CONDENSED AND BONDED QUINOXALINES

III.* SYNTHESIS OF SUBSTITUTED IMIDES OF 5,6-BENZOQUINOXALINE-2,3-DICARBOXYLIC ACID

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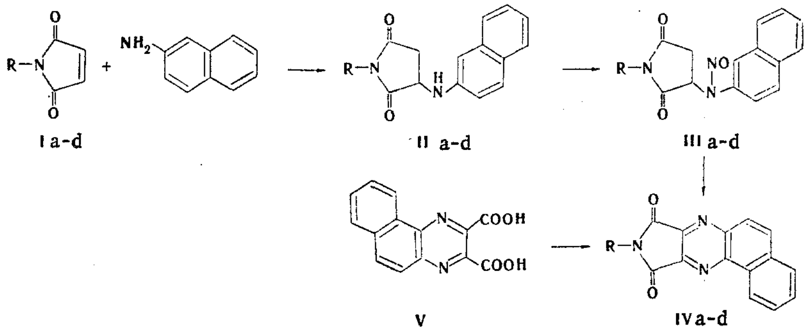
Under the influence of acetic anhydride, 3-(N-nitroso-2-naphthylamino)-1-R-pyrrolidine-2,5-diones are cyclized to substituted imides of 5,6-benzoquinoxaline-2,3-dicarboxylic acid, the structure of which was confirmed by alternative synthesis.

In the present paper we have investigated the conversion of 3-(N-nitroso-2-naphthylamino)-1-R-pyrrolidine-2,5-diones (III) to substituted imides (IV) of 5,6-benzoquinoxaline-2,3-dicarboxylic acid under the conditions that we discovered [1] for the cyclization of N-nitrosoarylamines to quinoxalines.



We have previously shown [1] that heating of 3-N-nitrosophenylamino-1-phenylpyrrolidine-2,5-diones in acetic anhydride gives quinoxaline-2,3-dicarboxylic acid N-phenylimide. The formation of a quinoxaline ring in the reaction under consideration may be due either to nitrosation of the methylene group of the pyrrolidine ring or – which is less likely – to isomerization of the nitrosamine to an o-nitrosoarylamine. It is known that aromatic nitrosamines are isomerized to p-nitrosoarylamino compounds (Fischer–Hepp rearrangement) on treatment with acids, while N-nitroso-N-alkyl-2-naphthylamines undergo ortho isomerization. In conformity with this, one might have expected a considerable increase in the rate of formation of IV for N-nitroso-2-naphthylamines III as compared with N-nitrosophenylamines, if the conversion of III to IV includes ortho isomerization of the nitrosamine. However, we found that only an insignificant increase in the reaction rate is observed for III as compared with benzonitrosamines, and the yields of cyclization products in both cases were almost the same. Attempts to synthesize 3-(1-nitroso-2-naphthylamino)-1-R-pyrrolidine-2,5-diones (VI) from nitrosamines III under the conditions that are typical for the Fischer–Hepp rearrangement were unsuccessful.

The information obtained confirms that the conversion of III to IV includes nitrosation of the methylene group; the cyclization of the resulting oximino derivative is apparently related to the recently observed [3] formation of a quinoline ring from oximes of 3-phenyl-Δ^2-unsaturated aldehydes under the influence of acetic anhydride.

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*See [1] for communication II.

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TABLE 1. Characteristics of the Compounds Obtained

Comp.	R	mp, °C	Empirical formula	N, %		IR spectrum, cm^{-1}			Yield, %
				found	calc.	$\nu_{C=O}$	ν_{N-NO}	ν_{N-H}	
IIa	Methyl	201—203	$C_{15}H_{14}N_2O_2$	11,2	11,0	1780; 1710		3390; 3360	46
IIb	Phenyl	227—230	$C_{20}H_{16}N_2O_2$	8,8	8,9	1770; 1712		3395; 3350	73
IIc	1-Naphthyl	189—190	$C_{24}H_{18}N_2O_2$	7,5	7,6	1790; 1720		3390; 3360	70
IId	2-Naphthyl	260—263	$C_{24}H_{18}N_2O_2$	7,6	7,6	1776; 1700		3345	65
IIIa	Methyl	170—173 (dec.)	$C_{15}H_{13}N_3O_3$	14,6	14,8	1780; 1720	1460; 1450; 1440		93
IIIb	Phenyl	155—156 (dec.)	$C_{20}H_{15}N_3O_3$	12,4	12,2	1790; 1720	1460; 1440; 1425		96
IIIc	1-Naphthyl	189—192 (dec.)	$C_{24}H_{17}N_3O_3$	10,7	10,6	1790; 1730	1450; 1440; 1410		97
IIId	2-Naphthyl	above 240 (dec.)	$C_{24}H_{17}N_3O_3$	10,4	10,6	1784; 1711	1465; 1450; 1430		93
IVa	Methyl	306—309	$C_{15}H_9N_3O_2$	16,0	16,0	1790; 1735			15
IVb	Phenyl	335—340	$C_{20}H_{11}N_3O_2$	12,6	12,9	1800; 1735			42
IVc	1-Naphthyl	318—321	$C_{24}H_{13}N_3O_2$	10,9	11,2	1795; 1740			45
IVd	2-Naphthyl	355—360	$C_{24}H_{13}N_3O_2$	11,1	11,2	1795; 1735			47

*The following solvents were used for crystallization: acetic acid (IIa,b), toluene (IIc), acetic acid + DMF (IId), butanol (IIIa-d), and DMF (IVa-d).

The structure of imides IV was proved by alternative synthesis from 5,6-benzoquinoxaline-2,3-dicarboxylic acid (V), which was obtained from 1,2-naphthylenediamine and dihydroxytartaric acid.

The synthesis of 3-(2-naphthylamino)-1-R-pyrrolidine-2,5-diones (II) was accomplished by the addition of 2-naphthylamine to N-R-maleinimides (I). Compound IId was obtained by condensation of 2-naphthylamine with maleic anhydride in diethylbenzene with heteroazeotropic distillation of the resulting water. Compound III was converted to IV by heating III in excess acetic anhydride at 90-100° for 10 h.

There are two absorption bands in the IR spectra of II, III, and IV in the carbonyl region, and the higher-frequency band appears as a shoulder on the principal band, while its intensity is considerably higher in the spectrum of IV and is comparable to the principal band in the spectrum of imide IVa. The appearance of a broad band that is split into a triplet is characteristic for nitrosamines III in the region of the N—NO stretching vibrations (1450-1500 cm^{-1}) [4].

EXPERIMENTAL

The IR spectra of KBr pellets were recorded with a UR-20 spectrometer.

3-(2-Naphthylamino)-1-R-pyrrolidine-2,5-diones (IIa-c). A solution of 0.1 mole of N-R-maleinimide in 50 ml of ethanol was mixed with a solution of 0.11 mole of 2-naphthylamine in 100 ml of aqueous ethanol (1 : 1), and the mixture was refluxed for 1 h. The resulting crystalline precipitate was removed by filtration from the hot solution (Table 1).

3-(2-Naphthylamino)-1-(2-naphthyl)pyrrolidine-2,5-dione (IId). A 24.5-g (0.25 mole) sample of maleic anhydride and 100 ml of diethylbenzene were placed in a flask equipped with a Dean—Stark trap, and 42.9 g (0.3 mole) of 2-naphthylamine was added with vigorous stirring. The mixture was then refluxed on an oil bath until the stoichiometric amount of water (4.5 ml) had separated (this required 1.5-2 h), after which it was poured into a beaker, cooled, and 100 ml of alcohol was added. The resulting crystalline precipitate was removed by filtration (Table 1).

3-(N-Nitroso-2-naphthylamino)-1-R-pyrrolidine-2,5-diones (IIIa-d). A solution of 0.025 mole of sodium nitrite in 20 ml of water was added at room temperature in the course of 30 min with vigorous stirring to a suspension of 0.02 mole of 3-(2-naphthylamino)-1-R-pyrrolidine-2,5-dione in 50 ml of acetic acid, and the mixture was stirred for another 30 min. The nitrosamine was then removed by filtration. Compounds III were yellowish crystalline substances that were only slightly soluble in ether and benzene but readily soluble on heating in acetic acid, dioxane, and alcohols (Table 1).

N-R-Imides of 5,6-Benzoquinoxaline-2,3-dicarboxylic Acid (IVa-d). A solution of 0.02 mole of 3-(2-naphthylnitrosamino)-1-R-pyrrolidine-2,5-dione in 75 ml of acetic anhydride (the amount of acetic anhydride should be such that the compound dissolves completely at 90-100°) was stirred vigorously at 90-100° for 10 h in a three-necked flask equipped with a stirrer, a reflux condenser, and a thermometer. The resulting precipitate was removed by filtration, washed on the filter with acetic anhydride, and dried. When the heating time was increased to 20 h, the yield was raised by 3-6%. Compounds IV were yellow crystalline substances that were only slightly soluble in most organic solvents.

5,6-Benzoquinoxaline-2,3-dicarboxylic Acid (V). A 12.6-g (0.08 mole) sample of 1,2-naphthylenediamine was dissolved in a mixture of 300 ml of water and 100 ml of alcohol by heating on a water bath, and 9.0 g (0.04 mole) of disodium dihydroxytartrate was added. The mixture was heated with stirring for 30 min and filtered. The filtrate was made strongly acidic with concentrated HCl or by passage of hydrogen chloride through the solution. The resulting crystalline substance was removed by filtration and washed thoroughly on the filter with water to give 5.5 g (51%) of a product with mp 228-230° (dec.). Found,%: N 10.2. $C_{14}H_8N_2O_4$. Calculated,%: N 10.4.

5,6-Benzoquinoxaline-2,3-dicarboxylic Acid Anhydride (VI). A 5.36-g (0.02 mole) sample of 5,6-benzoquinoxaline-2,3-dicarboxylic acid was refluxed in 40 ml of acetic anhydride for 10-15 min. The mixture was cooled, and the anhydride was crystallized to give 4.76 g (95%) of light-brown leaflets with mp 220-223° (dec.). Found,%: N 11.3. $C_{14}H_6N_2O_3$. Calculated,%: N 11.2. IR spectrum, cm^{-1}: $\nu_{C=O}$ 1870 and 1795 cm^{-1}.

N-R-Imides of 5,6-Benzoquinoxaline-2,3-dicarboxylic Acid (IV). Equimolecular amounts of the appropriate amine and anhydride VI were refluxed in alcohol for 10-15 min. The acylation products were slightly soluble in alcohol and crystallized during their formation. In the case of methylamine, an excess of the amine was used, and the reaction mass was then acidified. The isolated substances were dried and refluxed for 10-15 min in acetic anhydride to give compounds with physical constants and IR spectra that were identical to those of compounds obtained from nitrosamines III. The yields based on anhydride VI were usually 60-70%.

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