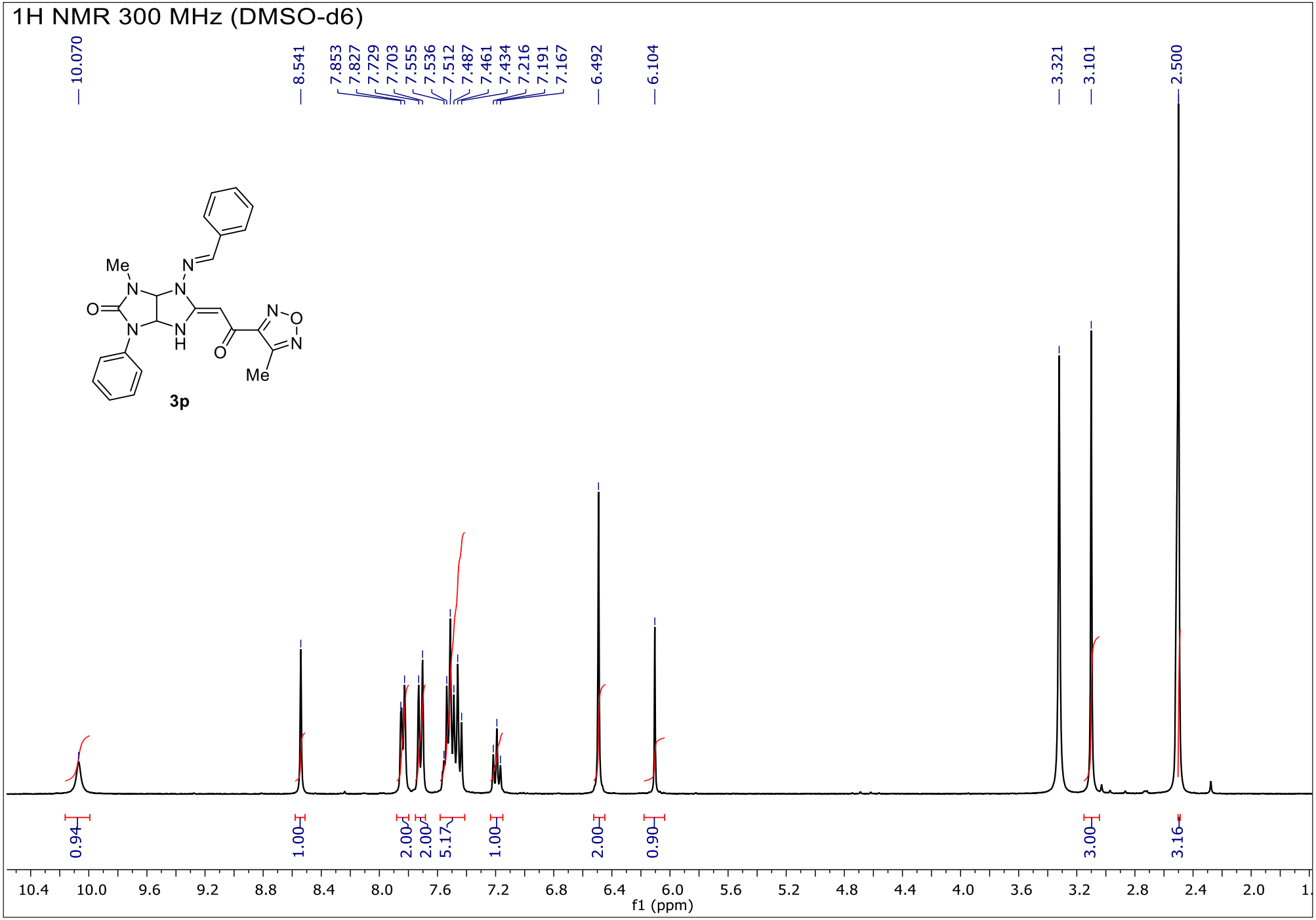
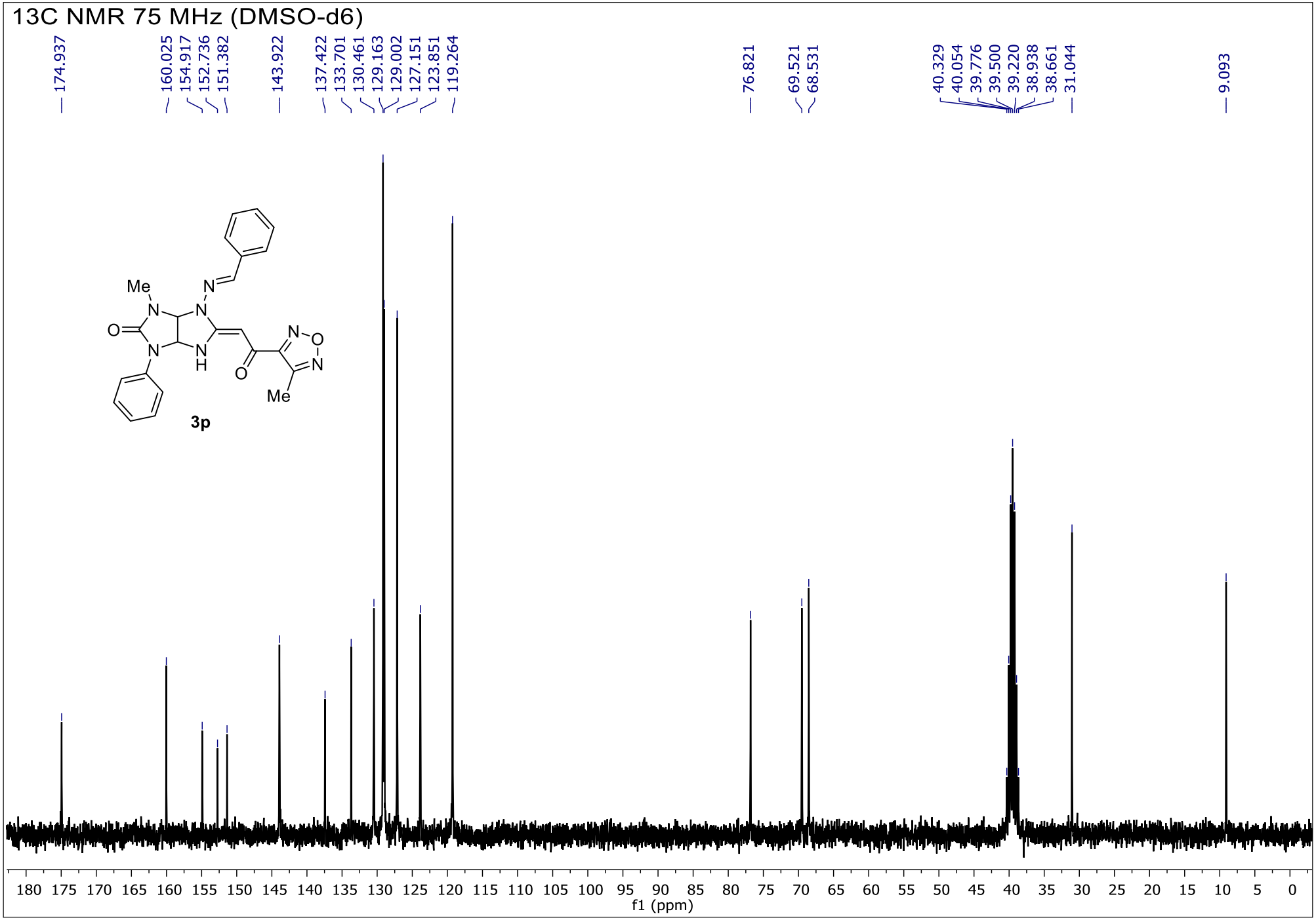
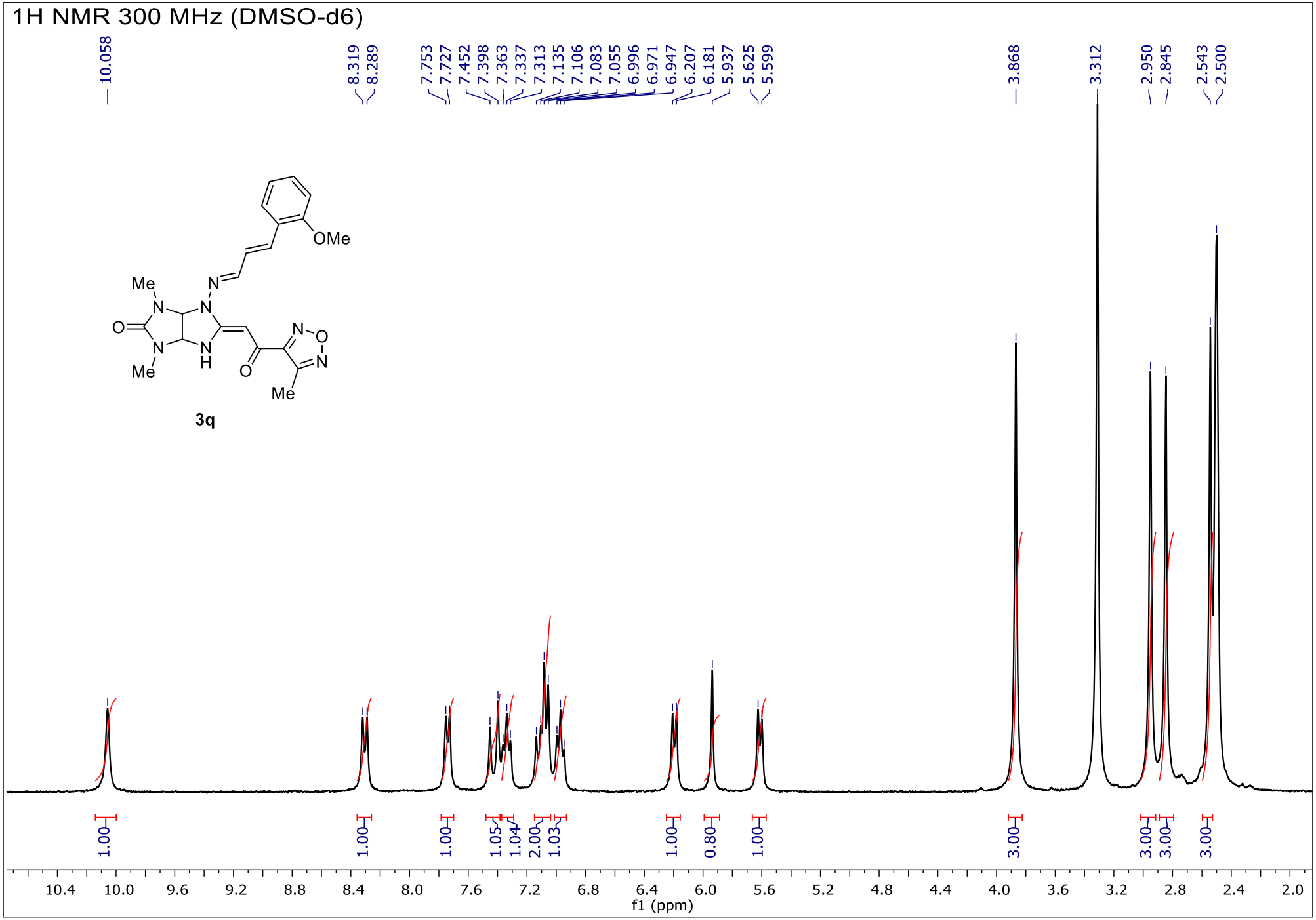
2.6
2.2
1.8
1.4
1.0
0.6
0.2
f1 (ppm)

3o


13C NMR 75 MHz (DMSO-d6)
174.279
159.248
156.990
152.900
151.379
142.887
133.711
130.337
129.032
126.945
76.427
68.914
68.847
40.333
40.056
39.777
39.500
39.222
38.943
38.667
38.285
35.918
13.932
13.366
9.114
Et
N
N
O
N
N
H
Et
O
N
O
N
Me
3o
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

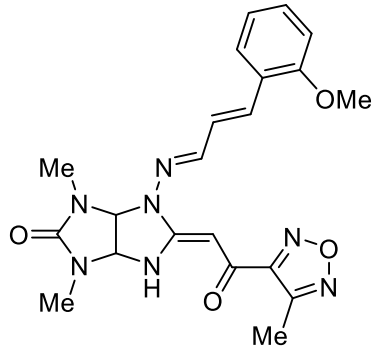

1H NMR 300 MHz (DMSO-d6)
10.070
8.541
7.853
7.827
7.729
7.703
7.555
7.536
7.512
7.487
7.461
7.434
7.216
7.191
7.167
6.492
6.104
3.321
3.101
2.500
Me
N
O
N
H
O
N
O
N
Me
3p
0.94
1.00
2.00
2.00
5.17
1.00
2.00
0.90
3.00
3.16
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)


13C NMR 75 MHz (DMSO-d6)
174.937
160.025
154.917
152.736
151.382
143.922
137.422
133.701
130.461
129.163
129.002
127.151
123.851
119.264
76.821
69.521
68.531
40.329
40.054
39.776
39.500
39.220
38.938
38.661
31.044
9.093
Me
N
N
N
O
N
H
O
N
O
N
Me
3p
180 175 170 165 160 155 150 145 140 135 130 125 120 115 110 105 100 95 90 85 80 75 70 65 60 55 50 45 40 35 30 25 20 15 10 5 0
f1 (ppm)

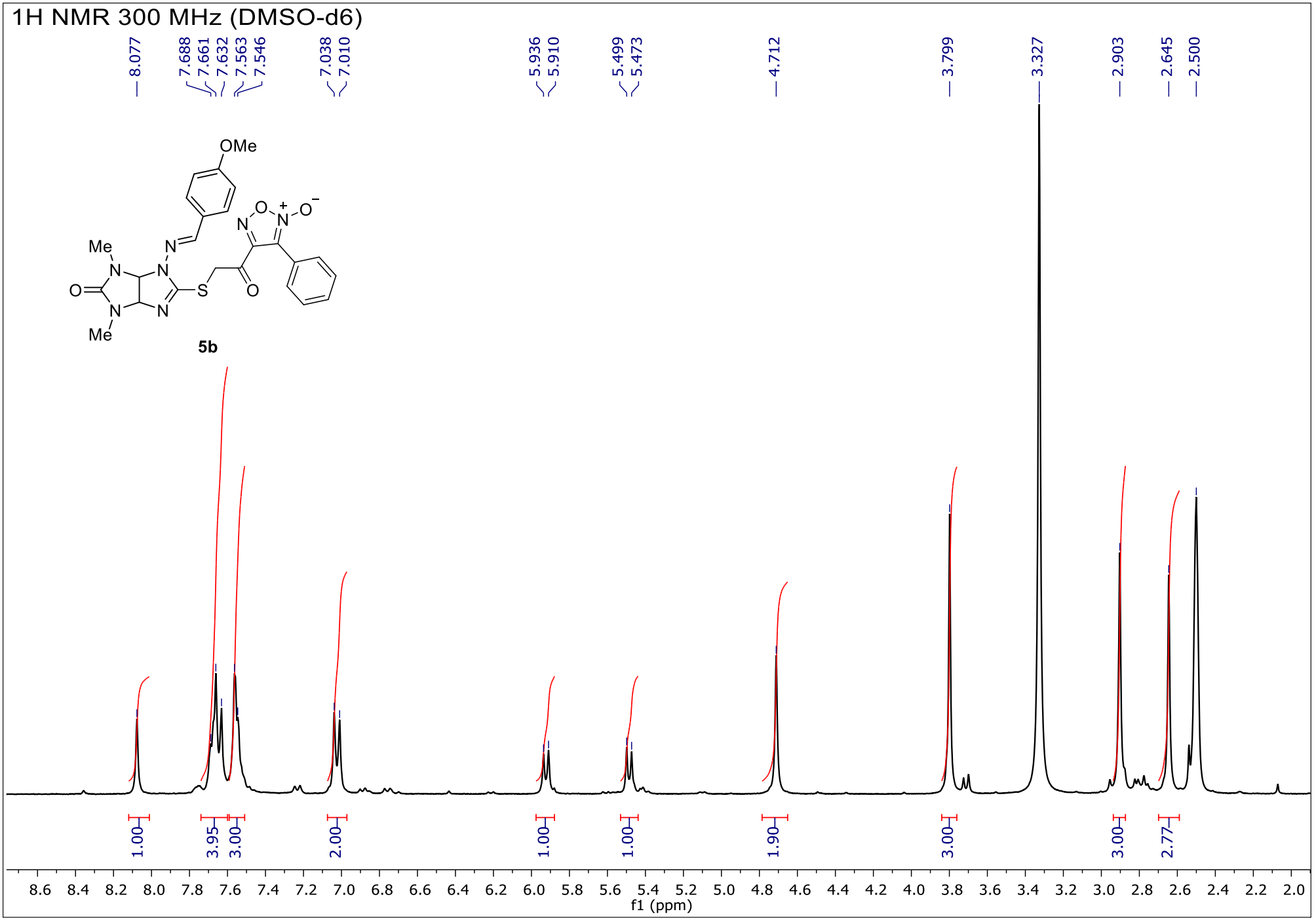

1H NMR 300 MHz (DMSO-d6)
10.058
8.319
8.289
7.753
7.727
7.452
7.398
7.363
7.337
7.313
7.135
7.106
7.083
7.055
6.996
6.971
6.947
6.207
6.181
5.937
5.625
5.599
3.868
3.312
2.950
2.845
2.543
2.500
OMe
Me
N
N
O
N
N
H
O
N
O
N
Me
Me
3q
1.00
1.00
1.00
1.05
1.04
2.00
1.03
1.00
0.80
1.00
3.00
3.00
3.00
3.00
10.4
10.0
9.6
9.2
8.8
8.4
8.0
7.6
7.2
6.8
6.4
6.0
5.6
5.2
4.8
4.4
4.0
3.6
3.2
2.8
2.4
2.0
f1 (ppm)

13C NMR 75 MHz (DMSO-d6)

174.004
159.056
157.643
156.798
152.858
151.402
146.493
134.301
130.447
127.150
125.315
124.025
120.716
111.539
76.393
70.305
69.795
55.514
40.332
40.056
39.778
39.500
39.222
38.944
38.669
31.042
28.385
9.121



3q


1H NMR 300 MHz (DMSO-d6)
8.077
7.688
7.661
7.632
7.563
7.546
7.038
7.010
5.936
5.910
5.499
5.473
4.712
3.799
3.327
2.903
2.645
2.500
OMe
Me
Me
O
S
5b
1.00
3.95
3.00
2.00
1.00
1.00
1.90
3.00
3.00
2.77
f1 (ppm)