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Nitrile Groups. IV. The Catalyzed Reaction of Nitriles with Amines in Water[1]

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The reaction of unsubstituted aliphatic nitriles, such as acetonitrile and benzonitrile, with amines in water is catalyzed by such different compounds as hydrochloric acid, acetic acid, and thiophenol and is particularly well catalyzed by hydrogen sulfide and thioacetamide. The hydrogen sulfide catalysis leads to either substituted amides (with primary amines at 100–150°, with morpholine at 100–150°, and with piperidine and diethylamine at 150°) or unsubstituted amides (with piperidine and diethylamine at 100°). These products are not produced in substantial amounts in uncatalyzed reactions at these temperatures. The reaction of acetonitrile with water in the presence of triethylamine and hydrogen sulfide at 100° gives acetamide.

The combined aminolysis-hydrolysis reaction of the nitrile group with primary and secondary amines in water, to give substituted amides and ammonia, does not take place with sufficient ease to be classified as a general reaction. When the nitrile group is activated by another substituent, or can form, together with the entering amine, a five- or six-membered ring, reaction takes place at reflux temperatures or less. However, it has been shown that simple aliphatic and aromatic nitriles do not take part in this reaction under such conditions.[2] The reaction has been stated to be general under catalyzed conditions at high pressures and temperatures,[3] and has been shown also to proceed between diamines and dinitriles at temperatures of 250° and above.[4]

The present work has necessitated a re-examination of the uncatalyzed reaction. This re-examination has confirmed the fact that the reaction does not occur between any pair of amine and nitrile in the presence of water at 100°. However, in some cases substantial reaction has been shown to take place at 150°. This reaction was complicated by the further hydrolysis of amide to acid at these high temperatures. The acid did not appear on fractionation of the reaction mixture, but it was shown to be present, associated usually with base (ammonia or amine), in the final product, with which it co-distilled. The use of non-aqueous titration with, respectively, perchloric acid in glacial acetic acid for base and sodium ethoxide in dimethyl formamide for acid,[5] allowed exact determination of these contaminants. The association was not a direct 1:1 ratio (salt), the acid usually being in excess. Since the results substantiate the catalytic effects to be shown in this paper, it was not thought necessary to probe this side-effect completely. In only one case, the reaction of acetonitrile with aqueous piperidine, was there any substantial amount of acid by-product formed in the *catalyzed* reactions studied and to be described, at either 100° or 150°.

Uncatalyzed reactions of amine (1 mole), acetonitrile (0.5 mole), and water (2.8 moles) were carried out at 150° in an autoclave. Methylamine gave ostensibly 47% N-methylacetamide, with correct boiling point and refractive index. Analysis for nitrogen gave 17.8% (theory 19.2%) and non-aqueous titration showed it contained 7.0% acetic acid associated with about one-fifth equivalent of a base. If this base is assumed to be methylamine, calculations show the rest of the material (92.4%) to be N-methylacetamide. Butylamine gave ostensibly 9% of N-butylacetamide, which however had a wide boiling range and high refractive index. It was not thought necessary to further examine this obviously impure product. There was recovered 84% of the butylamine and 71% of the acetonitrile (by analysis of distillates). Piperidine gave ostensibly 19% of 1-acetylpiperidine, which, although close-boiling, had a very low refractive index (n_{D}^{25} 1.4581 *vs.* about 1.4710). This product contained 21% of acetic acid, associated with one-third equivalent of base, and probably considerable amounts of acetamide (about 35%) on the basis of nitrogen analysis (13.7% *vs.* 11.0% theory). Benzylamine gave no reaction at 150°.

These experiments clearly show that only in the case of the reaction of methylamine with acetonitrile in water is any substantial amount of amide (substituted or unsubstituted) formed. If methylamine is accepted as the most likely of all amines to take part in this uncatalyzed reaction, it is clear that the reaction requires very little more activation to become general. The activation can be provided by higher temperatures, at some sacrifice of convenience and with increasing formation of acid by-product. Catalysis in the liquid phase is a more desirable alternative.

The acid-catalyzed addition of substances to the

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[1] Given in part at the First Delaware Valley Regional Meeting of the American Chemical Society, February 16, 1956. For the previous paper in this series, see de Benneville, Strong, and Elkind, *J. Org. Chem.*, **21**, 772 (1956).

[2] (a) Exner, Hurwitz, and de Benneville, *J. Am. Chem. Soc.*, **77**, 1103 (1955); (b) Hurwitz, Exner, and de Benneville, *J. Am. Chem. Soc.*, **77**, 3251 (1955).

[3] Mahan, U. S. Patent 2,476,500 (1949); *Chem. Abstr.*, **43**, 8398 (1949).

[4] Greenewalt, U. S. Patent 2,245,129 (1941); *Chem. Abstr.*, **35**, 6110 (1941).

[5] Fritz, *Acid Base Titrations in Nonaqueous Solvents*, published by G. Frederick Smith Chemical Co., P. O. Box 1611, Columbus, Ohio, 1952, pp. 13 and 29.

nitrile group has been shown to be dependent on the particular acid used. The use of aromatic sulfonic acids in at least molecular equivalents is recommended for the preparation of amidines from nitriles and anhydrous amines.[6] The acid-catalyzed hydrolysis of the nitrile group proceeds best with hydrochloric acid catalyst.[7] It has been speculated that this hydrolysis (and solvolysis in acetic acid) does not necessarily proceed through the addition of a proton to the nitrile group, and that with hydrochloric acid, for example, there is an alternate path through an iminochloride intermediate. Hydrogen sulfide has been recommended as a catalyst for the preparation of imidazolines from nitriles and ethylene diamine.[8]

The reaction of acetonitrile, benzylamine, and water therefore was studied at 150° in Carius tubes with a group of acidic catalysts. N-Benzylacetamide was isolated in the yields shown in Table I. Of the group of catalysts hydrogen sulfide was outstanding.

TABLE I

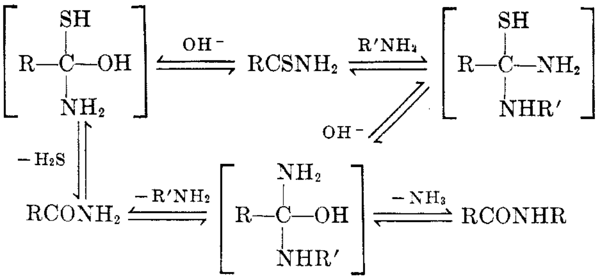
REACTION OF ACETONITRILE WITH BENZYLAMINE IN WATER

$$CH_3CN + C_6H_5CH_2NH_2 + H_2O \longrightarrow CH_3CONHCH_2C_6H_5 + NH_3$$

(150°, 0.25 mole of catalyst per mole of CH_3CN)

Catalyst	N-Benzylacetamide, %
None	0
H_3BO_3	0
CO_2	1
C_6H_5SH	10
HCl	20
CH_3COOH	40
H_2S	73

Hydrogen sulfide is a much more effective coreactant than is water for the reaction of amines with hydrogen cyanide.[1] Amines and ammonia act as catalysts for the addition of hydrogen sulfide to nitriles in non-aqueous systems, with the resultant formation of thioamides.[9] It is believed, therefore, that the hydrogen sulfide catalysis of the present reaction proceeds through a thioamide intermediate. On the other hand, hydrogen sulfide is easily displaced from thioacetamide in aqueous solutions, the latter compound being used as a source of hydrogen sulfide in such systems.[10] It is probable that reaction proceeds from the thioamide stage by a process of successive reversible displacements, as for example for one set of possible equilibria:



The final products which are isolated are those which are favored in these equilibria. This route finds a parallel in alkyl halide reactions where catalysis by halide ion is brought about by successive displacements.[11]

As would be expected, thioacetamide is an excellent and convenient catalyst for these reactions. When it was introduced in catalytic amount into a mixture of acetonitrile, benzylamine, and water, and the whole was brought to reflux, ammonia was evolved, and after 24 hours, there was isolated a 76% yield of N-benzylacetamide. Under the same conditions without thioacetamide, recovery of the original reactants was complete.

The use of hydrogen sulfide as a catalyst for this reaction was studied for a number of nitriles and amines, at both 100° and 150°. Data are given separately for primary amines (Table II) and for secondary amines (Table III). Products were identified by physical properties and by analysis (Table IV). Titration with sodium ethoxide in dimethylformamide showed acid to be substantially absent (less than 0.5 ml. of 0.1 *N* sodium ethoxide for 0.7 g. of amide) in the following products: N-methyl-

TABLE II

H_2S-CATALYZED REACTIONS OF PRIMARY AMINES, $R'NH_2$,[a] WITH NITRILES

RCN	R'	Temp., °C.	Yield of RCONHR', %
CH_3CN	H	100[b]	72
CH_3CN	CH_3	100	69
CH_3CN	n-C_4H_9	100	31
CH_3CN	n-C_4H_9	150	74
CH_3CN	n-$C_{12}H_{25}$	100	42
CH_3CN	Cyclo-C_6H_{11}	150[c]	71
CH_3CN	C_6H_5	150	16
CH_3CN	$HOCH_2CH_2$	150[d]	35
n-C_3H_7CN	CH_3	100	73
n-C_3H_7CN	n-C_4H_9	100	13[e]
n-C_3H_7CN	n-C_4H_9	150	83
n-$C_{15}H_{31}CN$	CH_3	150	65
C_6H_5CN	CH_3	150	63

[a] Mole Ratio: 1 nitrile:2 amine:5 water:0.25 H_2S. Reaction carried out in stainless-steel autoclave for eight hours at temperature shown. [b] Reactions labeled 100° were actually carried out by immersing the autoclave in a steam-bath. [c] At 100°, gave 15% N-cyclohexylacetamide. No acetamide was isolated. [d] At 100°, gave 36% N-β-hydroxyethylacetamide. [e] There was also isolated a 21% yield of n-butyramide.

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(6) Oxley and Short, *J. Chem. Soc.*, 147 (1946).

(7) Kilpatrick, *J. Am. Chem. Soc.*, 69, 42 (1947).

(8) (a) Ciba, Ltd., British Patent 608,295; *Chem. Abstr.*, **43,** 5048 (1949). (b) Isler, U. S. Patent 2,505,247; *Chem. Abstr.*, **44,** 6888 (1950).

(9) (a) Bernthsen, *Ann.*, **184,** 290 (1877); (b) Kindler, *Ann.*, **431,** 187 (1923); (c) Fairfull, Lowe, and Peak, *J. Chem. Soc.*, 742 (1952).

(10) Barber and Grzeskowiak, *Ind. Eng. Chem., Anal. Ed.*, 21, 192 (1949).

(11) Hammett *Physical Organic Chemistry,* McGraw-Hill & Co., New York, N. Y., 1940, p. 182.

acetamide, N-methylbutyramide, N-*n*-butylbutyramide, N-*n*-butylacetamide, and 1-acetylmorpholine. Analytical data and melting points show the absence of acid in other cases. 1-Acetylpiperidine produced by this method contained 7.0% acetic acid.

TABLE III

H_2S-CATALYZED REACTIONS OF ACETONITRILE WITH AQUEOUS SECONDARY AMINES

Amine	Temp., °C.	Time, Hours	Yields RCONR^{1}R^2, %	Yields RCONH$_2$, %
$(CH_3)_2NH$	100[a]	8	0	59
Piperidine	100	8	0	56
Piperidine	150	4	59[b]	0
Morpholine	100	8	41[c]	[b]
Morpholine	150	8	78	0

[a] See Table II, footnote *a*. [b] Impure product, see Table IV. [c] Analysis for N, 13.0% found *vs.* 10.9% calc'd implies some acetamide which could not be separated.

TABLE IV

PHYSICAL PROPERTIES AND ANALYSES OF AMIDES, RCONR^{1}R^2

Comp'd. No.	R	R^1	R^2	B.P., °C.	mm.	M.P., °C., or n_D^{25}	N Calc'd	N Found	S
I	CH_3	H	H			77–81[a]	23.8	23.3	0.6
II	CH_3	CH_3	H	112–113[b]	24	1.4311	19.2	19.1	
III	CH_3	*n*-C_4H_9	H	230[c]	atm.	1.4392	12.2	12.2	0.3
IV	CH_3	*n*-$C_{12}H_{25}$	H	224–229	17	58–59[d]	6.2	6.2	0
V	CH_3	Cyclo-C_6H_{11}	H			106[e]	9.9	10.0	0
VI	CH_3	C_6H_5	H			110–113[f]	10.4	10.6	1.5
VII	CH_3	$HOCH_2CH_2$	H	155–160[g]	3	1.4735	13.6	13.5	0
VIII	*n*-C_3H_7	H	H			114–115[h]	16.1	15.8	
IX	*n*-C_3H_7	CH_3	H	120–123[i]	22	1.4389	13.9	14.0	0.2
X	*n*-C_3H_7	*n*-C_4H_9	H	136–139	12	1.4419	9.8	9.9	0
XI	*n*-$C_{15}H_{31}$	CH_3	H			81–82[j]	5.2	5.2	0
XII	C_6H_5	CH_3	H			79–82[k]	10.4	10.4	0
XIII	CH_3	$-(CH_2)_5-$		222–226[m]	atm.	(1.4710)	(11.0)	11.0	trace
XIV	CH_3	$-CH_2CH_2OCH_2CH_2-$		239–242[n]	atm.	1.4803	10.9	11.3	0

[a] Footnote 12, m.p. 82—83°. [b] B.p. at atmospheric pressure, 205—208°. Footnote 12, b.p. 206°. Footnote 13, b.p. 141/90 mm., n_D^{26} 1.4296. [c] Footnote 14, b.p. 229°. [d] Footnote 15, m.p. 53—54°. [e] Footnote 16, m.p. 104°. [f] Footnote 17, m.p. 114°. [g] Footnote 18, b.p. 155–160° (2–3 mm.), n_D^{25} 1.4710. [h] Footnote 19, m.p. 115°. [i] Footnote 13, b.p. 156° (90 mm.) n_D^{25} 1.4365. [j] Footnote 13, m.p. 85.5°. [k] Footnote 20, m.p. 80–81°. [m] Footnote 21, b.p. 226–227°. This product contained 7% acetic acid, a small amount of base, and probably some acetamide. The close analytical agreement is fortuitous. [n] Footnote 22, b.p. 242–246°.

Substituted amides were generally obtained from primary amines. However, among the primary amine reactions, one led to appreciable quantities of an unsubstituted amide. This was the reaction of *n*-butylamine, butyronitrile, and water at 100°. It is possible, but unlikely, that appreciable amounts of unsubstituted amide were missed in working up the other reactions. 1,1,3,3-Tetramethylbutylamine gave no substituted amide and only 4% acetamide at 100°.

In the H_2S-catalyzed reaction at 100° of acetonitrile with, respectively, dimethylamine and piperidine in water, acetamide was the only product. At 150°, 1-acetylpiperidine was the major product; acetic acid and acetamide were probable contaminants but were not produced in quantities sufficient to be isolated. In these cases, at least, hydrolysis seems to precede aminolysis. The substituted amide may well be formed by amide interchange at the higher temperature.

Morpholine did not promote very much hydrolysis, and at 100°, the product by analysis seemed to be for the most part 1-acetylmorpholine contaminated with some acetamide. At 150°, the product was pure 1-acetylmorpholine.

The results at 100°, which were detailed in the preceding paragraphs, completely parallel the behavior of methyl cyanoacetate in uncatalyzed reactions at reflux temperatures.[2b] The stable product which results from the equilibria involved is therefore directly, and in a general way, a function of the amine used. Primary amines, which are known to react easily with esters, probably add before any substantial hydrolysis can take place. It is indicated by the single example of butyronitrile and aqueous *n*-butylamine, that if both the nitrile and amine are large enough to lead to slow addition, the hydrolysis product can be isolated. With a secondary amine of sufficient base strength hydrolysis occurs in preference to addition. However, a weak

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(12) Hofmann, *Ber.*, **14,** 2725 (1881).

(13) D'Alelio and Reid, *J. Am. Chem. Soc.*, **59,** 109 (1937).

(14) Sowa and Nieuwland, *J. Am. Chem. Soc.*, **59,** 1202 (1937).

(15) Hunter, *Iowa State Coll. J. Sci.*, **15,** 215 (1941); *Chem. Abstr.*, **36,** 4475 (1942).

(16) Baeyer, *Ann.*, **278,** 88 (1894).

(17) Mathews, *J. Am. Chem. Soc.*, **39,** 1125 (1917).

(18) D'Alelio and Reid, *J. Am. Chem. Soc.*, **59,** 111 (1937).

(19) Hemilian, *Ann.*, **176,** 7 (1875).

(20) Titherley, *J. Chem. Soc.*, **79,** 391 (1901).

(21) Wallach, *Ann.*, **214,** 193 (1882).

(22) Medard, *Bull. soc. chim.*, [5] **3,** 1343 (1936).

secondary amine like morpholine reacts almost exclusively by addition because it is not sufficiently basic to furnish a hydrolytic environment.[23]

This would indicate that if a tertiary amine of base strength comparable with the range of dimethylamine and piperidine were combined with a nitrile and water in the presence of hydrogen sulfide, it too would promote hydrolysis. And in fact, when acetonitrile, triethylamine, and water were heated with a catalytic amount of hydrogen sulfide at 100°, there was isolated a substantial amount of acetamide.

No study was made of the catalysts other than hydrogen sulfide which were effective in the work described in Table I. Since only a small amount of initial reaction need be involved, and since the route may concern primarily transition states, it is not unlikely that these catalysts work in the same way as hydrogen sulfide.

EXPERIMENTAL

Amines and nitriles used were commercial materials. Boiling points and melting points are uncorrected. Analyses were carried out under the direction of Mr. T. P. Callan. Autoclave reactions were carried out in a low-pressure, stirred, stainless steel autoclave.

N-Methylacetamide (II). Into a 700-ml. autoclave were introduced acetonitrile (20.5 g., 0.5 mole), and aqueous methylamine (81.6 g. of 38%, 1.0 mole). The solution was heated for eight hours at 150°. A pressure of 200 p.s.i.g. was developed, which was maintained to the end of reaction. The autoclave contents were stripped of low-boiling materials up to 80° (10 mm.) and then were distilled. There was obtained 28.6 g. (47%) of II, b.p. 108–111° (23 mm.). On the basis of nitrogen analyses (17.8%, calc'd 19.2) and non-aqueous titrations for acid and base,[5] this product is 92.4% II, 7.0% acetic acid, and 0.6% methylamine. In an identical reaction, maintained by use of a steam-bath at 95–100° for eight hours, nothing remained after the initial stripping of low-boiling materials. A third identical reaction mixture, to which hydrogen sulfide (4.5 g., 0.13 mole) had been added, was also heated at 95–100° for eight hours. The reaction mixture was stripped at 100° (30 mm.) to yield 30 g., m.p. 21–24°, b.p. 206°. Redistillation gave 25 g. (69%) of II, b.p. 112–113° (24 mm.), m.p. 24–27.5°.

N-Benzylacetamide (XV)[24]—*Catalysis study.* Gaseous catalysts were passed into the amine until the proper amount had been absorbed. Other catalysts were added directly. By these methods, mixtures were made of benzylamine (XVI) (21.4 g., 0.2 mole), acetonitrile (4.1 g., 0.1 mole), water (9.0 g., 0.5 mole), and various catalysts (0.025 mole except where noted). Each mixture was introduced into a standard Carius tube. The tube was sealed, placed in an iron jacket which was in turn completely immersed in an electrically-heated oil-bath to 150° (about one hour), and held at 150° for four hours. The tube then was allowed to cool, chilled in a Dry Ice-acetone mixture, and opened. The mixture was distilled directly from a 50-ml. distilling flask, first at atmospheric pressure to remove water and unreacted acetonitrile, and finally under a vacuum to give the following fraction: *No catalyst:* 19.0 g. of XVI, b.p. 71–74° (13 mm.); Liquid residue, 1.1 g. *Boric acid (1.6 g.):* 22.4 g. of XVI, b.p. 84–90° (20 mm.). Solid residue, 3.1 g. mostly borates. *Carbon dioxide (1.1 g.):* 16.4 g. of XVI b.p. 63–80° (13 mm.). Solid residue, 4.0 g., recrystallized from ether and ligroin, 0.2 g. of XV, m.p. 57–61°, mixture m.p. 57–62°. *Thiophenol (1.2 g., 0.01 mole)* 19.9 g., b.p. 32–97° (18 mm.) containing 13.5 g. of XVI by neutral equivalent (158). Mixed liquid-solid residue, 9.9 g. Recrystallized from 10 g. of toluene to give 1.5 g. of XV, m.p. 61–63°. *Hydrochloric acid (2.5 g. of 36%)* 20.0 g., b.p. 70–80° (13 mm.) contains 13.1 g. of XVI by neutral equivalent (164). Residue slurried with ether gave 2.1 g. of XVI hydrochloride. From the ether solution by addition of ligroin, and recrystallization from toluene, 3.0 g. of XV, m.p. 61–62°. *Acetic acid (1.6 g.)* 16.9 g. of b.p. 82–142° (23 mm.), contains 12.5 g. of XVI by neutral equivalent (145). Mushy residue, 7.8 g., recrystallized from toluene, 5.9 g. of XV, m.p. 60–62°. *Hydrogen sulfide (0.9 g.)* 9.4 g., b.p. 27–85° (12 mm.) contains 8.2 g. of XVI by neutral equivalent (122.5). Waxy residue 16.3 g., recrystallized from toluene, 10.8 g. of XV, m.p. 61–62°.

N-Benzylacetamide (XV), *catalyzed by thioacetamide.* A mixture of benzylamine (80.3 g., 0.75 mole), acetonitrile (20.5 g., 0.5 mole), water (18 g., 1 mole) and thioacetamide (3.7 g., 0.05 mole) was brought to reflux (82°) and refluxed for 24 hours.[25] The reflux temperature rose to 93°. Low-boiling materials were removed by distillation, and the residue was distilled from a Claisen flask to give 57 g., (77%) of XV, b.p. 175–180° (10 mm.), crystallizing in the receiver. After recrystallization from ethyl acetate it melted at 61–63°, N, found 9.3%; 9.4% calc'd. Another 0.5 mole run with mole ratios 1:1:1.1:0.1 gave 55 g. (74%), b.p. 173–178° (10 mm.). In a third run, identical with the first, except that the thioacetamide was omitted there was recovered on distillation at atmospheric pressure, 98% of acetonitrile and 95.5% of benzylamine (by nitrogen analysis and neutral equivalent).

Hydrogen sulfide-catalyzed reactions (*Ammonia and primary amines*). The following reaction is typical of the procedure: hydrogen sulfide (4.3 g., 0.125 mole) was led into a mixture of *n*-butylamine (73 g., 1 mole) and water (45 g., 2.5 moles) at 0–5°. This mixture was charged into a 1000-ml. stainless steel autoclave and acetonitrile (20.5 g., 0.5 mole) was added. The autoclave was closed and heated to 140°. The pressure rose to 130 p.s.i.g. Heating was continued at 140–150° for 8 hours. (Maximum pressure 180 p.s.i.g.). The autoclave was cooled and rinsed out with ethanol and the contents were worked up. Isolation details are given below for each of the reactions in Tables II and III, with variations as noted. Moles of acetonitrile, temperature and time are given in each case. *Acetonitrile and ammonia,* 0.57 mole, 95–100°, 8 hours. Distilled to 100° (atmospheric pressure). Residue, recrystallized from ethyl acetate, m.p. 77–81°, 24 g. of I (72%). *Acetonitrile and butylamine,* 0.63 mole, 95–100°, 8 hours. Distilled to give 30 g., b.p. 126–144° (20 mm.). Redistilled, b.p. 132–144° (20–27 mm.) 22.5 g. (31%) of III. In a second run, 0.5 mole, 150°, 8 hours, distilled to give 49 g., b.p. 118–144° (18–21 mm.) and redistilled b.p. 142–146° (30–32 mm.), 43 g. (74%) of III. *Acetonitrile and n-dodecylamine,* 0.25 mole, 95–100°, 8 hours. Distilled to give 55.5 g. of *n*-dodecylamine, b.p. 142–176° (32 mm.), 12.1 g. of intermediate cut, boiling at 168–208° (17 mm.), and 28.8 g. of almost pure IV, boiling at 224–229° (17 mm.), m.p. 53–55°. Recrystallized from ethyl acetate, m.p. 58–59°, 24 g. (42%). *Acetonitrile and cyclohexylamine,* 0.68 mole, 150°, 8 hours. Filtered to recover

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[23] It must be considered, however, that estimates of relative base-strength are based on determinations in dilute solution at 25°. These relationships are certainly not valid at 100–150° in solutions containing large amounts of amine. Solvation effects, which may be expected to vary extensively with structure, will also be much different under these conditions. Perhaps the most valid comparison shown here is therefore that between piperidine and morpholine.

[24] Amsel and Hofmann, *Ber.*, **19**, 1284 (1886), m.p. 60–61°.

[25] Hydrogen sulfide formed is probably retained as the amine salt. The implication of this experiment is that hydrogen sulfide can be used without the need for an autoclave technique.

9.7 g. of solid, recrystallized from ethyl acetate, m.p. 105–106°, 5.7 g. of V. After stripping the filtrate, there was recovered 44.5 g. of almost pure V, m.p. 99–103°. *Acetonitrile and aniline*, 0.5 mole, 150°, 4 hours. Distilled to recover 79.4 g. of aniline, b.p. 85–95° (23 mm.). Residue, 16.5 g., recrystallized from toluene, m.p. 110–113°, 10.5 g. (16%) of VI. *Acetonitrile and ethanolamine*, 0.5 mole, 100°, 8 hours. Distilled to recover 49.3 g of ethanolamine, and 20.6 g. of VII (36%), b.p. 150–157° (2 mm.). In a second run, 0.5 mole, 150°, 8 hours, the product was distilled to recover 20.6 g. ethanolamine, and 30.7 g. of crude VII, b.p. 140–155° (3 mm.). Redistillation, b.p. 155–160° (3 mm.), gave 18.4 g.[1] (35%) of VII. *Acetonitrile and 1,1,3,3-tetramethylbutylamine*, 0.5 mole, 100°, 8 hours. Distilled up to 145°, to recover, by neutral equivalent, 121 g. (94%) of 1,1,3,3-tetramethylbutylamine. In the last portion of distillate, some solid precipitated which from ethyl acetate melted at 81–83°, 1.2 g. (4%) of I. *n-Butyronitrile and methylamine*, 0.5 mole, 100°, 8 hours. Distilled to recover 40 g. of crude IX, b.p. 120–129° (20 mm.). Redistilled, b.p. 120–123° (22 mm.), 32.3 g. (64%). *n-Butyronitrile and n-butylamine*, 0.8 mole, 100°, 8 hours. Distilled the low-boiling materials up to 100°. The mushy residue was dissolved in 125 ml. of hot ligroin, treated with charcoal, cooled, and filtered to give 13 g. of waxy crystals, m.p. 112.5–113°, which were recrystallized (m.p. 114.5–115°) and identified by analysis (15.8 % N) and melting point as VIII (16.1 % N). The filtrate was distilled to recover 29.5 g. of an oil containing solid, b.p. 130–152° (20 mm.), from which by addition of ligroin, 1.5 g. more of VIII was recovered. The oil again was distilled to give 19.6 g., b.p. 136–150° (12 mm.), analyzing correctly for X (9.6 % N found, 9.8 % calc'd), n_{D}^{25} 1.4495. A second run, 0.5 mole, 140–150°, 8 hours, gave 52.2 g. (73%) of X, b.p. 136–139° (12 mm.), n_{D}^{25} 1.4419, with no VIII isolated. *Hexadecane nitrile and methylamine*, 0.3 mole, 145–160°, 8 hours. Filtered and recrystallized from ethyl acetate to yield 45 g. of XI, m.p. 79–80.5°, and 8 g. of XI (second crop) m.p. 79–80°. Recrystallized to give pure XI, m.p. 81–82°. *Benzonitrile and methylamine*, 0.5 mole, 145–155°, 8 hours. After removal of low-boiling substances up up to 80° (20 mm.) the residue crystallized. After two crystallizations from toluene, there was obtained 33.8 g. of pure XII, m.p. 79–82°, and 8.5 g. of somewhat impure XII, m.p. 74–81°.

Reaction of piperidine, acetonitrile, and water, uncatalyzed. a mixture of acetonitrile (20.5 g., 0.5 mole), piperidine (85 g., 1.0 mole), and water (50.5 g., 2.8 moles) was heated in an autoclave at 97° for eight hours. The entire reaction mixture distilled from 85–102° at atmospheric pressure, indicating no reaction. The reaction was repeated at 150° for eight hours. After removal of low-boiling products up to 108° at atmospheric pressure, the residue was distilled to give 12 g. of impure XIII, b.p. 99–105° (11 mm.), n_{D}^{25} 1.4581. This material contained 13.7% N (theory 11.0 %). Titration with sodium ethoxide in dimethyl formamide gave 21% acetic acid, associated with one-third equivalent of base.[5] The analysis, combined with these values, and assuming the base to be piperidine, indicates a composition of 21% acetic acid, 10% piperidine, 35% acetamide, and 34% 1-acetylpiperidine.

Reaction of acetonitrile, piperidine, and water, catalyzed by H_2S. To a solution of piperidine (85 g., 1.0 mole) in water (45 g., 2.5 moles) was added hydrogen sulfide (4.3 g., 0.125 mole) and then acetonitrile (20.5 g., 0.5 mole). The mixture was heated at 95–100° for eight hours in an autoclave. The contents were distilled to remove liquids volatile up to 100° at atmospheric pressure, and titration of the distillate gave a recovery of 86% of the piperidine. The residue, 37 g. of dark oil, crystallized on seeding with acetamide. Recrystallization from ethyl acetate gave 11.1 g., m.p. 80–83° and 5.5 g., m.p. 77–81°, which were identified as I by nitrogen analysis (found 23.2%, calc'd 23.7). In an exactly similar run at 150°, there was recovered 65% of the piperidine, the water and other low-boiling materials up to 100° at atmospheric pressure, and on distillation of the residue, 40.3 g., b.p. 95–104° (12 mm.) which on redistillation gave 37.5 g., b.p. 100–104° (11 mm.) and 222–226° at atmospheric pressure. This was identified as mostly XIII by analysis, but contained 7.0% of acetic acid associated with a small amount of base by non-aqueous titration.

Reaction of acetonitrile, dimethylamine, and water, catalyzed by H_2S. A mixture of dimethylamine (119 g. of 37.8% aqueous, 1.0 mole), acetonitrile (20.5 g., 0.5 mole), and hydrogen sulfide (4.3 g., 0.125 mole) was heated at 95–100° for eight hours. Low-boiling materials were stripped at 30 mm. and the residues were recrystallized from ethyl acetate. There was obtained a total of 17.3 g. (59%) of I, melting at 80–83°, N, found 23.3%; calc'd for I, 23.7%; b.p. 221° (reported b.p. for I, 222°).

1-Acetylmorpholine (XIV). A mixture of morpholine (87 g., 1.0 mole), acetonitrile (20.5 g., 0.5 mole), hydrogen sulfide (4.3 g., 0.125 mole), and water (45 g., 2.5 moles) was heated at 95–100° for eight hours and the low-boiling materials were removed. There was then recovered 36 g. of crude XIV, b.p. 117–138° (17 mm.) which when redistilled gave 26.5 g., b.p. 113–128° (17 mm.), n_{D}^{25} 1.4782. This contained some acetamide by nitrogen analysis (found 13.0%, calc'd for XIV, 10.9%). When the reaction was repeated at 150° for eight hours, there was isolated 52 g. of crude XIV, b.p. 113–140° (14 mm.) which on redistillation gave 51 g. (78%) of XIV, b.p. 115–122° (22 mm.), 239–242° at atmospheric pressure.

Reaction of n-butylamine, acetonitrile, and water, uncatalyzed. A mixture of *n*-butylamine (73 g., 1.0 mole), acetonitrile (20.5 g., 0.5 mole), and water (50.5 g., 2.8 moles) was heated at 150° for eight hours. The autoclave was rinsed with a small amount of water and the whole was distilled. The fraction boiling at 75–105° (151 g.) at atmospheric pressure had a neutral equivalent of 180.4, corresponding to 84% recovery of *n*-butylamine, and contained 11.1% N, calculating to 71% recovery of acetonitrile after allowance for *n*-butylamine. There was also obtained 3.3 g., b.p. 101–129° (15 mm.), N, 11.5%, and 3.1 g., b.p. 129° (15 mm.), N, 11.9%. Calc'd for N-*n*-butylacetamide, 12.2 % N.

Acetamide (I) *by the reaction of acetonitrile with water and triethylamine, H_2S-catalyzed.* A mixture of triethylamine (101 g., 1.0 mole), acetonitrile (20.5 g., 0.5 mole), water (50.5 g., 2.8 moles), and hydrogen sulfide (4.2 g., 0.125 mole) was heated at 100° for eight hours with good stirring. The reaction mixture, which was in two layers, was distilled. After removal of the low-boiling fractions, there was obtained 22 g. of a dark oil which solidified on cooling. This was redistilled from a small Claisen flask to give 19 g., b.p. 105–120° (15 mm.), m.p. 65–70°. Titration in nonaqueous media showed practically no acidic or basic substances. Recrystallized from ethyl acetate to give 13.5 g. (45%) of I, m.p. 78–80°, mixture m.p. 79–81°.

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