Effect of the Chain Length of *N*-Alkyl-*β*-alanine on Their Copper Complex Formation in Aqueous Solution

Akio Nakamura,* Masakatsu Koshinuma,† and Kazuo Tajima††
Nagoya Municipal Women's Junior College, Kitachikusa, Chikusa-ku, Nagoya 464
†Laboratory of Chemistry, Faculty of Informatics, Teikyo University of Technology, Uruido, Ichihara-shi, Chiba 290-01
††Department of Chemistry, Faculty of Engineering, Kanagawa University, Rokkakubashi, Kanagawa-ku, Yokohama 221

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The effects of the chain length of *N*-alkyl-*β*-alanine (NAA) (the number of carbon atoms in the alkyl chains; n=0, 2, 4, 6, 8, 10, 12) on the copper(II) complex formation and its properties were investigated. The complex formation constants for two-step reactions were determined by potentiometry using the selective electrodes of copper(II) and hydrogen ions. The values of the complex formation constants decreased with increasing chain length of the alkyl substituents, and became constant for the substituents longer than the butyl group. These results could be explained in terms of a steric hindrance effect of the *N*-alkyl substituents on these coordination reactions. Each logarithmic function of the solubility and of the solubility product of the 1(Cu) : 2(NAA)-complexes was found to be expressed, respectively, as a linear function of the number of carbon atoms in the alkyl group. From these data, the standard free energies of the formation and the precipitation of the 1 : 2-complexes from these constituent ions have been estimated, and a standard free energy diagram was constructed for 1 : 2-complex formation. It was concluded that the hydrophobic interaction is a driving force which promotes crystalline complex formation from the constituent ions.

One of the most unique characteristics of amphoteric surfactants of the amino acid type is to form stable complexes with the transition metal ions. These inherent properties, however, seem not to have been fully investigated so far, and have not been used for the industrial applications. In practice, there are very few documents which systematically describe how the chain length of the amphoteric surfactants affects the complex formation equilibria.

In a previous study concerning copper(II) complexes of *N*-alkyl-*β*-alanine (NAA),[1)] we demonstrated that the chain length of the alkyl groups in the 1 : 2-complexes is one of the significant factors which govern the configuration in a complex molecule and the molecular arrangement in a crystal. Moreover, it has also been emphasized that the hydrophobic interaction between alkyl chains incorporated in complex molecules plays an important role in the promotion of complex formation.

The present study was attempted in order to elucidate the effects of the hydrophobic interaction between alkyl groups of NAA on the copper(II)-NAA complex formation and also to clarify the energetic relation between complex formation and its precipitation.

Experimental

Materials. *N*-Alkyl-*β*-alanine (NAA) (i.e., 3-(alkylammonio)propionate) was used. The number of carbon atoms in the alkyl chain of NAA was 0 (*β*-Ala), 2 (NEtA), 4 (NBuA), 6 (NHeA), 8 (NOA), 10 (NDeA), and 12 (NDA). Details regarding the syntheses and purification of these compounds have been reported elsewhere.[1,2)] The copper salt ($CuCl_2 \cdot 2H_2O$) was purified by recrystallization from distilled water.

Dissociation Constants. The first and second dissociation constants of NAA were determined by the usual pH potentiometry in an atmosphere of nitrogen; the NAA solutions were titrated with carbonate-free sodium hydroxide solutions or with the hydrochloric acid. From the difference in the pH values between the NAA solution and the distilled water, the dissociation constants were calculated.

Complex Formation Constants. A given amount of pure NAA powder was added with stirring into the $CuCl_2$ solution. The activities of copper(II) and hydrogen ions in the solution were simultaneously measured as a function of the NAA concentration with the ion-selective electrodes connected to the ion meter (Orion Research, model 920). From data concerning the activities, the stepwise formation constants of copper(II)-NAA complexes were calculated. To minimize the influence of the photosensitivity of the copper(II) ion-selective electrode on the output current, the apparatus was set up and operated in a room that was as dark as possible. All measurements were made at 30±0.2 °C.

Results and Discussion

Dissociation Constants of NAA. The coordination reactions of amino acids and metal ions are usually accompanied by the dissociation of amino acids. It is therefore necessary to know the acid-base character of NAA in order to study its complex formation reactions. The dissociation reactions of NAA are expressed as

$$L^{+} \rightleftarrows L^{\pm} + H^{+} \qquad (1)$$

and

$$L^{\pm} \rightleftarrows L^{-} + H^{+}, \qquad (2)$$

where L^{+}, $L^{\pm}$, L^{-}, and H^{+} denote the cationic, the amphoteric, the anionic forms of NAA, and hydrogen ions, respectively. Then, the first and the second dissociation constants of NAA are defined by

$$C_{L^{\pm}} \cdot C_{H^{+}} / C_{L^{+}} = K_{A1} \qquad (3)$$

and

$$C_{L^{-}} \cdot C_{H^{+}} / C_{L^{\pm}} = K_{A2}, \qquad (4)$$

where C_i denotes the concentration of species i, and K_{A1} and K_{A2} express the first and the second dissociation constants of NAA, respectively. Since the concentration of each solute is sufficiently low, and since the activity coefficient of each ion is approximately unity according to the Debye-Hückel theory, hereafter the concentration expression for each solute is used instead of its activity. The pK_{A1} and pK_{A2} values determined by the pH potentiometry are listed in Table 1, together with the dissociation constants for some analogous compounds.[3]

From Table 1, it can be seen that though the pK_{A1} values are not affected by the introduction of an alkyl group into β-alanine, the pK_{A2} values decrease by about 0.5 compared to that of β-alanine, regardless of the chain length of the alkyl group. These facts can be explained in terms of an increase in the basicity of the nitrogen atom, owing to an introduction of the alkyl group which acts as an electron-releasing group. Similar results have been reported for glycine and its alkyl-substituted derivatives, as shown in Table 1.[3]

Formation Constants of Cu-NAA Complexes. Since most copper(II) complexes of amino acids generally have the 1(Cu):2(amino acid)-composition, the complex-formation equilibria of the copper(II) ion with NAA in a dilute aqueous solution are assumed to be established by the following two-step reactions:

$$M^{2+} + L^{\pm} \rightleftarrows ML^{+} + H^{+} \tag{5}$$

and

$$ML^{+} + L^{\pm} \rightleftarrows ML_2 + H^{+}, \tag{6}$$

Where M^{2+}, ML^{+}, and ML_2 denote the copper(II) ion, the 1(Cu):1(NAA)-complex ion, and the 1(Cu):2(NAA)-complex, respectively. Then, from Eqs. 5 and 6 we obtain

$$C_{ML^+} \cdot C_{H^+}/C_{M^{2+}} \cdot C_{L^\pm} = K_1, \tag{7}$$

and

$$C_{ML_2} \cdot C_{H^+}/C_{ML^+} \cdot C_{L^\pm} = K_2, \tag{8}$$

where K_1 and K_2 denote the stepwise formation constants of ML^+ and ML_2, and $C_{M^{2+}}$, $C_{L^\pm}$, C_{ML^+}, C_{ML_2}, and C_{H^+} denote the concentrations of M^{2+}, $L^\pm$, ML^+, ML_2, and H^+, respectively.

Table 1. Dissociation Constants of NAA and Formation Constants of Copper-NAA Complexes at 30 °C

NAA	pK_{A1}	pK_{A2}	$\log K_1$	$\log K_2$
β-Ala	3.70	10.1	−2.82	−4.23
NEtA	3.61	10.6	−3.98	−5.53
NBuA	3.57	10.6	−4.30	−5.90
NHeA	3.61	10.6	−4.29	−5.88
NOA	3.56	10.6	−4.27	—[a]
NDeA	3.57	10.6	−4.28	—[a]
NDA	3.55	10.6	−4.26	—[a]
Glycine[b]	2.35	9.78	−1.22	−2.74
	(2.36)	(9.57)	(−1.42)	(−2.72)
N-Methylglycine[b]	2.11	10.2	−2.06	−3.34
	(2.20)	(9.99)	(−2.05)	(−3.33)
N-Ethylglycine[b]	(2.30)	(10.1)	(−2.76)	(−3.94)
N-Propylglycine[b]	(2.28)	(10.0)	(−2.75)	(−3.95)

a) Not determined because of low solubilities of the 1:2-complexes. b) The data of glycine and its derivatives are obtained according to the relations, $K_1 = K_1^* \cdot K_{A2}$, and $K_2 = K_2^* \cdot K_{A2}$. The data of K_1^*, K_2^*, and K_{A2} for these compounds are cited from Ref. 4, where K_1^* and K_2^* are defined as: $K_1^* = [ML^+]/[M^{2+}][L^-]$, and $K_2^* = [ML_2][ML^+][L^-]$ at 25 °C and ionic strength=0. (Data in Parentheses: ionic strength =0.1.)

For such a system, in which the amount of complex is too small to be detected by a pH measurement, it has generally been emphasized that both the activities of the hydrogen and metal ions have to be measured simultaneously and independently in order to determine the formation constants.[4] Therefore, the activity measurements of both copper(II) ions and hydrogen ions in solution were made for determining the formation constants of the 1:1- and 1:2-complexes, especially for the systems of the lower homologs of NAA. The obtained results for the Cu-NHeA system, as a typical example, are shown in Fig. 1. The $C_{M^{2+}}$ and C_{H^+} values gradually decreased with increasing concentration of NAA, in common with other sytems.

Here, we conventionally introduce the total concentrations of copper(II) (C^M) and NAA (C^L) defined respectively as

$$C^M = C_{M^{2+}} + C_{ML^+} + C_{ML_2} \tag{9}$$

and

$$C^L = C_{L^\pm} + C_{ML^+} + 2C_{ML_2}. \tag{10}$$

Under the condition $C^L \gg C^M$, the combination of Eqs. 7 and 8 gives us

$$(C^M/C_{M^{2+}}) - 1 = K_1(C^L/C_{H^+}) + K_1K_2(C^L/C_{H^+})^2. \tag{11}$$

Thus, the application of Eq. 11 to the Cu-NHeA

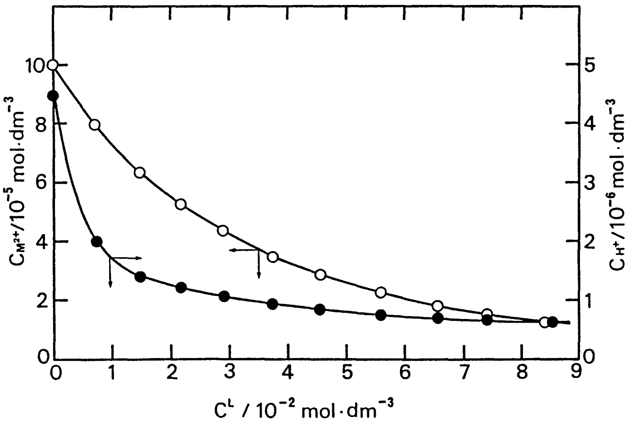

Fig. 1. Activities of copper(II) ions ($C_{M^{2+}}$) (○) or hydrogen ions (C_{H^+}) (●) vs. the concentration of NHeA (C^L).

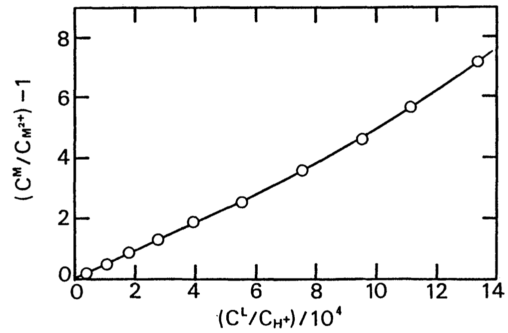

Fig. 2. $[(C^M/C_{M^{2+}})-1]$ vs. (C^L/C_{H^+}) plot according to Eq. 9.

system is indicated in Fig. 2. The value of K_1 was given from the initial slope at the origin; then, the value of K_2 was calculated from an appropriate set of data (K_1, $C_{M^{2+}}$, C^L, and C_{H^+}), where the observed activity values of copper(II) and hydrogen ions were used as the values of $C_{M^{2+}}$ and C_{H^+}, respectively. The values of K_2 for NOA, NDeA, and NDA could not be accurately determined because the solubilities of these 1 : 2-complexes in solution are very small.

The values of K_1 and K_2 for each complex are also listed in Table 1, together with the data concerning some analogous compounds.[3] These values initially decrease as the alkyl chain length increase, though the values become nearly constant for NAA with alkyl substituents longer than the butyl group, i.e., NAA is less reactive with copper(II) ions than *β*-alanine. This result can be explained by a steric hindrance effect of the alkyl substituents directly bonded to the nitrogen donor. A similar tendency has been observed for the formation of the copper(II) complexes of glycine and its *N*-alkyl-substituted derivatives,[3] as shown in Table 1. A systematic study of the steric hindrance effect of *N*-substitution has also been reported for the complex formation of ethylenediamine derivatives with copper(II) and nickel(II) ions.[5]

However, the electron-releasing effect of alkyl substituents, itself, can be considered to increase the basicity of the nitrogen donor and, as a result, to promote a favorable reaction of the ligands with copper(II) ions. In fact, the overall stability constant increases linearly with increasing pK_A as obtained, for instance, for the copper complexes of a series of phthalic acid derivatives[6] and a series of salicylic acid derivatives.[7] In these cases, however, because the substituent groups are incorporated into benzene ring, their steric hindrance effects seem not to play an important role in these coordination reactions.

As regards the second-step coordination of NBuA and NHeA, almost the same values of K_2 were obtained, as shown in Table 1. These results suggest that, when the 1 : 2-complex is formed with the 1 : 1-complex ion and a NAA molecule, the hydrophobic interaction does not occur between the alkyl chain of the 1 : 1-complex ion and that of the NAA molecule. Otherwise, we would have observed the K_2 value for NHeA larger than that for NBuA. The absence of the hydrophobic interaction mentioned above would be explained in terms of a definite directionality of coordinate bonds; i.e., the present 1 : 2-complexes have been supposed to have a planar square trans-configuration as to the four donor atoms (two nitrogen atoms and two oxygen atoms) around the copper(II) ion.[1] On account of this configuration, two alkyl chains in a 1 : 2-complex molecule would be forced to extend in the opposite directions to each other. In contrast to the complex formation, the hydrophobic interaction has been demonstrated to promote a molecular association cooperatively when an ion-pair is formed between two long alkyl chains having opposite charges, such as *N*-dodecyl-*β*-alanine ion and alkyl sulfate ion,[8] or decyltrimethylammonium ion and long-chain fatty acid ion.[9]

Solubility Product and Solubility of the 1 : 2-Complexes. The 1 : 2-complex formation equilibrium can be written from Eqs. 5 and 6 as

$$M^{2+} + 2L^{\pm} \rightleftarrows ML_2 + 2H^+, \qquad (12)$$

and from Eqs. 7 and 8, we have

$$C_{ML_2} \cdot C_{H^+}{}^2 / C_{M^{2+}} \cdot C_{L^\pm}{}^2 = K_1 \cdot K_2. \qquad (13)$$

At the precipitation equilibrium,

$$C_{ML_2} = S(\text{constant}). \qquad (14)$$

Then, from Eqs. 13 and 14, the solubility product (K_{sp}) of the 1 : 2-complex is written as

$$C_{M^{2+}} \cdot C_{L^\pm}{}^2 / C_{H^+}{}^2 = S/K_1 \cdot K_2 = K_{sp}, \qquad (15)$$

where the S value in Eq. 14 is defined as the intrinsic solubility of the 1 : 2-complex.

In order to determine the K_{sp} value, the activities of copper(II) and hydrogen ions were measured for solutions of copper dichloride with a constant concentration of 1.0×10^{-3} mol·dm^{-3} as a function of the added NAA concentration. In order to establish the precipitation equilibrium, the solutions were allowed to stand at least for 12 hours in a thermostat at 30 °C before measuring the activities. The generation of the precipitated particles of the 1 : 2-complex was confirmed by observing the scattered light of a He-Ne laser beam. The precipitation phenomena were not observed in the $CuCl_2$-NAA solutions of *β*-alanine, NEtA, and, NBuA, even when the NAA concentrations were increased up to 1.0 mol·dm^{-3}. Using the data of $C_{M^{2+}}$, C_{H^+}, and $C_{L^\pm}$, the K_{sp} values were calculated from Eq. 15. The results are listed in Table 2.

Figure 3 shows a plot of the logarithmic K_{sp} vs. the number of carbon atoms (n) in an alkyl chain of the 1 : 2-complex molecule. A linear relationship,

$$\ln K_{sp} = 32.7 - 1.50 \times 2n, \quad (n=6\text{—}12), \qquad (16)$$

was found.

Table 2. Solubility Product and Solubility of Copper-NAA Complexes at 30 °C

NAA	K_{sp}/mol · dm^{-3}	S/mol · dm^{-3}
NHeA	2.42×10^{6}	1.51×10^{-4}
NOA	6.00×10^{3}	3.74×10^{-7}
NDeA	2.22×10^{1}	1.38×10^{-9}
NDA	3.92×10^{-2}	2.54×10^{-12}

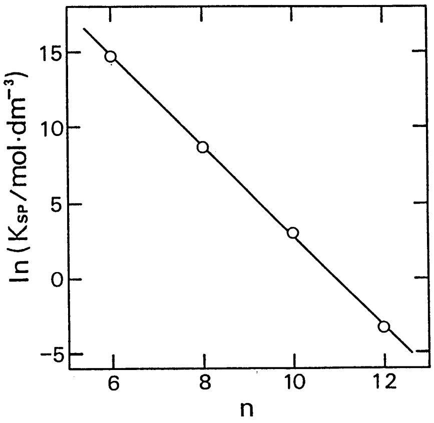

Fig. 3. Logarithmic solubility product (K_{sp}) vs. the number of carbon atoms (n) in an alkyl chain of the 1 : 2-complex.

Next, the intrinsic solubilities of the 1 : 2-complexes (n=6—12) in water were estimated from Eq. 15:

$$S=K_1\cdot K_2\cdot K_{sp}. \tag{17}$$

Here, the K_2 value of NHeA was used as that of NOA, NDeA, and NDA, assuming that the K_2 values are constant for NAA with an alkyl chain longer than the butyl group for the reason mentioned above. Thus, the calculated solubility is listed in Table 2. A linear relation between the logarithmic S and n was found to be

$$\log S=-0.65\times 2n+4.00, \quad (n=6—12). \tag{18}$$

Similar linear relations have been found for the solubilities of long-chain alcohols (n=5—8), amines (n=10—14), fatty acids (n=9—13), and sodium alkanesulfonates (n=8—18).[10)] The value of 0.65 in Eq. 18 indicates a decrease in the logarithmic solubilities per one methylene group in 1 : 2-complexes. This value is close to those of fatty acids (0.63) and amines (0.67), and larger than those of alcohols (0.58) and sodium alkanesulfonates (0.46).[10)]

Standard Free Energy of the Formation of the Crystalline 1 : 2-Complex. The standard free energy of the formation of the crystalline 1 : 2-complex (ΔG°_p/kJ · mol^{-1}) from the constituent ions can be calculated from

$$\Delta G^\circ_p=RT\ln K_{sp} \tag{19}$$

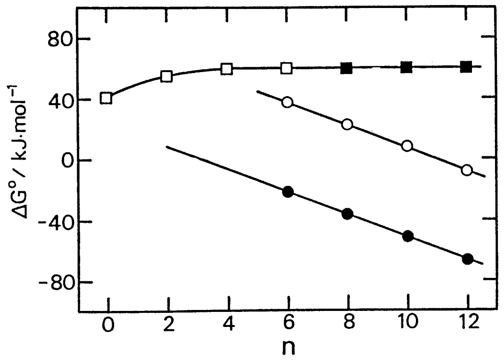

Fig. 4. The standard free energy change vs. the number of carbon atoms (n) in an alkyl chain of the 1 : 2-complex in each process: (see text) ΔG°_P; (○), ΔG°_F; (□), extrapolated values of ΔG°_F; (■), ΔG°_S; (●).

for systems of n=6—12. Figure 4 shows the ΔG°_p values as a function of n at 30 °C. The ΔG°_p values assume a linear relation with n as follows;

$$\Delta G^\circ_p=-3.77\times 2n+82.4, \quad (n=6—12). \tag{20}$$

The ΔG°_p values decrease by 3.77 kJ · mol^{-1} per one -(CH)$_2$- group in 1 : 2-complexes. This value is fairly larger than that of sodium alkanesulfonates (2.68 kJ · mol^{-1})[10)] and of calcium alkanesulfonates (3.36 kJ · mol^{-1}),[11)] and is close to that of long-chain fatty acids (3.65 kJ · mol^{-1}), and of long-chain amines (3.86 kJ · mol^{-1}). The values of the several divalent metal soaps range from 3.33 kJ · mol^{-1} for zinc soap to 3.97 kJ · mol^{-1} for manganese soap, including the value of 3.42 kJ · mol^{-1} for copper(II) soaps.[12)] Since these values primarily reflect the hydrophobic interaction between alkyl chains of adjacent molecules in the respective crystals, the alkyl chain arrangements in the copper(II)-NAA complexes seem to be packed in a manner similar to these metal soap compounds.

However, the metal soaps have been explained to generally assume a multibilayer tail-to-tail and head-to-head structure in crystals from the X-ray data of the long spacings, which are roughly twice as long as the alkyl chain length.[13)] In contrast to metal soaps, it has been supposed that the copper (II)-NAA com-

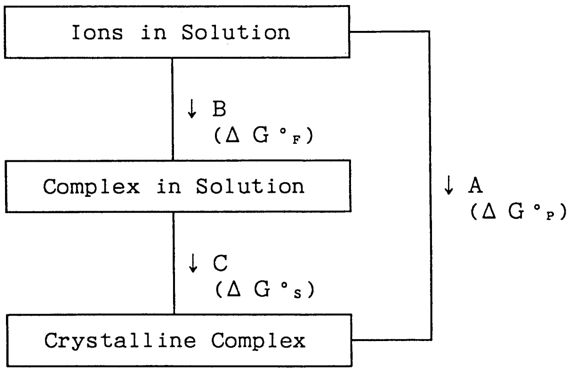

Fig. 5. A standard free energy diagram for the formation and the precipitation processes of the 1 : 2-complex.

plexes assume a multiunilayer structure in which alkyl groups interpenetrate one another by turns. This structure is supported by the observation of the definite regularity of the long spacing of these complexes, as shown by X-ray analyses for these complexes.1)

Standard Free Energy Diagram of the 1:2-Complex Formation. As shown in Fig. 5, the total process (called process A) of the formation of the crystalline 1:2-complex from the constituent ions should be divided energetically into two processes: i.e., process B regarding the formation of the 1:2-complex from constituent ions in the solution and process C regarding the precipitation of the resulting 1:2-complex from its saturated solution.

Here, the standard free energy (ΔG°_F/kJ·mol^{-1}) of process B can be calculated from Eq. 13 as

$$\Delta G^\circ_F = -RT\ln(K_1 \cdot K_2), \qquad (21)$$

for systems of n=0—6. The values for the systems of n=8—12 were also calculated, assuming that the K_2 values are invariable in systems of $n \geqq 4$, as mentioned above. The calculated values of ΔG°_F are plotted as a function of n in Fig. 4.

For process C, the standard free energy (ΔG°_S/kJ·mol^{-1}) can also be calculated from the solubility of the 1:2-complex as

$$\Delta G^\circ_S = RT\ln S, \qquad (22)$$

for systems of n=6—12. The results are shown in Fig. 4.

Therefore, the standard free energy (ΔG°_P/kJ·mol^{-1}: Eq. 19) of the total process A can be expressed as

$$\Delta G^\circ_P = \Delta G^\circ_F + \Delta G^\circ_S. \qquad (23)$$

As should be clear from Fig. 4, the ΔG°_P values decrease linearly with increasing n, and become negative when n is more than 11. This result corresponds to the experimental findings that since the complex formation equilibria are gradually shifted from the constituent ions toward the appearance of a precipitate, the amount of precipitate increases as n increases.

As regards the contribution of process B to the total process A, the ΔG°_F values are positive, regardless on n, and slightly increase with increasing n up to 4, and become close to a constant value of 59.1 kJ·mol^{-1}. Therefore, the introduction of alkyl substituents into the ligand molecules acts to shift the equilibrium in process B toward a direction rather opposite to the formation of the 1:2-complex.

On the contrary, the ΔG°_S values decrease linearly with n as

$$\Delta G^\circ_S = -3.77 \times 2n + 23.2, \quad (n=6\text{—}12), \qquad (24)$$

and are negative for n=6—12. Therefore, process C is largely shifted toward the precipitation as n increase.

These results show that the complex formation reaction of process B could not proceed appreciably without cooperative contribution of the hydrophobic interaction in precipitation process C. This is the reason why it is able to easily form 1:2-complexes having long alkyl chains (n=8—12), even in a dilute, weak acid solution.1,2)

In general, it should also be emphasized that the occurrence of a hydrophobic interaction between reactant molecules in an aqueous solution contributes not only to the hydrophobicity of the resulting products, but also to the promotion of a chemical reaction which does not proceed to any appreciable extent if the hydrophobic interaction does not occur.

References

1) A. Nakamura, M. Koshinuma, and K. Tajima, *Bull. Chem. Soc. Jpn.*, **63**, 116 (1990).

2) T. Okumura, K. Tajima, and T. Sasaki, *Bull. Chem. Soc. Jpn.*, **47**, 1067 (1974).

3) A. E. Martell and R. M. Smith, "Critical Stability Constants, Vol. 1," Plenum Press, New York (1974), p. 1, 66.

4) G. Anderegg, "Coordination Chemistry, Vol. 1," ACS Monograph Series Vol. 168, ed by M. E. Martell, Van Nostrand Reinhold, New York (1971), Chap. 8.

5) F. Basolo and R. K. Murmann, *J. Am. Chem. Soc.*, **74**, 5243 (1952); **76**, 211 (1954).

6) M. Yasuda, K. Suzuki, and K. Yamazaki, *J. Phys. Chem.*, **60**, 1649 (1956).

7) A. E. Martell and M. Calvin, "Chemistry of the Metal Chaelate Compounds," Prentice-Hall, New York (1952), p. 153.

8) A. Nakamura, *Bull. Chem. Soc. Jpn.*, **48**, 1720 (1975).

9) D. G. Oakenfull and D. E. Fenwick, *J. Phys. Chem.*, **78**, 1759 (1974).

10) I. J. Lin and P. Somasundaran, *J. Colloid Interface Sci.*, **37**, 731 (1971).

11) M. S. Celik and P. Somasundaran, *J. Colloid Interface Sci.*, **122**, 163 (1988).

12) K. A. Hunter and P. S. Liss, *J. Electroanal. Chem.*, **73**, 347 (1976).

13) P. A. Spegt and A. E. Skoulios, *Acta Crystallogr.*, **16**, 301 (1963); **17**, 198 (1964); R. Matsuura, *Nippon Kagaku Zasshi*, **86**, 560 (1965); K. Ogino and T. Saito, *Bull. Chem. Soc. Jpn.*, **50**, 1623 (1977).