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Palladium(II) complexes containing dipicolinic acid (DPA), iminodiacetic acid (IDA), and various biologically important ligands

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ABSTRACT

Ternary 1:1:1 complexes of Pd(II) with dipicolinic acid (DPA) or iminodiacetic acid (IDA) as a primary ligands and some selected mono- and dicarboxylic amino acids (glycine, α-alanine, leucine, valine, phenylalanine, tryptophan, methionine, histadiene aspartic acid, and glutamic acid), aromatic carboxylic acids (salicylic and phathalic), and aliphatic carboxylic acids (succinic, oxalic, malic, maleic, malonic, and tartaric) as a secondary ligands by potentiometric technique at T = 30 ºC and I = 0.1 mol·dm^{-3} $NaNO_3$. The ternary complexes are formed in a stepwise mechanism. Confirmation of the ternary complexes in solution has been carried out using conductometric measurements.

KEYWORDS

Stability constants;
Pd(II) complexes;
Dipicolinic acid;
Iminodiacetic acid;
Amino acids;
Carboxylic acids.

INTRODUCTION

Interest in the study of reaction of the Pd(II) ions with various donor atom ligands of biological importance began with the discovery of Rosenberg et al. that certain platinum complexes exhibit carcinostatic activity.[1] Among the first to be used for clinical trials against tumors, were the analogues to cisplatin, complexes of Pd(II), *cis*-Pd(en)Cl_2 and *cis*-Pd(DACH)$_2Cl_2$ because Pd (II) has a very similar chemistry to Pt(II) forming square planar complexes.[2] Both Pd(II) and Pt(II) are soft lewis acids and form stronger bonds with nitrogen or sulfur donors (soft bases) than oxygen donors (hard base). The difficulty in studying the platinium complexes directly is their kinetic inertness and due to the similarities in the general chemistry of Pt(II) and Pd(II), as well as the increased rates of reaction of Pd(II) ions (on average approximately 10^3 times faster than platinum), palladium analogues are studied instead of, or as well as, the platinum compounds. It was also suggest that the faster aquation of palladium (II) than of platinum (II) in *vitro*, makes the former a better model for studies of the reactions of the latter in *vivo*[3,4] with biological molecules, since these reactions always start with the aquation of the platinum (II) complexes. The Pd(II) ions are capable of interactioning with DNA.[5-7] Das and Livingstone[8] had suggest that S, N- chelate complexes of Pd(II) were expected to exhibit anti-tumor and anti-microbial activities, despite the non-activity and high toxicity of its complexs with mono-dentate ligands.

Dipicolinic acid (pyridine 2,6-dicarboxylic acid) is present in nature as an oxidative degradation product of vitamins, coenzymes and alkaloids. Dipicolinic acid shows various biological functions including activation/ inactivation of some metalloenzymes,[9,10] inhibition of electron transport system,[11] acts as a potent inhibitor of LDL oxidation.[12] Dipicolinic acid is adesirable metal ion ligand because of its low toxicity and amphophilic nature. Dipicolinic acid is furthermore related to pyridine-2,3- dicarboxylic acid (quinolinic acid), which is also an intermediate in the tryptophan degradation pathway and a precursor of NAD.

In the present work, we report a study on the solution equilibria involved in the formation of ternary Pd(II)complexes involving dipicolinic acid (DPA) and iminodiacetic acid (IDA), an important biological complexing agent, as a primary ligands and some amino acids (glycine, α-alanine, leucine, valine, phenylalanine, tryptophan, methionine, histadiene aspartic acid, and glutamic acid), aromatic carboxylic acids (salicylic and phathalic), and aliphatic carboxylic acids (succinic, oxalic, malic, maleic, malonic, and tartaric) as a secondary ligands by potentiometric technique at T = 30 ºC and I = 0.1 mol·dm^{-3}.

EXPERIMENTAL

Materials and Solutions

$PdCl_2$, dipicolonic acid (DPA), and iminodiacetic acid (IDA) were from fluke. Amino acids (glycine, α-alanine, leucine, valine, phenylalanine, tryptophan, methionine, histadiene aspartic acid, and glutamic acid), aromatic carboxylic acids (salicylic and phathalic), and aliphatic carboxylic acids (succinic, oxalic, malic, maleic, malonic, and tartaric) were analytical-grade (Aldrich or Merck) products. Stock solutions of Pd salt was prepared in deionized water. A carbonate-free sodium hydroxide (titrant, prepared in 0.1 mol·dm^{-3} $NaNO_3$ solution) was standardized potentiometrically with KH phthalate (Merck AG). A nitric acid solution (0.04 mol·dm^{-3}) was prepared and used after standardization. Sodium hydroxide, nitric acid, and sodium nitrate were from Aldrich.

Apparatus and Procedure

The titrations were performed at (30 ± 0.1) °C in a double-walled cell fitted with a thermostat CG 825 pH-meter using a glass electrode was used to monitor the pH changes. The titrant (CO_2-free standard NaOH) was added to the titration cell, and the pH changes were monitored through the pH meter. The pH meter was calibrated with standard buffer solutions (pH 4.0 and 10.0) before the pH measurements. The ionic strength was kept constant (0.10 mol·dm^{-3}) using a $NaNO_3$ solution, and a total volume of 50 cm^{-3} was used for each titration.

For the study of ternary (1:1:1) complexes, the different solutions titrated were as follows: 0.004 mol·dm^{-3} HNO_3 + 0.1 mol·dm^{-3} $NaNO_3$ (a), solution a + 0.001 mol·dm^{-3} DPA or IDA (b), solution b + 0.001 mol·dm^{-3} Pd(II) ion (c), solution a + 0.001 mol·dm^{-3} amino acid or carboxylic acid (d), solution d + 0.001 mol·dm^{-3} Pd (II) ion (e), and solution a + 0.001 mol·dm^{-3} M(II) ion + 0.001 mol·dm^{-3} DPA or IDA + 0.001 mol·dm^{-3} amino acid or carboxylic acid. The complexes are quite stable up to high pH values. In all cases, our calculations of stability constants have been determined successfully at the optimum pH region (usually low pH region); hence, the hydroxyl species likely to be formed after this point could not be studied. In analyzing the titration data for the determination of the proton dissociation constants of the free ligands and the stability constants of binary and ternary metal-ligand complexes in solution, Bjerrum-Calvin's pH titration technique,[13,14] as adopted by Irving and Rossotti[15,16] for binary systems and by Chidambaram and Bhattacharya[17] for ternary systems, has been used at (30 ± 0.1) ºC. It is worth mentioning that many papers related to the protonation constants of the lingands under investigation and their stability constants with Pd(II) ion, were extensively measured and discussed. e.g.[18-22] It is beyond the scope of this article to calculate the protonation constants and the stabiliy constant of the binary systems.

Conductometric titrations were followed with a HANNA HI 9835, Microprocessor conductivity / TDS Meter.

The following mixture was titrated conductometrically against a 0.10 mol·dm^{-3} NaOH solution: 0.01 mol·dm^{-3} Pd (II) (10 cm^3) + 0.01 mol·dm^{-3} DPA or IDA (10 cm^3) + 0.01 mol·dm^{-3} amino acid or carboxylic acid (10 ml).

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RESULTS AND DISCUSSION

Representative potentiometric titration curves are shown in Figure 1 for the Pd(II) + DPA + valine system.

When a solution contains two different ligands and a metal ion, they may exist in equilibria in which either (i) both the ligands may combine with the metal ion simultaneously or (ii) the two ligands may be combined one by one at different pH. As is evident from the titration curves in the present study, the addition of two ligands is stepwise. It was deduced that DPA or IDA interacts first with the Pd (II) ion, followed by the interaction of the amino acid or carboxylic acid ; that is, the ternary complex formation could be considered in stepwise complexation equilibria, i.e., the formation of a ternary complex can be represented by the stepwise equilibrium;

$$M + A \rightleftharpoons MA \quad (1)$$

$$MA + L \rightleftharpoons MAL \quad (2)$$

$$K_{MAL}^{MA} = [MAL] / [MA][L] \quad (3)$$

where M = Pd(II), A represents primary ligand (DPA or IDA) and L represents the secondary ligand (amino acid or carboxylic acid); for instance, examining Figure 1, one may observe that the curves obtained for the different 1:1:1 ternary complex solutions (curve f) overlap with the titration curve of the 1:1 binary Pd(DPA)- (curve c) at low pH values and a divergence of the ternary complex titration curve from that of the binary Pd(DPA)- is observed. This shows the coordination of the valine to the Pd(DPA)-binary complex in a stepwise manner as represented by the following equations:

$$Pd(II) + (DPA) \rightleftharpoons Pd(DPA) \quad (4)$$

$$Pd(DPA) + valine \rightleftharpoons Pd(DPA)(valine) \quad (5)$$

The stability constants for ternary complexes have been calculated at 30 ºC and I = 0.1 mol·dm^{-3}and are tabulated in Tables 1.

In general, the observed order of stability of ternary systems with respect to the primary ligand is dipicolinic acid > iminodiacetic acid, which might be a result of π acidic character in the dipicolinic acid, due to the possibility of $M \rightarrow N$ π bond formation. A similar behavior has been previously observed in M-dipyridyl-L] systems.[23]

TABLE 1 : Formation constant of the ternary complexes of pd(II) involving DPA and IDA as a primary ligands and amino acid or aliphatic and aromatic acid as a secondary ligand at 30 ºC and I = 0.1 mol·dm^{-3} ($NaNO_3$).

Ligands	$\log K_{Pd(DPA)(L)}^{Pd(DPA)}$	$\log K_{Pd(IDA)(L)}^{Pd(IDA)}$
Glycine	5.35 ± 0.06	5.24 ± 0.04
Alanine	5.30 ± 0.05	5.17 ± 0.07
Valine	5.93 ± 0.06	6.31 ± 0.05
Phenylalanine	5.49 ± 0.07	5.20 ± 0.05
Tryptophan	6.02 ± 0.05	5.96 ± 0.06
Methionine	6.16 ± 0.04	5.72 ± 0.05
Leucine	6.09 ± 0.05	5.92 ± 0.06
Aspartic acid	6.20 ± 0.07	5.64 ± 0.05
Glutamic acid	6.18 ± 0.04	6.23 ± 0.06
Histadiene	6.33 ± 0.06	6.31 ± 0.05
Phathalic acid	6.83 ± 0.04	6.62 ± 0.06
Salicylic acid	6.89 ± 0.03	6.54 ± 0.04
Succinic acid	6.70 ± 0.05	6.42 ± 0.04
Malonic acid	6.23 ± 0.04	6.03 ± 0.06
Malic acid	5.41 ± 0.06	5.10 ± 0.05
Oxalic acid	5.92 ± 0.05	5.80 ± 0.03
Tartaric acid	5.18 ± 0.07	5.09 ± 0.05

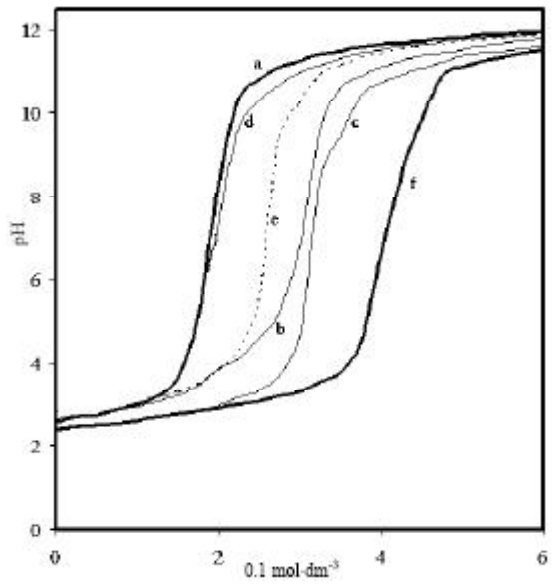

Figure 1 : Potentiometric titration curves for the Pd(II) + DPA + valine system at 30 0.1ºC and I = 0.1 mol·dm^{-3} $NaNO_3$.

In Figure 2, a conductometric titration curve for the ternary complex of Pd(II) with IDA and α-alanine is displayed, as a representative. The titration curve shows an initial decrease and an inflection at a = 2 (a = moles

of base added per mole of ligand). This probably corresponds to the neutralization of H^+ ions originating from the formation of the Pd(II) + IDA binary complex. In the $3 \geq a \geq 2$ range, the conductance increases slightly due to the formation of a ternary complex associated with the release of a H^+ ion from α-alanine. Beyond a = 3, the conductance increases appreciably due to the presence of an excess of NaOH.

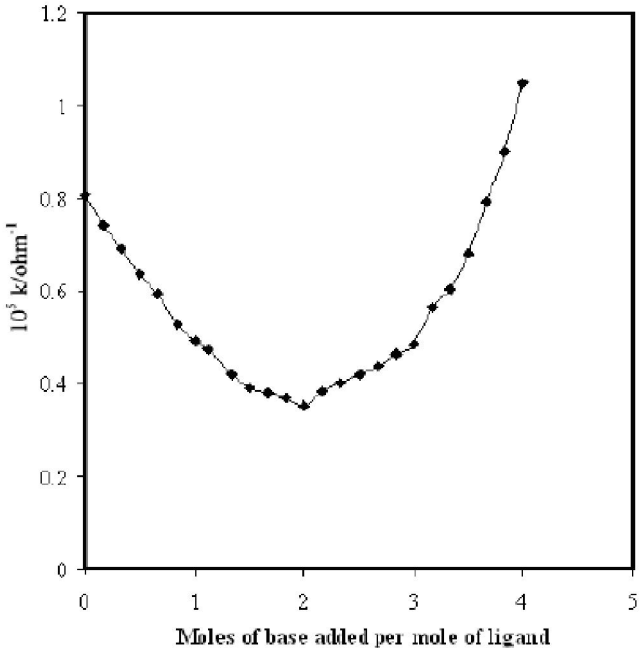

Figure 2 : Conductometric titration curve for Pd(II)-IDA- α-alanine systems at at 30 0.1°C and I = 0.1 mol·dm^{-3} $NaNO_3$.

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