Synthesis of 1,2,4-triazolium 4*N*-nitroimides by the nitration of 1-substituted 4-amino-1,2,4-triazolium nitrates

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A general method for the synthesis of 1,2,4-triazolium 4*N*-nitroimides with functionalized substituents in position 1 of the heterocycle was developed. The method is based on the nitration of the corresponding 1-*R*-4-amino-1,2,4-triazolium nitrates.

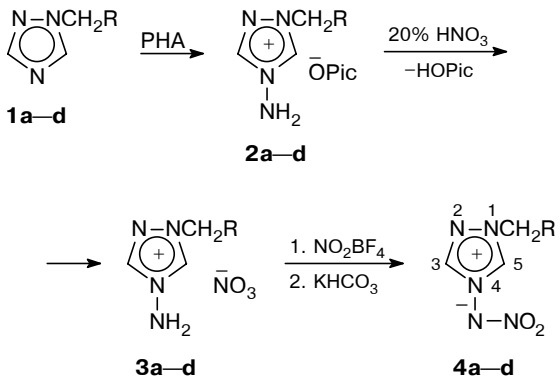
Key words: 1,2,4-triazolium 4*N*-nitroimides, 1-substituted 4-amino-1,2,4-triazolium salts, nitration, nitronium tetrafluoroborate.

The present work was done in continuation of systematic studies on the methods of preparing nitrogen—oxygen organic compounds containing rather long chains of heteroatoms directly bound to each other. Such structures can be most effectively created through involvement of nitroamino fragments in the reactions. However, schemes for the synthesis of new substances containing the nitroamino group mostly involve compounds in which the nitrogen atom of the nitroamino group is attached to carbon atoms. At the same time, it has been shown in some studies[1,2] that compounds with the nitroamino N atom bound to the tertiary nitrogen atom, namely, onium *N*-nitroimides, can also be synthesized.

One of the simplest methods for the synthesis of onium *N*-nitroimides and, in particular, 1,2,4-triazolium 4*N*-nitroimides, is to nitrate salts of the corresponding *N*-amino compounds.[3]

Up to the present study, 1,2,4-triazolium 4*N*-nitroimides with functionalized substituents bound to the N(1) atom of the heterocycle have not been synthesized in such a way.

Earlier,[3] we demonstrated that heterocyclic *N*-amino salts can easily be obtained by the reaction of the corresponding heterocycles with hydroxylamine derivatives. *O*-Picrylhydroxylamine (PHA) was chosen as an aminating agent since this compound is highly reactive with weakly basic amines, stable at room temperature, and convenient to handle. In the present work, the reactions with 1-nitromethyl-1,2,4-triazole **1a** and functionalized derivatives of (1,2,4-triazol-1-yl)acetic acid **1b—d** were studied as examples.



R = NO_2 (**a**); CN (**b**); COOMe (**c**); COOEt (**d**).
Pic — 2,4,6-trinitrophenyl.

Amination was carried out in CH_2Cl_2; the reagents were mixed at −10 to −15 °C and kept at room temperature. Picrates **2a—d** were obtained as nonhygroscopic yellow crystals poorly soluble in water and nonpolar organic solvents. However, 4-amino-1,2,4-triazolium nitrates **3a—d** are preferred to picrates for nitration because of the easier isolation of the final products. The picrates were converted to nitrates with an excess of 20% HNO_3 at −10 to 0 °C. Insoluble picric acid was filtered off, and compounds **3b—d** were isolated by concentrating aqueous mother liquors *in vacuo* at 40 °C. Compound **3a** was isolated by freezing it out of aqueous EtOH at −70 °C. The resulting nitrates **3b—d** are viscous liquids that cannot be

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distilled, while **3a** is a crystalline substance. Nitrates **3a—d** were converted into the corresponding *N*-nitroimides **4a—d** by treating them with NO_2BF_4 in anhydrous MeCN at −15 to −30 °C. The acids that formed (HNO_3 and HBF_4) were neutralized with $KHCO_3$. The resulting triazolium *N*-nitroimides **4a—d** are stable crystalline substances with limited solubility in water and alcohol, but they are insoluble in nonpolar organic solvents. The UV spectra of compounds **4a—d** show absorption bands at 247—251 nm; their IR spectra contain peaks at 1290—1300 cm^{-1} and 1385—1415 cm^{-1} characteristic of the *N*-nitroimido group.[1—4] In the ^1H NMR spectra of compounds **4a—d**, signals from the ring protons (δ 9.30—9.50 for HC(3) and 10.10—10.50 for HC(5)) are shifted downfield compared to the corresponding signals for compounds **1a—d** (δ 7.90—8.30 for HC(3) and 8.40—9.00 for HC(5)). In the ^{13}C NMR spectra of *N*-nitroimides **4a—d**, signals from the ring C(3) and C(5) atoms are shifted upfield by ~8.00 and ~2.60 ppm, respectively, compared to the starting triazoles **1a—d** (Table 1).

Table 1. ^{13}C NMR data for 1*R*-1,2,4-triazoles (**1a,b,d**), 1*R*-4-amino-1,2,4-triazolium picrates (**2a,b,d**), and 1*R*-1,2,4-triazolium 4*N*-nitroimides (**4a,b,d**) (CD_3SOCD_3, δ, *J*/Hz)

Compound	C(3)	C(5)	NCH_2	C≡N	C=O	OCH_2	Me	OPic
1a	153.0 (d, *J* = 209.4; d, *J* = 12.4)	147.6 (d, *J* = 216.3; d, *J* = 7.2; t, *J* = 3.1)	79.8 (t, *J* = 165.2)	—	—	—	—	—
1b	152.6 (d, *J* = 209.0; d, *J* = 12.0)	145.1 (d, *J* = 215.0; d, *J* = 7.0)	37.5 (t, *J* = 151.0)	115.0 (t, *J* = 9.0)	—	—	—	—
1d	151.5 (d, *J* = 206.2; d, *J* = 12.0)	145.4 (d, *J* = 212.7; d, *J* = 7.4; t, *J* = 2.8)	50.0 (t, *J* = 142.4)	—	167.4 m	61.4 (t, *J* = 148.9; q, *J* = 4.6)	13.8 (q, *J* = 127.6; t, *J* = 2.8)	—
2a	145.7 (d, *J* = 230.3±0.9; d, *J* = 3.7)	145.7 (d, *J* = 230.3±0.9; d, *J* = 3.7)	80.6 (t, *J* = 168.3)	—	—	—	—	124.1 (*p*-C) 124.8 (*m*-C) (d, *J* = 168.3; d, *J* = 5.5) 141.7 (*o*-C) 160.6 (C—O)
2b	145.4 (d, *J* = 229.3; d, *J* = 5.5±9)	143.7 (br.d, *J* = 230.3)	*	113.1 (t, *J* = 9.2)	—	—	—	124.1 (*p*-C) 124.9 (*m*-C) (d, *J* = 167.4; d, *J* = 5.5) 141.7 (*o*-C) 160.7 (C—O)
2d	145.1 (d, *J* = 227.5; d, *J* = 4.6)	144.0 (d, *J* = 232.1; d, *J* = 5.5)	52.6 (t, *J* = 146.1)	—	165.7 m	62.2 (t, *J* = 148.9; q, *J* = 4.6)	13.8 (q, *J* = 126.7)	124.2 (*p*-C) 125.1 (*m*-C) (d, *J* = 167.4; d, *J* = 4.6) 141.9 (*o*-C)
4a	145.0 (d, *J* = 230.3; d, *J* = 6.5)	145.0 (d, *J* = 230.3; d, *J* = 6.5)	80.8 (t, *J* = 168.3±0.9)	—	—	—	—	—
4b	144.4 (d, *J* = 229.3; d, *J* = 5.5±0.5)	142.5 (br.d, *J* = 232.1)	*	113.2 (t, *J* = 7.0)	—	—	—	—
4d	143.9 (d, *J* = 228,4; d, *J* = 6.5)	142.8 (d, *J* = 231.8; d, *J* = 2.8)	52.5 (t, *J* = 147.0)	—	165.7 m	62.1 (t, *J* = 148.9; q, *J* = 4.6)	13.8 (q, *J* = 127.6±0.9; t, *J* = 1.8)	—

* Overlap with a signal from the solvent.

The observed signal shifts, as well as a significant increase in $^1J_{H-C(3)}$ (by 20.0—22.0 Hz) and $^1J_{H-C(5)}$ (by 14.0—19.0 Hz) in onium imides **4a—d** compared to heterocycles **1a—d**, are probably due to the presence of a strong acceptor substituent in the heteroaromatic ring.

Experimental

Melting points were determined on a Boetius microscope stage. ^1H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument; ^1H and ^{13}C chemical shifts were referenced to DMSO-d_6 (δ 2.50 and 39.5, respectively). IR spectra were recorded on a UR-20 instrument (KBr), and UV spectra were taken on a Specord UV-VIS spectrometer with water as a solvent.

4-Amino-1-nitromethyl-1,2,4-triazolium picrate (2a). A solution of **1a** (1.24 g, 9.7 mmol) in 20 mL of CH_2Cl_2 was added dropwise to a stirred solution of *o*-picrylhydroxylamine (PHA) (2.36 g, 9.7 mmol) in 150 mL of CH_2Cl_2 at −20 °C. The reaction mixture was kept at 20 °C for 72 h, and the precipitate that formed was filtered off, washed with Et_2O, and dried to give compound **2a** (1.95 g, 54%), m.p. 151—153 °C (from EtOH). Found (%): C, 28.92; H, 2.24; N, 30.38. $C_9H_8N_8O_9$. Calculated (%): C, 29.03; H, 2.15; N, 30.11. IR, ν/cm^{-1}: 1320—1340 (s, NO_2); 1560—1570 (as, NO_2); 3380 (NH_2). ^1H NMR, δ: 7.10 (s, 2 H, CH_2); 8.57 (s, 2 H, Pic); 9.47 (s, 1 H, C(3)H); 10.37 (s, 1 H, C(5)H).

4-Amino-1-cyanomethyl-1,2,4-triazolium picrate (2b) was obtained analogously from PHA (4.52 g, 18.5 mmol) in 227 mL of CH_2Cl_2 and **1b** (2.00 g, 18.5 mmol) in 10 mL of CH_2Cl_2. The reaction mixture was kept for 24 h. The yield of compound **2b** was 3.05 g (47%), m.p. 164—165 °C (from EtOH). Found (%): C, 34.38; H, 2.03; N, 31.63. $C_{10}H_8N_8O_7$. Calculated (%): C, 34.10; H, 2.27; N, 31.82. IR, ν/cm^{-1}: 1340 (s, NO_2), 1575 (as, NO_2), 2280 (C≡N), 3360 (NH_2). ^1H NMR, δ: 5.77 (s, 2 H, CH_2); 7.05 (s, 2 H, NH_2); 8.60 (s, 2 H, Pic); 9.27 (s, 1 H, C(3)H); 10.15 (s, 1 H, C(5)H).

4-Amino-1-methoxycarbonylmethyl-1,2,4-triazolium picrate (2c) was obtained analogously from PHA (1.56 g, 6.4 mmol) in 117 mL of CH_2Cl_2 and **1c** (0.90 g, 6.4 mmol) in 5 mL of CH_2Cl_2. The yield of compound **2c** was 1.90 g (77%), m.p. 94—95.5 °C (from EtOH). Found (%): C, 34.85; H, 3.07; N, 25.03. $C_{11}H_{11}N_7O_9$. Calculated (%): C, 34.28; H, 2.85; N, 25.05. IR, ν/cm^{-1}: 1330 (s, NO_2), 1570 (as, NO_2), 1760 (C=O), 3310 (NH_2). ^1H NMR, δ: 3.70 (s, 3 H, Me); 5.40 (s, 2 H, CH_2); 7.00 (s, 2 H, NH_2); 8.55 (s, 2 H, Pic); 9.20 (s, 1 H, C(3)H), 10.10 (s, 1 H, C(5)H).

4-Amino-1-ethoxycarbonylmethyl-1,2,4-triazolium picrate (2d) was obtained analogously from PHA (2.00 g, 8.4 mmol) in 100 mL of CH_2Cl_2 and **1d** (1.27 g, 8.4 mmol). The yield of compound **2d** was 2.50 g (76%), m.p. 118—119 °C (from EtOH). Found (%): C, 35.96; H, 3.23; N, 24.98. $C_{12}H_{13}N_7O_9$. Calculated (%): C, 36.09; H, 3.26; N, 24.56. IR, ν/cm^{-1}: 1340 (s, NO_2), 1570 (as, NO_2), 1760 (C=O), 3320 (NH_2). ^1H NMR, δ: 1.20 (t, 3 H, Me); 4.20 (q, 2 H, CH_2); 5.46 (s, 2 H, CH_2); 7.04 (s, 2 H, NH_2); 8.58 (s, 2 H, Pic); 9.10 (s, 1 H, C(3)H); 10.30 (s, 1 H, C(5)H).

4-Amino-1-nitromethyl-1,2,4-triazolium nitrate (3a). Picrate **2a** (2.30 g, 6.2 mmol) was added to stirred 20% HNO_3 (8.1 mL) at −10 °C. Stirring was continued at 0 °C for 1 h and at 20 °C for 2 h. The precipitate of PicOH that formed was filtered off, and the rest of the picric acid was extracted from the mother liquor with benzene (3×20 mL). The aqueous layer was separated, diluted with one and half volumes of EtOH, and kept at −70 °C for 10 h. The precipitate that formed was filtered off. The yield of compound **3a** was 0.98 g (66%), m.p. 91 °C (from EtOH). Found (%): C, 17.39; H, 2.90; N 40.70. $C_3H_6N_6O_5$. Calculated (%): C, 17.48; H, 2.91; N, 40.78. IR, ν/cm^{-1}: 1390 (NO_3^-), 1590 (NO_2), 3360 (NH_2). ^1H NMR, δ: 7.08 (s, 2 H, CH_2); 9.42 (s, 1 H, C(3)H); 10.35 (s, 1 H, C(5)H).

4-Amino-1-cyanomethyl-1,2,4-triazolium nitrate (3b). Picrate **2b** (2.50 g, 7.1 mmol) was added to stirred 20% HNO_3 (8.5 mL) at −10 °C. Stirring was continued at 0 °C for 1 h. The precipitate of PicOH that formed was filtered off, and the rest of the picric acid was extracted from the mother liquor with benzene (3×20 mL). The aqueous layer was separated and concentrated *in vacuo* at a bath temperature no higher than 40—50 °C to a volume of 2 mL. Ethanol (5 mL) was added, the solvent was removed *in vacuo*, and the residue was evacuated at a pressure of 1 Torr to give compound **3b** (0.92 g, 55%) as an oil. IR, ν/cm^{-1}: 1390 (NO_3^-); 2280 (C≡N); 3360 (NH_2). ^1H NMR, δ: 5.90 (s, 2 H, CH_2); 7.05 (s, 2 H, NH_2); 9.20 (s, 1 H, C(3)H); 10.20 (s, 1 H, C(5)H).

4-Amino-1-methoxycarbonylmethyl-1,2,4-triazolium nitrate (3c) was obtained analogously from picrate **2c** (1.58 g, 3.9 mmol) and 20% HNO_3 (9.5 mL). The yield of compound **3c** (oil) was 0.65 g (76%). IR, ν/cm^{-1}: 1385 (NO_3^-); 1760 (C=O); 3160, 3350 (NH_2).

4-Amino-1-ethoxycarbonylmethyl-1,2,4-triazolium nitrate (3d) was obtained analogously from picrate **2d** (1.48 g, 3.7 mmol) and 20% HNO_3 (8 mL). The yield of compound **3d** (oil) was 0.80 g (93%). IR, ν/cm^{-1}: 1370 (NO_3^-); 1760 (C=O); 3160, 3350 (NH_2).

1-Nitromethyl-1,2,4-triazolium 4*N*-nitroimide (4a). Nitronium tetrafluoroborate NO_2BF_4 (0.39 g, 2.9 mmol) was added with stirring at −30 °C to nitrate **3a** (0.50 g, 2.4 mmol) in 10 mL of MeCN. The temperature was gradually elevated (no higher than −5 °C) until NO_2BF_4 was completely dissolved, and stirring was continued for 15 min. The temperature was decreased to −30 °C, and finely divided K_2CO_3 (0.59 g, 5.9 mmol) was added. The reaction mixture was stirred at 20 °C for 30 min. The precipitate that formed was filtered off, and the mother liquor was concentrated *in vacuo*. The resulting oil was dissolved in 5 mL of EtOH and cooled to −70 °C, and the precipitate that formed was filtered off to give compound **4a** (0.45 g, 98%), m.p. 154—155 °C (from EtOH). Found (%): C, 19.28; H, 2.18; N, 44.80. $C_3H_4N_6O_4$. Calculated (%): C, 19.15; H, 2.13; N, 44.68. IR, ν/cm^{-1}: 1300, 1405 (NO_2, imide); 1380 (s, NO_2), 1600 (as, NO_2). UV (EtOH), λ_{max}/nm (ε): 247 (8230). ^1H NMR, δ: 7.06 (s, 2 H, CH_2); 9.53 (s, 1 H, C(3)H); 10.50 (s, 1 H, C(5)H).

1-Cyanomethyl-1,2,4-triazolium 4*N*-nitroimide (4b) was obtained analogously from nitrate **3b** (0.50 g, 2.7 mmol) and NO_2BF_4 (0.39 g, 2.9 mmol). The yield of compound **4b** was 0.30 g (67%), m.p. 173—175 °C (EtOH—water, 2 : 1). Found (%): C, 28.55; H, 2.35; N, 50.44. $C_4H_4N_6O_2$. Calculated (%): C, 28.57; H, 2.38; N, 50.00. IR, ν/cm^{-1}: 1300, 1415 (NO_2, imide); 2270 (C≡N). UV (EtOH), λ_{max}/nm (ε): 251 (7500). ^1H NMR, δ: 5.83 (s, 2 H, CH_2); 9.38 (s, 1 H, C(3)H); 10.30 (s, 1 H, C(5)H).

1-Methoxycarbonylmethyl-1,2,4-triazolium 4*N*-nitroimide (4c) was obtained analogously from nitrate **3c** (0.58 g, 2.6 mmol) and NO_2BF_4 (0.39 g, 2.9 mmol). The yield of compound **4c** was 0.30 g (57%), m.p. 148—150 °C (from EtOH). Found (%): C, 30.28; H, 3.41; N, 34.77. $C_5H_7N_5O_4$. Calculated (%): C, 29.85; H, 3.68; N, 34.83. IR, ν/cm^{-1}: 1295, 1390 (NO_2, imide); 1755 (C=O). ^{1}H NMR, δ: 3.73 (s, 3 H, Me); 5.46 (s, 2 H, CH_2); 9.30 (s, 1 H, C(3)H); 10.25 (s, 1 H, C(5)H).

1-Ethoxycarbonylmethyl-1,2,4-triazolium 4*N*-nitroimide (4d) was obtained analogously from nitrate **3d** (0.94 g, 4.0 mmol) and NO_2BF_4 (0.59 g, 4.4 mmol). The yield of compound **4d** was 0.25 g (29%), m.p. 156—157 °C (from EtOH). Found (%): C, 33.01; H, 4.09; N, 32.41. $C_6H_9N_5O_4$. Calculated (%): C, 33.48; H, 4.19; N, 32.56. IR, ν/cm^{-1}: 1290, 1385 (NO_2, imide); 1750 (C=O). UV (EtOH) λ_{max}/nm (ε): 249 (7460). ^{1}H NMR, δ: 1.22 (t, 3 H, Me); 4.20 (q, 2 H, CH_2); 5.45 (s, 2 H, CH_2); 9.31 (s, 1 H, C(3)H); 10.23 (s, 1 H, C(5)H).

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