KINETICS AND MECHANISM OF BASE HYDROLYSIS OF A-AMINOACID ESTERS CATALYSED BY [Pd(1,3-DIAMINO-2-HYDROXYPROPANE)(H₂O)₂]²⁺ COMPLEX

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ABSTRACT

Amino acid esters (L) react with $[Pd(DHP(H_2O)_2]^{2+}$, (DHP = 1,3-diamino-2-hydroxopropane) giving mixed ligand $[Pd(DHP)L]^{2+}$ The kinetics of hydrolysis of $[Pd(DHP)L]^{2+}$ have been studied by pH-stat technique and rate constants were obtained. Rate acceleration observed for glycine methyl ester is high. The effect with methionine methyl ester and histidine methyl ester are much less marked, as the mixed-ligand complexes with these ligands do not involve alkoxycarbonyl donors. Possible mechanisms for these reactions are considered. Activation parameters have been determined for glycine methyl ester.
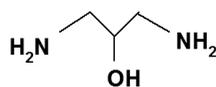
DHP

INTRODUCTION

Metal ions in metalloenzymes such as carboxypeptidase A[1], carbonic anhydrase[2] and alkaline phosphatase[3] play a key role in many biochemical processes.[4]   In these metalloenzymes, the metal ions at the active sites are considered to serve as a primary catalytic considered to serve as a primary catalytic centre for bringing substrate and nucleophile together through formation of a coordination complex, to activate the substrate carbonyl group facilitating attack of the nucleophile in caroxypeptodase A[5] or to activate the water molecule in the reversible hydrated process of carbon dioxide in carbonic anhydrase[6] and to activate the serine hydroxyl group in alkaline phosphatase.[7] In order to probe the mechanism by which the metalloenzyme may operate and consequently provide a theoretical base for designing high effective artificial metalloenzyme, previous reports[8-11] have developed biomimetic models for metalloenzyme which catalyse the hydrolysis of carboxylic acid esters in biomemetic models for certain metalloenzymes, as the metalloenzyme-substrate complex .

Work in our laboratory[12-17] has focused on catalysis of the hydrolysis of various amino acid esters by metal complexes. The mixed ligand complex $[Pd(en)L]^{2+}$, where a five-membered chelate ring is formed, undergoes hydrolysis by water and hydroxide ion.[18] It is therefore of considerable interest to extend this work to the mixed ligand complex with 1,3-diamino-2-hydroxypropane , where a six- membered chelate ring is formed. The increase of chelate ring size may affect the elecrophilicity of the Pd(II) ion and tune the reactivity of this metal centre in possible catalytic and biological applications as the hydrolysis of the ester group.

EXPERIMENTAL

Materials and reagent

All reagents were of Analar grade. K_2PdCl_4 and 1,3-diamine-2-hydroxopropane are provided by Aldrich. The glycine-, histidine-, and methionine methyl esters were purchased from Fluka. Carbonate-free NaOH was prepared and standardized against potassium hydrogen phthalate solution. All solutions were prepared in deionized H_2O.

Apparatus and measuring techniques

$Pd(DHP)Cl_2$ was prepared by dissolving K_2PdCl_4 (2.82 mmol) in 10 ml water with stirring. The clear solution of $[PdCl_4]^{2-}$ was filtered and 1,3-diamino-2-hydroxopropane (2.82 mmol), dissolved in 10 ml H_2O was added drop wise to the stirred solution. The pH was adjusted to 2-3 by the addition of HCl and/or NaOH. A yellowish -brown precipitate of $Pd(DHP)Cl_2$ was formed and stirred for a further 30 minute at 50 °C. After filtering off the precipitate, it was thoroughly washed with H_2O, ethanol and diethyl ether. A yellow powder was

obtained. Anal. Calcd. for $C_3H_{10}N_2OPdCl_2$ (267.3) :C, 13.6; H, 3.7; N, 10.5. Found: C, 13.5; H,4.0; N, 10.3%.

Aqueous solutions of the diaqua form of the $Pd(DHP)Cl_2$ complex were prepared *in situ* by the addition of slightly less than two mole equivalents of $AgNO_3$ to a solution of a known amount of the dichloro complex and stirred over night. The white precipitate of AgCl that formed was filtered off using a 0.1 mm pore membrane filter. Great care was taken to ensure that the resulting solution was free of Ag^+ ion and that the dichloro complex had been converted completely into the diaqua species. The ionic strength of the solutions was adjusted to 0.1 M with $NaNO_3$ (Acros, p.a.).
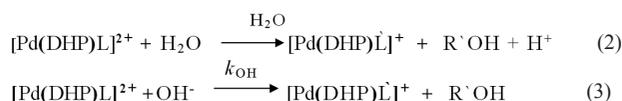
Kinetic measurements

The kinetics of hydrolysis was monitored using a Metrohm 751 Titrino operated with the SET mode (titration to a preset end point). The titroprocessor and electrode were calibrated with standard buffer solutions according to NIST.[19] Hydrolysis kinetics of glycine-, methionine-, and histidine methyl esters in the presence of $[Pd(DHP)(H_2O)_2]^{2+}$ is investigated by pH-stat technique[20,21]. After equilibrating a solution mixture (40 cm³) containing $[Pd(DHP)(H_2O)_2]^{2+}$ (2.5x10⁻³M) , ester (2.5x10⁻³M) and $NaNO_3$ (0.1M) at the required temperature under nitrogen flow and the pH was brought to the desired value by the addition of 0.05 M NaOH solution. The hydrolysis was then followed by the automatic addition of 0.05 M NaOH solution to maintain the given pH constant. The data fitting was performed with the OLIS KINFIT set of programs[22] as described previously[23]. The precision of the kinetic data was estimated from plot as obtained from the OLIS program output. The accepted residual values are less than 10⁻². Values of the hydroxide ion concentration were estimated from the pH using pK_w = 13.997 and an activity coefficient of 0.772 was determined from the Davies equation[24] . At the variable temperature studies, the following values of pK_w and g were employed[25], at 15ºC (pK_w = 14.35, g = 0.776), at 20º C (pK_w = 14.16, g = 0.774) at 25º C (pK_w = 14.00, g = 0.772) at 30ºC (pK_w = 13.83, g = 0.770), at 35ºC (pK_w = 13.68, g = 0.768)

RESULTS AND DISCUSSION

a-amino acid esters react with $[Pd(DHP)(H_2O)_2]^{2+}$ according to the equilibrium (1). The equilibrium constant is expected to be >> 1. This is due to the high affinity of Pd^{II} ion to react with N-ligands[26]. The resulting mixed-ligand complexes $[Pd(DHP)L]^{2+}$ $[L = NH_2CH(R)CO_2R`]$ undergo hydrolysis by water and hydroxide ion according to Eq. (2) and (3) .

$$[Pd(DHP)(H_2O)_2]^{2+} + L \rightleftharpoons [Pd(DHP)L]^{2+} + 2H_2O \qquad (1)$$

$$[Pd(DHP)L]^{2+} + H_2O \xrightarrow{\;H_2O\;} [Pd(DHP)\dot{L}]^+ + R`OH + H^+ \qquad (2)$$

$$[Pd(DHP)L]^{2+} + OH^- \xrightarrow{\;k_{OH}\;} [Pd(DHP)\dot{L}]^+ + R`OH \qquad (3)$$

Where $L = NH_2CH(R)CO_2R`$ and $\dot{L} = NH_2CH(R)CO_2$

The kinetic data, the volume of base added to keep the pH constant versus time, could be fitted by one exponential . Various other kinetic models were tested without leading to satisfying fits of the data. The values of $k_{obs.}$ (the observed first-order rate constant at constant pH) were obtained. Plots of $k_{obs.}$ versus the hydroxide ion concentration were linear with a positive intercept The precision of the data was evidenced by the correlation coefficient (R^2), Fig. (1). The rate expression is therefore of the form Eq. (4,5) .

$$\text{Rate} = k_{obs}[Pd(DHP)(ester)] \qquad (4)$$

$$k_{obs} = k_o + k_{OH}[OH] \qquad (5)$$

The term k_o arises due to water attack on the mixed-ligand complex. Values of $k_{H2O} = k_o/55.5$, where 55.5 mol dm⁻³ is the molar concentration of water, were determined from the intercept, and values of $k_{OH} = (k_{obs.} - k_o)/[OH]$ from the slopes of the plots. The various rate constants are given in Table (1) .

The linear dependence of k_{obs} on the OH^- concentration is consistent with the direct attack of OH^- ion on the coordinated ester carbonyl group. The rate acceleration denoted by the catalysis ratio (C = k_{OH}/k_{OH}^{ester}) is calculated Table 1) and found to be 2.25×10^4 for glycine methyl ester. Rate acceleration of this magnitude is fully consistent with the formation of mixed–ligand complex where there is a direct interaction between Pd(II) and the carbonyl group of the ester (structure I).[13,18] The isolation of complex (I) is not posssible as it is not stable as once the complex is formed the hydrolysis of the ester starts.

Table 1. Kinetics of hydrolysis of coordinated amino acid ester in aqueous solution at 25°C.

System	pH	$10^{10}[OH^-]$	$10^4 k_{obs}{}^a (s^{-1})$
Glycine methyl ester	4.2	2.06	2.39(0.04)
	4.4	3.28	3.19(0.02)
	4.6	5.19	4.03(0.03)
	4.8	8.23	5.80(0.05)

System	pH	$10^5[OH^-]$	$10^4 k_{obs} (s^{-1})$
Methionine methyl ester	8.8	0.82	4.11(0.06)
	9.0	1.30	5.46(0.08)
	9.2	2.06	7.14(0.14)
	9.4	3.27	8.47(0.18)
Histidine methyl ester	8.8	0.82	2.34(0.02)
	9.0	1.30	4.07(0.07)
	9.2	2.06	5.25(0.05)
	9.4	3.27	7.24(0.08)

ᵃ standard deviations are given in parentheses

I
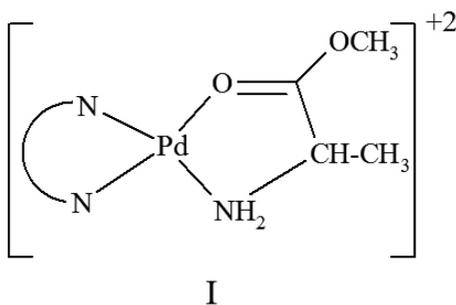
The formation of bidentate ester complexes with both copper(II) and cobalt(II) leads to rate accelerations[27,28] of 10^5- 10^6 and the situation with palladium(II) appears to be similar. The base hydrolysis of coordinated histidine and methionine esters was studied in the pH range 9-10. Throughout this pH range the reaction shows a first-order dependence on the hydroxide ion concentration. The relative catalysis ratio (C) observed with L-methylmethionate (L-MethOMe) [k_{OH}/k_{OH}^{ester} = 22.85] and methyl-L-histidinate (L-HisOMe) [k_{OH}/k_{OH}^{ester} = 30.64], table (1), suggests that in these cases the alkoxycarbonyl group is not bonded to the metal ion.
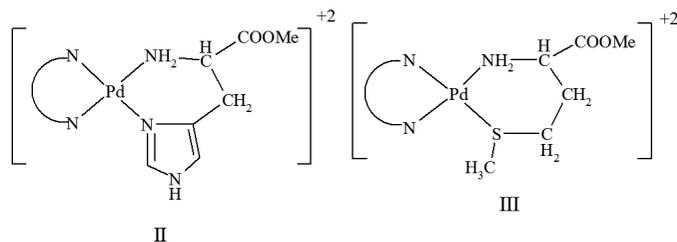
II   III

L-MethOMe complex is expected to have the structure (II), in which the donor atoms are thiolato-sulphur and the a-amino group. A similar situation (III) is likely with L-hisOMe, where the a-amino group and the pyridine nitrogen of the imidazole ring act as donors. Previous studies have shown that the formation of such complexes with non-bonded or pendant ester groups leads to only relatively small rate increases[27].

Table 2. Rate constant (k /dm³mol⁻¹s⁻¹) for base hydrolysis of amino acid esters and their complexes at 25°C in aqueous solution.

System	k_{OH}	k_{H2O}	$k_{OH}{}^{ester(a)}$	$k_{OH}/k_{OH}{}^{(ester)}$
Glycine methyl ester	5.42×10^5	9.76×10^{-6}	1.28	4.23×10^5
Methionine methyl ester	17.6	5.48×10^{-6}	0.77	22.85
Histidine methyl ester	19.0	2.14×10^{-6}	0.62	30.64

(a)   Ref. (20), (21)
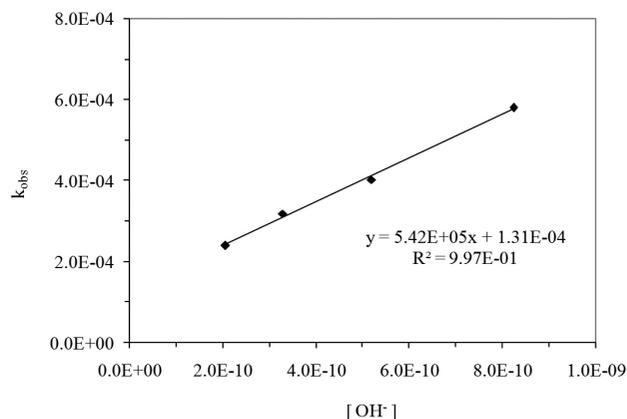
Fig. 1. Plot of k_{obs} vs. [OH^-] for the hydrolysis of coordinated glycine methyl ester at 25°C.

The relative catalysis ratio at 25°C for the base hydrolysis of the glycine methyl ester incorporated in [Pd(en)L]²⁺ is 3.81×10^4.[18] The corresponding value for [Pd(DHP)L]²⁺ (4.23×10^5) is higher than that of [Pd(en)L]²⁺. This may be explained on the premise that the [Pd(DHP)L]²⁺ complex is involving formation of more enlarged six-membered chelate ring and associated with increase of electrophilicity of the Pd(II) centre. The electrophilicity is one of the factors determining the donor-acceptor interaction between the ester and Pd(II) ion, the complex which binds the ester more tightly, would withdraw the most electron density from the ester making it more susceptible to OH^- attack. This will lead to increase of the respective catalysis ratio.
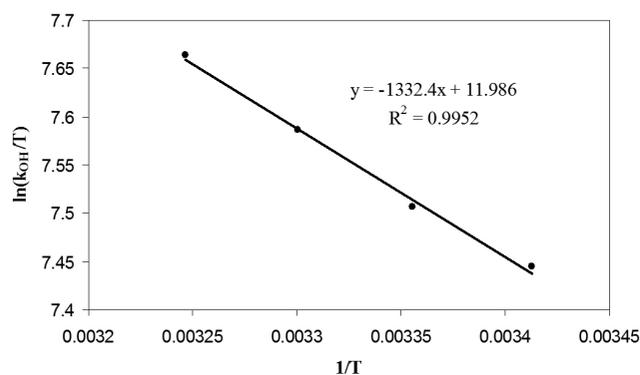
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Fig. 2. Plot of ln k_{OH}/T vs. 1/T for the hydrolysis of coordinated glycine methyl ester.

Table 3. Rate constant (k/dm^{3}mol^{-1}s^{-1}) for base hydrolysis of coordinated Glycine methyl ester at different temperatures in aqueous solution.

Temp. ºC	k_{OH}	k_{H2O}
20	5.01×10^5	2.25×10^{-6}
25	5.42×10^5	2.36×10^{-6}
30	5.97×10^5	2.48×10^{-6}
35	6.56×10^5	2.60×10^{-6}

The activation parameters (DH$^\#$ and DS$^\pm$) were determined for the hydrolysis of coordinated glycine methyl ester from the temperature dependence of the rates in Table 3. The activation parameters were obtained using the Eyring plot of (lnk_{OH}/T) versus 1/T, Fig. (2), from which the values DH$^\#$ = 11.07 kJmol^{-1} , DS$^\pm$ = -99.60 JK^{-1}mol^{-1} were calculated[25]. For the base hydrolysis of free glycinemethyl ester the activation parameters were found[10] to be DH$^\#$= 39.7 kJmol^{-1} and DS$^\#$ = -117 JK^{-1}mol^{-1}. The enhanced rate for base hydrolysis of the ester incorporated in the complex [Pd(DHP)L]$^{2+}$ is therefore due to a decreased DH$^\#$ and an increased DS$^\pm$ implies desolvation between the ground and transition states and is indicative of a mechanism involving nucleophilic attack by external OH$^-$ on the complexed ester group.

CONCLUSION

The hydrolysis of glycine methyl ester is catalyzed by [Pd(DHP)(H$_2$O)$_2$]$^{2+}$ complex with catalysis ratio C = 4.23×10^5. The catalytic effect is due to a direct interaction between Pd(II) and the alkoxycarbonyl group of the ester species. However, the hydrolysis of histidine and methionine methyl esters is not significantly catalyzed. The relative small catalysis-ratio values suggest that in these cases the alkoxycarbonyl group is not bonded to the metal ion . The activation parameters for the hydrolysis of coordinated glycine methyl ester were determined.