**Butylene with Benzene.**—One mole of benzene and 8.4 g. of dihydroxyfluoboric acid were weighed in a liter Florence flask which was connected to a butylene tank as previously described. Butylene was passed into the benzene until three moles were absorbed. The catalyst was removed by treatment with a small amount of a 10% caustic soda solution. The butyl substituted benzenes were separated by fractionation. The products were *s*-butylbenzene (32.1%) b. p. 173–176, and polysubstituted butylbenzenes (13.8%). The *s*-butylbenzene gave benzoic acid upon oxidation with dilute (1:3) nitric acid.

Similar attempts to condense propylene with benzene were unsuccessful.

**Rearrangement of Isopropyl Phenyl Ether.**—One hundred ninety grams of isopropyl phenyl ether and 5 g. of dihydroxyfluoboric acid were weighed in a 500-cc. flask fitted with a reflux condenser and the contents refluxed for two hours. The method of purification was the same as that described under "Propylene with Phenol."

Sixty-seven grams of product was obtained which consisted of phenol (21%), 2-isopropylphenol (58%), 4-isopropylphenol (20%) and a trace of 2,4-diisopropylphenol.

Butylene with Acetic Acid.—Butylene (about 80% isobutylene and about 20% *n*-butylene) was passed into one mole of acetic acid and 2 g. of hydroxyfluoboric acid. The mixture was agitated and maintained at about 30° until 10 g. of butylene was absorbed. The contents were then neutralized with sodium carbonate, dried over calcium chloride and distilled. A yield of 16 g. of *t*-butyl acetate, b. p. 97°, and a small quantity of *s*-butyl acetate, was isolated.

**Butylacetylene with Methyl Alcohol.**—The procedure was the same as described[8] previously except that 5 g. of hydroxyfluoboric acid with 5 g. of mercuric oxide was substituted for the boron fluoride. A yield of 75% of the theoretical of 2,2-dimethoxyhexane (b. p. 58–60° at 30 mm.) was obtained.

**Amylacetylene with Acetic Acid.**—The procedure was the same as previously described[4] except that hydroxyfluoboric acid was used in place of the boron fluoride catalyst. A yield of 32% of the theoretical of $\alpha$-amylvinyl acetate (b. p. 93° at 40 mm.) was isolated.

**Acidolysis of Esters.**—By treating *n*-propyl propionate with acetic acid in the presence of various catalysts[9] the yields of *n*-propyl acetate were: sulfuric acid 21%, zinc chloride 31%, boron fluoride 40% and dihydroxyfluoboric acid 60%.

## Summary

Dihydroxyfluoboric acid has been shown to function as a catalyst in most organic reactions that are catalyzed by boron fluoride.

Dihydroxyfluoboric acid is a milder catalyst than boron fluoride.

An explanation for the similarity between boron fluoride and dihydroxyfluoboric acid as catalysts has been proposed.

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[8] Hennion, Killian, Vaughn and Nieuwland, THIS JOURNAL, **56**, 1130 (1934).

[9] Sowa, *ibid.*, **60**, 654 (1938).

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[A COMMUNICATION FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF WISCONSIN]

# The Relative Reactivity of Amines in the Aminolysis of Amides[1]

BY MARTHA E. SMITH AND HOMER ADKINS

It was thought that a comparison of the effect of various alkyl groups in modifying the replacement value of amines in the aminolysis of amides would be of value for its own sake. In addition it would be of interest for a comparison of the values so obtained with the strength of the amines as bases in water solution, as well as with the effect of the same alkyl groups in the alcoholysis of esters.[2]

In order to attain these ends, equilibrium has been established in the reaction

$$\mathrm{AcNHR'} + \mathrm{RNH_2} \rightleftarrows \mathrm{AcNHR} + \mathrm{R'NH_2}$$

for a series of amines and amides, and the concentrations at equilibrium of the two amines determined. Equilibrium was established both by starting with $\mathrm{RNH_2}$ and with AcNHR, R′ being either *n*-amyl or phenethyl. These two amines were used for the purpose of the comparison of the amines because their boiling points enable one or the other of them to be separated readily by fractionation from the other amines investigated. They are the most readily available of alkyl primary amines with the exception of cyclohexylamine, whose boiling point is intermediate between them.

It seems unnecessary to describe the many preliminary experiments made before the procedure outlined below for aminolysis and analysis was developed. Equimolecular amounts (0.11 mole) of an amine and an amide were allowed to react in dodecylpiperidine within a steel vessel under hydrogen (100 atm.) for two to five days at 260°. The two lower boiling amines were then separated from each other and from the other reactants by fractional distillation. The reactants were so chosen that one of the amines could be distilled

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[1] This investigation was supported in part by a grant from the Wisconsin Alumni Research Foundation.

[2] Hatch and Adkins, THIS JOURNAL, **59**, 1694 (1937).

below 130° at atmospheric pressure while the other could be separated below 90° at a pressure of 7 to 15 mm.

The fact that aminolysis did not occur during fractionation and the quantitativeness of the separation were demonstrated by fractionation of mixtures of dodecylpiperidine, two amines and their acetyl derivatives. Amylamine, as a representative of the lower boiling amines, was recovered with losses of 0.03 to 0.07 g. from twelve such mixtures which contained 3.4 to 5.1 g. of that amine. From these same mixtures which contained phenethyl, 3-ethylheptyl, benzyl or 2-octyl amines, the higher boiling amine was recovered with a loss of from 0.0024 to 0.0058 mole, depending upon which amine was involved. The amount of this loss was added to the amount of higher boiling amine obtained by fractionation of reaction mixtures. The loss of amines due to side reactions during the period for aminolysis was less than 1%.

Dodecylpiperidine was used as a reaction medium because it is a good solvent for the reactants, is high boiling and so did not interfere with the fractionations, is inert toward amides and amines, is stable at 260°, and is as readily available as any compound known to the authors which possesses the properties given above.

A numerical comparison of the relative reactivity values was made on the basis of *n*-amylamine as 1.00, the ratio of the moles of amylamine to the moles of the other amine under consideration being calculated. For example, it was found that, in the system $CH_3CONHC_5H_{11} + C_6H_5CH_2CH_2NH_2 \rightleftarrows CH_3CONHCH_2CH_2C_6H_5 + C_6H_{11}NH_2$ starting with 0.115 mole of either *n*-amylamine or phenethylamine, at equilibrium the average number of moles of amylamine was 0.0555 and of 2-phenethylamine was 0.0551. The distillation loss to be added to the phenethylamine is 0.0058 mole, so that at equilibrium in this system the number of moles of phenethylamine is 0.609. From these results, it is apparent that phenethylamine is *less* reactive than *n*-amylamine; that is, there is relatively more of this amine present at equilibrium than of *n*-amylamine. This can be expressed numerically by the ratio 0.0555/0.0609 or 0.91. In the case of amines which were compared with phenethylamine, the ratio of the number of moles of phenethylamine to the number of moles of the amine under consideration was calculated, and in order to compare this with *n*-amylamine as 1.00, the ratio was multiplied by 0.91.

The acetyl derivatives of piperidine and neopentylamine distil at so low a temperature that phenethylamine could not be separated quantitatively from them so that the comparison was based on the lower boiling amine. In order to obtain a numerical value of the reactivity of piperidine, the average number of moles of piperidine present at equilibrium was compared with the number of moles of cyclohexylamine present at equilibrium in its reaction with acetylphenethylamine, since in setting up this equilibrium exactly the same number of moles of amine and amide had been used as in the case of piperidine. For example, starting with 0.111 mole of each of the reactants, there was found at equilibrium 0.0661 mole of piperidine, while in the case of cyclohexylamine there was 0.0633 mole of that amine at equilibrium. Piperidine is thus 0.0633/0.0661 or 0.96 as reactive as cyclohexylamine, which is known by direct comparison to be 0.72 as reactive as phenethylamine, while the latter is 0.91 as reactive as *n*-amylamine, therefore piperidine is 0.96 × 0.72 × 0.91, or 0.63 as reactive as *n*-amylamine. In a similar way the relative replacement value for neopentylamine was calculated through comparison with 2-ethylbutylamine.

The data on the relative replacing values of amines in aminolysis are summarized in Table I. With one exception these values are the average

TABLE I

RELATIVE REPLACEMENT VALUES OF AMINES

| Amine | Relative replacement value | $K_{eq.}$ | $pK_{H(25°)}$ |
|---|---|---|---|
| *n*-Amylamine | 1.00 | 1.00[b] | 10.6[3] |
| 3-Ethylheptylamine | 1.06 | 1.12 | ... |
| Isoamylamine | 1.05 | 1.10 | 10.6 |
| 2-Ethylbutylamine | 1.02 | 1.04 | ... |
| Neopentylamine | 0.98 | 0.96 | ... |
| 2-Phenethylamine | .91 | .83 | 9.8 |
| Benzylamine | .83 | .69 | 9.3 |
| Cyclohexylamine | .66 | .44 | 10.6 |
| Piperidine | .63 | .40 | 11.1 |
| 1,3-Dimethylbutylamine | .63 | .40 | ... |
| 1,2,2-Trimethylpropylamine | .54[a] | .29 | ... |
| 2-Octylamine | .55 | .30 | ... |
| Aniline | .11 | .012 | 4.6 |

[a] This value may be too low since it is based upon reaction from only one direction. [b] $K = \frac{AcNHR \times C_5H_{11}NH_2}{AcNHC_5H_{11} \times RNH_2}$ concentrations expressed in mole fractions.

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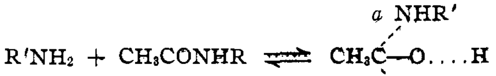
(3) Hall and Sprinkle, THIS JOURNAL, 54, 3469 (1932).

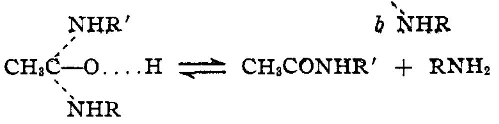
of several closely agreeing determinations carried out from both directions by the procedure described above. The experimental errors are such that differences of 0.03 in replacement values are hardly significant. The authors believe that a difference of as much as 0.05 is a definite indication of a difference in relative reactivity.

### Discussion of Results

The mechanism involved in the reaction between an amide, $CH_3CONHR$, and an amine, $R'NH_2$, may be the formation of an intermediate addition compound of the amide and amine, with subsequent decomposition into the amine and amide. That is, there may be at least two equilibria involved

(1) 

$$R'NH_2 + CH_3CONHR \rightleftharpoons CH_3\overset{a\ NHR'}{\underset{b\ NHR}{C}}—O\ldots H$$

(2) 

$$CH_3\overset{NHR'}{\underset{NHR}{C}}—O\ldots H \rightleftharpoons CH_3CONHR' + RNH_2$$

Whether the addition of the amine to the amide or the decomposition of the addition compound is the rate determining step is not known, but, since equilibrium concentrations are being compared and not relative rates of reaction, this does not need to be taken into consideration. For the purposes of this discussion, a high relative replacement value of the amine, $R'NH_2$, is considered as indicating a relatively stable carbon to nitrogen linkage, designated as *a*, as compared with the linkage *b*.

Whatever the mechanism of the reaction may be, there are certain significant differences in the behavior of the amines which may be pointed out. In general, amines in which the amino group is on a primary carbon atom are much more reactive than those in which it is substituted on a secondary carbon, 3-ethylheptylamine, isoamylamine, 2-ethylbutylamine and *n*-amylamine falling into the first class, and 1,3-dimethylbutylamine, 1,2,2-trimethylpropylamine and 2-octylamine in the latter. Branching on the α-carbon atom greatly decreases the reactivity of the amine.

On the other hand, substitution of a methyl or ethyl group in the 3-position seems to enhance the reactivity. 3-Ethylheptylamine has the highest replacement value of any of the amines. Isoamylamine, with a methyl group substituted in the 3-position, has a replacement value practically the same as that of 3-ethylheptylamine, and both of these are greater than the value for *n*-amylamine. Another example of the effect of branching on the 3-carbon atom may be found in a comparison of the values for 1,3-dimethylbutylamine and 2-octylamine, both of which have a methyl group substituted on the α-carbon atom, the 1,3-dimethylbutylamine having a methyl group in the 3-position also. The latter compound has a replacement value eight points higher than that of 2-octylamine. Branching of the chain in the 2-position seems to have no tendency to decrease the reactivity of the amine. 2-Ethylbutylamine and neopentylamine have replacement values almost the same as *n*-amylamine.

The effect of the phenyl group on the reactivity may be seen in a comparison of phenethylamine, benzylamine and aniline. When the amino group is attached directly to an unsaturated linkage, as in aniline, the relative replacement value is extremely low (0.11). This effect becomes much less as the phenyl group is removed from the amino group, and benzylamine has the fairly high value of 0.83, the value for phenethylamine being even greater.

Piperidine is the only secondary amine which has been investigated, and therefore no definite conclusions may be drawn concerning the reactivity of secondary amines on this basis. However, the replacement value 0.63 is in the same range as that of a primary amine in which the amino group is on a secondary carbon atom.

It is interesting to compare the relative replacement values of the amines with those of alcohols in the alcoholysis of esters.[3] It was not possible to measure the relative reactivity of the amines corresponding to methanol, ethanol, propanol and butanol because of the low boiling points of the amines. However, there seems to be some correlation between the relative reactivities of the amines studied and the corresponding members of the alcohol series. In the case of the alcohols which show the greatest reactivity, it is possible, from stereochemical considerations, for a methyl group at the end of a chain to come into juxtaposition with the functional group. Pentanol-1, pentanol-2, 2-ethylbutanol-1, and 2-ethylhexanol-1 have relatively high replacement values, and it is possible for all of these to assume such a position. A similar effect may be observed in the amines. By a coiling of the chain, it is possible, in *n*-amylamine, isoamylamine, 2-ethylbutylamine and 3-ethylheptylamine, for a methyl group at the end of the branched chain to come close to the functional group. If the methyl group, which is relatively positive, due to an inductive shift of electrons through the chain, can exert its influence directly on a group, then this would account for the relatively high values in these instances. This effect would also account for the value of 0.63 for 1,3-dimethylbutylamine, which is eight points higher than that of 2-octylamine where no such effect is possible.

The values for phenethylamine and benzylamine are much higher than the values for the corresponding alcohols. Phenol does not react in alcoholysis while aniline does give aminolysis. Evidently an aryl group is more effective in decreasing the reactivity of an alcohol than of an amine.

Hall and Sprinkle[3] have reported the basic strength in water solution of seven of the amines listed in Table I. Their values for the negative logarithms of the hydrolysis constant for the reaction $RNH_3^+ + H_2O \rightleftarrows RNH_2 + H_3O^+$ are given in the last column of Table I. Aniline has the lowest replacement value and is also the weakest base of the amines studied. However, cyclohexylamine and *n*-amylamine have the same base strength but very different replacement values. Piperidine, the strongest of the amines listed, has a replacement value of 0.63, as compared to the weaker isoamylamine, which has a value of 1.05. Thus there seems to be little correlation between the strength of amines as bases in water and their relative replacing power in aminolysis. Evidently steric effects have much more influence on the relative chemical reactivity of amines as determined in this way than they do on the basicity of amines in water solution.

Although no attempt has been made to determine the relative rates of reaction of different amines, there are certain facts which may be pointed out in this connection. The reaction is not a rapid one in any case, and requires a fairly high temperature and a catalyst in order that equilibrium be reached within a few days. The reactions involving *n*-amylamine, isoamylamine, 3-ethylheptylamine and benzylamine came to equilibrium in less time (twenty-six to forty-eight hours) than was required for some others. Piperidine was very slow in reacting (ninety-six hours) and the same length of time has not proved sufficient to establish equilibrium in the reaction involving 1,2,2-trimethylpropylamine. Steric factors have a marked effect on the rate at which equilibrium is established.

**Preparation of Materials.**—All of the amines, with the exception of aniline, were prepared by catalytic hydrogenation over nickel. Piperidine and cyclohexylamine were prepared from pyridine and aniline, respectively. *n*-Amyl-, isoamyl-, benzyl-, phenethyl-, 3-ethylheptyl-, and 2-ethylbutylamines were made by the hydrogenation of the corresponding cyanides over Raney nickel, at 125–150° under about 200 atm. pressure. 1,3-Dimethylbutyl-, 1,2,2-trimethylpropyl-, 2-octyl- and neopentylamines were obtained by the hydrogenation of oximes over Raney nickel.[4]

Pinacoloneoxime,[5] m. p. 75.5–76.0°, was prepared in 87% yield according to the procedure described for benzophenoneoxime.[6] Diethylketoxime,[7] b. p. 60–64 (7 mm.), methylhexylketoxime,[7] b. p. 102.0–102.5° (7 mm.) and methyl isobutylketoxime,[8] b. p. 68–70° (8 mm.), were prepared in 75–88% yields by the same method except that after extraction with ether the solution was treated with "Drierite" and fractionated through a Widmer column.

Trimethylacetaldehyde was prepared by dehydrogenating neopentyl alcohol (130 g.) over 70 ml. of pumice impregnated with copper–chromium oxide at 300°.[9] The alcohol recovered by the fractionation of the first run was again passed over the catalyst, a total of 84 g. of crude aldehyde being obtained. The oxime, b. p. 46–48° (9 mm.), was obtained in 80% yield according to the procedure for heptaldoxime.[10]

Pinacoloneoxime and methyl isobutylketoxime in quantities of about 0.25 mole in 100–120 ml. of methanol were hydrogenated over 2.5 g. of Raney nickel within less than forty-five minutes at 85° to give yields of 40 and 64%, respectively, of the corresponding amines. The oxime of methyl hexyl ketone was hydrogenated similarly in ethanol to give a 50% yield of 2-octylamine. The oxime of trimethylacetaldehyde (0.36 mole) in 100 ml. of ethylene glycol was hydrogenated in less than twenty minutes at 105° over 5 g. of catalyst to give a 45% yield of neopentylamine. The variations in the solvent were made in order to facilitate the separation of the amines by fractionation. When methanol or ethanol was used as the solvent, the reaction mixture, after the removal of the catalyst, was dried with anhydrous sodium sulfate and then with "Drierite" before it was fractionated slowly and carefully. Even so 1,2,2-trimethylpropylamine could not be separated from methanol without considerable loss, and neopentylamine could not be separated from methanol or ethanol. In this case the expedient of using ethylene glycol was tried, since the latter is a good solvent for the

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[4] Adkins, "Reactions of Hydrogen," University of Wisconsin Press, 1937, pp. 53, 91.

[5] Markownikoff, *Ber.*, **32**, 1448 (1899).

[6] "Organic Syntheses," Vol. X, John Wiley and Sons, Inc., New York, 1930, p. 10.

[7] Scholl, *Ber.*, **21**, 509 (1888).

[8] Obregia and Gheroghiu, *J. prakt. Chem.*, **128**, 239 (1930).

[9] Adkins and Peterson, THIS JOURNAL, **53**, 1513 (1931); Adkins, Kommes, Struss and Dasler, *ibid.*, **55**, 2992 (1933).

[10] "Organic Syntheses," Vol. XI, 1931, p. 54.

water (formed by the hydrogenation) which would otherwise stop the hydrogenation. In this case the water and neopentylamine were distilled out of the glycol. The amine was then dried with potassium hydroxide and fractionated.

Dodecylpiperidine was prepared by the hydrogenation of laurylpiperidine[11] or by the alkylation in dioxane of piperidine with dodecyl alcohol[12] over copper-chromium oxide.

The amides were prepared by the acetylation of the amines with acetic anhydride. Equimolecular quantities of the reactants were mixed slowly at a temperature slightly above 0°. The acetic acid was removed by distillation and the amides carefully fractionated through a Widmer column at the temperatures and pressures indicated in Table II. The yields were from 73 to 92%.

The analysis for nitrogen of certain amines and amides, which have not been hitherto reported, are given in Table III.

**Procedures.**—The reaction mixture for aminolysis was made up with equimolecular amounts of approximately 0.11 mole of an amide and of an amine, 15 to 16 g. of dodecylpiperidine, 0.05 to 0.08 g. of water, and 0.15 to 0.25 g. of anhydrous zinc chloride. The volume of the mixture was a little less than 50 ml. It was contained in a chrome-vanadium steel vessel having the same outside dimensions as have been given for a small bomb for quantitative hydrogenation.[24] However, the inside dimensions were larger, *i. e.*, 2.2 × 15.5 cm., the capacity being 62 ml. The bomb was closed in the usual manner, using a copper gasket. Hydrogen was then admitted, through a needle valve attached to the head of the bomb by a short nipple

TABLE II

AMINES AND AMIDES

| Amines and amides | B. p., °C. | Mm. | $n^{25}D$ or m. p. | Neutral equiv. Calcd. | Neutral equiv. Found |
|---|---|---|---|---|---|
| *n*-Amylamine | 103.5–103.7 | 749 | ........ | 87 | 88 |
| Acetyl-*n*-amylamine | 106.5–107.5 | 1 | 1.4412 | ... | ... |
| Isoamylamine | 96–97 | 742 | ........ | 87 | 89 |
| Acetyl-isoamylamine[13] | 96–98 | 1 | 1.4393 | ... | ... |
| Piperidine | 105–105.1 | 740 | ........ | 85 | 86 |
| Acetylpiperidine[14] | 105–105.5 | 14 | 1.4776 | ... | ... |
| Neopentylamine[15] | 81–82 | 741 | ........ | 87 | 90 |
| Acetylneopentylamine[16] | 114–115 | 10 | 65–66° | ... | ... |
| 1,3-Dimethylbutylamine[17] | 107–108 | 740 | ........ | 101 | 102 |
| Acetyl-1,3-dimethylbutylamine | 94.5–95 | 1 | 1.4378 | ... | ... |
| 1,2,2-Trimethylpropylamine[18] | 101.8–102 | 730 | ........ | 101 | 102 |
| Acetyl-1,2,2-trimethylpropylamine[19] | 110–111 | 8 | 66–67° | ... | ... |
| 2-Ethylbutylamine | 121–122 | 725 | ........ | 101 | 101 |
| Acetyl-2-ethylbutylamine | 107–108 | 1.5 | 1.4487 | ... | ... |
| 2-Octylamine[20] | 55–56 | 13 | ........ | 129 | 128 |
| Acetyl-2-octylamine | 129–129.2 | 1.5 | 1.4449 | ... | ... |
| 3-Ethylheptylamine | 73–73.5 | 11 | ........ | 143 | 143 |
| Acetyl-3-ethylheptylamine | 132.5–133 | 1 | 1.4518 | ... | ... |
| Cyclohexylamine | 132.8–133 | 740 | ........ | 99 | 100 |
| Acetylcyclohexylamine[21] | 137.5–138 | 7 | 104.5–105° | ... | ... |
| Benzylamine | 60.5–61 | 8 | ........ | 107 | 107.6 |
| Acetylbenzylamine[22] | ......... | | 61–62° | ... | ... |
| Phenethylamine | 70–71 | 7 | ........ | 121 | 121 |
| Acetylphenethylamine[23] | 143–146 | 1 | 53.5–54° | ... | ... |
| Dodecylpiperidine | 144–146 | 1 | ........ | 253 | 255 |

TABLE III

ANALYTICAL DATA

| Compound | Formula | Nitrogen, % Calcd. | Nitrogen, % Found |
|---|---|---|---|
| N-Acetyl-1,3-dimethylbutylamine | $C_8H_{17}ON$ | 9.79 | 9.71 |
| N-Acetyl-*n*-amylamine | $C_7H_{15}ON$ | 10.85 | 10.81 |
| N-Acetyl-2-ethylbutylamine | $C_8H_{17}ON$ | 9.79 | 9.76 |
| N-Acetyl-2-octylamine | $C_{18}H_{21}ON$ | 8.19 | 8.25 |
| N-Acetyl-3-ethylheptylamine | $C_{11}H_{23}ON$ | 7.57 | 7.73 |
| 3-Ethylheptylamine | $C_9H_{21}N$ | 9.78 | 9.90 |
| 2-Ethylbutylamine | $C_6H_{15}N$ | 13.86 | 13.75 |

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(11) Wojcik and Adkins, THIS JOURNAL, **56**, 2419 (1934).

(12) Paden and Adkins, *ibid.*, **58**, 2487 (1936).

(13) Erickson, *Ber.*, **59B**, 2665 (1926).

(14) Wallach, *Ann.*, **214**, 238 (1882).

(15) Freund and Lenze, *Ber.*, **23**, 2867 (1890).

(16) Ingold and Patel, *J. Chem. Soc.*, 67 (1933).

(17) Maihle, *Bull. soc. chim.*, **29**, 219 (1921).

(18) Markownikoff, *Ber.*, **32**, 1448 (1899).

(19) Drake, Kline and Rose, THIS JOURNAL, **56**, 2056 (1934).

(20) Levene, Rothen and Kuna, *J. Biol. Chem.*, **115**, 415 (1936).

(21) Baeyer, *Ann.*, **278**, 104 (1894).

(22) Hofmann, *Ber.*, **19**, 1286 (1886).

(23) Bischler and Napieralski, *ibid.*, **26**, 1905 (1893).

(24) Adkins, THIS JOURNAL, **55**, 4272 (1933).

of steel tubing, until the pressure was approximately 40 atm. The valve was then closed and the bomb placed in a thermostat held at 260 ± 1°.

The thermostat consisted of a steel block into which the bomb, a thermometer and a bimetallic helix fitted. The steel block was covered with asbestos paper and then wound with enough No. 18 nichrome wire so that the resistance was about 30 ohms. The block and heating unit were placed in a transite box and well insulated. The temperature of the steel block was readily and constantly controlled through the agency of the bimetallic helix acting through a relay upon the current passing through the nichrome wire.

After the reaction vessel had cooled to room temperature the contents was transferred to a 75-ml. flask with a ground glass joint and the two lower boiling amines fractionated through an electrically heated, modified Widmer column as described below.

**Fractionation.**—The experimental work described in this paper as well as in numerous others that have been and will be published from this Laboratory depends upon careful fractionation through suitable columns. In order that others may duplicate, if they care to, the results reported from this Laboratory it seems desirable to describe here the apparatus and method used. These have been developed for the semiquantitative separation of 3 to 500 g. of material distilling from 50° at 740 mm. to 200° at 1 mm.[25] It has seemed that the Widmer type of column among the several used was the most satisfactory for this wide range of pressures and temperatures considering the efficiency of separation and economy of material.

The essential unit in a Widmer column[26] is a core bearing a helix which, in the columns under consideration usually consists of a glass tube 8 mm. in diameter sealed at both ends, around which is wrapped a glass rod 2 mm. in diameter. The outside of the helix is ground so that it fits snugly into a Pyrex glass tube of 12 mm. internal diameter. The most generally useful helix is 15 cm. in length with twelve to fifteen turns in the helix. A helix with six to seven turns within a length of 15 cm. is particularly useful at high temperatures with low pressure. Helices varying from 8 to 58 cm. in length and from 7 to 27 mm. in diameter, made of glass or brass are in use in this Laboratory. The closeness of the turns of the helices varies from 1.5 to 0.4 per cm., while one has a double helix, thus permitting a steeper pitch, in order to prevent flooding at low pressures with high temperatures. All of these Widmers as well as many other types of columns have their special uses and advantages which cannot be considered here.

The characteristic feature of a Widmer column is that it consists of three concentric tubes so constructed that the vapors rise between the inside wall of the outer tube and the outside wall of the middle one, descend between the walls of the middle and inner tube, and then rise around the helix held within the third or inner tube. The objective of this circulation of vapors is of course to thermostat the helix around which almost if not all of the fractionation occurs. The column must be surrounded with a jacket, for the fractionation of materials boiling much higher than ethanol, in order to prevent excessive condensation. If the column is placed inside a glass jacket it may be used for distillations at atmospheric pressure at temperatures as high as about 170°, or 100° at 1 mm. For materials distilling at higher temperatures it is necessary to heat the jacket.

The chief advantages of a Widmer column so constructed are that it will probably give a fair separation even in the hands of a rather inexperienced operator. and that it may be used over a wide range of temperatures and pressures without external heating. The chief disadvantage is the rather large internal volume, which results in intermediate fractions and hold-up at the end larger than necessary. However, for the simpler mixtures and large quantities (100 ml.) it is quite satisfactory because of its wide range and the simplicity in operation.

The column may be simplified greatly in construction by eliminating the two outer concentric tubes which provide for the circulation of vapors about the inner tube holding the helix. This modification results in no loss in efficiency, with a considerable decrease in the size of intermediate fractions and final hold-up. However, it demands external heating of the column above about 150° at atmospheric pressure, or 50° at 10 mm., and it is not so "fool proof" in operation. That is, it requires more careful attention to avoid flooding and to ensure a good separation. Even under the best of attention it has not been possible to use this "modified Widmer" over so extensive a range as the original Widmer. The range may be extended by using a helix with only 0.4 turns per cm., but even so it has not been feasible to use this modified column at 1 mm. for temperatures higher than 170°, although at higher pressures it may readily be used at considerably higher temperatures.

The heater for a column should not interfere with the visibility of the helix and should permit a close control of the temperature about the column. The heaters used in this Laboratory consist of glass tubes having outside dimensions of 5.5 × 25 cm. for the Widmers and 4.5 × 20 cm. for the modified Widmers, each containing four lengths of no. 22 nichrome wire arranged parallel and close to the inner walls of the tubes. The wire is wound in a helix, on a rod 3 mm. in diameter, before being inserted in the heater. The resistance of the wire in a heater is 35 to 40 ohms. The wire is fastened to circular pieces of transite which cover the ends of the glass tube. These covers are so designed that the column readily may be inserted and removed from the heater. The space between the edges of the covers and the column is filled by cork or other readily removable insulating material. A thermometer is inserted so that the temperature of the air within the heater may be observed.

Successful fractionation in these or any other columns depends upon an accurate *control* and *maintenance*, sometimes for many hours, of the heating of the liquid and of the column. It is best to use electrical heating for both

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(25) The figures given in this paper to indicate the range in temperature and pressure of a column are only rough approximations, since the exact figures vary with the heats of vaporization and with other factors of the compound to be distilled. Ebullition has been prevented by the use of very small capillaries for the inlet of air or nitrogen but a roll of glass wool in the flask is possibly a better preventative.

(26) Widmer, *Helv. Chim. Acta*, **7**, 59 (1924).

purposes. A helix of no. 22 or 24 nichrome wire having a resistance of 23 to 27 ohms is immersed in cottonseed oil (or other high boiling stable oil), held in a casserole. The helix is attached to binding posts clipped on the edge of the casserole and connected to a source of current. The temperature of the bath and of the column heater is then controlled separately by means of two rheostats, each having a resistance of 44 ohms. A drawing of a Widmer column, visible heater, condenser and fraction cutter is shown in Fig. 1. A modified Widmer and a wiring diagram of an outfit for controlling the temperature of the bath or column are also shown. The switch is left open for the higher amperages and is closed when a low amperage is desired.

The temperature of the air about the column should be slightly below the boiling range of the fraction being taken off but high enough to avoid flooding. The temperature of the bath should be only high enough to bring about a slow but steady distillation of the order of 10 g. per hour. In some cases a much slower rate is advantageous, while in others a much faster rate may be justified by experience with the particular mixture involved. It cannot be emphasized too strongly that *slow* and *even* heating of the bath and column is essential to a good fractionation. Patience in the operator is at least as important as the construction of the column. Good fractionations *can* be made with gas heating but few operators have the patience and uninterrupted time to do so.

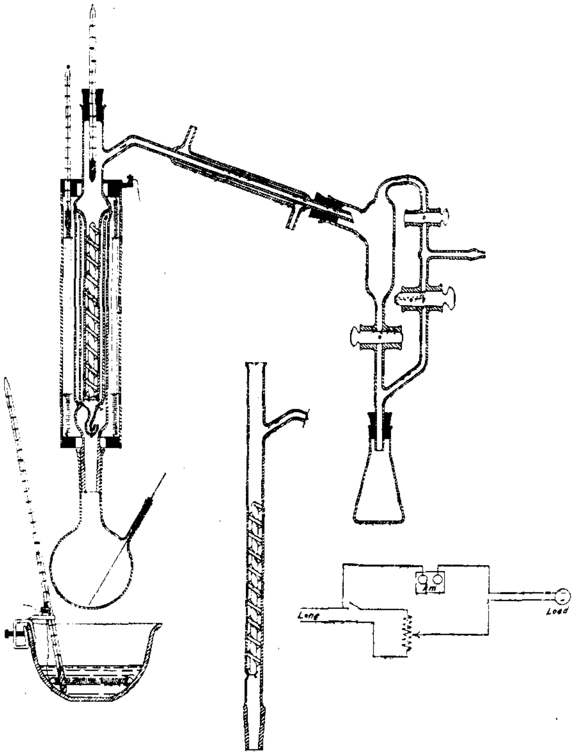

Fig. 1.—Apparatus for fractional distillation. A Widmer column with accessories is shown together with a modified Wldmer and a wiring diagram for connecting the column heater or bath heater to a source of current.

The foregoing is in large part a summary of the conclusions developed by several different investigators in this Laboratory. Acknowledgment is made especially to Karl A. Folkers and Frank Signaigo; to J. B. Davis, who constructed the columns; and to Lee Henke and Carl Baumann, who made the heaters. The columns are sealed to no. 15 interchangeable ground glass joints and small high-efficiency condensers. The spirals were obtained from Eck and Krebs, New York City. Widmer columns have been sold in Germany for several years and are now available from commercial glass blowers in this country. Philip Fehlandt, formerly of this Laboratory, now of Wittenberg College, has described the details of construction of spirals and columns.[27]

## Summary

It has been found that primary and secondary amines react with substituted amides of acetic acid at 260°. The reaction is reversible and takes place without side reactions under the conditions used. Procedures have been developed for the quantitative determination of the concentrations of various amines at equilibrium in this reaction. Numerical values have been assigned to the relative replacing power in aminolysis of thirteen amines. The relations of the structure of these amines to their relative replacement values and basicity have been discussed. A correlation has been made between the effect of various alkyl groups in the alcoholysis of esters and in the aminolysis of amides. Apparatus and procedures for the semiquantitative separation by fractional distillation of quantities varying from 3 g. upward of materials boiling over a wide range of temperatures and pressures have been described.

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(27) Fehlandt, *Chemist Analyst*, **25**, 28 (1936), published by J. T. Baker Chemical Co., Phillipsburg, New Jersey.