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Studies of the Substituent Effect on the Stability Constants of Bis(2-hydroxy-4 or 5-substituted acetophenonato)copper(II)

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The dissociation constants of eleven 2-hydroxy-4 or 5-substituted acetophenones were determined in a 22.5% water-dioxane-mixed solvent system at 25 and 40 °C by potentiometric titration. They were then discussed in terms of the electronic effect of the substituents and the linear-free-energy relationship. The stability constants bis(2-hydroxy-4 or 5-substituted acetophenonato)copper(II) were also determined under the same experimental conditions; a linear relationship between the dissociation constants and the stability constants was obtained for bis(2-hydroxy-4 or 5-substituted acetophenonato)copper(II). No significant difference has been found in the effects of 4- and 5-substituted groups on the stability constants.

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The values obtained were discussed in terms of the electronic effect of the substituents and the linear free-energy relationship. The stability constants of bis(2-hydroxy-4 or 5-substituted acetophenonato)copper (II) were also determined under the same experimental conditions, and a linear relationship between the dissociation constants and the stability constants was discussed in comparison with those of bis(4- or 5-substituted salicylaldehydato)copper(II).

Although several studies of the stability constants for metal complexes, especially copper complexes, of salicylaldehyde and its derivatives have been reported,[1–4] few studies of copper complexes of *o*-hydroxyacetophenone derivatives have appeared so far.[5] It would be interesting to study the stability constants of the copper complex of *o*-hydroxyacetophenone derivatives which have no steric factors in the course of the complex formation and to compare them with those of the copper complexes of the corresponding salicylaldehyde derivatives.

Since *o*-hydroxyacetophenone derivatives, salicylaldehyde derivatives, and their metal complexes are not very soluble in water, nonaqueous or mixed solvent systems are usually employed for the measurement of the equilibrium constants. The use of such solvents, however, raises the question of the interpretation of the potential obtained from a cell containing a glass electrode and a liquid junction error. Therefore, the calibration of the glass electrode must be made for the solvent system. An empirical calibration for pH-meter reading was made by the method reported by Van Uitert and Haas[6] for the 22.5% water–dioxane system at 25 and 40 °C.

The electronic effect of the substituent on the dissociation constants(pK_a) of 2-hydroxy-4 or 5-substituted acetophenones were interpreted in terms of the linear free-energy relationship.

The stability constants of bis(2-hydroxy-4 or 5-substituted acetophenonato)copper(II) were compared with those of bis(4- or 5-substituted salicylaldehydato)copper(II). A linear relationship between the pK_a and the stability constant has been predicted by Calvin,[1] assuming that the enthalpy change for the complex formation is predominant over the entropy change to the stability constant. On the contrary, Jones *et al.*[2] have shown a non-linear relationship between the pK_a's and the log K's for salicylaldehyde derivatives and their copper complexes; they explained their result in terms of the interaction of the d_ε-electron of the cupric ion. Since it has since been found, though, that the latter work involves some experimental errors together with the use of a ligand determined incorrectly,[7] the determination of the stability constants of bis(4- or 5-substituted salicylaldehydato)copper(II) should be reexamined in order to elucidate the electronic effect of the substituent on the complex formation.

Experimental

Materials. 2-Hydroxyacetophenone, 4-methyl, 5-methyl, 4-chloro, 5-chloro, 4-bromo, 5-bromo, and 4-nitro derivatives of 2-hydroxyacetophenone were prepared by the usual Fries-rearrangement of the corresponding substituted phenyl acetates. 4-Methoxy and 5-methoxy derivatives were obtained by the Friedel-Crafts reaction of acetyl chloride with resorcinol and hydroquinone dimethyl ether respectively.[8] 2-hydroxy-5-nitroacetophenone was synthesized by the nitration of 2-hydroxyacetophenone. All of these compounds were purified by recrystallization. Dioxane was purified by a previously reported method.[9] Sodium perchlorate was recrystallized twice from water at 50 °C. Potassium chloride was purified by the Pinching and Bates method.[10] Hydrochloric acid was distilled twice, and the middle fraction was used. Deionized water was distilled under a nitrogen atmosphere.

The other reagents employed in this study were commercially available and were used without further purification.

Preparation of Bis(2-hydroxy-4 or 5-substituted acetophenonato)-copper(II). The general procedure was as follows: About 0.5 g of the ligand was dissolved in methanol containing an equivalent amount of potassium hydroxide; then the mixture was diluted with the same volume of water. A one half equivalent of cupric chloride was dissolved in a small amount of water and added to the ligand solution. The copper chelate was collected by filtration, washed with 50% aqueous methanol, and dried at room temperature *in vacuo*. The results of elemental analyses are summarized in Table 4.

Titration. The titration apparatus employed was the same as that reported in a previous paper.[11] Titration was carried out by the method reported by Irving and Rossotti.[12] The ionic strength was maintained at 0.3 with potassium

Table 1. Dissociation constants of 2-hydroxy-4 or 5-substituted acetophenones in 22.5% aqueous dioxane at 25 and 40 °C

Substituent	$pK_{a25\,°C}$	$pK_{a40\,°C}$	$\Delta\Delta G_i$ (kcal/mol)
4-OCH_3	10.475	10.267	+0.43
5-OCH_3	10.849	10.631	−0.08
4-CH_3	11.127	10.902	−0.46
5-CH_3	11.395	11.162	−0.82
H	10.794	10.578	0.00
4-Cl	9.780	9.591	+1.38
5-Cl	10.148	9.948	+2.26
4-Br	9.680	9.494	+1.52
5-Br	9.959	9.766	+1.14
4-NO_2	8.617	8.460	+2.97
5-NO_2	7.265	7.144	+4.81

nitrate, while the temperatures were 25.0±0.1 °C and 40.0±0.1 °C. The metal solution was standardized by the usual EDTA-titration method.[13]

Correction of pH Meter Reading. An empirical calibration of the glass electrode in 22.5% aqueous dioxane at 25.0 and 40.0 °C (±0.1 °C) was carried out by the method reported by Van Uitert and Haas.[6]

A Hildebrand-type platinum electrode, 3000-10T, of the Hitachi-Horiba Manufacturing Co., was platinized[14] in each measurement and employed as a hydrogen electrode. A silver-silver chloride electrode** was used as the reference electrode.

The standard potential of the reference electrode and the mean activity coefficient of hydrogen chloride were obtained by interpolation from the data of Harned and Owen.[15] The conversion factors(U_H) were obtained by means of the relationship between the pH meter reading(B) and the hydrogen-ion concentration ([H]).

Determination of the Dissociation Constants(pK_a). The dissociation constants of 2-hydroxy-4 or 5-substituted acetophenones were obtained by the usual titration method with a pair of glass and calomel electrodes at 25.0 and 40.0 °C (±0.1 °C) and were calculated by means of Irving and Rossotti's equation.[16] The pK_a's were corrected by the Van Uitert and Haas method.[6b] The values thus obtained are shown in Table 1.

Calculation of the Stability Constants. The stability constants of bis(2-hydroxy-4 or 5-substituted acetophenonato) copper(II) were calculated by the method reported in a previous paper.[11]

Results and Discussion

The conversion factor and the correction factor for the 22.5% aqueous dioxane system were found to be reasonable in comparison with the values obtained by a graphic method.[6]

According to the generalized equation of the linear free-energy relationships,[17] the dissociation constants and the difference in the free energy change can be expressed as follows:

$$\log(K_i/K_0) \equiv X_i \text{ or } \sigma_i\rho_i$$

$$\Delta\Delta G_i = \Delta G_i - \Delta G_0 = -2.303RT\sigma_i\rho_i$$

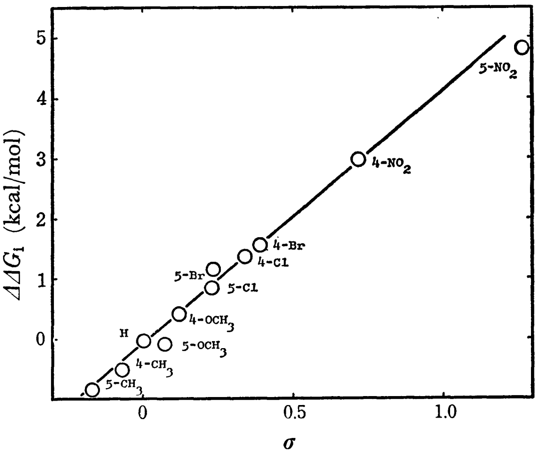

Fig. 1. Correlation of the difference of the free energy change ($\Delta\Delta G_i$) for the dissociation constant of 2-hydroxy-4 or 5-substituted acetophenones with Hammett σ constants.

where the i and 0 subscripts indicate the values for 2-hydroxy-4 or 5-substituted acetophenones and 2-hydroxyacetophenone respectively. Figure 1 shows the relation between the $\Delta\Delta G_i$ values of 2-hydroxy-4 or 5-substituted acetophenones and the Hammett σ constants. Bekkum's σ value(σ=0.076) for the 5-methoxy derivative[18] and the polarizability effect (σ=1.27) for the 5-nitro derivative[19] are used to evaluate the effect of those substituents. Those two plots deviate from the linear relationship.

In the case of the 5-nitro derivative, a remarkable precipitation of the complex was found in the course of titration, whereas no such precipitation was observed for the other ligands. Some experimental error may be involved in the stability constant for bis(2-hydroxy-5-nitroacetophenonato)copper(II) for the 5-nitro de-

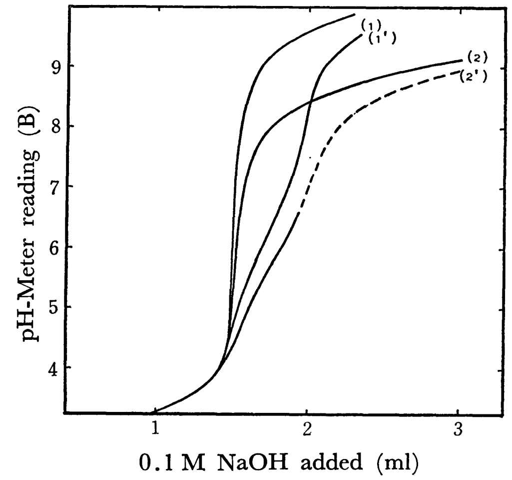

Fig. 2. Typical titration curves of 2-hydroxyacetophenone and their Cu(II) complexes in 22.5% aqueous dioxane at 25 °C.
(1); 5×10^{-3} M 2-hydroxyacetophenone, 1.9413×10^{-3} M HNO_3, 3×10^{-3} M KNO_3, (1′); Chelating agent, acid and salt as (1), 2.5042×10^{-4} M Cu(II), (2); 5×10^{-3} M 2-hydroxy-4-chloroacetophenone, acid and salt as (1), (2′); Chelating agent, acid and salt as (2), Cu(II) as (1′).

** Kindly prepared and provided by Toa Electronics, Ltd., Tokyo.

TABLE 2. STABILITY CONSTANTS OF 2-HYDROXY-4 OR 5-SUBSTITUTED ACETOPHENONES AND Cu(II) IN 22.5% AQUEOUS DIOXANE AT 25 °C AND IONIC STRENGTH 0.3 (KNO_3)

Substituent	pK_a	pA			β	log K_{MA}	log K_{MA_2}
		n=0.5	n=1.0	n=1.5			
4-OCH_3	10.47	7.35	6.72	6.15	2.75×10^{13}	7.27	6.23
5-OCH_3	10.85	7.37	6.76	6.19	3.27×10^{13}	7.29	6.28
4-CH_3	11.13	7.79	7.14	6.57	1.93×10^{14}	7.71	6.66
5-CH_3	11.39	7.74	7.12	6.41	1.72×10^{14}	7.66	6.47
H	10.79	7.58	6.94	6.30	7.48×10^{13}	7.50	6.37
4-Cl	9.78	7.10	6.53	5.98	1.14×10^{13}	6.99	6.06
5-Cl	10.15	7.30	6.93	6.07	1.41×10^{13}	7.21	6.16
4-Br	9.68	6.88	6.28	5.78	3.66×10^{12}	6.79	5.89
5-Br	9.96	7.00	6.39	5.89	6.08×10^{12}	6.91	6.00
4-NO_2	8.62	6.68	6.03	5.62	1.14×10^{12}	6.61	5.73
5-NO_2	7.26	4.54	3.89	3.49	6.08×10^{7}	4.46	3.61

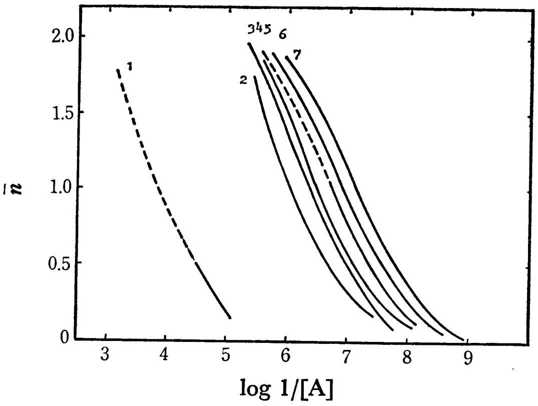

Fig. 3. Typical formation curves of 2-hydroxyacetophenone derivatives and Cu(II) complexes in 22.5% aqueous dioxane at 25 °C, and ionic strength 0.3 (KNO_3).
1; 2-OH-5NO_2-acetophenone, 2; 2-OH-4-NO_2-acetophenone, 3; 2-OH-5-Br-acetophenone, 4; 2-OH-4-Cl-acetophenone, 5; 2-OH-5-OCH_3-acetophenone, 6; 2-OH-acetophenone, 7; 2-OH-4-CH_3-acetophenone.

rivative under the conditions here employed. Typical titration curves for some complex formations are illustrated in Fig. 2, while in Fig. 3 the formation curves for typical complexes are presented, with a dotted line indicating the precipitation of the complex. Among these complexes, the 5-nitro and 4-chloro derivatives showed poor solubility under the present conditions. A comparison of the formation curves indicates that a similar type of complex formation may occur during the titration. The stability constants obtained are summarized in Table 2.

It has been reported that a linear relationship can be established for the dissociation constants of salicylaldehyde derivatives and the stability constants of bis(substituted salicylaldehydato)copper(II).[7] A similar trend was confirmed in the eleven bis(4- or 5-substituted salicylaldehydato)copper(II) complexes. Slightly convex curves were obtained in the cases of 2-hydroxyacetophenone derivatives and pentane-2,4-dione derivatives.[2,6c] These trends have been explained by Jones *et al.*[2] in terms of the σ and π-electronic effects of the substituents. That is, the nitro group acts as

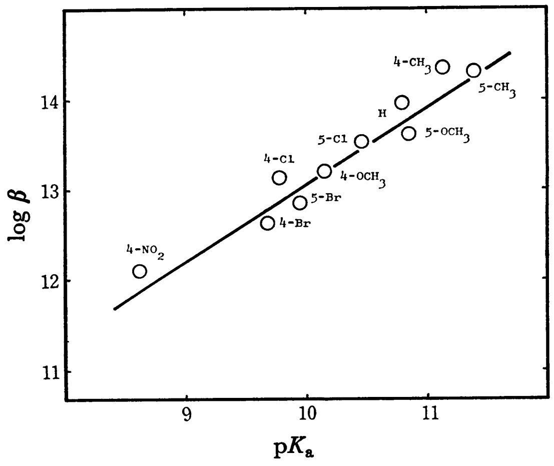

Fig. 4. The relation between the dissociation constants (pK_a) of 2-hydroxy-4 or 5-substituted acetophenones and the over-all stability constants (log β) of their copper(II) complexes.

a σ and π-electron acceptor, whereas the chloro group acts as a σ-acceptor and π-donor. Therefore, larger stability constants may be expected for the nitro derivatives than the chloro derivatives. The predominant stabilization of the complexes is attributed to the "back donation" of the d_π-electron of the copper ion. However, the above-mentioned hypothesis, which was proposed for the interpretation of the stability constants salicylaldehyde complexes, has been criticized by Postmus *et al.*,[7] since the structure of 4-chlorosalicylaldehyde was not correctly identified. Some experimental error may indeed be included in the determination of the stability constant of the 5-nitro derivative.

The linear relationship between the stability constants and the dissociation constants, which has been predicted by Calvin[1] in view of the thermodynamic functions for the formation of the complex, is expressed as follows:

$$\log K = a\,\mathrm{p}K_a + b$$

where log K is the stability constant(log K_{MA}, log K_{MA_2}, log β), pK_a is the dissociation constant of the ligand, and a and b are constants. The constants, a and b, obtained from the plot of the stability constant against pK_a are presented in Table 3, along with those of

TABLE 3. VALUES OF THE CONSTANTS(a, b) IN EQUATION $\log K = a\ \mathrm{p}K_a + b$, AND THE CORRELATION COEFFICIENTS(r) FOR COPPER(II) COMPLEXES OF 4 OR 5-SUBSTITUTED SALICYLALDEHYDES AND 2-HYDROXY-4 OR 5-SUBSTITUTED ACETOPHENONES IN 22.5% AQUEOUS DIOXANE AT 25 °C

	$\log K_{MA}$			$\log K_{MA_2}$			$\log \beta$		
	a	b	r	a	b	r	a	b	r
4 or 5-Substituted salicylaldehyde	0.79	−0.79	0.96	0.76	−1.50	0.96	1.51	−2.04	0.96
2-Hydroxy-4 or 5-substituted acetophenone	0.43	2.81	0.95	0.32	2.90	0.94	0.85	4.59	0.96

TABLE 4. ELEMENTAL ANALYSES OF BIS(2-HYDROXY-4 OR 5-SUBSTITUTED ACETOPHENONATO)COPPER(II)

Substituent	Formula	Found (%)					Calcd (%)				
		C	H	N	X	Cu[a]	C	H	N	X	Cu
4-OCH_3	$C_{18}H_{18}O_6Cu$	54.84	4.73	—	—	16.11	54.89	4.61	—	—	16.13
5-OCH_3	$C_{18}H_{18}O_6Cu \cdot 0.5H_2O$	53.33	4.60	—	—	16.03	53.66	4.75	—	—	15.77
4-CH_3	$C_{18}H_{18}O_4Cu \cdot H_2O$	56.44	5.09	—	—	17.02	56.91	5.31	—	—	16.73
5-CH_3	$C_{18}H_{18}O_4Cu \cdot H_2O$	57.00	4.98	—	—	17.10	56.91	5.31	—	—	16.73
H	$C_{16}H_{14}O_4Cu \cdot 0.5H_2O$	56.35	4.44	—	—	19.07	56.06	4.41	—	—	18.53
4-Cl	$C_{16}H_{12}O_4Cl_2Cu$	47.54	3.03	—	17.76	14.91	47.72	3.00	—	17.61	15.78
5-Cl	$C_{16}H_{12}O_4Cl_2Cu \cdot 0.5H_2O$	46.98	3.12	—	17.34	15.05	46.68	3.18	—	17.22	15.43
4-Br	$C_{16}H_{12}O_4Br_2Cu$	38.86	2.55	—	32.91	12.25	39.09	2.46	—	32.51	12.93
5-Br	$C_{16}H_{12}O_4Br_2Cu$	39.28	2.63	—	32.51	11.97	39.09	2.46	—	32.51	12.93
4-NO_2	$C_{16}H_{12}O_8N_2Cu$	45.69	3.08	6.47	—	13.84	45.34	2.85	6.61	—	14.99
5-NO_2	$C_{16}H_{12}O_8N_2Cu$	45.62	3.02	6.60	—	13.03	45.34	2.85	6.61	—	14.99

a) Obtained from per cent ash as copper oxide.

bis(4- or 5-substituted salicylaldehydato)copper(II).

The a constants for the salicylaldehyde derivative were found to be larger than those for the 2-hydroxyacetophenone derivative in all cases. This fact indicates that the effect of the substituent of the salicylaldehyde derivatives on the stability constant is more significant than the effect of that of the 2-hydroxyacetophenone derivatives. This finding may be interpreted in terms of the difference in polarizability between the two series of ligands induced by the cation.[20]

The stability constant of a metal complex is strongly dependent on the basicity of its ligand. An electron-donating substituent group increases the electron density on the keto oxygen atom or the phenolic oxygen atom; this, in turn, results in an enhancement of the stability constant of the metal complex. The position of the substituent does not make any essential difference in the stability constants. It seems that the 4-substituent group increases the electron density on the keto oxygen atom, whereas the 5-substituent group enhances the electron density on the phenolic oxygen atom. Therefore, these trends can be explained in terms of classical substituent effects as a whole, such as the Hammett σ values.

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