of a mixture of carbonyl derivatives, m.p. 130–195°, 0.5 g. of which was separated by chromatography on alumina into 0.40 g. (56% based on total products) of diphenylacetaldehyde 2,4-dinitrophenylhydrazone, m.p. 153–155°, showing no depression when mixed with an authentic sample, and 0.07 g. (10%) of the desoxybenzoin 2,4-dinitrophenylhydrazone, m.p. 202–204°, not depressed when mixed with an authentic sample.[27]

The gas evolved, 350 ml. (theory for 1 mole, 246 ml.), was shown to contain carbon dioxide and carbon monoxide (precipitate of metallic silver on shaking the mixture with ammoniacal silver hydroxide).[28] Nitric oxide was present as judged by the fact that the gas turned brown on exposure to air.

**5-Methyl-5-phenyl-3-nitroso-2-oxazolidone.**[2]—The decomposition of this material was carried out as described above. During the decomposition of 5.0 g. (0.024 mole), 410 ml. of gas (corrected to standard conditions) was evolved. This is approximately 75% of theory for one molecular equivalent. The gas proved to be largely nitric oxide. The product was extracted with petroleum ether (30–60°) leaving 310 g. (70.5%) of 5-methyl-5-phenyloxazolidone, m.p. 145–147° (reported[2] 146–147°).

After evaporation of the petroleum ether, the residue was treated with neutral 2,4-dinitrophenylhydrazine reagent. As no precipitate formed on refluxing, there was added 0.5 g. of mercuric sulfate and 2 ml. of concentrated sulfuric acid. On gentle refluxing an orange precipitate formed. After recrystallization from ethyl acetate–methanol 1.96 g. of propiophenone 2,4-dinitrophenylhydrazone, m.p. 186.5–188°, was not depressed when mixed with authentic sample.[29] These facts indicated the presence of 1-phenylpropyne in at least 26% yield.

**4,4-Diphenyl-3-nitroso-2-oxazolidone.**—In the manner previously described 1.00 g. of 4,4-diphenyl-3-nitroso-2-oxazolidone which had been dried *in vacuo* was thermally decomposed. The product was dissolved in ethanol–petroleum ether (30–60°) and cooled. There crystallized 0.81 g. (87%) of 4,4-diphenyl-2-oxazolidone, m.p. 175–177°.

**4,4-Dimethyl-3-nitroso-2-oxazolidone.**—The freshly prepared and dried nitroso compound (20 g., 0.14 mole) was heated to 200°. When the evolution of gas (mostly nitric oxide) was complete, the product was recrystallized from a mixture of ether and petroleum ether (30–60°) at low temperatures. There was obtained 13.5 g. (84%) of 4,4-dimethyl-2-oxazolidone, m.p. 54–56°. From a small amount of material collected in a Dry Ice trap during the decomposition, there was prepared 1.3 g. of isobutyraldehyde 2,4-dinitrophenylhydrazone, m.p. 172–174°.

(27) Reference 13, p. 365.

(28) G. Lunge and H. R. Ambler, "Technical Gas Analysis," Gurney and Jackson, London, 1934, p. 228.

(29) T. Thomson and T. S. Stevens, *J. Chem. Soc.*, 2607 (1932).

COLUMBUS, OHIO

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[CONTRIBUTION FROM THE NOYES CHEMICAL LABORATORY, UNIVERSITY OF ILLINOIS]

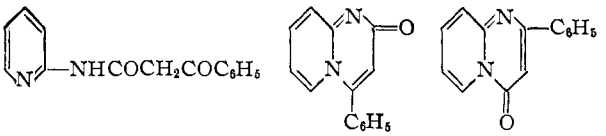
# The Action of Alkali on Bromopyridopyrimidones

BY ROGER ADAMS AND IRWIN J. PACHTER

RECEIVED MAY 27, 1953

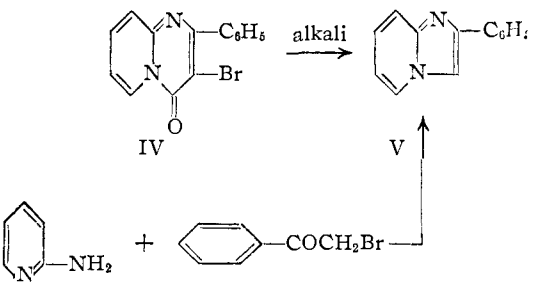
2-Substituted-3-bromo-4H-pyrido[1,2-a]pyrimidin-4-ones undergo rearrangement with ring contraction upon treatment with dilute alkali to yield imidazo[1,2-a]pyridine derivatives.

In a previous communication,[1] comparison of the ultraviolet absorption spectra of several pyridopyrimidones led to the conclusion that benzoylacetamidopyridine (I) does not cyclize in concentrated sulfuric acid to give 4-phenyl-2H-pyrido[1,2-a]pyrimidin-2-one (II), but instead rearranges and yields 2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one (III). A new reaction of some compounds of this series has now been discovered which provides chemical evidence to confirm this conclusion.



I II III

When 3-bromo-2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one (IV), obtained upon bromination of III with N-bromosuccinimide,[1] was heated with dilute aqueous sodium hydroxide, it was converted in 86% yield to a bromine-free base which was identical with 2-phenylimidazo[1,2-a]pyridine (V) prepared from 2-aminopyridine and phenacyl bromide.[2] The formation of V in this ring contraction reaction rather than the known 3-phenyl isomer[3] establishes unequivocally that the product obtained upon cyclization of I is III rather than II.



IV V

When 2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one is brominated with N-bromosuccinimide, an excellent yield of monobromo product results. This appears to be the 3-bromo-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one and not the possible isomeric 2-bromomethyl-4H-pyrido[1,2-a]pyrimidin-4-one. This conclusion is based on the fact that the 3-position in pyridopyrimidin-4-ones is highly reactive. The ease of bromination with NBS of the 2-phenyl-4H-pyrido[1,2-a]pyrimidin-4-one and the corresponding 2-chloro compound,[4] as reported in this communication, serves as an illustration. Khitrik[5] has demonstrated that nitration of the 2-methyl derivative results in substitution in the 3-position. It follows, therefore, that if the compound in hand were the 2-bromomethyl-4H-pyrido[1,2-a]pyrimidin-4-one, further bromination with NBS should convert the monobromo deriva-

(1) R. Adams and I. J. Pachter, THIS JOURNAL, **74**, 5491 (1952).

(2) A. E. Chichibabin, *Ber.*, **59**, 2048 (1926).

(3) Y. A. Goldfarb and M. S. Kondakova, *J. Applied Chem. (U.S.S.R.)*, **15**, 151 (1942) [*C. A.*, **37**, 2380 (1943)].

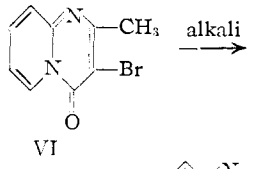
(4) H. R. Snyder and M. M. Robison, THIS JOURNAL, **74**, 4910 (1952); ref. 1.

(5) S. N. Khitrik, *J. Gen. Chem. (U.S.S.R.)*, **9**, 1109 (1939).

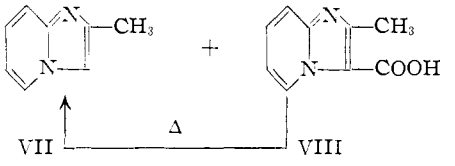
tive to the 3-bromo-2-bromomethyl analog. However, the monobromo derivative fails to react with NBS.

3-Bromo-2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one (VI) also underwent a reaction of the same type as the phenyl derivative when treated with alkali. In this case, however, two products were obtained: 2-methylimidazo[1,2-a]pyridine (VII) and 2-methylimidazo[1,2-a]pyridine-3-carboxylic acid (VIII). The former, synthesized from 2-aminopyridine and bromoacetone, has been reported as a liquid[2]; in this investigation it was obtained as a crystalline solid, m.p. 45–46°, the methiodide of which corresponds in melting point to that prepared by other investigators.[6] Compound VIII evolved gas upon melting and gave VII. When treated with alkali under conditions which caused conversion of VI to VII, compound VIII did not yield VII but was recovered unchanged. The acid VIII is therefore not an intermediate in the conversion of VI to VII.

Compound VIII was isolated directly from the alkaline treatment of VI as the potassium salt. The salt had the same infrared spectrum (Nujol mull) as the salt made by treating VIII with one molecule of potassium hydroxide. This eliminates the possibility that the potassium salt as originally isolated is that of a reaction intermediate different from VIII, but which cyclizes to give VIII upon acidification.

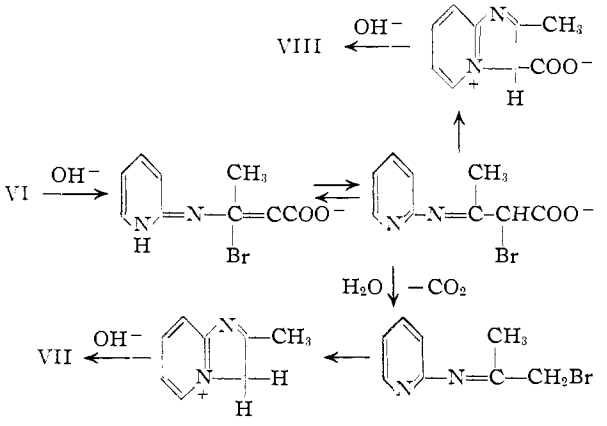



VI

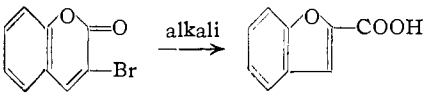



VII VIII

It is suggested that the products may be formed as illustrated.



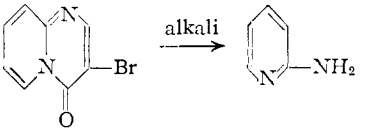

Related rearrangements of nitrogen heterocycles have not been reported. Perkin's conversion of 3-bromocoumarin (IX) to coumarilic acid (X) in alkali[7] bears resemblance to the conversion of VI to VIII. In this case, however, there appears to be no tendency for the intermediate to lose the carboxyl group in the presence of alkali with formation of 2,3-benzofuran.




IX X

Bromination of 4H-pyrido[1,2-a]pyrimidin-4-one with NBS is assumed to give the 3-bromo derivative. This is deduced on the basis of arguments similar to those presented for the structure of the mono bromo derivative of the 2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one. If the first bromine enters the 2-position, the molecule should be susceptible to further bromination with NBS to the 2,3-dibromo compound. This does not occur.

3-Bromo-4H-pyrido[1,2-a]pyrimidin-4-one (XI) did not behave in the same manner as the 2-substituted compounds when treated with alkali. The basic hydrolysis product proved to be 2-aminopyridine. Its formation is undoubtedly to be ascribed to increased susceptibility to hydrolytic attack of the 2-position of XI, or of the corresponding position of some hydrolysis intermediate derived from XI.




XI

**Acknowledgment.**—The authors are indebted to Mrs. Esther Fett, Mr. J. Nemeth and Mrs. Katherine Pih for the microanalyses.

## Experimental[8]

**Action of Alkali on 3-Bromo-2-phenyl-4H-pyrido[1,2-a]-pyrimidin-4-one (IV).**—A mixture of 0.500 g. of the bromo compound[1] IV and 15 ml. of 5% aqueous sodium hydroxide was heated under reflux for 2 hours.[9] The oil which formed during the reaction solidified upon cooling. A small additional yield of product was obtained by extraction of the mother liquor with chloroform followed by evaporation of the chloroform solution to dryness. The combined solids were recrystallized from cyclohexane to give 0.276 g. (86%) of 2-phenylimidazo[1,2-a]pyridine (V), m.p. 136–137°.

The same compound, m.p. 136–137°, was prepared from 2-aminopyridine and phenacyl bromide as described by Chichibabin.[2] No depression of melting point was observed upon admixture of the two samples.

**3-Bromo-2-methyl-3H-pyrido[1,2-a]pyrimidin-4-one (VI).**—A mixture of 8.0 g. of 2-methyl-4H-pyrido[1,2-a]pyrimidin-4-one,[1,10] 9.5 g. of N-bromosuccinimide and 70 ml. of carbon tetrachloride was heated under reflux for 30 minutes with stirring. The mixture was cooled and filtered. The crystalline precipitate was washed with water and recrystallized from ethanol to give 10.2 g. (85%) of VI, m.p. 181.5–182.5°. The carbon tetrachloride mother liquor was washed with water and evaporated to dryness to yield an additional 0.43 g. of crude product.

*Anal.* Calcd. for $C_9H_7BrN_2O$: C, 45.21; H, 2.95. Found: C, 45.29; H, 3.11.

(6) J. Takahashi and G. Shibasaki, *J. Pharm. Soc. Japan*, **69**, 496 (1949); *C. A.*, **44**, 4474 (1950).

(7) W. H. Perkin, *J. Chem. Soc.*, **24**, 37 (1871).

(8) All melting points are corrected.

(9) A quantity of unchanged starting material was isolated in an experiment where heating was continued for only 45 minutes.

(10) C. R. Hauser and M. J. Weiss, *J. Org. Chem.*, **14**, 453 (1949).

**Action of Alkali on 3-Bromo-2-methyl-4H-pyrido[1,2-a]-pyrimidin-4-one (VI).**—A mixture of 8.00 g. of bromo compound (VI) was heated under reflux with 80 ml. of 7% aqueous potassium hydroxide for 45 minutes. The pale yellow solution was cooled. Upon addition of 30 g. of potassium carbonate, an oil separated. The mixture was extracted with five 50-ml. portions of ether. The ethereal extract was dried over potassium carbonate and then treated with hydrogen bromide. A solid separated. The ethereal supernatant liquid was decanted and the residual solid was stirred with 20 ml. of acetone and filtered. The dry hydrobromide of 2-methylimidazo[1,2-a]pyridine (VII) weighed 3.84 g. (54%). After recrystallization from acetone–chloroform, the m.p. was 197–198°.

*Anal.* Calcd. for $C_8H_9BrN_2$: C, 45.99; H, 4.25. Found: C, 45.25; H, 4.27.

The hydrobromide of 2-methylimidazo[1,2-a]pyridine was treated with excess cold dilute potassium hydroxide. The resulting solution was extracted with several portions of ether. The ethereal extract was dried over potassium carbonate and distilled. 2-Methylimidazo[1,2-a]pyridine (VII) boiled at 262–263° at atmospheric pressure. It solidified when scratched and, upon recrystallization from ether, melted at 45–46°. It is very hygroscopic.

*Anal.* Calcd. for $C_8H_8N_2$: C, 72.69; H, 6.10; N, 21.19. Found: C, 71.77; H, 6.17; N, 20.56.

Compound VII rapidly forms a methiodide, m.p. 191–192°, when treated with methyl iodide at room temperature.

*Anal.* Calcd. for $C_9H_{11}IN_2$: C, 39.43; H, 4.05; N, 10.22. Found: C, 39.57; H, 4.46; N, 9.91.

The alkaline mother liquor from the hydrolysis of VI was saturated with carbon dioxide and evaporated to dryness. The residue was extracted with several portions of boiling absolute ethanol. Evaporation of the ethanol, extraction of the resulting residue with ethanol–isopropyl alcohol and re-evaporation to dryness yielded 2.15 g. (30%) of the potassium salt of VIII. A 10 *N* sulfuric acid solution was added dropwise to a solution of 1.20 g. of the potassium salt in 50 ml. of absolute ethanol until the solution was neutral to congo red paper. The resulting mixture of liquid and solid was heated to boiling and filtered. The precipitate was extracted with two 25-ml. portions of boiling absolute ethanol. The ethanolic solutions were combined, concentrated and cooled to give 0.69 g. of 2-methylimidazo[1,2-a]-pyridine-3-carboxylic acid (VIII). The compound decomposed at about 185° with evolution of gas. The decomposition point is largely dependent upon the rate of heating.

*Anal.* Calcd. for $C_9H_8N_2O_2$: C, 61.36; H, 4.58; N, 15.90. Found: C, 61.33; H, 4.31; N, 15.81.

Approximately 0.1 g. of VIII was heated above the decomposition temperature until gas evolution ceased. The residual liquid was dissolved in ether and treated with hydrogen bromide. A solid separated. The ethereal solution was decanted and the residual solid was washed with a little cold acetone and then recrystallized from acetone. The product melted at 197–198°. Its melting point was not depressed when mixed with a sample of the hydrobromide of VII prepared as described above.

**3-Bromo-2-chloro-4H-pyrido[1,2-a]pyrimidin-4-one.**—A mixture of 3.3 g. of 2-chloro-4H-pyrido[1,2-a]pyrimidin-4-one,[4] 40 ml. of carbon tetrachloride and 3.5 g. of NBS was heated under reflux with stirring for 30 minutes. The 3-bromo compound crystallized from solution as it was formed. The mixture was filtered and the product was washed with water, dried and concentrated to give a small additional yield. The combined solids were recrystallized from chloroform–ethanol to yield 4.3 g. (90%) of colorless needles, m.p. 225–228°.

*Anal.* Calcd. for $C_8H_4BrClN_2O$: C, 37.02; H, 1.55. Found: C, 37.26; H, 1.54.

**3-Bromo-4H-pyrido[1,2-a]pyrimidin-4-one (XI).**—To 40 ml. of carbon tetrachloride was added 1.46 g. of pyridopyrimidone and 1.92 g. of N-bromosuccinimide. The mixture was heated under reflux with stirring for 30 minutes. The product was isolated as described for compound VI. Upon recrystallization from ethanol there was obtained 1.36 g. (60%) of IX, m.p. 133–134°.

*Anal.* Calcd. for $C_8H_5BrN_2O$: C, 42.69; H, 2.24. Found: C, 42.69; H, 2.24.

**Action of Alkali on 3-Bromo-4H-pyrido[1,2-a]pyrimidin-4-one (XI).**—A mixture of 0.98 g. of IX and 15 ml. of 5% aqueous sodium hydroxide was heated under reflux for 45 minutes. The solution was cooled and extracted with ether. The ethereal extract was dried over potassium carbonate and evaporated to dryness. The residue, which possessed the odor of 2-aminopyridine, solidified. After two recrystallizations from cyclohexane containing a little carbon tetrachloride, it melted at 56° and its melting point was not depressed upon admixture with authentic 2-aminopyridine.

URBANA, ILLINOIS

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY OF THE UNIVERSITY OF PENNSYLVANIA]

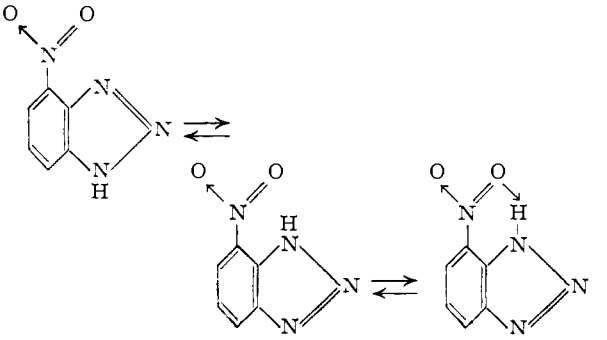
# Restriction of Tautomerism in the Triazole System by Hydrogen Bonding. The Case of 4(7)-Nitrobenzotriazole[1]

BY NORMAN L. MILLER AND E. C. WAGNER

RECEIVED SEPTEMBER 2, 1953

Comparative study of the isomeric nitrobenzotriazoles showed the vicinal isomer, 4(7)-nitrobenzotriazole, to be the more volatile, the more rapidly reduced polarographically, the weaker acid, and to be less associated in solution. These characteristics are attributed to existence of chelation in 4(7)-nitrobenzotriazole; as a consequence there is a corresponding restriction of the tautomerism of the benzotriazole system. The results of catalytic hydrogenation did not (as in earlier studies of analogous systems) parallel those of polarographic reduction, indicating the need for caution in the interpretation of results obtained for such systems by catalytic hydrogenation. The ultraviolet absorptions of the two nitrobenzotriazoles likewise proved to be non-committal with respect to chelation in the vicinal isomer.

This paper reports the results of the extension to the 1,2,3-triazole system, represented by the isomeric nitrobenzotriazoles, of the experimental methods used previously to secure inferential evidence for the restriction of tautomerism in other and analogous systems[2–4] owing to involvement of the labile hydrogen in chelation. Of the two nitrobenzotriazoles the 4(7)-nitro isomer has a structure that appears to permit chelation



(1) Paper constructed from the Ph.D. thesis of Norman L. Miller, University of Pennsylvania, 1953.

(2) M. E. Runner, M. L. Kilpatrick and E. C. Wagner, THIS JOURNAL, **69**, 1406 (1947).

(3) J. L. Rabinowitz and E. C. Wagner, *ibid.*, **73**, 3030 (1951).

(4) M. E. Runner and E. C. Wagner, *ibid.*, **74**, 2529 (1952).