COPPER(II) COMPLEXES OF N-SALICYLIDENE-α-AMINODICARBOXYLIC ACIDS; FACTORS CONTROLLING THE SYNTHESIS OF MONOMERIC SQUARE-PLANAR COMPLEXES*

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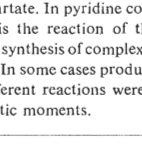
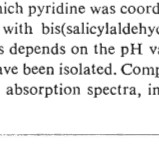
Condensation of salicylaldehyde with aspartic, glutamic, and α-aminoadipic acid gave Schiff's bases which represent tri or tetradentate ligand. Their behaviour toward Cu^{2+} ions depends on the distance of both carboxyls and in the case of aspartic acid also on whether it is optically active or racemic. In the case of (*S*)-aspartic acid hydrolysis takes place under formation of copper(II) aspartate. In pyridine complexes were obtained in which pyridine was coordinated. In contrast to this the reaction of the mentioned amino acids with bis(salicylaldehydato)copper(II) leads to the synthesis of complexes. The result of the synthesis depends on the pH value of the medium only. In some cases products of polymeric character have been isolated. Complexes prepared by two different reactions were characterised by electronic absorption spectra, infrared spectra, and magnetic moments.

The reaction of α-amino acids and their derivatives respectively with compounds containing active carbonyl in the molecule leads in the presence of metal ions to the synthesis of the complexes of Schiff's bases[1,2] which may belong to one of the following structural types:



I; R = alkyl, aryl; $R^1 = COOCH_3$
II; R = alkyl, aryl; $R^1 = CONH_2$



III; R = alkyl, aryl
X = H_2O, pyridine

Complexes of the type *I* and *II*, in which the amino acid, or its derivatives, is bound as a monodentate ligand undergo a series of reactions, both in the region

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of the carbonyl group of the amino acid[1,3–6], *i.e.* transesterification and amidation, or on the α-carbon atom of the amino acid, where racemisation takes place.

The majority of the papers published up to the present time from this field concerns complexes of the structure *I–III*, while only very little is known of the complexes of Schiff's bases derived from tridentate amino acids (type *III*, where R is $(CH_2)_n$.COOH or a carboxylic acid derivative), which can undergo the above mentioned reactions. In addition to this the presence of a polar side chain may have complications during the synthesis as a consequence, as for example polymerisation, hydrolysis *etc.* These complications are felt also in the work by Nakahara and co-workers[2] who described the synthesis of N-salicylidene((*S*)-(+)-aspartato)aquocopper(II) which we were unable to synthetise. Therefore, in the present paper we investigate more closely the question of the synthesis of complexes with ligands with varying distance of the polar side chain.

EXPERIMENTAL

Chemicals and Apparatus

The chemicals used were of Lachema make. Specific rotation of (*S*)-(+)-aspartic acid $[\alpha]_D$ +20° (in 2M-HCl), and of (*S*)-(+)-glutamic acid $[\alpha]_D$ +30° (in 5M-HCl). The IR spectra were measured in KBr on a Perkin-Elmer Model 137 apparatus, the electronic absorption spectra on an Optica-Milano spectrophotometer. The electrophoresis was carried out on paper Whatman No 4 in 0·01M-CH_3COONa at 300 V, using a Tatrachema (Kuklov, Czechoslovakia) apparatus.

Preparation of Complexes

Bis(salicylaldehydato)copper(II) was prepared in the conventional manner[7].

Direct Synthesis According to Charles[8]

N-*Salicylidene*((*S*)-(+)-*glutamato*)*aquocopper*(II). To a solution containing 3·22 g (0·02 mol) of (*S*)-(+)-glutamic acid, 2·12 ml (0·02 mol) of freshly distilled salicylaldehyde were added followed by as much methanol as necessary for a complete dissolution of the aldehyde. To the yellow solution formed 4 g (0·024 mol) of cupric acetate monohydrate were added and the green solution formed was heated at 60°C for 15 minutes. After cooling and concentration *in vacuo* methanol and ethyl acetate were added and the solution was cooled to 0°C. A green substance poorly soluble in water was separated which was filtered off, washed with water and methanol, and dried in air. For $C_{12}H_{13}NO_6Cu$ (329·8) calculated: 43·70% C, 3·94% H, 4·25% N; found: 44·00% C, 3·90% H, 4·64% N.

Potassium N-*salicylidene*((*S*)-(+)-*glutamato*)*cuprate*(II) was prepared according to the described procedure, slightly modified. Before the addition of salicylaldehyde 0·56 g of KOH (0·01 mol) were added. The green substance obtained was isolated from the aqueous solution by crystallisation without the use of methanol or ethyl acetate. For $C_{12}H_{12}NO_6CuK.2\,H_2O$ (409·9) calculated: 35·59% C, 3·98% H, 3·46% N; found: 35·96% C, 3·88% H, 3·53% N.

N-*Salicylidene* ((*S*)-(+)*glutamato*)*pyridinocopper*(II). The same procedure as before was applied, with the difference that it was carried out in 50% pyridine. A dark green water soluble

substance was obtained on crystallisation from aqueous solution. For $C_{17}H_{16}N_2O_5Cu$ (391·8) calculated: 52·10% C, 4·11% H, 7·15% N; found: 52·51% C, 4·25% H, 7·23% N.

N-*Salicylidene*((*S*)-(+)-*aspartato*)*pyridinocopper* (II). A green substance, soluble in water. It was prepared in the same manner as the preceding compounds. For $C_{16}H_{13}N_2O_5Cu$ (377·9) calculated: 51·01% C, 3·48% H, 7·44% N; found: 51·18% C, 3·58% H, 7·58% N.

N-*Salicylidene*((*RS*)-α-*aminoadipato*)*pyridinocopper*(II). By the method used for the preceding compounds a dark green, water soluble substance was obtained. For $C_{18}H_{18}N_2O_5Cu.H_2O$ (422·9) calculated: 51·12% C, 4·73% H, 6·62% N; found: 51·23% C, 4·60% H, 6·65%N.

N-*Salicylidene*((*S*)-(+)-*aspartato*)*aquocopper*(II). Using the first procedure mentioned above a water insoluble blue compound was obtained. Its elemental analysis corresponded to copper(II) aspartate. For $C_4H_5NO_4Cu.3\,H_2O$ (248·7) calculated 19·31% C, 4·46% H, 5·63% N; found: 19·06%C, 4·57% H, 5·38% N.

N-*Salicylidene*((*RS*)-*aspartato*)*aquocopper*(II). The procedure was the same as in the preceding case. A water insoluble olive-green substance was obtained. For $C_{11}H_{10}NO_6Cu.H_2O$ (333·7) calculated: 39·20% C, 3·56% H, 4·16% N; found: 39·23% C, 3·16% H, 4·29% N.

Indirect Method According to Pfeiffer[1]

N-*Salicylidene* ((*S*)-(+)-*aspartato*)*aquocopper*(II). For the preparation of this complex the method published by Nakahara[2] was used. For $C_{11}H_8NO_5Cu$ (297·7) calculated: 44·40% C, 2·69% H, 4·70% N; found: 44·52% C, 2·55% H, 4·59% N.

Potassium N-*salicylidene*((*S*)-(+)-*aspartato*)*aquocuprate*(II). To a solution containing 1·33 g (0·01 mol) of (*S*)-(+)-aspartic acid in 50 ml of water 0·56 g (0·01 mol) of KOH was added followed by 3·05 g (0·01 mol) of bis(salicyladehydato)copper(II) and the reaction mixture was heated at 50°C for 30 minutes. The reaction mixture was cooled, filtered and evaporated *in vacuo* to a small volume. After addition of methanol and standing overnight a dark green crystalline substance separated which was filtered off, washed with ethanol, and dried in air. For $C_{11}H_{10}NO_6CuK.2\,H_2O$ (390·9): calculated 33·77% C, 3·58% H, 3·58% N; found: 33·97% C, 3·65% H, 3·60% N.

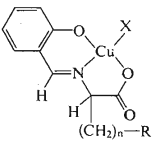
Potassium N-*salicylidene*((*RS*)-α-*aminoadipato*)*aquocuprate*(II). For the preparation of this complex the same procedure was used as in the preceding section. A green, water soluble substance was obtained. For $C_{13}H_{14}NO_6CuK.H_2O$ (400·9) calculated: 38·94% H, 4·02% H, 3·49% N; found: 39·10% C, 3·97% H, 3·4%N.

RESULTS AND DISCUSSION

Stereochemistry of the Complexes

The monomeric copper(II) complexes of N-salicylidene-α-aminodicarboxylic acids can assume some of the below given structures. From the known examples it follows that the stereochemistry of the complexes of Schiff's bases depends predominantly on two factors. First on the steric volume of the substituent on the nitrogen atom of the C=N group, and second, on the number of carbon atoms forming the bridge[9,10]. While the first case leads to deviations from the usual sterochemistry of the metal, the rigidity of the bridge affects the steric requirements of the ligands. From the X-ray study of N-salicylideneglycinatoaquocopper(II) (ref.[11]) it follows that the

chelate has a planar structure. The five-membered ring formed on coordination of the amino acid, which forms the non-rigid bridge, does not exclude a possible coordination of the ω-carbonyl protruding from the α-carbon atom of the aminodicarboxylic acid. In spite of this the coordination of this carboxyl in water solution is not very probable in view of the position of the carboxyl in the spectrochemical series[12]. From the rate with which the dehydrated complexes bind one molecule of water only the conclusion can be made that the ω-carboxyl is not coordinated in the solid phase either. For these reasons the structure of the complexes prepared corresponds to *IV* or *V*, depending on which medium the complexes were isolated from. We came to these conclusions, regarding the stereochemistry of the isolated complexes, on the basis of the results of elemental analysis and physico-chemical measurements.



IV; R = $COO^{(-)}$, X = H_2O
V; R = COOH, X = pyridine

The electronic absorption spectra (region of *d–d* transitions) of the prepared complexes are mutually identical and display a broad absorption band at $\lambda_{max} = 660$ nm. The absorption maxima of pyridine complexes show maxima at 650 nm. This shift of the maximum is caused by the change of the chromophore from $CuNO_3$ to CuN_2O_2 which is connected with the increase of the strength of the ligand field, which takes place when O is substituted by N. The comparison of the absorption spectra of complexes with coordinated water with the spectrum of N-salicylideneglycinatoaquocopper(II) confirms the arrangement of the $CuNO_3$ chromophore. The identical position of the maxima confirms that the complexes of the structure *IV* are aquo complexes (as is N-salicylideneglycinatoaquocopper(II) (ref.[13]). The values of magnetic moments which vary in the interval from 1·71 to 1·82 B.M. show that the complexes are monomeric (Table I).

The IR spectra of complexes are very complex and therefore we give here only the vibrations of such groups as are decisive for coordination. As it follows from Table I all complexes may be characterised by absorption bands in the 1600 cm^{-1} region, which correspond both to the antisymmetric valence vibration of the carboxyl and to the vibration of the C=N group[14–16] as well. The width of these bands demonstrates the presence of water, as do the maxima in the 3000 cm^{-1} region. The vibration of the C—H group of amino acids, if it was not superimposed by the band of the

adsorbed water, appears at about 2950 cm^{-1} (see[14]). In the case of pyridine complexes the IR spectra show an additional maximum at 1760 cm^{-1} which corresponds to the values for undissociated carboxyl. The bands corresponding to coordinated pyridine are mostly superimposed. Our proof of the coordination of pyridine is based on the results of elemental analysis and the comparison of infrared spectra of aquo and pyridino complexes. The position of absorption maxima assigned to pyridine agrees with the values from the literature[17].

Factors Affecting the Synthesis of the Complexes

For the preparation of the complexes of Schiff's bases two methods are used. The first (Charles' method[8]) consists in the addition of metal ions into the solution of the preformed Schiff's base, while in the second case (Pfeiffer's method[1]) the corresponding complex of the carbonyl compound reacts with the amino acid. While in the case of salicylaldehyde and α-monoaminomonocarboxylic acids both methods give products of the same composition, the amino acids which represent a polydentate ligand do not react in this way.

From the unsuccessful synthesis (see Experimental) of N-salicylidene((*S*)-(+)-aspartato)aquocopper(II) it follows that the behaviour of N-salicylidenedicarboxylic acids toward Cu^{2+} ions depends on the distance of both carboxyls, on whether the aspartic acid used is optically active or racemic, and on the polarity of the medium as well as on pH. In the case of (*S*)-(+)-aspartic acid ($n = 1$) we were unable to prepare from an aqueous solution complex *IV* in solid phase although the experimental

TABLE I
Magnetic Moments and Some Characteristic Vibrations of the Complexes

Substance	μ_{eff} B.M.	$\nu_{as}(COO^-)$	$\nu_s(COO^-)$, cm^{-1}	ν(COOH)	ν(C=N)
[Cusal((*S*)-Glu))H_2O][a,b]	1·26	—	—	—	—
K[Cusal((*S*)-Glu)H_2O]	1·72	1 580 s[c]	1 410 m[d]	—	1 635 s
[Cusal((*S*)-Glu)Pyr][e]	1·80	1 570 s	1 390 m	1 735 s	1 635 s
[Cusal((*S*)-Asp)Pyr][f]	1·79	1 590 s	1 440 m	1 730 s	1 630 s
Cusal(*RS*-Aad)Pyr][g]	1·81	1 590 s	1 405 m	1 710 s	1 610 s
[Cusal(*RS*-Asp)H_2O]	1·30	—	—	—	—
[Cusal((*S*)-Asp)]	1·74	1 600 s	1 360 m	—	1 640 s
K[Cusal((*S*)-Asp)H_2O]	1·76	1 595 s	1 445 m	—	1 635 s
K[Cusal(*RS*-Aad)H_2O]	1·76	1 590 s	1 402 m	—	1 610 s

[a] sal means salicylaldehyde anion. [b] Glu is glutamic acid. [c] s means strong. [d] m means medium. [e] Pyr is pyridine. [f] Asp is aspartic acid. [g] Aad is α-aminoadipic acid.

conditions, as for example pH or concentration, were varied. In all instances we isolated from the dark green solution copper(II) aspartate. The reason of this decomposition consists in the dissociation of Schiff's bases in aqueous solution which causes the nature of the products after the addition of metal ions to be dependent on the relative thermodynamic stabilities of complexes of all ligands, including intermediates. In agreement with the mechanism of formation of Schiff bases complexes[18] the role of metal ions consists in the shift of the equilibrium to the side of thermodynamically more stable products (the so-called equilibrium displacement[19]). In the considered system aspartic acid itself acts as a tridentate ligand even in a ternary complex which is the intermediary product of the reaction between Cu^{2+} ions and the mentioned ligands[18]. As this ternary complex is in principle a complex with mixed ligands, in which both ligands are bound to Cu(II) independently, its future fate is determined by factors affecting the stability of the complexes with mixed ligands. In this sense the coordination of the β-carboxyl of aspartic acid will destabilise the intermediate formed, thus causing its hydrolysis before the interligand condensation in the inner coordination sphere of Cu(II) (which is the rate determining process[20]) can take place. Copper(II) aspartate formed in the reaction displays a Cotton effect (region of *d–d* transitions) which confirms that during hydrolysis no racemisation of the optically active Schiff's base[21] has taken place. As was already mentioned the result of the synthesis also depends on the optical activity of aspartic acid. In the case of (*S*)-(+)-acid hydrolysis took place under formation of copper(II) aspartate, while in the case of (*RS*)-aspartic acid we isolated from the aqueous solution a complex in solid phase the magnetic moment of which demonstrates that the substance is of polymeric character. The different behaviour of both ligands may be explained by the stereospecific coordination of the (*S*)-amino acid. The results from the literature[22] show that there is no difference in thermodynamical stabilities between the copper(II) complexes of optically active and racemic monoaminomonocarboxylic acids. However, in the case of tridentate amino acids the stereospecific coordination may be expected. This will be evident by the increase of the thermodynamic stability of complexes of optically active ligands. For example, copper(II) (*S*)-asparaginate is much more stable than the asparaginate formed with a racemic ligand[23].

The above mentioned considerations may be supported first by the fact that (*S*)-(+)-glutamic acid, with the carboxyl group in the γ-position (its participation in the coordination is improbable), gave from an aqueous solution (pH 10) a complex of monomeric nature *IV*, and further by the fact, that when the reaction is carried out in pyridine which coordinates more easily than the β-carboxyl, a pyridine complex (*V*) may be isolated from aqueous solution. Eventually, if the synthesis is carried out in non-aqueous alkaline medium in which the dissociation of Schiff's bases is suppressed, a monomeric complex may be isolated even in the case of (*S*)-(+)-aspartic acid. In other cases, *i.e.* in the case of (*S*)-(+)-glutamic and (*RS*)-α-aminoadipic acid, complexes of a polymeric nature can be isolated from aqueous medium without

the adjustment of pH, having subnormal magnetic moment (Table I) and totally insoluble in water and other solvents of a non-donor character.

In contrast to this the reaction of bis(salicylaldehydato) copper(II) with amino acids (the so-called kinetic template reaction[19]) leads to successful synthesis of complexes *IV* and *V* even in the case of (*S*)-(+)-aspartic acid. The nature of the products, as well as the rate of their formation is dependent on pH. In acid medium (without the adjustment of pH) the isolated complex of (*RS*)-aspartic acid shows in its IR spectrum in the region of the carboxyl group absorption maxima at 1630, 1610, and 1360 cm^{-1}, corresponding to the absorption of the azomethine group C=N and also to the antisymmetrical and the symmetrical stretching vibration of the carboxyl[14-16]. In addition to this in the region of 2000–4000 cm^{-1} no absorption corresponding to the vibration of the OH group of water was found, which, together with the small width of the absorption band, about 1600 cm^{-1} indicates that the substance does not contain water. The absence of the absorption band at 1700 cm^{-1} which would indicate the undissociated carboxyl leads to the conclusion that in the anhydrous complex the fourth coordination site of copper is occupied by the oxygen atom of the β-carboxyl. In spite of the fact that the isolated complex has a normal value of the magnetic moment, corresponding to one unpaired electron of the copper atom (Table I), it is probably of polymeric character. The coordination of the β-carboxyl may then lead to a structure with a sufficient distance of copper atoms, which manifests itself in an independent orientation of each spin in an external magnetic field[24]. The low solubility of the complex in water and other solvents, with the exception of pyridine, excludes the possibility of the molecular weight determination. In no case does the elemental analysis of the complex correspond to the complex the structure of which is given by Nakahara and coworkers[2].

If the pH value is 10–12 during the reaction, it is possible to isolate from the aqueous solution both the complex of (*S*)- and the (*RS*)-aspartic acid, but also the complexes of other aminodicarboxylic acids which are soluble in water and methanol and which display a magnetic moment corresponding to one unpaired electron of copper atom. In these complexes the fourth coordination site of copper is occupied by a molecule of water (*IV*), while from a pyridine containing medium the corresponding pyridino-derivative (*V*) may be isolated without the adjustment of pH.

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