LXVII. THE DETERMINATION OF THE TERTIARY DISSOCIATION CONSTANT OF PHOSPHORIC ACID.

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QUANTITATIVE studies of the mechanism of calcification require a knowledge of the physico-chemical constants of the blood equilibria involved in the process [Kugelmass, 1924; Kugelmass and Shohl, 1924].
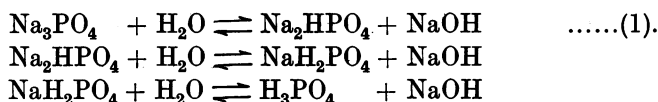
The values for the tertiary dissociation constant of phosphoric acid available at present are at variance. Abbott and Bray [1909] found K_3 to be $3·6 \times 10^{-13}$ at 18° for a total concentration of 0·026 M by means of conductivity and distribution ratios of ammonia between chloroform and solutions of sodium ammonium phosphate. This value seems incompatible with the apparent dissociation constant p_{K_3}, from the dissociation curve for the phosphates, which is of a higher order of magnitude.

The tertiary dissociation constant of phosphoric acid was determined from a study of the aqueous systems of the tertiary phosphates at equilibrium from the standpoint of hydrolysis.

The neutralisation of orthophosphoric acid by strong alkali has been studied by means of thermochemical, electrometrical, and conductance measurements. Thomsen has shown that the small heat effects that attend the addition of the third equivalent of base indicate that the third equivalent of hydrogen of the acid is far from completely replaced when the proportions of acid and base are those corresponding to the salt Na_3PO_4. Berthelot found that the decrease of conductance during neutralisation may be represented by a straight line up to the point at which the first hydrogen of the acid is replaced and by another straight line different in direction from the first up to the point corresponding to the replacement of the second hydrogen. Beyond this point further addition of alkali causes a change in the direction of the curve, which can no longer be represented by a straight line. Hence, the first and second equivalents of hydrogen in orthophosphoric acid are almost quantitatively replaced but the third equivalent is only gradually neutralised as the proportion of base increases. These results clearly indicate that the tertiary phosphate is hydrolysed to a considerable extent.

<div align="center">THEORETICAL.</div>

Derivation of equations. The tertiary dissociation constant may be evaluated from the degrees of hydrolysis of the tertiary phosphates. The hydrolysis occurs progressively in several stages, to each of which correspond definite equilibria represented by the following stoichiometric equations: ·

$$Na_3PO_4 \; + H_2O \rightleftharpoons Na_2HPO_4 + NaOH \qquad \ldots\ldots(1).$$
$$Na_2HPO_4 + H_2O \rightleftharpoons NaH_2PO_4 + NaOH$$
$$NaH_2PO_4 + H_2O \rightleftharpoons H_3PO_4 \quad + NaOH$$

The tertiary phosphate hydrolyses to a great extent, the secondary and primary salts inappreciably, as will be evident from the data below. Such an aqueous system probably also contains the intermediate ions, $Na_2PO_4^-$ and $NaPO_4^=$, but we know very little about their concentrations or activities. Hence, the first stage hydrolysis (equation (1)) may be considered as the essential equilibrium.

The mechanism of equation (1) may be expressed by the ionic equilibrium:

$$PO_4^\equiv + H_2O \rightleftharpoons HPO_4^= + OH^-.$$
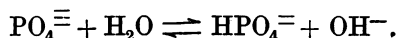
Applying the law of mass action,

$$\frac{[HPO_4^=][OH^-]}{[PO_4^\equiv]} = K_h \qquad \ldots\ldots(2),$$

where the brackets include the ion activities; K_h is the "activity" hydrolysis constant.

The degree of hydrolysis, h, is by definition,

$$h = \frac{[HPO_4^=]}{\gamma_S C} = \frac{[OH^-]}{\gamma_B C} \qquad \ldots\ldots(3)$$

and

$$1 - h = \frac{[PO_4^\equiv]}{\gamma_T C},$$

where γ_B, γ_S, γ_T are the activity coefficients of hydroxide, secondary and tertiary phosphates of sodium or potassium respectively and C is the total molar concentration of all phosphates. Substituting the values of OH^-, $HPO_4^=$ and $PO_4^\equiv$ from these relations in equation (2), we have

$$\frac{h^2 \gamma_B \gamma_S C^2}{(1-h)\gamma_T} = K_h \qquad \ldots\ldots(4).$$

Also, the condition obtains that

$$[H^+][OH^-] = K_w.$$

Dividing this by equation (2),

$$\frac{[H^+][PO_4^\equiv]}{[HPO_4^=]} = \frac{K_w}{K_h} = K_a \qquad \ldots\ldots(5),$$

where K_a is the tertiary ion activity or true constant.

The apparent dissociation constant may also be expressed in terms of the degree of hydrolysis of the tertiary salt

$$K_3' = \frac{[H^+][Na_3PO_4]}{Na_2HPO_4} \qquad \ldots\ldots(6).$$

Replacing for the secondary and tertiary salt concentrations their equivalents from the above relationships

$$K_3' = [H^+]\left(\frac{1-h}{h}\right) \qquad \qquad ......(7).$$

Expressed in logarithmic form

$$p_H = p_{K_a'} + \log\frac{1-h}{h} \qquad \qquad ......(8).$$

EXPERIMENTAL.

Method of procedure. Purely prepared sodium and potassium phosphates were made up to definite concentrations with conductivity water at 20° and kept in pyrex flasks. The hydrion concentrations of these solutions were measured potentiometrically in a thermostat maintained at 20° and 38° $\pm$ 0·02° respectively. The gas chain consisted of Pt—H_2—solution x—saturated KCl—HgCl—Hg. The hydrion potentials measured for these solutions at varying time intervals showed that the hydrolytic equilibria are established immediately on preparation of the solution.

The hydrion concentration measurements were standardised daily against 0·1 N HCl prepared from constant boiling acid. The p_H was 1·085 at 20° and 1·09 at 38°, extrapolated from the activity coefficients determined by Noyes and Ellis [1917]. The calculated E.M.F. values of the entire system against the acid standard were 0·3119 at 20° and 0·3022 volt at 38°. The average divergence in terms of p_H was 0·003. The observed voltages were corrected to one atmosphere of hydrogen.

Preparation and analysis of materials. The tertiary phosphates were recrystallised twice from distilled water free from CO_2 and finally again by the addition of an equal volume of 95 % alcohol and then cooling in ice water. Two liquid phases were formed upon addition of alcohol, crystallisation proceeded at the interface while the upper phase gradually disappeared. The upper layer in the closed system prevented the absorption of CO_2 which otherwise would have tended to form the secondary phosphate and carbonate. The $Na_3PO_4.12H_2O$ crystals are trigonal and the $K_3PO_4.2H_2O$ are needle-like. The crystals were filtered on a Büchner funnel with suction and washed several times with alcohol. They were dried on a glass plate and finally pulverised. No attempt was made to prepare constant hydrates but the crystals were dried to remove free moisture and analysed for water of hydration. The water content was determined by first weighing a sample of the material in a platinum crucible and then heating in the electric furnace until constant weight was obtained.

The dodecahydrated trisodium phosphate crystals were tested by determining the transition temperature, 73·4°, which Richards proposed as a fixed point in thermometry. Analysis of the phosphates gave the following results.

Percentage composition of the phosphates.

Salt	Water determined	P Determined	P Calculated
K_2HPO_4	27·41	13·82	13·86
Na_2HPO_4	45·65	12·70	12·77
K_3PO_4	34·84	9·50	9·47
Na_3PO_4	44·74	10·45	10·49

Experimental and calculated data.

[H+] is the activity of the hydrion taken as that determined by the hydrogen electrode.

γ_B, γ_S and γ_T are the activity coefficients of the hydroxide, secondary and tertiary phosphates, respectively of sodium or potassium. They are the thermodynamic degrees of dissociation obtained by dividing the mean activity of the ions or their effective concentrations by the molarity of the salt. The coefficients given were read from curves plotted from Lewis and Randall's data [1923] for uni-, bi- and ter-valent anions at the calculated ionic strengths. The validity of this procedure follows especially from recent work which indicates that the ratio of the activity coefficient of an ion of one valency to that of another is constant at a given ionic strength.

Table I. *The tertiary dissociation constant of phosphoric acid.*

Calculated from the hydrolysis of Na_3PO_4 at 20°.

C	H^+	OH^-	μ	γ_B	γ_S	γ_T	h	K_h	$K_a.10^{12}$	$K_a{'}.10^{-12}$
0·0250	$0·907 \times 10^{-12}$	$9·48 \times 10^{-3}$	0·126	0·79	0·23	0·18	0·480	$1·12 \times 10^{-2}$	0·77	0·98
0·0125	1·418 ,,	6·03 ,,	0·065	0·84	0·33	0·26	0·574	1·03 ,,	0·83	1·06
0·00625	2·263 ,,	3·80 ,,	0·029	0·88	0·42	0·33	0·691	1·08 ,,	0·80	1·01
0·00312	3·806 ,,	2·26 ,,	0·014	0·90	0·51	0·41	0·805	1·16 ,,	0·74	0·92

Calculated from the hydrolysis of K_3PO_4 at 20°.

C	H^+	OH^-	μ	γ_B	γ_S	γ_T	h	K_h	$K_a.10^{12}$	$K_a{'}.10^{-12}$
0·0250	$0·930 \times 10^{-12}$	$9·25 \times 10^{-3}$	0·124	0·80	0·24	0·19	0·468	$1·04 \times 10^{-2}$	0·83	1·06
0·0125	1·431 ,,	6·01 ,,	0·065	0·84	0·33	0·26	0·572	1·02 ,,	0·84	1·07
0·00625	2·278 ,,	3·77 ,,	0·029	0·88	0·43	0·33	0·685	1·04 ,,	0·82	1·04
0·00312	3·858 ,,	2·23 ,,	0·015	0·91	0·51	0·41	0·784	1·00 ,,	0·85	1·04

Calculated from the hydrolysis of Na_3PO_4 at 38°.

C	H^+	OH^-	μ	γ_B	γ_S	γ_T	h	K_h	$K_a.10^{12}$	$K_a{'}.10^{-12}$
0·0250	$2·591 \times 10^{-12}$	$1·29 \times 10^{-2}$	0·115	0·80	0·24	0·19	0·648	$3·02 \times 10^{-2}$	1·11	1·40
0·0125	4·203 ,,	0·797 ,,	0·056	0·84	0·33	0·27	0·759	3·07 ,,	1·09	1·33
0·00625	7·202 ,,	0·465 ,,	0·027	0·88	0·43	0·34	0·846	3·23 ,,	1·03	1·31
0·00312	1·305 ,,	0·257 ,,	0·013	0·91	0·52	0·43	0·914	3·33 ,,	1·00	1·22

Calculated from the hydrolysis of K_3PO_4 at 38°.

C	H^+	OH^-	μ	γ_B	γ_S	γ_T	h	K_h	$K_a.10^{12}$	$K_a{'}.10^{-12}$
0·0250	$2·681 \times 10^{-12}$	$1·26 \times 10^{-2}$	0·115	0·80	0·24	0·19	0·629	$2·70 \times 10^{-2}$	1·24	1·57
0·0125	4·312 ,,	0·77 ,,	0·056	0·84	0·33	0·27	0·740	2·71 ,,	1·24	1·52
0·00625	7·261 ,,	0·46 ,,	0·027	0·88	0·43	0·34	0·839	3·01 ,,	1·12	1·41
0·00312	1·332 ,,	0·25 ,,	0·013	0·91	0·52	0·43	0·887	2·39 ,,	1·39	1·68

Table II. *The tertiary dissociation constant of phosphoric acid.*

Calculated from K_2HPO_4—K_3PO_4 mixtures

$$K_3 = \frac{[H^+]\left[B - \frac{[OH^-]}{\gamma_B} + \frac{[H^+]}{\gamma_S}\right]}{C - B + \frac{[OH^-]}{\gamma_B} - [H^+]}.$$

C	B	p_H	H+	OH−	μ	γ_B	γ_S	γ_T	$K_a'.10^{-12}$
0·0313	0·0062	11·20	$6·31 \times 100^{-2}$	0·0016	0·11	0·80	0·25	0·20	1·06
0·0294	0·0118	11·55	2·82 ,,	0·0036	0·15	0·76	0·21	0·16	1·10
0·0278	0·0168	11·80	1·59 ,,	0·0063	0·12	0·78	0·23	0·19	0·94
0·0263	0·0211	11·95	1·12 ,,	0·0089	0·12	0·79	0·23	0·19	0·84

μ is the total ionic strength. The ionic strength is equal to the stoichiometric molarity of each ion multiplied by the square of its valence. The total ionic strength is equal to the sum of the strengths of the anions and cations divided by two. The activity coefficient of a strong electrolyte is the same in all dilute solutions of the same ionic strength.

K_h is calculated from equation (4), K_a from equation (5), and K_a' from equations (6), (7) or (8). K_w at 20° is $0·86 \times 10^{-14}$ and at 38° is $3·35 \times 10^{-14}$.

Discussion of K_3 calculated.

The tertiary dissociation constant may be calculated from the data obtained by the electrometric titration of phosphoric acid and from the formulae developed by Van Slyke [1922]. The equation for the dissociation of a weak acid in an alkaline system is No. 29 of Van Slyke's paper,

$$K_a' = \frac{[H^+]\left(B - \frac{[OH^-]}{\gamma_B} + \frac{[H^+]}{\gamma_S}\right)}{C - B + \frac{[OH^-]}{\gamma_B} - [H^+]}.$$

Table III of that paper gives K_a' calculated from the titration data of W. M. Clark for $H(K_2PO_4) + KOH$. The above equation was used in its simplified form assuming complete dissociation. A recalculation of K_2' using activity coefficients at the respective ionic strengths is given in Table III. These values are concordant with those obtained from the hydrolysis data.

The apparent tertiary constant may also be calculated from the apparent secondary dissociation constant knowing the hydrion concentration which defines the secondary phosphate. Replacing the secondary and tertiary salt concentrations in equation (6) by their equivalents,

$$[Na_3PO_4] = \frac{K_3'}{K_3' + [H^+]} \cdot [C],$$

$$[Na_2HPO_4] = \frac{K_2'}{K_2' + [H^+]} \cdot [C]$$

and solving the quadratic, we obtain,

$$K_3' = \frac{[H^+]^2}{K_2'}.$$

Therefore, the secondary phosphate ratio has a maximum when $[H^+]$ is the geometric mean of the apparent dissociation constants,

$$p_H = \frac{p_{K_3'} + p_{K_2'}}{2}.$$

The p_H of the secondary phosphate is difficult to localise experimentally. Clark's titration curve gives p_H 9·3 for 0·066 M K_2HPO_4, $p_{K_2} = 6·8$ and hence p_{K_3} is 11·8. The secondary phosphates prepared in this work had a p_H of 9·35 and hence p_{K_3} is 11·9.

Table III. *The tertiary dissociation constant of phosphoric acid.*

Calculated from titration data of W. M. Clark for $K_2HPO_4 + KOH$.

C	B	p_H	H	OH^-	U	γ_B	γ_S	γ_T	$K_a'.10^{-12}$
0·0313	0·0062	11·20	$6·31 \times 100^{-2}$	0·0016	0·11	0·80	0·25	0·20	1·06
0·0294	0·0118	11·55	2·82 ,,	0·0036	0·15	0·76	0·21	0·16	1·10
0·0278	0·0168	11·80	1·59 ,,	0·0063	0·12	0·78	0·23	0·19	0·94
0·0263	0·0211	11·95	1·12 ,,	0·0089	0·12	0·79	0·23	0·19	0·84

CONCLUSION.

The tertiary dissociation constant of phosphoric acid, determined from the hydrolysis of the tertiary phosphates, has been found to be $1·02 \times 10^{-12}$ at 20° and $1·48 \times 10^{-12}$ at 38°.

REFERENCES.

Abbott and Bray (1909). *J. Amer. Chem. Soc.* **31**, 729.
Kugelmass (1924). *J. Biol. Chem.* **60**, 237.
—— and Shohl (1924). *J. Biol. Chem.* **58**, 649.
Lewis and Randall (1923). Thermodynamics and the free energy of chemical substances.
Noyes and Ellis (1917). *J. Amer. Chem. Soc.* **39**, 2532.
Van Slyke (1922). *J. Biol. Chem.* **52**, 525.