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Unusual kinetics of poly(ethylene glycol) oxidation with cerium(IV) ions in sulfuric acid medium and implications for copolymer synthesis†

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The cerium(IV)-alcohol couple in an acidic medium is an example of a redox system capable of initiating free radical polymerization. When the alcohol has a polymeric nature, the outcome of such a process is a block copolymer, a member of a class of compounds possessing many useful properties. The most common polymer with a terminal -OH group is poly(ethylene glycol) (PEG); however, the detailed mechanism of its reaction with cerium(IV) remains underexplored. In this paper, we report our findings for this reaction based on spectrophotometric measurements and kinetic modeling. We find that both the reaction order and the net rate constant for the oxidation process depend strongly on the nature of the acidic medium used. In order to account for the experimental observations, we postulate that protonation of PEG decreases its affinity for some of the cerium(IV)-sulfate complexes formed in the system.

Free radical polymerization in its many forms is the easiest-to-implement protocol for the synthesis of most of the industrially and economically important polymers. The radicals are produced in situ by methods that depend on the particular system under consideration, especially the monomer and solvent being used.

One initiation (radical production) procedure that is particularly well-suited to an aqueous phase is based on redox chemistry. Here, the free radicals are produced in an oxidation-reduction process involving a redox pair usually comprising a metal cation and a substance featuring active oxygen-hydrogen or oxygen-carbon bonds, which are cleaved in the course of the process. A pair consisting of cerium(IV) ions in conjunction with an organic reductant, such as an alcohol, a ketone, a carboxylic acid or an amine is one of such redox systems and is potentially attractive because of the possibility of using a pre-formed polymeric substance containing one of the functional groups likely to interact with the metal ions and to furnish radicals. As an example, it is well known that the cerium(IV)-poly(ethylene glycol) (PEG) pair can play the role of a source of polymerization-initiating radicals, thus providing access to PEG-based copolymers, many of which exhibit amphiphilic character if the secondary monomer is hydrophobic.

Recently, there has been a renewed interest in various systems featuring macromolecules with hydroxyl groups amenable to cerium(IV) oxidation, especially in relation to surface-initiated polymerizations and to polymer chain grafting to and from sugar backbones. Our recent study points to potential utility of the cerium(IV)-PEG pair in emulsion polymerization to give vesicle-forming amphiphilic copolymers under mild conditions, including no degassing. In order to exploit to the fullest the properties of this redox pair in polymerization initiation, it is useful to have a good understanding of the mechanistic nature of the processes responsible for radical production, so that the reaction conditions can be appropriately modeled and therefore tuned.

Even though the presence of radicals among reaction products is not in dispute, the general mechanism of oxidation of polymeric alcohols with cerium(IV) is not fully understood. Most work on oxidations of small-molecule alcohols in either nitric or perchloric acid medium postulates complexation of cerium(IV) with hy-
droxyl groups\textsuperscript{13–16}, but the exact nature of these interactions remains elusive. Additionally, marked differences have been reported between reactions carried out in the sulfuric acid medium and in non-sulfonated media such as nitric or perchloric acid. In particular, no evidence of direct alcohol-cerium(IV) complex formation was observed in sulfuric acid\textsuperscript{17,18}, which was thought to be related to the presence of various types of sulfatocerium complexes in the system\textsuperscript{19,20}.

In the present Communication, we are concerned with elucidating the nature and kinetic characteristics of poly(ethylene glycol) oxidation by cerium(IV) in sulfuric acid medium and also getting insight into the influence exerted by sulfate ion concentration on the course of the process. We show that for certain initial concentrations oxidation proceeds relatively slowly and with zero-order kinetics with respect to cerium(IV) ions. Based on the experimental results, we then develop a simple kinetic model of the initiation steps.

The reaction of poly(ethylene glycol) with cerium(IV) was investigated in some detail by Nagarajan et al.\textsuperscript{21}, who reported first order kinetics with respect to both reductant and oxidant as well as influence of ionic strength and PEG chain length in addition to that of the sulfate ion concentration. Our initial, exploratory experiments were therefore designed taking into account a simple picture of interactions between aqueous cerium(IV) and PEG analogous to the one encountered in the literature for the case of kinetic modeling of this system in a non-polymerization context\textsuperscript{22}. The reaction scheme outlined therein involves a two-step process whereby cerium(IV) is able to react with both the PEG molecules and the intermediate radicals:

\[
\begin{align*}
\text{PEG} + \text{Ce}^{4+} & \xrightarrow{k_1} \text{PEG}^* + \text{Ce}^{3+} \\
\text{PEG}^* + \text{Ce}^{4+} & \xrightarrow{k_2} \text{Ce}^{3+} + \text{oxidation products}
\end{align*}
\]

\[k_1 = 5.0 \times 10^{-3}, \quad k_2 = 1.0 \times 10^{3}\]

The radicals produced can be assumed to have their free electron associated with the terminal carbon atom, as presented in Figure 1.

![Fig. 1 Structure of a polymeric PEG-based radical formed during oxidation of PEG with cerium(IV).](image)

Because the concentration of the PEG radicals changes on a much shorter timescale than those of the other reagents, we applied the quasi-stationary state approximation (QSSA) to these radicals and were expecting to find (for the situation in which the PEG concentration is considerably larger than that of cerium(IV)) first-order kinetics with respect to Ce\textsuperscript{4+} according to the formula (the complete derivation is given in the ESI\textsuperscript{†}):

\[
\frac{d[\text{Ce}(IV)]}{dt} = -2k_1[\text{PEG}][\text{Ce}(IV)]
\]

To our surprise, the kinetic measurements revealed a behavior that was markedly different from the one expected on the basis of equation 1. Specifically, the concentration of cerium(IV) ions decayed \textit{linearly}, indicating a zeroth-order kinetics and therefore a process which is considerably more complex than a simple two-step oxidation (Figure 2a, see also the changes in the appearance of the spectrum of the reacting solution in this regime presented in Figure S1 in the ESI\textsuperscript{†}).

Zeroth-order kinetics in the oxidation of organic material by cerium(IV), albeit originating from keto-enol tautomerism, was previously reported for an aldehyde, acrolein, in accordance with a proposed mechanism involving complexes of Ce\textsuperscript{4+} with sulfate ions\textsuperscript{23}. Although long-chain aldehydes might be expected to be present among the final reaction products, 100-fold excess of PEG employed in our initial experiments ensured that only a small percentage of the chains underwent complete oxidation. In light of this, we decided to focus our efforts on the complex aqueous phase equilibria involving Ce\textsuperscript{4+} and sulfate ions such as had postulated by previous researchers\textsuperscript{19,20}.

In general, various sulfatocerium(IV) species involving different numbers of sulfate anions can be present in solution. To gain some insight into the degree to which these species play a role during oxidation of PEG, we conducted a series of experiments in which the PEG, cerium ion and proton concentrations were kept constant, but the ratio \(R = [\text{HSO}_4^-]/[\text{H}^+]\) was manipulated by replacing some of the sulfuric acid content of the mixture with nitric acid,\textsuperscript{24} while taking into account the detailed ionic composition of sulfuric acid solutions as outlined in a paper by Robertson and Dunford\textsuperscript{25}. This allowed us to investigate mixtures with different concentrations of the HSO\textsubscript{4}\textsuperscript{-} ion while avoiding any secondary effects due to changes in the proton concentration. The absorbance of the reaction mixture due to cerium(IV) was recorded as it changed in time and the values of the apparent rate constant \(k_{app}\), and the reaction order \(n\) were arrived at through integration of the rate equation:

\[\text{Reaction order} = n = \frac{\log(1 - \text{absorbance})}{\log(1 - \text{absorbance})}\]
\[ \frac{d[\text{Ce(IV)}]}{dt} = -2k_{\text{app}}[\text{PEG}][\text{Ce(IV)}]^n \] (2)

(where the factor 2 originates in the QSSA, see above) and fitting the resulting formula (equation 3) to the experimental absorbance readings (details are provided in the ESI\(^\dagger\)):

\[ [\text{Ce(IV)}]_t^{1-n} = 2k_{\text{app}}[\text{PEG}]_0(n - 1)t + [\text{Ce(IV)}]_0^{1-n} \] (3)

Since we ensured that the initial concentration of PEG was two orders of magnitude greater than that of cerium(IV), the actual value of \(k_{\text{app}}\) was obtained by dividing the fitted pseudo-first-order rate constant \(2k_{\text{app}}[\text{PEG}]_0\) by twice the starting PEG concentration.

Beginning with a solution containing 0.1 M sulfuric acid, for which \([\text{H}^+] = 0.130 \text{ M}\) and \(R = 0.537^{25}\), we observed a gradual increase in the reaction order while decreasing \(R\). For \(R\) below 0.1, i.e. when the concentration of \(\text{HSO}_4^-\) became relatively low, the order started approaching one (Figure 2b and 3). In accordance with earlier studies involving various alcohols, a similar strong dependence on the ratio \(R\) was observed for the apparent rate constant of the PEG oxidation\(^\dagger\)\(^\dagger\). It is worth pointing out that in order to reach very low values of \(R\) (\(R < 0.02\)), the proton concentration had to be increased to account for the presence of small amount of sulfate ions introduced with the cerium(IV) solutions; as a result, ionic strength increased which lead to reaction rates being lower than expected.\(^\dagger\)\(^\dagger\)\(^\dagger\). When the oxidation was conducted with stock \(\text{Ce}^{4+}\) solution prepared in nitric acid, the reaction was purely first-order and comparatively very fast (\(k = 3.925 \text{ M}^{-2} \text{s}^{-1}\)).

Both data sets point to considerable influence of the state of the equilibria involving sulfate and cerium(IV) ions on the characteristics of the reaction. After verifying numerically (\textit{a posteriori}) that the equilibria involving sulfate ions described in ref. 25 do not influence the rate at which the sulfatocerate(IV) equilibria are established (since \([\text{Ce}^{4+}]_0 \ll [\text{H}_2\text{SO}_4]_0\)), the remaining steps to be considered were\(^\dagger\)\(^\dagger\):

\begin{align*}
(A) \text{Ce}^{4+} + \text{HSO}_4^- & \rightleftharpoons \text{CeSO}_4^{2+} + \text{H}^+ \\
(B) \text{CeSO}_4^{2+} + \text{HSO}_4^- & \rightleftharpoons \text{Ce(SO}_4)_2 + \text{H}^+ \\
(C) \text{Ce(SO}_4)_2 + \text{HSO}_4^- & \rightleftharpoons \text{Ce(SO}_4)_3^2^- + \text{H}^+
\end{align*}

with the equilibrium constants equal to \(K_A = 3500\), \(K_B = 200\) and \(K_C = 20\), respectively. Using these relations, the composition of the reaction medium with respect to

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different cerium(IV) species can be unambiguously described as a function of the total cerium(IV) and the ratio \( R \), see ESI1. Clearly, the contributions of the different metal species to the total cerium(IV) content will be different depending on the concentration of bisulfate ions and therefore on \( R \).

The above suggests that equation 1 might be rewritten in a way that takes into account the presence of several different cerium(IV) species, each of which could potentially interact with poly(ethylene glycol) at a rate \( k_i \). This would, however, replace one first-order term with four, and the solution of the resulting differential equation would still not predict the linear decay observed in the experiments. To deal with this, we have singled out the Ce(SO\(_4\))\(_{2}^{2-}\) species as the one whose domination of the reaction mixture at high \( R \) is the most probable cause for the zero-order kinetics. If contributions of this species are represented by a linear term \( K \), one obtains the following alternative form of equation 1:

\[
-\frac{d[\text{Ce(IV)}]}{dr} = \sum_{i=1}^{3} 2k_i[\text{Ce(SO}_4)_2^{-}\,][\text{PEG}]_0 + 2K \tag{4}
\]

where the summation, to take into account each of the three equilibria, takes place over the three species Ce\(^{3+}\), Ce(SO\(_4\))\(_{2}^{2-}\) and Ce(SO\(_4\))\(_{3}^{-}\) as well as over the respective rate constants. The factor 2 is again the consequence of applying a QSSA to the PEG radicals.

In an attempt to elucidate the nature of the term \( K \), we conducted additional experiments at constant HSO\(_4\) concentration, while varying PEG and proton concentrations. As shown in Table 1, increasing proton concentration decreases \( K \), whereas increasing PEG concentration has the opposite effect. In order to account for these observations, we have considered a possible PEG protonation step taking place in the system and its corresponding equilibrium constant \( K_{prot} \), viz.

\[
\text{PEG} + \text{H}^+ \leftrightarrow \text{PEGH}^+, \tag{5}
\]

where only the unprotonated PEG reacts with Ce(SO\(_4\))\(_{2}^{2-}\). The latter step is considerably faster than the rate at which the above equilibrium is established. In other words, the rate of the slow step only depends on the PEG and proton concentrations. This led us to suggest a further modification of equation 4:

\[
-\frac{d[\text{Ce(IV)}]}{dr} = \left(\frac{1}{K_{prot}[\text{H}^+]}\right) \sum_{i=1}^{3} 2k_i[\text{Ce(SO}_4)_2^{-}\,][\text{PEG}]_0 + 2k_d[\text{PEG}]_0/K_{prot}[\text{H}^+] \tag{6}
\]

We then set out to incorporate the proposed relationship into a numerical model. This, however, required knowledge of all the rate constants pertaining to equation 5 for all of the cerium species. Since for \( R > 0.02 \) the concentration of the cerium(IV) species with no sulfate ions in its coordination sphere, Ce\(^{4+}\), was three or more orders of magnitude smaller than the total initial concentration of oxidized metal ions, we first decided to leave it out of the summation and then compared equations 5 and 2. This yielded

\[
\frac{1}{K_{prot}[\text{H}^+]} \sum_{i=2}^{3} 2k_i[\text{Ce(SO}_4)_2^{-}\,][\text{PEG}]_0 + 2k_d[\text{PEG}]_0/K_{prot}[\text{H}^+] = 2k_{app}[\text{PEG}]_0[\text{Ce(IV)}]^n \tag{6}
\]

or, after substituting the relevant expressions for the relative concentrations of the cerium species and some simple algebra

\[
\frac{k_2[\text{Ce(IV)}][K_A R]}{K_{prot} \sigma[H^+]} + \frac{k_3[\text{Ce(IV)}][K_B R^2]}{K_{prot} \sigma[H^+]} + \frac{k_4}{K_{prot}[H^+]} = k_{app}[\text{Ce(IV)}]^n \tag{7}
\]

where

\[
\sigma = 1 + K_A R + K_A K_B R^2 + K_A K_B K_C R^3 \tag{8}
\]

If our hypothesis is correct, these two forms should in principle approximate each other. Consequently, we...
the reaction medium; (iii) the reaction of the Ce(SO$_4$) complex takes part in the oxidation. The results were modeled using a reaction mechanism which assumes the protonation of PEG. The resulting PEG-PEG$^+$ equilibrium is established on a time scale comparable to that of the subsequent reaction with the cerium(IV) species, except for the reaction of Ce(SO$_4$)$_2^-$ with PEG, which is much faster and therefore is not the rate-limiting step. It follows that zeroth-order kinetics results when the sulfate concentration is relatively high, such as for example in the emulsion polymerization system reported by us previously, and contributes to the improved efficiency of the initiation, because even when the free radicals initially produced in the mixture are consumed by oxygen, the slower kinetics provides a radical source active for longer periods of time. Further studies are currently in progress to elucidate the behavior of the system in the presence of monomers and specifically during the later polymerization stages.

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### References