Kinetics and mechanism of the reduction of chromium(VI) by D-ribose

Joaquin F. Perez-Benito,* Conchita Arias, Rosa M. Rodriguez and Marta Ros

Departamento de Quimica Fisica, Facultad de Quimica, Universidad de Barcelona,
Marti i Franques, 1, 08028 Barcelona, Spain

The reaction between $\mathrm{Cr^{VI}}$ and D-ribose in aqueous perchloric acid, studied by application of the initial-rates method, is first order in both oxidant and reductant, whereas the apparent order of $\mathrm{H^+}$ is a little lower than 2. At $[\mathrm{HClO_4}] = 0.366$ M and 25.0 °C the reaction with monomeric $\mathrm{Cr^{VI}}$ is 12.7 times faster than that with dimeric $\mathrm{Cr^{VI}}$. Under the same acidity conditions, the apparent activation parameters are $\Delta H^{0,\neq} = 40.1 \pm 0.6$ kJ mol^{-1} and $\Delta S^{0,\neq} = -155 \pm 2$ J K^{-1} mol^{-1}. At low $[\mathrm{Cr^{VI}}]_0$ the reaction is catalyzed by $\mathrm{Mn^{II}}$. The catalytic reaction pathway is zero order in $\mathrm{Cr^{IV}}$ and first order in both D-ribose and $\mathrm{H^+}$. At high $[\mathrm{Cr^{VI}}]_0$ the reaction is inhibited by $\mathrm{Mn^{II}}$ because it traps the intermediate $\mathrm{Cr^{VI}}$. In the presence of $\mathrm{Mn^{II}}$ the formation of $\mathrm{Mn^{III}}$ as an intermediate has been detected. Mechanisms for the uncatalyzed and catalyzed reaction pathways are proposed.

Chromium(VI) is a potent toxin and carcinogen[1,2] whose ability to produce DNA lesions and mutations has been established.[3,4] This accused mutagenicity might be rather specific to $\mathrm{Cr^{VI}}$, since the other members of the same periodic table group (molybdenum and tungsten) have failed to show a similar mutagenicity in some bacterial experiments.[5] Given that $\mathrm{Cr^{VI}}$ cannot react with isolated DNA *in vitro* under physiological conditions,[6,7] it seems reasonable to assume that one or several of the intermediates[8–10] or reaction products[11,12] formed in its intracellular metabolism must be directly responsible for the mutagenic properties. Hence, in the last decade the interest of many reseachers working on $\mathrm{Cr^{VI}}$ has oscillated from the traditional field of reactions with nonbiological reductants[13,14] to that of reactions with biologically relevant molecules. Thus, the reactions of $\mathrm{Cr^{VI}}$ with L-ascorbic acid,[15,16] with sulfhydryl-containing amino acids[17,18] and peptides[18–20] and with hydrogen peroxide[21,22] have received some attention lately.

The reactions of $\mathrm{Cr^{VI}}$ with carbohydrates might also be of some biological interest.[23–26] The $\mathrm{Cr^{III}}$ complexes formed as products of these reactions have been reported to cause DNA lesions.[27,28] In particular, our attention was called to the reaction between $\mathrm{Cr^{VI}}$ and D-ribose, in view of the fact that ribonucleotides (but not deoxyribonucleotides) reduce $\mathrm{Cr^{VI}}$ to $\mathrm{Cr^{V}}$,[29] an intermediate believed to be involved in the mechanism of chromium-induced carcinogenesis.[30–32] The results of the present work indicate that at physiological pH the $\mathrm{Cr^{VI}}$ plus D-ribose reaction is probably too slow to play anything but a minor role in the intracellular metabolization of $\mathrm{Cr^{VI}}$, although its contribution might be important under more acidic conditions, such as in stomach cells or tissues suffering from acute inflammation.[33] A notable feature of this kinetic system is the dual effect caused by $\mathrm{Mn^{II}}$ on the reaction rate: a catalyst at low concentrations of $\mathrm{Cr^{VI}}$ and an inhibitor at high concentrations.

Experimental

Materials and methods

The solvent used was water previously subject to deionization, distillation and further purification by circulation through a Millipore system. The other chemicals were employed as purchased from Merck [potassium dichromate, perchloric acid, sodium perchlorate, manganese(II) sulfate and sodium pyrophosphate] or Aldrich (D-ribose). The D-ribose stock solution was kept in a refrigerator and renewed daily. To measure the absorbances three different UV/VIS spectrophotometers (Shimadzu UV-120-02 and UV-160A, and Varian Cary 219) and thermostatted 1 cm glass cuvettes were used.

Stoichiometric experiments

To determine the reductant : oxidant stoichiometric ratio, a series of reacting mixtures with a fixed concentration of oxidant and different concentrations of reductant in the presence of perchloric acid were kept in the dark and at room temperature in well-stoppered volumetric flasks. Periodically, spectrophotometric readings were made to check the progress of the reaction. After 233 days, in those flasks still containing $\mathrm{Cr^{VI}}$, the reaction was already extremely slow and the absorbances of the solutions at 352 nm were measured.

Kinetic experiments

In most cases the oxidant concentration was low enough ($[\mathrm{Cr^{VI}}]_0 = 1.28 \times 10^{-4}$–$1.54 \times 10^{-3}$ M) for the progress of the reaction to be monitored by means of the decay of the absorbance at 352 nm, corresponding to the peak of $\mathrm{HCrO_4}^-$ in the visible region of the spectrum.[34] However, when the oxidant concentration was higher ($[\mathrm{Cr^{VI}}]_0 = 2.05 \times 10^{-3}$–$2.56 \times 10^{-2}$ M) we monitored the decay of the absorbance at 486 nm, corresponding to the foot of the visible band of $\mathrm{HCrO_4}^-$. The latter wavelength was selected because the molar absorption coefficient of $\mathrm{Cr^{VI}}$ was low enough to allow the measurement of the absorbance when the oxidant was very concentrated, yet the $\varepsilon(\mathrm{Cr^{VI}})/\varepsilon(\mathrm{Cr^{III}})$ ratio was high enough to attain a good variation of the solution absorbance ($A_0 - A_\infty$) during the kinetic runs.

Usually, the reactions were followed at the desired, constant temperature until 25% $\mathrm{Cr^{VI}} \rightarrow \mathrm{Cr^{III}}$ conversion. The solutions were then kept at room temperature and the A_∞ values were measured when the reactions were over (2–4 days later). All the kinetic data given in this article represent the averages of duplicate runs (typical standard deviation $\pm 3\%$, total number of experiments around 900) and they were obtained by application of the initial-rates method, using a nonlinear least-squares fit of the absorbance *vs.* time values to eqn. (1) in all cases except when pyrophosphate was present, and to eqn. (2) in the latter case.

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* Fax: +34 93 4021231; e-mail: j.perez@dept.qf.ub.es

$$\ln(A - A_\infty) = a_0 + a_1 t + a_2 t; \quad v_0 = -a_1[\mathrm{Cr^{VI}}]_0 \qquad (1)$$

$$(A - A_\infty)^m = a_3 + a_4 t; \quad v_0 = -\frac{a_4}{m a_3}[\mathrm{Cr^{VI}}]_0 \qquad (2)$$

Results and Discussion

Stoichiometry

The final oxidation state of the inorganic reactant was $\mathrm{Cr^{III}}$, whose spectrum was easily recognized by means of its two small d-d bands at around 410 and 580 nm, characteristic of $\mathrm{Cr^{III}}$ complexes.[22,35] With respect to the stoichiometric experiments (Fig. 1), the plot of the absorbance (352 nm) *vs.* the reductant : oxidant ratio was a curve with a first stretch almost linear. By tracing the tangent to the curve at $[\text{D-ribose}]_0/[\mathrm{Cr^{VI}}]_0 = 0$ it was concluded that the reductant : oxidant stoichiometric ratio was 0.192 ± 0.006. This means that, under conditions of strong excess of oxidant with respect to reductant, each molecule of D-ribose was able to transfer 15.6 ± 0.5 electrons to $\mathrm{Cr^{VI}}$. Considering that the correct value must be a whole, even figure, since the formation of organic free radicals as stable reaction products can be safely excluded, we can conclude that the actual number of electrons transferred is 16. Such a high value indicates that, under these conditions, there must occur oxidative cleavage of some C—C sugar bonds. This is consistent with the report that carbon dioxide is one of the reaction products from the oxidation of carbohydrates by $\mathrm{Cr^{VI}}$,[36] although its formation cannot be observed when the excess of saccharide with respect to oxidant is too large.[37,38]

Kinetic data

The reaction was autocatalytic and, under some experimental conditions, bell-shaped rate *vs.* $[\mathrm{Cr^{VI}}]$ plots were obtained. However, when $[\mathrm{Cr^{VI}}]_0$ was decreased while keeping $[\text{D-ribose}]_0$ constant, the plots approached closely the situation expected for pseudo first-order kinetics (Fig. 2).

The initial rate was directly proportional to the initial oxidant concentration in the range $[\mathrm{Cr^{VI}}]_0 = 0\text{–}1.28 \times 10^{-3}$ M (Fig. 3). This allowed the determination of a first-order rate constant as $k_1 = v_0/[\mathrm{Cr^{VI}}]_0$. The latter was also directly proportional to $[\text{D-ribose}]_0$ (Fig. 3, inset), but the second-order rate constant, calculated as $k_2 = k_1/[\text{D-ribose}]_0$, decreased when $[\mathrm{Cr^{VI}}]_0$ increased from 2.05×10^{-3} to 2.56×10^{-2} M (Fig. 4). This effect was caused by the dimerization of the

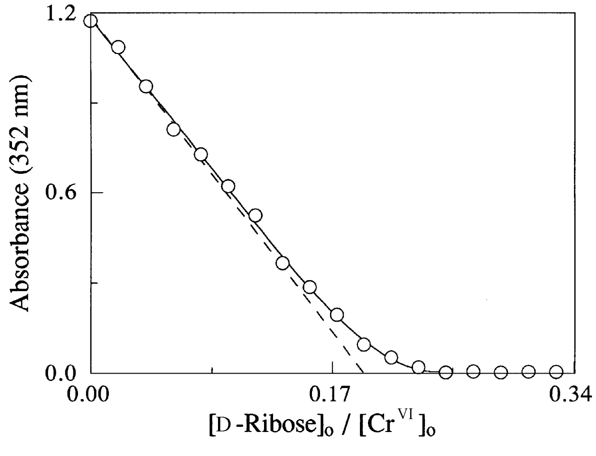

Fig. 1 Effect of the reductant : oxidant initial ratio on the absorbance at 352 nm at the end of the reaction between $\mathrm{Cr^{VI}}$ (7.68×10^{-4} M) and D-ribose (variable) in the presence of $\mathrm{HClO_4}$ (0.366 M) at room temperature. The dashed line is the tangent to the experimental curve at $[\text{D-ribose}]_0/[\mathrm{Cr^{VI}}]_0 = 0$

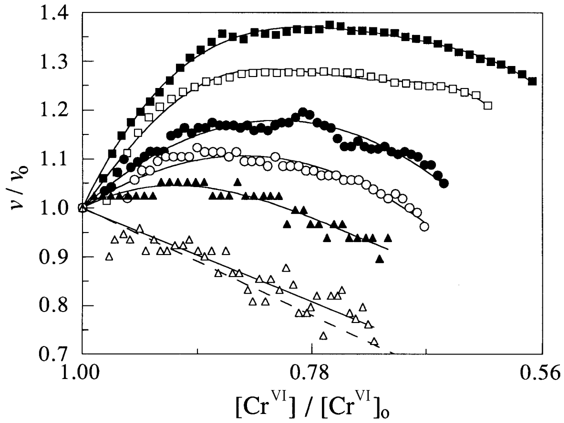

Fig. 2 Effect of the oxidant initial concentration on the v/v_0 *vs.* $[\mathrm{Cr^{VI}}]/[\mathrm{Cr^{VI}}]_0$ plot during the course of the reaction between $\mathrm{Cr^{VI}}$ and D-ribose (2.77×10^{-2} M) in the presence of $\mathrm{HClO_4}$ (0.366 M) at 25.0 °C. (△) $[\mathrm{Cr^{VI}}]_0 = 1.28 \times 10^{-4}$, (▲) 5.12×10^{-4}, (○) 3.07×10^{-3}, (●) 6.15×10^{-3}, (□) 1.23×10^{-2} and (■) 2.56×10^{-2} M. The dashed line represents the behavior expected for pseudo first-order kinetics

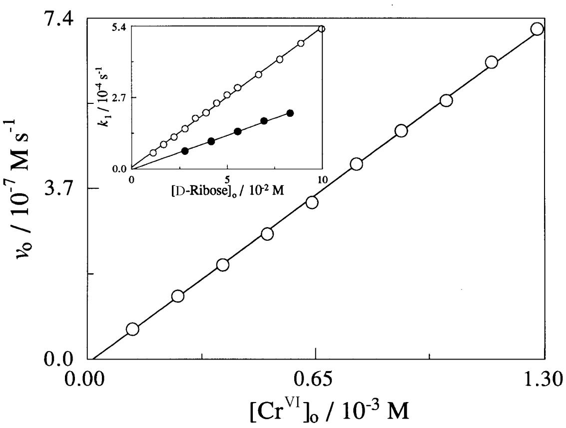

Fig. 3 Dependence of the initial rate on the initial concentration of oxidant for its reaction with D-ribose (9.99×10^{-2} M) in the presence of $\mathrm{HClO_4}$ (0.366 M) at 25.0 °C. Inset: Dependence of the first-order rate constant on the initial concentration of reductant at (○) $[\mathrm{Cr^{VI}}]_0 = 5.12 \times 10^{-4}$ and (●) 2.56×10^{-2} M, $[\mathrm{HClO_4}] = 0.366$ M and 25.0 °C

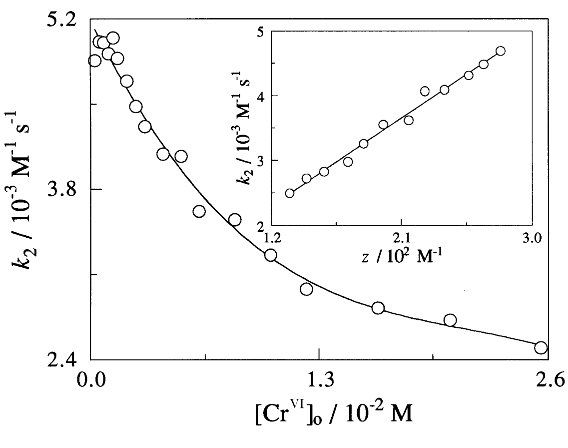

Fig. 4 Dependence of the second-order rate constant on the initial concentration of oxidant for its reaction with D-ribose (2.77×10^{-2} M) in the presence of $\mathrm{HClO_4}$ (0.366 M) at 25.0 °C. Inset: Linearization in the range $[\mathrm{Cr^{VI}}]_0 = (0.20\text{–}2.56) \times 10^{-2}$ M according to eqn. (5) with $z = (\sqrt{1 + 8K_d[\mathrm{Cr^{VI}}]_0} - 1)/[\mathrm{Cr^{VI}}]_0$

oxidant:

$$2\mathrm{HCrO_4^-} \xrightleftharpoons{K_\mathrm{d}} \mathrm{Cr_2O_7^{2-}} + \mathrm{H_2O} \tag{3}$$

We can write the initial rate as the global result of two parallel reaction pathways, one with a rate constant k_MR corresponding to the reaction of D-ribose with the monomeric form of the oxidant, and the other with a rate constant k_DR corresponding to the reaction with the dimeric form:

$$\begin{aligned} v_0 = -\left(\frac{\mathrm{d}[\mathrm{Cr^{VI}}]}{\mathrm{d}t}\right)_{t=0} &= (k_\mathrm{MR}[\mathrm{HCrO_4^-}]_0 \\ &\quad + 2k_\mathrm{DR}[\mathrm{Cr_2O_7^{2-}}]_0)[\text{D-ribose}]_0 \\ &= k_2[\mathrm{Cr^{VI}}]_0[\text{D-ribose}]_0 \end{aligned} \tag{4}$$

where $[\mathrm{Cr^{VI}}]_0 = [\mathrm{HCrO_4^-}]_0 + 2[\mathrm{Cr_2O_7^{2-}}]_0$. Then, the second-order rate constant should change with the total initial concentration of $\mathrm{Cr^{VI}}$ according to the law:

$$k_2 = k_\mathrm{DR} + \frac{(k_\mathrm{MR} - k_\mathrm{DR})(\sqrt{1 + 8K_\mathrm{d}[\mathrm{Cr^{VI}}]_0} - 1)}{4K_\mathrm{d}[\mathrm{Cr^{VI}}]_0} \tag{5}$$

which agrees well with the experimental data (Fig. 4, inset). By nonlinear least-squares we obtained $k_\mathrm{MR} = (5.2 \pm 0.1) \times 10^{-3}$ $\mathrm{M^{-1}\,s^{-1}}$, $k_\mathrm{DR} = (4.1 \pm 0.5) \times 10^{-4}$ $\mathrm{M^{-1}\,s^{-1}}$ and $K_\mathrm{d} = 86 \pm 7$ $\mathrm{M^{-1}}$ (at 0.37 M ionic strength and 25.0 °C), the latter value being consistent with those reported in the literature[39–41] for the dimerization equilibrium constant at 25.0 °C (35.5 $\mathrm{M^{-1}}$ at zero ionic strength, and 98 $\mathrm{M^{-1}}$ at 1.00 M ionic strength). Thus, the rate constant for the monomer is 12.7 times higher than that corresponding to the dimer (both expressed per chromium atom).

The second-order rate constant decreased as the ionic strength was raised at constant acidity (Table 1), whereas it increased when the acidity was raised at constant ionic strength. The apparent kinetic order of hydrogen ion was slightly lower than 2, and it seemed to depend only little on the experimental conditions: 1.84 ± 0.05 at 0.366 M ionic strength (Table 2) and 1.91 ± 0.01 at 0.731 M ionic strength (Fig. 5). This suggests the following rate law:

$$v_0 = \frac{k_\mathrm{obs}[\mathrm{H^+}]^2}{1 + K_\mathrm{p}[\mathrm{H^+}]}[\mathrm{Cr^{VI}}]_0[\text{D-ribose}]_0 \tag{6}$$

where K_p is the equilibrium constant corresponding to the protonation of hydrogen chromate ion:

$$\mathrm{HCrO_4^-} + \mathrm{H^+} \xrightleftharpoons{K_\mathrm{p}} \mathrm{H_2CrO_4} \tag{7}$$

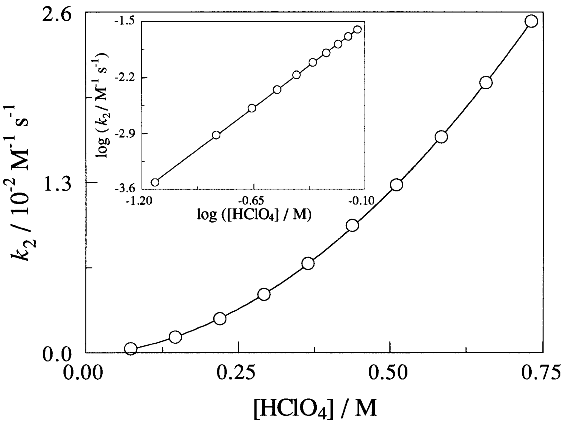

Fig. 5 Dependence of the second-order rate constant on the concentration of $\mathrm{HClO_4}$ for the reaction of $\mathrm{Cr^{VI}}$ (5.12×10^{-4} M) with D-ribose (2.77×10^{-2} M) at constant ionic strength (0.731 M, $\mathrm{NaClO_4}$) at 30.0 °C. Inset: Double-logarithmic plot (slope = 1.91 ± 0.01)

Effectively, according to eqn. (6), the apparent kinetic order of hydrogen ion is expected to be in the range: 1 < order < 2, and, given that K_p decreases as the ionic strength increases, taking the value of 0.83 $\mathrm{M^{-1}}$ at 1 M ionic strength and 25.0 °C,[39] that order is expected to approach its superior limit of 2 at higher ionic strengths. The acid–base properties of dimeric $\mathrm{Cr^{VI}}$ have not been taken into consideration in view of the fact that, under the conditions of low $[\mathrm{Cr^{VI}}]_0$ for which eqn. (6) has been obtained, the predominant reaction is that of monomeric $\mathrm{Cr^{VI}}$ with D-ribose. A quadratic dependence on $[\mathrm{H^+}]$ was also observed for a related reaction, the oxidation of D-gluconic acid by $\mathrm{Cr^{VI}}$ in aqueous perchloric acid.[42]

The reaction followed both the Arrhenius (Fig. 6) and Eyring (Fig. 6, inset) equations, leading to the apparent (associated with k_2) activation parameters: $E_\mathrm{a} = 42.7 \pm 0.5$ kJ $\mathrm{mol^{-1}}$, $\Delta H^{0,\neq} = 40.1 \pm 0.6$ kJ $\mathrm{mol^{-1}}$ and $\Delta S^{0,\neq} = -155 \pm 2$

Table 1 Dependence of the second-order rate constant on the concentration of sodium perchlorate[a]

$[\mathrm{NaClO_4}]$/M	$k_2/10^{-4}$ $\mathrm{M^{-1}\,s^{-1}}$
0.000	3.79 ± 0.17
0.028	3.36 ± 0.24
0.056	3.68 ± 0.16
0.084	3.71 ± 0.16
0.112	3.44 ± 0.04
0.140	3.42 ± 0.22
0.168	3.23 ± 0.17
0.196	3.02 ± 0.05
0.224	3.13 ± 0.30
0.252	3.06 ± 0.10

[a] $[\mathrm{Cr^{VI}}]_0 = 5.12 \times 10^{-4}$ M, [D-ribose] = 2.77×10^{-2} M, $[\mathrm{HClO_4}] = 7.31 \times 10^{-2}$ M, 30.0 °C.

Table 2 Effect of the acid concentration on the second-order rate constant[a,b]

$[\mathrm{HClO_4}]$/M	$k_2/10^{-3}$ $\mathrm{M^{-1}\,s^{-1}}$
0.219	1.72 ± 0.01
0.256	2.19 ± 0.02
0.292	2.94 ± 0.04
0.329	3.55 ± 0.07
0.366	4.35 ± 0.16

[a] $[\mathrm{Cr^{VI}}]_0 = 1.28 \times 10^{-4}$ M, [D-ribose] = 2.77×10^{-2} M, ionic strength = 0.366 M ($\mathrm{NaClO_4}$), 25.0 °C. [b] Slope of the log k_2 *vs.* log $[\mathrm{HClO_4}]$ plot: 1.84 ± 0.05.

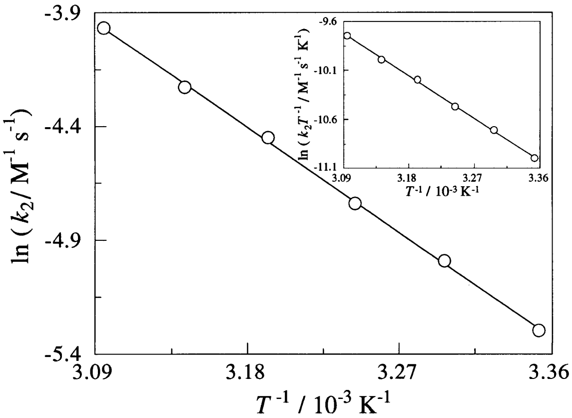

Fig. 6 Arrhenius plot for the reaction of $\mathrm{Cr^{VI}}$ (5.12×10^{-4} M) with D-ribose (2.77×10^{-2} M) in the presence of $\mathrm{HClO_4}$ (0.366 M). Inset: Eyring plot

J K^{-1} mol^{-1}. Given the apparent character of these activation parameters, they must be considered as valid only for the experimental conditions under which they have been deduced, and a certain dependence on the acidity of the medium can be anticipated. However, these activation parameters correspond essentially to the reaction between monomeric Cr^{VI} and D-ribose since, again, the value of $[Cr^{VI}]_0$ for the experiments on which Fig. 6 is based is low enough to allow that the fraction of oxidant present in its dimeric form can be considered negligible.

Addition of $MnSO_4$ to the solutions enhanced dramatically the autocatalytic bell-shaped pattern of the rate plots, even when the kinetic runs were done at a $[\text{D-ribose}]_0 : [Cr^{VI}]_0$ ratio so high that almost no autocatalysis could be observed in the absence of Mn^{II} (Fig. 7). From the initial rate values, it could be concluded that Mn^{II} has a dual effect on the reaction: at low $[Cr^{VI}]_0$ it behaves as a catalyst (Fig. 8, top) and at high $[Cr^{VI}]_0$ as an inhibitor (Fig. 8, bottom).

In the first case, the global initial rate can be written as the result of two contributions, one corresponding to the non-catalytic reaction pathway ($v_{0,n}$) and the other to the Mn^{II}-catalyzed reaction pathway ($v_{0,c}$):

$$v_0 = v_{0,n} + v_{0,c} \tag{8}$$

Given that the catalytic reaction pathway was of first order in Mn^{II} (Fig. 8, top) a catalytic first-order rate constant, defined as $k_{1,c} = v_{0,c}/[MnSO_4]$, could be calculated. This new rate constant was independent of the initial concentration of oxidant (Table 3) but directly proportional to that of the reductant (Table 4). The catalytic second-order rate constant, defined as $k_{2,c} = k_{1,c}/[\text{D-ribose}]_0$, showed a rough, directly proportional dependence on the hydrogen ion concentration (Table 5). Thus, the Mn^{II}-catalyzed reaction pathway followed the rate law:

$$v_{0,c} = k_{obs,c}[\text{D-ribose}]_0[H^+][Mn^{II}] \tag{9}$$

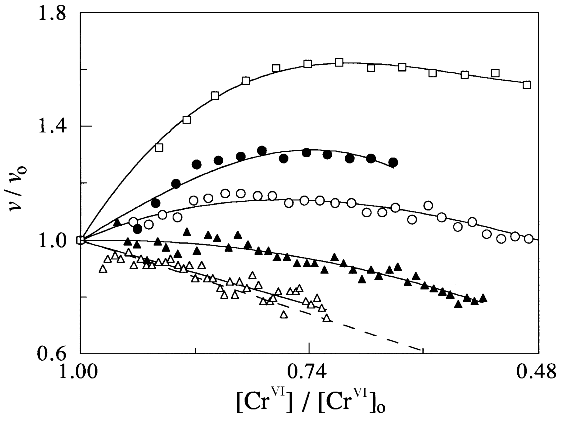

Fig. 7 Effect of the Mn^{II} concentration on the v/v_0 *vs.* $[Cr^{VI}]/[Cr^{VI}]_0$ plot during the course of the reaction between Cr^{VI} (1.28 × 10^{-4} M) and D-ribose (2.77 × 10^{-2} M) in the presence of $HClO_4$ (0.366 M) at 25.0 °C. (△) $[MnSO_4]$ = 0.00, (▲) 2.19, (○) 4.37, (●) 6.56 and (□) 9.84 × 10^{-3} M. The dashed line represents the behavior expected for pseudo first-order kinetics

Table 3 Effect of the initial concentration of Cr^{VI} on the catalytic first-order rate constant[a,b]

$[Cr^{VI}]_0/10^{-4}$ M	$k_{1,c}/10^{-6}$ s^{-1}
1.28	3.84 ± 0.10
2.56	4.69 ± 0.06
5.12	5.05 ± 0.10
7.68	4.52 ± 0.17
10.25	4.92 ± 0.14

[a] [D-ribose] = 2.77 × 10^{-2} M, $[HClO_4]$ = 0.366 M, 25.0 °C. [b] Slope of the log $k_{1,c}$ *vs.* log $[Cr^{VI}]_0$ plot: 0.10 ± 0.05.

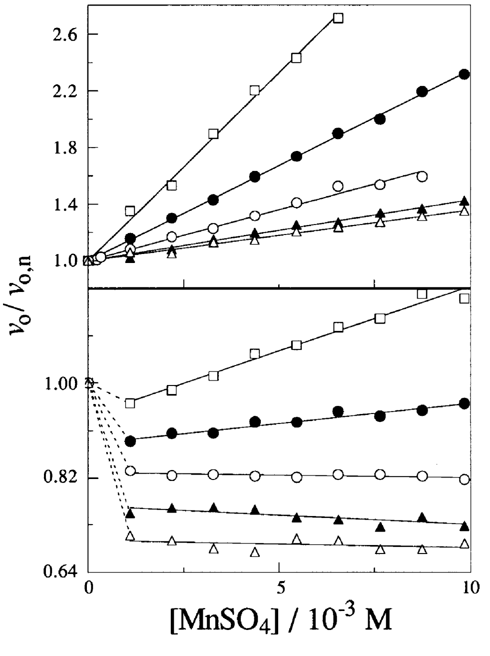

Fig. 8 Effect of the oxidant initial concentraton on the $v_0/v_{0,n}$ *vs.* $[MnSO_4]$ plots in the range of high Mn^{II} concentration for the reaction of Cr^{VI} with D-ribose (2.77 × 10^{-2} M) in the presence of $HClO_4$ (0.366 M) at 25.0 °C. Top: (□) $[Cr^{VI}]_0$ = 1.28 × 10^{-4}, (●) 2.56 × 10^{-4}, (○) 5.12 × 10^{-4}, (▲) 7.68 × 10^{-4} and (△) 1.02 × 10^{-3} M. Bottom: (□) $[Cr^{VI}]_0$ = 1.54 × 10^{-3}, (●) 3.07 × 10^{-3}, (○) 8.20 × 10^{-3}, (▲) 1.23 × 10^{-2} and (△) 2.56 × 10^{-2} M. The dashed lines indicate the inhibition found in the range of very low concentration of Mn^{II} and very high concentration of Cr^{VI}

Table 4 Effect of the D-ribose concentration on the catalytic first-order rate constant[a,b]

[D-ribose]/10^{-2} M	$k_{1,c}/10^{-6}$ s^{-1}
0.55	0.81 ± 0.05
1.11	1.66 ± 0.11
1.66	2.70 ± 0.09
2.22	3.34 ± 0.12
2.77	3.84 ± 0.10

[a] $[Cr^{VI}]_0$ = 1.28 × 10^{-4} M, $[HClO_4]$ = 0.366 M, 25.0 °C. [b] Slope of the log $k_{1,c}$ *vs.* log [D-ribose] plot: 0.99 ± 0.05.

Table 5 Effect of the acid concentration on the catalytic second-order rate constant[a,b]

$[HClO_4]$/M	$k_{2,c}/10^{-4}$ M^{-1} s^{-1}
0.219	0.69 ± 0.02
0.256	0.82 ± 0.02
0.292	1.03 ± 0.02
0.329	1.00 ± 0.03
0.366	1.38 ± 0.04

[a] $[Cr^{VI}]_0$ = 1.28 × 10^{-4} M, [D-ribose] = 2.77 × 10^{-2} M, ionic strength = 0.366 M ($NaClO_4$), 25.0 °C. [b] Slope of the log $k_{2,c}$ *vs.* log $[HClO_4]$ plot: 1.23 ± 0.22.

Addition of $Na_4P_2O_7$ to the solutions had a peculiar effect on the initial rates. Whereas at low concentration (2.46 × 10^{-3} M) the additive seemed to completely suppress the catalytic effect caused by Mn^{II}, so that a small inhibition

Table 6 Effect of the Mn^{II} concentration on the initial rate at various pyrophosphate concentrations[a]

	$v_0/10^{-8}$ M s^{-1}		
		$[Na_4P_2O_7]/10^{-3}$ M	
$[MnSO_4]/10^{-3}$ M	0	2.46	9.84
0.00	1.54 ± 0.06	1.65 ± 0.04	1.58 ± 0.08
1.09	2.02 ± 0.08	1.29 ± 0.01	1.29 ± 0.04
2.19	2.29 ± 0.20	1.22 ± 0.02	1.56 ± 0.08
3.28	2.83 ± 0.09	1.26 ± 0.04	1.79 ± 0.04
4.37	3.29 ± 0.07	1.30 ± 0.08	1.94 ± 0.04
5.47	3.63 ± 0.18	1.27 ± 0.04	2.30 ± 0.15
6.56	4.05 ± 0.06	1.26 ± 0.07	2.35 ± 0.03
7.65	4.24 ± 0.11	1.31 ± 0.02	2.62 ± 0.05
8.74	4.55 ± 0.33	1.26 ± 0.04	2.99 ± 0.16
9.84	4.74 ± 0.04	1.33 ± 0.08	3.47 ± 0.09

[a] $[Cr^{VI}]_0 = 1.28 \times 10^{-4}$ M, [D-ribose] $= 2.77 \times 10^{-2}$ M, $[HClO_4] = 0.366$ M, 25.0 °C.

effect was clearly visible, at high concentration of pyrophosphate (9.84×10^{-3} M), both inhibition (at low $[Mn^{II}]$) and catalytic (at high $[Mn^{II}]$) effects were observed (Table 6).

The inhibition found at high $[Cr^{VI}]_0$ in the presence of Mn^{II} and absence of pyrophosphate (Fig. 9) led to a dependence of the second-order rate constant on the inhibitor concentration of the type:

$$k_2 = \frac{a}{1 + b[Mn^{II}]} + c \qquad (10)$$

with parameter b (obtained by nonlinear least-squares) showing an inversely proportional dependence on the initial concentration of reductant (Fig. 9, inset), in agreement with previous reports.[43,44]

Detection of an intermediate

In experiments made in the presence of both $MnSO_4$ and $Na_4P_2O_7$, the use of difference UV/VIS spectroscopy allowed the identification of Mn^{III} as one of the intermediates involved in the mechanism. To this end, two experiments were performed, one in the presence of pyrophosphate and the other in its absence, the other conditions being identical, and periodic scans were recorded during the reaction. By subtracting the spectrum without $Na_4P_2O_7$ from that with $Na_4P_2O_7$ (with recording times such that the concentration of unreacted Cr^{VI} was exactly the same in both experiments), the difference spectrum showed a wide absorption band with a maximum at around 518 nm, typical of the $[Mn(P_2O_7)]^-$ complex.[45,46]

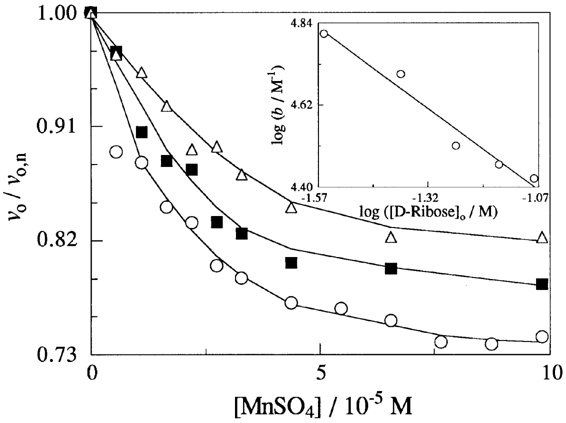

Fig. 9 Effect of the initial oxidant concentration on the $v_0/v_{0,n}$ *vs.* $[MnSO_4]$ plots in the range of low Mn^{II} concentration for the reaction of Cr^{VI} with D-ribose (2.77×10^{-2} M) in the presence of $HClO_4$ (0.366 M) at 25.0 °C. (△) $[Cr^{VI}]_0 = 1.23$, (■) 1.64 and (○) 2.56×10^{-2} M. Inset: log b *vs.* log $[D\text{-ribose}]_0$ plot at $[Cr^{VI}]_0 = 2.56 \times 10^{-2}$ M, $[HClO_4] = 0.366$ M and 25.0 °C; slope: -0.87 ± 0.10

Mechanism

In Table 7 the value of the second-order rate constant for the reaction between Cr^{VI} and D-ribose can be compared with those corresponding to the reactions between Cr^{VI} and other relevant organic compounds.[44] We can see that the rate constants for the reactions with aldehydes are much higher than those corresponding to the reactions with the related alcohols, since the value of k_2 for the reaction with formaldehyde is 426 times higher than that for the reaction with the alcohol having the same number of carbon atoms (methanol). Interestingly enough, the value of k_2 for the reaction with D-ribose (5.00×10^{-3} M^{-1} s^{-1}) closely resembles that expected from the combined, parallel reactions of Cr^{VI} with the four alcoholic groups (1 primary and 3 secondary) present in the reductant molecule. Effectively, if we assume that the corresponding reactivities are roughly similar to those for the reactions with 1-propanol and 2-propanol, respectively, we obtain: $k_2 = (1.48 + 3 \times 1.35) \times 10^{-3}$ M^{-1} $s^{-1} = 5.53 \times 10^{-3}$ M^{-1} s^{-1}. Hence, our results indicate that the molecule of D-ribose participates in the reaction in its cyclic form rather than in its free-aldehyde, linear form. This is consistent with the findings reported for the degradative oxidation of monosaccharides by Ce^{IV}.[47]

For the oxidation of D-ribose (symbolized by R_1R_2CHOH) at low $[Cr^{VI}]_0$ and in the absence of Mn^{II}, we propose the following mechanism:

$$R_1R_2CHOH + H_2CrO_4 \overset{K_{I,i}}{\rightleftharpoons} R_1R_2CH{-}O{-}CrO_3H + H_2O \qquad (11)$$

$$R_1R_2CH{-}O{-}CrO_3H + H^+ \xrightarrow[\text{slow}]{k_{II,i}} R_1R_2C{=}O + CrO^{2+} + OH^- + H_2O \qquad (12)$$

$$CrO^{2+} + R_1R_2CHOH \xrightarrow{k_{III,i}} Cr^{II} + R_1R_2C{=}O + H_2O \qquad (13)$$

$$Cr^{II} + Cr^{VI} \rightarrow Cr^{III} + Cr^{V} \qquad (14)$$

$$Cr^{V} + R_1R_2CHOH \rightarrow Cr^{III} + R_1R_2C{=}O \qquad (15)$$

The formation of ester-like condensation compounds between chromic acid and hydroxy-containing organic molecules (such as linear[48–50] and cyclic[51] alcohols, diols,[52] α-hydroxy acids[53] and saccharides[54,55]) in quasi-equilibrium reactions prior to the redox rate determining steps is widely accepted. The participation of Cr^{II} as an intermediate in the reduction of Cr^{VI} to Cr^{III} by alcohols and other organic two-electron reductants is now well-established.[43,44,56,57] This intermediate might play a certain role in the development of chromium-induced carcinogenesis.[58,59] In the particular case of the Cr^{VI}–saccharide reactions, the finding of Cr^{III} dimeric complexes among the reaction products[60,61] may be explained as a consequence of the addition, redox reaction between Cr^{II}

Table 7 Values of the second-order rate constant for the reactions between Cr^{VI} and some relevant organic substrates[a]

Substrate	$k_2/10^{-4}$ M^{-1} s^{-1}
Methanol[b]	0.587
2-Propanol[b]	13.5
1-Propanol[b]	14.8
D-Ribose[c]	50.0
Formaldehyde[b]	250

[a] $[HClO_4] = 0.366$ M, 25.0 °C. [b] $[Cr^{VI}]_0 = 8.74 \times 10^{-4}$ M, ref. 44. [c] $[Cr^{VI}]_0 = 7.68 \times 10^{-4}$ M, this work.

and CrO^{2+},[62,63] thus constituting an indirect proof of the involvement of both intermediates, whereas the participation of Cr^{V} has been demonstrated by EPR.[64]

The formation of carbonylic compounds by oxidation of the hydroxy groups can explain the autocatalysis observed in the absence of Mn^{II}. Effectively, the oxidation of the primary alcoholic group leads to an intermediate aldehyde and, given that aldehydes are much more reactive toward Cr^{IV} than alcohols, the accumulation of the aldehyde in the system will cause the rate to increase in the first stretch of the reaction. However, if $[\text{D-ribose}]_0$ is kept constant and $[Cr^{VI}]_0$ is decreased, the maximum concentration of aldehyde reached in the system will decrease too until the rate of the reaction of Cr^{VI} with aldehyde becomes negligible against the rate of the reaction with D-ribose, so that the behavior approaches that expected for pseudo first-order kinetics, exactly as observed in the experiments (see Fig. 2). Similar findings were reported for the Cr^{VI} oxidation of some primary alcohols.[65] The carboxylic compound formed from the oxidation of the intermediate aldehyde by Cr^{VI} is probably one of the main reaction products when the reaction is performed in the presence of a large excess of reductant with respect to oxidant, since it has been reported to be a ligand in the Cr^{III} dimeric complex isolated from the reaction between Cr^{VI} and D-ribose.[61]

We have seen that, under the experimental conditions corresponding to Fig. 4, the second-order rate constant for the reaction of D-ribose with dimeric Cr^{VI} is much lower than that for the reaction with monomeric Cr^{VI}. This decrease of reactivity associated with the dimerization of Cr^{VI} cannot be explained in terms of the electron density of the respective chromium atoms, since each chromium atom of $Cr_2O_7^{2-}$ has a higher positive charge than the chromium atom of $HCrO_4^-$.[66] Thus, considering only this criterion, one would expect a higher affinity for electrons in the case of the metal atoms of the dimer. Instead, the explanation might lie in the different tendency of the acid forms of the monomer (H_2CrO_4) and the dimer ($HCr_2O_7^-$) to suffer an esterification with D-ribose; presumably, this tendency might be higher in the case of H_2CrO_4.

The rate law deduced from the proposed mechanism is coherent with eqn. (6), the expression obtained for the observed rate constant being:

$$k_{\text{obs}} = 2K_{\text{p}} \sum_{i=1}^{4} K_{\text{I},i}\, k_{\text{II},i} \tag{16}$$

where the sum is extended to the four hydroxy groups present in the D-ribose molecule. The finding that the second-order rate constant decreased when sodium perchlorate was added to the solutions (see Table 1) can be explained by the decrease of K_{p} with increasing ionic strength,[39] which results in a decrease of the concentration of the active form of the oxidant (H_2CrO_4).

For the Mn^{II}-catalyzed reaction pathway we propose the following mechanism:

$$R_1R_2CHOH + Mn^{II} \overset{K_{IV}}{\rightleftharpoons} C \tag{17}$$

$$C + H^+ \underset{k_{-V}}{\overset{k_V}{\rightleftharpoons}} D + H_2O \tag{18}$$

$$D + Cr^{VI} \xrightarrow{k_{VI}} R_1R_2C{=}O + Mn^{III} + Cr^{III} \tag{19}$$

$$2Mn^{III} \rightarrow Mn^{II} + Mn^{IV} \tag{20}$$

$$Mn^{IV} + R_1R_2CHOH \rightarrow Mn^{II} + R_1R_2C{=}O \tag{21}$$

Polyhydroxylated compounds are known to interact strongly with metal ions. In particular, the existence of a complex between Mn^{II} and D-gluconic acid has been reported.[67] Notice that eqn. (19) presents an unusual feature, since we have proposed a direct, three-electron reduction from Cr^{VI} to Cr^{III}; one of the electrons transferred is given by the manganese atom and the other two by the organic substrate. Actually, we detected the formation of Mn^{III} as an intermediate when the reaction was performed in the presence of the stabilizing ligand pyrophosphate. Dismutation of this intermediate leads to both Mn^{II} and Mn^{IV},[46] whereas the two-electron reduction of the latter by a D-ribose molecule allows complete recuperation of the Mn^{II} acting as catalyst. The notable enhancement of the autocatalytic profile of the rate plots when Mn^{II} was added to the solutions (Fig. 7) might be caused by an accumulation in the system of the intermediate Mn^{IV}, since the soluble, colloidal form of the latter is known to autocatalyze many permanganate reactions.[68,69]

The finding that this reaction pathway is of zero order in Cr^{VI} suggests that the slow step is the forward direction of eqn. (18). Then, the rate law deduced from the proposed mechanism is coherent with eqn. (9) provided that the observed catalytic rate constant is:

$$k_{\text{obs, c}} = \frac{K_{IV}\, k_V\, k_{VI}[Cr^{VI}]_0}{k_{-V} + k_{VI}[Cr^{VI}]_0} \tag{22}$$

This expression can be reduced to $k_{\text{obs, c}} = K_{IV} k_V$ when the values of the initial oxidant concentration are high enough that k_{-V} is negligible against $k_{VI}[Cr^{VI}]_0$. Hence, under these conditions, the Mn^{II}-catalyzed reaction pathway would be of zero order in Cr^{VI}.

An important question is why the slow step should be the forward direction of eqn. (18) instead of eqn. (19), in spite of the fact that, in the case of redox reactions, the first redox step of the mechanism [apparently eqn. (19)] is usually the rate-determining one. The reason might be that eqn. (18) itself is a redox step. We regard the species D as a complex of the type $R_1R_2\dot{C}H{-}Mn^{3+}$, where the organic part has a certain free radical character. Since the formation of a free radical requires most often a high activation energy, this would explain the slowness of the reaction.

The mechanism proposed for the Mn^{II}-catalyzed reaction pathway might be applicable also to other chromic acid oxidations catalyzed by Mn^{II}, such as those of α-hydroxybutyric, malonic, mandelic and oxalic acids.[70,71] It is interesting to notice that for the Mn^{II}-catalyzed pathways of those reactions, apparent kinetic orders between 0 and 0.3 were found for Cr^{VI}. The mechanism given in eqns (17)–(21) accommodates well these findings, since, according to eqn. (22), apparent kinetic orders between 0 and 1 are expected for Cr^{VI}, depending on the relative values of k_{-V} and $k_{VI}[Cr^{VI}]_0$. In contrast, the mechanism proposed by Kemp and Waters[70] for the Mn^{II}-catalyzed reaction pathway would lead to a fixed kinetic order of 1/3 in Cr^{VI}, too high compared to the value obtained by us for the Cr^{VI} oxidation of D-ribose (0.10 ± 0.05). Moreover, the mechanism proposed by these authors would require the existence of a rapid quasi-equilibrium involving Cr^{VI} and Mn^{II} as reactants and Cr^{III} and Mn^{III} as products. This hypothesis seems to us very unlikely, given that the relative inertness of Cr^{III} might be incompatible with its rapid reoxidation by Mn^{III}.

We believe that the existence or not of catalysis of Mn^{II} in the Cr^{VI} oxidation of an organic substrate can be related to the ability of that substrate to behave as a stabilizing ligand for Mn^{III}. A polyhydroxylated substrate (such as D-ribose) might be a good example. The finding that at low concentrations pyrophosphate behaves as an inhibitor of the catalysis by Mn^{II} (Table 6) might be a consequence of the competition between D-ribose and pyrophosphate to act as ligands for Mn^{II}. The recuperation of the catalysis at higher concentrations of pyrophosphate might indicate that the latter is also capable of opening a new reaction pathway.

Given that the Mn^{II}-catalyzed reaction pathway is zero-order dependent on Cr^{VI}, whereas the uncatalyzed reaction pathway is first-order dependent on the same species, the contribution of the former to the global reaction becomes negligible at very high $[\mathrm{Cr^{VI}}]_0$, so that the inhibition effect cause by $\mathrm{Mn^{II}}$ becomes predominant over the catalysis. This inhibition is caused by the capacity of the latter to act as an efficient trapping agent for the intermediate $\mathrm{Cr^{IV}}$:

$$\mathrm{CrO^{2+} + Mn^{II} + H_2O \xrightarrow{k_{VII}} Cr^{III} + Mn^{III} + 2OH^-} \qquad (23)$$

thus suppressing the formation of $\mathrm{Cr^{II}}$ and its posterior oxidation by $\mathrm{Cr^{VI}}$.[44] This inhibition caused by $\mathrm{Mn^{II}}$ is probably present at all values of $[\mathrm{Cr^{VI}}]_0$, but it can be observed only when $[\mathrm{Cr^{VI}}]_0$ is high enough for the $\mathrm{Mn^{II}}$-catalyzed reaction pathway to give a negligible contribution to the global reaction. If we assume that $\mathrm{CrO^{2+}}$ is in steady state, the rate law obtained from the mechanism proposed [eqns (11)–(15) and (23)] is consistent with eqn. (10), and the inhibition parameter is given by:

$$b = \frac{k_{\mathrm{VII}}}{\sum_{i=1}^{4} k_{\mathrm{III},\,i}[\text{D-ribose}]_0} \qquad (24)$$

which is again consistent with the inversely proportional dependence on the reductant concentration found for this parameter (see Fig. 9, inset). Thus, we conclude that the inhibition by $\mathrm{Mn^{II}}$ can be taken as strong proof of the participation of $\mathrm{Cr^{IV}}$ (in the form of $\mathrm{CrO^{2+}}$) as an intermediate in the mechanism.

Finally, the finding that the reaction in the absence of added perchloric acid seems to be extremely slow suggests that under ordinary physiological conditions the reduction by D-ribose (and, probably, by other saccharides and their derivatives) might represent only a minor contribution to the intracellular metabolization of $\mathrm{Cr^{VI}}$.

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