KINETICS OF OXIDATION OF MONOSACCHARIDES WITH CERIUM(IV)*

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ABSTRACT

The kinetics of the oxidation of D-galactose, D-glucose, D-mannose, D-fructose, L-sorbose, L-arabinose, D-ribose, and D-xylose with cerium(IV) in perchloric acid were studied. Two complexes were found to form in each case. The first complex forms in a pre-equilibrium reaction during mixing in the stopped-flow apparatus. Michaelis-Menten kinetics were observed for this oxidation. The values of the complex-formation and dissociation rate-constants were determined in 1.0M HClO₄. The dissociation partly involves the oxidation of the first complex and partly, the formation of a second, more-stable complex. This second complex is oxidized much more slowly than the first, and the values of the pseudo-first-order rate-constant were again determined in 1.0M HClO₄. The values proved to be almost constant in the range of 0.1M to 1.0M [Sugar], from which it was concluded that practically all of the Ce(IV) was complexed.

INTRODUCTION

In earlier work¹, we reported rate constants, and the effects of salt, temperature, $[H^+]$, and $[HSO_4^-]$ on the rate of oxidation of several mono- and poly-hydric alcohols and monsaccharides with vanadium(V). Kale and Nand² recently studied the rate of oxidation of D-ribose with Ce(IV) in aqueous HClO₄, using conventional techniques for kinetic experiments. Employing a specifically designed mixing-tube in the cell of a recording spectrophotometer, Pottenger and Johnson³ had much earlier reported considerably higher rates for the oxidation of D-glucose with Ce(IV) in aqueous HClO₄. In view of the discrepancy in the results, we decided to carry out additional kinetic studies related to the oxidation of monosaccharides with Ce(IV). It was also of interest to compare the oxidizing properties of the two one-electron oxidants, the transition metal V(V) and the lanthanide Ce(IV).

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We used both stopped-flow and conventional techniques for kinetic studies on three aldohexoses, two ketohexoses, and three aldopentoses. All eight monosaccharides were found to have two oxidation rates, one in the stopped-flow and the other in the classical, time range. All experiments were conducted in perchloric acid solutions in order to minimize the number of Ce(IV) species⁴.

EXPERIMENTAL

Ceric ammonium nitrate, D-galactose, D-glucose, D-mannose, D-fructose, Lsorbose, L-arabinose, D-ribose, and D-xylose were analytical-grade *purissimum* p. a. reagents from Fluka AG, and were used without purification.

In a specially designed, 300-mL, glass-stoppered flask⁵, equipped with a sidearm with a sintered-glass funnel, ceric ammonium nitrate (5 g) was dissolved in de-ionized water. Hydrous ceric oxide (ceric hydroxide) was precipitated by the addition of 5M ammonium hydroxide (25 mL), and the precipitate filtered off (suction), washed with five 25-mL portions of water, and dissolved in aqueous HClO₄, to yield a stock solution of perchloratoceric acid (ceric perchlorate). The solution was preserved in a refrigerator, and [Ce(IV)] was determined daily. The method, similar to that⁶ used earlier for [V(V)], involved the addition of Ce(IV) to aqueous FeSO₄, followed by the addition of aqueous KSCN and the determination of the absorbance at 450 nm with a Cary Model 16 spectrophotometer equipped with a Varian Model G-2510 chart-recorder. Aqueous FeCl₃ was used as a blank. The amount of Ce(IV) was noted to be linearly related to the absorbance if [HClO₄] was at least⁷ 0.1M.

Kinetic experiments. — (a) For the determination of the rate constants of the fast oxidation, ceric perchlorate in aqueous $HClO_4$ was mixed with a monosaccharide in aqueous $HClO_4$ at 25° in a Gibson-Durrum type of stopped-flow apparatus⁸. The solutions were in contact only with glass, stainless steel (type 304), and Teflon. The data acquired from the apparatus were first registered in an online, Datalab transient-recorder DL 902 (Data Laboratories, Mitcham, Surrey, England), visibilized with an oscilloscope, and analyzed with an on-line microcomputer programmed in BASIC to optimize the values of the pseudo-first-order rate-constant.

(b) For the determination of the rate constants of the slow oxidation, the conventional technique was employed, based on the analysis of unreacted [Ce(IV)] in samples withdrawn from the reaction mixture.

All the rate constants were determined under pseudo-first-order conditions with the monosaccharide in excess, and they refer to the oxidation of the first alcohol group. Initial rates were used in the calculations for D-ribose.

RESULTS

Two complexes were found to form in the oxidation of each monosaccharide.

TABLE 1

variation of the first- and second-order rate-constants with the concentration of mono-saccharides in 1.0m aqueous $HCIO_4$ at 25°, measured by the stopped-flow technique. [Ce(IV)] = 3.0 mm

Sugar	[Sugar] (range, м)	k _{obs} (range, s ⁻¹)	k _{obs} ∕[Sugar] (range, M ⁻¹ ⋅ s ⁻¹)	No. of data points
D-Galactose	0.012→0.080	1.1→1.8	92→23	6
D-Glucose	$0.020 \rightarrow 1.0$	$0.30 \rightarrow 0.73$	$15 \rightarrow 0.73$	7
D-Mannose	$0.020 \rightarrow 0.30$	$0.15 \rightarrow 0.32$	$7.7 \rightarrow 1.1$	6
D-Fructose	$0.012 \rightarrow 0.060$	1.9→2.6	160→43	6
L-Sorbose	$0.011 \rightarrow 0.072$	1.4→2.3	$130 \rightarrow 32$	6
L-Arabinose	$0.024 \rightarrow 0.080$	2.0 → 2.8	83 → 35	6
D-Ribose	$0.00060 \rightarrow 0.0050$	$0.51 \rightarrow 1.1$	$850 \rightarrow 220$	6
D-Xylose	0.012 → 0.20	0.36 → 2.2	30→11	6

The first complex formed fast in a pre-equilibrium reaction during the mixing time (~3 ms) of the Gibson-Durrum type stopped-flow apparatus. This complex dissociated rapidly. The rate constants in 1.0M HClO₄ at 25° measured at the wavelength³ of 425 nm by the stopped-flow technique, are given in Table I. Because the first-order rate-constant, $k_{obs} = -d\ln [Ce(IV)]/dt$, increased continuously while the second-order rate-constant, $k_{obs}/[Sugar]$, decreased, the results indicate neither a zero- nor a first-order rate with respect to carbohydrate. The relatively high values of $k_{obs}/[Rib]$ are noteworthy.

The values of k_{obs} in Fig. 1, and those for D-ribose in Fig. 2, are presented as a function of the concentration of the monosaccharides. The shape of the curves shows that the second-order rate in low carbohydrate concentration changes to a pseudo-first-order rate when the carbohydrate concentration increases so much that no more complex can form. Kinetically⁹, this kind of situation follows Eq. 1,



Fig. 1. Effect of substrate concentration on the pseudo-first-order rate-constant for the oxidation of monosaccharides with 3.0mM Ce(IV) in aqueous 1.0M HClO₄ at 25°.



Fig. 2. Effect of D-ribose concentration on the pseudo-first-order rate-constant for the oxidation with 3.0mM Ce(IV) in aqueous 1.0M HClO₄ at 25°.

$$\frac{1}{k_{\rm obs}} = \frac{1}{k_{\rm diss}} + \frac{1}{k_{\rm diss}K_{\rm ass}} \times \frac{1}{[{\rm Sugar}]}.$$
 (1)

in which K_{ass} is the formation constant of the complex, and k_{diss} , its dissociation rate-constant. Employing Eq. 1, Eqs. 2-9 were obtained:

$$\frac{1}{k_{\rm obs}} = (5.14 \pm 0.45) \times 10^{-3} \times \frac{1}{[\text{Gal}]} + (4.98 \pm 0.20) \times 10^{-1}$$
(2)

$$\frac{1}{k_{\rm obs}} = (4.14 \pm 0.33) \times 10^{-2} \times \frac{1}{[\rm Glc]} + (1.39 \pm 0.08)$$
(3)

$$\frac{1}{k_{\rm obs}} = (7.54 \pm 0.36) \times 10^{-2} \times \frac{1}{[{\rm Man}]} + (2.88 \pm 0.10)$$
(4)

$$\frac{1}{k_{\rm obs}} = (2.35 \pm 0.16) \times 10^{-3} \times \frac{1}{[\rm Fru]} + (3.35 \pm 0.08) \times 10^{-1}$$
(5)

$$\frac{1}{k_{\rm obs}} = (3.34 \pm 0.20) \times 10^{-3} \times \frac{1}{[\text{Sor}]} + (3.94 \pm 0.10) \times 10^{-1}$$
(6)

$$\frac{1}{k_{\rm obs}} = (4.64 \pm 0.24) \times 10^{-3} \times \frac{1}{[\rm Ara]} + (3.07 \pm 0.07) \times 10^{-1}$$
(7)

$$\frac{1}{k_{\rm obs}} = (7.41 \pm 0.30) \times 10^{-4} \times \frac{1}{[\rm Rib]} + (7.38 \pm 0.27) \times 10^{-1}$$
(8)

$$\frac{1}{k_{\rm obs}} = (9.86 \pm 0.86) \times 10^{-3} \times \frac{1}{[\rm Xyl]} + (4.17 \pm 0.17) \times 10^{-1}$$
(9)

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Sugar	k _{diss} (s ⁻¹)	K _{ass} (M ⁻¹)	Oxidation ^a (mol %)	$\frac{\mathbf{k}_{ox}(I)}{(s^{-1})}$	k _{stab} (s ⁻¹)
D-Galactose	2.0	100	8.5	0.2	1.8
D-Glucose	0.72	34	8.5	0.06	0.64
D-Mannose	0.35	38	8.9	0.03	0.32
D-Fructose	3.0	140	10.7	0.3	2.7
L-Sorbose	2.5	120	10.3	0.3	2.2
L-Arabinose	3.3	67	9.8	0.4	2.9
D-Ribose	1.4	1000	9.2	0.1	1.3
D-Xylose	2.4	42	11.5	0.3	2.1

COMPLEX-FORMATION CONSTANT AND DISSOCIATION, OXIDATION, AND STABILIZATION RATE-CONSTANTS OF MONOSACCHARIDES IN 1.0M AQUEOUS $HClO_4$ at 25°. [Ce(IV)] = 3.0mM

 $e[Ce(IV)] = 6.8mM; [Sugar] = 1.0M; [HClO_4] = 1.0M; reaction time, 1 min.$

The values of k_{diss} and K_{ass} evaluated from Eqs. 2–9 are given in Table II. The dissociation comprises partly the oxidation and partly the formation of a second, more-stable complex. This second route of dissociation and its relative contribution were found by analyzing the [Ce(IV)] before and after the fast reaction and by assuming that the oxidation consumes two moles of Ce(IV) per mole of carbo-hydrate. These analyses allow estimation of the rate constant of the two reaction paths, $k_{ox}(1)$ for the fast oxidation and k_{stab} for the formation of the more-stable complex. Our value of 0.72 s⁻¹ at 25° for k_{diss} of D-glucose is slightly higher than, but of the same magnitude as, the value of 0.23 s⁻¹ at 20° in M HClO₄ measured by a modified, conventional mixing-technique by Pottenger and Johnson³. Our value of 34 M⁻¹ at 25° for K_{ass} is in excellent agreement with their value of 39.4 M⁻¹ at 20°. The high value of K_{ass} for D-ribose is noteworthy.

TABLE III

Sugar	$k_{ox}(2)$ (range, s ⁻¹)	$\begin{array}{c} \mathbf{k}_{ox}[V(V)]^{a}\\ (M^{-1} \cdot s^{-1}) \end{array}$	Reference
D-Galactose	$(7.7 \rightarrow 8.8) \times 10^{-5}$	6.3 × 10 ⁻⁴	10
D-Glucose	$(6.4 \rightarrow 7.8) \times 10^{-5}$	2.9×10^{-4}	11
D-Mannose	$(2.4 \leftarrow 3.7) \times 10^{-5}$	2.7×10^{-4}	11
D-Fructose	$(1.8 \rightarrow 4.5) \times 10^{-4}$	7.6×10^{-3}	12
L-Sorbose	$(5.1 \rightarrow 8.9) \times 10^{-4}$	1.1×10^{-2}	10
L-Arabinose	$(1.7 \rightarrow 2.3) \times 10^{-4}$	1.7×10^{-3}	13
D-Ribose	$(5.5 \leftarrow 6.6) \times 10^{-5}$	1.9×10^{-3}	13
D-Xylose	$(1.8 \rightarrow 2.3) \times 10^{-4}$	2.3×10^{-3}	13

variation of the first-order rate-constant with the concentration of monosaccharide in 1.0m aqueous $HClO_4$ at 50°, measured by the conventional technique. [Ce(IV)] = 14mm; range of [sugar] = 0.1-1.0m

 $a[\text{HClO}_4] = 1.5\text{M}.$

TABLE IV

t (°)	$k_{ox}(2) (s^{-1})$	r		
25	$(8.39 \pm 0.26) \times 10^{-6}$	0.9971		
35	$(2.62 \pm 0.07) \times 10^{-5}$	0.9980		
45	$(8.14 \pm 0.16) \times 10^{-5}$	0.9986		
50	$(1.38 \pm 0.02) \times 10^{-4}$	0.9994		

EFFECT OF TEMPERATURE ON THE RATE CONSTANT OF THE SLOW OXIDATION OF D-GLUCOSE WITH Ce(IV). $[Ce(IV)] = 14.1 \text{mm}; [HClO_4] = 2.000 \text{m}, [GLUCOSE] = 0.703 \text{m} \text{ at } 25^{\circ}$

The second complex is oxidized much more slowly than the first complex. The values of the pseudo-first-order rate constant $k_{ox}(2)$ in Table III were determined in the concentration range 0.1 to 1.0M carbohydrate in 1.0M HClO₄ at 50°. The oxidation is not first order with respect to the carbohydrate. The values of $k_{ox}(2)$ increase only slightly within the 10-fold concentration range. Kinetically, this shows that practically all of the Ce(IV) is complexed. For D-mannose and D-ribose, the rate constant was found to decrease slightly with increasing [Sugar].

For comparison, the second-order rate-constants $k_{ox}[V(V)]$ for oxidation of the same monosaccharides with V(V) are included in Table III. These values were calculated from experimental data obtained under identical experimental conditions, *i.e.*, 1.5M aqueous HClO₄ at 50°.

The effect of temperature on the rate of the slow oxidation of D-glucose is given in Table IV. The values of 87.3 ± 0.8 kJ·mol⁻¹ for the enthalpy of activation and -49.6 ± 2.5 J·K⁻¹.mol⁻¹ for the entropy of activation were evaluated from the values of the first-order rate-constant k_{obs} . The values 103.7 kJ·mol⁻¹ and 7.3 J·K⁻¹·mol⁻¹ have been reported¹¹ for the oxidation with V(V). The lower value for the entropy of Ce(IV) oxidation may indicate a stronger, or else a more-ordered, complex-formation.

The rate constants for D-glucose at 50° (in Tables III and IV) show that $k_{ox}(2)$ increases with increasing [HClO₄]. Qualitatively, we found that it also increases with increasing [NaClO₄]. Because of precipitation problems, salt effects were not studied more.

DISCUSSION

The monosaccharides studied in this work can exist in solution in pyranose, furanose, and open-chain forms. It can be estimated^{14,15} that, in 2M aqueous HClO₄, the rate of mutarotation of D-glucose is ~33,000 times the rate of oxidation with V(V). Because the rate constant¹¹ for the latter reaction in 0.5M HClO₄ is only $6.9 \times 10^{-5} \,\mathrm{M^{-1} \cdot s^{-1}}$ at 25° and $2.0 \times 10^{-3} \,\mathrm{M^{-1} \cdot s^{-1}}$ at 50°, it is highly probable that, in all of these experiments, mutarotational equilibrium was attained before the oxidation.

Kinetically, monosaccharides can be considered to be polyols in which the reactivities of the alcohol groups are increased by the carbonyl group. Michaelis-Menten kinetics, Eq. 1, have been observed for the oxidation of cyclic alcohols⁹ and diols¹⁶ with aqueous Ce(IV) in acid perchlorate solution. At 15°, the rate constants k_{diss} for the dissociation of the complex are, for example, $2.2 \times 10^{-3} \text{ s}^{-1}$ for cyclohexanol⁹, $5.8 \times 10^{-4} \text{ s}^{-1}$ for 1,3-propanediol¹⁶ and $9.9 \times 10^{-4} \text{ s}^{-1}$ for 1,6-hexanediol¹⁶. A comparison of the k_{diss} values in Table II with these values shows the great importance of the carbonyl group for the reaction rate and site.

The products obtained from the oxidation of D-glucose³ with Ce(IV) in 1.0M $HClO_4$ at 20° are D-arabinose and formic acid. One mole of D-arabinose is formed for every two moles of Ce(IV) reduced. These products are the same as in the oxidation¹¹ of D-glucose with V(V). Owing to the reactivity of the carbonyl group, it is likely that the products are the same in Ce(IV) oxidations as in V(V) oxidations. Aldohexoses yield aldopentoses and formic acid, and ketohexoses yield dicarbonyl compounds as the first oxidation products.

In the case of oxidation with V(V), the rate constant for hydroxyacetone¹⁷ is about 10⁴ times that for glycol¹, but the rate constants for D-glucose and Dmannose¹¹ are only about 15 times higher than that for glycol. Because, on a structural basis, sugars can be expected to react much faster, we earlier concluded¹¹ that at least a major part, if not all, of the oxidations with V(V) proceed through the open-chain forms of the sugars, and that the low apparent rates arise from the fast pre-equilibrium involving the open-chain forms.

For aldohexoses, the relative amount of the open-chain forms decreases in the order D-galactose > D-mannose > D-glucose, and, for aldopentoses, in the order D-ribose \gg L-arabinose > D-xylose¹⁸. Interestingly, the values of K_{ass} in Table II decrease in the same order. It may be of general importance that, in both series, the two properties¹⁸ mentioned decrease in the order described in Scheme 1.

To the best of our knowledge, the existence of two oxidation rates for monosaccharides has not been reported earlier. The present data do not allow us to describe the different reactions in detail. However, it is logical to suppose that the fast-forming complex is between Ce(IV) species and the open-chain form of the sugars. This complex then dissociates *via* two routes: it can either be oxidized, $k_{ox}(1)$, or be stabilized, k_{stab} , by forming a second complex. One possibility, but not



Scheme 1.

the only one, is that the second complex is formed between Ce(IV) species and a ring form of the sugars.

The value of K_{ass} is considerably higher for D-ribose than for the other sugars. D-Ribose differs from the other sugars in that, in aqueous solution, it exists to the extent of ~8.5% in the open-chain form¹⁸, as compared with 0.22% for L-arabinose and 0.022% for D-glucose, for example.

Ce(IV) is known to exist in aqueous $HClO_4$ in a variety of forms, such as aquated Ce⁴⁺, CeOH³⁺, and various dimeric species^{7,19}. Based on the strong affinity of Ce(IV) for water and on X-ray diffraction studies²⁰, the species of Cc(H₂O)⁴⁺_n has been recommended². Because the present reaction is acid-catalyzed, at least two reactive Ce(IV) species are likely to exist. Like Prakash *et al.*¹ⁿ. we give priority to Ce⁴⁺(aq) and CeOH³⁺(aq).

If all of the foregoing observations are taken into consideration, as well as the different characters of the complexes, the following, simplified mechanism can be proposed to explain the experimental data for the faster and slower oxidations.

$$Ce^{4+}(aq) + H_2O \rightleftharpoons CeOH^{3+}(aq) + H_3O^+$$
 (fast) (10)

Sugar + Ce⁴⁺(aq)
$$\rightleftharpoons$$
 {Complex}⁴⁺ (fast) (11)

Sugar + CeOH³⁺(aq)
$$\rightleftharpoons$$
 {Complex}³⁺₂ (fast) (12)

$$\{\text{Complex}\}_{1}^{4+} + \text{H}_{2}\text{O} \rightarrow \{\text{Radical}\} + \text{H}_{3}\text{O}^{+} + \text{Ce(III)} \quad (\text{slow}) \quad (13)$$

$${\text{Complex}}_{2}^{3+} \rightarrow {\text{Radical}} + {\text{H}}_{2}{\text{O}} + {\text{Ce(III)}}$$
 (slow) (14)

These rate-determining reactions are followed by the product-forming reaction, e.g.,

{Radical} + Ce(IV)
$$\rightarrow$$
 {Product} + H₃O⁺ + Ce(III), (fast) (15)

where Ce(IV) and Ce(III) are the preponderant Ce species under the experimental conditions.

This mechanism differs from that in which the substrate is oxidized directly with Ce(IV) and which follows simple second-order kinetics. Michaelis–Menten kinetics seem to be general for the oxidation of hydroxylic substrates with Ce(IV) in aqueous HClO₄, as has now been documented for mono- and di-hydric alcohols^{9,16}, 2-ketocarboxylic acids²⁰, monosaccharides³ (this work), cellulose³, and 2-hydroxycarboxylic acids²¹.

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