Research Article

Kinetics and Mechanism of Oxidation of Carbenicillin by Copper (III) Periodate Complex in Aqueous Alkaline Medium

Yuv Raj Sahu and Parashuram Mishra

Bio-Inorganic and Materials Chemistry Research Laboratory, Department of Chemistry, Mahendra Morang Adarsha Multiple Campus, Biratnagar, Tribhuvan University, Nepal

Correspondence should be addressed to Parashuram Mishra; prmmishra@rediffmail.com

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Kinetics and mechanism of oxidation of carbenicillin by diperiodatocuprate [DPC-III] in aqueous alkaline medium were studied spectrophotometrically at 298 K and an ionic strength of 0.10 mol dm$^{-3}$. The reaction between DPC (III) and carbenicillin in the alkaline medium showed (CRBC:DPC-III) 1:4 stoichiometry. The reaction products were identified by the CHNS test, FT-IR, and LC-MS spectral reports. The reaction was of pseudo-first order with respect to DPC (III) and fractional order with respect to carbenicillin as well as alkali but retarding effect with respect to periodate. Monoperiodatocuprate (MPC-III) was found to be the main active species in the alkaline medium in the form of $[Cu(H_2IO_6)(H_2O)_2]_x$. Activation and thermodynamic parameters with respect to uncatalyzed rate constants ($k_u$) and slow step rate constant ($k$) as well as equilibrium constants were determined. The plausible mechanism consistent with experimental results was proposed and discussed in detail.

1. Introduction

Penicillanic acid derivatives (PADs) are composed of beta lactam ring and thiazolidine ring as the integral part which have growing demands in daily life, medicines, health tonics, etc. [1]. Carbenicillin, one of the PADs, is the 4th generations’ semisynthetic [2] analogue of naturally occurring benzylpenicillin with carboxyl and benzyl group penicillin which is synthesized from the 6-amopenicillin acid nucleus, discovered at Beecham as “Pyopen.” It is active against Pseudomonas aeruginosa in vitro [3] and hence used successfully in the treatment of pseudomonal infections [4–6] due to sensitivities of many strains of P. aeruginosa to carbenicillin within a reasonably narrow range of concentrations which can be safely obtained in vivo [7]. It is an acid liable antibiotic that inhibits bacterial cell wall synthesis and is commonly used in place of ampicillin to reduce the production of satellite colonies. It is more stable than ampicillin at low pH, which usually arises during bacterial fermentation.

It is soluble in water (solubility 451 mg/L). Its molecular formula, molar mass, and IUPAC name are $C_{17}H_{18}N_2O_6S$, 378.401 g mol$^{-1}$, and (2S, 5R, 6R)-6-[(carboxy (phenyl) acetyl] amino]-3,3-dimethyl-7-oxo-thia-1-azabicyclo [3.2.0] heptanes-2-carboxylic acid or 6-(a-carboxy-phenyl acetamido) penicillanic acid), respectively. Its structure is given in Figure 1.

Ampicillin, amoxicillin, dicloxacillin, carbenicillin, tetracycline, etc. belong to PADs family that are widely applied in hospitals, households, sewages [8], veterinary drugs, cosmetics [9], and fragrances or nutraceutical products [10] against different diseases to improve quality of personal health for the whole ecosystem. Characteristics, distribution, and source analysis of the main persistent toxic substances in karst groundwater have been reported [11]. These PADs do not degrade and mix into aquatic environment directly/indirectly, accumulate in natural water reservoirs, and contaminate drinking water, discharge or wastes, surface water, and ground water as well as air and soil. These effects enhance bacterial or viral resistance [12, 13] against different
PADs, and hence, it is a great challenge before researchers and drug manufacturers [14] to modify their composition along with updated specific function with a view to get fast relief from the illness. Personal care products (PCPs) [15–17] and antibiotic resistance represent a serious health problem, and different advanced oxidation processes (AOPs) have to be applied to degrade such emergent chemical pollutants [18–20] because most of the intermediates, formed transiently, can be definitely mineralized into CO₂, water, and mineral species due to possible oxidation-degradation reactions. The proposed work will disclose a novel application in the field of pharmaceuticals as well as kinetics for degradation of drugs and will be adequately applied in wastewater treatment at the sites polluted by PADs antibacterial agents.

Transition metals can form stable complexes with polydentate ligands such as diperiodatocuprate (DPC-III) [21, 22], diperiodatogantcarte (DPA-III) [23], diperiodatonicelkate (DPN-IV) [24], dittelluricatocuprate (DTC-II) [25, 26], and hexacyanoferrate (HCF-III) [27]. At first, Malatesta had synthesized DPC (III) more than a half century ago, and Panigrahi and Pathy [28] followed that method. Determination of the nature of the diperiodatocuprate (III) species in the aqueous alkaline medium through a kinetic and mechanistic study on the oxidation of iodide ion has been reported in the previous literature [29]. DPC (III) has a square planar geometry with dsp² hybridization and diamagnetic nature. Cu (III) appears as an active intermediate species in many electron transfer reactions [30] and supports to know the role of Cu (III)/Cu (II) couple, as described in earlier literature [31]. Review of literature regarding carbencillin is quite scanty. Only limited previous literature studies could have been included herewith. Some studies are voltammetric oxidation of carbencillin and its electroanalytical applications at gold electrode [32], in vitro effects of carbencillin combined with Gentamicin or polymyxin B against Pseudomonas aeruginosa [33], interactions of carbencillin and Ticarcillin with gentamicin [34], interaction between aminoglycoside antibiotics and carbencillin or ticarcillin [35], effect of time and concentration upon interaction between gentamicin, tobramycin, netilmicin, or amikacin and carbencillin or ticarcillin [36], in vivo inactivation of gentamicin by carbencillin and ticarcillin [37], administration of carbencillin and ticarcillin—pharmaceutical aspects [38], Carbencillin and ticarcillin [39], synergy between Ticarcillin and Tobramycin against Pseudomonas aeruginosa and enterobacteriaceae in vitro and in vivo [40], Carbencillin administration in patients with severe renal failure [41], etc.

The present research work aimed to investigate the kinetics and mechanism of oxidation of carbencillin without any catalyst and thence to arrive at plausible mechanism including determination of order of reaction, activation, and thermodynamic properties with respect to uncatalyzed rate constant (k₃), slow step rate constant (k), and equilibrium constants (K₁, K₂, and K₃) at different temperatures.

2. Materials and Methods

2.1. Reagents and Chemicals. Chemicals used were of Analytical Reagent (AR) grade and double distilled water was used throughout the work. The stock solution of carbencillin (Sigma Aldrich (0.01 mol·dm⁻³)) was prepared by dissolving 0.378 g of recrystallized carbencillin in 100 ml double distilled water. Potassium periodate solution was prepared by dissolving 0.023 g (0.01 mol·dm⁻³) of KIO₄ (Sigma Aldrich) in 100 ml double distilled hot water and the solution was used only after 24 hours. The concentration of the potassium periodate solution was determined by the iodimetric method [42].

2.2. Instrumentation. The pH of the solution was measured by ELICO LI 613 pH meter. The electronic absorption spectra were recorded on Varian CARY 5000 UV-VIS spectrophotometer in the range of 200–1000 nm. The infrared spectra of the complexes were recorded on Thermo Nicolet, Avatar 370 FT-IR spectrometer, in the range of 4000–400 cm⁻¹ that was run as KBr disc. The mass spectrum of the products was recorded on the UPLC-TQD mass spectrometer in the positive mode in the range of 0–1000 m/z.

2.3. Synthesis of Reagents. (DPC-III) was prepared [43, 44] by mixing copper sulphate (3.54 g), potassium periodate (6.80 g), potassium persulphate (2.20 g), and potassium hydroxide (9.0 g) in a 250 ml double distilled water in a RB flask. After collecting all chemicals, the whole mixture was frequently shaken thoroughly and heated on a hot plate for about 2 hours. As the mixture turned to intense red, the flask was heated again further for 20 minutes to remove potassium persulphate completely from the mixture by decomposing persulphate. After completion of the reaction, the mixture was cooled and filtered through sintered glass crucible G-4 and the dark red-brown solution was diluted to 250 ml by adding double distilled water. The aqueous solution of DPC (III) was standardized by iodimetric titration (Na₂S₂O₃, starch, Ki, and K₂H₂PO₄) by the thio- cyanate method, and its exact concentration was ascertained. The existence of DPC (III) was verified by using a UV-visible spectrophotometer that showed an absorption band with a maximum peak at 415 nm. However, the accurate concentration of DPC was calculated by using a UV-visible spectrophotometer. Similarly, KOH (BDH) and the other required solutions were prepared and stored safely. A study on the synthesis of alkaline copper (III) periodate (DPC) complex with an overview of its
redox behavior in aqueous micellar media including stability and redox nature of Cu (III) periodate complex in a microheterogeneous environment has been reported in the recent literature [45].

2.4. Synthesis of Complex. 10 ml of carbenicillin solution (0.132 mol·dm⁻³) was taken in a 100 ml RB flask. To this, 10 ml DPC (III) (0.528 mol·dm⁻³) was mixed in 1:4 stoichiometric ratio along with 1.0 ml of KNO₃ (HiMedia) and KIO₄ (Sigma Aldrich) and 2.0 ml of KOH (HiMedia) solution of fixed molarities and stirred on a hot plate followed by restirring during refluxing with condensation for 24 hours. Then, the mixture was cooled naturally for 3 days and filtered by using a Whatman No. 1 filter paper. The products were purified and recrystallized in ethanol till the whole solvent evaporated, leaving behind crystals only. The appearance of peaks in UV-visible spectrophotometer showed the formation of the complex. The possible structures of DPC (III) and MPC (III) are given in Figure 2.

2.5. Kinetic Measurements. Since the reaction is very fast, its absorbance was taken quite rapidly along with the progress of the reaction by following pseudo-first-order state when the active mass of CRBC was greater than that of DPC (III) at 20°C, 25°C, 30°C, and 35°C ± 0.1°C unless specified. The reaction was initiated by mixing required quantities of previously thermostated solutions of CRBC into DPC (III) that already contained a definite concentration of KIO₄ along with KNO₃ and KOH. Data were obtained from a UV-visible spectrophotometer at pH (9.0–9.2) and 415 nm wavelength due to DPC (III) by monitoring the decrease in absorbance at the molar extinction coefficient (ε) of 6144 ± 50 dm³·mol⁻¹·cm⁻¹. The UV-visible spectrophotometer was run up to 85% reaction wherein initially added products and dielectric constant did not exhibit any interference in the reaction. There was no effect of ubiquitous contamination of initially added carbonate in the reaction. Fresh solutions were nevertheless used to carry out each kinetic run. Regression analysis of experimental data to obtain regression coefficient (r) and standard deviation(s) of points from the regression line was completed with the help of Origin 9.6 (2017) software. Plots of log (abs) versus time gave a straight line and hence uncatalyzed rate constants (kₒ) were calculated from slopes. The kₒ values agreed within ±5% error and were the average of at least three independent kinetic runs. A constant concentration of periodate was mixed into reaction mixture all the time. Finally, the total kinetic runs. A constant concentration of periodate was reacted with DPC(III) in alkaline medium, 2-phenylmalonic acid (C₉H₈O₄) and 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide (C₉H₁₂N₂O₃S) were formed as the main products which were recrystallized from ethanol, separated by Column Chromatography over neutral alumina by using 80% benzene and 20% chloroform as eluent. Side product CO₂ was qualitatively detected by bubbling N₂ gas through the acidified reaction mixture and passing the gas liberated through the tube filled with lime water.

The reaction between carbenicillin and diperiodatocuprate (III) in alkaline medium is given as

$$\text{[Cu(H₃IO₆)(H₂O)₂]}^-$$

Diperiodatocuprate (DPC)

$$\text{[Cu(H₂IO₄)₂(H₂O)₃]}^-$$

Monoperiodatocuprate (MPC)

![Figure 2: Structure of (a) DPC (III) and (b) MPC (III).](image)

3. Results and Discussion

3.1. Stoichiometry and Product Analysis. Several sets of reaction mixtures with varying ratio of DPC (III) to CRBC in presence of constant amounts of KOH and KNO₃ were kept for 2.5 hours in a closed vessel under N₂ atmosphere and the remaining concentration of DPC (III) was analyzed to confirm the accurate stoichiometry by Job’s method which was confirmed to be 1:4 for CRBC:DPC. When CRBC reacts with DPC (III) in alkaline medium, 2-phenylmalonic acid (C₉H₈O₄) and 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide (C₉H₁₂N₂O₃S) were formed as the main products which were recrystallized from ethanol, separated by Column Chromatography over neutral alumina by using 80% benzene and 20% chloroform as eluent. Side product CO₂ was qualitatively detected by bubbling N₂ gas through the acidified reaction mixture and passing the gas liberated through the tube filled with lime water.

The reaction between carbenicillin and diperiodatocuprate (III) in alkaline medium is given as
Scheme 1. Reaction showing the formation of complex.

Here, A is 2-phenylmalonic acid (C_9H_8O_4) and B is 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide (C_8H_12N_2O_4S).

The FT-IR and LC-MS are presented in Figures 4 and 5, respectively.

Both complex and products were characterized by LC-MS, which gave m/z at 703 for complex (C_{17}H_{24}CuIN_2O_6S): the first product (2-phenylmalonic acid) gave m/z at 182 (m + 2) and the second product (2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide) at 232 (m + 1), respectively. A sharp absorption peak was at 1641.2 cm\(^{-1}\) (due to ketonic/carboxylic C\(\sim\)O stretch), 1464.4 and 1386.6 cm\(^{-1}\) (due to CH\(_3\) stretch), 3413.5 cm\(^{-1}\) (due to carboxylic OH group), and 1276.7 cm\(^{-1}\) (due to carboxylic C=O stretch) and a broad peak was at 3380.7 cm\(^{-1}\) (due to N-H stretching). The MPC (III)-CRBC complex (C_{17}H_{24}CuIN_2O_{14}S) showed % elemental analysis as C- 41.37 (41.53), H-5.21 (5.37), N-12.06 (12.16), and S-13.81 (13.88) besides oxygen. The first product, 2-phenylmalonic acid (C_9H_8O_4), showed C-60.00 (60.11) and H-4.48 (4.55) besides oxygen. The second product, 2-(amino (carboxy) methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide (C_8H_{12}N_2O_4S), showed C-41.37 (41.53), H-5.21 (5.37), N-12.06 (12.16), and S-13.81 (13.88) besides oxygen.

3.2. Reaction Orders. The orders of reaction were determined from the slope of log \(k_{\text{abs}}\) versus log (concentration) from different time plots as given in Figure 6 and Table 1 by varying concentrations of carbenicillin, KIO\(_4\), and KOH while keeping the other parameters constant except the concentration of DPC (III).

3.3. Effect of [DPC (III)]. The DPC concentrate was varied in the range of 1.0 \times 10^{-5} to 1.0 \times 10^{-4} mol-dm\(^{-3}\). The linearity and almost parallelism plots of log absorbance versus time up to 85% completion of the reaction by keeping other concentrations remaining constant indicated a reaction order of unity in DPC (III). Table 1 and Figure 6 are in the support of pseudo-first-order reaction with respect to DPC (III).

3.4. Effect of [CRBC]. The effect of [CRBC] was studied within a range of 1 \times 10^{-4} to 1 \times 10^{-3} mol-dm\(^{-3}\). The rate constants (\(k_u\)) increased with increase in [CRBC] and order with respect to carbenicillin was found to be 0.718 (\(r \geq 0.997, s \leq 0.0014\)) which was also confirmed from the plot of (5+log \(k_u\)) vs. 4+log [CRBC], as shown in Figure 7 and Table 1.

3.5. Effect of Alkali. The effect of alkali was studied by varying \[OH^-\] in the range of 0.04 to 0.2 mol-dm\(^{-3}\) DPC (III) and CRBC, as well as ion strength. Rate constant (\(k_0\)) increased with increase in [alkali] and order of reaction with respect to alkali was found to be 0.50 (\(r \geq 0.999, s \leq 0.0005\)), confirmed by the linear plot of (5+log \(k_0\)) vs. 2+log [KOH]), as shown in Figure 8 and Table 1.

3.6. Effect of Periodate. The effect of [KIO\(_4\)] was observed by varying the concentration range from 1.0 \times 10^{-5} to 1.0 \times 10^{-4} mol-dm\(^{-3}\), while the other remaining active masses and conditions were constant. It was observed that rate constants decreased with an increase in [IO\(_4^-\)] and the order of reaction was -0.265 (\(r \geq 0.997, s \leq 0.0002\)) as presented in Figure 9 and Table 1.

3.7. Effect of Ionic Strength (I) and Dielectric Constant (D). Ionic strength is applied to know the participation of specific species in the reaction like ion-dipole, ion-ion, and dipole-dipole with the same or opposite charge, etc. The effect of ionic strength was studied by varying the concentration of KNO\(_3\) in the range of 0.1–0.2 M by keeping the concentration of DPC, CRBC, and KOH constant and we found that increasing ionic strength did not have any significant effect on the rate of reaction. The dielectric constant of the medium (D) can be studied by varying t-butyl alcohol at a constant concentration of DPC, CRBC, KOH, and KNO\(_3\) by using equation \(D = D_1V_1 + D_2V_2\), where \(D_1\) and \(D_2\) are the dielectric constants of water and t-butyl alcohol and \(V_1\) and \(V_2\) are volume fractions of those, respectively. There was no effect of dielectric constant on the rate of the catalyzed reaction.

3.8. Effect of Initially Added Products. Initially added product (CuSO\(_4\) (II)) did not show any significant effect on the rate of reaction.

3.9. Polymerization Study. A known quantity of acrylonitrile [46] monomer was initially added to the reaction mixture.
and allowed to remain in the inert atmosphere for 3.0 hours. The mixture gave no precipitate on dilution with methanol indicating the absence of free radicals.

3.10. Effect of Temperature. The effect of temperature on the rate of oxidation reaction was studied at four different temperatures under the constant concentration of CRBC, KOH, and DPC (III) keeping other conditions constant. Rate constants increased with the rise in temperature. The energy of activation and other activation parameters were calculated by the least square method from the plot of log $k_o$ versus $1/T$ and thence computed in Table 2 and Figure 10.

The energy of activation and other activation parameters were calculated by using least square method from the plot of $(4 + \log k)$ versus $1/T$ and thence computed in Table 3 and Figure 11.

Since DPC (III) is chelating as well as the oxidizing agent, oxidation of different β-lactam antibiotics has been carried out in an alkaline medium. The activity of DPC is a function of pH and is capable of subtle control.

DPC (III) is water-soluble oxidizing reagent that exists as $[\text{Cu} (\text{HIO}_6)_2 (\text{OH})_2]^{-}$ as well as $[\text{HIO}_6]^{4-}$ under higher pH condition. It has been evident that it can also exist as $[\text{Cu} (\text{H}_2\text{IO}_6)_2]$ or $[\text{Cu} (\text{H}_2\text{IO}_6) (\text{OH})_2]^{2-}$ or $[\text{Cu} (\text{H}_2\text{IO}_6) (\text{H}_2\text{O})_2]$ or $[\text{Cu} (\text{H}_2\text{IO}_6) (\text{H}_2\text{O})_2]$ in aqueous alkaline medium. Periodic acid exists as $\text{H}_3\text{IO}_6$ in acid medium. The main species most active for the title work is $[\text{Cu} (\text{H}_2\text{IO}_6) (\text{H}_2\text{O})_2]$ as reported in earlier literature. At higher alkali concentration, periodate ion tends to dimerize.
3.11. Probable Mechanism of Reaction. The oxidation reaction between MPC (III) and carbenicillin showed 1:2 stoichiometry and exhibited pseudo-first-order reaction with respect to DPC (III), fractional order with respect to carbenicillin and alkali, but negative fractional-order periodate. Based on this experimental evidence, a suitable mechanism is proposed along with the proper involvement of all species. In the first step, DPC (III) reacts with the hydroxide ion to form a deprotonated form of DPC (III) which in presence of water yields MPC (III) along with free periodate species. Hence fractional order with respect to carbenicillin presumably results due to the formation of the complex by the interaction between carbenicillin and MPC (III) species. This complex interacts with one mole of MPC (III) in a slow step to give intermediate A along with regeneration of free periodate ion and Cu$^{2+}$ ion. In the next step, intermediate A reacts with fresh mole of MPC (III) to

$$
\begin{align*}
\text{H}_3\text{IO}_6 & \Leftrightarrow \text{H}_3\text{IO}_6^- + \text{H}^+, K_1 = 5.1 \times 10^{-4} \\
\text{H}_4\text{IO}_6^- & \Leftrightarrow \text{H}_4\text{IO}_6^{2-} + \text{H}^+, K_2 = 4.9 \times 10^{-9} \\
\text{H}_5\text{IO}_6^{2-} & \Leftrightarrow \text{H}_5\text{IO}_6^{3-} + \text{H}^+, K_3 = 2.5 \times 10^{-12}
\end{align*}
$$

**Table 1**: Effect of variation of [DPC] *, [CRBC], and [KOH] on the oxidation of carbenicillin by diperiodatocuprate (III) in aqueous alkaline medium at 298 K and $I = 0.10$/mol dm$^{-3}$.

<table>
<thead>
<tr>
<th>[DPC] $\times 10^5$</th>
<th>[CRBC] $\times 10^4$</th>
<th>[OH$^-$] $\times 10^2$</th>
<th>[IO$_4$]$^- \times 10^5$</th>
<th>$k_u \times 10^{-4}$ (s$^{-1}$)</th>
<th>Order</th>
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</thead>
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*Concentrations are expressed in mol dm$^{-3}$. Bold values in [DPC] $\times 10^5$, [CRBC] $\times 10^4$, [OH$^-$] $\times 10^2$, and [IO$_4$]$^- \times 10^5$ signify the variable concentration of each solution for each kinetic run, whereas other values signify constant concentration of solutions used in experiments. Bold values in $k_u \times 10^{-4}$ (s$^{-1}$) signify the average rate constant calculated after conducting the experiment for the corresponding bold value (concentration) of that solution only. Bold values in order signify the exact order of reaction as obtained from the plot.
Table 2: Activation parameters with respect to uncatalyzed rate constant ($k_u$).

<table>
<thead>
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<th>Parameters</th>
<th>Values</th>
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<td>$E_a$ (K J mol$^{-1}$)</td>
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<tr>
<td>$\Delta H^#$ (K J mol$^{-1}$)</td>
<td>28 ± 1</td>
</tr>
<tr>
<td>$\Delta S^#$ (J K$^{-1}$ mol$^{-1}$)</td>
<td>$-205 \pm 3$</td>
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<td>$\Delta G^#$ (K J mol$^{-1}$)</td>
<td>89 ± 2</td>
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<tr>
<td>LogA</td>
<td>2.5 ± 0.6</td>
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Table 3: Activation parameters with respect to slow step rate constants ($\bar{k}$).

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$E_a$ (K J mol$^{-1}$)</td>
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<tr>
<td>$\Delta H^#$ (K J mol$^{-1}$)</td>
<td>48 ± 1</td>
</tr>
<tr>
<td>$\Delta S^#$ (J K$^{-1}$ mol$^{-1}$)</td>
<td>$-150 \pm 2$</td>
</tr>
<tr>
<td>$\Delta G^#$ (K J mol$^{-1}$)</td>
<td>92 ± 2</td>
</tr>
<tr>
<td>LogA</td>
<td>5.3 ± 0.2</td>
</tr>
</tbody>
</table>

Figure 7: Plot of $(5 + \log k_u)$ vs. $4 + \log$ [CRBC].

Figure 8: Plot of $(4 + \log k_u)$ vs. $2 + \log$ [KOH].

Figure 9: Plot of $(5 + \log k_u)$ vs. $5 + \log$ [KIO$_4$].

Figure 10: Plot of $(4 + \log k_u)$ vs. $(1/T) \times 10^3$.

Figure 11: Plot of $(4 + \log k)$ vs. $(1/T) \times 10^3$. 
form intermediate B which undergoes hydrolysis to yield the other final products, i.e., 2-phenylmalonic acid gave m/z at 182 (m + 2) and the second product 2-(amino (carboxy)methyl)-5, 5-dimethyl-4, 5-dihydrothiazole-4-carboxylic acid-1-oxide) as explained in Scheme 1.

\[
\begin{align*}
[Cu(H_2IO_6)_2]^+ + OH^- &\rightleftharpoons [Cu(H_2IO_6)(H_2IO_6)]^{2-} + H_2O \\
[Cu(H_2IO_6)(H_2IO_6)]^{2-} + 2H_2O &\rightleftharpoons [Cu(H_2IO_6)(H_2O)_2] + H_3IO_6^{2-}
\end{align*}
\]

The probable structure of complex C is given as follows:

Spectroscopic evidence for the complex formation between reagent DPC (III) and substrate (CRBC) was obtained from UV-visible spectra by resisting CRBC (5.0 \times 10^{-4} \text{ M}), KOH (0.12 \text{ M}), and a mixture of all. A bathochromic shift was obtained. The Michaelis–Menten plot is in great support for complex formation, Figure 9.

Scheme 1 leads to rate law equation (2) as

\[
\begin{align*}
\text{rate} &= \frac{d[DPC]}{dt} = k[C] \\
k_{\text{obs}} &= \frac{kK_1K_2K_3[DPC][CRBC][OH^-]}{[H_3IO_6^{2-}] + K_1[OH^-][H_2IO_6^{2-}] + K_1K_2[OH^-] + K_1K_2K_3[OH^-][CRBC]}
\end{align*}
\]
Equation (2) describes all kinetic orders observed for different species. The rate law equation (2) can be rearranged into equation (3) that suits for verification:

\[
\frac{1}{k_{\text{obs}}} = \frac{[\text{H}_3\text{IO}_6^{2-}]}{kK_1K_2K_3[\text{CRBC}][\text{OH}^-]} + \frac{[\text{H}_2\text{IO}_6^{3-}]}{kK_2K_3[\text{CRBC}]} + \frac{1}{kK_3[\text{CRBC}]} + \frac{1}{k}
\]  

(3)

The basic rule to calculate the activation energy and other activation parameters and the complete rate law derivation are given in Appendices A and B, respectively.

Figures 12–14 represent verification plots for oxidation of CRBC by DPC (III) in alkaline medium. According to equation (3), other remaining conditions being constant, the plots of $1/k_u$ vs. $1/\text{[KOH]}$ ($r \geq 0.999, \leq s 0.003$), $1/k_u$ vs. $1/\text{[CRBC]}$ ($r \geq 0.997, \leq s 0.004$), and $1/k_u$ vs. $[\text{H}_2\text{IO}_6^{3-}]$ ($r \geq 0.999, \leq s 0.003$) should be linear and are found to be so as in Figures 12–14.

Overall slow step rate constants and equilibrium constants are presented in Tables 4 and 5 including thermodynamic parameters at 298 K.

Scheme 1 clarifies the participation of neutral species in the reaction due to invariable ionic strength and dielectric constant. The modest values of both enthalpy and entropy of activation, within the range of electron pairing and unpairing process for the loss of degree of freedom and rigid transition state, are favourable for electron transfer reactions. The higher negative value of $\Delta S^\ddagger$ suggests that the intermediate complex is probably highly ordered compared to the reacting species. The above results, evidences,
and lower rate constant for slow steps indicate that the oxidation presumably occurs via an inner-sphere mechanism. The reducing property of the substrate is, probably, reduced in the absence of catalyst and the path of the uncatalyzed reaction is extended by increasing the activation energy.

4. Conclusions

The oxidation of carbenicillin by DPC (III) was studied experimentally in aqueous alkaline medium. (MPC-III) [Cu (H₂IO₆) (H₂O)₂] was considered to be the active species for the present work. Activation and thermodynamic parameters with respect to uncatalyzed rate constant (k_u), slow step rate constant (k), and equilibrium constants at different temperatures were calculated and computed. Overall sequences described here are inconsistent with all experimental evidences including product, spectral analysis, and mechanistic and kinetics studies.

Appendix

(A). Calculation of Activation Parameters

The energy of activation for the present reaction was calculated by

$$E_a = -2.303 \times R \text{ slope.}$$  \hspace{1cm} (A.1)

The Arrhenius factor “A” was calculated by

$$\log A = \log k_u + \frac{E_a}{2.303 RT}$$  \hspace{1cm} (A.2)

The entropy of activation was calculated by

$$\frac{\Delta S^\#}{4.576} = \log k_u - 10.753 - \log T + \frac{E_a}{4.576T}$$  \hspace{1cm} (A.3)

The enthalpy of activation was calculated by

$$\Delta H^\# = E_a - RT.$$  \hspace{1cm} (A.4)

The free energy of activation was calculated by

$$\Delta G^\# = \Delta H^\# - T\Delta S^\#,$$  \hspace{1cm} (A.5)

where $k_u/k_{obs}$ is uncatalyzed rate constant in sec⁻¹, $T$ is temperature in Kelvin, $E_a$ is energy of activation in calories, $R$ is universal gas constant, and $\#$ is activation parameter.

(B). Derivation of Rate Law

From scheme 1,

$$rate = -\frac{d[DPC]}{dt} = k[\text{complex}] = k[C].$$  \hspace{1cm} (B.1)

From the law of mass action, the third equilibrium constant can be given by

$$K_3 = \frac{[C]}{[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2]_{\text{CRBC}}}$$  \hspace{1cm} (B.2)

After rearrangement, we get

$$[C] = K_3[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2]_{\text{CRBC}}$$  \hspace{1cm} (B.3)

Substituting the value of C from equation (B.3), we get

$$rate = -\frac{d[DPC]}{dt} = K_1K_3[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2]_{\text{CRBC}}$$  \hspace{1cm} (B.4)

The second equilibrium constant can be given by

$$K_2 = \frac{[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2][\text{H}_3\text{IO}_6^{2-}]}{[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2]_{\text{CRBC}}[\text{H}_3\text{IO}_6^{2-}]}$$  \hspace{1cm} (B.5)

This can be rearranged into

$$[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2] = K_2[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2][\text{H}_3\text{IO}_6^{2-}]$$  \hspace{1cm} (B.6)

The first equilibrium constant can be given by

$$K_1 = \frac{[\text{Cu(H}_2\text{IO}_6)(\text{H}_2\text{O})_2][\text{OH}^-]}{[\text{Cu(H}_2\text{IO}_6)_2][\text{H}_3\text{IO}_6^{2-}]}$$  \hspace{1cm} (B.7)
This can be rearranged into
\[
[Cu(H_2IO_6)(H_3IO_6)]^{-2} = K_1 [Cu(H_2IO_6)_2]^{-} [OH^-}
\]  
(B.8)

Substituting equation (B.6) into (B.8) in equation (B.4), we get
\[
\text{Rate} = \frac{d[DPC]}{dt} = \frac{kK_1K_2K_3[CRBC][DPC][OH^-]}{[H_2IO_6]^2}
\]  
(B.9)

\[
[DPC]_T = [DPC]_f + K_1[DPC]_f[OH^-] + \frac{K_1K_2[DPC]_f[OH^-]}{[H_2IO_6]^2} + \frac{K_1K_2K_3[DPC]_f[OH^-]}{[H_2IO_6]^2}[CRBC]
\]  
(B.10)

\[
[DPC]_T = \frac{[DPC]_T[H_2IO_6^2]}{[H_2IO_6^2]} + K_1[OH^-][H_2IO_6^2] + K_1K_2[OH^-] + K_1K_3[OH^-][CRBC]
\]  
(B.11)

The total concentration of \([OH^-]\) can be given as
\[
[OH^-]_T = [OH^-]_f + [Cu(H_2IO_6)(H_3IO_6)]^{-2} + [Cu(H_2IO_6)(H_2O)] + [C]
\]  
(B.12)

\[
[OH^-]_T = [OH^-]_f + K_1[DPC][OH^-] + \frac{K_1K_2[DPC][OH^-]}{[H_2IO_6]^2} + \frac{K_1K_2K_3[DPC][OH^-]}{[H_2IO_6]^2}[CRBC]
\]  
(B.13)

\[
[OH^-]_T = [OH^-]_f \left(1 + K_1[DPC] + \frac{K_1K_2[DPC]}{[H_2IO_6]^2} + \frac{K_1K_2K_3[DPC][CRBC]}{[H_2IO_6]^2}\right)
\]  
(B.14)

\[
[CRBC]_T = [CRBC]_f
\]

Putting these values of \([DPC]_f\) from equation (B.11), \([OH^-]_f\) from equation (B.13), and \([CRBC]_f\) from equation (B.14) in equation (B.9) after omitting subscripts \(T\) and \(f\), we get
\[
\text{Rate} = \frac{d[DPC]}{dt} = \frac{kK_1K_2K_3[CRBC][DPC][OH^-]}{[H_2IO_6]^2 + [H_2IO_6^2] + K_1[OH^-][H_2IO_6^2] + K_1K_2[OH^-] + K_1K_3[OH^-][CRBC]}
\]  
(B.15)

Data Availability
The data used to support the findings of this study are available from the corresponding author upon request.

Conflicts of Interest
The authors declare that there are no conflicts of interest regarding the publication of this paper.
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