the theory of Brönsted of velocity of reactions catalyzed by strong electrolytes. It seems to be very difficult to find a thoroughly satisfactory explanation of the changes of the decomposition velocity of diacetone alcohol in various solutions of strong electrolytes.

PHILADELPHIA, PENNSYLVANIA

[CONTRIBUTION FROM THE MUSPRATT LABORATORY OF PHYSICAL AND ELECTROCHEMISTRY, UNIVERSITY OF LIVERPOOL]

THE SOLUBILITIES OF LEAD PHOSPHATES[1]

BY HORACE MILLET AND MAURICE JOWETT

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Although some measurements have been made of the solubilities of the secondary and tertiary phosphates of lead in water, no measurements have been made under conditions sufficiently well defined to allow of calculation of the solubility products of these salts, and hence to allow of calculation of the solubilities under various conditions.

The solubilities of these salts are of biological interest in connection with lead poisoning and the lead treatment of cancer. Some evidence has been obtained by Aub and others,[2] and by Brooks[3] that inorganic lead compounds are transformed into lead phosphate in the body, lead phosphate being regarded as the least soluble salt of lead under body conditions.

The solubility of lead phosphates is thus probably the limiting factor with regard to lead-ion concentrations in the body, and the subject has been discussed from this point of view by W. C. M. Lewis.[4] The work of Fairhall[5] shows that the primary phosphate of lead, $PbH_4(PO_4)_2$, is much more soluble than the other phosphates except in very acid solutions and this salt is thus of no great biological importance.

We are not concerned here primarily with the biological aspects of the subject, the purpose of the present paper being to present measurements undertaken to determine the solubility products of the secondary and tertiary phosphates of lead. We shall, however, show reason to correct the statement[2] that whereas the tertiary phosphate is the stable salt under normal body conditions, a slight shift of equilibrium to the acid side converts this salt to the secondary phosphate.

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[1] This investigation was undertaken on behalf of the Liverpool Medical Research Organization, Professor W. Blair Bell, Director, University of Liverpool.

[2] Aub, Fairhall, Minot and Reznikoff, "Monograph on Lead Poisoning," Williams and Wilkens Co., Baltimore, **1926**.

[3] Brooks, *Biochem. J.*, **21**, 766 (1927).

[4] W. C. M. Lewis, *J. Cancer Research*, **11**, 16 (1927).

[5] Fairhall, THIS JOURNAL, **46**, 1593 (1924).

Methods

Measurements of hydrogen-ion activity were carried out with the quinhydrone electrode, as described in an accompanying paper.[6]

Phosphates were estimated by the colorimetric method of Briggs,[7] which is accurate to 1–2% under the conditions maintained.

The lead-ion activity in the lead phosphate solutions has been determined by employing a lead electrode in a cell of the following type

Pb | Solution of lead salt ¦ Saturated KCl | Normal calomel electrode

Getman[8] has shown that lead can function as a reversible electrode, a finding which has been confirmed by us.

The value of E_0 for the lead electrode at 25° has been taken to be 0.122 volt;[9] hence the value of $p\text{Pb}^{++}$, the negative logarithm of the lead-ion activity, is obtained from the relation

$$p\text{Pb}^{++} = \frac{E - 0.4042}{0.02956}$$

where E is the observed e.m.f. of a cell of the type shown above.

The corresponding formula for 37.5° has been taken to be

$$p\text{Pb}^{++} = \frac{E - 0.4106}{0.03080}$$

As no value of E_0 for the lead electrode was available for 37.5°, this was determined by measurements on several dilute solutions of lead nitrate at both 25 and 37.5°, the activity coefficient of lead-ion being assumed to be the same in both cases.

The lead electrodes were made by depositing lead electrolytically upon platinum, using very weak currents. (For use in acid solutions, the electrodes were amalgamated.) The technique of the lead electrode will be described more fully elsewhere by one of the authors.

Tertiary lead phosphate was made, following Alders and Stähler,[10] by adding slowly in dilute solution an equivalent amount of Na_2HPO_4 to a dilute boiling solution of lead acetate, the precipitate being washed repeatedly.

Secondary lead phosphate was prepared by adding in the hot 16.5 g. of lead nitrate dissolved in 500 cc. of water to 8 g. of potassium dihydrogen phosphate dissolved in 500 cc. of $N/6$ nitric acid. The precipitate was kept in the mother liquor at 25° for two days and then washed and dried.

The solutions for solubility determinations, to which a considerable excess of the appropriate solid salt was added, were kept in a thermostat

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[6] Jowett and Millet, THIS JOURNAL, **51**, 1004 (1929).

[7] Briggs, *J. Biol. Chem.*, **59**, 255 (1924).

[8] Getman, THIS JOURNAL, **38**, 792 (1916); **40**, 611 (1918).

[9] Lewis and Randall, "Thermodynamics and the Free Energy of Chemical Substances," McGraw-Hill Book Co., Inc., New York City, 1923.

[10] Alders and Stähler, *Ber.*, **42**, 2261 (1909).

at the required temperature for several weeks before measurements were made, and evidence was obtained with each series that the lead-ion activities had reached practically constant values. Measurements of P_H were made on each solution on the same day that the lead-ion activity was measured and samples were simultaneously filtered for determination of phosphate.

General Considerations

In earlier measurements on the solubilities of the phosphates of lead[2] the importance of hydrogen-ion activity in determining the state of ionization of the phosphate was little considered. Since the solubility products of the phosphates are defined by the relations

$$S_2 = a_{Pb^{++}} \times a_{HPO_4^{--}} \tag{1}$$
$$S_3 = a^3_{Pb^{++}} \times a^2_{PO_4^{---}} \tag{2}$$

it is necessary to determine accurately the distribution of the total phosphate in solution between the various phosphate ions.

With this purpose in view the authors have determined values for the ionization constants of phosphoric acid.[3] The values required for our purposes are given in Table I. They are defined as follows

$$pK'_1 = pH^+ + pC_{H_2PO_4^-} - pC_{H_3PO_4} \tag{3}$$
$$pK'_2 = pH^+ + pC_{HPO_4^{--}} - pC_{H_2PO_4^-} \tag{4}$$
$$pK_2 = pH^+ + pHPO_4^{--} - pH_2PO_4^- \tag{4a}$$
$$pK_3 = pH^+ + pPO_4^{---} - pHPO_4^{--} \tag{5}$$

pK'_2 and $\gamma_{HPO_4^{--}}$ in dilute solutions are taken as given by the relations

$$pK'_2 = pK_2 - \frac{1.5\sqrt{\mu}}{1 + 1.5\sqrt{\mu}} \tag{6}$$
$$-\log \gamma_{HPO_4^{--}} = \frac{2.0\sqrt{\mu}}{1 + 1.5\sqrt{\mu}} \tag{7}$$

Table I

Ionization Constants of Phosphoric Acid

	25°	37.5°		25°	37.5°
pK_1	...	....	pK'_1 (μ = 0.16)	1.94	2.04
pK_2	7.127	7.058	pK'_2 (μ = 0.16)	6.680	6.589
pK_3	12.30	12.66[11]			

The third ionization constant is not known accurately but pK_3 enters into our calculations only in the form of an additive constant, since no measurements have been made in the region of P_H in which the tertiary phosphate ion is an appreciable fraction of the total phosphate concentration. Any alteration in the value of pK_3 chosen would simply necessitate a change in the value of pS_3 according to the equation

$$pS_3 = 3pPb^{++} + 2pHPO_4^{--} - 2pH^+ + 2pK_3 \tag{8}$$

which is derived by combining Equations 2 and 5.

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[11] Sendroy and Hastings, *J. Biol. Chem.*, **71**, 783 (1926–27).

Equation 1 similarly can be stated in a logarithmic form

$$pS_2 = p\text{Pb}^{++} + p\text{HPO}_4^{--} \tag{9}$$

Solubilities of the Tertiary Phosphate.—Measurements of the solubility of $Pb_3(PO_4)_2$ have been carried out at 25 and 37.5° in dilute solutions and at an ionic strength of 0.16.

The solutions which the lead phosphate was allowed to saturate contained in all these experiments 0.005 *M* phosphate, a value which remained constant throughout the time of saturation.

This phosphate concentration was attained by mixing solutions of KH_2PO_4 and Na_2HPO_4 in various proportions, so that the *P*H might be varied. It was found that during saturation the *P*H values of the solutions changed, and always in an acid direction. We have no explanation to offer for this change, which sometimes amounted to 0.2; it was, however, a slow effect and the *P*H was sensibly constant for a long enough time for saturation to take place under definite conditions. The constancy of the phosphate concentration shows that no transformation of the solid phase to or from secondary phosphate could be taking place, since in this process, $Pb_3(PO_4)_2 + H_3PO_4 \rightleftharpoons 3PbHPO_4$, the phosphate concentration would decrease or increase, respectively.

The solubilities observed are hence really those of the tertiary phosphate, a conclusion supported by the sensible constancy of the calculated values of pS_3 over a range of PO_4^{---} concentration of more than twenty times.

TABLE II

SOLUBILITY DATA IN DILUTE SOLUTIONS

Solid phase, $Pb_3(PO_4)_2$; *C*, phosphate, 0.005 *M*

No.	pH$^+$	pPb$^+$	μ (approx.)	No.	pH$^+$	pPb$^+$	μ (approx.)
	Temp., 25°				Temp., 37.5°		
1	7.194	8.819	0.0117	5	7.136	8.507	0.0117
2	6.868	8.539	.0100	6	6.795	8.177	.0100
3	6.692	8.326	.0083	7	6.639	7.984	.0083
4	6.346	7.927	.0070	8	6.261	7.580	.0070

The data obtained in dilute solutions are given in Table II. The values of μ are calculated from the initial composition of the solutions.

The calculation of pS_3 from these data is indicated in Table III. pK'_2 is obtained from Equation 6, and Equation 4 is then used to calculate the

TABLE III

CALCULATION OF pS_3 IN DILUTE SOLUTIONS

No.	$\gamma_{HPO_4^{--}}$	pHPO$_4^{--}$	pPO$_4^{---}$	pS_3	No.	$\gamma_{HPO_4^{--}}$	pHPO$_4^{--}$	pPO$_4^{---}$	pS_3
		Temp., 25°					Temp., 37.5°		
1	0.65	2.697	7.803	42.06	5	0.65	2.693	8.237	42.00
2	.67	2.845	8.277	42.17	6	.67	2.847	8.732	41.99
3	.69	2.948	8.556	42.09	7	.69	2.928	8.969	(41.89)
4	.71	3.203	9.157	42.10	8	.71	3.216	9.635	42.01

ratio $C_{HPO_4^{--}}/C_{H_2PO_4^-}$. The total phosphate concentration being known, $C_{HPO_4^{--}}$ is obtained.

$\gamma_{HPO_4^{--}}$ is calculated by the use of Equation 7 and hence $pHPO_4^{--}$ obtained. pPO_4^{---} is then derived from Equation 5, or alternatively pS is derived directly from Equation 8.

The mean values for pS_3 derived (omitting the bracketed value) are 42.10 at 25° and 42.00 at 37.5°.

A set of measurements similar to those in dilute solutions have been made at an ionic strength of 0.16. Solutions of alkali phosphates were raised to this ionic strength by addition of sodium chloride. The data obtained are given in Table IV.

TABLE IV

SOLUBILITY DATA AT $\mu = 0.16$

Solid phase, $Pb_3(PO_4)_2$; C, phosphate, 0.005 M

No.	pH^+	pPb^{++}	No.	pH^+	pPb^{++}
	Temp., 25°			Temp., 37.5°	
9	7.015	8.460	13	6.887	8.081
10	6.774	8.243	14	6.719	7.905
11	6.429	7.917	15	6.317	7.518
12	6.202	7.584	16	6.173	7.265

Values of pK_2' for $\mu = 0.16$ are given in Table I. The ratio $C_{HPO_4^{--}}/C_{H_2PO_4^-}$ is calculated with the aid of Equation 4 and the observed P_H. $C_{HPO_4^{--}}$ is next obtained. We leave $\gamma_{HPO_4^{--}}$ indeterminate for the present and hence derive values for $(pS_3 + 2 \log \gamma_{HPO_4^{--}})$ given in Table V.

TABLE V

CALCULATION OF $(pS_3 + 2 \log \gamma_{HPO_4^{--}})$, $\mu = 0.16$

No.	$(pHPO_4^{--} + \log \gamma_{HPO_4^{--}})$	$(pPO_4^{---} + \log \gamma_{HPO_4^{--}})$	$(pS_3 + 2 \log \gamma_{HPO_4^{--}})$	No.	$(pHPO_4^{---} + \log \gamma_{HPO_4^{--}})$	$(pPO_4^{---} + \log \gamma_{HPO_4^{--}})$	$(pS_3 + 2 \log \gamma_{HPO_4^{--}})$
	Temp., 25°				Temp., 37.5°		
9	2.466	7.743	40.87	13	2.478	7.531	40.74
10	2.558	8.076	40.88	14	2.542	7.767	40.69
11	2.745	8.608	40.97	15	2.759	8.382	40.76
12	2.904	8.994	40.74	16	2.858	8.625	(40.49)

The mean values for $(pS_3 + 2 \log \gamma_{HPO_4^{--}})$ derived are 40.86 at 25° and 40.73 at 37.5°. Hence, from the values of pS_3 already obtained, —log $\gamma_{HPO_4^{--}}$ has a value of about 0.62 at 25° and 0.635 at 37.5°.

Thus in the solutions of $\mu = 0.16$, $\gamma_{HPO_4^{--}}$ has the value 0.24 (25°) and 0.23 (37.5°). Making use of the values of pK_2 and pK_2' ($\mu = 0.16$) given in Table I, it can be calculated that $\gamma_{H_2PO_4^-}$ has values of about 0.67 and 0.68 at 25 and 37.5°. These values have already been shown[6] to agree with data obtained for pK_1 and pK_1' ($\mu = 0.16$). Thus it can be concluded that the two sets of data on the solubility of tertiary lead phosphate are in good agreement.

Solubilities of the Secondary Phosphate.—In an attempt to obtain the solubility product of $PbHPO_4$, a series of solutions similar to those above described ($\mu = 0.16$) and initially at similar *P*H values were saturated with solid $PbHPO_4$. It was observed, however, that the phosphate content of the solutions increased and the *P*H fell much more than was the case when the tertiary phosphate was the solid phase. There was thus reason to consider that the reaction $3\ PbHPO_4 \longrightarrow Pb_3(PO_4)_2 + H_3PO_4$ was taking place, and it appeared doubtful whether the solution would be truly saturated with $PbHPO_4$ or whether its lead-ion content would show a value intermediate between those corresponding to the solubilities of $PbHPO_4$ and $Pb_3(PO_4)_2$.

The observed phosphate concentrations were from 0.0057 to 0.0081 molar, the *P*H values ranged from 5.61 to 6.36, and the values of ($p\mathrm{Pb}^{++} + p\mathrm{HPO_4}^{--}$) were 11.40–11.64 at 25° and 11.16–11.29 at 37.5°. The lead-ion activities were higher than those corresponding to the solubility of $Pb_3(PO_4)_2$. The ionic product for the secondary phosphate was not, however, a constant, and we concluded that experiments should be undertaken under conditions where the secondary phosphate was the more stable salt. Such conditions were attained by employing *P*H values in the region 2.0–2.5.

As before, four solutions were studied at each temperature, mixtures of KH_2PO_4 and HCl being made and their ionic strength raised to the value 0.16 by adding sodium chloride. The data and calculation of pS_2 are given in Table VI. From the observed *P*H and phosphate concentrations, $p\mathrm{H_2PO_4}^-$ is calculated, using the values of pK_1' given in Table I, the values of $\gamma_{\mathrm{H_2PO_4}^-}$ obtained in the last section and Equation 3. $p\mathrm{HPO_4}^{--}$ is then obtained using the values of pK_2 given in Table I and Equation 4a.

TABLE VI

SOLUBILITIES OF $PbHPO_4$, $\mu = 0.16$

Temp., °C.	$p\mathrm{H}^+$	$p\mathrm{Pb}^{++}$	*C*, phosphate	$p\mathrm{H_2PO_4}^-$	$p\mathrm{HPO_4}^{--}$	pS_2
25	2.515	3.508	0.0320	1.770	6.382	9.89
	2.303	3.278	.0336	1.803	6.627	9.90
	2.494	3.345	.0173	2.042	6.675	10.02
	2.301	2.885	.0176	2.085	6.911	9.80
37.5	2.341	3.125	.0326	1.829	6.546	9.67
	2.156	2.763	.0344	1.876	6.778	9.54
	2.426	2.925	.0173	2.078	6.710	9.64
	2.067	2.438	.0181	2.196	7.187	9.62

The mean values derived for pS_2 are 9.90 at 25° and 9.62 at 37.5°. It can readily be calculated from the values of pS_3 previously obtained that the solubility of $Pb_3(PO_4)_2$ in the above solutions is greater than that observed for $PbHPO_4$. Thus the latter is the stable salt in these solutions.

From the values of pS_2 at the two temperatures it can be calculated that the heat of solution of $PbHPO_4$ at infinite dilution is about −10,000 cal. In view of the uncertainty in pK_3 it is not worth while to calculate a value for the heat of solution of $Pb_3(PO_4)_2$.

Equilibrium Conditions

The conditions under which both $PbHPO_4$ and $Pb_3(PO_4)_2$ will be in equilibrium with a solution can now be defined. The condition takes the form

$$\frac{S_2}{a_{HPO_4^{--}}} = \frac{S_3^{1/3}}{a_{PO_4^{---}}^{2/3}}$$

It may also be stated in the forms

$$a_{H^+}^2 \times a_{HPO_4^{--}} = \frac{K_3^2\,S_2^3}{S_3}$$

$$a_{H^+} \times a_{H_2PO_4^-} = \frac{K_3^2\,S_2^3}{K_2\,S_3}$$

Numerical values are given in Table VII.

TABLE VII

EQUILIBRIUM CONDITIONS FOR $PbHPO_4$ AND $Pb_3(PO_4)_2$

	25°	37.5°
$a_{H^+}^2 \times a_{HPO_4^{--}}$	$10^{-12.20}$	$10^{-12.18}$
$a_{H^+} \times a_{H_2PO_4^-}$	$10^{-5.07}$	$10^{-5.12}$

The conditions are very similar at both temperatures. The higher the phosphate concentration the lower the hydrogen-ion activity at equilibrium. Thus with M phosphate the pH$^+$ is about 5, with $M/1000$ phosphate the pH$^+$ is about 2.

This latter phosphate concentration is of the same order as is found in blood and in animal tissues, of which the pH$^+$ is about 7.0–7.3. Thus under these conditions $Pb_3(PO_4)_2$ is definitely the stable phosphate of lead and the statement[2] that a slight shift to the acid side converts it to $PbHPO_4$ is quite erroneous. This statement was based on arguments physicochemically unsound.

Making use of the data obtained, the solubilities in (human) blood serum will now be calculated. The activity coefficients are assumed to be the same in serum as in 0.16 M sodium chloride. For low concentrations of lead salts in the latter solution $\gamma_{Pb^{++}}$ was found to be 0.17. The pH$^+$ of serum is about 7.33, and its phosphate concentration about 1.2×10^{-3} molar. Hence it is calculated that the lead-ion concentration in serum saturated at 37.5° with $Pb_3(PO_4)_2$ is 5.5×10^{-8}, while the solubility of $PbHPO_4$ is much greater, namely, 6.3×10^{-6} molar.

In order to be able to calculate solubilities of $PbHPO_4$ and $Pb_3(PO_4)_2$ under various conditions in terms of lead-ion *concentrations* from the values obtained for pS_2 and pS_3, it is necessary to be able to evaluate $\gamma_{Pb^{++}}$. Data obtained by one of the authors, which will be published elsewhere,[12]

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[12] **Millet**, *Trans. Faraday Soc.*, **25**, (1929).

show that $\gamma_{Pb^{++}}$ is given fairly accurately by the Debye-Hückel expression in solutions of alkali chlorides up to 0.16 *M*.

Summary

Solubilities of $Pb_3(PO_4)_2$ and $PbHPO_4$ in aqueous solutions have been measured, lead-ion activities being determined with the lead electrode. The values of the solubility products deduced are as follows: $S_2 = a_{Pb^{++}} \times a_{HPO_4^{--}} = 10^{-9.90}$ at 25°; $10^{-9.62}$ at 37.5°. $S_3 = a^3_{Pb^{++}} \times a^2_{PO_4^{---}} = 10^{-42.10}$ at 25°, $10^{-42.00}$ at 37.5°, when K_3 (the third ionization constant of phosphoric acid) is taken to have the values $10^{-12.30}$ at 25° and $10^{-12.66}$ at 37.5°.

The conditions for equilibrium between the two salts are discussed and the biological bearing of the work is mentioned. $Pb_3(PO_4)_2$ is the more stable salt under body conditions.

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[CONTRIBUTION FROM THE MUSPRATT LABORATORY OF PHYSICAL AND ELECTROCHEMISTRY, UNIVERSITY OF LIVERPOOL]

THE IONIZATION CONSTANTS OF PHOSPHORIC ACID[1]

BY MAURICE JOWETT AND HORACE MILLET

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In the course of an investigation[2] on the solubilities of the secondary and tertiary phosphates of lead, it became evident that the values available in the literature for the ionization constants of phosphoric acid were insufficient for the purpose of that work.

We therefore have made measurements to determine the first ionization constant at 25 and 37.5°. A few measurements bearing on the second ionization constant are also reported. Relevant data of other observers are also considered and a value is derived for the third ionization constant. The activity concept is made use of throughout.

Methods

Measurements of hydrogen-ion activity were made by means of cells in which a quinhydrone electrode was connected with a normal calomel electrode by a bridge of saturated potassium chloride solution. This bridge is assumed to eliminate liquid–liquid P. D.'s.

At 25° the P_H is obtained by means of the relation[3]

$$pH^+ = \frac{0.4136 - E}{0.05911}$$

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[1] This investigation was undertaken on behalf of the Liverpool Medical Research Organization, Professor W. Blair Bell, Director, University of Liverpool.

[2] Millet and Jowett, THIS JOURNAL, **51**, 997 (1929).

[3] Millet, *Trans. Faraday Soc.*, **23**, 521 (1927).