Journal of Coordination Chemistry

ISSN: 0095-8972 (Print) 1029-0389 (Online) Journal homepage: http://www.tandfonline.com/loi/gcoo20

Thermal stability of Pd(1,4-bis(2-hydroxyethyl)piperazine)Cl_2 and its role in the catalysis of base hydrolysis of α-amino acid esters

Mohamed R. Shehata, Mohamed M. Shoukry, Shokry A. Shokry & Mahmoud A. Mabrouk

To cite this article: Mohamed R. Shehata, Mohamed M. Shoukry, Shokry A. Shokry & Mahmoud A. Mabrouk (2015) Thermal stability of Pd(1,4-bis(2-hydroxyethyl)piperazine)Cl_2 and its role in the catalysis of base hydrolysis of α-amino acid esters, Journal of Coordination Chemistry, 68:17-18, 3272-3281, DOI: 10.1080/00958972.2015.1061659

To link to this article: http://dx.doi.org/10.1080/00958972.2015.1061659

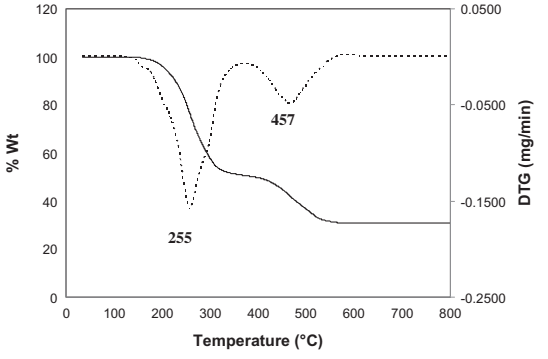
Journal of Coordination Chemistry, 2015
Vol. 68, Nos. 17–18, 3272–3281, http://dx.doi.org/10.1080/00958972.2015.1061659

Thermal stability of Pd(1,4-bis(2-hydroxyethyl)piperazine)Cl_2 and its role in the catalysis of base hydrolysis of α-amino acid esters

MOHAMED R. SHEHATA†, MOHAMED M. SHOUKRY*†, SHOKRY A. SHOKRY‡ and MAHMOUD A. MABROUK‡

†Faculty of Science, Department of Chemistry, Cairo University, Giza, Egypt
‡Science and Technology Center of Excellence (STCE), Ministry of Military Production, Cairo, Egypt

(*Received 27 February 2015; accepted 6 May 2015*)



The thermal stability of Pd(BHEP)Cl_2 complex was investigated. The role of the complex in the catalysis of amino acid esters was studied.

Pd(BHEP)Cl_2 was synthesized and characterized (BHEP = 1,4-bis(2-hydroxyethyl)piperazine). The complex decomposes in two steps, leaving a residue of palladium metal. Amino acid ester (L) reacts with $[Pd(BHEP)(H_2O)_2]^{2+}$ (BHEP = 1,4-bis(2-hydroxyethyl)piperazine), giving mixed-ligand complexes, $[Pd(BHEP)L]^{2+}$. The kinetics of hydrolysis of $[Pd(BHEP)L]^{2+}$ 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 is much less marked, as the mixed-ligand complexes with these ligands do not involve alkoxycarbonyl donors. Possible mechanisms for these reactions are considered.

Keywords: 1,4-Bis(2-hydroxyethyl)piperazine; Thermal stability; Amino acid ester hydrolysis; Pd(II); pH-stat technique

*Corresponding author. Email: shoukrymm@hotmail.com
Dedicated to Prof. Rudi van Eldik on the occasion of his 70th birthday.

1. Introduction

Piperazines or cyclizines are generally considered as ethylenediamine derivatives or cyclic ethylenediamines (cyclizines). Piperazines are a broad class of compounds with many important pharmacological properties. This dinitrogen moiety has been a component of a plethora of drugs. Piperazines have chemical similarity with piperidine, a constituent of piperine in the black piper plant (Piper nigrum). Piperazine was introduced into medicine as a solvent for uric acid [1]. Metal ions in metalloenzymes such as carboxypeptidase A [2], carbonic anhydrase [3] and alkaline phosphatase [4] play key roles in many biochemical processes [5]. In these metal-containing metalloenzymes, metal ions at the active sites are considered to serve as a primary catalytic center for bringing substrate and nucleophile together through formation of a coordination complex, to activate the substrate carbonyl group facilitating attack of the nucleophile as hydroxide. In order to probe the mechanism by which the metalloenzyme may operate and consequently provide a theoretical base for designing effective artificial metalloenzymes, previous reports [6–8] have developed biomimetic models for metalloenzyme, which catalyze the hydrolysis of carboxylic acid esters in biomimetic models.

Work in our laboratory [9–14] has focused on catalysis of the hydrolysis of various amino acid esters by metal complexes. $[Pd(en)L]^{2+}$ undergoes hydrolysis by water and hydroxide ion [15]. It is therefore of considerable interest to extend this work to study the thermal stability of Pd(II) complexes with 1,4-bis(2-hydroxyethyl)piperazine and its role in the catalysis of amino acid esters. The results of this investigation are expected to support the biological activity of the piperazine derivative.

2. Experimental

2.1. *Materials and reagent*

All reagents were of Analar grade. K_2PdCl_4 and 1,4-bis(2-hydroxyethyl)piperazine are provided by Aldrich. The glycine- 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.

2.2. *Preparation of the complex*

$Pd(BHEP)Cl_2$ was prepared by dissolving K_2PdCl_4 (0.92 g, 2.82 mmol) in 10 mL water with stirring. The clear solution of $[PdCl_4]^{2-}$ was filtered and 1,4-bis(2-hydroxyethyl) piperazine (0.491 g, 2.82 mmol) dissolved in 10 mL H_2O was added dropwise to the stirred solution. The pH was adjusted to 2–3 by addition of HCl and/or NaOH. A yellowish-brown precipitate of $Pd(BHEP)Cl_2$ was formed and stirred for a further 30 min at 50 °C. After filtering off the precipitate, it was thoroughly washed with H_2O, ethanol, and diethyl ether. An orange crystalline precipitate was obtained after recrystallization from 2 : 1 methanol/water mixture. (Found: C, 27.3; H, 5.3; N, 7.8%. Calcd for $C_8H_{18}N_2O_2PdCl_2$ (F.Wt = 351.55): C, 27.33; H, 5.17; N, 7.97%). IR: ν_{O-H} (st) at 3429 cm^{-1}, ν_{C-H} (st) at 3018, 2983, 2949, and 2891 cm^{-1}, ν_{Pd-N} at 472 cm^{-1}, ν_{Pd-Cl} at 333 and 324 cm^{-1}.

Aqueous solutions of the diaqua form of $Pd(BHEP)Cl_2$ were prepared *in situ* by addition of slightly less than two mole equivalents of $AgNO_3$ to a solution of a known amount of

the dichloro complex and stirred overnight. The white precipitate of AgCl that formed was filtered off using a 0.1-μm 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.

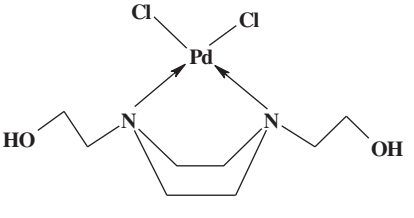
2.3. *Instrumentation and measurements*

IR spectra were recorded on a 8001-PC FT-IR Shimadzu spectrophotometer using KBr pellets. Thermogravimetric measurements (TGA, DTA, 20–1000 °C) were recorded on a DTG-50 Shimadzu thermogravimetric analyzer at a heating rate of 10 °C min^{-1} and nitrogen flow rate of 20 mL min^{-1}.

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 [16]. Hydrolysis kinetics of glycine- and methionine methyl esters in the presence of $[Pd(BHEP)(H_2O)_2]^{2+}$ are investigated by pH-stat technique [17, 18]. After equilibrating a solution mixture (40 cm^3) containing $[Pd(BHEP)(H_2O)_2]^{2+}$ (5.0×10^{-3} M) (the concentration of Pd complex was taken twice that of ester to ensure that the ester is completely coordinated), ester (2.5×10^{-3} M) and $NaNO_3$ (0.1 M) at the required temperature under nitrogen flow, the pH was brought to the desired value by the addition of 0.05 M NaOH solution. The hydrolysis was then followed by 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 [19] as described previously [20]. The precision of the kinetic data was estimated from the 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 [21]. At the variable temperature studies, the following values of pK_w and γ were employed [22] at 15 °C ($pK_w = 14.35$, $\gamma = 0.776$), at 20 °C ($pK_w = 14.16$, $\gamma = 0.774$), at 25 °C ($pK_w = 14.00$, $\gamma = 0.772$), at 30 °C ($pK_w = 13.83$, $\gamma = 0.770$) and at 35 °C ($pK_w = 13.68$, $\gamma = 0.768$).

3. Results and discussion

The analytical data indicated that the complex is of 1 : 1 stoichiometry and of formula Pd(BHEB)Cl_2, which is given in scheme 1. IR spectra of BHEP and Pd(BHEP)Cl_2 are compared (figures 1a and 1b). The stretching vibration of OH group of BHEP shows a broad band at 3151 cm^{-1}. This may be explained on the premise that the OH groups are involved



Scheme 1. Structure of [Pd(BHEP)Cl_2].

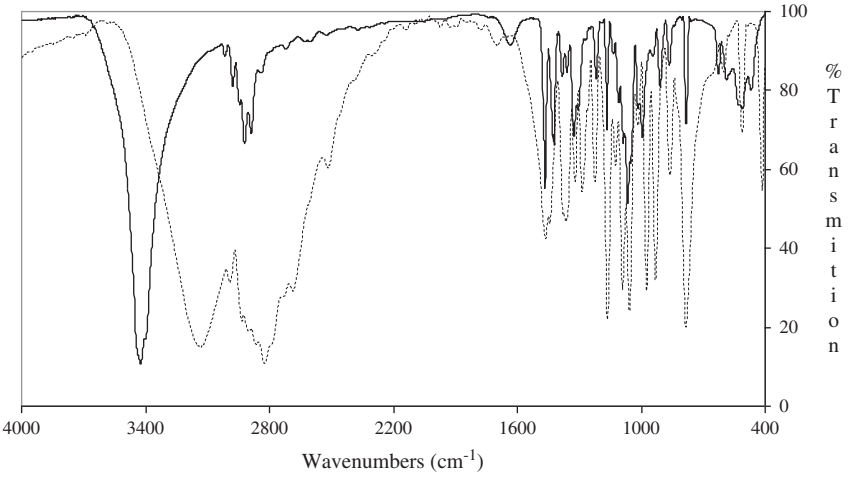


Figure 1a. Infrared spectrum of $[Pd(BHEP)Cl_2]$ (-) and ligand BHEP (. . .).

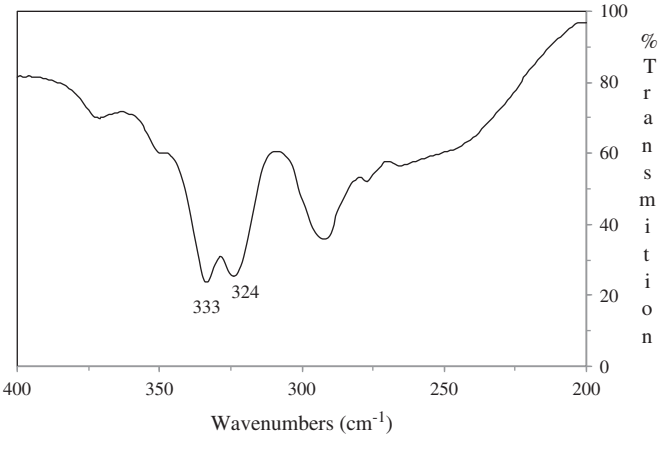


Figure 1b. Far-infrared spectrum of $[Pd(BHEP)Cl_2]$.

in hydrogen bonding. This band is sharp in the complex and occurs at 3429 cm^{-1}, which indicates that the OH groups are not involved in coordination. The stretching vibration band corresponding to ν_{Pd-N} was assigned at 472 cm^{-1}. The stretching vibration band corresponding to ν_{Pd-Cl} was found to be a doublet at 333 and 324 cm^{-1}, which confirm *cis* configuration of the two Pd–Cl bonds [23, 24].

3.1. *Thermal measurements*

Thermogravimetric studies (TG) for the complex were carried out from room temperature up to 1000 °C with a heating rate of 10° min^{-1}. TG data are displayed in figure 2.

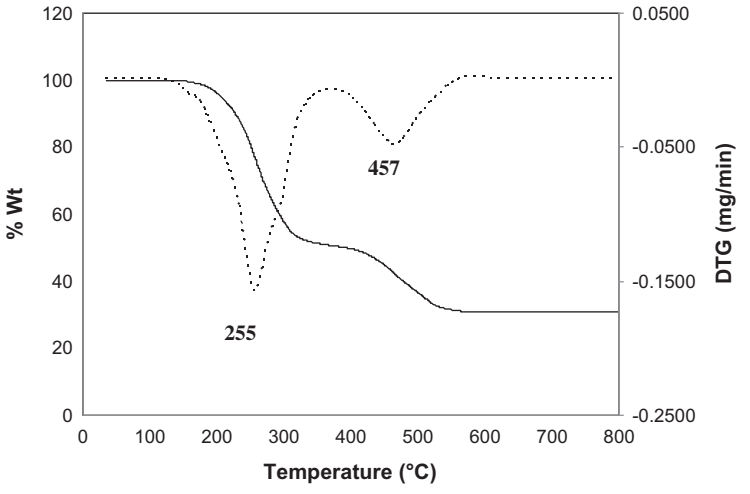


Figure 2. TGA (solid) and DrTGA (dotted) curves of $Pd(BHEP)Cl_2$.

Table 1. Scheme for TGA mass loss of $Pd(BHEP)Cl_2$ in the temperature range ~33–600 °C with heating rate of 10 min^{-1}.

Assignment loss	TGA (°C)	DrTGA (°C)	%Wt. Loss found (Calcd)
$L(C_8H_{18}N_2O_2)$	150–360	255	49.1 (49.56)
2Cl	360–560	457	20.3 (20.17)
Pd (residue)	>600		30.6 (30.26)

The determined temperature ranges and percent mass losses of the solid complex on heating are given table 1. Analysis of the data revealed the following findings:

The TG curve of $Pd(BHEP)Cl_2$ exhibits a first estimated mass loss of 49.1% (Calcd 49.56%) at 150–360 °C, which may be attributed to the liberation of $C_8H_{18}N_2O_2$ as gasses. The second estimated mass loss of 20.3% (Calcd 20.17%), at 360–560 °C, may be attributed to the liberation of 2Cl atoms as gasses. The residue corresponds to palladium metal 30.6% (Calcd 30.26%).

3.2. *The catalysis of base hydrolysis of α-amino acid esters*

α-Amino acid esters react with $[Pd(BHEP)(H_2O)_2]^{2+}$ according to equilibrium (1). The equilibrium constant is expected to be >>1. This is due to the high affinity of Pd^{II} to N-ligands [10]. The resulting mixed-ligand complexes $[Pd(BHEP)L]^{2+}$ $[L = NH_2CH(R)CO_2R']$ undergo hydrolysis by water and hydroxide ion according to equations (2) and (3).

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

$$[Pd(BHEP)L]^{2+} + H_2O \xrightarrow{H_2O} [Pd(BHEP)L']^{+} + R'OH + H^{+} \quad (2)$$

$$[\mathrm{Pd(BHEP)L}]^{2+} + \mathrm{OH}^- \overset{\mathrm{kOH}}{\rightarrow} [\mathrm{Pd(BHEP)L'}]^{+} + \mathrm{R'OH} \quad (3)$$

where $\mathrm{L} = \mathrm{NH_2CH(R)CO_2R'}$ and $\mathrm{L'} = \mathrm{NH_2CH(R)CO_2^-}$.

The kinetic data, *viz.* the volume of base added to keep the pH constant *versus* time, could be fitted by a single exponential function as shown in figure 3. Various other kinetic models were tested without satisfactory fits of the data. A plot of k_{obs} *versus* hydroxide ion

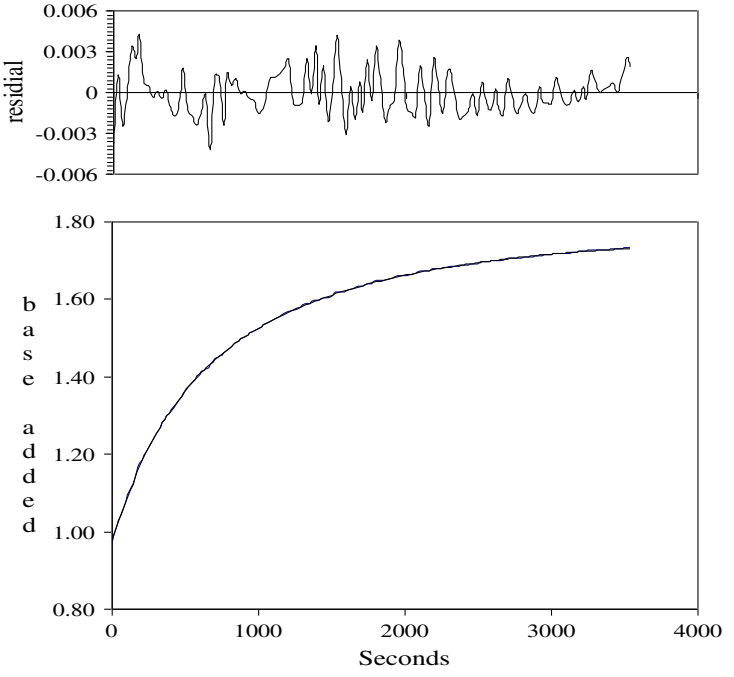


Figure 3. Typical plot of volume of base added *vs.* time in seconds fitted with a single exponential function for the hydrolysis of $[\mathrm{Pd(BHEP)(GlyOMe)}]^{2+}$ at 25 °C and 0.1 M ionic strength.

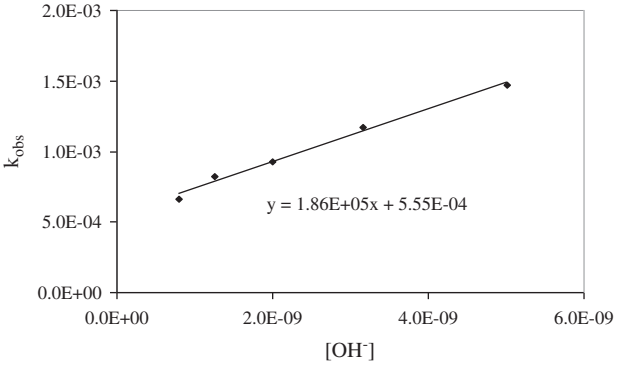


Figure 4. Kinetic data for the hydrolysis of Pd(BHEP)-glycine methyl ester at 25 °C and 0.1 M ionic strength.

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

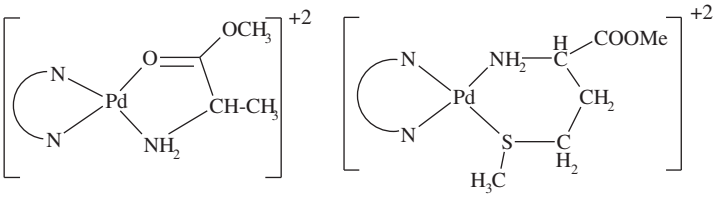
Ester	pH	$[OH^-]^a$	k_{obs} (s^{-1})
Glycine methyl ester	4.8	7.94E-10	6.64E-04
	5.0	1.26E-09	8.19E-04
	5.2	2.00E-09	9.28E-04
	5.4	3.16E-09	1.17E-03
	5.6	5.01E-09	1.47E-03
Methionine methyl ester	8.8	7.94E-06	1.66E-04
	9.0	1.26E-05	2.25E-04
	9.2	2.00E-05	2.89E-04
	9.4	3.16E-05	4.06E-04
	9.6	5.01E-05	5.97E-04

concentration is linear as shown in figures 4 and 5 (for data see table 2) and follows the rate expression given in equation (4):

$$k_{obs} = k_o + k_{OH}[OH^-] \tag{4}$$

The k_o term is suggested to arise from spontaneous hydrolysis with water. The linear dependence of the rate on the OH^- concentration is consistent with direct attack of OH^- on the ester group (figures 4 and 5).

For the coordinated glycine methyl ester, the catalytic ratio is 1.45×10^5. A catalytic ratio of this magnitude is consistent with the formation of the mixed-ligand complex of structure I, where there is a direct interaction between Pd^{II} and the carbonyl group of the ester.



I II

The catalytic ratio for methionine methyl ester complexes is 13.2 (table 3). The relatively low catalytic ratio suggests that the carbonyl group is not bound to Pd(II). The methionine methyl ester complex is expected to have structure II, where the amino and the sulfur are donors. Earlier studies [25–27] have shown that the formation of such complexes with a pendant ester group leads only to relatively small catalytic effects.

Comparative values of k_{OH} at 25 °C for the base hydrolysis of the glycine methyl ester incorporated in $[Pd(en)L]^{2+}$ is 4.88×10^4 dm^3 mol^{-1} s^{-1} [18], where en = ethylenediamine.

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

Ester	k_{OH}	k_{H_2O}	$k_{OH}^{(ester)a}$	$k_{OH}/k_{OH}^{(ester)}$
Glycine methyl ester	1.86E+05	1.00E-05	1.28	1.45E+05
Methionine methyl ester	10.1	1.71E-06	0.767	13.2

[a]Data from Ref. [9].

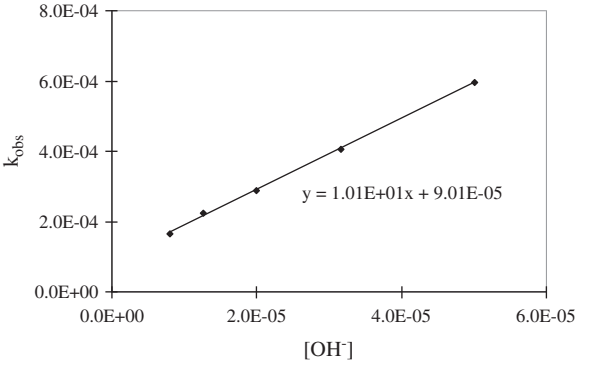


Figure 5. Kinetic data for the hydrolysis of Pd(BHEP)-methionine methyl ester at 25 °C and 0.1 M ionic strength.

The k_{OH} value for $[Pd(BHEP)L]^{2+}$ (1.85×10^5) is higher than that of $[Pd(en)L]^{2+}$. The enhanced hydrolysis is probably due to stabilization of the mixed-ligand complex through involvement of the OH groups of BHEP in hydrogen bonding with the coordinated amino acid ester.

The activation parameters for the hydrolysis of coordinated glycine methyl ester were determined using Eyring plots of ln(k/T) *versus* 1/T, figure 6 (for data, see table 4). The activation parameters for kOH were calculated to be $\Delta H^{\#} = 28.0(\pm 0.2)$ kJ mol^{-1} and

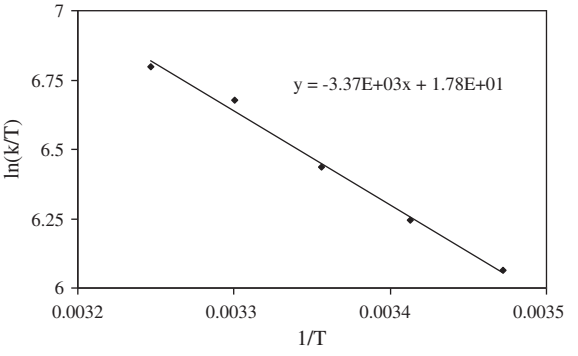


Figure 6. Effect of temperature on the hydrolysis of the coordinated glycine methyl ester.

Table 4. Hydrolysis data (dm^3 mol^{-1}s^{-1}) of $[Pd(BHEP)(GlyOMe)]^{2+}$ at different temperatures in aqueous solution at pH = 5.4.

T (°C)	k_{OH}	k_{H2O}
15	1.24E+05	9.664E-06
20	1.51E+05	9.832E-06
25	1.86E+05	1.000E-05
30	2.41E+05	1.017E-05
35	2.76E+05	1.034E-05

$\Delta S^{\#} = -49.5((\pm 0.3)\ JK^{-1}\ mol^{-1}$. The activation parameters for k_o may be inaccurate since the rate constants were determined by an extrapolation procedure. For base hydrolysis of the free glycine methyl ester, the activation parameters were reported [18, 28] to be $\Delta H^{\#} = 39.7$ kJ mol^{-1} and $\Delta S^{\#} = -117\ JK^{-1}\ mol^{-1}$. The enhanced rate for base hydrolysis of the ester coordinated to the complex is therefore due to a decrease in $\Delta H^{\#}$ and an increase in $\Delta S^{\#}$.

4. Conclusion

TG for $Pd(BHEP)Cl_2$ confirmed the structure and the absence of water of crystallization. The kinetic parameters (Supplementary Material) of thermal degradation process calculated using Coats–Redfern and Horowitz–Metzger methods show high values of the energy of activation of the complex reveal the high stability of such chelates, and all the decomposition steps are nonspontaneous processes. Also, the negative values of ΔS^* for the degradation process indicate more ordered activated complex than the reactants or the reaction is slow.

The hydrolysis of glycine methyl esters is catalyzed by $[Pd(BHEP)(H_2O)_2]^{2+}$ with catalysis ratio 1.45×10^5. The catalytic effect is due to a direct interaction between Pd(II) and the alkoxycarbonyl group of the ester species. The activation parameters for the hydrolysis of coordinated glycine methyl ester were determined and compared with those of free glycine methyl ester. The enhanced rate for base hydrolysis of the ester coordinated to the complex is due to a decrease in $\Delta H^{\#}$ and an increase in $\Delta S^{\#}$. The hydrolysis of methionine methyl ester is not significantly catalyzed. The relatively small catalysis ratio value suggests that the alkoxycarbonyl group is not bonded to the metal ion.

Supplementary material

The supplementary material for this article is available online at http://dx.doi.org/10.1080/00958972.2015.1061659.

Disclosure statement

No potential conflict of interest was reported by the authors.

References

[1] V.K. Jain, B. Jain, U.K. Sharma, D. Saha. *Int. J. Curr. Pharm. Res.*, **3**, 66 (2011).
[2] W.N. Lipscomb. *Acc. Chem. Res.*, **3**, 81 (1970).
[3] J.M. Pesando. *Biochemistry*, **14**, 681 (1975).
[4] T.W. Reid, I.B. Wilson. In *The Enzymes*, P.D. Boyer (Ed.), Vol. 4, 3rd edn, p. 373, Academic Press, New York (1971).
[5] D.S. Auld. In *Enzyme Mechanisms*, M.I. Page, A. Williams (Eds), p. 240, The Royal Society of Chemistry, London (1987).
[6] R. Jairam, M.L. Lau, J. Adorante, P.G. Potvin. *J. Inorg. Biochem.*, **84**, 113 (2001).

[7] X. Kou, X. Meng, J. Xie, X. Zeng. *Transition Met. Chem.*, **28**, 777 (2003).
[8] J. Xia, S. Li, Y. Shi, K. Yu, W. Tong. *J. Chem. Soc., Dalton Trans.*, 2109 (2001).
[9] M.R. Shehata, M.M. Shoukry, F.M.H. Nasr, R. van Eldik. *Dalton Trans.*, 779 (2008).
[10] M.R. Shehata, M.M. Shoukry, F.H. Abdel-Shakour, R. van Eldik. *Eur. J. Inorg. Chem.*, 3912 (2009).
[11] M.M.A. Mohamed, A.A. Shoukry, M.M. Shoukry. *Int. J. Chem. Kinet.*, **38**, 737 (2006).
[12] M.M.A. Mohamed, M.M. Shoukry. *Polyhedron*, **21**, 167 (2002).
[13] A.A. El-Sherif, M.M. Shoukry. *Inorg. Chim. Acta*, **360**, 473 (2007).
[14] M.M. Shoukry, E.M. Khairy, A. Saeed. *Transition Met. Chem.*, **12**, 315 (1987).
[15] R.W. Hay, P. Banerjee. *J. Chem. Soc., Dalton Trans.*, 362 (1981).
[16] R.G. Bates. *Determination of pH-Theory and Practice*, 2nd edn, Wiley Interscience, New York (1975).
[17] R.W. Hay, A.K. Basak. *J. Chem. Soc., Dalton Trans.*, 1819 (1982).
[18] R.W. Hay, P.J. Morris. In *Metal Ions in Biological Systems*, H. Sigel (Ed.), Vol. 5, pp. 173–243, Marcel Dekker, New York (1976).
[19] OLIS KIFET, Olis Inc., Borgart GA, 19 (1993).
[20] A.A. Shoukry, T. Rau, M.M. Shoukry, R. van Eldik. *J. Chem. Soc., Dalton Trans.*, 3105 (1998).
[21] C.W. Davis. *J. Chem. Soc.*, 2093, (1938).
[22] R.A. Robinson, R.H. Stokes. *Electrolyte Solutions*, 2nd edn, Butterworths, London (1959).
[23] S.N. Singh, M. Katyal, R.K. Agarwal. *Molecular Structure: A Spectroscopic Approach*, p. 62, Book Publisher, Discovery Publishing House, New Delhi (1990).
[24] P.-C. Kong, F.D. Rochon. *Can. J. Chem.*, **59**, 3293 (1981).
[25] R.W. Hay, P. Banerjee. *J. Chem. Soc., Dalton Trans.*, 362 (1981).
[26] R.W. Hay, L.J. Porter. *J. Chem. Soc. B*, 1261 (1967).
[27] R.W. Hay, A.K. Basak. *J. Chem. Soc., Dalton Trans.*, 1821, (1982).
[28] R.J. Angelici, J.W. Allison. *Inorg. Chem.*, **10**, 2238 (1971).