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Reactions of Acids with Diamines

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Hexamethylenediamine was condensed with various proportions of acids to give recovered diamine, monoamide, and diamide in yields close to those predicted based on randon distribution. Similarly, ethylenediamine with acids gave all three types of products, but the yields were in greater variation.

In spite of the large number of amides made by the reaction of acids on diamines, there still appears to be appreciable question about the nature of the products obtained. For example, the reaction of equimolar amounts of an acid and hexamethylenediamine could give the monoamide alone, the N,N′-diamide plus excess diamine, or a mixture of diamine, monoamide, and diamide. The relative amounts of acid and diamine employed should determine the distribution of products. Furthermore, after symmetrical disubstitution has been effected to give the N,N′-diamide, there is the possibility of placing a second acyl group on each of the nitrogen atoms. However, the decreased basicity[1] of the monoacylated nitrogen atom reduces the tendency to form the N,N-diamide. This research concerns a study of the distribution of products in a limited number of condensations between acids and diamines.

Many complex mixtures of amides and ammonium salts have been made, especially for various commercial applications, and are described mainly in the patent literature. The inconsistency of interpretation of the distribution of products as expressed in this literature is rather confusing and, as Ralston[2] states, "shows a trend towards the utilization of the amide and contributes little to our knowledge of the chemistry of these compounds." For example, Johnson and Brown[3] indicate that equimolar quantities of an acid and a diamine give only the monoamide, and other possible products are not mentioned. Bird and Jacoby[4] disclose that equimolar amounts of stearic acid and ethylenediamine give only the monoamide. In another patent,[5] stearic acid is heated with more than one mole of ethylenediamine hydrate to give the diamide, monoamide, and recovered diamine. Chitwood and Reid[6] show how the diamides can be made by heating ethylenediamine with excess acids or their esters. Mixed diamines are made[7] by heating diamines with one mole of acid to give the monoamide, which subsequently is converted to the N,N′-diamide by heating with one mole of a second acid. Gunderson and Denman[8] have shown that equimolar quantities of ethylenediamine and stearic acid give N,N′-distearylethylenediamine and recovered diamine. Many more examples could be cited, but it is evident that the identities of the products are not always definite.

Reactions between lauric acid and hexamethylenediamine could possibly give N,N′-dilaurylhexamethylenediamine (I), N-laurylhexamethylenediamine (II), recovered diamine, N,N,N′-trilaurylhexamethylenediamine (III), tetralaurylhexamethylenediamine (IV), and N,N-dilaurylhexamethylenediamine (V). Compound V is essentially eliminated by the reasoning of Gilman[1] while III and IV would be expected to form only under vigorous conditions and possibly in the presence of a large excess of acids or more reactive acid derivatives. The reaction most likely to be encountered is the following when equimolar quantities are employed.

$$\begin{aligned}&\mathrm{RCOOH} + \mathrm{H_2N(CH_2)_xNH_2} \longrightarrow\\&\qquad \mathrm{RCONH(CH_2)_xNHCOR} +\\&\qquad\qquad \mathrm{RCONH(CH_2)_xNH_2} + \mathrm{H_2N(CH_2)_xNH_2}\end{aligned}$$

In general, a bifunctional compound, AA, will react with a monofunctional compound, B, as follows: AA + bB → AA + AB-A + AB-AB, where b varies from zero to a maximum of two, for above this b would be present in stoichiometric excess. At least in the instance of hexamethylenediamine, in which the two reactive groups are widely separated in the chain, it can be fairly assumed that reaction is random and that the products will have an incidence predicted by probability. This is similar, for example, to the distribution of products in the Wurtz reaction.[9] It can be shown that when $b > 0$ and <2, the recovery of AA will be $\left(\frac{2\text{-}b}{2}\right)^2$, the formation of AB-AB will be $(b/2)^2$, and the yield of AB-A will be $(b\text{-}\frac{b^2}{2})$. When the reactants are

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(1) Gilman, *Organic Chemistry*, John Wiley & Sons, Inc., New York, 1938, p.682.

(2) Ralston, *Fatty Acids and Their Derivatives*, John Wiley & Sons, Inc., New York, 1948, p. 606.

(3) U. S. Patents 2,317,959 (1943); 2,426,220 (1947).

(4) Bird and Jacoby, Canadian Patent 443,431 (1946).

(5) German Patent 464,142 [*Chem. Abst.*, **22**, 4130 (1928)].

(6) Chitwood and Reid, *J. Am. Chem. Soc.*, **57**, 2424 (1935).

(7) British Patent 571,591 (1945).

(8) Gunderson and Denman, *Ind. Eng. Chem.*, **40**, 1363 (1948).

(9) Davis, Gilkerson and Hernandez, *J. Chem. Educ.*, **26**, 606 (1949).

TABLE I

CONDENSATIONS OF HEXAMETHYLENEDIAMINE WITH ACIDS

Acid	Value of b	Temp., °C.	Hours	Percent A-A[a] Found	Percent A-A[a] Calc'd	Percent AB-A[b] Found	Percent AB-A[b] Calc'd	Percent AB-AB[c] Found	Percent AB-AB[c] Calc'd
Lauric	0.75	175	6	35	39	44	47	15	14
Lauric	1.0	175	2	24	25	48	50	25	25
Lauric	1.0	180	21	22	25	50	50	25	25
Lauric	1.0	180	44	20	25	51	50	24	25
Lauric	1.5	175	5	4	6	40	37	51	56
Stearic	0.94	190	2	29	28	48	50	23	22
Enanthic	0.99	175	1	24	26	48	50	24	25

[a] A-A is recovered hexamethylenediamine. [b] AB-A is N-acylhexamethylenediamine. [c] AB-AB is N,N′-diacylhexamethylenediamine.

present in equimolar quantities and b is one, the diamine AA will be recovered to the extent of 25%, and will be converted 25% into the diamide and 50% into the monoamide. Results in Table I show that the yields of products obtained experimentally check reasonably well with this anticipated distribution.

Inspection of these data shows that in every instance in which an acid condensed with hexamethylenediamine, the yields were close to the predicted values. In the instance of lauric acid, three values of b were employed with consistent results. Prolonged heating (beyond the brief period of about one hour which gave essentially complete reaction) did not affect the distribution of products. The quantity of diamine recovered was determined by titration of the aqueous solution, using Methyl Orange indicator. The assumption that the base thus determined was the anticipated diamine was ascertained on occasion by converting the amine in near quantitative yield to a solid derivative. The monoamide was determined by isolating the material, frequently in somewhat impure state, and then by converting it into stable derivatives. The monoamide was readily titrated and thus the percent of titrable amino nitrogen was determined.

It appears fair to conclude that the consistent results obtained in these experiments would be encountered with other materials unless competing reactions might occur to affect the distribution of products. In the instance of ethylenediamine such an irregularity is encountered for cyclization can occur to give imidazolines. For example,[10,11] N-diethylacetylethylenediamine, formed by the reaction of ethyl diethylacetate on excess diamine, was converted into 2-amylimidazoline by heating with calcium oxide at 225° for 15 hours. Monoamides having no *alpha*-substitution in the acyl group[10] are relatively easily cyclized into the imidazolines by prolonged heating. The imidazolines also can be made from N,N′-diacylethylenediamines[6] alone or when heated with the monoamide,[11] again after prolonged heating. On the basis of these considerations, the condensation of ethylenediamine with an acid would be expected to give mainly four products: recovered diamine, monoamide, diamide, and the imidazoline. Possibly, as experienced above with hexamethylenediamine, there initially is a random distribution and subsequently, especially if the experimental conditions are rather forceful, one or both of the amides might gradually be converted into the imidazoline. The relative amounts of the four products ultimately obtained could thus be rather unpredictable. Continuous removal of unreacted diamine, such as was encountered in this work, would shift the distribution but not the identity of the products.

Table II contains results obtained by the condensation of ethylenediamine with various acids. The percentages of diamine converted to the monoamide, AB-A, include the imidazoline (if any) possibly formed. It is believed, however, that the selection of acids and the mild experimental conditions minimized ring formation. This is especially true for diphenylacetic acid and diethylacetic acid, for it has been shown[10] that *alpha*-branched chain acids minimize imidazoline formation.

It will be observed that in each instance a mixture of the three anticipated products was obtained. Whatever imidazoline might have formed, and the amount should be very low, would be included with the monoamide yield. There was no indication of any imidazoline, at least any appreciable amount, being present in any of the condensations. The high recovery of ethylenediamine is reflected in the variance of yields of the monoamides and diamides from those expected.

EXPERIMENTAL

Condensation of hexamethylenediamine and stearic acid. A mixture of 9.30 g. of hexamethylenediamine (0.080 mole) and 21.47 g. of stearic acid (0.075 mole) in a Claisen flask was heated in a bath at 190° for 2 hours and then at 150°/10 mm. for 15 minutes. A slow stream of dry natural gas helped carry over volatile materials. The residue weighed 26.75 g. The distillate weighed 4.06 g. and was indicated by titration to contain 2.71 g. (29%) of hexamethylenediamine.

Half the distillate with benzenesulfonyl chloride gave N,N′-dibenzenesulfonylhexamethylenediamine, m.p. 157–

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[10] Hill and Aspinall, *J. Am. Chem. Soc.*, **61**, 822 (1939).

[11] Aspinall, *J. Am. Chem. Soc.*, **61**, 3195 (1939).

TABLE II

CONDENSATIONS OF ETHYLENEDIAMINE WITH ACIDS

Acid	Value of b	Temp., °C.	Hours	Percent A-A[a] Found	Percent A-A[a] Calc'd	Percent AB-A[b] Found	Percent AB-A[b] Calc'd	Percent AB-AB[c] Found	Percent AB-AB[c] Calc'd
Lauric	1.0	200	3	30	25	37	50	30	25
Caprylic	1.0	200	4	31	25	36	50	29	25
Diphenylacetic	1.0	165	5.5	39	25	26	50	13	25
Diethylacetic	1.0	200	1.5	40	25	43	50	12	25

[a] A-A is recovered diamine. [b] AB-A is N-acyldiamine. [c] AB-AB is N,N'-diacyldiamine.

158°, from *n*-butyl alcohol (reported m.p. 154°).[12] The balance of the distillate with benzoyl chloride gave N,N'-dibenzoylhexamethylenediamine, m.p. 162–163°, from *n*-butyl alcohol (reported m.p. 158°).[13]

A portion of the residue (2.85 g.) dissolved in 200 cc. of ethanol-butanol gave 1.25 g. (23%) of N,N'-distearylhexamethylenediamine, m.p. 145–147° (reported m.p. 140°).[14]

Anal. Calc'd for $C_{42}H_{84}N_2O_2$: N, 4.32. Found: N, 4.35.

Evaporation of the solvent left 1.7 g. (48%) of impure stearylhexamethylenediamine, m.p. 73–85°.

Anal. Calc'd for $C_{24}H_{50}N_2O$: N, 3.6 (by titration). Found: N, 3.7 (by titration).

This *monoamide* (1 g.) with 1 cc. each of acetic acid and acetic anhydride gave N-acetyl-N'-stearylhexamethylenediamine, m.p. 135–136°, from ethanol.

Anal. Calc'd for $C_{26}H_{52}N_2O_2$: N, 6.60. Found: N, 6.4.

The *monoamide* (1.7 g.) in benzene with 0.45 g. of phenyl isocyanate gave N-stearyl-N'-phenylcarbamylhexamethylenediamine, m.p. 145–146°, from butyl alcohol.

Anal. Calc'd for $C_{31}H_{55}N_3O_2$: N, 8.33. Found: N, 8.1.

Condensation of hexamethylenediamine and lauric acid. A mixture of 12.25 g. of hexamethylenediamine (0.105 mole) and 21.05 g. of lauric acid (0.105 mole) was heated for 21 hours at 180° and then was evacuated to 5 mm. for 30 minutes. The distillate weighed 4.28 g. Titration of this distillate indicated the recovery of 2.68 g. (22%) of hexamethylenediamine. The residue, 28.47 g., m.p. 90–128°, contained 2.77% nitrogen by titration. Crystallization of 5.0 g. of this residue from 75 cc. ethanol gave 2.16 g. (25%) of N,N'-dilaurylhexamethylenediamine, m.p. 146–147°.

Anal. Calc'd for $C_{30}H_{60}N_2O_2$: N, 5.83. Found: N, 5.99.

Evaporation of the residual solvent overnight at about 50° and evacuation for 30 minutes at 1 mm. left 3.1 g. (50%) of a yellow, wax-like residue, N-laurylhexamethylenediamine. Recrystallization from ligroin failed to give a pure product but there was obtained a white *monoamide*, m.p. 68–75°.

Anal. Calc'd for $C_{18}H_{38}N_2O$: N, 9.39; N, 4.7 (by titration). Found: N, 9.20; 4.6 (by titration).

This *monoamide* (0.5 g.) heated at 100° for 30 minutes in 1 cc. each of acetic acid and acetic anhydride gave N-lauryl-N'-acetylhexamethylenediamine, m.p. 130–131°, from ethanol.

Anal. Calc'd for $C_{20}H_{40}N_2O_2$: N, 8.23. Found: N, 8.14.

The *monoamide* (0.54 g.) was treated in ligroin with 0.35 g. of phenyl isocyanate to give N-lauryl-N'-phenylcarbamylhexamethylenediamine, m.p. 143–144°, from ethanol.

Anal. Calc'd for $C_{25}H_{43}N_3O_2$: N, 10.06. Found: N, 9.98.

Condensation of hexamethylenediamine with enanthic acid. A mixture of 11.92 g. of hexamethylenediamine (0.103 mole) and 13.23 g. of enanthic acid (0.102 mole) was heated at 175° for 1 hour and then at 150/10 mm. for 30 minutes. Titration of the volatile material indicated 2.80 g. (24%) of the diamine. The residue weighed 20.63 g.

Crystallization of 10.36 g. of the residue from ethanol gave 4.2 g. (24%) of N,N'-dienanthylhexamethylenediamine, m.p. 141–143°.

Anal. Calc'd for $C_{20}H_{40}N_2O_2$: N, 8.23. Found: N, 8.36.

The residual oil after removal of the solvent weighed 6.2 g. (53%). This monoamide dissolved in 30 cc. dilute hydrochloric acid to give a clear solution. Excess sodium hydroxide liberated an oil which soon changed to a low melting solid, N-enanthylhexamethylenediamine, 5.6 g. (48%).

Anal. Calc'd for $C_{13}H_{28}N_2O$: N, 6.1 (by titration). Found: N, 5.8 (by titration).

This *monoamide* (1.09 g.) with excess benzoyl chloride in base gave N-benzoyl-N'-enanthylhexamethylenediamine, 1.3 g., m.p. 121–122°, from ethanol.

Anal. Calc'd for $C_{20}H_{32}N_2O_2$: N, 8.44. Found: N, 8.4.

Reaction of the *monoamide* with phenyl isocyanate gave N-enanthyl-N'-phenylcarbamylhexamethylenediamine, m.p. 139–141°

Anal. Calc'd for $C_{20}H_{33}N_3O_2$: N, 12.1. Found: N, 12.0.

The *monoamide* with acetic acid and acetic anhydride gave N-acetyl-N'-enanthylhexamethylenediamine, m.p. 120–121°.

Anal. Calc'd for $C_{15}H_{30}N_2O_2$: N, 10.3. Found: N, 10.3.

Condensation of ethylenediamine with diethylacetic acid. A mixture of 24 g. of ethylenediamine (0.40 mole) and 46.4 g. of diethylacetic acid (0.40 mole) in a Claisen flask was heated at 120° for 12 hours. Solubility characteristics of the material indicated that condensation was not complete, so heating was continued for $1^1/_2$ hours at 200°. Titration of the distillate indicated recovery of 9.6 g. (40%) of the diamine. Part of this recovered diamine was treated with benzoyl chloride to form N,N'-dibenzoylethylenediamine, m.p. 247–248° (reported m.p. 244°).[15]

A portion of the residue (17.8 g.) was treated with 25 cc. water to leave 5.3 g. (12%) of the diamide, N,N'-bis-diethylacetylethylenediamine, m.p. 234–235°, from ethanol.

Anal. Calc'd for $C_{14}H_{28}N_2O_2$: N, 10.9. Found: N, 10.8.

The aqueous solution was distilled under a vacuum to remove the water, and the residual yellow, viscous oil distilled at 135–138°/10–12 mm. (reported b.p. 113°/7 mm.).[11] This N-diethylacetylethylenediamine weighed 11.0 g. (43%).

A portion of the above *monoamide* with phenyl isocyanate gave N-diethylacetyl-N'-phenylcarbamylethylenediamine, m.p. 178–179°, from dilute alcohol (reported m.p. 179°).[11]

Anal. Calc'd for $C_{15}H_{23}N_3O_2$: N, 15.1. Found: N, 15.0.

A portion of the *monoamide* with benzoyl chloride in base gave N-diethylacetyl-N'-benzoylethylenediamine, m.p. 164–166°, from ethanol. The *picrate* melted at 120–122° (reported m.p. 123°).[11]

Condensation of ethylenediamine with lauric acid. A mixture of 4.22 g. of 95% ethylenediamine (0.067 mole) and 13.33 g. of lauric acid (0.067 mole) was heated at 200° for $3^1/_2$

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(12) Heilbron, *Dictionary of Organic Compounds*, Oxford University Press, 1943, Volume II, p. 178.

(13) Korshak and Rafikor, *J. Gen. Chem.* (*U.S.S.R.*), **14**, 974 (1944).

(14) Berchet, U. S. Patent 2,132,388 [*Chem. Abst.*, **33**, 174 (1939)].

(15) Refenence 12, p. 30.

hours. Titration of the distillate indicated 1.2 g. (30%) of the recovered diamine.

The residue, a white solid, weighed 14.30 g. Crystallization of 4.17 g. of this residue from ethanol gave 2.4 g. (30%) of N,N′-dilaurylethylenediamine, m.p. 159° (reported m.p. 158.8°).[6]

Evaporation of the solvent left N-laurylethylenediamine, 1.72 g. (37%), m.p. 80–82°, from ligroin (reported m.p. 51–52°).[16]

Anal. Calc'd for $C_{14}H_{30}N_2O$: N, 11.6. Found: N, 12.1.

The *monoamide* in ligroin with phenyl isocyanate gave N-lauryl-N′-phenylcarbamylethylenediamine, m.p. 156–158°.

Anal. Calc'd for $C_{21}H_{35}N_3O_2$: N, 11.5. Found: N, 11.1.

Condensation of ethylenediamine with caprylic acid. A mixture of 4.22 g. of 95% ethylenediamine (0.067 mole) and 9.66 g. of caprylic acid (0.067 mole) was heated at 200° for 4 hours. Titration of the distillate showed that 1.22 g. (31%) of ethylenediamine was recovered.

The residue was a white solid which weighed 10.0 g. Recrystallization of 3.0 g. from ethanol yielded 1.83 g. (29%) of N,N′-dicaprylethylenediamine, m.p. 168–169°, reported 171°.[6]

Anal. Calc'd for $C_{18}H_{36}N_2O_2$: N, 9.0. Found: N, 8.9.

Evaporation of the solvent left 1.2 g. (36%) of N-caprylylethylenediamine. This monoamide in benzene with phenyl isocyanate gave N-caprylyl-N′-phenylcarbamylethylenediamine, m.p. 152–154°.

Anal. Calc'd for $C_{17}H_{27}N_3O_2$: N, 13.8. Found: N, 13.8.

Condensation of ethylenediamine with diphenylacetic acid. A mixture of 3.0 g. of ethylenediamine (0.05 mole) and 10.6 g. of diphenylacetic acid (0.05 mole) was heated at 165° for 5 hours. Titration of the distillate indicated recovery of 1.18 g. (39%) of ethylenediamine. The residue weighed 8.4 g.

A portion of this yellow, gummy residue (0.95 g.) was treated with dilute hydrochloric acid to remove the monoamide. The white solid which remained was thoroughly washed and this N,N′-bis-diphenylacetylethylenediamine weighed 0.29 g. (13%), m.p. 207–209°, from benzene.

Anal. Calc'd for $C_{30}H_{28}N_2O_2$: N, 6.24. Found: N, 6.46.

The aqueous filtrate was made basic with sodium hydroxide and the precipitate of N-diphenylacetylethylenediamine, m.p. 124–130°, weighed 0.38 g. (26%).

Anal. Calc'd for $C_{16}H_{18}N_2O_2$: N, 5.5 (by titration). Found: N, 5.3 (by titration).

This *monoamide* with phenyl isocyanate gave N-diphenylacetyl-N′-phenylcarbamylethylenedimine, m.p. 218–219°, from ethanol.

Anal. Calc'd for $C_{23}H_{23}N_3O_2$: N, 11.3. Found: N, 11.3.

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(16) Weiner, U. S. Patent 2,387,201 [*Chem. Abst.*, 40, 596 (1946)].