Discussion

It is strange to find that with $FeCl_3$ the molecular weight increases with a diminution in the concentration of the solute. Similar results were also noticed by Kahlenberg and Lincoln.[4] The molecular weight obtained for the compound $FeCl_3 \cdot POCl_3$ is 344, while the calculated value is 316. The difference between the observed molecular weight (310) and the calculated value (785.5) for the compound $2FeCl_3 \cdot 3POCl_3$ is quite considerable. This may be due to the dissociation of the complex.

$$2FeCl_3 \cdot 3POCl_3 \rightleftharpoons 2(FeCl_3 \cdot POCl_3) + POCl_3 \quad (1)$$

This also explains the equality in conductivity of the two complexes for a given concentration of ferric chloride.

Table III indicates that the specific conductivity of the complex $FeCl_3 \cdot POCl_3$ is invariably higher than the sum of the conductivities of the individual components. This increase in the conductivity can be explained by assuming the dissociation of the complex as

$$FeCl_3 \cdot POCl_3 \rightleftharpoons FeCl_4^- + POCl_2^+ \quad (2)$$

The studies described above indicate the formation of the two complexes $2FeCl_3 \cdot 3POCl_3$ and $FeCl_3 \cdot POCl_3$. The existence of the compound $2FeCl_3 \cdot POCl_3$ reported in the literature, however, could not be confirmed.

Acknowledgment.—The authors wish to thank Prof. K. R. Krishnaswami, Head of the Department of General Chemistry, Indian Institute of Science, Bangalore, for his keen interest and helpful criticism during the progress of this investigation.

DEPARTMENT OF GENERAL CHEMISTRY
INDIAN INSTITUTE OF SCIENCE
BANGALORE-3 (INDIA)

An Aqueous Synthesis of Barium Titanate

BY STEWARD S. FLASCHEN

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High temperature calcination and reaction of titanium dioxide and barium as the oxide, nitrate, carbonate or hydroxide, or as the mixed oxalates are the usual bases for the preparation of barium titanate ($BaTiO_3$). In the method reported herein crystalline barium titanate as well as various titanate solid solutions are synthesized directly from aqueous solution. This method is based upon the precipitation of barium titanate upon addition of a titanium ester to an aqueous solution of a soluble barium salt. Analogous to the solution chemistry of the zirconates, vanadates and chromates, a strongly alkaline environment is found to be essential for the formation of the "meta" salt. Precipitation from neutral and acid solutions result in the formation of hydrated titanium dioxide only.

In this method a dilute propyl alcohol solution of a titanium ester such as tetrapropyltitanate or an ester of a higher alcohol is added dropwise and with vigorous stirring to a degassed water solution of barium hydroxide, pH 11 to 14. Reaction in a KOH solution is used where a controlled pH is desirable. No chemical or physical differences in the nature of the product could be detected by reaction in the presence of potassium ion or as a function of the pH over this range. Sufficient excess of the ester is added to result in a final 1:1 or greater molar ratio of BaO to TiO_2. A white, fine grained (1 to 5 μ), homogeneous phase readily precipitates on mixing over the temperature range 20 to 100°. Reaction above 80° yields a crystalline product directly. The low temperature precipitate must be aged for from one to two hours at the boiling point. The precipitate is filtered and then washed with hot, degassed distilled water to remove excess barium salt.

The X-ray diffraction pattern of the product is identical to that characteristic of the tetragonal modification of $BaTiO_3$ as synthesized by means of high temperature solid state reaction. This method has also been used successfully for the introduction of trace impurities and for the synthesis of homogeneous solid solutions in which partial substitution has been made for the barium ion.

BELL TELEPHONE LABORATORIES, INC.
MURRAY HILL, N. J.

Basicity of the Amide Bond[1,2]

BY A. R. GOLDFARB, A. MELE AND N. GUTSTEIN

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During the course of an investigation of the ultraviolet absorption spectra of amides and peptides it was observed that these compounds showed a marked lowering of the molar extinction coefficient (ϵ) in concentrated sulfuric acid solutions. The shape of the curves, ϵ *vs.* concentration of sulfuric acid, suggested that we were measuring the proton binding ability of the amide and peptide structures. Cryoscopic measurements[3,4] in 100% H_2SO_4 have indicated that amides and carboxylic acids bind one proton. Hall[5] using potentiometric methods, measured the acid dissociation constant for the acetamidonium ion and found pK_a[6] values of −0.5 in water and −1.65 in glacial acetic acid. More recently Lemaire and Lucas[7] determined the thermodynamic pK_a values of a number of weak bases, including acetamide, by use of an indicator method. The value of pK_a determined in the last instance was about −0.04. We have made a study of a series of acetamide derivatives, using a spectrophotometric method, to determine the effect of substituent on the nitrogen and of adjacent charge on the basicity of the amide bond.

Experimental

Materials.—Acetic acid, acetamide, methyl- and dimethylacetamide, glycinamide and acetylglycine were commercially available materials which were purified by fractional distillation or crystallization. The butylacetamides were prepared by mixing acetic anhydride (2 moles) with the

(1) Supported by Grant #NSF-G617 from the National Science Foundation.

(2) Reported, in part, at the Meeting of the American Chemical Society held in New York during March of 1954.

(3) A. Hantzsch, *Ber.*, **64**, 667 (1931).

(4) J. L. O'Brien and C. J. Niemann, THIS JOURNAL, **72**, 5348 (1950).

(5) N. F. Hall, *ibid.*, **52**, 5115 (1930).

(6) $pK_a = -\log K_a$, K_a = (acetamide)(H+)/(acetamide H+).

(7) H. Lemaire and H. J. Lucas, THIS JOURNAL, **73**, 5198 (1951).

TABLE I

EQUILIBRIUM CONSTANTS FOR AMIDONIUM COMPOUNDS IN AQUEOUS H_2SO_4

Compound	ϵ_B (2050 A)	pK_1	σ^a	$\epsilon_{BH_1^+}/\epsilon_B$	pK_2	σ^a	$\epsilon_{BH_2^+}/\epsilon_{BH_1^+}$
CH_3CONH_2	246	+0.37	0.10	0.60	−1.40	0.02	0.21
NH_3^+–CH_2CONH_2	328	−1.78	.28	.78	−6.10	.20	.26
$CH_3CONHCH_2COOH$	975	−1.92	.13	.71	−4.33	.08	.63
$CH_3CONHCH_3$	1400	−0.46	.07	.29	−3.70	.40	.21
$CH_3CONHC_4H_9$-n	2610	+0.15	.12	.51	−2.27	.30	.67
$CH_3CONHC_4H_9$-*iso*	2690	+0.01	.11	.61	−1.98	.20	.70
$CH_3CONHC_4H_9$-*sec*	2370	+0.10	.11	.58	....[b]	..	.90
$CH_3CONHC_4H_9$-*t*	2270	+0.32	.05	.44	....[b]	..	.90
$CH_3CON(CH_3)_2$	6166	−0.19	.06	.48	....[b]	..	.88
CH_3COOH	5.8	−6.10					

[a] σ is the standard deviation. No less than seven points were used in estimating the average pK and the standard deviation. [b] The amount of change of ϵ is too small to permit calculations of the pK_2 values. [c] ϵ_B, $\epsilon_{BH_1^+}$ and $\epsilon_{BH_2^+}$ are the molar extinctions for the free amide, the amidonium ion of the first kind (see Discussion) and the amidonium of the second kind in the equilibria $H^+ + B \rightleftarrows BH_1^+ \rightleftarrows BH_2^+$.

butylamine (1 mole) and fractionating the product 2 or 3 times. The properties and analyses for the acetyl butylamides are as follows: *n*-butyl, b.p. 103.5° at 3.5 mm., N (found) 12.17%; isobutyl, b.p. 97° at 3.5 mm., N (found) 12.09%; *sec*-butyl, b.p. 77° at 1.2 mm., N (found) 12.20%; *t*-butyl, m.p. 97–98°, N (found) 12.12%, N (calcd.) for butylacetamide is 12.17%. The sulfuric acid was an ACS grade.

Methods.—Test solutions were prepared of a known concentration of sulfuric acid, which contained a known amount of amide (concentration between 10^{-3} and 10^{-4} M). The values of H_0[8] were obtained from the concentration of H_2SO_4 and the data given by Hammett and Deyrup,[9] Hammett and Paul[10] and Deno and Taft.[11] The solutions were made up immediately before being studied spectrophotometrically. Precautions were taken to prevent the temperature from rising above 25° at any time during the experiment.

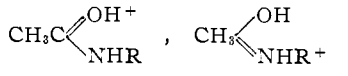
The optical densities of the solutions were determined at 2000, 2050 and 2100 Å. within 5 to 15 minutes after the solutions were prepared. The spectrophotometric procedures were those described previously.[12] To determine whether hydrolysis had occurred during the experiment, the test solutions were allowed to stand for 4 to 24 hours at room temperature and the optical densities read. In no case was there any observable change after 4 hours and after 24 hours the change was less than 10%. Since the ϵ for acetic acid is less than 3% of that for the amides and absorption for amine sulfates are negligible in this region of the spectra, we concluded that an insignificant amount of hydrolysis occurred during the experiment. The values of pK_a were determined from the spectral data as described by Flexser, Hammett and Dingwall,[13] using the expression $pK_a = H_0 - \log (\epsilon_B - \epsilon_{BH^+})/(\epsilon_B - \epsilon)$, where ϵ is the experimental absorption coefficient, and ϵ_B and ϵ_{BH^+} are the coefficients of the free base and proton bound from the amide.

Results and Discussion

In the early stages of this work when the molar extinction was plotted against H_0, typical sigmoid curves were obtained. However, when attempts were made to calculate pK it was soon evident that no single pK value fitted all of the data. Instead of assuming ϵ_{BH^+} to be the lowest experimental value, we calculated it by a method of approximations using the equation given above and assuming the value of ϵ_B to be the experimental value. The calculated value of $\epsilon_{BH_1^+}$, thus obtained, was always larger than the smallest value of ϵ obtained at large negative values of H_0. In a similar manner the value of $\epsilon_{BH_1^+}$ was calculated using the data at large negative H_0 values assuming $\epsilon_{BH_2^+}$ to be the lowest experimental value of ϵ. Both values of $\epsilon_{BH_1^+}$ agreed well within experimental error and we were led to conclude that the data were consistent with the presence of two equilibria. The values of pK_1 and pK_2 were obtained using these calculated estimates of ϵ_{BH_1} with the experimental values of ϵ_B and $\epsilon_{BH_2^+}$.

In Table I are summarized the results of these studies.[14] The value of pK_1 which was found for acetamide (+0.37) is in fair agreement with the previously reported values of −0.5 by Hall[5] and about −0.04 by Lemaire and Lucas.[7] The first equilibrium seems to correspond to the reaction $B + H^+ \rightleftarrows BH_1^+$. The values of pK_1 for all the amides are fairly close except for glycinamide and acetylglycine. The latter two compounds indicate the relatively strong inductive effect of an adjacent charge and carboxymethyl group.

The second equilibrium is not as easily assigned. In view of the cryoscopic measurements of Hantzsch[3] on acetamide and O'Brien and Niemann[4] on acetylglycine it is not possible that a second proton could have added to the amides. Operationally we have measured the change of spectra with increasing concentration of sulfuric acid. The change must be identified with some effect on the electronic structure of any portion of the amide bond. A generalized solvent effect due to a change of some property of the solvent does not seem reasonable in view of the wide range of values of pK_2. The basicity of the amide bond may be considered to be associated with the resonating forms



If it is assumed that one of the solvent species is

(8) H_0 is the acidity function described by L. P. Hammett, in "Physical Organic Chemistry," McGraw-Hill Book Co., New York, N. Y., 1940, p. 267.

(9) L. P. Hammett and A. J. Deyrup, THIS JOURNAL, **54**, 2721 (1932).

(10) L. P. Hammett and M. A. Paul, *ibid.*, **56**, 827 (1934).

(11) N. C. Deno and R. W. Taft, Jr., *ibid.*, **76**, 244 (1954).

(12) A. R. Goldfarb, L. J. Saidel and E. Mosovich, *J. Biol. Chem.*, **193**, 397 (1951).

(13) L. A. Flexser, L. P. Hammett and A. Dingwall, THIS JOURNAL, **57**, 2109 (1935).

(14) The validity of this study depends on the assumption that the data obtained on any portion of an absorption curve for a compound are equally valid for any other portion of the curve. The region which we have studied is the wave length of half maximum. This region is one which has been shown to correspond to strong absorption by amides.[15,16]

(15) H. Ley and B. Arends, *Z. physik. Chem. Abst.*, **B17**, 177 (1932).

(16) H. D. Hunt and W. T. Simpson, THIS JOURNAL, **75**, 4540 (1953).

bound to an amide by the free electron pair on the nitrogen through a H-bond[17] it is possible to account for the change of absorption spectra without requiring a value of "i" greater than 2. The amount of solvent bound would not be sufficiently large to be measurable by cryoscopic methods. The marked effect of nitrogen substituents on pK_2 might be theoretical support for assuming that the effect is on the electron pair on the nitrogen. The enormous effect of the ammonium group in glycinamide is not as clear.

The pK_a for acetic acid was determined since acetylglycine has a carboxylic acid group. The value of -6.1 is much too negative compared to the pK_2 of acetylglycine (-4.33) and it is not reasonable to correlate the pK_2 of acetylglycine with the proton binding by the COOH. We are continuing this study for simple and complex peptides and proteins and will report the results of these studies in the not too distant future.

(17) The authors feel that the comments of referee I should be incorporated here since they are of interest. With his permission we are reporting them without further comment.

"There is some question in my mind whether the hydrogen bond is discrete enough to be treated as a thermodynamic equilibrium. At least to my knowledge no one has yet shown that treating hydrogen bonding as a thermodynamic equilibrium correlates some physical property with concentration. A similar situation arose in the failure of the Arrhenius theory of ionization to treat association of solvated ions as equilibria."

"The fact that the C=O group exists primarily as $C{=}OH^+$ is no reason that it cannot be also in equilibrium with $C\begin{smallmatrix}OH\\OSO_3H\end{smallmatrix}$. A similar situation exists in the conversion of alcohols to alkyl hydrogen sulfates (THIS JOURNAL, **72**, 3852 (1950)) where the reaction does not become appreciable until concentrations of H_2SO_4 are reached at which the alcohols are primarily in the protonated form (private communication from Dr. Bartlett). Lest the authors feel that I am "pushing" this alternative explanation, let me hasten to emphasize that to me the data do not seem to favor either interpretation."

DEPARTMENT OF BIOCHEMISTRY
CHICAGO MEDICAL SCHOOL
CHICAGO 12, ILLINOIS

The Estimation of the Validity of Stepwise Association Constants[1]

BY J. W. GRYDER

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Several methods have been reported in the literature for the estimation of successive association constants of mononuclear complexes.[2] All of the methods involve successive approximations, graphical solution, or both. Frequently, less rigorous methods have also been employed and the set of constants obtained over-emphasize certain experimental points. The result is that the constants are not the best choices to fit all of the available data. The procedure discussed below is a quick and reliable method for determining the validity of constants derived by any procedure.

The following symbols, with parentheses indicating concentration, will be employed

A = ligand, M = central atom or ion
MA_i = formula for a complex species containing one M and i A's
γ_i = activity coefficient of complex MA_i
γ_a = activity coefficient of complex A
γ_M = activity coefficient of complex M
$\beta_i = \dfrac{\gamma_i(MA_i)}{\gamma_M\gamma_a{}^i(M)(A)^i}$ = association constant for species MA_i

If C_A is the total concentration of ligand and C_M is the total concentration of cation, we obtain the conservation equations

$$C_M = (M) + \sum_{i=1}^{n} \frac{\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(M)(A)^i \qquad (1)$$

$$C_A = (A) + \sum_{i=1}^{n} \frac{i\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(M)(A)^i \qquad (2)$$

Rearranging equations 1 and 2

$$0 = -\frac{(M) - C_M}{(M)} + \sum_{i=1}^{n} \frac{\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^i \qquad (3)$$

$$0 = -\frac{C_A}{(M)} + \left[\frac{1}{(M)} + \frac{\beta_1\gamma_M\gamma_a}{\gamma_1}\right](A) + \sum_{i=2}^{n} \frac{i\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^i \qquad (4)$$

It is assumed that C_A, C_M and (M) are the measured quantities and that the activity coefficients and the β's have been derived from these quantities. Equations 3 and 4 are seen to be power series in the concentration of free ligand, with the coefficients being functions of the experimental quantities, the equilibrium constants and the activity coefficients. The variable can be eliminated from two power series in the same variable by Sylvester's method of dialytic elimination.[3] This involves treating each power of the variable as an independent unknown and multiplying the equations through by the variable until there are the same number of equations as there are unknowns. Multiplying equations 3 and 4 by (A), n times we obtain the set of $2n$ equations 5.

$$0 = \frac{(M) - C_M}{(M)}(A) + \sum_{i=1}^{n} \frac{\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^{i+1}$$

$$0 = -\frac{C_A}{(M)}(A) + \left[\frac{1}{(M)} + \frac{\beta_1\gamma_M\gamma_a}{\gamma_1}\right](A)^2 + \sum_{i=2}^{n} \frac{i\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^{i+1}$$

$$\vdots \qquad \vdots \qquad \vdots \qquad \vdots$$

$$0 = \frac{(M) - C_M}{(M)}(A)^n + \sum_{i=1}^{n} \frac{\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^{i+n}$$

$$0 = -\frac{C_A}{(M)}(A)^n + \left[\frac{1}{(M)} + \frac{\beta_1\gamma_M\gamma_a}{\gamma_1}\right](A)^{n+1} + \sum_{i=2}^{n} \frac{i\beta_i\gamma_M\gamma_a{}^i}{\gamma_i}(A)^{i+n} \qquad (5)$$

In order to have a solution the determinant of the coefficients must vanish, *i.e.*,

(1) This work was supported by Grant G 3604(C2) from the National Institutes of Health, Department of Health, Education, and Welfare.

(2) These methods have been discussed critically and extended by J. C. Sullivan and J. C. Hindman, THIS JOURNAL, **74**, 6091 (1952), and by J. Z. Hearon and J. B. Gilbert, *ibid.*, **77**, 2594 (1955).

(3) See, for example, J. M. Thomas, "Theory of Equations," McGraw–Hill Book Co., New York, N. Y., 1938, pp. 171–175.