BULLETIN OF THE CHEMICAL SOCIETY OF JAPAN, VOL. 52 (1), 249—250 (1979)

Synthesis and Characterization of (Salicylideneaminoalkyl)phosphonatocopper(II) and [(*N*-Salicylideneglycylamino)alkyl]phosphonatocopper(II)

Ichiro MURASE* and Arthur E. MARTELL†

Laboratory of Chemistry, College of General Education, Kyushu University, Ropponmatsu, Chuo-ku, Fukuoka 810

† *Department of Chemistry, Texas A & M University, College Station, Texas 77843, U. S. A.*

(Received August 28, 1978)

Synopsis. The titled compounds have been synthesized by a template reaction of aminoalkylphosphonic acids or glycylaminoalkylphosphonic acids and salicylaldehyde with copper(II) ion. The square-planar structures have been proposed by analogy with corresponding structures of *N*-salicyclideneglycine or *N*-salicylideneglycylglycine chelates. The deprotonated peptide nitrogen coordination was confirmed by IR-spectra for the phosphonopeptides chelates.

Since (2-aminoethyl)phosphonic acid has been discovered from some living organisms,[1–6] the aminoalkylphosphonic acids have attracted chemical and biological interest in the recent years. Several investigations have been reported for the syntheses of phosphonopeptides[7–9] and phosphonolipids[10] as well as aminoalkylphosphonic acids.[11–13]

It is well known that amino acids or peptides form Schiff bases with salicylaldehyde in the presence of a metal ion as a template and the stable copper(II) chelates have been isolated.[14] Because aminoalkylphosphonic acids and phosphonopeptides are phosphonic analogues of amino acids and peptides, similar metal chelate formation can be expected for these compounds. In the present investigation we have isolated salicylidene derivatives of (aminomethyl)phosphonic acid, (2-aminoethyl)phosphonic acid, (glycylaminomethyl)phosphonic acid, and [2-(glycylamino)-ethyl]phosphonic acid as a copper(II) chelate. This paper deals with synthesis of the copper(II) chelates and characterization of their structural similarity with those of amino acids and peptides by means of electronic and infrared spectroscopy.

Experimental

Reagents. (Aminomethyl)phosphonic acid,[12] (2-aminoethyl)phosphonic acid,[11] (glycylaminomethyl)phosphonic acid,[8] and [2-(glycylamino)ethyl]phosphonic acid[8] were prepared by slight modification of the previous reports.

Sodium [2-(N-Salicylideneamino)ethyl]phosphonatocuprate(II), Na[Cu(saepo)]. (2-Aminoethyl)phosphonic acid (0.63 g, 5 mmol) and salicylaldehyde (0.61 g, 15 mmol) were dissolved in 50 ml of 50% ethanol containing sodium hydroxide (0.6 g, 15 mmol) and powdered copper(II) acetate monohydrate (1.0 g, 5 mmol) was added. The mixture was heated on a water bath for a few minutes and bright green crystals were formed. They were recrystallized from hot water and air dried. Yield 0.4 g. Found: C, 31.45; H, 3.68; N, 4.16%. Calcd for $C_9H_{11}NO_5PCuNa\cdot H_2O$: C, 30.98; H, 3.76; N, 4.02%.

Sodium [(Salicylideneamino)methyl]phosphonatocuprate(II), Na[Cu(sampo)]. The procedure was the same as given for the preparation of Na[Cu(saepo)], using (aminomethyl)-phosphonic acid in place of (2-aminoethyl)phosphonic acid and bright green crystals were obtained in a yield of 0.5 g. Found: C, 30.12; H, 2.93; N, 4.34%. Calcd for $C_8H_7NO_4PCuNa\cdot H_2O$: C, 30.34; H, 2.87; N, 4.42%.

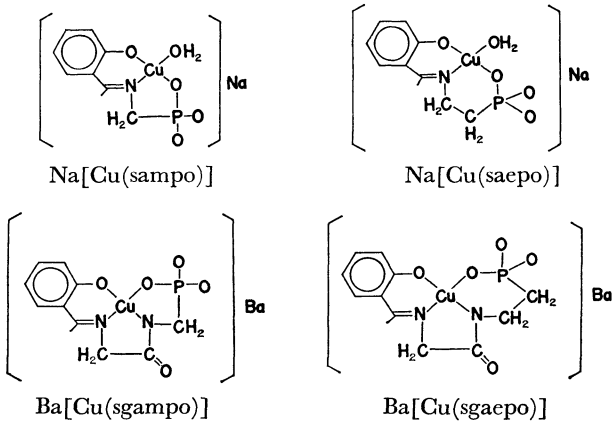
Barium [(N-Salicylideneglycylamino)ethyl]phosphonatocuprate(II), Ba[Cu(sgaepo)]. [2-(Glycylamino)ethyl]phosphonic acid (0.18 g, 1mmol) and salicylaldehyde (0.12 g, 1 mmol) were suspended in 20 ml of water and aqueous sodium hydroxide was added to give a clear solution. To this was added copper-(II) acetate monohydrate (0.2 g, 1 mmol) and the mixture was heated on a water bath, while aqueous sodium hydroxide was added to adjust a pH of 9. After ten minutes, the insoluble precipitate was filtered off and saturated barium chloride solution was added to the filtrate. The resulting blue-violet crystals were filtered and recrystallized from hot water and air dried. Yield 0.4 g. Found: C, 26.57; H, 2.67; N, 5.50%. Calcd for $C_{11}H_{11}N_2O_5PCuBa\cdot H_2O$: C, 26.36; H, 2.62; N, 5.59%.

Barium [(N-Salicylideneglycylamino)methyl] phosphonatocuprate-(II), Ba[Cu(sgampo)]. The procedure was the same as employed for the preparation of Ba[Cu(sgaepo)], but with (glycylaminomethyl)phosphonic acid in place of [2-(glycylamino)ethyl]phosphonic acid. Violet needles were obtained in a yield of 0.4 g. Found: C, 24.39; H, 2.51; N, 5.65%. Calcd for $C_{10}H_9N_2O_5PCuBa\cdot H_2O$: C, 24.66; H, 2.28; N, 5.75%.

Measurements. The infrared spectra were determined in potassium bromide disks by means of a Hitachi EPI-S2 spectrophotometer, while the electronic spectra were measured with a Hitachi EPS-3T spectrophotometer.

Results and Discussion

As described in the experimental section, copper(II) chelate formation is a typical template reaction and proceeded smoothly with equimolar aminoalkylphosphonic acid or glycylaminoalkylphosphonic acid, sali-



Na[Cu(sampo)] Na[Cu(saepo)]

Ba[Cu(sgampo)] Ba[Cu(sgaepo)]

Fig. 1. Structures of sodium [(salicylideneamino)alkyl]-phosphonatocuprate(II) and barium [(*N*-salycylidene-glycylamino)alkyl]phosphonatocuprate(II).

Table 1. Absorption spectra of the copper(II) chelates in water

Chelate	λ_{max} (nm)	log ε	Chelate	λ_{max} (nm)	log ε
Na[Cu(sampo)]	680	1.99	Ba[Cu(sgampo)]	566	2.10
Na[Cu(saepo)]	700[a]	—	Ba[Cu(sgaepo)]	596	2.08
Cu(sg)[b]	662	1.98	Na[Cu(sgg)]	575	2.20

a) Refrecting spectrum. b) Ref. 14.

Table 2. Infrared spectra of phosphonopeptides and their copper(II) chelates (cm^{-1})

Compound	Amide I	Amide II	$\left(P\langle^{O}_{O}\right)^{-}$	$\left(P\langle^{O}_{O}\right)^{2-}$
H_3(gampo)[a]	1665	1552	1116 1046	—
Ba[Cu(sgampo)]	1590	—	—	1104 1047
H_3(gaepo)[b]	1693	1584	1160 1145	—
Ba[Cu(sgaepo)]	1580	—	—	1096 1045

a) (Glycylaminomethyl)phosphonic acid. b) [2-(Glycylamino)ethyl]phosphonic acid.

cylaldehyde, and copper(II) acetate in an alkaline medium. The probable structures of these chelates are formulated in Fig. 1 by analogy with the corresponding structures of the amino acid and peptide chelates. The elemental analyses also agreed with these formulations.

The electronic spectra of the copper(II) chelates exhibit one broad band due to d-d transition in the visible region. They are shown in Table 1 and compared with those of *N*-salicylideneglycinatocopper(II), Cu(sg) and sodium *N*-salicylideneglycylglycinatocuprate(II), Na[Cu(sgg)]. The close similarity in the absorption maximum and the intensity between the phosphonatocopper and the glycinatocopper clearly indicates the same geometry around the metal ion, *i.e.* square-planar as previously discussed.[14] It is interesting to note that the ligand field strength of the amine-phosphonate coordination is nearly equal to that of amine-carboxylate coordination. In the case of the phosphonopeptide chelates, Ba[Cu(sgampo)] and Ba[Cu(sgaepo)], the amide nitrogen coordinates to the metal ion by deprotonation. This conclusion is supported by the similarity of the ligand field strength to that of Na[Cu(sgg)] in which the coordination of the deprotonated amide nitrogen has been recognized.[14]

Kim and Martell[15] have studied infrared spectra of coordinated peptide in D_2O by varying pD, and assigned the carbonyl band at different solution conditions. The peptide carbonyl band of glycylglycine which exists as a zwitter ion appears at 1665 cm^{-1} and it shifts to 1625 cm^{-1} on coordination through the carbonyl oxygen to the copper(II) ion in acidic solution. The 1625 cm^{-1} band further shifts to 1610 cm^{-1} in alkaline solution and this was interpreted as direct evidence for the ionization of the peptide NH hydrogen. Similar spectral changes were observed in the solid state for the phosphonopeptide chelates as shown in Table 2, and peptide nitrogen coordination in these complexes is indicated. The amide I band (C=O stretching vibration) in the free ligands shifts to lower wave number and the amide II band (NH deformation vibration) disappears on metal chelate formation. This indicates the deprotonation of the amide nitrogen and the resulting delocalization of charge in the $N{=}C{\swarrow}^{O}$ linkage. The P–O stretching bands of the monoanion in the free ligands also shift to lower wave number on metal chelate formation because of proton ionization to form the dianion.

It is concluded from the present investigation that aminoalkylphosphonic acids and their peptides with amino acids have properties that are similar to those of amino acids and peptides in metal chelate formation so far as copper(II) ion is concerned. Although aminophosphonate peptide derivatives have been described in this paper, there is another fundamentally different type of phosphonopeptide that may be formed; such as $H_2N(CH_2)_nP(O)(OH)NHCH_2COOH$ having a P–N linkage. Synthesis of such phosphonopeptides and investigation of their metal-chelating property are in progress at our laboratories.

References

1) M. Horiguchi and M. Kandatsu, *Nature(London)*, **184**, 901 (1959).
2) J. S. Kittredge, E. Roberts, and D. G. Simonsen, *Biochemistry*, **1**, 624 (1962).
3) L. D. Quin, *Biochemistry*, **4**, 324 (1966).
4) A. J. Koning, *Nature (London)*, **210**, 113 (1966)
5) T. Hori, O. Itasaka, H. Inoue, and K. Yamada, *J. Biochem. (Tokyo)*, **56**, 447 (1964).
6) J. A. Alhadeff and G. D. Davies, Jr., *Biochemistry*, **9**, 4866 (1970); *Biochim. Biophys. Acta*, **244**, 2111 (1971).
7) M. Hariharan, S. Chaberek, and A. E. Martell, *Synth. Commun.*, **3**, 375 (1973).
8) M. Hariharan, R. J. Motekaitis, and A. E. Martell, *J. Org. Chem.*, **40**, 470 (1975).
9) K. Yamauchi, M. Kinoshita, and H, Imoto, *Bull. Chem. Soc. Jpn.*, **45**, 2528; 2531 (1972).
10) E. Baer and N. Z. Stancev, *J. Biol. Chem.*, **239**, 3209 (1964).
11) G. M. Kosolapoff, *J. Am. Chem. Soc.*, **69**, 2112 (1947).
12) J. R. Chambers and A. F. Isbell, *J. Org. Chem.*, **29**, 832 (1964).
13) A. F. Isbell, J. P. Berry, and L. W. Tansey, *J. Org. Chem.*, **37**, 4399 (1972).
14) A. Nakahara, *Bull. Chem. Soc. Jpn.*, **32**, 1195 (1959).
15) M. K. Kim and A. E. Martell, *Biochemistry*, **3**, 1169 (1964).