*Russian Journal of Organic Chemistry, Vol. 37, No. 9, 2001, pp. 1253–1254. Translated from Zhurnal Organicheskoi Khimii, Vol. 37, No. 9, 2001, pp. 1321–1322.*


# Reaction of 1-Nitro-9,10-anthraquinone-2-carboxylic Acid with 2-Aminoethanol*

**T. I. Lavrikova, O. V. Podvyaznyi, and L. M. Gornostaev**

*Krasnoyarsk State Pedagogical University, ul. Lebedevoi 89, Krasnoyarsk, 660049 Russia*

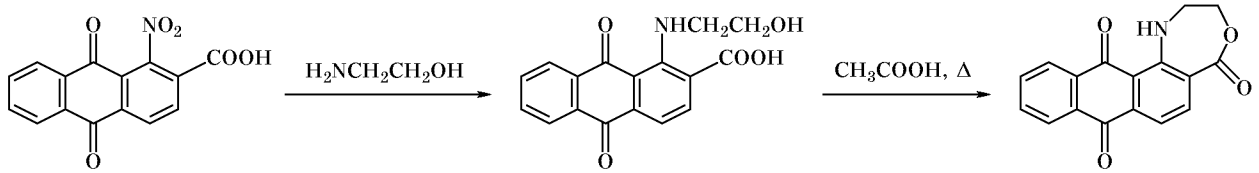
Received February 16, 2001

**Abstract**—1-Nitro-9,10-anthraquinone-2-carboxylic acid reacts with 2-aminoethanol to give 1-(2-hydroxyethylamino)-9,10-anthraquinone-2-carboxylic acid which undergoes intramolecular cyclization to 1,2,3,5,8,13-hexahydroanthra[1,2-*e*][1,4]oxazepine-5,8,13-trione on heating in acetic acid. Reactions of the cyclization product with amines result in cleavage of the seven-membered heteroring.

Some 1-(2-hydroxyethylamino)anthraquinones are known to exhibit antitumor activity [1]. Therefore, it seems reasonable to synthesize derivatives of such compounds having a substituent in position *2*. By reaction of 1-nitro-9,10-anthraquinone-2-carboxylic acid with 2-aminoethanol in dimethylformamide at 40–50°C we have synthesized 1-(2-hydroxyethylamino)-9,10-anthraquinone-2-carboxylic acid (**I**). At higher temperature the reaction was accompanied by formation of other products. On heating in boiling acetic acid compound **I** was converted into a product which, according to the $^1$H NMR and mass spectra, had the structure of 1,2,3,5,8,13-hexahydroanthra-[1,2-*e*][1,4]oxazepine-5,8,13-trione (**II**) (Scheme 1).

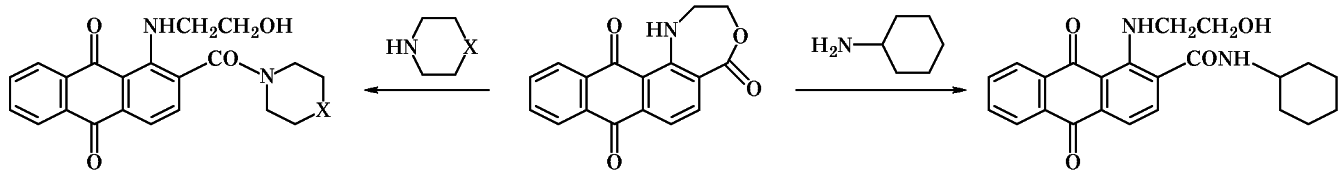
The $^1$H NMR spectrum of **II** differed from the spectrum of acid **I** by the absence of signals from the hydroxy and carboxy protons, which indicates the occurrence of condensation. In the mass spectrum of **II** a strong peak from the molecular ion was present (*m*/*z* 293), which counts in favor of the lactone

**Scheme 1.**




**I** **II**

**Scheme 2.**




**IIIa, IIIb** **II** **IV**

**III**, X = $CH_2$ (**a**), O (**b**).

* This study was financially supported by the Krasnoyarsk Region Science Foundation (grant no. 9F0158).

1070-4280/01/3709-1253 $25.00 © 2001 MAIK "Nauka / Interperiodica"

Yields, melting points, and elemental analyses of 1,2,3,5,8,13-hexahydroanthra[1,2-*e*][1,4]oxazepine-5,8,13-trione (**II**) and 1-(2-hydroxyethylamino)-9,10-anthraquinone-2-carboxamides **IIIa**, **IIIb**, and **IV**

| Comp. no. | Yield, % | mp, °C | Found, % | | | Formula | Calculated, % | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | C | H | N | | C | H | N |
| **II** | 86 | 238–240 | 69.18 | 3.61 | 4.51 | $C_{17}H_{11}NO_4$ | 69.62 | 3.78 | 4.78 |
| **IIIa** | 77 | 232–234 | 69.39 | 5.71 | 6.96 | $C_{22}H_{22}N_2O_4$ | 69.83 | 5.86 | 7.40 |
| **IIIb** | 78 | 235–237 | 65.80 | 5.40 | 6.90 | $C_{21}H_{10}N_2O_5$ | 66.31 | 5.30 | 7.36 |
| **IV** | 72 | 202–204 | 70.01 | 5.78 | 6.84 | $C_{23}H_{24}N_2O_4$ | 70.39 | 6.16 | 7.14 |

structure. Oxazepine **II** can be modified by conversion into 1-(2-hydroxyethylamino)-9,10-anthraquinone-2-carboxamides. Amides **IIIa**, **IIIb**, and **IV** were synthesized by heating of **II** with morpholine, piperidine, and cyclohexylamine, respectively (Scheme 2).

The structure of the products was proved by elemental analyses (see table) and $^1$H NMR spectra.

## EXPERIMENTAL

The $^1$H NMR spectra were recorded on a Bruker DRX-500 spectrometer (500 MHz) using DMSO-$d_6$ as solvent and TMS as internal reference. The progress of reactions was monitored, and the purity of products was checked, by TLC on Silufol UV-254 plates.

**1-(2-Hydroxyethylamino)-9,10-anthraquinone-2-carboxylic acid (I).** To a solution of 2.98 g (0.01 mol) of 1-nitro-9,10-anthraquinone-2-carboxylic acid in 20 ml of DMF we added 3 ml (0.05 mol) of 2-aminoethanol, and the mixture was stirred for 5 h at 50–60°C. It was then cooled and poured into water acidified with hydrochloric acid to a slightly acidic reaction. The precipitate was filtered off and washed with ethanol. Yield 2.83 g (91%). mp 180–182°C (from ethanol). $^1$H NMR spectrum, δ, ppm: 3.25 t (2H, $OCH_2$), 3.63 t (2H, $NCH_2$), 4.88 br.s (1H, $CH_2O$**H**), 7.45–8.23 m (6H, $H_{arom}$), 10.24 s (1H, NH), 13.25 br.s (1H, COOH).

**1,2,3,5,8,13-Hexahydroanthra[1,2-*e*][1,4]oxazepine-5,8,13-trione (II).** A solution of 1 g (0.003 mol) of acid **I** in 100 ml of acetic acid was refluxed for 60–90 min. The mixture was cooled, and the precipitate was filtered off, washed with water, and recrystallized from acetic acid. $^1$H NMR spectrum, δ, ppm: 3.95 t (2H, $CH_2$), 4.58 t (2H, $CH_2$), 7.44–8.27 m (6H, $H_{arom}$), 10.89 s (1H, NH). Mass spectrum, *m*/*z* ($I_{rel}$, %): 293 (100) $[M]^+$, 294 (22), 295 (2.5), 278 (5.8), 264 (21), 263 (93), 249 (5.7), 235 (95), 208 (74).

**1-(2-Hydroxyethylamino)-9,10-anthraquinone-2-carboxamides IIIa, IIIb, and IV.** A solution of 0.4 g (1.3 mmol) of compound **II** in 3.5–4 ml (~0.04 mol) of morpholine, piperidine, or cyclohexylamine was refluxed for 3–4 h. The mixture was cooled, and the precipitate was filtered off and recrystallized from ethanol or toluene.

**1-(2-Hydroxyethylamino)-2-piperidinocarbonyl-9,10-anthraquinone (IIIa).** $^1$H NMR spectrum, δ, ppm: 1.45–1.70 m [6H, $(CH_2)_3$], 3.25–3.85 m [8H, $CON(CH_2)_2$, $NHCH_2$, $CH_2OH$], 4.82 br.s (1H, $CH_2O$**H**), 7.43–8.25 m (6H, $H_{arom}$), 10.31 s (1H, NH).

**1-(2-Hydroxyethylamino)-2-morpholinocarbonyl-9,10-anthraquinone (IIIb).** $^1$H NMR spectrum, δ, ppm: 3.32–3.75 m [12H, $CON(CH_2CH_2)_2O$, $NHCH_2$, $CH_2OH$], 4.83 br.s (1H, $CH_2O$**H**), 7.48–8.27 m (6H, $H_{arom}$), 10.28 s (1H, NH).

**2-Cyclohexylaminocarbonyl-1-(2-hydroxyethylamino)-9,10-anthraquinone (IV).** $^1$H NMR spectrum, δ, ppm: 1.15–1.87 m [10H, $(CH_2)_5$], 3.38 t (2H, $CH_2OH$), 3.63 t (2H, $NHCH_2$), 3.72 m (1H, NHC**H**), 4.82 s (1H, $CH_2O$**H**), 7.45–8.28 m (6H, $H_{arom}$), 8.36 d (1H, CONH), 10.38 s (1H, N**H**$CH_2$).

## REFERENCE

1. Gorelik, M.V., *Khimiya antrakhinonov i ikh proizvodnykh* (Chemistry of Anthraquinones and Their Derivatives), Moscow: Khimiya, 1983.