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Synthesis of 2-substituted 6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridines and the formation of the related zwitterionic σ-adducts

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A method for the synthesis of 2-substituted 6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridines is proposed. The method includes the reaction of 2-chloro-3,5-dinitropyridine with the corresponding 5-substituted tetrazoles. The resulting compounds react with anhydro bases of α- and γ-methylazinium salts to give zwitterionic σ-adducts.

Key words: 2-substituted 6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridines, 2-chloro-3,5-dinitropyridine, 5-substituted tetrazoles, anhydro bases, zwitterionic σ-adducts.

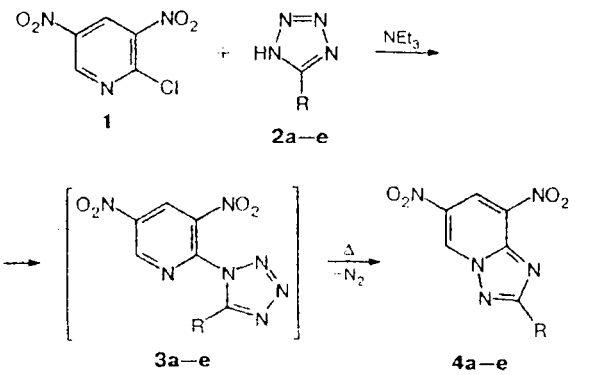
The addition products of nucleophilic agents to activated arenes (or hetarenes) (σ-adducts) are used as the starting compounds in some syntheses. However, they are mostly insufficiently stable, which precludes studies of these compounds. Earlier,[1] it was shown that introduction of nitro groups into the pyridine ring increases the rate of formation and stability of anionic σ-adducts. Stable zwitterionic σ-adducts were obtained by reaction of alkoxide-anionic σ-adducts of dinitrotetrazolo[1,5-*a*]pyridine with *N*-methylazinium salts as nucleophilic agents.[2] However, zwitterionic σ-adducts of azines are studied inadequately, and the influence of azoloannelation on their stability is still unclear.

The goal of this work is to synthesize the previously unknown 2-substituted 6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridines and their zwitterionic σ-adducts.

We could not obtain 2-hydrazino-3,5-dinitropyridine, a possible precursor of dinitrotriazolopyridine, because 2-chloro-3,5-dinitropyridine reacted with hydrazine vigorously to give a mixture of unidentified products.

For this reason, we developed a method for the synthesis of 2-substituted 6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridines (**4a—e**) that consists in the reaction of 2-chloro-3,5-dinitropyridine (**1**) with the corresponding 5-substituted tetrazoles **2a—e** in boiling acetonitrile in the presence of triethylamine (Scheme 1). Apparently, the formation of compounds **4a—e** proceeds *via* inter-

Scheme 1



R = phenyl (**a**), 4-chlorophenyl (**b**), 4-bromophenyl (**c**), 4-methoxyphenyl (**d**), 3,4-dimethoxyphenyl (**e**)

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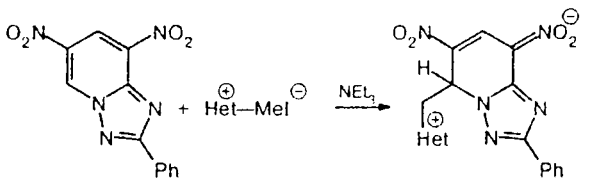
Scheme 2



4a **5—7**

Het = 1-methylquinolinio-4-yl (**5**), 1-methylquinolinio-2-yl (**6**), 1-methylpyridinio-2-yl (**7**)

mediates **3a—e**. The mechanism of this reaction was discussed in detail in connection with the synthesis of other triazoloannelated heterocycles.[3,4]

Triazolopyridines **4a—e** were introduced into reactions with anhydro bases of 1-methyllepidinium, 1-methylquinaldinium, and 1-methyl-α-picolinium salts, respectively. As with 6,8-dinitrotetrazolo[1,5-*a*]pyridine,[1] we observed the formation of stable zwitterionic σ-adducts **5**, **6**, and **7** (Scheme 2).

Zwitterions **5—7** are bright colored, poorly soluble in the majority of solvents, and acid- and heat-resistant. Their structures were proved by ^{1}H NMR spectroscopy, in particular, by the characteristic positions of signals for the Me—N$^+$ groups (δ 4.54, 4.61, and 4.28, respectively) and upfield shifts of signals for the H(5) atoms (δ 6.23—6.35, 6.35—6.50, and 6.25—6.40, respectively). The chemical shifts for these protons are virtually the same as those for the protons in zwitterionic C—σ-adducts based on dinitrotetrazolo[1,5-*a*]pyridine[2] (whose structures were confirmed by X-ray diffraction analysis).[2,5]

The formation of only σ-C(5)-adducts was also supported by the corresponding *ab initio* STO-3G calculations of 6,8-dinitrotetrazolo[1,5-*a*]pyridine (the charges on C(5) and C(7) are +0.114 and −0.010, respectively). Calculations of 6,8-dinitro-2-phenyl[1,2,4]triazolo-[1,5-*a*]pyridine (**4a**) also showed that the charge on the C(7) atom is negative (−0.017), which does not correlate with the common occurrence of reaction with C-nucleophiles (the charge on C(5) is +0.111).

The ^{1}H NMR spectra of compounds **5**, **6**, and **7** show the methylene protons of the CH$_2$—Het$^+$ group attached to the asymmetrical C(5) atom to be nonequivalent, which confirms the structures of these zwitterions. Otherwise, if the addition occurred at the C(7) atom, the methylene protons would be equivalent because the nearest environment of the C(7) atom is virtually alike.

Experimental

^{1}H NMR spectra were recorded on a Tesla BS-567A instrument (80 MHz). The chemical shifts are given with respect to Me$_4$Si as the internal standard in DMSO-d$_6$. The course of the reactions was monitored by TLC using Silufol UV-254 plates in a chloroform—methanol (9 : 1) system.

Synthesis of 2-substituted 6,8-dinitro[1,2,4]triazolo-[1,5-*a*]pyridines (4a—e) (general procedure). Equimolar amounts of 2-chloro-3,5-dinitropyridine, 5-substituted tetrazole, and Et$_3$N were refluxed in acetonitrile (2.5 mL per 1 mmol) for 25 min. The reaction mixture was cooled, and the precipitate that formed was filtered off and recrystallized from acetonitrile.

6,8-Dinitro-2-phenyl[1,2,4]triazolo[1,5-*a*]pyridine (4a). Colorless crystals, yield 65.9%, m.p. 271—272 °C. Found (%): C, 50.51; H, 2.49; N, 24.44. $C_{12}H_7N_5O_4$. Calculated (%): C, 50.53; H, 2.47; N, 24.55. ^{1}H NMR, δ: 7.60—7.67 (m, 3 H, Ph); 8.24—8.34 (m, 2 H, Ph); 9.18 (d, 1 H, H(7), J = 2.0 Hz); 10.65 (d, 1 H, H(5), J = 2.0 Hz).

2-(4-Chlorophenyl)-6,8-dinitro[1,2,4]triazolo[1,5-*a*]-pyridine (4b). Colorless crystals, yield 57.3%, m.p. 244—245 °C. Found (%): C, 45.05; H, 1.71; N, 21.88. $C_{12}H_6N_5O_4Cl$. Calculated (%): C, 45.09; H, 1.89; N, 21.91. ^{1}H NMR, δ: 7.63 (d, 2 H, *o*-C$_6$H$_4$, J = 8.41 Hz); 8.24 (d, 2 H, *m*-C$_6$H$_4$, J = 8.27 Hz); 9.15 (d, 1 H, H(7), J = 2.0 Hz); 10.55 (d, 1 H, H(5), J = 2.0 Hz).

2-(4-Bromophenyl)-6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridine (4c). Colorless crystals, yield 51.8%, m.p. 264—265 °C. Found (%): C, 39.63; H, 1.66; N, 19.31. $C_{12}H_6N_5O_4Br$. Calculated (%): C, 39.58; H, 1.66; N, 19.23. ^{1}H NMR, δ: 7.80 (d, 2 H, *o*-C$_6$H$_4$, J = 8.7 Hz); 8.19 (d, 2 H, *m*-C$_6$H$_4$, J = 8.5 Hz); 9.17 (d, 1 H, H(7), J = 2.0 Hz); 10.60 (d, 1 H, H(5), J = 2.0 Hz).

2-(4-Methoxyphenyl)-6,8-dinitro[1,2,4]triazolo[1,5-*a*]-pyridine (4d). Yellow crystals, yield 47.2%, m.p. 218—219 °C. Found (%): C, 48.46; H, 2.72; N, 22.22. $C_{13}H_9N_5O_5$. Calculated (%): C, 48.16; H, 2.80; N, 22.60. ^{1}H NMR, δ: 3.86 (s, 3 H, OMe); 7.14 (d, 2 H, C$_6$H$_4$, J = 8.9 Hz); 8.19 (d, 2 H, C$_6$H$_4$, J = 8.9 Hz); 9.12 (d, 1 H, H(7), J = 2.0 Hz); 10.53 (d, 1 H, H(5), J = 2.0 Hz).

2-(3,4-Dimethoxyphenyl)-6,8-dinitro[1,2,4]triazolo[1,5-*a*]pyridine (4e). Yellow crystals, yield 45.9%, m.p. 228—229 °C. Found (%): C, 48.74; H, 3.03; N, 20.21. $C_{14}H_{11}N_5O_6$. Calculated (%): C, 48.70; H, 3.21; N, 20.28. ^{1}H NMR, δ: 3.87 (s, 3 H, 4′-OMe); 3.89 (s, 3 H, 3′-OMe); 7.19 (d, 1 H, H(5′), C$_6$H$_3$, J = 8.3 Hz); 7.75 (d, 1 H, H(2′), C$_6$H$_3$, J = 2.0 Hz); 7.91 (dd, 1 H, H(6′), C$_6$H$_3$, J = 2.0 and 8.3 Hz); 9.13 (d, 1 H, H(7), J = 2.0 Hz); 10.54 (d, 1 H, H(5), J = 2.0 Hz).

Syntesis of zwitterionic adducts 5—7 (general procedure). Equimolar amounts of **4a**, the corresponding *N*-methylazinium salt, and Et$_3$N were stirred in acetonitrile (5 mL per 0.35 mmol) for 4 h and left overnight. The precipitate that formed was filtered off and washed with acetonitrile.

5*H*-5-(1-Methylquinolinio-4-ylmethyl)-6,8-dinitro-2-phenyl[1,2,4]triazolo[1,5-*a*]pyridinide (5). Yield 96.7%. Found (%): C, 62.09; H, 4.09; N, 18.60. $C_{23}H_{18}N_6O_4$. Calculated (%): C, 62.44; H, 4.10; N, 18.99. Decomp. temp. 200 °C. ^{1}H NMR, δ: 3.98—4.09 (m, 2 H, CH$_2$); 4.54 (s, 3 H, N$^+$—Me); 6.23—6.35 (m, 1 H, H(5)); 7.33—7.41 (m, 3 H, H(3′)—H(5′), Ph); 7.50—8.34 (m, 7 H, H(2′), H(6′), Ph, H(3′), H(5′)—H(8′), quinoline); 8.44 (s, 1 H, H(7)); 9.23 (d, 1 H, H(2′), quinoline, J = 5.7 Hz).

5*H*-5-(1-Methylquinolinio-2-ylmethyl)-6,8-dinitro-2-phenyl[1,2,4]triazolo[1,5-*a*]pyridinide (6). Yield 93.7%. Found (%): C, 62.49; H, 4.11; N, 18.88. $C_{23}H_{18}N_6O_4$. Calculated (%): C, 62.42; H, 4.10; N, 18.99. Decomp. temp. 180 °C. ^{1}H NMR, δ: 3.46—4.21 (m, 2 H, CH$_2$); 4.61 (s, 3 H, N$^+$—Me); 6.35—6.50 (m, 1 H, H(5)); 7.28—7.46 (m, 3 H, H(3′)—H(5′), Ph); 7.81—7.92 (d, 1 H, H(3′), quinoline, J = 8.5 Hz); 8.03—8.56 (m, 6 H, H(2′), H(6′), Ph and 4 H, quinoline); 8.69 (s, 1 H, H(7)); 8.93–9.04 (d, 1 H, H(4′), quinoline, J = 8.5 Hz).

5*H*-5-(1-Methylpyridinio-2-ylmethyl)-6,8-dinitro-2-phenyl-[1,2,4]triazolo[1,5-*a*]pyridinide (7). Yield 87.5%. Found (%): C, 58.12; H, 4.08; N, 21.51. $C_{19}H_{16}N_6O_4$. Calculated (%): C, 58.16; H, 4.11; N, 21.42. Decomp. temp. 250 °C. ^{1}H NMR, δ: 3.69—3.82 (m, 2 H, CH_2); 4.28 (s, 3 H, N^+—Me); 6.25—6.40 (m, 1 H, H(5)); 7.32—7.44 (m, 3 H, H(3′)—H(5′), Ph); 7.68—8.48 (m, 5 H, H(2′), H(6′), Ph, H(3′)—H(5′), pyridine); 8.65 (s, 1 H, H(7)); 8.91—8.99 (d, 2 H, H(6′), pyridine, J = 5.7 Hz).

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