C–H Bond Activation by Metal Oxo Species: Chromyl Chloride Oxidations of Cyclooctane, Isobutane, and Toluene

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Abstract: Chromyl chloride, CrO_2Cl_2, oxidizes cyclooctane, isobutane, and toluene under mild conditions (25–60 °C). The reactions give chlorinated products (chlorocyclooctane, *tert*-butyl chloride, and benzyl chloride) and a dark chromium-containing precipitate. Hydrolysis of the precipitate yields oxygenated products, such as ketones, aldehydes, chloro ketones, epoxides, and alcohols. Kinetic data show that all of the reactions are first order in CrO_2Cl_2 and first order in substrate, with no sign of an induction period. Primary isotope effects have been observed for t-d_1-isobutane and d_8-toluene. The kinetic and mechanistic data indicate that the reactions proceed by initial hydrogen atom transfer from the substrate to CrO_2Cl_2. The rates of hydrogen atom abstraction by CrO_2Cl_2 vary in the order cyclohexane < cyclooctane ≃ isobutane < toluene and are directly related to the strength of the C–H bond being cleaved. A correlation is observed between $\Delta H^\ddagger$ and $\Delta S^\ddagger$, indicating a common mechanism for the four substrates. The pathways leading from the initially formed alkyl radicals to the observed products are described. The ability of CrO_2Cl_2 to abstract a hydrogen atom from alkanes is remarkable, as it is a closed-shell, diamagnetic species, not a radical. It is proposed that the hydrogen atom abstracting ability derives from the strong O–H bond formed on hydrogen atom transfer, in $[Cl_2(O)Cr(OH)]$. The rates of the CrO_2Cl_2 reactions correlate with rates of hydrogen atom abstraction by oxygen radicals, assuming a CrO–H bond strength of 83 kcal/mol (similar to that in $HMnO_4^-$). The implications of this perspective for transition metal mediated hydrogen atom transfer reactions are discussed.

Introduction

The selective oxidation of hydrocarbons is of importance in the production of fuels, commodity chemicals, and fine chemicals.[1] Metal oxo complexes and metal oxide surfaces are common reagents or catalysts for hydrocarbon oxidations, in the laboratory, in the industrial plant, and in metalloenzyme active sites (for instance, in cytochrome P-450 enzymes).[1–4] It has been known for over a century that chromyl chloride (CrO_2-Cl_2), permanganate (MnO_4^-), and other metal oxo compounds oxidize alkanes and arylalkanes.[3,5,6] Organic radical intermedi-

ates have been implicated in homogeneous, heterogeneous, and enzymatic hydrocarbon oxidations,[2–8] but in general the mechanisms are not well understood and, perhaps most importantly, it is not clear what features of these oxidants enable them to oxidize C–H bonds. In many cases the details of the C–H activation step are clouded by an inability to observe and study the reactive species.

We recently reported a detailed study of the oxidation of cyclohexane by chromyl chloride as a model system for C–H bond activation by high-valent metal oxo species.[9] CrO_2Cl_2 oxidizes cyclohexane by initial abstraction of a hydrogen atom

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(eq 1). The resulting cyclohexyl radical is then rapidly trapped
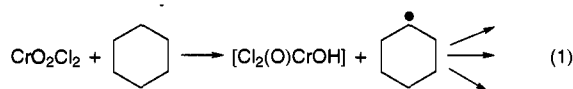
by high oxidation state chromium by one of three pathways: chlorine atom transfer to give chlorocyclohexane, carbon−oxygen bond formation leading to cyclohexanone, or transfer of a second hydrogen atom to give cyclohexene, which is further oxidized under the reaction conditions.

The observation that a diamagnetic species such as CrO_2Cl_2 is capable of cleaving the strong C−H bond in cyclohexane is surprising. Hydrogen atom abstraction mechanisms have been viewed as the domain of radical species (with a few exceptions[10]). This bias derives from our foundation in organic chemistry but has found its way into the inorganic, organometallic, and enzymatic literature as well.[1−8] We suggested that radical character is not a factor in determining propensity for reaction by hydrogen atom abstraction.[9] Chromyl chloride is able to abstract a hydrogen atom primarily because of the strength of the O−H bond formed in [Cl_2(O)CrOH]. We proposed that the reactivity of CrO_2Cl_2 is quite similar to that of an oxygen centered radical, such as *tert*-butylperoxy ($^tBuOO^\bullet$) and *tert*-butoxy ($^tBuO^\bullet$) radicals, based on the strength of the O−H bond formed rather than any radical character.

We report here studies of the oxidations of cyclooctane, isobutane, and toluene by CrO_2Cl_2. This expansion of the original study was undertaken to test the conclusions concerning both the C−H activation step as well as the subsequent steps leading to the observed products. Many studies have examined the oxidation of toluene and related alkyl aromatics by CrO_2-Cl_2 (and chromic acid in various forms).[5] A variety of mechanisms have been suggested, including radical (chain and nonchain) pathways, carbocation routes, and concerted mechanisms. The nature of the chromium product has also been much discussed. A charge-transfer complex is observed in reactions of CrO_2Cl_2 with arenes,[5d,11] but the extent of complex formation and its possible effect on the oxidation mechanism have not been addressed. Only approximate kinetic parameters and isotope effects are available[12,13] and a mass balance for the reaction has not been reported. In sum, a clear picture of the oxidation of toluene by CrO_2Cl_2 has not emerged. The oxidations of isobutane and cyclooctane by CrO_2Cl_2 or chromic acid have received only cursory attention.[14]

The studies reported here demonstrate that the CrO_2Cl_2 oxidations of cyclooctane, cyclohexane, isobutane, and toluene are very similar. All four reactions proceed via nonchain radical

mechanisms, and different aspects of the radical trapping and its cascade to products are revealed by the different substrates. Most importantly, this study allows a comparison of the absolute and relative rates of hydrogen atom abstraction by CrO_2Cl_2. This confirms that CrO_2Cl_2 exhibits radical-like selectivity. The absolute rates correlate with the exo- or endothermicity of the hydrogen atom transfer step, as predicted by the Polanyi equation. Thus the rates correlate with the strength of the C−H bond being cleaved, comparing the reactions of secondary (cyclohexane, cyclooctane), tertiary (isobutane), and benzylic hydrogens (toluene). The rates also correlate with the rates of hydrogen atom abstraction from these substrates by $^tBuOO^\bullet$ and $^tBuO^\bullet$ radicals. The implications of these correlations are discussed.

Experimental Section

General. All reaction mixtures were prepared in a drybox (N_2 atmosphere) or by vacuum transfer of the necessary reagents. Reactions were run in greaseless Pyrex (or quartz) reaction vessels, sealed with a Teflon valve with ground glass joint attachment, and stirred with Teflon-coated stir bars. Reactions were prepared in the dark with the aid of photographic safe-lights and run under N_2 or *in vacuo* shielded from exposure to light. CrO_2Cl_2 (99.99%, Aldrich) was stored in a greaseless, light-free glass vessel and was vacuum transferred prior to use in a vacuum line greased with KRYTOX fluorinated grease (DuPont). *Caution: CrO_2Cl_2 is a corrosive and carcinogenic volatile liquid that should be handled with extreme caution.* Cyclohexane (99+%, Aldrich) was purified[15] by washing with concentrated H_2SO_4/ HNO_3, followed by 5% aqueous NaOH and deionized H_2O until the washings were neutral. The material was then passed down a column of activated silica, predried with P_2O_5, and vacuum transferred onto sodium metal, from which it was vacuum transferred before use. Cyclooctane (Columbian Carbon Co.) was purified[15] by washing with concentrated H_2SO_4 followed by saturated aqueous $NaHCO_3$ and deionized H_2O until the washings were neutral. The material was then dried over $MgSO_4$ and filtered, and the resulting filtrate was fractionally distilled and the middle fraction collected. After passing this material down a column of activated silica it was further dried over sodium metal then distilled under N_2. The liquid collected was degassed on the vacuum line before storage in a greaseless, Teflon-valve-sealed container in a drybox. Isobutane (Aldrich, 99%) and isobutylene (Aldrich, 99+%) were used as received. *tert*-Butyl alcohol (Baker, 99%) and isopropyl alcohol (Aldrich, 99.9%) were dried over sieves and vacuum transferred prior to use. Toluene (Baker, 99.9%) was purified[15] by washing with concentrated H_2SO_4 while being cooled in an ice bath. This was followed by washing with saturated aqueous $NaHCO_3$ then deionized H_2O until the washings were neutral. The material was then pre-dried with P_2O_5 and vacuum transferred onto sodium metal, from which it was vacuum transferred before use. d_8-Toluene (Cambridge Isotope) was dried over sieves, stored over CaH_2, and vacuum transferred before use. *tert*-Butylbenzene (Aldrich, 99%) was purified[15] in the same manner as toluene except after washing with cold concentrated H_2SO_4 the material was washed repeatedly with 4% aqueous NaOH and then deionized H_2O until neutral. The material was then dried over $MgSO_4$ and filtered, and the resulting filtrate was further dried over sodium metal from which it was fractionally distilled under N_2 and the middle fraction collected. This liquid was degassed

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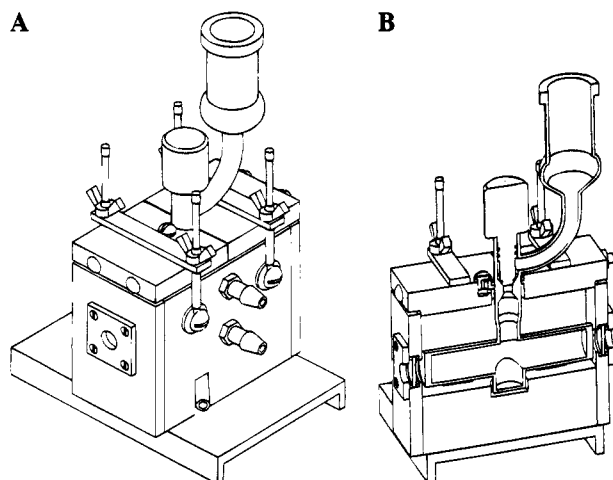
C—H Bond Activation by Metal Oxo Species

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A   **B**

Figure 1. Drawings of the long-path UV−vis cell and cell holder used in the kinetic experiments: (A) exterior view: (B) cut-away view of cell and cell holder, showing the well for the reaction solution at the bottom of the cell and the Teflon stopcock and 24/40 glass joint at the top. The air-driven stir motor is not shown. The apparatus is mounted in the spectrometer such that the light path proceeds through the vapor above the reaction solution.

on the vacuum line before storage in a greaseless, Teflon-valve-sealed container in a drybox. All the other reagents were used as received.

Organic oxidation products were identified and quantified by application of a variety of techniques depending on the substrate (see below). GC/FID analyses were performed on a Hewlett Packard 5790A instrument connected to a Hewlett Packard 3390A integrator. Products were identified by comparison of their GC retention times with authentic samples and by GC/MS using a Kratos Profile mass spectrometer. Product quantification by GC/FID was done by one-point calibration to an internal standard. ^{1}H NMR spectra were obtained using a Bruker AM-300 spectrometer. Chemical shifts are referenced to residual protons in the solvent or (in D_2O) to DSS ($Me_3SiCH_2CH_2CH_2SO_3Na$, sodium 2,2-dimethyl-2-silapentane-5-sulfonate, MSD Canada), which was also used as an internal standard for quantitation of the products. IR analyses for CO_2 were performed using an 8 cm quartz gas IR cell in a Perkin-Elmer 1720 FT-IR flushed with N_2. HPLC analyses were accomplished with a Hitachi L-6200 pump connected to a Hitachi L-4250 UV/vis detector set at 250 nm and a Hitachi D-2500 integrator. HPLC separation was accomplished using a Beckman 25 cm/4.6 mm Ultrasphere ODS column running 80% Millipore H_2O (0.1% TFA) and 20% acetonitrile. Products were identified and quantified by comparison of their HPLC retention times and intensities with authentic samples using potassium hydrogen phthalate (KHP) as an internal standard.

Kinetics. Reactions were followed by UV/vis analysis of the CrO_2Cl_2 in the vapor phase above the reaction solution. This general method for kinetic data collection has been described for the reaction of CrO_2Cl_2 with cyclohexane.[9a] Cyclooctane, isobutane, and toluene react at lower temperatures than cyclohexane, so longer pathlength cells were used to make up for the lower vapor pressure of CrO_2Cl_2 above the reaction solutions. An 8 cm path length quartz cell (total volume = 21.6 mL) sealed to a Teflon needle valve was used for the cyclooctane reactions, and a similar thick-walled Pyrex cell (8 cm path length, total volume = 17.1 mL) was used for toluene and isobutane reactions (the latter were run at elevated pressures, 3−4 atm). Reaction temperatures were regulated by complete immersion of the cell volume and headspace in a water-tight chamber with quartz windows (Figure 1) connected to a circulating water bath (Lauda Model K-2/R). Complete immersion is required to prevent refluxing within the cell. Rapid equilibration between the vapor and liquid phases is facilitated by continuous stirring of the reaction solution using an air-driven stirring plate mounted in the base of the cell holder. This apparatus, like the original,[9] is mounted in the sample compartment of a Hewlett Packard 8452A diode array spectrophotometer. The CrO_2Cl_2 absorbance in the vapor at λ_{max} = 292 and 408 nm was shown to be linearly related to the CrO_2Cl_2

concentration in cyclohexane solution at 25 °C. A spectrum of the vapor of the appropriate solvent at the fixed temperature was used as the blank.

Analysis of the kinetics data was performed as described previously for reactions of cyclohexane with CrO_2Cl_2.[9a] The use of the 8 cm path length cells greatly reduced the contribution to the apparent absorbance due to precipitate (Étard complex) forming in the light path. For reactions employing the Pyrex cell, which cuts off the peak with λ_{max} = 292 nm, the CrO_2Cl_2 concentration at time t, $[CrO_2Cl_2]_t$, was calculated using the CrO_2Cl_2 λ_{max} at 408 nm in conjunction with a single reference wavelength, 352 nm.

Iodometric Titrations of Étard Complexes. Iodometric titrations were performed under a flow of N_2, following the procedures of Vogel.[16] using soluble starch as the indicator. The same procedure was used on isolated Étard complexes derived from cyclooctane, isobutane, and toluene; a sample procedure follows. After heating a reaction mixture of 0.123 mmol of CrO_2Cl_2 in 1.00 mL of cyclooctane for 5 h at 40 °C, the volatiles were removed *in vacuo*. To the brown solid remaining in the reaction vessel was added 4 mL of 0.92 M aqueous KI. followed immediately by 2 mL of 0.35 M aqueous H_2SO_4 and 5 mL of deionized H_2O, giving a clear brown/green solution. A buret containing 25.5(3) mM aqueous $Na_2S_2O_3$ solution (concentration determined by titration of $K_2Cr_2O_7$ primary standard done the same day) was connected to the reaction vessel via a rubber septum. After addition of 2 mL of the $Na_2S_2O_3$ solution from the buret to the solution in the reaction vessel, the buret was momentarily disconnected as 3 drops of a near-saturated solution of aqueous soluble starch (prepared shortly before the titration, by addition of soluble starch to boiling H_2O) was added to the solution in the reaction vessel. This resulted in a color change to clear navy blue. The buret was reconnected to the reaction vessel and the titration was continued to the end point, a rapid color change from navy blue to pale green, upon addition of 4.10 ± 0.07 mL of $Na_2S_2O_3$ solution. A repeat of this procedure on a second sample of complex resulting from an identical reaction required 4.25 ± 0.07 mL. It has been shown previously, for titrations of Étard complex resulting from reaction of cyclohexane, that varying the concentration of the KI solution by a factor of 15 has no significant effect on the results, indicating that chromium is efficiently reduced by I^- rather than by the organic matter present.[9]

Reactions of CrO_2Cl_2 with Cyclooctane. In a typical procedure, 1.00 ± 0.02 mL of cyclooctane was measured out using a volumetric flask and added to a reaction vessel containing a stir bar. Into the flask was syringed 10.0 ± 0.2 μL of CrO_2Cl_2 (0.123 mmol). The needle valve on the reaction flask was quickly closed and the vessel was removed from the glovebox. The flask was then stirred for 5 h in a light-free, temperature-controlled circulating water bath at 40 °C, over which time a brown precipitate formed and the solution turned from clear red to colorless. The flask was removed from the water bath and opened to the atmosphere, and 1 mL of 0.2 M aqueous $Na_2S_2O_3$ was added to give a clear green aqueous layer and a colorless organic phase. After addition of 5 mL of diethyl ether and 10.0 ± 0.2 μL of *tert*-butylbenzene standard, the resulting mixture was allowed to stir for several minutes. An aliquot of the organic layer was then removed and analyzed by GC/FID and GC/MS. Yields are given in Table 1.

For reactions of CrO_2Cl_2 with cyclooctane diluted with cyclohexane, a stock cyclooctane/cyclohexane solution was first prepared in the glovebox from 2.457 ± 0.001 g of cyclohexane (0.02919 mol) and 3.898 ± 0.001 g of cyclooctane (0.03474 mol) for a total volume of 7.88 ± 0.05 mL. Reactions mixtures were prepared and worked up as described above. At 40 °C reactions of 10.0 ± 0.2 μL of CrO_2Cl_2 (0.123 mmol) in 1.00 ± 0.02 mL of the cyclooctane/cyclohexane stock solution proceed to completion in 9 h.

Syntheses of Oxidation Products. Chlorocyclooctane was synthesized from cyclooctene by hydrochlorination[17] and isolated as a clear liquid after chromatography on silica gel with pentane. The product was 97% pure by GC/FID. GC/MS: M^+ = 146. ^{1}H NMR (C_6D_6): δ

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Table 1. Product Yields from Reactions of CrO_2Cl_2 and Cyclooctane

$[CrO_2Cl_2]_i$[a]	$[C_8H_{16}]$[b]	Temp.			% yield versus CrO_2Cl_2 reacted[c]		Av. Cr oxidation state[d]	Yield in oxidative equiv.	estimated % Yield of $^-O_2C(CH_2)_6CO_2^-$[e]	moles CrO_2Cl_2[e] / moles products
0.123M	neat (7.42M)	25°C	14.5(2)	19(1)	3.0(1)	3.4(1)	2.6(2)	3.94(3)	68(2)%	6.6%	2.04(6)
0.123M	neat (7.31M)	40°C	13.9(5)	19.6(6)	3.6(2)	3.6(2)	2.7(1)	3.87(3)	68(2)%	6.7%	2.00(6)
0.123M	+ C_6H_{12} (4.35M)	40°C	12.8(5)	19.9(2)	4.0(2)	1.5(2)	2.8(6)	3.88(3)	67(2)%	6.9%	2.09(6)
0.123M	neat (7.18M)	58°C	14.5(3)	19.6(4)	4.4(1)	3.0(2)	2.3(2)	3.74(3)	66(2)%	7.7%	1.94(6)

% yields versus cyclooctene reacted[c]

	Temp.					Undetected Cyclooctene oxidation products
0.308 mmol CrO_2Cl_2, 0.0384 mmol C_8H_{14}, in 1.25 mL C_6H_{12}	40 °C	--	trace	34(2)	--	20(3)	46(4)
0.247 mmol CrO_2Cl_2 0.0384 mmol C_8H_{14} in 1.60 mL C_6H_{12}	25 °C	--	trace	29(3)	--	19(4)	52(5)

[a] Initial concentration of CrO_2Cl_2. [b] Molar concentration of neat cyclooctane calculated from its density, from ref 20. The concentration of cyclooctane in cyclohexane assuming ideal behavior in both liquid and vapor phases. [c] Yields averaged from at least two reactions; the value in parentheses is one standard deviation. Average chromium oxidation state in the isolated precipitate (Étard complex) determined by iodometric titration. Value reported is the average from two experiments. [d] Yield calculated from oxidative equivalents unaccounted for in the observed products. [e] The average number of moles of CrO_2Cl_2 consumed per mole of cyclooctane product formed (the reaction stoichiometry).

3.93 (m, 1 H), 1.85 (m, 4 H), 1.1−1.7 (m, 10 H). **2-Chlorocyclooctanone:** In the glovebox, a solution of 0.5 g (4.5 mmol) of cyclooctene in 5 mL of cyclohexane was added dropwise to a stirred solution of 1.4 g (9 mmol) of CrO_2Cl_2 in 5 mL of cyclohexane over the course of 10 min. A brown precipitate formed immediately. This mixture was heated to 50 °C for 3 h before the reaction was quenched (in the air) with 10 mL of 0.1 M aqueous $Na_2S_2O_3$ solution. After extraction with Et_2O, 2-chlorocyclooctanone was isolated by column chromatography on silica gel, eluting with pentane then with 5% (v/v) EtOAc in pentane. Further purification with a second column, using 2% EtOAc in pentane, gave ca. 100 mg of a clear, colorless, liquid that was 84(1)% 2-chlorocyclooctanone by GC/FID, with a 10(1)% cyclooctanone impurity. GC/MS: M^+ = 160. ¹H NMR (C_6D_6): δ 3.95 (dd, 6 Hz, 4 Hz, 1 H), 2.35 (m, 1 H), 1.6−2.1 (m, 3 H), 0.8−1.6 (m, 8 H). **Cyclooctanol** was formed virtually quantitatively by reduction of cyclooctanone by $NaBH_4$ in methanol.[18] >98% pure by GC/FID. GC/MS: M^+ = 128. ¹H NMR (C_6D_6): δ 3.62 (m, 1 H), 1.1−1.9 (m, 15 H). **Cyclooctene oxide:** *m*-Chloroperbenzoic acid oxidation of cyclooctene in CH_2Cl_2, following standard procedures,[19] gave material that was 91(1)% cyclooctene oxide and 6(1)% *m*-chlorobenzoic acid by GC/FID. GC/MS: M^+ = 126. ¹H NMR (C_6D_6): δ 2.61 (m, 2 H), 1.94 (m, 2 H), 1.0−1.4 (m, 10 H).

Reaction of CrO_2Cl_2 with Cyclooctene. A reaction vessel was charged with 0.308 mmol of CrO_2Cl_2, 1.00 mL of cyclohexane, a stir bar, and a sealed breakseal vial containing 0.038 mmol of cyclooctene in 250 µL of cyclohexane, which had been sealed under vacuum. After 10 min of stirring in a 40 °C water bath, the reaction flask was quickly shaken, breaking the vial containing the cyclooctene solution, and returned to the bath. Every 30 min the reaction flask was periodically removed from the bath and vigorously shaken to ensure complete mixing. After 2 h, a significant quantity of brown precipitate was visible in the bottom of the flask but the supernatant remained clear red in color suggesting that some of the CrO_2Cl_2 remained unreacted. The reaction was quenched by the addition of 1 mL of 1 M aqueous

$Na_2S_2O_3$, followed by 5 mL of Et_2O and 5.0 ± 0.2 µL of *tert*-butylbenzene. The Et_2O layer was analyzed by GC/FID (Table 1). A similar reaction of CrO_2Cl_2 with cyclooctene at 25 °C was accomplished in the glovebox by adding 50-µL aliquots of a solution of 0.038 mmol of cyclooctene in 300 µL of cyclohexane, every 5−10 min. to a solution of 0.247 mmol of CrO_2Cl_2 in 1.00 mL of cyclohexane that had been initially stirred for 40 min. After six aliquots, the cyclooctene vial was rinsed with 300 µL of cyclohexane, these washings were added, and the solution was stirred for 20 min prior to workup as above.

Kinetics of CrO_2Cl_2 Oxidation of Cyclooctane. Solutions were prepared in the glovebox by dilution of the appropriate volume of CrO_2Cl_2 to 1.00 ± 0.02 mL with either cyclooctane or cyclooctane/ cyclohexane solution. The solution and a Teflon covered stir bar were added to the 8 cm quartz cell. The cell was evacuated on the vacuum line, after the reaction solution had been cooled to −78 °C. Reaction solutions were allowed to thaw prior to placing the cuvette in the special cell holder, as described above. Spectra were taken from 250 to 600 nm. The data analysis was performed as described above. The cyclooctane concentrations of neat cyclooctane were calculated from the molar densities at the appropriate temperatures.[20] Concentrations in cyclooctane/cyclohexane mixtures were calculated using the molar densities of the pure liquids, assuming ideal behavior. Reaction conditions and rate constants are reported in Table 2.

Reactions of CrO_2Cl_2 with Isobutane. Reaction vessels with consistent internal volumes (with stir bar, 26.8(7) mL) were constructed to ensure reproducible isobutane concentrations. In the glovebox, a reaction vessel was charged with 1.00 ± 0.02 mL of cyclohexane, a stir bar, and 10.0 ± 0.2 µL of CrO_2Cl_2 (0.123 mmol). The vessel was attached to the vacuum line, cooled to −78 °C, and evacuated. The vacuum manifold (internal volume = 1.078 L) was filled to 130 Torr with isobutane (7.61 mmol, assuming ideal behavior). The isobutane was condensed into the reaction vessel cooled in liquid N_2. The reaction vessel was stirred for 18 h in a light-free, temperature-controlled water bath at 60 °C, forming a brown precipitate while the solution turned

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(20) Design Institute for Physical Property Data (DIPPR) file, American Institute of Chemical Engineers (AIChE), provided by the *Scientific & Technical Information Network (STN)*.

C–H Bond Activation by Metal Oxo Species

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Table 2. Rate Constants for Reactions of CrO_2Cl_2 with Cyclooctane, Isobutane, and Toluene

	reaction	temp[a] °C	initial $[CrO_2Cl_2]$, mol/L	substrate concn,[b] mol/L	k_{obs},[c,d] $\times 10^{-4}$ s^{-1}	$k^e \times 10^{-5}$ M^{-1} s^{-1}
			Cyclooctane[f]			
1	$CrO_2Cl_2 + C_8H_{16}$	25.00	0.123	7.42	0.729(±0.006)	0.983(±0.08)
2a	$CrO_2Cl_2 + C_8H_{16}$	32.97	0.123	7.36	1.67(±0.03)	2.27(±0.04)
2b	$CrO_2Cl_2 + C_8H_{16}$	32.97	0.123	7.36	1.63(±0.07)	2.21(±0.09)
3a	$CrO_2Cl_2 + C_8H_{16}$	40.00	0.123	7.31	3.31(±0.02)	4.53(±0.03)
3b	$CrO_2Cl_2 + C_8H_{16}$	40.00	0.123	7.31	3.38(±0.07)	4.62(±0.10)
4	$CrO_2Cl_2 + C_8H_{16}$ in C_6H_{12}[g]	40.00	0.123	4.35	1.77(±0.01)	4.07(±0.03)
5a	$CrO_2Cl_2 + C_8H_{16}$	50.00	0.0987	7.24	8.78(±0.39)	12.1(±0.5)
5b	$CrO_2Cl_2 + C_8H_{16}$	50.00	0.0987	7.24	9.02(±0.19)	12.5(±0.3)
6a	$CrO_2Cl_2 + C_8H_{16}$	57.80	0.0617	7.18	19.20(±0.06)	26.7(±0.1)
6b	$CrO_2Cl_2 + C_8H_{16}$	57.80	0.0617	7.18	18.36(±0.13)	25.6(±0.2)
			Isobutane[h]			
7a	$CrO_2Cl_2 + C_4H_{10}$	40.00	0.0719	3.70	1.15	0.311
7b	$CrO_2Cl_2 + C_4H_{10}$	40.05	0.0652	4.21	1.31	0.312
8a	$CrO_2Cl_2 + C_4H_{10}$	50.00	0.0630	4.21	4.18	0.992
8b	$CrO_2Cl_2 + C_4H_{10}$	50.10	0.0834	2.67	2.58	0.967
9a	$CrO_2Cl_2 + C_4H_{10}$	60.00	0.0763	3.05	8.12	2.66
9b	$CrO_2Cl_2 + C_4H_{10}$	60.00	0.0753	3.12	7.19	2.30
10a	$CrO_2Cl_2 + C_4H_{10}$	68.50	0.0371	3.08	16.30	5.29
10b	$CrO_2Cl_2 + C_4H_{10}$	68.50	0.0374	3.03	15.82	5.22
11	$CrO_2Cl_2 + C_4H_9D^i$	59.90	0.0736	3.25	4.61	1.42
12	$CrO_2Cl_2 + C_4H_{10}$ gas phase reaction	80.00	4.8×10^{-5}	0.161	0.69	43
			Toluene[h]			
13a	$CrO_2Cl_2 + C_7H_8$	29.40	0.122	1.85	3.53	19.1
13b	$CrO_2Cl_2 + C_7H_8$	29.36	0.122	1.85	3.45	18.7
14a	$CrO_2Cl_2 + C_7H_8$	40.12	0.0843	1.37	5.96	43.7
14b	$CrO_2Cl_2 + C_7H_8$	40.12	0.0843	1.83	7.70	42.1
14c	$CrO_2Cl_2 + C_7H_8$	40.14	0.0603	1.19	4.95	41.7
15a	$CrO_2Cl_2 + C_7H_8$	49.93	0.0596	1.17	11.56	98.7
15b	$CrO_2Cl_2 + C_7H_8$	49.93	0.0596	1.17	11.25	96.1
16a	$CrO_2Cl_2 + C_7H_8$	59.90	0.0588	1.16	25.32	219
16b	$CrO_2Cl_2 + C_7H_8$	59.90	0.0588	1.16	25.14	217
17a	$CrO_2Cl_2 + C_7D_8$	50.00	0.0596	1.17	1.48	12.6
17b	$CrO_2Cl_2 + C_7D_8$	50.00	0.0596	1.17	1.44	12.3
			tert-Butylbenzene			
18	$CrO_2Cl_2 + PhCMe_3$	60.00	0.123	6.46	0.407	0.63

[a] Temperature ±0.10 °C. [b] The calculation of substrate concentrations is presented in the Experimental Section. [c] The errors reported for cyclooctane are the spread of the individual data treatments (see Experimental Section). For the other substrates, the data treatment does not generate an estimate of error; errors are estimated at ±3%. [d] The rate constants reported for reactions of isobutane are based on initial rates and have been adjusted to account for competitive attack at the cyclohexane solvent. [e] Second-order rate constants calculated by dividing k_{obs} by the concentration of substrate at the stated temperature. [f] Reactions of cyclooctane were run in neat substrate unless otherwise noted. [g] Reaction run in the presence of 46% by mole cyclohexane. [h] Reactions run in cyclohexane, except for the gas-phase reaction. [i] Deuterated at the tertiary position: $(CH_3)_3CD$.

colorless. These steps were all performed in the dark with the aid of a photographic safe-light.

The volatiles were collected by short-path vacuum transfer directly from the reaction vessel. Toluene (0.7 mL) and methylcyclohexane standard (5.0 ± 0.2 μL) were added to the isolated volatiles, which were analyzed by GC/FID and GC/MS. CD_3CN (0.5 mL) was vacuum transferred into the reaction vessel containing the Étard complex and, after stirring for several minutes, the volatiles were collected by short-path vacuum transfer into a flask containing 1.81 μmol of DSS standard. To the solid remaining in the reaction flask, 0.5 mL of 1 M $Na_2S_2O_3$ in D_2O was added by syringe, under flow of N_2. After degassing the reaction flask, the volatiles were collected by short-path vacuum transfer to the flask already containing the CD_3CN solution. In this manner, organic products in the Étard complex such as acetone, *tert*-butyl alcohol, and cyclohexanone were quantitatively recovered, as verified by control experiments. Initial treatment with CD_3CN *before* hydrolysis is necessary to avoid oxidation of aldehyde products during aqueous $Na_2S_2O_3$ workup. This could be avoided by employing the more efficient Cr(VI) reductant, KI; however, the I_2 that vacuum transfers with the products created other problems. The CD_3CN/D_2O solution collected was analyzed by ^1H NMR. Products were identified and quantified by ^1H NMR spectra and by comparison with authentic samples (see below) whenever possible (Table 4). The reaction mixtures and authentic samples were stable in the CD_3CN/D_2O solution.

Reactions of CrO_2Cl_2 with t-d_1-isobutane, $(CH_3)_3CD$, were performed and analyzed in the same manner as described above, with longer reaction times because of the mild isotope effect (Table 4). t-d_1-

Isobutane was prepared as follows. A solution of 23 mL of 2 M ^tBuMgCl in Et_2O (Aldrich) in 50 mL of dry triglyme was left under dynamic vacuum for 3 h to remove all traces of the Et_2O solvent. D_2O (0.39 g, Cambridge Isotope, 99.9%) was vacuum transferred into the reaction vessel cooled in liquid N_2. The reaction was stirred at 25 °C for 15 h, then cooled to 0 °C, and the t-d_1-isobutane was vacuum transferred into a flask at −196 °C. Yield: 1.16 g, 43% based on ^tBuMgCl. GC/MS: 59. ^1H NMR (C_6D_6): δ 0.84 (1:1:1 t, $^3J_{HD}$ = 1 Hz). No tertiary proton resonance is observed, so the enrichment is estimated to be >98%.

Syntheses of Oxidation Products. 2-Chloro-2-methylpropionaldehyde was prepared following the procedure in ref 21. GC/MS: 106. ^1H NMR (D_2O): δ 4.91 (s, 1 H), 1.54 (s, 6 H). **2-Hydroxy-2-methylpropionaldehyde** was produced in D_2O solution by H_2SO_4-catalyzed hydrolysis of its dimethylacetal.[21] ^1H NMR (D_2O): 4.76 (s, 1 H), 1.17 (s, 6H). **1,2-Hydroxy-2-methylpropane** was generated *in situ* by addition of 0.5 equiv of KOH to a solution of isobutylene oxide in D_2O.[22] ^1H NMR (D_2O): 3.40 (s, 2H), 1.18 (s, 6H). Attempts to synthesize **2-chloro-2-methyl-1-propanol**[23] were not successful. Singlets at δ = 3.52 and 1.52 in the ^1H NMR (CD_3CN/D_2O) of the isobutane reaction products are assigned to this compound because (i) they were consistently in a 1:3 ratio, (ii) the upfield chemical shift is

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Table 3. Rates. Isotope Effects, and Activation Parameters for the Initial Step of Reactions of CrO_2Cl_2 with Cyclohexane, Cyclooctane, Isobutane, and Toluene

substrate[a]	$k(340\ K)$, $M^{-1}\ s^{-1}$ [b]	k_H/k_D	$\Delta H^\ddagger$ kcal/mol	$\Delta S^\ddagger$ {per H}[c] eu	$\Delta G^\ddagger$ {per H}[c] kcal/mol	$D(C-H)$,[d] kcal/mol
C_6H_{12}[a]	1.38×10^{-7}	$2.2(2)^e$	26.6(8)	$-7(2)$ {$-12(2)$}	30.0(7) {30.7(7)}	95.5(10)
C_8H_{16}	1.86×10^{-5}		19.4(2)	$-17.9(5)$ {$-22.8(5)$}	25.5(3) {27.4(3)}	92.6(15)
$(CH_3)_3CH$	2.33×10^{-5}	$2.3(3)^f$	20.4(8)	$-20(5)$ {$-20(5)$}	27.2(7) {27.2(7)}	92.0(10)
$C_6H_5CH_3$	7.03×10^{-4}	$8.0(8)^g$	15.5(4)	$-25(1)$ {$-28(1)$}	24.2(5) {24.9(5)}	87.9(15)

[a] Data for cyclohexane from ref 9a. [b] Rate constant per reactive hydrogen (12 per molecule of cyclohexane. 16 for cyclooctane, 1 for isobutane. and 3 for toluene). [c] At 340 K. Values in { } are activation parameters on a per hydrogen basis. [d] See text. [e] $k_{C_6H_{12}}/k_{C_6D_{12}}$ measured at 75.00 °C. [f] Determined from the yields of $(CH_3)_3CCl$ and $C_6H_{11}Cl$ in reactions of $(CH_3)_3CH$ and $(CH_3)_3CD$ in cyclohexane at 59.90 °C. [g] $k_{C_6H_5CH_3}/k_{C_6D_5CD_3}$ measured at 50.00 °C.

Table 4. Product Yields from Reactions of CrO_2Cl_2 with Isobutane and Related Substrates

reaction	conditions	Cl	O	⟍O	Cl O	Cl OH	OH	OH Cl	OH O	HO OH	(CO₂ + CO₃²⁻)	other products	Av. Cr oxidation state[b]
1. CrO_2Cl_2 (0.0762M) + Me_3CH (3.07M) in cyclohexane (5.69M)	60°C	7.6(7)	3.9(2)	5.7(5)	0.70(6)	0.43(2)	0.28(2)	0.40(9)	0.20	0.13	0.61	2.0(3)% chloro-cyclohexane[c]	3.49(3)
2. CrO_2Cl_2 (0.0736M) + Me_3CD (3.25M) in cyclohexane (5.51M)	60°C	4.5	3.5	4.5	0.7	0.2	0.3	0.3	0.3	0.3	d	2.7% chloro-cyclohexane[e]	d
3a. CrO_2Cl_2 (0.247mmol) + $Me_2C=CH_2$ (52μmol) in cyclohexane (1.00mL)	60°C, 1 h	—	12.5	27.4	3.9	3.3	--	2.5	0.5	0.8	d	d	d
b. CrO_2Cl_2 (0.247mmol) + $Me_2C=CH_2$ (54μmol) in cyclohexane (1.00mL)	60°C, 10 min	--	9.3	37.7	5.0	10.3	--	2.9	0.5	1.7	d	d	d
4. CrO_2Cl_2 (0.247mmol) + Me_3COH (64μmol) in cyclohexane (1.00mL)	60°C, 4 h	--	5.3	2.4	0.7	1.4	6.1	0.9	0.1	0.5	d	d	d
5. CrO_2Cl_2 (0.185mmol) + Me_2CHOH (65μmol) in cyclohexane (1.00mL)	25°C, 1 h; then 60°C, 2 h	—	100	--	—	--	--	--	—	—	d	d	d

[a] Yields reported versus moles of the limiting reagent, CrO_2Cl_2 in entries 1 and 2 and the organic reagent in entries 3—5. Errors reported from the average of two or more experiments. [b] Average chromium oxidation state in the isolated precipitate (Étard complex) determined by iodometric titration. Value reported is the average from two experiments. [c] Cyclohexanone and 2-chlorocyclohexanone also observed but could not be quantified separately by ^1H NMR. Total yield of the two products = 2.6(2)%. [d] Products were not quantified. [e] Cyclohexanone and 2-chlorocyclohexanone were also observed but could not be quantified separately by ^1H NMR. Total yield of the two products = 3%.

within 0.05 ppm of that of 2-chloro-2-methylpropionaldehyde and ≥0.3 ppm downfield from the tertiary alcohol products, and (iii) they were only observed upon hydrolysis of the Étard complex, not in the CD_3-CN volatiles prior to hydrolysis, suggesting that the product is an alcohol.

Determination of CO_2 Yield. The volatiles from a standard reaction were vacuum transferred into the 8 cm path length quartz cell. The cell was mounted in the chamber of the IR spectrometer under a nitrogen flow and vigorous purging was continued until absorbance at 2360 cm^{-1} became constant. Spectra were taken of the headspace above the cyclohexane/isobutane solution using the evacuated cell under N_2 purge as the blank. Absorbance due to isobutane in the headspace was subtracted independently using a stored spectrum. Spectra showed the presence of CO_2 ($\nu_{max} = 2360$ cm^{-1}) but not CO. CO_2 was quantified (0.34(2)% versus CrO_2Cl_2) by addition of a known quantity of CO_2 from a gas addition bulb to the cell still containing the reaction volatiles and determination of an extinction coefficient by comparison of the change in the CO_2 absorbance with the moles added.

To determine the amount of carbonate or bicarbonate. the Étard complex from a standard reaction was treated with 164 mg of solid $Na_2S_2O_3 \cdot 5H_2O$ under flow of N_2, the reaction vessel was evacuated. and 0.5 mL of degassed 0.1 M aqueous HCl solution was added by vacuum transfer. After the solution was stirred for several minutes, the volatiles were vacuum transferred into the 8-cm path length quartz cell and analyzed for CO_2 as above, giving a yield of 0.25(2)%. Using the above procedures on a sample of K_2CO_3 gave quantitative recovery of carbonate as CO_2.

Reactions of CrO_2Cl_2 with Isobutylene. In the glovebox. a reaction vessel was charged with 0.247 mmol of CrO_2Cl_2, 1.00 mL of cyclohexane. a stir bar. and a sealed breakseal vial containing 52.4 μmol of isobutylene gas. The reaction vessel was degassed on the vacuum line and stirred for 1 h at 60 °C and then quickly shaken. breaking the isobutylene vial. After an additional hour of stirring at 60 °C, a brown solid had formed in the bottom of the reaction vessel but the supernatant remained red. suggesting that not all of the CrO_2-Cl_2 had reacted. Workup was as described above for isobutane reactions. A similar reaction was done with stirring for only 10 min after the breaking of the vial. Yields are reported in Table 4.

Reaction of CrO_2Cl_2 with *tert*-Butyl Alcohol and Isopropyl Alcohol. In the glovebox. 0.247 mmol of CrO_2Cl_2 was added to a standard reaction vessel containing 63.6 μmol *tert*-butyl alcohol in 1.00 mL of cyclohexane and a stir bar. The reaction vessel was attached to the vacuum line and evacuated while being cooled to -78 °C. The reaction was stirred at 60 °C for 4 h and worked up as described for isobutane. A similar reaction of 0.185 mmol of CrO_2Cl_2 and 65.3 μmol of isopropyl alcohol was stirred at 25 °C for 1 h and at 60 °C for 2 h.

(24) From a third-order polynomial fit to the isobutane vapor pressure vs temperature data in: Stull. D. R. *Ind. Eng. Chem.* **1947.** *39,* 517—550.

Table 5. Product Yields from Reactions of CrO_2Cl_2 with Toluene and Toluene-d_8

CrO_2Cl_2 +									
$[CrO_2Cl_2]_{in}$	[Toluene]	Temp.		% Yield[a]		Av. Cr oxidation state[b]	Yield in oxidative equiv.	estimated % Yield[c]	$\frac{\text{moles } CrO_2Cl_2}{\text{moles products}}$[d]
0.0995M	1.67M	29°C	15.8(6)	31(2)	8(1)	3.93(3)	83(4)%	5.9%	1.65(6)
0.103M	1.18M	50°C	18(1)	32.0(7)	5(1)	3.92(3)	84(3)%	5.6%	1.65(6)
0.060M	1.18M d_8-toluene	50°C	21(2)	28(2)	4.4(1)		*78(4)%* [e]	*7.5%* [e]	*1.64(6)* [e]

[a] Yields averaged from at least two reactions and reported versus moles of CrO_2Cl_2 reacted. [b] Average chromium oxidation state in the isolated precipitate (Étard complex) determined by iodometric titration. Value reported is the average from two experiments. [c] Yield calculated from oxidative equivalents unaccounted for in the observed products. [d] Represents stoichiometry of reaction in terms of average moles of CrO_2Cl_2 consumed per mole of product formed. [e] Value calculated assuming the same average chromium oxidation state observed for the protio reaction (3.92).

Procedures for workup and analysis were as described for reactions of isobutylene; yields are reported in Table 4.

Kinetics of CrO_2Cl_2 Oxidation of Isobutane. Reaction solutions were prepared in an 8 cm path length thick-walled Pyrex cell (to withstand the isobutane pressure), in the same manner as described above for reactions of cyclooctane. Data were collected and analyzed using the same techniques and apparatus employed to follow the kinetics of cyclooctane oxidation. Scans were taken over the wavelength range from 300 to 700 nm using the cyclohexane solvent as a blank (vapor phase, at the appropriate temperature).

The solution-phase isobutane concentrations for the various reactions were calculated from eq 2, derived using Raoult's law and the Ideal Gas law, assuming ideal behavior for both isobutane and cyclohexane in both the liquid and gas phases (including that molar densities of pure cyclohexane and isobutane are accurate for the mixed solvent). In eq 2, n = moles of isobutane in the vapor, P_0 = vapor pressure of

$$0 = n^2\left(\frac{P_0}{d_x} - RT\right) + n\left(xRT + cRT - \frac{2xP_0}{d_x} + P_0V - \frac{cP_0}{d_x}\right) + xP_0\left(\frac{x}{d_x} + \frac{c}{d_c} - V\right) \quad (2)$$

pure isobutane at the appropriate temperature,[24] x = moles of isobutane added, d_x = molar density of pure isobutane at the appropriate temperature.[20] R = gas constant. T = temperature. c = moles of cyclohexane added, d_c = molar density of pure cyclohexane at the appropriate temperature,[20] and V = volume of the empty cell (or reaction vessel). The expression accounts for the decrease in headspace volume due to the increase in solution volume from isobutane dissolving in the cyclohexane solvent. However, it does not account for partitioning between liquid and gas of the cyclohexane, which should represent a very modest perturbation. Observed rate constants and second order rate constants calculated from the isobutane concentrations are reported in Table 2.

Reactions of CrO_2Cl_2 with Toluene. In the glovebox, a reaction vessel was charged with 1.00 ± 0.02 mL of cyclohexane, a stir bar. 150 ± 1 μL of toluene (1.41 mmol), and finally 10.0 ± 0.2 μL of CrO_2Cl_2 (0.123 mmol). The reaction vessel was removed from the glovebox, cooled to −78 °C, and evacuated on the vacuum line. The flask was stirred at 50 °C for 1.5 h, over which time a brown precipitate formed while the solution turned colorless. The volatiles were collected by short-path vacuum transfer while the reaction vessel was gently heated to 40−50 °C for 5 min. Cyclohexane (1.0 mL) and *tert*-butylbenzene standard (10.0 ± 0.2 μL) were added to the isolated volatiles and the solution was analyzed by GC/FID, showing benzyl chloride as the only volatile product. The isolated Étard complex was dissolved in 2 mL of 0.9 M aqueous KI, followed by 2 mL of CH_3CN, and diluted to 10.00 ± 0.08 mL with deionized H_2O washings from the reaction vessel. A 1.00 ± 0.01 mL aliquot of this solution was added to a 1.00 ± 0.01 mL aliquot of a 0.05051 M aqueous potassium hydrogen phthalate solution (KHP) as an internal standard and analyzed

by HPLC, showing benzaldehyde and benzyl alcohol. Reactions of d_8-toluene were done in the same manner. HPLC detector responses to the deuterated products were assumed to be the same as for the corresponding protiotoluene oxidation product. Yields are given in Table 5.

Detection of Benzoate from Toluene Oxidation. Zn/HCl reductions of isolated Étard complex were performed following standard procedures.[25] Under flow of N_2, 2 mL of 0.9 M aqueous KI was added to isolated Étard complex from reaction of 0.123 mmol of CrO_2Cl_2 with 1.41 mmol of toluene in 1.00 mL of cyclohexane at 50 °C. After allowing the resulting solution to stir for several minutes the volatiles were removed *in vacuo* while the reaction vessel was warmed to 40−50 °C. Under flow of N_2, 600 mg of Zn metal was added to the brown solid remaining in the reaction vessel and 5 mL of 9 M aqueous HCl was added dropwise to the reaction vessel by cannula, resulting in H_2 evolution and a slow color change from clear emerald green to clear robin's egg blue. Another 100 mg of Zn metal was added under flow of N_2, followed by 4 mL of CH_3CN by cannula. Once all of the Zn had been consumed (30 min later), the solution was analyzed by HPLC in the presence of KHP as described above, showing a 0.5% yield of benzoic acid (vs CrO_2Cl_2). An identical Zn/HCl reduction procedure on 0.36 mmol of basic chromium acetate $[Cr_3(O)(OAc)_7 \cdot xH_2O^{26}]$ did not result in a detectable color change from the emerald green of the starting material.

Kinetics of CrO_2Cl_2 Oxidation of Toluene and *tert*-Butylbenzene. Reaction solutions were prepared in the glovebox by addition of the appropriate volume of CrO_2Cl_2 to a solution of toluene (or d_8-toluene) diluted to 1.00 ± 0.02 mL with cyclohexane in an 8 cm path length thick-walled Pyrex cell containing a stir bar. Addition of clear red CrO_2Cl_2 to toluene resulted in an immediate color change. forming a dark brown/black solution. Reaction solutions were degassed on the vacuum line while being cooled to −78 °C before the cell was mounted in the spectrometer. Data were collected and analyzed using the same techniques and apparatus employed above. Spectra were taken over the wavelength range from 300 to 700 nm using the cyclohexane solvent as a blank (vapor phase. at the appropriate temperature). Toluene concentrations were calculated assuming molar densities of the components in the solution are unchanged from the molar densities of the respective pure liquids at the appropriate temperature.[20] Reaction conditions and rate constants are reported in Table 2.

Addition of clear red CrO_2Cl_2 to *tert*-butylbenzene resulted in an immediate color change forming a dark brown/black solution. Kinetic data were collected following the procedures used for cyclooctane. The plot of $\ln[CrO_2Cl_2]$ vs time is linear out to as long as data were collected (2.5 half-lives). The *tert*-butylbenzene concentration was taken from reported values for the molar density of the pure material.[20] Reaction conditions and rate constants are reported in Table 2.

(25) Balthis. J. H.. Jr.; Bailar. J. C.. Jr. *Inorganic Syntheses*; McGraw-Hill: New York. 1939; Vol. 1, pp 122−124.

(26) An old bottle of "Chromium Acetate $Cr(C_2H_3O_2)_3 \cdot xH_2O$" (Matheson. Coleman & Bell) contained the basic acetate on the basis of its optical spectrum: Dubicki. L.; Martin. R. L. *Aust. J. Chem.* **1969.** *22.* 701−7.

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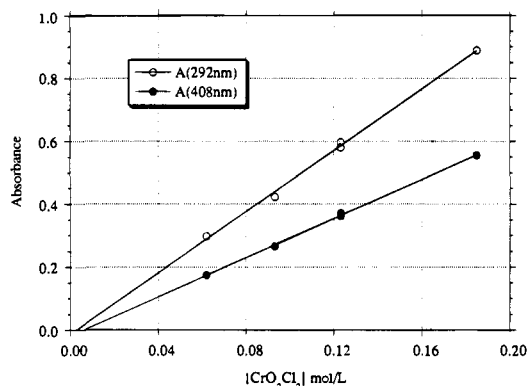
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Figure 2. Vapor-phase absorbance at 292 and 408 nm vs CrO_2Cl_2 concentration in cyclohexane solution at 25 °C.

Estimation of K_{eq} for the $CrO_2Cl_2 \cdot C_6H_5C(CH_3)_3$ CT Complex. The 8 cm quartz cell was charged in the glovebox with CrO_2Cl_2, cyclohexane. and a stir bar and evacuated as described above. Vapor-phase spectra were taken using the apparatus described above. against a neat cyclohexane blank (vapor phase. at 25.0 °C). The CrO_2Cl_2 absorbance at 292 and 408 nm in the vapor phase at 25.0 °C was found to be proportional to the concentration of CrO_2Cl_2 in the solution. as shown in the Beer's law plot of Figure 2 (at 25 °C the reaction of CrO_2Cl_2 with cyclohexane was too slow to detect). From the slope of the plot, $\epsilon_{292nm} = 0.078(3)$ M^{-1} cm^{-1} and $\epsilon_{408nm} = 0.049(2)$ M^{-1} cm^{-1} (these values relate the vapor-phase absorbance to the path length and the *solution* molarity and hence are not true extinction coefficients). Preparation and analysis of a solution of 0.123 M CrO_2Cl_2 in *tert*-butylbenzene at 25 °C in the same manner gives essentially the same values. $\epsilon_{292nm} = 0.078(3)$ M^{-1} cm^{-1} and $\epsilon_{408nm} = 0.047(2)$ M^{-1} cm^{-1}, so complexation of CrO_2Cl_2 by *tert*-butylbenzene must be quite weak: $K_{eq} \leq 0.02$ M^{-1}.

Results

Reactions of CrO_2Cl_2 with cyclooctane, isobutane, and toluene were carried out in the dark in sealed containers under vacuum in neat substrate or in cyclohexane solvent. Solutions were prepared in the glovebox and handled in the dark with the aid of photographic safe-lights. All reagents and solvents were vacuum transferred prior to use and cyclooctane, toluene, and cyclohexane were stringently purified prior to use (see Experimental Section).

The reactions all form brown precipitates, commonly referred to as Étard complexes.[5] Chlorinated products, such as benzyl chloride from oxidation of toluene, are detected in the solution, while other organic products are bound in the precipitate. Aldehyde and ketone products are liberated on workup of the isolated Étard complex upon addition of a coordinating solvent such as acetonitrile or water. Alcohol products are only produced upon aqueous workup, usually done in conjunction with a mild reductant (KI or $Na_2S_2O_3$).

I. Oxidation of Cyclooctane by CrO_2Cl_2. A. Products. The reaction of CrO_2Cl_2 with neat cyclooctane over the temperature range 25−60 °C gives chlorocyclooctane, cyclooctanone, 2-chlorocyclooctanone, cyclooctanol, and cyclooctene oxide (eq 3, Table 1).
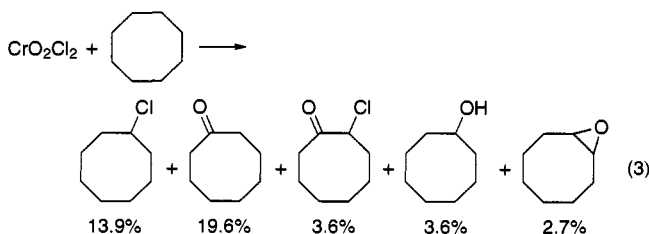
The yields in eq 3 are from reactions at 40 °C and are reported as moles of product vs moles of CrO_2Cl_2 reacted; identification and quantitation was by GC/FID and GC/MS. Essentially the same yields are observed on reaction of CrO_2Cl_2 with a 4.35 M solution of cyclooctane in cyclohexane (54 mol % cyclooctane, Table 1). No cyclohexane oxidation products are observed, indicating that cyclooctane is substantially more reactive than cyclohexane, as is also evident from the kinetic studies described below. The oxidation of pure cyclohexane by CrO_2Cl_2 gives similar products (chlorocyclohexane, cyclohexanone, and 2-chlorocyclohexanone), although no epoxide and only a trace of cyclohexanol are observed.[9]

The average oxidation state of the chromium in the isolated complex from the reaction of CrO_2Cl_2 with cyclooctane, determined by iodometric titration, varies from 3.94(3) for reactions run at 25 °C to 3.74(3) for reactions at 58 °C (Table 1). The presence of cyclohexane again has no effect. From the average final chromium oxidation state, the number of chromium oxidative equivalents expended in the reaction can be calculated. Comparing this value with the extent of oxidation of the organic products shows that the yield of observed cyclooctane products in oxidative equivalents is 66−68% (Table 1). There must therefore be other, unobserved oxidation products. The oxidative equivalent yield shows little if any variation with temperature or when the cyclooctane is diluted with cyclohexane, implying that the branch ratios leading to the observed and unobserved products are not very sensitive to temperature or cyclooctane concentration.
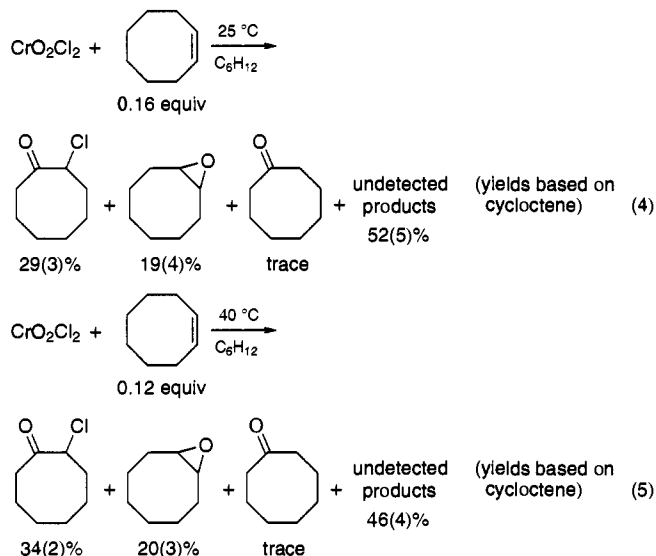
A similar lack of mass balance in terms of oxidative equivalents in the oxidation of cyclohexane by CrO_2Cl_2 was explained by the formation of ring-opened compounds, primarily adipate $\{^-O_2C(CH_2)_4CO_2^-\}$.[9] Adipate was not observed but there was extensive indirect evidence for its formation. Adipate is formed by CrO_2Cl_2 oxidation of the cyclohexene intermediate. By analogy, the cyclooctane oxidations most likely form ring-opened products, presumably octanedioate $\{^-O_2C(CH_2)_6CO_2^-\}$, via the intermediacy of cyclooctene. While no cyclooctene is observed directly in these reactions (trace cyclohexene *is* observed in the reaction of cyclohexane), the detection of both 2-chlorocyclooctanone and cyclooctene oxide points directly to cyclooctene as an intermediate. Epoxides are well established as major products produced in reactions of alkenes with CrO_2Cl_2[27] and, in cyclohexane oxidation, it has been shown that the alkene intermediate is the only viable source of the α-chloro ketone product, 2-chlorocyclohexanone.[9] Carboxylate products such as adipate and octanedioate are tightly bound to the resulting substitution inert Cr(III) and are not liberated by the standard workup procedures (aqueous KI or aqueous $Na_2S_2O_3$). Carboxylate-containing products can sometimes be displaced from the chromium after Zn/HCl reduction but even this procedure is not quantitative (see below).

Reactions of cyclooctene with CrO_2Cl_2 support the contention that cyclooctene is an intermediate on the pathway to the unobserved products in the oxidation of cyclooctane. To model reaction conditions under which cyclooctene is formed and consumed in cyclooctane oxidations at 25 °C, aliquots of a dilute solution of cyclooctene in cyclohexane were added periodically to CrO_2Cl_2 in cyclohexane. For cyclooctene oxidations at 40 °C, a breakseal vial containing the cyclooctene/cyclohexane

(27) (a) Sharpless. K. B.: Teranishi. A. Y.: Backvall. J.-E. *J. Am. Chem. Soc.* **1977.** *99.* 3120−3128. (b) See also ref 5 and the discussion in Miyaura. N.: Kochi. J. K. *J. Am. Chem. Soc.* **1983.** *105.* 2368−2378.

(28) The k_{obs} is not exactly proportional to $[C_8H_{16}]$ as the second-order rate constant is 11% lower than expected based on the change in cyclooctane concentration. While this is larger than the uncertainty in the measurement. it may be due to small solvent effects or to the slightly different mix of products formed (Table 1).

solution was broken into a CrO_2Cl_2/cyclohexane solution within a sealed reaction vessel at the appropriate temperature. Substantially the same results are obtained at the two temperatures, with about half of the cyclooctene reacted being observed as chlorocyclooctanone and cyclohexene oxide (eqs 4 and 5). The

$$CrO_2Cl_2 + \quad \overset{25\,°C}{\underset{C_6H_{12}}{\longrightarrow}}$$

0.16 equiv

(4)

 29(3)% 19(4)% trace + undetected products (yields based on cycloctene)

52(5)%

$$CrO_2Cl_2 + \quad \overset{40\,°C}{\underset{C_6H_{12}}{\longrightarrow}}$$

0.12 equiv

(5)

 34(2)% 20(3)% trace + undetected products (yields based on cycloctene)

46(4)%

ratios of 2-chlorocyclooctanone to cyclooctene oxide of 1.5(4):1 at 25 °C and 1.7(3):1 at 40 °C are in good agreement with the ratios of 1.2(1):1 and 1.4(1):1 observed in the reactions of cyclooctane at the same temperatures (Table 1). This supports the conclusion that these products in the cyclooctane reaction derive from a cyclooctene intermediate.

From eqs 4 and 5, roughly 50% of the cyclooctene reacted is oxidized to undetected product(s). The ratios of unobserved product(s) to 2-chlorocyclooctanone are 1.8(3):1 at 25 °C and 1.4(2):1 at 40 °C. From these branch ratios and the measured yields of 2-chlorocyclooctanone in the cyclooctane reactions, we can calculate the yield of undetected products derived from cyclooctene in the cyclooctane oxidation. The cyclooctene pathway accounts for 5.4(8)% and 4.9(6)% yields of unobserved products at 25 and 40 °C. These yields are only slightly lower than the predicted 6.7% yields of octanedioate, calculated on mass balance considerations assuming that octanedioate is the sole unobserved product (Table 1). Thus a consistent picture of the reaction is derived (Scheme 1, see Discussion), accounting for ≥90% of the chromium oxidative equivalents consumed.

B. Kinetics of Cyclooctane plus CrO_2Cl_2. Reactions of CrO_2Cl_2 with cyclooctane were followed by UV/vis spectroscopy, monitoring the disappearance of red CrO_2Cl_2 vapor from the headspace above the reaction mixture. The specific techniques and the special UV/vis cell employed (Figure 1) are discussed in the Experimental Section. There is a first-order dependence on $[CrO_2Cl_2]$ under pseudo-first-order reaction conditions, in neat cyclooctane or in a solution of cyclooctane in cyclohexane. Plots of $\ln[CrO_2Cl_2]$ versus time are linear to approximately 4 half-lives (Figure 3). Varying the concentration of cyclooctane by addition of cyclohexane results in a proportional drop in the observed rate constant (k_{obs}) demonstrating the reaction to be first order in substrate as well (Table 2).[28] This substrate dependence was assumed but could not be tested in the cyclohexane study.[9]

The activation parameters for the reaction of CrO_2Cl_2 with cyclooctane, from an Eyring plot of $\ln(k/T)$ vs $1/T$, are $\Delta H^{\ddagger} = 19.1(2)$ kcal/mol and $\Delta S^{\ddagger} = -17.5(5)$ eu. These values are derived from the rate at which CrO_2Cl_2 is consumed. This is not the same as the rate of the initial activation of cyclooctane,
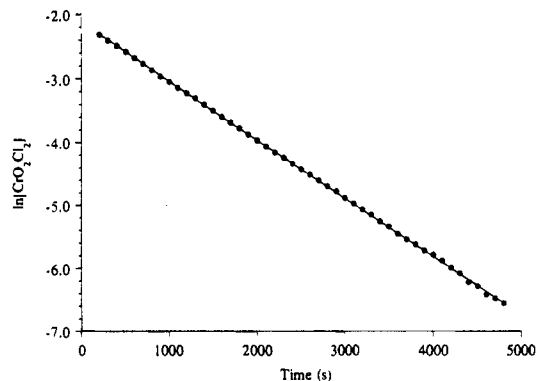

Figure 3. A plot of $\ln[CrO_2Cl_2]$ vs time for the reaction of CrO_2Cl_2 with cyclooctane at 50.0 °C.

because more than one CrO_2Cl_2 is consumed for each cyclooctane oxidized. (Cyclooctanone, 2-chlorocyclooctanone, and cyclooctene oxide each require >1 equiv of CrO_2Cl_2.) The linearity of the $\ln[CrO_2Cl_2]$ vs time plots indicates that the subsequent steps are much faster than the rate of cyclooctane activation and that the stoichiometry of the reaction does not change over time. Under these conditions, the observed rate of CrO_2Cl_2 disappearance is equal to the rate of initial activation times the reaction stoichiometry, the average number of CrO_2-Cl_2 molecules consumed per cyclooctane activated. Values for the reaction stoichiometry vary very little with temperature or cyclooctane concentration (less than the estimated uncertainty, Table 1),[29] consistent with the observation above that the product branch ratios are not very sensitive to conditions. This supports the assumption of a constant reaction stoichiometry that was made in the study of cyclohexane oxidation by CrO_2Cl_2.[30] The temperature dependence of the calculated rate constants for the initial step (Figure 4A)[31] gives the activation parameters $\Delta H^{\ddagger} = 19.4(2)$ kcal/mol and $\Delta S^{\ddagger} = -17.9(5)$ eu (Table 3). These are only slightly different from the values derived from the disappearance of CrO_2Cl_2 (see above).

II. Oxidation of Isobutane by CrO_2Cl_2. A. Products. Reactions of CrO_2Cl_2 with isobutane were carried out in cyclohexane solvent under pressure by condensing the isobutane into the reaction vessels from a gas addition bulb of known volume. A typical reaction was run at 60 °C in a solvent of 3.07 M isobutane and 5.69 M cyclohexane. Under these conditions, attack at cyclohexane is competitive with attack at isobutane. Calculations of the isobutane concentration in the cyclohexane solutions assume ideal behavior of isobutane and cyclohexane liquid and vapor phases (e.g., Raoult's law).

Because of the pressurized reaction mixtures and the volatility of the isobutane oxidation products, detection and quantification required different procedures than were employed for reactions of cyclooctane or toluene. The volatiles were collected by short-path vacuum transfer, yielding a cyclohexane/isobutane solution containing *tert*-butyl chloride and chlorocyclohexane (quantified by GC/FID). The isolated Étard complex containing the bulk of the products was worked up by addition of dry d_3-acetonitrile to displace aldehyde and ketone products which were then collected by short-path vacuum transfer. The remaining chromium-containing solid was hydrolyzed with $Na_2S_2O_3$ in D_2O, yielding alcohol products which vacuum transferred into the acetonitrile solution already collected. The CD_3CN/D_2O solution was analyzed by ^1H NMR.

Workup of a reaction of 0.0762 M CrO_2Cl_2 with 3.07 M isobutane in cyclohexane (5.69 M) at 60 °C gives three major isobutane oxidation products—*tert*-butyl chloride {7.6(7)%}, acetone {3.9(2)%}, and isobutyraldehyde {5.7(5)%}—plus a variety of minor products (eq 6, Table 4). The concurrent
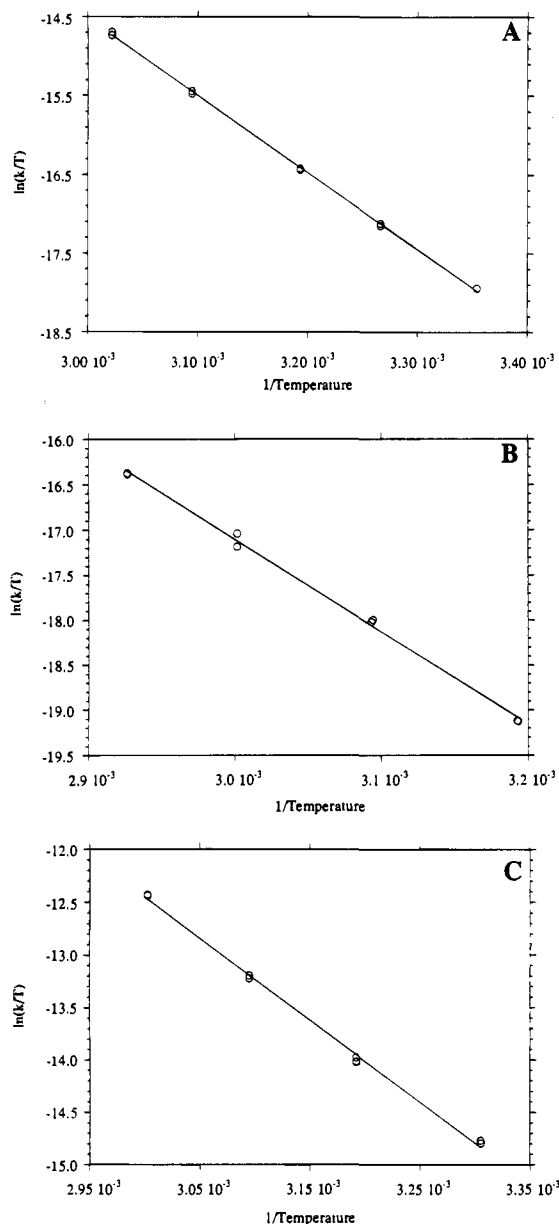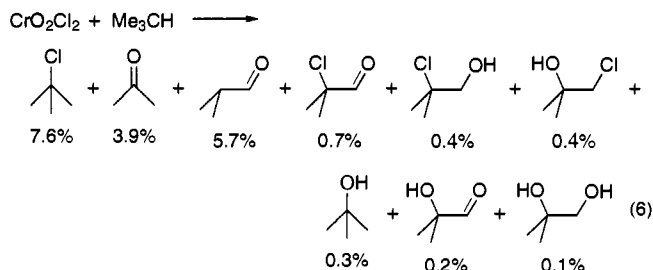
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Figure 4. Eyring plots, $\ln(k/T)$ vs $1/T$, of second-order rate constants for the C−H bond activation steps in the reactions of CrO_2Cl_2 with (A) cyclooctane. (B) isobutane. and (C) toluene.


oxidation of cyclohexane also yields chlorocyclohexane {2.0-(3)%} and cyclohexanone plus 2-chlorocyclohexanone, which could not be quantified independently because their ¹H NMR spectra overlap. The combined 2.6(2)% yield of cyclohexanone and 2-chlorocyclohexanone is 1.3 times the yield of chlorocyclohexane, the same ratio as observed in independent reactions of CrO_2Cl_2 with neat cyclohexane.[9] Thus the reaction of CrO_2Cl_2 with isobutane does not appear to affect the concurrent oxidation of cyclohexane.

The formation of acetone from isobutane requires cleavage

of a carbon−carbon bond. This supports the proposal of carbon−carbon bond cleavage in the oxidations of cyclohexane and cyclooctane, for which there is only indirect evidence (see above). Acetone formation also indicates the production of a 1-carbon product. FTIR analysis of the volatiles stripped from the product mixture shows a small yield of CO_2, 0.34(2)%. This is considerably less than the 3.9(2)% yield of acetone. The possibility that CO_2 could be bound in the Étard complex as carbonate was tested by acid workup of the precipitate (0.1 M HCl with $Na_2S_2O_3$), which gave only an additional 0.25% yield of CO_2. Control experiments on solid K_2CO_3 gave quantitative recovery of CO_2. The 1-carbon fragment unaccounted for apparently remains bound to Cr(III), presumably as formate.

Isobutyraldehyde is a surprising product because it appears to derive from attack at a methyl group rather than the tertiary hydrogen. Similarly, CrO_2Cl_2 oxidation of 2-methylbutane gives 3-methyl-2-butanone (and 3-chloro-3-methyl-2-butanone).[14a] However, the oxidation of t-d_1-isobutane, $(CH_3)_3CD$, shows that isobutyraldehyde does not derive from initial attack at a primary C−H bond. The same products are observed from $(CH_3)_3CD$ as from $(CH_3)_3CH$ (Table 4), though in lower yields because reaction with cyclohexane is more competitive (see below). The isobutyraldehyde product observed by ¹H NMR shows a clean doublet for the isobutyraldehyde methyl protons—*no deuterium is observed at the tertiary position* (eq 7). This indicates that
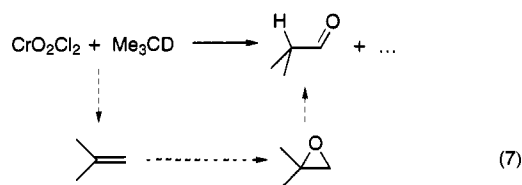
the product is not formed from direct attack at the primary position. A likely pathway involves isobutylene as an intermediate, followed by epoxidation and electrophilic ring opening (eq 7). In fact, isobutyraldehyde is the major product of isobutylene oxidation (see below), and while epoxide is not observed in the reaction of isobutane, it is observed in the reaction of cyclooctane described above. These same steps have been proposed to account for the formation of benzyl methyl ketone in the CrO_2Cl_2 oxidation of n-propylbenzene.[32]

The average oxidation state of the chromium in the precipitated Étard complex from the reaction of Me_3CH is +3.49(3) (Table 4). The observed isobutane oxidation products account for only 40(2)% of the oxidative equivalents used in the oxidation of isobutane, even after taking into account the concurrent cyclohexane oxidation and the unobserved formate produced with acetone.[33] The "missing" oxidative equivalents are likely consumed in the formation of carboxylate products,

(29) Calculation of these values assumes that the oxidative equivalents unaccounted for in the observed products are used in the formation of octandioate.

(30) Yields of the observed products for the reaction of cyclohexane with CrO_2Cl_2 are much lower[9a] such that precise determination of the reaction stoichiometry and its temperature dependence is not possible.

(31) Rate constants for the C−H activation step are calculated by dividing the second-order rate constants by the reaction stoichiometry calculated at the corresponding temperature. A second-order polynomial fit to a plot of reaction stoichiometry vs temperature yielded reaction stoichiometry values at 32.97 and 50.00 °C. This variation in the reaction stoichiometry with temperature is an insignificant perturbation on the activation parameters.

(32) (a) Wiberg. K. B.; Marshall. B.; Foster. G. *Tetrahedron. Lett.* **1962.** *8.* 345. (b) Rentea. C. N.; Necsoiu. I.; Rentea. M.; Ghenciulescu. A.; Nenitzescu. C. D. *Tetrahedron* **1966.** *22.* 3501−3513.

(33) It is not possible to calculate the oxidative equivalents consumed in the formation of acetone from isobutane without knowing the state of the remaining fragment. so it is assumed that the 1-carbon product not accounted for as CO_2 or $CO_3{}^{2-}$ is present as formate.

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which, as noted above, are not liberated from chromium by our workup procedures. Carboxylate products could be formed by further oxidation of one of the many observed isobutane products. Hence we have examined the stability of the observed products under the reaction conditions.

Addition of isopropyl alcohol to 3 equiv of CrO_2Cl_2 in cyclohexane (Table 4, entry 5) rapidly forms a dark precipitate, similar in appearance to the Étard complex, in which acetone is coordinated to chromium.[9] This more closely approximates the conditions under which acetone is present in the isobutane reactions than would simple addition of free ketone. After 2 h at 60 °C the reaction was quenched by removal of the volatiles *in vacuo*, including the unreacted CrO_2Cl_2. Application of the standard workup procedures on the isolated precipitate followed by analysis of the products by ^{1}H NMR showed 100% recovery of the isopropyl alcohol starting material as acetone product. None of the acetone produced in this fashion had undergone further oxidation.

The stabilities of isobutyraldehyde, 2-chloroisobutyraldehyde (2-chloro-2-methylpropionaldehyde), and other products were also tested under the reaction conditions, by examining the oxidation of isobutylene. Introduction of isobutylene from a breakseal vial to a solution of 4.8 equiv of CrO_2Cl_2 in cyclohexane that had been preheated for an hour at 60 °C results in rapid formation of a brown precipitate, similar to the Étard complex. Quenching of the unreacted CrO_2Cl_2 after 10 min followed by workup of the isolated complex yields primarily isobutyraldehyde (37.7%), along with considerable acetone (9.3%), 2-chloroisobutyraldehyde (5.0%), and its chlorohydrin precursor,[9] 2-chloro-2-methyl-1-propanol (10.3%) (yields vs isobutylene reacted, see Table 4, entry 3a). When an identical reaction mixture is allowed to continue to heat for 1 h after rupturing of the breakseal vial, the observed molar yield of isobutylene oxidation products decreases, from 67.4% after 10 min to 51.0% after 1 h (see Table 4, entry 3b). The yields of primary alcohols (2-chloro-2-methylpropanol and 1,2-dihydroxy-2-methylpropane) are reduced by factors of 2—3 upon further heating. The aldehyde yields also decrease with longer reaction times, although less dramatically; the chloro- and hydroxy-isobutyraldehydes may be continually generated by alcohol oxidation. In contrast, acetone is a product of this further oxidation, as its yield increases with further heating. This is consistent with the observation that acetone is not susceptible to further oxidation under the reaction conditions (see above). Clearly, the primary alcohol and aldehyde products are susceptible to further oxidation, presumably to the corresponding carboxylate. The difficulties of observing carboxylate products are described below.

tert-Butyl alcohol has also been found to be further oxidized under the reaction conditions. A solution of Me_3COH and 3.9 equiv of CrO_2Cl_2 in cyclohexane was heated to 60 °C for 4 h and worked up in the usual manner (Table 4, entry 4). Only 6.1% of the *tert*-butyl alcohol is recovered but another 11.3% is observed as a variety of other oxidation products. These products are identical to those obtained in the isobutylene reaction. This is consistent with elimination of isobutylene from a chromium *tert*-butoxy species. Loss of isobutylene from *tert*-butoxide complexes has been previously observed[34] and such eliminations have been proposed in other CrO_2Cl_2 reactions,[5b-d]
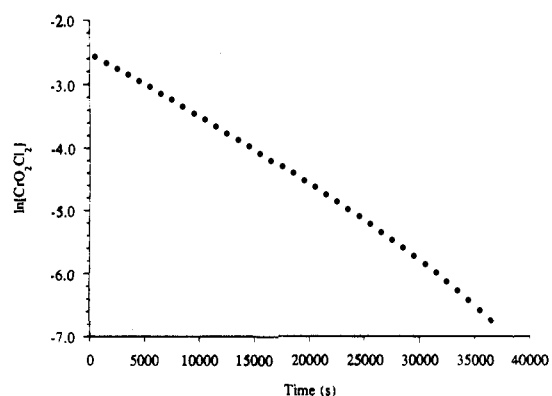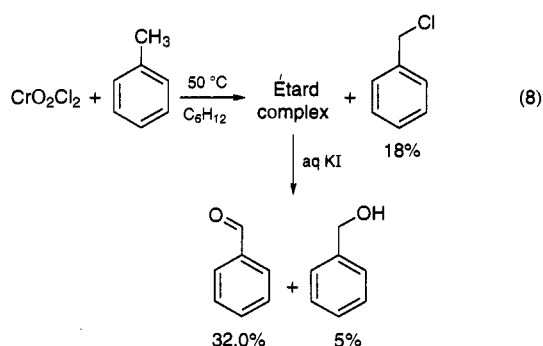
(34) (a) Budzichowski. T. A.; Chisholm. M. H.; Strieb. W. E. *J. Am. Chem. Soc.* **1994.** *116.* 389—390. (b) Bradley. D. C.; Gaur. D. P.; Mehrotra. R. C. *Metal Alkoxides*; Academic Press: New York. 1978: p 69. (c) Alyea. E. C.; Basi. J. S.; Bradley. D. C.; Chisholm. M. H. *J. Chem. Soc. A* **1971.** 772—780. (d) Mayer. J. M. *Polyhedron* Submitted for publication. (e) For a related discussion. see: Nugent. W. A.; Mayer. J. M. *Metal—Ligand Multiple Bonds*; Wiley-Interscience: New York. 1988: pp 64—65.

Figure 5. A plot of $\ln[CrO_2Cl_2]$ vs time for the reaction of CrO_2Cl_2 with isobutane in cyclohexane solvent at 60.0 °C.

although they have not been reported for either $CrO_2(O^tBu)_2$ or $CrO_2(OH)(O^tBu)$.[35]

In sum, the isobutane reactions are complicated by the continued oxidation of most of the observed products. Isobutylene is indicated as an intermediate in the formation of most of the observed products, including isobutyraldehyde. Chlorohydrins and α-chloro ketones are common products of olefin oxidation by CrO_2Cl_2[5b-e,27a] and were shown to derive from cyclohexene in the cyclohexane oxidation.[9] Isobutylene is formed on further reaction of chromium *tert*-butoxy complexes and perhaps by other paths as well (see Discussion).

B. Kinetics of Isobutane plus CrO_2Cl_2. Reactions of CrO_2Cl_2 with excess isobutane (or t-d_1-isobutane) in cyclohexane were followed as described previously for the reaction of cyclooctane. Plots of $\ln[CrO_2Cl_2]$ versus time are not linear but curve downward (Figure 5), with an increase of as much as 50% in slope over the first 3 half-lives. Thus the reactions do not display simple first-order behavior under the pseudo-first-order reaction conditions. This is presumably due to competitive attack at the isobutane oxidation products, such as isobutyraldehyde, formed over the course of the reaction (see above). This problem is not encountered in the cyclohexane, cyclooctane, or toluene oxidations. The rate constants reported in Table 2 are the initial rates, adjusted to account for reaction with the cyclohexane solvent (5—17% of the observed rate of CrO_2Cl_2 disappearance, based on the previously determined rates of CrO_2Cl_2 oxidation of cyclohexane[9]). The initial reaction of CrO_2Cl_2 with isobutane is first order in both reagents (Table 2). Second-order rate constants are obtained by dividing k_{obs} for the initial reaction by the isobutane concentration (Table 2). Deuteration at the tertiary position (t-d_1-isobutane, Me_3CD) results in a modest deuterium kinetic isotope effect, $k_{(CH_3)_3CH}/k_{(CH_3)_3CD} = 1.7$ at 59.9 °C.

A rate constant for the gas-phase oxidation of isobutane by CrO_2Cl_2 was also determined, using limited amounts of reagents such that no liquid phase was present. The disappearance of gas-phase CrO_2Cl_2 (4.8×10^{-5} M) reacting with isobutane (0.161 M) at 80 °C was followed using the same apparatus as employed for solution-phase reactions (Figure 1). The $\ln[CrO_2Cl_2]$ vs time plot is mostly linear, with a very slight downward curve noticeable after 4 half-lives. From the slope of the initial linear portion of the plot and the isobutane concentration, the second-order rate constant is 4.3×10^{-4} M^{-1} s^{-1}. This value is quite close to (2.9 times larger than) the solution rate constant calculated for this temperature.

(35) (a) Sharpless. K. B.; Akashi. K. *J. Am. Chem. Soc.* **1975.** *97.* 5927—5928. (b) Richer. J. C.; Hachey. J. M. *Can. J. Chem.* **1974.** *52.* 2475. (c) See also: Stavropoulos. P.; Bryson. N.; Youinou. M.-T.; Osborn. J. A. *Inorg. Chem.* **1990.** *29.* 1807—1811 and references therein.

From the temperature dependence of the initial rates, $\Delta H^{\ddagger} = 20.4(8)$ kcal/mol and $\Delta S^{\ddagger} = -19(5)$ eu. As noted above, these do not refer to the rate of CrO$_2$Cl$_2$ attack on isobutane because of the stoichiometry of the reaction: more than one CrO$_2$Cl$_2$ is consumed per isobutane activated. This stoichiometry is not constant throughout the reaction as demonstrated by the downward curvature in the ln[CrO$_2$Cl$_2$] vs time plot. We estimate the initial reaction stoichiometry to be roughly 2.0, by analogy with the other systems studied. Dividing the rate constants by this constant factor and redoing the Eyring plot (Figure 4B) gives a slightly more negative entropy of activation, $\Delta S^{\ddagger} = -20(5)$ eu, but the enthalpy is unaffected (Table 3).

The measured kinetic isotope effect on the initial rate ($k_{(CH_3)_3CH}/k_{(CH_3)_3CD} = 1.7$) is also not simply the isotope effect for attack at the tertiary hydrogen because the reaction stoichiometry is likely to be different for Me$_3$CH and Me$_3$CD. The stoichiometry depends on the rate of attack at the alkane (faster for Me$_3$CH than for Me$_3$CD) versus the rate of further oxidation of products or intermediates formed, which is the same for the two substrates. Thus initial reaction stoichiometry is expected to be higher for the Me$_3$CD reaction and the kinetic isotope effect is most likely a lower limit for the isotope effect on the hydrogen atom abstraction step. The isotope effect is better determined from the product yields, using the competitive reaction of the cyclohexane solvent as an internal reference. The same *tert*-butyl radical is formed from Me$_3$CH and Me$_3$-CD, so its rate of trapping by CrO$_2$Cl$_2$ to give Me$_3$CCl is the same in both cases. The ratio of *tert*-butyl chloride to chlorocyclohexane yields is therefore directly related to the relative rates of formation of *tert*-butyl and cyclohexyl radicals. Comparing this ratio of yields from reactions of Me$_3$CH and Me$_3$CD run under the same conditions (Table 4) directly gives the isotope effect on the hydrogen atom abstraction step as 2.3(4) at 60 °C.

III. Oxidation of Toluene by CrO$_2$Cl$_2$. A. Products. The oxidation of toluene by CrO$_2$Cl$_2$ was studied over the temperature range 29−60 °C in cyclohexane solvent. At 50 °C the reaction of 0.103 M CrO$_2$Cl$_2$ with 1.18 M toluene gives a 18(1)% yield of benzyl chloride (by GC) and a brown precipitate. Aqueous KI workup of the isolated Étard complex gives benzaldehyde and benzyl alcohol, in 32.0(7)% and 5(1)% yields by HPLC (eq 8, Table 5). Benzyl chloride and benzal-

dehyde have long been identified as the products of toluene oxidation by CrO$_2$Cl$_2$.[5] The average oxidation state of the chromium in the isolated complex is +3.93(3), as determined by iodometric titrations on complexes from reactions at 29 and 50 °C. This supports the Cr(IV) oxidation state assignment favored by most of the earlier work (on the more tenuous basis

of ambient temperature magnetic susceptibility and EPR signal intensity).[5,9,36]

The three major toluene oxidation products, benzyl chloride, benzaldehyde, and benzyl alcohol, account for 84(3)% of the chromium oxidative equivalents consumed in reactions run at 50 °C. Thus these products represent the large majority of the reaction. The missing oxidative equivalents could result from CrO$_2$Cl$_2$ attack at the aromatic ring, yielding products that might not be detected by our workup and analytical methods. CrO$_2$-Cl$_2$ is known to oxidize benzene[5] but ring attack appears to be too slow to compete with benzylic oxidation as toluene reacts more than 350 times faster than *tert*-butylbenzene at 60 °C (Table 2). More likely, given the isobutane results above, is that some of the benzaldehyde product is further oxidized to benzoate.

Carboxylate products are not freed from the Étard complex by application of the standard aqueous KI or aqueous Na$_2$S$_2$O$_3$ workup procedure, as noted above. This is presumably due to the difficulty of displacing such products from substitution inert Cr(III). To circumvent this problem, the solid remaining after a standard aqueous KI workup of a CrO$_2$Cl$_2$ plus toluene reaction was reduced with zinc and aqueous HCl. This turned the reaction solution from green to blue, and benzoic acid was observed in 0.5% yield by HPLC, demonstrating the formation of carboxylate products. However, this is only a tenth of the expected yield of benzoate assuming that its formation accounts for all of the missing oxidative equivalents. It is not clear whether carboxylates can be observed quantitatively by application of the Zn/HCl workup procedure, as basic chromic acetate, Cr$_3$(O)(OAc)$_7$·xH$_2$O, is not reduced under the same conditions nor is the Étard complex from CrO$_2$Cl$_2$ oxidation of cyclohexane.[9] Zn/HCl reduces most of the chromium in the complex isolated from CrO$_2$Cl$_2$ oxidation of toluene, as evidenced by the color change, but little can be said with certainty since only a very small percentage of the chromium present can possibly be bound to benzoate (the maximum benzoate yield is only 5−6% based on mass balance considerations, Table 5). The observed products, including the small yield of benzoate detected, account for 85(2)% of the oxidative equivalents for reaction at 50 °C.

The nature of the precipitate, the Étard complex, has been a subject of considerable speculation. Most workers have written a simple stoichiometric structure for this material, but our data clearly indicate it to be a heterogeneous, oligomeric material. The aldehyde (or ketone) products have been shown to be present intact in the complex, as ligands to chromium, by IR spectroscopy[9,37] and Cr−C bonds have been excluded.[38] Therefore, assuming that the 15% unobserved oxidative equivalents form benzoate, the isolated complex has the approximate composition CrO$_{1.5}$Cl$_{1.83}$(C$_6$H$_5$CHO)$_{0.32}$(C$_6$H$_5$CH$_2$O)$_{0.06}$(C$_6$H$_5$-CO$_2$)$_{0.06}$ (the oxo or alkoxide ligands could be protonated). The empirical formula, C$_{3.08}$H$_{2.49}$CrO$_{2.00}$Cl$_{1.83}$, is in reasonable agreement with reports[5,36a] that analytical results are consistent with the formula C$_7$H$_8$·2CrO$_2$Cl$_2$. The chromium begins the reaction with four ligands (CrO$_2$Cl$_2$) but is most likely five or six coordinate in the product.[39] Since no new ligands are

(36) (a) Wheeler, O. H. *Can. J. Chem.* **1960**, *38*, 2137−2142. (b) Necsoiu, I.; Balaban, A. T.; Pascaru, I.; Sliam, E.; Elian, M.; Nenitzescu, C. D. *Tetrahedron* **1963**, *19*, 1133−1142 reinterpreted in: (c) Wiberg, K. B.; Eisenthal, R. *Tetrahedron* **1964**, *20*, 1151−1161.

(37) (a) Duffin, H. C.; Tucker, R. B. *Tetrahedron* **1968**, *24*, 6999−7003.

(38) Hydrolysis by D$_2$O did not result in any deuterium incorporation in the products observed here or by: Sulima, L. V.; Gragerov, I. P. *J. Gen. Chem. USSR* **1959**, *29*, 3787.

(39) Larkworthy, L. F.; Nolan, K. B.; O'Brien, P. In *Comprehensive Coordination Chemistry*; Winkinson, G., Ed.; Pergamon: New York, 1987; Vol. 3, pp 699−969.

generated, some fraction of the oxide, chloride, alkoxide, or carboxylate groups most likely act as bridging ligands. In sum, the Étard "complex" should not be viewed as a homogeneous, molecular species with a definite composition or structure.

B. Kinetics of Toluene plus CrO_2Cl_2. Addition of toluene to a solution of CrO_2Cl_2 in cyclohexane results in an immediate color change from the clear red of CrO_2Cl_2/cyclohexane to a very dark brown/black. This color change does not reflect consumption of the CrO_2Cl_2: while the color change occurs instantly, disappearance of CrO_2Cl_2 from the vapor phase above the solution is very much slower (see below). Similar behavior is observed for CrO_2Cl_2 plus *tert*-butylbenzene. The formation of dark CrO_2Cl_2/toluene solutions has been previously observed and ascribed to formation of a "π complex" between CrO_2Cl_2 and the arene;[36a] a charge-transfer complex between CrO_2Cl_2 and benzene has also been described.[11] We find that the initial vapor-phase absorbance at 408 nm for CrO_2Cl_2 in 1.83 M toluene in cyclohexane at 40 °C is the same within experimental error (4%) as that for CrO_2Cl_2 in neat cyclooctane. Similarly, no significant difference in absorbance is observed between a solution of CrO_2Cl_2 in neat *tert*-butylbenzene and a CrO_2Cl_2/cyclohexane solution of identical CrO_2Cl_2 concentration. Since the vapor-phase absorbance of CrO_2Cl_2 is directly proportional to the solution concentration (Figure 2), less than 4% of the CrO_2Cl_2 in solution can be present as a charge-transfer complex, or $K_{eq} < 0.02$ M^{-1} at 40 °C for $CrO_2Cl_2 \cdot C_7H_8$.

The reaction of CrO_2Cl_2 with toluene in cyclohexane solvent is first order in both reactants, as plots of $\ln[CrO_2Cl_2]$ versus time are linear to greater than 3.5 half-lives and the psuedo-first-order rate constants vary linearly with toluene concentration (Table 2). The rate constant for oxidation of d_8-toluene is 8.0(8) times slower than that for C_7H_8 at 50 °C. This value is equal to the isotope effect on the C—H activation step because the reaction stoichiometries are the same for protio- and deuterio-toluene (Table 5). Reaction of CrO_2Cl_2 with a 1:1 mixture of toluene and d_8-toluene in cyclohexane gave a 7.4:1 ratio of benzyl chloride to d_7-benzyl chloride, in good agreement with the isotope effect determined kinetically. The isotope effect we measure is consistent with the "considerable kinetic isotope effect" reported for CrO_2Cl_2 oxidation of $XC_6H_4CH_2D$ (X = H, NO_2)[40] but much larger than the "approximate" value of 2.4 reported previously.[13] This last value was determined from the percent deuterium in the unreacted toluene remaining from reaction of CrO_2Cl_2 with a mixture of $C_6H_5CH_3$ and $C_6H_5CD_3$ in CS_2 at 0 °C, an approach which depends on an accurate reaction stoichiometry (which was not available) and quantitative recovery of unreacted toluene. Loss of unreacted toluene, imperfect separation from the CS_2 solvent, and incomplete deuteration of $C_6H_5CD_3$ would all reduce the apparent isotope effect.[41]

The activation parameters for the C—H bond activation step are calculated, as in the cyclooctane case, from an Eyring plot of the second-order rate constants adjusted for the reaction stoichiometry (Figure 4C), yielding $\Delta H^{\ddagger} = 15.5(4)$ kcal/mol and $\Delta S^{\ddagger} = -25(1)$ eu (Table 3). The reaction stoichiometry was calculated assuming that the oxidative equivalents unaccounted for in the observed products are lost to formation of benzoate, and it appears to be constant at 1.65 over the temperature range studied (Table 5). The activation parameters reported here are quite similar to those reported by Stairs for

Scheme 1. Oxidation of Cyclooctane by CrO_2Cl_2
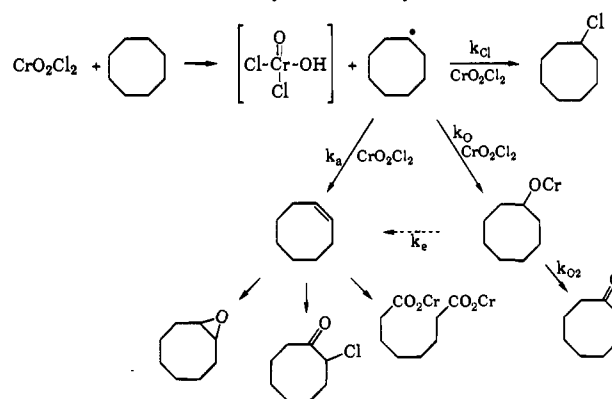
toluene oxidation by CrO_2Cl_2 in CCl_4 (as monitored by iodometric titration), $\Delta H^{\ddagger} = 14.3$ kcal/mol and $\Delta S^{\ddagger} = -28$ eu.[12]

Discussion

We have shown previously that the activation and functionalization of cyclohexane by CrO_2Cl_2 involves initial hydrogen atom abstraction leading to cyclohexyl radical and $Cl_2(O)CrOH$ (eq 1).[9] The cyclohexyl radical intermediate can be trapped by $CBrCl_3$, and the observed products are consistent with the reaction pathways available to a radical intermediate. The results presented above suggest CrO_2Cl_2 oxidations of cyclooctane, isobutane, and toluene proceed by similar mechanisms, based on the types of products observed and the relative reactivities of the substrates (see below). Benzyl radicals (and related benzylic radicals) have been previously suggested as intermediates in the CrO_2Cl_2 oxidation of toluene on the basis of product analyses and broad EPR spectra.[5,42,43] A comparison of all four substrates provides a comprehensive view of the pathways from the radicals to the observed products, the "Product Cascade".

I. Product Cascade. A general scheme to account for the products observed from CrO_2Cl_2 oxidations must include three elements: (a) a chlorine atom transfer pathway, leading to the corresponding alkyl chloride product; (b) a second pathway involving attack of the alkyl radical at oxygen leading to oxygenated products; and (c) a pathway forming an alkene intermediate. This third pathway requires a C—H bond β to the radical, and hence is not operative in reactions of toluene. The product distributions in all of the reactions except that of isobutane are constant over the course of the reaction, indicating that the various reaction pathways all have the same kinetic dependence on CrO_2Cl_2 concentration. Mechanisms for the oxidations of cyclooctane and isobutane that obey these constraints are presented in Schemes 1 and 2, together with products observed upon hydrolysis.

A. Trapping by Chlorine Atom Transfer. Alkyl chlorides such as chlorocyclooctane, *tert*-butyl chloride, and benzyl chloride are observed as products in all CrO_2Cl_2 oxidations of alkanes and arylalkanes.[5,42] These products result from the alkyl radical abstracting a chlorine atom from CrO_2Cl_2 (k_{Cl} in Schemes 1 and 2), which was previously shown to occur at 10^9 M^{-1} s^{-1} for cyclohexyl radicals.[9] Chlorine atom transfer to carbon radicals is well-precedented for oxidizing metal halides.[44] In

(40) Gragerov, I. P.; Ponomarchuk, M. P. *J. Gen. Chem. USSR* **1962**, *32*, 3501.

(41) For an excellent discussion of incomplete deuteration on apparent isotope effects, see: Sorokin, A.; Robert, A.; Meunier, B. *J. Am Chem. Soc.* **1993**, *115*, 7293—7299.

(42) Stephenson, L. M.; Egnatchik, J.; Speth, D. R. *J. Org. Chem.* **1979**, *44*, 346—349.

(43) Gragerov, I. P.; Ponomarchuk, M. P. *J. Org. Chem. USSR* **1969**, *5*, 1125; *Chem. Abstr.* **1969**, *71*, 76079u.

(44) (a) Kochi, J. K. *Acc. Chem. Res.* **1974**, *7*, 351. (b) See also: Asmus, K.-D.; Bonifacic, M. In *Radical Reaction Rates in Liquids*; Landolt-Börnstein New Series; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984; Vol. 13, subvol. b, Carbon-centered Radicals II.

Scheme 2. Oxidation of Isobutane by CrO_2Cl_2
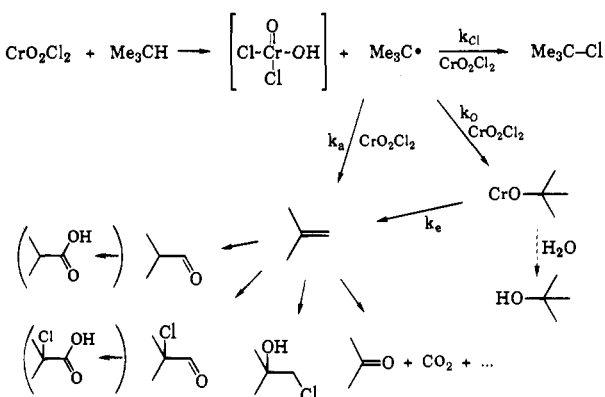
the reaction of cyclohexane, chlorocyclohexane was shown to represent a reaction dead end, not susceptible to further oxidation under the reaction conditions. With this assumption for all four substrates, the percentage of each intermediate radical that is trapped by chlorine atom transfer is given by the moles of alkyl chloride formed versus the total molar yield of oxidation products.[45] For cyclooctyl radical, 28% is trapped by chlorine atom transfer; for cyclohexyl radical, 25%; for *tert*-butyl radical, 20%; and for benzyl radical, 28%. There is little variation in these percentages with changes in reaction temperature and substrate concentration as indicated by the product yields from cyclooctane and toluene (Tables 1 and 5).

B. Trapping by C—O Bond Formation. The formation of cyclooctanol, *tert*-butyl alcohol, cyclohexanol, and benzyl alcohol on hydrolysis of the Étard complexes indicates that the alkyl radicals can be trapped by C—O bond formation (k_O in Schemes 1 and 2). While many of the observed oxygenated products could be accounted for via an alkene intermediate (see below), simple alcohols are not observed to be products of alkene oxidation by CrO_2Cl_2, either in our hands or in related studies.[27] Addition of R• to an oxo ligand (eq 9) is likely to be very exothermic as H• addition is estimated to be downhill by ca. 83 kcal/mol (see below).

$$R• + CrO_2Cl_2 \rightarrow Cr^V(O)(OR)Cl_2 \qquad (9)$$
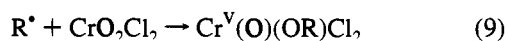
Chromate and permanganate trap radicals in aqueous solution at close to the diffusion limit, presumably by formation of a C—O bond.[46] Cyclohexyl radicals add to an oxo group of CrO_2-Cl_2 competitively with chlorine atom abstraction, at a rate of 10^9 M^{-1} s^{-1}.[9]

The yields of cyclooctanol, cyclohexanol, and benzyl alcohol upon hydrolysis reflect a competition between the formation of chromium alkoxides by eq 9 and the rate of consumption of these alkoxide ligands, by oxidation to ketones or aldehydes or by some other pathway (Schemes 1 and 2). This is evident from the decrease in cyclooctanol yield comparing CrO_2Cl_2 oxidation of neat cyclooctane versus cyclooctane in cyclohexane (Table 1, entries 2 and 3). Dilution of the cyclooctane slows the rate of cyclooctane attack but not the rate of cyclooctanol conversion.

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(45) It is assumed for this calculation that the oxidative equivalents unaccounted for in the observed products were lost to formation of the carboxylate or dicarboxylate products, as described above. This assumption is likely the largest source of error in the calculations, which are therefore least accurate for the reactions with lower mass balances, cyclohexane and isobutane.

(46) (a) Al-Sheikhly, M.; McLaughlin, W. L. *Radiat. Phys. Chem.* **1991**, *38*, 203–211. (b) Steenken, S.; Neta, P. *J. Am. Chem. Soc.* **1982**, *104*, 1244–8.

Independent reactions of cyclohexanol, isopropyl alcohol, and *tert*-butyl alcohol with CrO_2Cl_2 suggest two mechanisms for decomposition of chromium alkoxide intermediates. Alcohols react with CrO_2Cl_2 via chromate esters such as $Cr^{VI}(O)_2(OR)$-Cl,[5,35] similar to the $Cr^V(O)(OR)Cl_2$ species formed in eq 9 although with a different chromium oxidation state. Primary and secondary alcohols are readily oxidized by CrO_2Cl_2; for instance, isopropyl alcohol gives a quantitative yield of acetone. A similar decomposition pathway is available to $Cr^V(O)(OR)$-Cl_2 (from eq 9) when the alkoxide is primary or secondary, as evidenced by the formation of benzaldehyde, cyclohexanone, and cyclooctanone (k_{O_2} in Scheme 1). Note that even though cyclohexanone and cyclooctanone are also generated via the corresponding cycloalkene intermediates, this only accounts for a tiny fraction of the ketone yields from the alkanes, based on the product ratios from independent alkene reactions (Table 1).[9]

The reaction of *tert*-butyl alcohol with CrO_2Cl_2 suggests that the second pathway for decomposition of chromium alkoxides is elimination of alkene. The *tert*-butoxide ligand cannot be oxidized by removal of a β hydrogen, so there is no k_{O_2} pathway. Still, *tert*-butyl alcohol is consumed on reaction with CrO_2Cl_2, forming the same products as observed from reaction of isobutylene (though in lower yields). This suggests that isobutylene can be eliminated from $Cr^{VI}(O)_2(O^tBu)_nCl_{2-n}$ intermediates. If the Cr(V) intermediate expected from trapping of the *tert*-butyl radical at oxygen, $Cr^V(O)(O^tBu)Cl_2$ (eq 9), displays similar reactivity to $Cr^{VI}(O)_2(O^tBu)_nCl_{2-n}$, this could account for the low yield of *tert*-butyl alcohol (k_e in Scheme 2). The oxidation of isobutane gives only 0.3% ^tBuOH, compared to 7.6% for ^tBuCl (Table 4), even though trapping of the *tert*-butyl radical by C—O bond formation should be significant as this is a major trapping path for the other three substrates (C—O bond formation could be disfavored for $Me_3C•$ by steric effects).

No products of alkene elimination are observed in reactions of the secondary alcohols cyclohexanol[9] and isopropyl alcohol (Table 4), which suggests that elimination from the secondary alkoxides $Cr^{VI}(O)_2(OR)Cl$ is not competitive with oxidation to ketones. This appears to be similarly true for $Cr^V(O)(OR)Cl_2$, from eq 9, as cyclohexanone and cyclooctanone generated via the corresponding alkoxide intermediate are major products observed from CrO_2Cl_2 oxidations of cyclohexane and cyclooctane. The k_e pathway in Scheme 1 for cyclooctane is represented by a dashed arrow to indicate the apparently reduced significance of this pathway relative to k_{O_2}.

C. Alkene Intermediates. CrO_2Cl_2 oxidations of cyclohexane, cyclooctane, and isobutane yield products indicative of alkene intermediates: chlorohydrins, chloro ketones, and epoxide (cyclooctene oxide).[27] Trace cyclohexene is observed in the reaction of cyclohexane, and cyclohexene was shown to be the only competent precursor to 2-chlorocyclohexanone, one of the major cyclohexane oxidation products.[9] While cyclooctene is not observed directly in reactions of cyclooctane with CrO_2Cl_2, its independent oxidation gives 2-chlorocyclooctanone and cyclooctene oxide in the same ratio as observed in the reaction of cyclooctane. Similar arguments indicate that isobutylene is an intermediate in the isobutane oxidation. Of particular note is that the isobutyraldehyde derived from *t-d₁*-isobutane {$(CH_3)_3CD$} is protio at the tertiary position, implying that initial attack occurs at the weaker tertiary C—D bond and consistent with aldehyde formation via electrophilic ring-opening of the epoxide (eq 7).

The alkene intermediate could be formed by two pathways. We have proposed that cyclohexene is generated directly from the cyclohexyl radical by loss of a second hydrogen atom.[9] Since
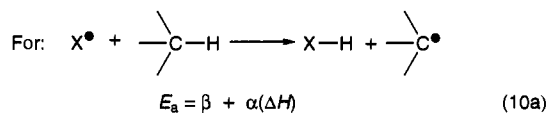
C—H Bond Activation by Metal Oxo Species

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CrO_2Cl_2 is able to abstract a hydrogen atom from the 99 kcal/mol C—H bond in cyclohexane, it is not surprising that abstraction of the second hydrogen, from a ca. 35 kcal/mol C—H bond, is facile. This path is denoted as k_a in Schemes 1 and 2. At least in some cases alkenes can also be formed by elimination from $Cr^V(O)(OR)Cl_2$ as described above for isobutylene (k_e in Schemes 1 and 2). The difference in product yields for cyclohexane vs d_{12}-cyclohexane was explained on the basis of a primary isotope effect of 1.5 on k_a. However, the yields of benzyl chloride from toluene and d_8-toluene are different (Table 5), so there may be significant secondary isotope or other effects as well, which were not taken into account in the cyclohexane study.

The oxidations of cyclooctene, cyclohexene, and isobutylene by CrO_2Cl_2 give a variety of observed products, but in each case a significant portion of the alkene is oxidized to products that are not observed. Mass balance considerations indicate that the alkenes are oxidatively cleaved—isobutylene to acetone, cyclohexene to adipate, and cyclooctene to octanedioate—which is a well-precedented reaction of CrO_2Cl_2, for instance in the formation of benzaldehyde from styrene and 1-phenyl-1-propene.[5] The observed products from oxidations of cyclohexane (at 80 °C) and cyclooctane (at 25 °C) account for only 26% and 68% of the chromium oxidizing equivalents used. However, virtually complete mass balance is achieved for both substrates assuming that the unrecovered products are dicarboxylates formed from the corresponding alkenes. For instance, oxidation of cyclooctene gives a 1:1.8 ratio of 2-chlorocyclooctanone to unrecovered product. Thus, from the 3.0% yield of 2-chloro-cyclooctanone observed in the reaction of cyclooct*ane*, 5.4% of the unrecovered product must also have been produced. If the unrecovered product is octanedioate, then the sum of all the products account for 94(4)% of the chromium oxidative equivalents consumed. Applying similar assumptions to reaction of cyclohexane accounts for 90(10)% of the oxidative equivalents.[9] This comparison is particularly persuasive because reactions of cyclohexane and cyclohexene give very different product yields and distributions than the corresponding reactions of cyclooctane and cyclooctene.

II. Rates and Activation Parameters.

The rates of reactions of CrO_2Cl_2 with cyclooctane, cyclohexane,[9] isobutane, and toluene are first order in CrO_2Cl_2 and first order in substrate. A primary kinetic isotope effect is observed, ranging from 2.2(2) for cyclohexane at 75 °C to 8.0(8) for toluene at 50 °C (Table 2). From the stoichiometries of the reactions, the observed rates are converted into the rates of the initial hydrocarbon activation steps, and the activation parameters for these steps are calculated (Table 2). The data are completely consistent with rate limiting hydrogen atom abstraction by CrO_2Cl_2 from the alkane substrates.[9] Alkanes containing more than one type of C—H bond are attacked by CrO_2Cl_2 selectively at the site with the weakest C—H bond, isobutane at the 3° position and toluene at the benzylic position. Some oxidation products appear to suggest that CrO_2Cl_2 can attack at less reactive C—H bonds, such as isobutyraldehyde from isobutane, benzyl methyl ketone from *n*-propylbenzene,[32] and 1-decalone from *trans*-decaline,[47] but as shown above these products derive from oxidation of alkene intermediates, which are generated by initial attack at the site of the weaker C—H bond. The selectivity is also observed in the relative reactivities of the four substrates studied: on a per active C—H bond basis, the rate constants increase in the order cyclohexane < cyclooctane < isobutane < toluene, varying by a factor of more than 5000 (Table 2).

A cornerstone of organic radical chemistry is that rates of hydrogen atom abstraction are closely related to the strength of C—H bonds being broken. In 1936, Evans and Polanyi showed a correlation between rate and thermodynamic driving force for hydrogen atom transfer reactions, stated in eq 10a, where α and β are constants.[48] ΔH is the exo- or endothermicity of the hydrogen atom transfer step, simply the difference in the strengths of the bonds being formed and broken, $D(X—H) - D(C—H)$. This relationship between E_a and ΔH was originally established assuming that the Arrhenius pre-exponential factor A shows little or no variation in hydrogen atom abstraction reactions for a given radical, $X^\bullet$.[49] An alternative and often more accurate and accessible formulation of the Polanyi relationship correlates ΔH with the free energy of activation, $\Delta G^\ddagger$ (eq 10b) or, equivalently, with the log of the rate constant ($k = [K\kappa T/h]e^{-\Delta G^\ddagger/RT}$). Rate constants or free energies are more easily determined than activation energies, and the same linear correlation holds.[50] (For the reactions examined here, $\Delta H^\ddagger$ correlates with $\Delta S^\ddagger$ (see below), so these treatments are equivalent.)

For: $X^\bullet + \overset{\diagdown}{\underset{\diagup}{C}}{-}H \longrightarrow X{-}H + \overset{\diagdown}{\underset{\diagup}{C}}{}^\bullet$

$$E_a = \beta + \alpha(\Delta H) \tag{10a}$$

$$\log k \propto \Delta G^\ddagger = \beta + \alpha(\Delta H) \tag{10b}$$

If hydrogen atom abstraction by CrO_2Cl_2 is analogous to hydrogen atom abstraction by main group radicals, then the rates of cyclooctane, cyclohexane, isobutane, and toluene oxidations should correlate with the C—H bond strengths, following eqs 10. There is, unfortunately, no up-to-date table of C—H bond strengths that includes the four substrates studied here. The values we have used for C—H bond strengths are as follows: 88.5 ± 1.5 kcal/mol for $C_6H_5CH_2—H$, 96.5 ± 0.4 kcal/mol for $Me_3C—H$, 95.7 ± 1.5 kcal/mol for $C_8H_{15}—H$, and 99.3 ± 1.5 kcal/mol for $C_6H_{11}—H$. The first two are taken from a very recent compilation,[51] but the latter two are from older literature, adjusted to account for the recent re-evaluation of C—H bond strengths (see footnote 52). Even after the adjustment, the value for the C—H bond strength in cyclooctane may be too low as it is unlikely that this bond is weaker than $D(Me_3C—H)$.[54]

The 3.6 kcal/mol difference in $D(C—H)$ between cyclooctane and cyclohexane manifests itself in the 100-fold faster reaction of cyclooctane than cyclohexane at 340 K (Table 3). This is why no cyclohexane oxidation products are observed in roughly equimolar C_8H_{16}/C_6H_{12} solutions. Similarly, cyclooctane and isobutane have very similar rate constants for hydrogen atom

(47) Rentea, C. N.; Rentea, M.; Necsoiu, I.; Nenitzescu, C. D. *Tetrahedron* **1968**, *24*, 4667—4676.

(48) (a) Ingold, K. U. Chapter 2, pp 69ff in: (b) Vol.1 of *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973. (c) Russell, G. A. Chapter 7, Vol. 1 of ref 48b, pp 283—293. (d) The correlation of rates with driving force holds for similar kinds of radicals, when polar effects are not significant.[48c,e] (e) Tedder, J. M. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 401—410. (f) A discussion of free energy relationships in radical reactions is also given in: Korzekwa, K. R.; Jones, J. P.; Gillette, J. R. *J. Am. Chem. Soc.* **1990**, *112*, 7042—6.

(49) For leading references see: (a) Hendry, D. G.; Mill, T.; Piszkiewicz, L.; Howard, J. A.; Eigenmann, H. K. *J. Phys. Chem. Ref. Data* **1974**, *3*, 937—978. (b) Knox, J. H. In *Oxidation of Organic Compounds*; Gould, R. F., Ed.; American Chemical Society: Washington, DC, 1968; Vol. II, pp 1—57.

(50) (a) Korcek, S.; Chenier, J. H. B.; Howard, J. A.; Ingold, K. U. *Can. J. Chem.* **1972**, *50*, 2285. (b) Exner, O. *Prog. Phys. Org. Chem.* **1973**, *10*, 411—482, especially pp 466ff contains a general discussion of linear free energy correlations with ΔH vs ΔG.

(51) Berkowitz, J.; Ellison, G. B.; Gutman, D. *J. Phys. Chem.* **1994**, *98*, 2744—2765.

transfer on a per hydrogen basis (isobutane is 10% faster) because the C—H bonds being cleaved are of similar strength. These results show that caution should be applied to mechanistic arguments based on relative reactivity of 1°, 2°, and 3° positions (as is common in metal-mediated hydrocarbon oxidations). On a per mole basis, cyclooctane is fifteen times more reactive then isobutane. A similar caution applies to discussions of the selectivity of reagents based on their relative reactivity with 1°, 2°, and 3° positions. CrO_2Cl_2 is extremely selective, reacting a hundred times faster per hydrogen with cyclooctane than with cyclohexane, as compared to chlorine atoms which react 1.6 times faster with cyclooctane.[53c]

The rate constants and free energies of activation for hydrogen atom abstraction by CrO_2Cl_2 correlate fairly well with the C—H bond strengths: Figure 6 is a Polanyi plot of $\Delta H^{\ddagger}$ versus $D(C-H)$. This is good evidence for a common mechanism for all four substrates, involving direct transfer of a hydrogen atom from the hydrocarbon to CrO_2Cl_2. Alternative mechanisms would not show such a correlation. Isobutane and toluene would react much more rapidly than cycloalkanes in hydride transfer reactions, because of the much greater stability of tertiary and benzylic carbocations.[55] A concerted pathway, such as the 2 + 2 addition of a C—H bond across a Cr=O bond suggested by theoretical studies[56] and in recent experimental work on manganate oxidations[57] should be affected by steric effects as
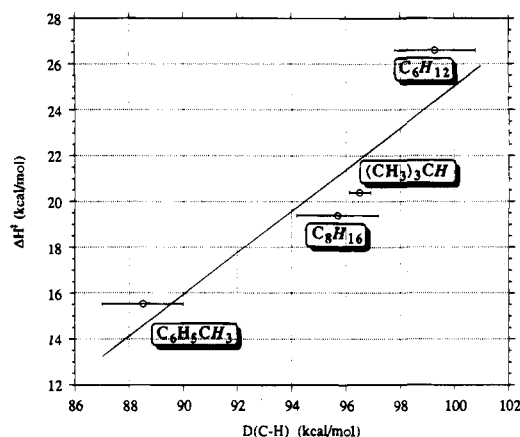

Figure 6. Plot of $\Delta H^{\ddagger}$ vs $D(C-H)$ for reactions of CrO_2Cl_2 with cyclohexane, cyclooctane, isobutane, and toluene.

well as C—H bond strengths: making a five coordinate carbon in the transition state is much less favorable for isobutane than for toluene. Mechanisms involving Cl•, such as dissociation of CrO_2Cl_2 to a caged radical pair {$CrO_2Cl + Cl$}, would not show this selectivity nor the large isotope effects. The hydrogen atom transfer pathway is supported by a number of lines of evidence—for instance, the similarity of gas- and solution-phase oxidation of isobutane and the trapping of cyclohexyl radicals by $CBrCl_3$—but the linearity of the Polanyi plot is powerful mechanistic evidence.

The Polanyi correlation between $\Delta H^{\ddagger}$ and $D(C-H)$ for oxidations of cyclohexane, cyclooctane, isobutane, *and* toluene indicates a common hydrogen atom abstraction mechanism for alkanes and arylalkanes. A common mechanism is also indicated by the correlation of $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$, described below. This indicates that the weak charge transfer complex formed between toluene and CrO_2Cl_2[5d,11] does not affect the mechanism; in other systems it has been argued that charge-transfer complex formation indicates the availability of an electron transfer mechanism.[58] An electron transfer path would be substantially more facile for toluene with its much lower oxidation potential,[59] and would not be expected to show the large primary kinetic isotope effect. Other studies have shown that there is little charge buildup in the transition state, as revealed by the small dependence of the rate on the solvent polarity[12b] and the modest ϱ value of -1.58 for CrO_2Cl_2 plus substituted toluenes at 40 °C.[12c] A similar small ϱ value of -0.78 has been reported for $^tBuOO•$ abstractions of hydrogen atoms from substituted toluenes at 30 °C.[60]

The slope of the plot of $\Delta H^{\ddagger}$ vs $D(C-H)$, α in eq 10b, is 0.9, which means that an increase in endothermicity (ΔH) of 1 kcal/mol gives a corresponding increase in $\Delta H^{\ddagger}$ of 0.90 kcal/mol. Hydrogen atom transfer from these substrates to CrO_2Cl_2 is estimated to be 5−16 kcal/mol uphill, so by the Hammond postulate the transition state should look more like the products than the reactants. Thus a slope approaching one is expected for Polanyi plots of endothermic reactions, as observed here.[48–50] For highly exothermic reactions, such as hydrogen atom abstraction by OH•, α → 0 as the reactions approach the diffusion limit. This pattern has been observed in a number of different radical reactions.[49b]

(52) (a) Values for $D(C-H)$ bond strengths have been recently re-evaluated substantially upward: the current value of $D(Me_3C-H)$ of 96.5 kcal/mol[51] is 3−4 kcal/mol higher than the value reported in earlier reviews.[52c] The reported values (1971)[52b] for cyclohexane (95.5 kcal/mol) and cycloheptane[53] (92.5 kcal/mol) have not been re-examined and are clearly too low vs isobutane. These bond strengths were measured from rates of hydrogen atom abstraction by Br•, using the assumption that the reverse reaction (R• + HBr) has a small positive activation energy. The re-evaluation, documented in ref 51, is based on the determination that these E_a values are actually negative (-0.4 to -1.9 kcal/mol depending on R•). The revised bond strengths for cyclohexane and cyclooctane[53] used here were calculated using the reported method,[52d] using the E_a values for RH + Br•[52b] and assuming that the E_a for R• + HBr are the same as the value for R• = *sec*-butyl (-1.1 kcal/mol).[52d] This last assumption adds little error since the entire reported range of such E_a values (excluding CH$_3$•) is only 0.9 kcal/mol. Correction from ΔH_{375} to ΔH_{298} was done using the correction for *t*-C$_4$H$_9$ over the same temperature range.[52e] (b) Ferguson, K. C.; Whittle, E. *Trans. Faraday Soc.* **1971**, *67*, 2618. (c) Golden, D. M.; Benson, S. W. *Chem. Rev.* **1969**, *69*, 125. McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493−532. Wayner, D. D. M.; Griller, D. In *Advances in Free Radical Chemistry*; JAI Press Inc.: Greenwich, 1990; Vol. 1, pp 159−192. (d) Seetula, J. A.; Gutman, D. *J. Phys. Chem.* **1990**, *94*, 7529−7533. (e) Russel, J. J.; Seetula, J. A.; Timonen, R. S.; Gutman, D.; Nava, D. F. *J. Am. Chem. Soc.* **1988**, *110*, 3084−3091.

(53) (a) $D[c$-C$_8$H$_{15}$−H] does not appear in the standard tables, but it can be calculated from $D_\beta(C-H)$ for cyclooctyl radical (33.9 kcal/mol: Roginskii, V. A. *J. Org. Chem. USSR* **1989**, *25*, 403−413) and the heat of hydrogenation of cyclooctene in cyclohexane (-22.4 kcal/mol: Jensen, J. L. *Prog. Phys. Org. Chem.* **1976**, *12*, 189−228). The value obtained, 92.6 ± 1.5 kcal/mol, was very close to the old literature value for cycloheptane (92.5 ± 1.0 kcal/mol[52b]). If anything, $D(C-H)$ for cyclooctane should be slightly lower than that for cycloheptane since cyclooctane is the more reactive substrate toward hydrogen atom transfer.[53b,c] though the distinction is likely smaller than the stated errors. For these reasons, we have used the re-evaluated number for cycloheptane[52] as the value for cyclooctane: the uncertainty in $D(C_8H_{15}$−H) = 95.7 ± 1.5 kcal/mol is estimated. (b) Alfassi, Z. B.; Feldman, L. *Int. J. Chem. Kinet.* **1981**, *13*, 517−526. (c) Russel, G. A. In *The Chemistry of Alkanes and Cycloalkanes*; Patai, S., Rappoport, Z., Eds.; Wiley: New York, 1992; pp 963−997, especially p 975.

(54) Attack at the tertiary position of isobutane by Cl• is faster than attack at cycloheptane (Hendry, D. G.; Mill, T.; Piszkiewicz, L.; Howard, J. A.; Eigenmann, H. K. *J. Phys. Chem. Ref. Data* **1974**, *3*, 937−978), indicating that the tertiary C—H bond in isobutane is weaker than $D(C-H)$ for cycloheptane and, by analogy,[53] than $D(C-H)$ for cyclooctane.

(55) (a) March, J. *Advanced Organic Chemistry*, 4th ed.; Wiley-Interscience: New York, 1992; pp 166ff. (b) For example, hydride affinities of 2° vs 3° carbocations differ by ∼17 kcal/mol: Houle, F. A.; Beauchamp, J. L. *J. Am. Chem. Soc.* **1979**, *101*, 1239−1248. Arnett, E. M.; Hofelich, T. C. *J. Am. Chem. Soc.* **1983**, *105*, 2889−2895.

(56) (a) Rappé, A. K.; Goddard, W. A., III *J. Am. Chem. Soc.* **1982**, *104*, 3287−3294. (b) Ziegler, T.; Li, J. *Organometallics* **1995**, *14*, 214−223.

(57) Lee, D. G.; Chen, T. *J. Am. Chem. Soc.* **1993**, *115*, 11231−11236.

(58) Wallis, J. M.; Kochi, J. K. *J. Am. Chem. Soc.* **1988**, *110*, 8207−8223 and references therein.

(59) Kochi, J. K., pp 849−890 in ref 3f. Ross, S. D.; Finkelstein, M.; Rudd, E. J. *Anodic Oxidation*; Academic Press: New York, 1975; p 117ff.

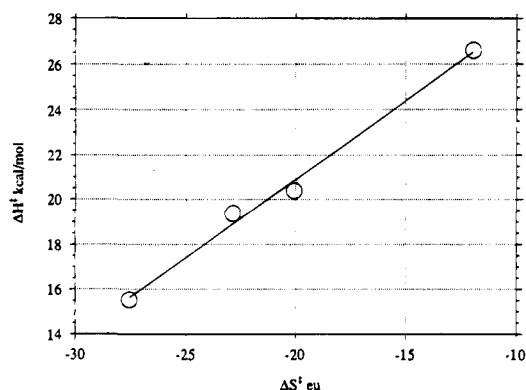(60) Howard, J. A.; Chenier, J. H. B. *J. Am. Chem. Soc.* **1973**, *95*, 3054−3055.

Figure 7. Plot of $\Delta H^{\ddagger}$ vs $\Delta S^{\ddagger}$ (per hydrogen) for reactions of CrO_2Cl_2 with cyclohexane, cyclooctane, isobutane, and toluene at 340 K.

Additional evidence that the correlation in Figure 6 is a true linear free energy relationship is provided in the observation of a linear correlation between $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ values for the four substrates (Figure 7). Such a correlation is additional evidence of mechanistic similarity and is a necessary condition for a linear free energy relationship to hold for a reaction series for which the entropy is not constant.[50b] $\Delta H^{\ddagger}/\Delta S^{\ddagger}$ correlations are referred to as "isokinetic relationships" or "compensation effects",[50b] the latter used when $\Delta H^{\ddagger}$ and $\Delta S^{\ddagger}$ change in the same direction, as in Figure 7. As the enthalpic barrier $\Delta H^{\ddagger}$ decreases, the entropy of activation becomes more unfavorable, in part compensating for the change in $\Delta H^{\ddagger}$. Because of this compensation effect, a Polanyi plot of $\Delta G^{\ddagger}$ vs $D(C-H)$, analogous to the $\Delta H^{\ddagger}$ plot of Figure 6, has a slope α of only 0.47.

The Polanyi relation correlates not only the rates of different substrates with the same oxidant but also the rates of a series of oxidants with the same substrate. It is important that the oxidants be similar to avoid polar effects,[48c,e] so we have chosen to compare hydrogen atom abstraction by CrO_2Cl_2 with reactions of the oxygen radicals $HO^{\bullet}$, $^tBuO^{\bullet}$, and $^tBuOO^{\bullet}$. The strengths of the $O-H$ bonds formed by the radicals are well-known: $HO-H$, 119 kcal/mol; $^tBuO-H$, 105 kcal/mol; and $^tBuOO-H$, 89 kcal/mol.[61] We estimate that the $Cl_2(O)CrO-H$ bond strength is similar to that for $[O_3MnO-H]^-$, 83 kcal/mol.[9b] This is not unreasonable as the hydrogen atom abstraction reactivities of CrO_2Cl_2 and MnO_4^- are similar, CrO_2Cl_2 being a little more reactive.[62] The $[O_3MnO-H]^-$ bond strength is calculated from experimental redox potential and pK_a values, following the method of Bordwell;[63] a recent quantum chemical study[56b] supports the similarity of bond strengths in $[O_3MnOH]^-$ and $Cl_2(O)CrOH$, but suggests much lower values (63 and 66 kcal/mol, respectively).

Using the value of 83 kcal/mol for the $Cl_2(O)CrO-H$ bond strength, *the absolute rate constants for hydrogen atom abstrac-*

tion by CrO_2Cl_2 correlate with the rates of hydrogen atom abstraction by oxygen radicals. Correlations are observed (Figures 8A—C) between CrO_2Cl_2 and oxygen radical reactions[64] with toluene, isobutane,[65] and cyclohexane (a revised version of the plot in ref 9 based on the corrected $Cl_2(O)CrO-H$ bond strength). The correlations show that CrO_2Cl_2 abstracts hydrogen atoms from hydrocarbons at roughly the rates predicted for an oxygen radical capable of forming an 83 kcal/mol $O-H$ bond. Thus the rate of CrO_2Cl_2 oxidation of a new substrate can be predicted, either from its $C-H$ bond strength, following Figure 6, or from its rates of hydrogen atom abstraction by oxygen radicals, following Figure 8. It should be emphasized that these correlations are crude—the plots in Figure 8 cover almost twenty orders of magnitude in $\log k$—so this analysis is not going to explain factors of 2 or even 10. The plots are not really linear and should not be, based on the discussion above: at left the reactions are endothermic and the slope α approaches 1 while at right the hydroxyl radical rates approach the diffusion limit ($\alpha \rightarrow 0$).

III. Implications. The correlations of Figures 6 and 8 show that CrO_2Cl_2 abstracts hydrogen atoms just like an oxygen radical, but CrO_2Cl_2 is not a radical, it is a diamagnetic, d^0 complex. There is no evidence for radical character in the ground state of CrO_2Cl_2 nor evidence for a thermally accessible excited state.[66] The correlations therefore support our proposal that radical character is not relevant to the ability of an oxidant to abstract a hydrogen atom from a substrate.[9] The key feature of such an oxidant is its ability to form a strong bond to a hydrogen atom. This is a new perspective on oxidation reactions that proceed by initial hydrogen atom transfer, with potential implications from metalloenzyme active sites to surface sites in heterogeneous catalysts.

The reaction of two spin-paired molecules to give two radicals is rare in organic chemistry, although "molecule assisted homolysis" and "molecule-induced radical formation" were discussed twenty years ago.[10b,c] Recently, clear examples of hydrogen atom transfer between two closed-shell organic molecules were reported, in the reactions of α-methylstyrene with dihydroanthracene and xanthine at 300 °C.[10a] These reactions are spin allowed because they can form the singlet radical pair. It should be noted that the formation of odd-electron complexes from spin-paired reagents is not foreign to an inorganic chemist: for instance, the diamagnetic low-spin d^6 reagents $Co(NH_3)_6^{3+}$ and $Ru(NH_3)_6^{2+}$ readily react by outer-sphere electron transfer to give paramagnetic $Co^{2+}(aq)$ and $Ru-(NH_3)_6^{3+}$ complexes.[67]

The observation that the rates of hydrogen atom abstraction for CrO_2Cl_2 and oxygen radicals are related does not mean that the reactions are identical in their intimate details. In a formal sense, transfer of a hydrogen atom to $RO^{\bullet}$ results in one-electron
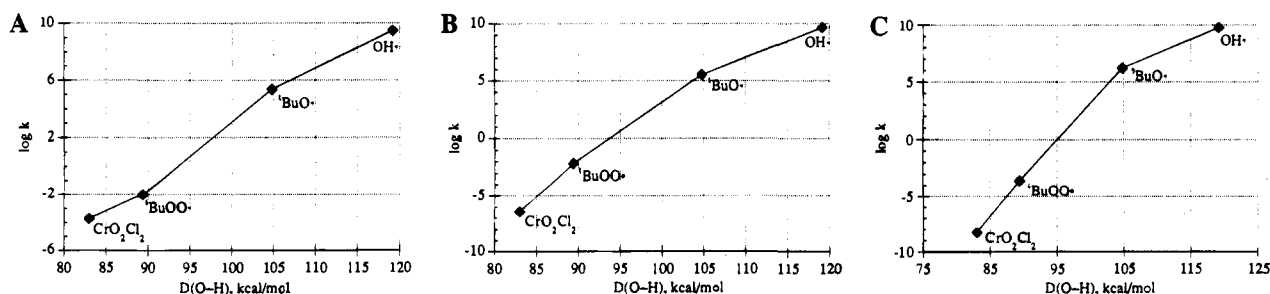

Figure 8. Rates of hydrogen atom abstraction by $OH^{\bullet}$, $^tBuO^{\bullet}$, $^tBuOO^{\bullet}$, and CrO_2Cl_2 at 25—30 °C in cyclohexane solvent vs the $O-H$ bond strength formed for (A) toluene, (B) isobutane, and (C) cyclohexane. The bond strengths were taken from ref 61, except $D[Cl_2(O)CrO-H]$ was taken as that of permanganate, 83 kcal/mol.[9b] Kinetic data are from ref 64 except for CrO_2Cl_2, for which the rate was extrapolated from slightly higher temperature data. Kinetic data for $^tBuO^{\bullet}$ and $^tBuOO^{\bullet}$ plus isobutane are not available, so Figure 8B uses the rate constant for $^tBuOO^{\bullet}$ + Me_2CHR and half the rate constant for $^tBuO^{\bullet}$ + $Me_2CHCHMe_2$ (see ref 65).

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Scheme 3
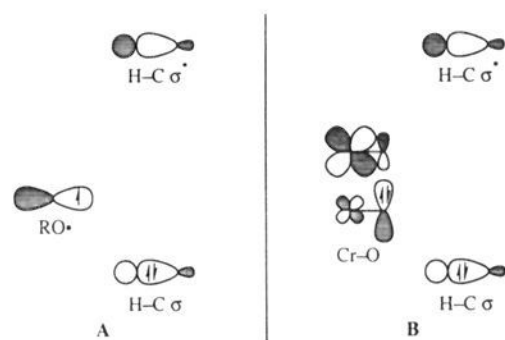
reduction at oxygen and the new O−H bond includes the electron that is a part of the transferred hydrogen atom (eq 11). In contrast, hydrogen atom addition to CrO_2Cl_2 is a formal reduction at the chromium center, even though bond formation occurs at oxygen (eq 12). Since the proton portion of the

$$RO^\bullet + H-R' \rightarrow RO-H + R'' \qquad (11)$$

$$Cr^{VI}O_2Cl_2 + H-R' \rightarrow Cr^V(O)(OH)Cl_2 + R'' \qquad (12)$$
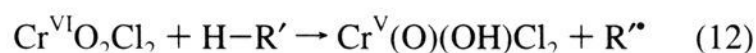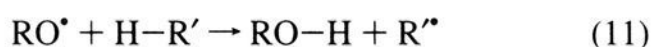
hydrogen atom attaches to oxygen while the electron moves to chromium, reaction 12 could be termed proton-coupled electron transfer. In spite of these differences, reactions 11 and 12 are essentially equivalent kinetically, as indicated by the Polanyi correlations.

Metal oxo species such as CrO_2Cl_2 are ideal candidates for proton-coupled electron transfer processes, because addition of an electron to a metal−oxygen π antibonding orbital significantly increases the basicity of the oxo group.[68] Alternatively, protonation of an oxo ligand makes the complex a much stronger electron acceptor. Meyer and co-workers have previously proposed a distinction between hydrogen atom transfer and proton-coupled electron transfer, defining the latter as reactions in which the proton and electron come from "orbitally different sites".[69] The difference between eqs 11 and 12 is not in the origins of the proton and electron but in their destinations.

The distinction between eqs 11 and 12 is best illustrated in the orbital descriptions of these processes. Reactions of main group radicals with alkanes are quite adequately described by the interactions of the frontier orbitals (Scheme 3).[70] The singly occupied orbital on the radical (the SOMO) interacts with the HOMO and LUMO of the alkane, which are C−H bonding and antibonding (**A**). The SOMO in electrophilic radicals such as RO• interacts primarily with the alkane HOMO, but a proper treatment requires consideration of all three orbitals. In contrast,

hydrogen atom abstraction by CrO_2Cl_2 must involve both the HOMO and LUMO of the oxidant, as well as the HOMO and LUMO of the alkane (**B** in Scheme 3). The HOMO in CrO_2-Cl_2 is primarily an oxygen lone pair orbital, with some Cr−O π bonding character, and the LUMO is a Cr−O π^* orbital, mostly chromium d in character, that lies only 2.4 eV above the HOMO.[67] The HOMO formally accepts the proton while the LUMO accepts the electron. Thus, unlike the radical abstraction in eq 11, which involves three electrons and three orbitals, the reaction in eq 12 involves four electrons and four orbitals.

Given the difference in the molecular orbital descriptions of hydrogen abstraction by RO• and CrO_2Cl_2, the correlation of abstraction rates in Figure 8 is remarkable. It should be repeated that these correlations are based on an estimated bond strength for CrO_2Cl_2. A clearer test of this approach and evidence of its generality will be provided by ongoing studies of oxidations by permanganate and other species. Preliminary results are quite supportive.[62]

Conclusions

Chromyl chloride oxidizes cyclooctane, isobutane, and toluene by initial hydrogen atom abstraction. The resulting organic radical is trapped by chlorine atom transfer, by C−O bond formation, or (in some cases) by a second hydrogen atom transfer to give the corresponding alkene. The relative rates of hydrogen atom abstraction (on a per hydrogen basis) are in the order toluene > isobutane $\cong$ cyclooctane > cyclohexane, varying by a factor of more than 5000 (Table 2). These relative rates correlate well with the strength of the C−H bond being cleaved (Figure 6), as is typical of radical reactions (in the absence of polar effects). Thus a secondary C−H bond in cyclooctane is abstracted roughly as fast as the tertiary C−H bond in isobutane, because they have similar bond strengths. An increase in the C−H bond strength of 1 kcal/mol increases the enthalpy of activation ($\Delta H^\ddagger$) by 0.9 kcal/mol. In further support of a common mechanism for all four substrates, a linear correlation of $\Delta H^\ddagger$ and $\Delta S^\ddagger$ is observed (Figure 7). The absolute rates of hydrogen atom abstraction by CrO_2Cl_2 also correlate with analogous reactions of oxygen radicals (Figure 8), based on the strength of the O−H bond each oxidant forms, with the O−H bond in Cr(O)(OH)Cl_2 taken as 83 kcal/mol. In sum, CrO_2Cl_2 abstracts hydrogen atoms just like an oxygen radical, despite the fact that CrO_2Cl_2 has no unpaired spins. Bond strength and not radical character appears to be the primary determinant of reactivity in hydrogen atom abstractions.

(61) (a) D(HO−H) = 119.2 kcal/mol, derived from data in: *JANAF Thermochemical Tables*, 3rd ed.; *J. Phys. Chem. Ref. Data* **1985**, *14*, Suppl. 1. (b) D($^tBuO-H$) = 104.8, D(MeO−H) = 104.4, and D($^tBuOO-H$) = 89.4 kcal/mol from: Colussi, A. J. In *Chemical Kinetics of Small Organic Radicals*; Alfassi, Z. B., Ed.; CRC Press: Boca Raton, FL, 1988; p 33.

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