

Influence of copper(II) catalyst on the oxidation of L-histidine by platinum(IV) in alkaline medium: a kinetic and mechanistic study

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Abstract The kinetics of oxidation of L-histidine (His) by platinum(IV) in the absence and presence of copper(II) catalyst was studied using spectrophotometry in alkaline medium at a constant ionic strength of 0.1 mol dm^{-3} and at $25 \text{ }^\circ\text{C}$. In both cases, the reactions exhibit a 1:1 stoichiometry ($[\text{His}]:[\text{Pt}^{\text{IV}}]$). The rate of the uncatalyzed reaction is dependent on the first power of each of the concentrations of oxidant, substrate and alkali. The catalyzed path shows a first-order dependence on both $[\text{Pt}^{\text{IV}}]$ and $[\text{Cu}^{\text{II}}]$, but the order with respect to both $[\text{His}]$ and $[\text{OH}^-]$ is less than unity. The rate constants increase with increasing ionic strength and dielectric constant of the medium. The catalyzed reaction has been shown to proceed via formation of a copper(II)-histidine intermediate complex, which reacts with the oxidant by an inner-sphere mechanism leading to decomposition of the complex in the rate-determining step. Platinum(IV) is reduced to platinum(II) by the substrate in a one-step two-electron transfer process. This is followed by other fast steps, giving rise to the oxidation products which were identified as 2-imidazole acetaldehyde, ammonia and carbon dioxide. A tentative reaction mechanism is suggested, and the associated rate laws are deduced. The activation parameters with respect to the slow step of the mechanism are reported and discussed.

Keywords Kinetics · Mechanism · Platinum(IV) · L-histidine · Copper(II) catalysis

Introduction

There is growing interest in the chemistry of six-coordinate platinum(IV) complexes because of their anticancer activity [1–3]. It is generally believed that platinum(IV) compounds are inert in ligand substitution reactions relative to their platinum(II) analogues [4]. They require reduction to Pt^{II} species to act as potential anticancer drugs. The anticancer activity of such complexes is likely to be due to effective Pt^{IV} transport into the cell, followed by reduction to the more reactive Pt^{II} compounds.

Kinetic investigations of the oxidation of organic [5–8] and inorganic substrates [9–12] by platinum(IV) have been reported. The reduction of platinum(IV) complexes can be carried out with both outer-sphere [13] and inner-sphere [14–17] single-electron reductants. Although the reduction of some platinum(IV) complexes by various substrates proceeds via a free radical mechanism, i.e., one-electron transfer process [13, 18–20], the alternative path where platinum(IV) undergoes a two-electron reduction has also been proposed [16].

The study of the oxidation of amino acids is of interest because of their biological significance and selectivity toward oxidants to yield different products [21, 22]. L-histidine (His) is an essential amino acid that finds extensive applications as a reducing agent in chemical and biochemical systems. The oxidation of histidine with several different reagents has been reported [23–28]. Copper(II) complexes of histidine [29] play an essential role in biochemistry and pharmacology, because copper is an essential trace element and histidine plays a pivotal role in

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copper transport before its entry into cellular transport systems and incorporation into enzymes and proteins. A small fraction of Cu^{II} bound to histidine maintains an exchangeable pool of copper in equilibrium with albumin in human blood. Copper(II) acts as a catalyst in the oxidation of several amino acids [30]. The mechanism of catalysis can be quite complicated due to formation of different intermediate complexes. Although the mechanism of catalysis depends on the nature of the substrate, oxidant and the experimental conditions, it has been shown [31] that metal ions act as catalysts by a few different paths such as the formation of complexes with reactant, or direct oxidation of the substrate, or through the formation of free radicals.

To the best of my knowledge, no studies have been reported on the oxidation of histidine by Pt^{IV} in alkaline medium in either the absence or presence of a catalyst. The present report deals with the title reactions in order to understand the active species of oxidant and catalyst, to examine the activity of the catalyst and to propose an appropriate mechanism.

Experimental

Reagent grade chemicals and doubly distilled water were used throughout the work. A stock solution of L-histidine (Merck) was prepared afresh as required in bidistilled water. Chloroplatinic acid solution (Johnson Matthey) was used without further purification. The required solution of oxidant was freshly prepared before each experiment by proper dilution of the stock solution, which was standardized spectrophotometrically [32]. The solution was stored away from light and re-standardized periodically. All other reagents were of analytical grade, and their solutions were prepared by dissolving requisite amounts of the samples in doubly distilled water.

Kinetic measurements

The kinetic studies were carried out under pseudo-first-order conditions with the concentration of His in a large excess (0.01 mol dm^{-3}) relative to that of Pt^{IV} . The ionic strength, I , of the reaction mixture was adjusted to 0.1 mol dm^{-3} using NaClO_4 . The reaction temperature ($25.0 \text{ }^\circ\text{C}$) was controlled to within $\pm 0.1 \text{ }^\circ\text{C}$. The rate of disappearance of Pt^{IV} was followed spectrophotometrically by monitoring the decrease in the absorption maximum at 262 nm. The spectrophotometer, Shimadzu UV-1800 PC automatic scanning double-beam, had a cell compartment kept at constant temperature by circulating water from a thermostat. The applicability of Beer's law was verified at 262 nm under the reaction conditions, and the determined

molar extinction coefficient ($\epsilon = 1.26 \pm 0.026 \times 10^4 \text{ dm}^3 \text{ mol}^{-1} \text{ cm}^{-1}$) was found to be in a good agreement with that reported previously [32]. Solutions of Pt^{IV} and the mixture containing His and alkali (and Cu^{II} catalyst where required) were separately thermostatted for ca. 1 h. The solutions were then mixed and transferred to the cell of path length 1 cm, and 3–4 experimental readings were taken for each run. Good straight lines were obtained for at least three half-lives. The pseudo-first-order rate constants of the uncatalyzed (k_{U}) and catalyzed (k_{C}) reactions were calculated from plots of $\ln(\text{absorbance})$ versus time. The gradients of the plots were calculated by the least-squares method. The rate constants were reproducible to within 4 %. The total rate constant (k_{T}) is equal to the sum of the rate constants k_{U} and k_{C} .

Results

Spectral changes

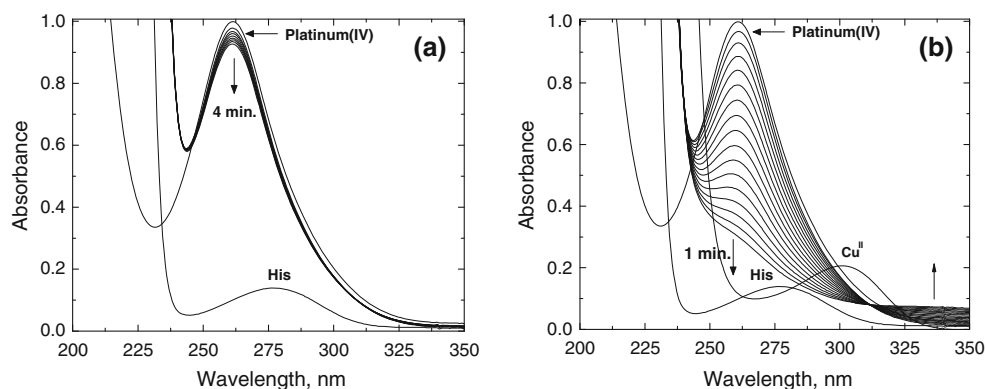
Spectra recorded during the course of the reactions in alkaline medium in the absence and presence of Cu^{II} catalyst are shown in Fig. 1. The figure shows a gradual disappearance of the Pt^{IV} band at 262 nm, with a slow rate in the case of the uncatalyzed reaction, Fig. 1a, but a significantly faster one in the presence of Cu^{II} catalyst, Fig. 1b. The simultaneous appearance of a new broad band in the region above 330 nm was observed with an isosbestic point located at 310 nm.

Stoichiometry and product analysis

Reaction mixtures containing a known excess of $[\text{Pt}^{\text{IV}}]$ over $[\text{His}]$ at fixed $[\text{OH}^-]$ were kept overnight, until the reactions had gone to completion, and then filtered to remove the solid black residue. The unreacted platinum(IV) was determined spectrophotometrically by measuring the absorbance at 262 nm, showing that one mole of histidine consumed one mole of platinum(IV). The reactions may thus be represented stoichiometrically as in Scheme 1.

The stoichiometric equation shown in Scheme 1 is consistent with the results of product analysis. The aldehyde product was estimated quantitatively as its 2,4-DNP derivative [33]. The ammonia by-product was identified by Nessler's reagent [34], and CO_2 was qualitatively detected by bubbling nitrogen gas through the acidified reaction mixture, followed by a tube containing lime water. Similar oxidation products with different experimental conditions have been reported earlier [23–28]. The formation of Pt^{II} was confirmed by the black precipitate obtained after standing of the reaction mixture for several hours. This

Fig. 1 Spectral changes in the oxidation of histidine by platinum(IV) in alkaline medium. [His] = 0.01, $[Pt^{IV}] = 8 \times 10^{-5}$, $[OH^-] = 0.05$ and $I = 0.1 \text{ mol dm}^{-3}$ at 25°C , **a** in the absence of Cu^{II} , **b** in the presence of $1 \times 10^{-5} \text{ mol dm}^{-3} Cu^{II}$



Scheme 1 The stoichiometric equation

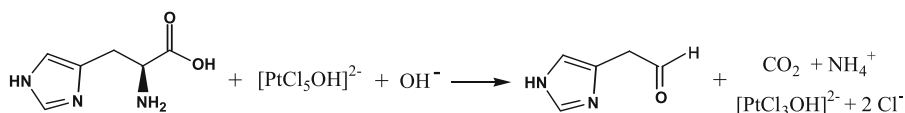
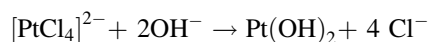


Table 1 Effects of $[Pt^{IV}]$, $[His]$, $[OH^-]$ and ionic strength, I , on the pseudo-first-order rate constant value in the uncatalyzed oxidation of histidine by platinum(IV) in alkaline medium at 25°C ^a

$10^5 [PtCl_6^{2-}]$ (mol dm^{-3})	$10^2 [His]$ (mol dm^{-3})	$10^2 [OH^-]$ (mol dm^{-3})	I (mol dm^{-3})	$10^5 k_U$ (s^{-1})
4.0	1.0	5.0	0.1	3.21
6.0	1.0	5.0	0.1	3.39
8.0	1.0	5.0	0.1	3.32
10.0	1.0	5.0	0.1	3.35
12.0	1.0	5.0	0.1	3.33
8.0	0.6	5.0	0.1	1.88
8.0	0.8	5.0	0.1	2.46
8.0	1.0	5.0	0.1	3.32
8.0	1.2	5.0	0.1	3.93
8.0	1.4	5.0	0.1	4.54
8.0	1.0	1.0	0.1	0.73
8.0	1.0	3.0	0.1	1.96
8.0	1.0	5.0	0.1	3.32
8.0	1.0	7.0	0.1	4.39
8.0	1.0	10.0	0.1	6.30
8.0	1.0	5.0	0.10	3.32
8.0	1.0	5.0	0.12	3.88
8.0	1.0	5.0	0.15	4.51
8.0	1.0	5.0	0.17	5.45
8.0	1.0	5.0	0.20	6.32

^a Experimental error $\pm 3\%$

black precipitate is formed as a result of transformation of $[PtCl_4]^{2-}$ in alkaline medium into hydrated PtO, as indicated by thermogravimetric and IR spectral analysis [35].



There is literature evidence [36] to indicate that platinum(II) oxide exists as $Pt(OH)_2$.

Reactions order and reagents effects

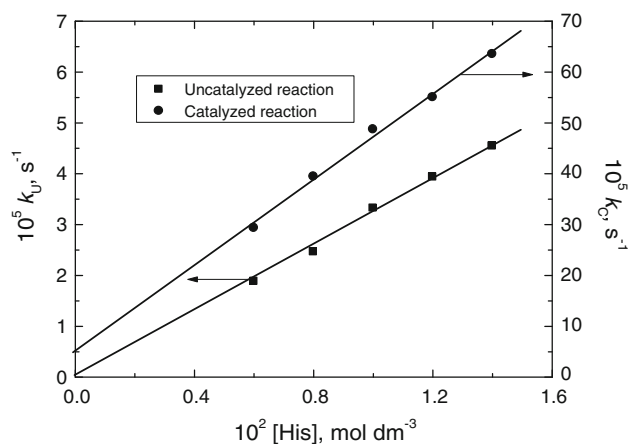
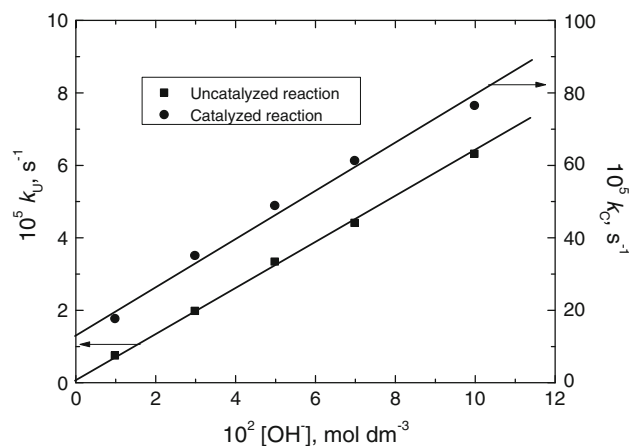
The orders with respect to the reactants for both the uncatalyzed and catalyzed reactions were determined from the slopes of the $\log k_U$ and $\log k_C$ versus $\log(\text{concentration})$ plots using the relationship ($\log k = \log k' + n \log C$) by varying the concentrations (C) of substrate, alkali and catalyst, in turn, while keeping other conditions constant.

The pseudo-first-order rate constants (k_U and k_C) were determined at different $[Pt^{IV}]$ in the region: $(4-12) \times 10^{-5} \text{ mol dm}^{-3}$ but at constant $[His]$, $[OH^-]$, ionic strength, temperature and $[Cu^{II}]$ for the catalyzed reaction. The values of k_U and k_C were independent of initial $[Pt^{IV}]$, Tables 1 and 2. Hence, the order of the reactions with respect to the oxidant is confirmed to be one.

In order to determine the effect of $[His]$, the rate constants were determined at different initial $[His]$ keeping all other reactants concentrations constant, including that of the copper(II) catalyst for the catalyzed reaction. The values of the rate constants for both the uncatalyzed and catalyzed reactions increased with increasing concentration of histidine, as listed in Tables 1 and 2. In the uncatalyzed path, the plot of k_U versus $[His]$ was found to be fairly linear passing through the origin, whereas the plot of k_C versus $[His]$ gave a straight line with a positive intercept on the k_C axis (Fig. 2). These results confirm that the order with respect to histidine thus changes from first to less than unity from the uncatalyzed path to the catalyzed one.

Table 2 Effects of $[\text{Pt}^{\text{IV}}]$, $[\text{His}]$, $[\text{OH}^-]$, $[\text{Cu}^{\text{II}}]$ and ionic strength, I , on the pseudo-first-order rate constant value in the copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium at 25 °C

$10^5 [\text{PtCl}_6^{2-}]$ (mol dm ⁻³)	$10^2 [\text{His}]$ (mol dm ⁻³)	$10^2 [\text{OH}^-]$ (mol dm ⁻³)	$10^5 [\text{Cu}^{\text{II}}]$ (mol dm ⁻³)	I (mol dm ⁻³)	$10^5 k_{\text{C}}$ (s ⁻¹)
4.0	1.0	5.0	1.0	0.1	47.3
6.0	1.0	5.0	1.0	0.1	49.9
8.0	1.0	5.0	1.0	0.1	48.7
10.0	1.0	5.0	1.0	0.1	47.5
12.0	1.0	5.0	1.0	0.1	50.2
8.0	0.6	5.0	1.0	0.1	29.3
8.0	0.8	5.0	1.0	0.1	39.4
8.0	1.0	5.0	1.0	0.1	48.7
8.0	1.2	5.0	1.0	0.1	55.0
8.0	1.4	5.0	1.0	0.1	63.5
8.0	1.0	1.0	1.0	0.1	17.5
8.0	1.0	3.0	1.0	0.1	34.9
8.0	1.0	5.0	1.0	0.1	48.7
8.0	1.0	7.0	1.0	0.1	61.1
8.0	1.0	10.0	1.0	0.1	76.3
8.0	1.0	5.0	0.5	0.1	21.5
8.0	1.0	5.0	1.0	0.1	48.7
8.0	1.0	5.0	1.5	0.1	68.9
8.0	1.0	5.0	2.0	0.1	92.3
8.0	1.0	5.0	2.5	0.1	119.1
8.0	1.0	5.0	1.0	0.10	48.7
8.0	1.0	5.0	1.0	0.12	59.3
8.0	1.0	5.0	1.0	0.15	71.4
8.0	1.0	5.0	1.0	0.17	79.2
8.0	1.0	5.0	1.0	0.20	88.2

Experimental error $\pm 4\%$ **Fig. 2** Plots of k_{U} and k_{C} versus $[\text{His}]$ in the uncatalyzed and copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$, $[\text{OH}^-] = 0.05$ and $I = 0.1$ mol dm⁻³ at 25 °C. $[\text{Cu}^{\text{II}}] = 1 \times 10^{-5}$ mol dm⁻³**Fig. 3** Plots of k_{U} and k_{C} versus $[\text{OH}^-]$ in the uncatalyzed and copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$, $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$ and $I = 0.1$ mol dm⁻³ at 25 °C. $[\text{Cu}^{\text{II}}] = 1 \times 10^{-5}$ mol dm⁻³

Next, the reaction rates were measured at constant $[\text{His}]$, $[\text{Pt}^{\text{IV}}]$, $[\text{Cu}^{\text{II}}]$ (for the catalyzed reaction), ionic strength and temperature but with various $[\text{OH}^-]$ (0.01–0.1 mol dm⁻³). The rates of both the reactions were found to increase with

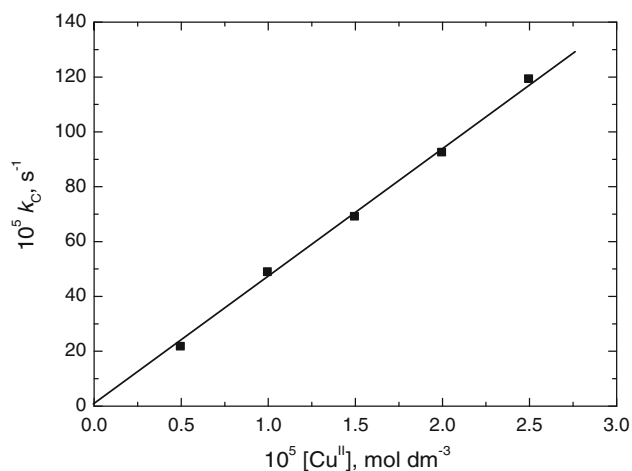


Fig. 4 A plot of k_C versus $[\text{Cu}^{\text{II}}]$ in the copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$, $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$, $[\text{OH}^-] = 0.05$ and $I = 0.1 \text{ mol dm}^{-3}$ at 25 °C

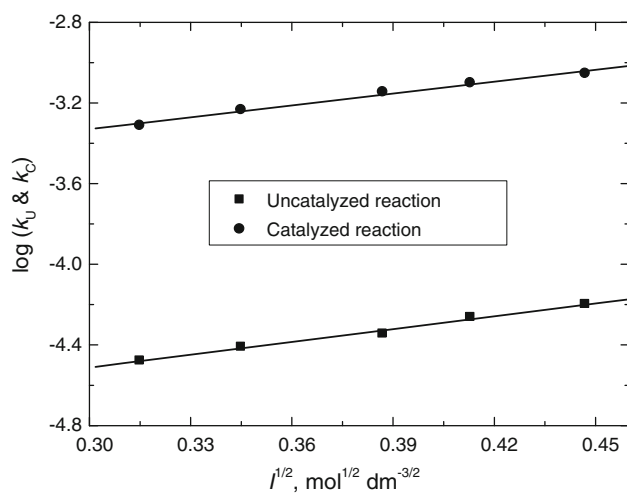


Fig. 5 Debye–Hückel plots in the uncatalyzed and copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$, $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$ and $[\text{OH}^-] = 0.05 \text{ mol dm}^{-3}$ at 25 °C. $[\text{Cu}^{\text{II}}] = 1 \times 10^{-5} \text{ mol dm}^{-3}$

$[\text{OH}^-]$, Tables 1 and 2. Similar to the case of histidine, the order with respect to $[\text{OH}^-]$ changes from first to less than unity from the uncatalyzed path to the catalyzed one, as also illustrated in Fig. 3.

The copper(II) catalyst concentration was varied from 5×10^{-6} to $25 \times 10^{-6} \text{ mol dm}^{-3}$, at constant concentrations of platinum(IV), histidine and alkali and at constant ionic strength and temperature. The rate of the reaction was directly proportional to $[\text{Cu}^{\text{II}}]$ as listed in Table 2 and shown in Fig. 4, showing that the order in $[\text{Cu}^{\text{II}}]$ is unity. This was also confirmed from the linearity of the plot of $\log k_C$ versus $\log[\text{Cu}^{\text{II}}]$ with a slope ≈ 1 .

The effect of ionic strength was investigated. At constant concentrations of Pt^{IV} , His, Cu^{II} and OH^- , and at constant temperature, the addition of NaClO_4 to the reaction medium was found to accelerate the reactions. The results, presented in Tables 1 and 2, show that the pseudo-first-order rate constants k_U and k_C increase with increasing ionic strength of the medium, and the Debye–Hückel plots were found to be linear with positive slopes (Fig. 5).

The dielectric constant of the medium, D , was varied by varying the ratio of *t*-butyl alcohol to water in the solvent. The D values were calculated from equation (1):

$$D = D_w V_w + D_B V_B \quad (1)$$

where D_w and D_B are dielectric constants of pure water and *t*-butyl alcohol, respectively, and V_w and V_B are the volume fractions of components water and *t*-butyl alcohol, respectively, in the total mixture. Decreasing the dielectric constant of the reaction medium decreased the rate of reactions. Plots of $\log k_U$ and $\log k_C$ versus $1/D$ gave straight lines with negative slopes.

The effect of chloride ion on the reaction was investigated by the addition of different concentrations of NaCl solution ranging from 1×10^{-3} to $1 \times 10^{-2} \text{ mol dm}^{-3}$, keeping other variables constants. The values of the rate constants were found to be independent of NaCl concentration.

The influence of temperature on the value of k_U was studied at 20, 25, 30 and 35 °C. It was found that raising the temperature increases the k_U value. The activation parameters for the second-order constant of the slow step of the mechanism, k_1 , were obtained from the

Table 3 Activation parameters of the second-order rate constant (k_1) in the uncatalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$, $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$, $[\text{OH}^-] = 0.05$ and $I = 0.1 \text{ mol dm}^{-3}$ ^b

Temp. K	293	298	303	308
$10^4 k_1, \text{ dm}^3 \text{ mol}^{-1} \text{ s}^{-1}$	2.31	3.42	4.29	5.27
$\Delta S^\ddagger, \text{ J mol}^{-1} \text{ K}^{-1}$		$\Delta H^\ddagger, \text{ kJ mol}^{-1}$	$\Delta G^\ddagger, \text{ kJ mol}^{-1}$	$E_a^\ddagger, \text{ kJ mol}^{-1}$
-177.50	39.99	82.38	40.58	$A, \text{ mol}^{-1} \text{ s}^{-1}$
				4.14×10^3

^b Experimental errors $\pm 5 \%$

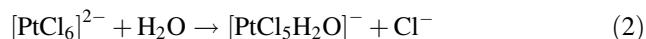
Arrhenius and Eyring equations by the least-squares method and are presented in Table 3.

Finally, the possibility of involvement of free radicals was examined as follows; the reaction mixture, to which a known quantity of acrylonitrile monomer had been added, was kept in an inert atmosphere for 2 h. On diluting the reaction mixtures with methanol, no white precipitate was formed, indicating the absence of free radicals in these reactions.

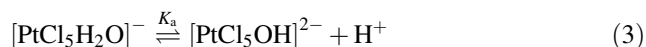
Discussion

The mechanism of reduction of platinum(IV) by different reductants has been the subject of much discussion [13] centered mainly on the possibility of platinum(III) formation as an intermediate. The reductions of some platinum(IV) complexes by different reductants have been shown to proceed via a free radical mechanism in two successive one-electron transfer steps [37]. However, alternative mechanistic paths whereby platinum(IV) undergo a simultaneous two-electron reduction have also been reported [10, 16]. In the present study, the absence of free radical intervention in the reactions suggests the possibility of a two-electron transfer mechanism.

It has been reported [38] that hexachloroplatinate(IV) is hydrolyzed in aqueous solutions according to the following equation:



The hydrolysis can be followed by rapid deprotonation of the aqua-complex upon increasing pH to form $[\text{PtCl}_5\text{OH}]^{2-}$;

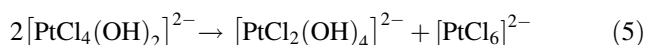


where K_a is the acid dissociation constant ($K_a = 3.5$) [39]

Furthermore, there is literature evidence [40] to indicate that in alkaline medium ($\text{pH} > 8$), $[\text{PtCl}_6]^{2-}$ is converted to $[\text{PtCl}_5\text{OH}]^{2-}$ in a fast step as follows:

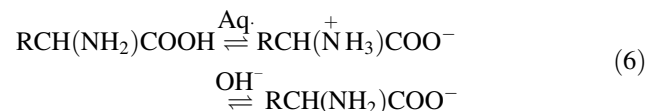


In the present work, addition of Cl^- to the reaction mixture failed to inhibit the rate, indicating that step (4) is irreversible. A metathesis reaction between $[\text{PtCl}_5\text{OH}]^{2-}$ and OH^- to give $[\text{PtCl}_4(\text{OH})_2]^{2-}$, followed by the oxidation of histidine by $[\text{PtCl}_4(\text{OH})_2]^{2-}$ can be ruled out, since the dihydroxy platinum(IV) complex is unstable in aqueous solution and readily disproportionates [41] according to the following equation:



Consequently, under the present experimental conditions, $[\text{PtCl}_5\text{OH}]^{2-}$ is probably the sole oxidizing species.

It is well known in aqueous solutions [42], amino acid exists as zwitterions, whereas in aqueous alkaline media, they exist in anionic form according to the following equilibria:



The observed enhancement of the reaction rates with increasing pH of the medium suggests deprotonation of histidine prior to the rate-determining step, such that the deprotonated form is the principal reactive species.

Mechanism of uncatalyzed oxidation

Since platinum(IV) complexes are generally substitution inert [4], initial complex formation prior to electron transfer does not normally take place in reductive-elimination reactions [43], [44] and electron transfer by a substitution controlled inner-sphere mechanism is unlikely. Halide-mediated reductive-elimination reactions of platinum(IV) complexes involving various inorganic [45, 46] and biological [47] reductants have been suggested to take place via nucleophilic attack of the reductant on a halide ligand on a good leaving center such as Pt^{IV} . Such reactions are formally equivalent to a transfer of Cl^+ from the oxidizing Pt^{IV} center to the reducing nucleophile followed by loss of the trans-ligand [45, 46].

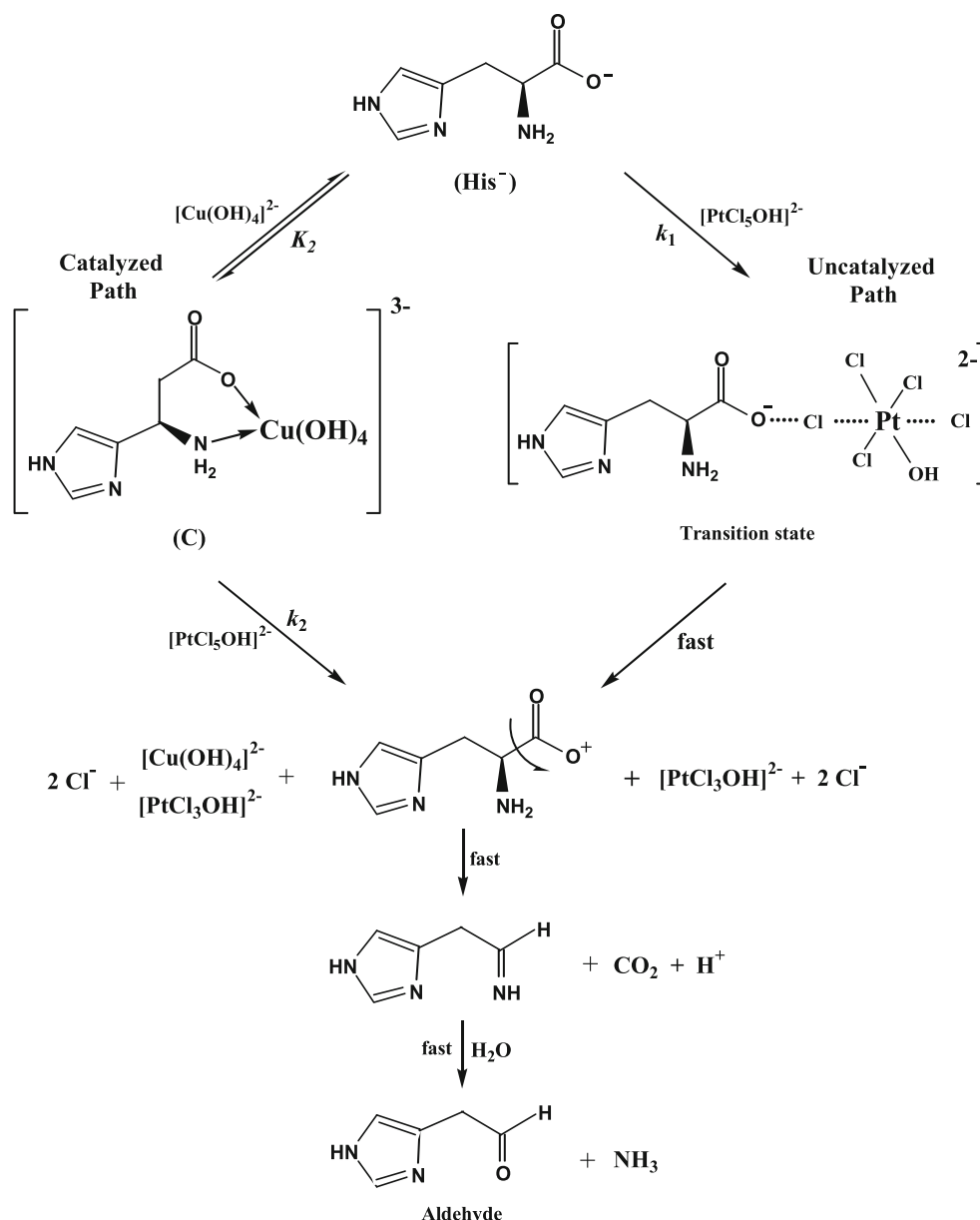
Under the present experimental conditions, initial complex formation between $[\text{PtCl}_5\text{OH}]^{2-}$ and histidine can be excluded because of the substitution inertness of Pt^{IV} complexes. This is confirmed by the absence of any spectroscopic evidence for the formation of such a complex in the UV-Vis spectra, as shown in Fig. 1a. Furthermore, the independence of $[\text{His}]$ with respect to the well-known Michaelis-Menten kinetics, $1/k_{\text{U}}$ versus $1/[\text{His}]$, is considered as kinetic evidence against intermediate formation.

The reaction between platinum(IV) and histidine in alkaline medium in the absence of catalyst exhibits a stoichiometry of 1:1, with first-order dependences on $[\text{Pt}^{\text{IV}}]$, $[\text{His}]$ and $[\text{OH}^-]$. Based on the experimental results and product analysis, a mechanism can be proposed as discussed below. Thus, the amino acid substrate is first deprotonated by the alkali,

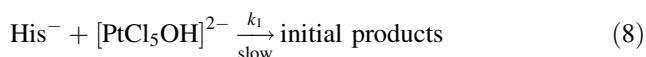


followed by its attack on the active oxidant species, $[\text{PtCl}_5\text{OH}]^{2-}$, in the rate-determining step to give rise to

Scheme 2 Mechanism of uncatalyzed and copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium



the initial oxidation products in a one-step two-electron transfer process



This was indicated by the absence of free radicals during the reaction. The observed kinetic behavior on varying the ionic strength and dielectric constant confirms that the reaction is between two similarly charged ions [48, 49], consistent with $[\text{PtCl}_5\text{OH}]^{2-}$ and His^- . This is followed by other fast steps to yield the final oxidation products as illustrated in Scheme 2.

Histidine has both carboxylate and amine groups which may act as nucleophiles toward a chloride ligand in the platinum(IV) complex, depending on the pH. At high pH,

where the carboxylate group is deprotonated, it should be able to attack $[\text{PtCl}_5\text{OH}]^{2-}$. Such a reaction may be visualized as a nucleophilic substitution on the halogen, with the platinum moiety as the leaving group. As already pointed out [50, 51], there is no sharp distinction between a two-electron redox change involving atom transfer and such a nucleophilic substitution.

The redox reaction follows the second-order rate law given by

$$-\frac{d[\text{PtCl}_5\text{OH}^{2-}]}{dt} = \frac{+d[\text{Pt}^{\text{II}}]}{dt} = k_1[\text{His}][\text{PtCl}_5\text{OH}^{2-}] \quad (9)$$

Under pseudo-first-order conditions, the rate law can be expressed by Eq. (10)

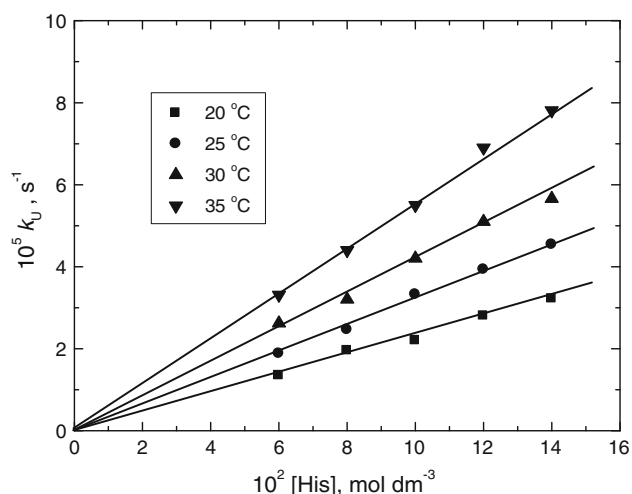


Fig. 6 Plots of k_U versus $[\text{His}]$ at different temperatures in the uncatalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$, $[\text{OH}^-] = 0.05$ and $I = 0.1 \text{ mol dm}^{-3}$

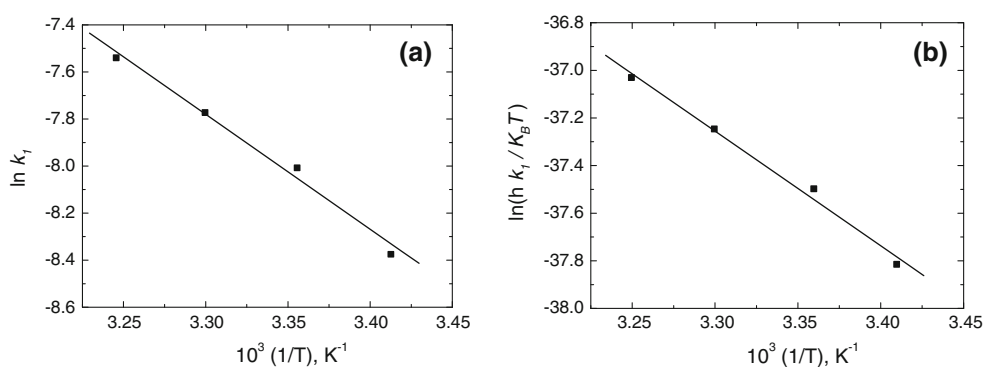
$$\frac{-d[\text{PtCl}_5\text{OH}^{2-}]}{dt} = k_U[\text{PtCl}_5\text{OH}^{2-}]^2 \quad (10)$$

Comparing Eqs. (9) and (10), the following relationship is obtained

$$k_U = k_1[\text{His}] \quad (11)$$

According to Eq. (11), plots of k_U against $[\text{His}]$ at constant $[\text{H}^+]$ should be linear passing through the origin, as was observed experimentally at four different temperatures (Fig. 6). The pH-dependent second-order rate constant, k_1 , obtained from the slopes of these plots, along with its activation parameters which were calculated by the least-squares method from Arrhenius and Eyring plots (Fig. 7a, b), is listed in Table 3. The observed large negative value of ΔS^\ddagger suggests that the reactants form a transition state which is more ordered than the reactants, while the positive values of both ΔH^\ddagger and ΔG^\ddagger indicate endothermic formation of the transition state and its non-spontaneity, respectively.

Fig. 7 **a** Arrhenius and **b** Eyring plots for the rate constant of the slow step (k_1) in the uncatalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$, $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$, $[\text{OH}^-] = 0.05$ and $I = 0.1 \text{ mol dm}^{-3}$

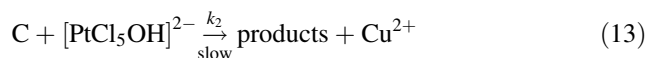


Mechanism of copper(II)-catalyzed reaction

It has been reported [29, 30] that copper(II) acts as an efficient catalyst in some redox reactions involving amino acids, particularly in alkaline media. In aqueous alkaline media [52], Cu^{II} is known to give the tetrahydroxycuprate(II) ion, $[\text{Cu}(\text{OH})_4]^{2-}$. The reaction between $[\text{PtCl}_5\text{OH}]^{2-}$ and histidine in the presence of microquantities of copper(II) catalyst is similar to that of the uncatalyzed reaction with respect to stoichiometry and effects of ionic strength and dielectric constant, addition of Cu^{II} changed the order in both $[\text{His}]$ and $[\text{OH}^-]$ from unity to less than unity. In addition, the reaction is first-order with respect to copper(II) catalyst.

The observed order in $[\text{His}]$ of less than unity presumably results from complex formation between the copper(II) catalyst and substrate prior to reaction with the oxidant. Spectroscopic evidence to support complex formation between Cu^{II} and histidine was obtained from the UV–Vis spectra, which showed a new band with an isosbestic point as shown in Fig. 1b. The formation of the complex was also indicated kinetically by a nonzero intercept in the plot of $[\text{Cu}^{\text{II}}]/k_C$ versus $1/[\text{His}]$ (Fig. 8). Similar complexes between histidine and copper(II) catalyst have been reported in earlier studies [30].

I suggest that the deprotonated histidine combines with $[\text{Cu}(\text{OH})_4]^{2-}$ to form an intermediate complex, $[\text{His}-\text{Cu}(\text{OH})_4]^{3-}$, which then reacts in a slow step with one mole of $[\text{PtCl}_5\text{OH}]^{2-}$ to give the initial products. This is followed by other fast steps to yield the final oxidation products. The results are accommodated in the following sequence



According to the proposed mechanism, the rate of disappearance of $[\text{PtCl}_5\text{OH}]^{2-}$ or formation of the intermediate complex (C) can be expressed by the following rate law equation:

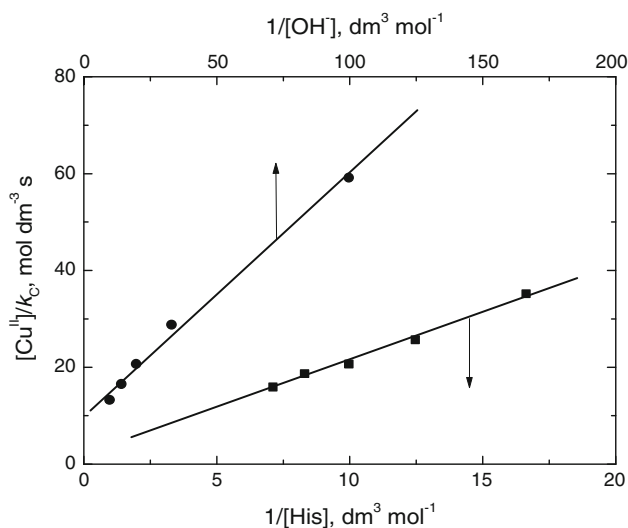


Fig. 8 Verification of the rate law (15) in the form of Eq. (17) in the copper(II)-catalyzed oxidation of histidine by platinum(IV) in alkaline medium. $[\text{His}] = 0.01$ (when varying $[\text{OH}^-]$), $[\text{OH}^-] = 0.05$ (when varying $[\text{His}]$), $[\text{Pt}^{\text{IV}}] = 8 \times 10^{-5}$ and $I = 0.1 \text{ mol dm}^{-3}$ at 25°C

$$\text{Rate}_{(\text{C})} = \frac{-d[\text{Pt}^{\text{IV}}]}{dt} = \frac{+d[\text{C}]}{dt} = k_2[\text{C}][\text{Pt}^{\text{IV}}] \quad (14)$$

$$\text{Rate} = \frac{k_2 K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}][\text{Pt}^{\text{IV}}]}{(1 + K_1[\text{OH}^-])(1 + K_1 K_2 [\text{His}][\text{OH}^-])} \quad (15)$$

Under pseudo-first-order conditions,

$$\frac{-d[\text{Pt}^{\text{IV}}]}{dt} = k_{\text{C}}[\text{Pt}^{\text{IV}}] \quad (16)$$

Comparing Eqs. (15) and (16) and rearranging, we obtain

$$\frac{[\text{Cu}^{\text{II}}]}{k_{\text{C}}} = \left(\frac{1 + K_1[\text{OH}^-]}{k_2 K_1 K_2 [\text{OH}^-]} \right) \frac{1}{[\text{His}]} + K' \quad (17)$$

where $K' = (1 + K_1[\text{OH}^-])/k_2$.

According to Eq. (17), plots of $[\text{Cu}^{\text{II}}]/k_{\text{C}}$ versus $1/[\text{His}]$, at constant $[\text{OH}^-]$, and of $[\text{Cu}^{\text{II}}]/k_{\text{C}}$ versus $1/[\text{OH}^-]$, at constant $[\text{His}]$, should be linear with positive intercepts on $[\text{Cu}^{\text{II}}]/k_{\text{C}}$ axes. The experimental results satisfied this requirement, as shown in Fig. 8.

The rate constant for the slow step (k_2) could not be evaluated because of non-availability of the deprotonation constants of histidine (K_1) and/or the formation constants of the copper(II)-histidine complex (K_2) under the present experimental conditions and at different temperatures. Some attempts were made to evaluate these constants from the experimental data, but the results were unsatisfactory. The overall mechanisms indicated by this work is shown in Scheme 2.

Appendix

According to the suggested mechanism for copper(II)-catalyzed oxidation reaction,

$$\text{Rate}_{(\text{C})} = \frac{-d[\text{Pt}^{\text{IV}}]}{dt} = \frac{+d[\text{C}]}{dt} = k_2[\text{C}][\text{Pt}^{\text{IV}}] \quad (14)$$

From reaction (7),

$$K_1 = \frac{[\text{His}^-]}{[\text{His}][\text{OH}^-]} \quad (18)$$

Therefore,

$$[\text{His}^-] = K_1[\text{His}][\text{OH}^-] \quad (19)$$

From reaction (12) and Eq. (19),

$$K_2 = \frac{[\text{C}]}{[\text{His}^-][\text{Cu}^{\text{II}}]} = \frac{[\text{C}]}{K_1[\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}]} \quad (20)$$

Therefore,

$$[\text{C}] = K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}] \quad (21)$$

Substituting Eq. (21) into Eq. (14) yields

$$\text{Rate}_{(\text{C})} = k_2 K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}][\text{Pt}^{\text{IV}}] \quad (22)$$

The total concentration of histidine is given by

$$[\text{His}]_{\text{T}} = [\text{His}]_{\text{F}} + [\text{His}^-] + [\text{C}] \quad (23)$$

where $[\text{His}]_{\text{T}}$ and $[\text{His}]_{\text{F}}$ stand for total and free concentrations of histidine.

Substituting Eqs. (19) and (21) into Eq. (23) gives

$$[\text{His}]_{\text{T}} = [\text{His}]_{\text{F}} + K_1[\text{His}]_{\text{F}}[\text{OH}^-] + K_1 K_2 [\text{His}]_{\text{F}}[\text{OH}^-][\text{Cu}^{\text{II}}] \quad (24)$$

$$[\text{His}]_{\text{T}} = [\text{His}]_{\text{F}}(1 + K_1[\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{Cu}^{\text{II}}]) \quad (25)$$

Therefore,

$$[\text{His}]_{\text{F}} = \frac{[\text{His}]_{\text{T}}}{1 + K_1[\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{Cu}^{\text{II}}]} \quad (26)$$

Similarly,

$$[\text{Cu}^{\text{II}}]_{\text{T}} = [\text{Cu}^{\text{II}}]_{\text{F}} + [\text{C}] \quad (27)$$

Substituting Eq. (21) into Eq. (27) and rearrangement gives

$$[\text{Cu}^{\text{II}}]_{\text{F}} = \frac{[\text{Cu}^{\text{II}}]_{\text{T}}}{1 + K_1 K_2 [\text{His}][\text{OH}^-]} \quad (28)$$

In view of the concentrations of $[\text{OH}^-]$ and $[\text{Pt}^{\text{IV}}]$ used

$$[\text{OH}^-]_{\text{T}} = [\text{OH}^-]_{\text{F}} \quad (29)$$

and,

$$[\text{Pt}^{\text{IV}}]_{\text{T}} = [\text{Pt}^{\text{IV}}]_{\text{F}} \quad (30)$$

Substituting Eqs. (26), (28), (29) and (30) into Eq. (21) (and omitting “T” and “F” subscripts), we get

$$\text{Rate}_{(\text{C})} = \frac{k_2 K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}][\text{Pt}^{\text{IV}}]}{(1 + K_1[\text{OH}^-] + K_1 K_2 [\text{OH}^-][\text{Cu}^{\text{II}}])(1 + K_1 K_2 [\text{His}][\text{OH}^-])} \quad (31)$$

In view of low concentration of $[\text{Cu}^{\text{II}}]$ and $[\text{OH}^-]$ used, the term $K_1 K_2 [\text{OH}^-][\text{Cu}^{\text{II}}]$ in the denominator of Eq. (31) can be neglected. Therefore, Eq. (31) becomes

$$\text{Rate}_{(\text{C})} = \frac{k_2 K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}][\text{Pt}^{\text{IV}}]}{(1 + K_1[\text{OH}^-])(1 + K_1 K_2 [\text{His}][\text{OH}^-])} \quad (32)$$

Under pseudo-first-order conditions, the rate law can be expressed as

$$\text{Rate}_{(\text{C})} = \frac{-d[\text{Pt}^{\text{IV}}]}{dt} = k_{\text{C}} [\text{Pt}^{\text{IV}}] \quad (33)$$

Comparing Eqs. (32) and (33), the following relationship is obtained

$$k_{\text{C}} = \frac{k_2 K_1 K_2 [\text{His}][\text{OH}^-][\text{Cu}^{\text{II}}]}{(1 + K_1[\text{OH}^-])(1 + K_1 K_2 [\text{His}][\text{OH}^-])} \quad (34)$$

and with rearrangement, it becomes

$$\frac{[\text{Cu}^{\text{II}}]}{k_{\text{C}}} = \left(\frac{1 + K_1[\text{OH}^-]}{k_2 K_1 K_2 [\text{OH}^-]} \right) \frac{1}{[\text{His}]} + \frac{1 + K_1[\text{OH}^-]}{k_2} \quad (35)$$

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