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KINETICS, MECHANISM AND DFT CALCULATIONS ON BASE HYDROLYSIS OF α-AMINO ACID ESTERS CATALYZED BY $[Pd(TMPDA)(H_2O)_2]^{2+}$

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Abstract

$Pd(TMPDA)Cl_2$ (TMPDA = *N,N,N`,N`*-tetramethyl-1,3-propanediamine) was synthesized and characterized by elemental analysis. $[Pd(TMPDA)(H_2O)_2]^{2+}$ reacts with amino acid esters (L) to form mixed ligand $[Pd(TMPDA)L]^{2+}$ complexes. The kinetics of base hydrolysis of $[Pd(TMPDA)L]^{2+}$ was studied by pH-stat technique and the corresponding rate constants are reported. The coordinated glycine methyl ester is efficiently hydrolyzed, whereas the coordinated methionine methyl ester is hydrolysed with a much lower catalytic activity. The catalytic influence is depended on the mode of coordination of the ester to the palladium complex. Probable mechanisms for these reactions are considered. Activation parameters for the hydrolysis of the coordinated glycine methyl ester were determined experimentally. DFT calculations (B3LYP/LANL2DZ) were applied to determine the possible mechanism of the base hydrolysis of the amino acid esters. The calculations are discussed in reference to the reported experimental data.

Keywords: N,N,N`,N`-tetramethyl-1,3-propanediamine; amino acid ester; catalytic hydrolysis; Pd(II), pH-stat technique; DFT calculations

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1. Introduction

Metal ions incorporated in metalloenzymes such as carbonic anhydrase [1], carboxypeptidase A [2] and alkaline phosphatase [3], play a significant role in many biological processes [4]. Metal ions in the site of metalloenzymes act as catalytic center by carrying substrate and nucleophile together during formation of a coordination complex to stimulate the substrate carbonyl group and hence facilitate attack of the nucleophile in carboxypeptidase A [5]. To elucidate the mechanism by which the metalloenzyme may function and consequently provide a theoretical base for designing highly effective artificial metalloenzymes. Former reports [6,7] have examined biomimetic models for metalloenzymes which catalyze the hydrolysis of carboxylic acid esters in biomimetic models for certain metalloenzymes, e.g. the metalloenzyme-substrate complex. Palladium(II) complexes are used as functional mimics of hydrolytic enzymes (hydrolases) and oxidoreductases [8]. Also, a soft metal ion as Pd(II) stimulates the hydrolysis of amino acid esters that have a soft donor sulfur atom as in the case of esters having the biologically active methionine moiety [9].

Diamine complexes may undergo catalytic hydrolysis of the ester group, existing as functional group in biological fluids. Work in our laboratory [10-19] has dedicated on study of ternary complexes of biological significance and its catalytic activity for hydrolysis of various amino acid esters. Based on the above, it is of considerable interest to study the catalysis of base hydrolysis of amino acid esters by $[Pd(TMPDA)(H_2O)_2]^{2+}$. DFT (B3LYP/LANL2DZ) calculations were used to account for the catalytic activity of ester hydrolysis, where every species in the DFT calculated mechanism for hydrolysis were treated as a different isomer of the same compound.

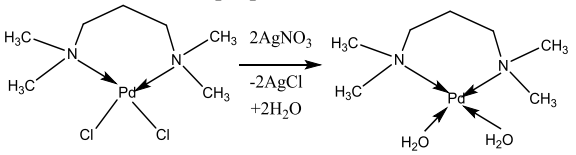
2. Experimental

2.1 Materials and reagents

All the reagents used are of AR grade. $PdCl_2$ and N,N,N`,N`-tetramethyl-1,3-propanediamine were provided by Aldrich. The glycine methyl ester (GlyOMe) and methionine methyl ester (MethOMe) were obtained from Fluka.

$[Pd(TMPDA)Cl_2]$ was prepared by heating $PdCl_2$ (177.33 mg; 1.0 mmol) and KCl (149.1mg; 2.0 mmol) in the least amount of water to 70˚C with stirring. The clear solution of $[PdCl_4]^{2-}$ solution was cooled to 25ºC, filtered and N,N,N`,N`-tetramethyl-1,3-propane diamine, (130.23 mg; 1.0 mmol) was added to the stirred solution. The solution was evaporated to a small volume (20ml) under vacuum then an orange crystalline precipitate of $[Pd(TMPDA)Cl_2]$ was formed on cold. The precipitate was filtered off and washed with H2O, ethanol and ether. An orange crystalline precipitate was obtained; yield 92%. Anal. Calcd. for $C_7H_{18}N_2PdCl_2$ (%) (MW = 307.56): C, 27.34; H, 5.90; N, 9.11. Found: C, 27.3; H, 5.8; N, 9.2.

$[Pd(TMPDA)Cl_2]$ is converted into the diaqua complex by treating with two equivalents of $AgNO_3$ as described before [20].



$Pd(TMPDA)Cl_2$ $Pd(TMPDA)(H_2O)_2$

2.2. Kinetic measurements

Metrohm 751 Titrino was used to monitor the kinetics of hydrolysis using SET mode (titration with preset end point). The electrode and titroprocessor were calibrated according to NIST [21], with standard buffer solutions. Hydrolysis kinetics of glycine- and methionine -methyl esters coordinated to $[Pd(TMPDA)(H_2O)_2]^{2+}$ were investigated by pH-stat technique [22, 23]. A solution mixture (40 cm^3) containing $[Pd(TMPDA)(H_2O)_2]^{2+}$ (2.5 x 10^{-3} M), ester (2.5 x 10^{-3} M) and $NaNO_3$ (0.1 M) was equilibrated at the required temperature under nitrogen atmosphere and the pH was brought to the desired value by the addition of 0.05 M NaOH solution. NaOH solutions (carbonate-free) were prepared and standardized against solutions of potassium hydrogen phthalate. All solutions were prepared in deionized water. The hydrolysis was then followed by the addition of 0.05 M NaOH solution to maintain a constant pH. The fitting of the data was done using the OLIS KINFIT program [24] as previously described [10]. The precision of the data was tested from plots obtained from the OLIS program where the accepted residual values were less than 3 mV. The hydroxide ion concentration values were estimated from the pH using $pK_w = 13.997$, and an activity coefficient (γ) of 0.772 that was determined from the Davies equation [25]. For the variable temperature studies, the following values of pK_w and γ were employed [21], at 15 ^oC (pK_w = 14.35, γ = 0.776), at 20 ^oC (pK_w = 14.16, γ = 0.774) at 25 ^oC (pK_w = 14.00, γ = 0.772), at 30 ^oC (pK_w = 13.83, γ = 0.770), and at 35 ^oC (pK_w = 13.68, γ = 0.768).

2.3. Quantum Chemical Method

For all calculations, the B3LYP functional in combination with the LANL2DZ basis set [27] was applied. The characterization as minima was done by computation of vibrational frequencies at the same level. All calculations were performed using the Gaussian 09 program package [28].

3. Results and discussion

The reaction between α-amino acid esters and $[Pd(TMPDA)(H_2O)_2]^{2+}$ can be presented as in equilibrium (1):

$$[Pd(AEMP)(H_2O)_2]^{2+} + {}^{+}NH_3CH(R)CO_2R` \rightleftharpoons [Pd(AEMP)\{NH_2CH(R)CO_2R`\}]^{2+} + H_3O^{+} + H_2O \quad (1)$$

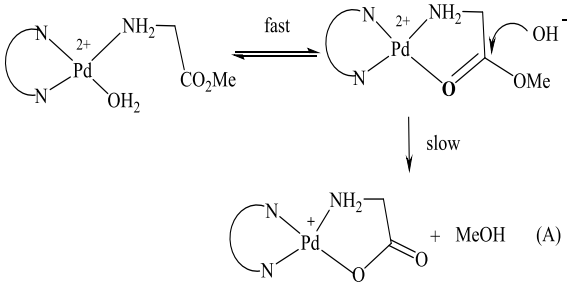
The equilibrium constant K is sufficiently large that in a medium with pH larger than 5.0 for 1:1 ratios of the palladium complex to α-amino acid esters, formation of the mixed-ligand complex is effectively complete [22]. Thus one mole of base is consumed per mole of complex formed and $NH_2CH(R)CO_2R`$ is bound almost entirely as [Pd(TMPDA) $\{NH_2CH(R)CO_2R`\}$]. The possible hydrolysis of uncoordinated α-amino acid ester may be neglected.

The coordinated α-amino acid ester can be hydrolyzed by H_2O and OH^- as given in eq. (2) and (3), respectively.

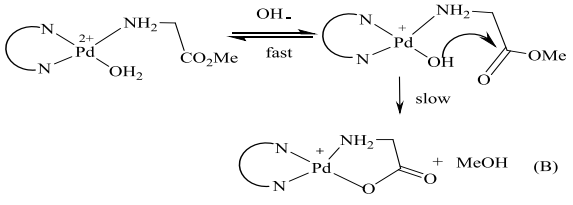
$$[Pd(TMPDA)\{NH_2CH(R)CO_2R`\}]^{2+} + H_2O \xrightarrow{k_o} [Pd(TMPDA)NH_2CH(R)COO]^{+} + R`OH + H^{+} \quad (2)$$

$$[Pd(TMPDA)\{NH_2CH(R)CO_2R`\}]^{2+} + OH^- \xrightarrow{k_{OH}} [Pd(TMPDA)NH_2CH(R)COO]^{+} + R`OH \quad (3)$$

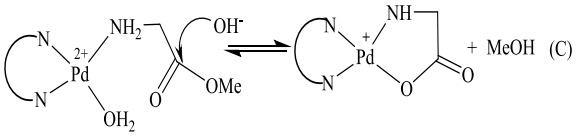
Under the conditions used here the $NH_2CH(R)CO_2R`$ is bound almost entirely as [Pd(TMPDA)$\{NH_2CH(R)$ $CO_2R`\}]^{2+}$. Therefore, the observed rate law represents steps (2), (3). The first-order dependence on OH^- concentration may be accounted for by three mechanisms [29]. One involves a rapidly established equilibrium in which the carbonyl oxygen of ester group coordinates to the metal, followed by rate determining OH^- attack, mechanism (A).



The second involves rapid equilibrium formation of a Pd-OH complex, followed by intramolecular OH^- attack, mechanism (B).



The third involves only OH^- attacks at the ester carbonyl carbon of a non-coordinated ester group, mechanism (C).



The data fitting was performed with OLIS KINFIT Set of programs [24]. A typical volume of base-time trace for the hydrolysis of coordinated glycine methyl ester fitted with one exponential function using OLIS KINFIT is shown in Fig 1.

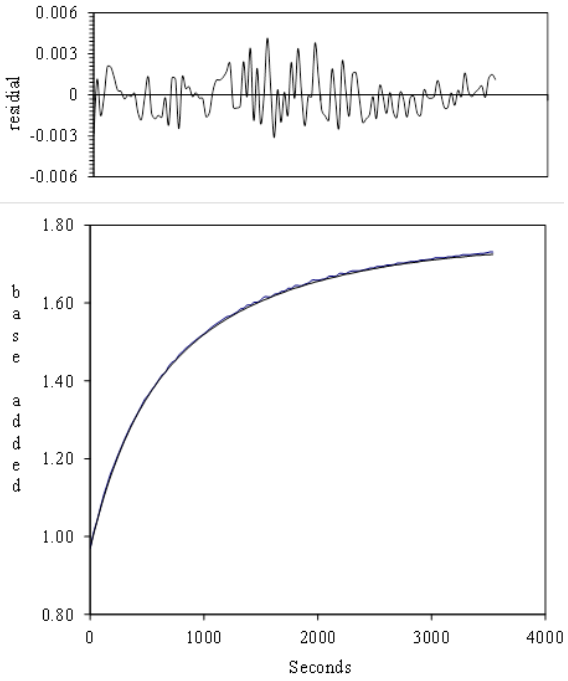


Fig. 1. Typical volume of base vs. time trace, fitted with one exponential, for the hydrolysis reaction of $[Pd(TMPDA)GlyOMe]^{2+}$ at 25^0C and 0.1M ionic strength.

The values of $k_{obs.}$ (the observed pseudo-first-order rate constant at constant pH) were obtained and summarized in Table 1. Plots of k_{Obs} versus the hydroxide ion concentration were linear with a positive intercept, Figures 2 and 3.

Various other kinetic models were tested without leading to satisfying fits of the data. The rate expression is therefore of the form Eq. (4) & (5).

$$Rate = k_{Obs.}[Pd(TMPDA)(ester)] \quad (4)$$

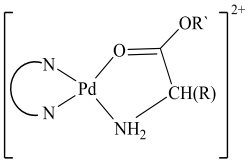
$$k_{Obs} = k_o + k_{OH}[OH^-] \quad (5)$$

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 linear dependence of the rate on the OH^-

concentration is consistent with the direct attack of OH^- ion on the coordinated ester carbonyl group as given in mechanism (A). On the other hand, mechanism (B) requires that the plot of $k_{obs.}$ versus the hydroxide ion concentration is not linear, while a plot of $1/k_{Obs.}$ versus $1/[OH^-]$ should be linear. The rate constants k_{OH}^{ester} previously reported [30] for the base hydrolysis reaction, equation (6) are given in Table 3.

$$NH_2CH(R)CO_2R` + OH^- \xrightarrow{k_{OH}^{free\ ester}} NH_2CH(R)CO_2^- + R`OH \qquad (6)$$

For the α-amino acid esters "glycine methyl ester (GlyOMe) the rate of accelerations denoted by the rate ratio (k_{OH}/k_{OH}^{ester}) is quite substantial, 1.45×10^5 for (GlyOMe) with $[Pd(TMPDA)ester]^{2+}$ (Table 3). Rate acceleration of this magnitude are fully consistent with the formation of the mixed-ligand complex as in mechanism (A), where there is a direct interaction between Pd(II) and the alkoxycarbonyl group of the ester species (Structure I). Methionine ester act as bidentate without invoking any interaction with alkoxycarbonyl group. The kinetic data of MethOMe complexe (the volume of base added to keep the pH constant versus time) could be fitted by applying only one exponential. Values of $k_{Obs.}$ versus the hydroxide ion concentration are allotted in Table 1.



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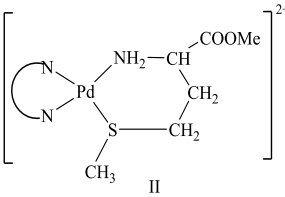

II

The linear plots of k_{Obs} versus the hydroxide ion concentrations are represented in Figures 2 and 3. They reveal that hydrolysis proceeds by intermolecular mechanism. The catalysis ratio of methionine-methyl ester (MethOMe) complexe amounts to 13.2 for $[Pd(TMPDA)ester]^{2+}$, Table 3. The relatively small catalysis-ratio values suggest that in these cases the alkoxycarbonyl group is not bonded to the metal ion.

A number of previous studies [30-32] have shown that the formation of such complexes with ester groups lead only to relatively small rate accelerations, i.e. if the ester carbonyl was otherwise, directly bonded to Pd(II), we would have found much higher catalysis ratios.

In order to distinguish between these mechanisms; activation parameters for the hydrolysis of coordinated ester were determined using the Eyring plot [31] of $(\ln k_{OH}/T)$ versus $1/T$, according to equation (7):

$$\ln(k_{OH}/T) = (\ln(k/h) + \Delta S^{\neq}/R) - \Delta H^{\neq}/R(1/T) \qquad (7)$$

Where: $h = 6.626\times10^{-34}$ J.s. Planck's constant

$k = 1.381\times10^{-23}$ $J.K^{-1}$ is Boltzmann's constant

$R = 8.314$ $J.mol^{-1}$ K^{-1} is the universal gas constant

T is the absolute temperature

$\Delta H^{\neq}$ and $\Delta S^{\neq}$ are the activation parameters of enthalpy change and entropy change, respectively. The slope is $-\Delta H^{\neq}/R$ and the intercept is related to $\Delta S^{\neq}$ by equation (8) where k, h and R are the Boltzmann, Plank and gas constants, respectively.

Table.1. Kinetic of hydrolysis of $[Pd(TMPDA)(ester)]^{2+}$ at 25°C and 0.1M ionic strength.

Ester	pH	$[OH^-]$	k_{obs} (s^{-1})
Glycine methyl ester			
	4.8	7.94E-10	6.47E-04
	5.0	1.26E-09	7.28E-04
	5.2	2.00E-09	8.90E-04
	5.4	3.16E-09	1.04E-03
	5.6	5.01E-09	1.27E-03
Methionine methyl ester			
	8.8	7.94E-06	1.57E-04
	9.0	1.26E-05	2.12E-04
	9.2	2.00E-05	2.79E-04
	9.4	3.16E-05	4.05E-04
	9.6	5.01E-05	5.63E-04

Table 2. Hydrolysis data ($dm^3mol^{-1}s^{-1}$) of $[Pd(TMPDA)(GlyOMe)]^{2+}$ at different temperatures in aqueous solution at pH=5.4.

t ºC	k_{OH}	k_{H2O}
15	9.65E+04	1.015E-05
20	1.19E+05	1.032E-05
25	1.41E+05	1.049E-05
30	1.91E+05	1.065E-05
35	2.29E+05	1.082E-05

Table 3. Hydrolysis data ($dm^3mol^{-1}s^{-1}$) of $[Pd(TMPDA)(ester)]^{2+}$ at 25°C and 0.1M ionic strength.

Ester	k_{OH}	k_{H2O}	$k_{OH}^{(ester)a}$	$k_{OH}/k_{OH}^{(ester)}$
Glycine methyl ester				
	1.41E+05	1.05E-05	1.28	1.10E+05
Methionine methyl ester				
	9.61	1.59E-06	0.767	12.5

[a]Data from [ref. 32].

The values of $\Delta H^{\neq}$ and $\Delta S^{\neq}$ were calculated to be $\Delta H^{\neq}$ = 29.9(±0.2) $kJmol^{-1}$, $\Delta S^{\neq}$ = -45.4(±0.3) $JK^{-1}mol^{-1}$ respectively. For the base of hydrolysis free glycine methyl ester the activation parameter were found [32] to be $\Delta H^{\neq} = 39.7$ $kJmol^{-1}$, $\Delta S^{\neq} = -117$ $JK^{-1}mol^{-1}$.

$$\Delta S^{\neq} = [\text{intercept}-\ln(k/h)]R \qquad (8)$$

The enhanced rate for base hydrolysis of the ester incorporated in the complex $[Pd(N\text{-}N)L]^{2+}$ is

therefore due to contributions from a decreased $\Delta H^{\neq}$ and an increased $\Delta S^{\neq}$. The increase in $\Delta S^{\neq}$ implies disolvation between the ground and transition states and is revealing of a mechanism comprising nucleophilic attack by external OH^- on the complexed ester group as shown in mechanism (A).

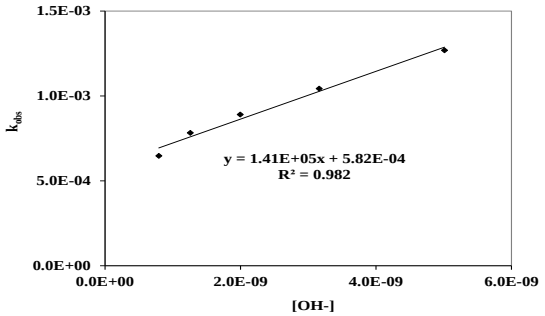

Fig. 2. Kintetics hydrolysis of Pd(TMPDA)-glycine methyl ester.

DFT Calculations

Molecular Modelling of Amino Acid Esters

DFT calculations have been carried out to investigate the equilibrium geometry of glycine methyl ester (GME) and methionine methyl ester (MME) and their complex species $[Pd(TMPDA)GME]^{2+}$ and $[Pd(TMPDA)MME]^{2+}$ before hydrolysis. Also, DFT calculations have been carried out to their products after base hydrolysis: $[Pd(TMPDA)Gly]^{+}$ and $[Pd(TMPDA)MME]^{+}$ using Gaussian 09 program [28] at the B3LYP//LANL2DZ level of theory.

Figures 4 and 5 show the optimized structures of the above species as the most stable configurations. Figure 6 shows the optimized structures of the coordinated GME and MME after hydrolysis.

The palladium centre has a typical square-planar geometry with some distortion.

Glycine methyl ester (GME) and methionine methyl ester (MME) act as bidentate chelates, forming a five and six-membered rings, respectively. The optimized bond lengths and bond angles of GME and MME compared to their complexes before and after base hydrolysis are listed in Tables 4 and 5.

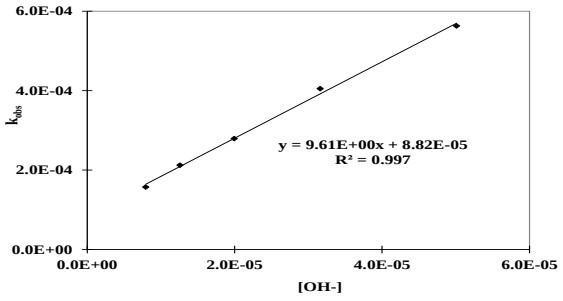

Fig. 3. Kintetics hydrolysis of Pd(TMPDA)-methionine methyl ester.

The values of angles around Pd atom are close to 90°, see Table (5). The distance between N1- - -O1 = 2.848Å, in free GME is lower upon complex formation to N3- - -O1 = 2.735Å in $[Pd(TMPDA)GME]^{2+}$. Similarly, the distance between N1- - -S= 4.757Å, in free MME is lower upon complex formation to N3- - -S = 2.922Å in $[Pd(TMPDA)MME]^{2+}$.

The following conclusions were obtained confirming the proposed mechanism of hydrolysis and the larger catalytic hydrolysis in case of coordinated GME ($k_{OH} = 1.41x10^{+5}$) compared to coordinated MME ($k_{OH} = 9.61$):

1. The charges on carbonyl carbons of the coordinated ester in $[Pd(TMPDA)GME]^{2+}$ and $[Pd(TMPDA)MME]^{2+}$ are more positive and those the free esters indicating enhancing hydrolysis through the attack of OH^- on carbonyl carbons as proposed mechanism.
2. The larger catalytic hydrolysis of coordinated GME ($k_{OH} = 1.41x10^{+5}$) compared to coordinated MME ($k_{OH} = 9.61$) was attributed to direct involvement of carbonyl oxygen in case of the coordinated GME ($[Pd(TMPDA)GME]^{2+}$) and this is confirmed by larger positive formal charge on C7=+0.890 (more than that of free GME by, 0.890-0.806 = 0.084) compare to smaller positive charge, in case of MME, on C7=+0.841 (more than that of free MME by only, 0.841-0.836 = 0.005).
3. The bonds involving the coordination are elongated in coordinated GME ($[Pd(TMPDA)GME]^{2+}$) (C8=O1) and (N3-C9) compared to those in free GME, Table(4).
4. The more negative values of total energies of the complexes of coordinated esters $[Pd(TMPDA)GME]^{2+}$ (-836.972 a.u.) and $[Pd(TMPDA)MME]^{2+}$ (-964.995 a.u.) before hydrolysis compared to those of free esters (-323.671 and -451.700 a.u., respectively) indicate that the formers are more stable, Table (6).
5. Pathway (A) involves first a fast ring-closure reaction to displace the weakly coordinated water molecule, followed by base hydrolysis of the ester. In the case of GlyOMe, the carbonyl group of the ester coordinates to the metal, whereas in the other two cases the aliphatic nitrogen atom is involved in the ring-closure process. The next step is the rate-determining attack by OH^-.
6. The alternative path B involves rapid formation of a Pd-OH complex, followed by an intra-molecular attack by OH^-. This path cannot be correct since the Pd-OH bond is known to be extremely strong such that in the case of all three α-amino acid esters an intermediate is formed that is much more stable than the species formed in path (A). Therefore, path (A) seems to be the more logic option from a chemical point of view. This is also in agreement with the experimental data since the reaction shows

a linear dependence on the OH^- concentration with a significant intercept in the case of the glycine methyl ester, which can be ascribed to the parallel water reaction path.

Table 4. Important optimized bond lengths (Å) of {GME, $[Pd(TMPDA)GME]^{2+}$ and $[Pd(TMPDA)Gly]^{+}$} and {HME, $[Pd(TMPDA)MME]^{2+}$ and $[Pd(TMPDA)Meth]^{+}$}.

GME	$[Pd(TMPDA)GME]^{2+}$ before hydrolysis	$[Pd(TMPDA)Gly]^{+}$ after hydrolysis
N1-C2 = 1.456	N3-C8 = 1.511	N3-C8 = 1.515
C1=O1 = 1.235	C7=O1 = 1.277	C8=O1 = 1.237
-	Pd-N1 = 2.129	Pd-N1 = 2.140
-	Pd-N2 = 2.136	Pd-N2 = 2.170
-	Pd-N3 = 2.179	Pd-N3 = 2.135
-	Pd-O1 = 2.116	Pd-O2 = 2.012
N1- - -O1 = 2.848	N3- - -O1 = 2.721	
MME	$[Pd(TMPDA)MME]^{2+}$ before hydrolysis	$[Pd(TMPDA)Meth]^{+}$ after hydrolysis
N1-C2 = 1.464	N3-C9 = 1.518	N3-C9 = 1.517
C1=O1 = 1.243	C10=O1 = 1.249	C10=O1 = 1.242
-	Pd-N1 = 2.195	Pd-N1 = 2.194
-	Pd-N2 = 2.153	Pd-N2 = 2.151
-	Pd-N3 = 2.127	Pd-N3 = 2.134
-	Pd-S = 2.584	Pd-S = 2.582
N1- - -S = 4.757	N3- - -S = 2.922	N3- - -S = 2.925

Table 5. Important optimized bond angles (°) of GME, [Pd (TMPDA)GME]$^{2+}$ and [Pd(TMPDA)Gly]$^{+}$.

$[Pd(TMPDA)GME]^{2+}$ before hydrolysis	$[Pd(TMPDA)Gly]^{+}$ after hydrolysis
N1-Pd-O1 = 89.70	N1-Pd-O2 = 85.10
N1-Pd-N2 = 96.48	N1-Pd-N2 = 98.57
N2-Pd-N3 = 95.31	N2-Pd-N3 = 95.59
N3-Pd-O1 = 78.45	N3-Pd-O2 = 80.78
N1-Pd-N3 = 168.1	N1-Pd-N3 = 165.8
N2-Pd-O1 = 171.6	N2-Pd-O2 = 175.1
N1-N2-N3-O1 = -3.494*	N1-N2-N3-O2 = -2.577*
$[Pd(TMPDA)MME]^{2+}$ before hydrolysis	$[Pd(TMPDA)Meth]^{+}$ after hydrolysis
N1-Pd-N2 = 97.19	N1-Pd-N2 = 97.22
N2-Pd-S = 97.0	N2-Pd-S = 97.21
N1-Pd-N3 = 88.93	N1-Pd-N3 = 88.95
N3-Pd-S = 75.96	N3-Pd-S = 75.97
N2-Pd-N3 = 173.3	N2-Pd-N3 =173. 4
N1-Pd-S = 163.3	N1-Pd-S =163.2
N1-N2-S-N3 = 3.737*	N1-N2-S-N3 = 4.140*

*dihedral angle

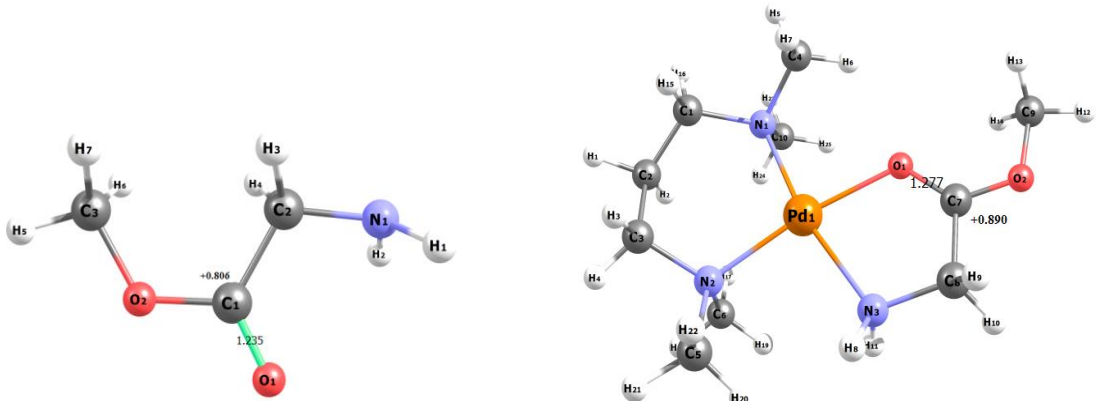

Fig. 4. Optimized structures of GME (upper) and coordinated GME ($[Pd(TMPDA)GME]^{2+}$) (lower) by DFT method using B3LYP/LANL2DZ functional.

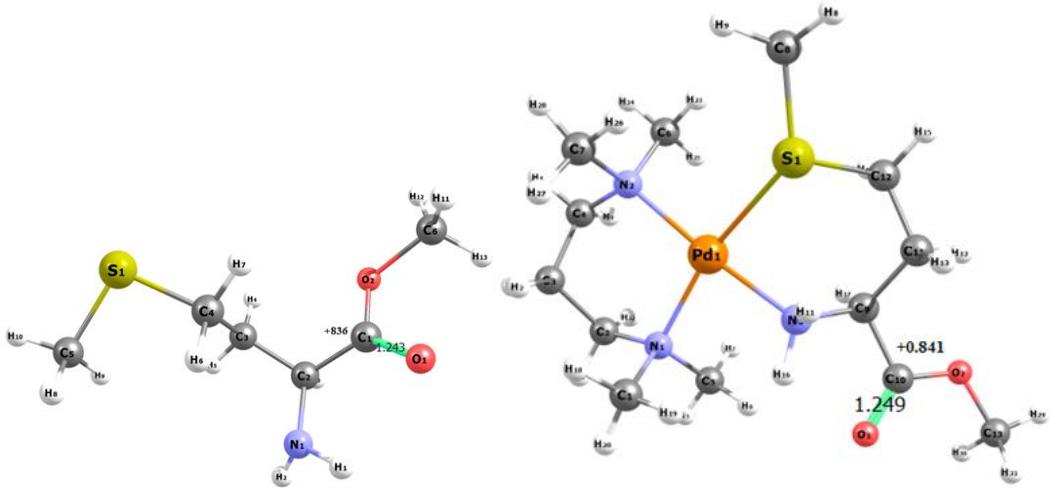

Fig. 5. Optimized structures of Methionine (upper) and $[Pd(TMPDA)MME]^{2+}$ (lower) by DFT method using B3LYP/LANL2DZ functional.

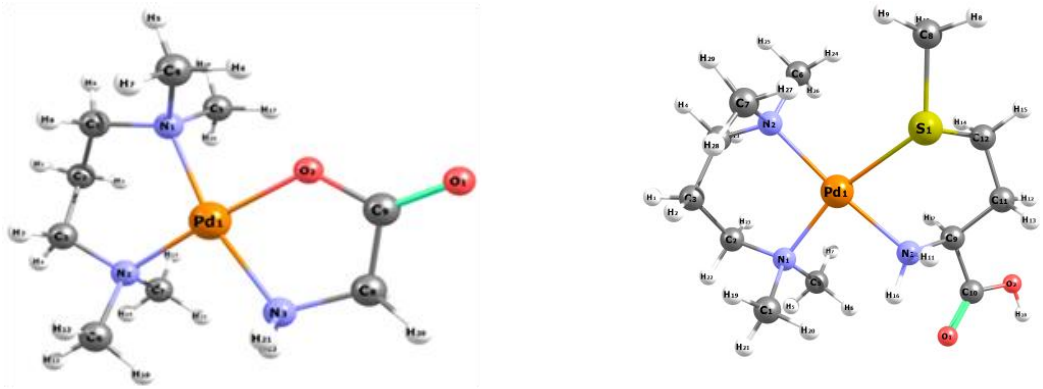

Fig. 6. Optimized structure of coordinated esters after hydrolysis $[Pd(TMPDA)Gly]^{+}$ (left) and $[Pd(TMPDA)Meth]^{+}$ (right), by DFT method using B3LYP/LANL2DZ functional.

Table 6. Calculated energies of GME, MME and their complexes $[Pd(TMPDA)\ GME]^{2+}$, $[Pd(TMPDA)Gly\text{-}H]^{+}$, $[Pd(TMPDA)MME]^{2+}$ and $[Pd(TMPDA)MME\text{-}H]^{+}$ at B3LYP/LANL2DZ.

	E[a]	HOMO[b]	LUMO[c]	ΔE[d]	Dipole moment[d]
GME	-323.671	-6.5232	-0.3660	6.1572	4.0481
$[Pd(TMPDA)GME]^{2+}$	-836.972	-14.1049	-9.8925	4.2124	2.2715
$[Pd(TMPDA)Gly\text{-}H]^{+}$	-797.401	-9.9505	-5.8718	4.0787	10.1326
MME	-451.700	-5.7460	-0.5665	5.1795	2.6129
$[Pd(TMPDA)MME]^{2+}$	-964.995	-13.7016	-9.6963	4.0053	3.7281
$[Pd(TMPDA)Meth\text{-}H]^{+}$	-925.691	-13.8216	-9.8261	3.9955	3.2826

[a]E: the total energy (a.u.). [b] HOMO: highest occupied molecular orbital (eV).
[c]LUMO: lowest unoccupied molecular orbital (eV).
[d]ΔE:E_{LUMO}- E_{HOMO} (eV). [e]Dipole: dipole moment calculated (Debye).

Conclusions

The present investigation draws a more general picture of biological applications of Pd(II) complexes as outlined in the Introduction. The reaction of the diaqua species $Pd(TMPDA)(H_2O)_2^{2+}$ with amino acid esters leads to the formation the complex with a chelated ester. The concentration of each species depends on the pH of the medium and the stability constant of the complex. The hydrolysis of the

glycine methyl ester is catalyzed significantly by $[Pd(TMPDA)(H_2O)_2]^{2+}$ with a catalytic ratio of 1.10 x 10^5. This is due to the binding of the Pd(II) complex directly to the carbonyl group of the ester which accounts for the enormous catalytic effect. However, the catalytic effect of the complex on the methionine-methyl esters is not strong with catalytic ratios of 12.5 for the mentioned esters, due to the extended distance of the carbonyl group away from the metal center. The mechanism of hydrolysis was discussed in detail. A mechanism involving the direct interaction of OH^- with the carbonyl carbon atom was suggested. The activation parameters were determined for the hydrolysis of the coordinated glycine methyl ester. The values were compared to those of the free ester and the proposed mechanism was supported. DFT calculations allowed the optimization of the structure of the glycine- and methionine-methyl ester complexes before, during and after hydrolysis. The calculations throw light on the mechanism of the base hydrolysis process.

5. Conflicts of interest

There are no conflicts to declare.

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الملخص العربي

دراسة حركية وميكانيكية وحسابات DFT للتميؤ القاعدى لاسترات الاحماض الامينية المحفز بواسطة المتراكب $[Pd(TMPDA)(H_2O)_2]^{2+}$

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اهتم هذا البحث بدراسة حركية وميكانيكية التميؤ القاعدى لاسترات الاحماض الامينية المحفز بواسطة المتراكب $[Pd(TMPDA)(H_2O)_2]^{2+}$. لقد تم تحضير المتراكب $Pd(TMPDA)Cl_2$ والتعرف على تركيبه بتحليل العناصر كما تم تفاعل $[Pd(TMPDA)(H_2O)_2]^{2+}$ مع استرات الاحماض الامينية مكونا متراكبات مختلطة المرافق $[Pd(TMPDA)L]^{2+}$. وتم دراسة حركية التميؤ القاعدى لها وحساب ثابت التميؤ. ووجد ان الميثيل جليسين استر التناسقى يتميؤ بكفاءة عالية مقارنة بالميثيل ميسونين استر التناسقى و يعزى ذلك الى ان النشاط التحفيزى يعتمد على كيفية ارتباط الاستر بمتراكب البالديوم. وقد تم تعيين ثوابت التنشيط الحفزى لتميؤ الميثيل جليسين استر التناسقى عمليا. كما تم تطبيق حسابات DFT لتحديد الميكانيكية المحتملة للتميؤ القاعدى لاسترات الاحماض الأمينية كما تم مناقشة القيم المحسوبة مع ماتم تعينه عمليا.