January, 1973] BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 46, 187—190 (1973)

The Stability of Fused Rings in Metal Chelates. IX. Copper(II) and Nickel(II) Complexes of Schiff Bases Derived from Salicylaldehyde and Dipeptides Containing Glycine and/or β-Alanine

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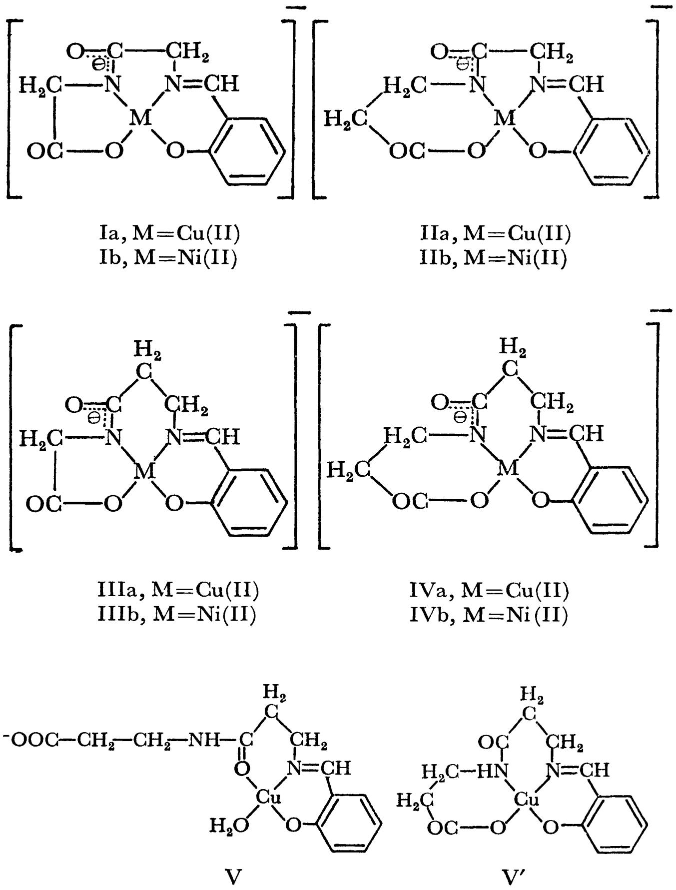
(Received April 24, 1972)

Copper(II) and nickel(II) complexes of Schiff bases derived from salicylaldehyde(Sal) and dipeptides containing glycine and/or β-alanine have been prepared. It has been found that Schiff base ligands containing glycylglycine (Gly·Gly), glycyl-β-alanine (Gly·β-Ala) or β-alanylglycine (β-Ala·Gly) as the peptide moieties give rise to square-planar, quadridentate copper(II)- and nickel(II)-chelates, while the *N*-salicylidene-β-alanyl-β-alanine (Sal=β-Ala·β-Ala) does not form the same type of copper(II)- or nickel(II)-chelate. It is concluded on the basis of spectrophotometric, polarographic and other measurements that the stability decreases in the order 6-5-5-([Cu(Sal=Gly·Gly)])$\geqq$6-5-6-([Cu(Sal=Gly·β-Ala)])$\geqq$6-6-5-([Cu(Sal=β-Ala·Gly)])$\gg$6-6-6-([Cu(Sal=β-Ala·β-Ala)])fused-ring system.

In a previous paper,[1] it was reported as the result of a comparative study on copper(II) complexes of Schiff bases derived from 2-acetylpyridine or 2-pyridinecarbaldehyde and some dipeptides that the stability of fused-ring systems in metal Schiff base chelates decreases in the order 5-5-6-$\simeq$5-6-5-$>$5-5-5-$>$5-6-6-membered ring system.[2] As an extension of our previous investigations we have studied the copper(II) and nickel(II) complexes of Schiff bases produced from salicylaldehyde and dipeptides such as glycylglycine, glycyl-β-alanine, β-alanylglycine, and β-alanyl-β-alanine. Structural formulas of these chelates are shown in Fig. 1, (Ia—V′). In this paper we describe the relationship between the structures of the chelates and their relative stabilities.

Copper(II) Complexes of the Schiff bases Derived from Salicylaldehyde and Glycylglycine, Glycyl-β-alanine, β-Alanylglycine or β-Alanyl-β-alanine (Ia—IVa). The sodium and potassium salts of *N*-salicylideneglycylglycinatocuprate(II) (Ia) were reported in detail.[3] In the present study we have newly prepared copper(II) chelates of Schiff bases obtained from salicylaldehyde and glycyl-β-alanine, β-alanylglycine, or β-alanyl-β-alanine (IIa, IIIa, and IVa, respectively). The chelates were prepared by reactions of each dipeptide with bis(salicylaldehydato)copper(II) in the pH range 9—11. Of these IIa and IIIa have been isolated as either potassium, calcium, or barium salts. The color of these salts is violet, and their IR spectra revealed that the structure of each complex is essentially the same as that in Ia regardless of the kind of cation. On the other hand, preparation of the copper(II) chelate of *N*-salicylidene-β-alanyl-β-alanine by the same method has resulted in the formation of a bright green complex. The decomposition temperature, absorption maximum for the *d-d* transition band and the half-wave potentials for the reduction of copper(II) at the dropping mercury electrode of a green complex are given in Table 1, together with those of three violet complexes, Ia—IIIa. A comparison of some properties in Table 1 shows that the structure of the green complex may differ from that of the three violet complexes which have similar properties to each other. Since



Ia, M=Cu(II)
Ib, M=Ni(II)

IIa, M=Cu(II)
IIb, M=Ni(II)

IIIa, M=Cu(II)
IIIb, M=Ni(II)

IVa, M=Cu(II)
IVb, M=Ni(II)

V

V′

Fig. 1. Structural formulae of copper(II) and nickel(II) chelates of Schiff bases derived from salicylaldehyde and dipeptides.

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[1] Y. Nakao, H. Ishibashi, and A. Nakahara, This Bulletin, **43**, 3457 (1970).

[2] The notations "5-5-6" etc. represent the skeletal structure of fused-chelate-rings in metal multidenate chelates in view of the numbers of ring members, starting from the metal chelate ring containing the carbonyl compound moiety.

[3] A. Nakahara, This Bulletin, **32**, 1195 (1959).

Table 1. Properties of copper(II) complexes Ia—IIIa, V (or V′)

	Complex	Decomp. temp.	Absorp. max. $\tilde{\nu}_{\max}$ ($\times 10^3$) cm^{-1}	Half-wave potential *vs.* SCE, 25°C
Ia	Ba/2[Cu(Sal=Gly·Gly)]·$4H_2O$	263—275°C	17.7(log ε, 2.21)	−0.61 V
IIa	Ba/2[Cu(Sal=Gly·β-Ala)]·$4.5H_2O$	265—280	17.5(log ε, 2.24)	−0.59
IIIa	Ba/2[Cu(Sal=β-Ala·Gly)]·$3.5H_2O$	290—297	17.4(log ε, 1.93)	−0.55
V (or V′)	[Cu(Sal=β-Ala·β-Ala)(OH_2)]	210—220	15.2(log ε, 1.75)[a]	b)

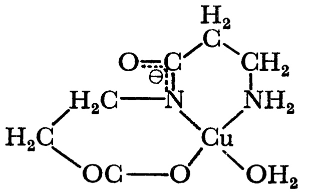
a)

pH	$\tilde{\nu}_{\max}$($\times 10^3$)cm^{-1}
6.5	15.2
8.4	16.4
10.3	16.8
11.2	16.8

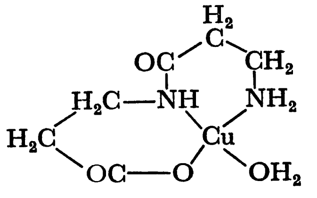
b)

pH	$E_{1/2}^{(1)}$	$E_{1/2}^{(2)}$
6.3	−0.16V	−0.42V
7.9	−0.16	−0.42
8.7	−0.18	−0.43
9.4	−0.20	−0.43
10.0	−0.21	−0.43
11.4		−0.43

such properties as the color and decomposition temperature of the crystals and the absorption maximum for the *d-d* band in the 20% dimethyl sulfoxide aqueous solution are similar to those of *N*-salicylideneaminoacidatoaquocopper(II),[4] the green complex seems to be better explained by the structure V or V′ rather than by IVa. The result of elemental analysis also supports the presumption. We have recently demonstrated from a pH-titration study that the deprotonation of amide >NH to CuL from $CuHL^+$ in the β-alanyl-β-alanine-Cu(II) chelate is more difficult than that in copper(II) chelate with glycylglycine, glycyl-β-alanine, or β-alanylglycine.[5] The difficulty in isolating copper(II) chelate of IVa-structure can be explained as due to the result described above and the increasing steric strain in 6-6-6-fused-ring system. Thus it can be concluded that the copper(II) complex IVa is less stable than complexes Ia—IIIa.



CuL



$CuHL^+$

From the decomposition temperatures, the absorption maxima of *d-d* transition bands and the polarographic half-wave potentials (nearly constant in the pH range 6—10) corresponding to the reduction of copper(II) in the chelates Ia—IIIa (Table 1), we see that the stability of the three copper(II) complexes differs only slightly. On the other hand, the polarographic behavior of the bright green complex is entirely different from that of the other violet complexes Ia—IIIa. The polarograms of the green complex corresponding to various pH values are given in Fig. 2. The reduction wave for the green complex consists of two steps, in which the ratio of the wave-height of the first and second reduction wave varies with pH values. The wave-height of the first reduction wave decreases but that of the second reduction wave increases with the rise in pH, the total wave-heights remaining unchanged. Thus, it is considered that two kinds of complexes exist in the pH range 6—11, and the ratio of their abundance changes with pH. The second wave on the polarogram can be estimated as the reduction wave due to the species IVa, as judged from the value of the half-wave potential and the increase of its wave-height with the rise in pH. On the other hand, the first wave is considered to be the reduction wave for the green complex V (or V′). The effect of pH on the *d-d* absorption band for the green complex was also examined. The results are shown in Table 1. We see that the *d-d* absorption band is hypsochromically shifted with increasing pH values. The absorption maximum at pH 6.5 is almost the same as those of *N*-salicylideneaminoacidatoaquocopper(II) complexes.[4]

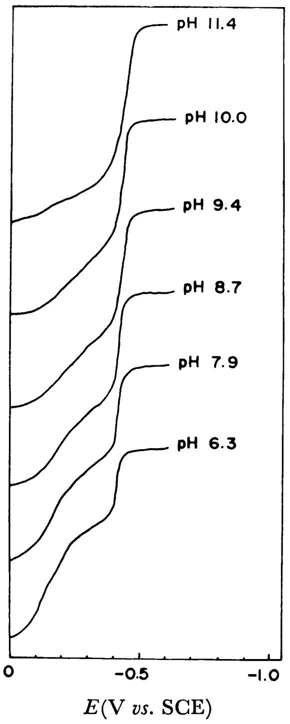


Fig. 2. Polarograms of salicylaldehyde-β-alanyl-β-alanine-copper(II) in various pH-values.

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[4] Y. Nakao, K. Sakurai, and A. Nakahara, This Bulletin, **40**, 1536 (1967).

[5] O. Yamauchi, Y. Hirano, Y. Nakao, and A. Nakahara, *Can. J. Chem.*, **47**, 3441 (1969).

In the pH region 10.3—11.2 the absorption maximum is observed at 16.8×10^3 cm^{-1}, showing the formation of a structure similar to that of copper(II) chelates Ia—IIIa. Thus, it can be considered that the most predominant structure of chelate in aqueous solution at around pH 11 should be the one represented by IVa. The reason why the species IVa cannot be isolated in the preparation of salicylaldehyde-β-alanyl-β-alanine-copper(II) chelate in aqueous solution in the pH range 9—11 was found to be as follows: V (or V′) are preferentially separated from the solution because of its comparatively poor solubility when the equilibrium V (or V′)$\leftrightarrows$IVa takes place in an alkaline solution. From a comparison of the easiness of preparation and of the numerical data in Table 1, it may be concluded that the relative stability in the copper(II) chelates Ia—IVa decreases in the order: Ia(6-5-5)$\geqq$IIa(6-5-6)$\geqq$IIIa(6-6-5)$\gg$IVa(6-6-6). It is of interest to note that the chelate produced from copper(II), β-alanyl-β-alanine and 2-pyridinecarbaldehyde or 2-acetylpyridine (instead of salicylaldehyde) can easily be isolated as stable crystals,[1] but not IVa. This contrast is understood by taking the increasing strain in the 6-6-6-fused-ring system into consideration.

Nickel(II) Complexes of the Schiff Bases Derived from Salicylaldehyde and Glycylglycine, Glycyl-β-alanine, β-Alanylglycine or β-Alanyl-β-alanine (Ib—IVb). Nickel(II) complexes of Schiff bases derived from salicylaldehyde and dipeptides (Gly·Gly, Gly·β-ala, β-Ala·Gly, and β-Ala·β-Ala) were prepared. The nickel(II) complex Ib containing glycylglycine residue was isolated as potassium, calcium or barium salts. Their IR spectra showed no essential difference and were in good agreement with those for the corresponding salts of *N*-salicylideneglycylglycinatocuprate(II). From these IR-studies and the elemental analyses, it is evident that the structure of nickel(II) complex produced from salicylaldehyde, glycylglycine, and nickel(II) is of Ib. Similar findings were confirmed also for nickel(II) complexes of *N*-salicylidene-glycyl-β-alaninate and -β-alanylglycinate. Hence, the structures of those chelates are concluded to be of IIb and IIIb, respectively. The nickel(II) complex of Schiff base derived from salicylaldehyde and β-alanyl-β-alanine could not be isolated. During the course of preparation of nickel(II) complexes Ib—IIIb the original green solution turned orange with the rise in pH, giving orange crystals. The visible and ultraviolet absorption spectra for nickel(II) chelates Ib—IIIb in dimethyl sulfoxide-water (1: 1 by volume) are shown in Fig. 3. The absorption curves resemble those observed for nickel(II) complexes which are considered to have a square-planar structure.[6] In the case of salicylaldehyde-β-alanyl-β-alanine-nickel(II) complex, the color of reaction solution does not change during the course of preparation regardless of pH (5—11). Thus, all efforts to obtain the complex in crystal were unsuccessful. However, it may be considered from the absorption spectrum of the reaction solution diluted with water that the nickel(II) complex of *N*-salicylidene-β-alanyl-β-alaninate in solution have an octahedral structure.[6] This suggests that the complex is more stabilized in high-spin form (sp^3d^2) than in square-planar form. This is because of the rather weak ligand field of *N*-salicylidene-β-alanyl-β-alaninate, which contains a considerable strain in 6-6-6-fused-ring system IVb.

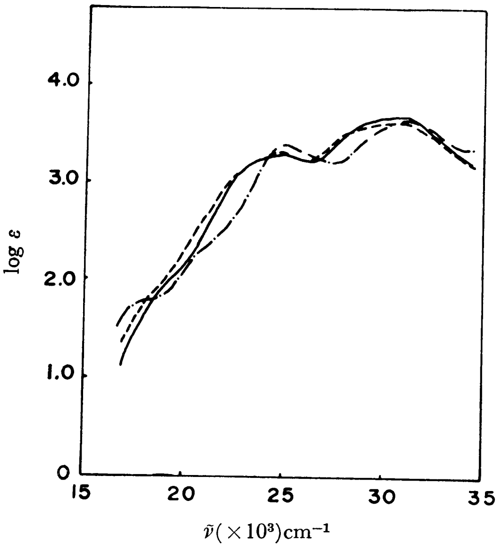

Fig. 3. VIS-UV spectra of Ba/2[Ni(Sal=Gly·Gly)]·H_2O (—), Ba/2[Ni(Sal=Gly·β-Ala)]·$3H_2O$ (---), and Ba/2[Ni(Sal=β-Ala·Gly)]·$2H_2O$ (-—-).

Experimental

Dipeptides[1] and Bis(salicylaldehydato)copper(II)[7] were prepared according to the directions described previously. *Bis(salicylaldehydato)nickel(II)* was obtained by the same method as that for the corresponding copper(II) complex, using nickel acetate instead of copper acetate. *Potassium N-salicylideneglycylglycinatocuprate(II)* was prepared by the known method.[3] *Potassium* N-*salicylideneglycylglycinatonickelate(II), Ib.* Into 15 ml of a water: ethanol mixture (2:1 by volume) were dissolved 0.34 g of glycylglycine and 0.78 g of bis(salicylaldehydato)nickel(II). The resulting mixture was adjusted to pH 9—10 by 1N-KOH solution and stirred at 25°C for an hour. The reaction product was deposited as orange powders and was recrystallized from water-ethanol. The results of elemental analyses are shown in Table 2.

Barium Salts of Copper(II) Chelates of Schiff Bases Derived from Salicylaldehyde and Dipeptides (Ia—IIIa), and Copper(II) Chelate Containing β-alanyl-β-alanine as Dipeptide Moiety (V or V′). *Method A*: To a mixture of 0.0025 mol of each dipeptide and 15 ml of water: ethanol (2: 1 by volume) was added 0.0025 mol of bis(salicylaldehydato)copper(II). The pH-values of each reaction solution were adjusted to 9—11 by using 1N-KOH solution. After it had been stirred at 25°C for an hour, the reaction mixture was filtered. The filtrate was passed through a column of the cation exchanger Amberlite IR-120B (Ba form). The column was washed with water, and the violet crystalline product adsorbed on the resin layer was extracted by hot water. The solution which had passed through the cation exchanger and the extracted aqueous solution were combined and concentrated *in vacuo* until violet crystals were considerably deposited. This was recrystallized from hot water (90°C). In the case of reaction system containing β-alanyl-β-alanine as dipeptide, the solution

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[6] S. Yamada and H. Nishikawa, This Bulletin, **36**, 755 (1963).

[7] A. Nakahara, K. Hamada, I. Miyachi, and K. Sakurai, *ibid.*, **40**, 2826 (1967).

TABLE 2. ANALYTICAL DATA FOR THE POTASSIUM AND CALCIUM SALTS OF $[M(Sal{=}dipeptide)]^-$ (M=Cu(II), Ni(II))

Complex	C, %		H, %		N, %	
	Found	Calcd	Found	Calcd	Found	Calcd
K[Ni(Sal=Gly·Gly)]·H_2O	38.03	37.85	2.54	3.18	8.27	8.03
Ca/2[Cu(Sal=Gly·Gly)]·3.5H_2O	34.86	34.78	4.07	4.25	7.53	7.38
Ca/2[Cu(Sal=Gly·β-Ala)]·4.5H_2O	35.11	34.99	4.66	4.90	6.51	6.80
Ca/2[Ni(Sal=Gly·Gly)]·2H_2O	37.99	37.96	3.72	3.77	8.26	8.05
Ca/2[Ni(Sal=Gly·β-Ala)]·2.5H_2O	39.04	38.84	4.30	4.36	7.99	7.55

TABLE 3. ANALYTICAL DATA FOR Ba/2[M(Sal=dipeptide)] (M=Cu(II), Ni(II))

Complex	Cu or Ni, %		N, %	
	Found	Calcd	Found	Calcd
Ba/2[Cu(Sal=Gly·Gly)]·4H_2O	14.34	14.53	6.26	6.40
Ba/2[Cu(Sal=Gly·β-Ala)]·4.5H_2O	13.54	13.80	6.00	6.08
Ba/2[Cu(Sal=β-Ala·Gly)]·3.5H_2O	14.23	14.36	6.11	6.33
Ba/2[Ni(Sal=Gly·Gly)]·H_2O	15.26	15.50	7.29	7.40
Ba/2[Ni(Sal=Gly·β-Ala)]·3H_2O	13.75	13.69	6.68	6.54
Ba/2[Ni(Sal=β-Ala·Gly)]·2H_2O	14.24	14.29	7.20	6.82

which had passed through a column was evaporated to dryness *in vacuo*. The green products were recrystallized from water-acetone. Its aqueous solution gave no white precipitate by the addition of dilute sulfuric acid. Analytical data of the violet complexes are given in Table 3. Analytical data of the green complex are as follows: Found: C, 45.54; H, 4.70; N, 8.19%. Calcd for $Cu(C_{13}H_{14}N_2O_4)\cdot H_2O$: C, 45.41; H, 4.70; N, 8.15%.

Method B. Almost the same procedure as that in Method A was applied. After filtration of reaction mixture, the saturated solution of barium chloride (0.63 g) was added to the filtrate. Upon cooling the solution violet crystals were deposited, which were filtrated by suction and recrystallized from hot water (90°C).

Calcium Salts of Copper(II) Chelates of Schiff Bases Derived from Salicylaldehyde and Dipeptides (glycylglycine, glycyl-β-alanine) Ia—IIa. These complexes were obtained in a similar manner to method B using calcium chloride instead of barium chloride. Recrystallization from water or water-ethanol gave violet crystals, whose analytical data are given in Table 2.

Barium Salts and Calcium Salts of Nickel(II) Chelates of Schiff Bases Derived from Salicylaldehyde and Dipeptides (glycylglycine, glycyl-β-alanine, β-alanycine) Ib—IIIb. The same method of preparation as that for copper(II) complexes was employed. The results of elemental analyses are shown in Table 2 and 3.

Measurements. The VIS-UV absorption spectra were obtained with a Shimadzu spectrophotometer QR-50 at room temperature. The solvent used was 20% or 50% dimethyl sulfoxide aqueous solution. The IR spectra were recorded with a Hitachi EPI-2 infrared spectrophotometer. The measurements were carried out at room temperature using the pressed KBr disk technique in the wave number range 700—4000 cm^{-1} with a rock-salt prism. Polarographic measurements were carried out by the same method as already described.[1] Water was used as solvent. Concentration of the copper(II) chelates used was 5×10^{-4}M. The supporting electrolyte and the maximum suppressor used were 0.1M-KNO_3 and Triton X-100 (0.0018%), respectively. The pH-value of each solution was adjusted by KOH solution.

This work was supported in part by a grant from the Ministry of Education.