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Design and synthesis of pyrazolo[3,4-*d*]pyridazine 5,6-dioxides as novel NO-donors

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Table of Contents

S1. Synthetic procedures S2

1.1 General remarks S2

1.2 Synthesis of *N*-aryl-2-oxopropanehydrazonoyl chlorides **9a-f** (general procedure) S2

1.3 Synthesis of *N*-(1,2,5-oxadiazol-3-yl)-2-oxopropanehydrazonoyl chlorides **9g-k** (general procedure) S3

1.4 Synthesis of 3,4-diacetyl-5-methyl-1*H*-pyrazoles **4** (general procedure) S4

1.5 Synthesis of 3,4-bis[(1-hydroximino)ethyl]-5-methyl-1*H*-pyrazoles **5** (general procedure) S6

1.6 Synthesis of 3,4,7-trimethyl-2*H*-pyrazolo[3,4-*d*]pyridazine 5,6-dioxides **3** (general procedure) S8

S2. NO release assay S10

S3. References S10

S4. Crystallographic data S11

S5. Copies of NMR spectra S28

S1. Synthetic procedures

1.1 General remarks

All reactions were carried out in well-cleaned oven-dried glassware with magnetic stirring. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker AM-300 (300.13 and 75.47 MHz, respectively) spectrometer and referenced to residual solvent peak. The chemical shifts are reported in ppm (δ); multiplicities are indicated by s (singlet), d (doublet), t (triplet), q (quartet), m (multiplet) and br (broad). Coupling constants, *J*, are reported in Hertz. The IR spectra were recorded on a Bruker "Alpha" spectrometer in the range 400-4000 cm^{-1} (resolution 2 cm^{-1}). High resolution mass spectra were recorded on a Bruker microTOF spectrometer with electrospray ionization (ESI). All measurements were performed in a positive (+MS) ion mode (interface capillary voltage: 4500 V) with scan range *m/z*: 50-3000. External calibration of the mass spectrometer was performed with Electrospray Calibrant Solution (Fluka). A direct syringe injection was used for all analyzed solutions in MeCN (flow rate: 3 μl min^{-1}). Nitrogen was used as nebulizer gas (0.4 bar) and dry gas (4.0 dm^3 min^{-1}); interface temperature was set at 180 °C. All spectra were processed by using Bruker DataAnalysis 4.0 software package. The melting points were determined on Stuart SMP20 apparatus and are uncorrected. Analytical thin-layer chromatography (TLC) was carried out on Merck 25 TLC silica gel 60 F_{254} aluminum sheets. The visualization of the TLC plates was accomplished with a UV light. Column chromatography was performed on silica gel 60 A (0.060-0.200 mm, Acros Organics). All solvents were purified and dried using standard methods prior to use. All standard reagents were purchased from Aldrich or Acros Organics and used without further purification. Amino-1,2,5-oxadiazoles **7g-l** were prepared according to a described procedure [S1].

X-ray diffraction data were collected at 100 K on a Bruker Quest D8 diffractometer equipped with a Photon-III area-detector (graphite monochromator, shutterless φ- and ω-scan technique), using Mo K_α-radiation (0.71073 Å). The intensity data were integrated by the SAINT program [S2] and corrected for absorption and decay using SADABS [S3]. The structure was solved by direct methods using SHELXS-2013 [S4] and refined on F^2 using SHELXL-2018 [S5]. All non-hydrogen atoms were refined with anisotropic displacement parameters. Hydrogen atoms were placed in ideal calculated positions and refined as riding atoms with relative isotropic displacement parameters. The SHELXTL program suite [S2] was used for molecular graphics. CCDC 2021356 and 2021357 contain the supplementary crystallographic data for **4h** and **3h**. These data can be obtained free of charge via http://www.ccdc.cam.ac.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB21EZ, UK; or deposit@ccdc.cam.ac.uk).

1.2 Synthesis of *N*′-aryl-2-oxopropanehydrazonoyl chlorides 9a-f (general procedure)

A solution of $NaNO_2$ (1.42 g, 20 mmol) in H_2O (20 ml) was added dropwise to a mixture of the corresponding aniline (20 mmol) in 6*M* HCl (12 ml) at 0-5 °C and stirred for 1 h. The formed suspension of arenediazonium salt **6a-e** was added dropwise to a solution of 3-chloropentane-2,4-dione **8** (2.69 g, 20 mmol) and AcONa (1.64 g, 20 mmol) in EtOH (100 ml) at 0-5 °C. The reaction mixture was stirred for 45 min at 0-5 °C and kept at the same temperature

for 6 h. The formed precipitate was filtered off, washed with water and crystallized from EtOH. *N*-(Pyridin-4-yl)-2-oxopropanehydrazonoyl chloride **9f** was prepared analogously from the previously synthesized [S6] (pyridin-4-yl)diazonium tetrafluoroborate **6f**.

N-(4-Chlorophenyl)-2-oxopropanehydrazonoyl chloride **9a**. Yield 3.37 g (73%) as yellow solid, mp 177-178 °C (lit. [S7] 178-179 °C).

N-Phenyl-2-oxopropanehydrazonoyl chloride **9b**. Yield 2.91 g (74%) as yellow solid, mp 143 °C (lit. [S7] 143 °C).

N-(3-Chlorophenyl)-2-oxopropanehydrazonoyl chloride **9c**. Yield 3.20 g (69%) as beige solid, mp 184-185 °C (lit. [S6] 190 °C), R_f 0.65 ($CHCl_3$); υ_{max} (KBr) 3243, 1681, 1596, 1529, 1482, 1219, 1165, 1095, 1029, 881 cm^{-1}; δ_H (300 MHz, DMSO-d_6): 2.49 (s, 3H, Me), 7.04 (d, 1H, J = 7.0 Hz, H Ar), 7.32-7.45 (m, 3H, H Ar), 10.76 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 25.4, 113.4, 114.4, 122.2, 123.9, 130.9, 133.8, 144.0, 187.9; Found (%): C 47.00, H 3.41, N 12.02, calc. for $C_9H_8Cl_2N_2O$ (%): C 46.78, H 3.49, N 12.12.

N-(4-Ethoxyphenyl)-2-oxopropanehydrazonoyl chloride **9d**. Yield 3.32 g (69%) as light green solid, mp 111-112 °C, R_f 0.64 ($CHCl_3$); υ_{max} (KBr) 3235, 1674, 1519, 1222, 1182, 1028 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.30 (t, 3H, J = 6.9 Hz, CH_2CH_3), 2.46 (s, 3H, Me), 3.97 (q, 2H, J= 6.9 Hz, CH_2Me), 6.92 (d, 2H, J = 8.8 Hz, H Ar), 7.36 (d, 2H, J = 8.8 Hz, H Ar), 10.57 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 14.7, 25.2, 63.2, 115.1, 116.1, 121.7, 136.0, 154.6, 187.5; Found (%): C 55.02, H 5.50, N 11.47, calc. for $C_{11}H_{13}ClN_2O_2$ (%): C 54.89, H 5.44, N 11.64.

N-(4-Nitrophenyl)-2-oxopropanehydrazonoyl chloride **9e**. Yield 4.30 g (89%) as yellow solid, mp 216-217 °C, R_f 0.39 ($CHCl_3$); υ_{max} (KBr) 3260, 1688, 1606, 1551, 1333, 1230, 1171, 1111, 1025, 850 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.52 (s, 3H, Me), 7.56 (d, 2H, J = 9.0 Hz, H Ar), 8.20 (d, 2H, J = 9.0 Hz, H Ar), 11.17 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 25.5, 114.7, 125.6, 126.3, 141.8, 148.2, 188.1; Found (%): C 44.70, H 3.55, N 17.19, calc. for $C_9H_8ClN_3O_3$ (%): C 44.74, H 3.34, N, 17.39.

N-(Pyridin-4-yl)-2-oxopropanehydrazonoyl chloride **9f**. Yield 2.70 g (68%) as light cream solid, mp 210-211 °C, R_f 0.11 ($CHCl_3$-EtOAc = 1:2); υ_{max} (KBr) 3252, 3141, 1701, 1642, 1556, 1521, 1369, 1247, 1155, 1071, 945, 799 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.58 (s, 3H, Me), 7.78 (d, 2H, J = 7.0 Hz, H Het), 8.61 (d, 2H, J = 7.0 Hz, H Het); δ_C (75.5 MHz, DMSO-d_6) 25.8, 110.8, 131.6, 142.3, 155.3; 188.6; Found (%): C 48.40, H 4.23, N 21.09, calc. for $C_8H_8ClN_3O$ (%): C 48.62, H 4.08, N 21.26.

1.3 Synthesis of *N*-(1,2,5-oxadiazol-3-yl)-2-oxopropanehydrazonoyl chlorides 9g-k (general procedure)

Method A. The corresponding 1.2.5-oxadiazolyl diazonium tetrafluoroborate **6g,h** (5 mmol) [S8] was added to a solution of 3-chloropentane-2,4-dione **8** (0.68 g, 5 mmol) in MeOH-AcOH mixture (1:1, 5 ml) at -10 °C, and the reaction mixture was stirred for 30 min at -10 °C and for 1.5 h at 20 °C. Then H_2O (20 ml) was added dropwise for 20 min, the solid formed was filtered off, washed with water, 20% EtOH and dried in air.

Method B. $NOBF_4$ (0.58 g, 5 mmol) was added to a magnetically stirred solution of the corresponding amino-1,2,5-oxadiazole [S1] **7i-k** (5 mmol) in TFA (5 ml) at 0-5 °C. The mixture was stirred for additional 20 min at 0-5 °C, then a solution of 3-chloropentane-2,4-dione **8** (0.68 g, 5 mmol) in MeOH (5 ml) was added dropwise. The mixture was stirred for 30 min at -10 °C and for 1 h at 20 °C, the solid formed was filtered off, washed with cold MeOH, pentane and dried in air.

4-[2-(1-Chloro-2-oxopropylidene)hydrazinyl]-3-phenyl-1,2,5-oxadiazole **9g** (prepared by method A). Yield 1.15 g (87%) as beige solid, mp 132-133 °C, R_f 0.45 ($CHCl_3$); υ_{max} (KBr) 3159, 1703, 1566, 1529, 1477, 1360, 1304, 1247, 1164, 1023, 937, 887, 768 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.85 (s, 3H, Me), 7.55-7.58 (m, 3H, H Ph), 7.66-7.69 (m, 2H, H Ph), 11.55 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 24.5, 125.4, 128.7, 128.8, 128.9, 130.3, 148.5, 153.5, 188.0; Found (%) C 49.73, H 3.48, N 21.01, calc. for $C_{11}H_9ClN_4O_2$ (%) C 49.92, H 3.43, N 21.17.

4-[2-(1-Chloro-2-oxopropylidene)hydrazinyl]-3-phenyl-1,2,5-oxadiazole 2-oxide **9h** (prepared by method A). Yield 1.29 g (92%) as beige solid, mp 133-134 °C, R_f 0.29 ($CHCl_3$); υ_{max} (KBr) 3247, 1678, 1611, 1570, 1526, 1464, 1246, 1177, 1055, 846 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.78 (s, 3H, Me), 7.48-7.60 (m, 3H, Ph), 7.62-7.70 (m, 2H, Ph), 11.65 (br.s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 24.4, 110.3, 123.1. 128.7, 128.8, 130.3, 154.6, 187.9; Found (%) C 47.03, H 3.43, N 20.12, calc. for $C_{11}H_9ClN_4O_3$ (%) C 47.07, H 3.23, N 19.96.

3-(4-Bromophenyl)-4-[2-(1-chloro-2-oxopropylidene)hydrazinyl]-1,2,5-oxadiazole **9i** (prepared by method B). Yield 1.53 g (89%) as beige solid, mp 159-160 °C, R_f 0.35 ($CHCl_3$); υ_{max} (KBr) 3211, 2962, 1703, 1614, 1555, 1490, 1418, 1226, 1184, 1025, 938, 861 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.90 (s, 3H, Me), 7.64 (d, 2H, J = 8.4 Hz, H Ar), 7.77 (d, 2H, J = 8.4 Hz, H Ar), 11.57 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 24.4, 124.0, 124.7, 128.5, 130.8, 131.8, 147.7, 153.5, 187.9; Found (%) C 38.56, H 2.42, N 16.56, calc. for $C_{11}H_8BrClN_4O_2$ (%) C 38.46, H 2.35, N 16.31.

3-(3-Bromophenyl)-4-[2-(1-chloro-2-oxopropylidene)hydrazinyl]-1,2,5-oxadiazole 2-oxide **9j** (prepared by method B). Yield 0.93 g (52%) as beige solid, mp 151-152 °C, R_f 0.26 ($CHCl_3$); υ_{max} (KBr) 3252, 1708, 1652, 1600, 1532, 1481, 1410, 1163, 1017, 952, 868, 776 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.82 (s, 3H, Me), 7.52 (t, 1H, J = 8.0 Hz, H Ar), 7.68 (d, 1H, J = 8.0 Hz H Ar), 7.74 (d, 1H, J = 8.0 Hz H Ar), 7.89 (s, 1H Ar), 11.73 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 24.3, 109.5, 121.6, 125.6, 128.3, 130.9, 131.7, 133.1, 135.6, 154.6, 187.8; Found (%) C 36.90, H 2.18, N 15.75, calc. for $C_{11}H_8BrClN_4O_3$ (%) C 36.73, H 2.24, N 15.58.

3-(4-Bromophenyl)-4-[2-(1-Chloro-2-oxopropylidene)hydrazinyl]-1,2,5-oxadiazole 2-oxide **9k** (prepared by method B). Yield 1.53 g (85%) as cream solid, mp 157-158 °C, R_f 0.24 ($CHCl_3$); υ_{max} (KBr) 3209, 1695, 1604, 1584, 1558, 1503, 1476, 1394, 1251, 1162, 1021, 981, 936, 842, 650 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.85 (s, 3H, Me), 7.63 (d, 2H ^3J = 8.4 Hz H Ar), 7.78 (d, 2H ^3J = 8.4 Hz H Ar), 11.67 (s, 1H, NH); δ_C (75.5 MHz, DMSO-d_6) 24.4, 109.9, 122.5, 123.9, 128.8, 131.0, 131.8, 154.6, 187.9; Found (%) C 36.65, H 2.27, N 15.49, calc. for $C_{11}H_8BrClN_4O_3$ (%) C 36.73, H 2.24, N 15.58.

1.4 Synthesis of 3,4-diacetyl-5-methyl-1*H*-pyrazoles 4 (general procedure)

Method A (for aryl derivatives). Acetylacetone (1.00 g, 10 mmol) was added to a solution of EtONa, prepared from 0.23 g Na (10 mmol) in absolute EtOH (10 ml). Then the corresponding *N*-aryl-2-oxopropanehydrazonoyl chloride **9a-e** (10 mmol) was added, and the reaction mixture was stirred for 7 h at 35 °C and then for 12 h at 20 °C. The formed precipitate was filtered off, washed with water, dried in air and crystallized from EtOH.

Method B (for heteroaryl derivatives). Acetylacetone (0.50 g, 5 mmol) was added to a solution of EtONa, prepared from 0.12 g Na (5 mmol) in absolute EtOH (5 ml). Then the corresponding *N*-heteroaryl-2-oxopropanehydrazonoyl chloride **9f-k** (5 mmol) was added at 0-2 °C. The reaction mixture was stirred for 1 h at 0 °C and for 4 h at 20 °C. The solvent was evaporated and water (5 ml) was added to the residue. The product was extracted with ether (3x5 ml), the

combined organic extracts were washed with water and dried over $MgSO_4$. Filtration and evaporation of the solvent afforded diacetyl derivatives **4f-k**.

3,4-Diacetyl-1-(4-chlorophenyl)-5-methyl-1H-pyrazole **4a**. Yield 1.94 g (70%) as cream solid, mp 152 °C (lit. [S9] 152 °C).

3,4-Diacetyl-5-methyl-1-phenyl-1H-pyrazole **4b.** Yield 1.86 g (77%) as cream solid, mp 132 °C (lit. [S10] 132 °C). δ_H (300 MHz, DMSO-d_6) 2.31 (s, 3H, Me), 2.44 (s, 3H, Me), 2.57 (s, 3H, Me), 7.58 (br. s, 5H, H Ar), δ_C (75.5 MHz, DMSO-d_6) 11.4, 27.4, 31.1, 121.5, 125.6, 129.3, 129.5, 138.0, 143.0, 148.7, 194.4, 196.6.

3,4-Diacetyl-1-(3-chlorophenyl)-5-methyl-1H-pyrazole **4c**. Yield 1.99 g (72%) as cream solid, mp 117-118 °C, R_f 0.54 ($CHCl_3$); υ_{max} (KBr) 3435, 1687, 1676, 1591, 1531, 1480, 1415, 1361, 1180, 1150, 1010, 873, 779 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.33 (s, 3H, Me), 2.44 (s, 3H, Me), 2.58 (s, 3H, Me), 7.62 (br. s, 3H, H Ar), 7.75 (s, 1H, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.3, 27.4, 31.0, 121.6, 124.4, 125.5, 129.3, 131.1, 133.7, 139.1, 143.2, 148.9, 194.3, 196.5; Found (%) C 60.60, H 4.47, N 9.83, calc. for $C_{14}H_{13}ClN_2O_2$ (%) C 60.77, H 4.74, N 10.12.

3,4-Diacetyl-1-(4-ethoxyphenyl)-5-methyl-1H-pyrazole **4d.** Yield 2.26 g (79%) as white solid, mp 104-105 °C, R_f 0.49 ($CHCl_3$); υ_{max} (KBr) 2981, 1687, 1518, 1350, 1259, 1183, 1150, 1048, 836, 820 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.36 (t, 3H, J = 7.1 Hz, CH_2*Me*), 2.27 (s, 3H, Me), 2.44 (s, 3H, Me), 2.56 (s, 3H, Me), 4.10 (q, 2H, J = 7.1 Hz, *CH_2*Me), 7.09 (d, 2H, J = 8.5 Hz, H Ar), 7.48 (d, 2H, J = 8.5 Hz, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.3, 14.5, 27.4, 31.0, 63.5, 114.9, 121.1, 127.0, 130.6, 143.0, 148.4, 158.9, 194.3, 196.5; Found (%) C 67.29, H 6.27, N 9.66, calc. for $C_{16}H_{18}N_2O_3$ (%) C 67.12, H 6.34, N 9.78.

3,4-Diacetyl-5-methyl-1-(4-nitrophenyl)-1H-pyrazole **4e**. Yield 2.10 g (73%) as beige solid, mp. 213-214 °C, R_f 0.49 ($CHCl_3$); υ_{max} (KBr) 3119, 1697, 1679, 1595, 1531, 1427, 1346, 1148, 864 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.40 (s, 3H, Me), 2.45 (s, 3H, Me), 2.59 (s, 3H, Me), 7.94 (d, 2H, J = 8.4 Hz, H Ar), 8.42 (d, 2H, J = 8.4 Hz, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.6, 27.4, 31.1, 122.3, 124.9, 125.4, 142.8, 143.3, 147.2, 149.4, 194.3, 196.5; Found (%) C 58.41, H 4.41, N 14.55, calc. for $C_{14}H_{13}N_3O_4$ (%) C 58.53, H 4.56, N 14.63.

3,4-Diacetyl-5-methyl-1-(pyridin-4-yl)-1H-pyrazole **4f.** Yield 1.29 g (53%) as brown solid, mp 125-126 °C, R_f 0.18 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3434, 3043, 1690, 1633, 1590, 1537, 1418, 1374, 1260, 1149, 1005, 826, 702 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.44 (s, 6H, 2 Me), 2.60 (s, 3H, Me), 7.72 (d, 2H, J = 3.9 Hz, H Het), 8.80 (d, 2H, J = 3.9 Hz, H Het); δ_C (75.5 MHz, DMSO-d_6) 11.7, 27.6, 31.3, 119.3, 122.7, 143.3, 145.0, 149.7, 151.4, 194.5, 196.9; Found (%) C 63.89, H 5.51, N 17.02, calc. for $C_{13}H_{13}N_3O_2$ (%) C 64.19, H 5.39, N 17.27.

4-(3,4-Diacetyl-5-methyl-1H-pyrazol-1-yl)-3-phenyl-1,2,5-oxadiazole **4g**. Yield 0.99 g (64%) as yellow solid, mp 62-63 °C, R_f 0.37 ($CHCl_3$); υ_{max} (KBr) 1687, 1567, 1534, 1485, 1433, 1355, 692 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.35 (s, 3H, Me), 2.45 (s, 6H, 2Me), 7.51-7.61 (m, 5H, H Ph); δ_C (75.5 MHz, DMSO-d_6) 10.9, 27.2, 31.0, 122.4, 123.4, 128.8, 128.9, 131.3, 145.9, 150.1, 150.5, 151.0, 193.7, 196.1; Found (%) C 62.20, H 4.34, N 17.93, calc. for $C_{16}H_{14}N_4O_3$ (%) C 61.93, H 4.55, N 18.05.

4-(3,4-Diacetyl-5-methyl-1H-pyrazol-1-yl)-3-phenyl-1,2,5-oxadiazole 2-oxide **4h.** Yield 1.14 g (70%) as beige solid, mp 129-130 °C, R_f 0.35 ($CHCl_3$); υ_{max} (KBr) 1702, 1677, 1604, 1539, 1436, 1357, 1162, 1011,826, 765 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.37 (s, 3H, Me), 2.45 (s, 3H, Me), 2.46 (s, 3H, Me), 7.46-7.55 (m, 5H, H Ph); δ_C (75.5 MHz, DMSO-d_6) 10.7, 27.3, 31.0, 111.7, 121.0, 122.3, 128.0, 128.8, 131.1, 145.7, 150.6, 150.7, 193.7, 196.0; Found (%) C 58.53, H 4.04, N 17.00, calc. for $C_{16}H_{14}N_4O_4$ (%) C 58.89, H 4.32, N 17.17.

4-(3,4-Diacetyl-5-methyl-1H-pyrazol-1-yl)-3-(4-bromophenyl)-1,2,5-oxadiazole **4i**. Yield 1.63 g (84%) as white solid, mp 103-104 °C, R_f 0.36 ($CHCl_3$); υ_{max} (KBr) 3437, 1690, 1559, 1523, 1426, 1382, 1353, 1160, 995, 952, 895, 825 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.35 (s, 3H, Me), 2.45 (s, 3H, Me), 2.48 (s, 3H, Me), 7.57 (d, 2H, *J* = 8.0 Hz, H Ar), 7.77 (d, 2H, *J* = 8.0 Hz, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.0, 27.2, 31.0, 122.5, 122.8, 125.0, 131.0, 131.8, 145.9, 147.9, 150.0, 150.4, 193.6, 196.1; Found (%) C 49.50, H 3.25, N 14.19, calc. for $C_{16}H_{13}BrN_4O_3$ (%) C 49.38, H 3.37, N 14.40.

4-(3,4-Diacetyl-5-methyl-1H-pyrazol-1-yl)-3-(3-bromophenyl)-1,2,5-oxadiazole 2-oxide **4j**. Yield 1.38 g (68%), mp 91-92 °C, R_f 0.51 ($CHCl_3$); δ_H (300 MHz, acetone-d_6) 2.45 (s, 3H, Me), 2.49 (s, 3H, Me), 2.57 (s, 3H, Me), 7.49-7.60 (m, 2H, H Ar), 7.74-7.77 (m, 1H, H Ar), 7.84 (s, 1H, H Ar); δ_C (75.5 MHz, acetone-d_6) 10.4, 26.6, 30.5, 108.6, 110.8, 121.9, 123.9, 127.2, 130.8, 131.0, 133.9, 146.1, 150.8, 151.1, 193.3, 195.6; Found (%) C 47.19, H 3.44, N 13.56, calc. for $C_{16}H_{13}BrN_4O_4$ (%) C 47.43, H 3.23, N 13.83.

4-(3,4-Diacetyl-5-methyl-1H-pyrazol-1-yl)-3-(4-bromophenyl)-1,2,5-oxadiazole 2-oxide **4k**. Yield 1.26 g (62%), mp 104-105 °C, R_f 0.55 ($CHCl_3$); δ_H (300 MHz, $CDCl_3$) 2.48 (s, 3H, Me), 2.53 (s, 3H, Me), 2.60 (s, 3H, Me), 7.45 (d, 2H, *J* = 8.7 Hz, H Ar), 7.63 (d, 2H, *J* = 8.7 Hz, H Ar); δ_C (75.5 MHz, $CDCl_3$) 11.3, 27.5, 31.5, 108.7, 122.5, 128.7, 130.0, 132.3, 146.5, 149.6, 150.3, 150.8, 193.6, 196.6; Found (%) C 47.59, H 3.39, N 13.62, calc. for $C_{16}H_{13}BrN_4O_4$ (%) C 47.43, H 3.23, N 13.83.

1.5 Synthesis of 3,4-bis[(1-hydroximino)ethyl]-5-methyl-1*H*-pyrazoles 5 (general procedure)

Method A. A mixture of the corresponding diacetyl derivative **4a-f** (5 mmol) and $NH_2OH{\cdot}HCl$ (0.7 g, 10 mmol) in EtOH (10 ml) was refluxed for 7 h and kept at 20 °C for 12 h. The formed precipitate was filtered off, washed with EtOH, water and dried in air.

Method B. A mixture of the corresponding diacetyl derivative **4g-k** (5 mmol) and hydroxylamine hydrochloride (0.7 g, 10 mmol) in EtOH (10 ml) was stirred for 1-4 h at 70 °C. Then the solvent was evaporated, water (5 ml) was added, and the product was extracted with ether (3x5 ml). The combined organic extracts were washed with water and dried over $MgSO_4$. Filtration from the drying agent and evaporation of the solvent afforded title compounds **5g-k**.

3,4-Bis[(1-hydroximino)ethyl]-1-(4-chlorophenyl)-5-methyl-1H-pyrazole **5a.** Yield 1.30 g (85%) as white solid, mp 178-179 °C, R_f 0.52 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3374, 3185, 1501, 1384, 1372, 1091, 1076, 1012, 838, 736 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.98 (s, 3H, Me), 2.16 (s, 3H, Me), 2.26 (s, 3H, Me), 7.60 (br. s, 4H, H Ar), 11.27 (br. s, 2H, 2 NOH); δ_C (75.5 MHz, DMSO-d_6) 11.2, 11.7, 16.3, 116.9, 126.4, 129.2, 132.3, 138.0, 138.7, 147.4, 148.9, 150.0; Found (%) C 54.70, H 5.03, N 18.33, calc. for $C_{14}H_{15}ClN_4O_2$ (%) C 54.82, H 4.93, N 18.26.

3,4-Bis[(1-hydroximino)ethyl]-5-methyl-1-phenyl-1H-pyrazole **5b**. Yield 1.17 g (86%) as white solid, mp 190-191 °C, R_f 0.42 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3476, 1505, 1431, 1368, 1192, 1153, 1076, 990, 925, 908, 760 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.98 (s, 3H, Me), 2.15 (s, 3H, Me), 2.24 (s, 3H, Me), 7.45-7.55 (m, 5H, H Ph), 10.83 (br. s, 1H, OH), 11.24 (br. s, 1H, OH); δ_C (75.5 MHz, DMSO-d_6) 11.2, 11.7, 16.4, 116.4, 124.8, 128.0, 129.3, 138.6, 139.1, 147.2, 149.0, 150.5; Found (%) C 61.45, H 5.77, N 20.80, calc. for $C_{14}H_{16}N_4O_2$ (%) C 61.75, H 5.92, N 20.57.

3,4-Bis[(1-hydroximino)ethyl]-1-(3-chlorophenyl)-5-methyl-1H-pyrazole **5c.** Yield 1.27 g (83%) as white solid, mp 175-176 °C, R_f 0.58 ($CHCl_3$-EtOAc = 2:1); υ_{max} (KBr) 3377, 3067, 2668, 1588, 1488, 1418, 1380, 1174, 1080, 1029, 763 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.98 (s, 3H, Me),

2.15 (s, 3H, Me), 2.27 (s, 3H, Me), 7.49-7.68 (m, 3H, H Ar), 7.67 (s, 1H, H Ar), 11.05 (br. S, 2H, 2 NOH); δ_C (75.5 MHz, DMSO-d_6) 11.4, 11.6, 16.5, 117.1, 123.5, 124.6, 128.0, 131.1, 133.7, 139.0, 140.5, 147.7, 149.1, 150.2; Found (%) C 54.56, H 5.00, N 18.03, calc. for $C_{14}H_{15}ClN_4O_2$ (%) C, 54.82; H, 4.93; N, 18.26.

3,4-Bis[(1-hydroximino)ethyl]-1-(4-ethoxyphenyl)-5-methyl-1H-pyrazole **5d**. Yield 1.39 g (88%) as white solid, mp197-198 ºC, R_f 0.49 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3364, 3224, 1520, 1368, 1253, 1006, 924, 842 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.35 (t, 3H, J = 7.0 Hz, CH_2*Me*), 1.98 (s, 3H, Me), 2.14 (s, 3H, Me), 2.19 (s, 3H, Me), 4.07 (q, 2H, J = 7.0 Hz, *CH_2*Me), 7.04 (d, 2H, J = 8.7 Hz, H Ar), 7.43 (d, 2H, J = 8.7 Hz, H Ar), 11.18 (br. s, 2H, 2 NOH); δ_C (75.5 MHz, DMSO-d_6) 11.0, 11.7, 14.6, 16.3, 63.5, 114.7, 116.1, 126.4, 132.0, 138.4, 146.5, 149.1, 150.1, 158.1; Found (%) C 60.51, H 6.19, N 17.88, calc. for $C_{16}H_{20}N_4O_3$ (%) C 60.75, H 6.37, N 17.71.

3,4-Bis[(1-hydroximino)ethyl]-5-methyl-1-(4-nitrophenyl)-1H-pyrazole **5e**. Yield 1.50 g (95%) as yellow solid, mp 184-185 ºC, R_f 0.44 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3574, 3290, 3211, 1597, 1519, 1349, 995, 943, 858, 756 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.00 (s, 3H, Me), 2.20 (s, 3H, Me), 2.38 (s, 3H, Me), 7.92 (d, 2H, J = 8.3 Hz, H Ar), 8.38 (d, 2H, J = 8.3 Hz, H Ar), 10.93 (s, 1H, OH), 11.40 (s, 1H, OH); δ_C (75.5 MHz, DMSO-d_6) 11.6 (2 C), 16.2, 118.2, 124.6, 124.8, 139.2, 144.2, 145.9, 148.5, 148.8, 149.7; Found (%) C 53.20, H 4.69, N 21.94, calc. for $C_{14}H_{15}N_5O_4$ (%) C 52.99, H 4.76, N 22.07.

3,4-Bis[(1-hydroximino)ethyl]-5-methyl-1-(pyridin-4-yl)-1H-pyrazole **5f**. Yield 1.05 g (74%) as grey-brown solid, mp 224-225 ºC, R_f 0.13 ($CHCl_3$-EtOAc, 1:2); υ_{max} (KBr) 3406, 1633, 1514, 1444, 1372, 1185, 1132, 992, 942, 819, 752 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.97 (s, 3H, Me), 2.20 (s, 3H, Me), 2.52 (s, 3H, Me), 8.22 (d, 2H, J = 6.4 Hz, H Py), 8.92 (d, 2H, J = 6.4 Hz, H Py), 11.05 (br. s, 1H, OH), 11.59 (br. s, 1H, OH); δ_C (75.5 MHz, DMSO-d_6) 11.6, 12.5, 16.4, 118.3, 120.5, 141.2, 144.2, 148.5, 149.3, 150.6, 151.1; Found (%) C 56.80, H 5.56, N 25.45, calc. for $C_{13}H_{15}N_5O_2$ (%) C 57.13, H 5.53, N 25.63.

4-[3,4-Bis(1-hydroximino)ethyl)-5-methyl-1H-pyrazol-1-yl]-3-phenyl-1,2,5-oxadiazole **5g**. Yield 1.50 g (88%) as beige solid, mp. 136-137 ºC, R_f 0.58 ($CHCl_3$: EtOAc, 1:1). IR (KBr) 1762, 1571, 1533, 1484, 1379, 1003, 919, 773, 691 cm^{-1}. δ_H (300 MHz, DMSO-d_6) 1.93 (s, 3H, Me), 1.98 (s, 3H, Me), 2.34 (s, 3H, Me), 7.42-7.68 (m, 5H, Ph), 11.00 (s, 1H, NOH), 11.49, (s, 1H, NOH); ^{13}C NMR spectrum was not recorded since this compound was obtained as a mixture of *E*/*Z* isomers. Calc. for $C_{16}H_{16}N_6O_3$ (%): C, 56.47; H, 4.74; N, 24.69. Found (%): C, 56.28; H, 4.; N, 24.62.

4-[3,4-Bis(1-hydroximino)ethyl)-5-methyl-1H-pyrazol-1-yl]-3-phenyl-1,2,5-oxadiazole 2-oxide **5h**. Yield 1.39 g (78%) as beige solid, mp 130-131 ºC, R_f 0.50 ($CHCl_3$: EtOAc, 1:1); υ_{max} (KBr) 3465, 3342, 1608, 1552, 1509, 1474, 1435, 1368, 1177, 999, 922 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.90 (s, 3H, Me), 1.96 (s, 3H, Me), 2.32 (s, 3H, Me), 7.46-7.52 (m, 5H, Ph); δ_C (75.5 MHz, DMSO-d_6) 10.5, 11.3, 16.2, 111.9, 118.1, 121.7, 128.4, 128.7, 131.0, 141.7, 148.3, 149.1, 150.0, 151.5. Found (%): C, 53.66; H, 4.78; N, 23.40, calc. for $C_{16}H_{16}N_6O_4$ (%): C, 53.93; H, 4.53; N, 23.58. HRMS (ESI): *m/z* for $C_{16}H_{16}N_6O_4$ $(M+H)^+$: calcd 357.1307, found 357.1306.

4-[3,4-Bis(1-hydroximino)ethyl)-5-methyl-1H-pyrazol-1-yl]-3-(4-bromophenyl)-1,2,5-oxadiazole **5i**. Yield 1.90 g (91%) as white solid, mp 204-205 ºC, R_f 0.63 ($CHCl_3$: EtOAc, 1:1); υ_{max} (KBr) 3403, 3072, 3007, 2661, 1584, 1557, 1529, 1478, 1431, 1384, 1166, 1085, 996, 833, 738 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 1.90 (s, 3H, Me) 1.96 (s, 3H, Me), 2.36 (s, 3H, Me), 7.57 (d, 2H, J = 8.1 Hz H Ar), 7.74 (d, 2H, J = 8.1 Hz, H Ar), 10.43 (s, 1H, OH), 11.50 (br. s, 1H, OH). δ_C (75.5 MHz, DMSO-d_6) 10.7, 11.1, 16.1, 118.2, 123.4, 124.7, 131.1, 131.6, 141.9, 148.1, 149.0, 149.7,

150.2, 150.7; Found (%) C 46.10, H 3.46, N 19.91, calc. for $C_{16}H_{15}BrN_6O_3$ (%) C 45.84, H 3.61, N, 20.05.

4-[3,4-Bis(1-hydroximino)ethyl)-5-methyl-1H-pyrazol-1-yl]-3-(3-bromophenyl)-1,2,5-oxadiazole 2-oxide **5j**. Yield g (83%) as pale yellow solid, mp 64-65 °C, R_f 0.57 ($CHCl_3$: EtOAc, 1:1); δ_H (300 MHz, DMSO-d_6) 1.93 (s, 3H, Me) 1.99 (s, 3H, Me), 2.42 (s, 3H, Me), 7.46-7.58 (m, 2H, H Ar), 7.70-7.76 (m, 2H, H Ar), 11.03 (s, 1H, OH), 11.55 (br. s, 1H, OH). δ_C (75.5 MHz, DMSO-d_6) 11.1, 11.6, 16.6, 109.2, 111.5, 118.6, 121.7, 124.6, 128.1, 131.0, 131.9, 134.0, 142.1, 148.5, 149.3, 151.8. Found (%) C 44.42, H 3.31, N 19.09, calc. for $C_{16}H_{15}BrN_6O_4$ (%) C 44.15, H 3.47, N, 19.31.

4-[3,4-Bis(1-hydroximino)ethyl)-5-methyl-1H-pyrazol-1-yl]-3-(4-bromophenyl)-1,2,5-oxadiazole 2-oxide **5k**. Yield g (78%) as pale yellow solid, R_f 0.54 ($CHCl_3$: EtOAc, 1:1); δ_H (300 MHz, DMSO-d_6) 1.93 (s, 3H, Me) 1.99 (s, 3H, Me), 2.39 (s, 3H, Me), 7.61 (d, 2H, J = 8.6 Hz H Ar), 7.77 (d, 2H, J = 8.6 Hz, H Ar), 11.01 (s, 1H, OH), 11.51 (s, 1H, OH). δ_C (75.5 MHz, DMSO-d_6) 11.2, 11.6, 16.6, 109.0, 118.6, 123.9, 125.2, 131.6, 132.1, 142.4, 148.7, 149.5, 150.6, 151.2; Found (%) C 43.92, H 3.69, N 19.03, calc. for $C_{16}H_{15}BrN_6O_4$ (%) C 44.15, H 3.47, N, 19.31.

1.6 Synthesis of 3,4,7-trimethyl-2*H*-pyrazolo[3,4-*d*]pyridazine 5,6-dioxides 3 (general procedure)

A solution of N_2O_4 (0.92 g, 10 mmol) in dry ether (5 ml) was added dropwise to a stirred mixture of the corresponding dioxime **5a-k** (5 mmol) in dry ether (20 ml) at 20 °C. The reaction mixture was stirred for 1 h at 20 °C, the precipitate formed was filtered off, washed with ether, hexane and dried in air.

2-(4-Chlorophenyl)-3,4,7-trimethyl-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3a.** Yield 1.26 g (83%) as light cream solid, mp 220-221 °C, R_f 0.15 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3444, 3051, 1500, 1370, 1227, 1198, 1092, 1009, 842, 803, 706 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.63 (s, 3H, Me), 2.66 (s, 3H, Me), 2.76 (s, 3H, Me), 7.51 (d, 2H, J = 7.5 Hz, H Ar), 7.57 (d, 2H, J = 7.5 Hz, H Ar); δ_C (75.5 MHz, $CDCl_3$) 12.8, 13.4, 15.9, 109.3, 125.7, 125.9, 127.4, 129.8, 134.8, 135.9, 136.9, 138.1; Found (%) C 55.12, H 4.23, N 18.29, calc. for $C_{14}H_{13}ClN_4O_2$ (%) C 55.18, H 4.30, N 18.39.

2-Phenyl-3,4,7-trimethyl-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3b**. Yield 1.00 g (74%) as light cream solid, mp 220-221 °C, R_f 0.12 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3049, 1501, 1225, 1197, 950, 777, 702 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.63 (s, 3H, Me), 2.64 (s, 3H, Me), 2.75 (s, 3H, Me), 7.47-7.60 (m, 5H, H Ph); δ_C (75.5 MHz, $CDCl_3$) 12.8, 13.5, 15.9, 109.3, 126.0, 126.2, 126.3, 129.7, 129.8, 134.8, 138.0, 138.4; Found (%) C 62.02, H 5.05, N 20.56, calc. for $C_{14}H_{14}N_4O_2$ (%) C 62.21, H 5.22, N 20.73.

2-(3-Chlorophenyl)-3,4,7-trimethyl-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3c**. Yield 1.34 g (88%) as light cream solid, mp 232-233 °C, R_f 0.29 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3433, 3063, 1595, 1504, 1430, 1368, 1227, 781, 707 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 2.69 (s, 3H, Me), 2.70 (s, 3H, Me), 2.80 (s, 3H, Me), 7.40-7.46 (m, 1H, H Ar), 7.52-7.60 (m, 3H, H Ar); ^{13}C NMR spectrum was not recorded due to the very low solubility of this compound in common solvents ($CDCl_3$, acetone-d_6, CD_3CN, DMSO-d_6, acetic acid-d_4). Found (%) C 55.33, H 4.07, N 18.14, calc. for $C_{14}H_{13}ClN_4O_2$ (%) C 55.18, H 4.30, N 18.39. HRMS (ESI): M^+, found: 327.0615 $[C_{14}H_{13}{}^{35}ClN_4NaO_2]^+$ $(M+Na)^+$ requires 327.0619.

2-(4-Ethoxyphenyl)-3,4,7-trimethyl-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3d**. Yield 1.21 g (77%) as light cream solid, mp 213-214 °C, R_f 0.14 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3449, 3054,

1609, 1516, 1476, 1253, 1225, 1176, 1046, 842 cm^{-1}; δ_H (300 MHz, $CDCl_3$) 1.45 (t, 3H, *J* = 6.7 Hz, CH_2*Me*), 2.61 (s, 3H, Me), 2.64 (s, 3H, Me), 2.75 (s, 3H, Me), 4.10 (q, 2H, *J* = 6.7 Hz, *CH_2*Me), 7.03 (d, 2H, *J* = 8.1 Hz, H Ar), 7.39 (d, 2H, *J* = 8.1 Hz, H Ar); δ_C (75.5 MHz, $CDCl_3$) 12.6, 13.5, 14.7, 15.8, 64.1, 109.1, 115.2, 126.1, 126.3, 127.3, 131.0, 134.8, 137.8, 159.9; Found (%) C 61.33, H 5.62, N 18.00, calc. for $C_{16}H_{18}N_4O_3$ (%) C 61.14, H 5.77, N 17.82.

3,4,7-Trimethyl-2-(4-nitrophenyl)-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3e**. Yield 1.42 g (90%) as yellow solid, mp 227-228 ºC, R_f 0.10 ($CHCl_3$-EtOAc, 2:1); υ_{max} (KBr) 3449, 1613, 1596, 1516, 1348, 1228, 1105, 869, 701 cm^{-1}; δ_H (300 MHz, $CDCl_3$-DMSO-d_6) 2.58 (s, 3H, Me), 2.76 (s, 6H, 2 Me), 7.86 (d, 2H, *J* = 9.0 Hz, H Ar), 8.42 (d, 2H, *J* = 9.0 Hz, H Ar); ^{13}C NMR spectrum was not recorded due to the very low solubility of this compound in common solvents ($CDCl_3$, acetone-d_6, CD_3CN, DMSO-d_6, acetic acid-d_4). Found (%) C 53.55, H 4.08, N 22.03, calc. for $C_{14}H_{13}N_5O_4$ (%) C 53.33, H 4.16, N 22.21. HRMS (ESI): M^+, found: 338.0857 $[C_{14}H_{13}N_5NaO_4]^+$ $(M+Na)^+$ requires 338.0860.

3,4,7-Trimethyl-2-(pyridin-4-yl)-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3f**. Yield 0.73 g (52%) as yellow solid, mp 174-175 ºC, R_f 0.26 (EtOAc-DMSO, 40:1); υ_{max} (KBr) 3436, 2754, 1633, 1505, 1380, 1193, 1062, 823 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.56 (s, 3H, Me), 2.69 (s, 3H, Me), 2.82 (s, 3H, Me), 8.16 (d, 2H, *J* = 5.7 Hz, H Py), 9.04 (d, 2H, *J* = 5.7 Hz, H Py); 12.8, 13.1, 15.6, 110.0, 121.1, 123.8, 124.5, 137.1, 138.9, 146.5, 146.7; HRMS (ESI): M^+, found: 294.0962 $[C_{13}H_{13}N_5NaO_2]^+$ $(M+Na)^+$ requires 294.0961.

3,4,7-Trimethyl-2-(3-phenyl-1,2,5-oxadiazol-4-yl)-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3g**. Yield 0.74 (44%) as light cream solid, mp 163-164 ºC, R_f 0.11 ($CHCl_3$); υ_{max} (KBr) 3433, 1618, 1553, 1531, 1451, 1384, 1279, 1246, 1203, 1001, 792 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.39 (s, 3H, Me), 2.66 (s, 3H, Me), 2.70 (s, 3H, Me), 7.49-7.59 (m, 5H, H Ph); δ_C (75.5 MHz, DMSO-d_6) 11.5, 12.9, 15.4, 109.0, 123.0, 123.2, 123.8, 128.3, 129.0; 131.5, 139.1, 139.4, 150.2, 151.1; Found (%) C 56.70, H 4.03, N 24.91, calc. for $C_{16}H_{14}N_6O_3$ (%) C 56.80, H 4.17, N 24.84.

3,4,7-Trimethyl-2-(2-oxido-3-phenyl-1,2,5-oxadiazol-4-yl)-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3h**. Yield 1.33 g (75%) as light cream solid, mp 198-199 ºC, R_f 0.19 ($CHCl_3$: EtOAc, 1:1); υ_{max} (KBr) 3445, 1600, 1533, 1436, 1363, 1246, 1201, 1111, 976, 791 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.41 (s, 3H, Me), 2.66 (s, 3H, Me), 2.72 (s, 3H, Me), 7.37-7.40 (m, 2H, H Ph), 7.44-7.52 (m, 3H, H Ph); δ_C (75.5 MHz, DMSO-d_6) 11.6, 13.2, 15.7, 109.2, 112.1, 120.9, 123.6, 124.3, 127.6, 129.2, 131.4, 139.3, 139.8, 150.9; Found (%) C 53.99, H 3.80, N 23.83, calc. for $C_{16}H_{14}N_6O_4$ (%) C 54.24, H 3.98, N 23.72.

2-[3-(4-Bromophenyl)-1,2,5-oxadiazol-4-yl]-3,4,7-trimethyl-2H-pyrazolo[3,4-d]pyridazine 5,6-dioxide **3i**. Yield 1.33 g (64%) as yellow solid, mp 195-196 ºC, R_f 0.60 (EtOAc-DMSO, 40:1); υ_{max} (KBr) 3086, 2749, 1630, 1525, 1375, 1242, 1194, 1069, 997, 830, 793, 710 cm^{-1}; δ_H (300 MHz, DMSO-d_6) 2.41 (s, 3H, Me), 2.68 (s, 3H, Me), 2.73 (s, 3H, Me), 7.48 (d, 2H, *J* = 8.2 Hz H Ar), 7.71 (d, 2H, *J* = 8.2 Hz, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.6, 12.9, 15.4, 109.1, 122.4, 123.2, 123.7, 125.2, 130.5, 132.0, 139.1, 139.4, 150.1, 150.4; Found (%) C 45.90, H 3.32, N 20.31, calc. for $C_{16}H_{13}BrN_6O_3$ (%) C 46.06, H 3.14, N 20.14.

2-[3-(3-Bromophenyl)-2-oxido-1,2,5-oxadiazol-4-yl]-3,4,7-trimethyl-2H-pyrazolo[3,4-d]-pyridazine 5,6-dioxide **3j**. Yield 1.17 g (54%) as yellow solid, mp 171-172 ºC, R_f 0.10 ($CHCl_3$); δ_H (300 MHz, DMSO-d_6) 2.40 (s, 3H, Me), 2.66 (s, 3H, Me), 2.79 (s, 3H, Me), 7.31 (d, 1H, *J* = 7.4 Hz, H Ar), 7.43 (t, 1H, *J* = 7.4 Hz, H Ar), 7.73 (d, 1H, *J* = 7.4 Hz, H Ar), 7.82 (s, 1H, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.5, 12.9, 15.5, 109.0, 111.2, 121.5, 123.0, 123.3, 123.7, 127.0,

130.5, 130.9, 133.8, 139.1, 139.4, 150.7; Found (%) C 44.45, H 3.12, N 19.27, calc. for $C_{16}H_{13}BrN_6O_4$ (%) C 44.36, H 3.02, N 19.40.

2-[3-(4-Bromophenyl)-2-oxido-1,2,5-oxadiazol-4-yl]-3,4,7-trimethyl-2H-pyrazolo[3,4-d]-pyridazine 5,6-dioxide **3k**. Yield 1.02 g (47%) as beige solid, mp 68-69 °C, R_f 0.18 ($CHCl_3$-EtOAc, 20:1); δ_H (300 MHz, DMSO-d_6) 2.42 (s, 3H, Me), 2.66 (s, 3H, Me), 2.75 (s, 3H, Me), 7.33 (d, 2H, J = 8.2 Hz, H Ar), 7.70 (d, 2H, J = 8.2 Hz, H Ar); δ_C (75.5 MHz, DMSO-d_6) 11.4, 13.0, 15.5, 109.0, 111.6, 120.2, 123.3, 123.8, 124.6, 129.4, 132.0, 139.0, 139.6, 150.6; Found (%) C 44.30, H 2.93, N 19.50, calc. for $C_{16}H_{13}BrN_6O_4$ (%) C 44.36, H 3.02, N 19.40.

S2. NO release assay

A test compound (0.1 mmol) was dissolved in DMSO (50 ml). A 20 μl aliquot of the resulted solution was diluted with phosphate buffer solution (180 μl, pH 7.4, containing 2 μmol L-cysteine). The final concentration of the furoxan derivative was $2 \cdot 10^{-4}$ M. The mixture was incubated at 37 °C for 1 h. Then a 50 μl aliquot of the Griess reagent (prepared by mixing sulfanilamide (4 g), *N*-naphthylethylenediamine dihydrochloride (0.2 g) and 85% H_3PO_4 (10 ml) in distilled and deionized water (final volume 100 ml)) was added, and this was incubated for 10 min at 37 °C. UV absorbance at 540 nm was measured using a Multiskan GO Microplate Photometer and calibrated using a standard curve prepared from standard solutions of $NaNO_2$ to give the nitrite concentration. All measurements were made in triplicate.

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S4. Crystallographic data

Table S1. Crystal data and structure refinement for **4h**.

Empirical formula	C16 H14 N4 O4	
Formula weight	326.31	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Triclinic	
Space group	P-1	
Unit cell dimensions	a = 8.0831(4) Å	α= 81.3641(11)°.
	b = 9.0099(4) Å	β= 73.0382(11)°.
	c = 11.4421(5) Å	γ = 66.2132(10)°.
Volume	728.85(6) $Å^3$	
Z	2	
Density (calculated)	1.487 g cm^{-3}	
Absorption coefficient	0.110 mm^{-1}	
F(000)	340	
Crystal size	0.59 x 0.46 x 0.38 mm^3	
Theta range for data collection	2.472 to 31.682°.	
Index ranges	-11<=h<=11, -13<=k<=13, -16<=l<=16	
Reflections collected	25671	
Independent reflections	4887 [R(int) = 0.0451]	
Observed reflections	3936	
Completeness to theta = 25.242°	100.0 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.8498 and 0.7864	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	4887 / 0 / 221	
Goodness-of-fit on F^2	1.039	
Final R indices [I>2sigma(I)]	R1 = 0.0438, wR2 = 0.1012	
R indices (all data)	R1 = 0.0603, wR2 = 0.1134	
Extinction coefficient	0.010(3)	
Largest diff. peak and hole	0.455 and -0.260 e.$Å^{-3}$	

Table S2. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **4h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	6988(1)	-686(1)	8262(1)	18(1)
O(2)	6680(1)	926(1)	9730(1)	19(1)
O(3)	1126(1)	4287(1)	3631(1)	20(1)
O(4)	-1751(1)	1939(1)	6752(1)	24(1)
N(1)	6058(1)	835(1)	8890(1)	15(1)
N(2)	6121(1)	-570(1)	7373(1)	17(1)
N(3)	3642(1)	1316(1)	6633(1)	14(1)
N(4)	4034(1)	2191(1)	5584(1)	15(1)
C(1)	4801(2)	869(1)	7440(1)	14(1)
C(2)	4693(2)	1807(1)	8378(1)	13(1)
C(3)	3446(2)	3447(1)	8772(1)	14(1)
C(4)	2157(2)	4429(1)	8110(1)	17(1)
C(5)	950(2)	5978(1)	8484(1)	18(1)
C(6)	1020(2)	6581(1)	9506(1)	19(1)
C(7)	2296(2)	5616(2)	10167(1)	21(1)
C(8)	3501(2)	4059(2)	9810(1)	19(1)
C(9)	2576(2)	2576(1)	5117(1)	14(1)
C(10)	1222(2)	1971(1)	5881(1)	14(1)
C(11)	1957(2)	1172(1)	6856(1)	14(1)
C(12)	2543(2)	3638(1)	3982(1)	15(1)
C(13)	4312(2)	3903(2)	3331(1)	22(1)
C(14)	-618(2)	2054(1)	5809(1)	16(1)
C(15)	-1049(2)	2203(2)	4598(1)	21(1)
C(16)	1268(2)	249(2)	7946(1)	17(1)

Table S3. Bond lengths [Å] and angles [°] for **4h**.

O(1)-N(2)	1.3641(13)
O(1)-N(1)	1.4513(13)
O(2)-N(1)	1.2342(12)
O(3)-C(12)	1.2136(14)
O(4)-C(14)	1.2173(15)
N(1)-C(2)	1.3303(14)
N(2)-C(1)	1.3011(14)
N(3)-N(4)	1.3624(13)
N(3)-C(11)	1.3672(14)
N(3)-C(1)	1.4069(14)
N(4)-C(9)	1.3326(14)
C(1)-C(2)	1.4252(15)
C(2)-C(3)	1.4617(15)
C(3)-C(4)	1.3989(16)
C(3)-C(8)	1.4017(16)
C(4)-C(5)	1.3856(16)
C(4)-H(4)	0.9500
C(5)-C(6)	1.3857(17)
C(5)-H(5)	0.9500
C(6)-C(7)	1.3878(18)
C(6)-H(6)	0.9500
C(7)-C(8)	1.3859(17)
C(7)-H(7)	0.9500
C(8)-H(8)	0.9500
C(9)-C(10)	1.4281(15)
C(9)-C(12)	1.4925(16)
C(10)-C(11)	1.3838(15)
C(10)-C(14)	1.4847(15)
C(11)-C(16)	1.4886(16)
C(12)-C(13)	1.5026(17)
C(13)-H(13A)	0.9800
C(13)-H(13B)	0.9800
C(13)-H(13C)	0.9800
C(14)-C(15)	1.4994(17)
C(15)-H(15A)	0.9800
C(15)-H(15B)	0.9800
C(15)-H(15C)	0.9800
C(16)-H(16A)	0.9800

C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800

N(2)-O(1)-N(1)	107.69(8)
O(2)-N(1)-C(2)	135.96(10)
O(2)-N(1)-O(1)	115.77(9)
C(2)-N(1)-O(1)	108.27(9)
C(1)-N(2)-O(1)	106.28(9)
N(4)-N(3)-C(11)	113.21(9)
N(4)-N(3)-C(1)	119.48(9)
C(11)-N(3)-C(1)	126.63(10)
C(9)-N(4)-N(3)	104.35(9)
N(2)-C(1)-N(3)	118.72(10)
N(2)-C(1)-C(2)	113.65(10)
N(3)-C(1)-C(2)	127.61(10)
N(1)-C(2)-C(1)	104.11(9)
N(1)-C(2)-C(3)	123.93(10)
C(1)-C(2)-C(3)	131.96(10)
C(4)-C(3)-C(8)	118.97(10)
C(4)-C(3)-C(2)	119.69(10)
C(8)-C(3)-C(2)	121.34(10)
C(5)-C(4)-C(3)	120.22(11)
C(5)-C(4)-H(4)	119.9
C(3)-C(4)-H(4)	119.9
C(4)-C(5)-C(6)	120.56(11)
C(4)-C(5)-H(5)	119.7
C(6)-C(5)-H(5)	119.7
C(5)-C(6)-C(7)	119.60(11)
C(5)-C(6)-H(6)	120.2
C(7)-C(6)-H(6)	120.2
C(8)-C(7)-C(6)	120.48(11)
C(8)-C(7)-H(7)	119.8
C(6)-C(7)-H(7)	119.8
C(7)-C(8)-C(3)	120.17(11)
C(7)-C(8)-H(8)	119.9
C(3)-C(8)-H(8)	119.9
N(4)-C(9)-C(10)	111.53(10)
N(4)-C(9)-C(12)	117.11(10)
C(10)-C(9)-C(12)	131.16(10)
C(11)-C(10)-C(9)	105.07(10)

C(11)-C(10)-C(14)	120.92(10)
C(9)-C(10)-C(14)	134.01(10)
N(3)-C(11)-C(10)	105.82(10)
N(3)-C(11)-C(16)	121.94(10)
C(10)-C(11)-C(16)	132.21(10)
O(3)-C(12)-C(9)	120.88(11)
O(3)-C(12)-C(13)	122.12(11)
C(9)-C(12)-C(13)	116.97(10)
C(12)-C(13)-H(13A)	109.5
C(12)-C(13)-H(13B)	109.5
H(13A)-C(13)-H(13B)	109.5
C(12)-C(13)-H(13C)	109.5
H(13A)-C(13)-H(13C)	109.5
H(13B)-C(13)-H(13C)	109.5
O(4)-C(14)-C(10)	118.67(11)
O(4)-C(14)-C(15)	120.34(11)
C(10)-C(14)-C(15)	120.95(10)
C(14)-C(15)-H(15A)	109.5
C(14)-C(15)-H(15B)	109.5
H(15A)-C(15)-H(15B)	109.5
C(14)-C(15)-H(15C)	109.5
H(15A)-C(15)-H(15C)	109.5
H(15B)-C(15)-H(15C)	109.5
C(11)-C(16)-H(16A)	109.5
C(11)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(11)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5

Table S4. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **4h**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	16(1)	15(1)	21(1)	-1(1)	-9(1)	-2(1)
O(2)	19(1)	24(1)	18(1)	1(1)	-10(1)	-8(1)
O(3)	21(1)	18(1)	21(1)	2(1)	-10(1)	-7(1)
O(4)	18(1)	37(1)	20(1)	6(1)	-5(1)	-16(1)
N(1)	14(1)	16(1)	15(1)	1(1)	-4(1)	-6(1)
N(2)	17(1)	17(1)	19(1)	-1(1)	-8(1)	-5(1)
N(3)	13(1)	15(1)	14(1)	1(1)	-5(1)	-7(1)
N(4)	16(1)	16(1)	14(1)	1(1)	-4(1)	-8(1)
C(1)	13(1)	15(1)	15(1)	1(1)	-4(1)	-7(1)
C(2)	12(1)	15(1)	14(1)	2(1)	-4(1)	-6(1)
C(3)	13(1)	15(1)	16(1)	0(1)	-3(1)	-7(1)
C(4)	18(1)	16(1)	16(1)	0(1)	-6(1)	-6(1)
C(5)	19(1)	15(1)	18(1)	1(1)	-4(1)	-5(1)
C(6)	20(1)	16(1)	20(1)	-1(1)	-2(1)	-7(1)
C(7)	23(1)	21(1)	22(1)	-6(1)	-5(1)	-9(1)
C(8)	18(1)	20(1)	20(1)	-3(1)	-7(1)	-7(1)
C(9)	14(1)	14(1)	14(1)	0(1)	-4(1)	-6(1)
C(10)	14(1)	14(1)	14(1)	-1(1)	-4(1)	-6(1)
C(11)	14(1)	14(1)	16(1)	-1(1)	-4(1)	-6(1)
C(12)	18(1)	14(1)	15(1)	0(1)	-5(1)	-7(1)
C(13)	22(1)	26(1)	20(1)	6(1)	-4(1)	-14(1)
C(14)	15(1)	16(1)	19(1)	2(1)	-7(1)	-7(1)
C(15)	19(1)	29(1)	19(1)	2(1)	-9(1)	-13(1)
C(16)	19(1)	21(1)	16(1)	4(1)	-6(1)	-11(1)

Table S5. Hydrogen coordinates (x 10^4) and isotropic displacement parameters ($Å^2$x 10^3) for **4h**.

	x	y	z	U(eq)
H(4)	2110	4032	7401	20
H(5)	68	6631	8036	22
H(6)	198	7648	9753	23
H(7)	2345	6027	10869	26
H(8)	4365	3405	10270	22
H(13A)	5354	2851	3166	33
H(13B)	4568	4521	3845	33
H(13C)	4167	4510	2557	33
H(15A)	81	1571	3998	31
H(15B)	-1480	3346	4319	31
H(15C)	-2030	1788	4684	31
H(16A)	972	-581	7683	26
H(16B)	141	994	8482	26
H(16C)	2238	-274	8393	26

Table S6. Torsion angles [°] for **4h**.

N(2)-O(1)-N(1)-O(2)	179.88(9)
N(2)-O(1)-N(1)-C(2)	-0.17(11)
N(1)-O(1)-N(2)-C(1)	0.23(12)
C(11)-N(3)-N(4)-C(9)	-1.43(12)
C(1)-N(3)-N(4)-C(9)	-172.61(9)
O(1)-N(2)-C(1)-N(3)	-178.85(9)
O(1)-N(2)-C(1)-C(2)	-0.22(13)
N(4)-N(3)-C(1)-N(2)	-96.61(13)
C(11)-N(3)-C(1)-N(2)	93.51(14)
N(4)-N(3)-C(1)-C(2)	84.97(14)
C(11)-N(3)-C(1)-C(2)	-84.91(15)
O(2)-N(1)-C(2)-C(1)	179.97(12)
O(1)-N(1)-C(2)-C(1)	0.04(11)
O(2)-N(1)-C(2)-C(3)	-0.2(2)
O(1)-N(1)-C(2)-C(3)	179.84(10)
N(2)-C(1)-C(2)-N(1)	0.11(13)
N(3)-C(1)-C(2)-N(1)	178.60(10)
N(2)-C(1)-C(2)-C(3)	-179.66(11)
N(3)-C(1)-C(2)-C(3)	-1.2(2)
N(1)-C(2)-C(3)-C(4)	174.50(11)
C(1)-C(2)-C(3)-C(4)	-5.77(19)
N(1)-C(2)-C(3)-C(8)	-5.96(17)
C(1)-C(2)-C(3)-C(8)	173.77(12)
C(8)-C(3)-C(4)-C(5)	-0.41(17)
C(2)-C(3)-C(4)-C(5)	179.13(11)
C(3)-C(4)-C(5)-C(6)	0.87(18)
C(4)-C(5)-C(6)-C(7)	-0.71(19)
C(5)-C(6)-C(7)-C(8)	0.10(19)
C(6)-C(7)-C(8)-C(3)	0.35(19)
C(4)-C(3)-C(8)-C(7)	-0.19(18)
C(2)-C(3)-C(8)-C(7)	-179.74(11)
N(3)-N(4)-C(9)-C(10)	1.01(12)
N(3)-N(4)-C(9)-C(12)	176.44(9)
N(4)-C(9)-C(10)-C(11)	-0.28(13)
C(12)-C(9)-C(10)-C(11)	-174.87(11)
N(4)-C(9)-C(10)-C(14)	179.53(11)
C(12)-C(9)-C(10)-C(14)	4.9(2)
N(4)-N(3)-C(11)-C(10)	1.29(12)

C(1)-N(3)-C(11)-C(10)	171.71(10)
N(4)-N(3)-C(11)-C(16)	179.32(10)
C(1)-N(3)-C(11)-C(16)	-10.26(17)
C(9)-C(10)-C(11)-N(3)	-0.58(12)
C(14)-C(10)-C(11)-N(3)	179.58(10)
C(9)-C(10)-C(11)-C(16)	-178.33(12)
C(14)-C(10)-C(11)-C(16)	1.83(19)
N(4)-C(9)-C(12)-O(3)	-166.11(11)
C(10)-C(9)-C(12)-O(3)	8.25(19)
N(4)-C(9)-C(12)-C(13)	11.82(15)
C(10)-C(9)-C(12)-C(13)	-173.83(11)
C(11)-C(10)-C(14)-O(4)	25.32(16)
C(9)-C(10)-C(14)-O(4)	-154.47(13)
C(11)-C(10)-C(14)-C(15)	-152.06(11)
C(9)-C(10)-C(14)-C(15)	28.16(19)

Table S7. Crystal data and structure refinement for **3h**.

Empirical formula	C16 H14 N6 O4	
Formula weight	354.33	
Temperature	100(2) K	
Wavelength	0.71073 Å	
Crystal system	Monoclinic	
Space group	$P2_1/c$	
Unit cell dimensions	a = 10.5233(2) Å	α= 90°.
	b = 17.6418(3) Å	β= 96.0130(10)°.
	c = 8.28210(10) Å	γ = 90°.
Volume	1529.11(4) $Å^3$	
Z	4	
Density (calculated)	1.539 g/cm^3	
Absorption coefficient	0.115 mm^{-1}	
F(000)	736	
Crystal size	0.27 x 0.11 x 0.08 mm^3	
Theta range for data collection	2.263 to 34.989°.	
Index ranges	-16<=h<=16, -28<=k<=27, -13<=l<=12	
Reflections collected	41217	
Independent reflections	6713 [R(int) = 0.0866]	
Observed reflections	4087	
Completeness to theta = 25.242°	99.7 %	
Absorption correction	Semi-empirical from equivalents	
Max. and min. transmission	0.7469 and 0.7146	
Refinement method	Full-matrix least-squares on F^2	
Data / restraints / parameters	6713 / 0 / 238	
Goodness-of-fit on F^2	1.014	
Final R indices [I>2sigma(I)]	R1 = 0.0671, wR2 = 0.1454	
R indices (all data)	R1 = 0.1249, wR2 = 0.1755	
Largest diff. peak and hole	0.450 and -0.359 $e.Å^{-3}$	

Table S8. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$x 10^3) for **3h**. U(eq) is defined as one third of the trace of the orthogonalized U^{ij} tensor.

	x	y	z	U(eq)
O(1)	9076(1)	2868(1)	2655(2)	28(1)
O(2)	7854(1)	3372(1)	480(2)	23(1)
O(3)	6459(1)	8346(1)	1006(2)	26(1)
O(4)	4580(1)	8034(1)	2526(2)	25(1)
N(1)	8424(1)	3418(1)	2154(2)	20(1)
N(2)	7190(2)	4025(1)	140(2)	21(1)
N(3)	6787(1)	5162(1)	1410(2)	16(1)
N(4)	7482(1)	5742(1)	841(2)	17(1)
N(5)	6333(1)	7646(1)	1211(2)	19(1)
N(6)	5164(1)	7454(1)	2125(2)	18(1)
C(1)	9062(2)	3807(1)	5595(2)	21(1)
C(2)	9391(2)	4040(1)	7172(2)	24(1)
C(3)	9128(2)	4772(1)	7651(2)	24(1)
C(4)	8534(2)	5279(1)	6527(2)	22(1)
C(5)	8216(2)	5056(1)	4933(2)	19(1)
C(6)	8465(2)	4313(1)	4444(2)	17(1)
C(7)	8087(2)	4076(1)	2767(2)	16(1)
C(8)	7329(2)	4432(1)	1453(2)	16(1)
C(9)	4822(2)	4816(1)	2678(2)	20(1)
C(10)	5703(2)	5380(1)	2063(2)	15(1)
C(11)	5689(2)	6166(1)	1914(2)	15(1)
C(12)	6784(2)	6350(1)	1142(2)	16(1)
C(13)	7092(2)	7107(1)	756(2)	17(1)
C(14)	8219(2)	7337(1)	-82(2)	23(1)
C(15)	4873(2)	6742(1)	2421(2)	17(1)
C(16)	3737(2)	6629(1)	3323(2)	20(1)

Table S9. Bond lengths [Å] and angles [°] for **3h**.

O(1)-N(1)	1.2342(19)
O(2)-N(2)	1.3610(19)
O(2)-N(1)	1.453(2)
O(3)-N(5)	1.2547(18)
O(4)-N(6)	1.2564(18)
N(1)-C(7)	1.330(2)
N(2)-C(8)	1.299(2)
N(3)-C(10)	1.368(2)
N(3)-N(4)	1.3702(19)
N(3)-C(8)	1.407(2)
N(4)-C(12)	1.338(2)
N(5)-C(13)	1.322(2)
N(5)-N(6)	1.548(2)
N(6)-C(15)	1.320(2)
C(1)-C(2)	1.379(3)
C(1)-C(6)	1.405(2)
C(1)-H(1)	0.9500
C(2)-C(3)	1.389(3)
C(2)-H(2)	0.9500
C(3)-C(4)	1.390(3)
C(3)-H(3)	0.9500
C(4)-C(5)	1.385(2)
C(4)-H(4)	0.9500
C(5)-C(6)	1.404(2)
C(5)-H(5)	0.9500
C(6)-C(7)	1.465(2)
C(7)-C(8)	1.426(2)
C(9)-C(10)	1.486(2)
C(9)-H(9A)	0.9800
C(9)-H(9B)	0.9800
C(9)-H(9C)	0.9800
C(10)-C(11)	1.393(2)
C(11)-C(12)	1.413(2)
C(11)-C(15)	1.422(2)
C(12)-C(13)	1.418(2)
C(13)-C(14)	1.491(2)
C(14)-H(14A)	0.9800
C(14)-H(14B)	0.9800

C(14)-H(14C)	0.9800
C(15)-C(16)	1.488(2)
C(16)-H(16A)	0.9800
C(16)-H(16B)	0.9800
C(16)-H(16C)	0.9800

N(2)-O(2)-N(1)	107.60(12)
O(1)-N(1)-C(7)	135.88(16)
O(1)-N(1)-O(2)	115.91(14)
C(7)-N(1)-O(2)	108.21(13)
C(8)-N(2)-O(2)	106.52(14)
C(10)-N(3)-N(4)	115.05(13)
C(10)-N(3)-C(8)	126.83(14)
N(4)-N(3)-C(8)	117.59(13)
C(12)-N(4)-N(3)	102.23(13)
O(3)-N(5)-C(13)	126.36(15)
O(3)-N(5)-N(6)	112.52(13)
C(13)-N(5)-N(6)	121.11(13)
O(4)-N(6)-C(15)	126.52(15)
O(4)-N(6)-N(5)	112.74(13)
C(15)-N(6)-N(5)	120.73(13)
C(2)-C(1)-C(6)	120.23(17)
C(2)-C(1)-H(1)	119.9
C(6)-C(1)-H(1)	119.9
C(1)-C(2)-C(3)	120.66(17)
C(1)-C(2)-H(2)	119.7
C(3)-C(2)-H(2)	119.7
C(2)-C(3)-C(4)	119.74(17)
C(2)-C(3)-H(3)	120.1
C(4)-C(3)-H(3)	120.1
C(5)-C(4)-C(3)	120.20(17)
C(5)-C(4)-H(4)	119.9
C(3)-C(4)-H(4)	119.9
C(4)-C(5)-C(6)	120.40(16)
C(4)-C(5)-H(5)	119.8
C(6)-C(5)-H(5)	119.8
C(5)-C(6)-C(1)	118.76(16)
C(5)-C(6)-C(7)	119.95(15)
C(1)-C(6)-C(7)	121.29(15)
N(1)-C(7)-C(8)	104.10(15)

N(1)-C(7)-C(6)	123.66(15)
C(8)-C(7)-C(6)	132.23(15)
N(2)-C(8)-N(3)	118.37(15)
N(2)-C(8)-C(7)	113.56(15)
N(3)-C(8)-C(7)	128.00(15)
C(10)-C(9)-H(9A)	109.5
C(10)-C(9)-H(9B)	109.5
H(9A)-C(9)-H(9B)	109.5
C(10)-C(9)-H(9C)	109.5
H(9A)-C(9)-H(9C)	109.5
H(9B)-C(9)-H(9C)	109.5
N(3)-C(10)-C(11)	104.27(13)
N(3)-C(10)-C(9)	121.61(14)
C(11)-C(10)-C(9)	134.08(15)
C(10)-C(11)-C(12)	105.50(14)
C(10)-C(11)-C(15)	133.39(15)
C(12)-C(11)-C(15)	121.04(14)
N(4)-C(12)-C(11)	112.93(14)
N(4)-C(12)-C(13)	124.72(15)
C(11)-C(12)-C(13)	122.35(15)
N(5)-C(13)-C(12)	116.95(15)
N(5)-C(13)-C(14)	118.10(15)
C(12)-C(13)-C(14)	124.94(15)
C(13)-C(14)-H(14A)	109.5
C(13)-C(14)-H(14B)	109.5
H(14A)-C(14)-H(14B)	109.5
C(13)-C(14)-H(14C)	109.5
H(14A)-C(14)-H(14C)	109.5
H(14B)-C(14)-H(14C)	109.5
N(6)-C(15)-C(11)	117.72(15)
N(6)-C(15)-C(16)	115.83(15)
C(11)-C(15)-C(16)	126.40(15)
C(15)-C(16)-H(16A)	109.5
C(15)-C(16)-H(16B)	109.5
H(16A)-C(16)-H(16B)	109.5
C(15)-C(16)-H(16C)	109.5
H(16A)-C(16)-H(16C)	109.5
H(16B)-C(16)-H(16C)	109.5

Table S10. Anisotropic displacement parameters ($Å^2 x\ 10^3$) for **3h**. The anisotropic displacement factor exponent takes the form: $-2\pi^2[\ h^2\ a^{*2}U^{11} + ...\ + 2\ h\ k\ a^*\ b^*\ U^{12}\ ]$.

	U^{11}	U^{22}	U^{33}	U^{23}	U^{13}	U^{12}
O(1)	31(1)	20(1)	34(1)	0(1)	0(1)	12(1)
O(2)	28(1)	19(1)	23(1)	-3(1)	1(1)	5(1)
O(3)	27(1)	12(1)	39(1)	4(1)	4(1)	-4(1)
O(4)	27(1)	13(1)	36(1)	-3(1)	7(1)	3(1)
N(1)	20(1)	17(1)	23(1)	-1(1)	3(1)	2(1)
N(2)	24(1)	17(1)	22(1)	-2(1)	3(1)	4(1)
N(3)	15(1)	14(1)	18(1)	2(1)	2(1)	1(1)
N(4)	16(1)	16(1)	18(1)	2(1)	2(1)	-2(1)
N(5)	18(1)	15(1)	24(1)	2(1)	2(1)	-4(1)
N(6)	18(1)	14(1)	23(1)	0(1)	3(1)	0(1)
C(1)	17(1)	21(1)	24(1)	5(1)	3(1)	2(1)
C(2)	20(1)	30(1)	23(1)	8(1)	0(1)	0(1)
C(3)	20(1)	32(1)	18(1)	1(1)	0(1)	-4(1)
C(4)	19(1)	24(1)	23(1)	-2(1)	2(1)	-2(1)
C(5)	16(1)	19(1)	21(1)	1(1)	0(1)	1(1)
C(6)	13(1)	18(1)	19(1)	1(1)	3(1)	0(1)
C(7)	14(1)	14(1)	22(1)	1(1)	4(1)	1(1)
C(8)	15(1)	16(1)	19(1)	1(1)	3(1)	0(1)
C(9)	21(1)	16(1)	25(1)	1(1)	6(1)	-1(1)
C(10)	15(1)	15(1)	17(1)	0(1)	2(1)	0(1)
C(11)	14(1)	14(1)	17(1)	0(1)	1(1)	0(1)
C(12)	16(1)	15(1)	16(1)	1(1)	1(1)	-1(1)
C(13)	16(1)	16(1)	19(1)	1(1)	0(1)	-1(1)
C(14)	20(1)	24(1)	25(1)	4(1)	4(1)	-5(1)
C(15)	16(1)	15(1)	20(1)	-1(1)	2(1)	-1(1)
C(16)	18(1)	19(1)	24(1)	-3(1)	6(1)	0(1)

Table S11. Hydrogen coordinates ($x\ 10^4$) and isotropic displacement parameters ($Å^2 x\ 10^{\ 3}$) for **3h**.

	x	y	z	U(eq)
H(1)	9240	3303	5284	25
H(2)	9803	3695	7940	29
H(3)	9353	4927	8742	28

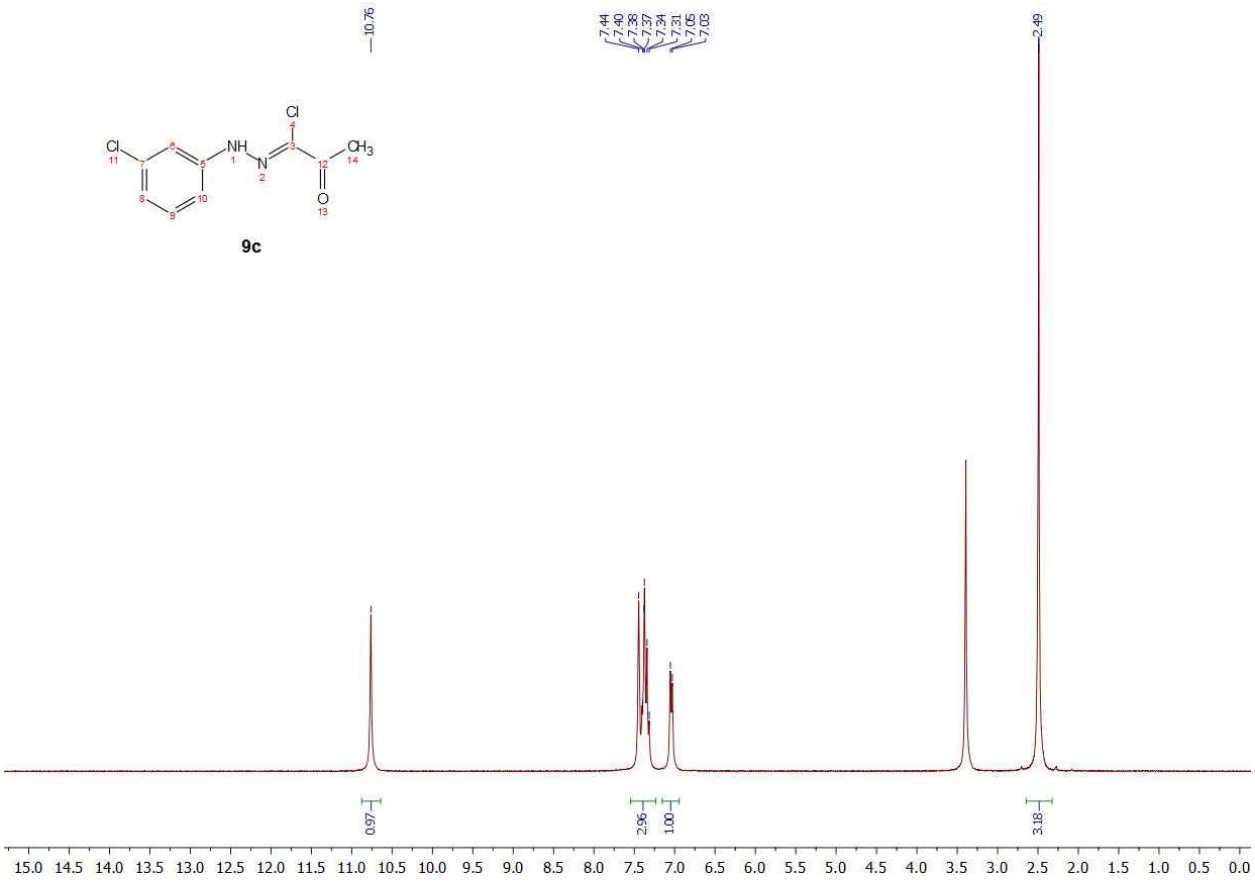
H(4)	8345	5779	6854	26
H(5)	7827	5408	4165	23
H(9A)	4678	4944	3796	31
H(9B)	5201	4310	2654	31
H(9C)	4005	4823	1991	31
H(14A)	8541	6897	-636	34
H(14B)	8891	7531	719	34
H(14C)	7964	7733	-879	34
H(16A)	3479	6095	3256	30
H(16B)	3032	6946	2844	30
H(16C)	3951	6770	4463	30

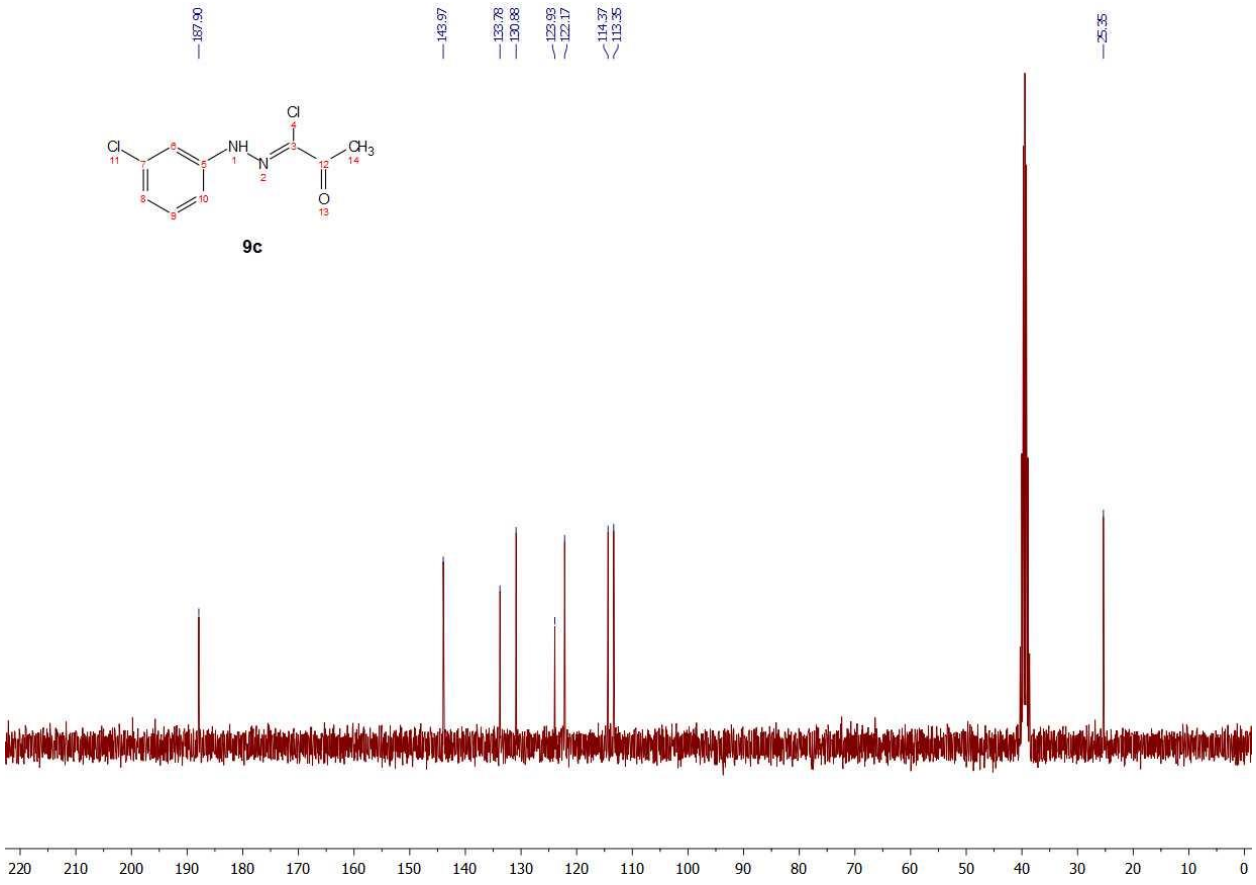
Table S12. Torsion angles [°] for **3h**.

N(2)-O(2)-N(1)-O(1)	-179.29(14)
N(2)-O(2)-N(1)-C(7)	0.55(17)
N(1)-O(2)-N(2)-C(8)	-0.04(17)
C(10)-N(3)-N(4)-C(12)	-0.66(18)
C(8)-N(3)-N(4)-C(12)	-172.89(14)
O(3)-N(5)-N(6)-O(4)	-1.6(2)
C(13)-N(5)-N(6)-O(4)	177.14(16)
O(3)-N(5)-N(6)-C(15)	178.78(16)
C(13)-N(5)-N(6)-C(15)	-2.5(2)
C(6)-C(1)-C(2)-C(3)	0.6(3)
C(1)-C(2)-C(3)-C(4)	-0.4(3)
C(2)-C(3)-C(4)-C(5)	-0.6(3)
C(3)-C(4)-C(5)-C(6)	1.4(3)
C(4)-C(5)-C(6)-C(1)	-1.1(2)
C(4)-C(5)-C(6)-C(7)	178.02(15)
C(2)-C(1)-C(6)-C(5)	0.2(2)
C(2)-C(1)-C(6)-C(7)	-179.00(16)
O(1)-N(1)-C(7)-C(8)	179.03(19)
O(2)-N(1)-C(7)-C(8)	-0.77(17)
O(1)-N(1)-C(7)-C(6)	-1.5(3)
O(2)-N(1)-C(7)-C(6)	178.73(14)
C(5)-C(6)-C(7)-N(1)	171.47(16)
C(1)-C(6)-C(7)-N(1)	-9.4(2)
C(5)-C(6)-C(7)-C(8)	-9.2(3)
C(1)-C(6)-C(7)-C(8)	169.96(17)
O(2)-N(2)-C(8)-N(3)	176.74(13)

O(2)-N(2)-C(8)-C(7)	-0.46(19)
C(10)-N(3)-C(8)-N(2)	104.5(2)
N(4)-N(3)-C(8)-N(2)	-84.27(19)
C(10)-N(3)-C(8)-C(7)	-78.7(2)
N(4)-N(3)-C(8)-C(7)	92.5(2)
N(1)-C(7)-C(8)-N(2)	0.81(19)
C(6)-C(7)-C(8)-N(2)	-178.63(17)
N(1)-C(7)-C(8)-N(3)	-176.07(15)
C(6)-C(7)-C(8)-N(3)	4.5(3)
N(4)-N(3)-C(10)-C(11)	-0.17(19)
C(8)-N(3)-C(10)-C(11)	171.21(15)
N(4)-N(3)-C(10)-C(9)	177.76(15)
C(8)-N(3)-C(10)-C(9)	-10.9(3)
N(3)-C(10)-C(11)-C(12)	0.89(17)
C(9)-C(10)-C(11)-C(12)	-176.65(18)
N(3)-C(10)-C(11)-C(15)	-176.16(18)
C(9)-C(10)-C(11)-C(15)	6.3(3)
N(3)-N(4)-C(12)-C(11)	1.26(18)
N(3)-N(4)-C(12)-C(13)	-179.29(15)
C(10)-C(11)-C(12)-N(4)	-1.42(19)
C(15)-C(11)-C(12)-N(4)	176.08(15)
C(10)-C(11)-C(12)-C(13)	179.12(15)
C(15)-C(11)-C(12)-C(13)	-3.4(2)
O(3)-N(5)-C(13)-C(12)	178.70(16)
N(6)-N(5)-C(13)-C(12)	0.1(2)
O(3)-N(5)-C(13)-C(14)	0.2(3)
N(6)-N(5)-C(13)-C(14)	-178.43(14)
N(4)-C(12)-C(13)-N(5)	-176.70(16)
C(11)-C(12)-C(13)-N(5)	2.7(2)
N(4)-C(12)-C(13)-C(14)	1.7(3)
C(11)-C(12)-C(13)-C(14)	-178.88(16)
O(4)-N(6)-C(15)-C(11)	-177.72(16)
N(5)-N(6)-C(15)-C(11)	1.8(2)
O(4)-N(6)-C(15)-C(16)	-0.1(3)
N(5)-N(6)-C(15)-C(16)	179.41(14)
C(10)-C(11)-C(15)-N(6)	177.61(18)
C(12)-C(11)-C(15)-N(6)	0.9(2)
C(10)-C(11)-C(15)-C(16)	0.3(3)
C(12)-C(11)-C(15)-C(16)	-176.39(16)

S5. Copies of NMR spectra

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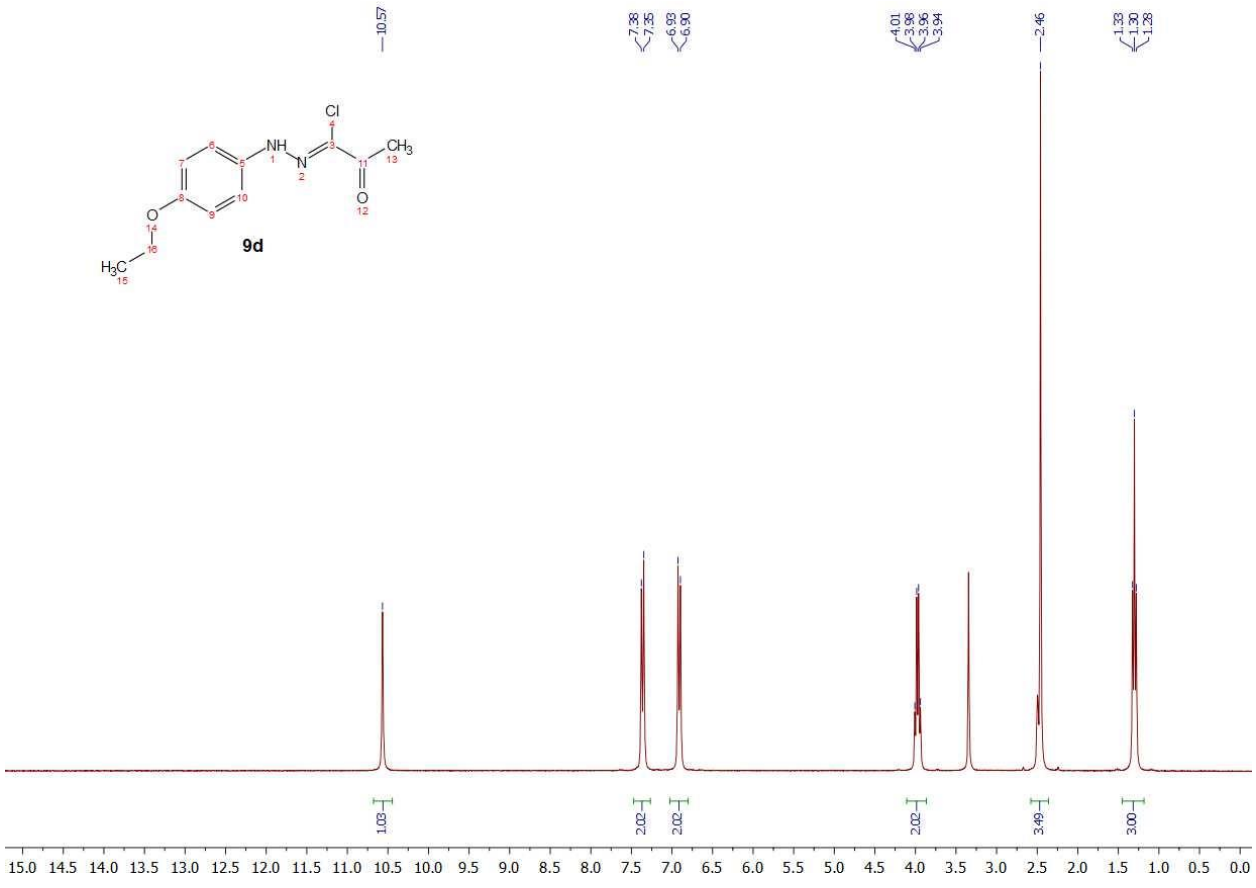
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O
9d
H3C
1.03
2.02
2.02
2.02
3.49
3.00
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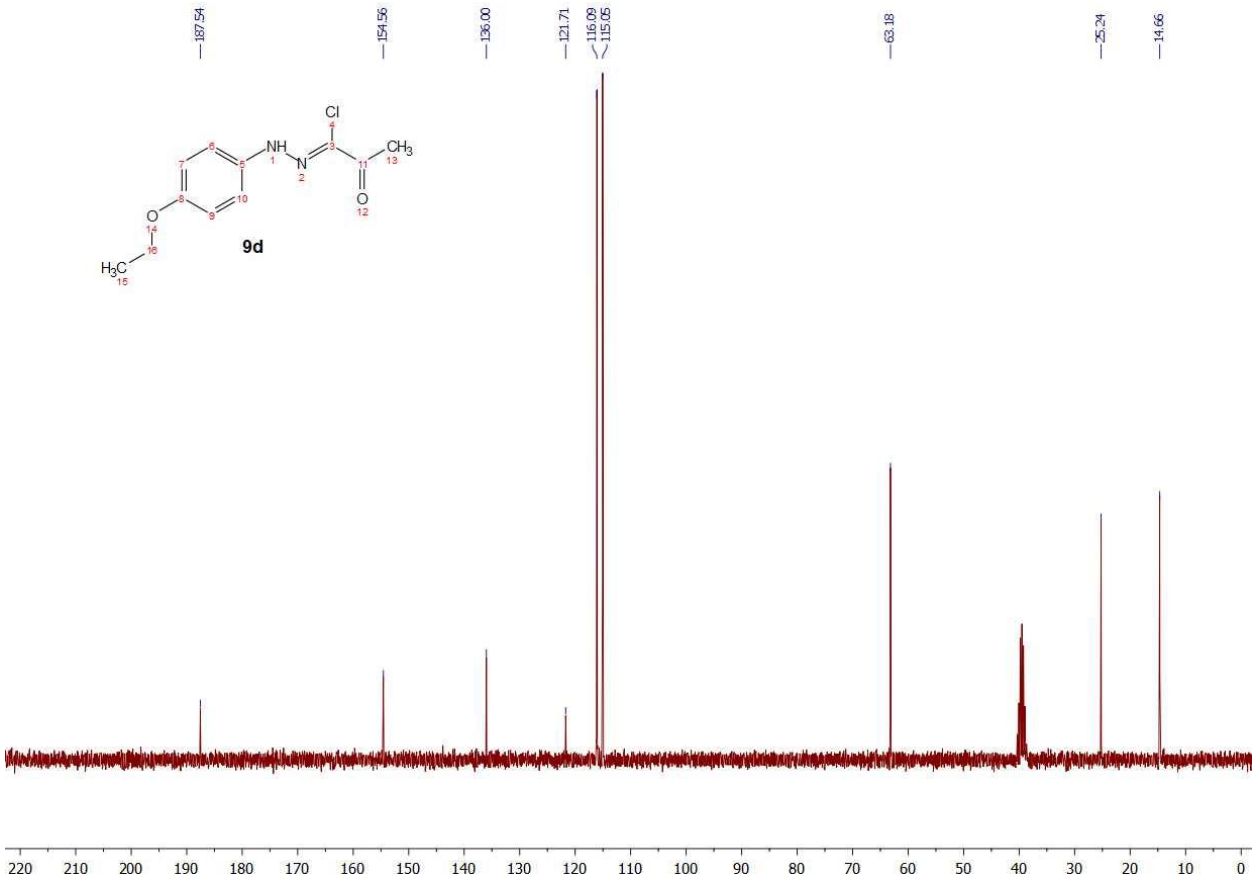
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9d
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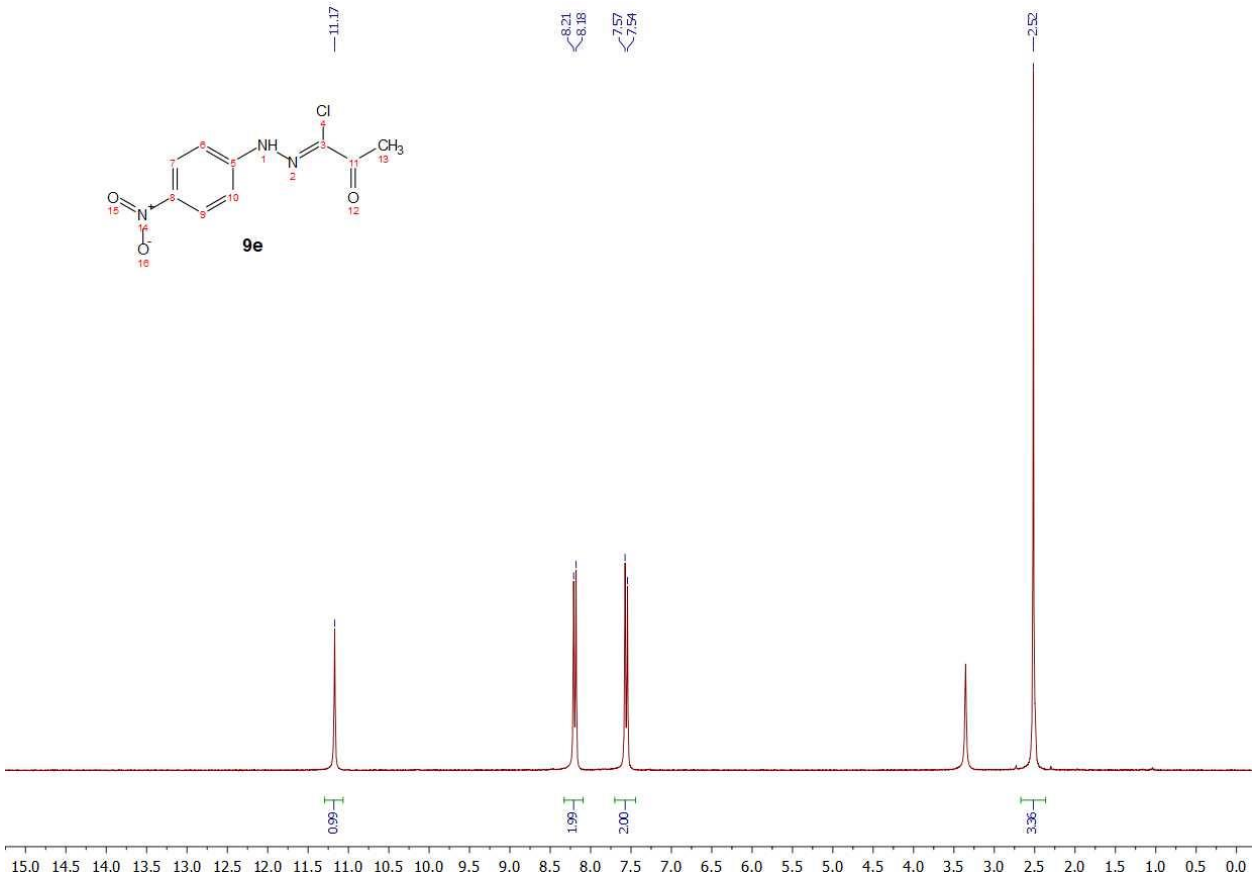
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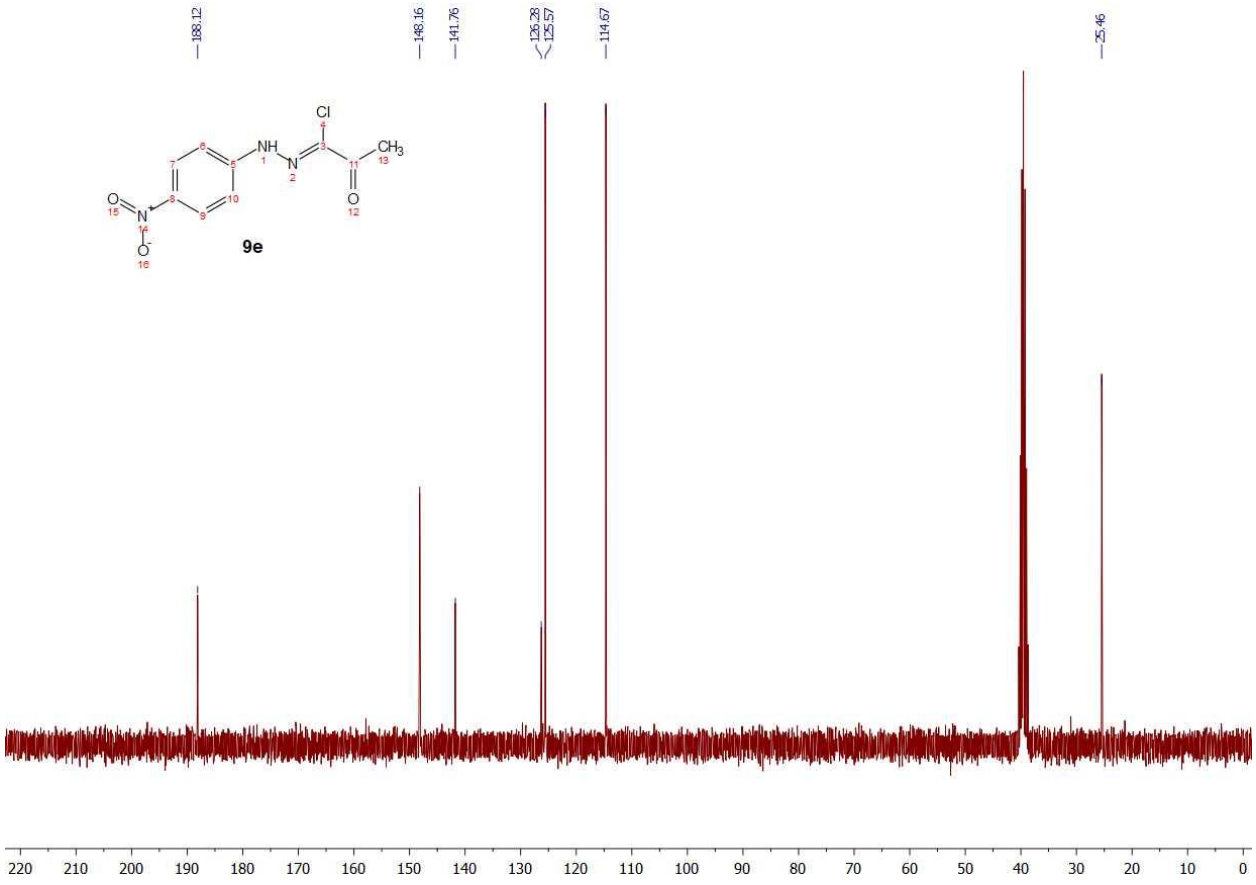
2.00
3.36
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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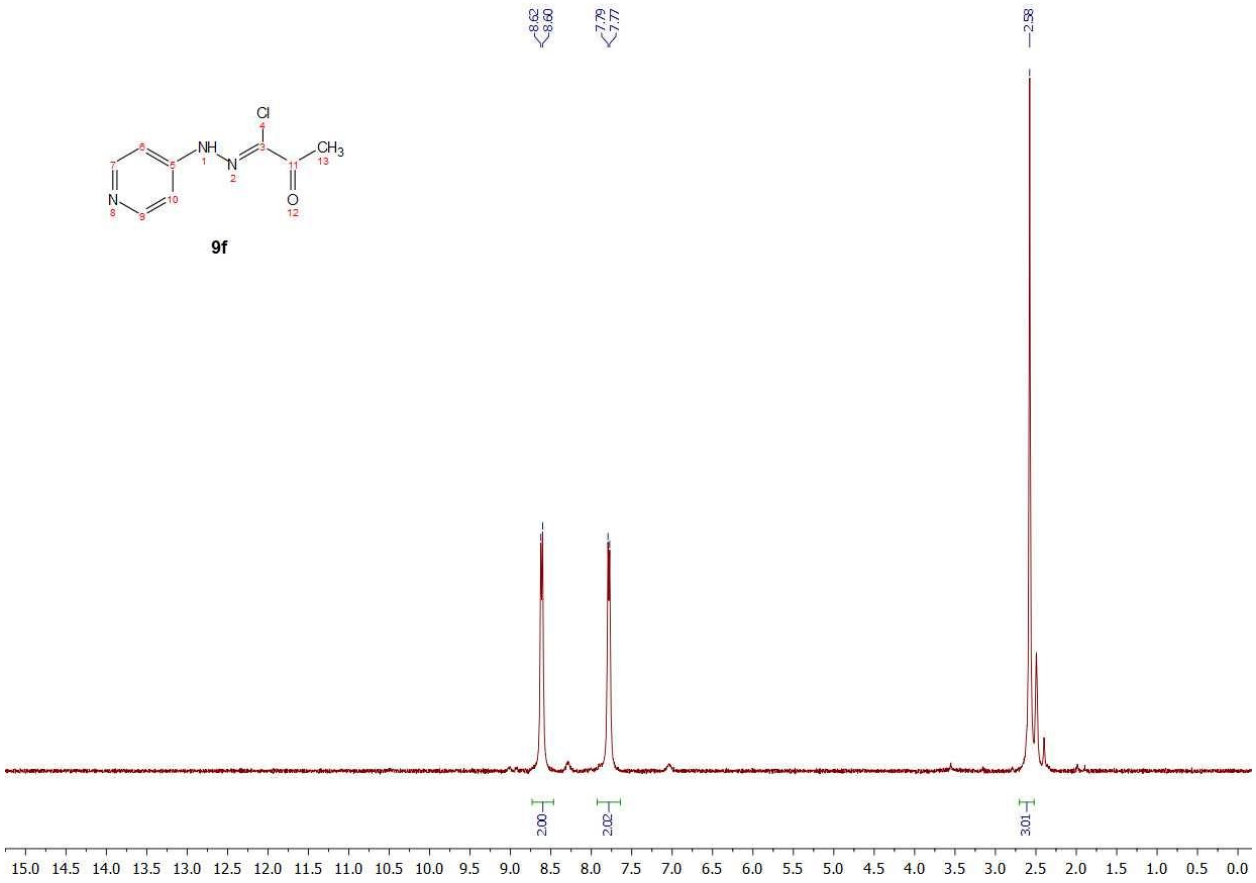
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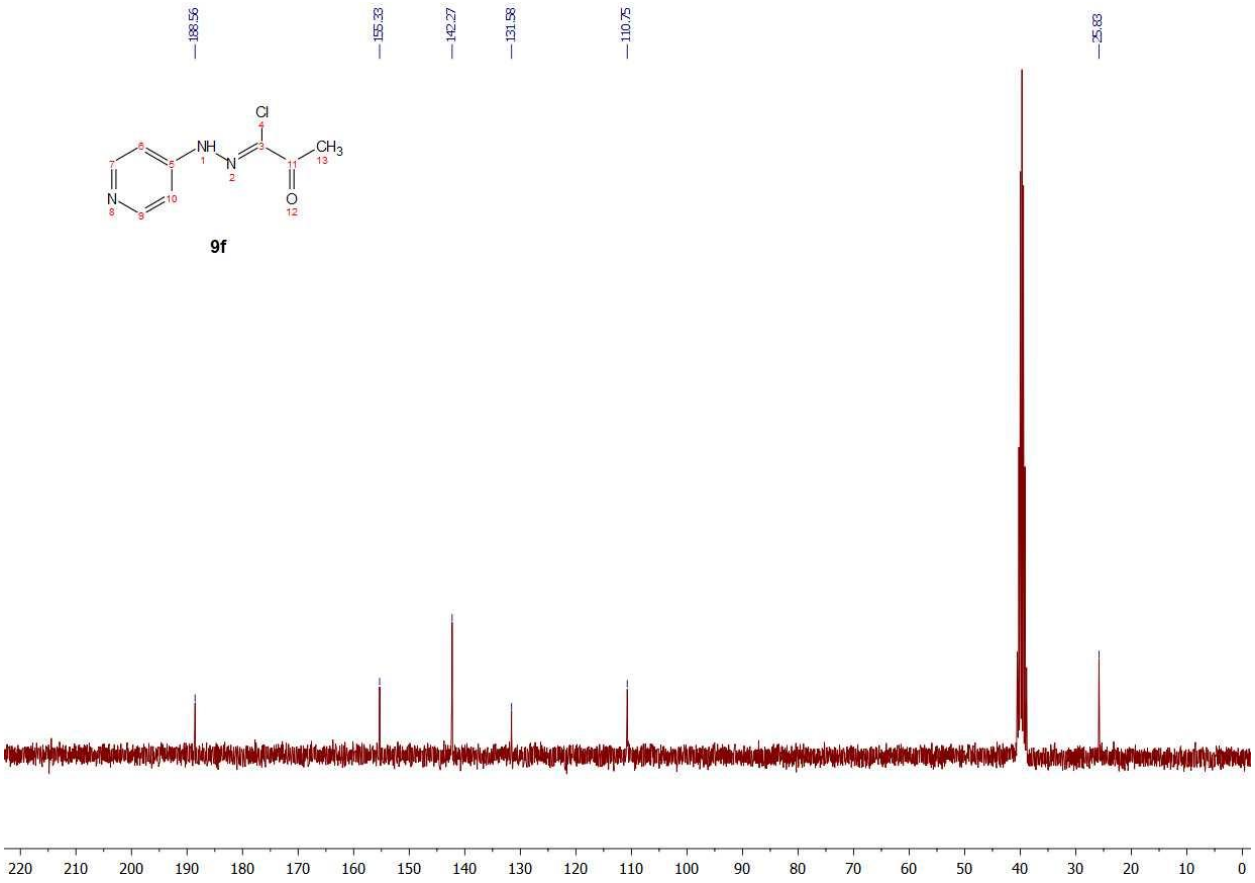
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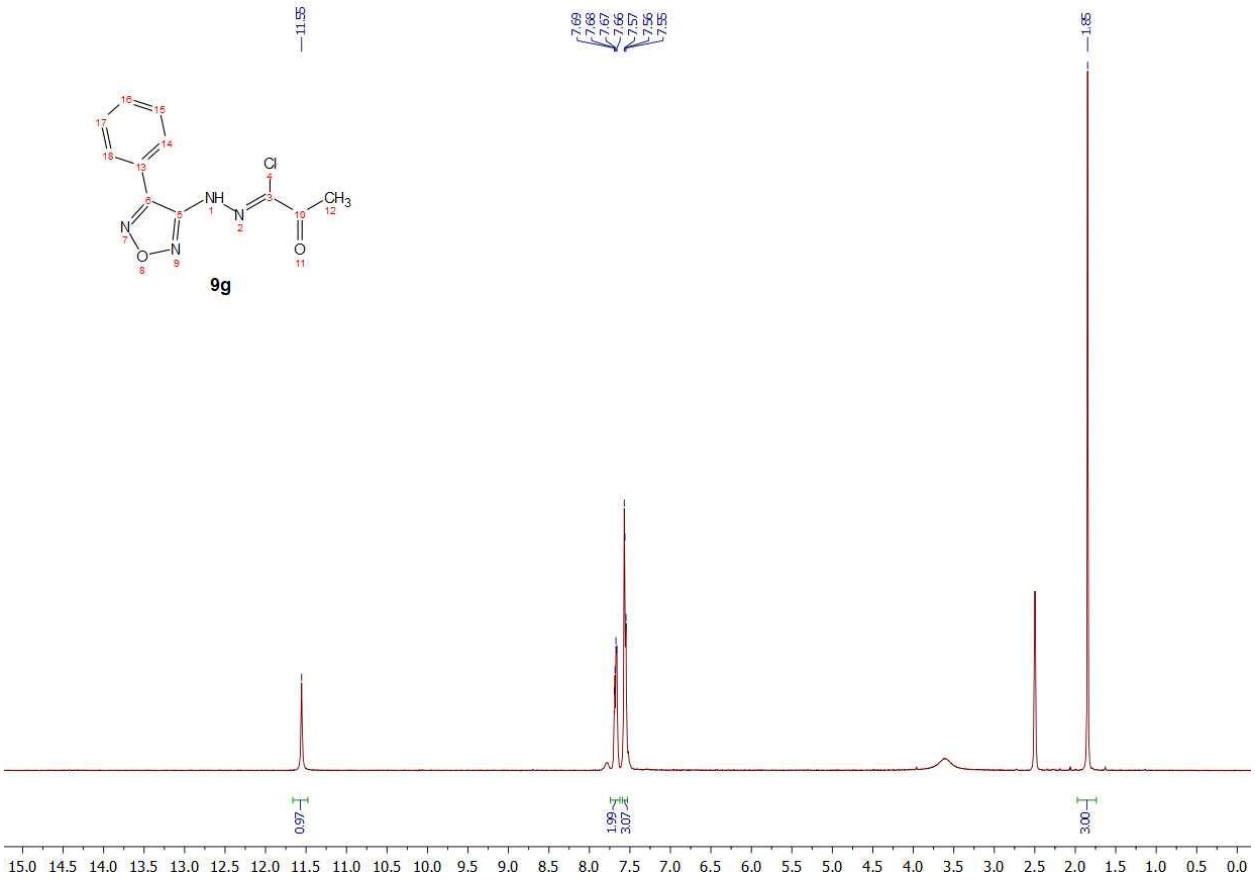
9f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N
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3.00
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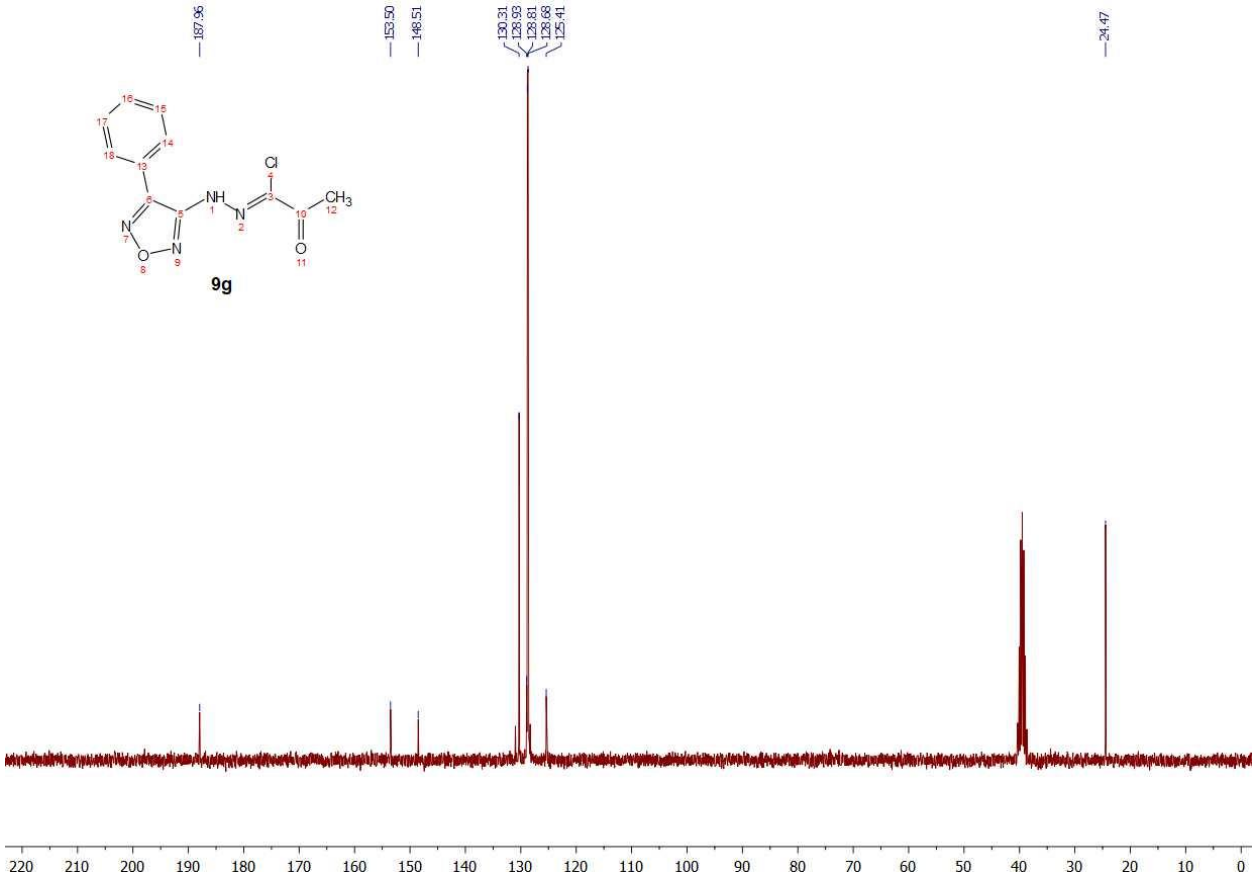
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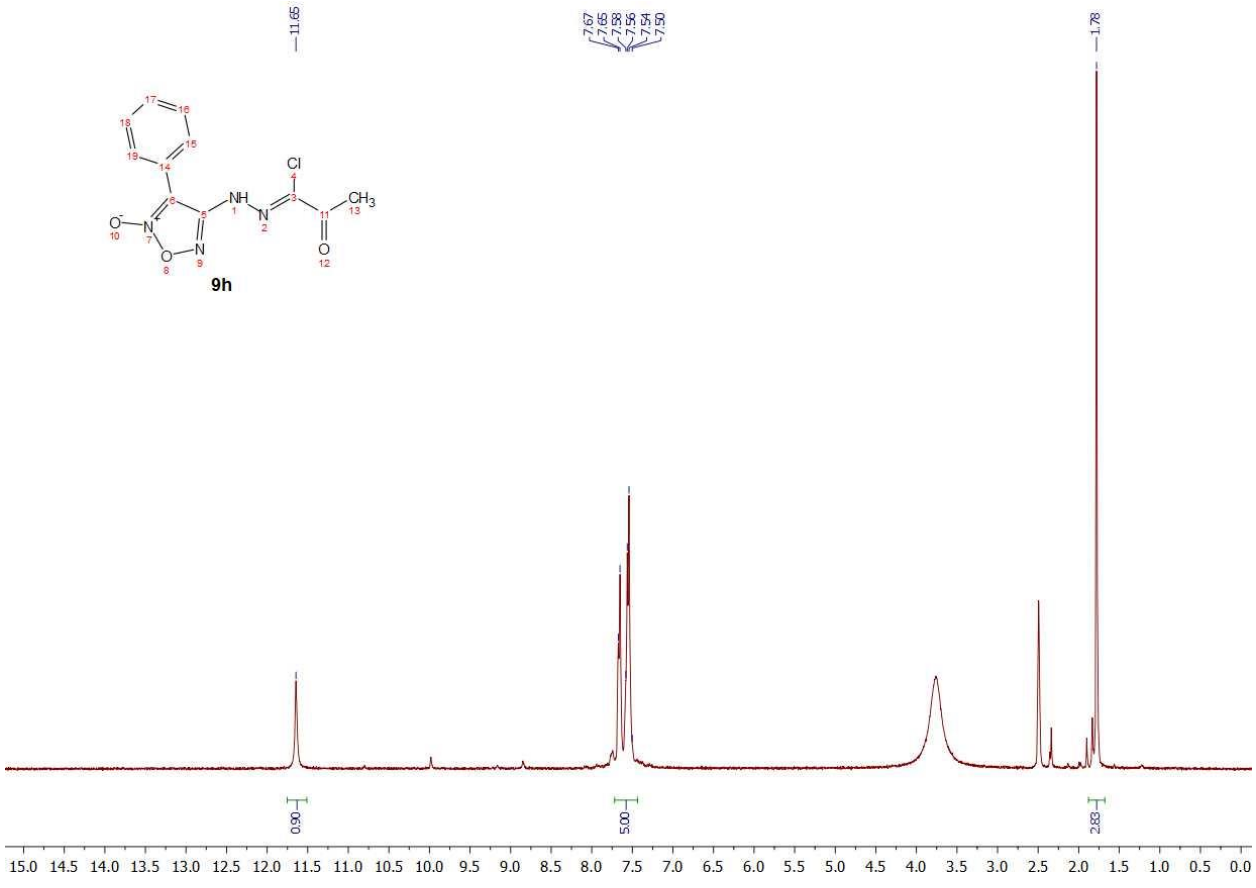
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2.83
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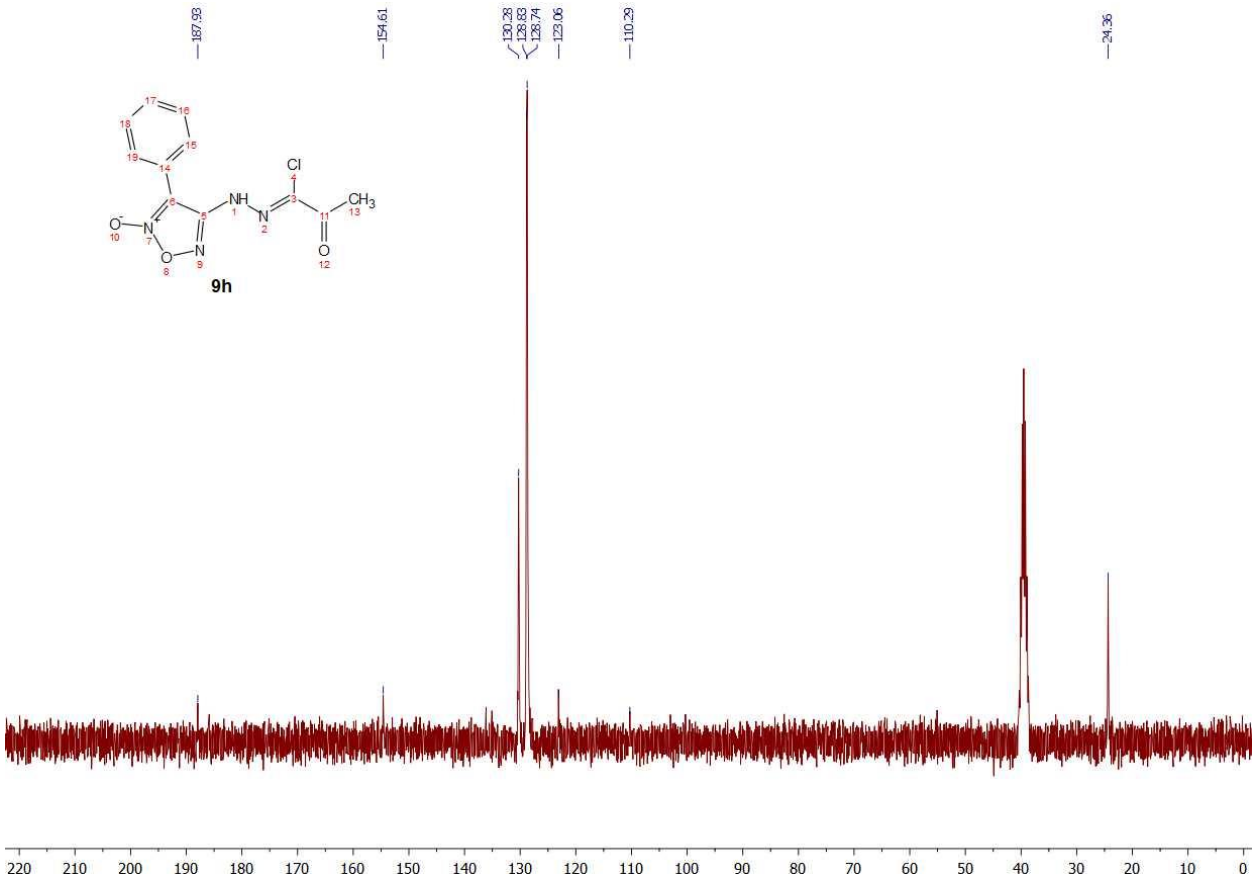
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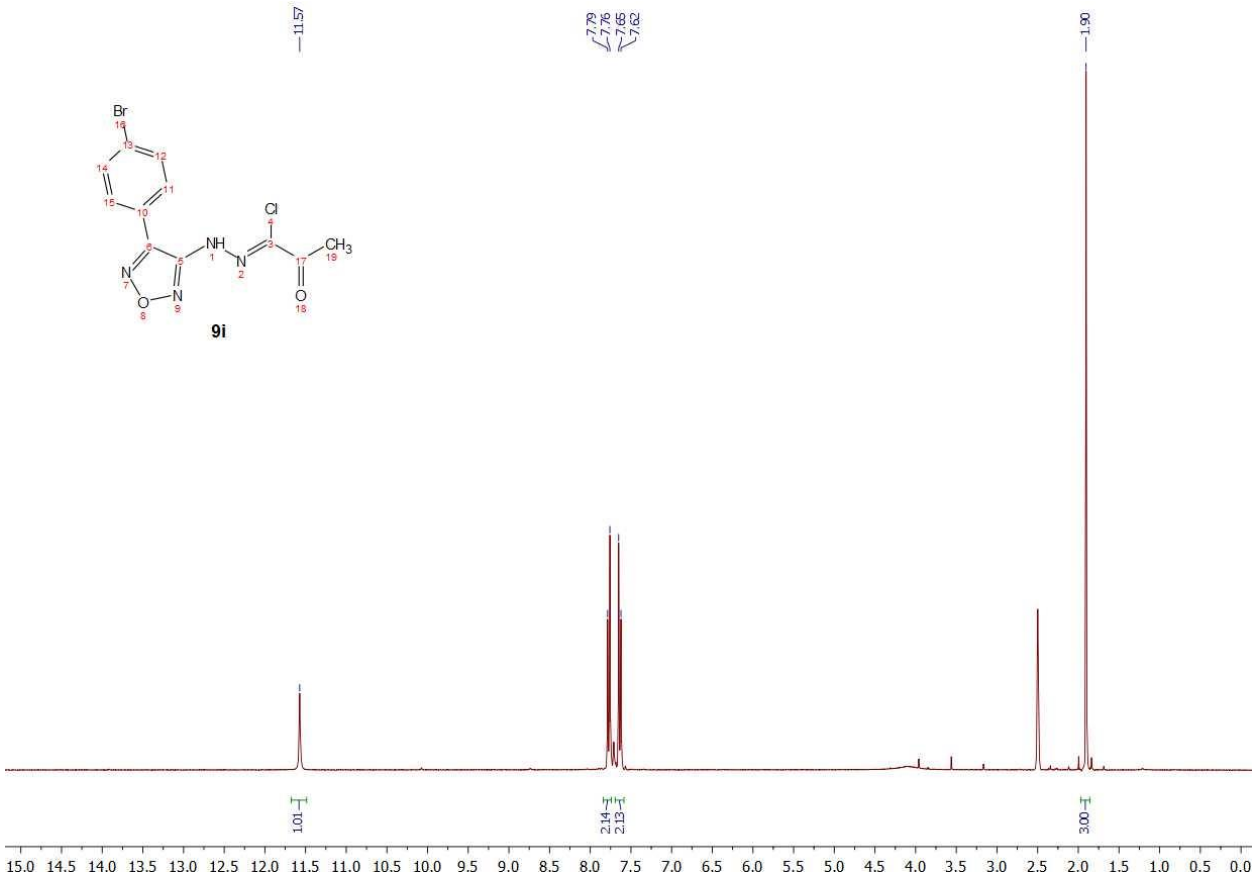
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2.13
3.00
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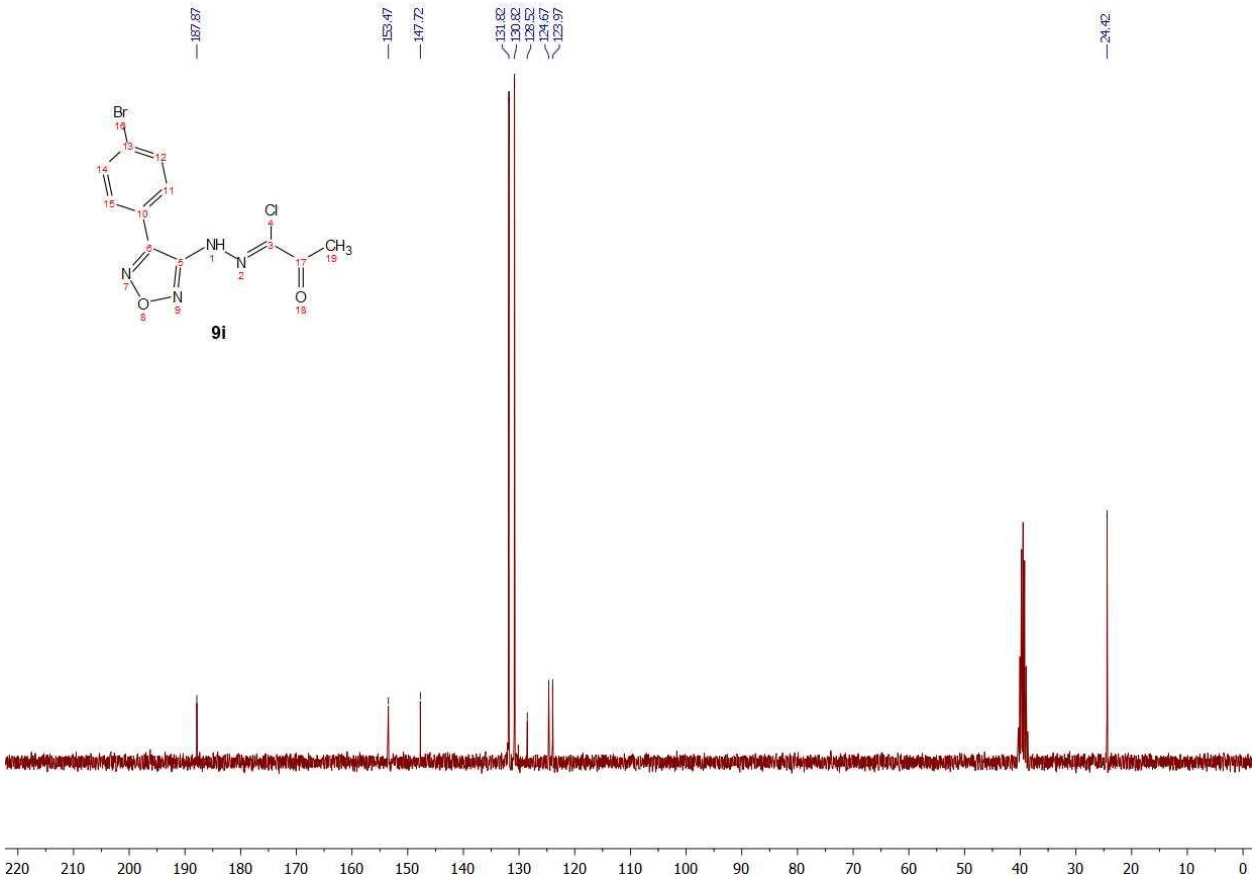
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Cl
NH
N
CH3
O
9i
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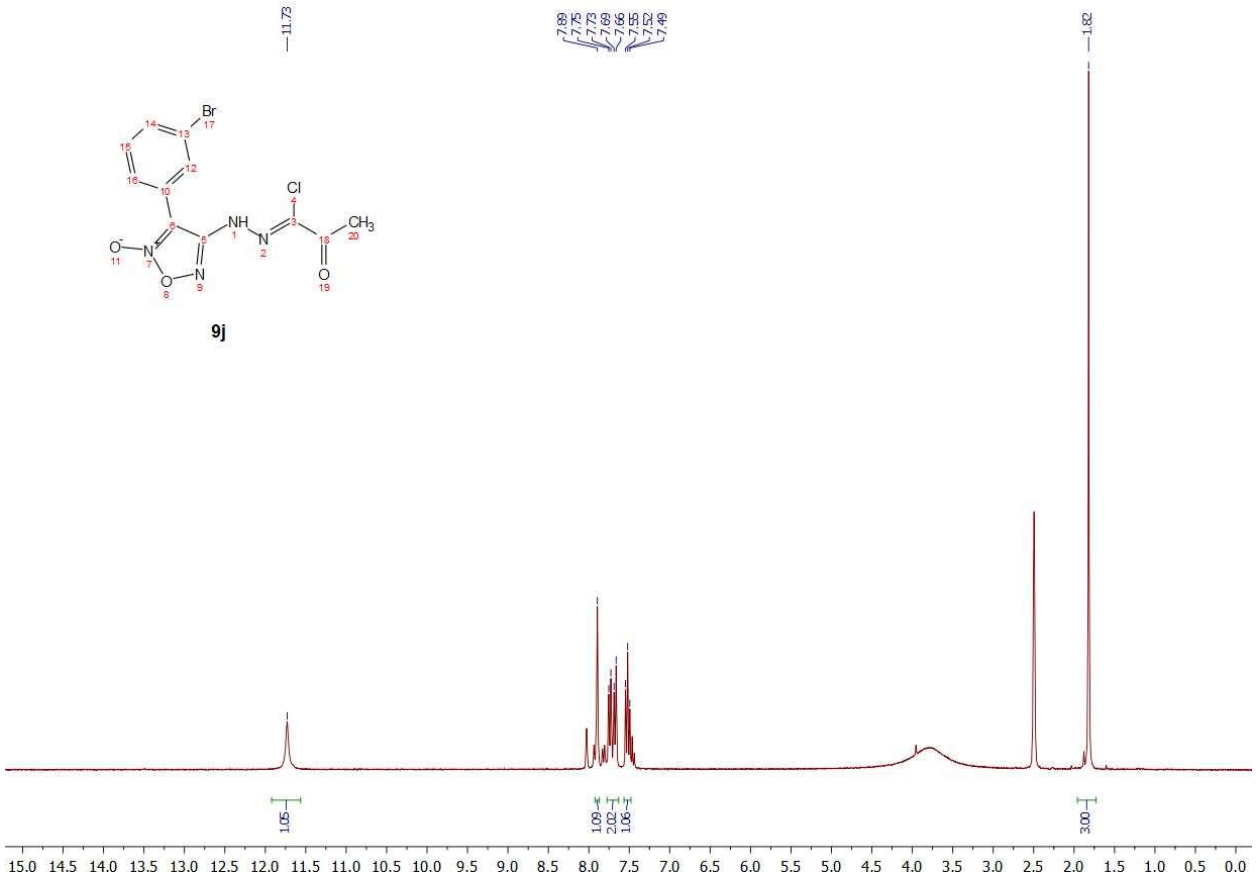
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7.52
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Cl
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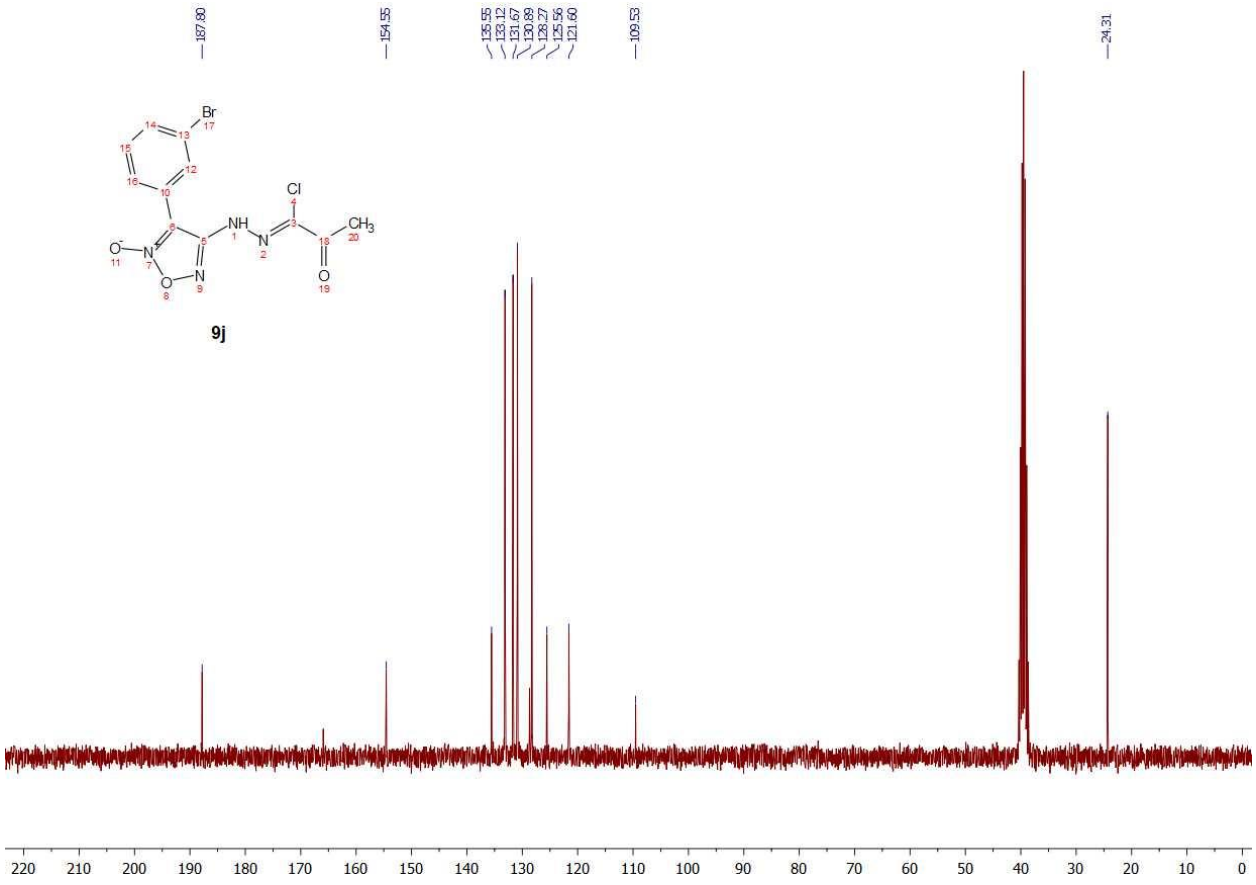
N
CH3
O
9j
1.05
1.09
2.02
1.06
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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Br
Cl
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N
O
CH3
9j
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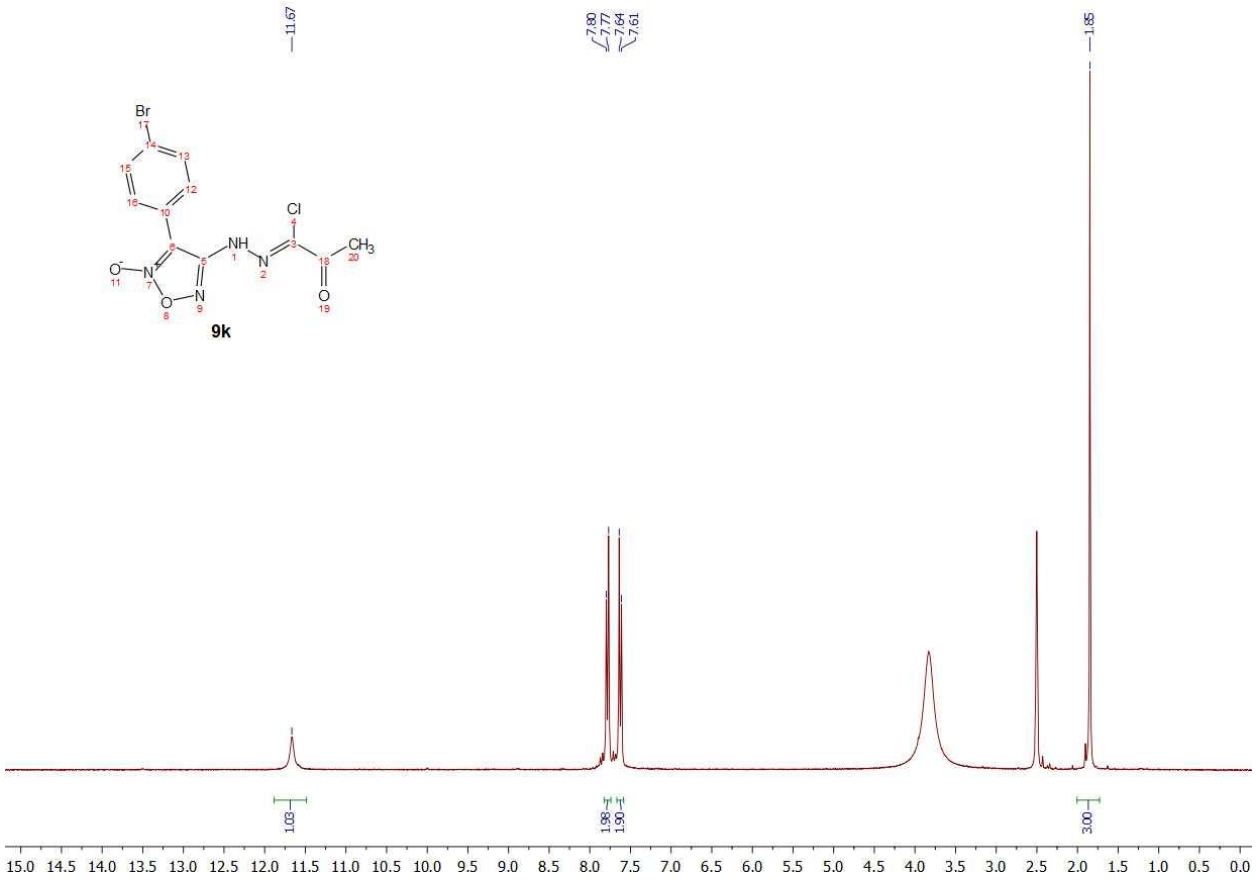
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9k
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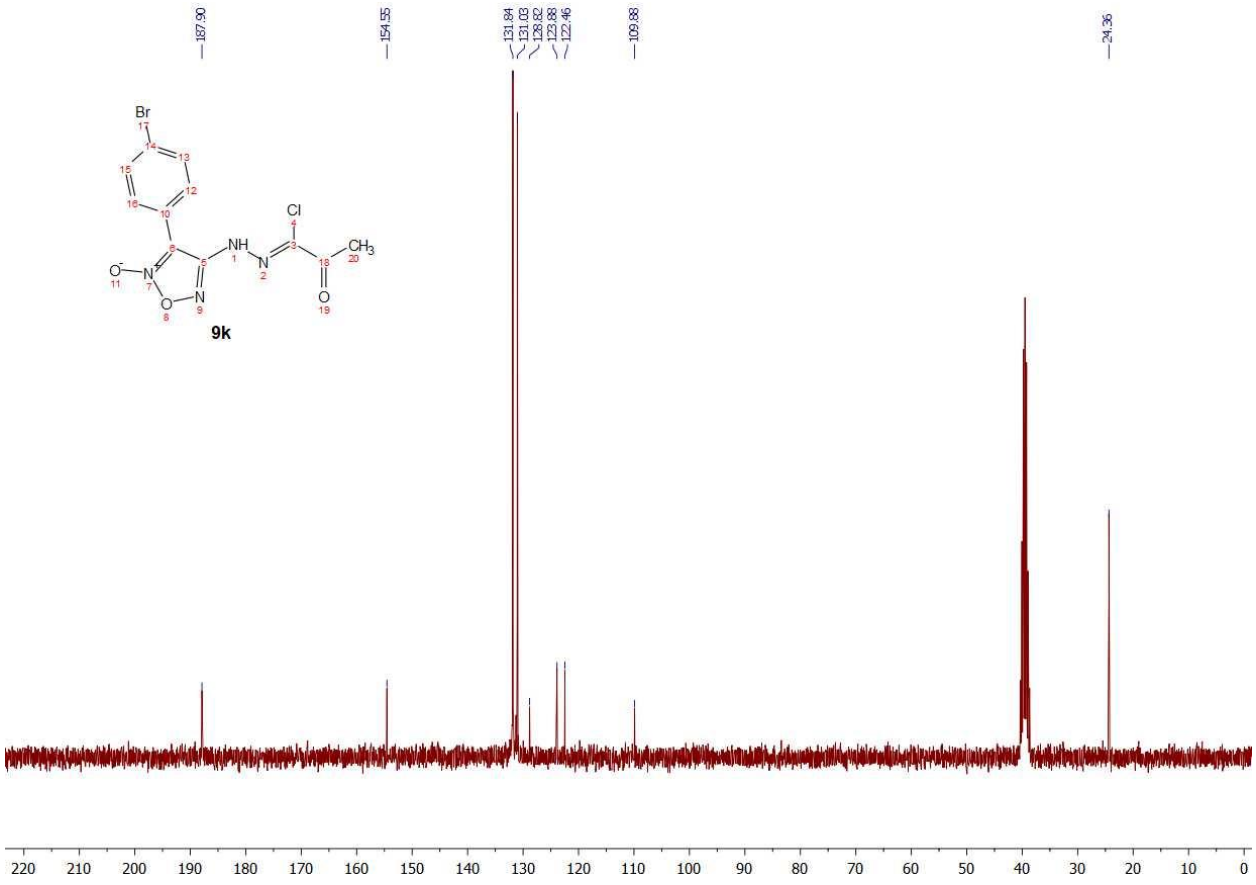
1.98
1.90
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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Cl
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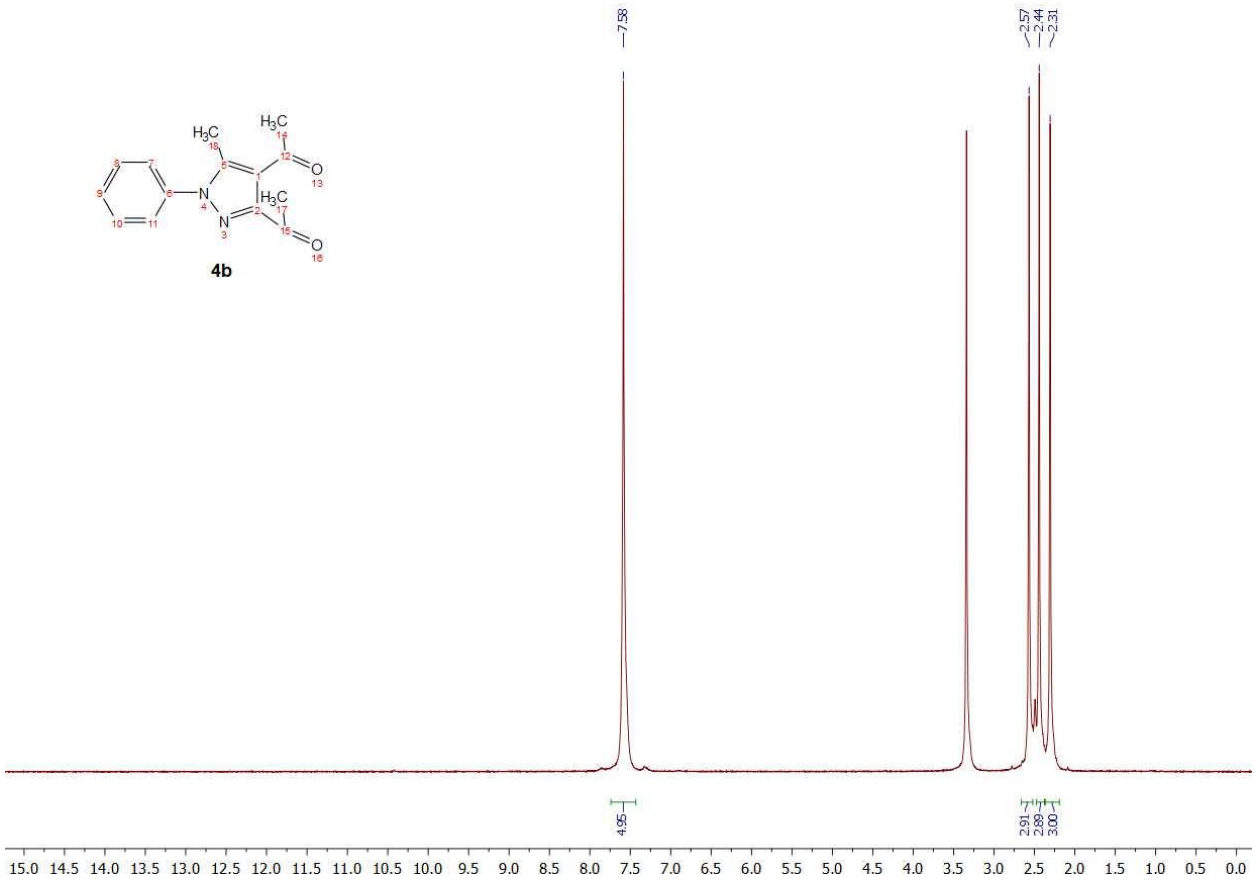
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2.44
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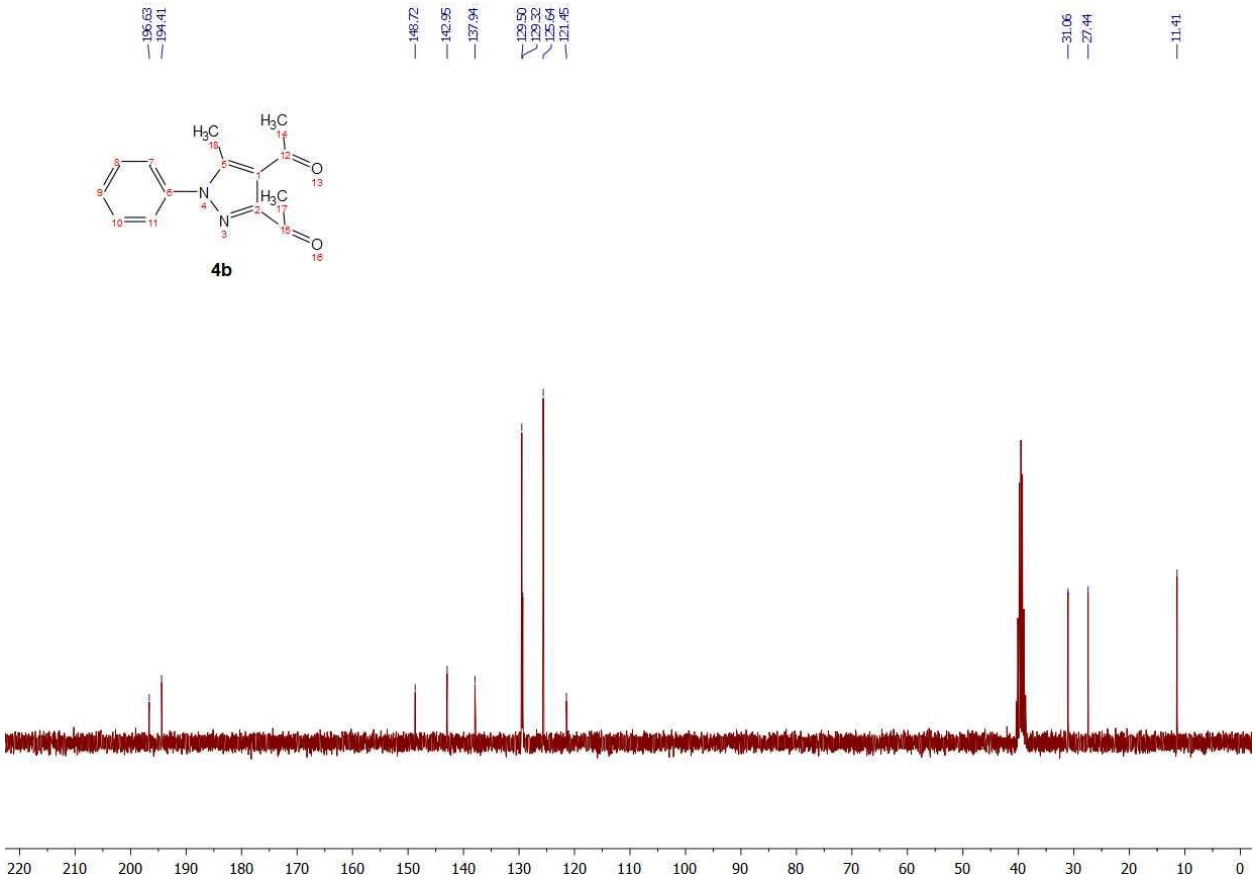
O
N
4b
4.95
2.91
2.89
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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27.44
11.41
4b
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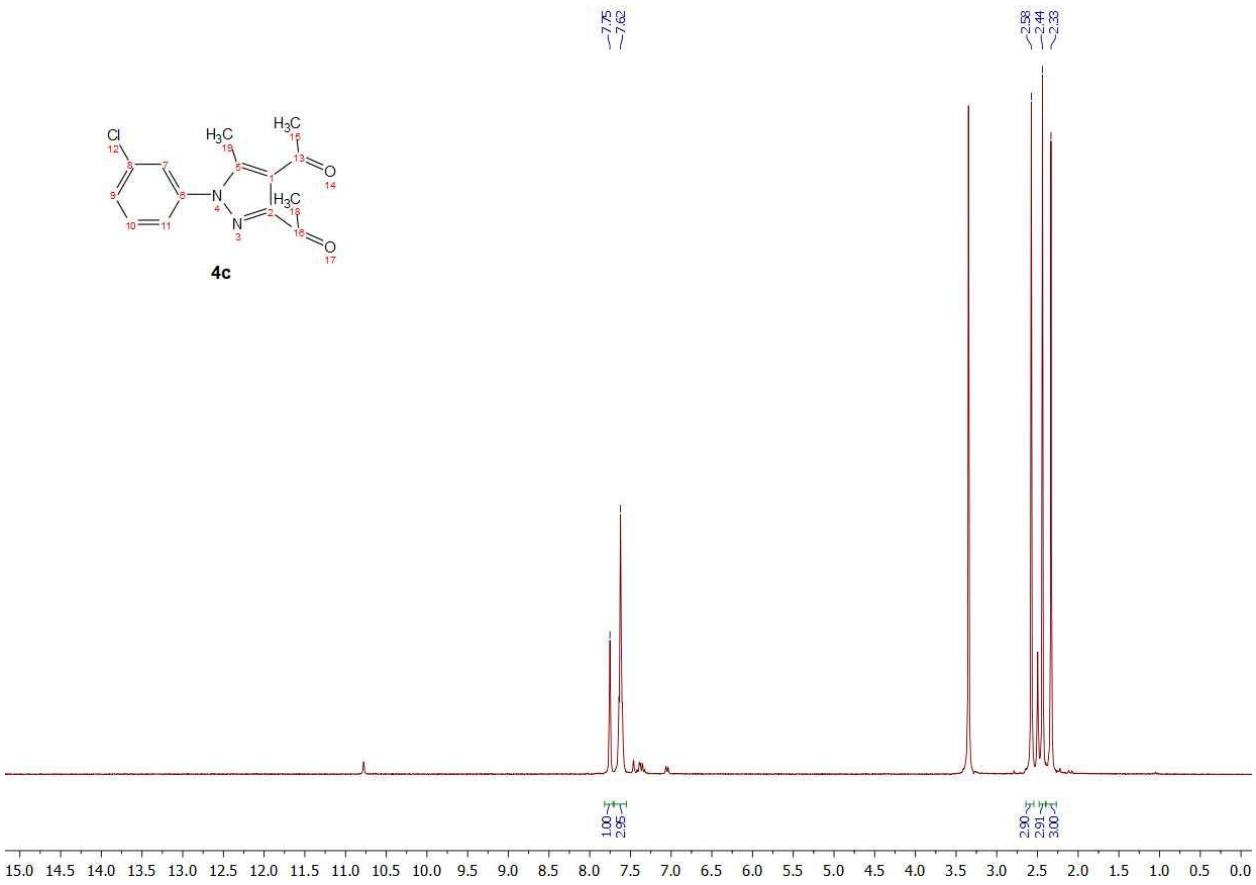
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2.95
2.90
2.91
3.00
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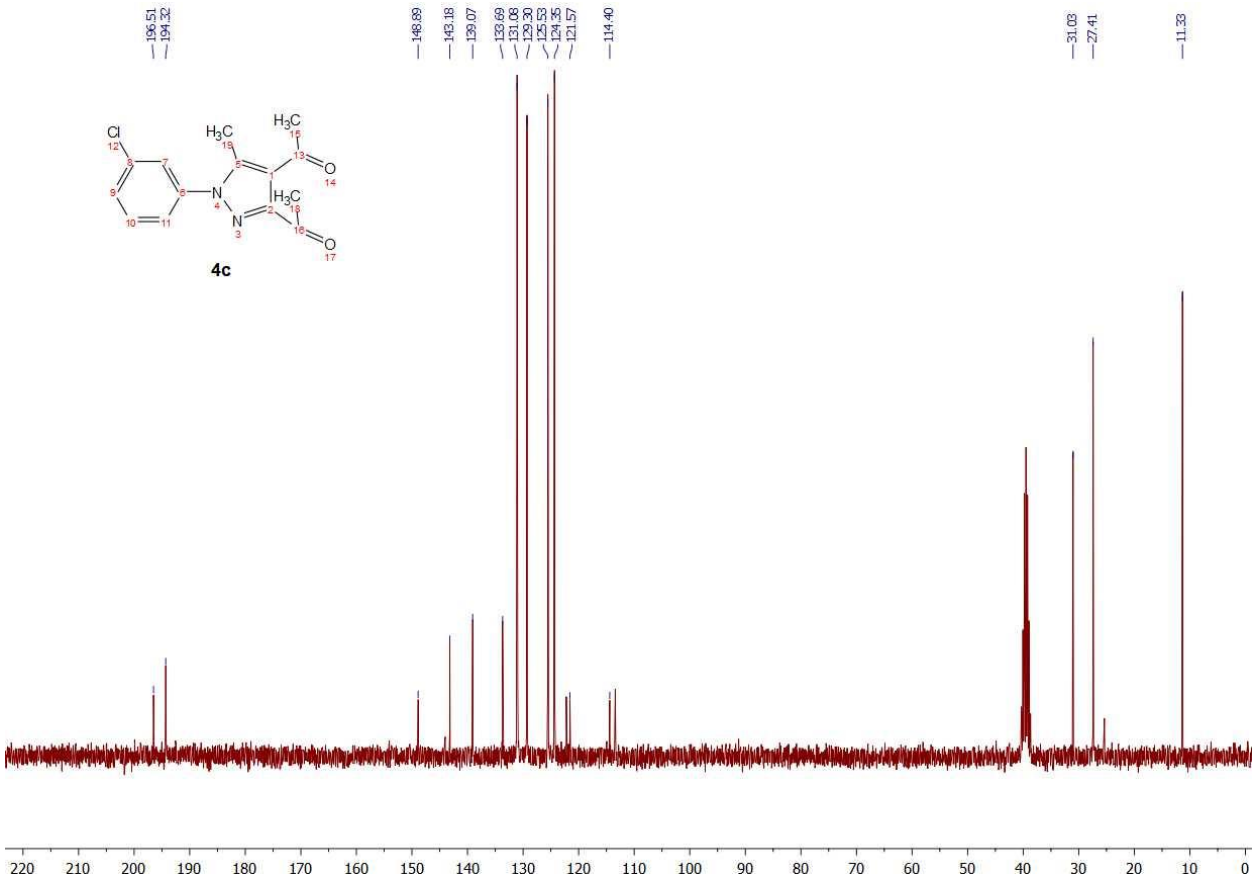
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114.40
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11.33
4c
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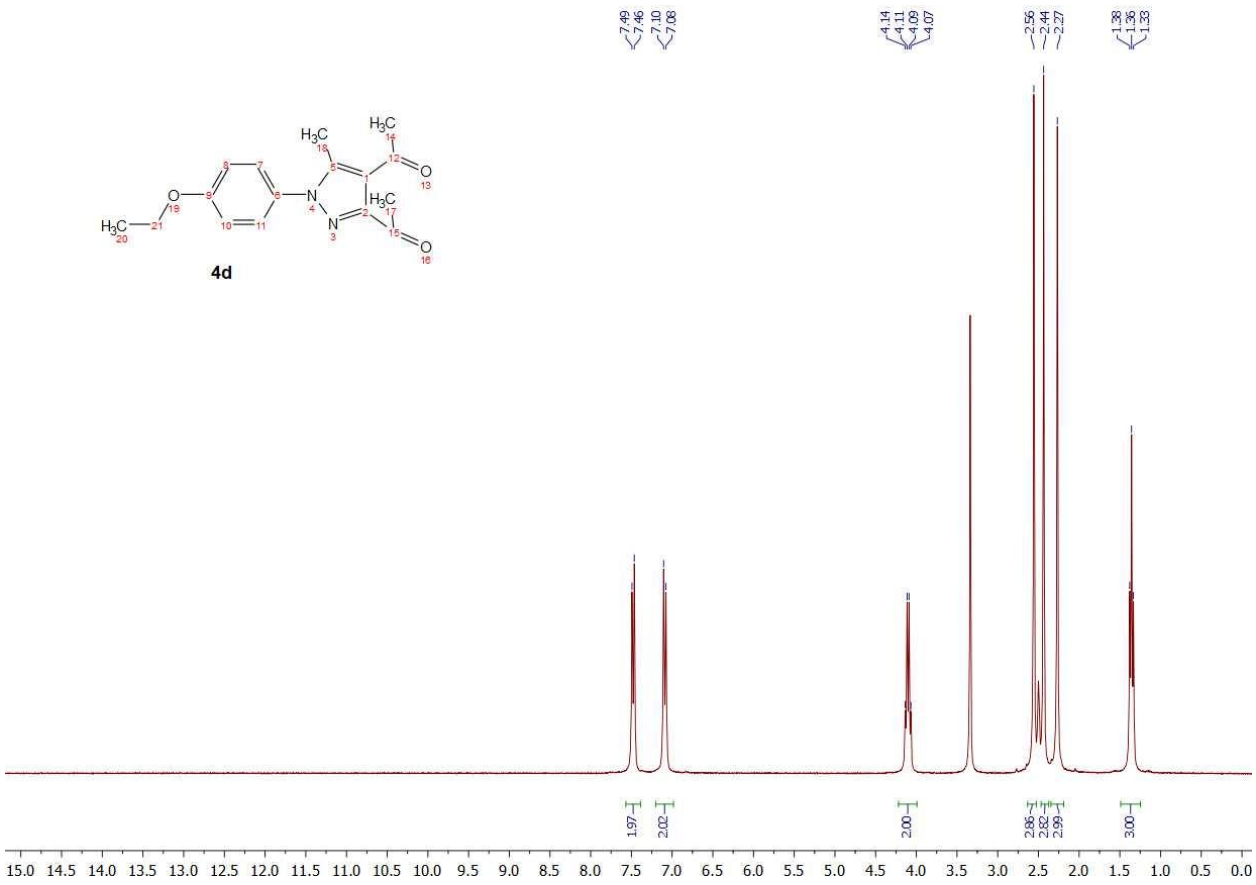
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4.07
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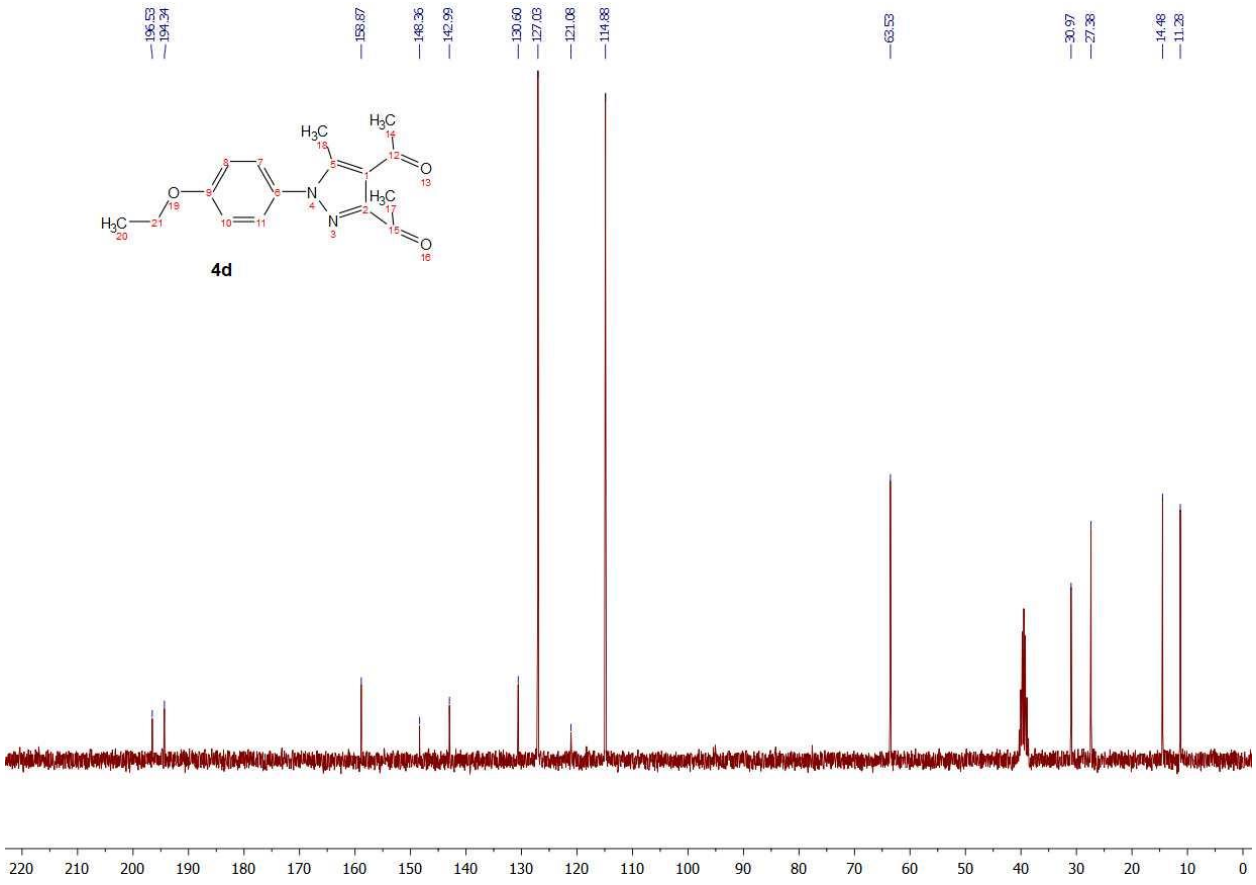
2.44
2.27
1.38
1.36
1.33
4d
1.97
2.02
2.00
2.86
2.82
2.99
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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27.38
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4d
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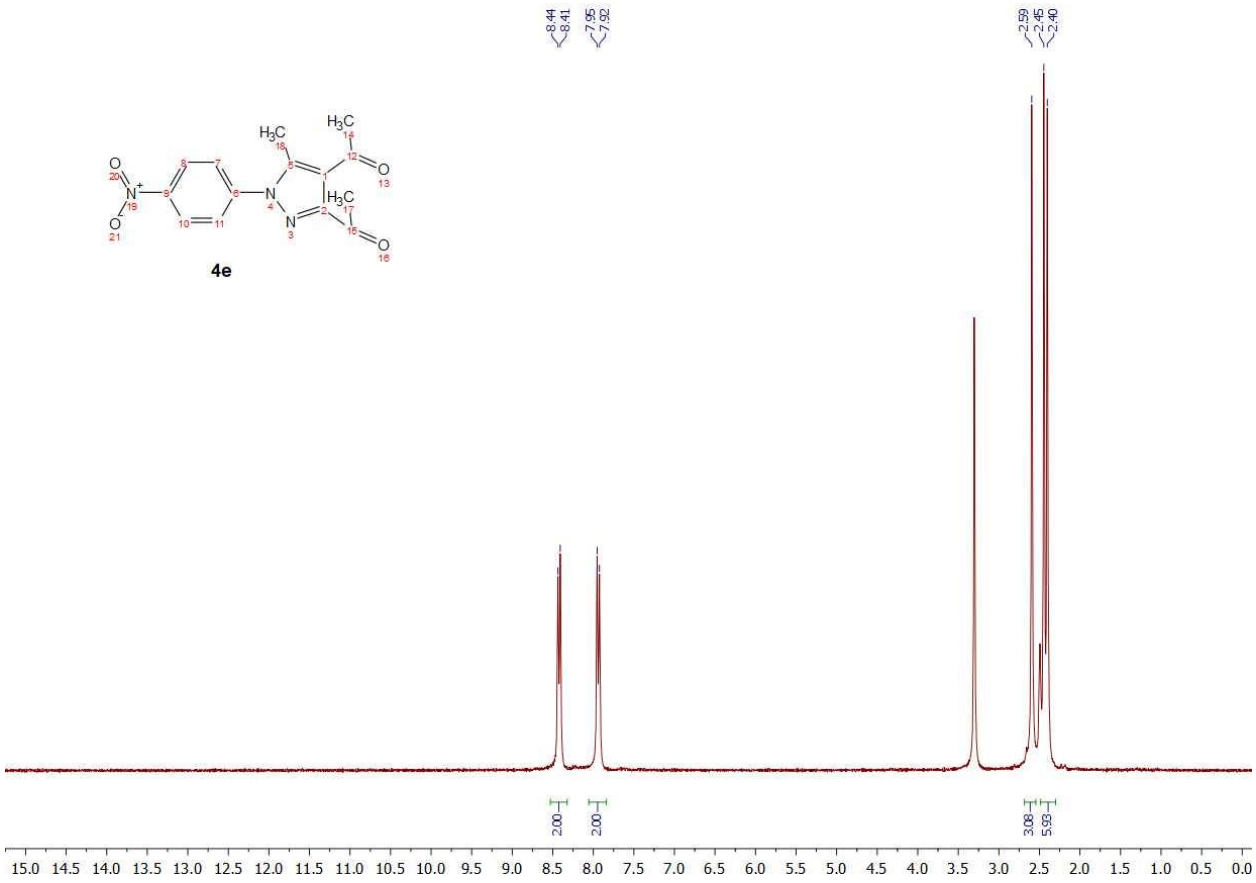
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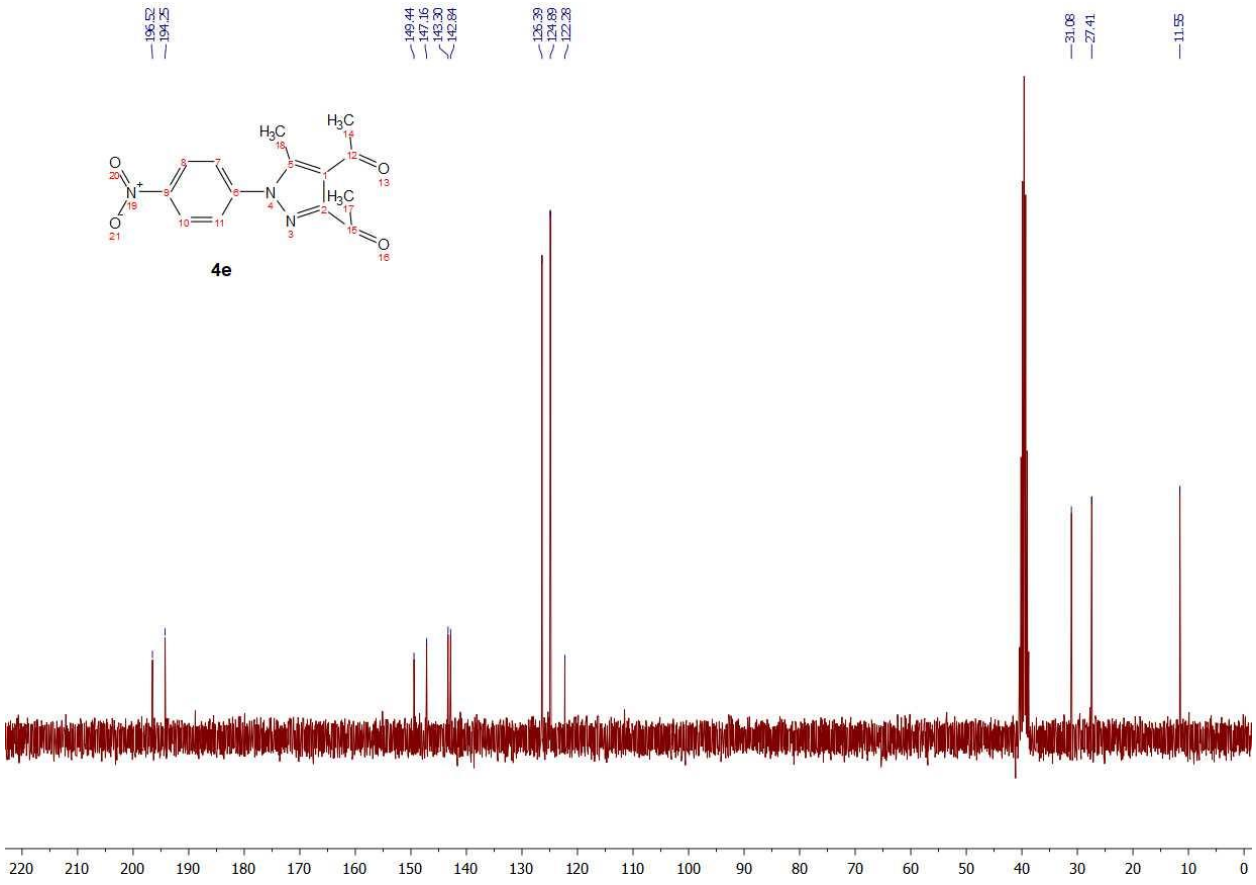
8.41
7.95
7.92
2.59
2.45
2.40
4e
2.00
2.00
3.08
5.99
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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31.08
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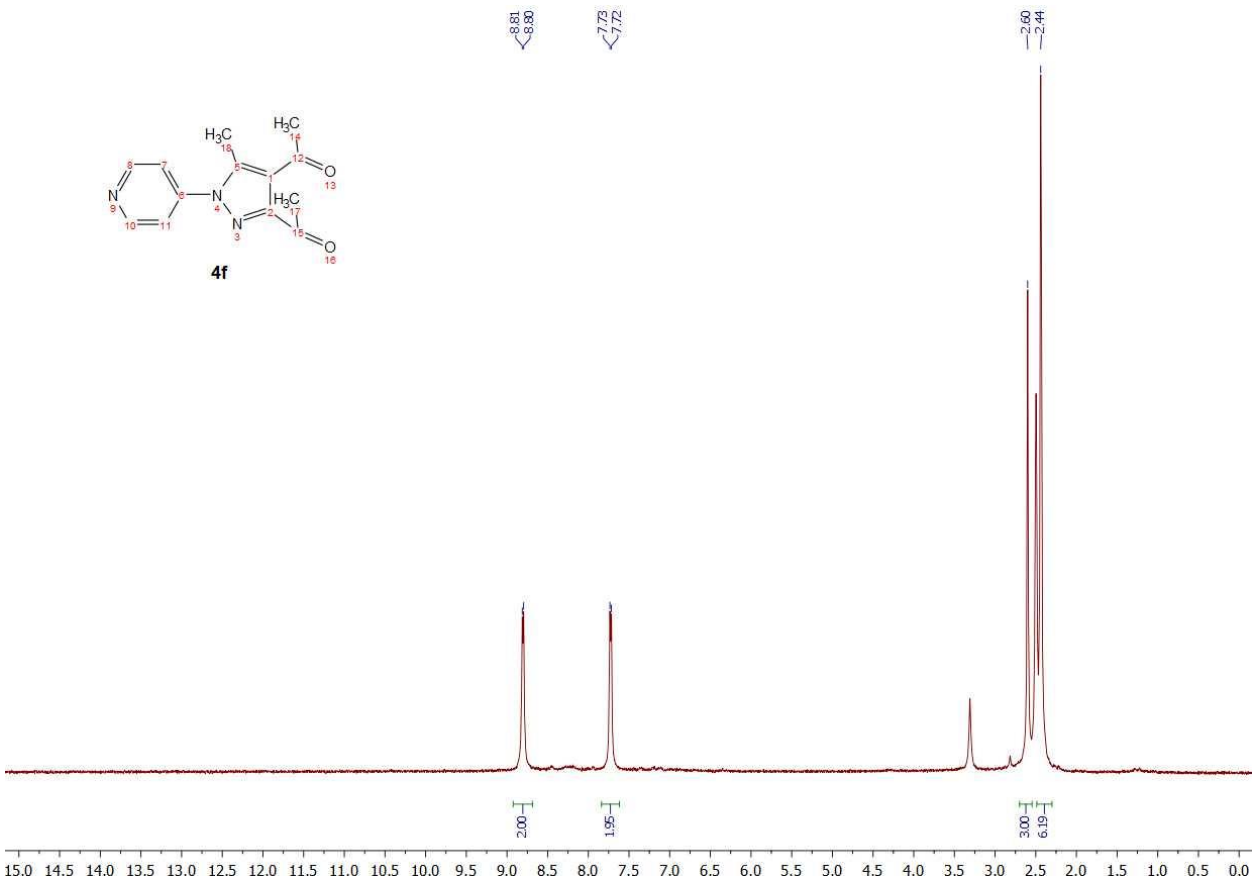
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7.72
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4f
2.00
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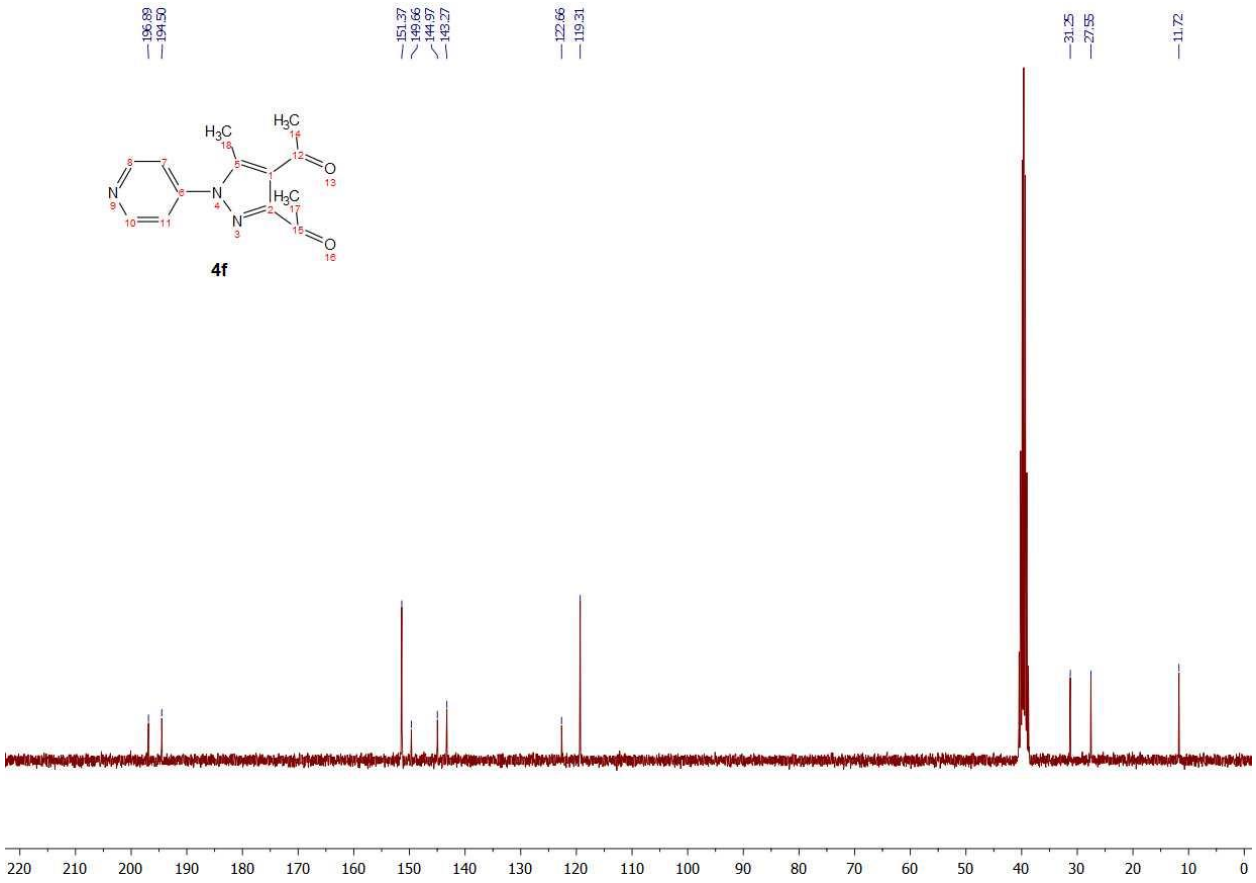
3.00
6.19
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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4f
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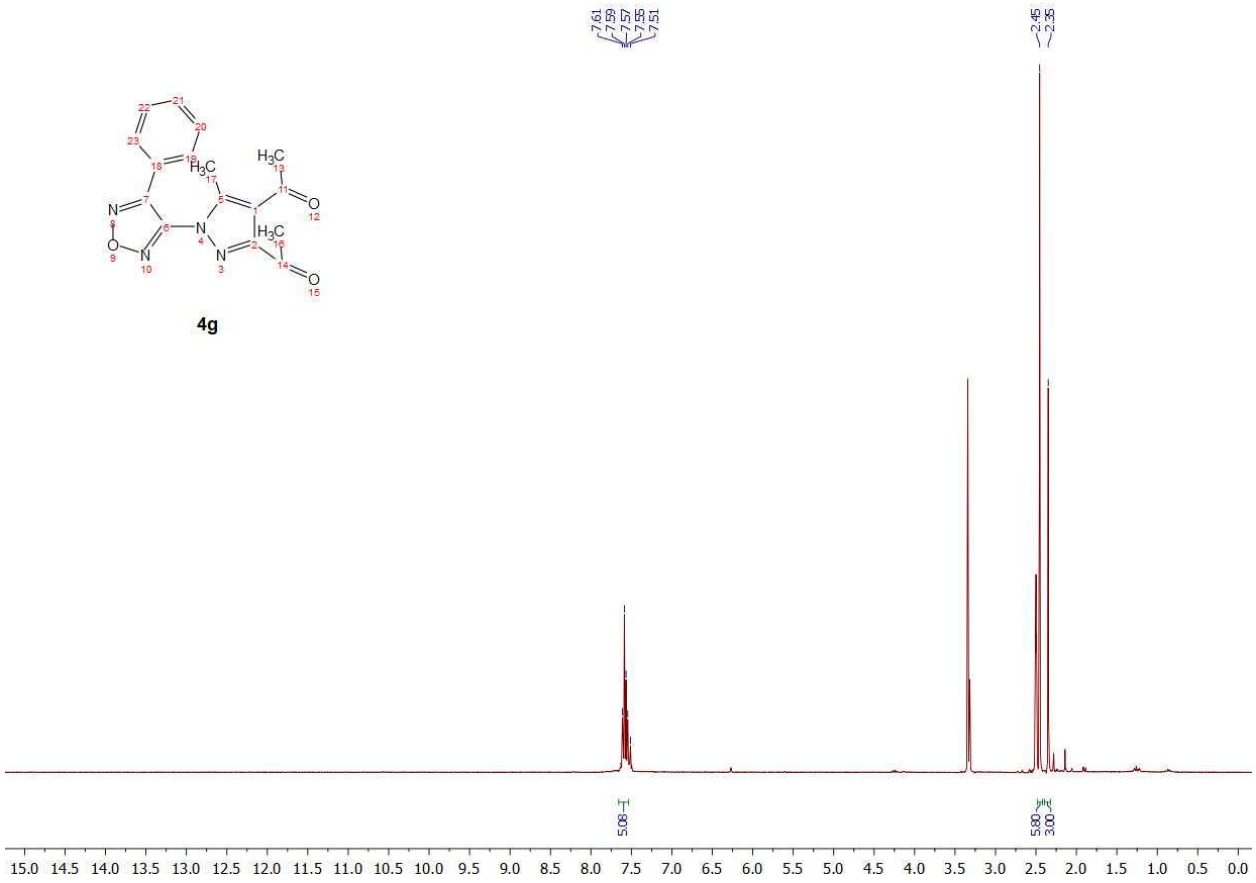
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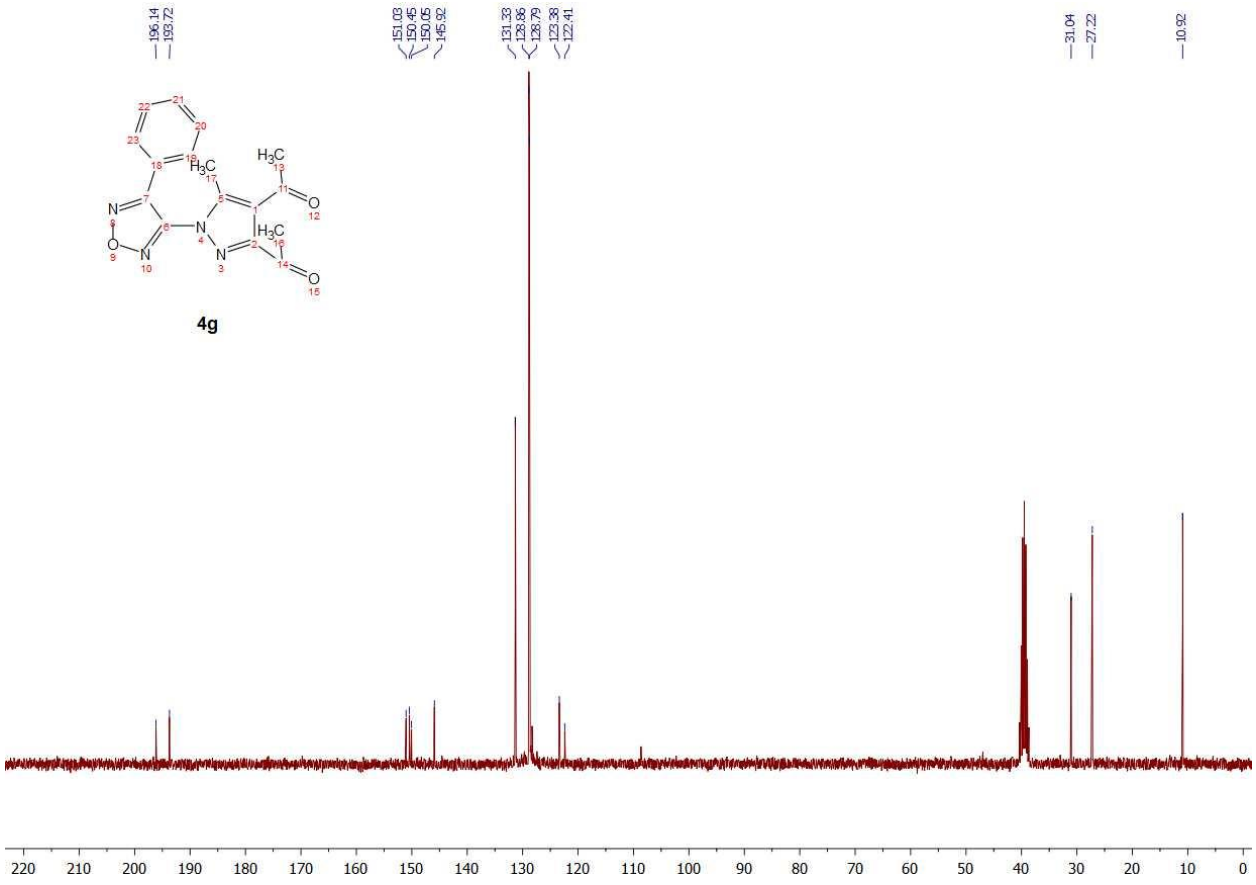
7.57
7.55
7.51
2.45
2.35
4g
5.00
5.80
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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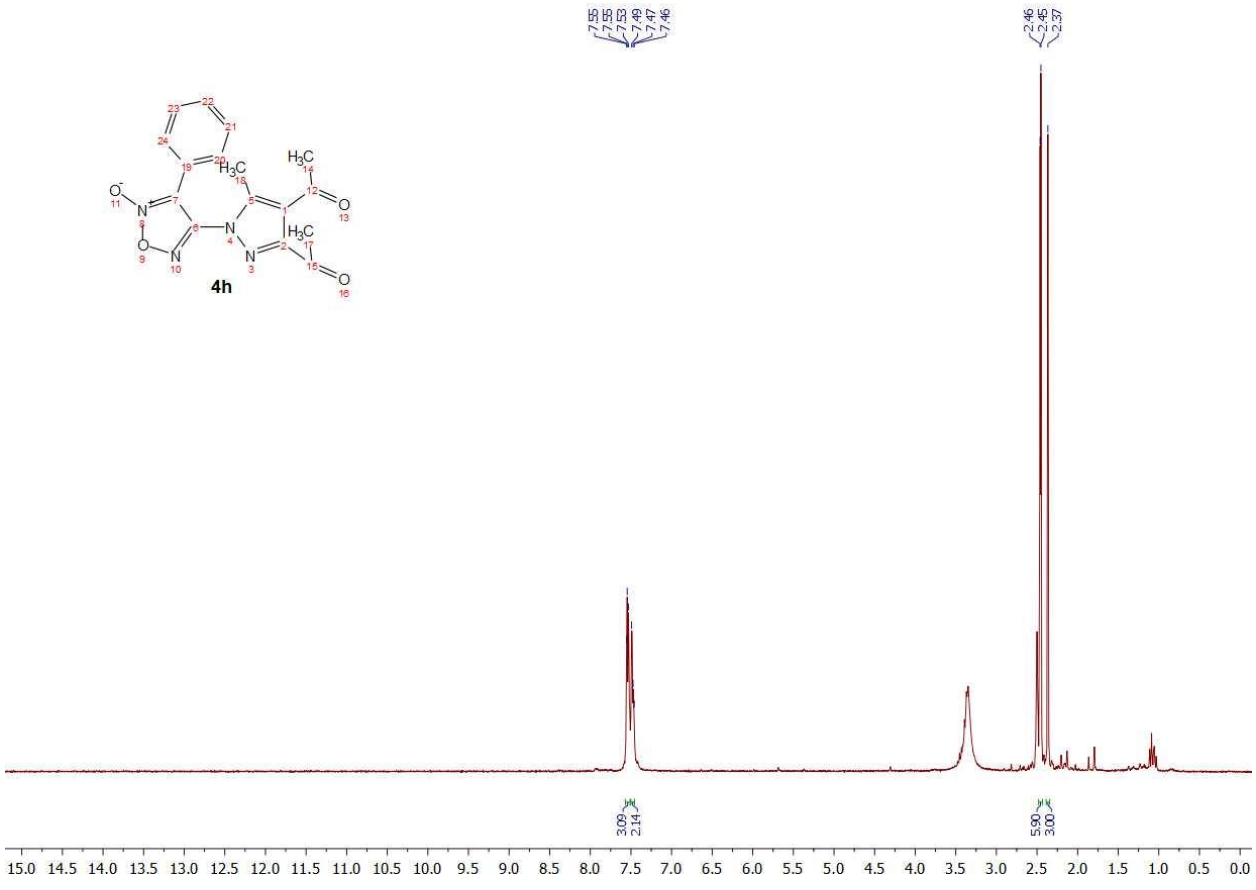
4g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7.55
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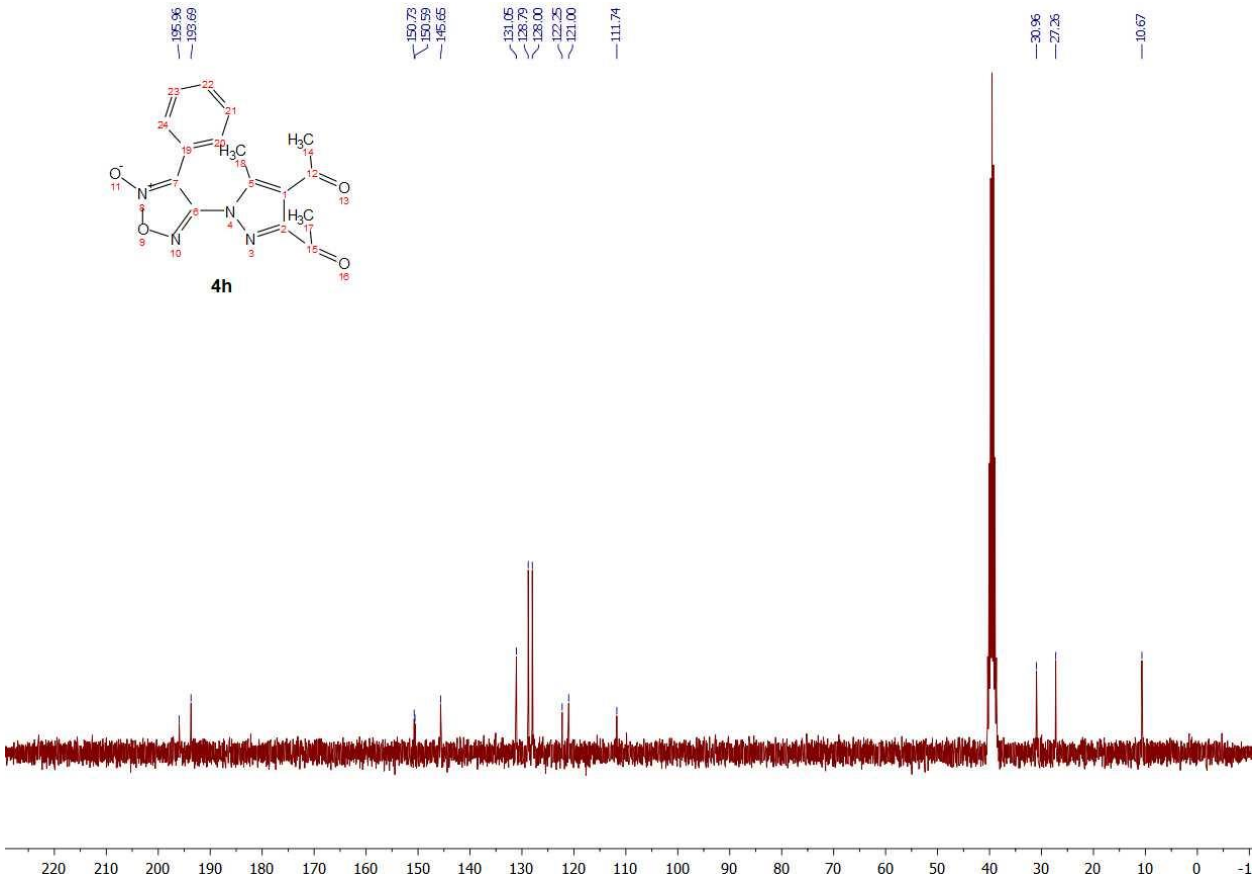
7.46
2.46
2.45
2.37
4h
3.09
2.14
5.90
3.00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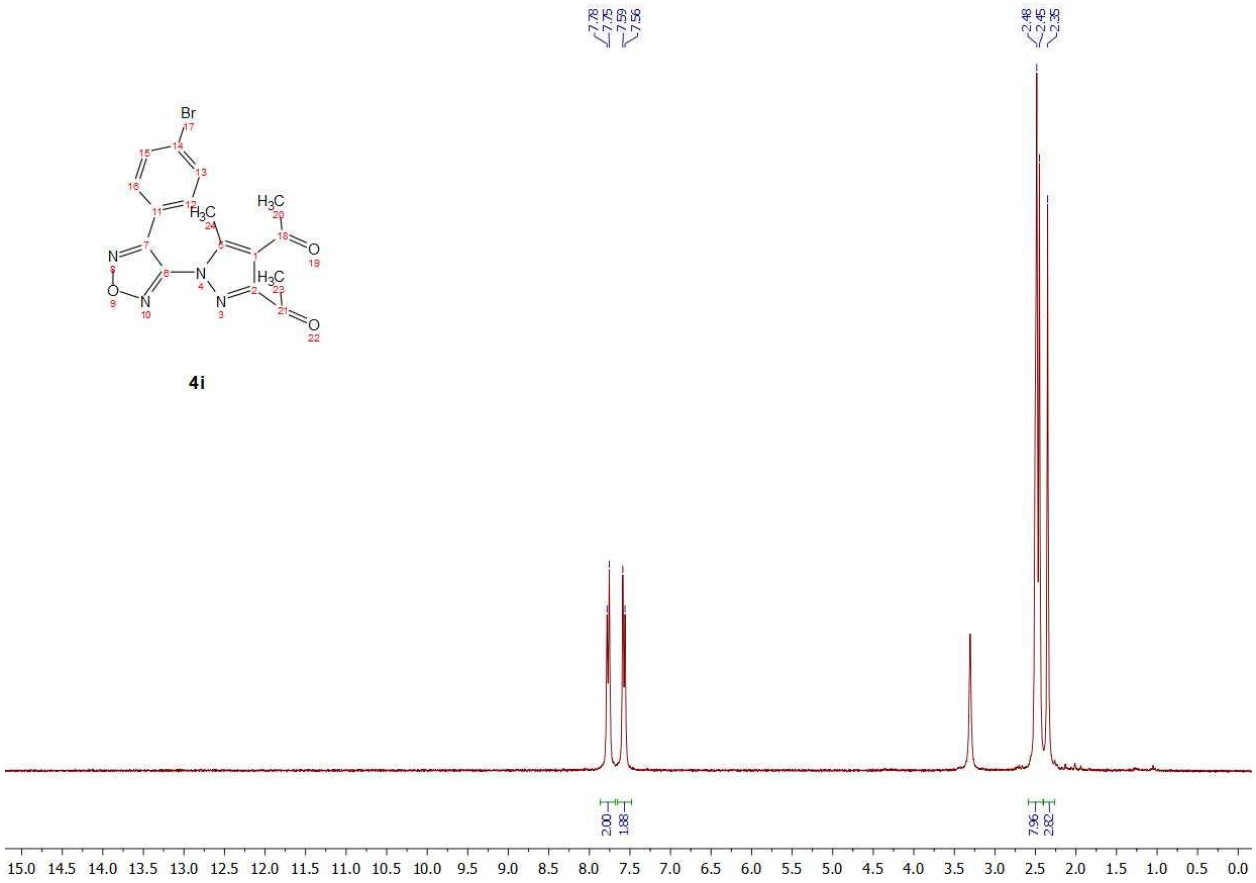
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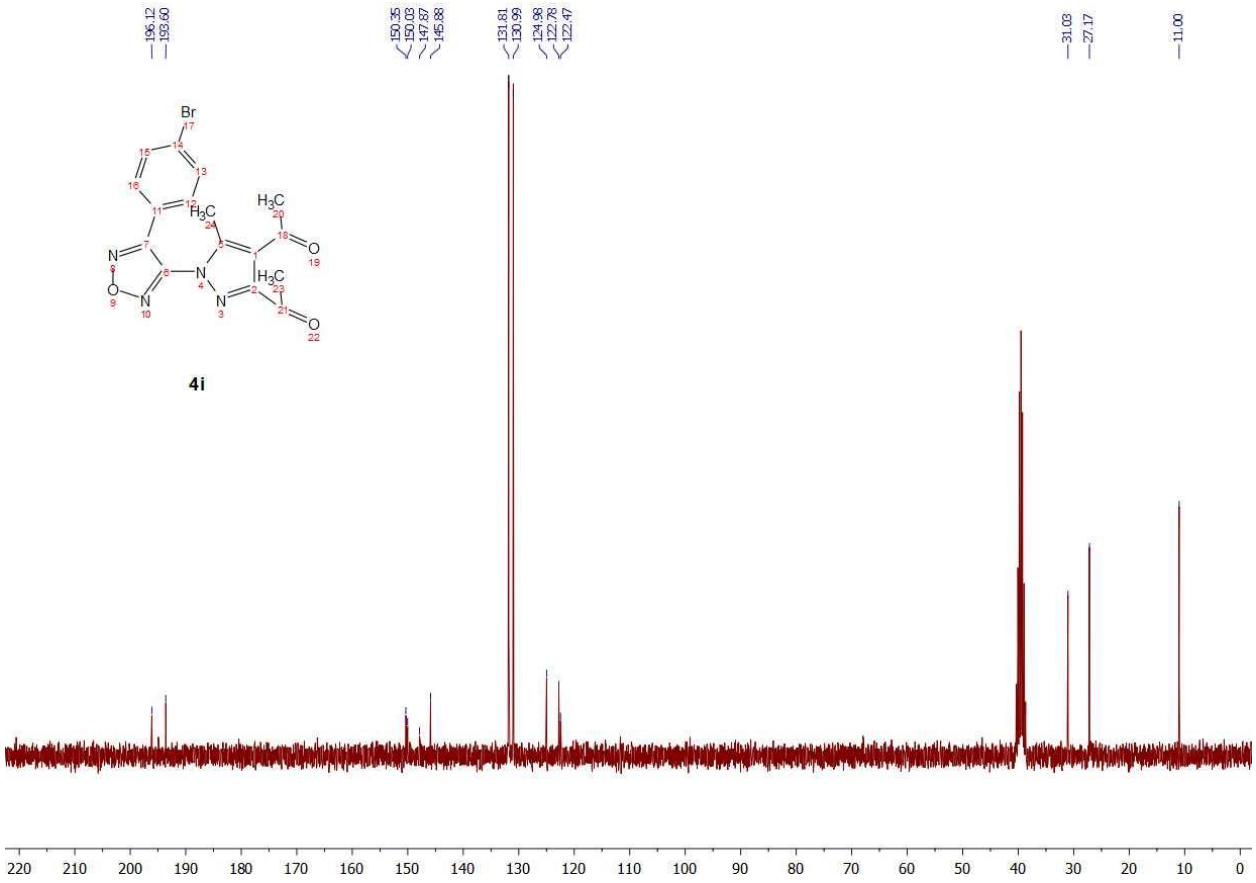
2.35
4i
2.00
1.88
7.96
2.82
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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122.78
122.47
31.03
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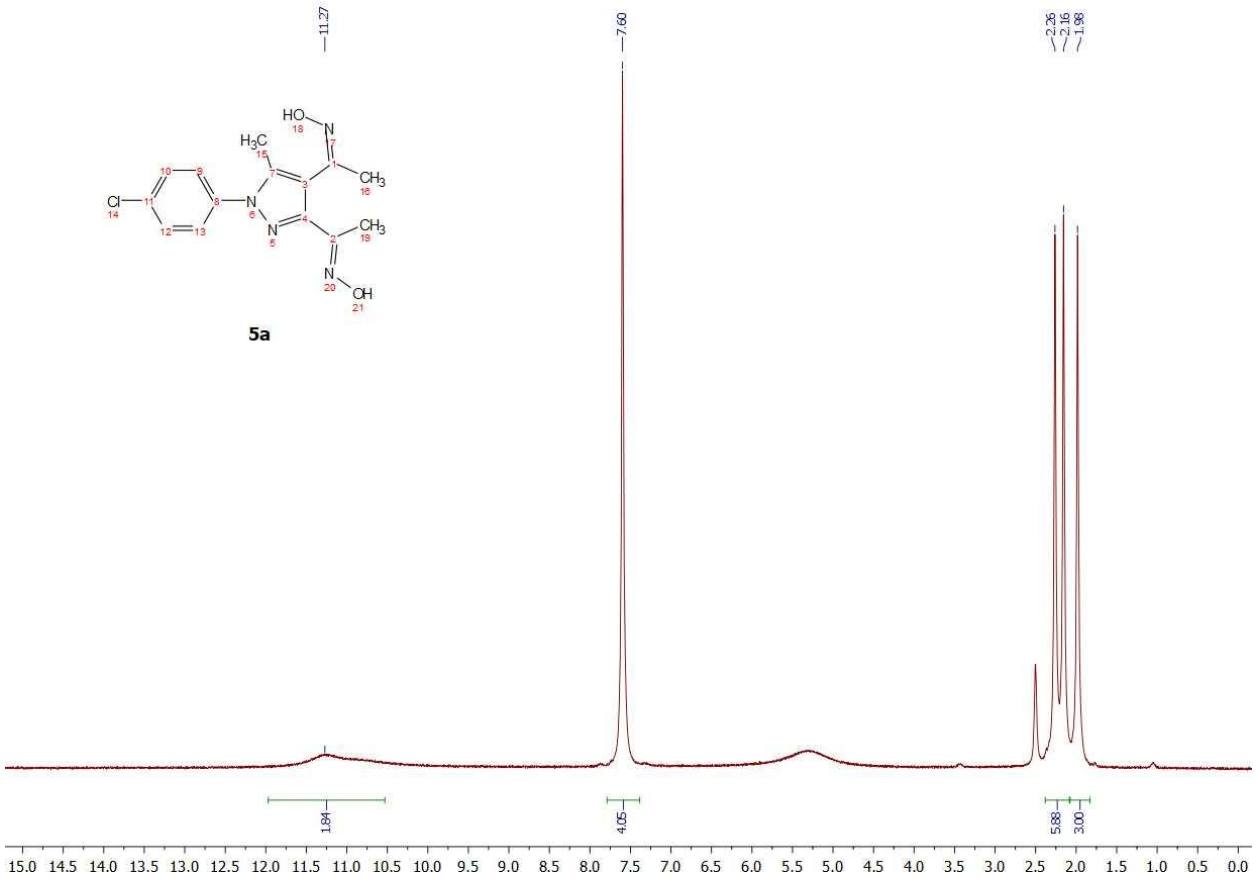
O
N
O
N
N
N
O
4i
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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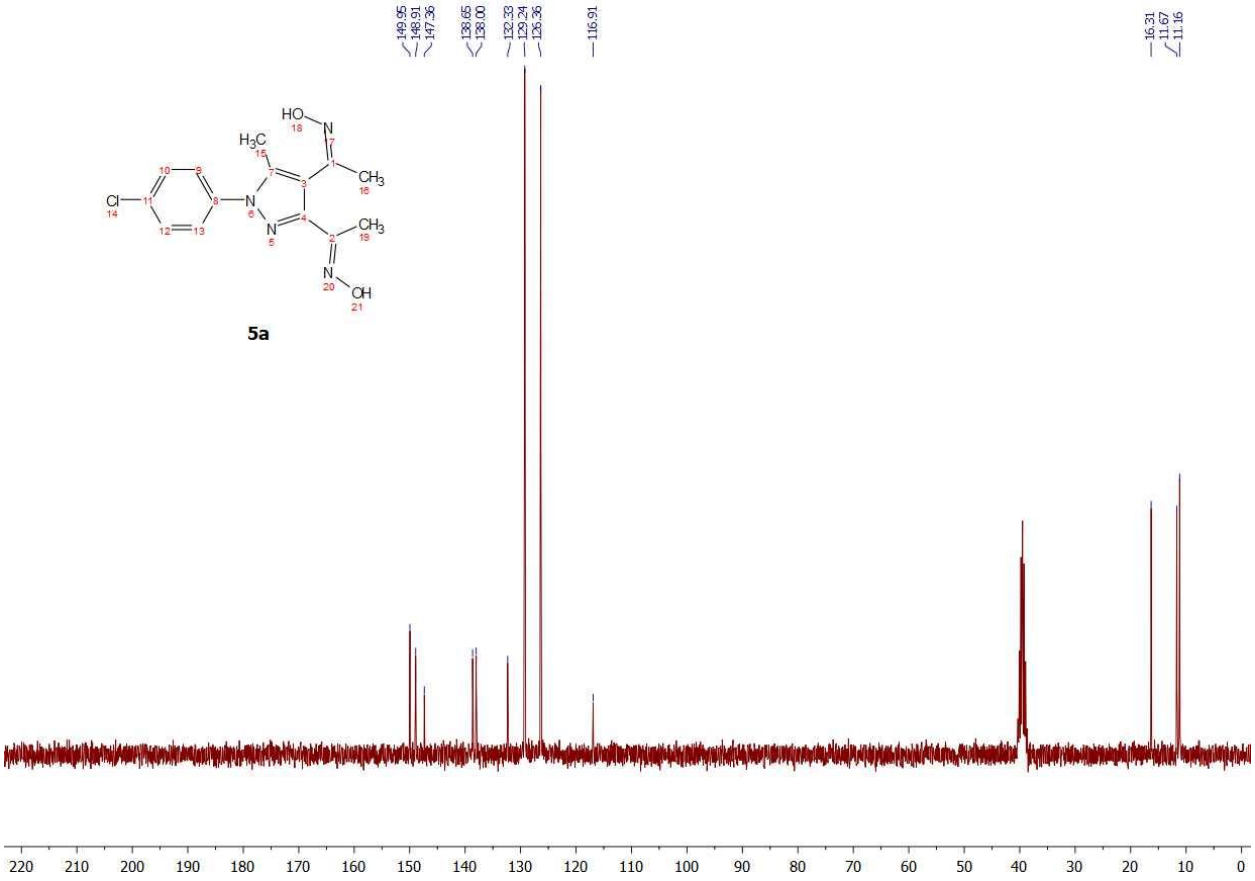
Cl
N
N
N
OH
5a
1.84
4.05
5.88
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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16.31
11.67
11.16
HO
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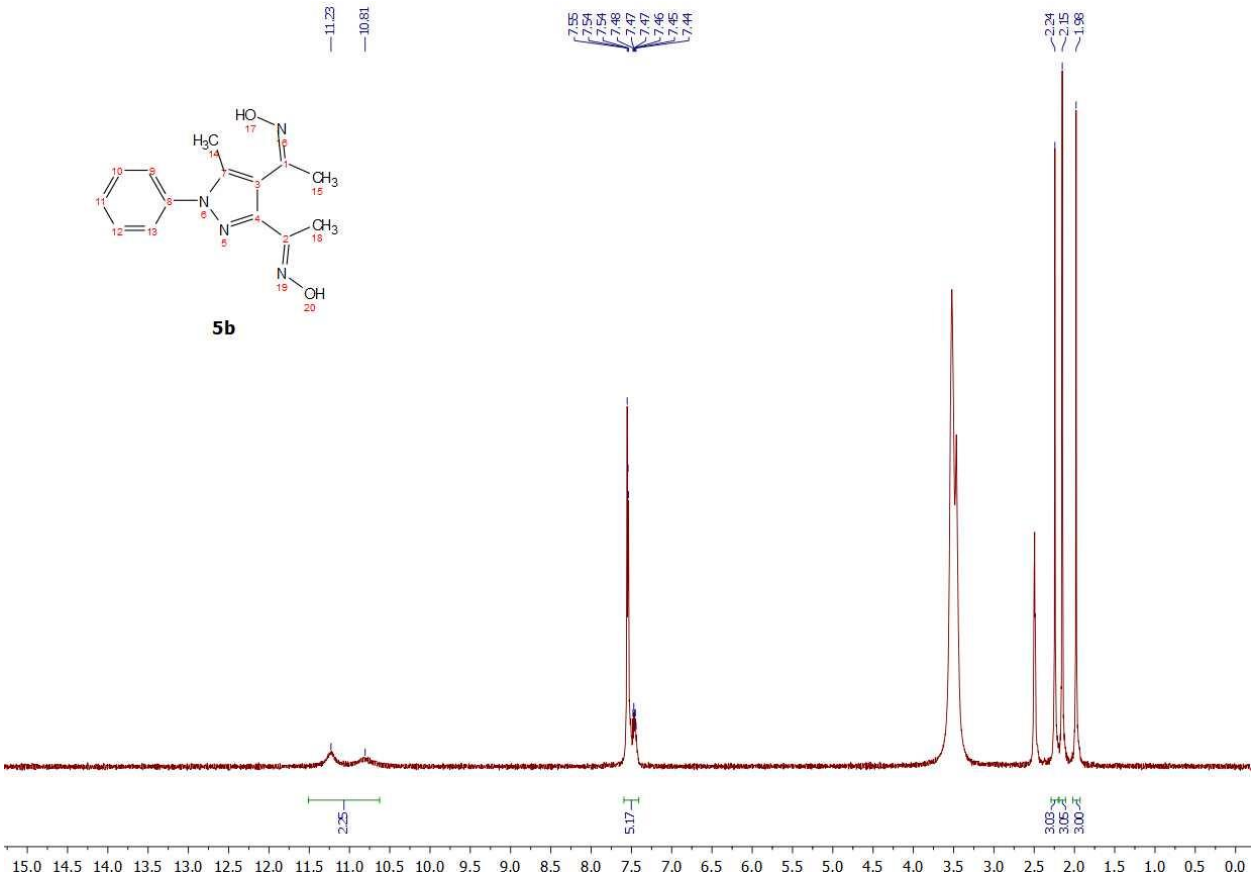
H3C
CH3
Cl
N
N
CH3
N
OH
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

5a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7.47
7.46
7.45
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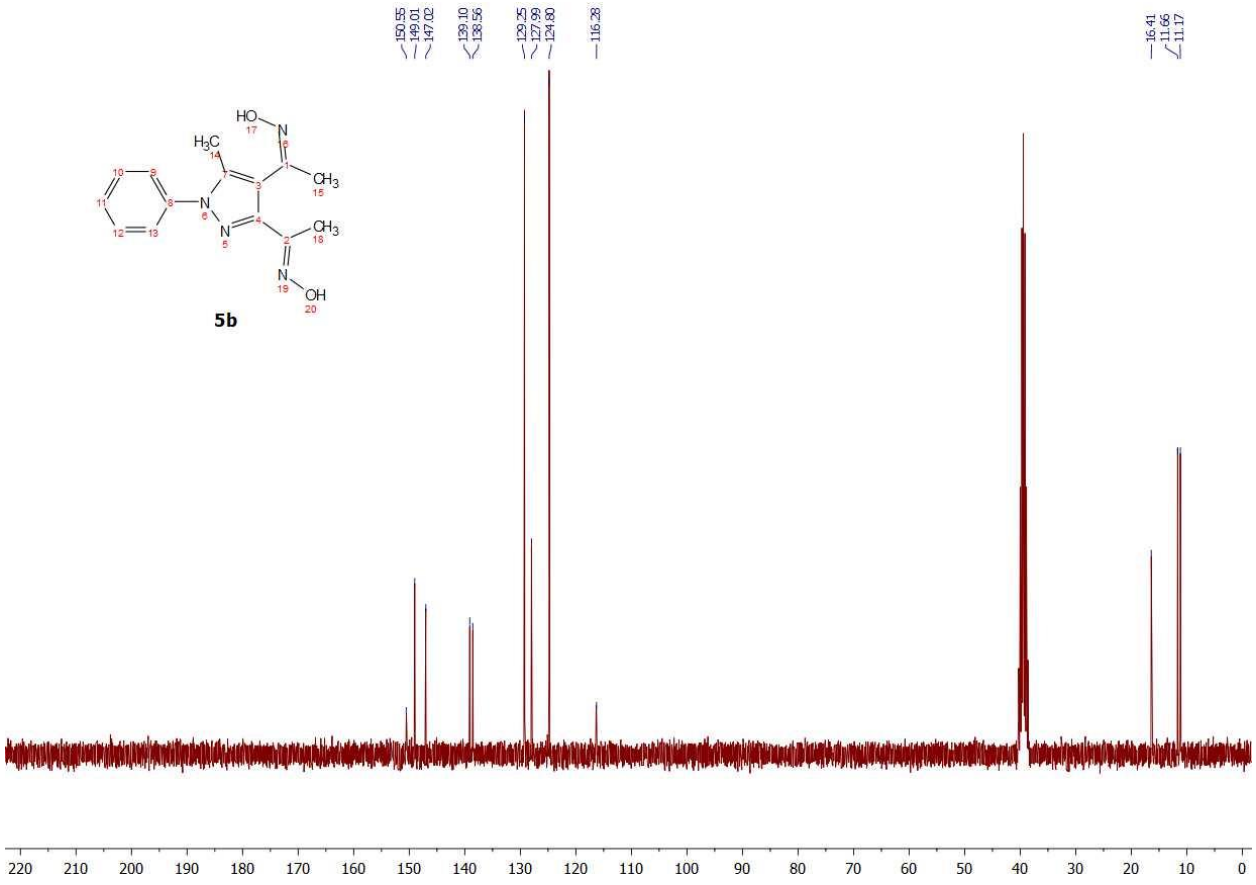
HO
N
H3C
CH3
N
N
CH3
N
OH
2.25
5.17
3.03
3.05
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

5b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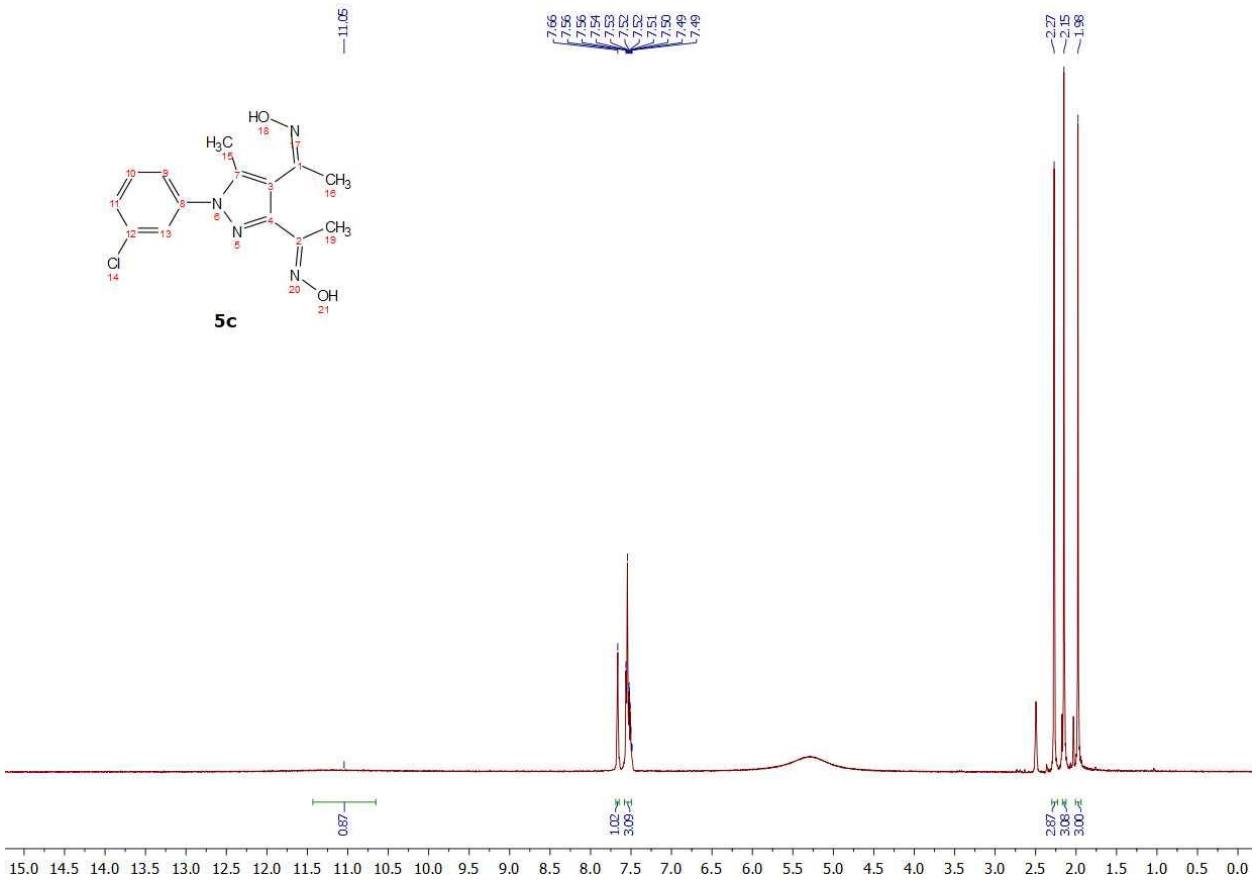
16.41
11.66
11.17
HO
N
17
16
H3C
14
CH3
15
10
9
11
8
N
6
12
13
N
5
4
3
2
CH3
18
N
19
OH
20
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

5b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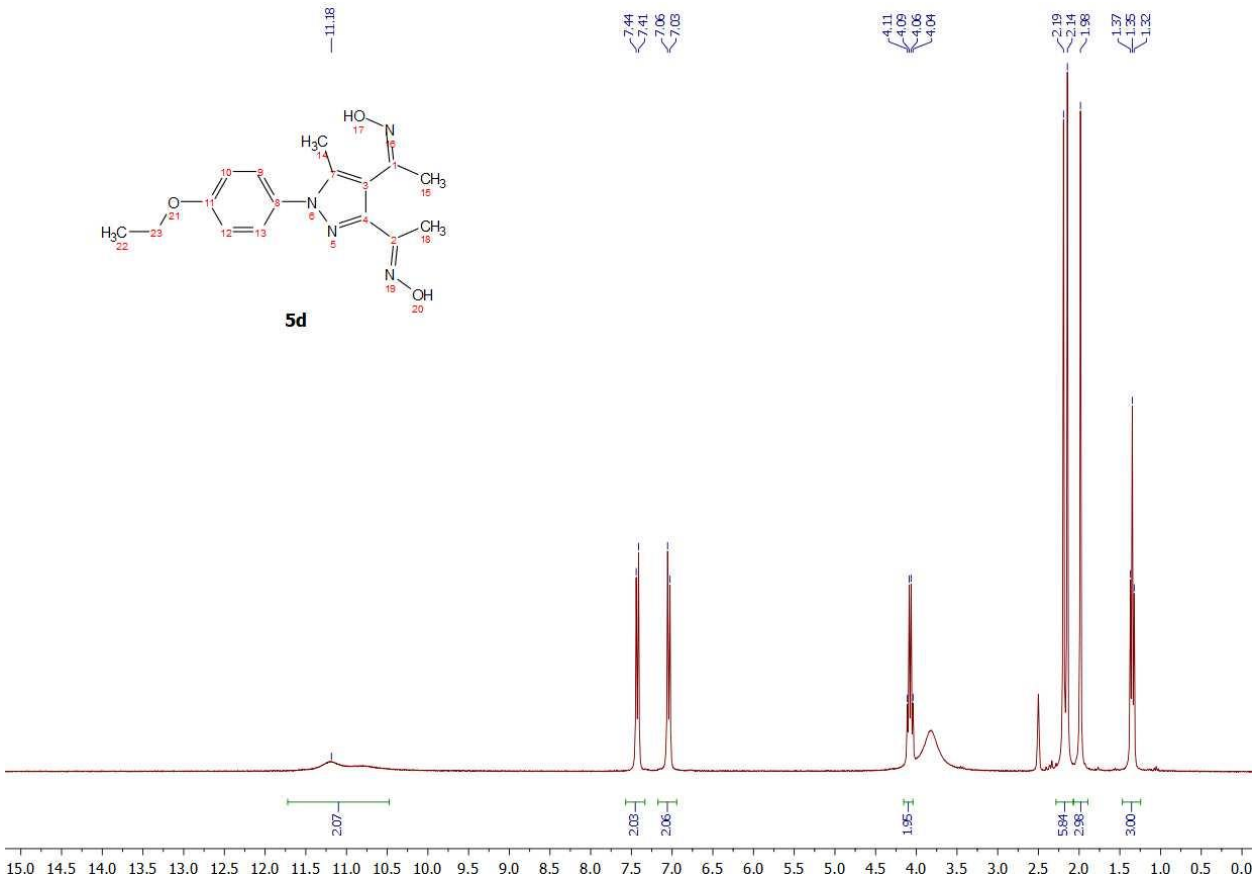
7.50
7.49
7.49
2.27
2.15
1.98
HO
18
N
17
16
H3C
15
CH3
7
3
10
9
11
8
N
6
12
13
Cl
14
N
5
4
2
CH3
19
N
20
OH
21
0.87
1.02
3.09
2.87
3.08
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

5c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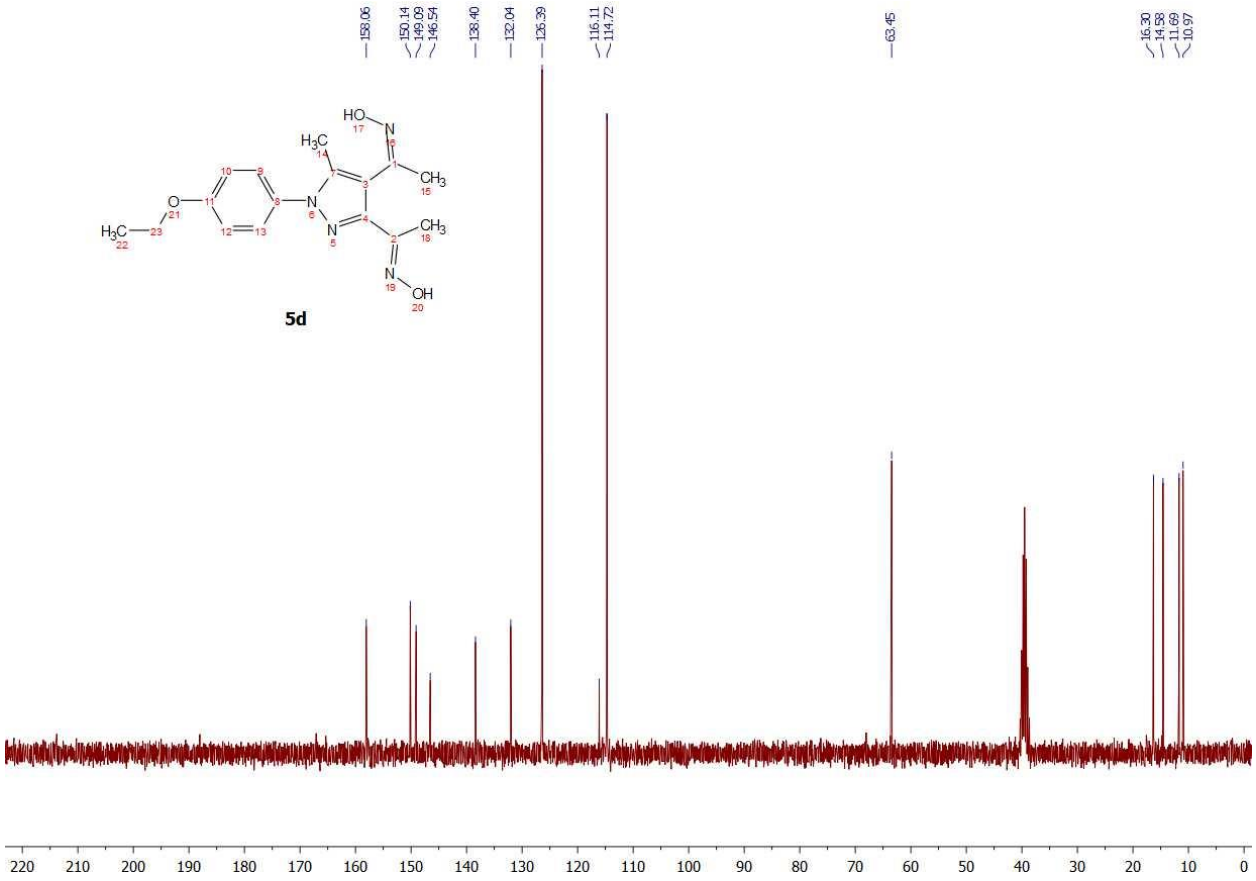
7.06
7.03
4.11
4.09
4.06
4.04
2.19
2.14
1.98
1.37
1.35
1.32
HO
N
H3C
CH3
O
N
N
CH3
H3C
N
OH
5d
2.07
2.03
2.06
1.95
5.84
2.98
3.00
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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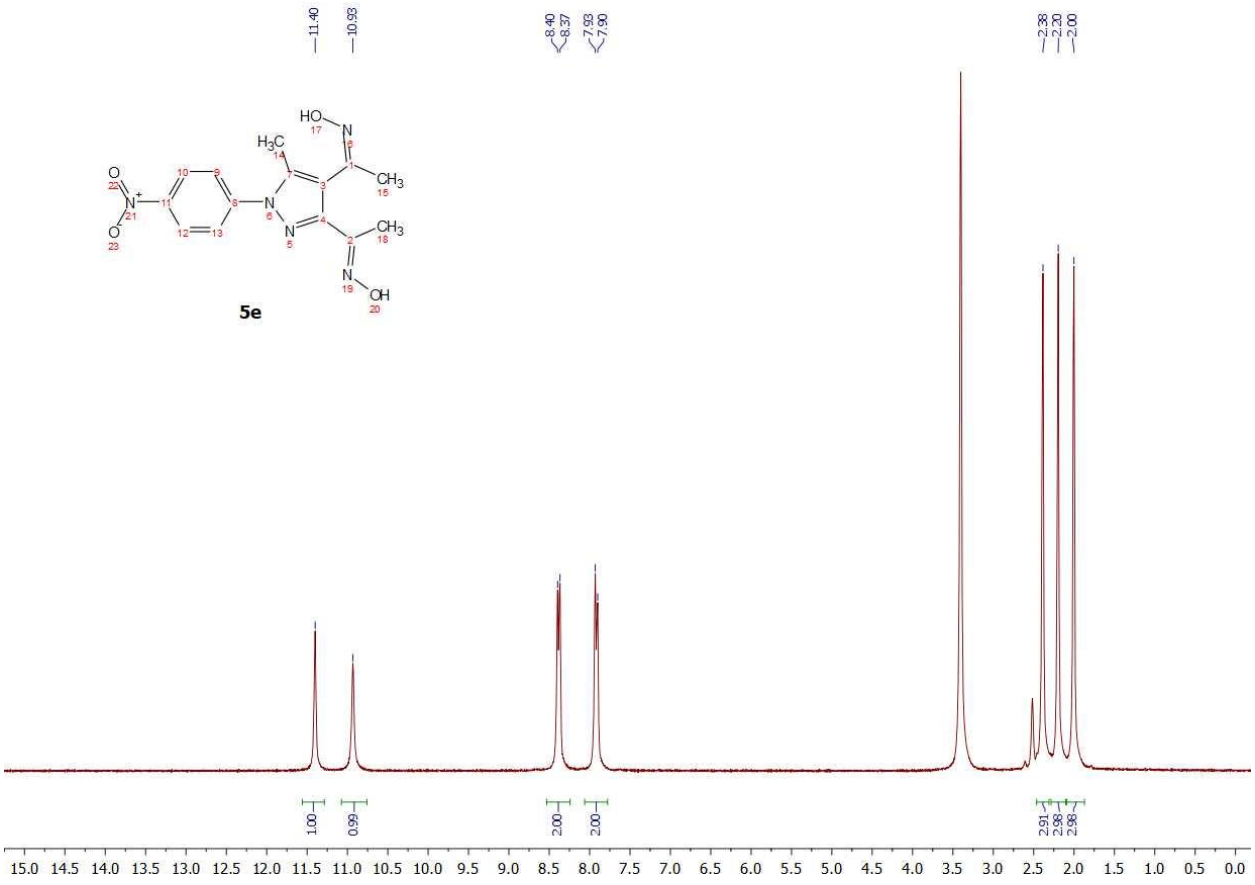
149.09
146.54
138.40
132.04
126.39
116.11
114.72
63.45
16.30
14.58
11.69
10.97
HO
N
H3C
CH3
O
N
N
CH3
H3C
N
OH
5d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0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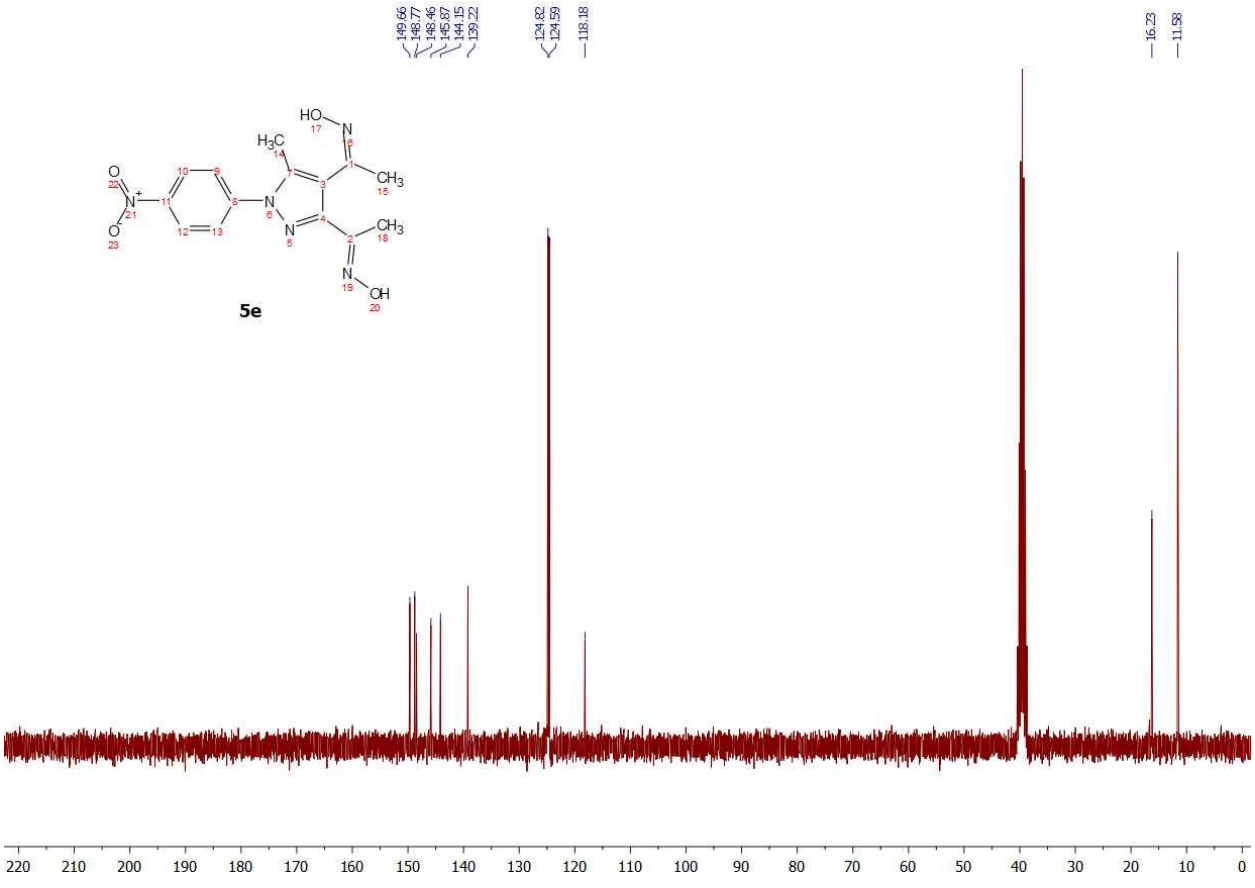
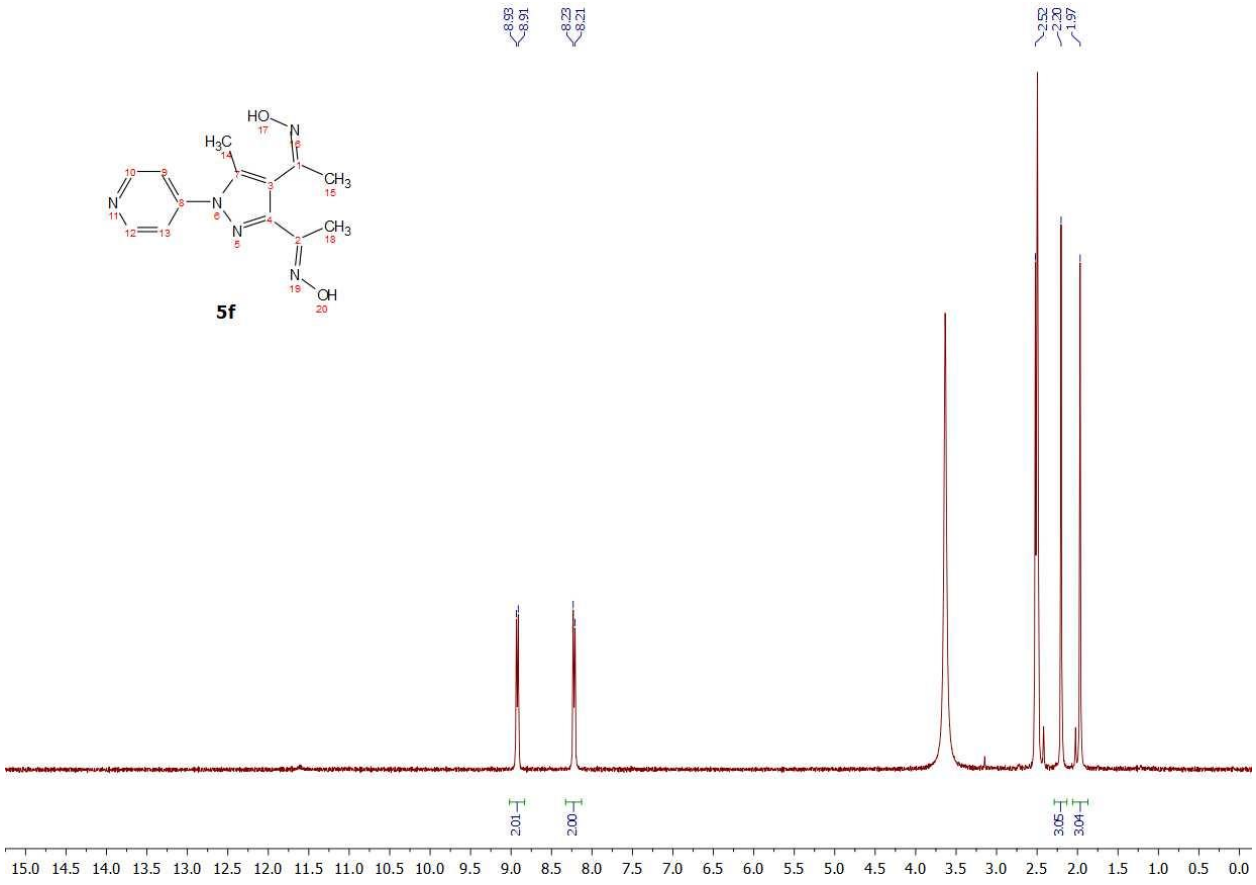
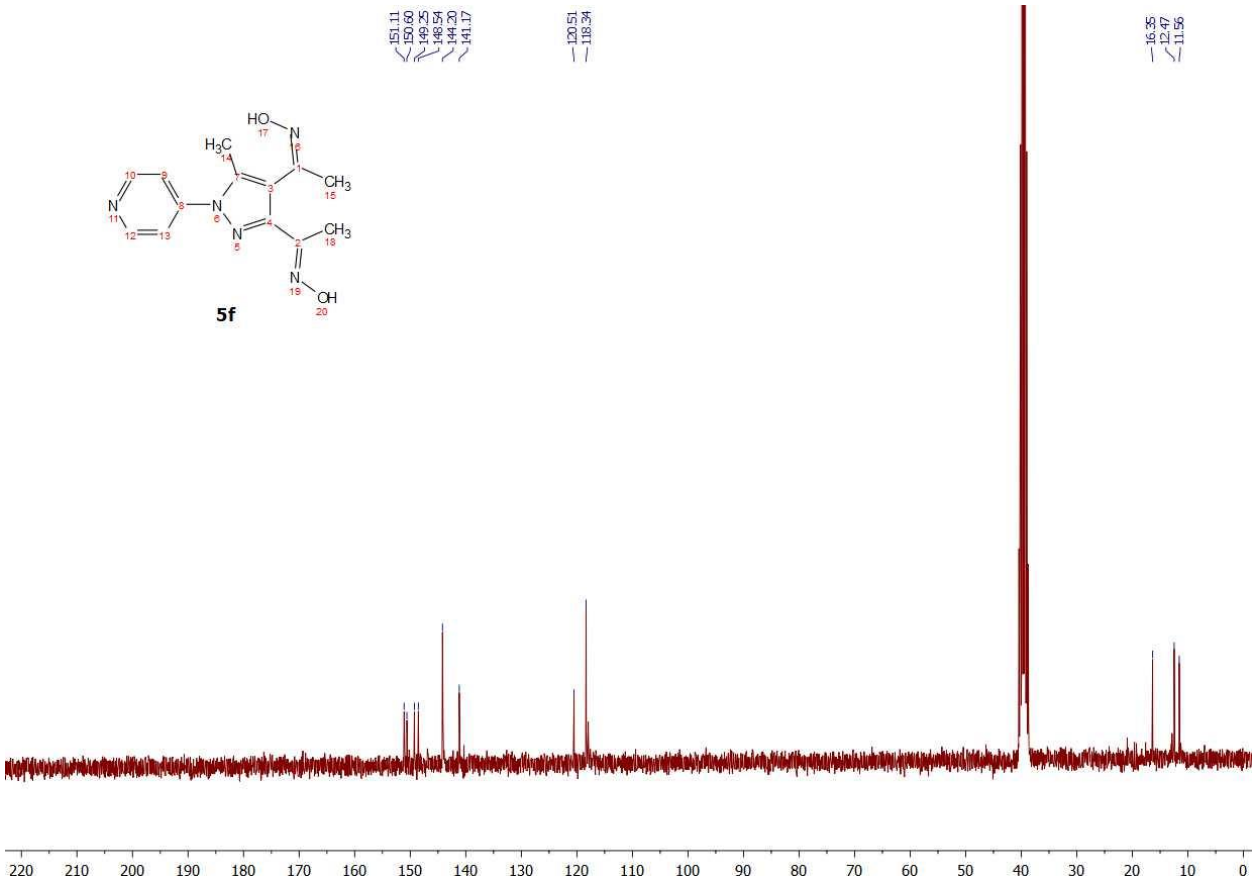
7.93
7.90
2.38
2.20
2.00
HO
N
17
H3C
14
CH3
15
O
22
N+
21
O
23
10
9
11
8
N
6
7
3
4
N
5
2
CH3
18
N
19
OH
20
12
13
1.00
0.99
2.00
2.00
2.91
2.98
2.98
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

5e


149.66
148.77
148.46
145.87
144.15
139.22
124.82
124.59
118.18
16.23
11.58
HO
N
17
H3C
14
CH3
15
O
22
N+
21
O
23
10
9
11
8
N
6
7
3
4
N
5
2
CH3
18
N
19
OH
20
12
13
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

5e


8.93
8.91
8.23
8.21
2.52
2.20
1.97
5f
2.01
2.00
3.05
3.04
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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150.60
149.25
148.54
144.20
141.17
120.51
118.34
16.35
12.47
11.56
5f
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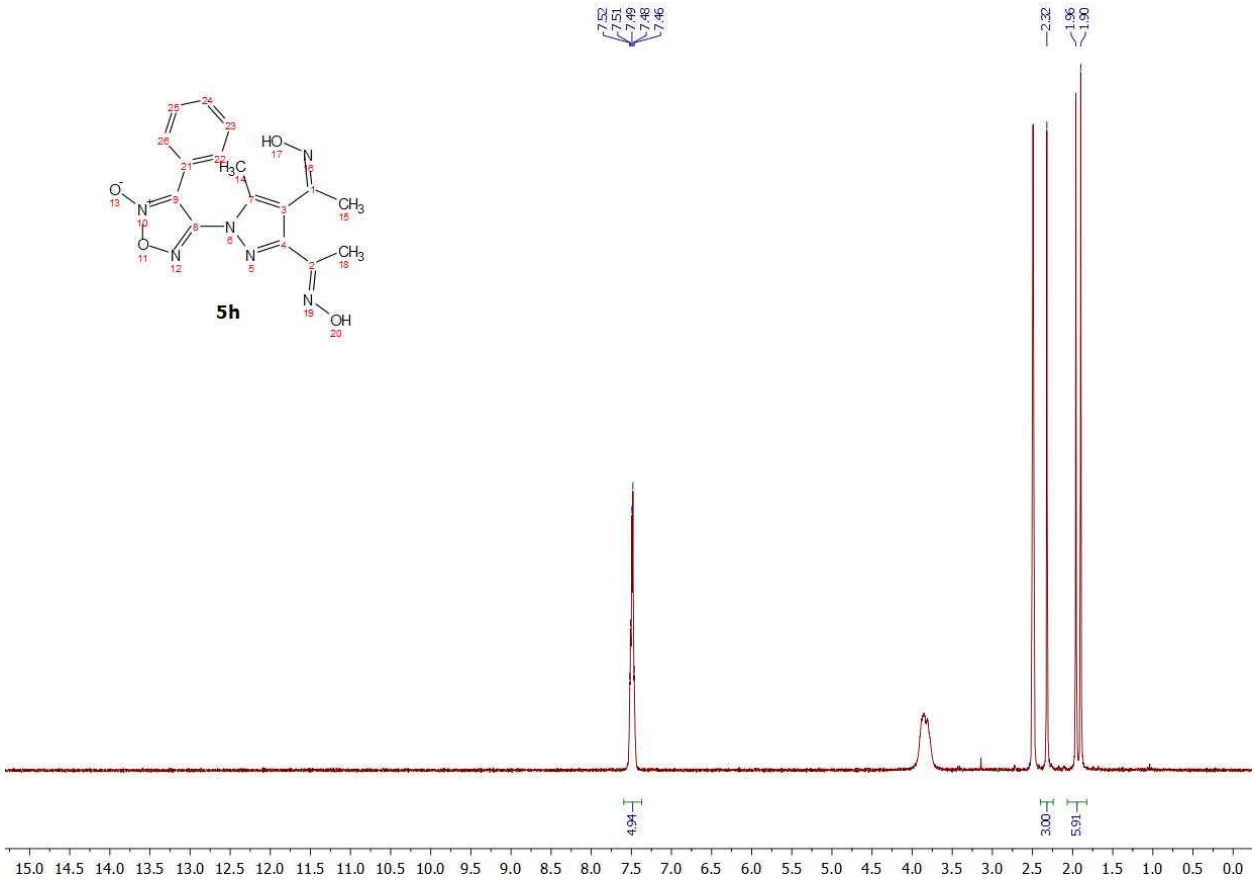
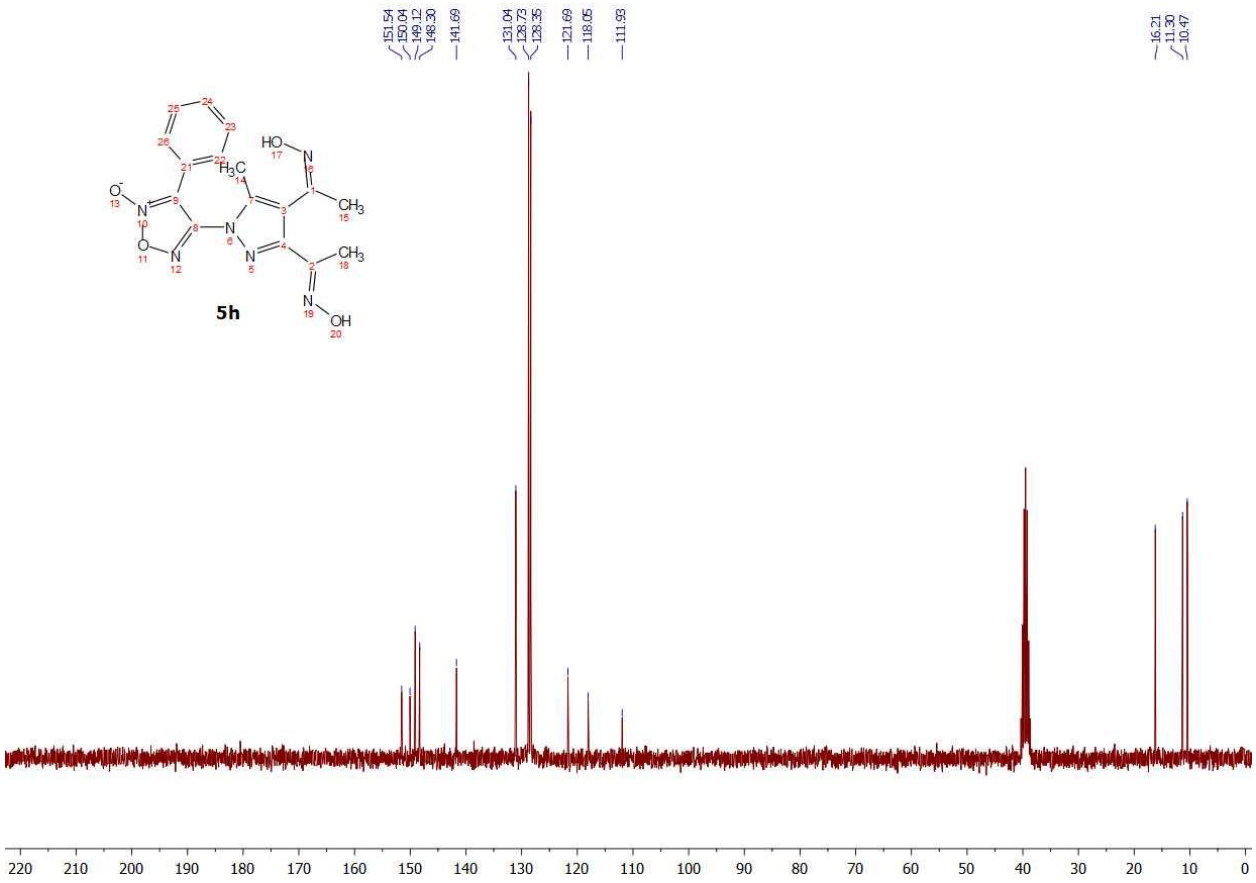

7.52
7.51
7.49
7.48
7.46
2.32
1.96
1.90
4.94
3.00
5.91
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

5h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150.04
149.12
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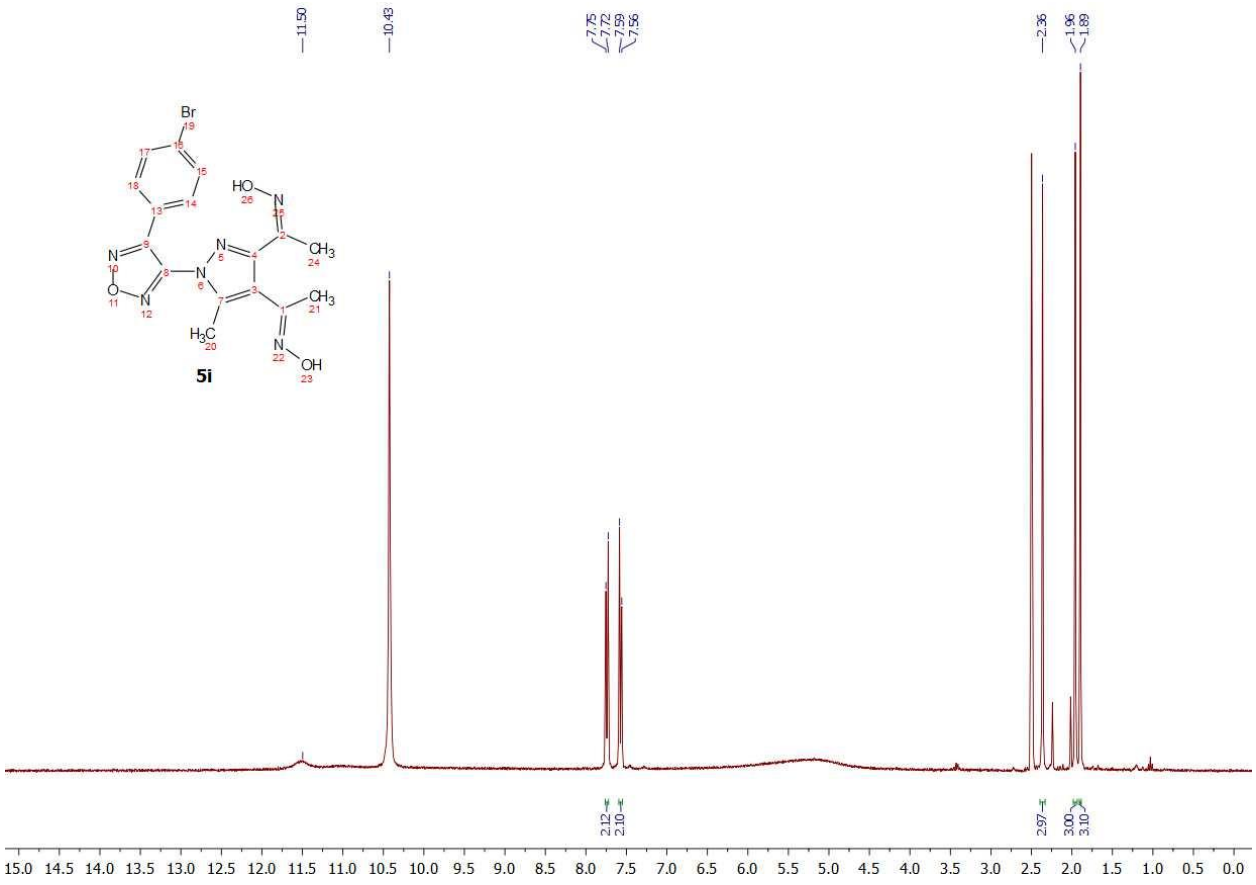
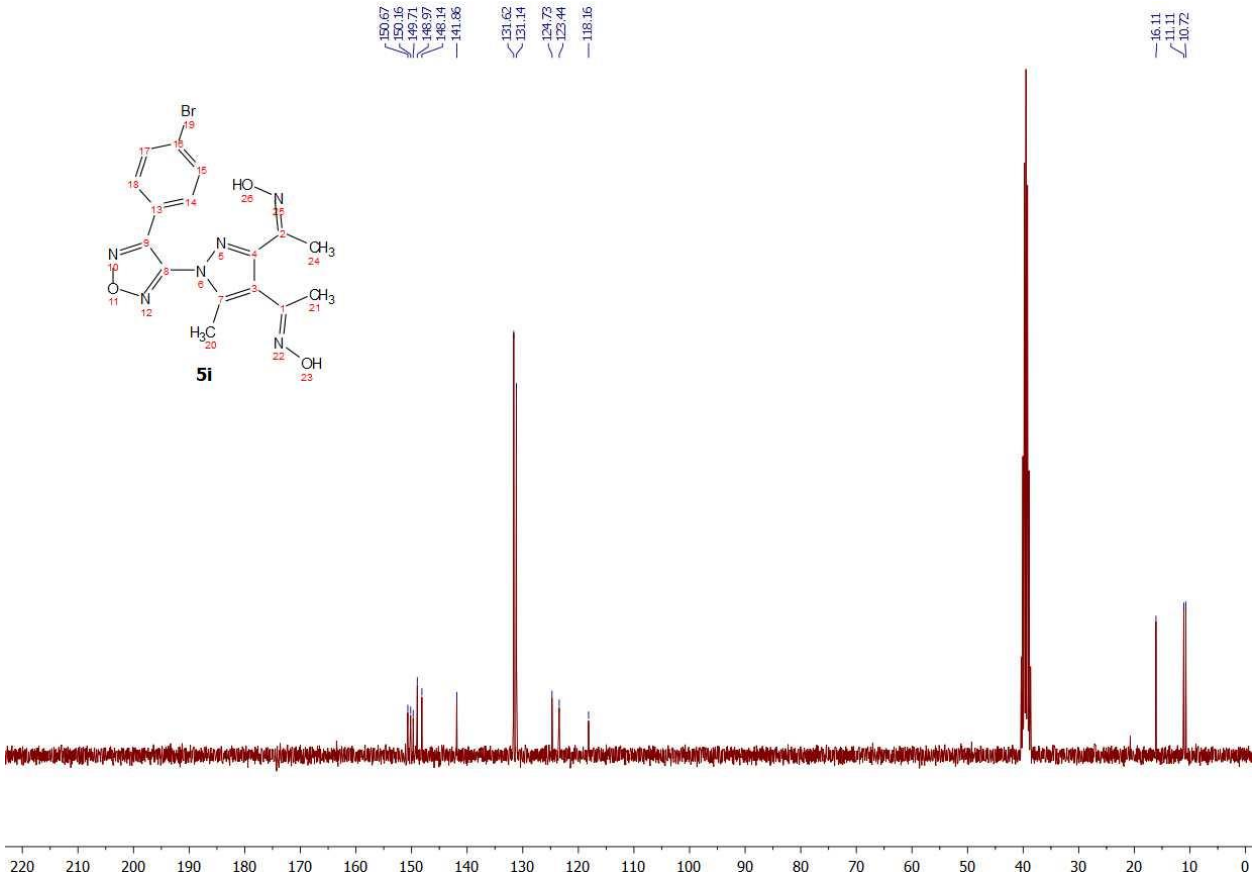
141.69
131.04
128.73
128.35
121.69
118.05
111.93
16.21
11.30
10.47
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

5h


11.50
10.43
7.75
7.72
7.59
7.56
2.36
1.96
1.89
Br
HO
N
CH3
H3C
OH
5i
2.12
2.10
2.97
3.00
3.10
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0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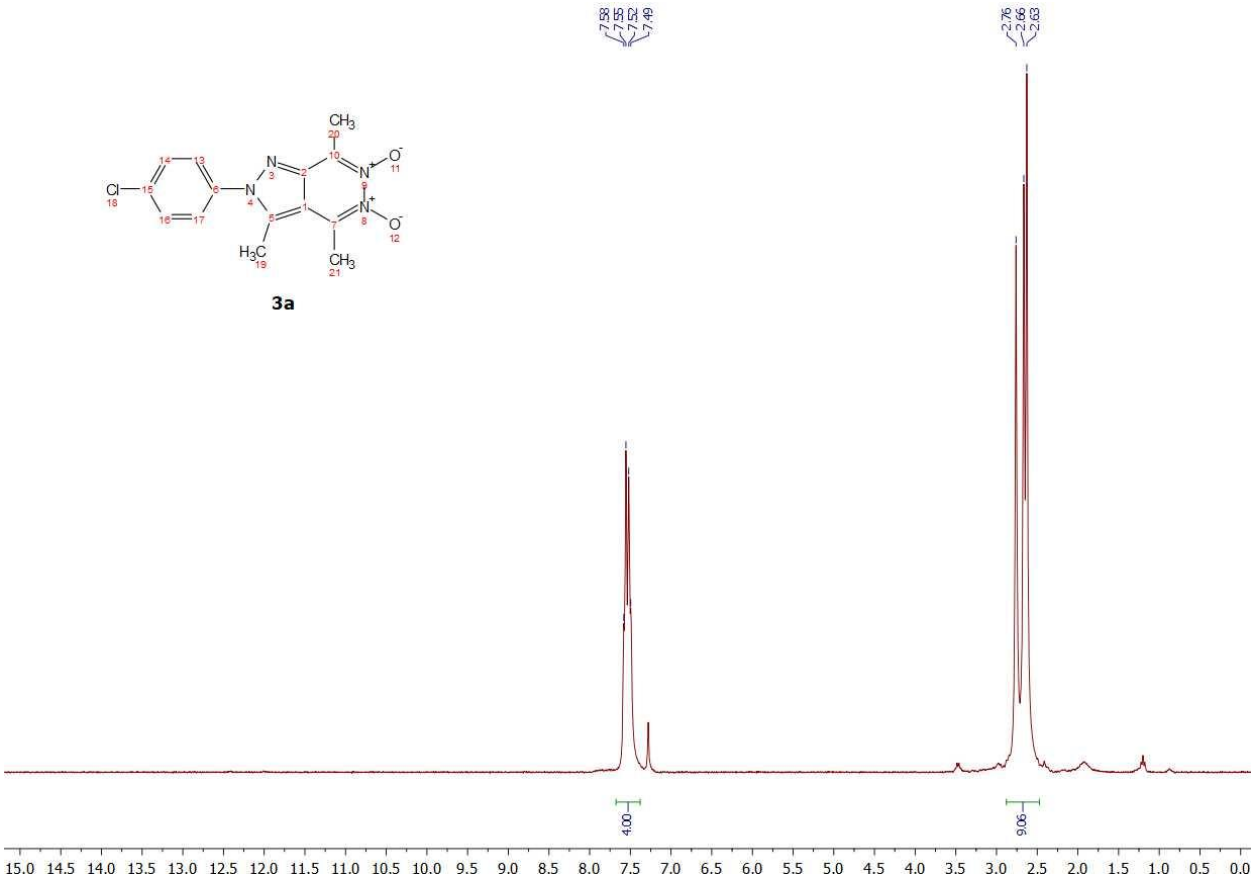
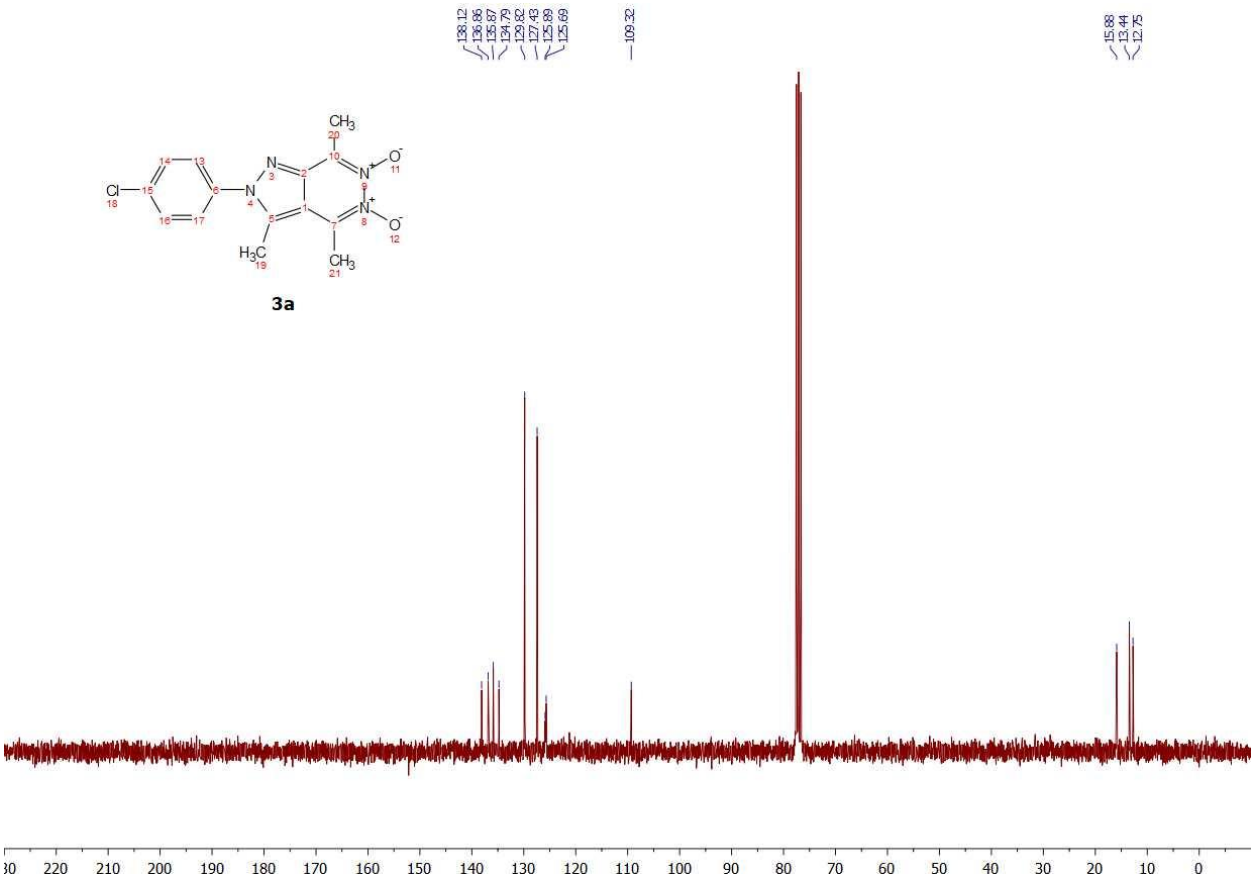
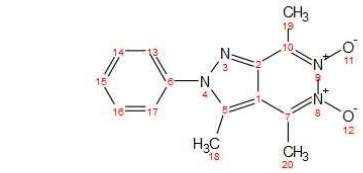
150.16
149.71
148.97
148.14
141.86
131.62
131.14
124.73
123.44
118.16
16.11
11.11
10.72
Br
HO
N
CH3
H3C
OH
5i
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0


7.58
7.55
7.52
7.49
2.76
2.66
2.63
4.00
9.06
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3a

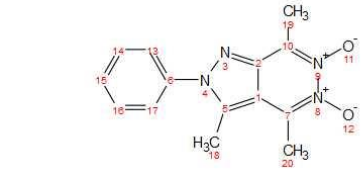

138.12
136.86
135.87
134.79
129.82
127.43
125.89
125.69
109.32
15.88
13.44
12.75
30 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

3a



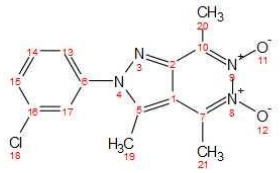
3b

7.55
7.52
2.75
2.64
2.63
5.00
9.09
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0



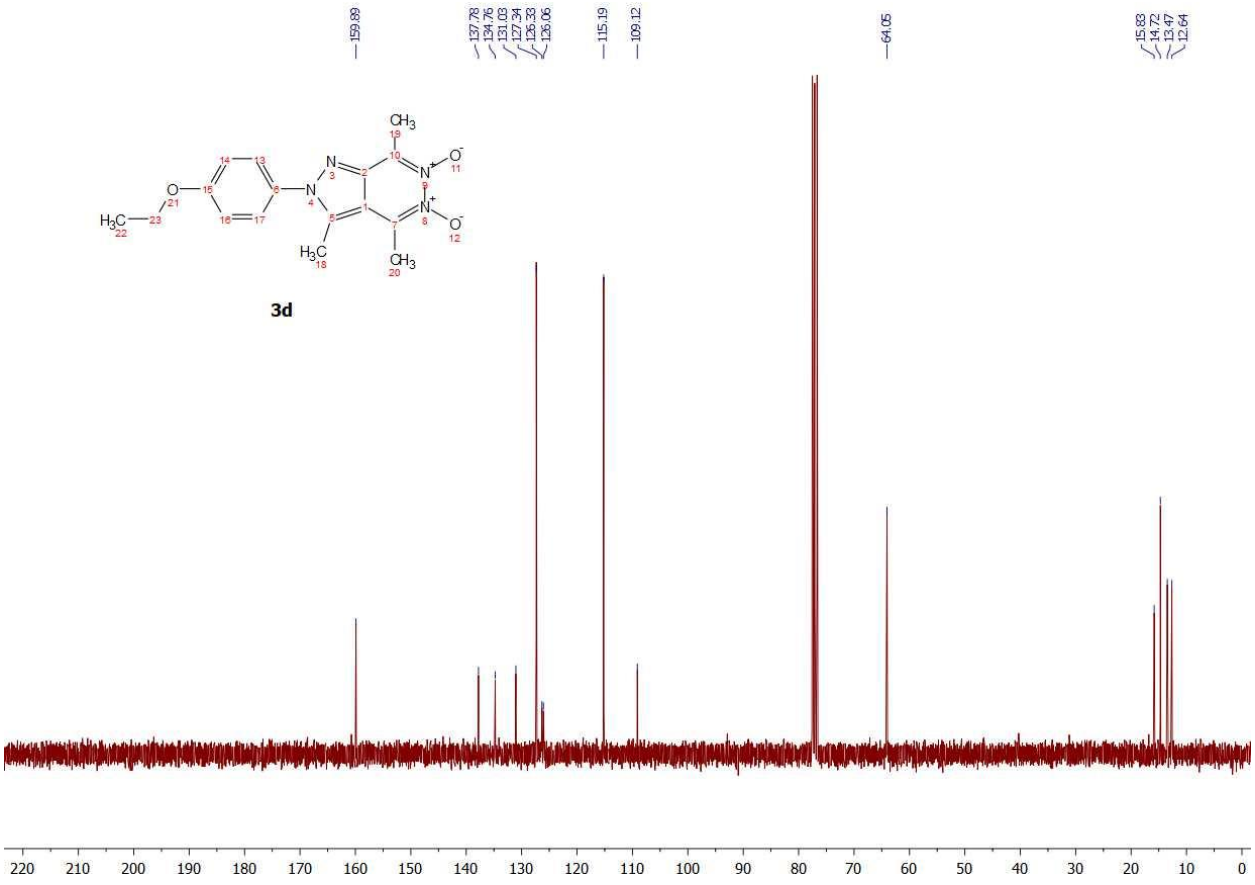
3b

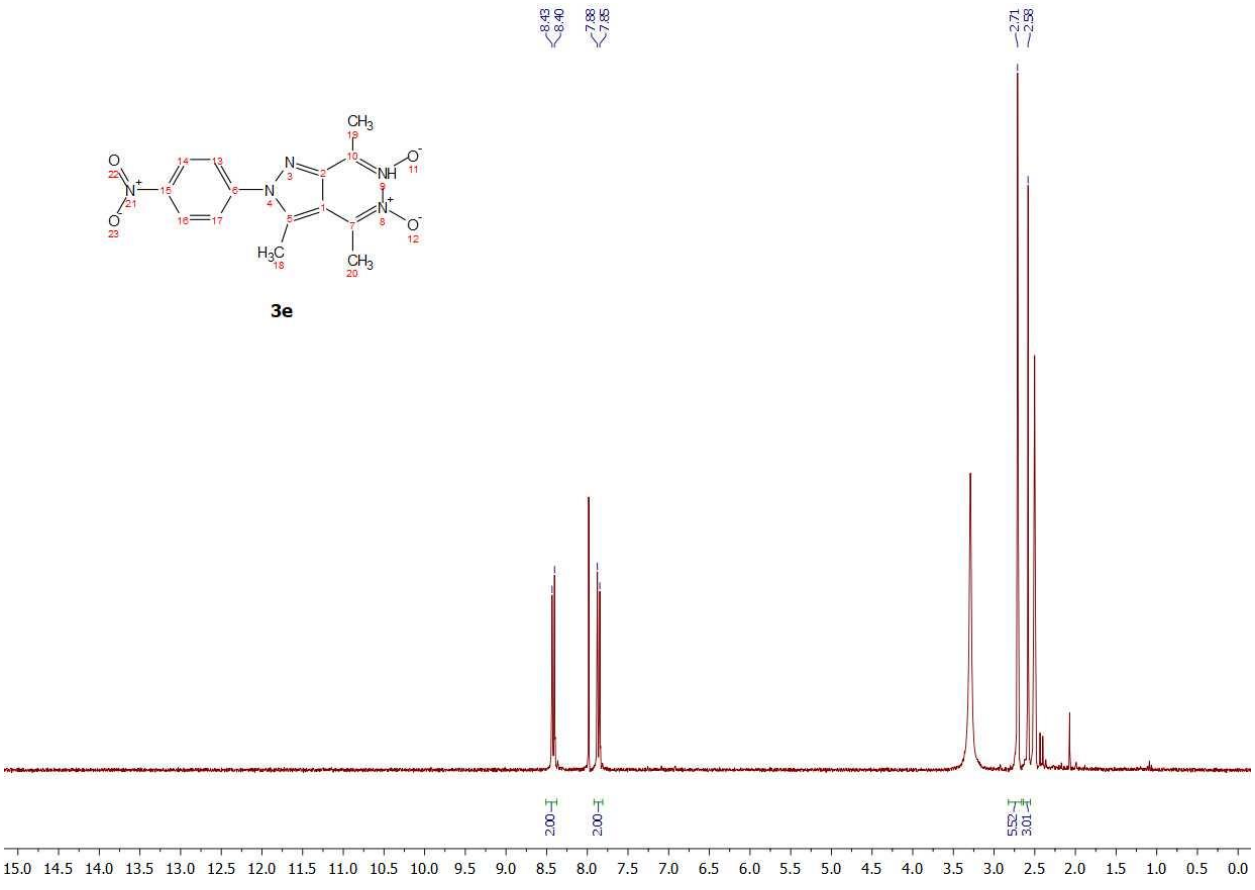
138.42
138.03
134.84
129.84
129.65
126.31
126.17
126.01
109.32
15.91
13.51
12.76
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

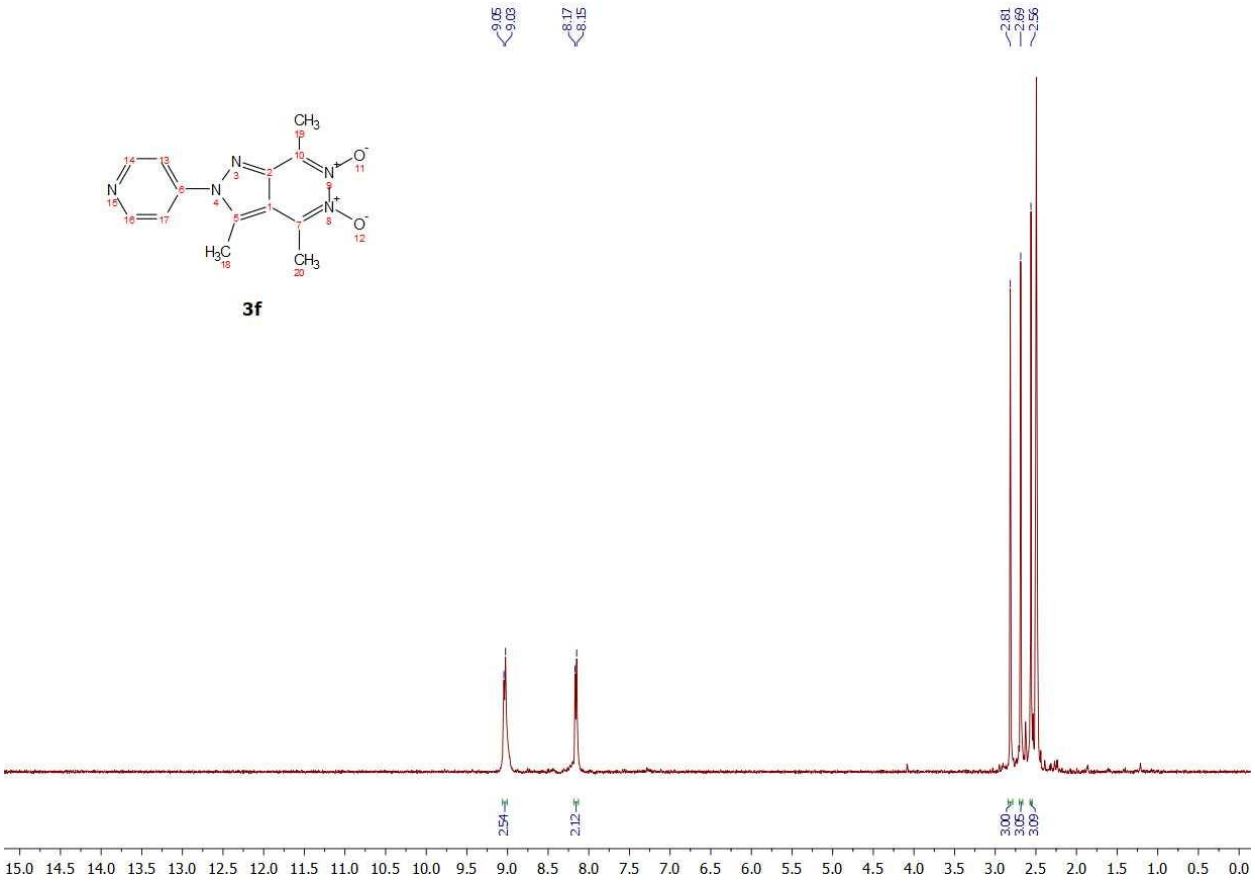


3c

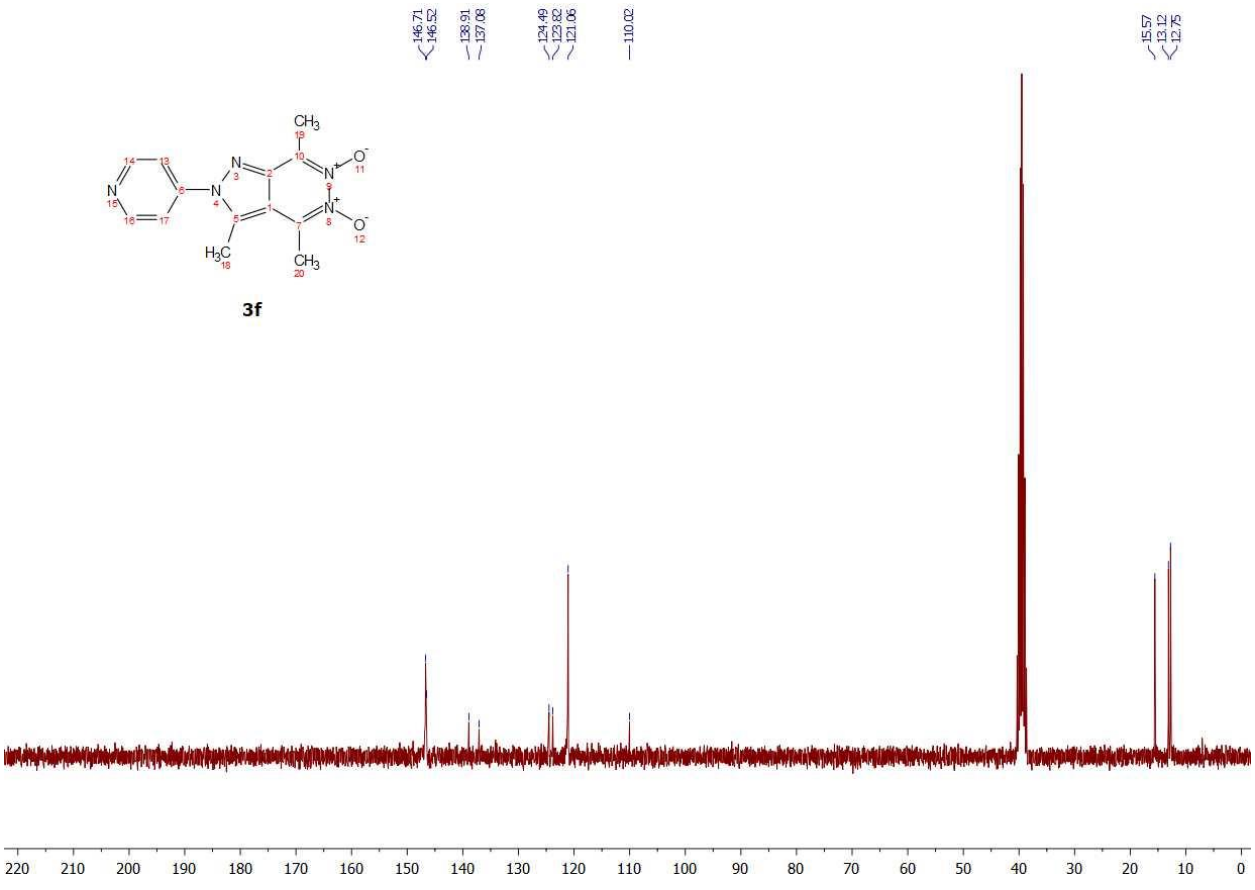
3d


159.89
137.78
134.76
131.03
127.34
126.33
126.06
115.19
109.12
64.05
15.83
14.72
13.47
12.64
3d
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

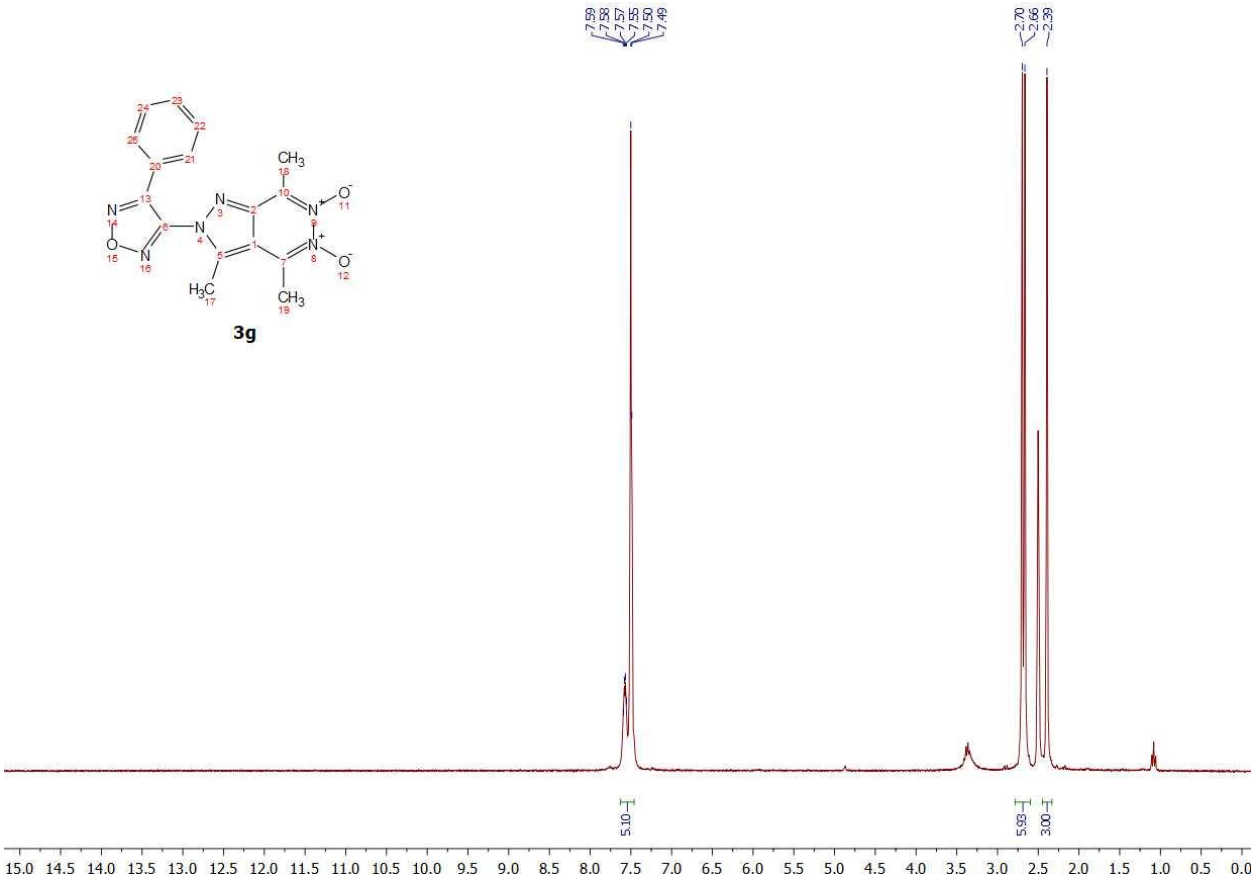

8.43
8.40
7.88
7.85
2.71
2.58
3e
2.00
2.00
5.52
3.01
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0


9.05
9.03
8.17
8.15
2.81
2.69
2.56
2.54
2.12
3.00
3.05
3.09
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3f


146.71
146.52
138.91
137.08
124.49
123.82
121.06
110.02
15.57
13.12
12.75
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

3f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7.57
7.55
7.50
7.49
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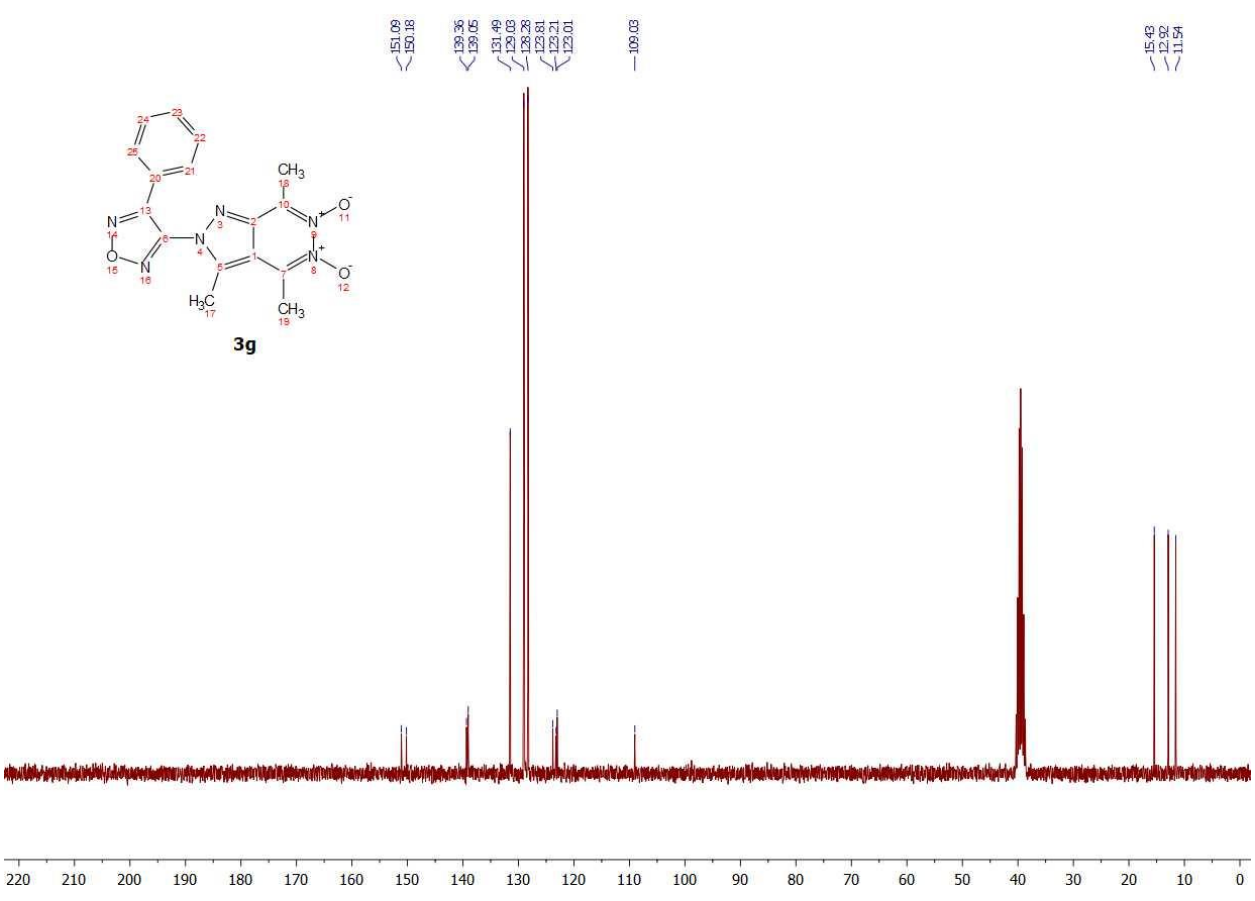
2.66
2.39
5.10
5.93
3.00
3g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109.03
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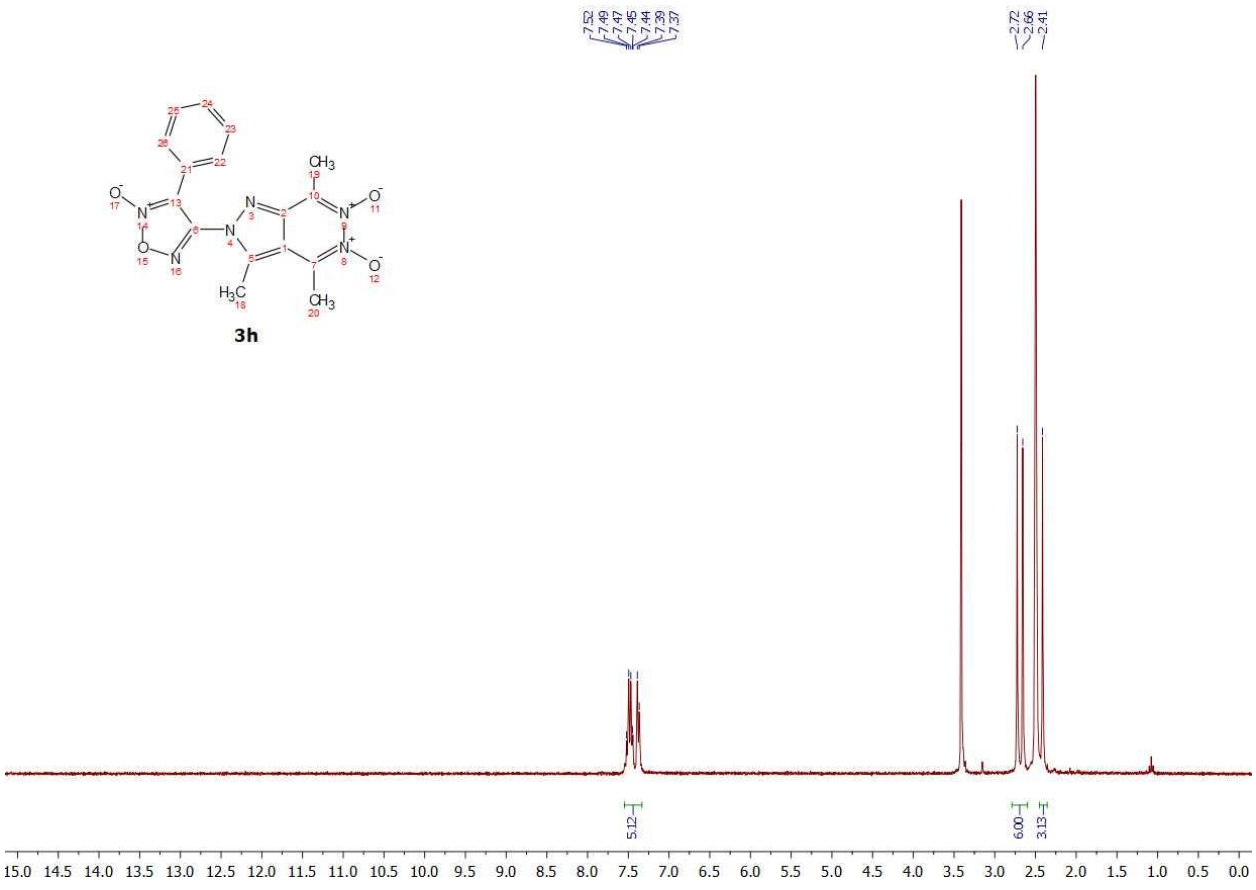
12.92
11.94
3g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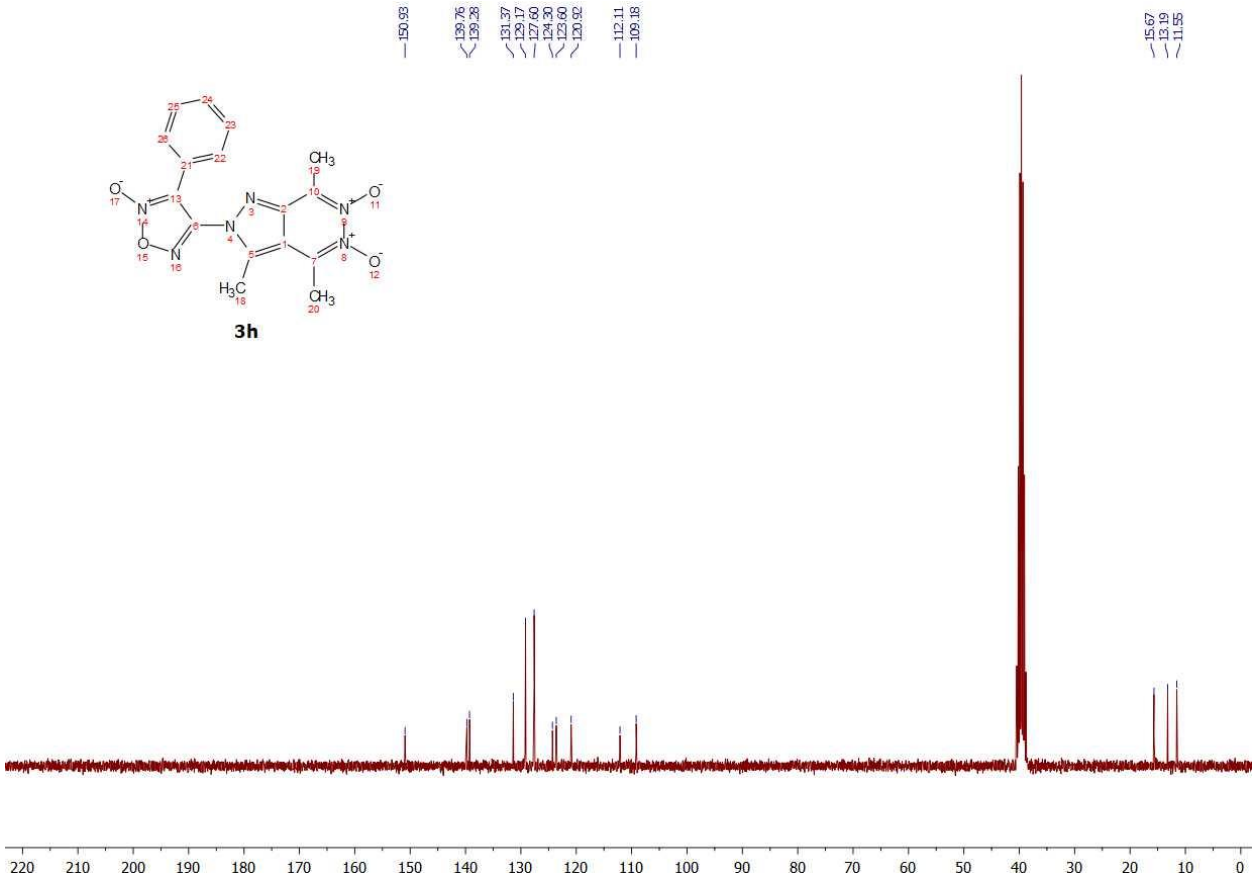
7.49
7.47
7.45
7.44
7.39
7.37
2.72
2.66
2.41
5.12
6.00
3.13
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3h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131.37
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127.60
124.30
123.60
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109.18
15.67
13.19
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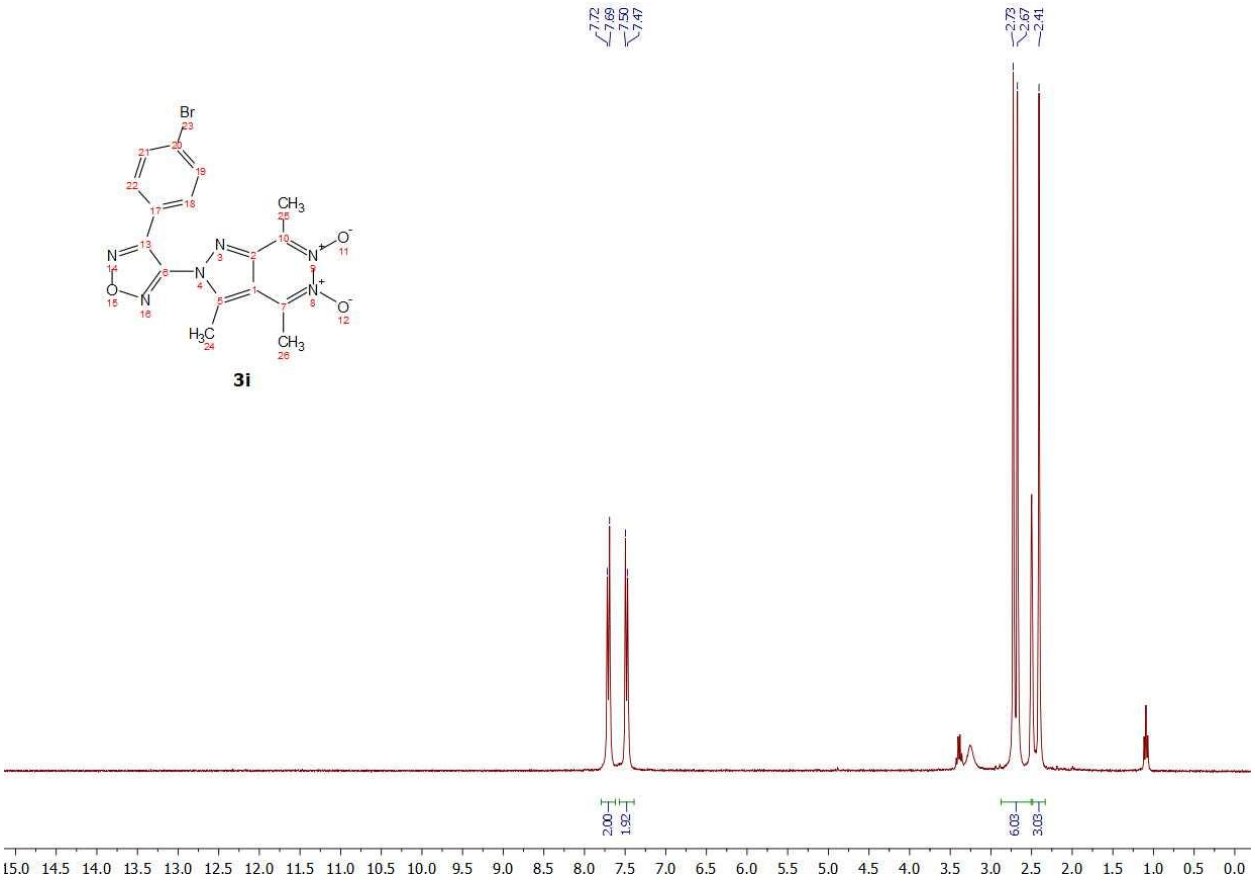
3h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7.47
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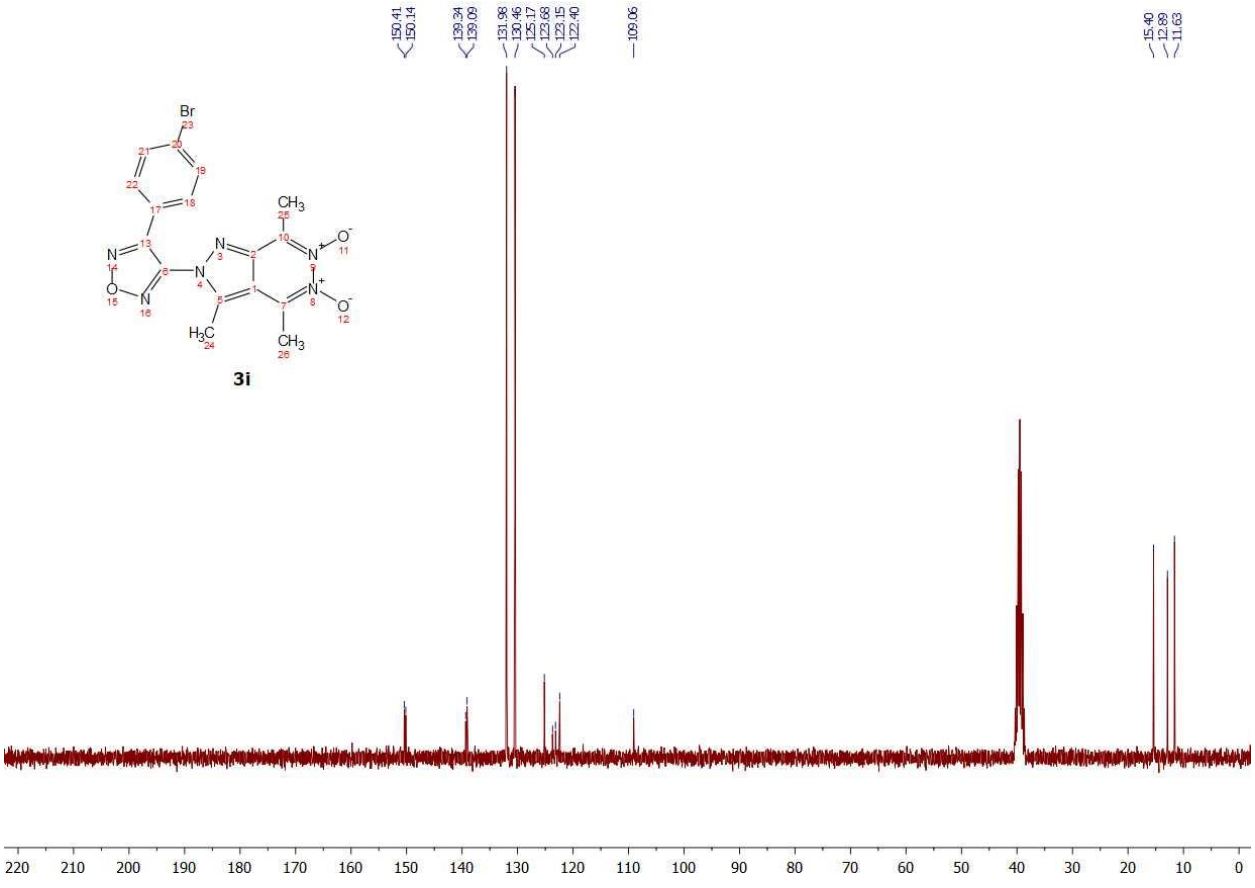
2.67
2.41
2.00
1.92
6.08
3.03
3i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123.15
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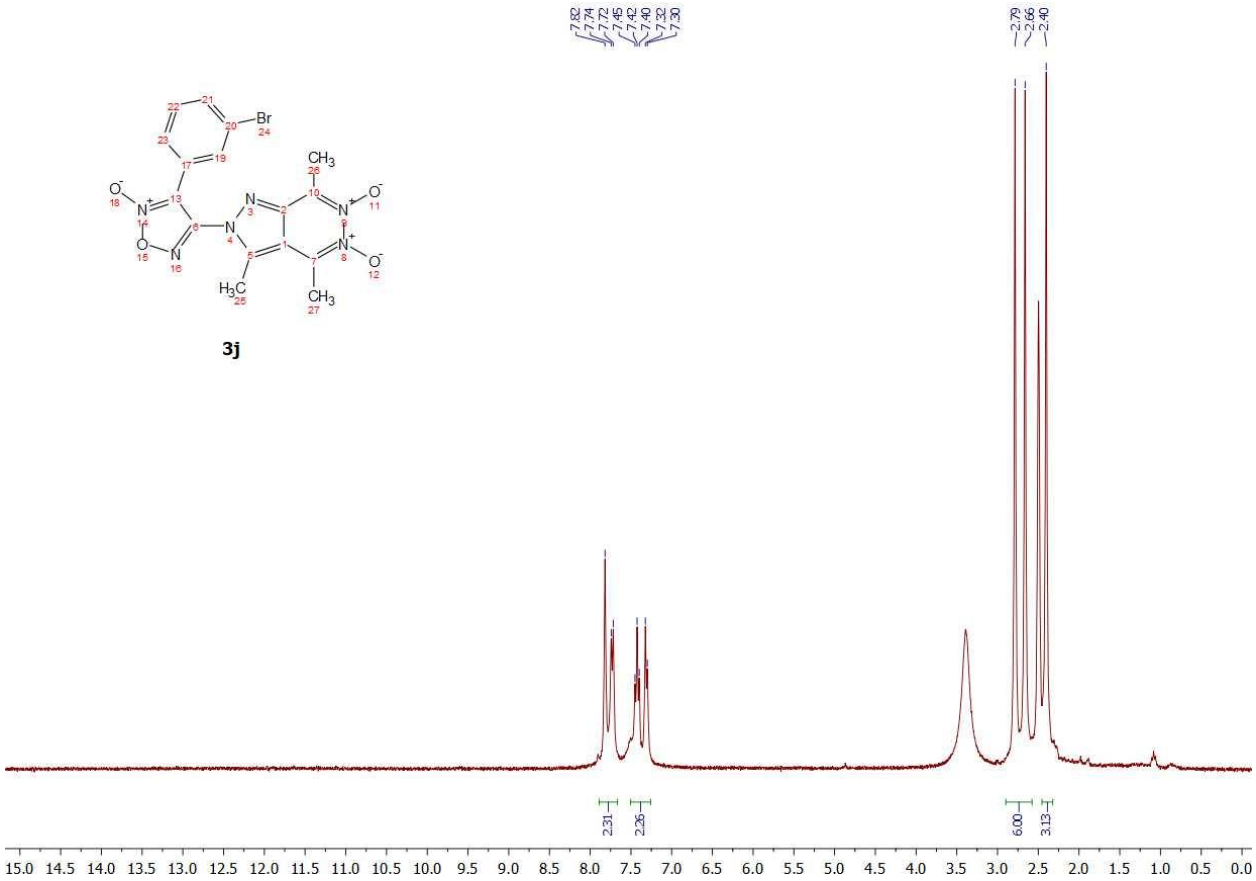
109.06
15.40
12.89
11.63
3i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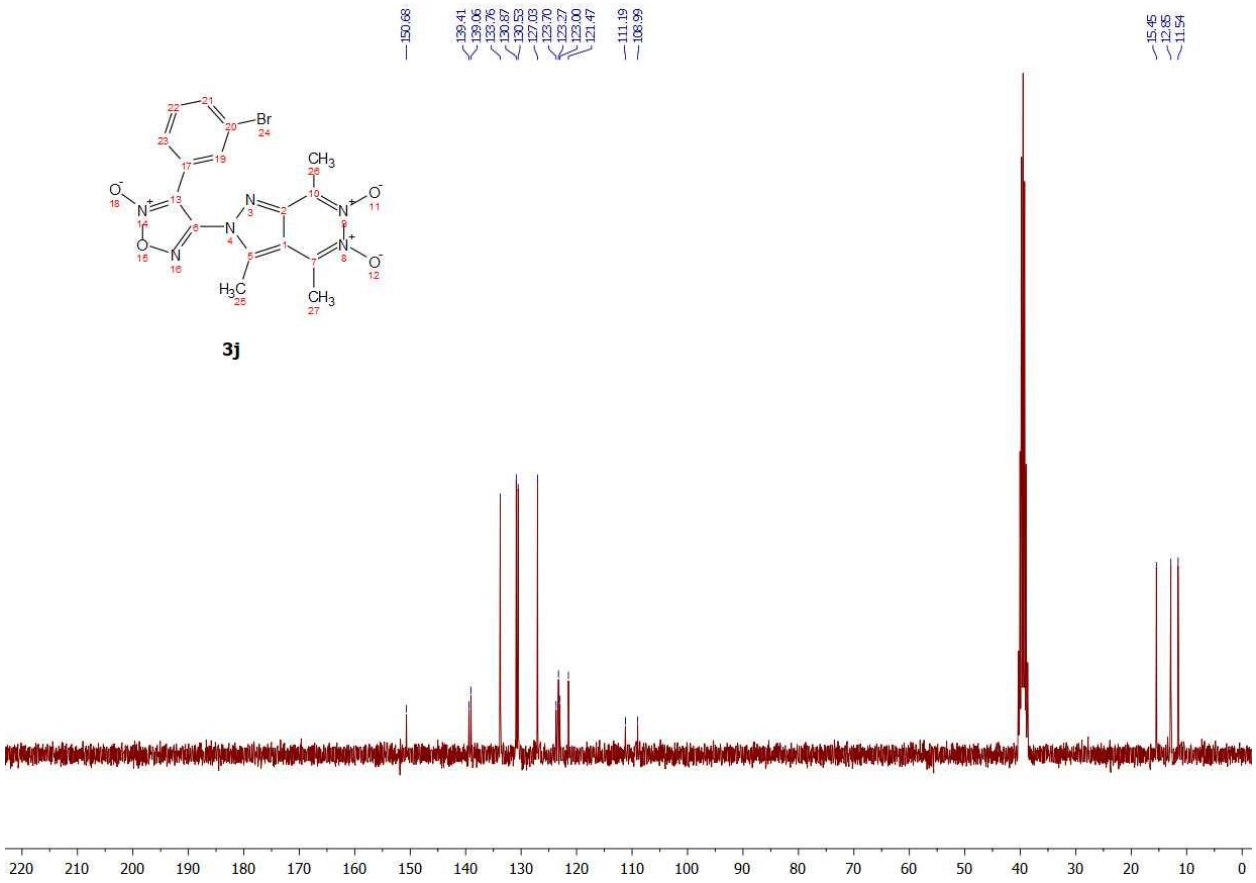
7.40
7.32
7.30
2.79
2.66
2.40
2.31
2.26
6.00
3.13
15.0 14.5 14.0 13.5 13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0

3j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139.06
133.76
130.87
130.53
127.03
123.70
123.27
123.00
121.47
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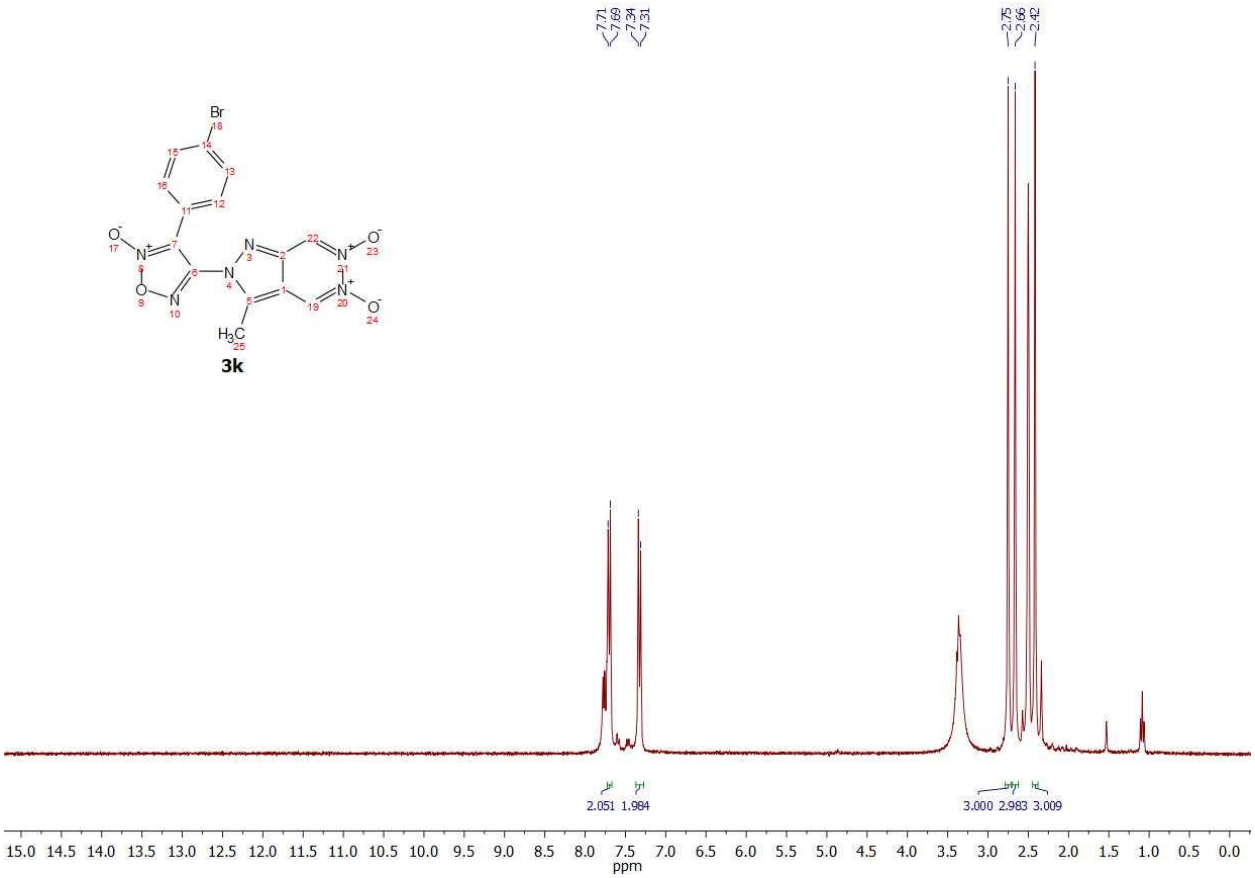
108.99
15.45
12.85
11.54
220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

3j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2.66
2.42
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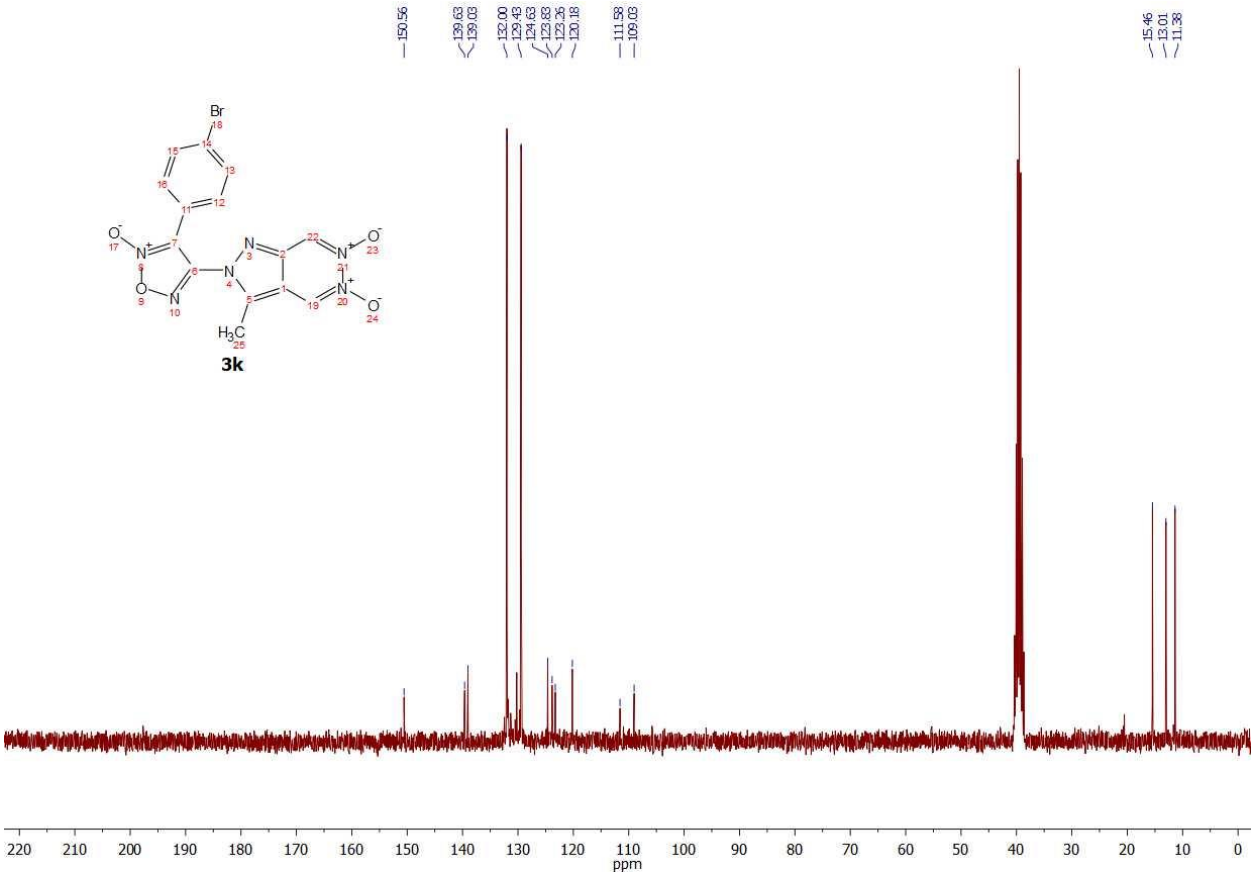
3.000 2.983 3.009
ppm

3k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111.58
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15.46
13.01
11.38
ppm

3k