

Cyclization of 2-Azido-3-(alkyl-*N*-nitrosoamino)-1,4-naphthoquinones to 1-Alkyl-1*H*-naphtho[2,3-*d*][1,2,3]triazole-4,9-dione 2-Oxides

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Abstract—Thermolysis of 2-azido-3-(alkyl-*N*-nitrosoamino)-1,4-naphthoquinones gives rise to compounds belonging to a new quinoid fused heterocyclic system, 1-alkyl-1*H*-naphtho[2,3-*d*][1,2,3]triazole-4,9-dione 2-oxides.

It is known that aromatic azides containing a carbonyl, azo, or nitroso group in the *ortho* position with respect to the azido group undergo intramolecular ring closure with elimination of nitrogen and formation of the corresponding nitrogenous heterocycles on heating or irradiation [1]. Heterocyclization of compounds possessing an azido group in the *ortho* position with respect to an *N*-nitrosoamino group was not reported previously.

By reaction of 2-(alkyl-*N*-nitrosoamino)-3-chloro-1,4-naphthoquinones **Ia–Id** with sodium azide in ethanol we obtained the corresponding 2-azido-3-(alkyl-*N*-nitrosoamino)-1,4-naphthoquinones **IIa–IIId** and examined their thermal transformations. By heating in boiling benzene for a short time, azides **IIa–IIId** were converted into 1-alkyl-1*H*-naphtho[2,3-*d*][1,2,3]-

triazole-4,9-dione 2-oxides **IIIa–IIIId** via elimination of nitrogen (Scheme 1).

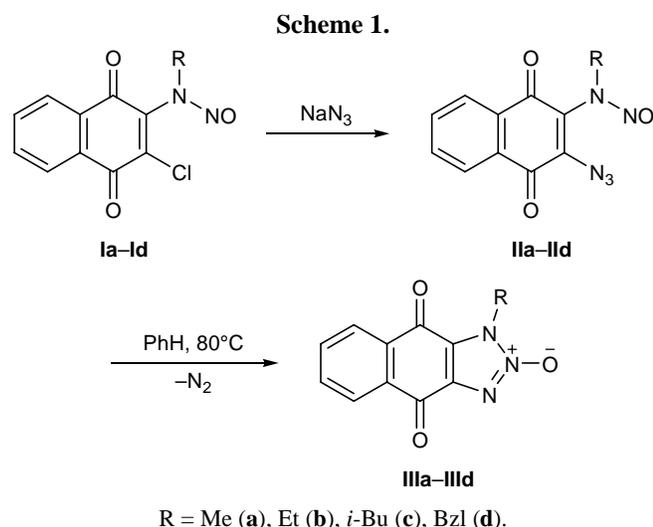
Transformations of azides possessing a double bond in the *ortho* position may occur according to several paths either involving or not involving formation of nitrenes [2] (Scheme 2). In particular, nitrene (*a*) and concerted (*b*) heterocyclization mechanisms were proposed, as well as preliminary intramolecular 1,3-dipolar cycloaddition with subsequent elimination of nitrogen molecule (*c*).

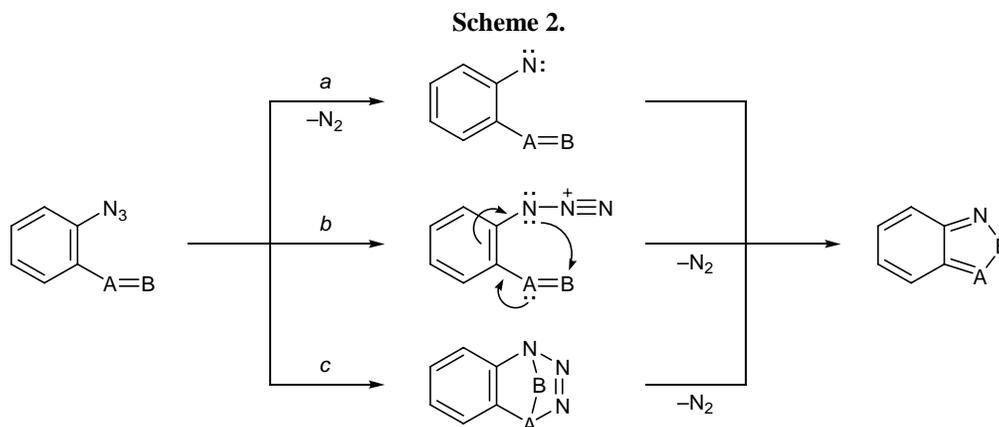
We believe that the high yield of oxides **III** and the absence of by-products indicate that the cyclization **II** → **III** follows either path *b* or path *c*. Comparison of the ¹H NMR spectra of products **III** with those of azides **II** shows that the latter exist as mixtures of *Z* and *E* isomers. This is typical of many *N*-nitroso compounds [2], including quinones **I** [3]. Naturally, *Z,E* isomerism is not inherent to products **III**; therefore, signals from protons in the R radical are not split and are displaced downfield due to the presence of positive charge in the triazole fragment.

Some polycyclic aza quinones are known to exhibit antitumor activity [4]. Taking this into account, we believe it promising to extend the scope of the above described heterocyclization via involvement of other quinoid *N*-nitroso compounds and functionalization of the R substituent in *N*-oxides **III**.

EXPERIMENTAL

The ¹H NMR spectra were recorded on Bruker DRX-500 (500 MHz; compounds **IIa**, **IIb**, and **IIIa–IIIId**) and Bruker WP-200 spectrometers (200 MHz;





IIc) from solutions in DMSO- d_6 and $CDCl_3$ using TMS as internal reference. The melting points were determined on a Boetius melting point apparatus. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates using toluene–acetone (10:1) as eluent. The mass spectrum was obtained on a Finnigan MAT-8200 instrument.

2-Azido-3-(alkyl-N-nitrosoamino)-1,4-naphthoquinones IIa–IIId (general procedure). 2-(Alkyl-N-nitrosoamino)-3-chloro-1,4-naphthoquinone **Ia–Id**, 0.004 mol, was dissolved in a mixture of 8 ml of ethanol and 2 ml of water. A solution of 0.01 mol of sodium azide in 3 ml of water was added, and the mixture was stirred for 30–40 min. The yellow precipitate was filtered off, washed with water, and dried.

2-Azido-3-(methyl-N-nitrosoamino)-1,4-naphthoquinone (IIa). Yield 90%, mp 131–133°C. 1H NMR spectrum ($CDCl_3$), δ , ppm: 3.29 s and 4.10 s (3H, CH_3), 7.75–7.85 m (2H, 6-H, 7-H), 8.10–8.25 m (2H, 5-H, 8-H). Found, %: C 51.15; H 2.27; N 26.89. $C_{11}H_7N_5O_3$. Calculated, %: C 51.36; H 2.72; N 27.24.

2-Azido-3-(ethyl-N-nitrosoamino)-1,4-naphthoquinone (IIb). Yield 85%, mp 99–100°C. 1H NMR spectrum ($CDCl_3$), δ , ppm: 1.10 t and 1.41 t (3H, CH_3 , $J = 8.0$ Hz), 3.88 q ($J = 8.0$ Hz), 4.51 m (2H, CH_2), 7.75–7.85 m (2H, 6-H, 7-H), 8.08–8.26 m (2H, 5-H, 8-H). Found, %: C 52.86; H 3.34; N 25.55. $C_{12}H_9N_5O_3$. Calculated, %: C 53.14; H 3.32; N 25.83.

2-Azido-3-(isobutyl-N-nitrosoamino)-1,4-naphthoquinone (IIc). Yield 85%, mp 69–70°C. 1H NMR spectrum (DMSO- d_6), δ , ppm: 0.88 d [6H, (CH_3) $_2$, $J = 6.8$ Hz], 2.18–2.30 m (1H, CH, $J = 6.8$ Hz), 4.33 d (2H, CH_2 , $J = 7.4$ Hz), 7.82–7.91 br.m (2H, 6-H, 7-H), 8.02–8.12 br.m (2H, 5-H, 8-H). Found, %: C 55.88; H 4.29; N 23.15. $C_{14}H_{13}N_5O_3$. Calculated, %: C 56.19; H 4.35; N 23.41.

1-Alkyl-1H-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxides IIIa–IIId (general procedure). A mixture of 0.004 mol of azidonaphthoquinone **IIa–IIId** in 10 ml of benzene was heated for 30–40 min under reflux. The mixture was cooled to room temperature, and the yellow–orange precipitate was filtered off, washed with ethanol, and dried.

1-Methyl-1H-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxide (IIIa). Yield 84%, mp 295–296°C. 1H NMR spectrum (DMSO- d_6), δ , ppm: 4.07 s (3H, CH_3), 7.93 m (2H, 6-H, 7-H), 8.10–8.16 br.m (2H, 5-H, 8-H). Found, %: C 57.67; H 2.96; N 18.30. $C_{11}H_7N_3O_3$. Calculated, %: C 57.64; H 3.05; N 18.34.

1-Ethyl-1H-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxide (IIIb). Yield 70%, mp 201–203°C. 1H NMR spectrum ($CDCl_3$), δ , ppm: 1.50 t (3H, CH_3 , $J = 7.8$ Hz), 4.75 q (2H, CH_2 , $J = 7.8$ Hz), 7.80 m (2H, 6-H, 7-H), 8.17 d and 8.25 d (2H, 5-H, 8-H, $J = 6.4$ Hz). Found, %: C 59.30; H 3.69; N 16.82. $C_{12}H_9N_3O_3$. Calculated, %: C 59.26; H 3.70; N 17.28.

1-Isobutyl-1H-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxide (IIIc). Yield 81%, mp 229–230°C. 1H NMR spectrum ($CDCl_3$), δ , ppm: 1.03 d (6H, CH_3 , $J = 8.4$ Hz), 2.41 m (1H, CH), 4.46 d (2H, CH_2 , $J = 8.0$ Hz), 7.78 m (2H, 6-H, 7-H), 8.14 d and 8.25 d (2H, 5-H, 8-H, $J = 8.0$ Hz). Found, %: C 62.00; H 4.86; N 15.53. $C_{14}H_{13}N_3O_3$. Calculated, %: C 61.99; H 4.79; N 15.49.

1-Benzyl-1H-naphtho[2,3-d][1,2,3]triazole-4,9-dione 2-oxide (IIId). Yield 82%, mp 249–252°C. 1H NMR spectrum ($CDCl_3$), δ , ppm: 5.82 s (2H, CH_2), 7.33–7.37 br.m, 7.55–7.59 br.m (5H, H_{arom}), 7.76–7.81 m (2H, 6-H, 7-H), 8.18–8.25 m (2H, 5-H, 8-H). Mass spectrum, m/z (I_{rel} , %): 305 (6.9) [M] $^+$, 275 (3.9), 158 (8.8), 104 (4.4), 91 (100), 77 (2.9), 65 (18.6), 28 (44.6). Found, %: C 66.44; H 3.53; N 13.61. $C_{17}H_{11}N_3O_3$. Calculated, %: C 66.88; H 3.61; N 13.77.

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