Electronic supplementary materials *Mendeleev Commun.*, 2021, **31**, 865-866

Anticancer activity of new benzofuroxan–imidazolone hybrids

Elena A. Chugunova, Andrey V. Smolobochkin, Almir S. Gazizov, Alexander R. Burilov, Alexandra D. Voloshina, Anna P. Lyubina, Syumbelya K. Amerhanova, Tatyana A. Melnikova, Alena I. Tulesinova, Nurgali I. Akylbekov, Nurlybek A. Akhatayev and Victor V. Syakaev

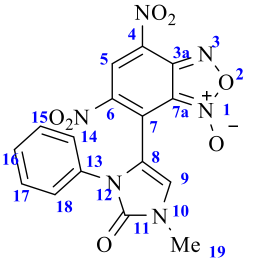
Contents

General

IR spectra were recorded on a UR-20 spectrometer in the 400–3600 cm^{-1} range in KBr. ^{1}H-NMR spectra were recorded on IR spectra were recorded on a UR-20 spectrometer in the 400–3600 cm^{-1} range in KBr. The ^{1}H- and ^{13}C-NMR spectra were recorded on a Bruker Avance 600 spectrometer (Bruker BioSpin, Rheinstetten, Germany) operating at 600 MHz (for ^{1}H NMR) and 151 MHz (for ^{13}C NMR) and Bruker AVANCE*III*-500 (Bruker BioSpin, Rheinstetten, Germany) operating at 500.1 MHz for ^{1}H, 125.8 MHz for ^{13}C and 50.7 MHz for ^{15}N. Chemical shifts were measured in δ (ppm) with reference to the solvent (δ = 2.06 ppm and 28.94 ppm for $(CD_3)_2CO$ for ^{1}H and ^{13}C NMR, respectively). The ^{15}N NMR spectra are referenced to external urea and converted to the liquid anhydrous ammonia scale ($(NH_2)_2C(O)$ δ(^{15}N)=75 ppm). The pulse programs of the COSY, HSQC and HMBC experiments were taken from Bruker software library. Elemental analysis was performed on a CHNS-O Elemental Analyser EuroEA3028-HT-OM (EuroVector S.p.A., Milan, Italy). The melting points were determined in glass capillaries on a Stuart SMP 10 instrument. All solvents were purified and dried according to standard procedures. 7-Chloro-4,6-dinitrobenzofuroxan **1** and imidazol-2-ones **2a-c** were synthesized according to the literature [Norris, W. P.; Chafin, A.; Spear, R. J.; Read, R. W. *Heterocycles* **1984**, *22*, 271; Burilov, A. R.; Khakimov, M. S.; Gazizov, A. S.; Pudovik, M. A.; Syakaev, V. V; Krivolapov, D. B.; Konovalov, A. I. *Mendeleev Commun.* **2008**, *18*, 54].

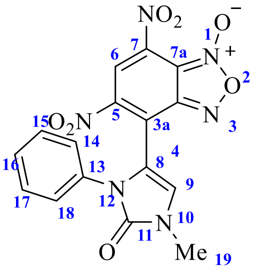
Synthetic procedures and compound characterization data

Reaction between 7-chloro-4,6-dinitrobenzofuroxan **1** and 1*H*-imidazol-2(3*H*)-ones **2a-c**. To a solution of 7-chloro-4,6-dinitrobenzofuroxan **1** (0.1 g, 0.4 mmol) in $CHCl_3$ (5 mL) at room temperature was added a solution of 1*H*-imidazol-2(3*H*)-one **2** (0.4 mmol) in $CHCl_3$ (5 mL) and $NaHCO_3$ (0.04 g, 0.48 mmol). The reaction was carried out at room temperature and under magnetic stirring, and the conversion was monitored through TLC analysis (eluent: toluene/ethyl acetate, 2:1). The mixture was stirred at room temperature overnight, after removal of the solvent under reduced pressure, the crude products were purified by column chromatography on 230-400 mesh silica (eluent: toluene/ethyl acetate, 2:1) to give target compounds.

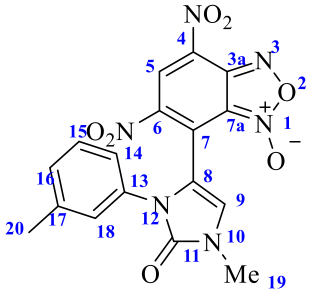


7-(1-Methyl-2-oxo-3-phenyl-2,3-dihydro-1H-imidazol-4-yl)-4,6-dinitrobenzo[c][1,2,5]oxadiazole 1-oxide **3a**. Blue solid. Yield 0.088 g (55%). M.p.: 98-100 °C. IR (ν, cm^{-1}): 1714 (CO), 1625 (furoxan ring), 1556 (NO_2 asymm), 1372 (NO_2 symm). Anal. calcd (%) for $C_{16}H_{10}N_6O_7$: C 48.25; H 2.53; N 21.10. Found: C 48.38; H 2.66; N 21.06.

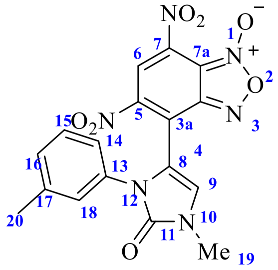
^{1}H NMR (500 MHz, acetone-d_6) δ 8.76 (s, 1H, H5), 7.68 (s, 1H, H9), 7.29 (s, 5H, H14-H18), 3.52 (s, 3H, H19). **^{13}C{^{1}H} NMR** (126 MHz, acetone-d_6) δ 152.17 (C11), 145.22 (C3a), 141.60 (C6), 134.61(C13), 134.24 (C4), 128.87 (C16/C18), 128.12 (C5), 127.10 (C17), 125.72 (C13/C15), 123.71 (C9), 121.43 (C7), 114.41 (C7a), 108.32 (C8), 30.54 (C19). **^{15}N NMR** (51 MHz, acetone-d_6) δ 362.5 (N6), 358.7 (N4), N3 (n/o), N1 (n/o), 142.8 (N12), 131.9 (N11).



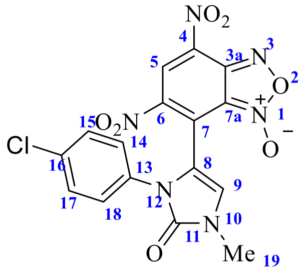
The spectrum also contained minor characteristic signals for tautomeric 4-(1-methyl-2-oxo-3-phenyl-2,3-dihydro-1*H*-imidazol-4-yl)-5,7-dinitrobenzo[*c*][1,2,5]oxadiazole 1-oxide **3'a**. Ratio of tautomers 8:1. **^{1}H NMR** (500 MHz, acetone-d_6) δ 8.31 (s, 1H, H6), 7.99 (s, 1H, H9), 7.20-7.28 (m, 5H, H14-H18), 3.56 (s, 3H, H19). ^{13}C NMR (126 MHz, acetone-d_6) δ 152.47, 141.95, 132.80, 129.00, 128.63, 127.95, 123.52, 122.02, 121.27, 118.53, 116.28, 111.37, 110.01, 30.46.



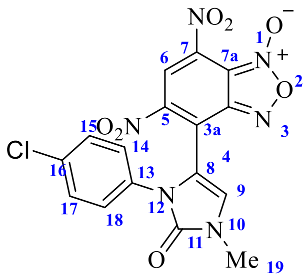
7-(1-Methyl-2-oxo-3-m-tolyl-2,3-dihydro-1H-imidazol-4-yl)-4,6-dinitrobenzo[c][1,2,5]oxadiazole 1-oxide **3b**. Dark green solid. Yield 0.107 g (65%). M.p.: 108-110 °C. IR (ν, cm^{-1}): 1707 (CO), 1622 (furoxan ring), 1563 (NO$_2$ asymm), 1377 (NO$_2$ symm). Anal. calcd (%) for $C_{17}H_{12}N_6O_7$: C 49.52; H 2.93; N 20.38. Found: C 49.54; H 2.88; N 20.33. **^{1}H NMR** (600 MHz, acetone-d_6) δ 8.75 (s, 1H), 7.67 (s, 1H), 7.01-7.14 (m, 4H), 3.51 (s, 3H), 2.24 (s, 3H). **^{13}C NMR** (151 MHz, acetone-d_6) δ 152.20, 145.24, 141.53, 138.94, 134.17, 134.09, 128.67, 128.13, 128.11, 127.88, 126.38, 123.77, 122.80, 121.51, 114.40, 108.46, 30.56, 20.30.



The spectrum also contained minor characteristic signals for tautomeric 4-(1-methyl-2-oxo-3-(m-tolyl)-2,3-dihydro-1*H*-imidazol-4-yl)-5,7-dinitrobenzo[*c*][1,2,5]oxadiazole 1-oxide **3'b**. Ratio of tautomers 7:1. **^{1}H NMR** (600 MHz, acetone-d_6) δ 8.31 (s, 1H), 7.98 (s, 1H), 7.01-7.14 (m, 4H), 3.55 (s, 3H), 2.26 (s, 3H). ^{13}C NMR (151 MHz, acetone-d_6) δ 152.48, 141.94, 139.08, 134.52, 129.29, 128.78, 127.79, 125.70, 125.06, 123.53, 123.02, 121.29, 119.50, 111.48, 106.94, 31.40, 20.57.



7-(3-(4-Chlorophenyl)-1-methyl-2-oxo-2,3-dihydro-1H-imidazol-4-yl)-4,6-dinitrobenzo[c][1,2,5]oxadiazole 1-oxide **3c**. Purple solid. Yield 0.046 g (28%). M.p.: 153-154 °C. IR (ν, cm^{-1}): 1705 (CO), 1622 (furoxan ring), 1563 (NO$_2$ asymm), 1377 (NO$_2$ symm). Anal. calcd (%) for $C_{16}H_9ClN_6O_7$: C 44.41; H 2.10; Cl 8.19; N 19.42. Found: C 44.45; H 2.07; Cl 8.22; N 19.50. **^{1}H NMR** (600 MHz, acetone-d_6) δ 8.78 (s, 1H), 7.68 (s, 1H), 7.33 (m, 4H), 3.51 (s, 3H). **^{13}C NMR** (151 MHz, acetone-d_6) δ 152.04, 145.28, 141.78, 133.13, 132.26, 129.02, 128.17, 127.25, 123.88, 121.15, 120.44, 114.48, 108.03, 30.59.



The spectrum also contained minor characteristic signals for tautomeric 4-(3-(4-chlorophenyl)-1-methyl-2-oxo-2,3-dihydro-1*H*-imidazol-4-yl)-5,7-dinitrobenzo[*c*][1,2,5]oxadiazole 1-oxide **3'c**. **^{1}H NMR** (600 MHz, acetone-d_6) δ 8.35 (s, 1H), 7.68 (s, 1H), 7.33 (m, 4H), 3.51 (s, 3H). **^{1}H NMR** (600 MHz, acetone-d_6) δ 8.78 (s, 1H), 8.00 (s, 1H), 7.26-7.68 (m, 4H), 3.55 (s, 3H). Unfortunatly, part of carbon atoms for the minor tautomer is not possible to determine due to its low concentration. **^{13}C NMR** (151 MHz, acetone-d_6) δ 134.45, 129.11, 128.84, 128.51, 125.93, 123.54, 122.51, 121.46.

Copies of NMR and IR spectra

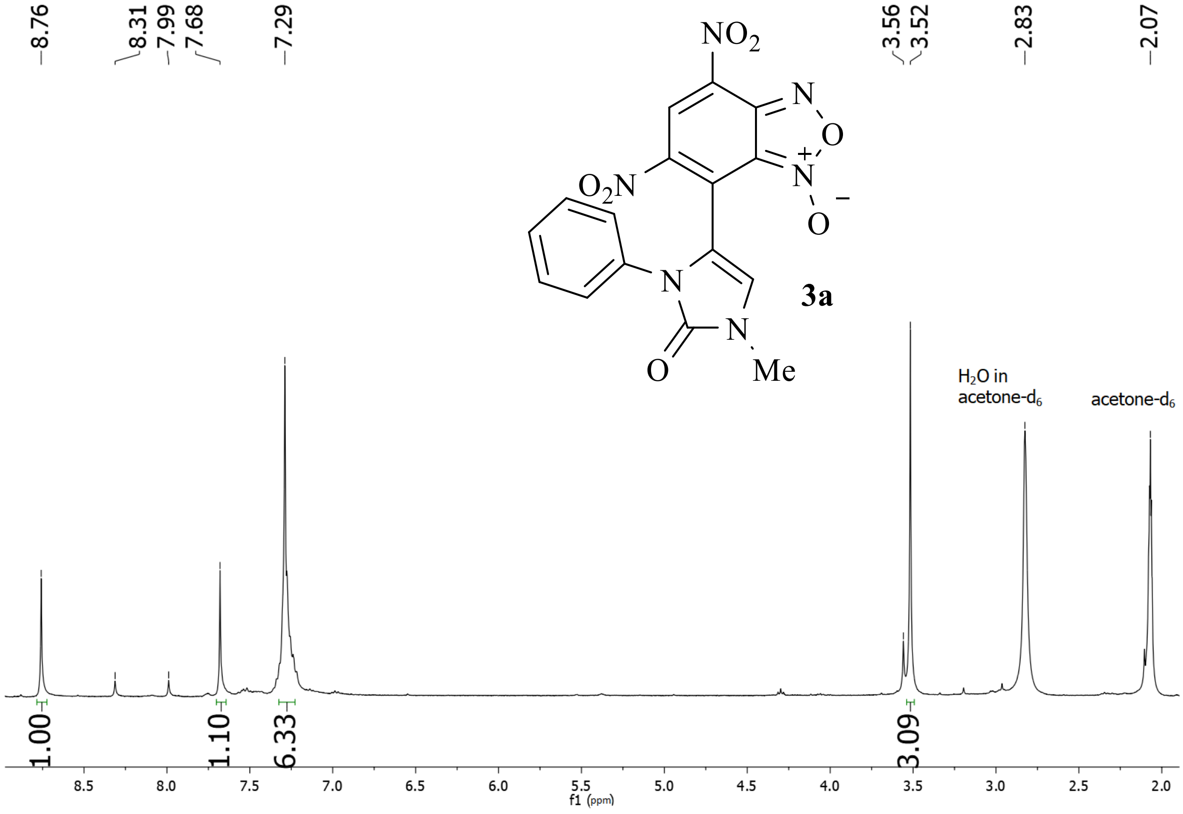


Figure S1. ^{1}H NMR (acetone-d_6, 500 MHz, 25 °C) of compound **3a**.

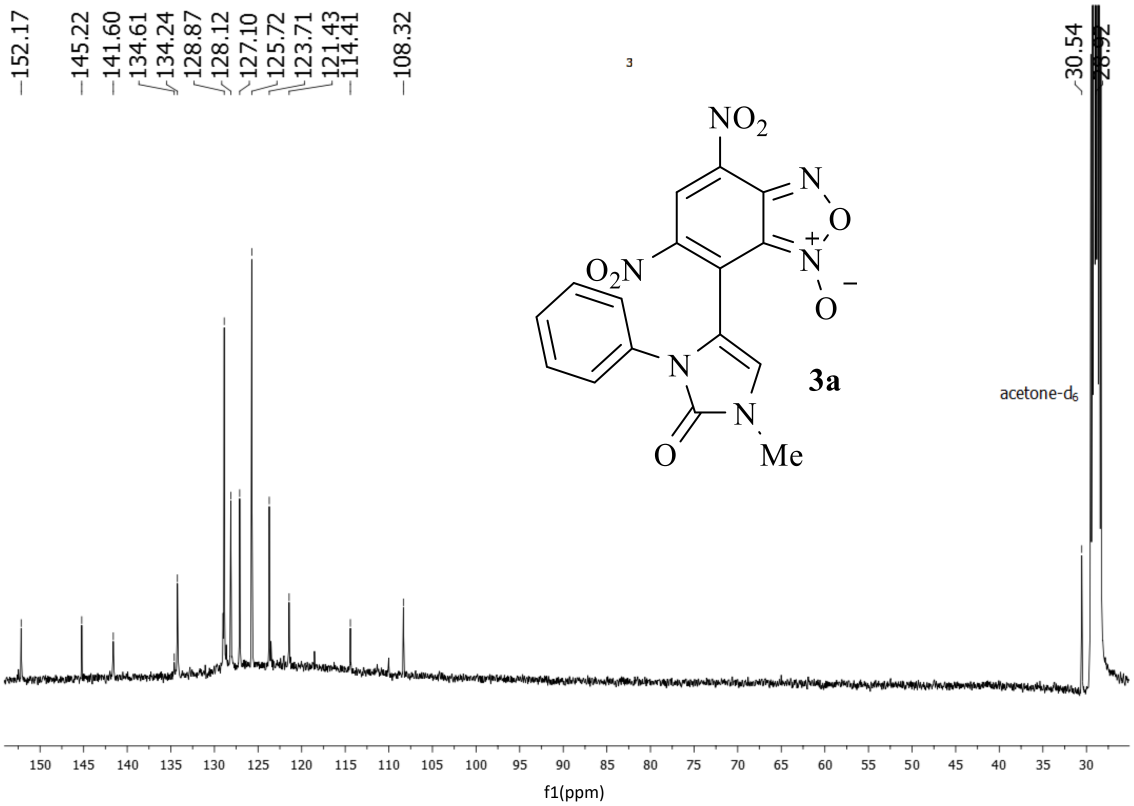


Figure S2. ^{13}C{1H} NMR (acetone-d_6, 126 MHz, 25 °C) of compound **3a**

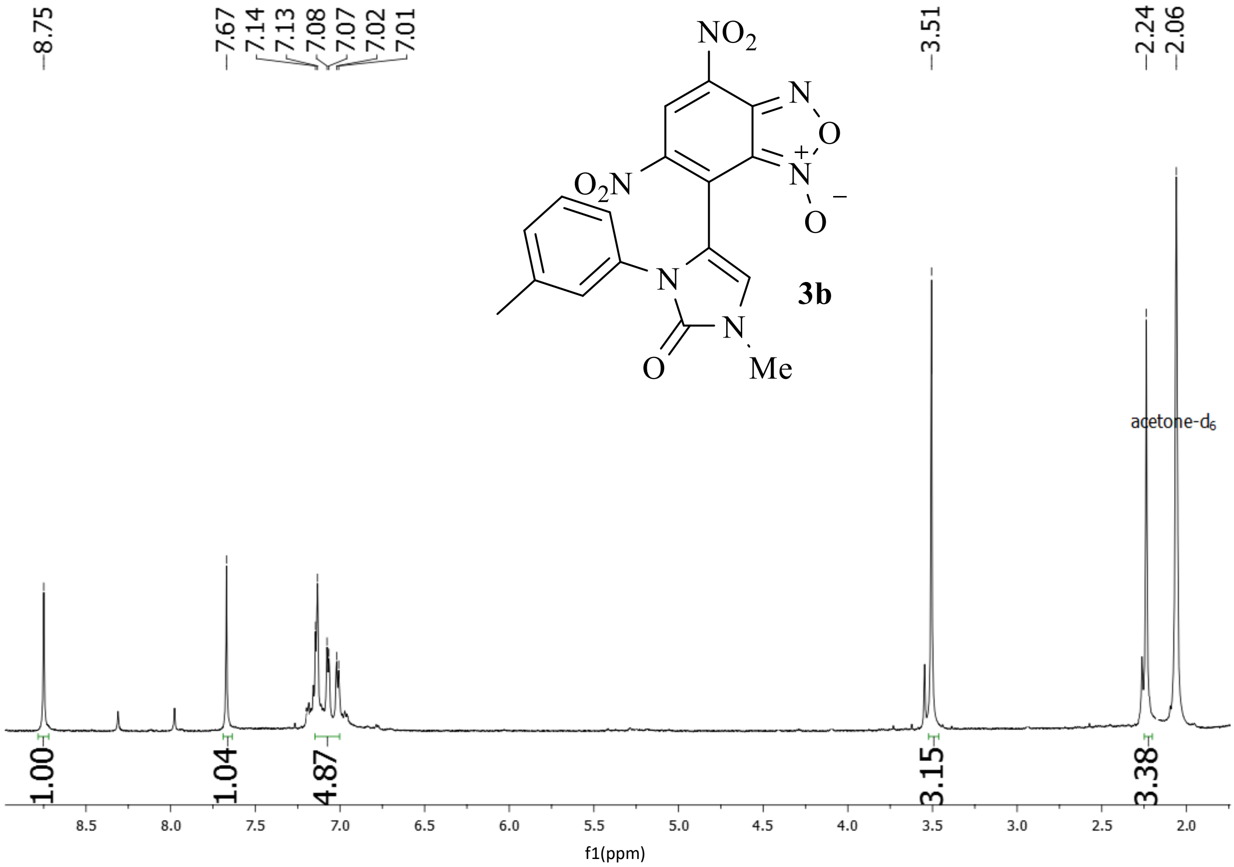


Figure S3. ^{1}H NMR (acetone-d$_6$, 600 MHz, 25 °C) of compound **3b**.

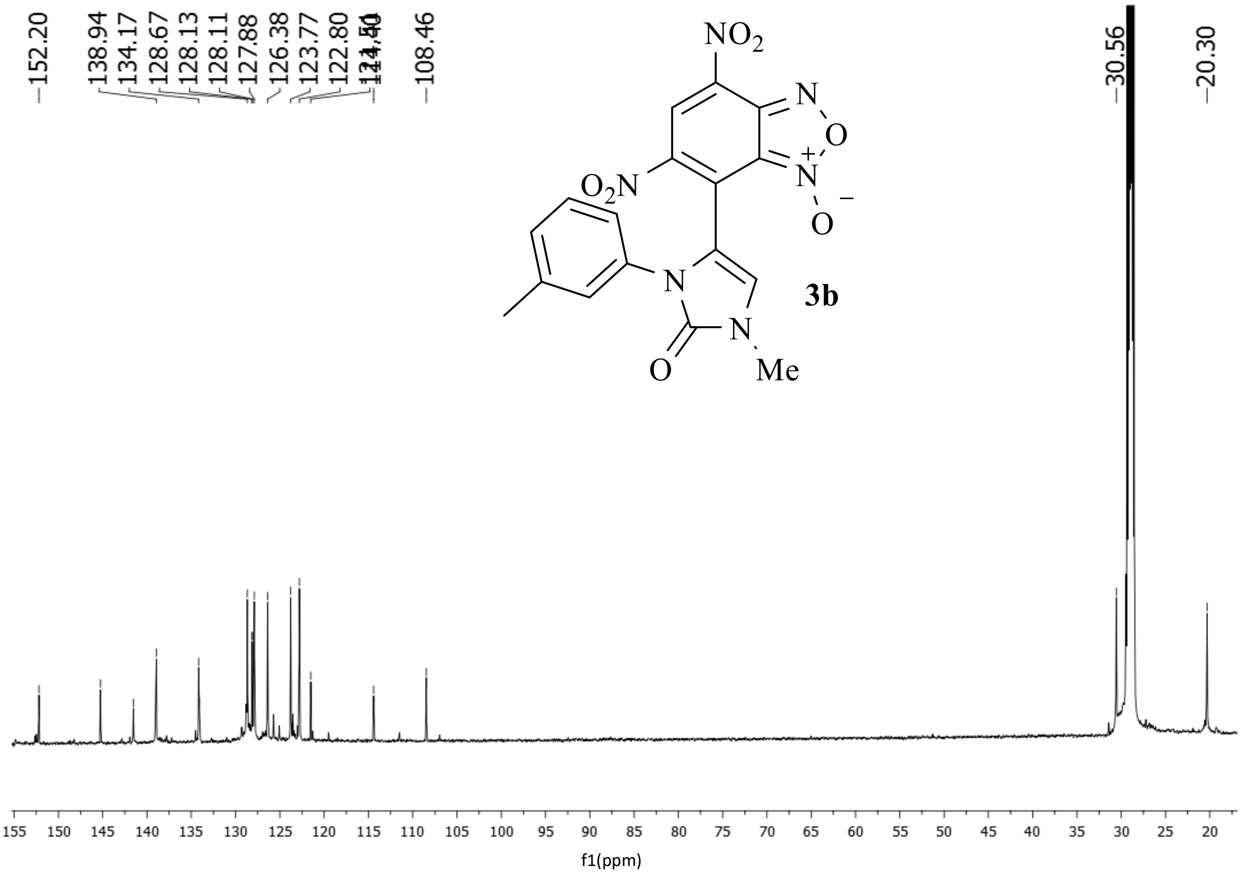


Figure S4. ^{13}C{1H} NMR (acetone-d$_6$, 151 MHz, 25 °C) of compound **3b**

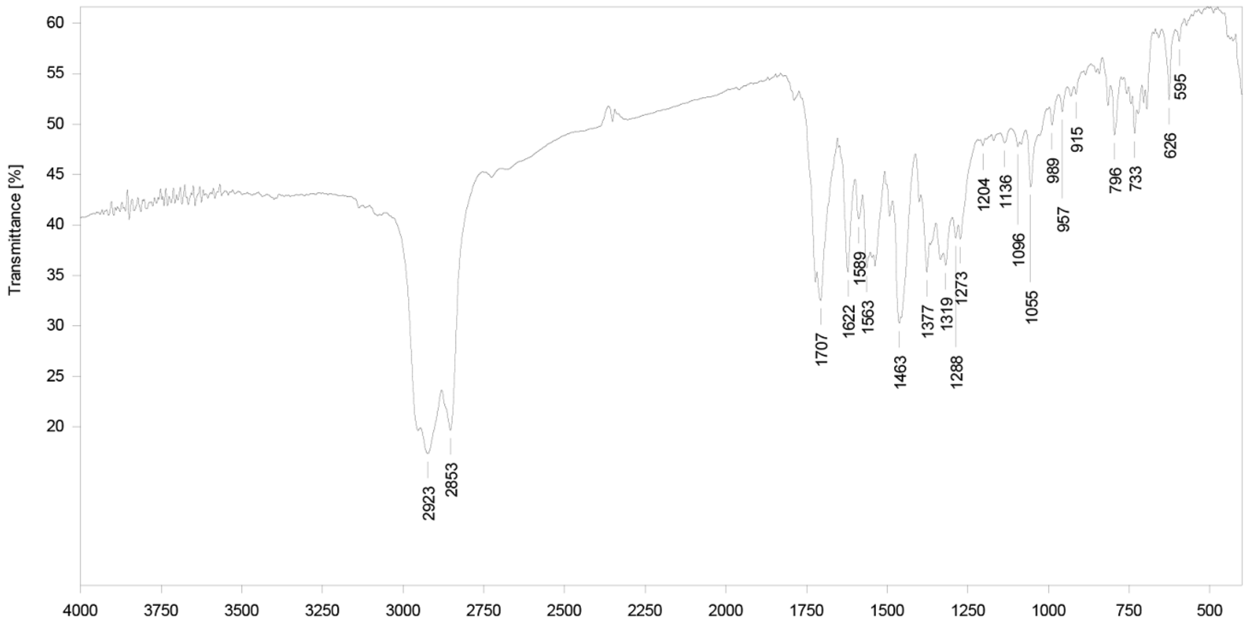


Figure S5. IR spectrum of compound **3b**

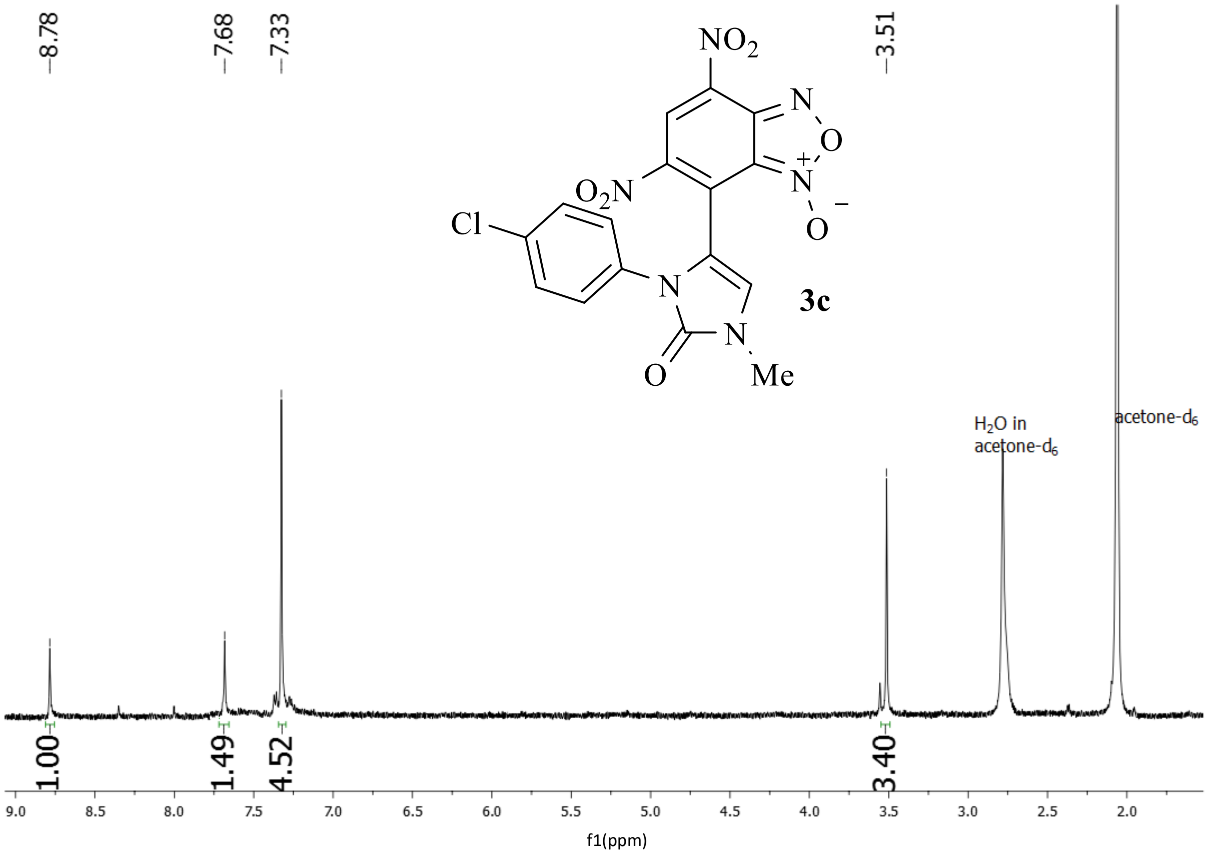


Figure S6. ^{1}H NMR (acetone-d$_6$, 600 MHz, 25 °C) of compound **3c**.

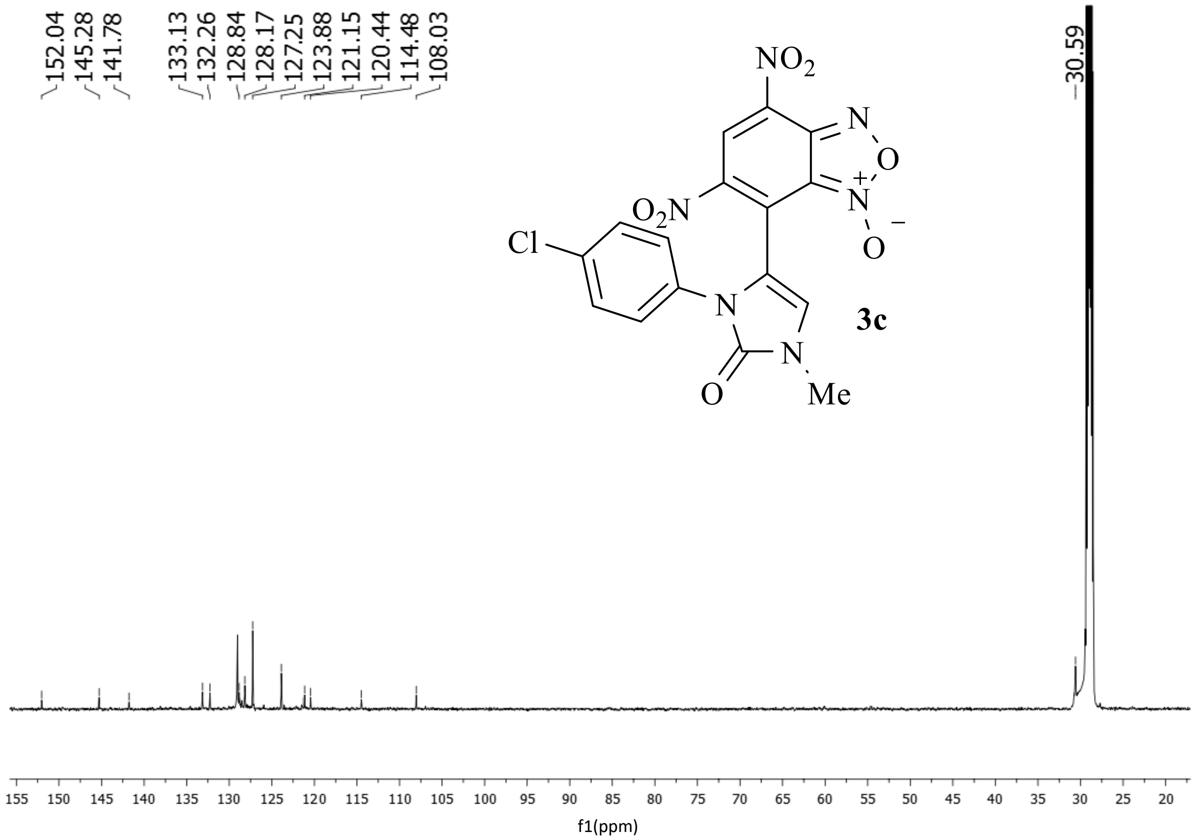


Figure S7. ^{13}C{1H} NMR (acetone-d$_6$, 151 MHz, 25 °C) of compound **3c**