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Some Oxidations with Cr(V)

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The reactions of $CrOCl_4^-$ *with triphenylphosphine, sulfite, aldehydes, 1,3,7-trimethylxanthine (caffeine) and several alcohols have been examined. The reaction with* Ph_3P *results in the two-electron reduction of Cr(III) to give* Ph_3PO *and* $Cr_2Cl_9^{3-}$*. Transfer of the oxo ligand also occurs in the reaction of* $CrOCl_4^-$ *with sulfite and aldehydes. The oxidation of caffeine did not produce detectable quantities of the corresponding uric acid, but rather 8-chlorocaffeine. The organic products from the reaction of alcohols and aldehydes with* $CrOCl_4^-$ *are in agreement with those generally attributed to Cr(V) intermediates which are generated during the oxidation of these substrates by Cr(VI). The enhanced oxidative ability of* $CrOCl_4^-$ *relative to* $MoOCl_4^-$ *has also been demonstrated.*

Introduction

Our interest [1–3] in the chemistry of those molybdoenzymes which serve as oxidases has led us to consider the ability of $CrOCl_4^-$ to act as an oxo-transfer agent in reactions with sulfite, aldehydes, and 1,3,7-trimethylxanthine (caffeine). Xanthine could not be used due to its poor solubility. The reaction of $CrOCl_4^-$ with triphenylphosphine, a reagent which is known to bring about oxo ligand abstraction from Mo(VI) [4, 5], was also considered. Since Cr(V) is recognized as an active intermediate in oxidations of alcohols by Cr(VI) [6], but has never been examined separately, we have also briefly examined the reactions of $CrOCl_4^-$ with two primary alcohols and one secondary alcohol.

Experimental

Materials

Reagent grade chemicals were generally used without further purification. However, benzaldehyde was distilled to remove benzoic acid and stored under argon while CH_2Cl_2 was dried over P_2O_5 and distilled under vacuum directly into the reaction flasks. A sample of 1,3,7-trimethyluric acid was obtained from Tridom Chemical. Literature methods were used to prepare $(R_4N)(CrOCl_4)$ (R = Et or n-Bu) [7], $(Bu_4N)(MoOCl_4)$ [8], $(Bu_4N)_3(Cr_2Cl_9)$ [9], and 8-chlorocaffeine [10]. The tetraethylammonium salts of SO_3^{2-} and SO_4^{2-} were prepared by passing concentrated solutions of $(Et_4N)Cl$ through anion exchange columns which were charged with SO_3^{2-} and SO_4^{2-} respectively. The $(Et_4N)_2SO_3$ and $(Et_4N)_2SO_4$ solutions were evaporated to dryness under vacuum. The resulting white solids were dried overnight at 60 °C. The syntheses were confirmed by infrared spectra of the products. Tetraethylammonium sulfite is sensitive to oxidation by air and must be stored under air-free conditions if used over a long period of time.

Methods

All reactions were conducted at room temperature, under a positive pressure of argon and in CH_2Cl_2. Proton NMR spectra were obtained with either a Varian T-60 or a Varian HR-200 NMR spectrometer. Phosphorous-31 NMR spectra were obtained using a Varian XL-100-15 FT NMR spectrometer. Mass spectral analysis was performed on a Varian Associates CH-7 mass spectrometer. Infrared spectra were recorded with a Perkin-Elmer 283 spectrometer. A Varian Aerograph Series 1700 gas chromatograph equipped with a flame ionization detector was used for the analysis of all volatile materials. Weighed quantities of organic liquids were diluted to known concentration and used for instrument calibration. Retention times and peak heights were used as criteria for identifaction and quantitation. A Porapak R column (6 ft × 1/8 in) was used for the benzaldehyde, benzyl alcohol and 2-butanol reactions; a Porapak Q column (6 ft × 1/8 in) was used for the butanal and 1-butanol reactions.

Results

The reaction of $(R_4N)(CrOCl_4)$ (R = Et or n-Bu) with Ph_3P led to an immediate color change from

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TABLE. Reactions of $(Et_4N)(CrOCl_4)$ with Alcohols.[a]

Alcohol	[Alcohol] (*M*)	$[CrOCl_4^-]$ (*M*)	Alcohol[b] Consumed (%)	Product[b] Yield (%)	Time (h)	Other Products
1-Butanol	0.08	0.09	100	11	2.3	Butyric acid[c] Butyl butyrate
	0.24	0.07	142[d]	31	2.5	Butyraldehyde dibutyl acetal[e] Butyric acid Butyl butyrate
Benzyl	0.09	0.10	100	66	12.0	Benzoic acid[f] Benzyl benzoate
	0.24	0.08	150[d]	88	2.0	g
2-Butanol	0.21	0.07	93	93	16.0[g]	g

[a] Twenty five mL of solvent were used for all reactions. [b] Alcohol consumption and product (aldehyde or ketone) yields were determined by VPC. The percentages are based upon the limiting reagent. [c] All volatile materials were removed by vacuum distillation to give an oily residue. The residue was extracted with a mixture of H_2O and CH_2Cl_2. Although the acetal was not isolated, any acetal formed was presumably hydrolyzed during the aqueous work up procedure. Aqueous solutions of unreacted $CrOCl_4^-$ are sufficiently acidic (pH = 1.0) to catalyze hydrolysis. Although all the butanol was utilized during the reaction, the extracted organic material contained ~20% butanol. [d] The excessive consumption of alcohol is attributed to coordination of the alcohol to the Cr(III) product. [e] Products recovered by vacuum distillation of the reaction mixture at 60 °C. [f] Products recovered by precipitation of the chromium species with 100 mL Et_2O. [g] No other products were isolated.

brownish red to violet. High yields of pure $(Bu_4N)_3(Cr_2Cl_9)$ were obtained when the reaction was carried out in the presence of excess $(Bu_4N)Cl$. The addition of water to the reaction caused hydrolysis and extraction of the Cr(III) into the aqueous layer. Integration of the ^{31}P NMR spectrum of the organic phase, using a known excess of Ph_3P as an internal standard for quantitation, indicated that the quantitative formation of one equivalent of Ph_3PO per equivalent of Cr(V) had occurred.

The reaction of roughly stoichiometric amounts of $(Et_4N)(CrOCl_4)$ and $(Et_4N)_2SO_3$ in the presence of $(Et_4N)Cl$ led to an immediate color change to deep wine red. Hydrolysis and passage of the aqueous layer through a cation exchange column (Na^+ form) removed all of the green Cr(III). When the resulting solution was reduced to dryness, the infrared spectrum of the white solid contained a broad absorption at 1120 cm^{-1} which is characteristic of SO_4^{2-}, whereas the strong absorption at 960 cm^{-1} due to SO_3^{2-} was completely absent. We presume that the product of the redox reaction is the sulfato-Cr(III) complex, $Cr(O_2SO_2)Cl_4^{3-}$, which is subsequently destroyed by hydrolysis.

The reactions of benzaldehyde and butanal with $(Et_4N)(CrOCl_4)$ were followed by VPC as shown in Fig. 1. The reaction in each case was slow with 88% of the benzaldehyde consumed after 20 h and 91% of the butanal consumed after 15 h. Precipitation of all chromium species with Et_2O allowed the recovery and the identification of the corresponding carboxylic acids.

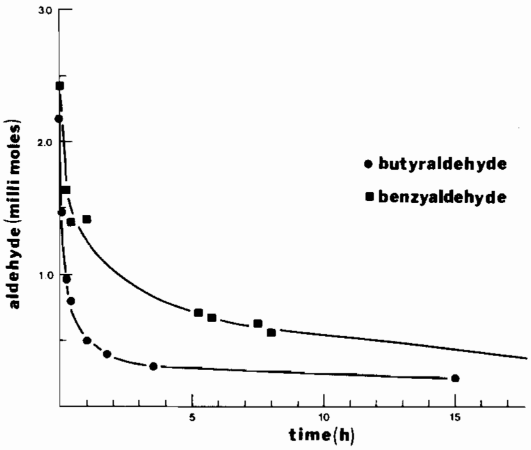

Fig. 1. Oxidation of butyraldehyde and benzaldehyde by $(Et_4N)(CrOCl_4)$. In the oxidation of butyraldehyde, the reactant concentrations were 0.087 *M* butyraldehyde and 0.097 *M* $(Et_4N)(CrOCl_4)$. The consumption of butyraldehyde after 15 h was 91%. In the oxidation of benzaldehyde, the reactant concentrations were 0.097 *M* benzaldehyde and 0.128 *M* $(Et_4N)(CrOCl_4)$. The consumption of benzaldehyde after 20 h was 88%.

The results of the reaction of $(Et_4N)(CrOCl_4)$ with 1-butanol, benzyl alcohol and 2-butanol are summarized in Table I. In the presence of either excess alcohol or excess oxidant, benzyl alcohol displayed greater reactivity [3] and resulted in larger yields of the corresponding aldehyde than 1-butanol. The oxidation of 1-butanol was complicated by the formation of a variety of side products which were identified at the completion of the reaction, but which could not be quantitated during the course of the reaction by VPC due to insufficient volatility. These products, butyric acid, butyl butyrate, and the dibutyl acetal of butanal, are the result of the subsequent oxidation of the aldehyde, the reaction of the alcohol and the aldehyde to form the hemiacetal which is subsequently oxidized [6a, b], and the reaction of the alcohol with the hemiacetal, respectively. Butyric acid and butyl butyrate were also detected in a reaction which contained a slight excess of the Cr(V) reagent with the yield of aldehyde decreasing to about one-third of the previous value. Small amounts of benzoic acid and only trace amounts of benzyl benzoate were detected during benzyl alcohol oxidations. The larger yields of aldehyde and the smaller amounts of side products during oxidations of benzyl alcohol are consistent with the greater reactivity of benzyl alcohol toward oxidation, the diminished reactivity of benzaldehyde toward oxidation (see Fig. 1), and the reduced tendency of conjugated aldehydes to undergo alcohol-addition reactions [11, 12].

In contrast to primary alcohols, secondary alcohols are oxidized to ketones which are less reactive toward oxidation and alcohol-addition reactions than aldehydes. The reaction of excess 2-butanol with $(Et_4N)(CrOCl_4)$, shown in Fig. 2, results in a 93% consumption of the alcohol and a 93% yield of methyl ethyl ketone after 16 h. No other products were detected by VPC or by other means.

The reaction of caffeine with excess $(Et_4N)(CrOCl_4)$ over a period of 48 h led to the formation of a brown solution and a dark precipitate. Five aqueous washings of the reaction mixture led to the recovery of 8-chlorocaffeine (~20% yield) whose melting point, infrared spectrum, mass spectrum, and ^1H NMR spectrum were identical to those obtained from an authentic sample. We have found no indications of the formation of 1,3,7-trimethyluric acid, the analog of the product formed in the reaction catalyzed by xanthine oxidase.

We have also made a brief comparison of $CrOCl_4^-$ and $MoOCl_4^-$. Although $Mo_2Cl_9^{3-}$ is known [13], $MoOCl_4^-$ does not react with Ph_3P in the presence of excess Cl^- under either thermal or photolytic conditions. Similarly, alkylammonium salts of $MoOCl_4^-$ may be recrystallized from alcohols without any apparent reaction.

Discussion

This investigation has shown that $CrOCl_4^-$ will oxidize a variety of compounds, including several substrates of molybdoenzymes. The reaction with Ph_3P quantitatively demonstrates that a two-electron reduction of Cr(V) has occurred according to equation (1). Transfer of the oxo ligand is apparent in

$$2CrOCl_4^- + 2Ph_3P + Cl^- \rightarrow Cr_2Cl_9^{3-} + Ph_3PO \qquad (1)$$

this reaction as well as the oxidations of sulfite and aldehydes so that the products are (not unexpectedly) those observed in the enzymic reactions [1]. Interestingly, the oxidations of caffeine did not produce detectable quantities of the corresponding uric acid but 8-chlorocaffeine instead. The C(8) position in purines is susceptible to attack by both nucleophilic and electrophilic reagents depending on the number and placement of substituents on the rings and their inductive effects [14]. The electron-rich environment at C(8) in caffeine is demonstrated by its ability to undergo electrophilic attack by Cl_2 to give 8-chlorocaffeine [10]. We also note that monooxo complexes, including $CrOCl_3$, will oxidize carbon–carbon double bonds to give only chlorinated products [15]. In addition, it is conceivable that the products of oxo-transfer are formed initially but react further in the reaction medium or during the aqueous work up. In this regard, methylated uric acids can be converted to the corresponding 8-chloro derivatives with $POCl_3$ [14].

There are two other facets which deserve comment. First, the organic products from the reaction of alcohols and aldehydes with $CrOCl_4^-$ are in agreement with those generally attributed to Cr(V) which has been generated by the oxidation of these substrates with aqueous Cr(VI) [6, 16]. Second, the enhanced oxidative ability of Cr relative to Mo, which is often quoted [17], has been demonstrated again.

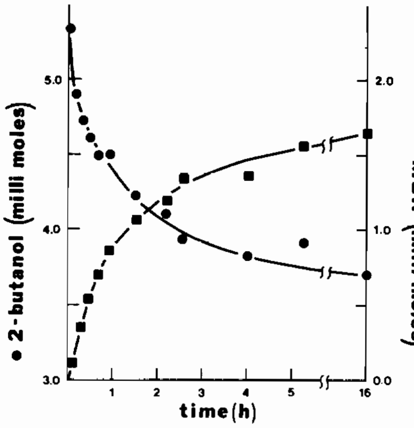

Fig. 2. Alcohol utilization and ketone formation during the oxidation of 2-butanol by $(Et_4N)(CrOCl_4)$. The reactant concentrations were 0.21 *M* 2-butanol and 0.081 *M* $(Et_4N)(CrOCl_4)$. The consumption of 2-butanol after 16 h was 93% while the yield of methyl ethyl ketone was also 93%.

Acknowledgment

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