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1-Morpholino-2-nitroethylene as a precursor of nitroacetaldehyde in the synthesis of azolo[5,1-*c*][1,2,4]triazines

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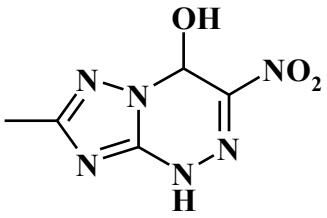
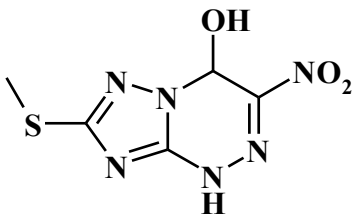
General. Unless otherwise indicated, all common reagents and solvents were used as purchased. Melting points were determined on a Staffordshire ST15 OSA apparatus. ^{1}H, ^{13}C, ^{19}F NMR spectra were recorded on a Bruker Avance-400 spectrometer, using DMSO-d_6 with TMS as internal reference. Elemental analysis was performed on a Perkin Elmer 2400 CHNS instrument. IR spectra were recorded on the IR spectrometer Bruker Alpha, ZnSe (FTIR). Monitoring of the reaction course was carried out by TLC on Silufol UV-254 plates using EtOAc as eluent. Silica gel is Merck Grade 9385.

7-Methyl-3-nitro-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4-ol 5b.



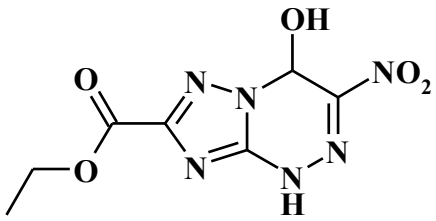
To a mixture of 5-amino-3-methyl-1,2,4-triazole (0.98 g, 0.01 mol), water (3 ml), acetonitrile (3 ml) and 12 *M* HCl (4.6 ml, 0.055 mol) a solution of KNO_2 (0.936 g, 0.011 mol) water (3 ml) is added portionwise at -7..-10 °C. The reaction mixture is kept at this temperature for 10 min, and then freshly prepared solution A (1.5 equiv.) is added thereto. The mixture is kept at room temperature for 1 h, the precipitate is filtered off, washed with cold *tert*-butyl methyl ether. In the case of observing a material on TLC with $R_f = 0$, the chromatography like for **5a** is performed. The product is recrystallized from water, filtered and dried. The yield is 0.81 g (41%), pale yellow powder, mp = 200-202 °C (decomp.). ^{1}H NMR, δ, ppm: 2.30 (s, 3H, CH_3), 6.87 (d, *J* = 7.5 Hz, 1H, CH), 7.93 (d, *J* = 7.5 Hz, 1H, OH), 13.14 (br.s., 1H, NH). ^{13}C NMR, δ, ppm: 13.91 (C7'), 72.03 (C4), 142.20 (C3), 146.14 (C8a), 160.11 (C7). Found (%): C 30.19; H 3.05; N 42.44. Calc. for $C_5H_6N_6O_3$ (%): C 30.31; H 3.05; N 42.41. IR, ν, cm^{-1}: 572, 706, 734, 836, 918, 1056, 1177, 1251, 1340, 1391, 1444, 1540, 1589, 1632, 2859, 3098, 3135.

7-Methylsulfanyl-3-nitro-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4-ol 5c.



To a mixture of 3-amino-5-methylsulfanyl-1,2,4-triazole (1.30 g, 0.01 mol), water (5 ml), acetonitrile (5 ml) and 12 *M* HCl (7.5 ml, 0.09 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10 °C. The mixture is kept at this temperature for 10 min and then freshly prepared solution A (3 equiv.) is added thereto. The mixture is kept at room temperature for 1 h, the precipitate is filtered off, washed with cold *tert*-butyl methyl ether. In the case of observing a material on TLC with R_f =0, the chromatography like for **5a** is performed. The product is recrystallized from 7:3 mixture water – acetonitrile, filtered and dried. The yield is 1.035 g (45%), dark orange powder, mp = 194-196 °C (decomp.). ^{1}H NMR, δ, ppm: 2.56 (s, 3H, SCH_3), 6.89 (d, *J* = 7.6 Hz, 1H, CH), 7.99 (d, *J* = 7.6 Hz, 1H, OH), 13.22 (s, 1H, NH). ^{13}C NMR, δ, ppm: 13.53 ($H_3\underline{C}$-S-), 72.29 (C4), 142.44 (C3), 146.71 (C8a), 161.31 (C7). Found (%): C 25.96; H 2.54; N 36.45. Calc. for $C_5H_6N_6O_3S$ (%): 26.09; H 2.63; N 36.51. IR, ν, cm^{-1}: 678, 700, 723, 753, 824, 904, 1066, 1113, 1181, 1240, 1276, 1328, 1389, 1536, 2804, 2862.

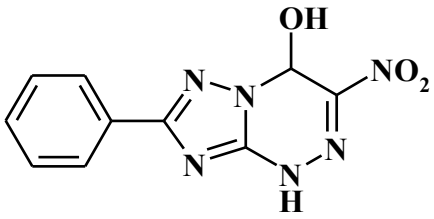
Ethyl 4-hydroxy-3-nitro-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-7-carboxylate 5d.



To a mixture of ethyl 5-amino-1,2,4-triazole-3-carboxylate (1.56 g, 0.01 mol), water (3 ml), acetonitrile (5 ml) and 12 *M* HCl (7.5 ml, 0.09 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10. The mixture is kept at this temperature for 10 min, and then freshly prepared solution A (3 equiv.) is added thereto. The mixture is kept at room temperature for 1 h, the precipitate is filtered off, washed with cold acetonitrile (10 ml) and water (5 ml) and dried. The product is purified by chromatography on silica gel (ethyl acetate as the eluent), the most mobile fraction is separated, the solvent is removed to dryness. The residue is recrystallized from water, filtered and dried. The yield is 0.282 g (11%), light orange powder, mp = 224-227 °C (decomp.). ^{1}H NMR, δ, ppm: 1.38 (t, *J* = 7.1 Hz, 3H, $COOCH_2C\underline{H_3}$), 4.36 (q, *J* = 7.1 Hz, 2H, $COOC\underline{H_2}CH_3$) 7.02 (d, *J* = 7.4 Hz, 1H, CH), 8.30 (d, *J* = 7.4 Hz, 1H, OH), 13.42 (s, 1H, NH). ^{13}C NMR, δ, ppm: 14.18 ($COOCH_2\underline{C}H_3$), 61.75 ($COO\underline{C}H_2CH_3$), 73.40 (C4), 142.60 (C3), 146.84 (C8a), 153.40 (C7), 159.24 (C7'). Found (%): C 32.97; H 3.19; N 32.72. Calc. for $C_7H_8N_6O_5$ (%): C 32.82; H 3.15;

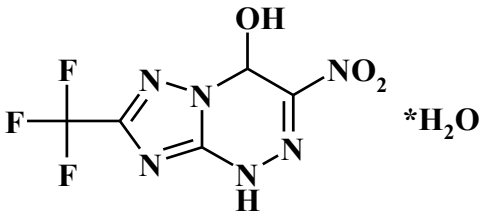
N 32.81. IR, ν, cm^{-1}: 667, 846, 911, 1026, 1074, 1197, 1337, 1788, 1541, 1576, 1733, 3211, 3222, 3231, 3243.

3-Nitro-7-phenyl-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4-ol 5e.



To a mixture of 3-phenyl-5-amino-1,2,4-triazole (1.60 g, 0.01 mol), water (5 ml), acetonitrile (8 ml) and 12 *M* HCl (7.5 ml, 0.09 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10 °C. The reaction mixture is kept at this temperature for 10 min, and then freshly prepared solution A (3 equiv.) is added thereto. The mixture is kept at room temperature for 1 h, the precipitate is filtered off, washed with cold 1:1 mixture acetonitrile – water. The wet cake is reprecipitated. For this, it is treated sequentially with 2 *M* solution of Na_2CO_3 until gas evolution ceased, and then with concentrated HCl to reach pH = 0-1. The precipitate is filtered off, washed with water and dried. The product is purified by chromatography on silica gel (ethyl acetate as the eluent), the most mobile fraction is separated, the solvent is removed to dryness. The yield is 0.468 g (18%), pale yellow powder, mp =214-216 °C (decomp.). ^{1}H NMR, δ, ppm: 7.01 (d, *J* = 7.8 Hz, 1H, CH), 7.39-7.49 (m, 3H, 3CH), 8.02 (d, *J* = 1.5 Hz, 1H, CH), 8.04 (d, *J* = 1.9 Hz, 1H, CH), 8.10 (d, *J* = 7.8 Hz, 1H, OH), 13.34 (s, 1H, NH). ^{13}C NMR, δ, ppm: 72.55 (C4), 125.86 (C2' and C6'), 128.72 (C3' and C5'), 129.76 (C4'), 130.06 (C1'), 142.35 (C3), 146.69 (C8a), 160.60 (C7). Found (%): C 46.27; H 3.05; N 32.46. Calc. for $C_{10}H_8N_6O_3$ (%): C 46.16; H 3.10; N 32.30. IR, ν, cm^{-1}: 694, 720, 910, 1070, 1196, 1247, 1332, 1357, 1435, 1479, 1532, 1556, 1590, 2849, 2871, 3138.

3-Nitro-7-trifluoromethyl-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4-ol 5f.



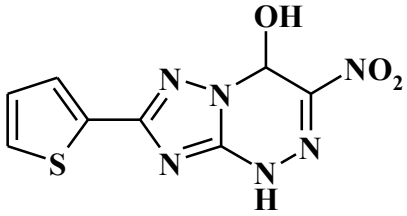
Method 1.

To a mixture of 3-trifluoromethyl-5-amino-1,2,4-triazole (1.52 g, 0.01 mol), water (10 ml) and 12 *M* HCl (12.5 ml, 0.15 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10 °C. The mixture is kept at this temperature for 10 min, and then freshly prepared solution A (5 equiv.) is

added thereto. The mixture is kept at room temperature until the diazonium salt is fully consumed (about 1 h).

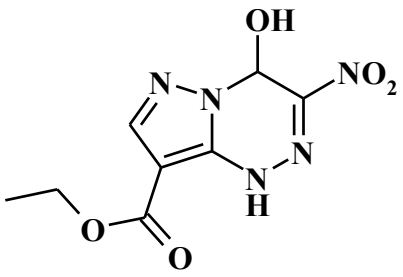
The product is extracted with diethyl ether (50 ml). The extract is dried over Na_2SO_4 and evaporated. The residue is purified by chromatography on silica gel (ethyl acetate as the eluent), the most mobile fraction is separated, the solvent is removed to dryness. The precipitate is recrystallized from water. The yield is 0.675 g (25%). Pale yellow powder, mp =185-187 °C (decomp.). ^{1}H NMR, δ, ppm: 7.06 (d, *J* = 7.2 Hz, 1H, CH), 8.50 (d, *J* = 7.2 Hz, 1H, OH), 13.75 (1H, c, NH). ^{13}C NMR, δ, ppm: 73.32 (C4), 118.84 (q, *J* = 270.1 Hz, $\underline{C}F_3$), 142.76 (C3), 147.22 (C8a), 151.72 (q, *J* = 39.2 Hz, C7). ^{19}F NMR, δ, ppm: 64.89 (CF_3). Found (%): C 22.30; H 1.74; N 30.99. Calc. for $C_5H_3F_3N_6O_3*H_2O$ (%): C 22.23; H 1.87; N 31.11. IR, ν, cm^{-1}: 704, 753, 909, 1007, 1080, 1156, 1206, 1224, 1340, 1531, 1557, 1582, 2815, 3246, 3610.

3-Nitro-7-(2-thienyl)-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazin-4-ol 5g.



To a mixture of 3-(2-thienyl)-5-amino-1,2,4-triazole (1.66 g, 0.01 mol), water (4 ml), acetonitrile (6 ml) and 12 *M* HCl (7.5 ml, 0.09 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10 °C. The reaction mixture is kept at this temperature for 10 minutes, and then freshly prepared solution A (2 equivalents) is added thereto. The mixture is kept at room temperature for 1 hour, the precipitate is filtered off, washed with cold acetonitrile (10 ml) and water (5 ml) and dried. The yield of crude product is 1.04 g (39%). In the case of observing a material on TLC with R_f = 0, the chromatography like for **5a** is performed. The precipitate is re-precipitated. For this, it is treated sequentially with 2 *M* solution of Na_2CO_3 until gas evolution ceased, and then with concentrated HCl to reach pH = 0-1. The precipitate is filtered off, washed with water and dried. The yield is 0.250 g (9%), light orange powder, mp =223-225 °C (decomp.). ^{1}H NMR, δ, ppm.: 7.00 (d, *J* = 3.9 Hz, 1H, CH), 7.18 (dd, *J* = 4.8, 3.8 Hz, 1H, CH), 7.67 (dd, *J* = 7.7, 4.3 Hz, 2H, 2CH), 8.24 (d, *J* = 5.7 Hz, 1H, OH), 13.48 (s, 1H, NH). ^{13}C NMR, δ, ppm.: 72.64 (C4), 126.93 (C5'), 128.13 (C3'), 128.16 (C4'), 132.77 (C2'), 142.48 (C3), 146.56 (C8a), 156.96 (C7). Found (%): C 35.94; H 2.33; N 31.67. Calc. for $C_8H_6N_6O_3S$ (%): C 36.09; H 2.27; N 31.57. IR, ν, cm^{-1}: 721, 744, 1073, 1251, 1344, 1376, 1543, 1569, 1590, 2844, 2956, 3128, 3148.

Ethyl 4-hydroxy-3-nitro-1,4-dihydropyrazolo[5,1-*c*][1,2,4]triazine-8-carboxylate 5h.



To a mixture of ethyl 3-aminopyrazole-4-carboxylate (1.53 g, 0.01 mol), water (3 ml) and 12 *M* HCl (2.5 ml, 0.03 mol) a solution of KNO_2 (0.936 g, 0.011 mol) in water (3 ml) is added portionwise at -7..-10 °C. The reaction mixture is kept at this temperature for 10 minutes, and then freshly prepared solution A (1 equivalent) is added thereto. The mixture is kept at room temperature for 1 hour, the precipitate is filtered off, washed with water and dried. The precipitate is recrystallized from acetonitrile, filtered and dried. The product is purified by chromatography on silica gel (ethyl acetate as the eluent), the most mobile fraction is separated, the solvent is removed to dryness. The residue is recrystallized from water, filtered and dried. The yield is 1.24 g (49%), pale yellow powder, mp = 199-201 °C (decomp.). ^{1}H NMR, δ, ppm.: 1.30 (t, *J* = 7.0 Hz, 3H, $COOCH_2C\underline{H}_3$), 4.29 (q, *J* = 7.0, 2H, $COOC\underline{H}_2CH_3$), 6.89 (d, *J* = 7.8 Hz, 1H, CH), 8.00 (s, 1H, CH), 8.11 (d, *J* = 7.8 Hz, 1H, OH), 12.73 (s, 1H, NH). ^{13}C NMR, δ, ppm.: 14.36 ($COOCH_2\underline{C}H_3$), 59.95 ($COO\underline{C}H_2CH_3$), 71.05 (C4), 96.47 (C8), 137.54 (C7), 141.60 (C3), 142.77 (C8a), 161.34 (C8'). Found (%): C 37.64; H 3.63; N 27.31. Calc. for $C_8H_9N_5O_5$ (%): C 37.65; H 3.55; N 27.44. IR, ν, cm^{-1}: 653, 673, 716, 776, 829, 905, 1032, 1086, 1169, 1204, 1294, 1327, 1416, 1446, 1479, 1535, 1587, 1626, 1677, 3228, 3267.

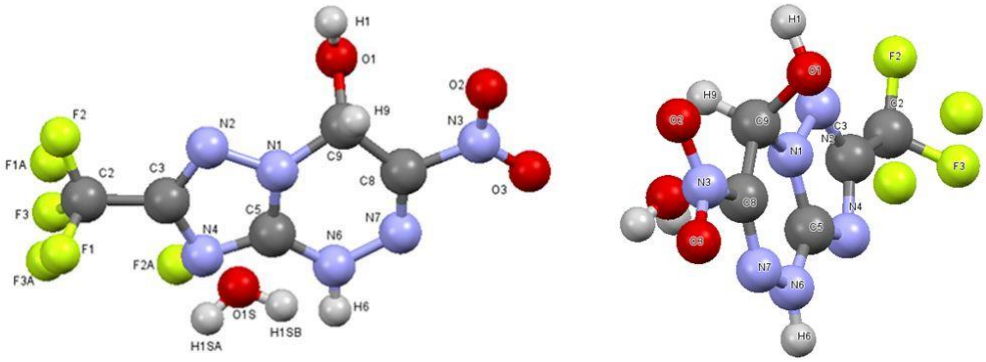


Figure S1 Molecular structure of 3-nitro-7-trifluoromethyl-1,4-dihydro-1,2,4-triazolo[5,1-*c*][1,2,4]triazine-4-ol **5f.**

Bond lengths, Å: F1-C2 1.327; F2-C2 1.297; F3-C2 1.315; C2-C3 1.499; C3-N2 1.318; C3-N4 1.350; N1-N2 1.365; N1-C5 1.341; N4-C5 1.325; C5-N6 1.351; N6-H6 0.901; N6-N7 1.341; N7-C8 1.274; C8-C9 1.508; N1-C9 1.466; C8-N3 1.470; N3-O2 1.223; N3-O3 1.211; C9-H9 0.998; C9-O1 1.391; O1-H1 0.941. Angles, °: F1-C2-F2 109.21; F2-C2-F3 109.19; F1-C2-F3 104.42; F1-C2-C3 111.33; F2-C2-

C3 111.80; F3-C2-C3 110.62; C2-C3-N2 120.88; C2-C3-N4 121.92; N2-C3-N4 117.20; C3-N2-N1 101.27; N2-N1-C5 109.08; N1-C5-N4 111.61; C5-N4-C3 100.84; C5-N1-C9 127.45; N1-C9-C8 102.59; C9-C8-N7 130.60; C8-N7-N6 119.02; N7-N6-C5 120.35; N6-C5-N1 119.81; N7-N6-H6 115.97; N7-C8-N3 113.92; C8-N3-O2 116.15; C8-N3-O3 119.78; O2-N3-O3 124.02; C9-C8-N3 115.48; C8-C9-O1 110.97; C8-C9-H9 109.35; C9-O1-H1 107.06.

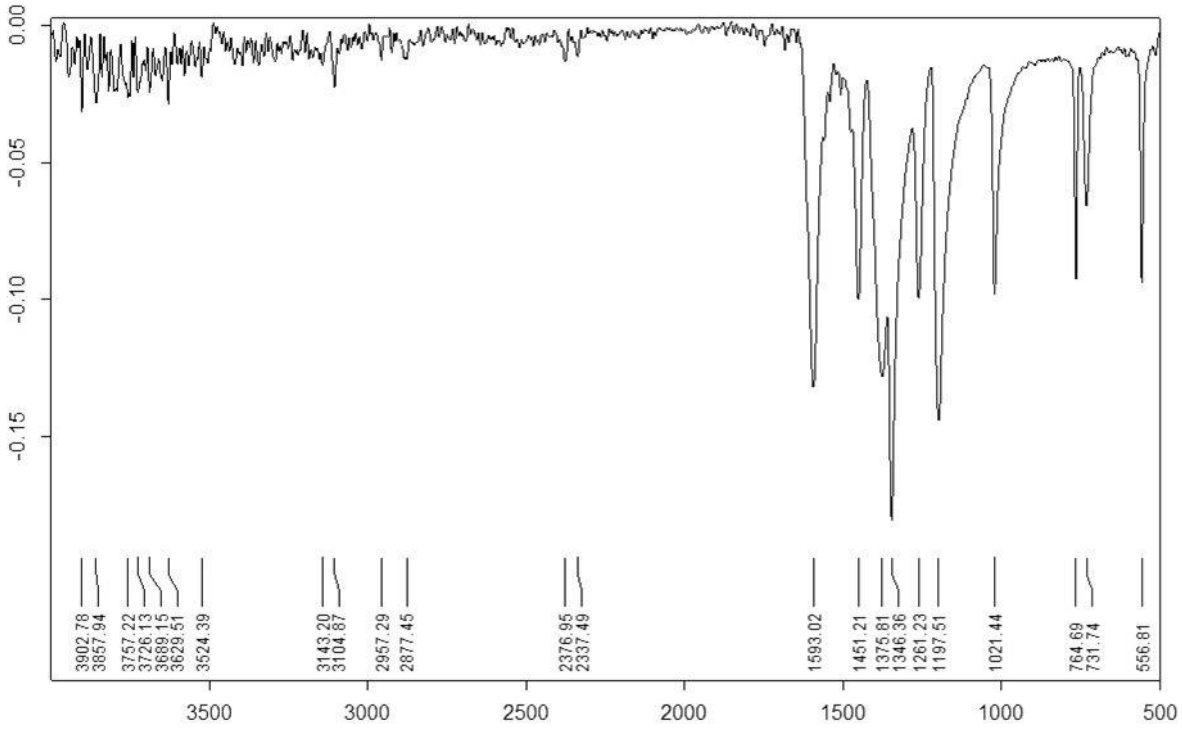


Figure S2 IR spectrum of nitroacetaldehyde potassium salt **2**.

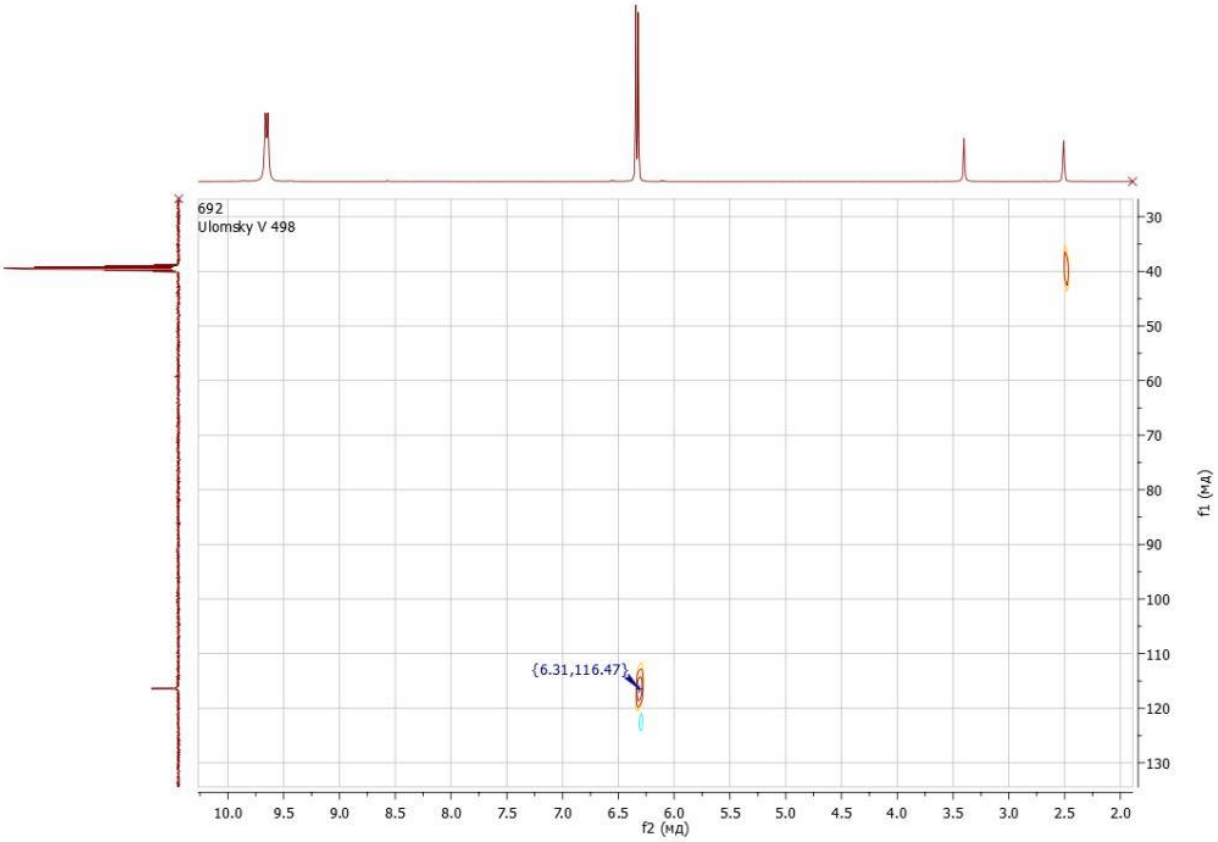


Figure S3 ^{1}H-^{13}C HMQC spectrum of nitroacetaldehyde potassium salt **2**.

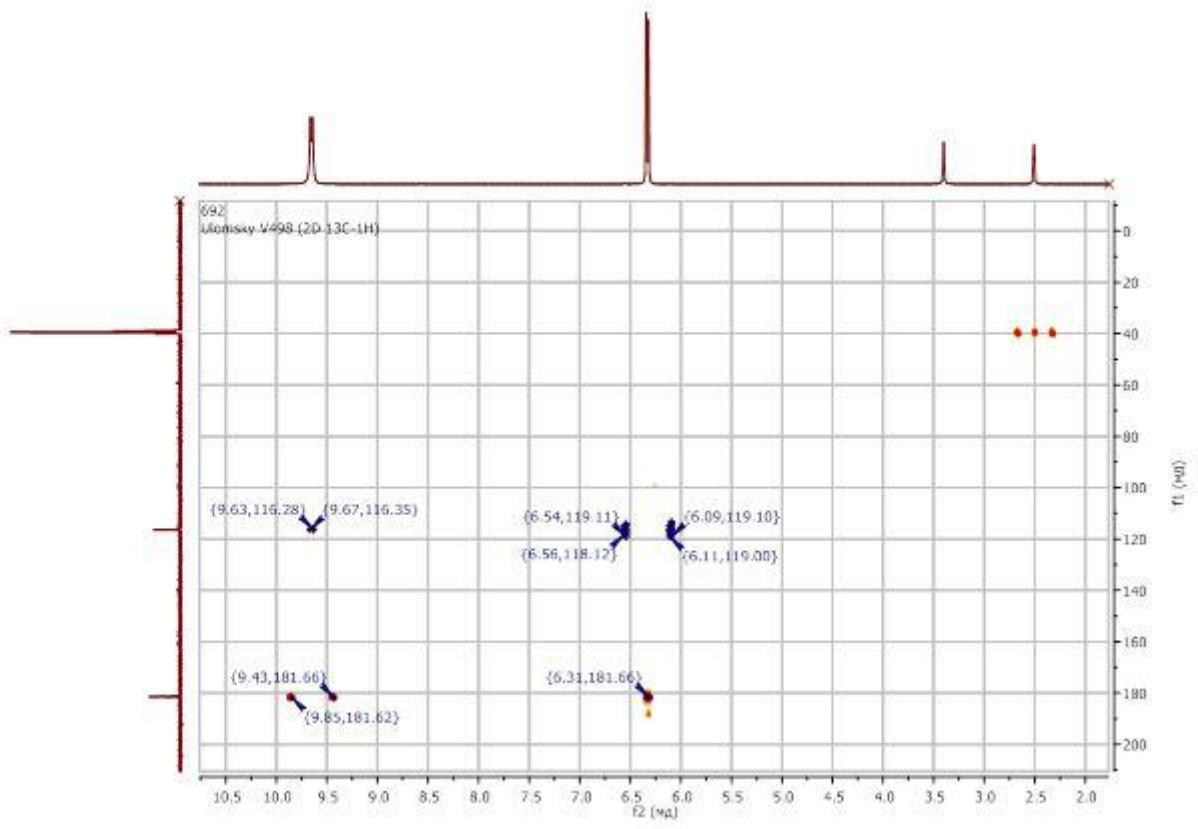


Figure S4 ^{1}H-^{13}C HMBC spectrum of nitroacetaldehyde potassium salt **2**.

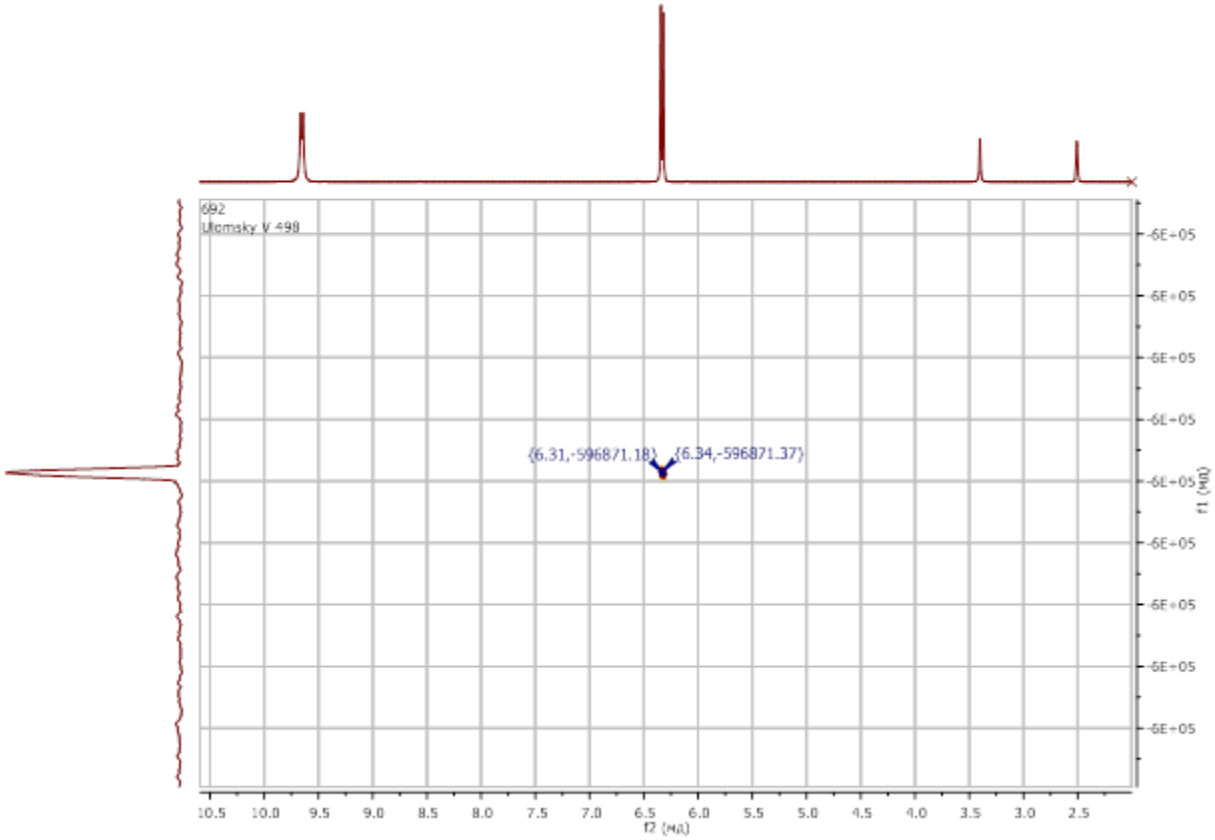


Figure S5 ^{1}H-^{15}N NMR spectrum of nitroacetaldehyde potassium salt **2**.