Asian Journal of Chemistry; Vol. 34, No. 10 (2022), 2657-2663

ASIAN JOURNAL OF CHEMISTRY

https://doi.org/10.14233/ajchem.2022.23898

Kinetics of Pd(II)-Catalyzed Oxidation of Ampicillin by Using $Cu(Bipy)_2^{2+}$ as Oxidant in Alkaline Medium: A Spectrophotometric Study

RUPAM YADAV, JAYA SRIVASTAVA, BRIJESH KUMAR PRAJAPATI, RAKESH PATEL and SHAHLA RAHMANI*

Department of Chemistry, University of Allahabad, Allahabad-211002, India

*Corresponding author: Fax: +91 532 2462266; E-mail: shahlaau@rediffmail.com

Received: 5 May 2022; *Accepted*: 5 July 2022; *Published online*: 19 September 2022; AJC-20970

The kinetic and mechanistic study of homogeneously Pd(II)-catalyzed oxidation of ampicillin by $Cu(Bipy)_2^{2+}$ in alkaline medium have been conducted at 35 ± 0.1 ºC. Spectrophotometric titrations show that the stoichiometry of the reaction is 1:4 ([ampicillin]:[$Cu(Bipy)_2^{2+}$] = 1:4). The first order kinetics is observed regarding [$Cu(Bipy)_2^{2+}$] and [Pd(II)] however, less than unity order exhibited by [OH^-]. On varying [ampicillin] and [bipyridyl], velocity of reaction remains unchanged. Reaction rate unaffected by changing ionic strength of the medium while with dielectric constant, it shows inverse relation. Various thermodynamic properties of reaction were calculated such as activation energy, activation entropy, *etc.* Oxophenyl acetic acid and 2-formyl-5,5-dimethylthiazolidine-4-carboxylic acid were identified as reaction product. With the help of kinetic observation, spectrophotometric data an appropriate reaction mechanism and rate law derived for aforesaid reaction.

Keywords: Alkaline medium, Ampicillin, Catalysis, Copper-bipyridyl complex, Spectrophotometric study.

INTRODUCTION

Ampicillin is a penicillin β-lactam broad spectrum antibiotic used in the treatment of bacterial infections caused by many Gram-positive and Gram-negative organisms [1]. There were a number of antibiotics that coordinate with metal ions to enhance their biological activities [2]. The coordinated metal ions toward these antibiotics play an important role in maintaining proper structure and/or function of these antibiotics. The oxidation of antibiotics has been studied in detail by using copper bipyridyl [3], cerium(IV) [4], *N*-bromosuccinimide [5], chloromine-T [6], sodium metaperiodate [7] and hexacynoferrate [8] as oxidants in alkaline/acidic medium. The chemistry of biologically active palladium complexes has become of fundamental importance in the last few decades, due to their antimicrobial and anticancer properties [9]. Some of them have shown better activity than platinum compounds [10]. For example, Pd(II)-NHC complexes (NHCs = *N*-heterocyclic carbenes) with *trans*-geometry [11], mononuclear cyclopalladate complexes with nitrogen-, carbon-, sulfur- and phosphorous-donor multidentate ligands, dinuclear dipalladium complexes and heterometallic palladium-containing complexes are the most promising compounds [12]. Literature survey reveals that kinetic studies of ampicillin in basic medium oxidized by $Cu(Bipy)_2^{2+}$ have no information till date.

This prompted us to study the kinetics of oxidation of ampicillin by $Cu(Bipy)_2^{2+}$ in alkaline medium. The purpose of this investigation is to study (i) the behaviour of reaction velocity on varying concentration of prime reactants *i.e.* $Cu(Bipy)_2^{2+}$, ampicillin and alkaline medium; (ii) Pd(II) acts as weak or strong catalyst; (iii) trace the all possible complex formed in between reaction path, and (iv) the oxidative potential of $Cu(Bipy)_2^{2+}$, for the same reaction.

EXPERIMENTAL

Reagent grade chemicals were used throughout the work. The standard solution of ampicillin was prepared freshly. The solutions of cupric sulphate, 2,2′-bipyridyl, 25% ethyl alcohol and potassium chloride were prepared in double distilled water. A stock standard solution of Pd(II) chloride was prepared in a known acidic strength. The overall kinetic investigation made by using Varian Carry Win UV-vis spectrophotometer. The pH of solution also maintained by using EUTECH pH 510 instruments. Initially for measuring the maximum absorbance of

This is an open access journal, and articles are distributed under the terms of the Attribution 4.0 International (CC BY 4.0) License. This license lets others distribute, remix, tweak, and build upon your work, even commercially, as long as they credit the author for the original creation. You must give appropriate credit, provide a link to the license, and indicate if changes were made.

products, the spectra was scanned over the range of 700 to 350 nm (Fig. 1) and the molar extinction coefficient is calculated as 5.00×10^3 dm^3 mol^{-1} cm^{-1} (Fig. 2). Thus, the wavelength 410 nm was obtained at which the product $Cu(Bipy)_2^+$ absorbs maximum radiation.

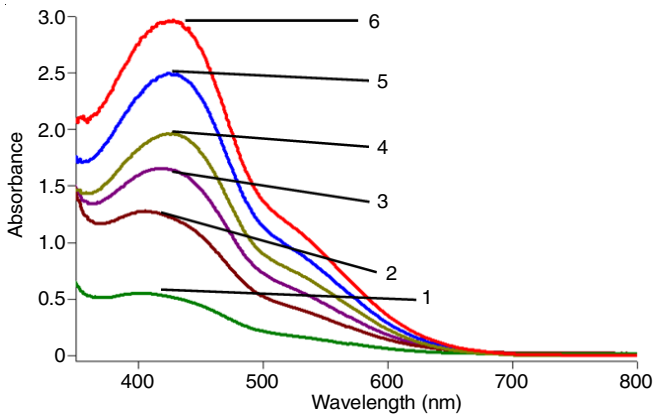


Fig. 1. Spectra of $Cu(Bipy)_2^+$ solutions at different concentrations are recorded at room temperature

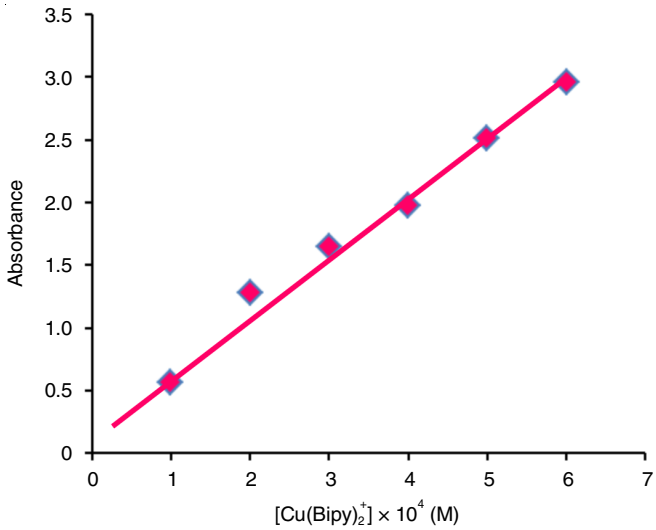
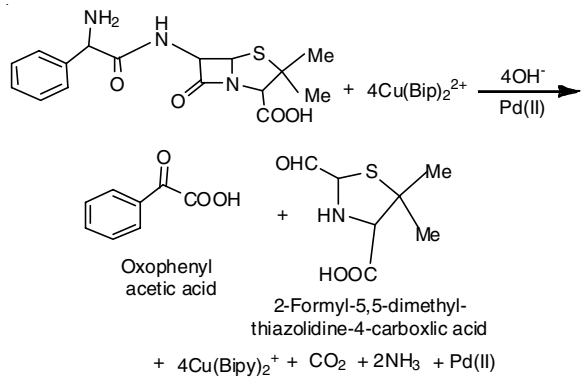


Fig. 2. Plot between absorbance (Abs) and [Cu(I)*]

One set of reaction mixture prepared by mixing $CuSO_4$, 2,2′-bipyridyl, Na_2CO_3, Pd(II) chloride and KCl whereas a separate set of mixture having same reactant except $CuSO_4$ also make and placed in same thermostatic waterbath to acquire required temperature. Ampicillin solution also put in same waterbath in a different conical flask to maintain temperature of reaction. The initiation of the reaction was carried out by mixing the requisite volume of ampicillin to the reaction mixture. After 0.5 h when all solutions attain the temperature of waterbath *i.e.* 35 ºC, the initiation of reaction was carried out by mixing the requisite volume of ampicillin to the reaction mixture. The new mixture shakes gently and quickly and fills in the cuvette and put at sample point into the spectrophotometer. This reaction mixture shows absorbance of $Cu(Bipy)_2^+$ at 410 nm whereas mixture without $CuSO_4$ solution used as reference solution. During the whole process, temperature of reaction maintained at 35 ºC.

Stoichiometry and product analysis: Different sets of reactions containing excess [$Cu(Bipy)_2^{2+}$] over [ampicillin] with constant concentrations of Pd(II) and [OH] were kept for 72 h and then estimated. Assessment of remaining concentration of $Cu(Bipy)_2^{2+}$ indicate that 4 mol of oxidant (*i.e.* $Cu(Bipy)_2^{2+}$) required for each mole of ampicillin. The results showed 1:4 stoichiometry according to eqn. 1:



(1)

RESULTS AND DISCUSSION

The expected mechanism and rate equations for the observed reaction have been derived by studying the effect of varying concentration of reactants on the reaction rate. The Ostwald's isolation method along with van't Hoff differential method was used to determine the order of reaction.

With the help of slope of tangent of graph between unused concentration of $Cu(Bipy)_2^{2+}$ and time the velocity of reaction *i.e.* (-dc/dt) was calculated for each set of reaction. On plotting graph for oxidant variation taken, a fixed time while in the variation of other reactants concentration graph is plotted at fixed concentration of [$Cu(Bipy)_2^{2+}$]. The value of k_1 was calculated by using following equation:

$$k_1 = -\frac{dc/dt}{[Cu(II)^*]}$$

where Cu(II)* represents $Cu(Bipy)_2^{2+}$ and k_1 is pseudo first order rate constant.

The order of reaction with respect to Cu(II)* was determined by keeping ampicillin concentration in large excess. Under such conditions, the velocity of reaction will mainly be determined by the variation in concentration of Cu(II)*. The first-order dependence of the reaction on Cu(II)* throughout its ten-fold variation is demonstrated by the plot of -dc/dt *versus* [Cu(II)*], which gives a straight line passing through origin (Fig. 3). Uniform values of k_1 presented in Table-1 against varying concentration of Cu(II)*, also confirmed the first-order kinetics with respect to [Cu(II)*]. Approximate constant values of first order rate constant (k_1) against varying [ampicillin] clearly shows that order with respect to ampicillin is zero throughout its ten-fold variation *i.e.* from 1.00×10^{-3} M to 10.00×10^{-3} M (Table-1). The value of first-order rate constant, (k_1) increases linearly as the concentrations of Pd(II) are increased. This shows that the first order for [Pd(II)] is observed (Table-1). The value of k_1 does not increase in the same proportion in which the concentration of OH^- is increased indicating fractional positive order kinetics with respect to OH^- (Table-1).

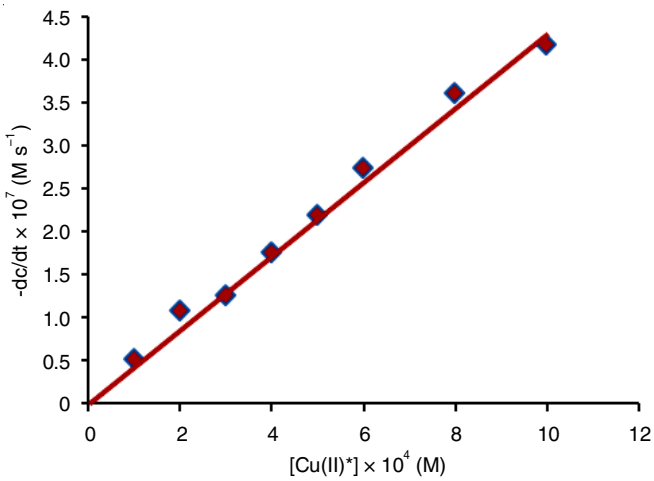


Fig. 3. Plot between -dc/dt and [Cu(II)*] at 35 °C

TABLE-1
EXPERIMENTAL VALUES OF THE RATE CONSTANT FOR THE VARIATIONS OF [Cu(II)*], [Amp] [Pd(II)] AND [OH^-] IN THE Pd(II) CATALYZED OXIDATION OF AMPICILLIN BY $Cu(Bipy)_2^{2+}$ AT 35 °C

[Cu(II)*] × 10^4 (M)	[Amp] × 10^3 (M)	[Pd(II)] × 10^6 (M)	$[OH]^-$ × 10^5 (M)	k_1 (s^{-1})
1.00	2.00	6.00	9.01	6.87
2.00	2.00	6.00	9.01	6.00
3.00	2.00	6.00	9.01	5.56
4.00	2.00	6.00	9.01	5.46
5.00	2.00	6.00	9.01	6.70
6.00	2.00	6.00	9.01	6.68
8.00	2.00	6.00	9.01	6.81
10.00	2.00	6.00	9.01	6.30
4.00	1.00	6.00	9.01	5.13
4.00	2.00	6.00	9.01	5.56
4.00	4.00	6.00	9.01	6.80
4.00	6.00	6.00	9.01	6.43
4.00	8.00	6.00	9.01	5.13
4.00	10.00	6.00	9.01	4.90
4.00	2.00	3.00	9.01	3.00
4.00	2.00	6.00	9.01	5.87
4.00	2.00	9.00	9.01	9.03
4.00	2.00	12.00	9.01	12.4
4.00	2.00	18.00	9.01	16.13
4.00	2.00	24.00	9.01	23.60
4.00	2.00	30.00	9.01	26.03
4.00	2.00	6.00	4.40	3.13
4.00	2.00	6.00	9.01	5.97
4.00	2.00	6.00	14.79	9.40
4.00	2.00	6.00	17.86	11.50
4.00	2.00	6.00	21.04	12.63
4.00	2.00	6.00	24.40	15.43

Solution conditions; [Free Bipy] = 1.20×10^{-3} M, m = 0.80 M

There is no change in (-dc/dt) value on varying [bipyridyl] in reaction mixture further nearly same value of k_1 also support zero order kinetic with respect to [bipyridyl]. Reaction velocity was not changed by varying ionic strength of medium. Ethyl alcohol was used to altered the dielectric constant of reaction mixture by 5-20% and ensure that ethyl alcohol does not react itself in given condition. The velocity of reaction decreases as the dielectric constant of medium increases, which demonstrated that reaction is occurring between appositely charged ions. This is further confirmed by the plot of log k_1 *vs.* 1/D, which gave a straight line, having a positive intercept on *y*-axis (Fig. 4). The rate constants have been calculated at four different temperatures *i.e.* 30, 35, 40 and 45 ºC and with the help of these values various activation parameters have been calculated (Table-2).

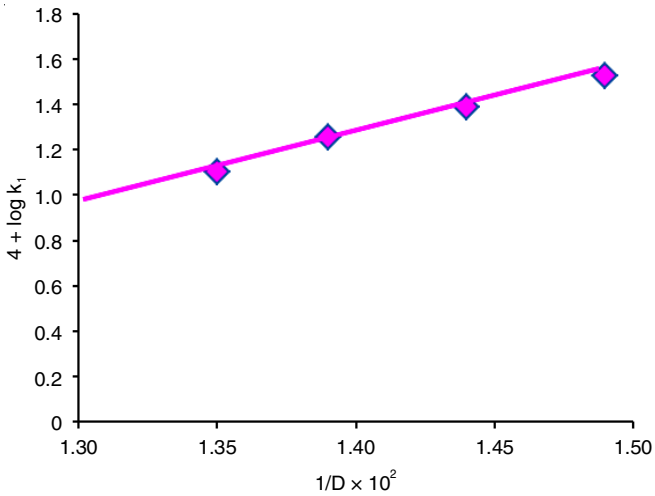


Fig. 4. Plot between 1/D and log k_1 at 35 °C

Reactive species of Cu(II) in alkaline medium: Upon analysis of spectrophotometric and kinetic outcome, it is clear that $[Cu(Bipy)_2]^{2+}$ was acted as reactive form of Cu(II) not free Cu(II) ion. The absorption band appeared at λ_{max} = 670 nm shows the $[Cu(Bipy)_2]^{2+}$ complex have molar extinction coefficient 0.59×10^2 dm^3 mol^{-1} cm^{-1}, which also reported in literature [13] (Fig. 5).

Reactive species of Pd(II) chloride in alkaline medium: It is reported that Pd(II) chloride is rather insoluble in aqueous solution but does dissolve in the presence of chloride ion as $PdCl_3(H_2O)^-$ and $PdCl_4^{2-}$ [14]. Several publications are available in the literature [15-19] where the equilibrium constants for the following equilibria have been determined and found in agreement with a value of log β_4 between 11 and 12 at 25 ºC.

$$Pd^{2+} + Cl^- \rightleftharpoons PdCl^+ \quad (K_1)$$

$$PdCl^+ + Cl^- \rightleftharpoons PdCl_2 \quad (K_2)$$

$$PdCl_2 + Cl^- \rightleftharpoons PdCl_3^- \quad (K_3)$$

$$PdCl_3^- + Cl^- \rightleftharpoons PdCl_4^{2-} \quad (K_4)$$

The study for the stability constants and rates of reaction has been made by Edling [20]. Edling studied both the stability constant and rates of reaction and determined value of log k_1

TABLE-2
ACTIVATION PARAMETERS FOR Pd(II) CATALYZED OXIDATION OF AMPICILLIN BY $Cu(Bipy)_2^{2+}$ IN ALKALINE MEDIUM AT 35 °C

Reducing substrate	k_r (mol^{-2} dm^6 s^{-1})	$\Delta H^{\#}$ (kJ mol^{-1})	$\Delta G^{\#}$ (kJ mol^{-1})	$\Delta S^{\#}$ (eu)	A (mol^{-3} dm^9 s^{-1})
Ampicillin	8.34×10^5	64.53	43.34	16.38	1.51×10^{17}

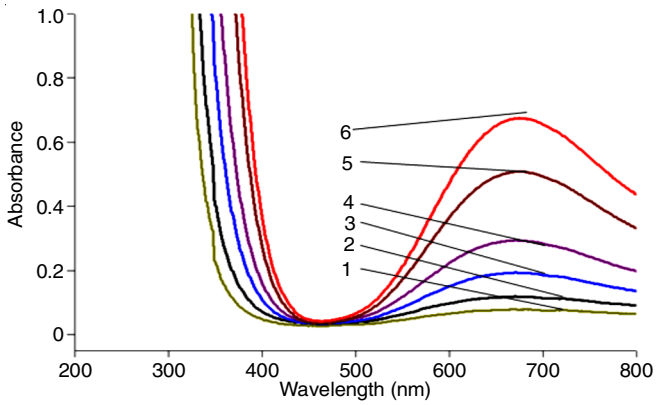


Fig. 5. Spectra of $Cu(Bipy)_2^{2+}$ solutions at different concentrations recorded at room temperature

to log k_4 as 4.47, 3.29, 2.41 and 1.37, respectively, with log β_4 equal to 11.5. A comparison can be made with values of 4.3, 3.54, 2.68 and 1.68 determined by Grinberg & Kiselever [18].

On the basis of above equilibrium, we can write:

$$Pd^{2+} + 4Cl^- \overset{\beta_4}{\rightleftharpoons} PdCl_4^{2-}$$

where β_4 is equal to K_1, K_2, K_3, K_4

The existence of Pd(II) chloride exclusively in the form of $PdCl_4^{2-}$ is supported by Ayres [21], who has observed that when a reaction ratio of 2:1 for sodium chloride to palladium chloride is maintained, it will result in the formation of tetrachlropalladate(II), [$PdCl_4^{2-}$]. Since throughout the study of oxidation of ampicillin, the aforesaid constant ratio was maintained, hence it is reasonable to assume that the starting species of Pd(II) chloride is $[PdCl_4]^{2-}$. Furthermore, since the study for the catalyzed oxidation of ampicillin has been made in alkaline medium, a decision about the reactive species of Pd(II) chloride can be made only after taking into account the effect of [OH^-] on the rate of oxidation. To support this, spectra of solutions containing Pd(II) chloride alone, Pd(II) chloride with two different concentration of OH^- solution have been taken (Fig. 6). From Fig. 6, it is apparent that when OH^- solution of two different concentration (20×10^{-2} M & 40×10^{-2} M) is added to the solution of Pd(II) chloride, an increase in absorbance from 0.09 to 0.12 and 0.16 with a shift in λ_{max} towards longer wavelength is observed. On the basis of this, an inference about the existence of following equilibrium can very easily be drawn.

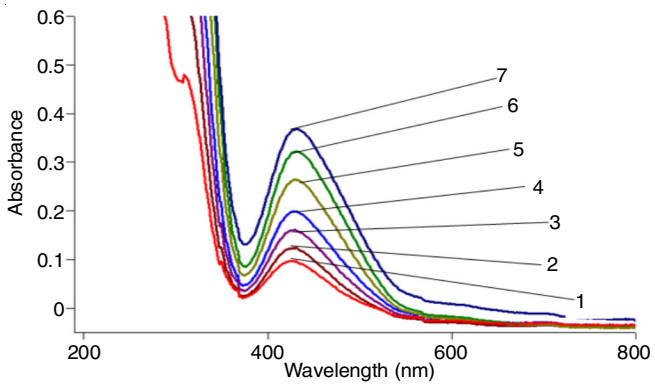


Fig. 6. Spectra of solutions recorded at room temperature

$$[PdCl_4]^{2-} + OH^- \rightleftharpoons [PdCl_4(OH)]^{3-} \quad (1)$$

With the addition of OH^- solution to the solution of Pd(II) chloride, the equilibrium (1) will shift towards right hand side and as a result, there will be more and more formation of the species $[PdCl_4(OH)]^{3-}$. Kinetic data demonstrated that there is an increase in pseudo-first-order rate constant (k_1) with the increase in Pd(II) chloride concentration hence, it can safely be assumed that $[PdCl_4(OH)]^{3-}$ is the reactive species of Pd(II) chloride in alkaline medium. Our assumption for the species $[PdCl_4(OH)]^{3-}$ in alkaline medium also finds support from the reported literature [22].

Spectral information for the formation of complex or complexes during the course of reaction for the oxidation of ampicillin by $Cu(Bipy)_2^{2+}$ in alkaline medium using Pd(II) as homogeneous catalyst: Further in order to verify the existence of a complex between $[PdCl_4(OH)]^{3-}$ and $Cu(Bipy)_2^{2+}$ in the oxidation of ampicillin, when a solutions of $Cu(Bipy)_2^{2+}$ were added to Pd(II) chloride solution and OH^-, it was observed that with the addition of $Cu(Bipy)_2^{2+}$ solution, there is increase in absorbance from 0.16 to 0.20, 0.26, 0.32 and 0.37 with a shift in λ_{max} towards longer wavelength (Fig. 6). The increase in absorbance with the addition of $Cu(Bipy)_2^{2+}$ solution can be attributed due to the formation of a new complex between $[PdCl_4(OH)]^{3-}$ and $Cu(Bipy)_2^{2+}$ according to the following equilibrium:

$$[PdCl_4(OH)]^{3-} + Cu(Bipy)_2^{2+} \rightleftharpoons \left[Cl_4Pd\text{–}\overset{H}{O}\text{–}Cu(Bipy)_2\right]^- \quad (2)$$

The shift in wavelength towards longer wavelength and increase in absorbance and above contention support that there is a formation of a new complex $\left[Cl_4Pd\text{–}\overset{H}{O}\text{–}Cu(Bip)_2\right]^-$, which is entirely different from the complex $[PdCl_4(OH)]^{3-}$.

The formation of 1:1 complex between the complex species C_1 and $Cu(II)^*$ was further verified by Job's plot [23,24] ($1/\Delta A$ *vs.* $1/[Cu(II)^*]$) where a straight line with positive intercept on *y*-axis was obtained (Fig. 7). The ΔA values on *y*-axis indicates the difference in absorbance of the solution containing Pd(II), OH^- and $Cu(Bipy)_2^{2+}$ and solution containing Pd(II) and OH^-.

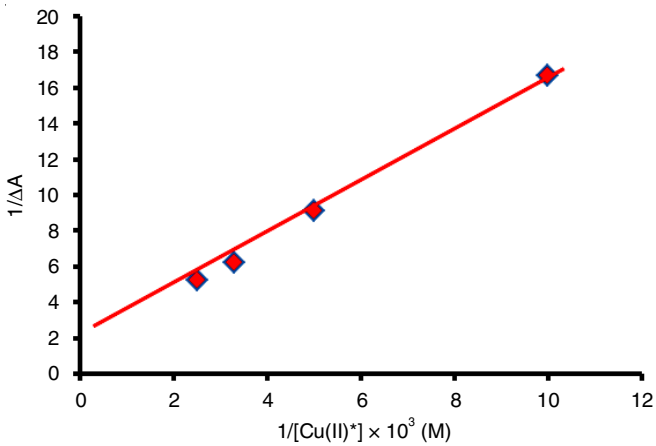


Fig. 7. Plot between $1/\Delta A$ and $1/[Cu(II)^*]$ at 35 °C

Mechanism and derivation of rate law: On the basis of kinetic orders with respect to each reactant taking part in the reaction, spectral information collected for the formation of the complex or complexes in the reaction and taking the effect of dielectric constant of the medium on the rate of reaction as well as activation parameters, a reaction **Scheme-I** for the reaction under investigation can be proposed in the following way:

On the basis of reaction **Scheme-I** and considering the stoichiometry of the reaction for the oxidation of ampicillin, the rate in terms of decrease in concentration of $Cu(II)^*$ can be expressed as:

$$\text{rate} = -\frac{d[Cu(II)^*]}{dt} = 4k_2[C_1][Cu(II)^*] \quad (1)$$

On applying the law of chemical equilibrium to steps (I), we have

$$K_1 = \frac{[C_1]}{[Pd(II)][OH^-]} \quad (2)$$

The equations for the concentrations of C_1 can be written as:

$$[c_1] = K_1[Pd(II)]\,[OH^-] \quad (3)$$

According to **Scheme-I**, the total concentration of Pd(II) *i.e.* $[Pd(II)]_T$ can be expressed as:

$$[Pd(II)]_T = [Pd(II)] + [C_1] \quad (4)$$

On substituting the value of $[C_1]$ from eqns. 3-4, we have eqn. 5:

$$[Pd(II)] = \frac{[Pd(II)]_T}{1 + K_1[OH^-]} \quad (5)$$

From eqns. 3 and 5

$$[C_2] = \frac{K_1[OH^-][Pd(II)]_T}{1 + K_1[OH^-]} \quad (6)$$

On substituting the value of $[C_2]$ from eqn. 6 to eqn. 1, we obtained eqn. 7:

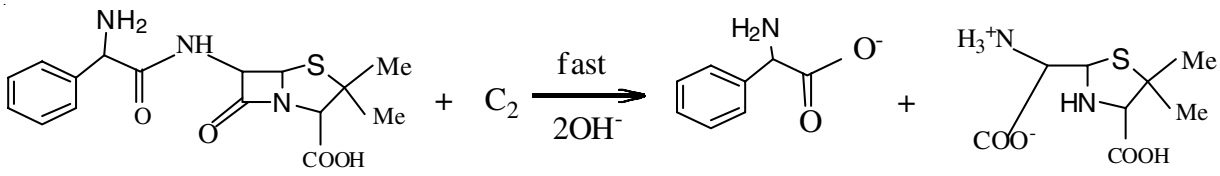
$$\text{Rate} = -\frac{d[Cu(II)^*]}{dt} = \frac{4K_1k_2[Cu(II)^*][Pd(II)]_T[OH^-]}{1 + K[OH^-]} \quad (7)$$

Eqn. 7 is the final rate law, which is in complete accordance with the present experimental findings.

Eqn. 7 can also be written as eqn. 8:

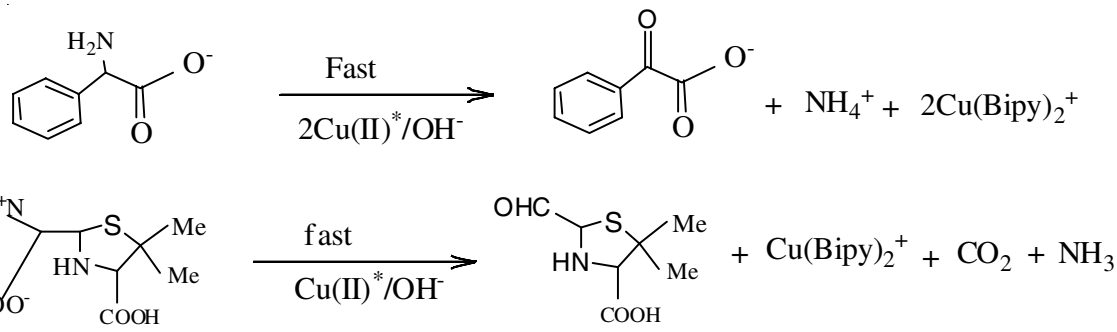
$$\underset{Pd(II)}{[PdCl_4]^{2-}} + [OH^-] \underset{}{\overset{K_1}{\rightleftharpoons}} \underset{C_1}{[PdCl_4(OH)]^{3-}} \quad (I)$$

$$[PdCl_4(OH)]^{3-} + Cu(Bipy)_2^{2+} \xrightarrow[\text{slow \& r.d.s}]{k_2} \underset{C_2}{\left[Cl_3Pd\text{—}O\text{—}Cu(Bipy)_2\right]^-} \quad (II)$$



Ampicillin

$$+ Cu(Bipy)_2^+ + [PdCl_3OH]^{2-} + Cl^- \quad (III)$$



Scheme-I

$$\frac{[Pd(II)]_T[Cu(II)^*]}{rate} = \frac{1}{4K_1k_2[OH^-]} + \frac{1}{4k_2} \quad (8)$$

According to eqn. 8, if a plot is made betweenand 1/[OH] and $\frac{[Pd(II)]_T[Cu(II)^*]}{Rate}$, a straight line having an intercept on *y*-axis will be obtained (Fig. 8). This clearly proves the validity of rate law (eqn. 7) and hence the proposed **Scheme-I**. From the slopes and intercepts of the straight line, the value of k_2 and K_1 have been calculated and found as 0.83×10^3 mol^{-1} dm^3 s^{-1} and 1.12×10^3 mol^{-1} dm^3. Utilizing these values, the rates of reaction for variation of [Pd(II)] and [OH$^-$] in the oxidation of ampicillin has been calculated and found very close to the rates of reaction observed experimentally (Table-3). The close similarity between the observed and calculated rates further confirms the validity of rate law (eqn. 7).

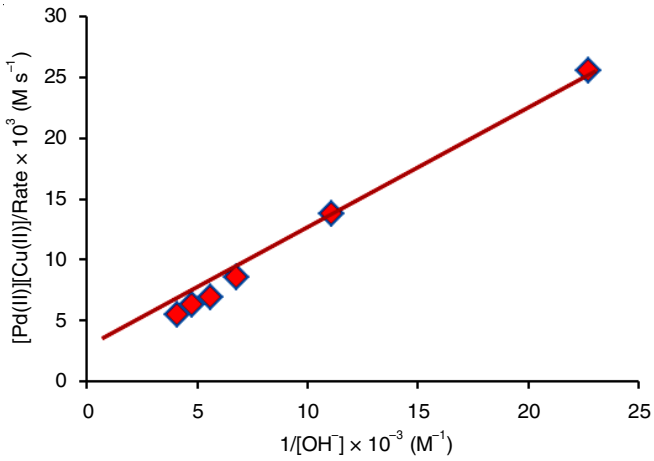


Fig. 8. Plot between $\frac{1}{[OH^-]}$ *vs.* $\frac{[Pd(II)]_T[Cu(II)^*]}{Rate}$ at 35 °C

It is a known fact that when reaction takes place between two ions of opposite charges, there will be an increase in the rate with the decrease in dielectric constant (D) of the medium. In the present study of Pd(II) catalyzed oxidation of ampicillin, the plot made between log k and 1/D, where a straight line having an intercept with positive slope was obtained, clearly supports the involvement of an ionic species $[PdCl_4(OH)]^{3-}$ and $Cu(Bipy)_2^{2+}$ in the rate determining step of the reaction (**Scheme-I**). Support to the rate determining step can also be given by the observed positive entropy of activation where transition state is less polar than the initial state.

Comparative study: The results of present investigation were compared with the results reported for Pd(II)-catalyzed oxidation of tetracycline hydrate by alkaline copper bipyridyl [3] and of paracetamol by chloramine-T [25] in alkaline medium, it was found that the observed unity order in oxidant concen-tration is similar to reported Pd(II)-catalyzed oxidation of para-cetamol [25] and differ from Pd(II)-catalyzed oxidation of tetracycline [3] where fractional positive order in Cu(II)* concen-tration was observed. When efforts were made to find out the effect of substrate concentration on the rate of oxidation, it was found that the zero-order kinetics observed in the present study differs from two other reported studies where first order and fractional positive order were observed in tetracycline hydrate and paracetamol concentration, respectively. As for as order with respect to Pd(II) concentration is concerned, it is first order in the present as well as in the reported Pd(II)-catalyzed oxidation of paracetamol [25], but it differs from fractional positive order observed in reported Pd(II)-catalyzed oxidation of tetracycline hydrate [3]. In present study, the observed fractional positive order in OH$^-$ concentration differs entirely from other two reported [3,25] studies where in one [3] zero-order kinetics in OH$^-$ concentration and in other [25] negative effect of [OH$^-$] on the rate of oxidation was observed. As for as the effect of dielectric constant of the medium on the rate of oxidation is concerned, it is found that the increase in rate constant of the reaction with decreasing dielectric constant of the medium in the present study is contrary to the reported nil effect of dielectric constant of medium in Pd(II)-catalyzed oxidation of tetracycline hydrate [3] and observed the direct proportionality between the rate and dielectric constant of the

TABLE 3
EXPERIMENTAL AND CALCULATED VALUES OF THE RATE FOR THE VARIATIONS OF [Pd(II)] AND [OH$^-$] IN THE Pd(II)-CATALYZED OXIDATION OF AMPICILLIN BY $Cu(Bipy)_2^{2+}$ AT 35 °C

[Pd(II)] × 10^6 (M)	[OH]$^-$ × 10^5 (M)	-dc/dt × 10^7 (M s^{-1})		
		Experimental rate	Rate calculated on the basis of rate law (eqn. 7)	Rate calculated on the basis of multiple regression analysis
3.00	9.01	0.90	0.91	0.92
6.00	9.01	1.76	1.83	1.78
9.00	9.01	2.71	2.74	2.63
12.00	9.01	3.72	3.65	3.46
18.00	9.01	4.84	5.48	5.09
24.00	9.01	7.08	7.31	6.70
30.00	9.01	7.81	9.14	8.30
6.00	4.40	0.94	0.94	0.93
6.00	9.01	1.79	1.82	1.78
6.00	14.79	2.82	2.83	3.13
6.00	17.86	3.45	3.30	3.32
6.00	21.04	3.79	3.80	3.86
6.00	24.40	4.63	4.28	4.39

Solution conditions; [Cu(II)*] = 4.00×10^{-4}M, [Free Bipy] = 1.20×10^{-3} M, m = 0.80 M

medium in Pd(II)-catalyzed oxidation of paracetamol [25]. Observed positive entropy of activation in the present study and in the reported Pd(II)-catalyzed oxidation of tetracycline hydrate [3] supports the interaction between two appositively charged species in the rate determining step whereas the large negative effect of entropy of activation in reported Pd(II)-catalyzed oxidation of paracetamol [25] provides evidence for the formation of a compact activated complex with fewer degrees of freedom. In view of the fact mentioned above, it can be said that the present study is different in many respects from other two studies reported earlier.

Conclusion

On the basis of observed kinetic data and spectral studies, the oxidation of ampicillin by $Cu(Bipy)_2^{2+}$ using Pd(II) as homogeneous catalyst in alkaline medium were derived. Ampicillin participates in the reaction after the rate determining step as the reaction follows zeroth-order kinetics with respect to [Amp]. The species $[PdCl_4OH]^{3-}$ has been assumed as the reactive species of Pd(II) chloride in alkaline medium for the oxidation of ampicillin. The formation of 1:1 complex between reactive species of Pd(II) chloride and $Cu(Bipy)_2^{2+}$ is supported by observed kinetic and spectrophotometric data and the Job's plots. In step (II) of **Scheme-I**, an interaction between a charged species, $[PdCl_4OH]^{3-}$ and $Cu(Bipy)_2^{2+}$ resulted in the formation of most reactive activated complex, which is well supported by the observed positive entropy of activation and the effect of dielectric constant of the medium on the rate of oxidation.

CONFLICT OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this article.

REFERENCES

1. R.S. Satoskar and S.D. Bhandarkar, Pharmacology and Pharmacotherapeutics, Popular Prakashan: Bombay, Ed. 11., vol. II (1990).
2. L.J. Ming, *Med. Res. Rev.*, **23**, 697 (2003); https://doi.org/10.1002/med.10052
3. A.K. Singh, M. Singh, S. Rahmani, J. Srivastava and J. Singh, *Ind. Eng. Chem. Res.*, **51**, 5728 (2012); https://doi.org/10.1021/ie300306a
4. S.S. Badi and S.M. Tuwar, *Arab. J. Chem.*, **10**, 1469 (2017); https://doi.org/10.1016/j.arabjc.2013.04.025
5. A.P. Khan, A. Khan, A.M. Asiri and S.A. Khan, *J. Mol. Liq.*, **218**, 604 (2016); https://doi.org/10.1016/j.molliq.2016.02.051
6. M.S. Veena, M.K. Prashanth, Y. Kumar, H.B. Muralidhara and Y.A. Nayaka, *J. Chil. Chem. Soc.*, **60**, 3063 (2015); https://doi.org/10.4067/S0717-97072015000300019
7. A.E.M. Abdel-Hady and A.M. Taha, *Transition Met. Chem.*, **40**, 379 (2015); https://doi.org/10.1007/s11243-015-9927-0
8. A.K. Durgannavar, M.B. Patgar and S.A. Chimatadar, *Indian J. Chem.*, **54A**, 1085 (2015).
9. J.A. Klaus, T.M. Brooks, M. Zhou, A.J. Veinot, A.M. Warman, A. Palayew, P.T. Gormley, B. Ninh Khuong, C.M. Vogels, J.D. Masuda, F.J. Baerlocher and S.A. Westcott, *Transition Met. Chem.*, **42**, 263 (2017); https://doi.org/10.1007/s11243-017-0130-3
10. S. Prince, S. Mapolie and A. Blanckenberg, Encyclopedia of Cancer, pp. 1-9 (2015).
11. S. Ray, R. Mohan, J.K. Singh, M.K. Samantaray, M.M. Shaikh, D. Panda and P. Ghosh, *J. Am. Chem. Soc.*, **129**, 15042 (2007); https://doi.org/10.1021/ja075889z
12. A.R. Kapdi and I.J.S. Fairlamb, *Chem. Soc. Rev.*, **43**, 4751 (2014); https://doi.org/10.1039/C4CS00063C
13. E. Prenesti, P.G. Daniele, S. Berto and S. Toso, *Polyhedron*, **25**, 2815 (2006); https://doi.org/10.1016/j.poly.2006.04.026
14. P.M. Henry, Palladium Catalyzed Oxidation of Hydrocarbons, D. Reidel Publishing Company, Dordrecht, Holland, pp. 11-12 (1928).
15. A.A. Biryukov and V.A. Schlenskaya, *Russ. J. Inorg. Chem.*, **9**, 450 (1964).
16. K. Burger, D. Dyrssen, L. Johansson, B. Norén and J. Munch-Petersen, *Acta Chem. Scand.*, **17**, 1489 (1963); https://doi.org/10.3891/acta.chem.scand.17-1489
17. H.A. Droll, B.P. Block and W.G. Fernelius, *J. Phys. Chem.*, **61**, 1000 (1957); https://doi.org/10.1021/j150553a036
18. A.A. Grinberg and N.V. Kiseleva, *Dokl. Acad. Nauk. SSSR*, **153**, 1327 (1963).
19. E.D. Weed, *Diss. Abstr.*, **25**, 795 (1964).
20. L.I. Elding, *Inorg. Chim. Acta*, **6**, 647 (1972); https://doi.org/10.1016/S0020-1693(00)91874-7
21. G.H. Ayres, *Anal. Chem.*, **25**, 1622 (1953); https://doi.org/10.1021/ac60083a013
22. A.K. Singh, S. Yadav, R. Srivastava, J. Srivastava and S. Rahmani, *J. Organomet. Chem.*, **695**, 2213 (2010); https://doi.org/10.1016/j.jorganchem.2010.06.009
23. P. Job, *Ann. Chim. (Paris)*, **10(9)**, 113 (1928).
24. P. Job, *Ann. Chim. (Paris)*, **11(6)**, 97 (1936).
25. A.K. Singh, R. Negi, B. Jain, Y. Katre, S.P. Singh and V.K. Sharma, *Ind. Eng. Chem. Res.*, **50**, 8407 (2011); https://doi.org/10.1021/ie101661m