

# POLAROGRAPHIC STUDIES ON METAL COMPLEXES OF IMIDAZOLE, 2-METHYL-IMIDAZOLE and 2-(1-NAPHTHYLMETHYL)-IMIDAZOLE\*

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金俊容·柳京秀·白南豪 : Imidazole 및 그誘導體의 金屬錯體에 關한 Polarograph 研究

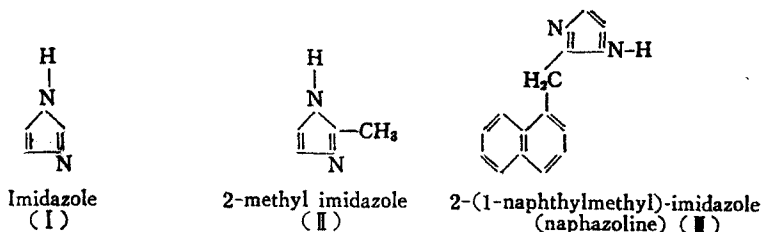
Imidazole 및 類似化合物과 遷移元素間의 錯體形成은 生化學的으로도 重要な 問題다. 본 論文은 Cd, Ni, Mn, Co 等과 錯體形成을 Polarograph法으로 究明하였으며 錯體形成 恒數는 Deford 및 Hume의 數學的方法을 適用하여 計算하였다. 錯體形成에서의 enthalpy 變化,  $\Delta H^\circ$ , 및 entropy 變化,  $\Delta S^\circ$ 를 25°C 와 35°C의 實驗에서 얻은 結果로부터 求하였다.

## INTRODUCTION

The reactivity of the imidazole groups and amino acids in proteins has assumed great importance for the understanding of interaction between proteins and several transition metal ions.

Many workers have been reported on the copper imidazole complexes,<sup>1)</sup> zinc imidazole complexes<sup>2)</sup>, cobalt and nickel complexes<sup>3)</sup>, and Cr, Ag<sup>4)</sup> and Hg<sup>5)</sup> complexes. If this is so, the binding constant for the reaction of a metal with imidazole itself should be of the same order of magnitude as the intrinsic constant found for the association of the same metal and serum albumin.

This paper presents the results on the cadmium, nickel, manganese, and cobalt complexes of imidazole groups, using the method of polarography. As far as the authors know, there



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have been no published reports on the 2-methylimidazole (II) and 2-(1-naphthylmethyl)-imidazole (III). The naphazoline<sup>6)</sup> have vasoconstrictor properties very similar to those of epinephrine and other phenylethylamines, although its structure differs from that of most sympathomimetic agents.

The authors, also, present the results on the metal imidazole complexes using the mathematical treatment for the determination of the successive formation constants of metal-complexes which are similar to the Deford and Hume<sup>7)</sup> approach to the evaluation of consecutive formation constants of complex ions. The coordination numbers were evaluated for each of the imidazole complexes from the plotting of the shifts of half-wave potential,  $\Delta E_{\frac{1}{2}}$ , and  $\beta_n$  fraction of metal ion in uncomplexed from metal ions. Finally, the change of enthalpy and entropy were determined by polarographic measurements on these systems.

## EXPERIMENTAL

### Material,

Reagent grade chemicals and polarographic mercury were used without further purification. Ionic strength was adjusted with potassium chloride which evidently form a weak chloride complex with metal ions.

### Apparatus,

Polarographic measurements were made with a Yanagimoto PA-102 recording polarograph. A Yokogawa potentiometer D-1B was used to obtain voltage readings. The pH was measured with a Beckman pH meter, 9602 Zeromatic. Solutions were maintained in a constant temperature by means of constant temperature bath at  $25 \pm 0.5^\circ\text{C}$ .

### Experimental Procedure,

Metal ions standard solutions were made a definite concentration  $5 \times 10^{-4}\text{M}$ , and  $1 \times 10^{-3}\text{M}$  to 0.1M (in case of naphazoline, 0.01M contained with 20% alcohol) solution of ligand were added to it. In each case of the measurements, potassium chloride was added to maintain an ionic strength of 0.1.

## RESULTS AND DISCUSSION

### General Polarographic Characteristics,

Relative decomposition potentials of the imidazole groups in the presence of 0.1M KCl solution have been measured as shown in Table 1. These potentials are independent on the pH range from 1 to 7. From the results measured, the decomposition potentials of imidazole, 2-methylimidazole, and naphazoline are to be -1.780, -1.770 and -1.542 volts versus saturated calomel reference electrode, respectively. It is assumed that the shifts of the more positive

A plot of  $\Delta E_{\frac{1}{2}}$  vs  $\Delta \log C_x$  in the concentration range from  $1 \times 10^{-3} M$  to  $1.5 \times 10^{-1} M$  shows that the curve can be interpreted as a composite of four straight lines, as shown in Figure 1. When the concentration of imidazole is higher than 0.1M the line is steepest, and yield  $p=4.0$  This is represented as  $Cd^{++} + 4 Im \rightleftharpoons CdIm_4^{++}$ . The value for  $p$ , given in Figure 1 and Table 2 were obtained from a least squares treatment of the polarographic data. Figure 1 indicates that there exists a mixture of complexes. However, it is difficult to determine the formula of medium order cadmium complexes of the imidazole. Because the range of the complexes formation between  $CdIm_2^{++}$  and  $CdIm_3$  is so small in graphically. With this calculation, the values obtained at medium order complexes are inaccurate that it is difficult to tell what the formation constants of medium complexes are.

For this reason, the mathematical treatment of polarographic data for the determination of the formation constants of successive complexes using the method of Deford and Hume<sup>7)</sup> was applied. To interpret the experimental data, we must evaluate the four successive formation constants for the complexes,  $CdIm_1^{++}$ ,  $CdIm_2^{++}$ ,  $CdIm_3^{++}$  and  $CdIm_4^{++}$ .

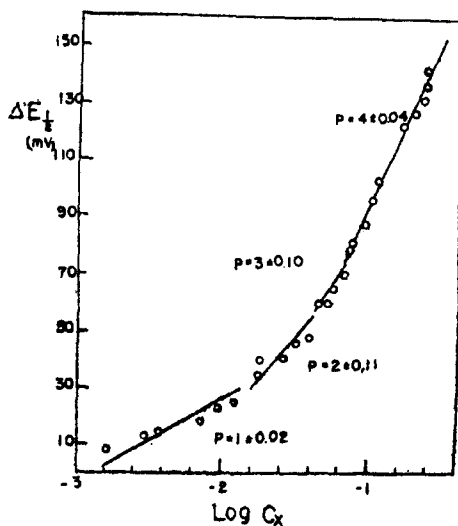
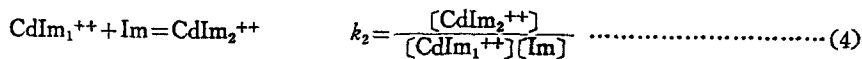
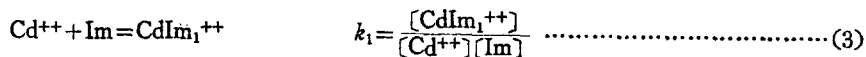


Fig 1. Cd(II)-imidazole complexes

If the formation of complex ion is rapid and reversible, then for each individual complex there exists an individual formation constant  $k$ .





In general,

$$K_j = \frac{[MX_j^{+n-j}]}{(k_1 k_2 k_3 \dots k_{j-1}) [M^{+n}] [X^-]^j} \dots\dots\dots(7)$$

where,  $k_j$  is the individual constant of the complex. On the other hand,  $C_{MX_i}$  is the concentration of complex forming substance, the fraction  $\beta_n$  of metal ion in uncomplexed form  $[M^{+n}]$  are as follows;

$$\frac{1}{\beta_n} = \frac{C_{MX}}{[M^{+n}]} = \sum_{j=0}^{j=n} K_j C_x^j f_x^j / f_{MX_i} \dots\dots\dots(8)$$

where, by definition  $K_0=1$ .

In case of the reduction to the metallic state(amalgam) of a complex ion of ametal, the equation which related  $K_j$  to the shift in half-wave potential due to complex formation is given below at 25°C.

$$(E_{\frac{1}{2}})_s - (E_{\frac{1}{2}})_c = \frac{0.0591}{n} \log \frac{I_c}{I_s} + \frac{0.0591}{n} \log \sum_j \frac{K_j C_x^j f_x^j}{f_{MX_i}} \dots\dots\dots(9)$$

If the symbol  $F(X)$  is introduced for convenience to represent,

$$F(X) = \frac{K_0}{f_x} + \frac{k_1 C_x f_x}{f_{MX1}} + \frac{k_2 C_x^2 f_x^2}{f_{MX2}} + \dots + \frac{K_j C_x^j f_x^j}{f_{MXj}} \dots\dots\dots(10)$$

Then, the equation is rearranged as follows,

$$F_0(X) = \frac{K_j C_x^j f_x^j}{f_{MXj}} = \text{antilog} \left[ \frac{n}{0.0591} \left\{ (E_{\frac{1}{2}})_s - (E_{\frac{1}{2}})_c \right\} + \log \frac{I_s}{I_c} \right] \dots\dots\dots(11)$$

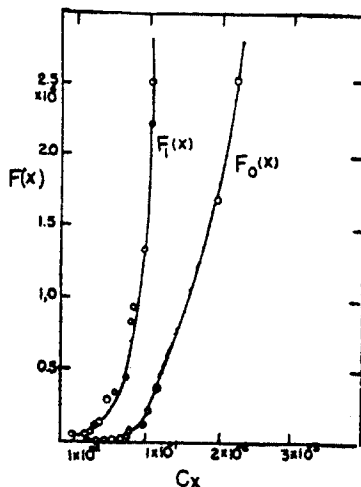


Fig 2.  $F_0(X)$  and  $F_1(X)$  as functions of the imidazole concentrations at 25°C

where,  $I_s$  and  $I_c$  are the diffusion current constant of the simple metal ion and complex ion, respectively.

If  $F_0(X)$ , as calculated from equation 11 is plotted versus  $C_x$ , curve is obtained whose intercept is equal to  $k_0(\text{unity})$  as shown in Figure 2.

Correspondingly,  $F_1(X)$  is derived from equation 10 and defined in the following manner,

$$F_1(X) = \frac{F_0(X) - k_0/f_x}{C_x f_x} = \frac{k_1}{f_{MX1}} + \frac{k_2 C_x f_x}{f_{MX2}} + \frac{k_3 C_x^2 f_x^2}{f_{MX3}} + \dots + \frac{k^j C_x^{j-1} f_x^{j-1}}{f_{MXj}} \dots (12)$$

As before, if  $F_1(X)$  is plotting versus  $C_x$  and extrapolated to  $C_x=0$ , the value of  $F_1(X)$  at the intercept is equal to the  $k_1/f_{MX1}$ , where  $k_1$  is the first formation constant. This process is repeated until all the constants have been determined.

$$F_2(X) = \frac{F_1(X) - k_1/f_{MX1}}{C_x f_x} = \frac{k_2}{f_{MX2}} + \frac{k_3 C_x f_x}{f_{MX3}} + \dots + \frac{k^j C_x^{j-1} f_x^{j-1}}{f_{MXj}} \dots (13)$$

Finally, for the high complex, in this case the neutral species;

$$F_n(X) = \frac{F_{n-1}(X) - k_{j-1}/f_{MX_{j-1}}}{C_x f_x} = k_1 k_2 k_3 \dots k_j / f_{MX_j} = K_j / f_{MX_j} \dots (14)$$

It can be seen from equation 11, 12, 13 and 14 that each succeeding expression in the series of  $F_0(X)$ ,  $F_1(X)$ , etc., may be represented by a successively lower order equation. Thus, if  $F_0(X)$  is a quadric equation,  $F_1(X)$  will be a cubic,  $F_2(X)$  quadratic,  $F_4(X)$  will be a constant. The evidence given here shows that the maximum coordination number of cadmium ion for imidazole molecule is 4, a finding completely in accordance with the evidence derived with other complexes of these ion. In Table 3, the formation constants are represented.

Table 3. Constants for the Cd-imidazole Complex

	CdIm <sub>1</sub> <sup>++</sup>	CdIm <sub>2</sub> <sup>++</sup>	CdIm <sub>3</sub> <sup>++</sup>	CdIm <sub>4</sub> <sup>++</sup>
Formation constants,* at 25°C	2.79	4.45	5.96	7.03
$\rho k_j$ at 35°C	—	4.48	5.87	6.88
Relative coordination mean	1	2.09	3.24	3.98
number, $\rho$ at $\Delta E_{\frac{1}{2}} = 30\text{mV}$ .	1	1.96	3.20	4.10

\* By application of Deford and Hume method.

On the other hand, as mentioned in equation 8, let us define a set of functions,  $\beta_1$  to  $\beta_n$ , which will represent the ratio of the concentration of the metal containing species to the analytical concentration of metal,  $C_{M^{+n}}$ . In the case of the equilibrium concentration of ligand and successive formation constant are known, the equation which relates to the shift in half-wave potential of the cadmium-imidazole complexes due to complexes formation given as follows at 25°C.

$$C_{M^{+n}} = \frac{[M_n^{+n}]}{\beta_n} = [M^{+n}] \sum_{j=0}^{j=n} K_j C_x^j f_x^j / f_{MX_j} \dots (15)$$

and

$$\left\{ (E_{\frac{1}{2}})_s - (E_{\frac{1}{2}})_c \right\} = \frac{0.0591}{n} \log \frac{I_s}{I_c} - \frac{0.591}{n} \log \beta_n C_M^{+n} \dots\dots\dots (16)$$

The mean coordination number with respect to imidazole ion were estimated from the logarithmic diagram of the  $\beta_n$  function versus  $\Delta E_{\frac{1}{2}}$  as shown in Table 3.

#### Calculation of $\Delta H^\circ$ and $\Delta S^\circ$ for the Formation of Cd-Complex.

From the data of the formation constant  $k_f$  at temperature of 25°C and 35°C. The value of  $\Delta H^\circ$  can be readily calculated using the Arrhenius equation,

$$\frac{d \ln k}{dT} = \frac{\Delta H^\circ}{RT^2} \dots\dots\dots (17)$$

On the other hand, the entropy change has been calculated by the following equations,

$$\Delta F^\circ = -RT \ln k \dots\dots\dots (18)$$

$$\Delta F^\circ = \Delta H^\circ - T \Delta S^\circ \dots\dots\dots (19)$$

The values of the heat of activation energy  $\Delta H^\circ$  and entropy change  $\Delta S^\circ$  are found to be -13.41 Kcal/mole, and -10.7 cal/mole, deg., respectively. These values are agreed well with the values of White and Doody<sup>8)</sup>.

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