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Synthesis of 3-Alkyl-5-arylamino-6,11-dihydro-3*H*-anthra[1,2-*d*]-[1,2,3]triazole-6,11-dione 2-Oxides by Nitrosation of 3-Alkylamino-5-arylamino-6*H*-anthra[1,9-*cd*]isoxazol-6-ones

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Abstract—Nitrosation of 3-alkylamino-5-arylamino-6*H*-anthra[1,9-*cd*]isoxazol-6-ones with sodium nitrite in acetic acid leads to the formation of the corresponding unstable *N*-nitroso derivatives which are converted into 3-alkyl-5-arylamino-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxides on heating.

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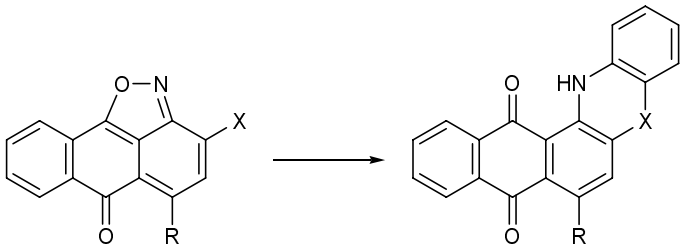
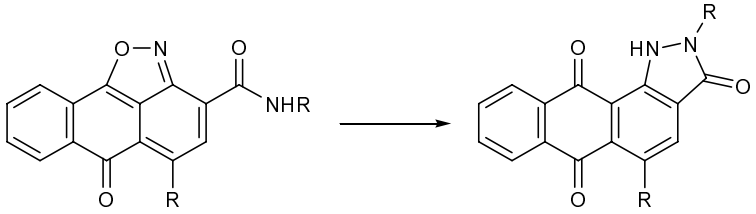
It is known that 6*H*-anthra[1,9-*cd*]isoxazoles possessing various substituents in the 3-position are capable of undergoing isomerization into derivatives of 9,10-anthraquinone fused at the 1,2-positions with a five- or six-membered nitrogen-containing ring (Scheme 1). These isomerizations can be promoted by heating, irradiation, or treatment with bases [1–4]. In some cases, the process is accompanied by profound change of color, so that the initial compounds may be used as thermal indicators [5]. We believed it to be appropriate to search for such 6*H*-anthra[1,9-*cd*]isoxazole derivatives whose isomerization would give rise to heterocyclic derivatives of 9,10-anthraquinone that are difficult to obtain by other methods.

We have found that 3-alkylamino-5-arylamino-6*H*-anthra[1,9-*cd*]isoxazol-6-ones **Ia**–**Ie** readily undergo nitrosation with sodium nitrite in acetic acid and that the primary products, 3-alkyl(nitroso)amino-5-arylamino-6*H*-anthra[1,9-*cd*]isoxazol-6-ones **IIa**–**IIe**, are converted into new compounds. On the basis of the UV, NMR, and mass spectra, the final products were assigned the structure of 3-alkyl-5-arylamino-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazol-6,11-dione 2-oxides **IIIa**–**IIIe** (Scheme 2). Intermediate *N*-nitroso compounds **IIa**–**IIe** turned out to be unstable under conditions of chromatographic separation, and we failed to isolate them as analytically pure substances. Their formation was detected by TLC, as well as by

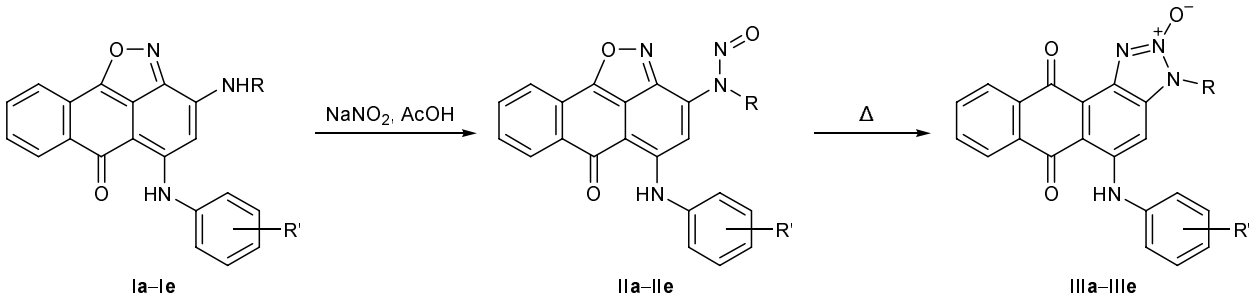
Scheme 1.



R = HO, ArNH; X = OPh, SPh, SePh.



Scheme 2.



R = *i*-Bu (**a**, **d**), Et (**b**, **c**), Bu (**e**); R' = H (**a**), 4-Me (**b**, **e**), 3-Me (**c**, **d**).

spectrophotometry. For example, the UV spectrum of the reaction mixture obtained by nitrosation of compound **Ib** contained long-wave absorption maxima at λ 515 and 540 nm, whose position almost coincided with the absorption maxima of 5-arylamino-3-bromo-6*H*-anthra[1,9-*cd*]isoxazol-6-ones (λ_{max} 515, 535 nm). Taking into account similar effects of bromine atom and *N*-nitrosoalkylamino group on chromophore systems, this fact also indicates the site of nitrosation. The heterocyclization of *N*-nitroso compounds **IIa**–**IIe** to triazole *N*-oxides **IIIa**–**IIIe** was completed by heating the reaction mixture obtained after nitrosation for 20–30 min at 50–70°C.

The UV spectra of compounds **IIIa**–**IIIe** in the visible region were similar to those of 5-arylamino-3-aryl-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-diones [6]. The ^{1}H NMR spectra of initial isoxazoloanthrones **Ia**–**Ie** and triazole *N*-oxides **IIIa**–**IIIe** differ mainly in the position of signals from the alkyl groups on the nitrogen atom and from 4-H. The 4-H signal in the spectrum of **Ib** appears as a singlet at δ 6.15 ppm, while the corresponding triazole *N*-oxide **IIb** is characterized by the 4-H signal located at δ 6.91 ppm; the downfield shift is induced by electron-acceptor effect of the triazole oxide moiety. The same factor is responsible for the downfield shift of signals from protons of the 3-CH_2 groups in compounds **III**, as compared to initial isoxazole derivatives **I**.

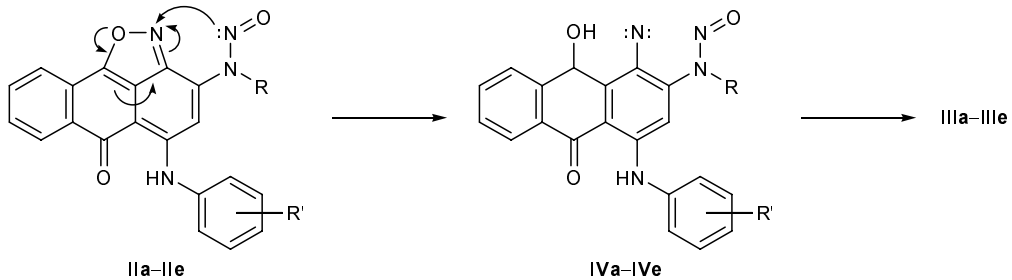
In the mass spectrum of triazole *N*-oxide **IIIb**, the most abundant ions were $[M]^+$ (*m*/*z* 398) and $[M-30]^+$, the latter resulting from elimination of the NO group. In addition, an ion peak with *m*/*z* 382 was present due to deoxygenation of the molecular ion. Ions with *m*/*z* 340 and 354 are likely to be formed by decarbonylation of the primary fragment ions with *m*/*z* 368 and 382. A strong peak with *m*/*z* 91 corresponds to the $[C_7H_7]^+$ ion originating from the 4-methylphenylamino fragment.

The transformation **II**→**III**, as well as the cyclization of 2-azido-3-alkyl(nitroso)amino)-1,4-naphthoquinones to 1-alkyl-4,9-dihydro-1*H*-naphtho[2,3-*d*]-[1,2,3]triazole-4,9-dione 2-oxides described previously [7] (it occurs at 80°C), may involve intermediate formation of nitrenes **IVa**–**IVe** (Scheme 3). However, isomerizations typical of 6*H*-anthra[1,9-*cd*]isoxazol-6-ones usually require more severe conditions, namely heating of the substrates above 100°C [1–3]. Therefore, a concerted path of the isomerization without participation of nitrene species cannot be ruled out.

EXPERIMENTAL

The ^{1}H NMR spectra were recorded from solutions in DMSO-d_6 or $CDCl_3$ on a Bruker DRX-500 spectrometer using tetramethylsilane as internal reference. The electronic spectra were measured on a Helios

Scheme 3.



Epsilon spectrophotometer in toluene ($c = 1 \times 10^{-4}$ M) using 1-cm cells. The progress of reactions and the purity of products were monitored by TLC on Silufol UV-254 plates. The melting points were determined on a Boetius melting point apparatus. The mass spectra were run on a Finnigan MAT-8200 instrument.

3-Alkylamino-5-arylamino-6*H*-anthra[1,9-*cd*]-isoxazol-6-ones Ia–Ie (*general procedure*). The corresponding amine, 10 mmol, was added under stirring to a solution of 5 mmol of 5-arylamino-3-bromo-6*H*-anthra[1,9-*cd*]isoxazol-6-one in 8 ml of DMF, and the mixture was stirred for 20–40 min at 40–50°C until the initial reactants disappeared. The mixture was cooled to 5–10°C, and the precipitate was filtered off, washed in succession with 5–10 ml of ethanol, 10–15 ml of 50% aqueous ethanol, and 20–30 ml of water, and recrystallized from DMF heated to 60°C.

3-Isobutylamino-5-phenylamino-6*H*-anthra-[1,9-*cd*]isoxazol-6-one (Ia). Yield 1.65 g (90%), mp 200°C. UV spectrum, λ_{max} (logε): 395 (3.92), 485 (4.31), 515 (4.37). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.95 s (6H, CH_3), 2.00 br.s (1H, CH), 3.25 (2H, CH_2), 6.25 br.s (1H, 4-H), 7.25–7.55 m (5H, C_6H_5), 7.60–8.60 m (4H, H_{arom}), 8.15 d (1H, $CH_2N\mathbf{H}$, J = 5 Hz), 11.75 s (1H, NH). Found, %: C 75.09; H 5.47; N 10.82. $C_{24}H_{21}N_3O_2$. Calculated, %: C 75.19; H 5.48; N 10.97.

3-Ethylamino-5-(4-methylphenylamino)-6*H*-anthra[1,9-*cd*]isoxazol-6-one (Ib). Yield 1.60 g (87%), mp 185–187°C. UV spectrum, λ_{max} (logε): 390 (3.96), 485 (4.32), 515 (4.38). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.25 t (3H, $C\mathbf{H}_3CH_2$), 2.36 s (3H, $C\mathbf{H}_3C_6H_4$), 3.46 br.s (2H, CH_2), 6.15 s (1H, 4-H), 7.30–7.40 m (4H, C_6H_4), 7.60-8.50 (4H, H_{arom}), 8.36 s (1H, $CH_2N\mathbf{H}$), 11.75 s (1H, NH). Found, %: C 74.49; H 5.19; N 11.41. $C_{23}H_{19}N_3O_2$. Calculated, %: C 74.79; H 5.15; N 11.38.

3-Ethylamino-5-(3-methylphenylamino)-6*H*-anthra[1,9-*cd*]isoxazol-6-one (Ic). Yield 1.55 g (85%), mp 183–185°C. UV spectrum, λ_{max} (logε): 390 (3.95), 485 (4.31), 515 (4.38). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 1.25 t (3H, $C\mathbf{H}_3CH_2$), 2.38 s (3H, $C\mathbf{H}_3C_6H_4$), 3.45 br.s (2H, CH_2), 6.20 s (1H, 4-H), 7.10–7.45 m (4H, C_6H_4), 7.60–8.50 (4H, H_{arom}), 8.39 s (1H, $CH_2N\mathbf{H}$), 11.75 s (1H, NH). Found, %: C 74.20; H 5.13; N 11.06. $C_{23}H_{19}N_3O_2$. Calculated, %: C 74.79; H 5.15; N 11.38.

3-Isobutylamino-5-(3-methylphenylamino)-6*H*-anthra[1,9-*cd*]isoxazol-6-one (Id). Yield 1.75 g (90%), mp 188–190°C. UV spectrum, λ_{max} (logε): 395 (3.94), 485 (4.32), 515 (4.38). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.90 s [6H, $(C\mathbf{H}_3)_2CH$], 2.00 br.s (1H, CH), 2.40 s (3H, $C\mathbf{H}_3C_6H_4$), 3.20 br.s (2H, CH_2), 6.25 br.s (1H, 4-H), 7.10–7.40 m (4H, C_6H_4), 7.65–8.55 (4H, H_{arom}), 8.16 d (1H, $CH_2N\mathbf{H}$, J = 6 Hz), 11.70 s (1H, NH). Found, %: C 75.52; H 5.85; N 10.56. $C_{25}H_{20}N_3O_2$. Calculated, %: C 75.56; H 5.08; N 10.58.

3-Butylamino-5-(4-methylphenylamino)-6*H*-anthra[1,9-*cd*]isoxazol-6-one (Ie). Yield 1.60 g (84%), mp 190°C. UV spectrum, λ_{max} (logε): 395 (3.92), 485 (4.33), 515 (4.39). ^{1}H NMR spectrum (DMSO-d_6), δ, ppm: 0.90 t (3H, $C\mathbf{H}_3CH_2$), 1.30–1.70 (4H, CH_2), 2.38 s (3H, $C\mathbf{H}_3C_6H_4$), 3.40 br.s (2H, CH_2N), 6.15 br.s (1H, 4-H), 7.25–7.40 m (4H, C_6H_4), 7.60–8.50 (4H, H_{arom}), 8.35 s (1H, $CH_2N\mathbf{H}$), 11.70 s (1H, NH). Found, %: C 75.52; H 5.85; N 10.56. $C_{25}H_{20}N_3O_2$. Calculated, %: C 75.56; H 5.08; N 10.58.

3-Alkyl-5-arylamino-6,11-dihydro-3*H*-anthra-[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxides IIIa–IIIe (*general procedure*). Compound **Ia**–**Ie**, 25 mmol, was dissolved in 20 ml of acetic acid, and 0.5–0.8 g of sodium nitrite was added in small portions under stirring. The mixture was stirred for 20–40 min until the initial compound disappeared, heated to 60–70°C, and kept for 20–30 min at that temperature until a blue–violet solid separated. The mixture was cooled, and the precipitate was filtered off, washed in succession with 70–80 ml of water, 10–15 ml of 50% aqueous ethanol, and 5–10 ml of ethanol, and recrystallized from *p*-xylene.

3-Isobutyl-5-phenylamino-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxide (IIIa). Yield 0.7 g (68%), mp 242–245°C. UV spectrum, λ_{max} (logε): 340 (4.14), 545 (3.91). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.92 d [6H, $(C\mathbf{H}_3)_2CH$, J = 6 Hz], 2.24 (1H, CH), 4.06 d (2H, CH_2, J = 6.8 Hz), 7.00 s (1H, 4-H), 7.20–7.5 (5H, C_6H_5), 7.7–8.30 (4H, H_{arom}), 11.50 s (1H, NH). Found, %: C 69.42; H 4.68; N 13.27. $C_{24}H_{20}N_4O_3$. Calculated, %: C 69.90; H 4.85; N 13.59.

3-Ethyl-5-(4-methylphenylamino)-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxide (IIIb). Yield 0.6 g (61%), mp 273–274°C. UV spectrum, λ_{max} (logε): 345 (4.07), 545 (3.86). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 t (3H, $C\mathbf{H}_3CH_2$), 2.40 s (3H, $C\mathbf{H}_3C_6H_4$), 4.31 q (2H, CH_2), 6.91 s (1H, 4-H), 7.05 m (4H, C_6H_4), 7.75–8.30 (4H, H_{arom}), 11.40 s (1H, NH). Found, %: C 69.11; H 4.41; N 14.02. $C_{23}H_{18}N_4O_3$. Calculated, %: C 69.35; H 4.52; N 14.07. *M* 398.41.

3-Ethyl-5-(3-methylphenylamino)-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxide (IIIc). Yield 0.7 g (70%), mp 224–226°C. UV spectrum, λ_{max} (logε): 340 (4.06), 545 (3.79). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 1.35 t (3H, C**H**$_3$CH$_2$), 2.39 s (3H, C**H**$_3$C$_6$H$_4$), 4.44 q (2H, CH$_2$), 6.99 s (1H, 4-H), 7.10–7.4 (4H, C$_6$H$_4$), 7.75–8.25 (4H, H$_{arom}$), 11.75 s (1H, NH). Found, %: C 74.20; H 5.13; N 11.06. $C_{23}H_{19}N_3O_2$. Calculated, %: C 74.79; H 5.15; N 11.38.

3-Isobutyl-5-(3-methylphenylamino)-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxide (IIId). Yield 0.75 g (70%), mp 205–208°C. UV spectrum, λ_{max} (logε): 340 (4.13), 550 (3.86). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.95 d [6H, (C**H**$_3$)$_2$CH, J = 6 Hz], 2.24 m (1H, CH), 2.40 s (3H, C**H**$_3$C$_6$H$_4$), 4.06 d (2H, CH$_2$, J = 6 Hz), 7.05 s (1H, 4-H), 7.00–7.40 (4H, C$_6$H$_4$), 7.7–8.40 (4H, H$_{arom}$), 11.50 s (1H, NH). Found, %: C 69.98; H 4.95; N 12.54. $C_{25}H_{22}N_4O_3$. Calculated, %: C 70.42; H 5.16; N 13.14.

3-Butyl-5-(4-methylphenylamino)-6,11-dihydro-3*H*-anthra[1,2-*d*][1,2,3]triazole-6,11-dione 2-oxide (IIIe). Yield 0.70 g (65%), mp 199–201°C. UV spectrum, λ_{max} (logε): 340 (4.14), 545 (3.79). ^{1}H NMR spectrum ($CDCl_3$), δ, ppm: 0.90 t (3H, C**H**$_3$CH$_2$), 1.30–1.75 (4H, CH$_2$), 2.40 s (3H, C**H**$_3$C$_6$H$_4$), 4.25 t (2H, CH$_2$N), 7.20 s (1H, 4-H), 7.20–7.40 (4H, C$_6$H$_4$), 7.70–8.40 (4H, H$_{arom}$), 11.45 s (1H, NH). Found, %: C 69.92; H 4.95; N 12.61. $C_{25}H_{22}N_4O_3$. Calculated, %: C 70.42; H 5.16; N 13.15.

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