[CONTRIBUTION FROM THE STAMFORD RESEARCH LABORATORIES OF THE AMERICAN CYANAMID COMPANY]

Cyanuric Chloride Derivatives. IX. Dissociation Constants of Substituted Melamines and Related Triazines

BY JAMES R. DUDLEY

The dissociation constants of a number of substituted melamines and related triazines have been determined by electrometric titration. The values show that the introduction of alkyl substituents on amino nitrogen increases the basicity of the melamine molecule, and modification with negative substituents decreases basicity. Replacement of amino nitrogen by other groups also decreases basicity. Evidence is presented to substantiate the conclusion that melamine itself exists in neutral solution in the normal rather than the iso form.

Although it is not always recognized, melamine is a weak base,[1,2] whose strength is about equal to dimethylaniline and quinoline. Substitution on or modification of the triazine molecule affects the basicity in various ways, and it became of interest in connection with studying the uses of such compounds to measure their dissociation constants.

Experimental

Materials Used.—The preparation of the substituted melamines for this work has been described in a previous paper.[3] The method of preparation of the other compounds is referred to individually in Table I. All compounds were purified by at least one crystallization.

Procedure.—The electrometric titration method described by Dixon, *et al.*,[1] was used to determine the dissociation constants of the compounds.[4]

Results

Substitution on Amino Nitrogen.—The introduction of aliphatic substituents on amino nitrogen of the melamine molecule increases the basic strength, and the increase appears to be directly related to the number of substituents present. This relationshp is indicated by the dissociation constants of the ethylmelamines.

Unfortunately, the dissociation constants could not be obtained for a complete series because of the insolubility of the more highly substituted compounds. Direct titration measurements were made on all the ethylmelamines with the exception of the tetraethylmelamine, whose hydrochloride was back titrated with sodium hydroxide. Even the hydrochloride was very sparingly soluble, however, and precipitation occurred early in the back titration. As a consequence, only a few points corresponding to a unit slope were obtained in plotting the data. The hydrochloride of pentaethylmelamine was too insoluble to permit the plotting of the data obtained in the back titration.

TABLE I

DISSOCIATION CONSTANTS OF AMINO-*s*-TRIAZINES

Compound	K_b
Melamine	1.0×10^{-9}
Ethylmelamine	1.7×10^{-9}
N^2,N^4-Diethylmelamine	3.4×10^{-9}
N^2-Diethylmelamine	4.2×10^{-9}
N^2,N^4,N^6-Triethylmelamine	6.9×10^{-9}
N^2,N^4-Tetraethylmelamine	1.9×10^{-8}
γ-Hydroxypropylamine	7.1×10^{-5}
N^2-Di-β-hydroxyethylmelamine	1.3×10^{-9}
N^2,N^4-Di-β-hydroxyethylmelamine	1.5×10^{-9}
N^2,N^4,N^6-Tri-β-hydroxyethylmelamine	1.6×10^{-9}
N^2,N^4-Tetra-β-hydroxyethylmelamine	1.4×10^{-9}
Hexa-β-hydroxyethylmelamine	5.0×10^{-10}
N^2,N^4,N^6-Trimethylolmelamine	1.0×10^{-10}
N^2,N^4,N^6-Tri-γ-hydroxypropylmelamine	3.0×10^{-9}
Ethylisomelamine[a]	3.5×10^{-4}
Phenylmelamine	4.5×10^{-10}
Formoguanamine[b]	7.6×10^{-9}
2-Amino-*s*-triazine[c]	Too weak to measure
Acetoguanamine[d]	4.0×10^{-10}
2-Allyloxy-4,6-diamino-*s*-triazine[e]	2.7×10^{-11}
2-Amino-4,6-dimethoxy-*s*-triazine[e]	Too weak to measure

[a] Prepared by Dr. D. E. Nagy of these laboratories according to the method given by D. W. Kaiser and D. E. Nagy, U. S. Patent 2,481,758 (1949). [b] Prepared by Dr. V. P. Wystrach of these laboratories according to the method of K. Rackmann, *Ann.*, **376**, 180 (1910). [c] Prepared by Dr. W. N. Oldham of these laboratories according to the method of J. Paden and J. P. English, U. S. Patent 2,334,162. [d] Prepared by Dr. D. W. Kaiser of these laboratories according to the method of W. Zerweck and W. Brunner, U. S. Patent 2,302,162. [e] J. R. Dudley, *et al.*, THIS JOURNAL, **73**, 2986 (1951).

On the other hand, the dissociation constant of hexa-β-hydroxyethylmelamine, which is quite water-soluble, was determined, and it is compared to those of other hydroxyalkylmelamines in Table I. That the basicity of hexa-β-hydroxyethylmelamine is less than that of melamine appears to contradict the conclusions drawn from the dissociation constants of the ethylmelamines. However, the hydroxyl group in the β-position moderates the effect of the alkyl group in the melamine molecule. This influence is clearly evident in simple aliphatic amines if the dissociation constant of ethanolamine,[5] 7.6×10^{-7}, is compared to that of ethylamine,[6] 5.6×10^{-4}. While the introduction of a β-hydroxyl group in the ethylmelamine molecule does not markedly decrease basicity, it is understandable that the effect is less in view of the greater complexity of the melamine molecule. In contrast to the simple amines, the melamine molecule offers several possible centers of basicity in its various resonance forms. Consequently, the introduction of a few β-hydroxyethyl groups increases the basicity of the melamine, although not as markedly as alkyl groups. However, as the number of the β-hydroxyethyl groups is increased, the effect of the hydroxyl group then becomes more

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[1] J. K. Dixon, N. T. Woodberry and G. Costa, THIS JOURNAL, **69**, 599 (1947).

[2] A. Albert, R. J. Goldacre and J. Phillips, *J. Chem. Soc.*, 2240 (1948).

[3] D. W. Kaiser, *et al.*, THIS JOURNAL, **73**, 2984 (1951).

[4] The titrations were made at 25 ± 3° by Mrs. M. Sermet of these laboratories.

[5] N. F. Hall and M. R. Sprinkle, THIS JOURNAL, **54**, 3469 (1932).

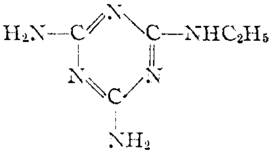
[6] G. Bredig, *Z. physik. Chem.*, **13**, 289 (1894).

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

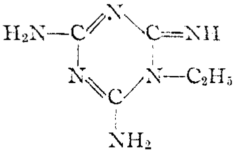
It is also interesting to note that the effect of the hydroxyl group is decreased as it is further removed from the basic group. This was demonstrated in the case of the alkanolamines by measuring the dissociation constant of γ-hydroxypropylamine. This amine was found to be much more strongly basic than ethanolamine[5] (7.6×10^{-7}). While not as marked, a similar effect is shown in the symmetrically substituted trialkanolmelamines. 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.



Ethylmelamine



Ethylisomelamine

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).

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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 hydroxyaponucidine[1] it was necessary to prepare considerable quantities of brucidine (V, $R_1 = R_2 = OCH_3$), which is obtained by the electrolytic reduction of brucine[2] (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 last available. This expectation was justified by the later success of Karrer in converting strychnine (I, $R_1 = R_2 = H$) to strychnidine (V, $R_1 = R_2 = H$) 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 ($C_{23}H_{28}N_2O_3$) 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.

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(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).

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