[CONTRIBUTIONS FROM THE LABORATORY OF ORGANIC CHEMISTRY OF THE UNIVERSITY OF ILLINOIS.]

MOLECULAR REARRANGEMENTS OF CARBON COMPOUNDS. II. AROMATIC (N) ACYLAMINES AND THE BECKMANN REARRANGEMENT.[1]

BY C. G. DERICK AND J. H. BORNMANN.

Received July 23, 1913.

CONTENTS: 1. Introduction. 2. Application of the Criterion for Non-reversible Intramolecular Rearrangements to Aromatic (N) Diacyl and Monacylamines. 3. Beckmann Rearrangement. 4. Experimental. 5. Conclusions.

1. Introduction.

Non-reversible intramolecular rearrangements (true rearrangements) of carbon compounds must proceed in the direction to produce substances more stable toward rearrangement than the initial substances. Since the reaction proceeds spontaneously (or may so take place if sufficient time is given), the initial substance is unstable with respect to the final and there is a decrease in free energy in the reaction. Since it is difficult, or at present practically impossible, to measure this decrease in free energy, it seems desirable to seek some criterion of stability in such rearrangements. One of us[2] has found that non-reversible intramolecular rearrangements of carbon compounds take place in the direction to decrease the ionization constant, if the substances are electrolytes, and that some function of the ionization constant may be taken as a criterion of the stability of such a compound, that is, as a criterion of the possibility of a rearrangement of this type. In the former paper[3] the logarithm of the ionization constant was chosen and the criterion stated, that rearrangements of this type went in the direction to decrease the free energy of ionization. For the purpose of this paper the criterion may be more simply stated thus: *Non-reversible intramolecular rearrangements of carbon compounds take place in the direction to decrease the ionization constant.*

To compare the relative stabilities of two isomeric substances toward rearrangements of this type we need only compare their ionization constants. The substance possessing the greater ionization constant is most unstable toward rearrangement and possesses the possibility of rearranging into its isomers. This fact is supported by all of the data given in the previous paper.[3] In this paper further experimental confirmation, of this criterion is given.

[1] Submitted to the Graduate School of the University in partial fulfilment of the requirements for the degree of Master of Science in Chemistry by Mr. Bornmann. Presented at the March meeting of the American Chemical Society at Milwaukee, Wisconsin, 1913.

[2] Derick, THIS JOURNAL, 32, 1333 (1910); see also W. A. Rothe and R. Stoermer, *Ber.*, 46, 260 (1913), who found that the heat of combustion may be used as a criterion of similar rearrangements.

[3] Derick, THIS JOURNAL, 32, 1337 (1910). First five columns of Table I.

Chattaway and his students[1] have shown from their experimental study of aromatic (N) diacylamines that, if the acyl radicals are formyl (HCO—), acetyl (CH_3CO—), propionyl (C_2H_5CO—), benzoyl (C_6H_5CO—) or any one of these acyl radicals with halogen, one acyl radical will rearrange into the ring when the diacyl amine is treated with zinc chloride or hydrochloric acid gas. The latter substances were considered as catalysts. Blanksma[2] has studied the rate of change of (N) chloroacetanilide into *p*-chloroacetanilide and found the reaction to be monomolecular, thus proving the catalytic nature of zinc chloride and hydrochloric acid gas for non-reversible intramolecular rearrangements of this group.

Chattaway[3] further states that "the transference of more than one acyl group into the nucleus has, however, not yet been effected" and yet "this process of intramolecular rearrangements, which follows a precisely similar course to the other well-known migrations of groups from the aminic nitrogen atom into the ortho and para positions of the ring, could, in all probability, be carried to the further stage in which two acyl groups would be introduced into the nucleus." From these statements it is not clear whether Chattaway and Lewis considered it possible to rearrange a single acyl radical from the aminic nitrogen atom of monacyl aromatic amine, as in the case of acetanilide, or, if dealing with the (N) diacylanilides, to rearrange both acyl radicals into the ring. The idea that such might be the truth appears to receive support from the fact that Bamberger[4] has shown that the nitro group of phenyl nitramine will rearrange into the nucleus, giving ortho- and paranitranilines. Likewise Bamberger and Hindermann[5] found that phenyl sulfamic acid easily changes to aniline-ortho-sulfonic acid. That is, the single substitution of the acid radicals, nitro or sulfonyl, upon the aminic nitrogen atom of aniline produce substances that will undergo non-reversible intramolecular rearrangements.

It is evident from experimental knowledge that very strongly negative radicals, like the nitro and sulfonyl, require only monosubstitution upon the aminic nitrogen atom of aromatic amines, while the weaker negative radicals (organic acyl radicals) require disubstitution before non-reversible intramolecular rearrangements are possible. The application of the above criterion to the possibility of such rearrangement is, therefore, highly desirable, for it should predict whether or not disubstitution will be required before a rearrangement of this type is possible.

Further, it is desirable to ascertain how negative any acyl radical must

[1] Chattaway, *J. Chem. Soc.*, **75**, 1046 (1899); **77**, 134, 789, 797 (1900); **85**, 386, 589, 1181 (1904).

[2] Blanksma, *Rec. trav. chim.*, **21**, 366; **22**, 290; *Chem. Zentr.*, **1903**, I, 414; II, 241.

[3] Chattaway and Lewis. See above references.

[4] Bamberger, *Ber.*, **26**, 471, 482 (1893); **27**, 359 (1894); **39**, 1248 (1897).

[5] Bamberger and Hindermann, *Ber.*, **30**, 654 (1897).

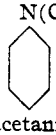
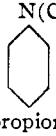
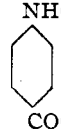
be in order that monosubstitution upon the aminic nitrogen atom of aromatic amines will make possible rearrangements of this type. One of us[1] has developed a quantitative measure of polarity which may be used to answer this question, as will be seen in the following section.

2. Application of the Criterion for Non-Reversible Intramolecular Rearrangements to Aromatic (N) Diacyl and Monacyl Amines.

Since Chattaway and his students have found that the aminic nitrogen atom of aniline must be twice substituted by the acyl radicals, formyl acetyl, propionyl and benzoyl, producing the corresponding (N) diacylamines before rearrangements to the isomeric acylaminoketones would be possible and since all attempts to rearrange the (N) monacyl aromatic amines, where the acyl group was one of the above, have failed, the criterion applied to these rearrangements must show that the ionization constants of the (N) diacylamines are greater than those of the corresponding isomeric acylaminoketone, while the ionization constants of the (N) monacylamines must be smaller than those of the corresponding isomeric aminoketones. The following tables will give the ionization constants of these substances as determined in the experimental part which follows:

In Table I, the first column gives the name and formulas of the (N) diacylamines that rearrange, while the third gives the products obtained from the rearrangement. Similarly, in Table II, the first column gives the name and formulas of the (N) monacylaromatic amines while the third gives the names and formulas of the isomeric aminoketone which would be obtained if the (N) monacylamine could be rearranged. The second and fourth columns, in each table, give the respective ionization constants of the substances given in the first and third columns:

TABLE I.

(N) Diacylamine.		Isomeric acylaminoketone.	
Name and formulas.	Ionization constant.	Name and formulas.	Ionization constant.
 Diacetanilide	$k_a^{25^\circ} = 7 \times 10^{-9}$	 *p*-Acetylamino-acetophenone	$k_b^{28^\circ} = 2 \times 10^{-13}$
 Dipropionan-ilide	$k_a^{26.5} = 5 \times 10^{-9}$	 *p*-Propionyl amino-propiophenone	$k_b^{24^\circ} = 4 \times 10^{-12}$

[1] Derick, THIS JOURNAL, 33, 1152 (1911).

TABLE II.

(N) Monacylamine.		Isomeric acylaminoketone.	
Name and formulas.	Ionization constant.	Name and formulas.	Ionization constant.
 Acetanilide	$k_b^{28^\circ} = 1 \times 10^{-13}$	 *p*-Aminoacetophenone	$k_b^{29^\circ} = 4.5 \times 10^{-10}$
 Propionanilide	$k_b^{30^\circ} = 3 \times 10^{-13}$	 *p*-Aminopropiophenone	$k_b^{30^\circ} = 2.4 \times 10^{-10}$
 Benzanilide	$k_b^{26^\circ} = 2 \times 10^{-13}$	 *p*-Aminobenzophenone	$k_b^{26^\circ} = 5.7 \times 10^{-10}$
 Chloroacetanilide	$k_b^{26^\circ} = 2 \times 10^{-13}$	 *p*-Aminochloroacetophenone	$k_b^{26^\circ} = 2.3 \times 10^{-10}$

Table I shows that each (N) diacylamine has a greater ionization constant than its corresponding acylaminoketone and therefore rearrangements into the acyl aminoketones are possible, as Chattaway has shown experimentally. Unfortunately, dibenzanilide is too insoluble to allow accurate measurements of its ionization constant and for this reason is not included in the study.

Table II shows that each (N) monacylamine has a smaller ionization constant than its corresponding aminoketone and therefore rearrangements into the aminoketone is impossible, as Chattaway found for acetanilide and the authors for (N) chloroacetanilide. Hence *the criterion for the possibility of non-reversible intramolecular rearrangements, namely that these rearrangements take place in the direction to decrease the ionization constant, holds for mono and diacyl aromatic amines.*

Since the ionization constant is influenced by the negative nature of the acyl radical, further conclusions concerning the possibility of rearrangements of aromatic (N) acyl amines may be drawn. From the negativity

tables given by one of us[1] it will be seen, quantitatively, how each acyl group affects the ionization. These tables show that the acetyl radical has a negativity of 211 at ordinary temperature (25°), the propionyl radical 206, and the benzoyl 240. Hence we may state that *all acyl radicals with a negativity between 206 and 240 will require disubstitution upon the aminic nitrogen atom of aromatic amines before rearrangements into the corresponding acylaminoketones are possible.*

Table II shows that (N) chloroacetanilide will not rearrange into the corresponding *p*-aminochloroacetophenone according to the criterion. Experimentally, using the methods that Chattaway has developed for performing such rearrangements, we have been unable to rearrange (N) chloroacetanilide. Unfortunately, we have been unable to prepare the corresponding diacylamine, (N) dichloroacetanilide, and its rearrangement has not been studied. But from analogy to the other cases, we feel safe in stating that the limits of negativity, given above in the comment upon Table I, may be stated as 206 and 355 instead of 206 and 240 for acyl radicals that will require disubstitution upon the aminic nitrogen atom of aniline in order that rearrangements shall be possible. The negativity of the chloroacetyl radical is 355. From the negativity tables referred to above it is evident, therefore, that the following radicals fall within these limits and that the corresponding (N) diacylamines must be formed before rearrangements are possible:

Acyl radicals.	θ.	Acid.	$k_a^{25°}$.
Formyl	272	Formic	2.14×10^{-5}
Acetyl	211	Acetic	1.86×10^{-5}
Propionyl	206	Propionic	1.45×10^{-5}
n-Butyryl	208	*n*-Butyric	1.56×10^{-5}
Isobutyryl	208	Isobutyric	1.60×10^{-5}
n-Pentyl	208	*n*-Pentanoic	1.60×10^{-5}
Acrylyl	235	Acrylic	5.6×10^{-5}
α,β-Pentenyl	207	α,β-Pentenonic	1.48×10^{-5}
β,γ-Pentenyl	223	β,γ-Pentenonic	3.35×10^{-3}
α-Chlorobutyryl	350	α-Chlorobutyric	1.39×10^{-5}
β-Chlorobutyryl	246	β-Chlorobutyric	8.59×10^{-5}
γ-Chlorobutyryl	221	γ-Chlorobutyric	3.0×10^{-3}
α-Bromopropionyl	349	α-Bromopropionic	1.38×10^{-3}
β-Bromobutyryl	249	β-Bromobutyric	9.8×10^{-5}
Iodoacetyl	320	Iodoacetic	7.5×10^{-4}
α-Hydroxypropionyl	259	α-Hydroxypropionic	1.38×10^{-4}
β-Hydroxypropionyl	259	β-Hydroxypropionic	3.1×10^{-5}
Benzoyl	240	Benzoic	6.9×10^{-5}
o-Toluyl	256	*o*-Toluic	1.25×10^{-4}
m-Toluyl	233	*m*-Toluic	5.1×10^{-5}
p-Toluyl	233	*p*-Toluic	5.1×10^{-5}
o-Chlorobenzoyl	341	*o*-Chlorobenzoic	1.32×10^{-5}
Salicyl, etc	325	Salicylic	1.04×10^{-3}

[1] Derick, THIS JOURNAL, **33**, 1151 (1911).

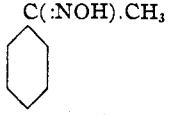
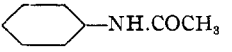
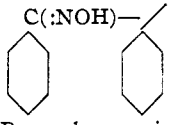
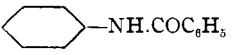
From this table it is obvious that the conclusions concerning the limits of negativity of acyl radicals for disubstitution upon the aminic nitrogen atom of aromatic amines, in order that rearrangements shall be possible, may be stated as follows: Disubstitution upon the aminic nitrogen atom of aromatic amines will be required, in order that intramolecular rearrangements are possible, by the acid radicals of all acids whose ionization constants lie between 1.45×10^{-5} and 1.55×10^{-3}.

From the above tables and discussion, it is evident that, for aromatic monacylamines to possess the possibility of intramolecular rearrangements of the type discussed, the negative acyl radicals must be capable of overcoming the weak basic nature of aniline and rendering the monacylamines acid with ionization constants greater, numerically, than the basic constants of the corresponding isomeric aminoketones. Tables I and II show that all aromatic monacyl amines, where the acyl group has a negativity less than 355, have ionization constants in the next order to the zone of neutrality for aqueous solutions, that is, in the order of 10^{-13}. If, however, these same acyl radicals with negativity between 206 and 355 are twice substituted upon the aminic nitrogen atom of aromatic monamines the basic natures of the latter are overcome and the resulting (N) diacylamines are weak acids whose ionization constants fall within the order of 10^{-9}. That a single acyl radical may be negative enough to completely mask the basic nature of the amino group when substituted into it to form the (N) monacylamine is seen from the following: Nitramine (NH_2NO_2), methylnitramine ($CH_3NH.NO_2$) and sulphamic acid ($NH_2.SO_3H$) give the ionization constants $k_a^{\circ} = 2 - 3 \times 10^{-7}$, $k_a^{\circ} = 3 \times 10^{-7}$ and $k_a^{25^{\circ}} = 1 \times 10^{-1}$, respectively. The nitro and sulfonyl radicals may overcome completely the basic nature of the free amino group rendering the resulting substances fairly strong acids. In the case of the weakly basic substance aniline, the substitution of these radicals upon the nitrogen atom, once, will produce fairly strong acids also. The ionization constant of phenylsulfamic acid by analogy is in the order of 10^{-1}, while those of aniline-*o*-sulfonic and aniline-*p*-sulfonic acids are at 25° 3.3×10^{-3} and 5.81×10^{-4}, respectively. The criterion states that phenyl sulfonic acid may rearrange into aniline-ortho or para-sulfonic acid, as Bamberger has shown. The nitro and sulfonyl radicals possess the negativity of approximately 750 and 740, respectively. Obviously, the limit, beyond which monosubstitution upon the nitrogen atom of aniline will produce (N) monacylamines that will rearrange to aminoketones and below which disubstitution will be required, is possessed by acyl radicals whose negativities are somewhere between 355 and 740. It is the purpose to continue this investigation until the limit is definitly determined.

3. Beckmann Rearrangement.

In the two cases of the Beckmann rearrangement investigated the

criterion for non-reversible intramolecular rearrangements is found to apply, as the following table will show:

Oxime.		Isomeric Acylamine.	
Name and formulas.	Ionization constant.	Name and formulas.	Ionization constant
 Acetophenonoxime	1.16×10^{-10}	 Acetanilide	1×10^{-13}
 Benzophenonoxime	2.0×10^{-11}	 Benzanilide	2×10^{-13}

4. Experimental.

General.—Since the acylamines do not give a sufficiently strong concentration of ions to be measured accurately by the direct conductivity method and, similarly, since the preparation of their pure salts of a strong mineral acid is practically impossible, due to hydrolysis, the indirect conductivity methods could not be employed. The colorimetric method for the determination of their ionization constants was therefore chosen. This choice was made, since a high degree of accuracy was not necessary in order to show whether or not the acylamine possessed a greater ionization constant than its isomeric aminoketone and since rapidity of experimentation was possible.

Colorimeter.—The colorimeter used in this work consisted of a wooden case with a removable front and top, by which means all light except that which entered the Nessler tubes could be excluded. The Nessler tubes were about one inch apart and rested upon a glass plate, which was covered with a sheet of black paper, perforated so as to allow equal amounts of light to enter both tubes. The light was reflected up through the tubes by an adjustable mirror. Observations of the color tints of the two tubes were made very sensitive by means of the monomolecular telescope of the Duboscq colorimeter which was fitted onto the instrument. This arrangement assured rapidity of manipulation and a high degree of accuracy in matching the color tints in the two tubes.

Method of Measuring the Hydrogen Ion Concentration.

Standard hydrogen ion concentrations were prepared according to the directions of A. A. Noyes.[1] For the color comparisons the standard hydrogen ion concentration was chosen somewhat weaker than that of the unknown solution. To each solution, contained in its respective Nessler tube of the colorimeter, was added the same amount of indicator

[1] THIS JOURNAL, **32**, 815 (1910).

and the unknown solution was diluted with water from a buret until the two matched in color tint, after thorough stirring. The final matching in color tint was made, after the standard solution was brought to the same level as the unknown solution, by adding its isohydric solution so that the concentration of the indicator and the height of the columns of solution in each tube were the same. Diffused daylight was found the most favorable light, since it allowed the use of small amounts of indicator, thus giving greater sensitiveness to the color matching. Eijkmann[1] and others have used artificial light but found they must work with fairly concentrated solutions of indicator.

Method for the Determination of the Hydroxyl Ion Concentration.—Since the ionization constants of aniline[2] are known over a wide range of temperature, allowing the curve (see Fig. 2) of the ionization constant against the temperature to be plotted with a fair degree of accuracy, aniline solutions of varying concentrations were used as the standard hydroxyl ion concentrations. In the measurements of the basic constants it was found advisable to dilute the standard, due to the slight solubility of the acylamines and aminoketones. The slight solubility of the basic acylamines makes it doubtful if their basic constants are known with an accuracy better than a complete order, although the ionization constants of aminoketones were measured with a mean error of 2%.

The advantage of this method of colorimetry is that the experimenter is independent of the knowledge of the ionization constants of the indicator, and is concerned to have an indicator that gives large color changes with small changes in the hydrogen or hydroxyl ion concentrations.

Indicators.—Red proved to be the best color for indicators which, for acids, were used at the concentrations where the red tint changed rapidly with the change in the hydrogen ion concentration. One or two drops of a 0.1% aqueous solution of methyl red were sufficient to give to the volume of the acyl amine solutions used a faint red coloration. The same was true for a 0.1% aqueous solution of methyl orange. The excellent work of Tizard[3] has clearly shown that methyl orange should be used for concentrations of hydrogen ions between the limits 10^{-2} and 10^{-4}, while methyl red should be used between the limits 10^{-4} to 10^{-6}. It was very difficult to find a suitable indicator for measuring the hydroxyl ion concentration, but finally litmus was chosen. Litmus gave a faint blue coloration to the volume of the aminoketones and basic acylamines solutions used, which tint is not as sensitive as the red used with the acids. This fact, combined with the fact of the slight solubility of these basic

[1] *Rec. trav. chim.*, **25**, 83 (1906). See also Veley, *J. Chem. Soc.*, **91**, 1153, 1246 (1907); **93**, 652 (1908) and Tizard, *Ibid.*, **97**, 2477 (1910).

[2] See Affinitätmessungen," H. Lundén, p. 87.

[3] *J. Chem. Soc.*, **97**, 2477 (1910).

substances, made it impossible to measure thier ionization constants with any great accuracy.

Accuracy of Color Matching.—A test of the accuracy with which the color tints could be matched by means of this method of colorimetry was made, using acetic acid solutions to produce the hydrogen ion concentrations and methyl orange as the indicator. In order to make sure that conditions were exactly alike in both tubes, equal quantities of the same solution were introduced into each tube, to each was added the same amount of indicator, and then the contents of one (Tube I) was diluted with a measured volume of water. Theoretically the color tints should match when the contents of the other tube (Tube II) were diluted with the same amount of water. This was done by adding water from a covered buret until the colors appeared of equal tint in the monocular telescope. The cover was then removed from the buret and the amount of water added determined. In all the measurements care was taken to use water of the same degree of purity for standard and unknown solutions. In this manner the following results were obtained:

TABLE III.

Normality of acetic acid, 0.00133. Concentration of indicator. Methyl orange, one drop of 0.1% aqueous solution.

Tube I.		Tube II.		Per cent. diff.
Cc. acid.	Cc. H_2O added.	Cc. acid.	Cc. H_2O added.	
5.00	12.80	5.00	12.85	+0.3
10.00	9.75	10.00	9.50	—1.0
10.00	9.40	10.00	8.90	—2.7
10.00	10.70	10.00	10.00	—3.4
10.00	6.20	10.00	6.50	+1.8
10.00	9.70	10.00	10.00	+1.5
10.00	6.60	10.00	7.00	+2.4
10.00	4.30	10.00	4.00	—2.1
10.00	9.20	10.00	9.00	—1.0
10.00	13.50	10.00	13.00	—2.1
Average error				0.6
Mean error				1.9

From Table III it is evident that this method of colorimetry is accurate enough for the conclusions which have been drawn from the ionization constants that follow.

Diacetanilide.

Preparation.—Diacetanilide was prepared by the method of Chattaway.[1] Equimolecular amounts of pure dry acetanilide and acetyl chloride were heated together under a reflux condenser, fitted with a calcium chloride tube, in an oil bath at 170°–190° for three hours. By this time the evolution of hydrochloric acid gas had ceased and the brown liquid left was distilled under a vacuum. After the fourth distillation it came

[1] *J. Chem. Soc.*, **85**, 386, 589 (1904).

over colorless at 147°–149° under 13 mm. pressure. This product was desiccated over calcium chloride and when cold it formed large plates which melted at 37.5° (corr.).

Ionization Constants.—Owing to the hydrolysis of diacetanilide into acetanilide and acetic acid, it was necessary to dissolve and determin the amount of water added to cause a match in color tints of the standard and diacetanilide solutions as quickly as possible after the solutions were prepared. Solution was difficult, however, for when the water was added the diacetanilide collected together on a compact mass, as if hydrating, and then slowly dissolved. The least time required for complete solution in any experiment was fifteen minutes. The amount of water necessary to add to cause a match in color tints was determined with fresh samples of the same diacetanilide solution at different time intervals after complete solution, as shown in Tables IV and V. From these results the amount of water necessary to add to the diacetanilide solution to make its color tint match that of the standard solution was obtained for zero time, when no hydrolysis had occurred, by extrapolation (see Fig. 1). However it was difficult to decide whether to call zero time the moment of adding the water to the solid (times T in Tables IV and V) or the moment of complete solution (times T_2 in Table IV and V). Obviously, the true zero time is somewhere between these limits. Fortunately, as Fig. 1 shows, taking either as zero time does not affect a significant figure in the result. Tables IV and V that follow give the results of the measurements.

TABLE IV.

Concentration of diacetanilide, N = 0.0179. Indicator, two drops of 0.1% aqueous solution of methyl red. Standard hydrogen ion concentration, $H^+ = 1 \times 10^{-5}$N. Temperature, 26°.

T_1. (Minutes.)	T_2. (Minutes.)	Diacetanilide. Cc.	Water added in cc.
15	5	5	2.0
25	15	5	3.0
34	24	5	4.0
44	34	5	4.5
65	55	5	6.0
80	70	5	8.0
100	90	5	11.0
120	110	5	13.5

In Fig. 1, the curves (*a*) and (*b*) show the extrapolation to zero time for the times T_1 and T_2, respectively. It is seen that when $T_1 = 0$, the water addition should be 1.3 cc. Similarly, when $T_3 = 0$, the result is 2.0 cc.

Calculations.–From the weak electrolytes dealt with in this paper, the mass law may be a stated as $\frac{(C\alpha)^2}{C} = k_a$, in which $(C\alpha)$ is the concentra-

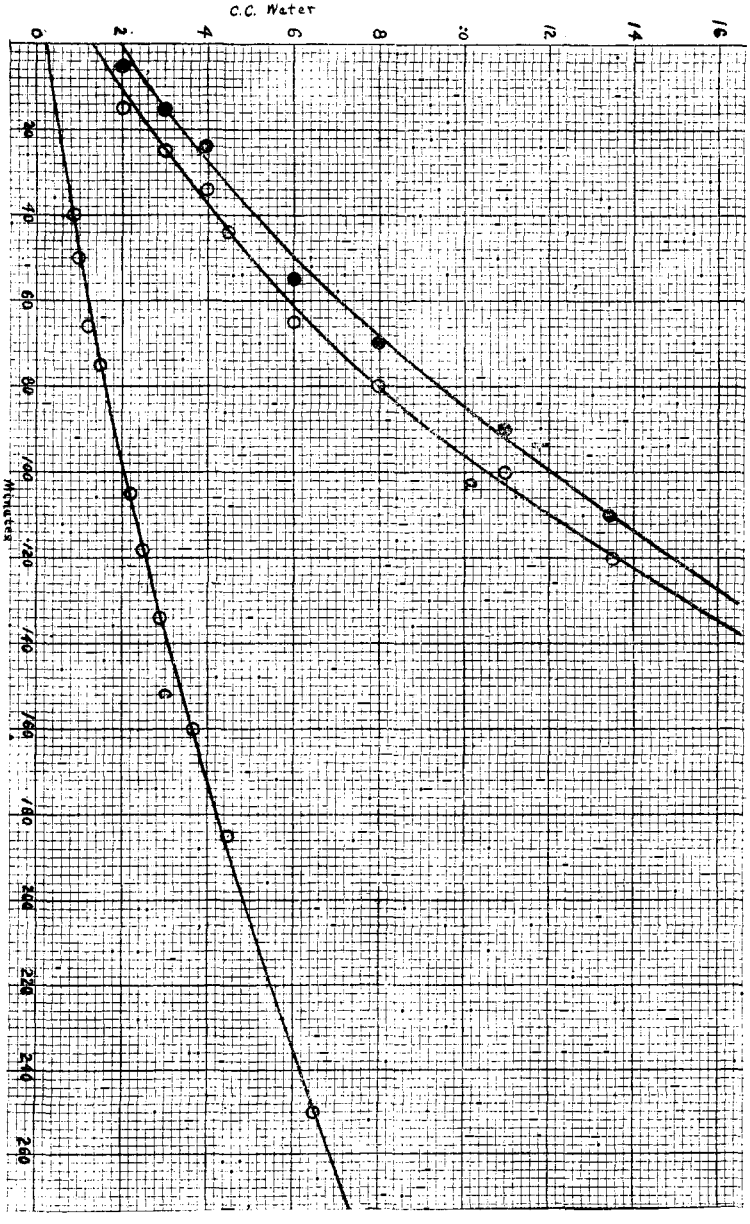


Fig. 1.

tion of the hydrogen ion (that of the standard solution and of the acidic amines, when the color tints are matched), C is the concentration of the acidic amine, and k_a its ionization constant. In the case of diacetanilide, using the times T_1, the expression becomes at zero time:

$$k_a = \frac{(\text{Conc. of } H^+ \text{ of standard solution})^2}{(\text{Initial conc. of diacetanilide solution}) \times \frac{(\text{cc. diacetanilide solution})}{(\text{cc. diacetanilide soln.} + \text{cc. water added at } T_1 = 0)}}$$

from which, by substitution, we have:

$$k_a^{26^\circ} = \frac{(1 \times 10^{-5})^2 \times (6.3)}{0.0179 \times 5} = 7.0 \times 10^{-9}.$$

Similarly, when $T_2 = 0$, then

$$k_a^{26^\circ} = \frac{(1 \times 10^{-5})^2 \times 7}{0.0179 \times 5} = 7.8 \times 10^{-9}.$$

The correct value for k_a lies somewhere between these results and nearer to that of 7.0×10^{-9}, but it is doubtful if the measurements warrant an accuracy greater than one unit, hence k_a is chosen as 7×10^{-9}.

Hydrolysis of Diacetanilide.—Curves (*a*) and (*b*), Fig. 1, show that these diacylamines are easily hydrolyzed by water at ordinary temperature. The form of each shows that the hydrogen ion produced by the hydrolysis becomes catalytic to the speed of hydrolysis. From curves (*a*) and (*c*) it is evident that the rate of hydrolysis of the diacetanilide is much greater than that of dipropionanilide. As one would expect from the fact that diacetanilide is more unstable toward rearrangement than acetanilide, diacetanilide is more unstable toward other reactions as solubility, melting, etc. If a saturated solution of diacetanilide is treated with a drop of sodium hydroxide solution (1–10), there is an immediate precipitation of the more stable (therefore less soluble) acetanilide illustrating the enormous catalytic effect of the hydroxyl ion on the speed of this hydrolysis. This test is a very convenient one in detecting the diacetanilide.

Rearrangement of Diacetanilide.—Following the method outlined by Chattaway[1] for the rearrangement of diacylamines, 26 grams of pure diacetanilide were intimately mixed with three grams of pure, dry zinc chloride and heated at 150° in an oil bath for twelve hours, when a brown liquid resulted. This reaction mass was boiled with water to remove the zinc chloride, and the oil which formed was separated. The oil was boiled for six hours with 60 cc. of ethyl alcohol and 20 cc. of hydrochloric acid (1.19). The resulting mixture was treated with sodium hydroxide solution (1–10) and the brown oil formed was subjected to steam distillation, which removed ethyl acetate and traces of aniline, benzoic ester, and isocyanide. The alkalin residue, remaining in the boiling flask after steam distillation, was extracted with ether. The ether extract, upon evaporation, gave a crystallin substance melting at 105°, which was identified as *p*-aminoacetophenone, thus substantiating the work of Chattaway.

[1] *J. Chem. Soc.*, **85**, 386, 389 (1904).

Dipropionanilide Preparation.—The dipropionanilide was prepared according to the method of Kay.[1] Ten grams of phenyl mustard oil and ten grams of propionic anhydride were heated together on an oil bath for 10 hours at 180°, carefully excluding all moisture. The reaction product was fractionally distilled in a vacuum. The dipropionanilide came over at 179°–185° (corr.) at 32 mm. pressure. This was not pure, and for the measurements of its hydrogen ion concentration it was crystallized twice from petroleum ether, from which it separated in beautiful rhombohedra which melted at 44° (corr.).

Ionization Constant.—The measurements were carried out exactly as described under diacetanilide, since hydrolysis interfered. However, it was found desirable to use a standard intermediate between 10^{-5} and 10^{-6}, which was prepared by adding 0.2 of a mol. of hydrated sodium acetate ($NaOOC-CH_3.3H_2O$) to a liter of 0.05 normal acetic acid which gave the result 4.6×10^{-6} for the hydrogen ion concentration at 25°. From the data given in Table V, Curve (*c*), Fig. 1 was drawn and by extrapolation to zero time the value 0.2 cc. (bracketed in the table) was obtained for the water necessary to add in order to have a match in color tints between the unknown and standard when no hydrolysis has occurred. From this the value 5×10^{-9} is obtained as the ionization constant of dipropionanilide at 28°. Curve (*c*), Fig. 1, shows that the rate of hydrolysis of dipropionanilide is much less than that of diacetanilide.

TABLE V.

Concentration of dipropionanilide, N = 0.00417. Indicator, one drop of 0.1% aqueous solution of methyl red. Standard hydrogen ion concentration, $H^+ = 4.6 \times 10^{-6}$ N. Temperature, 28°.

T_1. (Minutes.)	Dipropionanilide. Cc.	Water added in cc.
40	5	0.9
50	5	1.0
55	5	1.0
66	5	1.2
75	5	1.5
105	5	2.2
118	5	2.5
134	5	3.1
160	5	3.7
185	5	4.5
250	5	6.5
400	5	10.5
0	5	(0.2)

p-Acetylaminoacetophenone.

Preparation.—The compound is produced as the direct product of the rearrangement of diacetanilide. For our measurements it was prepared by acetylating *p*-aminoacetophenone with acetyl chloride.

[1] *Ber.*, **26**, 2853 (1893).

The crude product was crystallized from water, from which it separates, when pure, in almost colorless needles, which melt at 167° (corr.).

Ionization Constant.—Since this substance is so slightly soluble in water, the solution used in the measurement of its hydroxyl ion concentration was 0.003 molal, which necessitated the use of such a dilute standard aniline solution that little accuracy can be claimed for the results, yet sufficient to satisfactorily differentiate it from the ionization

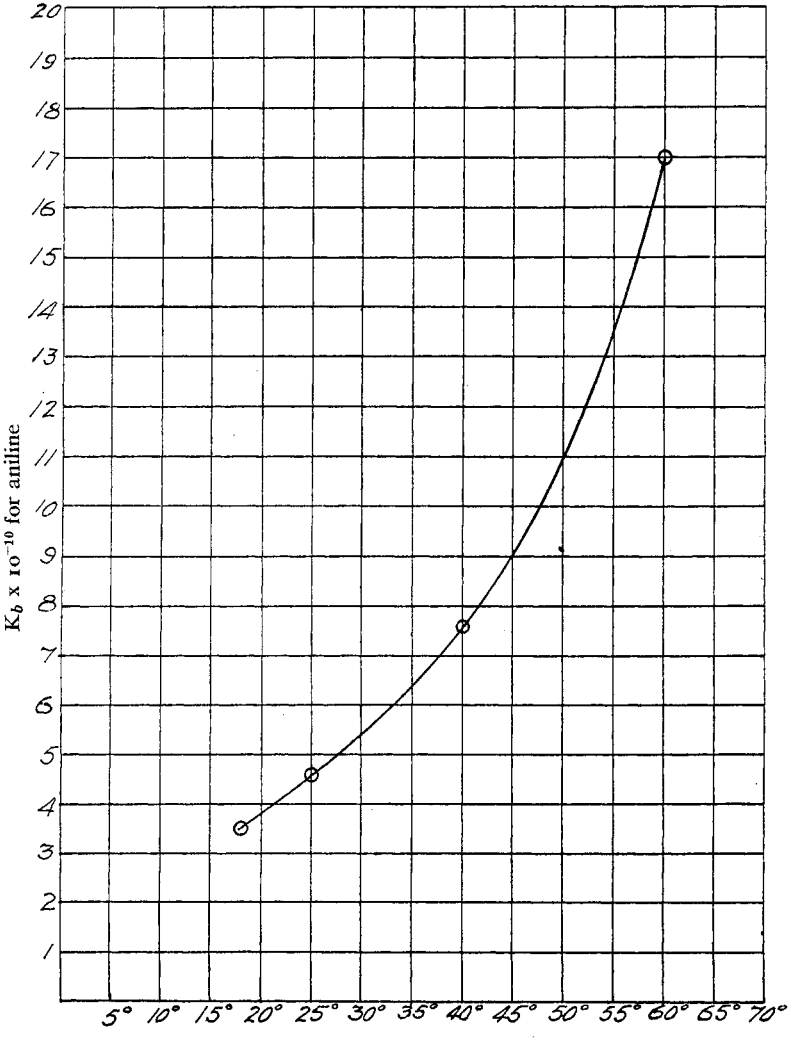


Fig. 2

constant of the isomeric diacetanilide. The results obtained are given in Table VI:

TABLE VI.

Concentration of *p*-acetylaminoacetophenone, C_1 = 0.003 N. Standard hydroxyl ion concentration, C_0 = 0.000592 N aniline solutions. Indicator, 10 drops of litmus solution. Temperature, 28°. $k_b^{28°} = 5.1 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{28°}$
1	0.2	12	2×10^{-12}
2	0.2	10	2×10^{-12}
3	0.2	10	2×10^{-12}
4	0.2	10	2×10^{-12}

Calculations.—Since the above table gives the concentration of the standard solution when the color tints match and since the ionization constant of aniline can be read off the curve in Fig. 2 for the desired temperature, the hydroxyl ion concentration of the standard can be quickly calculated and from that the ionization constant of the unknown. The mass law for weak electrolytes takes the form $kC = (C\alpha)^2$. When the color tints for the standard and unknown match, it follows that $(C\alpha)^2 = kC = k_1C_1$ or $k_1 = \frac{kC}{C_1}$, in which C is the concentration of the standard when the color tints match.

α is the degree of ionization of the standard solution
k is the ionization constant of the standard
C_1 is the concentration of the unknown
k_1 is the desired ionization constant of the unknown

As the experiments are actually carried out, C_0 is the concentration of the standard aniline solution before its dilution and is known, so when the color tints match, $C = C_0 \times \frac{\text{cc. standard}}{\text{cc. standard} + \text{cc. water added}}$.

Equation I becomes:

$$k_1 = k \times C_0/C_1 \times \frac{\text{cc. standard}}{\text{cc. standard} + \text{cc. water added}}.$$

For Experiment 2, in Table VI, the calculation is:

$$k_1 = 5.1 \times 10^{-10} \times \frac{5.92 \times 10^{-4}}{3 \times 10^{-3}} \times \frac{0.2}{10.2} = 1.97 \times 10^{-12}.$$

This calculation illustrates the method used for all the basic constants.

p-Propionylaminopropiophenone.

Preparation.—This compound is not described in the literature, so that it was prepared by two different methods. In the first method, the propionyl group was introduced into *p*-aminopropiophenone by means of propionyl chloride. The method of preparation of similar substances described by Kunchell[1] was followed in

[1] *Ber.*, 33, 2641, 2644 (1900).

the second case, in which 4 grams of propionyl anilide, 8 grams of propionyl chloride and 15 grams of carbon bisulfide were placed in a flask connected to a reflux condenser. Through the condenser about 15 grams of dry aluminium chloride were added in small portions. The mixture was heated on the water bath for ninety minutes. A red syrup separated which was poured slowly onto chopped ice, causing a violent reaction. The brownish substance which separated was recrystallized from hot water repeatedly until it gave the maximum melting point 151° (corr.). When pure, *p*-propionylaminopropiophenone crystallizes in long colorless needles. Its structure is evident from the fact that boiling with hydrochloric acid (1.14) and subsequent neutralization gave *p*-aminopropiophenone.

Ionization Constant.—Concentration of *p*-propionylaminopropiophenone, $C_1 = 5.03 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-6}$ N. Indicator, two drops of aqueous litmus solution. Temperature, 24°. $k_b^{24°} = 4.4 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{24°}$
1.....	5	2.0	4×10^{-12}
2.....	5	2.0	4×10^{-12}
3.....	10	4.0	4×10^{-12}
4.....	10	4.0	4×10^{-12}

It should be noted here also that the great dilution employed, required by the slight solubility of the acylamine, destroys the ordinary accuracy of this colorimetric method.

Acetanilide.

Preparation.—Carefully purified Kahlbaum acetanilide which melted at 113° (corr.) was used in the following measurements:

Ionization Constant.—Concentration of acetanilide, $C_1 = 2.3 \times 10^{-2}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-4}$ N. Indicator, 10 drops of aqueous solution of litmus. Temperature, 28°, $k_b^{28°} = 5.1 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{28°}$
1[1].....	0.2	25	1×10^{-13}
2[1].....	0.4	50	1×10^{-13}
3[1].....	0.2	25	1×10^{-13}
4.....	0.1	12	1×10^{-13}
5.....	0.2	24	1×10^{-13}
6.....	0.2	25	1×10^{-13}

[1] Used 15 drops of aqueous litmus solution. It should be noted that this value does not agree very closely with that obtained by Wood.[1]

Propionanilide.

Preparation.—The propionanilide was prepared by treating one molecular weight of aniline with one molecular weight of propionic

[1] *J. Chem. Soc.*, **83**, 568 (1903); **89**, 1831, 1839 (1906).

anhydride. After careful purification, by crystallization from water, it melts at 105° (corr.).

Ionization Constant.—Concentration of propionanilide, $C_1 = 8.62 \times 10^{-3}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-4}$ N. Indicator, 15 drops of aqueous litmus solution. Temperature, 30°. $k_b^{30°} = 5.4 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{28°}$.
1.....	0.2	25	3×10^{-13}
2.....	0.2	25	3×10^{-13}
3.....	0.2	25	3×10^{-13}
4.....	0.4	50	3×10^{-13}

Benzanilide Preparation.—Carefully purified Kahlbaum benzanilide which melted at 163° (corr.) was used for the measurement of its ionization constant.

Ionization Constant.—Concentration of benzanilide, $C_1 = 2.2 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-6}$ N. Indicator, 2 drops of an aqueous solution of litmus. Temperature, 26°. $k_b^{26°} = 4.8 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{26°}$.
1.....	0.2	10	2×10^{-13}
2.....	0.5	25	2×10^{-13}
3.....	0.5	25	2×10^{-13}

Chloroacetanilide.

Preparation.—Attempts to prepare chloroacetanilide by the method of Cech[1] resulted in very poor yields. In his method equimolar proportions of aniline and chloroacetic acid were mixed when a vigorous reaction occurs, resulting in a paste of crystallin compounds. The paste was heated with phosphorus pentoxide to cause dehydration. The dark paste resulting gave very little chloroacetanilide, which required repeated bone-blacking and recrystallization in order to obtain the pure product. A much more successful method was developed for the preparation of this compound. An ethereal solution of chloroacetic acid is added to an ethereal solution of aniline, drop by drop, with constant stirring, while the whole is cooled in an ice bath. A perfectly colorless product of aniline chloroacetate was obtained as a precipitate. The colorless aniline chloroacetate soon becomes yellow when exposed to the air. The finely crystallin aniline chloroacetate was mixed with the calculated amount of phosphorus pentoxide and allowed to stand tightly stoppered for about a month (it is doubtful if this time is always necessary). The product was then purified by crystallization from hot water. Treatment with boneblack was unnecessary, for after several crystallizations from water, a beautiful white product, which melted at 136° (corr.), was obtained.

[1] *Ber.*, 10, 1376 (1877).

Ionization Constant.—Concentration of chloroacetanilide, $C_1 = 6.76 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-6}$ N. Indicator, 2 drops of an aqueous solution of litmus. Temperature, 26°. $k_b^{26°} = 4.8 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{26°}$
1.....	1	25	2×10^{-13}
2.....	1	25	2×10^{-13}
3.....	1	25	2×10^{-13}

p-Aminoacetophenone.

Preparation.—The Kahlbaum product was purified by crystallization from alcohol by carefully diluting with water. A fairly colorless product was obtained which melted at 110° (corr.).

Ionization Constant.—Concentration of *p*-aminoacetophenone, $C_1 = 4.97 \times 10^{-3}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-3}$ N. Indicator, 10 drops of an aqueous solution of litmus. Temperature, 29°. $k_b^{29°} = 5.35 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{29°}$
1.....	20	8.0	4.5×10^{-10}
2.....	30	12.0	4.5×10^{-10}
3.....	20	8.0	4.5×10^{-10}
4.....	5	2.0	4.5×10^{-10}

p-Aminopropiophenone.

Preparation.—The method of Kunckell referred to above was used for the preparation of *p*-aminopropiophenone. Ten grams of acetanilide and 15 grams of propionyl chloride were dissolved in 30 cc. of carbon disulfide, to which solution were added 20 grams of aluminium chloride in small portions. The mixture was heated for an hour and a half upon the steam bath. The dark red syrup resulting was poured into fine ice when a brown substance precipitated. This product was *p*-acetylaminopropiophenone. It was hydrolyzed with hydrochloric acid and the *p*-aminopropiophenone separated after making the solution alkalin. It was purified by crystallization from hot water and when pure melted at 140° (corr.).

Ionization Constant.—Concentration of *p*-aminopropiophenone, $C_1 = 1.74 \times 10^{-3}$ N. Standard hydroxyl ion concentration, $C_0 = 2.36 \times 10^{-3}$ N. Indicator, 15 drops of an aqueous solution of litmus. Temperature, 30°. $k_b^{30°} = 5.44 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{30°}$
1.....	5	10	2.4×10^{-10}
2.....	5	10	2.4×10^{-10}
3.....	5	10	2.4×10^{-10}

p-Aminobenzophenone.

Preparation.—*p*-Aminobenzophenone was obtained by Döbner's[1]

[1] *Annalen*, 210, 266 (1881).

synthesis. It was purified by crystallization from dilute alcohol. It melted at 124° (corr.) when pure.

Ionization Constant.—Concentration of *p*-aminobenzophenone, $C_1 = 1.64 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-4}$ N. Indicator, 3 drops of an aqueous solution of litmus. Temperature, 26°. $k_b^{26°} = 4.8 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{26°}$
1.....	5	11	5.4×10^{-10}
2.....	5	10	5.7×10^{-10}
3.....	5	10	5.7×10^{-10}

p-Aminochloroacetophenone.

Preparation.—The product was prepared by the method of Kunckell[1] from acetanilide and chloroacetyl chloride. It was purified by crystallization from hot water from which it was obtained in faintly yellow needles which melted at 148° (corr.) when pure.

Ionization Constant.—Concentration of *p*-aminochloroacetophenone, $C_1 = 2.42 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-4}$ N. Temperature, 26°. $k_b^{26°} = 4.8 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_{b_1}^{26°}$
1.....	5	20	2.3×10^{-10}
2.....	5	20	2.3×10^{-10}
3.....	5	20	2.3×10^{-10}

Methylphenylketoxime.

Preparation.—Methylphenylketoxime was prepared by the action of hydroxylamine upon acetophenone in alcoholic solution. It was purified by crystallization from hot water and when pure it melted at 59° (corr.).

Ionization Constant.—Concentration of methylphenylketoxime, $C_1 = 1.09 \times 10^{-2}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-2}$ N. Indicator, 2 drops of an aqueous solution of litmus. Temperature, 27°. $k_b^{27°} = 4.9.3 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_b^{27°}$
1.....	1	22.0	1.16×10^{-10}
2.....	1	22.5	1.16×10^{-10}
3.....	1	23.0	1.16×10^{-10}

Diphenylketoxime.

Preparation.—Diphenylketoxime, which rearranges benzanilide, was obtained by the method of Beckmann,[2] using benzophenone and hydroxylamine hydrochloride in alcohol potash solution. It was purified by crystallization from dilute alcohol and when pure melted at 140° (corr.).

[1] *Ber.*, **33**, 2641, 2644 (1900).

[2] *Ber.*, **20**, 2581 (1887).

Ionization Constant.—Concentration of diphenylketoxime, $C_1 = 8.8 \times 10^{-4}$ N. Standard hydroxyl ion concentration, $C_0 = 5.92 \times 10^{-4}$ N. Indicator, 2 drops of an aqueous solution of litmus. Temperature, 24°. $k_b^{24°} = 4.4 \times 10^{-10}$ for aniline.

Experiment.	Standard solution. Cc.	Water added to standard. Cc.	$k_b^{24°}$
1.....	5	2.0	2×10^{-11}
2.....	5	2.0	2×10^{-11}
3.....	5	2.0	2×10^{-11}
4.....	5	2.0	2×10^{-11}

5. Conclusions.

1. The rearrangements of diacetanilide and dipropionanilide into the corresponding acylaminoketones are found to obey the criterion of intramolecular rearrangements, namely, that such arrangements shall proceed in the direction to decrease the numerical value of the ionization constant or to produce substances that are more neutral (*i. e.*, stable) toward ionization.

2. In order that intramolecular rearrangements of this type may take the aminic nitrogen atom of aniline or similar aromatic amine must be twice substituted by acyl radicals of negativity, varying from 206 to 355, *i. e.*, by acid radicals derived from organic acids whose ionization constants are from 1.4×10^{-5} to 1.55×10^{-3} at 25°.

3. The ionization constants of diacetanilide and dipropionanilide are found to be 7×10^{-9} and 5×10^{-9}, respectively, at ordinary temperature in aqueous solution, showing that acyl radicals derived from acids whose ionization constants fall between the limits 1.8×10^{-5} and 1.4×10^{-5} must be twice substituted upon the aminic nitrogen atom of aniline before its basic nature is changed to that of an acid.

4. The ionization constants of *p*-acetylaminoacetophenone and *p*-propionylaminopropiophenone are found to be basic and of the order 10^{-12}, showing that the single substitution upon the aminic nitrogen atom of aromatic aminoketones of acyl radicals, derived from acids of strengths varying from that of acetic acid ($k_a^{25°} = 1.8 \times 10^{-5}$) to that of propionic acid ($k_a^{25°} = 1.4 \times 10^{-5}$), is not sufficient to overcome the initial basic nature of the aminoketones.

5. The ionization constants of acetanilide, propionanilide, benzanilide and chloroacetanilide are found to be basic and of the order 10^{-13}, showing that single substitution upon the aminic nitrogen atom of aniline of acyl radicals, derived from acids of strengths varying from that of propionic acid ($k_a^{25°} = 1.4 \times 10^{-5}$) to that of chloroacetic acid ($k_a^{25°} = 1.55 \times 10^{-5}$), is not sufficient to overcome the initial basic nature of aniline.

6. The ionization constants of the following bases were determined:

p-aminoacetophenone..... $k_b^{29°} = 4.5 \times 10^{-10}$
p-aminopropiophenone..... $k_b^{30°} = 2.4 \times 10^{-10}$
p-aminobenzophenone..... $k_b^{26°} = 5.7 \times 10^{-10}$
p-aminochloroacetophenone..... $k_b^{26°} = 2.3 \times 10^{-10}$

showing the aromatic aminoketones to be bases with ionization constants of the same order as that of aniline.

7. Acetophenonoxime and benzophenonoxime are bases, the former has $k_b^{27^\circ} = 1.16 \times 10^{-10}$ while the latter has $k_b^{24^\circ} = 2.0 \times 10^{-11}$. The Beckmann rearrangements of these oximes obey the criterion for the non-reversible intramolecular rearrangements.

8. A colorimetric method is developed by means of which the ionization constant of sufficiently soluble acids and bases may be determined with a mean error of 2%.

URBANA, ILLINOIS.

THE ENZYMES OF THE TOBACCO PLANT.

BY J. DU P. OOSTHUIZEN AND O. M. SHEDD.

Received June 12, 1913.

There are a great many changes taking place in the tobacco plant throughout its growth, as well as during the curing and fermentation periods. Certain chemical compounds are formed and others are broken down to form new products. It is the result of these which give the color, texture, aroma, etc., to the finished product. Yet all these changes can be easily stopped by subjecting the tobacco to unfavorable conditions during the curing, and a whole crop can easily become worthless. Again, a crop may undergo some of these changes under favorable conditions and still one of its desirable qualities may be lacking. The causes of these changes have been studied by several scientists and numerous treatises have been published in regard to this subject.

The theory that bacteria are largely instrumental in bringing about the many changes of the different stages of the curing process, has been advanced by Suchsland[1] and other scientists.[2] Some scientists have even advanced the idea that the bacteria produced on the aromatic Vuelta Abajo (a variety of tobacco noted for its aroma) could be transferred to some of our American varieties and that the fermentative processes initiated by this would develop an aroma equal to that of the Cuban tobacco. If this was the case, then all the differences in the various types of tobacco due to soil, climate and localities would have been broken down, and all that would be necessary to grow a fine crop of tobacco would be to inoculate our tobacco with some of these aroma-producing bacteria.

Recently, however, Dr. Loew,[3] formerly of the United States Department of Agriculture, has proven that the fermentation and curing of tobacco is not caused by bacteria, nor is the aroma of tobacco due to the

[1] *Ber. bot. Ges.*, 9, 79–81 (1891).

[2] O. Loew disproves this theory in Report No. 59, Div. of Veg. Physiology and Pathology, U. S. Dept. of Agriculture.

[3] Reports Nos. 59 and 65, Div. of Veg. Physiology and Pathology, U. S. Dept. of Agr.