

# Transition metal-catalyzed oxidation of L-asparagine by platinum(IV) in acid medium: a kinetic and mechanistic study

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Abstract Kinetic investigations of Pt(IV) oxidation of L-asparagine catalyzed by transition metals with different valencies, namely Ag(I), Pd(II), Cr(III) and Zr(IV), were studied spectrophotometrically in sulfuric acid medium at constant ionic strength and temperature. The reaction was first order in [Pt(IV)], while the orders with respect to the concentrations of Asn, sulfuric acid and transition metal were less than unity over the concentration range studied. The rate constants decreased with increasing ionic strength and dielectric constant, while increasing temperature enhanced the rate. The order of catalytic efficiency was: Ag(I) > Cr(III) > Pd(II) > Zr(IV). A mechanism involving the formation of a complex between the catalyst and substrate is proposed. Oxidation by Pt(IV) is suggested to take place by an inner-sphere mechanism in which Pt(IV) is reduced to Pt(II) on the catalyst-bound substrate in a onestep two-electron transfer process. The oxidation products of Asn were identified as  $\alpha$ -formyl acetamide, ammonium ion and carbon dioxide. The rate law associated with the reaction mechanism was deduced. Activation parameters of the reactions were evaluated and discussed.

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## Introduction

Many transition metal complexes are good oxidants in acidic, basic and neutral media. The oxidation capacity depends on the redox potential of the metal, which in turn, depends on the pH of the medium. The chemistry of biologically active Pt(IV) complexes has become increasingly important over the last few decades due to their anticancer properties [1, 2]. Such complexes are usually substitution inert, requiring reduction to more labile Pt(II) species before they can act as potential anticancer drugs. The reduction of Pt(IV) complexes by various reductants generally proceeds via a free radical one-electron transfer mechanism [3-7]. An alternative path, whereby Pt(IV) undergoes a two-electron reduction process, has also been reported [8]. The experimental conditions and choice of reductant determined whether a two-electron reduction process could occur.

Hexachloroplatinate(IV) (HCP),  $[PtCl_6]^{2-}$ , has been used to oxidize a limited number of organic [9–16] and inorganic [17–19] compounds in different media. Knowledge of the reactivity of Pt(IV) compounds and their reduction by potential bioreductants, such as amino acids, is important for understanding the mechanism of antitumor activity as well as for designing new compounds with fewer side effects. It has been reported [20] that there is a correlation between the rate of reduction and the anticancer activity in a series of homologous Pt(IV) complexes. However, no details about the reaction mechanism were provided.

Oxidation of amino acids is of interest both from a chemical point of view and for its bearing on the mechanism of amino acid metabolism. Amino acids can be oxidized by a variety of reagents and often undergo oxidative decarboxylation and deamination [14-16].

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The rate of reduction by L-asparagine (Asn) depends on the nature of the oxidant and pH of the medium. Studies of the reaction of Asn with the following systems have been reported: sodium N-chloro-p-toluene sulfonamide catalyzed by Cu(II) in alkaline media [21], alkaline diperiodatonickelate(IV) [22], peroxydisulfate in acid medium [23] and permanganate in both acid [24] and alkaline [25] media. In most of these studies, the final oxidation products of Asn were  $\alpha$ -formyl acetamide, ammonium ion and carbon dioxide. Fawzy [15] reported the kinetics of the oxidation of Asn by hexachloroplatinate(IV) in sulfuric acid medium in both the absence and presence of Cu(II). Fawzy's work suggested that Asn combines with Cu(II) to form an intermediate complex. This complex then reacts in a slow step with HCP to give the products and regenerates the Cu(II) catalyst.

Transition metal ions, M(Y), where M is the metal and Y is its valency, have been widely employed as homogenous catalysts for oxidation of organic and inorganic substrates by reaction pathways such as formation of complexes with the reactants, oxidation of substrate or the formation of free radicals [26, 27]. Kinetic investigations on the homogeneously catalyzed oxidation of amino acids in liquid phase are limited [14–16, 28, 29]. Therefore, the mechanistic study of such reactions is considered an important research field due to the role played by metals in biological systems.

The present study deals with the redox reaction of HCP with Asn in the presence of transition metals with different valencies, namely Ag(I), Pd(II), Cr(III) and Zr(IV). These metals were investigated as catalysts in order to explore the kinetic and mechanistic aspects of the redox reactions in strong acid media. Our goal was to determine the mechanism of these redox reactions.

## **Experimental**

### Materials and methods

All chemicals used were analytical reagent grade, and water was double distilled. L-asparagine (Merck) was used as received. Solutions of Asn were prepared fresh for each experiment by dissolving a known amount of Asn in water. Solutions of chloroplatinic acid (Johnson Matthey) were freshly prepared before each experiment by dilution of a stock solution and standardized spectrophotometrically [30]. The stock solution was stored in a dark bottle to protect it from light and re-standardized periodically. Solutions of silver(I) nitrate, palladium(II) chloride, chromium(III) sulfate and zirconium(IV) nitrate were prepared by dissolving known amounts of each salt separately in a suitable solvent, then diluting with water.

#### **Kinetic measurements**

Kinetic investigations of the reaction between HCP and an excess of Asn were conducted under pseudo-first-order conditions. The ionic strength, I, of the reaction mixture was adjusted to 2.0 mol  $dm^{-3}$  using sodium sulfate. The reaction temperature (25.0 °C) was controlled within  $\pm 0.1$  °C using a thermostat, unless otherwise stated. The reaction was initiated by a rapid addition of a known amount of pre-equilibrated HCP to the reaction mixture containing the required amounts of Asn, sulfuric acid, transition metal salt, sodium sulfate and water. The solutions were then mixed and transferred to a cell of path length 1.0 cm. The course of the reaction was followed spectrophotometrically by monitoring the decrease in the absorbance of HCP at  $\lambda = 262$  nm, its absorption maximum, as a function of time. All spectra were recorded using an automatic scanning double-beam spectrophotometer (Shimadzu UV-1800 PC). The cell compartment was maintained at a constant temperature by circulating temperature-controlled water using a thermostat.

It has been reported that, in the absence of transition metal ion catalysts, Pt(IV) oxidation of Asn in sulfuric acid can be detected and measured [15]. The total rate constant ( $k_T$ ) for these reactions was thus equal to the sum of the pseudo-first-order rate constants of the catalyzed ( $k_C$ ) and uncatalyzed ( $k_U$ ) reactions ( $k_C = k_T - k_U$ ). Hence, during a calculation of  $k_C$ , the uncatalyzed rate constant  $k_U$  must be taken into account and kinetic runs under similar conditions in the absence of catalyst were also carried out to allow for this. The reactions were followed for more than three half-lives. The values of  $k_C$  were obtained from the slopes of log(absorbance) versus time plots. The average of at least three independent kinetic runs was calculated. The runs were reproducible to within  $\pm 4 \%$ .

The effect of dissolved oxygen on the reaction rate was also checked by preparing another batch of reaction mixture then conducting the same set of reactions under a nitrogen atmosphere. No significant differences in the results were seen with and without atmospheric oxygen.

## Results

## **Time-resolved spectra**

Time-resolved spectra are displayed in Fig. 1 for, as an example, the Ag(I)-catalyzed oxidation of Asn by HCP in sulfuric acid medium. The absorbance of HCP at its  $\lambda_{max}$  (262 nm) decreased gradually with time suggesting that Pt(IV) was reduced to Pt(II) by Asn.



**Fig. 1** Time-resolved spectra for the Ag(I)-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium. [Asn] =  $5.0 \times 10^{-2}$ , [HCP] =  $7.6 \times 10^{-5}$ , [H<sup>+</sup>] = 1.0, [Ag(I)] =  $5.0 \times 10^{-5}$ , and I = 2.0 mol dm<sup>-3</sup> at 25 °C. Scan time interval was 2 min

## Reaction stoichiometry and product identification

Reaction mixtures with different sets of reactant concentrations containing various amounts of HCP and Asn at a fixed pH, ionic strength and temperature were allowed to react for 24 h in an inert atmosphere. After completion of each reaction, the unreacted HCP was assayed spectrophotometrically. The results indicated that one mole of Asn consumed one mole of HCP, as represented in Eq. (1),

$$\begin{aligned} & \operatorname{RCH}(\operatorname{NH}_2)\operatorname{COOH} + \left[\operatorname{Pt}^{\operatorname{IV}}\operatorname{CI}_6\right]^{2-} + \operatorname{H}_2\operatorname{O} \xrightarrow{\operatorname{M}(\operatorname{Y})} \\ & \operatorname{RCHO} + \operatorname{NH}_4^+ + \operatorname{CO}_2 + \left[\operatorname{Pt}^{\operatorname{II}}\operatorname{Cl}_4\right]^{2-} + 2\operatorname{Cl}^- + \operatorname{H}^+ \end{aligned} \tag{1}$$

where  $R = -CH_2(CO)NH_2$  and RCHO is the corresponding aldehyde ( $\alpha$ -formyl acetamide), which was identified by a spot test [31]. Other oxidation products of the amino acid were identified as the ammonium ion (Nessler's reagent) [32] and carbon dioxide (lime water test). The corresponding aldehyde was also detected quantitatively as its 2,4-dinitrophenylhydrazine derivative (2,4-dinitrophenylhydrazine test) [32]. The aldehyde does not undergo further oxidation under the present experimental conditions, since a test for carboxylic acid was negative. Similar oxidation products obtained under different experimental conditions have been reported previously [14-16, 23]. Formation of  $[Pt^{II}Cl_4]^{2-}$  was confirmed [33] by the observation of a black precipitate [platinum(II) hydroxide] upon addition of alkali to the reaction mixture, according to Eq. (2).

$$[PtCl_4]^{2-} + 2OH^{-} = Pt(OH)_2 + 4Cl^{-}$$
(2)

## **Reaction orders**

Reaction orders were determined from the slopes of plots of log  $k_{\rm C}$  versus log (conc.) obtained by individually varying the concentrations of the reductant, sulfuric acid and transition metal ion in turn, while keeping the other parameters constant.

The concentration of oxidant HCP was varied over the range of  $4.0 \times 10^{-5}$ – $12.0 \times 10^{-5}$  mol dm<sup>-3</sup>, while keeping the concentration of other components constant. The first-order plots were found to be linear, and  $k_{\rm C}$  values for different [HCP] did not vary (Table 1), indicating an order of unity with respect to [HCP].

Kinetic runs were carried out by varying the initial concentration of Asn, while keeping the concentrations of oxidant, transition metal ion and sodium sulfate constant. The pH and temperature were also kept constant. Plots of  $k_{\rm C}$  versus [Asn] in the presence of different transition metal ions were linear with positive intercepts (figure not shown), suggesting that the order with respect to [Asn] was less than unity.

The reaction rates were measured at constant [Asn], [HCP], [M(Y)], ionic strength and temperature but with various [H<sup>+</sup>] (0.2–2.0 mol dm<sup>-3</sup>). The rate of reaction increased as [H<sup>+</sup>] increased. Plots of  $k_{\rm C}$  versus [H<sup>+</sup>] in the presence of different transition metal ions were linear with positive intercepts (figure not shown), confirming that the order with respect to [H<sup>+</sup>] was less than unity.

To evaluate the reaction orders using different transition metal ion catalysts, the reaction rate was measured with the following [M(Y)]:  $(1.0-9.0) \times 10^{-5}$  mol dm<sup>-3</sup> for Ag(I) and Cr(III) and  $(1.0-9.0) \times 10^{-4}$  mol dm<sup>-3</sup> for Pd(II) and Zr(IV). All other variables were kept constant. The reaction rates increased as [M(Y)] increased (Table 1). The catalytic efficiency increased in the order: Ag(I) > Cr(III) > Pd(II) > Zr(IV). The orders with respect to Ag(I), Cr(III), Pd(II) and Zr(IV) were 0.89, 0.79, 0.38 and 0.19, respectively, as determined from plots of log  $k_{\rm C}$  versus log [M(Y)] (Fig. 2).

#### Effects of ionic strength and dielectric constant

By addition of sodium sulfate to the reaction medium at constant [Asn], [HCP], [M(Y)], pH and temperature, it was found that increasing the ionic strength of the medium increased the rate of reaction. Debye–Hückel plots were linear with negative slopes (Figure shown in supplementary material).

In order to determine the effect of the dielectric constant (D) of the medium on the rate, the oxidation of Asn by HCP was studied at different solvent compositions (vol%) of acetic acid and water. The dielectric constant of the medium at different compositions was calculated

10 <sup>5</sup> [HCP]	$10^2$ [Asn]	[H <sup>+</sup> ]	$10^{x} [M(Y)]$	$I \pmod{\mathrm{dm}^{-3}}$	$10^5 k_{\rm C} ({\rm s}^{-1})$			
$(\text{mol } \text{dm}^{-3})$	$(\text{mol } \text{dm}^{-3})$	$(\text{mol } \text{dm}^{-3})$	$(\text{mol } \text{dm}^{-5})^{a}$		Ag(I) Pd(II)	Pd(II)	Cr(III)	Zr(IV)
4.0	5.0	1.0	5.0	2.0	538	59	263	35
6.0	5.0	1.0	5.0	2.0	534	57	364	39
7.6	5.0	1.0	5.0	2.0	545	58	260	37
10.0	5.0	1.0	5.0	2.0	557	58	258	36
12.0	5.0	1.0	5.0	2.0	549	59	256	37
7.6	1.0	1.0	5.0	2.0	156	16	78	12
7.6	3.0	1.0	5.0	2.0	340	37	177	25
7.6	5.0	1.0	5.0	2.0	545	58	260	37
7.6	7.0	1.0	5.0	2.0	721	79	339	50
7.6	9.0	1.0	5.0	2.0	909	101	425	64
7.6	5.0	0.2	5.0	2.0	271	27	123	18
7.6	5.0	0.5	5.0	2.0	402	42	195	28
7.6	5.0	1.0	5.0	2.0	545	58	260	37
7.6	5.0	1.5	5.0	2.0	662	65	311	43
7.6	5.0	2.0	5.0	2.0	749	81	366	51
7.6	5.0	1.0	1.0	2.0	128	35	77	29
7.6	5.0	1.0	3.0	2.0	319	48	169	33
7.6	5.0	1.0	5.0	2.0	545	58	260	37
7.6	5.0	1.0	7.0	2.0	730	71	351	41
7.6	5.0	1.0	9.0	2.0	912	82	439	44
7.6	5.0	1.0	5.0	2.0	545	58	260	37
7.6	5.0	1.0	5.0	2.5	516	54	246	35
7.6	5.0	1.0	5.0	3.0	480	51	231	33
7.6	5.0	1.0	5.0	3.5	451	47	218	30
7.6	5.0	1.0	5.0	4.0	425	45	205	28

**Table 1** Effect of [HCP], [Asn],  $[H^+]$ , [M(Y)] and ionic strength, *I*, on the first-order rate constant  $k_C$  in the transition metal ion-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium at 25 °C

Experimental error  $\pm 4$  %

<sup>a</sup> x = 5 for Ag(I) and Cr(III), x = 4 for Pd(II) and Zr(IV); Y is the valence of M

using the dielectric constants of water (78.5) and acetic acid (6.15) at 25 °C. The rate constant clearly increased as the dielectric constant of the solvent decreased (i.e., increasing acetic acid content). Plots of log  $k_{\rm C}$  versus 1/D were linear with positive slopes (Figure shown in supplementary material).

# Effect of temperature

The effect of temperature on the reaction rate was studied at 15, 20, 25, 30 and 35 °C while keeping other variables constant. The first-order rate constants were found to increase as the temperature increased. The activation parameters for the second-order rate constant,  $k_2$  ( $k_2 = k_C/$ [Asn]), were calculated using Arrhenius, Fig. 3a, and Eyring, Fig. 3b, plots and are listed in Table 2.

# Test for free radicals

To study the possible intervention of free radicals during the oxidation reaction, a known amount of acrylonitrile was added to the reaction mixture which was then kept for 6 h in an inert atmosphere. On diluting the mixtures with methanol, no white precipitate was formed, thus confirming the absence of free radical intervention in these reactions.

# Discussion

In acid media, it is thought [34] that  $[PtCl_6]^{2-}$  is the principal form of platinum(IV) species. During the redox reaction,  $[PtCl_6]^{2-}$  is reduced as shown in Eq. (3),

$$[PtCl_6]^{2-} + 2e^- = [PtCl_4]^{2-} + 2Cl^-$$
(3)



Fig. 2 Plots of log  $k_{\rm C}$  versus log [M(Y)] in the transition metal ioncatalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium. [Asn] =  $5.0 \times 10^{-2}$ , [HCP] =  $7.6 \times 10^{-5}$ , [H<sup>+</sup>] = 1.0 and I = 2.0 mol dm<sup>-3</sup> at 25 °C

In this redox reaction, octahedral Pt(IV) is reduced to square planar Pt(II) with the release of two  $Cl^-$  ions. Therefore, this reaction can be classified as a reductive elimination [35]. Since Pt(IV) complexes are generally substitution inert [36], initial complex formation between Pt(IV) and the reductant prior to the electron transfer can be excluded in reductive elimination reactions [37].

On the other hand, Martell and Smith [38] reported that in acid media, amino acids exist as zwitterions and tend to protonate at high acid concentration according to the following equilibria:

$$\begin{array}{l} \operatorname{RCH}(\operatorname{NH}_2)\operatorname{COOH} \equiv \operatorname{RCH}({}^+\operatorname{NH}_3)\operatorname{COO}^- + \operatorname{H}^+ \\ \operatorname{Amino\,acid} & \operatorname{Zwitterion} \\ \stackrel{K_1}{\rightleftharpoons} \operatorname{RCH}({}^+\operatorname{NH}_3)\operatorname{COOH} \\ \operatorname{Protonated\,form} \end{array}$$
(4)



Fig. 3 a Arrhenius plots and b Eyring plots for the transition metal ion-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium. [Asn] =  $5.0 \times 10^{-2}$ , [HCP] =  $7.6 \times 10^{-5}$ ,

where  $K_1$  is the stepwise protonation constant of the amino acid.

Since the reaction rates were observed to increase upon increasing the acid concentration, the protonated Asn<sup>+</sup> form may be the reactive species in the rate-determining step. It has also been reported [39] that amino acids form adducts with some transition metal ions, owing to the availability of an electron pair on the carboxylate oxygen [40] under conditions where the amine group is protonated.

There are two suggested mechanisms for the oxidation of amino acids by HCP. The first involves a simultaneous twoelectron transfer in a single step, while the second involves two successive one-electron transfer steps. If the transition states of the reductant and/or oxidant are unstable, a simultaneous two-electron transfer mechanism occurs, as observed in the oxidation of uranium(IV) by  $[PtCl_6]^{2-}$  [41]. In the present study, addition of acrylonitrile to the reaction mixture failed to give polymerized products. It is possible that a free radical such as a Pt(III) species was too short-lived to interact with acrylonitrile under our experimental conditions. Nevertheless, the two-electron transfer mechanism seems most likely in our study.

## **Reaction mechanism**

The reaction between HCP and Asn in the presence of small amounts of transition metal catalysts had a stoichiometry of 1:1, with a first-order dependence on [HCP] and less than unit order each with respect to [Asn],  $[H^+]$  and [M(Y)]. The rates of the reactions decreased as the ionic strength and dielectric constant of the medium increased, suggesting reactions between oppositely charged ions [42].

The observed less than unit order for both [Asn] and [M(Y)] suggests the formation of a complex between the



 $[H^+] = 1.0$  and I = 2.0 mol dm<sup>-3</sup>.  $[M(Y)] = 5.0 \times 10^{-5}$  mol dm<sup>-3</sup> for Ag(I) and Cr(III); and  $5.0 \times 10^{-4}$  mol dm<sup>-3</sup> for Pd(II) and Zr(IV)

Transition metal ion	Parameter							
	$\Delta S^{\neq} (\text{J mol}^{-1} \text{ K}^{-1})$	$\Delta H^{\neq}$ (kJ mol <sup>-1</sup> )	$\Delta G_{298}^{\neq}$ (kJ mol <sup>-1</sup> )	$E_a^{\neq}$ (kJ mol <sup>-1</sup> )				
Ag(I)	-152.98	32.82	78.41	35.71				
Cr(III)	-140.84	38.27	80.24	41.24				
Pd(II)	-146.74	40.18	83.91	43.09				
Zr(IV)	-160.62	37.27	85.14	40.21				

**Table 2** Activation parameters for the second-order rate constants  $k_2$  in the transition metal ion-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium

<sup>a</sup> [Asn] =  $5.0 \times 10^{-2}$ , [HCP] =  $7.6 \times 10^{-5}$ , [H<sup>+</sup>] = 1.0 and I = 2.0 mol dm<sup>-3</sup>. [M(Y)] =  $5.0 \times 10^{-5}$  mol dm<sup>-3</sup> for Ag(I) and Cr(III); and  $5.0 \times 10^{-4}$  mol dm<sup>-3</sup> for Pd(II) and Zr(IV). Experimental error  $\pm 4 \%$ 

catalyst and substrate prior to reaction with the oxidant. Complex formation is also indicated kinetically by the nonzero intercepts of the plots of  $[M(Y)]/k_C$  versus 1/[Asn], as shown in Fig. 4a–d. The failure to

spectrophotometrically detect such intermediate complexes might be explained by either the low concentrations of the reactants or fast subsequent decomposition of the intermediates relative to their rates of formation. However,





**Fig. 4 a–d** Verification of the rate law in the form of Eq. (14) in the transition metal ion-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium. [HCP] =  $7.6 \times 10^{-5}$ 

and  $I = 2.0 \text{ mol dm}^{-3}$  at 25 °C for **a** Ag(I), **b** Cr(III), **c** Pd(II) and **d** Zr(IV)

Scheme 1 Mechanism of transition metal ion-catalyzed oxidation of L-asparagine by hexachloroplatinate(IV) in sulfuric acid medium.  $R = H_2NC(O)CH_2^-$ , M(Y) = Ag(I), Pd(II), Cr(III) orZr(IV)

$$R \stackrel{H}{\longrightarrow} C \stackrel{H}{\longrightarrow} R \stackrel{H}{\longrightarrow} R \stackrel{H}{\longrightarrow} R \stackrel{H}{\longrightarrow} R \stackrel{H}{\longrightarrow} (5)$$

$$N \stackrel{H}{\longrightarrow} N \stackrel{H}{\longrightarrow$$

$$\begin{array}{c} H & H & O \\ R - C - COOH + M(Y) & \swarrow & R - C - C - O \rightarrow M(Y) \\ \downarrow & MH_3 & NH_3 & H \end{array}$$
(6)

$$C + [PtCl_{6}]^{2^{-}} \xrightarrow[k_{1}]{k_{1}} \approx R \xrightarrow[k_{1}]{|l|}{R - C - C - C - O^{+}} + H^{+} + [PtCl_{4}]^{2^{-}} + 2C\overline{l} + M(Y)$$
(7)

$$\begin{array}{cccc} R-C-H &+ H_2O & \xrightarrow{fast} & R-C-H &+ NH_4^+ \\ & & & & \\ NH_2 & & O \end{array} \tag{9}$$

complexes between amino acids and Ag(I) [16, 31, 35], Pd(II) [43, 44], Cr(III) [45–47] and Zr(IV) [48] have been reported in the literature.

A reaction mechanism consistent with the experimental results is given in Scheme 1. It is suggested that the protonated asparagine  $(Asn^+)$  combines with M(Y) to form an intermediate complex,  $[Asn-M]^{Y+1}$ , which then reacts in a slow step with one mole of HCP to give rise to the oxidation products with regeneration of the catalyst, as illustrated in the Scheme.

The proposed mechanism leads to the following rate law,

$$\frac{-\mathrm{d}[\mathrm{HCP}]}{\mathrm{d}t} = k_1[C][\mathrm{HCP}] \tag{10}$$

The relationship between the rate of complex formation and the substrate, hydrogen ion, catalyst and oxidant concentrations has been deduced (Appendix shown in supplementary material) to give the following rate law expression,

Rate = 
$$\frac{k_1 K_1 K_2 [\text{Asn}][\text{H}^+][\text{M}(\text{Y})][\text{HCP}]}{(1 + K_1 [\text{H}^+] + K_1 K_2 [\text{H}^+][\text{M}(\text{Y})])(1 + K_1 K_2 [\text{Asn}][\text{H}^+])}$$
(11)

In view of the low concentrations of [M(Y)] used, the term  $K_1$   $K_2[H^+][M(Y)]$  in the denominator can be neglected. Therefore, Eq. (11) becomes,

$$Rate = \frac{k_1 K_1 K_2 [Asn] [H^+] [M(Y)] [HCP]}{(1 + K_1 [H^+])(1 + K_1 K_2 [Asn] [H^+])}$$
(12)

Then, under pseudo-first-order conditions,

$$\frac{-\mathrm{d}[\mathrm{HCP}]}{\mathrm{d}t} = k_C[\mathrm{HCP}] \tag{13}$$

On comparing Eqs. (12) and (13) and rearrangement, Eq. (14) is obtained,

$$\frac{[\mathbf{M}(\mathbf{Y})]}{k_C} = \left(\frac{1+K_1[\mathbf{H}^+]}{k_1K_1K_2[\mathbf{H}^+]}\right)\frac{1}{[\mathbf{A}\mathbf{s}\mathbf{n}]} + \frac{1}{k_1}$$
(14)

According to Eq. (14), plots of  $[M(Y)]/k_C$  against 1/[Asn] at constant  $[H^+]$  and  $[M(Y)]/k_C$  against 1/[H<sup>+</sup>] at constant [Asn] should be linear with positive intercepts on the  $[M(Y)]/k_C$  axes. The experimental results satisfied this requirement, as shown in Fig. 4a–d.

Unfortunately, the value of the rate constant for the slow reaction step  $(k_1)$  and its associated activation parameters could not be determined because the protonation constant  $(K_1)$  for Asn and/or the formation constants  $K_2$  are unknown for M(Y)–Asn complexes under the present experimental conditions. Attempts to determine these constants from the experimental data were unsuccessful.

The activation parameters listed in Table 2 lead to the following conclusion. The large negative values of  $\Delta S^{\neq}$  indicate the compactness of the Asn-M(Y) complexes

formed. These activated complexes are more ordered than the reactants due to the loss of some degrees of freedom. The values of  $\Delta H^{\neq}$  and  $\Delta S^{\neq}$  are both favorable for an electron transfer process. The positive value of  $\Delta H^{\neq}$ indicates an endothermic transition state. This mechanism is also consistent with the proposition made by Stewart et al. [49, 50]. They reported that the entropy of activation tends to be more positive for outer-sphere mechanisms, whereas it is more negative for inner-sphere reactions.

## Conclusion

The reaction between Asn and HCP in sulfuric acid proceeds with a measurable rate in the absence of transition metal ion catalysts but is significantly faster in their presence. The catalytic efficiencies of the metals increase in the order: Ag(I) > Cr(III) > Pd(II) > Zr(IV). Electron transfer is facilitated by adducts between metal and the carboxylate oxygen on Asn. The reaction mechanism proposed here is consistent with product, kinetic and mechanistic studies.

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