Oxidation of Some Sustainable Sulfated Natural Polymers: Kinetics and Mechanism of Oxidation of Water-Soluble Chondroitin-4-Sulfate Polysaccharide by Hexachloroiridate(IV) in Aqueous Solutions

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ABSTRACT: The kinetics and mechanism of hexachloroiridate(IV) oxidation of chondroitin-4-sulfate as a sustainable coordination biopolymer macromolecule (CS) in aqueous acidic solutions at a constant ionic strength of 0.1 mol dm$^{-3}$ has been investigated spectrophotometrically. Pseudo first-order plots gave sigmoidal curves of S-shape nature, indicating that the kinetics is complex. Two distinct stages have been observed. The first stage was relatively fast corresponding to the autoacceleration period, followed by a slow stage which became linear at a longer time period called the induction period. First-order dependence with respect to the [OX] and fractional first order in [CS] was observed for both stages. Kinetic evidence for formation of the 1:1 intermediate complex within the two stages has been revealed. The influence of [H$^+$] on the rate constants indicated that the oxidation was of acid inhibition nature. The kinetic parameters have been evaluated, and a suitable reaction mechanism is suggested and discussed in terms of the nature of the electron-transfer process.

1. INTRODUCTION

Study of electron-transfer processes in macromolecules, in particular sustainable coordination natural polymers, is considered as a new criterion in the field of kinetic research.$^{1,2}$

Chondroitin-4-sulfate (CS) is a natural polymer that belongs to sulfated polysaccharides. It is composed of a chain of alternating sugars ($N$-acetylgalactosamine and glucuronic acid).$^3$ It is usually found to be attached to the proteins as a part of proteoglycan as a carrier for heparin. The nature of polysaccharides including the CS substrate as water-soluble, sustainable, and biodegradable natural polymers makes this kind of polymers of high importance from environmental and medical points of view.$^5,6$ Therefore, it has a wide therapeutic application owing to its high anticoagulant and antithrombotic activity.$^5,7$ Recently, the CS substrate has been successfully applied as an inhibitor for metal corrosion because of its safety, low cost, nontoxicity, nondegradability, and ecofriendly characterizations.$^8$

The literature survey indicated that a few reports have been published on the oxidation kinetics of sulfated macromolecules,$^9$ in particular chondroitin-4-sulfate. This fact may be attributed to the complex kinetic study of oxidation. However, the kinetics of oxidation by CS by a multiequivalent oxidant such as chromic acid$^9$ and a one-equivalent oxidant such as hexacyanoferrate(III)$^{10}$ has been reported earlier. A lack of information on the nature of the electron-transfer mechanism and transition states in the rate-determining steps for redox systems involving the CS substrate is recognized, which makes the kinetics and mechanisms of the electron-transfer process remains not complete and poor understand.

Preliminary experiments on the oxidation of CS by $[\text{IrCl}_6]^{2-}$ in aqueous solutions indicated that the kinetics were of complex nature and behave in a different trend from that studied by the other oxidants.$^9,10$

In view of the above argument and our interest in the oxidation of either sustainable natural polymers such as polysaccharides,$^{11-17}$ in particular chondroitin-4-sulfate,$^9,10$ or synthetic polymer such as poly(vinyl alcohol)$^{18}$ by various oxidants, we have prompted to undertake the present investigation of oxidation of CS by hexachloroiridate(IV) as an inert oxidant of one-equivalent nature with the aim at shedding more light on the oxidation kinetics in terms of the nature of electron transfer and transition states in the rate-determining step with special focus on the influence of the molar concentration ratio of reactants on the nature of oxidation products. Moreover, a novel synthesis of keto-acid derivatives as a renewal chelating agent for removal of toxic heavy metal ions from contaminated matters or as an inhibitor for metal corrosion.

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2. EXPERIMENTAL SECTION

2.1. Materials and Preparations. Chondroitin-4-sulfate (ICN Biomedicals, Inc.) was used without further purification. A stock solution of CS was prepared by stepwise addition of the reagent powder to doubly distilled water while vigorously stirring the solution to avoid the formation of aggregates, which swell with difficulty as described earlier. The measured viscosity using an Ubbelohde viscometer was found to be 1.12 dL/g for the reduced viscosity and 3.11 dL/g for the inherent viscosity, respectively, for 5% solution (w/v) in water at 25 °C.

Sodium hexachloroiridate(IV) of Analar quality (Wako Chemical Reagent) was used without further purification. Solutions of this reagent were freshly prepared before each experiment to minimize the interference from other reagents at this wavelength. This was followed by recording the decrease in absorbance of the formed labile hexachloroiridate(III). The measurements of optical density against concentration plots for 

\[ \text{[IrCl}_6\text{]}^{2-} \]

were conducted under pseudo first-order conditions to check the producibility of the pseudo first-order kinetic data obtained.

2.2. Kinetic Measurements. All kinetic measurements were conducted under pseudo first-order conditions where [CS] was present in a large excess over that of hexachloroiridate(IV) concentration. The course of reaction was followed by recording the decrease in absorbance of 

\[ \text{[IrCl}_6\text{]}^{2-} \]

at a wavelength of 489 nm, its absorption maximum, as a function of time. It was verified that there was no interference from other reagents at this wavelength. This means that all other reagents do not absorb significantly at this wavelength. The absorption measurements were made in a thermostated cell compartment at the desired temperature within ±0.05 °C on a Shimadzu UV-2101/3101 PC automatic scanning double-beam spectrophotometer fitted with a wavelength program controller using cells of pathlength 1.0 cm. The spectral changes during the progress of the oxidation reaction are displayed in Figure 1.

Some kinetic measurements were conducted under second-order conditions to check the producibility of the pseudo first-order kinetic data obtained.

3. RESULTS

3.1. Stoichiometry. Because this reaction seems to be of noncomplementary nature as well as of complexity kinetics, determination of the stoichiometry of the overall reaction becomes greatly significant. The stoichiometry of this redox reaction was performed by using reaction mixtures of different initial concentrations of the two reactants at [H⁺] = 1 × 10⁻³ and I = 0.1 mol dm⁻³ equilibrated in dark bottles away from light to avoid the photoreduction of 

\[ \text{[IrCl}_6\text{]}^{2-} \]

. The unreacted 

\[ \text{[IrCl}_6\text{]}^{2-} \]

was estimated periodically until it reached a constant value, that is, reaction completion. The results of various ratios of the equilibrated reactants indicate that 1 mol of CS consumed 8 ± 0.1 mol of 

\[ \text{[IrCl}_6\text{]}^{2-} \]

. This result indicates that the stoichiometry of the overall reaction conforms to the following equation

\[ (C_{14}H_{21}NO_{15}S)_n + 8[\text{IrCl}_6]^{2-} + H_2O = (C_{14}H_{19}NO_{14}S)_n + 8[\text{IrCl}_6]^{3-} + 8H^+ \] (1)

where 

\[ C_{14}H_{19}NO_{14}S \]

and 

\[ C_{14}H_{17}NO_{14}S \]

are corresponding to chondroitin-4-sulfate and its diketo-acid oxidation precursor derivative, respectively. The oxidation products were identified by elemental analysis and spectral data as described earlier. Under our experimental conditions of the presence of [CS] ≫ [IrCl₆]²⁻, the product was identified as the monoketo-derivative product of CS. This means that the product is dependent on the molar ratios between the reactants as follows

\[ (C_{14}H_{21}NO_{14}S)_n + 2[\text{IrCl}_6]^{2-} = (C_{14}H_{19}NO_{14}S)_n + 2[\text{IrCl}_6]^{3-} + 2H^+ \] (2)

\[ (C_{14}H_{21}NO_{14}S)_n + 4[\text{IrCl}_6]^{2-} = (C_{14}H_{17}NO_{14}S)_n + 4[\text{IrCl}_6]^{3-} + 4H^+ \] (3)

where 

\[ C_{14}H_{19}NO_{14}S \]

and 

\[ C_{14}H_{17}NO_{14}S \]

represent mono- and diketo-derivatives of oxidation of CS, respectively. These products could be separated and identified as mentioned above.

3.2. Reaction Time Curves. Pseudo first-order plots [ln (absorbance) vs time] or second-order plots [1/(absorbance) vs time] were much surprising which gave curves of inverted S-shape nature, indicating that the oxidation kinetics are complex throughout the entire course of reaction progression. At the early stages, the rates were relatively fast, followed by slow stages which became linear at longer time periods. This means that the oxidation reaction takes place through two distinct stages, namely, autoacceleration and induction periods, respectively. This behavior may obey to the following rate law expression

\[ (A_t - A_\infty) = P_0 e^{-kt} + B_0 e^{-kt} \] (4)
values of pseudo-first-order plots (Figure 2) may confirm the formation of such intermediate complexes. The Michaelis–Menten kinetic plots for both autoacceleration and induction periods were calculated by the method of least-squares and are summarized in Table 1.

### Table 1. Dependence of the Rate Constants on Variable Factors of [CS], [H⁺], and [Ox] in the Oxidation of CS by [IrCl₆]²⁻ through Both Autoacceleration and Induction Periods at 40 °C

| [CS], mol dm⁻³ | 10³[k₇]⁺, s⁻¹ | 10⁴[k₈]⁻, s⁻¹ | 10⁴[H⁺], mol dm⁻³ | 10³[k₁]⁺, s⁻¹ | 10⁴[k₂]⁻, s⁻¹ | 10⁴[Ox]⁺, mol dm⁻³ | 10³[k₃]⁺, s⁻¹ | 10⁴[k₄]⁻, s⁻¹ |
|---------------|----------------|----------------|-----------------|----------------|----------------|-----------------|----------------|----------------|
| 1.5 | 1.0 | 2.0 | 1.5 | 1.35 | 2.90 | 1.0 | 1.19 | 2.4 |
| 3.0 | 1.35 | 2.9 | 3.0 | 1.00 | 1.83 | 9.0 | 1.19 | 2.4 |

where Aᵣ and Aᵢ are the absorbances at time t and infinity, respectively; P₀ and B₀ are the absorbance change for the fast and slow reacting species, respectively. The rate constants for the autoacceleration period can be obtained by drawing a straight line throughout the fast stage and extrapolating the line back to zero time P₀. The rate constant of the induction period was obtained from plots of the form ln ([Aᵣ] − Aᵢ) versus time. The quantity (Aᵣ − Aᵢ) represents the experimental point and (Aᵢ − Aᵢ) represents the extrapolating point at time t. A typical plot is shown in Figure 2. The values of pseudo-first-order rate constants k₁ and k₂ for both autoacceleration and induction periods were calculated by the method of least-squares and are summarized in Table 1.

### 3.3. Dependence of the Reaction Rate on [IrCl₆]²⁻ and [CS].

The experimental results indicated that both first-order rate constants (k₁ and k₂) were independent on the concentration of the oxidant in the range of (1−8)×10⁻⁴ mol dm⁻³. The results are summarized in Table 1. This independency along with the linearity observed for pseudo-first-order plots (Figure 2) may confirm that the reaction is first order in [IrCl₆]²⁻ in both autoacceleration and induction stages, respectively.

The dependence of observed first-order rate constants kobs on the substrate concentration (where kobs = k₁ or k₂) was deduced from the measurements of such observed pseudo-first-order rate constants at various initial concentrations of CS and fixed concentrations of all other reagents. The nonconstancy values obtained by dividing kobs by [CS] indicates the fractional order with respect to [CS]. The order in [CS] was evaluated from the relation (log rate = n log[CS] plots).

Again, the double reciprocal plots of kobs versus [CS] were found to be linear with positive intercepts on 1/kobs axes in both two stages as shown in Figure 3. This behavior is indicative to the Michaelis–Menten kinetics for formation of 1:1 intermediate complexes. The existence of two isobestic points at wavelengths of about 390 and 320 nm during the reaction progression (Figure 1) may confirm the formation of such intermediate complexes. The Michaelis–Menten constants were found to be 0.55×10⁻² and 0.63×10⁻² dm⁻³ mol⁻¹ at 40 °C for the autoacceleration and induction periods, respectively.

### 3.4. Dependence of the Reaction Rate on [H⁺].

Some kinetic runs were conducted in HClO₄−NaClO₄ solutions of different [H⁺] and constants of all other reagent concentrations in order to examine the influence of [H⁺] on the oxidation rates in order to elucidate a suitable reaction mechanism. It was surprising to observe a decrease in the rate constants with increasing the hydrogen ion concentration because all alcoholic polysaccharides including the CS substrate possess high tendency for protonation in acidic solutions. The experimental results showed an inverse fractional order in [H⁺] in both two stages (Rate = [H⁺]ⁿ plots). Again, plots of observed pseudo-first-order rate constants against [H⁺]⁻ gave curvature lines passing through the origin as shown in Figure 4a,b.
3.5. Dependence of the Reaction Rate on Ionic Strength. Some kinetic runs were performed to examine the influence of the ionic strength on the reaction rates in order to shed some light on the reactive species in the rate-determining steps; this takes place by measuring the reaction rates with increasing the NaClO₄ added at constant [H⁺] and fixed concentration of all other reagents. It was found that the reaction rates (kf and ks) were decreased with increasing the ionic strength. Plots of ln kf versus either of √I or √I/(1 + √I) according to the Debye–Huckel or extended Bronsted–Debye–Huckel equations were found to be linear with negative slopes as shown in Figure 5a. However, the present measurements of necessity lie outside the Bronsted–Debye–Huckel region, covering a range over which the activity coefficients of many electrolytes are known to be fairly dependent on the ionic strength. The ionic strength dependence of the rate constants is qualitative as expected when considering the charges involved in the present redox reaction. ²⁹

3.6. Polymerization Test. Of course, the intervention of free radicals throughout the course of reaction was highly expected because the present reaction was of noncomplementary type. Therefore, the possibility of free-radical formation has been examined by adding 10% (v/v) of the acrylonitrile monomer to the partially oxidizing reaction mixture. The failure of the polymerization test after lapse of a long time period was much surprising which was found to be on contrary to our expectation. ³⁰ Such a result will be discussed later.

3.7. Dependence of the Reaction Rate on Temperature. Some experimental measurements were performed at various temperatures and fixed concentration of all other reagents in order to evaluate the kinetic parameters of the rate constants. The rate constants (kf and ks) were found to increase with increasing temperature and were fitting both Arrhenius and Eyring equations for the temperature dependence of the rate constants.

4. DISCUSSION
The experimental observations in the present redox reactions indicated that the behavior of reaction kinetics was complex with respect to both autoacceleration (initial first stage) and induction periods (slow second stage), respectively. This is because the plots of pseudo first-order or second-order rate constants were deviated from linearity and exhibited some curvature of inverted S-shape nature. This complicated behavior may suggest the existence of either two consecutive first-order reactions.
Oxidation of CS by [IrCl₆]²⁻ and the Rate Constants of the Elementary Reaction (the product. D and E are their respective reactants, respectively, and C is the oxidation of CS by [IrCl₆]²⁻ where the symbol kf and ks represent the observed pseudo or two parallel reactions as follows

\[ a \]

\[ a + b \overset{k_i}{\rightarrow} d + e \overset{k_i}{\rightarrow} c \]  

or two parallel reactions as follows

\[ A + B \overset{k_i}{\rightarrow} C \]  

\[ D + E \overset{k_i}{\rightarrow} C \]  

where the symbol kf and k, represent the observed pseudo first-order rate constants (kobs and Kobs) in the two stages, A and B; D and E are their respective reactants, respectively, and C is the product.

Table 2. Values of the Apparent Rate Constants (k′ and kₐ) and the Rate Constants of the Elementary Reaction (kₐ and kₕ) and the Hydrolysis Constants (K₂ and K₃) in the Oxidation of CS by [IrCl₆]²⁻

| Constants | temp, °C | 35 °C | 40 °C |
|-----------|----------|-------|-------|
| 10⁻¹kₕ mol⁻¹ s⁻¹ | 2.17 | 2.39 |
| 10⁻¹kₐ mol⁻¹ s⁻¹ | 1.21 | 1.83 |
| 10⁻¹kₐ mol⁻¹ s⁻¹ | 3.09 | 4.13 |
| 10⁻¹kₕ s⁻¹ | 3.16 | 3.34 |
| 10⁻¹K₁ dm³ mol⁻¹ | 5.38 | 3.90 |
| 10⁻¹K₂ dm⁻³ mol⁻¹ | 0.098 | 1.20 |

“Experimental errors (±3%).”

Table 3. Activation and Thermodynamic Parameters for the Rate Constants and the Hydrolysis Constants in the Oxidation of CS by [IrCl₆]²⁻

| Parameters | DH₀ kJ mol⁻¹ | DS₀ J mol⁻¹ K⁻¹ | DG₀ kJ mol⁻¹ | ET₀ kJ mol⁻¹ |
|------------|-------------|-----------------|-------------|-------------|
| kₕ | 13.39 | -271.65 | 94.34 | 16.0 |
| kₐ | 50.16 | -137.67 | 91.19 | 52.77 |
| kₜ | 38.17 | -207.60 | 100.03 | 40.40 |
| kₜ | 12.17 | -271.14 | 92.96 | 15.44 |

| DH | 0.19 | -17.35 | 5.07 |
| DG | -35.60 | 20.15 | 28.70 |
| ET | -19.33 | 29.08 | 48.41 |

“Experimental errors (±3%).” Estimated at 30 °C.

A + B \overset{k_i}{\rightarrow} D + E \overset{k_i}{\rightarrow} C \]  

or two parallel reactions as follows

\[ A + B \overset{k_i}{\rightarrow} C \]  

\[ D + E \overset{k_i}{\rightarrow} C \]  

The experimental kinetic results seem best interpreted in favor of the first type reaction pathway. This suggestion may be supported by the observed curvature lines passing through the origin obtained from the plots of kobs versus [H⁺]⁻². However, the second reaction path cannot be exclusively eliminated.

In view of the above interpretation and the experimental observations of the inverse first order in [H⁺] and the obedience of the [CS] dependence of the reaction rates to the Michaelis-Menten kinetics for formation of 1:1 intermediate complexes, the most suitable reaction mechanism to be suggested should involve the release of protons from at least one of the reaction paths prior to the rate-determining step. This suggestion is supported by the observed protons released in the stoichiometric equations. Because hexachloroiridate-(IV) is known to be extremely inert, then, the CS substrate is only responsible for releasing such protons.

All alcoholic polysaccharides involving chondroitin-4-sulfate are known to have a high tendency for either protonation in acidic solutions to give the more reactive alkyloxonium ions or deprotonation in alkali forming the more reactive alkoxide ions

\[(PS-OH)ₙ + H⁺ \overset{K}{\rightarrow} (PS-OH₂⁺)ₙ \]  

or

\[(PS-OH)ₙ + OH⁻ \overset{K}{\rightarrow} (PS-O⁻)ₙ + H₂O \]  

where PS-OH represents alcoholic polysaccharides, PS-O⁻ represents alkyl oxonium ions, and PS-O⁻ is the alkoxide ion, respectively.

Under our experimental conditions of lower acid concentrations (0.5–4.0) x 10⁻³ mol dm⁻³ where the pHs ranging between 2.4 and 3.3, the possibility of protonation of CS may be negligible small. Hence, the most suitable reaction mechanism which may be suggested involves the attack of the oxidant on the center of the CS substrate, forming an intermediate complex C with subtracting a proton ion by the water molecule prior to the rate-determining step as follows

\[ CS + [IrCl₆]²⁻ \overset{K}{\rightarrow} C + H₂O^⁺ \]  

Figure 6. Plots [CS]/kobs vs [H⁺] for the autoacceleration period in the oxidation of CS by [IrCl₆]²⁻. [IrCl₆]²⁻ = 2 x 10⁻⁴, [CS] = 3 x 10⁻³, and I = 0.1 mol dm⁻³ at various temperatures.

Figure 7. Plots 1/kobs vs [H⁺] for the induction period in the oxidation of CS by [IrCl₆]²⁻. [IrCl₆]²⁻ = 2 x 10⁻⁴, [CS] = 3 x 10⁻², and I = 0.1 mol dm⁻³ at various temperatures.
This reaction is followed by the transfer of electrons from the CS substrate to the oxidant in the rate-determining step to give a substrate radical (C₁•) and the reduced form of the oxidant (Red) as initial oxidation products in the initial fast stage (autoacceleration period).

\[
C₁ \xrightarrow{k₁} C₁• + \text{Red}
\]  

(11)

Because the oxidant is of one-equivalent nature, it needs to accept only one electron to give its corresponding reduced form [IrCl₆]⁻⁻ (Red). This means that the rate-determining step should involve the intervention of free radicals.

Therefore, the delay of formation of free radicals in the polymerization test during the progress of the oxidation process may be attributed to either the rapid oxidation of the formed free radical compared with its formation that could mask polymerization of acrylonitrile or to the oxidation of the vinyl compounds themselves under our experimental conditions. These reasons may be responsible for the observed negative test of polymerization.

The change of the rate constants with the change of both \([H^+]\) and \([CS]\) can be expressed by the following rate-law equation

\[
\text{Rate} = \frac{-d[\text{Ox}]}{dt} = \frac{k_{\text{f}}[H^+]^{-1}[CS][\text{Ox}]_{\text{a}}}{1 + K_2[H^+]^{-1}[CS]}
\]  

(12)

where \([\text{Ox}]_{\text{a}}\) is the analytical total concentration of the oxidant. Under pseudo first-order conditions of \([CS] \gg [\text{Ox}]\), the rate constant is generally written as

\[
\text{Rate} = k_{\text{obs}}[\text{Ox}]
\]  

(13)

Comparing eqs 12 and 13 and rearrangement, one concludes that

\[
\frac{1}{k_{\text{obs}}} = \frac{[H^+]^{-1}}{k_{\text{f}}K_2[CS]} + \frac{1}{k_a}
\]  

(14)

where \(k_{\text{obs}}\) corresponds to \(k_0\). According to eq 14, at constant \([H^+]\), a plot of \(1/k_{\text{obs}}\) versus \(1/[CS]\) should be linear with a positive intercept on the \(1/k_{\text{obs}}\) axis as shown in the Michaelis–
Scheme 2. Mechanism of Oxidation of Protonated Chondroitin-4-Sulfate by Hexachloroiridate (IV)

Following the attack of the oxidant on the center of that alxonium ion forming (Ct) complex with release of two protons as follows

\[
\text{CS} + H^+ \xrightarrow{K} \text{CSH}^+ \quad (15)
\]

In a similar manner for derivation of the abovementioned rate-law expression, one may conclude the following relationship

\[
k_{\text{obs}} = \frac{k_a' K K_1 [\text{CS}]_T}{1 + K [H^+] + [\text{Ox}] K K_2}
\]

where \([\text{CS}]_T\) is the analytical total concentration of the substrate. Rearrangement of eq 17 yields

\[
\frac{1}{k_{\text{obs}}} = \left( \frac{1}{k_a' K K_1} + \frac{[H^+]}{k_a' K K_2} \right) \frac{1}{[\text{CS}]} + A
\]

Assuming that the third term (\(A = [\text{Ox}] / k_a' [\text{CS}]\)) of the denominator of eq 18 is negligibly small, rearrangement yields

\[
\frac{[\text{CS}]}{k_{\text{obs}}} = \frac{1}{k_a' K K_1} + \frac{[H^+]}{K K_2 k_a'}
\]

The evaluated values of the protonation constant (K) in such plots were found to be in good accord to those reported for the protonation of the CS substrate\(^7\) or other polysaccharides\(^8-14\) in acidic solutions.\(^8-14\)

Plots of \([\text{CS}] / k_{\text{obs}}\) against \([H^+]\) were found to be linear with positive intercepts on \(Y\)-axes as shown in Figure 6. The values of the apparent rate constants \(k_a'\) (where \(k_a' = k_a K K_1\)) and \(k_a''\) (where \(k_a'' = k_a K K_2\)) can be evaluated from the slopes and intercepts of such plots, respectively. These values were calculated by the method of least-squares and are summarized in Table 2. The activation parameters of \(k_a'\) and \(k_a''\) were
calculated from the Arrhenius and Eyring equation using the least-squares method and are summarized along with the thermodynamic parameters of $K$ in Table 3.

Moreover, the observed inverse fractional order in $[H^+]$ for the rate constant dependency in the induction period along with formation of the 1:1 intermediate complexes in terms of the Michaelis–Menten kinetic plots of $1/k_b$ versus $1/[CS]$ means that the formed radical ($C_1^*$) in the initial stage also releases a proton ion prior to its picking up of a further oxidant molecule to form an intermediate complex $C_2^*$ as follows:

$$C_1^* \xrightleftharpoons{k'_1} H_2O + H^+$$

followed by electron transfer from the substrate radical to the oxidant to give rise to the final oxidation product as follows:

$$C_2^* + [\text{IrCl}_6^{2-}] + \xrightarrow{k_2} \text{product} + \text{Red}$$

In a similar manner to the derivation of the above rate-law expression of (eq 12) in the former mechanism, the change of the rate constant ($k_b$) with changing both the concentration of the substrate radical and $[H^+]$ (considering that $[C_2^*]$ equals to the initial $[CS]$, and $k_{obs}$ equals $k_b$) can be expressed by the following relationship:

$$k_{obs} = \frac{k_bK_3[C_2][H^+]^{-1}}{1 + K_b[H^+]^{-1}[CS]}$$

Equation 23 on rearrangement can be reformulated to eq 24

$$\frac{1}{k_{obs}} = \frac{[H^+]}{k_bK_3K_3}[CS] + \frac{1}{k_b}$$

Equation 24 requires that plots of $1/k_{obs}$ against either $1/[CS]$ or $[H^+]$ to be linear with positive intercepts on $1/k_{obs}$ axes as was experimentally observed in Figures 3 and 7, respectively. The agreement between the values of the elementary rate constants ($k_b$) obtained from the intercepts of such two plots may also confirm the validity of the suggested mechanism for the induction period. The values of the apparent rate constants ($k'_b = k_bK_3K_3$) and the elementary rate constant $k_b$ can be evaluated from the slopes and intercepts of $1/k_{obs} - [H^+]$ plots at constant $[CS]$. These values were calculated by the least-squares method and are summarized in Table 2. The activation parameters of these values were calculated from Arrhenius and Eyring equations using the least-squares method and are summarized in Table 3.

The observed protonation values ($K$) for the CS substrate were found to be in good agreement with that reported for either other sulfated polysaccharides or the oxidation of the CS substrate with other oxidants. The small values observed for the activation energies ($E^*$) in the initial rapid step means that the energy of attraction forces between the reactants is strong enough to overcome the energy barrier needed for reaching the transition state or the formation of the intermediate, that is, it does not need more energy for such purpose. This may be explained by the formation of bridges between one chloride ligand from $[\text{IrCl}_6^{2-}]$ anion and the CS substrate. Thus, in turn, the formation of such bridges will facilitate the transfer of electrons from the substrate and the oxidant. The negative and neutral molecules as reactive species in the rate-determining step may be confirmed by the negative slopes observed in the plots of ionic strength dependency of the rate constant in terms of the Bronsted–Debye–Huckel equation (Figure 5a,b). The large negative values of entropies of activation ($\Delta S^*$) indicate the compactness of the intermediates formed, that is, the intermediates are more ordered than the reactants which were stabilized by the solvation of the electron-transfer process. Again, the positive values of $\Delta G^*$ obtained may confirm the spontaneity of the complex formed prior to the rate-determining step.

In view of the above interpretation and the kinetic results, it may suggest that the oxidation of CS by $[\text{IrCl}_6^{2-}]$ proceeds by the one electron-transfer process of inner sphere nature, which is supported by the observed large negative entropies of activation (Table 3). Consequently, a suitable reaction mechanism for oxidation of chondroitin-4-sulfate by hexachloroiridate(IV) for both autoacceleration and induction periods may be speculated in Schemes 1 and 2. It involves the attack of the inert hexachloroiridate(IV) oxidant on the center of either the unprotonated or protonated CS substrate forming the intermediate complexes ($C_1^*$) with subtraction of one or two protons, respectively, by water molecules prior to the rate-determining step to give free-radical substrates ($C_2^*$) and the reduced form of the oxidant (Red) as initial oxidation products in the fast first stage. The substrate radicals were also picking up further oxidant molecules forming intermediate complexes ($C_2^*$), with releasing one proton prior to the rate-determining step of the slow second stage, followed by transfer of electrons from the intermediate radical substrates to the oxidant to give rise to the final oxidation products.

5. CONCLUSIONS

The kinetics and mechanism of hexachloroiridate(IV) oxidation of chondroitin-4-sulfate (CS) in aqueous acidic solutions at constant ionic strength of 0.1 mol dm$^{-3}$ has been investigated spectrophotometrically. Pseudo first-order plots gave sigmoidal curves of S-shape nature, indicating that the kinetics is of complexity nature. Two distinct stages have been observed. The first stage was relatively fast corresponding to the autoacceleration period, followed by a slow stage. The influence of $[H^+]$ on the rate constants indicated that the oxidation was of acid inhibition nature. The kinetic parameters have been evaluated, and a suitable reaction mechanism is suggested and discussed.

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Notes
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REFERENCES

(1) Hassan, R. M.; Alaraifi, A.; Fawzy, A.; Zaafarany, I. A.; Khairou, K. S.; Ikeda, Y.; Takagi, H. D. Acid-catalyzed oxidation of some sulfated polysaccharides. Kinetics and mechanism of oxidation of kappa-carrageenan by cerium(IV) in aqueous perchlorate solutions. J. Mol. Catal. A: Chem. 2010, 332, 138–144.

(2) Khan, Z.; Raju; Kabir-ud-Din. Oxidation of 4-(1,1,3,3-Tetramethybutyl)phenyl Polyethylene Glycol (TritionX-100) by Cerium(IV) in Presence of Sulfuric Acid. Colloids Surf., A 2003, 225, 78–83.

(3) Advances in Pharmacology Vol. 30. Chondroitin-4-Sulfate Structure, Role and Pharmacological Activity; Volpi, N., Ed.; Elsevier Inc.: USA, 2006.

(4) Thakur, V. K.; Thakur, M. K. Recent Advances in Graft Copolymerization and Applications of Chitosan: A Review. ACS Sustainable Chem. Eng. 2014, 2, 2637–2652.

(5) Thakur, M. K.; Thakur, V. K.; Gupta, R. K.; Pappu, A. Synthesis and Applications of Biodegradable Soy Based Graft Copolymers: A Review. ACS Sustainable Chem. Eng. 2016, 4, 1–17.

(6) Silvestri, L.; Baker, J. R.; Roden, L.; Stroud, R. M. The C1q Inhibitor in Serum Is a Chondroitin-4Sulfate Proteoglycan. J. Biol. Chem. 1981, 256, 7383–7387; http://www.jbc.org/content/256/14/7383.full.pdf.

(7) Yamada, S.; Sugahara, K. Potential Therapeutic Application of Chondroitin Sulfate/Dermatan Sulfate. Curr. Drug Discovery Technol. 2008, 5, 289–301.

(8) Hassan, R. M.; Ibrahim, S. M.; Takagi, H. D.; Sayed, S. A. Kinetics of Corrosion Inhibition of Aluminum in Acidic Media by Water-Soluble Natural Polymers. Chondroitin-4-Sulfate as Anionic Polyelectrolyte Inhibitor. Carbohydr. Polym. 2018, 192, 356–363.

(9) Hassan, R.; Ibrahim, S.; Dahy, A. R.; Zaafarany, I.; Tirkistani, F.; Takagi, H. Kinetics and Mechanism of Oxidation of Chondroitin-4-Sulfate Polysaccharide by Chromic Acid in Aqueous Perchlorate Solutions. Carbohydr. Polym. 2013, 92, 2321–2326.

(10) Ibrahim, S. M.; Althagafi, I.; Takagi, H. D.; Hassan, R. M. Kinetics and mechanism of oxidation of chondroitin-4-sulfate polysaccharide as a sulfated polysaccharide by hexacyanoferrate(III) in alkaline solutions with synthesis of novel coordination biopolymer chelating agent. J. Mol. Liq. 2017, 244, 353–359.

(11) Hassan, R. M. Algin polysaccharide polyelectrolyte ionotropic gels. XVIII. Oxidation of alginate polysaccharide by potassium permanganate in alkaline solutions: Kinetics of decomposition of intermediate complex. J. Polym. Sci. 1993, 31, 1147–1151.

(12) Khairou, K. S.; Hassan, R. M. Pectate polyelectrolyte ionotropic gels. Eur. Polym. J. 2000, 36, 2021–2030.

(13) Zaafarany, I. A.; AlArifi, A. A. S. N.; Fawzy, A.; Ahmed, G. A.; Ibrahim, S. A.; Hassan, R. M.; Takagi, H. D. Further evidence for detection of short-lived transient hypomanganate(V) and manganate-(VI) intermediates during oxidation of some sulfated polysaccharides by alkaline permanganate using conventional spectrophotometric techniques. Carbohydr. Res. 2010, 345, 1588–1593.

(14) Abdel-Hamid, M. I.; Khaifour, K. S.; Hassan, R. M. Kinetics and Mechanism of Permanganate Oxidation of Pectin in Acid Perchlorate Medium. Eur. Polym. J. 2003, 39, 381–387.

(15) Hassan, R. M.; Ahmed, S. M.; Fawzy, A.; Abdel-Kader, D. A.; Ikeda, Y.; Takagi, H. D. Acid-catalyzed oxidation of carboxymethyl cellulose polysaccharide by chromic acid in aqueous perchlorate solutions. A kinetics study. Catal. Commun. 2010, 11, 611–615.

(16) Hassan, R.; Dahy, A. R.; Ibrahim, S.; Zaafarany, I.; Fawzy, A. Oxidation of Some Macromolecules. Kinetics and Mechanism of Oxidation of Methyl Cellulose Polysaccharide by Permanganate Ion in Acid Perchlorate Solutions. Ind. Eng. Chem. Res. 2012, 51, 5424–5432.

(17) Hassan, R. M.; Alaraifi, A.; Fawzy, A.; Zaafarany, I. A.; Khaifour, K. S.; Ikeda, Y.; Takagi, H. D. Acid-catalyzed oxidation of some sulfated polysaccharides. Kinetics and mechanism of oxidation of kappa-carrageenan by cerium(IV) in aqueous perchlorate solutions. J. Mol. Catal. 2010, 332, 138–144.

(18) Abdel-Hamid, M. I.; Ahmed, G. A.-W.; Hassan, R. M. Kinetics and mechanism of oxidation of poly(vinyl alcohol) macromolecule by chromic acid in aqueous perchlorylic acid. Eur. Polym. J. 2001, 37, 2201–2206.

(19) Poulsen, I. A.; Garner, C. S. A Thermodynamic and Kinetic Study of Hexachloro and Aquopentachloro Complexes of Iridium(III) in Aqueous Solutions. J. Am. Chem. Soc. 1962, 84, 2032–2037.

(20) Martinez, M. R. Ph.D. Thesis, Dissertation U.C.L.A., Los Angeles, USA, 1958.

(21) Hassan, R. M. Kinetics of reaction of uranium(IV) and hexachlororidate(IV) in acid perchlorate solutions. Evidence for a binuclear intermediate. J. Chem. Soc., Dalton Trans. 1991, 3003–3008.

(22) Sykes, A. G.; Thorneley, R. N. F. Identification of Inner- and Outer-Sphere Paths in The Reaction of Chromium(II) with Hexachloroiridate(IV), and the Kinetics of the Decomposition of the Binuclear Intermediate. J. Chem. Soc. A 1970, 232–238.

(23) Hicks, K. W.; Hurless, M. A. An Investigation of the Vanadium(V)Oxyanomolybdate(VI) Reaction. Inorg. Chem. Acta 1983, 74, 229–234.

(24) Lawani, S. A.; Sutter, J. R. Kinetic Studies of Permanganate Oxidation Reactions. IV. Reaction with Bromide Ion. J. Phys. Chem. 1973, 77, 1547–1551.

(25) Hassan, R. M.; Wahdan, M. H.; Hassan, A. Kinetics and mechanism of sol-gel transformation on polyelectrolytes of nickel alginate ionotropic membranes. Eur. Polym. J. 1988, 24, 281–283.

(26) Pol, P. D.; Kathari, C. P.; Nandiwloor, S. T. Kinetics and Mechanism of Ruthenium(III)-Catalysed Oxidation of Tellurium(IV) by Alkaline Diperiodatonickelate(IV). Transition Met. Chem. 2003, 28, 209–216.

(27) Hassan, R. M.; Fawzy, A.; Ahmed, G. A.; Zaafarany, I. A.; Asghar, B. S.; Khaifour, K. S. Acid-catalyzed oxidation of some sulfated macromolecules. Kinetics and mechanism of oxidation of kappa-carrageenan polysaccharide by permanganate ion in acid perchlorate solutions. J. Mol. Catal. A: Chem. 2009, 309, 95–102.

(28) Singh, H. S.; Singh, V. P.; Pandey, D. P. Mechanism of Hexacyanoferrate(III) Oxidation of 1-Propanol and 2-Propanol in Aqueous Alkaline Medium. Monatsh. Chem. 1979, 110, 1455–1460.

(29) Laidler, K. Chemical kinetics; McGraw-Hill: New York, 1965.

(30) Upadhyay, S. K.; Agrawal, M. S. Kinetics of Oxidation of Os(VIII)-Catalyzed Oxidation of Some α-Amino Acids in the Presence of Excess of Ferricyanid. Indian J. Chem., Sect. A: Inorg., Phys., Theor. Anal. 1977, 15, 709–715; https://eurekamag.com/research/005/784/005784040.php.

(31) Morris, D. F. C.; Ritter, T. J. Oxidization of Hydrazine by Halogeno Complexes of Iridium (IV) in Acidic Perchloric Solutions. J. Chem. Soc., Dalton Trans. 1979, 216–219.