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Kinetics and Mechanism of Oxidation of Chloramphenicol – an Antibiotic Drug by Diperiodatocuprate(III) in Aqueous Alkaline Medium

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Chloramphenicol / Diperiodatocuprate(III) / Oxidation / Kinetics

The kinetics of oxidation of chloramphenicol (CHP) by diperiodatocuprate(III) (DPC) in aqueous alkaline medium at a constant ionic strength of 0.10 mol dm^{-3} was studied spectrophotometrically. The reaction between DPC and CHP in alkaline medium exhibits 1:2 stoichiometry (CHP: DPC). The main oxidation products were identified by spot test, IR, NMR and GCMS spectral studies. The reaction is of first order in DPC and CHP concentrations. As the alkali concentration increases the rate of reaction increases with fractional order dependence on alkali concentration. Increase in periodate concentration decreases the rate. A suitable mechanism is proposed. The reaction constants involved in the different steps of the mechanism were calculated. The activation parameters with respect to slow step of the mechanism are computed and discussed. Thermodynamic quantities are also determined.

1. Introduction

In recent years the study of highest oxidation states of transition metals has intrigued many researchers. Transition metals in a higher oxidation state can be stabilized by chelating with suitable polydentate ligands. Metal chelates such as diperiodatocuprate(III) [1], diperiodatoargentate(III) [2], diperiodatonickelate(IV) [3] are good oxidants in a medium with a appropriate pH value. Periodate and tellurate complexes of copper in its trivalent state have been extensively used in the analysis of several organic compounds [4]. The kinetics of self-decomposition of these complexes was studied in detail [5]. Copper(III) is shown

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to be an intermediate in the copper(II) catalysed oxidation of amino acids by peroxydisulphate [6]. The oxidation reaction usually involves the copper(II)-copper(I) couple and such aspects are dealt in different reviews [7,8]. The use of diperiodatocuprate(III) (DPC) as an oxidant in alkaline medium is new and restricted to a few cases due to its limited solubility in aqueous medium. DPC is a versatile one-electron oxidant for various organic compounds in alkaline medium and its use as an analytical reagent is well recognized [9].Copper complexes have occupied a major place in oxidation chemistry due to their abundance and relevance in biological chemistry [10–14]. Copper(III) is involved in many biological electron transfer reactions [15]. When copper(III) periodate complex is an oxidant, multiple equilibrium steps between different copper(III) species are involved, it would be interesting to know which of the species is the active oxidant.

Chloramphenicol(2,2-dichloro-*N*-[(1*R*,2*R*)-2-hydroxy-(hydroxymethyl)-nitrophenyl)-ethyl]acetamide) is a bacteriostatic antimicrobial. Chloramphenicol(CHP) is effective against a wide variety of Gram-positive and Gram-negative bacteria, including most anaerobic organisms. It is considered a prototypical broad band spectrum antibiotic, alongside the tetracycline's. The clinical application of chloramphenicol was in the treatment of typhoid. The most serious adverse effect associated with chloramphenicol treatment is bone marrow toxicity. Due to their extensive usage, chloramphenicol may enter the environment via wastewater effluent and biosolids from sewage treatment plants and via manure and litters from food-producing animal husbandry. The presence and accumulation of chloramphenicol antibiotics in aquatic environments, albeit at low concentrations, may pose threats to the ecosystem and human health by inducing increase and spread of bacteria drug-resistance due to long-term exposure. This necessitates development of the various advanced oxidation processes for the transformation of chloramphenicol in water. In view of potential pharmaceutical importance of chloramphenicol and lack of literature on the oxidation of this drug by any oxidant and the complexity of the reaction, a detailed study of the reaction becomes important. Hence the title reaction is undertaken.

2. Experimental

2.1 Chemicals and materials

All chemicals used were of A. R. grade and double distilled water was used throughout the work. The solution of chloramphenicol (Sisco Chem) was prepared by dissolving known amount of the samples in distilled water. The purity of the samples was checked by their melting point 150°C. (Literature: 149°C–153°C). The copper(III) periodato complex was prepared [16] and standardized by a standard procedure [17]. The copper(II) solution was made by dissolving the known amount of copper sulphate (BDH) in distilled water. Periodate solu-

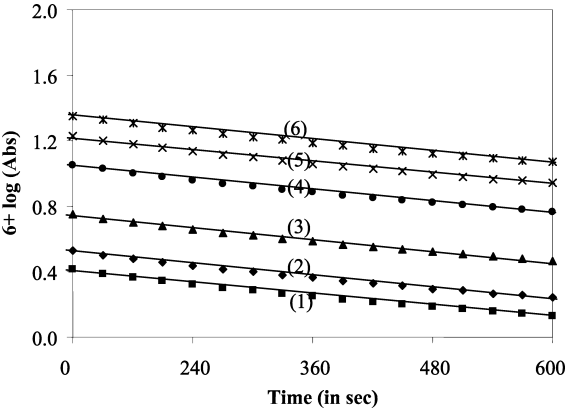


Fig. 1. First order plots of oxidation of chloramphenicol by DPC at 25°C [CHP] = 5.0×10^{-4}; $[OH^-] = 0.05$; I = 0.10/mol dm^{-3} = (1) 0.5, (2) 1.0, (3) 2.0, (4) 3.0, (5) 4.0, (6) 5.0.

tion was prepared by weighing out the required amount of sample in hot water and used after 24h. Its concentration was ascertained iodometrically [18] at neutral pH by a phosphate buffer. Since periodate is present in excess in DPC and also in the reaction mixture, the possibility of oxidation of chloramphenicol by periodate on alkaline medium in 25°C was checked. However, it was found that there was no significant reaction under the experimental conditions employed compared to the DPC oxidation of chloramphenicol. KOH and KNO_3 solutions were employed to maintain the required alkalinity and ionic strength respectively.

2.2 Kinetic measurements

The oxidation of CHP by DPC was followed under pseudo-first order conditions, where [CHP] > [DPC] at 25 ± 0.1°C. The reaction was initiated by adding DPC to chloramphenicol which also contained the required concentration of KNO_3, KOH and KIO_4. The progress of the reaction was followed spectrophotometrically at 415 nm by monitoring the decrease in absorbance of DPC. Earlier the extinction coefficient was determined at 415 nm for different concentrations and was found to be ε = 6235 ± 250 dm^3 mol^{-1} cm^{-1}. It was verified that there is negligible interference from other species present in the reaction mixture at this wavelength.

The pseudo-first order rate constants, k_{obs} were determined from log(absorbance) versus time plots (Fig. 1). The plots were linear up to 80% completion of the reaction. The rate constants were reproducible within ±5% and are the average of atleast three independent kinetic runs. During the kinetics a constant concentration of KIO_4 viz. 5.0×10^{-5} mol dm^{-3} was used throughout the study unless otherwise stated and excess periodate is present in DPC, the possibility

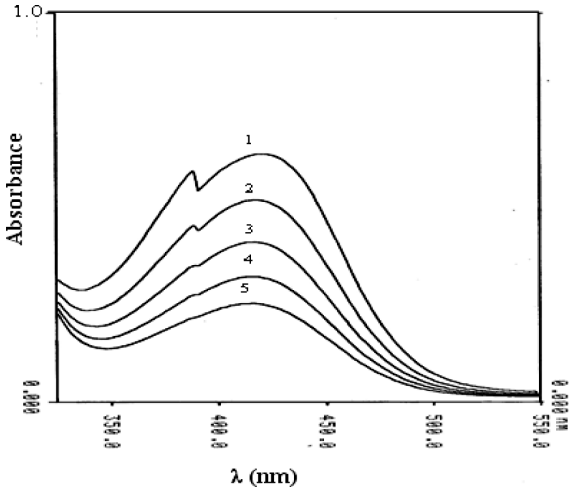
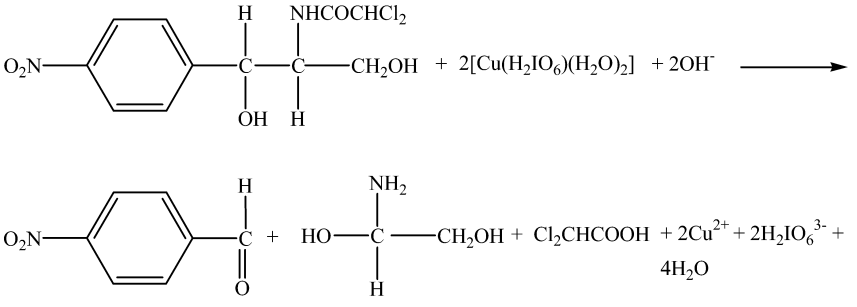


Fig. 2. Spectral changes during the oxidation of chloramphenicol by DPC at 25.0°C; [DPC] = 5.0×10^{-5}, [CHP] = $5.0 \times 10^{-4,}$ [OH^-] = 0.05 and I = 0.10 / mol dm^{-3} (scanning time interval is 1.0 min).

of the oxidation of chloramphenicol by periodate in alkaline medium at 25°C was checked. It was found that there is no significant reaction between CHP and periodate under the experimental conditions employed compared to the DPC oxidation of chloramphenicol. The concentration of periodate and OH^- was calculated by considering the amount present in the DPC solution and that additionally added. Kinetic runs were also carried out in N_2 atmosphere in order to understand the effect of dissolved oxygen on the reaction. No significant difference in the results was obtained in the N_2 atmosphere and in presence of air. In view of the ubiquitous contamination of carbonate in the basic medium, the effect of carbonate was also studied. Added carbonate has no effect on the reaction rates. The spectral changes during the reaction are shown in Fig. 2. It is evident from the figure that the concentration of DPC decreases at 415nm.

2.3 Stoichiometry and product analysis

Different sets of reaction mixtures containing excess of DPC to chloramphenicol in presence of constant amount of OH^- and KNO_3 were kept for 6h in a closed vessel under inert atmosphere. The remaining DPC concentration was estimated



Scheme 1. Stoichiometric equation for the oxidation of chloramphenicol by alkaline diperiodatocuprate.

by spectrophotometrically at 415nm. The results, indicated that one mole of CHP requires two moles of DPC as shown in Scheme 1.

After completion of the reaction, the reaction mixture was acidified, concentrated and extracted with ether. The ether layer was subjected to column chromatography [19] and fractions are subjected to spectral investigations. From the IR, (Fig. 3) GCMS (Fig. 4) and NMR (Fig. 5) spectra, the main oxidation product was identified as p-nitrobenzaldehyde. IR spectrum showed C = O stretching for aldehydic functional group at 1708 cm^{-1},while $-NO_2$ stretching observed at 1349 cm^{-1}. The presence of p-nitrobenzaldehyde was also confirmed by GC-MS analysis (Fig. 4), obtained on a Shimadzu 17A gas chromatograph with a Shimadzu XP- 5000A mass spectrometer using EI ionization technique. The mass spectrum showed the base peak at 151 amu consistent with the molecular ion of 151 amu. All other peaks observed in the GC-MS can be interpreted in accordance with the structure of p-nitrobenzaldehyde. Further p-nitrobenzaldehyde was characterized by its ^{1}HNMR spectra (Fig. 5) (DMSO): 10.17 (s.1H, CHO), 8.18 (d, 2H, ArH), 7.67(d, 2H, ArH).Another product 2-Amino, hydroxyethanol was confirmed by GCMS spectra which showed the molecular ion peak at 77amu. Chloro-acetic acid is confirmed by spot test [20].

3. Results

3.1 Reaction orders

The reaction orders were determined from the slope of log k_{obs} versus log (concentration) plots by varying the concentrations of chloramphenicol, alkali and periodate in turn while keeping all other concentrations and conditions constant.

3.2 Effect of [diperiodatocuprate (III)]

The oxidant DPC concentrations was varied in the range of 5.0×10^{-6} to 5.0×10^{-5} mol dm^{-3} and fairly constant k_{obs} values indicates that order with

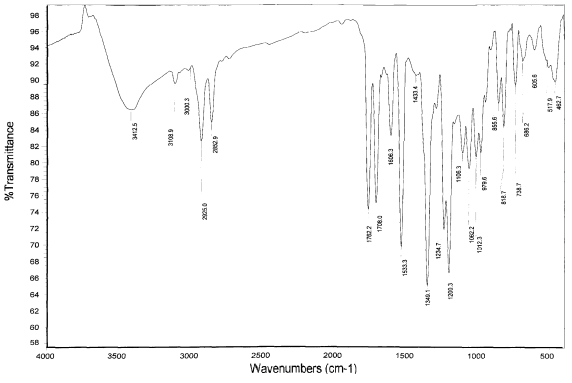


Fig. 3. FT-IR spectra of p-nitrobenzaldehyde, the product of oxidation of chloramphenicol by DPC.

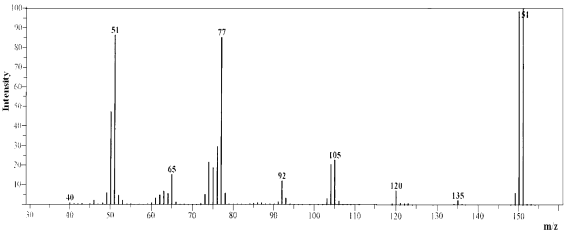


Fig. 4. GC-MS spectra of the product p-nitrobenzaldehyde showed molecular ion peak and base peak at m/z 151 amu.

respect to DPC concentration was unity (Table 1). This was also confirmed by linearity of the plots of log(absorbance) versus time up to 80% completion of the reaction as shown in Fig. 1.

3.3 Effect of [chloramphenicol]

The effect of chloramphenicol on the rate of reaction was studied at constant concentrations of alkali, DPC and periodate at a constant ionic strength of 0.10 mol dm^{-3}. The substrate CHP was varied in the range of 1.0×10^{-4} to 1.0×10^{-3} mol dm^{-3}. The k_{obs} values increased with increases in the concentration of CHP (Table 1). The order with respect to CHP concentration was found to be unity. This was also confirmed by the plot of k_{obs} versus CHP concentration (Fig. 6.), which is a straight line passing through the origin.

3.4 Effect of [alkali]

The effect of alkali concentration on the reaction was studied in the range 0.01 to 0.1 mol dm^{-3} at constant concentrations of chloramphenicol, DPC and perio-

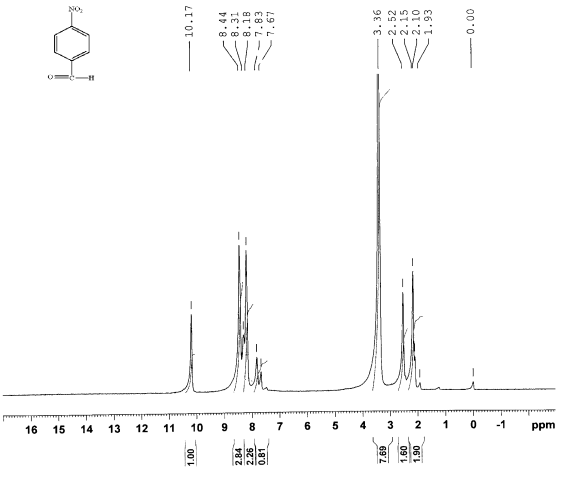


Fig. 5. ^{1}H NMR spectra of p-nitrobenzaldehyde, the product of oxidation of chloramphenicol by DPC.

date at constant ionic strength of 0.10 mol dm^{-3} at 25°C. The rate constants increased with the increase in the alkali concentration (Table 1). The order was found to be less than unity (0.32).

3.5 Effect of [periodate]

The effect of periodate was studied by varying the periodate concentration from 1.0×10^{-5} to 1.0×10^{-4} mol dm^{-3} keeping all other reactant concentrations constant. It was found that the added periodate had a retarding effect on the rate of reaction (Table 1).

3.6 Effect of ionic strength and dielectric constant

The effect of ionic strength was studied by varying the potassium nitrate concentration. Ionic strength was varied from 0.01 to 1.0 mol dm^{-3} at constant concentration of DPC, chloramphenicol, periodate and alkali. It was found that increasing ionic strength had negligible effect on the rate constant. The effect of dielectric constant (D) was studied by varying the t-butanol-water (v/v) content in the reaction mixture with all the other conditions being kept constant. Decreasing the dielectric constant of the medium had no effect on the rate of the reaction.

3.7 Effect of initially added products

The externally added products, p-nitrobenzaldehyde and copper(II) ($CuSO_4$) in the concentration range 1.0×10^{-6} to 1.0×10^{-5}, did not have any significant effect on the rate of reaction.

Table 1. Effect of variation of [DPC], [CHP] and [OH^-] on the oxidation of chloramphenicol by DPC at 25°C and I = 0.10 mol dm^{-3}.

[DPC] × 10^5 (mol dm^{-3})	[CHP] × 10^4 (mol dm^{-3})	[OH^-] (mol dm^3)	[$H_3IO_6^{2-}$] × 10^5 (mol dm^3)	k_{obs} × 10^3 (s^{-1})		$k_2 = k_{obs}/[CHP]$ ($dm^3 mol^{-1} s^{-1}$)
				Found	Calc.	
0.5	5.0	0.05	5.0	2.33	2.31	-
1.0	5.0	0.05	5.0	2.20	2.10	-
2.0	5.0	0.05	5.0	2.33	2.43	-
3.0	5.0	0.05	5.0	2.25	2.20	-
4.0	5.0	0.05	5.0	2.31	2.34	-
5.0	5.0	0.05	5.0	2.53	2.53	-
5.0	1.0	0.05	5.0	0.50	0.52	5.00
5.0	3.0	0.05	5.0	1.51	1.55	5.03
5.0	5.0	0.05	5.0	2.53	2.53	5.06
5.0	7.0	0.05	5.0	3.54	3.54	5.05
5.0	9.0	0.05	5.0	4.55	4.55	5.05
5.0	10.0	0.05	5.0	5.06	5.06	5.06
5.0	5.0	0.01	5.0	1.33	1.30	-
5.0	5.0	0.03	5.0	2.20	2.24	-
5.0	5.0	0.05	5.0	2.53	2.53	-
5.0	5.0	0.07	5.0	2.70	2.72	-
5.0	5.0	0.09	5.0	2.81	2.84	-
5.0	5.0	0.10	5.0	2.85	2.81	-
5.0	5.0	0.05	1.0	3.09	3.10	-
5.0	5.0	0.05	3.0	2.78	2.75	-
5.0	5.0	0.05	5.0	2.53	2.53	-
5.0	5.0	0.05	7.0	2.32	2.30	-
5.0	5.0	0.05	9.0	2.14	2.16	-
5.0	5.0	0.05	10.0	2.06	2.09	-

3.8 Polymerization study

The intervention of free radicals in the reaction was examined as follows: The reaction mixture, to which a known quantity of acrylonitrile monomer was initially added, was kept for 2h in an inert atmosphere. On diluting the reaction mixture with methanol, a white precipitate was formed, indicating the intervention of free radical in the reaction. The blank experiments of either DPC or chloramphenicol alone with acrylonitrile did not induce any polymerization under the same conditions as those induced for reaction mixture. Initially added acrylonitrile decreased the rate of reaction indicating free radical intervention.

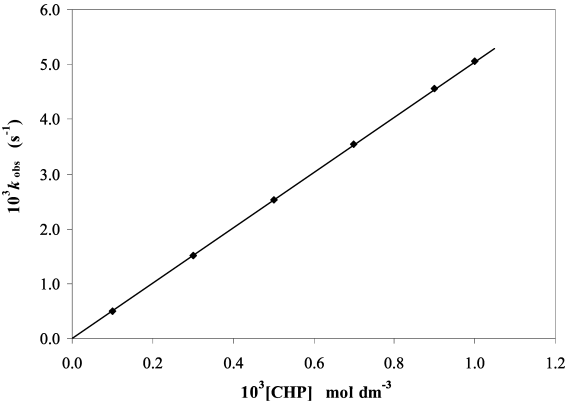


Fig. 6. Plot of k_{obs} versus [CHP] (Conditions as in Table 1).

3.9 Effect of temperature

The kinetics was studied at four different temperatures under varying concentrations of chloramphenicol, alkali and periodate, keeping other conditions constant. The rate of reaction was found to increases with increase in temperature. The rate constants (k) of the slow step of Scheme 1 were obtained from the slopes and intercepts of $[\text{CHP}]/k_{obs}$ versus $1/[\text{OH}^-]$ and $[\text{CHP}]/k_{obs}$ versus $[H_3IO_6^{2-}]$ (Fig. 7.) plots at four different temperatures. The energy of activation corresponding to these rate constants was evaluated from the Arrhenius plot of log k versus $1/T$ and from which other activation parameters were calculated (Table 2).

4. Discussion

The water soluble copper(III) periodate complex is reported [21] $[Cu(HIO_6)_2(OH)_2]^{7-}$. However in an aqueous alkaline medium and at high pH range employed in the study, periodate is unlikely to exist as HIO_6^{4-} is evident from its involvement in the multiple equilibria [22–24] (1)–(3), depending on the pH of the solution.

$$H_5IO_6 \overset{K_1}{\rightleftharpoons} H_4IO_6^- + H^+ \qquad K_1 = 5.1\times10^{-4}\ \text{mol dm}^{-3} \tag{1}$$

$$H_4IO_6^- \overset{K_2}{\rightleftharpoons} H_3IO_6^{2-} + H^+ \qquad K_2 = 4.9\times10^{-9}\ \text{mol dm}^{-3} \tag{2}$$

$$H_3IO_6^{2-} \overset{K_3}{\rightleftharpoons} H_2IO_6^{3-} + H^+ \qquad K_3 = 2.5\times10^{-12}\ \text{mol dm}^{-3} \tag{3}$$

Periodic acid exists as H_5IO_6 in acid medium and as $H_4IO_6^-$ near pH 7. Thus, under the conditions employed in alkaline medium, main species are

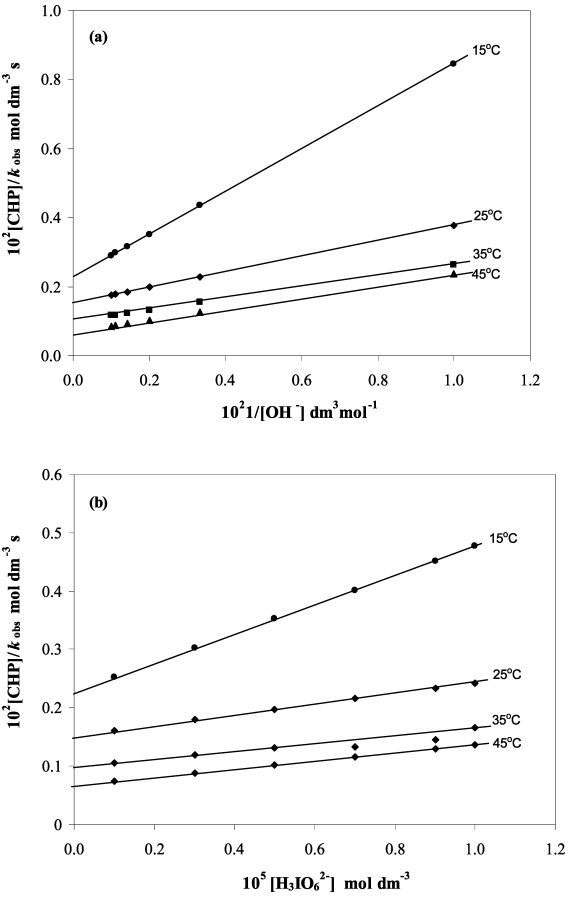


Fig. 7. (a) Plots of [CHP]/k_{obs} versus 1/[OH^-] at four different temperatures (Conditions as in Table 1). (b) Plots of [CHP]/k_{obs} versus [$H_3IO_6^{2-}$] at four different temperatures (Conditions as in Table 1).

expected to be $H_3IO_6^{2-}$and $H_2IO_6^{3-}$. Thus, at pH employed in this study, the soluble copper(III) priodate complex exist as diperiodatocuprate(III), $[Cu(OH)_2(H_3IO_6)_2]^{2-}$, a conclusion also supported by literature [23,24].

The reaction between the diperiodatocuprate(III) complex and chloramphenicol in alkaline medium has stiochiometry 1:2 (CHP: DPC) with first order dependence on DPC and CHP concentrations and an apparent order less than unit order in alkali concentration, a negative fractional order dependence on the periodate concentration. No effect of added products was observed. Based on the experimental results, a mechanism is proposed for which all the observed orders in each constituent such as [oxidant], [reductant]. [OH^-] and [IO_4^-] may be well accommodated. Lister [25] proposed three forms of copper(III) periodate

Table 2. Effect of temperature on the oxidation of chloramphenicol by DPC in aqueous alkaline medium.

(a) Rate constant with respect to slow step of Scheme 2.

Temperature (K)	k ($dm^3\ mol^{-1}s^{-1}$)
288	2.345
298	6.562
308	10.12
318	14.68
Parameter	Values
Activation parameters	
Ea	46 ± 1 kJ mol^{-1}
$\Delta H^{\#}$	43 ± 1 kJ mol^{-1}
$\Delta S^{\#}$	−84 ± 4 J $K^{-1}mol^{-1}$
$\Delta G^{\#}$	68 ± 2 kJ mol^{-1}
log A	8 ± 0.02 s^{-1}

(b) Effect of temperature on first and second equilibrium step of Scheme 2.

Temperature (K)	$K_4 \times 10^3$(dm^{-3} mol^{-1})	$K_5 \times 10^2$(mol dm^{-3})
288	1.63 ± 0.02	2.12 ± 0.02
398	2.11 ± 0.03	1.62 ± 0.03
308	2.68 ± 0.03	1.12 ± 0.04
318	3.12 ± 0.04	0.65 ± 0.02

(c) Thermodynamic quantities with respect to first and second step of Scheme 2.

Thermodynamic quantities	Values from K_4	Values from K_5
ΔH kJ mol^{-1}	16.7 ±1.2	−29.6 ± 0.5
ΔS J $K^{-1}mol^{-1}$	43 ± 2.4	−135.5 ± 3
ΔG kJ mol^{-1}	3.1 ± 0.01	11.75 ± 0.5

in alkaline medium as diperiodatocuprate(III)(DPC), monoperiodatocuprate(III)(MPC) and tetraperiodatocuprate(III). The latter is ruled out, as its equilibrium constant is 8.0×10^{-11} at 40°C. In the present kinetic study, DPC and MPC are to be considered as active forms of copper(III) periodate complex. It may be expected that lower periodate complex such as MPC is more important in the reaction than the DPC. The results of increase in the rate with increase in alkali concentration suggests that equilibia of copper(III) periodate complexes are possible as in Eqs (4) and (5).

$$[Cu(H_3IO_6)_2]^- + [OH^-] \overset{K_4}{\rightleftharpoons} [Cu(H_2IO_6)(H_3IO_6)]^{2-} + H_2O \quad (4)$$

$$[Cu(H_2IO_6)(H_3IO_6)]^{2-} + 2H_2O \overset{K_5}{\rightleftharpoons} [Cu(H_2IO_6)(H_3IO_6)] + [H_3IO_6]^{2-} \quad (5)$$

In the present study, the oxidation reaction proceeds via the formation of a free radical derived from chloramphenicol, in the slow step. The formation of such free radical is also observed in literature [26]. This free radical in a subse-

quent fast steps decomposes to give p-nitrobenzaldehyde and another free radical. In the next fast step thus formed free radical reacts with another mole of MPC in presence of OH^- to form 2, 2-Dichloro-N-(1, 2-dihydroxy-ethyl)-acetamide. In the further fast steps 2, 2-Dichloro-N-(1,2-dihydroxy-ethyl)-acetamide undergoes hydrolysis to give the final products 2,2-amino, hydroxy-ethanol and dichloroacetic acid. So, the detailed mechanistic Scheme for the oxidation of CHP by diperiodatocuprate(III) is presented in Scheme 2.

Since the Scheme 2 is in accordance with the generally well-accepted principle of non-complementary oxidations taking place in sequence of one-electron steps, the reaction between the substrate and oxidant would afford a free radical intermediate. A free radical scavenging experiment revealed such a possibility. This type of radical intermediate has also been observed in literature [27,28]. Scheme 2 leads to rate law (12) as follows. According to Scheme 2,

$$\text{Rate} = \frac{-\mathrm{d}[\mathrm{DPC}]}{\mathrm{d}t} = k[\mathrm{Cu(H_2IO_6)(_{H_2}O)2}][\mathrm{CHP}] = \frac{kK_5[\mathrm{Cu(H_2IO_6)(H_3IO_6)}]^{2-}[\mathrm{CHP}]}{[\mathrm{H_3IO_6}^{2-}]} = \tag{6}$$

$$= \frac{kK_4K_5[\mathrm{CHP}][\mathrm{DPC}]_f[\mathrm{OH}^-]_f}{[\mathrm{H_3IO_6}^{2-}]} \tag{7}$$

The total [DPC] can be written as

$$[\mathrm{DPC}]_t = [\mathrm{DPC}]_f + [\mathrm{Cu(H_2IO_6)(H_2IO_6)}]^{2-} + [\mathrm{Cu(H_2IO_6)(H_2O)_2}] = \tag{8}$$

$$= [\mathrm{DPC}]_f\left\{\frac{[\mathrm{H_3IO_6}^{2-}]+K_4[\mathrm{H_3IO_6}^{2-}][\mathrm{OH}^-]+K_4K_5[\mathrm{OH}^-]}{[\mathrm{H_3IO_6}^{2-}]}\right\} \tag{9}$$

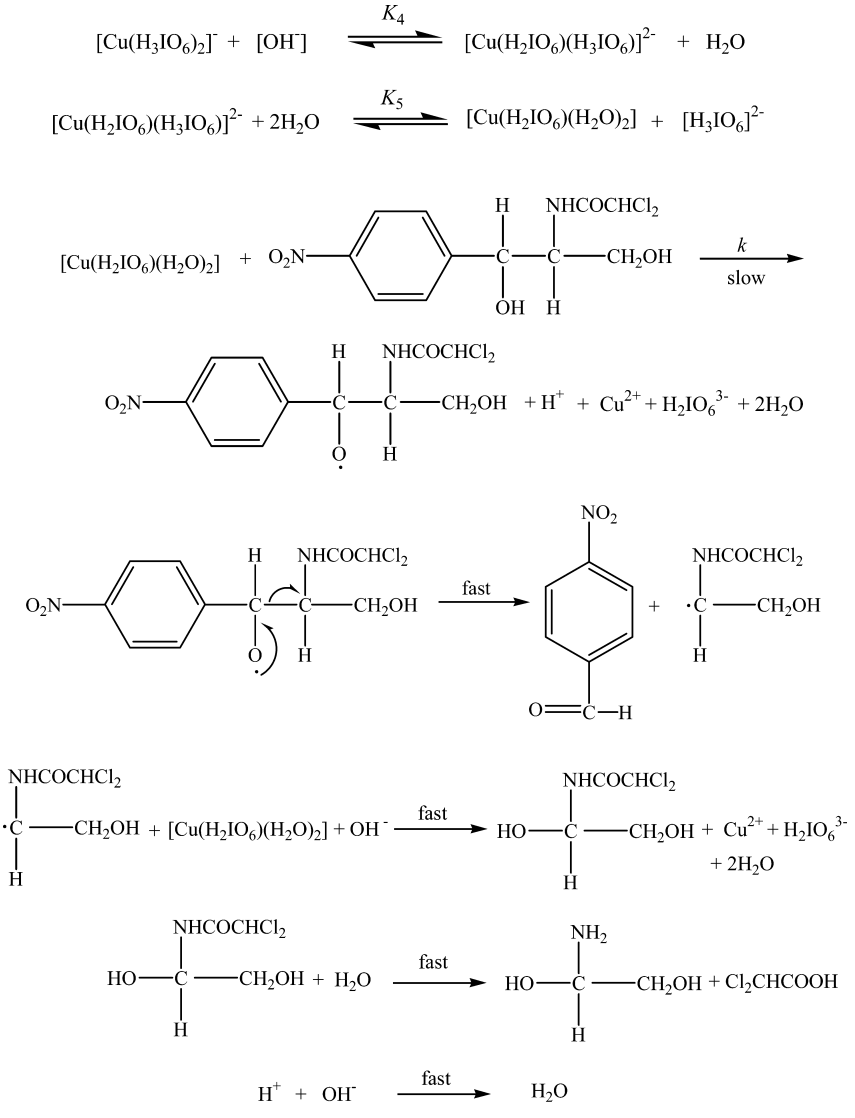
Where, $[\mathrm{DPC}]_t$ and $[\mathrm{DPC}]_f$ refer to total and free DPC concentrations respectively. Therefore free [DPC] is given by,

$$[\mathrm{DPC}]_f = \frac{[\mathrm{DPC}]_t[\mathrm{H_3IO_6}^{2-}][\mathrm{OH}^-]}{[\mathrm{H_3IO_6}^{2-}] + K_4[\mathrm{H_3IO_6}^{2-}] + K_4K_5[\mathrm{OH}^-]} \tag{10}$$

Similarly, the total $[\mathrm{OH}^-]$ can be written as

$$[\mathrm{OH}^-]_t = [\mathrm{OH}^-]_f + [\mathrm{Cu(H_2IO_6)(H_2IO_6)}]^{2-} + [\mathrm{Cu(H_2IO_6)(H_2O)_2}]$$

$$[\mathrm{OH}^-]_t = [\mathrm{OH}^-]_f\left\{1 + K_4[\mathrm{DPC}] + \frac{K_4K_5[\mathrm{DPC}]}{[\mathrm{H_3IO_6}^{2-}]}\right\}$$



Scheme 2. Detailed Scheme for the oxidation of chloramphenicol by alkaline diperiodatocuprate.

In view of low concentration of [DPC] and $[H_3IO_6^{2-}]$ above equation reduced to

$$[OH^-]_t = [OH^-]_f \quad (11)$$

Substituting Eqs. (10) and (11) in Eq. (7) and omitting t and f we get,

$$\text{Rate} = \frac{kK_4K_5[\text{CHP}][\text{DPC}][\text{OH}^-]}{[\text{H}_3\text{IO}_6{}^{2-}] + K_4[\text{H}_3\text{IO}_6{}^{2-}][\text{OH}^-] + K_4K_5[\text{OH}^-]}$$
$$\frac{\text{Rate}}{[\text{DPC}]} = k_{\text{obs}} = \frac{kK_4K_5[\text{CHP}][\text{OH}^-]}{[\text{H}_3\text{IO}_6{}^{2-}] + K_4[\text{H}_3\text{IO}_6{}^{2-}][\text{OH}^-] + K_4K_5[\text{OH}^-]} \quad (12)$$

The rate law (12) can be arranged in to the following form, which is suitable for verification.

$$\frac{[\text{CHP}]}{k_{\text{obs}}} = \frac{[\text{H}_3\text{IO}_6{}^{2-}]}{kK_4K_5[\text{OH}^-]} + \frac{[\text{H}_3\text{IO}_6{}^{2-}]}{kK_5} + \frac{1}{k} \quad (13)$$

According to Eq. (13), other conditions being constant, plots of $[\text{CHP}]/k_{\text{obs}}$ versus $1/[\text{OH}^-]$and $[\text{CHP}]/k_{\text{obs}}$ versus $[\text{H}_3\text{IO}_6^{2-}]$ should be linear and found to be so (Fig.7). The slopes and intercept of such plots lead to the values of K_4, K_5 and k are 2.11×10^{-1} dm^3 mol^{-1}, 1.62×10^{-2} mol dm^{-3} and 6.56 dm^3 mol^{-1} s^{-1} respectively at 25°C. The values of K_4 and K_5 are in good agreement with earlier literature [29]. The equilibrium constant K_4 is far greater than K_5. This may be attributed to the greater tendency of DPC to undergo hydrolysis compared to the dissociation of hydrolyzed species in alkaline medium. Using these rate constants under the experimental conditions were calculated according to Equation (12) and compared with experimental data (Table 1). The experimental and calculated rate constants are in good agreement. This fortifies the proposed mechanism.

The thermodynamic quantities for the first and second equilibrium steps of Scheme 2 can be calculated as follows. The $[\text{H}_3\text{IO}_6^{2-}]$ and $[\text{OH}^-]$ (as in Table 2) were varied at four different temperatures. The plots of $[\text{CHP}]/k_{\text{obs}}$ versus $1/[\text{OH}^-]$ and $[\text{CHP}]/k_{\text{obs}}$ versus $[\text{H}_3\text{IO}_6^{2-}]$ (Fig.7) should be linear. From the slopes and intercepts, the values of K_4 and K_5 were calculated at different temperatures and these values are given in Table 2. Van't Hoff plots were made for K_4 and K_5 with temperatures (log K_4 versus $1/\text{T}$ and log K_5 versus $1/\text{T}$) and the values of enthalpy of reaction ΔH, entropy of reaction ΔS and free energy of reaction ΔG, were calculated (Table 2) for the first and second equilibrium steps of Scheme 2. A comparison of the latter values with those obtained from the slow step of the reaction shows that these values mainly refer to the rate limiting step, supporting the fact that the reaction before rate determining step is fairly slow involves high activation energy.

The moderate values of $\Delta\text{H}^{\#}$ and $\Delta\text{S}^{\#}$ were both favorable for the electron transfer process. The values of $\Delta\text{S}^{\#}$ within the range of radical reaction has been ascribed to the nature of electron pairing and unpairing processes and to the loss of degrees of freedom formerly available to the reactants upon the formation of rigid transition state [30]. The observed modest enthalpy of activation and relatively low value of the entropy of activation as well as a higher rate constant of slow step indicate that the oxidation presumably occurs via inner-sphere mechanism. The conclusion is supported by earlier observation [31].

5. Conclusion

Among various species of DPC in alkaline medium, monodiperiodatocuprate(III) (MPC), $(Cu(H_2IO_6)(H_2O)_2)$ is considered as active species for the title reaction. The results demonstrate that in carrying out the reaction, the role of pH in the reaction medium is crucial. Rate constant of the slow step and other equilibrium constants involved in the mechanism were evaluated and activation parameters with respect to slow step of the mechanism were computed. The overall mechanistic sequence described here is consistent with product, mechanistic and kinetic studies.

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