

Potentiometric Study of 1, 2-Diphenylethylenediamine Palladium (II) Complex with Some Selected Amino Acids

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A potentiometric titration technique has been used to determine the stability constants for various complexes of $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$, with some selected amino acids (L). The stepwise formation of the complexes has been established in the pH region studied. The results show the formation of 1:1 complexes with amino acids. Stoichiometries and stability constants of the complexes were determined at 37°C and 0.1 mol dm⁻³ NaNO₃. The concentration distribution of the complexes in solution was evaluated .

Keywords: Amino acids; Potentiometric studies; Stability constants; Bioligands

1. INTRODUCTION

1, 2-Diphenylethylenediamine is an organic compound with the formula H₂NCHPhCHPhNH₂, where Ph is C₆H₅, phenyl. This diamine is a precursor to a ligand for certain homogeneous hydrogenation catalysts. It can be prepared from benzil by reductive amination[1]. Some papers deal with the complex formation of 1, 2-diphenylethylenediamine with metals, such as Cu (II) [2], Ni(II) [2] and Pt(II)[3]. Pt(II) complexes containing 1, 2-diphenylethylenediamine (stein) isomers has been synthesized and tested for their antitumor activity against leukemia L1210 [3]. In terms of complex formation and acid dissociation constants, Pt(II) and Pd(II) complexes behave very similarly, notwithstanding the fact that Pd(II) complexes are about 10³-10⁵ times as reactive as their platinum analogs because of their similar thermodynamic parameters and structures. Pt(II) and Pd(II) form square planar complexes forming *cis* and *trans* isomers. The *cis*-complexes are very active. Amino acids are biologically important molecules and do not possess toxicity. Several ternary complexes of

platinum(II) and palladium(II) with amino acids and other bioligands have been reported [4-10]; some of them are biologically active against human pathogens. In the present study, the equilibrium studies of the interaction of $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$ and amino acids were determined using potentiometric method under physiological-like conditions ($0.1 \text{ mol dm}^{-3} \text{ NaNO}_3$ - 37°C). The concentration distribution relations of the various complex species will be evaluated.

2. EXPERIMENTAL

2.1. Materials and Solutions

All the chemicals used were of analytical grade reagents. 1, 2-diphenylethylenediamine and PdCl_2 were obtained from Sigma. Amino acids and related compounds investigated are: glycine, β -phenylalanine, alanine, serine, methylamine, methionine, S-methylcysteine, histidine·HCl, histamine·2HCl, imidazol, pencillamine, lysine, ornithine HCl, mercaptoethylamine and cysteine. These materials were provided by Sigma-Aldrich (Germany). All these chemical are used as received without any further purification, their purities ranged from 99-99.9%. For equilibrium studies, $[\text{Pd}(\text{Ph}_2\text{en})\text{Cl}_2]$ was converted into the diaquo complex by treating it with two equivalents of AgNO_3 as described before for $[\text{Pd}(\text{en})\text{Cl}_2]$ [11]. Carbonate-free sodium hydroxide, (titrant) solution was standardized potentiometrically with potassium hydrogen phthalate (Merck Chem. Co.). All solutions were prepared with bi-distilled water.

2.2. Synthesis of $[\text{Pd}(\text{Ph}_2\text{en})\text{Cl}_2]$

$[\text{Pd}(\text{Ph}_2\text{en})\text{Cl}_2]$ was prepared by heating PdCl_2 (531.9 mg, 3.0 mmole) in 50 mL water and KCl (447.3 mg, 6.0 mmole) to 50.0°C for 30.0 min. After the $\text{K}_2[\text{PdCl}_4]$ solution was cooled, 1,2-diphenyl-ethylenediamine (636.9 mg, 3.0 mmole), dissolved in 10.0 mL water, was added dropwise to the stirred solution. A yellow precipitate formed and the mixture was stirred for a further 1 h at 25.0°C . After the precipitate was filtered off, it was washed sequentially with water, ethanol and diethyl ether. Analysis: Calc. for $\text{C}_{14}\text{H}_{14}\text{N}_2\text{Cl}_2\text{Pd}$: C, 43.4; H, 3.6; N, 7.2. Found: C, 43.7; H, 3.2; N, 7.5.

2.3. Apparatus

The titrimetric data were obtained using a Metrohm 686 titroprocessor equipped with a 665 dosimat (Switzerland). The glass electrode was calibrated before each with standard buffer solutions prepared according to NBS specifications [12]. Elemental microanalyses of the separated solid for C, H and N were performed in the microanalytical Center, Cairo University. The analyses were performed twice to check the accuracy of the analytical data.

2.4. Procedure

For the determination of the acid dissociation constants of all ligands, aqueous solutions ($1.25 \times 10^{-3} \text{ mol dm}^{-3}$) of the ligands were titrated with $0.1 \text{ mol dm}^{-3} \text{ NaOH}$ at 37.0°C under ionic strength of 0.1 mol dm^{-3} solution of NaNO_3 .

Table 1. Formation constants of Pd (Ph₂en) complexes with amino acids at 37.0 °C and 0.1 mol dm⁻³ ionic strength

System	<i>p</i>	<i>q</i>	<i>r</i> ^a	<i>logβ</i> ^b	<i>S</i> ^c
Pd (Ph ₂ en)-OH	1	0	-1	-4.08(0.03)	3.5E-8
	1	0	-2	-13.96(0.02)	
	2	0	-2	-5.33(0.02)	
Glycine	0	1	1	9.24(0.02)	2.0E-7
	0	1	2	11.09(0.01)	5.0E-7
	1	1	0	14.13(0.01)	
β-phenylalanine	0	1	1	9.14(0.02)	7.2E-8
	0	1	2	11.07(0.01)	1.5E-8
	1	1	0	14.43(0.03)	
Alanine	0	1	1	9.17(0.01)	9.3E ⁻⁸
	0	1	2	12.23(0.02)	4.0E-8
	1	1	0	14.83(0.01)	
Serine	0	1	1	8.93(0.01)	1.7E-8
	0	1	2	11.01(0.01)	8.1E-8
	1	1	0	14.87(0.01)	
	1	1	-1	3.23(0.03)	
1	1	0	16.12(0.01)		
Methylamine	0	1	1	9.44(0.01)	1.7E-7
	1	1	0	8.22(0.06)	8.1E-8
	1	2	0	16.12(0.01)	
Methionine	0	1	1	8.87(0.01)	8.7E-8
	0	1	2	11.01 (0.04)	2.4E-8
	1	1	0	14.02(0.02)	
S-methylcysteine	0	1	1	8.77(0.03)	3.4E-8
	1	1	0	14.98(0.04)	7.3E-8
Histidine	0	1	1	8.80(0.01)	1.8E-7
	0	1	2	14.55 (0.03)	9.5E-8
	0	1	3	16.65 (0.06)	
	1	1	0	18.83(0.04)	
	1	1	1	23.98(0.03)	
1	1	1	23.98(0.03)		
Histamine	0	1	1	9.14(0.01)	2.9E-8
	0	1	2	15.23(0.02)	6.3E-8
	1	1	0	18.72(0.01)	
	1	1	1	22.45(0.03)	
1	1	1	22.45(0.03)		
Imidazol	0	1	1	6.03(0.02)	1.7E-8
	1	1	0	7.33 (0.03)	8.2E-8
	1	2	0	13.65(0.03)	
Pencillamine	0	1	1	10.00(0.02)	3.0E-8
	0	1	2	17.66(0.03)	1.6E-8
	1	1	0	20.22(0.03)	
	1	1	1	26.11(0.02)	
1	1	1	26.11(0.02)		
Lysine	0	1	1	9.88(0.01)	1.4E-8
	0	1	2	18.76(0.01)	9.0E-8
	1	1	0	19.12(0.01)	
	1	1	1	22.44(0.02)	
1	1	1	22.44(0.02)		
Ornithine	0	1	1	9.98(0.00)	1.0E-8
	0	1	2	18.65(0.02)	1.8E-8
	1	1	0	19.65(0.03)	
	1	1	1	21.44(0.01)	
1	1	1	21.44(0.01)		
Mercaptoethylamine	0	1	1	10.00(0.04)	3.7E-8
	0	1	2	18.13(0.02)	1.6E-8
	1	1	0	21.29(0.04)	
	1	1	1	25.96(0.01)	
1	1	1	25.96(0.01)		
Cysteine	0	1	1	9.87(0.03)	3.7E-8
	0	1	2	17.12(0.04)	5.0E-8
	1	1	0	20.97(0.03)	
	1	1	1	24.98(0.01)	
1	1	1	24.98(0.01)		

^a *p*, *q* and *r* are the stoichiometric coefficient corresponding to Pd(Ph₂en), amino acid, and H⁺, respectively

^b Standard deviations are given in parentheses.

^c Sum of square of residuals.

The acid dissociation constants of the coordinated water molecules in [Pd (Ph₂en)(H₂O)₂]²⁺ were determined by titrating a (1.25×10⁻³ mol dm⁻³) solution of the complex. The formation constants

of the complexes were determined by titrating solution mixtures of $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$ (1.25×10^{-3} mol dm⁻³) and the ligand in concentration ratio of 1:1.

The titration solution mixtures had a volume of 40 cm³. $[\text{OH}^-]$ value was calculated using a pK_w value of 13.60 [13]. The equilibrium constants evaluated from the titration data (summarized in Table 1) are defined by Eqs. (1) and (2), where M, L and H stand for the $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$ ion, ligand and proton, respectively.



$$\beta_{pqr} = \frac{[\text{M}_p\text{L}_q\text{H}_r]}{[\text{M}]^p [\text{L}]^q [\text{H}]^r} \quad (2)$$

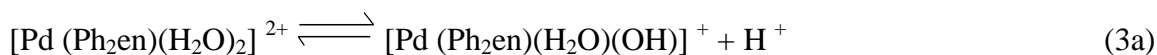
The calculations were performed using the computer program SUPERQUAD [14]. The stoichiometries and stability constants of the complex species formed in solution were determined by examining various possible composition models for the systems studied. The model selected gave the best statistical fit and was chemically consistent with the titration data without giving any systematic drifts in the magnitudes of various residuals, as described elsewhere [15]. The fitted model was tested by comparing the experimental titration data points and the theoretical curve calculated from the values of the acid dissociation constant of the ligand and the formation constants of the corresponding complexes. The species distribution diagrams were obtained using the program SPECIES [16] under the experimental conditions employed.

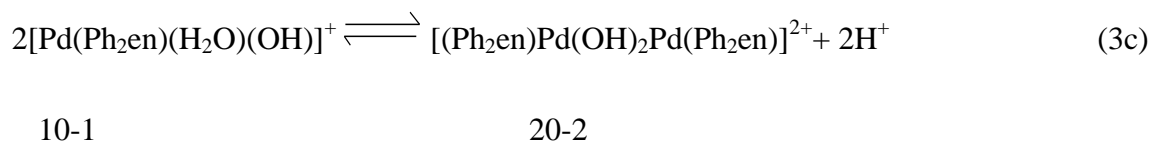
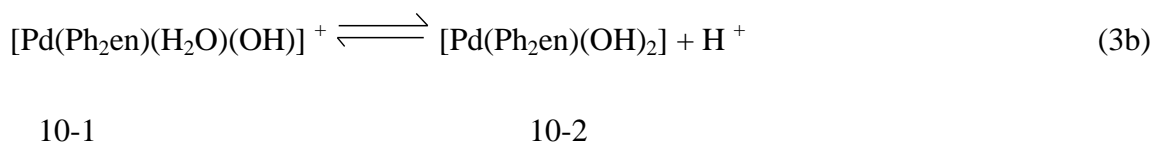
3. RESULTS AND DISCUSSION

The proton dissociation constants of the ligands studied have been redetermined at 37.0 °C and $I = 0.1$ mol dm⁻³ NaNO₃ to obtain values using the same experimental procedures as used in the determining of stability constants of the palladium(II) complexes are in good agreement with data found in the literature [8].

3.1. The Hydrolysis of $[\text{Pd}(\text{ph}_2\text{en})(\text{H}_2\text{O})_2]^{+2}$

The hydrolysis of the $[\text{Pd}(\text{ph}_2\text{en})(\text{H}_2\text{O})_2]^{+2}$ complex is characterized by fitting the potentiometric data by various models. The best-fit model was found to be consistent with the species 10-1, 10-2 and 20-2, as given in Eq. (3).





The pK_{a1} and pK_{a2} values were found to be 4.12 and 8.96, respectively. The equilibrium constant for the dimerization reaction (3c) can be calculated with Eq. (4) and amounts to 2.83.

$$\log_{10} K_{\text{dimer}} = \log \beta_{20-2} - 2 \log \beta_{10-1} \quad (4)$$

The species distribution diagram for $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$ and its hydrolyzed species is shown in Fig 1.

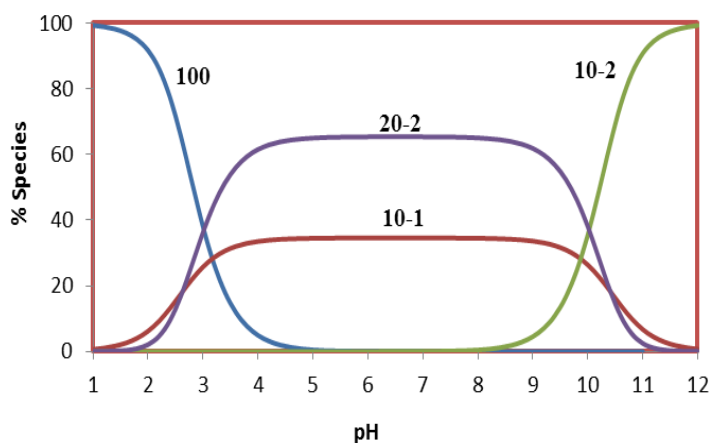


Figure 1. Concentration distribution of various species as a function of pH in the $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})_2]^{2+}$ system

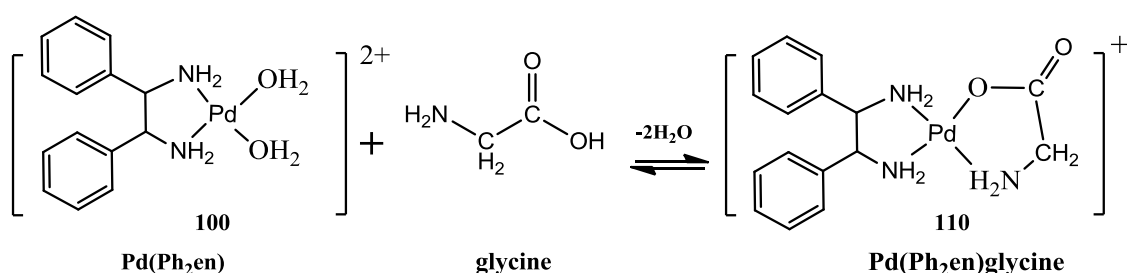
The concentration of the monohydroxo, 10-1, and the dimeric species, 20-2, increase with increase of pH, attaining a maximum of 36.5 and 65.5% at pH ca. 7.0, respectively. Further increase in pH is accompanied by a decrease in concentration of the monohydroxo species and an increase in that of the dihydroxo species. The main species present under physiological condition is calculated to be $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})(\text{OH})]^+$ and $[\text{Pd}(\text{Ph}_2\text{en})(\text{H}_2\text{O})(\text{OH})]_2$ which can interact with DNA constituents.

3.2. Complex Formation Equilibria

The stoichiometry and stability constants of the complexes formed have been determined by trying different possible composition models for the system. According to the method of calculation

applied, the model of the best fit for the complexes under investigation has been found to be Pd(Ph₂en)(L). Imidazole and methylamine are monodentate ligands, the stability constant value of the monodentate methylamine complex is higher than that of the imidazole complex. The observed extra stability of the methylamine complex may be due to the higher basicity of its amino group (as is reflected by their pK_a values).

The stability constant of the monodentate methylamine complex is lower than that of glycine, as seen in Table (1), indicating that glycine most likely coordinates with Pd(Ph₂en) as a bidentate ligand through the amino and carboxylate groups, rather than as a monodentate ligand. Proposed formation equilibria for complex of Pd(Ph₂en) with glycine is shown in *scheme I*.



Scheme (I)

The potentiometric titration curves for the Pd(Ph₂en)-serine system, representative, is significantly lower than the serine titration curve (Fig. 2).

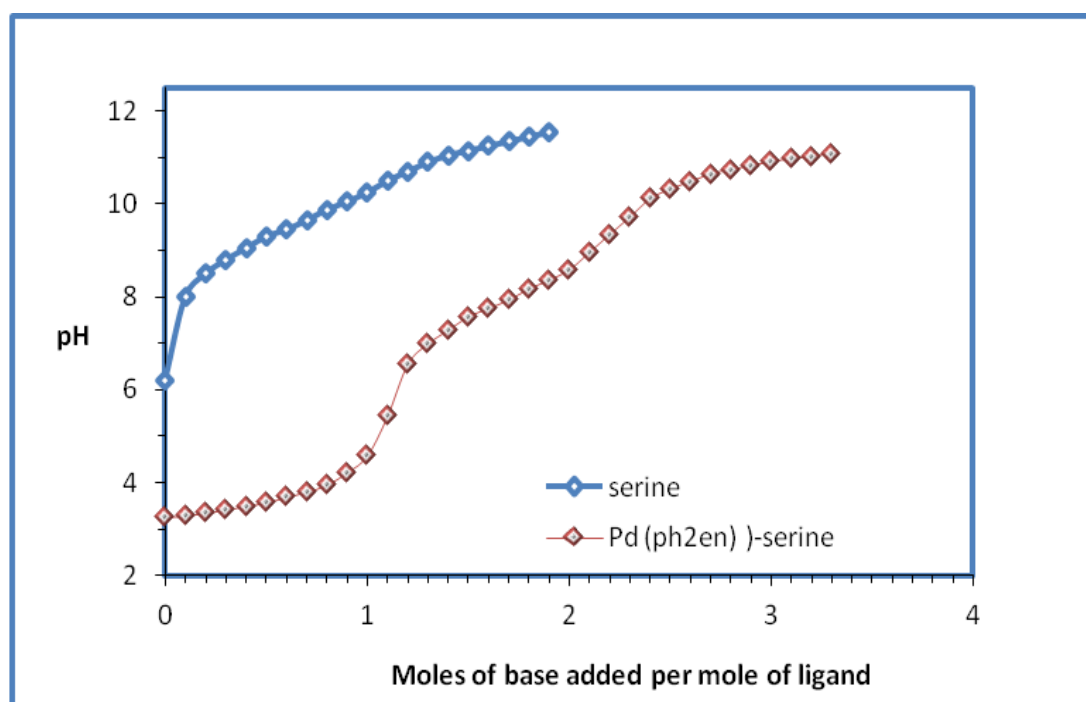
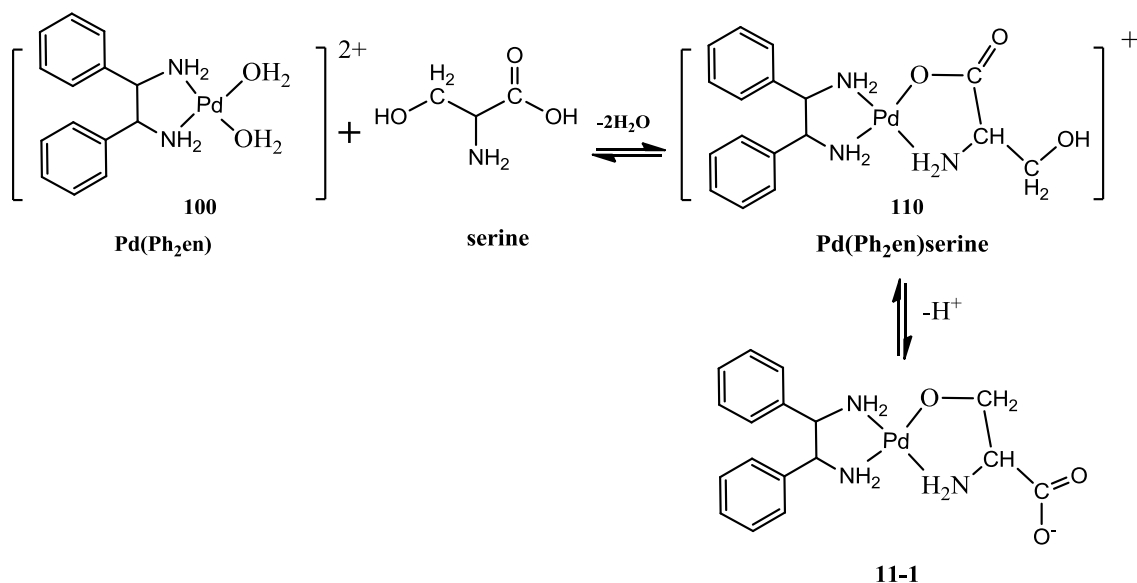


Figure 2. Potentiometric titration curve of the Pd(Ph₂en)-serine system

This corresponds to the formation of a complex species via release of a hydrogen ion. Serine forms in addition to the $\text{Pd}(\text{Ph}_2\text{en})(\text{L})$ complex, the $\text{Pd}(\text{Ph}_2\text{en})(\text{LH}-1)$ species. The latter complex is formed through induced ionization of the β -alcohol group as mentioned in the literature [17] according to *scheme II*, the alcohol group in serine is competing with the carboxylate group in binding to $\text{Pd}(\text{Ph}_2\text{en})^{2+}$ ion. Due to coordination of the alcohol group by donation of the electron pair on the oxygen to the metal centre, the OH bond is considerably weakened, and thus the ionization of a proton occurs at fairly low pH. The distribution diagram for the serine complex reveals that the complex species with coefficients 110 reaches the maximum degree of formation ($\sim 98\%$ in the pH range of 4.0-8.9); the hydroxo complex $[\text{Pd}(\text{Ph}_2\text{en})(\text{OH})]$ plays a minor role in that region. This means that in the physiological pH range the OH^- ion does not compete with amino acids in the reaction with the palladium(II) complex. However the species 11-1 predominates after pH 8.5 and attains the maximum concentration of $\sim 90\%$ at pH ~ 10.8 .



Scheme (II)

Histidine is a tridentate ligand having amino, imidazole and carboxylate groups as binding sites. With $[\text{Pd}(\text{ph}_2\text{en})(\text{H}_2\text{O})_2]^{+2}$ only two of the three binding sites are involved in complex formation. The stability constant of the histidine complex is higher than those of amino acids. This reveals that histidine interacts with $[\text{Pd}(\text{ph}_2\text{en})(\text{H}_2\text{O})_2]^{+2}$ by the amino and imidazole nitrogen atoms.

The imidazole group in histidine increases the stability of the complex due to the high affinity of Pd (II) for the nitrogen donor group. The acid dissociation constant of the protonated species is given by the following Eq. 5.

$$pK_a = \log \beta_{111} - \log \beta_{110} \quad (5)$$

The pK_a for the histidine complex amounts to 5.15, being lower than that of the protonated amino group NH_3^+ ($pK_a = 8.80$), but closer to that of the protonated imidazole group ($pK_a = 6.03$), suggesting the proton in the protonated complex would be located mainly on the imidazole group.

Lysine and ornithine may bind to Pd (II) ion as α -amino acid (N,O-donor set) or by α - and ω -amino groups (N,N-donor set). The stability constants of their complexes are higher than those of α -amino acids, indicating that lysine and ornithine ligating by the two amino groups. This formulation is supported by the great affinity of palladium to nitrogen donor centers.

Phenylalanine forms a less stable complex than alanine. This may be due to the steric effect exerted between the phenyl group of phenylalanine and the two phenyl groups of Ph_2en , as well as the lower basicity of the amino group of phenylalanine compared to that of alanine. This will contribute to the decreased stability of the complex formed.

S-methylcysteine has the lowest pK_a value (8.77) among the amino acids studied. Its complex has a higher stability constant than that for amino acids such as glycine. This may be taken as evidence that the sulfur atom participates in the complex formation process. Also, S-methylcysteine forms a more stable complex than methionine, plausibly due to the fact that the five-membered chelate ring in the former complex is energetically more favored than six-membered chelate ring in the latter complex.

The formation constants of ternary complexes with thiol-containing ligands as penicillamine, cysteine and mercaptoethylamine, were determined by fitting potentiometric data on the basis of possible composition models. The selected model with the best statistical fit was found to consist of 110 and 111 complexes.

Penicillamine has three binding sites, carboxylic, amino and sulfhydryl groups. It forms the complexes 110 and 111. The stability constant of the 110 complex is in fair agreement with that of mercaptoethylamine, (where the binding sites are the amino and sulfhydryl groups) and higher than those α -amino acids (where the binding sites are the amino and carboxylate groups). This indicates that penicillamine interacts with Pd(II) ion by the amino and deprotonated-SH group

Cysteine present three potential coordination sites for metal bonding the sulphoryl, amino, and carbonyl groups. All three sites have been observed in complexes [18-22]. It forms the complexes 110 and 111. It is well known that both $-SH$ and $-NH_2$ groups can coordinate to Pd(II). The acid dissociation constants of the protonated ternary complex ($\log \beta_{111} - \log \beta_{110}$) obtained with penicillamine, cysteine and mercaptoethylamine are 5.89, 4.01 and 4.67 respectively. These values obtained in the present study are less than the previously reported microscopic acid dissociation constants [23], revealing that the $[-NH_3]^+$ and $-SH$ groups most likely take part in complex formation.

The species distribution for ornithine complex, taken as a representative, is given in Figure (3).

The protonated species 111 complex predominates (22.20% at pH ca-2.4), the deprotonated species 110 complex predominates (93.8% at pH ca. 6.6) and the hydroxo- complex, makes a minor contribution in that range. This means that in the physiological pH range the OH^- ion does not compete with amino acids for reaction with the palladium (II) complex.

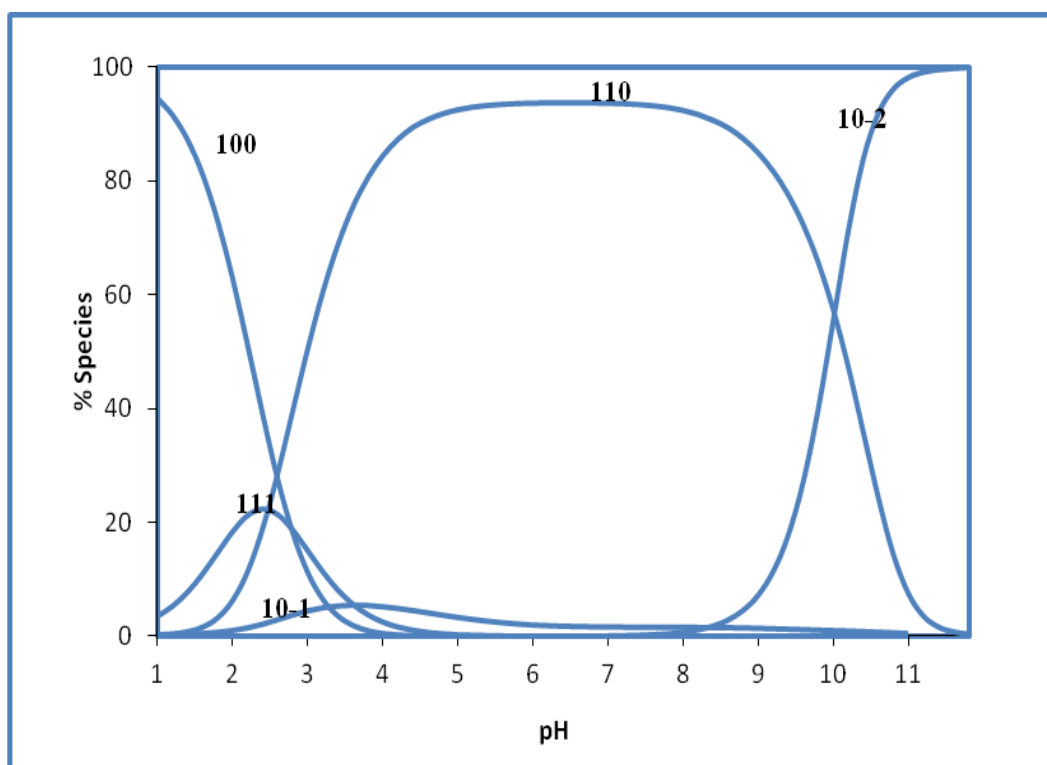


Figure 3. Concentration distribution of various species as a function of pH in the Pd (Ph₂en)- ornithine system.

4. CONCLUSION

The Potentiometric data for the system consisting of [Pd(Ph₂en)] and amino acids showed the formation of 1:1 complexes. The accepted model of Pd (Ph₂en)-serine consist of the formation of the species 110, followed by the formation of 11-1 complex. The sulphur ligands, (penicillamine, cysteine and mercaptoethylamine), form the protonated and the deprotonated complexes with Pd (II) ion. The concentration distribution curves of the various complex species existing in solution were evaluated.

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