in Table V; analyses of new compounds and their picrates are reported in Table VI.

In preliminary experiments sodium and potassium were used interchangeably; however, it soon became evident that the use of potassium gave generally better yields. Comparison of experiments 7 and 8 shows that starting from 2-*sec*-butylpyridine and ethyl bromide, a 5% yield of 2-(methylethylpropyl)-pyridine was obtained when sodium amide was used; however, when potassium amide was employed, a 39% yield was obtained. The absence of recovered starting material shows that the more active potassium compound is subject to a competitive reaction, most probably condensation of the carbanion at the azomethine position of another molecule of alkylpyridine.

Unsuccessful attempts were made to synthesize 2- or 4-(methylethylisobutyl)-pyridine starting with 2- or 4-(methylisobutyl)-pyridine (expts. 9 and 20, Table V). The desired alkylpyridines were however, obtained when the reactants were 2- and 4-*sec*-butylpyridine and isopropyl bromide (expts. 10 and 21, Table V). The condensation reaction could be explained as taking place through an intermediate formation of a carbanion with subsequent condensation with an alkyl halide.

The yields of 4-alkylpyridines usually were higher than those of the corresponding 2-alkylpyridines. This also probably is related to the greater stability in liquid ammonia medium of 4-picolyl carbanion as compared with the 2-picolyl carbanion.[6]

## Experimental Part

**I. Alkylation of Alkylpyridines.**—The alkylation reactions were carried out in either a 100- or 250-ml. capacity Magne-Dash autoclave[11] according to the procedure described previously.

The product was analyzed by means of infrared spectroscopy, comparing the alkylated product with the synthetically prepared alkylpyridines and by gas chromatography using as a stationary phase ethyltrihydroxypropylethylenediamine on Chromosorb.[12]

The kinetic experiments were carried out in a 100-ml. Magne-Dash autoclave. The 4-isopropylpyridine and sodium were placed in the autoclave which then was flushed with nitrogen. The autoclave was attached to an ethylene storage tank of about 125-ml. capacity which was kept in a constant temperature bath. The tank was equipped with a precision pressure gauge. The autoclave was heated to 125°. At this point the ethylene was introduced to the desired pressure and the agitating device on the Magne-Dash was started. The pressure in the Magne-Dash was kept constant and the drop in the pressure in the ethylene tank was recorded at frequent intervals. From the rate of pressure drop it was possible to determine the rate of reaction. The rate of ethylene consumption remained constant over the length of the experiment which usually lasted from 0.75 to 1.0 hour.

**II. Synthesis of Alkylpyridines.**—The alkylpyridines were prepared according to the general procedure described by Brown and Murphey.[8] The following describes a typical synthesis: to a solution of 0.2 g. of ferric nitrate in 200–300 ml. of liquid ammonia was added 0.5 g. atom of clean potassium metal. The solution turned dark blue. After all the potassium had dissolved (10–15 minutes) 0.5 mole of alkylpyridine was added and the solution was allowed to stir for about 15 minutes. To this was added over a period of 1–1.5 hours 0.5 mole of alkyl halide. The reaction was maintained at the boiling temperature of liquid ammonia.

The solution was allowed to warm up slowly to room temperature and the contents of the flask was added slowly into water. The pyridine layer was decanted and the water layer was extracted thrice each time with 20 ml. of ether. The ether and pyridine layers were combined and the ether was removed by distillation. Benzene was added to the alkylpyridines and distilled to remove the dissolved water as an azeotrope. The dry alkylpyridines then were distilled on a Podbielniak Hypercal or on a Whirling Band column.[13]

**Acknowledgment.**—The authors wish to thank Mr. Ed. M. Lewicki for technical assistance rendered and Miss Hildegard E. Beck for the elemental analyses.

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(11) Autoclave Engineers, Inc., Erie, Pa.

(12) A. W. Decora and G. V. Dinnen, paper presented before the Analytical Division, American Chemical Society Meeting, September, 1958, Chicago, Ill.

(13) Podbielniak, Inc., Chicago, Ill.

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[CONTRIBUTION FROM THE CHEMISTRY DEPARTMENT, TULANE UNIVERSITY]

# The Preparation of 6,7-Disubstituted Quinoxalines[1]

BY J. H. BOYER, R. S. BURIKS[2] AND U. TOGGWEILER

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Reduction of 1,2-dinitroso-4-nitroso-5-azidobenzene (III) with an insufficient amount of hydrogen iodide produces 1,2-diamino-4-nitro-5-azidobenzene (IV), whereas an excess of hydrogen iodide produces 2,4,5-triaminonitrobenzene (I). Condensation with 1,2-dicarbonyl derivatives gives 6-azido-7-nitroquinoxalines (VIII) from IV and 6-amino-7-nitroquinoxalines (VII) from I. The azides VIII also are obtained from corresponding diazotized amines VII and sodium azide. Certain 6-chloro-7-nitroquinoxalines are unreactive toward nucleophilic displacement of chlorine.

Condensation of an aromatic *o*-diamine with a 1,2-dicarbonyl compound, a preparative method for quinoxalines bearing carbocyclic substituents, has provided certain 6,7-disubstituted quinoxalines required for other purposes. The synthesis of 6-amino-7-nitroquinoxaline, an attractive goal since amino and nitro groups are easily transformed into other functional groups, requires initial preparation of 2,4,5-triaminonitrobenzene (I).

Each of two different methods for the preparation of I starts with 1,5-dichloro-2,4-dinitrobenzene obtained by nitrating *m*-dichlorobenzene. Transformation into 1,5-diazido-2,4-dinitrobenzene (II) and then, by pyrolysis, into 1,2-dinitroso-4-nitro-5-azidobenzene (III) has been reported previously.[3] In a one-step operation, an excess of hydrogen

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(2) The work described here is abstracted from a part of the thesis of R. S. Buriks submitted to Der Rijks-Universiteit, Leiden, Holland, in partial fulfillment of the requirements for the Ph.D. degree. Now at Peter Stuyvesant College, Willemstad, Curacao, The Netherlands Antilles.

(3) R. J. Gaughran, J. P. Picard and J. V. R. Kaufman, THIS JOURNAL, **76**, 2233 (1954).

TABLE I

2,3-DISUBSTITUTED-6-AMINO-7-NITROQUINOXALINES (VII) FROM 2,4,5-TRIAMINONITROBENZENE AND DICARBONYLS

| Dicarbonyl | VII, R = | Color | M.p., °C. | Molecular formula | Carbon, % Calcd. | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found | Nitrogen, % Calcd. | Nitrogen, % Found | Oxygen, % Calcd. | Oxygen, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| Glyoxal (as bisulfite adduct) | H | Red | 249 | $C_8H_6N_4O_2$ | 50.55 | 50.25 | 3.16 | 3.29 | 29.46 | 29.22 | 16.48 | 16.74 |
| Biacetyl | $CH_3$ | Red | 238–240 | $C_{10}H_{10}N_4O_2$ | 55.01 | 55.72 | 4.59 | 4.70 | 25.63 | 25.86 | ... | ... |
| Benzil | $C_6H_5$ | Purple-red | 238–240 | $C_{20}H_{14}N_4O_2$ | 70.16 | 70.31 | 4.12 | 4.07 | 16.37 | 16.19 | 9.35 | 9.70 |
| α-Pyridil | α-$C_5H_4N$ | Purple-red | 226–228 | $C_{18}H_{12}N_6O_2$ | 62.80 | 63.10 | 3.49 | 3.72 | 24.41 | 23.57 | 9.31 | 9.35 |

TABLE II

2,3-DISUBSTITUTED-6-AZIDO-7-NITROQUINOXALINES (VIII)[a]

$$ArNH_2 \xrightarrow{HONO} \xrightarrow{NaN_3} ArN_3$$

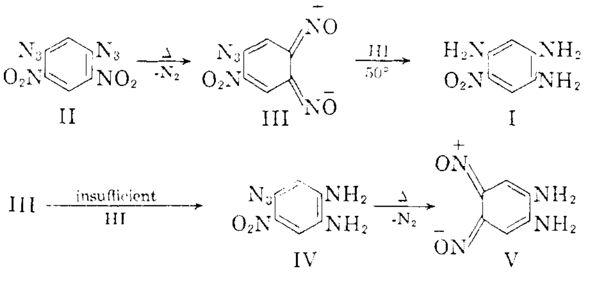
| R | Reacn. temp., °C. | Dec., °C. | Molecular formula | Carbon, % Calcd. | Carbon, % Found | Hydrogen, % Calcd. | Hydrogen, % Found | Nitrogen, % Calcd. | Nitrogen, % Found | Oxygen, % Calcd. | Oxygen, % Found |
|---|---|---|---|---|---|---|---|---|---|---|---|
| H | −15 | 135–145 | $C_8H_4N_6O_2$ | 44.45 | 44.49 | 1.87 | 1.99 | 38.88 | 38.55 | 14.80 | 14.80 |
| $CH_3$ | −30 | 120–130 | $C_{10}H_8N_6O_2$ | 49.18 | 49.35 | 3.30 | 3.40 | 34.42 | 34.20 | 13.10 | 13.19 |
| $C_6H_5$ | −10 | [b] | $C_{20}H_{12}N_6O_2$ | 65.21 | 65.50 | 3.28 | 3.27 | 22.82 | 21.17 | 8.69 | 9.50 |
| α-$C_5H_4N$ | −15 | 100 | $C_{18}H_{10}N_8O_2$ | 58.38 | 58.25 | 2.70 | 2.62 | 30.27 | 29.94 | 8.65 | 8.80 |

[a] Color of VIII, yellow-orange. [b] Turns purple, 100–200°.

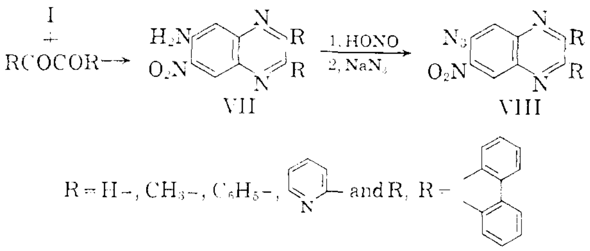
iodide reduces nitroso and azido groups in III with the formation of the desired 2,4,5-triaminonitrobenzene (I).

With an insufficient amount of hydrogen iodide, the nitroso groups but not the azido group are reduced with the formation of 1,2-diamino-4-azido-5-nitrobenzene (IV), identified by its condensation products with phenanthrenequinone and with biacetyl. Instability of the azide IV does not permit purification. Upon storage, this yellow-red product changes into a nicely crystalline purple substance which appears to be 1,2-dinitroso-4,5-diaminobenzene (V).

In an alternate procedure partial reduction of 1,5-diamino-2,4-dinitrobenzene (VI), from the corresponding dichloride and ammonia, gives 2,4,5-triaminonitrobenzene (I). Over-all yields of the two methods are comparable and each may be used for the preparation of a few grams of the triamine I. The second method is one step shorter and may be applied more safely to larger quantities of material.



6-Amino-7-nitroquinoxaline (VII, R = H) results from the condensation between glyoxal and the triamine I. In similar condensations with biacetyl, benzil, α-pyridil or phenanthrenequinone, corresponding quinoxalines are obtained with substituents also in the 2,3-positions (Table I). Five azidonitroquinoxalines (VIII) (Table II) are obtained from corresponding diazonium salts and sodium azide. In a future report pyrolysis of these nitroazido quinoxalines will be described.



## Experimental[4]

**1,5-Dinitro-2,4-dichlorobenzene.**—The following preparation was developed from a footnote statement of Zincke.[5] To a well stirred solution of 140.0 g. (1.39 moles) of potassium nitrate in 500 ml. of concentrated sulfuric acid, 100.0 g. (0.680 mole) of *m*-dichlorobenzene was added all at once. The temperature of the reaction mixture rose to 140°, slowly dropped to 125° and was kept between 120–135° for an additional hour. After cooling to 90°, the reaction mixture was poured over 1500 g. of crushed ice. The filtered product recrystallized from 1 liter of boiling ethanol as yellow needles, 115 g. (71%), m.p. 103–104°, of 1,5-dinitro-2,4-dichlorobenzene. This dinitrodichlorobenzene is a powerful skin irritant and may cause severe blisters.

**1,5-Dinitro-2,4-diazidobenzene** (II).—The following method was developed from a previously reported procedure.[3] To a well stirred solution of 18.0 g. (0.076 mole) of 1,5-dinitro-2,4-dichlorobenzene in 500 ml. of acetone, 10.0 g. (0.154 mole) of sodium azide, dissolved in a mixture of 180 ml. of water, 100 ml. of acetone and 180 ml. of ethanol, was added dropwise at room temperature over a period of 45 minutes. The reaction mixture was cooled in a Dry Ice–acetone-bath, whereupon 15.4 g. (81%) of faintly yellow crystals of 1,5-dinitro-2,4-diazidobenzene separated, m.p. 96–97°,[6] after recrystallization from methanol below 40°.

When the reaction was carried out with 18.0 g. (0.076 mole) of 1,5-dinitro-2,4-dichlorobenzene in 500 ml. of acetone and 5.0 g. (0.077 mole) of sodium azide there was obtained 8.4 g. (44%) of **1,5-dinitro-2-azido-4-chlorobenzene**, m.p. 86–87° dec.[6] From diazotized 2,4-dinitro-5-chloroaniline and sodium azide this product, m.p. 86–87° dec., was obtained in 60% yield. Photochemical decomposition of the product was immediately observed.

**1,2-Dinitroso-4-azido-5-nitrobenzene** (III).—Instead of dry decomposition,[3] the following procedure was used. To

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[4] Semi-micro analyses by Alfred Bernhardt, Microanalytisches Laboratorium Mülheim (Ruhr), Germany. Melting points are uncorrected.

[5] Th. Zincke, *Ann.*, **370**, 302 (1909), footnote **7**.

[6] A. S. Bailey and J. R. Case, *Tetrahedron*, **3**, 113 (1958).

400 ml. of boiling isopropyl alcohol, 25.0 g. (0.1 mole) of 1,5-dinitro-2,4-diazidobenzene was added in portions within a 30-minute period. Upon completion of gas evolution, the reaction mixture was cooled, whereupon 14.5 g. (65%) of crude 1,2-dinitroso-4-azido-5-nitrobenzene separated, m.p. 85–87°. It crystallized from ethanol as dark yellow needles, m.p. 89° (lit.[3] m.p. 89°).

In a similar manner, yellow crystalline 1,2-dinitroso-4-chloro-5-nitrobenzene, m.p. 87–89°,[6] was obtained (82%) from 1,5-dinitro-2-azido-4-chlorobenzene in 1-propanol, refluxing for 45 minutes or until completion of gas evolution.

*Anal.* Calcd. for $C_6H_2N_3O_4Cl$: C, 33.43; H, 0.94; N, 19.50; Cl, 16.45. Found: C, 33.36; H, 1.22; N, 19.61; Cl, 16.71.

**2,4,5-Triaminonitrobenzene (I).**—To 70 ml. of vigorously stirred 50% hydrogen iodide, 2.2 g. (0.010 mole) of 2-azido-4,5-dinitrosonitrobenzene was added slowly as the temperature was kept below 55°. Free iodine was removed with a saturated sodium bisulfite solution and 30% sodium hydroxide was added until the mixture became deep red and alkaline as the temperature rose to 75°. Upon cooling, 0.80 g. (47%) of the triamine I, m.p. 193–200°, separated and was recrystallized from boiling water as red needles, m.p. 204–206°.

*Anal.* Calcd. for $C_6H_8N_4O_2$: C, 42.86; H, 4.79; N, 33.32; O, 19.03. Found: C, 42.87; H, 4.88; N, 32.45; O, 19.90.

**1,2-Diamino-4-azido-5-nitrobenzene** was obtained from a reduction of 1,2-dinitroso-4-azido-5-nitrobenzene (0.06 mole) by 50% hydrogen iodide (0.48 mole) in ethanol. The orange-yellow product recrystallized from 50% methanol as purple crystals, no definite m.p., which appeared to be a 1:1 molecular complex of starting material and product.

*Anal.* Calcd. for $C_{12}H_{12}N_{10}O_4$: C, 40.00; H, 3.36; N, 38.88; O, 17.76. Found: C, 39.88; H, 3.39; N, 37.38; 37.36; O, 17.77.

Presence of 1,2-diamino-4-azido-5-nitrobenzene in the complex was confirmed by condensation with phenanthrenequinone into 7-nitro-8-azido-1,2,3,4-dibenzphenazine (see below) and with biacetyl into 6-nitro-7-azido-2,3-dimethylquinoxaline (see below), dec. 120–130°.

The blue-black compound that was formed upon storage of the complex for a period of several months appeared to be **1,2-dinitroso-4,5-diaminobenzene.**

*Anal.* Calcd. for $C_6H_6N_4O_2$: C, 43.37; H, 3.61; N, 33.73; O, 19.29. Found: C, 43.12; H, 3.53; N, 33.60; O, 19.49.

**1,5-Dinitro-2,4-diaminobenzene (VI.)**—Ammonia was bubbled into a well stirred, clear yellow solution of 60.0 g. (0.253 mole) of 1,5-dinitro-2,4-dichlorobenzene in 400 ml. of ethylene glycol at 140° at such a rate that it just remained absorbed. Within 30 minutes the color of the solution changed *via* orange to deep red. One hour after the start of the reaction an orange, crystalline precipitate started to form. Heating was continued for an additional two hours as a slow stream of ammonia gas was led through the reaction mixture. After cooling the reaction mixture, the product was filtered, washed with boiling water and boiling ethanol and dried. The yield of orange-brown crystals, m.p. 300°[7] (subl.), was 48 g. (95%).

**2,4,5-Triaminonitrobenzene.**—A well stirred slurry of 22.5 g. (0.114 mole) of 1,5-dinitro-2,4-diaminobenzene (previously pulverized in a mortar) in 150 ml. of water was heated to the boiling point. To this vigorously stirred refluxing mixture, a clear orange-red solution of sodium polysulfide (prepared by heating a mixture of 30.0 g. of sodium sulfide nonahydrate, 7.25 g. of sulfur and 125 g. of water) was added dropwise during a 90-minute period. After the addition, the well stirred reaction mixture was refluxed for an additional 90 minutes. The deep red mixture then was cooled to 0° and filtered. The residue (product, sulfur and some starting material) was thoroughly extracted with 1 liter of boiling water. Upon cooling, the extract yielded 9.9 g. (51%) of 2,4,5-triaminobenzene as red needles, m.p. and mixed m.p. 206–207°.

**7-Chloro-8-nitro-1,2,3,4-dibenzphenazine.**—Impure 1,2-diamino-4-chloro-5-nitrobenzene, m.p. 208–209°, was prepared in 44% yield in a reaction between 15 ml. of 50% hydrogen iodide solution and 1.3 g. (0.0006 mole) of 1,2-dinitroso-4-chloro-5-nitrobenzene. In 125 ml. of hot ethanol 1.90 g. (0.010 mole) of 1,2-diamino-4-chloro-5-nitrobenzene was mixed with a solution of 2.08 g. (0.010 mole) of 9,10-phenanthrenequinone in 300 ml. of acetic acid. The mixture was heated on a steam-bath as a finely divided precipitate separated. After 20 minutes the solution was diluted with four times its volume of water. The precipitate upon recrystallization from toluene yielded 2.5 g. (75%) of 7-chloro-8-nitro-1,2,3,4-dibenzphenazine as yellow needles, m.p. 284–286°. The compound gave a deep red color with concentrated sulfuric acid.

*Anal.* Calcd. for $C_{20}H_{10}N_3O_2Cl$: C, 66.77; H, 2.80; N, 11.62; Cl, 9.86. Found: C, 66.52; H, 2.79; N, 11.62; Cl, 8.61. C, 67.32; H, 2.55; N, 9.42; Cl, 9.89.

In a similar manner, **6-chloro-7-nitro-2,3-dimethylquinoxaline** was prepared from 1,2-diamino-4-chloro-5-nitrobenzene and biacetyl in 50% acetic acid. The product was obtained in 83% yield after recrystallization from aqueous acetone as colorless needles, m.p. 170–172°.

*Anal.* Calcd. for $C_{10}H_8N_3ClO_2$: C, 50.45; H, 3.36; N, 17.67; Cl, 14.93. Found: C, 50.71; H, 5.41; N, 17.55; Cl, 14.80.

Sodium azide did not react with either 7-chloro-8-nitro-1,2,3,4-dibenzphenazine or 6-chloro-7-nitro-2,3-dimethylquinoxaline.

**7-Amino-8-nitro-1,2,3,4-dibenzphenazine.**—A solution of 1.68 g. (0.010 mole) of 2,4,5-triaminonitrobenzene in 75 ml. of boiling ethanol was mixed with a solution of 2.08 g. (0.010 mole) of 9,10-phenanthrenequinone in 250 ml. of hot acetic acid. A dark purple reaction product was washed with hot ethanol and recrystallized from boiling acetic acid; 3.0 g. (89%), m.p. above 300°. It gave a deep red color with concentrated sulfuric acid.

*Anal.* Calcd. for $C_{20}H_{12}N_4O_2$: C, 70.57; H, 3.55; N, 16.46; O, 9.40. Found: C, 70.11; H, 3.56; N, 16.79; O, 9.58.

Additional examples of 6-amino-7-nitroquinoxalines are found in Table I.

**7-Azido-8-nitro-1,2,3,4-dibenzphenazine.**—A suspension of 4.0 g. (0.012 mole) of 6-nitro-7-amino-1,2,3,4-dibenzphenazine in 250 ml. of acetic acid was added to a well stirred solution of 7.0 g. (0.10 mole) of sodium nitrite in 10 ml. of concentrated sulfuric acid and 10 ml. of acetic acid. During the diazotization the temperature was held under 20°. The diazonium compound was stable enough to be filtered and dried. Attempts to recrystallize this orange diazonium salt from boiling methanol were unsuccessful. Excess nitrous acid was removed with urea. Upon dropwise addition of a solution of 1.3 g. (0.020 mole) of sodium azide in 100 ml. of water, the azide, 4.0 g. (91%), was formed with evolution of gas. Recrystallization from nitrobenzene below 115° gave golden yellow crystals which gradually turned dark brown to purple without melting. They gave a purple color with concentrated sulfuric acid.

*Anal.* Calcd. for $C_{20}H_{10}N_6O_2$: C, 65.57; H, 2.75; N, 22.94; O, 8.74. Found: C, 65.76; H, 2.77; N, 22.86; O, 8.66.

Additional examples of 6-azido-7-nitroquinoxalines are found in Table II.

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(7) R. Nietzki and A. Schedler, *Ber.*, **30**, 1666 (1897); R. Ruggli and R. Fischer, *Helv. Chim. Acta*, **28**, 1270 (1946).