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Studies on Metal Complex Formation in Solution. I. Cryptotanshinone-$FeCl_3$ Complex

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Cryptotanshinone was isolated from tanshinone III as a Fe(III) complex. The cryptotanshinone-Fe(III) complex was obtained by mixing anhydrous $FeCl_3$ with cryptotanshinone in glacial acetic acid, and it decomposed to its original components on addition of water. Elemental analysis and measurements of the molar conductance, molecular weight and infrared and far-infrared spectra of this complex suggested that it is an equimolar complex [Fe(cryptotanshinone)Cl_3] in which cryptotanshinone is a bidentate ligand of the *o*-quinone type.

This complex exhibited an absorption maximum at 560 nm in benzene, and was shown to have a 1: 1 composition by the continuous variation, slope ratio and molar ratio methods. Similar complexes of related compounds were also 1: 1. The apparent stability constants of these complexes, measured by molar ratio method, were compared; results suggested that the ether oxygen of cryptotanshinone contributes to the stability of this complex.

Keywords——*Salvia miltorrhiza* BUNGE (Tan-shen); cryptotanshinone; *o*-quinone; Fe(III) complex; five coordinate complex; stability constant; continuous variation method; molar ratio method; slope ratio method

Introduction

Nakamoto and Fukushima[2] isolated three pigments, tanshinone I, II and III from the roots of *Salvia miltorrhiza* BUNGE (Chinese drug, Tan-shen). Later Takiura[3] showed that tanshinone III was a mixture of tanshinone II (consisting of II–A (**1**) and II–B (**2**)) and a new pigment, cryptotanshinone (**3**). Cryptotanshinone was isolated from tanshinone III as a cryptotanshinone-Fe (III) complex by adding anhydrous $FeCl_3$ in glacial acetic acid. The complex was obtained as black needles, and decomposed easily into its original components in water. Tanshinone II has a similar structure to cryptotanshinone, but does not react with anhydrous $FeCl_3$ under the same conditions. Being interested in the complex formation for use in separation of compounds with similar structures, in this work we examined the structure of cryptotanshinone-Fe(III) complex, and the apparent stability constants of the Fe(III) complexes of cryptotanshinone and related compounds in solution.

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[2] M. Nakamoto and M. Fukushima, *Yakugaku Zasshi*, **54**, 154 (1934).

[3] K. Takiura, *Yakugaku Zasshi*, **61**, 475 (1941).

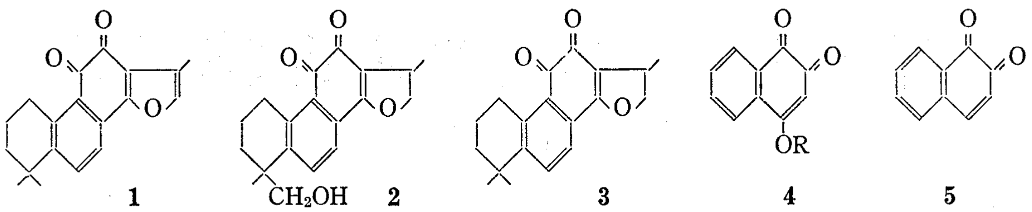

Chart 1

Experimental

Complex Formation and Chemical Analysis——Cryptotanshinone in glacial acetic acid was added to anhydrous $FeCl_3$ in the same solvent. The black needles of complex that rapidly formed were filtered, washed with the same solvent, and recrystallized from glacial acetic acid.

With the addition of water the black complex decomposed and became orange yellow. The insoluble orange yellow needles of cryptotanshinone were filtered off, washed thoroughly with water, dried and weighed. A sample of the filtrate was used to determine iron by chelatometric titration with 0.01 M EDTA, and chlorine by precipitation titration with 0.05 N $AgNO_3$ and 0.05 N NH_4CNS by the method of Volhard. *Anal.* Calcd. for cryptotanshinone($C_{19}H_{20}O_3$)$FeCl_3$: cryptotanshinone, 64.53; Fe, 12.18; Cl, 23.19. Found: cryptotanshinone, 64.14; Fe, 12.02; Cl, 22.56.

Physical Constants——The molar conductance of this complex was determined in nitrobenzene at 25° with a Toa Denpa CM-1DB conductance meter. $\Lambda_m = 9.9$ mho·cm² (1.7×10^{-3} M), 10.1 (1.0×10^{-3} M), 11.6 (0.2×10^{-3} M).

The molecular weight was determined in benzene with a Hitachi 115 vapor pressure osmometer. Calcd. for Cryptotanshinone($C_{19}H_{20}O_3$)$FeCl_3$: 458.56. Found: 462.5.

The infrared spectra of cryptotanshinone and its complex were obtained in nujol mull with a Hitachi EPI-S spectrophotometer. Cryptotanshinone, ν cm^{-1}: 2920, 1680, 1650, 1625, 1560, 1400, 1330, 1190, 1165, 1140, 940, 840, 700. Cryptotanshinone-$FeCl_3$, ν cm^{-1}: 2930, 1640, 1610, 1585, 1525, 1330, 1190, 1140, 940, 820, 720.

The far-infrared spectrum of the cryptotanshinone-$FeCl_3$ was obtained in nujol mull with a Hitachi EPI-L spectrophotometer. ν cm^{-1}: 590, 545, 510, 430 (ligand), 375 (Fe-Cl), 335 (Fe-Cl), 330 (ligand), 305 (ligand).

Spectrophotometric Studies on the Complexes——Molar compositions were determined by the following procedures. Visible spectra were measured with a Shimazu UV-200 spectrophotometer.

Ligand: Cryptotanshinone was isolated from Tan-shen. 4-Alkoxy-1,2-naphthoquinone (**4**) was synthesized by the method of Fieser.[4] 1,2-Naphthoquinone (**5**) was purchased and purified. 0.1 M Fe^{3+} solution in glacial acetic acid standardized by chelatometric titration was diluted to the required concentration with benzene.

Continuous Variation Method[5]: Cryptotanshinone-Fe(III) complex, $[\text{ligand}]+[Fe^{3+}]=4.0\times10^{-4}$ M. 1,2-Naphthoquinone-Fe(III) complex, $[\text{ligand}]+[Fe^{3+}]=3.0\times10^{-3}$ M.

Slope Ratio Method[6]: Cryptotanshinone- and 4-alkoxy-1,2-naphthoquinone-Fe(III) complexes; $[\text{constant component}]=1.0\times10^{-3}$ M, $[\text{variable component}]=0.5$—$2.0\times10^{-4}$ M.

Molar Ratio Method[6]: Cryptotanshinone-, 4-alkoxy-1,2-naphthoquinone- and 1,2-naphthoquinone-Fe(III) complexes; $[Fe^{3+}]=2.0\times10^{-4}$ M, $[\text{ligand}]=1.0$—20.0×10^{-4} M. Absorbance was measured at three wavelengths within 5 minutes after preparing the solution: Cryptotanshinone-Fe(III) complex; 560, 600 and 630 nm. 4-Alkoxy-1,2-naphthoquinone-Fe(III) complexes; 500, 530 and 560 nm. 1,2-Naphthoquinone-Fe(III) complex; 460, 480 and 500 nm. In the case that the absorption of ligand was not negligible, the absorbance was corrected.

Evaluation of Apparent Stability Constants[6]: Dissociation was expressed as

$$\begin{array}{lcccl} ML_n & \rightleftarrows & M & + \; nL & \\ C & & 0 & 0 & \text{initial concn.} \\ C(1-\alpha) & & C & n\alpha C & \text{equilibrium concn.} \end{array}$$

where C is the total concentration of the complex when there is no dissociation, and α is the degree of dissociation. The values of n for each complex were established as 1 by the continuous variation method and slope ratio method. The apparent stability constant is written as

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[4] L.F. Fieser, *J. Am. Chem. Soc.*, **48**, 2922 (1926).

[5] W.C. Vosburgh and G.R. Cooper, *J. Am. Chem. Soc.*, **63**, 437 (1941).

[6] A.E. Harvey and D.L. Manning, *J. Am. Chem. Soc.*, **72**, 4448 (1950).

$$K = [ML_n]/[M][L]^n = C(1-\alpha)/(\alpha C)(n\alpha C)^n = (1-\alpha)/\alpha^2 C$$

The values of α and C were obtained from the curves in Fig. 4 by the following equation

$$\alpha = (E_m - E_s)/E_m$$

where E_m is the maximum absorbance obtained from the horizontal portion of the curve and E_s is the absorbance at [ligand]/[Fe^{3+}]$=1$.

Results and Discussion

The cryptotanshinone-Fe(III) complex was obtained as black needles by mixing anhydrous $FeCl_3$ with cryptotanshinone in glacial acetic acid. The complex was slightly soluble in benzene, chloroform and ethyl acetate, practically insoluble in cyclohexane, and soluble in methanol in which it decomposed. Its decomposition in polar solvents were similar to those of the phenanthraquinone- and benzanthrone-Fe(III) complexes.[7,8]

The complex decomposed on addition of water, liberating cryptotanshinone quantitatively in a pure form. This is the basis of the gravimetric method for determination of cryptotanshinone in this complex. Samples of the filtrate were used for determination of iron and chlorine by chelatometric and precipitation titrations, respectively. The results showed that the ratio of cryptotanshinone: iron: chlorine was 1: 1: 3.

The molar conductance of a millimolar solution of this complex in nitrobenzene was in order of 9—11 mho·cm² mol⁻¹, indicating that the complex is a non-electrolyte which dissociate slightly in solution, because the value for a uni-univalent electrolyte should be higher.[9] The molecular weight in benzene suggested that the complex is monomeric species.

The infrared spectra of cryptotanshinone and its complex were compared. The band of free cryptotanshinone at 1650 cm⁻¹ attributed to a carbonyl streching vibration was a higher frequency than that of the complex (*ca.* 40 cm⁻¹) indicating that the complex is formed through the carbonyl group. In the far-infrared spectrum of this complex, the ν (Fe-Cl) absorptions (375 and 355 cm⁻¹) were consistent with those of five coordinate complexes.[10] These results

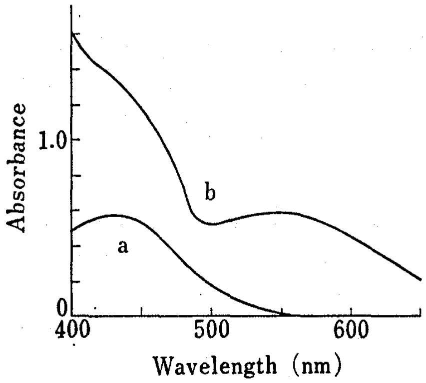

Fig. 1. Visible Absorption Spectra of (a) Cryptotanshinone (2.0×10^{-4} M) and (b) the Cryptotanshinone-$FeCl_3$ Complex (2.0×10^{-4} M) in Benzene

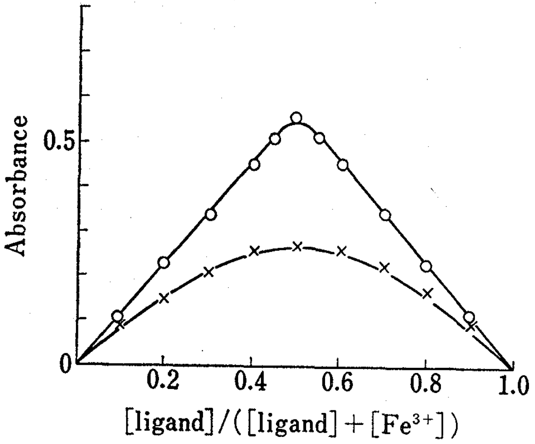

Fig. 2. Continuous Variation Method

—○—=cryptotanshinone-Fe(III) complex at 560 nm, [ligand]+[Fe^{3+}]$=4.0\times10^{-4}$ M; —×—=1,2-naphthoquinone-Fe(III) complex at 500 nm, ligand]+[Fe^{3+}]$=3.0\times10^{-4}$ M.

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7) K.H. Meyer, *Chem. Ber.*, **41**, 2568 (1908); P.J. Crowley and H.M. Haendler, *Inorg. Chem.*, **1**, 904 (1962).
8) R.C. Paul, R. Parkash, and S.S. Sandhu, *Z. Anorg. Allg. Chem.*, **352**, 322 (1967).
9) P.A. McCuster, T.J. Lane, and S.M. Kennard, *J. Am. Chem. Soc.*, **81**, 2974 (1959); S.A. Cotton and J.F. Gibson, *J. Chem. Soc.* (*A*), **1970**, 2105.
10) S.W.A. Fowles, D.A. Rice, and R.A. Walton, *J. Chem. Soc.* (*A*), **1968**, 1842; *idem*, *J. Inorg. Nucl. Chem.*, **31**, 3119 (1969).

suggest that cryptotanshinone is a bidentate ligand of *o*-quinone type in this complex, so that the complex is five coordinate.

Formation of the complex between cryptotanshinone and $FeCl_3$ cannot be studied spectrophotometrically in glacial acetic acid, because the complex precipitates. However, the complex showed an absorption maximum at 560 nm in benzene (Fig. 1). Thus in benzene, containing a trace of glacial acetic acid to dissolve anhydrous $FeCl_3$, it was possible to show that it was a 1: 1 complex by the method of continuous variation, slope ratio and molar ratio (Fig. 2—4).

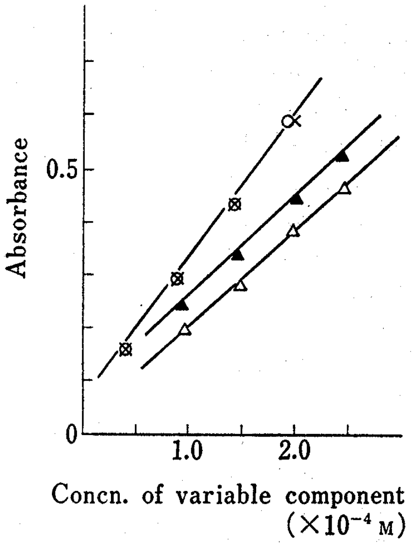

Fig. 3. Slope Ratio Method

Cryptotanshinone-Fe(III) complex; —○—= [ligand] is variable, —×—=[Fe^{3+}] is variable, [constant component]=1.0×10^{-3} M, at 560 nm: 4-methoxy-1,2-naphthoquinone-Fe(III) complex; —△—=[ligand] is variable, —▲—= [Fe^{3+}] is variable, [constant component]=1.0×10^{-3} M, at 500 nm.

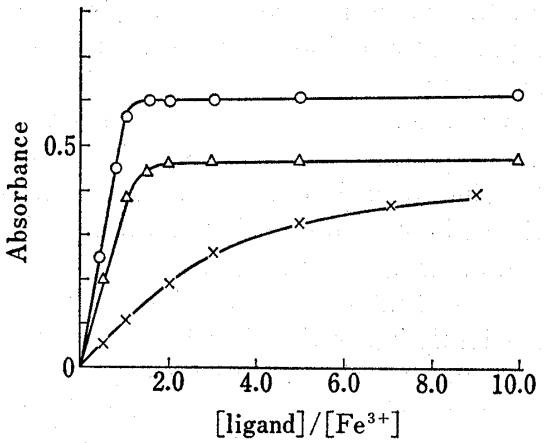

Fig. 4. Molar Ratio Method

—○—=cryptotanshinone-Fe(III) complex at 560 nm, —△—=4-methoxy-1,2-naphthoquinone-Fe(III) complex at 500 mn, —×—=1,2-naphthoquinone-Fe (III) complex at 480 nm, [Fe^{3+}]=2.0×10^{-4} M.

4-Alkoxy-1,2-naphthoquinone with similar functional groups to cryptotanshinone also form Fe(III) complexes, with the same spectra as that of cryptotanshinone-Fe(III) complex and λ_{max} at 500 nm. They were shown to be 1: 1 complexes by the slope ratio method (Fig. 3). 1,2-Naphthoquinone also form Fe(III) complex, and was assumed to be 1: 1 complex by continuous variation method (Fig. 2).

The apparent stability constants of Fe(III) complexes of cryptotanshinone and related compounds, estimated by molar ratio method, are shown in Table I. Formation of the complexes was affected by moisture, and results varied with the conditions used for measurements. Although it was impossible to determine the values exactly, the values measured at the same time showed similar tendencies. As shown in Table I, the complex of cryptotanshinone with

TABLE I. Apparent Stability Constants of Fe (III) Complexes

Fe (III) complex	log *K*
Cryptotanshinone	7.18 ± 0.33
4-Methoxy-1,2-naphthoquinone	5.23 ± 0.08
–Ethoxy–	5.41 ± 0.08
–(*n*-Propoxy)–	5.51 ± 0.08
–(iso-Propoxy)–	5.66 ± 0.06
–(*n*-Butoxy)–	5.26 ± 0.08
1,2-Naphthoquinone	<3.40

an ether link had larger stability constant than those of 4-alkoxy-1,2-naphthoquinone without an ether link. And, the complex of 1,2-naphthoquinone without an ether oxygen had smaller value than others. The difference of the values of the cryptotanshinone- and 4-alkoxy-1,2-naphthoquinone-Fe(III) complexes is attributed to the substituent effect of the alkyl group adjacent to the carbonyl group. The smaller value of 1,2-naphthoquinone-Fe(III) complex is ascribed to the ligand without electron-releasing group.

We conclude from this work that ether oxygen in cryptotanshinone contributes to the stability of the complex.

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