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The Synthesis of Phosphonophenylazochromotropic Acids and the Stability Constants of Its Alkaline Earth Metal Chelates

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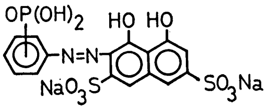
The acid dissociation constants of the three isomeric phosphonophenylazochromotropic acids and their chelate stability constants with alkaline earth metals have been measured by the pH titration method at an ionic strength of 0.10 and at 25.0±0.1°C. The stability order with respect to the ligands is as follows: *ortho*-$>$*meta*-$>$*para*-, and the stability constant of each ligand decreases in the order: Mg$>$Ca$>$Sr$>$Ba; this order is parallel to the reciprocal of the ionic radii of the metal ions. From a comparison between the chelate stability of *o*-phosphonophenylazochromotropic acid and that of Neo-Thorin, it has been concluded that the magnesium ion forms a more stable chelate bond with the phosphonic group than with the arsonic group.

A large number of azo compounds were synthesized and used as metal indicators. As a phenylazo derivative of chromotropic acid, Neo-Thorin, which has an arsonic group adjacent to the azo link, is well-known as a colorimetric reagent for thorium, zirconium, and uranium.

The present authors synthesized the *o*-phosphonophenylazochromotropic acid, which has a phosphonic group in place of the arsonic group of the Neo-Thorin, and two isomers (*m*-, *p*-) of this one. The structural formula for phosphonophenylazochromotropic acid disodium salt is given below:



Phosphonophenylazochromotropic acid

The measurement of its chelate stability constants with alkaline earth metals was carried out by means of the pH titration method.

Experimental

Synthesis of Phosphonophenylazochromotropic Acid. Three isomeric phosphonophenylazochromotropic acids were obtained form the corresponding diazonium salt by coupling with chromotropic acid dissolved in a sodium hydroxide solution. After the coupling reaction, the reaction mixture was added, drop by drop, to well-chilled concentrated hydrochloric acid; a reddish precipitate was thus obtained. This precipitate was recrystallized several times from an acidic solution by the salting-out method. These reagents, which are obtained as disodium salt, are all fine, reddish needles. Figure 1 shows the synthetic routes of the three isomeric diazo components.

o-Aminophenylphosphonic acid has been prepared by the use of the method of Route I. Triethylphosphite (25 g) and *o*-dinitrobenzene (16.8 g) were refluxed in acetonitrile for 8 hr.⁽¹⁾ After releasing the solvent under reduced pressure, diethyl *o*-nitrophenylphosphonate (mp 55°C) can be obtained as yellow needles by letting it stand over-night in an ice-box; then it was hydrolyzed in boiling concentrated hydrochloric acid (5 hr).⁽²⁾ The *o*-nitrophenylphosphonic acid thus obtained was reduced with the use of ferrous hydroxide. After the precipitated ferric hydroxide was removed by filtration, *o*-aminophenyl-phosphonic acid, mp 186°C, rapidly crystallized as white needles when the alkaline filtrate was acidified with concentrated hydrochloric acid. Two other isomers, *m*- and *p*-aminophenylphosphonic acids, were prepared by the use of the methods of Routes II, and III; the details of the procedure have been described in a previous paper.⁽⁶⁾

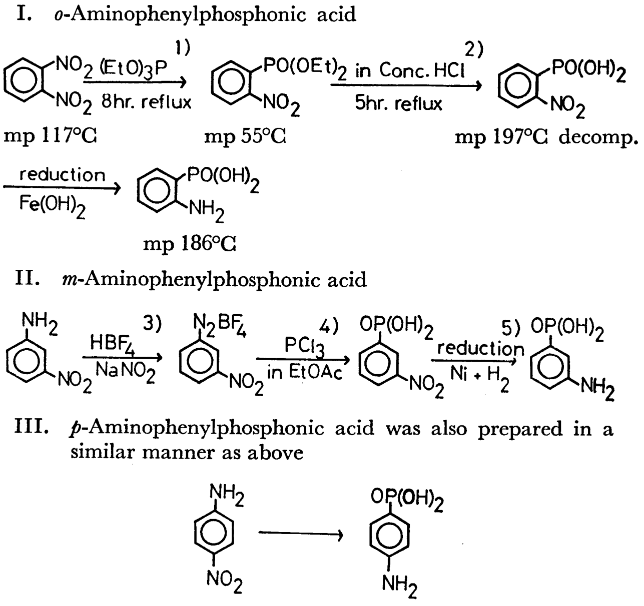


Fig. 1. Synthetic routes of diazo components.

Reagent Solutions. The stock solutions of these ligand were standardized by potentiometric titration with standard 0.10N potassium hydroxide. Carbonate-free 0.10N potassium hydroxide was prepared by the method of ion exchange and was standardized by potassium hydrogen phthalate titrimetrically. The stock solutions of the metal ion were prepared by dissolving $Mg(NO_3)_2 \cdot 6H_2O$, $Ca(NO_3)_2 \cdot 4H_2O$, $Sr(NO_3)_2$, and $Ba(NO_3)_2$ of a guaranteed reagent grade in distilled water. The concentrations of the Mg(II) and Ca(II) solutions were determined by chelatemetric titration, while the concentrations of the Ba(II) and Sr(II) solutions were determined by the usual gravimetric method.

pH Titration Method. The acid dissociation and the chelate stability constants were calculated from titration

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1) J. I. G. Cadogan, *Chem. Comm.*, **1966**, 491.

2) G. M. Kosolopoff, *J. Amer. Chem. Soc.*, **71**, 4022 (1949).

3) *Org. Reactions*, **2**, 427.

4) G. O. Doak and L. D. Freedman, *J. Amer. Chem. Soc.*, **73**, 5658 (1951).

5) *ibid.*, **74**, 753, 754 (1952).

6) H. Miyata, This Bulletin, **36**, 127 (1963).

curves obtained by titrating solutions (5 m*l*) in the presence and in the absence of metal ions, with 0.10N potassium hydroxide in a double-walled glass vessel with a 5-m*l* capacity, and maintained at 25.0±0.1°C by the circulation of water from a thermostat bath. All the measurements were carried out by the use of the micro-titration apparatus, presented in Fig. 2, and the alkali was added by means of a calibrated 0.50-m*l* micrometer syringe.

Solutions under titration were kept in a nitrogen atmosphere by the circulation of carbon dioxide-free nitrogen through the titration vessel. The ionic strength was adjusted to 0.10 with potassium nitrate. The hydrogen-ion concentration was measured by means of an HRL-Model P pH meter (Horiba Instruments Co., Ltd.) with a combined glass electrode (Metrohm, EA-125 U type, Herisaw, Switzerland). The observed pH meter readings were converted into the actual hydrogen-ion concentration by comparison with the stoichiometric dissociation constant of acetic acid. The pH ($-\log[H^+]$) region above 11.0 was calibrated by measurements in the KOH solution.

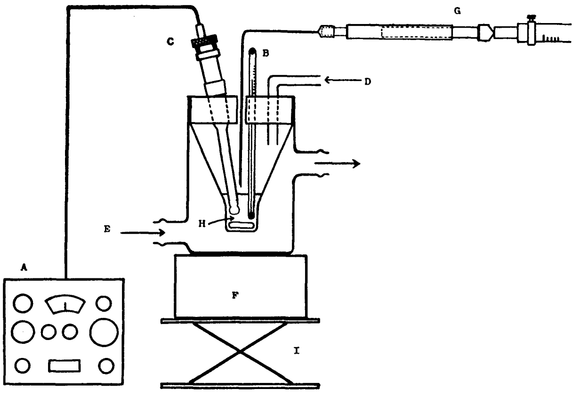

Fig. 2. Micro-titration apparatus.

A:	HRL-Model P pH meter (Horiba)
B:	Thermometer
C:	"Metrohm" combined glass electrode
D:	N_2 gas
E:	25°C water from a thermostat bath
F:	Magnetic stirrer
G:	Micro-meter outfit
H:	Volume 5 m*l*
I:	Laboratory jack

Calculation of Acid Dissociation Constants and Chelate Stability Constants. The dissociation constants of the triprotic acid are defined as follows:

$$K_{a1}=[H][H_2L]/[H_3L],$$
$$K_{a2}=[H][HL]/[H_2L],$$
$$K_{a3}=[H][L]/[HL],$$

where the ionic charge was neglected for the sake of convenience. In general, the following relationship holds among the step-by-step acid dissociation constants of the polyprotic acid:

$$\sum_{i=1}^{n}\frac{iT_L-f}{f[H]^i}K_{a1}\cdot K_{a2}\cdots K_{ai}=1,$$
$$f=T_{OH}+[H]-[OH],$$

where T_L represents the total concentration of ligand species, and T_{OH} the total concentration of the base added to the system. T_L, T_{OH}, and f are entirely of known or measurable quantities; therefore, K_{a1}, K_{a2}, and K_{a3} can be obtained by solving the simultaneous equation in principle. In practice, the ligands were treated as monoprotic acid until $a=1$, and treated as diprotic acid after $a=1$; since a clear inflection is observed, the first dissociation process can be separated from the subsequent dissociation. The chelate stability constants were calculated by the following equation:

$$K_{ML}=(T_L-F)/[L](F+T_M-T_L),$$

where:

$$[L]=(3T_L-T_{OH}-[H]+[OH])/\{[H]/K_{a3}+2[H]^2/K_{a3}K_{a2}$$
$$+3[H]^3/K_{a3}K_{a2}K_{a1}\},$$
$$F=[L]\{1+[H]/K_{a3}+[H]^2/K_{a3}K_{a2}+[H]^3/K_{a3}K_{a2}K_{a1}\},$$

where T_M represents the total concentration of the metal species.

Results and Discussion

Titration Curves. The titration curves are illustrated in Figs. 3—5 for phosphonophenylazochromotropic acid in the presence and in the absence of alkaline earth metal ions. According to the results of the measurement of the pK_a of phenylphosphonic acid, the first dissociation constant was not obtained because of

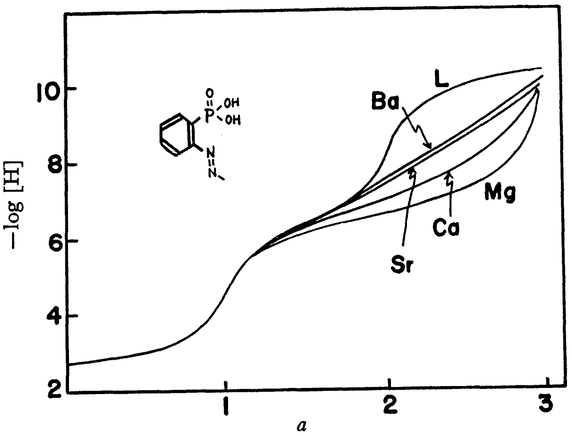

Fig. 3. Titration of *o*-phosphonophenylazochromotropic acid chelate system at 25°C, μ=0.10.
L, ligand only, [Ligand]=1.338×10^{-3}M, [Mg]=2.216×10^{-3}M, [Ca]=2.256×10^{-3}M, [Sr]=2.078×10^{-3}M, [Ba]=2.048×10^{-3}M,
a=moles of base added per mole of ligand

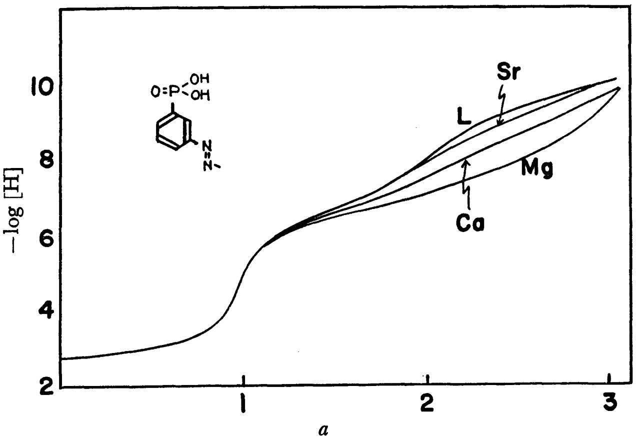

Fig. 4. Titration of *m*-phosphonophenylazochromotropic acid chelate system at 25°C, μ=0.10.
L, Ligand only, [Ligand]=1.600×10^{-3}M. [Mg]=2.216×10^{-3}M, [Ca]=2.256×10^{-3}M, [Sr]=2.078×10^{-3}M, [Ba]=2.048×10^{-3}M,
a=moles of base added per mole of ligand

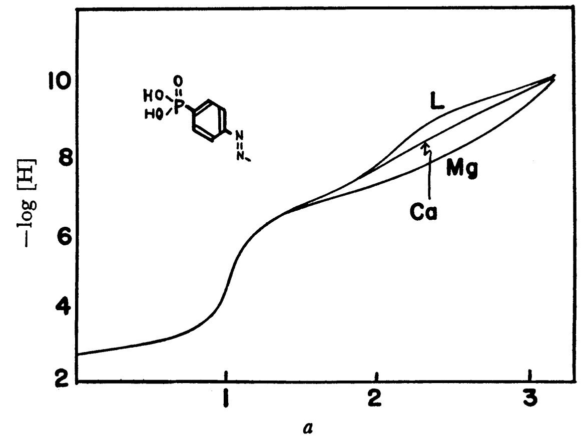

Fig. 5. Titration of *p*-phosphonophenylazochromotropic acid chelate system at 25°C, $\mu=0.10$.
L, Ligand only, [Ligand]$=1.374\times10^{-3}$M, [Mg]$=2.216\times10^{-3}$M, [Ca]$=2.256\times10^{-3}$M, [Sr]$=2.078\times10^{-3}$M, a=moles of base added per mole of ligand

the very strong acid; however, the second dissociation constant, pK_{a2}, is 6.90. Therefore, the inflections at $a=1$ and $a=2$ on the ligand-only titration curve were identified with the dissociation of two phosphonic protons. The third dissociation step corresponds to the naphtholic hydroxyl proton.

As is shown in Figs. 3—5, a depression of the pH on the titration curves is observed in the presence of the metal ion when compared with that of the ligand only; this depression is due to the formation of a chelate. Therefore, the stability order can be judged by the extent of the pH drop. The order with respect to metal ions is as follows: Mg>Ca>Sr>Ba; that is, the stability constants, log K_{ML}, increase with a decrease in the ionic radii. Therefore, the order with respect to ligands is as follows: *ortho*->*meta*->*para*-. The ligand-only titration curve of *o*-phosphonophenylazochromotropic acid has a well-defined inflection at $a=2$ in comparison with those of the two isomers, and the third dissociation step is separated from the second dissociation step; therefore, the calculation of pK_{a3} can be performed like that of monoprotic acid after $a=2$.

Acid-dissociation Constants. The acid-dissociation constants of phosphonophenylazochromotropic acid are listed in Table 1. The pK_{a1} and pK_{a2} values correspond to the dissociation of the phosphonic group; the pK_{a3} value corresponds to the dissociation of the naphtholic hydroxyl group. The pK_{a1} values were not obtained in practice, because the first dissociation is almost complete, as in the case of the sulfonic group. Phenylazochromotropic acid derivatives have two naphtholic protons; however, one proton is not dissociated under ordinary conditions because of the very strong hydrogen bond between the oxygen atoms.[7] Another proton is also combined with one of the nitrogen atoms of the azo link by a hydrogen bonding; that is, in spite of the fact that the pK_a value of the naphtholic proton of chromotropic acid is 5.44,[8] those of the azo derivatives are increased to an order of magnitude of 9—10. The *o*-phosphonophenylazochromotropic acid has a higher pK_{a3} value (=10.12) than the other *m*- and *p*-isomers. This is attributed to the ortho effect of the phosphonic group. Such phenomena have been also observed with regard to *o*-sulfophenylazochromotropic acid.

Table 1. Acid-dissociation constants of phosphonophenylazochromotropic acids and stability constants of their chelates ($t=25$°C; $\mu=0.10$ by KNO$_3$)

Ligand	Acid-dissociation constants			Stability constants, log K_{ML}			
	pK_{a1}	pK_{a2}	pK_{a3}	Mg	Ca	Sr	Ba
ortho-	a)	6.43	10.12	5.71	4.95	4.34	4.15
meta-	a)	6.78	9.46	4.34	3.48	2.72	a
para-	a)	6.88	9.42	3.93	3.04	1.8	a
Neo-Thorin				5.57	5.20	4.39	4.22

a) not measurable owing to very strong acid or unstable chelate

Stability Constants. The chelate stability constants are also listed in Table 1. The chelate stability constants, log K_{ML}, decrease with respect to metal ions as follows: Mg>Ca>Sr>Ba. This order is parallel to the reciprocal of the ionic radii of the metal ions. *o*-Phosphonophenylazochromotropic acid forms a more stable chelate than the *m*- and *p*-isomers; this stabilization is due to the increase in the coordination number produced by the phosphonic group. The log K_{ML} values of Neo-Thorin (*o*-arsonophenylazochromotropic acid) with respect to Mg, Ca, Sr, and Ba are 5.57, 5.20, 4.39, and 4.22 respectively. The calcium, strontium, and barium chelate stability constants of Neo-Thorin are greater than those of *o*-phosphonophenylazochromotropic acid, while the magnesium chelate of *o*-phosphonophenylazochromotropic acid is more stable than that of Neo-Thorin; therefore, it may be concluded that the coordination bond of Mg with the phosphonoic group is stronger than that with the arsonic group.

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[7] S. Nakashima, H. Miyata, and K. Tôei, This Bulletin, **41**, 2632 (1968).

[8] M. Sakaguchi, A. Mizote, H. Miyata, and K. Tôei, *ibid.*, **36**, 885 (1963).