

A Method to Correct the pH and Acid Dissociation Constants of Weak Aqueous Acid Solutions with Temperature

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Algumas aproximações razoáveis permitem a correção do pH ou pK_a de soluções aquosas tamponadas, com a temperatura. Para calcular a variação da atividade protônica, foram considerados a dissociação da água e do tampão e a variação dos coeficientes de atividade do ácido fraco e da correspondente base conjugada. As equações obtidas permitem o cálculo de pK'_a a uma certa temperatura, quando o pH'_a essa temperatura é conhecido, junto com o pH e pK_a a uma temperatura de referência. O procedimento inverso permite o cálculo do pH' quando o pK'_a é conhecido. Os resultados, usando o método em sete soluções padrões de pH, onde o pK_a do tampão é conhecido a várias temperaturas, concordam com os valores experimentais com uma aproximação de ±0,01 unidades de pK' (ou pH). O anion hidrogênio ftalato mostrou um desvio positivo sistemático, que pode ser explicado pela formação do enlace de hidrogênio intramolecular, e as duas cargas adjacentes da base conjugada.

Some reasonable assumptions allow the correction of pH or pK'_a of buffered aqueous solutions with temperature. In order to calculate the change of proton activity, the dissociation of water and buffer and the change of activity coefficients of the weak acid and the corresponding conjugate base were considered. The equations obtained permit the calculation of pK'_a at a certain temperature when the pH' at that temperature is known, and the pH and pK'_a at a reference temperature as well. The inverse procedure allows the calculation of pH' when pK'_a is known. The results using the method in seven pH standard solutions, where the pK_a of the buffer is known at several temperatures, agree with the experimental values within ±0.01 pK (or pH) units. Hydrogen phthalate anion showed a systematic positive deviation which can be ascribed as due to intramolecular hydrogen bonding, and to the two adjacent charges of the conjugated base.

Key words: *dissociation constant, pH, pK_a, buffer.*

The pH of an aqueous solution or the pK_a of a weak electrolyte used as buffer, are important parameters for acid-base catalytic studies¹⁻⁴. However, many times they cannot be measured under the reaction conditions, specially if the reaction is carried out at different temperature from that at which the pH (or the pK_a) was measured⁵⁻⁷. The change of temperature modifies the excess (or deficiency) of protons in the solution, depending on the autoprotolysis constant of water, K_w, the acid dissociation constant of the weak electrolyte, K_a, and the activity coefficients of the species involved.

The change of the pH with temperature for some buffers can be calculated from (1), where T is the temperature in kelvins, when the constants A, B, C, D are known.⁸ This equation is based on the assumption that the change of free energy with temperature can be represented by a power series.⁹

$$\text{pH}(S) = \frac{A}{T} + B + CT + DT^2 \quad (1)$$

Since there is no theoretical equation for expressing the ionization constant as a function of temperature¹⁰, by a

similar assumption, Harned and Embree¹¹ related the pK_a 's at different temperatures of a weak electrolyte, according to (2), where

$$pK_a - pK_m = a(t - t_m)^2 \quad (2)$$

a is a constant characteristic of each acid, t_m is the temperature at which the pK_a has a minimum value equal to pK_m , and t is the Celsius temperature.

The method we propose in this paper is based on the fact that pH-temperature curves are expected to be the same as those of the pK_a versus temperature, although small changes of the temperature minima of the two curves might occur because of the change of activity coefficients with temperature.¹²

Conceptually, the pH is defined as the negative logarithm of the (relative) single hydrogen ion activity (3), which is also related to the molality and activity coefficient of the hydrogen ion.¹³

$$pH = -\log a_H = -\log m_H \gamma_H \quad (3)$$

Hydrogen ion concentration can also be expressed as molarity, and for most purposes, the difference between both scales for dilute solutions, can be ignored because the density of water between 25 to 100°C changes only 3.91%.¹³

The definition of pH is operational and it is measured by comparison between two hydrogen cells using platinum electrodes. The most common method to measure the pH in laboratories where kinetics, reaction mechanisms or catalysis are studied, is to replace the platinum electrode with a glass electrode attached to a pHmeter. This means that the precision with which the pH is measured is not greater than a hundredth of a pH unit.

A number of standard solutions have been chosen¹³ to assign a value of pH at different temperatures, in the range of 0-95°C¹³. These sets of solutions provide the best available values of pH at different temperatures and some of them were used to test this method. We note, however, that even for these pH values there are some discrepancies at the level of a thousandth of a unit of pH depending on the type of cell used for the measurements.¹³

In this work we developed an approximate method of calculating the pK'_a of a weak acid at a certain temperature when then pH' of a solution of the acid is known at that temperature and the pH and pK_a are known at a reference temperature. Conversely the method allows the correction of the pH of such solution with temperature, if the pK_a is known under the same conditions.

The water contribution to the change of pH of aqueous solutions of strong acids or bases with temperature. The pH of aqueous solutions of strong acids or bases changes mainly due to the high temperature coefficient of pK_w as compared to the change of the activity coefficients with temperature¹² and it is the major contributor to the change of the activity of protons. The pH of these solutions is obtained by adding a strong acid (or base), that is considered totally dissociated. At the reference temperature of 25°C, the pH is given by (3) and the auto-protolysis constant of water by (4).

$$K_w = a_H \cdot a_{OH} = m_H \cdot m_{OH} \gamma_H \gamma_{OH} \quad (4)$$

When the temperature changes, the number of dissociated molecules of water also changes and the new value of K'_w is given by (5), where m_x is the change of molality of the proton and hydroxide

$$K'_w = a'_H \cdot a'_{OH} = (m_H + m_x)(m_{OH} + m_x) \gamma'_H \gamma'_{OH} \quad (5)$$

ion. The change of dissociation of water, measured by the concentration product, is much greater than the ionic activity coefficient function at constant ionic strength^{14,15} and we will assume that $m_x \gamma'_H \approx m_x \gamma'_{OH}$. We can rewrite (5) as (6), where $x = m_x \gamma'_H$, $i = H^+$, OH^- . Substituting $K'_w = a'_H \cdot a'_{OH}$ and $p = 10^{-pH} + 10^{-(pK_w - pH)}$ in (6), and solving for x , (7) can be obtained. The new pH' will

$$K'_w = (a_H + x)(a_{OH} + x) \quad (6)$$

$$x = -\frac{1}{2} p + \frac{1}{2} [p^2 + 4(K'_w - K_w)]^{1/2} \quad (7)$$

be related to that measured at the reference temperature by eq. 8.

$$pH' = -\log(10^{-pH} + x) \quad (8)$$

Correction of pH of aqueous solutions of buffers, and their pK'_a with temperature. In dilute solutions of buffers the effect of temperature on the pH is mainly due to the change of the acid dissociation constant and the autoprotolysis constant of water. The proton activity changes because of the dissociation of water and weak electrolyte molecules (9). We will call y the change of proton activity due to the dissociation of the weak electrolyte with temperature.



The acid dissociation constant K_a , corresponding to equilibrium (9), at 25°C, is given by (10), at any pH, where for

$$K_a = a_H \cdot \frac{m_A}{m_{HA}} \cdot \frac{\gamma_A}{\gamma_{HA}} = K_i \cdot \frac{\gamma_A}{\gamma_{HA}} \quad (10)$$

generality, the charges are omitted, and K_i is called the "incomplete" ("unvollständige") constant, according to Brønsted.^{16,17} The total molality of the weak electrolyte is $m_o = m_A + m_{HA}$ and assuming that at 25°C, $K_a \approx K_i$, m_{HA} can be calculated from (11). This

$$m_{HA} = m_o \left(\frac{a_H}{K_a + a_H} \right) \quad m_A = m_o \left(\frac{K_a}{K_a + a_H} \right) \quad (11)$$

approximation is usually made in catalytic studies.^{3,18}

When the temperature changes to t , K_i becomes K'_i (12), while the corresponding values of K'_w and the new pH' are given by (13) and (14),

$$K'_i = (a_H + x + y) \left(\frac{m_A + m_y}{m_{HA} - m_y} \right) = K'_a \frac{\gamma_{HA}}{\gamma_A} \quad (12)$$

$$K'_w = (a_H + x + y)(a_{OH} + x) \quad (13)$$

$$pH' = -\log(a_H + x + y) \quad (14)$$

Considering that the temperature coefficient of pK_w is much greater than that of the pK_a of weak acids,¹² y will be smaller than x and as a first approximation, y can be calculated assuming that $y \approx m_y$ (eq. 15), where q and r are given by (16) and (17).

$$y = \frac{1}{2} [-q + (q^2 - 4r)^{1/2}] \quad (15)$$

Calculation of K'_i is shown in the next section.

$$q = K_a + a_H + x + m_o \frac{K_a}{K_a + a_H} \quad (16)$$

$$r = \frac{(a_H + x)m_o K_a - K'_i \cdot m_o a_H}{K_a + a_H} \quad (17)$$

Correction of the activity coefficients with temperature. Equations (10) and (12) can be combined as eq. 18. Assuming that $pK_a \approx pK'_i$, as was done in (11), but considering the terms that determine the change of γ'_i s with temperature for the acid conjugated base species, one can approximate (18) to (19) (a, b).

$$pK'_a = (pK_a - pK'_i) + pK'_i + \log \gamma'_{HA} / \gamma_{HA} - \log \gamma'_A / \gamma_A \quad (18)$$

gated base species, one can approximate (18) to (19) (a, b).

$$pK'_a \approx pK'_i + \log \gamma'_{HA} / \gamma_{HA} - \log \gamma'_A / \gamma_A \quad (19a)$$

$$pK'_a \approx pK'_i + \Delta pK \quad (19b)$$

The molality of any salt added to the solution to reach a certain ionic strength I , does not change with temperature and when comparing I at two temperatures, the concentration of the salt will cancel out. If the solution contains also a weak acid, the change of I will depend on the change of the proton molality due to the dissociation of water (m_x) and the buffer (m_y), and therefore $I' - I = \Delta I = m_x + m_y z$. Since m_x and m_y are very small as compared to the total ionic strength, I can be considered constant at different temperatures.

The term ΔpK (eq. 19b) can be calculated from the Debye-Hückel equation 20, where z_i is the charge of the ionic species.¹⁹

$$-\log \gamma_i = \frac{Az_i^2 I^{1/2}}{1 + B\bar{a}_i I^{1/2}} \quad (20)$$

the activity coefficient function ΔpK (19b) can be calculated according to (20), substituting z_i for the corresponding charges of HA and A species (9). Since B varies very little with temperature^{20,21}, for the range 25-0°C or 25-100°C we will consider it as constant, and ΔpK can then be written as (21), or as (22).

$$\Delta pK \approx \frac{(A-A')(1+z)^2 I^{1/2}}{1 + B\bar{a} I^{1/2}} - \frac{(A-A')z^2 I^{1/2}}{1 + B\bar{a} I^{1/2}} \quad (21)$$

$$\Delta pK \approx \frac{(A-A')(1+2z)I^{1/2}}{1 + B\bar{a} I^{1/2}} \quad (22)$$

Methodology

All the calculations were carried out through appropriate programs in a Microcraft II Plus computer. Experimental pH and pK_a at different temperatures were taken from the literature.

Calculation of pH' . In order to calculate pH' of a buffered solution, pK'_i was calculated first from the experimental pK'_a , according to (22) and (19b) using the

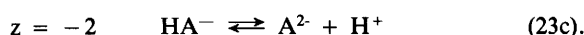
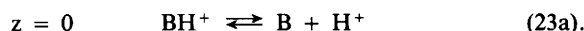
corresponding ion-size parameter.²² Finally, pH' was calculated from (7), (15) and (14).

Calculation of pK'_a . Considering pH and pH' values, y was calculated from (7) and (14) and therefore K'_i was obtained from (12) and corrected for the activity coefficient change according to (22) and pK'_a was then calculated from (19b).

Results and discussion

Eqs. 12 and 13 can be solved simultaneously for x and y , but the solution is cumbersome. When they are calculated by successive approximations, for $pH > 7$, x and y do not converge²³, whereas for $pH < 7$ no improvement was obtained, considering the experimental error, when compared with the results of the proposed method. Perusal of (7) and (15) shows that the first calculates x by zero order approximation with respect to y , and the second calculates y by first order approximation with respect to x .

The pH reference standards were chosen because their pK'_{as} are known at different temperatures with reasonable accuracy. These standards can be classified from (9), according to the charge z as shown in (23).



In Table 1 are summarized the parameters that allow the correction of pK'_a for the activity coefficients, at different temperatures (ΔpK). For Tris and borax, whose ionic radii are not known, the term $B\bar{a}$ was assumed to be equal to unity^{24,25}. In general, the slope of the straight line defined by (22), is negative for $z = 0$, and positive for all $z < 0$. In the last case the slope increases when z decreases and therefore, the correction is more important for divalent anions than for monovalent anions.

Table 1. Characteristic of the Activity Coefficient Correction for the Change of pK'_a with Temperature of Some Weak Electrolytes^a.

Compound	z	I	$\bar{a}, \text{\AA}^b$	m	n
Tris	0	0.16	c	-0.286	0.146
Acetate	-1	0.10	4.5	0.216	-0.110
Citrate	-1	0.041	3.5	0.164	-0.084
Phosphate	-2	0.10	4.5	0.646	-0.330
Tetraborate	-2	0.017	c	0.442	-0.226
Carbonate	-2	0.10	4.5	0.646	-0.330
Phthalate	-2	0.053	6.0	0.475	-0.243

$$a. \Delta pK = mA' + n, \text{ from (22), } m = - \frac{(1+2z)I^{1/2}}{1 + B\bar{a}I^{1/2}};$$

$$n = - \frac{A(1+2z)I^{1/2}}{1 + B\bar{a}I^{1/2}}$$

b. Reference 22.

c. $B\bar{a} = 1$.

Values of experimental pK'_a at different temperatures²⁶⁻²⁹ and the calculated pK'_i from pH values¹³ can be used to obtain ΔpK (19b) in order to compare these values with the ones calculated from (22). As shown in Fig. 1, the agreement is good, within ± 0.01 pK units, and can be considered as a fair estimate of the method.

Phthalate shows a clear positive deviation from the

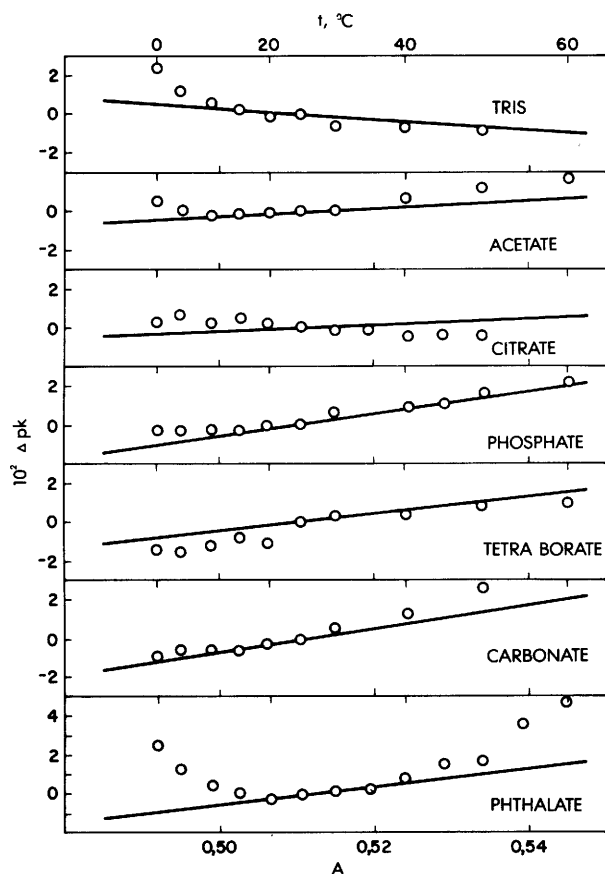


Figure 1. Activity coefficient correction for the change of pK_a with temperature. Straight lines drawn according to Table I; A: Debye-Hückel constant; open circles: ΔpK calculated from eq. 19b.

calculated ΔpK . At 25°C the phthalate monoanion presents a pK_a about 0.6 pK units higher than the terephthalate monoanion. This decrease of the dissociation constant might be due to the increase of the free energy of the dianion because of the two adjacent negative charges³⁰.

Table 2. Values of pH and pK_a for Tris-(hydroxymethyl) aminomethane ("TRIS") Standard Solution (0.01667m Tris + 0.05m Tris. HCl).

°C	pH _{exp} ^a	pH ^b	pK _{a(exp)} ^c	pK' _a ^b
0	8.399	8.418	8.850	8.831
5	8.238	8.246	8.677	8.669
10	8.083	8.086	8.516	8.513
15	7.933	7.933	8.362	8.362
20	7.788	7.786	8.214	8.216
25	7.648	7.648	8.075	8.075
30	7.513	7.508	7.934	7.939
35		7.376	7.803	
40	7.257	7.254	7.677	7.680
45		7.132	7.554	
50	7.018	7.017	7.437	7.438
55				
60	6.794			7.211

a. Reference 13.
b. This work.
c. Reference 26.

The higher pK_a of phthalate monoanion indicates also a lower rate constant for proton transfer to water by the acid³¹ because of the formation of intramolecular hydrogen bonding³².

Table 3. Values of pH and pK_a for Acetate Standard Solution (0.1 M AcOH + 0.1 M AcONa).

°C	pH _{exp} ^a	pH ^b	pK _{a(exp)} ^c	pK' _a ^b
0	4.664	4.673	4.781	4.772
5	4.657	4.661	4.770	4.766
10	4.652	4.653	4.762	4.761
15	4.647	4.648	4.758	4.757
20	4.645	4.645	4.756	4.756
25	4.644	4.644	4.756	4.756
30	4.643	4.644	4.757	4.756
35		4.648	4.762	
40	4.650	4.654	4.769	4.765
45		4.661	4.777	
50	4.663	4.670	4.787	4.780
55		4.681	4.799	
60	4.684	4.694	4.813	4.803
65				
70	4.713			4.835
75				
80	4.75			4.87
85				
90	4.80			4.93
95	4.83			4.96

a. Reference 13.
b. This work.
c. Reference 27.

Table 4. Values of pH and pK_a of the Citrate Standard Solution (0.05 m KH_2 citrate).

°C	pH _{exp} ^a	pH ^b	pK _{a(exp)} ^c	pK' _a ^b
0	3.863	3.869	3.220	3.214
5	3.840	3.849	3.200	3.190
10	3.820	3.824	3.175	3.171
15	3.802	3.808	3.160	3.154
20	3.788	3.791	3.142	3.139
25	3.776	3.776	3.128	3.128
30	3.766	3.763	3.116	3.119
35	3.759	3.756	3.109	3.112
40	3.753	3.746	3.099	3.106
45	3.750	3.743	3.097	3.104
50	3.749	3.740	3.095	3.104

a. Reference 13.
b. This work.
c. Reference 28.

Table 5. Values of pH and pK_a for Phosphate Standard Solution (0.025m Na_2HPO_4 + 0.025m KH_2PO_4).

°C	pH _{exp} ^a	pH' ^b	$pK_{a(exp)}$ ^c	pK'_a ^b
0	6.984	6.990	7.313	7.306
5	6.951	6.955	7.280	7.275
10	6.923	6.926	7.253	7.249
15	6.900	6.900	7.230	7.229
20	6.881	6.881	7.213	7.212
25	6.865	6.865	7.200	7.200
30	6.853	6.854	7.192	7.190
35	6.844	6.845	7.186	7.185
40	6.838	6.838	7.182	7.181
45		6.834	7.181	
50	6.833	6.832	7.182	7.182
55		6.832	7.185	
60	6.836	6.834	7.191	7.192
65				
70	6.845			7.208
75				
80	6.859			7.230
85				
90	6.876			7.257
95	6.886			7.271
100	6.896 ^d			7.285

- a. Reference 13.
 b. This work.
 c. Reference 27.
 d. Calculated from eq. 1.

Table 6. Values of pH and pK_a for Tetraborate Standard Solution (0.01m disodium tetraborate).

°C	pH _{exp} ^a	pH' ^b	$pK_{a(exp)}$ ^c	pK'_a ^b
0	9.464	9.458	9.508	9.513
5	9.395	9.385	9.436	9.445
10	9.332	9.325	9.377	9.384
15	9.276	9.270	9.325	9.329
20	9.225	9.223	9.278	9.287
25	9.180	9.180	9.237	9.237
30	9.139	9.140	9.199	9.198
35		9.101	9.162	
40	9.068	9.066	9.129	9.131
45		9.036	9.101	
50	9.011	9.009	9.076	9.078
55		8.981	9.052	
60	8.962	8.956	9.028	9.034
65				
70	8.921			8.998
75				
80	8.885			8.968
85				
90	8.850			8.938
95	8.833			8.924

- a. Reference 13.
 b. This work.
 c. Reference 27.

Table 7. Values of pH and pK_a for Carbonate Standard Solution (0.025m $NaHCO_3$ + 0.025m Na_2CO_3).

°C	pH _{exp} ^a	pH' ^b	$pK_{a(exp)}$ ^c	pK'_a ^b
0	10.317	10.298	10.625	10.622
5	10.245	10.245	10.557	10.572
10	10.179	10.147	10.490	10.488
15	10.118	10.083	10.430	10.430
20	10.062	10.062	10.377	10.376
25	10.012	10.012	10.329	10.329
30	9.966	9.963	10.290	10.286
35		9.912	10.250	
40	9.889	9.899	10.220	10.215
45		9.866	10.195	
50	9.828	9.839	10.172	10.160

- a. Reference 13.
 b. This work.
 c. Reference 29.

Table 8. Values of pH and pK_a for Potassium Hydrogen Phthalate Standard Solution (0.05m $KH.phthalate$).

°C	pH _{exp} ^a	pH' ^b	$pK_{a(exp)}$ ^c	pK'_a ^b
0	4.000	4.034	5.432	5.397
5	3.998	4.017	5.417	5.397
10	3.997	4.008	5.408	5.397
15	3.998	4.002	5.404	5.400
20	4.001	4.000	5.404	5.405
25	4.005	4.005	5.411	5.411
30	4.011	4.011	5.419	5.419
35	4.018	4.017	5.428	5.429
40	4.027	4.030	5.443	5.440
45	4.038	4.045	5.462	5.455
50	4.058	4.064	5.484	5.478
55	4.064	4.087	5.510	5.487
60	4.080	4.111	5.538	5.506
65	4.097			5.527
70	4.116			5.549
75	4.137			5.575
80	4.159			5.599
85	4.183			5.628
90	4.210			5.659
95	4.240			5.693
100	4.250 ^d			5.706

- a. Reference 13.
 b. This work.
 c. Reference 27.
 d. Extrapolated from eq. 1.

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References

1. M.L. Bender, *Mechanisms of Homogeneous Catalysis from Protons to Proteins*, (Wiley, New York, 1971), ch. 3.
2. W.P. Jencks, *Catalysis in Chemistry and Enzymology*, (Mc Graw-Hill, New York, 1969), ch. 3.
3. T.C. Bruice and S.J. Benkovic, *Bioorganic Mechanisms*, (Benjamin, New York, 1966), Vol. 1, ch. 1.
4. R.D. Gandour and R.L. Schowen, *Transition States of Biochemical Processes*, (Plenum Press, New York, 1978).
5. C.A. Bunton and H. Chaimovich, *J. Am. Chem. Soc.* **88**, 4082-90 (1966).
6. Ch. Degani and M. Halman, *J. Am. Chem. Soc.* **88**, 4075-82 (1966); *ibid.*, **90**, 1313-17 (1968).
7. C.A. Bunton and E. Humeres, *J. Org. Chem.* **34**, 572-76 (1969).
8. R.G. Bates, *Determination of pH. Theory and Practice*, (Wiley, New York, 1973, 2nd ed.), ch. 4.
9. H.S. Harned and R.A. Robinson, *Trans. Faraday Soc.* **36**, 973 (1940); Noyes, Kato, Sosman, *Publications Carnegie Institution*, Washington, **63**, **153**, **193** (1907).
10. H.S. Harned and B.B. Owen, *The Physical Chemistry of Electrolytic Solutions*, (Reinhold, New York, 1958), ch. 15.
11. H.S. Harned and N.D. Embree, *J. Am. Chem. Soc.* **56**, 1050-3 (1934).
12. Reference 8, ch.5.
13. A.K. Covington, R.G. Bates and A. Durst, *Pure & Appl. Chem.* **57**, 531-47 (1985).
14. H.S. Harned and W.J. Hamer, *J. Am. Chem. Soc.* **55**, 2194-2206 (1933).
15. H.S. Harned and R.H. Copson, *J. Am. Chem. Soc.* **55**, 2206-15 (1933).
16. Reference 8, ch. 9.
17. J.N. Bronsted, *Chem. Rev.* **5**, 231-338 (1928).
18. Reference 2, ch. 11.
19. P. Debye and E. Hückel, *Physik. Z.* **24**, 305-325 (1923).
20. R.A. Robinson and R.H. Stokes, *Electrolyte Solutions* (Butter-worths, London, 1970) p. 468.
21. G.N. Lewis and M. Randall, *J. Am. Chem. Soc.* **43**, 1112-54 (1921).
22. J. Kielland, *J. Am. Chem. Soc.* **59**, 1675-8 (1937).
23. N. Ya. Velenkin, *Método de Aproximaciones Sucesivas*, (MIR, Moscow, 1978), p. 88.
24. C.W. Davies, *J. Am. Chem. Soc.* 2093-8 (1938).
25. E. Gütelberg, *Z. Phys. Chem.* **123**, 199 (1926).
26. R.G. Bates and H.B. Hetzer, *J. Phys. Chem.* **65**, 667-71 (1961).
27. R.G. Bates and R. Gary, *J. Res. Nat. Bur. Stand.* **65A**, 495-505 (1961).
28. R.G. Bates, G.D. Pinching, *J. Am. Chem. Soc.* **71**, 1274-83 (1949).
29. H.S. Harned and S.R. Scholes, *J. Am. Chem. Soc.* **63**, 1706-9 (1941).
30. R.P. Bell, *The Proton in Chemistry* (Chapman and Hall, London, 1973), p. 96.
31. M.L. Bender, *Mechanisms of Homogenous Catalysis from Protons to Proteins* (Wiley - Interscience, New York, 1971), p. 23.
32. M. Eigen, *Angew. Chem. Intern. Ed.* **3**, 1-19 (1964).