A Comparison of 4-Hydroxynaphthalene-2,7-disulfonic Acid with Chromotropic Acid as a Coupling Component of Azo-type Metallochromic Indicators

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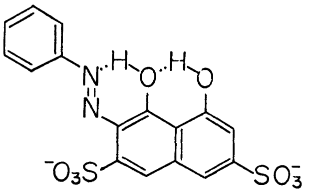
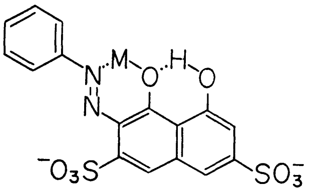
In order to clarify the effect of the hydroxyl group at the 5-position of chromotropic acid on the chelate stabilization, the following six reagents were synthesized by the coupling with 4-hydroxynaphthalene-2,7-disulfonic acid or 4,5-dihydroxynaphthalene-2,7-disulfonic acid(chromotropic acid): 2-(*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid(I), 2-(*o*-methoxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid(II), 2-(*o*-hydroxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid(III), 2-(*m*-sulfophenylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid(IV), 2-(*o*-methoxy-*m*-sulfophenylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid (V), and 2-(*o*-hydroxy-*m*-sulfophenylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid(VI). The acid dissociation constants of these reagents and the stability constants of their metal chelates with magnesium and calcium were measured by the pH titration method at an ionic strength of 0.10 and at 25°C. From the results obtained, it has become apparent that the hydroxyl group at the 5-position exerts a remarkable influence on the chelation of metal ions with the bidentate ligand, such as 2-(*m*-sulfophenylazo)-chromotropic acid, but that it has very little effect on those ions with the terdentate ligand, such as 2-(*o*-hydroxy-*m*-sulfophenylazo)-chromotropic acid. Such an effect appears even in the bidentate ligand with the methoxy group at the *ortho*-position of the benzene ring. That is to say, it may be concluded that the effect of the number of the chelate ring formed with a metal ion is preferred to stabilize the metal chelate over the effect of the hydroxyl group at the 5-position in the terdentate ligand.

Heller and Schwarzenbach[1] have reported that the values of the acid dissociation constants for the two hydroxyl groups of chromotropic acid are 5.36 and 15.6 respectively (pK_a values). The larger value of the latter dissociation of hydroxyl group results from a strong hydrogen bond between two oxygen atoms of chromotropic acid. On the other hand, the pK_{a_1} value of phenylazochromotropic acid is 9.15,[2] which corresponds to the 5.36 value of chromotropic acid; the pK_{a_2} value could not be determined under ordinary experimental conditions because of a strong intramolecular hydrogen bond. It is considered that the phenylazochromotropic acid and its metal chelate have the structures indicated by Formulas (1) and (2) respectively, and that the hydroxyl group at the 5-position of the naphthalene ring probably does not produce chelation with metal ion.



Formula (1)



Formula (2)

The present work will compare the chelate formation ability of 4-hydroxynaphthalene-2,7-disulfonic acid with that of chromotropic acid (4,5-dihydroxynaphthalene-2,7-disulfonic acid) as a coupling component. Namely, 2-(*m*-sulfophenylazo)-, 2-(*o*-methoxy-*m*-sulfophenylazo)- and 2-(*o*-hydroxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acids as well as 2-(*m*-sulfophenylazo)-, 2-(*o*-methoxy-*m*-sulfophenylazo)- and 2-(*o*-hydroxy-*m*-sulfophenylazo)-chromotropic acids were synthesized, and the acid dissociation constants and the stability constants of their chelates with magnesium and calcium were determined by the pH titration method at an ionic strength of 0.10 and at 25°C. The effect of the hydroxyl group at the 5-position will be discussed in comparison with the constants thus obtained.

Experimental

Reagents. The azo compounds, 2-(*m*-sulfophenylazo)-, 2-(*o*-methoxy-*m*-sulfophenylazo)-, and 2-(*o*-hydroxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acids, and 2-(*m*-sulfophenylazo)-, 2-(*o*-methoxy-*m*-sulfophenylazo)-, and 2-(*o*-hydroxy-*m*-sulfophenylazo)-chromotropic acids, were synthesized by the coupling reaction of 4-hydroxynaphthalene-2,7-disulfonic acid or chromotropic acid with each diazotized *m*-aminophenylsulfonic acid, 2-aminophenol-4-sulfonic acid and *o*-anisidine-*p*-sulfonic acid respectively. After the purification of these six reagents, their disodium salt were obtained as fine crystals by salting out. The stock solutions of these reagents were standardized by pH titration with a standard 0.10N potassium hydroxide solution.

The stock solutions of magnesium and calcium were prepared by dissolving $Mg(NO_3)_2 \cdot 6H_2O$ and $Ca(NO_3)_2 \cdot 4H_2O$ of a guaranteed reagent grade in distilled water; these solutions were then standardized by chelatometric titration.

pH Titration Method. The apparatus and the procedure

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[1] J. Heller and G. Schwarzenbach, *Helv. Chim. Acta*, **34**, 1876 (1951).

[2] S. Nakashima, H. Miyata, and K. Tôei, This Bulletin **41** 2635 (1968).

for the pH titration were described in a previous paper[2]; the temperature and ionic strength of a solution were maintained at 25°C and at 0.10 respectively with potassium nitrate.

Calculations

Acid Dissociation Constants of the Reagents. The reagents I(2-(*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid), II(2-(*o*-methoxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid), IV(2-(*m*-sulfophenylazo)-chromotropic acid), and V(2-(*o*-methoxy-*m*-sulfophenylazo)-chromotropic acid) are considered to be monobasic acids, while the reagents III(2-(*o*-hydroxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid) and VI(2-(*o*-hydroxy-*m*-sulfophenylazo)-chromotropic acid are considered to be dibasic acids. The acid dissociation constants, K_a, of these reagents are defined as follows:

(1) Monobasic acid,

$$\mathrm{HL} \rightleftarrows \mathrm{H} + \mathrm{L}$$

$$K_a = \frac{[\mathrm{H}][\mathrm{L}]}{[\mathrm{HL}]} = \frac{[\mathrm{H}](T_{\mathrm{OH}}+[\mathrm{H}]-[\mathrm{OH}])}{T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}]}$$

where T_{L} and T_{OH} represent the total concentrations of the ligand and the alkali added to the system respectively; the ionic charge is disregarded for the sake of convenience.

(2) Dibasic acid,

$$\mathrm{H_2L} \rightleftarrows \mathrm{H} + \mathrm{HL} \qquad K_{a_1} = \frac{[\mathrm{H}][\mathrm{HL}]}{[\mathrm{H_2L}]}$$

$$\mathrm{HL} \rightleftarrows \mathrm{H} + \mathrm{L} \qquad K_{a_2} = \frac{[\mathrm{H}][\mathrm{L}]}{[\mathrm{HL}]}$$

$$1/K_{a_1} = AK_{a_2} + B$$

where:

$$A = \frac{2T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}]}{[\mathrm{H}]^2(T_{\mathrm{OH}}+[\mathrm{H}]-[\mathrm{OH}])}$$

$$B = \frac{T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}]}{[\mathrm{H}](T_{\mathrm{OH}}+[\mathrm{H}]-[\mathrm{OH}])}$$

Stability Constants of the Chelates. The stability constants, K, of the chelates are defined as follows:

$$\mathrm{M} + \mathrm{L} \rightleftarrows \mathrm{ML}$$

$$K = \frac{[\mathrm{ML}]}{[\mathrm{M}][\mathrm{L}]} = \frac{T_{\mathrm{L}}-F}{[\mathrm{L}](F+T_{\mathrm{M}}-T_{\mathrm{L}})}$$

where T_{M} represents the total concentration of the metal ion, and where [L] and F represent as follows:

(1) Monobasic acid

$$[\mathrm{L}] = \frac{K_a}{[\mathrm{H}]}(T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}])$$

$$F = \left(\frac{K_a}{[\mathrm{H}]}+1\right)(T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}])$$

(2) Dibasic acid

$$[\mathrm{L}] = \frac{2T_{\mathrm{L}}-T_{\mathrm{OH}}-[\mathrm{H}]+[\mathrm{OH}]}{\frac{[\mathrm{H}]}{K_{a_2}}+\frac{2[\mathrm{H}]^2}{K_{a_1}K_{a_2}}}$$

$$F = [\mathrm{L}]\left(1+\frac{[\mathrm{H}]}{K_{a_2}}+\frac{[\mathrm{H}]^2}{K_{a_1}K_{a_2}}\right)$$

Results and Discussion

Titration Curves. The titration curves for Reagent I in the presence and in the absence of calcium and magnesium ions are illustrated in Fig. 1, while for Reagents II and III the curves are shown in Figs. 2 and 3 respectively. The titration curves for Reagents

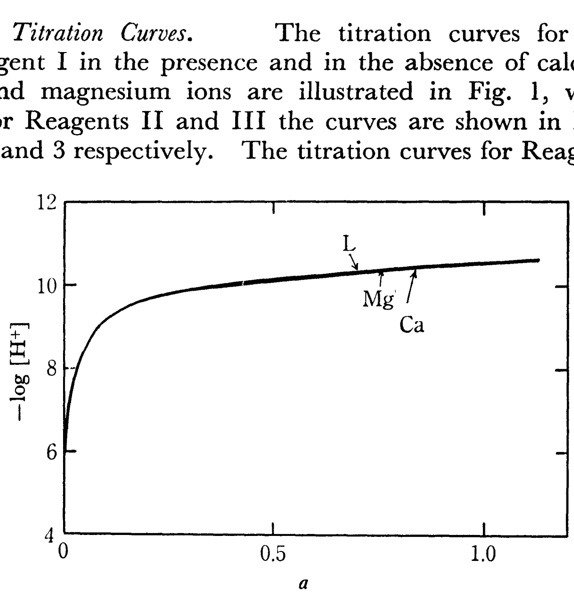


Fig. 1. Titration of 2-(*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid chelate system at 25°C and at μ= 0.10 L; ligand only, [L]=1.265×10^{-3}M, [Mg]=1.677×10^{-3}M, [Ca]=1.824×10^{-3}M.

a: mols of base added per mol of ligand.

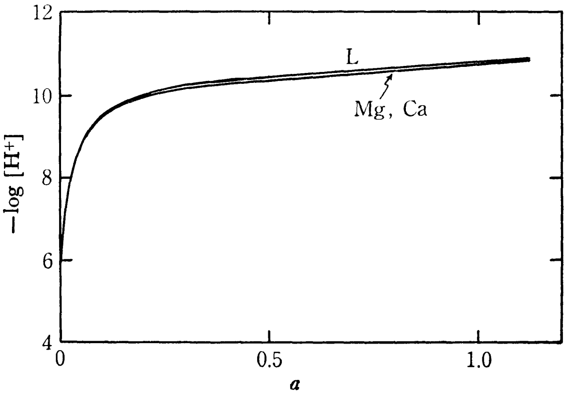


Fig. 2. Titration of 2-(*o*-methoxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid chelate system at 25°C, μ=0.10 [L]=1.228×10^{-3}M, [Mg]=1.677×10^{-3}M, [Ca]=1.824×10^{-3}M.

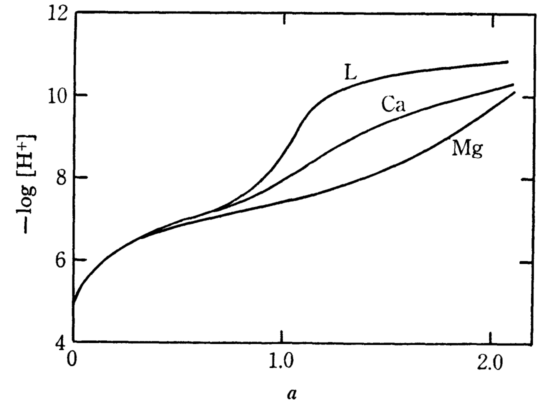


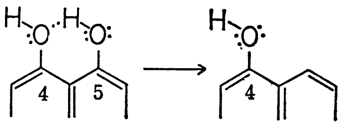
Fig. 3. Titration of 2-(*o*-hydroxy-*m*-sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid chelate system at 25°C, μ=0.10 [L]=1.143×10^{-3}M, [Mg]=1.108×10^{-3}M, [Ca]=1.134×10^{-3}M.

TABLE 1. ACID DISSOCIATION CONSTANTS OF THE REAGENTS AND THE STABILITY CONSTANTS OF THEIR MAGNESIUM AND CALCIUM CHELATES (t=25°C, μ=0.10)

Reagents	Acid dissociation constant		Stability constant, log K	
	pK_{a_1}	pK_{a_2}	Mg	Ca
2-(*m*-Sulfophenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid (I)		10.33	1.8	1.4
2-(*o*-Methoxy-*m*-sulfophenylazo)-1-hydroxy-naphthalene-3,6-disulfonic acid (II)		10.88	2.30	2.70
2-(*o*-Hydroxy-*m*-sulfophenylazo)-1-hydroxy-naphthalene-3,6-disulfonic acid (III)	6.92	10.94	6.08	4.87
2-(*m*-Sulfophenylazo)-1,8-dihydroxynaphthalene-3,6-disulfonic acid (IV)		8.97	3.62	2.89
2-(*o*-Methoxy-*m*-sulfophenylazo)-1,8-dihydroxy-naphthalene-3,6-disulfonic acid (V)		9.64	4.00	2.90
2-(*o*-Hydroxy-*m*-sulfophenylazo)-1,8-dihydroxy naphthalene-3,6-disulfonic acid (VI)	6.68	10.20	6.08	5.04

IV, V and VI are similar to those of Reagent I, II, and III in Figs. 1, 2, and 3 respectively. The acid dissociation constants of these reagents can be calculated by the use of the titration curve of the ligand only. As is shown in Figs. 1, 2, and 3, those curves for Reagents I and II are almost the same as that of phenylazochromotropic acid,2) and the curve for Reagent III corresponds to that of phenolazochromotropic acid.2) The inflection at a=1 in the titration curve of the ligand in Fig. 3 shows the dissociation of the phenolic proton of Reagent III. No inflection is observed at all on the neutralization of the naphtholic proton of the reagents. The titration curve in the presence of the metal ion shows a lower pH value than that of the ligand only. Such a depression of the titration curves indicates the formation of the metal chelate species; the chelate stability order, calcium$<$magnesium, can easily be expected from the extent of the depression of pH. Evidently, Reagents III and VI formed a more stable chelate with calcium and magnesium than did the other reagents investigated.

Acid Dissociation Constants. The acid dissociation constants of the six reagents are summarized in Table 1. In Table 1, the pK_{a_1} and pK_{a_2} values correspond to the dissociation of the phenolic and naphtholic protons respectively. The other naphtholic proton of chromotropic acid in the reagents is not dissociated by the presence of a strong hydrogen bridge between two oxygen atoms. The basicities of these reagents are expressed as a sum of the dissociation constants, pK_A= pK_{a_1}+pK_{a_2}; these values for the reagents decrease as follows: Reagent III>VI>II>I>V>IV. On the effect of the substituents, the sulfo group at the 5-position of the benzene ring decreases the pK_a value for the reagent by means of its electron-withdrawing effect, as is shown in Table 2. On the other hand, the elimination of the naphtholic hydroxyl group at the 5-position of Reagent IV, V, and VI shows a depression of the dissociation of the naphtholic proton at the 4-position of the reagent. This means that the oxygen atom at the 4-position will become more electron-rich than that of chromotropic acid, as is indicated by the following scheme;



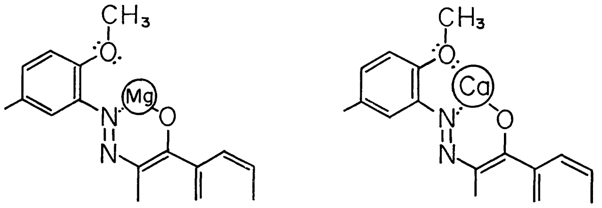
The dissociation of the hydroxyl group is disturbed for this reason.

Stability Constants. The chelate stability constants of their 1:1 chelates with magnesium and calcium ions are also listed in Table 1. Reagents I, II, IV, and V are considered to be bidentate ligands, and Reagents III and VI are considered to be terdentate ligands for metal ions. In these studies, the stabilization of the metal chelate depends mainly on the following factors: (1) the basicity of the reagent, (2) the number of rings formed with a metal ion, and (3) the stabilizing resonance interaction. As for Factor (1), from the concept of Lewis acids and bases, it seems that the strong basic ligand would form the more stable chelate. However, the order of the stability constants of these reagents, VI>III>V>IV>II>I, is not proportional to the basicities of the reagents, III>VI>II>I>V>IV. (2): In the case of Reagents III and VI, the pK_a values of the reagents and the stability

TABLE 2. THE EFFECT OF m-SO_3H GROUP ON THE pK_a OF THE REAGENTS

Reagents	pK_a	Reagents	pK_a
2-(Phenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid	10.48	→ I	10.33
2-(*o*-Methoxyphenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid	11.05	→ II	10.88
Phenylazochromotropic acid	9.19	→ IV	8.97
o-Methoxyphenylazochromotropic acid	9.92	→ V	9.64
o-Hydroxyphenylazochromotropic acid	7.60	→ VI	6.68
	10.60		10.20

constants, log *K*, of magnesium and calcium chelates is almost the same as shown in Table 1. This means that the number of chelate rings exerts a remarkable influence upon the stabilization of their chelates. (3): The effect of the oxygen atom as a donor atom is considered to be almost the same in each reagent. However, the very large difference in the values of log *K* between Reagents I and IV appeared as the effect of having or not having the naphtholic hydroxyl group at the 5-position. This may be caused by a stabilizing resonance of the chelate ring. The same tendency appears in the difference in the stability constants between the copper chelate of phenylazochromotropic acid and that of 2-(phenylazo)-1-hydroxynaphthalene-3,6-disulfonic acid; these log *K*'s values are 17.23 and 8.84 respectively.[3] In the case of Reagents II and V, the values of the stability constants are between Reagents I and III, or Reagents IV and VI, respectively. Such a stable deviation of the reagent with the OCH_3 group at the *o*-position would be due to the coordination of the oxygen atom of the group to metal ions; this coordination is more suitable for calcium ionic radii than for magnesium ones, as is shown in the following scheme:



Therefore, the calcium chelate with Reagent II behaves a bidentate ligand or, rather, a terdentate one. In fact, from the comparison of the stability constants of the magnesium or calcium chelate of Reagent II with those of Reagent IV, it can be assumed that the effect of the number of the chelate ring is preferable to the calcium chelate with Reagent II; on the contrary, the effect of the stabilizing resonance interaction by the hydroxyl group at the 5-position is preferred to that of the magnesium chelate with the same reagent.

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[3] J. Bjerrum *et al.*, "Stability Constants" (Part I, Organic), The Chemical Society, London (1957), p. 95.