ment, National Cancer Institute. High resolution and field desorption mass spectra were obtained on a mass spectrometer provided by grants from the National Cancer Institute (CA 11,388) and National Institute of General Medical Sciences (GM 16864). Carbon magnetic resonance spectra were obtained on a spectrometer purchased with an instrumentation grant from the National Science Foundation.

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Stable Chromium(V) Compounds[1]

Sir:

Chromium(V) is known in the form of several solid compounds.[2,3] Solutions of chromium(V) compounds in nonaqueous media, like fuming sulfuric acid[4] or ethylene glycol, have also been prepared; the latter have received a great deal of attention during recent years.[5] Aqueous solutions of chromium(V) are very unstable and undergo rapid disproportionation to chromium(VI) and chromium(III). Thus, although chromium(V) is well known to be formed as an intermediate in the course of chromic acid oxidations, it normally does not accumulate in detectable concentrations. The formation and decay of a chromium(V) intermediate, however, becomes observable in the chromic acid oxidation of oxalic[6-9] and glycolic[10] acids, which seem able to combine with chromium(V) to form relatively stable complexes.

We now wish to report that tertiary hydroxyacids 2-hydroxy-2-methylbutyric acid and citric acid form chromium(V) complexes of considerable stability, permitting for the first time the preparation and storage of aqueous solutions of chromium(V) compounds for extended periods of time.

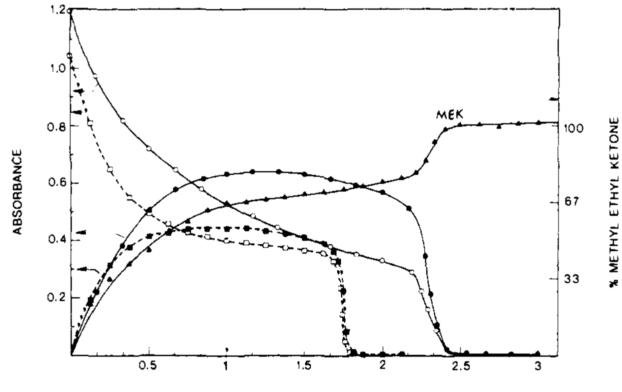


Figure 1. Time dependence of absorbance at 350 and 750 nm and of the formation of methyl ethyl ketone. Only chromium(V) absorbs at 750 nm, both chromium(VI) and chromium(V) absorb at 350 nm. Conditions: 2-hydroxy-2-methylbutyric acid = 0.5 M, $HClO_4$ = 0.5 M, chromium(VI) = 7.75×10^{-3} M, 50 °C; 350 nm, 0.1-cm cell (○); 750 nm, 5-cm cell (●); methyl ethyl ketone (▲); citric acid = 0.5 M, $HClO_4$ = 0.1 M, chromium(VI) = 7.0×10^{-3} M, 70 °C; 350 nm, 0.1-cm cell (□); 750 nm, 5-cm cell (■).

When chromic acid is allowed to react with 2-hydroxy-2-methylbutyric acid at 50 °C or with citric acid at 70 °C and the reaction is monitored spectrophotometrically, an unusual kinetic behavior is observed (Figure 1). At 350 nm (λ_{max} for chromium(VI)), the absorption first decreases almost asymptotically to about 35–40% of the original value, whereupon the reaction starts again and proceeds rapidly to completion. The absorption curve taken at 750 nm, a wavelength at which only chromium(V) absorbs,[10] shows that the concentration of chromium(V) increases until it reaches a maximum value at about the same time when the absorption curve at 350 nm has reached the plateau, and then decreases to an essentially zero value.

The chromic acid oxidation of 2-hydroxy-2-methylbutyric acid (HMBA) yields methyl ethyl ketone (MEK) and carbon dioxide according to eq 1.

$$2\mathrm{Cr(VI)} + 3\mathrm{HMBA} \rightarrow 2\mathrm{Cr(III)} + 3\mathrm{MEK} + 3\mathrm{CO_2} \quad (1)$$

The stoichiometry requires the formation of 1.5 mol of methyl ethyl ketone for each molecule of chromium(VI) reduced to chromium(III). Curve MEK in Figure 1 shows that about two-thirds of the expected amount of methyl ethyl ketone is formed by the time the 750-nm curve has reached its maximum.

This behavior indicates the formation of a relatively stable intermediate of chromium in almost quantitative yields at the time when two-thirds of the product has been formed. As at this point only two-thirds of the oxidizing power of chromium(VI) is utilized, chromium(VI) is reduced either to chromium(IV) (Scheme I) or to an equimolar mixture of chromium(V) and chromium(III) (Scheme II or Scheme III).

Scheme I

$$\mathrm{Cr(VI)} + \mathrm{HMBA} \rightarrow \mathrm{Cr(IV)} + \mathrm{MEK} + \mathrm{CO_2}$$

Scheme II

$$\mathrm{Cr(VI)} + \mathrm{HMBA} \rightarrow \mathrm{Cr(IV)} + \mathrm{MEK} + \mathrm{CO_2}$$

$$\mathrm{Cr(IV)} + \mathrm{HMBA} \rightarrow \mathrm{MEK} + \cdot\mathrm{CO_2H} + \mathrm{Cr(III)}$$

$$\mathrm{Cr(VI)} + \cdot\mathrm{CO_2H} \rightarrow \mathrm{Cr(V)} + \mathrm{CO_2}$$

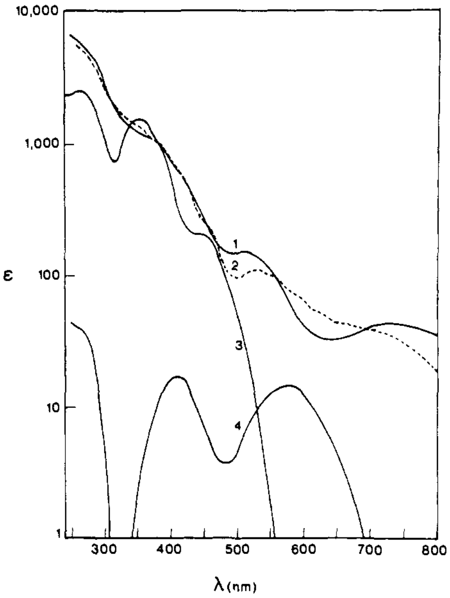


Figure 2. Spectra of chromium(VI), chromium(V), and chromium(III) in water at 25 °C: chromium(V) complex with 2-hydroxy-2-methylbutyric acid (1), chromium(V) complex with citric acid (2), chromium(VI) at the beginning (3) and chromium(III) at the end (4) of the oxidation of 2-hydroxy-2-methylbutyric acid by chromic acid under conditions given in Figure 1.

Scheme III

$$Cr(VI) + 2HMBA \rightarrow Cr(III) + 2MEK + CO_2 + \cdot CO_2H$$

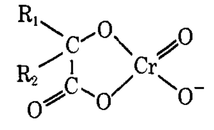
$$Cr(VI) + \cdot CO_2H \rightarrow Cr(V) + CO_2$$

The nature of the intermediates formed in the first phase of the reaction can be conveniently examined when the oxidation is interrupted by cooling the reaction mixture down to room temperature. At this point the color has changed from the original yellow to red-brown. The absorption spectra (corrected by subtracting the chromium(III) absorption), shown in Figure 2, together with the spectra of chromium(VI) and chromium(III) are in good agreement with the spectrum previously obtained for the chromium(V)-oxalic acid complex[8] and are completely different from the spectra of any known chromium(IV) compounds.[11,12] The conclusion that the intermediates are chromium(V) species is also consistent with the known extreme instability and reactivity of chromium(IV) in aqueous solutions.[13-18]

The solutions of the chromium(V) complexes are stable at room temperature for several hours, at 0 °C for about 1 day, and can be stored frozen at −20 °C for several weeks. Their stability can be extended considerably by careful deaeration. The solution obtained in the chromic acid oxidation of 2-hydroxy-2-methylbutyric acid has been further purified by passing it through a cation exchange column (Dowex 50W-X8) which did not affect the chromium(V) complex, but completely removed chromium(III). The chromium(III)-free solution was analyzed iodometrically (a) directly and (b) after oxidation to chromium(VI) by hydrogen peroxide in alkaline solution. The ratio of the I_3^- yields in procedures (a) and (b) were 1:1.52 providing additional proof that the complex is a chromium(V) compound.

While chromium(V) resembles in many respects chromium(VI),[8,19,20] its reactivity towards iodide ions is greater by a factor of more than 50 (for HMBA). This observation permitted the development of a method for the quantitative analysis of chromium(V)-chromium(VI) mixtures.[21]

Although insufficient information about the nature of the chromium(V) complexes is available at this time, the following structures appear plausible and are consistent with



I, $R_1 = CH_3$; $R_2 = CH_2CH_3$
II, $R_1 = R_2 = CH_2CO_2H$

the need for two functional groups to stabilize the chromium(V) valence state. Kinetic data[21] suggest that the chromium(V) compound first produced is a 1:1 complex, although it is entirely possible that the stable complex contains an additional molecule of hydroxyacid. The negative charge is consistent with the observation that the complexes are not absorbed by a cation-exchange resin, but are retained by an anion-exchange column (Dowex 2-X8).

The second phase of the reaction in which chromium(V) is rapidly reduced to chromium(III) appears to involve a free radical chain reaction initiated by traces of oxygen and inhibited by chromium(VI).

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Chemistry of Superoxide Ion. II. Reaction with Hydroperoxides[1]

Sir:

The elegant work of Fridovich and his group[2] has clearly demonstrated the damaging effects of superoxide ion ($O_2\cdot^-$) in biological systems. However, little work has yet appeared on the chemical reactions which superoxide can undergo with simple organic substrates.[1,3-11]

Both H_2O_2 and $O_2\cdot^-$ are formed in the reaction of xanthine oxidase with its substrates, and the system is destructive to organisms.[12] However, neither H_2O_2 nor $O_2\cdot^-$ alone is sufficient to account for the damage, and it has been hypothesized that OH·, a powerful oxidizing agent, is produced in the reaction of H_2O_2 and $O_2\cdot^-$.[12-14]

$$H_2O_2 + O_2\cdot^- \rightarrow OH\cdot + OH^- + O_2$$

As a model for this reaction, we have studied the reaction