Studies on Metal Chelate Compounds of Anthraquinone Derivatives

Part I. Magnesium Chelate Compounds of 1-Hydroxy and 1,4-Dihydroxyanthraquinone

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Structures, absorption spectra, and stabilities of magnesium chelates of 1-hydroxyanthraquinone and 1,4-dihydroxyanthraquinone were examined by the spectrophotometric method. 1-Hydroxyanthraquinone reacts with magnesium in alcoholic solution to form a 2:1 chelate compound (I), while 1,4-dihydroxyanthraquinone forms a 1:1 chelate compound, which is probably a polymer (II).

INTRODUCTION

Studies on metal chelates have been noticed with keen interests not only in the field of analytical chemistry, but of pharmacy, biology, and high molecular chemistry. For example, 8-hydroxyquinoline¹⁾ (oxine), which had originally been used for analytical reagent, its derivatives, and phenazine derivatives²⁾ show antibacterial action. But pyridine derivatives such as 2-methylpyridine-4-carboxylic acid³⁾ and 2-butylpyridine-6-carboxylic acid⁴⁾ (fusaric acid) are known to have remarkable injurious action on plant growth. Tamari⁵⁾ reported that injurious effects of these acids on plant growth were caused by their intermolecular chelation with metal ion which are essentially necessary for the formation of Fe-porphyrion oxidase, cytochrome and other enzymes containing metal

ions.

It is of interest that some of metabolic products produced by microorganisms especially by pathogenic organisms, are found to be chelate reagents such as kojic acid⁶⁾, fusaric acid⁷⁾, and hydroxyanthraquinones.

Flumiani⁸⁾ has reported on the copper chelates of some hydroxyanthraquinones, in which he concluded that the presence of a hydroxyl group at the α -position is decisive for the formation of normal chelate of 2:1, whereas for the formation of an addition compound the presence of a hydroxyl group at the β -position is decisive.

Recently Korshark⁹⁾ has reported that coordination chain polymers of quinizarine (1,4-dihydroxyanthraquinone) and Zn, Cu, Mn, Ni, Co and Cd (bivalent, co-ordination No. 4) were synthesized by treating quinizarin with metal acetylacetonates.

1) A. Albert, *J. Biochem.*, **41**, 534 (1947).

2) Y. Kawakami, et al., *J. Antibiotics, Ser. A*, **8**, 51 (1955).

3) K. Tamari, *Nippon Nogei Kagaku Kaishi*, **27**, 144 (1953).

4) T. Yabuta, K. Kambe and T. Hayashi, *ibid.*, **10**, 1059 (1934).

5) K. Tamari, *ibid.*, **27**, 144, 147, 159, 245, 249, 302 (1953).

6) R.V. Davies, et al., *J. Appl. Chem.*, **9**, 368 (1950).

7) K. Tamari, *Nippon Nogei Kagaku Kaishi*, **26**, 223 (1952).

8) Flumiani, *Monatsh.*, **72**, 368 (1939); **74**, 92 (1942).

9) Korshark, et al., *Vysokomolekulyarnye Soedineniya*, **2**, 492 (1960).

Shibata¹⁰⁾ found that alcoholic solutions of α -hydroxyanthraquinones form beautiful internal complex salts by treating with magnesium acetate.

And this color reaction is commonly used for detecting the position of hydroxyl group in the anthraquinone ring, but it is not clarified in the view of chelate compound.

In this paper, properties of magnesium chelate of 1-hydroxyanthraquinone, which possesses one functional group, was studied spectrophotometrically in ethanol solution, and quinizarin, having two functional groups in it, was also dealt with at the same time.

EXPERIMENTAL

Apparatus. pH measurements were carried out with a Yanagimoto glass electrode pH-meter, direct reading type. Measurements of absorbance were carried out with a Shimadzu electro-spectrophotometer, Model QB-50, direct reading type.

Materials. (a) Solvents: Since anthraquinone derivatives are insoluble in water, ethanol was used as a solvent. Ethanol was purified by treatment with conc. H_2SO_4 , KOH-alkaline $AgNO_3$, and CaO, followed by distillation.

(b) 1-Hydroxyanthraquinone¹¹⁾ was synthesized by means of diazo-reaction of 1-amino anthraquinone; m.p. 200~203°C.

(c) 1,4-Dihydroxyanthraquinone¹²⁾ (quinizarin) was synthesized by means of condensation of phthalic anhydride with hydroquinone; m.p. 196~198°C.

(d) Magnesium Acetate: Special grade for analytical use was used.

Procedure. Preparation of solution for absorption spectral measurements.

(a) 5×10^{-5} M solution of 1-hydroxyanthraquinone was prepared by dissolving 1.12 mg of the reagent in 100 ml of ethanol.

(b) 5×10^{-5} M solution of 1,4-dihydroxyanthraquinone was prepared by dissolving 1.20 mg of reagent in 100 ml of ethanol.

(c) Mg-chelate solution of reagents were prepared as follows. A few drops of saturated ethanol solution

of magnesium acetate were added to 5 ml of the reagent.

(d) pH adjustment: For the absorption spectral measurements, acidity or alkalinity was changed by adding a few drops of ethanol solution of acetic acid or potassium hydroxide, and change in pH of the solution was measured by a pH-meter.

(e) Molar Ratio Method: To 5 ml of 5×10^{-5} M magnesium acetate ethanol solution, ethanol solutions of the reagent was added at a molar ratio, followed by dilution with ethanol to 10 ml. When two, three and four molars weight of reagents are added, the theoretical amounts of reagents which they should combine with Mg^{2+} were discounted.

RESULTS

I. 1-Hydroxyanthraquinone-Magnesium Chelate.

(1) **Absorption Spectra.** In Figs. 1 and 2, absorption curves of both 1-hydroxyanthraquinone and its magnesium chelate compound are shown. The curve represented by I is in acidic (pH 5.6), II in neutral¹³⁾ (8.3), and III in alkaline (pH 11.9) solution. The curves of I and II seem to be nearly the same but III is very different. This phenomenon may be ascribed to changes in the structure caused by ionization. Three kinds of absorption curves of magnesium chelate are shown in Fig. 2, that is, in acidic (pH 4.5), neutral (pH 8.1), and alkaline (pH 12.0) solutions. The curves of II and III seem to be nearly the same but I in acidic solution is very different. The band which is characteristic in chelates is found in 500 $m\mu$ both in neutral and alkaline solution, but not in acidic solution.

(2) **Effect of pH Change.** The absorption of the magnesium chelate solution in various pH is shown in Fig. 3. The maximum absorption is shown at pH of about 8.1 to 8.5, measured at 500 $m\mu$.

(3) **Composition of the Chelate.** The determination of composition of the chelate was carried out by means of continuous variation

10) S. Shibata, *J. Am. Chem. Soc.*, **72**, 2789 (1956); *J. Pharm. Soc. Japan*, **61**, 103 (1941).

11) H. Roemer, *Ber.*, **15**, 1793 (1882).

12) C. Liebermann, *Ann.*, **212**, 10 (1882).

13) The term "neutral" means an intermediate solution between acidic and alkaline ethanol solutions.

FIG. 1. Absorption Spectra of 1-Hydroxyanthraquinone (5×10^{-5} M).

Acidic I —○—
Neut. III —●—
Alkali. II —×—

method and molar ratio method.

(a) Continuous Variation Method¹⁴): The molar ratio of the chelate was determined at 500 $m\mu$ and pH 8.1. The experimental data clearly indicated that molar ratio of the reagent to magnesium in chelate was 2:1 (Fig. 4).

(b) Molar Ratio Method¹⁵): Under the same condition of ethanol solution at pH 8.1 and 500 $m\mu$. When the reagent is 2 moles/Mg, the break was observed; the molar ratio of the reagent to magnesium was found to be 2:1 (Fig. 5).

II. 1,4-Dihydroxyanthraquinone Magnesium Chelate.

(1) Absorption Spectra. In Figs. 6 and 7, the absorption of both 1,4-dihydroxyanthraquinone and its magnesium chelate are shown. The curves of reagent in acidic and neutral media are almost the same but the one in

FIG. 2. Absorption Spectra of 1-Hydroxyanthraquinone Magnesium Chelate (5×10^{-5} M).

Acidic I —×—
Neut. II —●—
Alkali. III —○—

alkaline medium shows a marked difference. On the other hand, the curves of magnesium chelate in acidic medium is very different from what are in neutral and alkaline media. The band which is characteristic in chelation is at 580 $m\mu$ both in neutral and alkaline solution, but nothing is found in acidic medium.

(2) Effect of pH Change. The maximum absorption is shown at a pH of about 9 as shown in Fig. 8, measured at 580 $m\mu$.

(3) Composition of the Chelate.

(a) Continuous Variation Method: By this method, the composition of 1,4-dihydroxy-

14) W.C. Vosburgh, et al., *J. Am. Chem. Soc.*, **63**, 437 (1941).

15) A.E. Harvey, et al., *ibid.*, **72**, 4488 (1950).

FIG. 3. Effect of pH Change on 1-Hydroxyanthraquinone Magnesium Chelate (500 m μ).

anthraquinone to magnesium was 1:1 at pH 9 and 580 m μ (Fig. 9).

(b) Molar Ratio Method: Under similar conditions, the same results as by the former method (Fig. 10) was obtained.

III. Degree of Dissociation and Dissociation Constants of the Chelate Compounds. From the molar ratio method, degree of dissociation (α) is calculated from equation (1):

$$\alpha = \frac{E_m - E_s}{E_m} \quad (1)$$

16) M. Ishidate and Y. Yamane, *J. Pharm. Soc. Japan*, **79**, 389 (1957).

FIG. 4. Absorption Curve of 1-Hydroxyanthraquinone Magnesium Chelate (Job's Method).

FIG. 5. Absorption Curve of 1-Hydroxyanthraquinone Magnesium Chelate (Molar Ratio Method).

FIG. 6. Absorption Spectra of 1,4-Dihydroxyanthraquinone (5×10^{-5} M).

Acidic I —×—, Neut. II —○—
Alkali. III —●—

FIG. 7. Absorption Spectra of 1,4-Dihydroxyanthraquinone Magnesium Chelate (5×10^{-5} M).

Acidic I —×—, Neut. II —●—
Alkali. III —○—

FIG. 8. Effect of pH Change on 1,4-Dihydroxyanthraquinone Magnesium Chelate ($580 \text{ m}\mu$).

FIG. 9. Absorption Curve of 1,4-Dihydroxyanthraquinone Magnesium Chelate (Job's Method).

FIG. 10. Absorption Curve of 1-Hydroxyanthraquinone Magnesium Chelate (Molar Ratio Method).

where E_m is the maximum extinction and E_s is the extinction at the stoichiometric molar ratio of the reagent to magnesium in the chelate.

Since the ratio of the reagent to magnesium is 2:1, the equilibrium constant may be written as

$$K = \frac{\alpha(2\alpha c)^2}{1-\alpha} \quad c: \text{total concentration} \quad (2)$$

Similarly, in the case of 1:1 chelate, K is obtained as follows.

$$K = \frac{\alpha^2 c}{1-\alpha} \quad (3)$$

The degree of dissociation (α) and dissociation constant (K) of magnesium chelate of 1-hydroxyanthraquinone and 1,4-dihydroxyanthraquinone calculated from the formulas (1), (2), and (3) are shown in Table I.

TABLE I.

Compound	α	Reag. : Mg	$-\log K$	pH
1-Hydroxyanthraquinone	0.06	2 : 1	11.64	8.1
1,4-Dihydroxyanthraquinone	0.38	1 : 1	4.93	9.0

IV. Structure of the Chelate. From the results obtained here, 1-hydroxyanthraquinone forms a stable six membered, 2:1, normal chelate compound, but 1,4-dihydroxyanthraquinone forms a 1:1 chelate compounds; and structures of [I] and [II] are assigned.

DISCUSSION AND CONCLUSION

It is well known that hydroxyanthraquinones are produced by microorganisms and some of them are produced by pathogenic organisms as metabolic products. The question in regards to the role played by the

pigments in vivo has not been clarified yet. α -Hydroxyanthraquinone possesses one functional group, a hydroxyl peri to carbonyl, forming a chelate ring. Raistrick¹⁷⁾ has reported a general rule concerning the position of substituents in the anthraquinone ring, in

which pigments produced by micro-organisms have at least one α -hydroxyl group in it and many pigments have hydroxyl groups both at 4 and 5 position. In this paper, magnesium chelates of 1-hydroxyanthraquinone having one functional group and 1,4-dihydroxyanthraquinone having two functional groups were studied by spectrophotometric method concerning their properties and compositions in solution, as well as their dissociation constants. In neutral and alkaline media 1-hydroxyanthraquinone forms a six-membered chelate ring, indicating the molar ratio of 2:1; 1,4-dihydroxyanthraquinone forms a chelate believed to be a polymer with molar ratio of 1:1 in neutral and alkaline media. 1-Hydroxyanthraquinone forms a fairly stable magnesium chelate, showing the dissociation constant of 11.64.

In these results, it might be said that there are some relationship between the formation of chelate and pathogeny in the plant tissue.

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17) H. Howard and H. Raistrick, *Biochem. J.*, **46**, 49 (1950).