Palladium(II) Complexes of *N*-Sulfonylamino Acids. Part 3.[1] Ternary Adducts with 2,2'-Bipyridine

Gianantonio Battistuzzi,[a] Eleonora Gozzoli,[a] Marco Borsari,[a] Ledi Menabue,*[,a] Monica Saladini[a] and Marco Sola[b]

[a] *Department of Chemistry, University of Modena, via Campi 183, 41100 Modena, Italy*

[b] *Department of Chemistry, University of Basilicata, via N. Sauro 85, 85100 Potenza, Italy*

The equilibria involved in the formation of ternary adducts of Pd^{2+} with *N*-sulfonylamino acids (H_2L) and 2,2'-bipyridine were investigated through d.c. polarography, ^1H NMR and electronic spectroscopy in aqueous solution starting from strongly acidic conditions. The formation of the ternary species appears to proceed through the initial binding of the heteroaromatic base to Pd^{2+} followed, at higher pH values, by ligation of one amino acid dianion. The pK_{NH} value of the latter, ranging from 3.2 to 4.7 for the different amino acids, is unchanged or slightly higher compared to that observed in the formation of the $[PdL_2]^{2-}$ species from the precursor [PdL] in the binary Pd^{2+}–L^{2-} systems. A comparison is made with the corresponding ternary complexes of Cu^{2+}, Cd^{2+} and Zn^{2+}.

Metal substitution for the sulfonamide nitrogen-bound hydrogen in amino acids N-protected by a sulfonic group, occurring at acidic or slightly alkaline pH values, has been extensively characterized for metals such as Cu^{2+}, Cd^{2+} and Pd^{2+}.[2] In the ternary systems with Cu^{2+} and Cd^{2+} containing 2,2'-bipyridine (bipy) the additional heteroaromatic ligand is found to promote the above substitution, leading to pK_{NH} values for the amino acid ligand 0.4–3 units lower than those detected in the corresponding binary systems.[2,3] This effect, paralleled by positive $\Delta \log K$ values ($\Delta \log K = \log \beta^{[Pd(bipy)]}_{[Pd(bipy)(LNO)]} - \log \beta^{Pd}_{[Pd(LNO)]}$),[2] is thought to be related to a preferential binding of the carboxylate group, acting as primary ligating group, to the $[M(bipy)]^{2+}$ species as compared to the solvated metal ion, and to a metal-mediated π–π conjugation between the aromatic moieties of the amino acid ligand and of the heteroaromatic base.[3] The Pd^{2+} ion possesses an outstanding effectiveness as a promoter of amide-nitrogen deprotonation in this class of *N*-substituted amino acids,[4] leading to apparent pK_{NH} values as low as 1 (see Part 2[1]). This makes the role of the carboxylate group as primary ligating group seriously questionable. Hence it is of interest to determine whether the effect of the heteroaromatic base on the nitrogen-deprotonation equilibrium is maintained also in this case which differs from those previously characterized.

Experimental

Materials.—The amino acids used were as described in Part 2.[1]

Polarographic Analysis.—The ternary systems Pd^{2+}–bipy–H_2L (H_2L = *N*-protected amino acid) were investigated as aqueous solutions with 1×10^{-4} mol dm^{-3} metal ion and Pd:bipy:H_2L molar ratios from 1:1:2 to 1:1:20. The pH of the solutions were adjusted by adding small amounts of concentrated aqueous $HClO_4$ or NaOH. Sodium perchlorate was used as base electrolyte, and the ionic strength was kept constant (I = 0.1 mol dm^{-3}). Polarographic measurements were carried out with an Amel 472 Multipolarograph at 25 ± 0.1 °C. A saturated calomel electrode (SCE) was used as the reference and a platinum sheet as the counter electrode. All the $E_{\frac{1}{2}}$ values are referred to the SCE. An Ingold HA 405-60-K1 pH combination electrode was used for pH measurements. The electron-transfer processes were analysed as in Part 2.[1] The reversibility of the processes was determined by semilogarithmic analysis of the polarographic waves. Quasi-reversible reduction processes were invariably observed. The reversible $E_{\frac{1}{2}}$ values were determined according to Matsuda and Ayabe.[5]

Spectroscopy.—Proton NMR and UV/VIS measurements were carried out as described in Part 2.[1]

Results

Polarography.—All the Pd^{2+}–bipy–H_2L systems show the same polarographic behaviour. Two reduction waves are observed: one (wave I), with $E_{\frac{1}{2}}$ values from −0.3 to −0.4 V, is quasi-reversible and diffusion controlled, while the second (wave II), at more negative $E_{\frac{1}{2}}$ values (lower than −0.62 V), is adsorption controlled. Waves I and II do not show any pH dependence in the range 3.5–11.5. Wave I shifts toward more negative values with increasing amino acid concentration, while II does not show any such dependence. The former wave can be attributed to the reduction of the ternary complex,[3] where the ligands act as bidentate nitrogen-deprotonated dianions (see below), while the latter, being due to the absorption of the complex on the electrode surface, and hence unrelated to the complex stability, was not considered further. Below pH 3.5 a new wave (wave 0) appears, which increases to the detriment of wave I upon decreasing the pH from 3.5 to 1.5. The sum of the currents of waves I and 0 remains nearly constant (the irreversible redox reaction between the Hg of the electrode and Pd^{2+} below pH 3.5 prevented quantitative analysis of these polarographic waves[2]). In parallel, the current of wave II remains unchanged up to pH about 2.4, then undergoes a steep decrease and completely disappears at pH about 2. The stability constants reported in Table 1 were determined using the DeFord–Hume method[6] on wave I, and are referred to the species $[Pd(bipy)]^{2+}$, for which a literature log K value of 19.8 was used.[7] Lingane plots[8] (Fig. 1) at different pH values invariably indicate the presence of a species with a Pd:bipy:L ratio of 1:1:1.

Amino acids N-protected by an RCO group, like acetyl-, benzoyl- and benzyloxycarbonyl-glycine, show a polarographic behaviour closely similar to that described above for the RSO_2 N-protected amino acids. This finding is significant because it is indicative of the occurrence of metal-promoted deprotonation

Table 1 Values of log β[a] for ternary complexes [Pd(bipy)(LNO)] in aqueous solution, I = 0.1 mol dm^{-3}, 25 °C; the estimated error in log β is ±0.1

Ligand L[b]	log β	log X[c]
tsgly	30.3	8.5
bsgly	30.7	8.3
dnsgly	29.3	8.1
ts-α-ala	30.8	9.6
bs-α-ala	31.1	10.5
ts-β-ala	24.9	0.6
bs-β-ala	25.2	0.9
acgly	22.7	—
PhCO-gly	23.2	—
$PhCH_2OCO$-gly	23.1	—

[a] β is the overall stability constant. [b] dnsgly = (*N*-5-Dimethylamino-naphthylsulfonyl)glycinate; acgly = *N*-acetylglycinate. [c] See text.

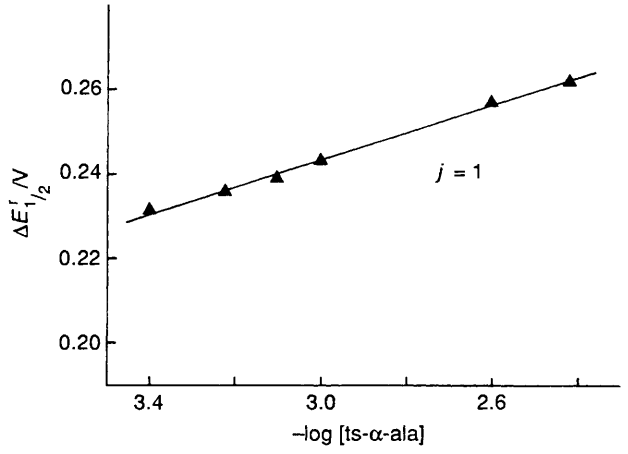

Fig. 1 Plot of $\Delta E_{\frac{1}{2}}{}^r$ *vs.* −log [ts-α-ala] (where $\Delta E_{\frac{1}{2}}{}^r = E_{\frac{1}{2}}{}^{[Pd(bipy)]} - E_{\frac{1}{2}}{}^{[Pd(bipy)(LNO)]}$) for the ternary system Pd^{2+}–bipy–ts-α-ala at pH 7.2. A similar qualitative trend was observed for the other ligands; j = maximum ligand co-ordination number

of the peptide nitrogen, never observed before for these ligands interacting with other metals either in binary or in ternary systems with heteroaromatic bases.

NMR Spectra.—The pH dependence of the ^{1}H NMR spectral features of the ternary bipy complexes was studied in the range pH 1–7. In all cases the resonances of the amino acid ligands remains unchanged from pH of about 1 up to 3–3.5. At higher pH the singlet corresponding to the CH_2 group of *N*-tosyl- (tsgly) and *N*-benzoyl-glycinate (PhCO-gly) and the two triplets of the two CH_2 groups of *N*-phenylsulfonyl-β-alaninate (bs-β-ala) show a titration pattern indicative of an equilibrium most probably involving the free amino acid and the nitrogen-deprotonated metal complex [Pd(bipy)(LNO)] in rapid exchange on the NMR time-scale (Fig. 2). These patterns were fitted by a single acid–base equilibrium and apparent pK_a values of 3.7 ± 0.1, 3.6 ± 0.1 and 4.7 ± 0.1 were obtained for tsgly, PhCO-gly and bs-β-ala, respectively. For the bs-α-ala system only the resonances corresponding to the $CHCH_3$ moiety of the free amino acid are observed from pH 1 to 2.8. At higher pH these resonances decrease in intensity, while another set of $CHCH_3$ peaks in slow exchange on the NMR time-scale appears. These new resonances are independent of pH and coincide with those observed for the crystalline complexes dissolved in D_2O. Hence they can be safely assigned to the [Pd(bipy)(LNO)] species. A plot of the peak area *vs.* pH yields an apparent pK_a value of 3.2 ± 0.1.

Electronic Spectra.—Aqueous solutions obtained by dissolving the crystalline ternary complexes invariably show the same pH-dependent spectral features. In particular, the broad shoulder at about 360 nm present in the spectra at around neutrality decreases in intensity with decreasing pH following a titration pattern with an apparent pK_a value of about 2.

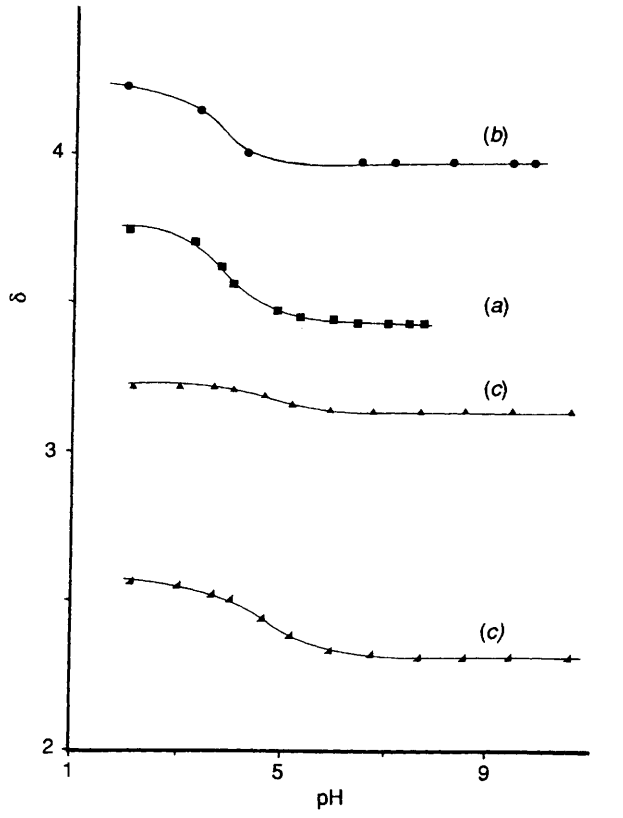

Fig. 2 The pH dependence of the ^{1}H NMR resonances of the amino acid moiety in the 400 MHz ^{1}H NMR spectra of the ternary complexes formed by tsgly, PhCO-gly and bs-β-ala in D_2O: (*a*) methylene singlet of tsgly; (*b*) methylene singlet of PhCO-gly; (*c*) central peak of the two methylene triplets of bs-β-ala

Discussion

In the range pH 3.5–11 all the amino acids yield only one ternary adduct containing the metal and the amino acid in a 1:1 molar ratio, as indicated by the Lingane plot in Fig. 1. X-Ray crystallography of the complexes separated in the solid state in this pH range identify this ternary complex as [Pd(bipy)(LNO)] (see Part 1[9]).

The binding of amino acids N-protected by an RCO group (acetyl-, benzoyl- or benzyloxycarbonyl-glycine) to Pd^{2+} as nitrogen-deprotonated dianions is worthy of note. Metal-promoted amide-nitrogen deprotonation in this class of ligands, which contain a peptide group, was previously observed only in a ternary NH_3 complex of acetylglycine with Pt^{2+}.[10] Since these amino acids were found not to bind to Pd^{2+} in the binary systems (Part 2[1]), it appears that bipy favours substitution of Pd^{2+} for the amide nitrogen-bound hydrogen, as previously observed for RSO_2 N-protected amino acids interacting with Zn^{2+},[2] Co^{2+} and Ni^{2+}.[11] This is possibly due to metal ligation of bipy at low pH which successfully competes with metal hydroxide precipitation and allows attainment of pH values in which the above substitution can occur.

The apparent pK_a values determined from the pH dependence of the ^{1}H NMR resonances of the RSO_2 N-substituted glycines and β-alanines can reasonably be assigned to the two-proton equilibrium from the neutral to the metal-bound dianionic form of the acid. The slow exchange on the NMR time-scale between the [Pd(bipy)(LNO)] species and the free amino acid for the substituted α-alanines is probably a

consequence of the higher stability of these ternary complexes as compared to those of the above glycines and β-alanines (see Table 1). No evidence for the formation of additional species was obtained. This most probably applies also to the above systems in rapid exchange. As a consequence, metal complexation of these amino acids appears to take place through concomitant deprotonation of the carboxylic and amide groups, without the apparent formation of stable carboxylate complexes, unlike that previously observed for the same ligands interacting with Cu^{2+} and Cd^{2+}. The NMR data unequivocally indicate that the equilibrium with a pK_a of about 2 invariably detected in the electronic spectra of all the ternary systems does not involve the amino acid ligand. As a consequence, the electronic spectra monitor the formation of the $[Pd(bipy)]^{2+}$ complex. The subsequent formation of the ternary species, leading to a PdN_3O chromophore, appears not to induce major spectral changes. Also the polarographic wave 0 is most probably due to bipy ligation to the Pd^{2+} ion.

The overall stability constants for these ternary complexes are much higher than those for the homologous species formed with Cu^{2+}, Zn^{2+} and Cd^{2+}. The order of stability $Pd^{2+} > Cu^{2+} > Cd^{2+}$ parallels that observed for the binary systems.[2] Inspection of Table 1 reveals that the stability constants of the ternary complexes formed by the *N*-substituted β-alanines are much lower than those for the corresponding α-alanines. In particular, step constants K and $\log X$ values[12] $\{\log X = 2 \log \beta^{Pd}_{[Pd(LNO)(bipy)]} - \log \beta^{Pd}_{[Pd(LNO)_2]^{2-}} + \log \beta^{Pd}_{[Pd(bipy)_2]^{2+}}\}$ lower by six and 10 orders of magnitudes, respectively, are observed. This effect can be attributed to two concomitant factors: the intrinsic higher stability of the five-membered chelate ring formed by the nitrogen-deprotonated dianions of the α-amino acids as compared to the six-membered one of the β derivatives, and the planarity of the five-membered chelate ring which allows π conjugation of the aromatic system of bipy, the chelate ring of the amino acid ligand and the π system of the N-protecting group. Conjugation is transmitted to the aromatic moiety of the N-protecting group by the SO_2 group.[13] The difference between step constants in binary and ternary bipy systems is not so dramatic for other metals like Cu^{2+} and Cd^{2+}.[2] This is probably related to the fact that, at least for Cu^{2+}, the metal is removed from the co-ordination plane, being inserted in a square-pyramidal geometry, hence π conjugation should play a minor role. The step constants for binding of the second nitrogen-deprotonated molecule to Pd^{2+} in the binary systems are only one order of magnitude greater for *N*-substituted α-alanines as compared to β-alanines (see Part 2[1]). This can be explained by the lack of the second factor described above, related to π conjugation involving the bipy molecule.

The pK_a values for the Pd^{2+}-promoted amide-nitrogen deprotonation in binary and ternary systems deserves some comment. It is apparent that, unlike what was previously observed for Cu^{2+} and Cd^{2+},[2] the apparent pK_{NH} values of the ternary bipy complexes are comparable or higher than those determined for the binary systems. This behaviour parallels that observed for binary and ternary bipy complexes of small peptides with all the above metals.

Although the step constant for the equilibrium (1) is

$$[M(bipy)]^{2+} + L^{2-} \rightleftharpoons [M(bipy)(LNO)] \quad (1)$$

remarkably higher than that corresponding to the binary system (2) as previously observed also for Cu^{2+} and Cd^{2+}, the

$$[M(LNO)] + L^{2-} \rightleftharpoons [M(LNO)_2]^{2-} \quad (2)$$

deprotonation of the sulfonamide nitrogen appears not to be favoured by the presence of bipy, while for Cu^{2+} and Cd^{2+} we observed a lowering of the pK_{NH} value as compared to the binary systems. With the last two metal ions this effect was attributed to preferential binding of the carboxylate group, acting as a primary ligating group, to the $[M(bipy)]^{2+}$ species as compared to the free metal ion, and possibly to a favourable effect of π conjugation between the aromatic system of bipy and that of the aromatic moiety of the N-protecting group of the amino acid ligand. The reverse effect observed for Pd^{2+} cannot be unambiguously explained. It may be of some relevance in this respect that the mechanism of amide-nitrogen deprotonation appears to be different from that observed for Cu^{2+} and Cd^{2+} since the involvement of carboxylate complexes as stable intermediates appears unlikely.[1] Moreover, the involvement of elusive hydroxide complexes at low pH values in the mechanism of Pd^{2+}-promoted amide deprotonation, with their unpredictable effect on the observed pK_{NH} value, cannot be excluded. Finally, the 'softer' acid nature of the Pd^{2+} ion,[14] as compared to Cu^{2+} and, to a lesser extent, to Cd^{2+}, may play a role in differentiating the behaviour of Pd^{2+} toward substitution of the NH proton in these systems.

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