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Novel Heterocyclic Compounds from 2-Nitromethylquinoxaline. (1)

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In a previous paper in this series it was shown that 2-nitromethylquinoxaline (II) can be conveniently obtained by the reaction of sodium 2-nitro-3-oxosuccinaldehyde (I) with *o*-phenylenediamine (3). As an extension of this work, we have undertaken a study of further reactions of II, leading to the synthesis of some novel heterocyclic compounds.

As suggested by the work of Kröhnke (4), we have found that an excellent yield of α -(*p*-dimethylamino-phenylimino)-2-quinoxalineacetonitrile (III) is obtained by heating II with *p*-nitrosodimethylaniline and sodium cyanide in aqueous alcoholic solution.

The reaction of III with *o*-phenylenediamine in boiling glacial acetic acid resulted in the formation of 3-amino-2,2'-biquinoxaline (V), which may be rationalized as occurring via an intermediate IV, with inclusion of the nitrile carbon atom in the subsequent ring-closure step. Analogous reactions occurred when toluene-3,4-diamine or 2,3-naphthalenediamine were used in place of *o*-phenylenediamine, but failed when 4-nitro-*o*-phenylenediamine, 3,4-diaminobenzoic acid, 2,3-diaminopyridine, or 4,5-diaminopyrimidine were used. Apparently the latter, weakly basic amines are unable to displace *p*-dimethylaminoaniline from III to give an intermediate analogous to IV.

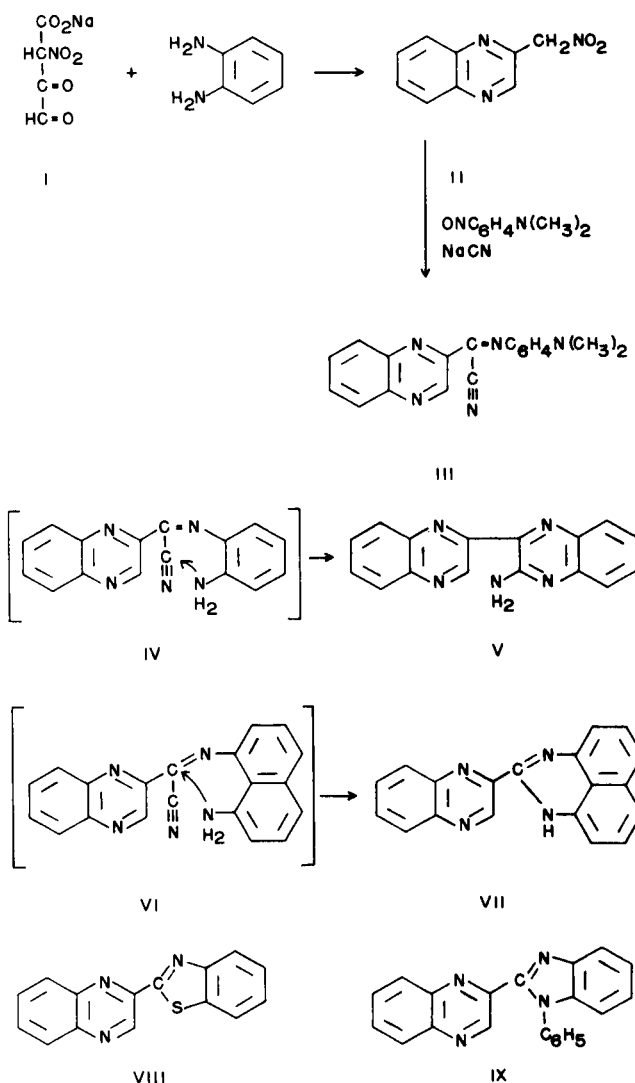
When compound III was treated with 1,8-naphthalenediamine the reaction occurred with the elimination of *p*-dimethylaminoaniline and hydrogen cyanide, corresponding to the ring-closure of the intermediate VI to give the six-membered perimidine ring derivative VII. Similarly, the reaction of III with *o*-aminothiophenol resulted in the closure of a five-membered ring with the loss of hydrogen cyanide to give the benzothiazole derivative VIII, and with *N*-phenyl-*o*-phenylenediamine to give the benzimidazole derivative IX.

We also wish to report a simplified procedure for the preparation of quinoxaline-2-aldoxime, utilizing the reaction of compound II with sodium ethoxide and benzyl bromide, (5) and the dehydration of the oxime to 2-cyanoquinoxaline, a new compound.

EXPERIMENTAL

 α -(*p*-Dimethylaminophenylimino)-2-quinoxalineacetonitrile (III).

A solution of 200 mg. (4 mmoles) of sodium cyanide in 1 ml. of water was added to a solution of 378 mg. (2 mmoles) of 2-nitromethylquinoxaline in 2 ml. of ethanol. The mixture was heated quickly to 70°, a solution of 400 mg. (2.6 mmoles) of *p*-nitrosodimethylaniline in 3 ml. of acetone was added, it was kept at 70° for an additional 45 minutes, 6 ml. of water was slowly added, and it was stored in



the refrigerator overnight. The resulting red precipitate was recrystallized several times from ethyl acetate to give an 85% yield of purple needles, m.p. 262-264°. The nmr spectrum in trifluoroacetic acid showed a one proton singlet at $\tau = 0$, and two four proton multiplets at $\tau = 1.5$ and $\tau = 2.0$.

Anal. Calcd. for $C_{18}H_{15}N_5$: C, 71.74; H, 5.02. Found: C, 71.60; H, 5.02.

Preparation of 2-Quinoxaline Derivatives.

In a typical procedure, a solution of compound III and the appropriate aromatic diamine (or *o*-aminobenzenethiol) in acetic acid was boiled for one half hour and water was added. After cooling, the resulting precipitate was recrystallized from a suitable solvent. The results are summarized in Table I.

Quinoxaline-2-aldoxime.

First 20 g. of 2-nitromethylquinoxaline, then 18 g. of benzyl bromide were added with stirring at room temperature to a solution of sodium

TABLE I
2-Quinoxaline Derivatives

Name (Formula)	Yield, Appearance, Solvent, m. p.	Calcd.		Found	
		C	H	C	H
3-amino-2,2'-biquinoxaline (V)	50%, yellow needles, ethyl acetate-tetrahydrofuran, 260-261°	70.31	4.06	70.55	4.22
3-amino-5(or 6)-methyl-2,2'- biquinoxaline	85%, yellow needles, alcohol-tetrahydrofuran, 235-240°	71.06	4.56	71.66	4.70
3-amino-2-(2-quinoxalyl)- benzo[g]quinoxaline	60%, orange needles, ethyl acetate, 300°	74.29	4.05	74.54	4.12
2-(2-perimidyl)quinoxaline (VII)	45%, black powder ethyl acetate, 286-288°	77.01	4.08	77.07	4.25
2-(2-benzothiazolyl)- quinoxaline (VIII)	20%, yellow prisms, tetrahydrofuran, 234-236°	68.42	3.45	68.57	3.61
2-(1-phenyl-2-benzimidazolyl)- quinoxaline (IX)	45%, orange needles, methanol-tetrahydrofuran, 150-151°	78.24	4.38	78.46	4.51

ethoxide prepared by dissolving 3 g. of sodium metal in 120 ml. of absolute alcohol. The solution became warm and solid sodium bromide was formed. After 4 hours the precipitate was removed by filtration and the filtrate was concentrated on the steam bath. The residue was shaken with 50 ml. of chloroform and 75 ml. of water. The water extract was discarded and the chloroform solution was extracted with 3 x 15 ml. portions of 10% aqueous sodium hydroxide. Neutralization of the combined alkaline extract gave a 32% yield of crystalline oxime, m. p. 202° (lit. (6) 202°).

2-Cyanoquinoxaline.

The oxime was heated for two hours under reflux with an excess of acetic anhydride and anhydrous sodium acetate. Most of the acetic anhydride was removed by distillation under vacuum and the oily residue was poured into water and cooled to give a yellowish, crystalline product. Recrystallization from alcohol gave a 17% yield of pale yellow needles, m. p. 123-124°.

Anal. Calcd. for $C_9H_5N_3$: C, 69.57; H, 3.26; N, 27.07. Found: C, 69.47; H, 3.56; N, 26.81.

The following nmr spectra observed in trifluoroacetic acid solution are all in accord with the assigned structures (values are in τ units): for V, a one proton singlet at 0, and two four proton multiplets at 1.5 and 2.0; for VII, a one proton multiplet at 0, a four proton multiplet at 1.5, and a six proton multiplet at 2.6; for VIII a one proton singlet at 0, and an eight proton multiplet at 1.7.

REFERENCES

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