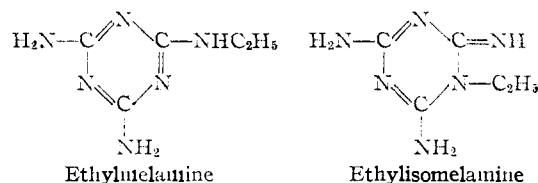


pronounced and basicity is decreased until the completely substituted hexa- β -hydroxyethylmelamine is a weaker base than melamine itself.

It is also interesting to note that the effect of the hydroxyl group is decreased as it is further removed from the basic group. This was demonstrated in the case of the alkanolamines by measuring the dissociation constant of γ -hydroxypropylamine. This amine was found to be much more strongly basic than ethanolamine⁵ (7.6×10^{-7}). While not as marked, a similar effect is shown in the symmetrically substituted tri-alkanolmelamines. N^2, N^4, N^6 -Tri- β -hydroxyethylmelamine is a weaker base than N^2, N^4, N^6 -tri- γ -hydroxypropylmelamine; and N^2, N^4, N^6 -trimethylolmelamine, although it may be abnormal in some respects, is a much weaker base than either and, in fact, weaker than melamine itself. Thus the effect of the hydroxyl group becomes increasingly pronounced as its position on the alkyl substituent is moved toward the nucleus.

A reduction in the basicity of melamine is also caused by a phenyl group on amino nitrogen, as shown by the dissociation constant of phenylmelamine.

Substitution on Ring Nitrogen.—It has been recognized that the substituted isomelamines are stronger bases than the substituted normal melamines, but the magnitude of the difference has not been known. Measurement of the dissociation constants of the isomeric ethylmelamines, each of which is represented below in the form of one of the possible resonance structures shows that the basicities in this case differ by a factor of 10^5 , and that the basicity of this isomelamine compares to those of the strongest aliphatic amines. These data substantiate the



conclusion^{7,8} that melamine itself, which might conceivably exist in the normal or iso form, exists in solution in the weakly basic normal form.

Replacement of Amino Nitrogen.—Replacement of one of the amino groups of melamine by another group results in a decrease in basicity, perhaps due to the reduction in symmetry and the change in resonance. The replacement of one of the amino groups by hydrogen produces a substantial reduction in basicity, and the replacement of two amino groups by hydrogen decreases the basicity to such an extent that it could not be measured by the method employed. The weakly basic character of acetoguanamine indicates that an alkyl group in place of the amino group produces a similar effect, although the reduction is not as great as that produced by replacement with hydrogen. This might be expected in view of the fact that the electronegative character of hydrogen is more pronounced than that of alkyl groups. A similar reduction in basicity is also produced by the replacement of an amino group with an alkoxy group. Thus 2-allyloxy-4,6-diamino-*s*-triazine is a very weak base and the basicity of 2-amino-4,6-dimethoxy-*s*-triazine is too weak to be measured by the method used.

(7) I. M. Klotz and T. Askounis, *THIS JOURNAL*, **69**, 801 (1947).

(8) G. Costa, R. C. Hirt and D. J. Salley, *J. Chem. Phys.*, **18**, 434 (1950).

STAMFORD, CONNECTICUT

RECEIVED JULY 14, 1950

[CONTRIBUTION FROM THE EXPERIMENTAL BIOLOGY AND MEDICINE INSTITUTE, NATIONAL INSTITUTES OF HEALTH, PUBLIC HEALTH SERVICE, FEDERAL SECURITY AGENCY]

A New Reduction Product of Brucine

BY STEPHEN P. FINDLAY

It has been discovered that the amide linkage of brucine is only partially reduced by lithium aluminum hydride, a new reduction product, dehydrobrucidine, having been obtained. Other strychnos alkaloids, strychnine, α -colubrine and β -colubrine, as well as the dihydro derivative of brucine, are reduced in the expected manner with this reagent. The suspected identity of the ring structure of the colubrines with that of strychnine and brucine has been established.

In connection with an investigation of the chemistry of hydroxyapoucinidine¹ it was necessary to prepare considerable quantities of brucidine (V, $R_1 = R_2 = \text{OCH}_3$), which is obtained by the electrolytic reduction of brucine² (I). This procedure is, however, tedious and the yields are not especially good. The finding that acylated amines are reducible in good yield to more highly substituted amines by means of the versatile lithium aluminum hydride reagent^{3,4} aroused the hope that a practical method for obtaining brucidine was at

(1) H. Leuchs and F. Kröhnke, *Ber.*, **64**, 1307 (1931).

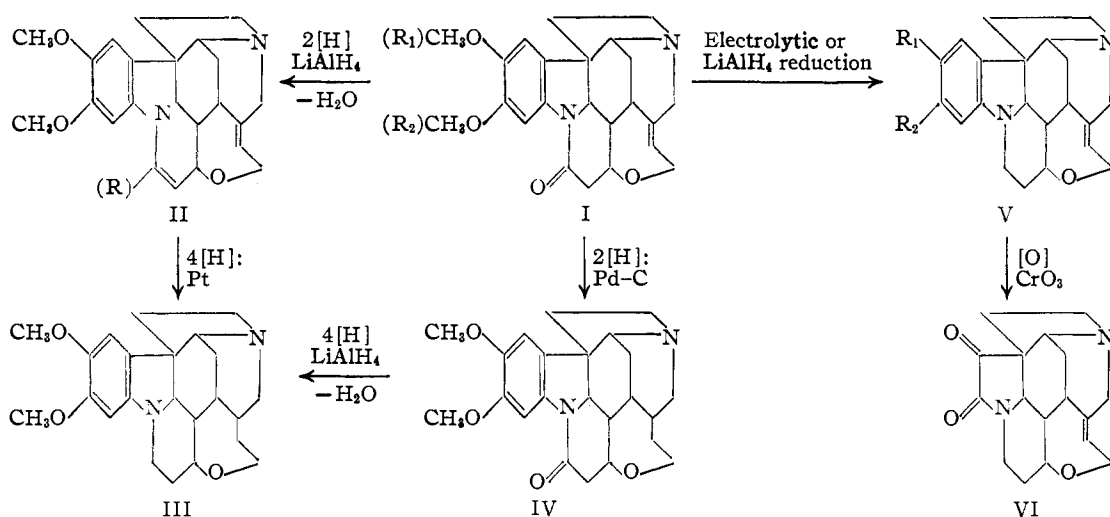
(2) J. M. Gulland, W. H. Perkin and R. Robinson, *J. Chem. Soc.*, 1627 (1927).

(3) A. Uffer and E. Schlittler, *Helv. Chim. Acta*, **31**, 1397 (1948).

(4) J. Ehrlich, *THIS JOURNAL*, **70**, 2286 (1948).

last available. This expectation was justified by the later success of Karrer in converting strychnine (I, $R_1 = R_2 = \text{H}$) to strychnidine (V, $R_1 = R_2 = \text{H}$) with this reagent.⁵ It is another instance of the unpredictability of chemical reactions that brucine is not thus converted to brucidine but instead is reduced only partially. The product contains two hydrogen atoms fewer than brucidine ($\text{C}_{23}\text{H}_{28}\text{N}_2\text{O}_3$) and has therefore been named dehydrobrucidine. It melts higher than brucine (178°) and lower than brucidine (203°) at 188 – 189° . It could not be identified with any known derivative of brucine and apparently has not been described before.

(5) P. Karrer, C. H. Eugster and P. Waser, *Helv. Chim. Acta*, **32**, 2381 (1949).



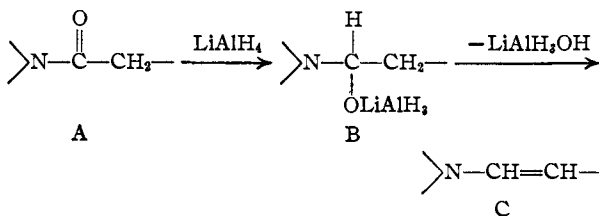
Because of its composition it was inferred that dehydrobrucidine had structure II ($R = H$), in agreement with which is the observation that it absorbs nearly two equivalents of catalytic hydrogen to give a corresponding yield of dihydrobrucidine (III).⁶ Insofar as they indicate the absence of the *N*-alkyl-5,6-dimethoxydihydroindole structure of brucidine, the color reactions of dehydrobrucidine also favor structure II. Brucidine (V, $R_1 = R_2 = \text{OCH}_3$) and dihydrobrucidine (III) are oxidized by acidic dichromate or ferric chloride to green products which in hue and intensity of color are nearly indistinguishable, whilst dehydrobrucidine is converted to products having a blue-green coloration. It is also worth noticing that from the reaction of brucine with methylmagnesium iodide Wieland and Hölischer isolated a more highly unsaturated compound, which they called the methiodide of desoxymethylbrucine (II, $R = \text{CH}_3$).⁷

Because of its relative instability, well-defined derivatives of the new base were difficult to obtain. Treated in ethyl acetate solution with excess methyl iodide it appeared to undergo oxidation simultaneously with methiodide formation. When its solution in methanol was treated with one equivalent of methyl iodide, a somewhat more satisfactory derivative was obtained. The hydrochloride, dihydrochloride and picrate salts precipitated with solvent of crystallization; they were unstable in solution.

This appears to be the first recorded instance in which lithium aluminum hydride has effected a partial reduction of the kind described. To obtain, if possible, an explanation of this abnormality, dihydrobrucine⁷ (IV) and the rare strychnos bases, α -colubrine⁸ (I, $R = H$, $R_2 = \text{OCH}_3$) and β -colubrine⁸ (I, $R_1 = \text{OCH}_3$, $R_2 = H$), were reduced with this reagent. The products were the expected ones: dihydrobrucidine (III), α -colubridine (V, $R_1 = H$, $R_2 = \text{OCH}_3$), and β -colubridine (V, $R_1 = \text{OCH}_3$, $R_2 = H$), respectively. It seems, therefore, that in this reaction brucine is peculiar,

not merely among amides generally, but even among the strychnos alkaloids.

It is worth noting that dehydrobrucidine (II, $R = H$) may be considered the dehydration product of an intramolecular aldehyde ammonia. Its formation can then be accounted for somewhat as follows



The exceptional behavior of brucine may be attributed to the fact that the intermediate structure (B) undergoes an elimination reaction to dehydrobrucidine (partial structure C) in preference to further reduction.

α -Colubridine and β -colubridine were readily obtained by the action of lithium aluminum hydride on the corresponding colubrines. These two bases had not been isolated and characterized hitherto. They have nearly the same melting point (170 – 172°) and, like brucidine, separate from methanol with solvent of crystallization. Their color reactions are distinctive and resemble those of solutions obtained by heating one or other of the colubrines in hydrochloric acid with amalgamated zinc.⁹ Like strychnidine and brucidine¹⁰ α - and β -colubridine are oxidized by chromic acid to diketonucidine (VI), and hence there is no longer any doubt¹¹ concerning the identity of the ring structures of the colubrines with those of strychnine and brucine.¹²

Acknowledgment.—The author is indebted to the Microanalytical Laboratory, directed by Mr. William C. Alford of this Institute, for the analytical data reported herein.

(6) O. Achmatowicz, R. C. Fawcett, W. H. Perkin and R. Robinson, *J. Chem. Soc.*, 1769 (1930).

(7) H. Wieland and F. Hölischer, *Ann.*, **500**, 70 (1951).

(8) K. Warnat, *Helv. Chim. Acta*, **14**, 997 (1931).

(9) H. L. Holmes and R. Robinson, *J. Chem. Soc.*, 910 (1946).

(10) H. Leuchs and W. Wegener, *Ber.*, **63B**, 2215 (1930); H. Leuchs and H. S. Overberg, *ibid.*, **64A**, 1007 (1931).

(11) T. A. Henry, "The Plant Alkaloids," The Blakiston Company, Philadelphia, Penna., 1949, p. 560.

(12) A. Hanssen, *Ber.*, **18**, 1917 (1885).

Experimental¹³

Dehydrobrucidine.—Dry, powdered brucine (24 g.) was placed in a Soxhlet extractor¹⁴ and reduced with a solution of 37 ml. of 1.8 *M* ethereal lithium aluminum hydride in 800 ml. of dry ether. After four days the refluxing reaction mixture was decomposed slowly with a mixture of 30 ml. of ethyl acetate and 200 ml. of ether. Nearly three-quarters of the solvent was distilled out, the white precipitate dissolved in chloroform (300 ml.), and 60 ml. of 90% alcohol added. The boiling solution was mixed with Super-Cel and filtered. The residue was leached once with boiling chloroform (200 ml.). The combined filtrates were dried (Na₂SO₄) and the solvents removed *in vacuo*. The red, oily residue was dissolved in 65 ml. of hot methanol. Rosettes of prisms separated from the cold solution: 12.5 g. (54%), m.p. 186.5–188.5°. From the mother liquors a second crop of 3.8 g., m.p. 185–186°, was obtained; total yield 71%. After one or two recrystallizations from methanol the base was pure; m.p. 187.5–189°. It crystallizes from methanol in irregular flakes and prisms, from ethyl acetate as stout prisms. It is quite soluble in chloroform and benzene, somewhat less so in alcohols, and still less so in ligroin. In alcohol the base mutarotates; initially it had $[\alpha]^{20}_D +242^\circ$ (*c*, 0.9); after 24 hours, $[\alpha]^{20}_D +210^\circ$.

Anal. Calcd. for C₂₃H₂₆N₂O₃: C, 72.9; H, 6.93; N, 7.40; CH₃O, 16.4. Found: C, 72.9; H, 6.85; N, 7.25; CH₃O, 16.6.

When a trace of dichromate was added to dehydrobrucidine in dilute sulfuric acid solution a chlorophyll green coloration resulted which changed rapidly to opaque bluish-green. Under the same conditions both brucidine and dihydrobrucidine yielded a permanent chlorophyll green. When its solution in dilute hydrochloric acid was treated with ferric chloride solution, a bluish-black coloration was obtained. In the same circumstances the other two bases furnished greenish-black colors. When their solutions in dilute hydrochloric acid were treated with a trace of sodium nitrite, dehydrobrucidine gave a deep green fading at once to yellow and then turning red, brucidine gave a deep green which quickly became pale greenish-yellow, and dihydrobrucidine gave a deep green which faded immediately to yellow and then became orange. Its solution in either alcoholic salicylic or alcoholic tartaric acid gradually turned pink but gave no crystals.

Dehydrobrucidine hydrochloride was obtained by chilling a mixture of 0.20 g. of base and 1.0 ml. of 0.50 *N* hydrochloric acid to 0°. The voluminous precipitate of asbestos-like crystals was crystallized twice from water.

Anal. Calcd. for C₂₃H₂₆N₂O₃·HCl·2H₂O: C, 61.2; H, 6.93; Cl, 7.87. Found: C, 61.3; H, 6.96; Cl, 8.11.

Dehydrobrucidine dihydrochloride separated when dry hydrogen chloride was admitted to a solution of the base in 99% alcohol. The salt was purified from this solvent: small prisms, m.p. 287° *in vacuo*. The salt soon turns red. Dried *in vacuo* at 110° it suffered the weight loss, 18.4% (theory for 3.5 molecules of water and one of hydrogen chloride, 19.4%).

Anal. Calcd. for C₂₃H₂₆N₂O₃·2HCl·3½H₂O: C, 53.7; H, 6.87; Cl, 13.8; CH₃O, 12.1. Found: C, 53.9; H, 7.32; Cl, 13.5; CH₃O, 11.7.

Dehydrobrucidine picrate was prepared from stoichiometric quantities of base and picric acid and purified from alcohol: small orange prisms, m.p. about 185°. Intelligible analytical data for this compound were not obtained. Treated in ethyl acetate solution with excess methyl iodide, dehydrobrucidine furnished a precipitate which was purified from methanol: white, very fine needles, m.p. above 400°. The analytical data suggest that methiodide formation was accompanied by absorption of one oxygen atom.

Anal. Calcd. for C₂₄H₂₈IN₂O₄: C, 53.73; H, 5.45; I, 23.64; N, 5.22. Found: C, 53.86; H, 5.63; I, 23.75; N, 5.20.

When stoichiometric quantities of base and methyl iodide were combined in methanol at room temperature, a white precipitate was obtained almost immediately. It was recrystallized twice from methanol from which it separated as

gossamer aggregates of long, very fine needles: m.p. 297° *in vacuo*. It closely resembled the product described above but had a composition nearer to that of dehydrobrucidine methiodide.

Anal. Calcd. for C₂₄H₂₈IN₂O₃: C, 55.4; H, 5.61; I, 24.4. Found: C, 55.1; H, 6.00; I, 24.1.

Dihydrobrucine.⁶—A mixture of palladium chloride (0.30 g.), activated charcoal (2.0 g.) and water (500 ml.) was shaken with hydrogen until no more was absorbed. A solution of brucine (10 g.) in 20% acetic acid (160 ml.) was added and the mixture shaken 24 hours. The consumption of hydrogen was 112% of the theoretical quantity. The catalyst-free solution was made alkaline with carbonate and extracted with ethyl acetate. Removal of the solvent from the dried extract afforded a gum which slowly crystallized. One recrystallization from a small volume of ethyl acetate furnished 7.5 g. of product, m.p. 180–182° (reported 179–181°).

Dihydrobrucidine (a) from Dehydrobrucidine.—A solution of dehydrobrucidine (4.5 g.) in 200 ml. of methanol was hydrogenated for 24 hours with 0.10 g. of platinum oxide. The hydrogen consumption was 82% of the theoretical quantity for two moles. The pink, catalyst-free solution was concentrated *in vacuo* to a red gum. This was dissolved in hot acetone and the solution cooled: 1.7 g. of nearly colorless flakes, m.p. 170–172°. From the mother liquors a second crop (0.7 g.) and a small third crop were obtained.

(b) **From Dihydrobrucine.**—Dihydrobrucine (7.5 g.) was reduced with lithium aluminum hydride in 47% yield according to the procedure for the preparation of dehydrobrucidine. The product separated from acetone as yellowish-brown rods: m.p. 172–172.5° (reported, 172–172.5°), $[\alpha]^{21}_D +10.7 \pm 0.6^\circ$ (*c*, 0.98). When mixed with the product from the catalytic hydrogenation (a), its melting point was not depressed. When the product from either reduction was treated in methanol with one equivalent of methyl iodide, **dihydrobrucidine methiodide** separated as colorless rods, m.p. 302° *in vacuo* (reported 298°).

Anal. Calcd. for C₂₂H₂₄IN₂O₃: C, 55.1; H, 6.35. Found: C, 55.3; H, 6.38.

α -Colubrine Hydrochloride.—Impure α -colubrine hydrochloride¹⁵ was purified from water. Heated *in vacuo* at 117° the salt lost 11.6% of its weight. Calcd. for C₂₂H₂₄N₂O₃·HCl·3H₂O: H₂O, 11.9.

Anal. Calcd. for C₂₂H₂₄N₂O₃·HCl: C, 65.8; H, 6.28. Found: C, 65.8; H, 6.53.

α -Colubrine, generated from the purified hydrochloride, crystallized from ethyl acetate as pyramids. As in the case of strychnine, the melting point depends upon the rate of heating. In an open tube, the base melted as high as 189–193° with decomposition; *in vacuo* at 192.5–195° with little or no decomposition (reported 184°). It had $[\alpha]^{20}_D -72.4^\circ$ (*c*, 0.9) (reported –76.5°, 80% alcohol⁸).

Anal. Calcd. for C₂₂H₂₄N₂O₃: C, 72.6; H, 6.65. Found: 72.6; H, 6.78.

α -Colubridine.— α -Colubrine (1.6 g.) was converted to crude α -colubridine in about 90% yield according to the procedure for the preparation of dehydrobrucidine. The pure base separated from methanol as large rhombic laths which lost methanol of crystallization when dried cautiously *in vacuo*. It sublimed about 120° (1 min.). The dried base had m.p. 170–172° and $[\alpha]^{20}_D -18^\circ$ (*c*, 0.9).

Anal. Calcd. for C₂₂H₂₈N₂O₂·CH₃OH: C, 72.2; H, 7.90; N, 7.32. Found: C, 72.3; H, 7.74; N, 7.48. Calcd. for C₂₂H₂₄N₂O₂: C, 75.39; H, 7.48; CH₃O, 8.96. Found: C, 75.68; H, 7.64; CH₃O, 8.98.

α -Colubridine methiodide, prepared from stoichiometric amounts of α -colubridine and methyl iodide, was purified from methanol: very fine, colorless needles, m.p. 322–323° *in vacuo*.

Anal. Calcd. for C₂₃H₂₈IN₂O₂: C, 56.10; H, 5.94; I, 25.8. Found: C, 56.29; H, 6.13; I, 26.0.

β -Colubrine Sulfate.—Impure β -colubrine sulfate¹⁵ was purified from water from which it separated as colorless needles.⁸ It was dried at 110° (1 mm.); weight loss 14.8%. Calcd. for (C₂₂H₂₄N₂O₃)₂·H₂SO₄·8H₂O, 14.8.

(13) All melting points are corrected and all measurements of optical rotation are for solutions in 95% alcohol.

(14) R. P. Nyström and W. G. Brown, *THIS JOURNAL*, **69**, 1197 (1947).

(15) Samples of α -colubrine hydrochloride and β -colubrine sulfate were kindly provided by Hoffmann-La Roche & Co., A.-G., Basel.

Anal. Calcd. for $(C_{22}H_{24}N_2O_3)_2 \cdot H_2SO_4$: C, 63.9; H, 6.09. Found: C, 63.5; H, 6.26.

β -Colubrine, recovered from the purified sulfate, was crystallized from ethyl acetate, from which it separated slowly as large, rhombic tablets, m.p. 219.5–220.5°, $[\alpha]^{20}_D -104^\circ$ (*c*, 1.1) (reported -108° , 80% alcohol⁸).

Anal. Calcd. for $C_{22}H_{24}N_2O_3$: C, 72.6; H, 6.65. Found: C, 72.3; H, 6.86.

β -Colubridine.— β -Colubrine (1.0 g.) was reduced with lithium aluminum hydride, according to the procedure for dehydrobrucidine, to β -colubridine (80% yield of crude product). Purified from methanol, it consisted of faintly yellow aciculae containing methanol of crystallization. It sublimed about 135° (1 mm.); m.p. 170–171.5°, $[\alpha]^{21}_D -41^\circ$ (*c*, 0.9).

Anal. Calcd. for $C_{22}H_{26}N_2O_2$: C, 75.4; H, 7.48; CH_3O , 8.96. Found: C, 75.3; H, 7.69; CH_3O , 8.92.

β -Colubridine methiodide was prepared in and purified from methanol using stoichiometric amounts of base and methyl iodide: slender, faintly yellow prisms, m.p. 309° *in vacuo*.

Anal. Calcd. for $C_{23}H_{29}IN_2O_2$: C, 56.10; H, 5.94; I, 25.8. Found: C, 56.24; H, 6.19; I, 25.6.

Diketonucidine (a) from α -Colubridine.¹⁶— α -Colubridine (0.59 g.) was dissolved in water (8.7 ml.) and sulfuric acid (0.70 ml., sp. gr. 1.84), and the cold mixture treated with two-thirds of a solution of chromium trioxide (0.77 g.) in

water (3.1 ml.). The dark reddish-purple salt which separated became yellowish and gradually dissolved as the mixture was warmed. After heating 35 minutes at 65–70° with occasional stirring the remainder of the aqueous chromium trioxide was added slowly, and heating maintained an additional 30 minutes. The hot mixture was made strongly ammoniacal and filtered from precipitated chromium hydroxide. The residue was leached once with hot water. The red filtrates were extracted with chloroform (4 × 50 ml.). The reddish-brown residue recovered from the extracts was converted to the perchlorate salt and decolorized with charcoal. Recovered from the perchlorate, the base was crystallized once from alcohol: 50 mg. of stout tan prisms, m.p. 268–271°; mixed m.p. with authentic diketonicidine, 267.5–270°.

(b) From β -Colubridine.—In similar manner β -colubridine (0.34 g.) was converted to diketonicidine: 30 mg., m.p. 263–266°; methiodide, m.p. 315° *in vacuo*; $[\alpha]^{20}_D +82^\circ$ (*c*, 0.7).

Color Reactions of α - and β -Colubridine.³—When ferric chloride was added to α -colubridine in 0.1 *N* hydrochloric acid, a crimson coloration was produced which changed immediately to orange and then to yellow. Under the same conditions β -colubridine gave an orange-red color. When a trace of potassium dichromate was added to a solution of α -colubridine in dilute sulfuric acid, the solution acquired a purplish-red color which slowly underwent a transition to green. β -Colubridine gave a red color soon changing to yellowish-brown under these conditions.

(16) Cf. H. Leuchs and H. S. Overberg, *Ber.*, **64**, 1009 (1931).

BETHESDA 14, MD.

RECEIVED NOVEMBER 24, 1950

[CONTRIBUTION FROM THE RESEARCH LABORATORIES OF PARKE, DAVIS & CO.]

Arylaminoheterocycles. VI. Trisubstituted Pyrimidines

BY MARIE-JO LANGERMAN AND C. K. BANKS¹

The preparation and properties of a number of 2,4,6-trisubstituted pyrimidines are reported.

As an extension of a previous investigation concerning 2-amino-4-arylamino-pyrimidines² it was considered of interest to prepare some trisubstituted pyrimidines which would be isosteric with several groups of symmetrical triazines of pharmaceutical interest.^{3,4,5} For this purpose 2,4,6-trichloropyrimidine was chosen as the starting material. Barbituric acid has been converted to the trichloropyrimidine⁶ using phosphorus oxychloride in sealed tubes. The use of dimethylaniline in catalytic amounts obviated the necessity of pressure and gave excellent yields of the desired compound.⁷ Since the reaction of ammonia and other amines with 2,4,6-trichloropyrimidine does not lead to unique compounds, it was convenient to convert certain aminohydroxypyrimidines of known structure to the corresponding aminochloropyrimidines by the same method. Both 2-amino-4,6-dihydroxypyrimidine and 2,4-diamino-6-hydroxypyrimidine chlorinated without difficulty but 4-amino-2,6-dihydroxypyrimidine failed to yield a dichloro compound under similar conditions. 4-Amino-2,6-dichloropyrimidine was obtained by separating it from 2-amino-4,6-dichloropyrimidine in the mixture

obtained by amination of 2,4,6-trichloropyrimidine with ammonia.⁸

Dimethylamine, diethylamine and morpholine reacted with the aminodichloropyrimidines to yield chlorodiaminopyrimidines. 2-Amino-4-diethylamino-6-chloropyrimidine has been prepared previously by the reaction of diethylamine and 2-amino-4,6-dichloropyrimidine under pressure at 120–130° or at reflux temperature with copper-bronze as a catalyst.⁹ It was found that dimethylamine and morpholine required no catalyst for the reaction. Arylamines reacted with the third halogen in slightly acid suspension under conditions established previously for this type of reaction.² While alkylamines normally do not replace the third halogen below 200°,^{8,9} morpholine behaved similarly to the arylamines. This behavior of morpholine has been noted previously in reactions with 2-amino-4-chloropyrimidine and 2,4-diamino-6-chlorotriazine.^{2,5}

Several alkoxydiaminopyrimidines were prepared for antihistaminic studies but, unlike the isosteric triazines,⁴ they were inactive.

Comparison of the reactivities of the halogens of 2,4,6-trichloropyrimidine with the halogens of cyanuric chloride (2,4,6-trichloro-*s*-triazine) indicates that in general the halogens of the triazine are more reactive than those of the pyrimidine.

(1) Metal and Thermit Corporation, Rahway, N. J.

(2) Banks, *THIS JOURNAL*, **66**, 1131 (1944).

(3) Controulis and Banks, *ibid.*, **67**, 1946 (1945).

(4) Pearlman, Mitulski and Banks, *ibid.*, **71**, 3248 (1949).

(5) Walker, L'Italien, Pearlman and Banks, *J. Amer. Phar. Assn.*, **39**, 393 (1950).

(6) Gabriel, *Ber.*, **33**, 3066 (1900).

(7) Baddeley and Topham, *J. Chem. Soc.*, 678 (1944).

(8) Büttner, *Ber.*, **36**, 2228 (1903).

(9) Braker, Pribyl, Sheehan, Spitzmiller and Lott, *THIS JOURNAL*, **69**, 3077 (1947).