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C–H Bond Activation by Metal Oxo Species: Oxidation of Cyclohexane by Chromyl Chloride

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Abstract: Chromyl chloride (CrO_2Cl_2) reacts with cyclohexane solvent at 75 °C to give a dark precipitate along with chlorocyclohexane and a small amount of cyclohexene (in 10.0 and ca. 0.3% yields based on chromium). Hydrolysis of the precipitate, or treatment with a coordinating organic solvent such as acetonitrile, yields cyclohexanone (8.0%) and chlorocyclohexanone (2.5%). Spectroscopic studies of the precipitate indicate that the ketone products are present intact as σ-only ligands. Iodometric titrations of the complex show the average chromium oxidation state to be 3.41. The observed organic products account for only 26% of the chromium oxidizing equivalents used in the reaction; the remainder are most likely consumed in the formation of ring-opened products such as adipic acid. The three major organic products grow in concurrently during the course of the reaction and are not substantially oxidized further under the reaction conditions. Cyclohexene, however, is readily oxidized by CrO_2Cl_2 to give mostly ring-opened products with some 2-chlorocyclohexanone and cyclohexanone. The rate of reaction of CrO_2Cl_2 with cyclohexane, monitored via the optical absorbance of the CrO_2Cl_2 vapor above the solution, is first order in chromium; assuming first-order behavior in cyclohexane as well gives $k = 1.07 \times 10^{-5}\ M^{-1}\ s^{-1}$ at 75 °C, $\Delta H^* = 26.6$ (8) kcal/mol, and $\Delta S^* = -5$ (2) eu. Rates were reproducible with no sign of an induction period. Reaction in the presence of the radical trap $CBrCl_3$ gave some bromocyclohexane. The data indicate that the reaction proceeds by initial hydrogen atom transfer from cyclohexane to CrO_2Cl_2. The cyclohexyl radical is rapidly trapped by oxidizing chromium species via one of three pathways: (i) chlorine atom abstraction, (ii) formation of a C–O bond, and (iii) transfer of a second hydrogen atom. The mass balance of the reaction and results from reactions of cyclohexane-d_{12} are consistent with this mechanism. The ability of CrO_2Cl_2 to abstract a hydrogen atom from cyclohexane 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 ability of CrO_2Cl_2 to make a strong O–H bond by accepting a hydrogen atom. The strength of the analogous O–H bond made by permanganate can be calculated from a thermodynamic cycle to be 80 kcal/mol. Using this value for CrO_2Cl_2 provides both a qualitative and a quantitative understanding of the hydrogen atom transfer step. The implications of this perspective for transition metal mediated hydrogen atom transfer reactions are discussed.

Introduction

The activation and functionalization of hydrocarbons is a subject of both fundamental and technological significance.[2] Hydrocarbons are primary industrial feedstocks for the production of fuels and commodity chemicals, often by oxidation—the removal of hydrogen and/or the addition of oxygen. Examples include the oxidations of butane to maleic anhydride and cyclohexane to adipic acid.[2,3] The oxidation of C–H bonds is also important in the synthesis of the fine chemicals and in enzymatic reactions.[2,4] The reagents or catalysts in these processes are often transition-metal species: on surfaces (as in the butane oxidation), as complexes in solution (as in the cyclohexane oxidation), or at an enzyme active site (as in cytochrome P-450 enzymes). Despite the importance of hydrocarbon oxidation reactions, mechanistic understanding of most processes is limited, both because of the complexity of the reactions and because of a lack of well-understood model systems.

The activation of C–H bonds by organometallic compounds has attracted much recent attention and an excellent understanding is emerging for oxidative addition, σ-bond metathesis, and other pathways.[2,5] Functionalization of hydrocarbons in this manner has however proven challenging. Conversely, there is a wide range of transition-metal species which are known to be

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capable of mediating organic oxidations: biomimetic species which act as models for cytochrome P-450, methane monooxygenase, and other enzymes;[4] novel GIF and heteropolyanion reagents;[6] aqueous cobalt(III) carboxylates;[3d] and well-known oxidants such as permanganate and the Jones reagent (CrO_3 in aqueous sulfuric acid/acetone).[7] While these systems do form oxygenated products, in general details of the C–H activation steps are usually clouded by an inability to isolate the active oxidant, because the reactive species is generated *in situ* or because of the complexity of the system.

We report here a mechanistic study of the oxidation of cyclohexane by chromyl chloride. Hydrocarbon oxidation by chromyl compounds has been known for many years, including CrO_2Cl_2, $CrO_2(NO_3)_2$, and $CrO_2[OC(O)CF_3]_2$ (which oxidizes *n*-hexane on mixing at −50 °C!).[8,9] Early mechanistic studies of alkane and arylalkane oxidations by chromium(VI) oxidants[10–15] were summarized in a 1965 review which suggested the intermediacy of organic free radicals.[16] Both radical chain and nonchain pathways were consistent with the available data, the former invoking Cr(V) as the reactive species, the latter pathway using Cr(VI).[16] In more recent experimental[17–19] and theoretical studies,[20] radical, carbocation, and concerted pathways have all been proposed. A charge transfer complex is observed on reaction of CrO_2Cl_2 with arylalkanes.[17] Surprisingly, there are no previous mechanistic studies of the CrO_2Cl_2 oxidation of alkanes or cycloalkanes (only product studies[10–19]), even though this is the simplest case for mechanistic study, avoiding charge transfer complexes and the complicated speciation of chromic acid solutions. CrO_2Cl_2 is a well-defined species, a dark red, volatile, molecular liquid.[8,21] It is stable under an inert atmosphere and miscible with nonpolar solvents including alkanes.[8] The studies reported here, for the first time, paint a comprehensive picture of an alkane oxidation by a chromium reagent, including the activation step, pathways leading to the observed oxidation products, and the mass balance. The data strongly indicate that CrO_2Cl_2 is the reactive species and that it abstracts a hydrogen atom from cyclohexane. The remarkable reactivity of CrO_2Cl_2 is explained, both qualitatively and quantitatively, on the basis of its ability to form a strong O–H bond to $H^\bullet$.

Experimental Section

General. All reaction mixtures were prepared in a drybox (N_2 atmosphere) under N_2 or *in vacuo* in Teflon sealed Pyrex or quartz reaction vessels and shielded from exposure to light. CrO_2Cl_2 (99.99% grade, Aldrich) was stored in a greaseless, light-free glass vessel and was vacuum transferred prior to use in a vacuum line greased in KRYTOX fluorinated grease (DuPont). *Caution: CrO_2Cl_2 is a corrosive and carcinogenic volatile liquid that should be handled with extreme caution.* While early literature reports[8] cite Cl_2 as a common impurity in CrO_2Cl_2, our material gave no apparent reaction with mercury, and exposure to mercury prior to use (to remove any traces of chlorine) has no effect on its reactivity.

Cyclohexane (99+%, Aldrich) was purified[22] 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. $CBrCl_3$ (99%, Aldrich) was vacuum transferred before storage in the glovebox in a glass vessel taped to exclude light. Prior to use, $CBrCl_3$ was filtered through a pipet column of activated alumina in the dark, to remove trace Br_2 and other possible initiators. Cyclohexane-d_{12} (Cambridge Isotope), cyclohexene (Aldrich), and cyclohexene-d_{10} (MSD) were dried over sodium metal, acetonitrile (Baker) was dried over molecular sieves and then CaH_2, and acetone (Baker) was dried over sieves; all were vacuum transferred prior to use. All the other reagents were used as received and vacuum transferred prior to use if sufficiently volatile.

Organic oxidation products were identified by comparison of their GC retention times with authentic samples and by GC/MS. The products were quantified by GC/FID using an internal standard (*n*-heptane) referenced to authentic product samples by one-point calibration. GC/FID analyses utilized a Hewlett Packard 5790A connected to a Hewlett Packard 3390A integrator. GC/MS analyses were performed on a Kratos Profile mass spectrometer. IR spectra were taken as either Nujol mulls or KBr pellets (prepared in the glovebox) on a Perkin-Elmer 1600 FT-IR.

Reaction of CrO_2Cl_2 with Cyclohexane. Reactions were run in greaseless Pyrex reaction vessels, sealed with a Teflon valve with ground glass joint attachment. A standard procedure follows. In the glovebox, 1.00 ± 0.01 mL of purified cyclohexane was measured out using a volumetric flask and added to a reaction vessel containing a Teflon covered stir bar. Into the flask was syringed 20.0 ± 0.3 μL of CrO_2Cl_2 (0.247 mmol). The needle valve on the reaction flask was quickly closed and the reaction mixture was removed from the glovebox. The flask was then placed in a light free, temperature controlled circulating water bath at 80 °C, and the reaction mixture was set stirring. Over approximately 8 h, a brown solid formed in the bottom of the reaction flask while the solution turned from clear red to colorless. The reaction flask was removed from the hot water and immediately frozen in a dry ice/acetone bath followed by addition of 1.5 mL of 0.1 M aqueous $Na_2S_2O_3$, yielding a clear-green aqueous layer and a colorless organic phase. $CHCl_3$ (4 mL) and 10.0 ± 0.3 μL of *n*-heptane standard were added. After this mixture was allowed to stir for 10–15 min, a 1-mL aliquot of the organic layer was pipetted into a vial followed by 30 μL of *N,N,N′,N′*-tetramethylethylenediamine (TMEDA). The resulting solution was analyzed by GC/FID and GC/MS. Yields are given in Table 1. The TMEDA was added to sequester any chromium still remaining in the organic layer, and its presence resulted in a marked increase in the reproducibility of the GC/FID quantification, especially with regard to the cyclohexanone product. Continuous ether extraction of the cyclohexane/aqueous $Na_2S_2O_3$ mixture followed by GC/FID analysis of the ether extract plus *n*-heptane standard gave the same products and yields.

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Table 1. Yields of Reactions of CrO_2Cl_2 with Cyclohexane and Related Substrates

		yields[b]				
reaction	conditions	chlorocyclohexane	cyclohexanone	2-chlorocyclohexanone	other products	Cr oxidation state[a]
1. CrO_2Cl_2 (0.247 mmol) + C_6H_{12} (1.00 mL)	80 °C	10.0(4)%	8.0(3)%	2.5(2)%	~0.3% cyclohexene	3.41(2)
2. CrO_2Cl_2 (0.247 mmol) + C_6D_{12} (1.00 mL)	80 °C	{14.2(4)%} d_{11}	{13.6(4)%} d_{10}	{5.7(6)%} d_9	<0.1% cyclohexene-d_{10}	3.53(2)
3. CrO_2Cl_2 (0.370 mmol) + C_6H_{12} (1.00 mL) in a 250-mL flask; reaction *in the gas phase*	100 ± 5 °C	3.8%	3.5%	1.0%	2.1% cyclohexene	
4. CrO_2Cl_2 (0.247 mmol) + chlorocyclohexane (0.169 mmol) + C_6H_{12} (5.00 mL)	70 °C	0.181 mmol (107% recovery)	7.3%	2.0%	*c*	
5. CrO_2Cl_2 (0.618 mmol) + 2-chlorocyclohexanone (0.35 mmol) + C_6H_{12} (5.00 mL)	70 °C	7.6%	6.4%	0.318 mmol (91% recovery)	*c*	
6. CrO_2Cl_2 (0.308 mmol) + cyclohexanone (0.241 mmol) + C_6D_{12} (5.00 mL)	70 °C	– {1.7%} d_{11}	53.9%[g] {1.8%}[h] d_{10}	4.0%[g] {0.8%} d_9	7.5%[g] 2-hydroxycyclohexanone[c]	
7a. CrO_2Cl_2 (0.247 mmol) + cyclohexanol (0.038 mmol) + C_6D_{12} (5.00 mL)	25 °C, 3.3 h[d]	–	62%[h]	–	(no cyclohexanol)[c]	
7b. CrO_2Cl_2 (0.247 mmol) + cyclohexanol (0.038 mmol) + C_6D_{12} (5.00 mL)	25 °C, 3.3 h; then 80 °C	– {9.3%} d_{11}	31%[h] {7.7%} d_{10}	– {3.7%} d_9	*c*	
8a. CrO_2Cl_2 (0.308 mmol) + cyclohexene (0.049 mmol) + C_6D_{12} (1.5 mL)	80 °C	– {7.8%} d_{11}	4.3%[i] {7.1%} d_{10}	8.6%[i] {3.0%} d_9	3.5%[i] $C_6H_{10}(OH)Cl$[e]	3.49(2)
8b. CrO_2Cl_2 (0.308 mmol) + cyclohexene (0.049 mmol) + C_6D_{12} (1.5 mL)	80 °C, 1 h[d]	– {0.010 mmol} d_{11}	3.5%[i] {0.010 mmol} d_{10}	10.4%[i] {0.003 mmol} d_9	5.5%[i] $C_6H_{10}(OH)Cl$[e]	
9a. CrO_2Cl_2 (0.308 mmol) + cyclohexene-d_{10} (0.049 mmol) + C_6H_{12} (1.5 mL)[f]	80 °C	– 7.3(5)%	{5.9(3)%}[j] d_{10} 5.4(4)%	{25(3)%}[j] d_9 1.7(2)%	13(2)%[j] $C_6D_{10}(OH)Cl$[e]	3.34(2)
9b. CrO_2Cl_2 (0.370 mmol) + cyclohexene-d_{10} (0.049 mmol) + C_6H_{12} (1.5 mL)	80 °C, 0.5 h[d]	– 0.012 mmol	{1.8%}[j] d_{10} 0.011 mmol	{10%}[j] d_9 0.003 mmol	31%[j] $C_6D_{10}(OH)Cl$[e]	

[a] Average chromium oxidation state in the precipitate formed (the Étard complex) determined by iodometric titration. [b] Yields vs CrO_2Cl_2, unless otherwise indicated. Errors in parentheses are one standard deviation (in the last decimal place) of the values obtained in repeated experiments. [c] Cyclohexene not measured. [d] Reaction was not run to complete conversion of CrO_2Cl_2. [e] *cis*- and *trans*-2-chlorocyclohexanol (cyclohexene chlorohydrin). [f] Average of three runs. [g] Yields based on cyclohexanone. [h] Yields based on cyclohexanol. [i] Yields based on cyclohexene reacted. [j] Yields based on cyclohexene-d_{10} reacted.

Analysis of the volatiles from the reaction mixture, isolated by short path vacuum transfer at ~60 °C, showed only chlorocyclohexane and cyclohexene, in yields as found above. Cyclohexanone and 2-chlorocyclohexanone were detected in the volatiles only after addition of 1 mL of dry acetonitrile or acetone to isolated precipitate from the product mixture. Filtration of the product mixture under an inert atmosphere and analysis of the filtrate by GC/FID showed only chlorocyclohexane and cyclohexene.

Reactions of CrO_2Cl_2 with Substrates in Cyclohexane Solvent. Reactions were run and worked up in the same manner as described in the standard procedure above except as noted. Substrate, CrO_2Cl_2, and cyclohexane (or cyclohexane-d_{12}) were added to the reaction vessel in the glovebox. Chlorocyclohexane, 2-chlorocyclohexanone, cyclohexanone, cyclohexanol, cyclohexene, and cyclohexene-d_{10} were measured out by syringe, except 2-chlorocyclohexanone which was weighed. Reagent amounts and product yields are given in Table 1. Special procedures for certain substrates are described below.

Cyclohexanol: Two identical reactions of CrO_2Cl_2 with 0.15 equiv of cyclohexanol in C_6D_{12} were set up as described above (Table 1, entries 7a,b). Both were stirred for 3.3 h at ambient temperatures, then one was cooled in a dry ice/acetone bath and worked up by the standard procedures and the other was heated to 80 °C, run to completion, and worked up. In neither case was any cyclohexanol observed on workup; C_6D_{12} oxidation products were observed only for the reaction that was heated (Table 1).

Cyclohexene: Special procedures were used for reactions of cyclohexene because of its extremely high reactivity toward CrO_2Cl_2 even at room temperature. In the glovebox, a solution of 0.049 mmol of cyclohexene in 0.5 mL of C_6D_{12} was prepared and loaded into a breakable glass vial with needle-valve attachment. This vial was degassed on the vacuum line and sealed with a torch. The sealed vial was returned to the glovebox and loaded into a standard reaction vessel containing 0.308 mmol of CrO_2Cl_2 in 1.00 mL of C_6D_{12}. The reaction vessel was placed in the circulating water bath set at 80 °C. After 10 min, the reaction flask was quickly shaken, breaking the glass vial containing the cyclohexene solution, and returned to the bath. After the reaction had run to completion the product mixture was worked up and analyzed by the standard procedures (Table 1). Simultaneously a second, identical reaction was run and the product mixture was titrated to determine the average oxidation state of the chromium (see Iodometric Titrations below).

Reactions in the Presence of $CBrCl_3$. Purified $CBrCl_3$ (see above) was found to be sensitive to heat and light, so these reactions were prepared, run, worked up, and analyzed in the dark, with the help of photographic safe-lights. Decomposition of $CBrCl_3$ also occurred on extended heating, so reactions were not run to complete conversion of the CrO_2Cl_2. A typical example follows.

$CBrCl_3$ (863 ± 3 mg) was weighed out in the drybox in the dark and diluted with 4.00 ± 0.08 mL of cyclohexane yielding a 10.5 mol % $CBrCl_3$ solution. Aliquots (1.00 ± 0.02 mL each) of this solution were added to each of four standard reaction vessels wrapped in aluminum foil. CrO_2Cl_2 was added to three of the reaction vessels, and the fourth was left as a control. The four reaction mixtures were stirred at 80 °C for 4.3 h, then worked up and analyzed using the standard procedures, except that 200 mg of I_2 was added to each reaction vessel prior to addition of the aqueous $Na_2S_2O_3$ solution. Reagent amounts and product yields are given in Table 3. No oxidation products were detected in the control experiment run in the absence of CrO_2Cl_2 (<0.3 μmol). The same yield of bromocyclohexane was observed when the precipitate (Étard complex) was removed from the product mixture by suction filtration prior to workup of the filtrate with I_2 and aqueous $Na_2S_2O_3$.

In the absence of added iodine, quenching of unreacted CrO_2Cl_2 in $C_6H_{12}/CBrCl_3$ with aqueous $Na_2S_2O_3$ yielded small amounts of bromocyclohexane (no bromocyclohexane was observed on quenching the Étard complex in $CBrCl_3/C_6H_{12}$ in the absence of CrO_2Cl_2). Presumably the CrO_2Cl_2 quench initiates radical chain oxidation of cyclohexane by

$CBrCl_3$ in the organic layer.[23] The added iodine apparently terminates any radical chains,[24] as treatment of a solution of 0.062 mmol of CrO_2Cl_2 in 1.00 ± 0.02 mL of 10.5 mol % $CBrCl_3/C_6H_{12}$ with 210 mg of I_2 and then treatment with aqueous $Na_2S_2O_3$ yielded no detectable bromocyclohexane.

Gaseous Products. CrO_2Cl_2 (1.23 mmol) was reacted with 3.00 ± 0.03 mL of cyclohexane under standard conditions at 80 °C. The reaction vessel was attached to the vacuum line and cooled to −78 °C. The volatiles were allowed to expand into a gas-phase IR cell. The IR spectrum showed no detectable CO or HCl. A very small quantity of CO_2 was detected (5 μmol, 0.4% vs CrO_2Cl_2, quantified by multipoint calibration), but this amount is on the same order of magnitude as the background levels of CO_2, and thus may not be due entirely to product formed from the reaction of CrO_2Cl_2 with cyclohexane.

Detection of Acid Products. CrO_2Cl_2 (0.247 mmol) was reacted with 1.00 ± 0.02 mL of cyclohexane under standard conditions at 80 °C. The mixture resulting from standard aqueous workup was subjected to continuous ether extraction followed by addition of diazomethane to the extract; no dimethyl adipate (or any other ester) was detected in the extract by GC/FID. The same procedure applied to a similar product mixture spiked with adipic acid gave quantitative recovery of the added adipic acid in the form of dimethyl adipate.

The product mixtures resulting from two reactions of 0.493 mmol of CrO_2Cl_2 in 2.00 ± 0.02 mL of cyclohexane run to completion at 80 °C were stripped to dryness on the vacuum line and 2.0 mL of 0.1 M aqueous $Na_2S_2O_3$ solution was added. Concentrated HCl (2.0 mL) was added to the first reaction vessel, while the second vessel received 0.940 mmol of Na_2H_2EDTA (H_4EDTA = ethylenediaminetetraacetic acid), 10.0 mL of deionized H_2O, and 20 mg of NaOH. Both reaction mixtures were stirred at 100 °C for 20 days. The clear green solution from the first reaction flask was concentrated to 2.5 mL followed by continuous ether extraction. Esterification of the extract with diazomethane yielded 9.6 μmol of dimethyl adipate, a 2% yield vs CrO_2Cl_2 reacted. The clear purple solution from the second reaction (purple is the color of Cr^{III}–EDTA complexes) was concentrated to 3 mL before acidifying with 1 mL of concentrated HCl. Continuous ether extraction of this solution followed by esterification of the extract with diazomethane yielded 3.6 μmol of dimethyl adipate, a 0.7% yield vs CrO_2Cl_2.

Iodometric Titrations. Iodometric titrations were performed, following Vogel,[25] under a flow of N_2 using soluble starch as the indicator. The results are given in Table 1; a sample procedure is described: A reaction of 0.247 mmol of CrO_2Cl_2 and 1.00 mL of C_6H_{12} was heated at 80 °C for 12 h and the volatiles were removed *in vacuo*. To the brown precipitate remaining in the reaction vessel was added 3.0 mL of 0.88 M aqueous KI, followed immediately by 2.0 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 2.47 (±0.04) × 10^{-2} M $Na_2S_2O_3$ 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 to the solution in the reaction vessel, 3 drops of a near saturated solution of soluble starch in deionized water (prepared shortly before the titration, by addition of soluble starch to boiling H_2O) were added to the solution resulting in a color change to clear navy blue. The titration with the $Na_2S_2O_3$ solution was continued until the end point was reached, a rapid change from navy blue to pale green, at 4.06 ± 0.07 mL. A repeat of this procedure on a second sample of complex resulting from an identical reaction required 4.03 ± 0.07 mL of the same $Na_2S_2O_3$ solution. Varying the concentration of the KI solution used by a factor of 15 had no significant effect on the results, indicating that chromium is being efficiently reduced by I^- (rather than by the organic matter present).

Kinetics. Solutions were prepared in the glovebox by dilution of the appropriate volume of CrO_2Cl_2 to 1.00 ± 0.01 mL with C_6H_{12} (or C_6D_{12}). The solution and a Teflon covered stir bar were added to a 1 cm quartz cuvette sealed to a Teflon needle valve. The cuvette was placed on a vacuum line, the solution cooled to 77 K, and the cuvette evacuated. Reaction solutions were warmed to near room temperature prior to mounting of the cuvette in the specially designed cell holder in the spectrometer, already at the required temperature. Reaction temperature was regulated by complete immersion of the cell volume and headspace in a water-tight chamber with quartz windows, connected to a circulating water bath (Lauda Model K-2/R). Complete immersion was required to prevent refluxing within the cell. The reaction solutions were stirred continuously by means of an air-driven stirring plate mounted in the base of the cell holder. With this apparatus, the light from the spectrophotometer passes through the vapor above the reaction solution. The light travels through a quartz window of the cell holder, the circulating water, the cell, and the circulating water and window on the other side of the cell, before reaching the detector. Spectra were taken using a Hewlett Packard 8452A diode array spectrophotometer scanning over the wavelength range from 250 to 600 nm using a neat cyclohexane blank (vapor phase, at the appropriate temperature). Tests using solutions of toluene in cyclohexane with this apparatus showed that the liquid/vapor equilibrium is fairly rapid: at 75 °C the absorbance due to the toluene in the vapor phase stabilized (equilibrium was established) within 300 s of introduction of a cell containing solution at −78 °C. For CrO_2Cl_2 reactions, 300 s was taken as t_0. A typical set of spectra are shown in Figure 1.

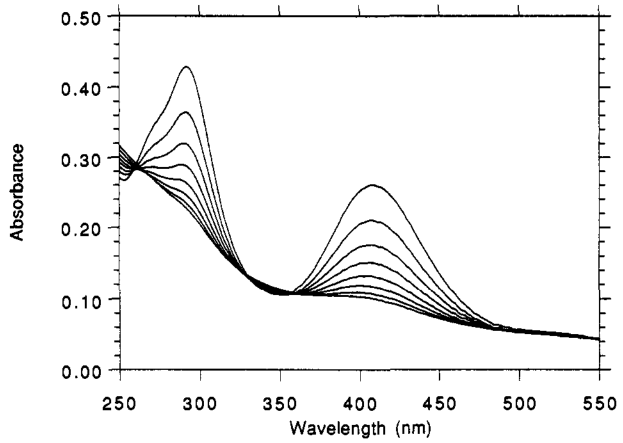

Figure 1. UV/vis spectra of the vapor over the reaction of CrO_2Cl_2 and cyclohexane at 80.3 °C taken at 1000-s intervals.

Data analysis required taking into account the presence of a thin film of reaction solution on the cell faces under the reaction conditions, such that a small amount of precipitate (Étard complex) formed in the light path. Fortunately, the scattering due to the precipitate under these conditions was moderately well behaved as illustrated by the presence of the isosbestic points in Figure 1. The scattering due to the precipitate was therefore treated as an absorbing compound, so that the absorbance at wavelength x is given by eq 1.

$$A_x = [CrO_2Cl_2]\epsilon_{Cr,x} + [precipitate]\epsilon_{P,x} \qquad (1)$$

The concentration of CrO_2Cl_2 can then be determined from the absorbance at two different wavelengths, x and y (eq 2).

$$[CrO_2Cl_2] = \left(A_x - A_y\frac{\epsilon_{P,x}}{\epsilon_{P,y}}\right)\Big/\left(\epsilon_{Cr,x} - \epsilon_{Cr,y}\frac{\epsilon_{P,x}}{\epsilon_{P,y}}\right) \qquad (2)$$

In eq 2 only the *ratio* of the absorptivities of the second species need be known, rather than a "concentration" for the precipitate. The observance of isosbestic points (Figure 1) suggests that the *relative* degree of light scattering by the precipitate versus wavelength stays fairly constant over the course of the reaction. In addition, this effective absorbance is roughly proportional to the amount of precipitate.

Typically reactions were run to completion and the absorbance spectrum at t_f was treated as the absorbance spectrum of the precipitate. In the few cases when the reactions were not run to completion, the precipitate spectrum was modeled using the absorbances at the isobestic points and absorbances at wavelengths where CrO_2Cl_2 absorbance was negligible (from spectra taken as close to the end of the reaction as possible). Interpolation yielded a model absorbance spectrum of the solid that was quite similar to the t_f spectra determined for other reactions.

The concentration of CrO_2Cl_2 at time t ($[CrO_2Cl_2]_t$) was calculated with eq 2 using an absorbance at a wavelength where CrO_2Cl_2 strongly absorbs (λ_{max} = 292 and 408 nm) and an absorbance at a reference

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(23) (a) Poutsma, M. L. in ref 23b, Vol. II, pp 159–230, especially 216ff. (b) *Free Radicals*; Kochi, J. K., Ed.; Wiley: New York, 1973.

(24) (a) I_2 is an extremely rapid radical trap, reacting with cyclohexyl radical with a rate constant $k = 1.2 \times 10^{10}$ M^{-1} s^{-1} at 23 °C: (b) Asmus, K.-D.; Bonifacic, M. Carbon-centered Radicals II. In *Radical Reaction Rates in Liquids*; Landolt-Börnstein New Series; Fischer, H., Ed.; Springer-Verlag: Berlin, 1984; Vol. 13, Subvol. b, p 13.

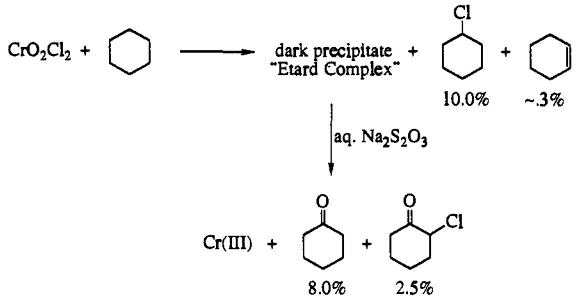
(25) Jefferey, G. H.; Bassett, J.; Mendham, J.; Denney, R. C. In *Vogel's Textbook of Quantitative Chemical Analysis*, 5th ed.; Wiley: New York, 1989; pp 384–393.

Table 2. Rate Constants for Reactions of CrO_2Cl_2 with C_6H_{12} and C_6D_{12}

reaction	temp[a]	initial $[CrO_2Cl_2]$, mol/L	$10^{-5}\ k_{obs}$,[b] s^{-1}	$10^{-5}\ k$,[c] $M^{-1}\ s^{-1}$
1. $CrO_2Cl_2 + C_6H_{12}$	75.00	0.0617	9.28 (±0.99)	1.08 (±0.12)
2. $CrO_2Cl_2 + C_6H_{12}$	75.00	0.123	9.17 (±0.32)	1.063 (±0.037)
3. $CrO_2Cl_2 + C_6H_{12}$	75.08	0.123	9.40 (±0.42)	1.089 (±0.048)
4. $CrO_2Cl_2 + C_6H_{12}$	80.30	0.0617	15.81 (±0.43)	1.846 (±0.050)
5. $CrO_2Cl_2 + C_6H_{12}$	85.00	0.0617	27.81 (±0.61)	3.268 (±0.072)
6. $CrO_2Cl_2 + C_6H_{12}$	91.20	0.0617	51.8 (±2.6)	6.14 (±0.30)
7. $CrO_2Cl_2 + C_6D_{12}$	75.00	0.123	3.74 (±0.26)	0.433 (±0.030)
8. $CrO_2Cl_2 + C_6H_{12}$ + 1-octene[d]	80.50	0.123	17.3 (±1.4)	2.02 (±0.16)

[a] Temperature ±0.05 °C. [b] Average of four data treatments for a single run. The errors reported are the spread of the individual data treatments; the k_{obs} values are likely more reproducible than these errors would suggest (see Experimental Section). [c] Second-order rate constants calculated by dividing k_{obs} by the concentration of cyclohexane at the stated temperature (C_6H_{12} densities from ref 33). [d] Reaction run in the presence of 0.03 equiv of 1-octene per CrO_2Cl_2.

Scheme 1. CrO_2Cl_2 Oxidation of Cyclohexane



wavelength close to a minimum in the CrO_2Cl_2 spectrum (250 nm and either 340 or 350 nm). Using two different peak absorbances with two reference wavelengths yields four distinct $[CrO_2Cl_2]_t$ data sets per data collection (292 vs 250; 408 vs 250; 292 vs 340/350; and 408 vs 340/350). Each data set was manipulated independently, resulting in determination of four apparent rate constants. The rate constant for the reaction, as given in Table 2, is taken as the average of these four values and the reported error reflects their spread; the use of four comparisons should lead to partial cancellation of any errors resulting from inaccurate values for the absorptivity of the precipitate.

Product Formation vs Time. In the glovebox, 1.85 mmol of CrO_2Cl_2 was diluted to 10.00 ± 0.05 mL with cyclohexane. Nine vessels were loaded with a stir bar and 1.00 ± 0.02 mL aliquots of this solution. The reaction mixtures were simultaneously placed in a water bath heated to 79.5 ± 0.5 °C with a copper coil connected to a Lauda K-2/R circulating water bath and stirred. Individual flasks were removed from the bath sequentially and worked up by the standard procedures described above. Data are shown in Figure 4. For reactions worked up at short times, the presence of significant quantities of unreacted CrO_2Cl_2 necessitated quenching with 0.5 M aqueous $Na_2S_2O_3$, rather than 0.1 M. The change in the ratio of chlorocyclohexane to cyclohexanone over time was fit with a second order polynomial which indicated an initial ratio of cyclohexanone to chlorocyclohexane of 0.98 (vs 0.76 by the end of the reaction).

Gas-Phase Reaction of CrO_2Cl_2 with Cyclohexane. A 205 ± 1 mL Pyrex reaction vessel capped by a Teflon needle valve was charged in the glovebox with 1.00 ± 0.02 mL of cyclohexane and 0.370 mmol of CrO_2Cl_2. After the flask was evacuated on the vacuum line, the reaction vessel was completely immersed in an oil bath heated to 100 ± 5 °C. After 164 h, the headspace was colorless, indicating that the reaction had reached completion, and a brown solid was visible on the walls of the flask. Standard workup and analysis gave the yields shown in Table 1.

Results

Chromyl chloride (CrO_2Cl_2) reacts with cyclohexane, slowly at ambient temperatures but with a half life of a few hours at 70–80 °C.[14] Our studies have been under conditions as simple as possible, in sealed containers under N_2 or *in vacuo*, using cyclohexane as both reactant and solvent. Solutions were prepared in a glovebox. High-purity cyclohexane and chromyl chloride were used and were vacuum transferred prior to use; cyclohexane was purified to remove any alkene impurities and CrO_2Cl_2 was checked for any chlorine impurity.[8]

The CrO_2Cl_2/cyclohexane reaction (Scheme 1) forms a brown precipitate, commonly called an Étard complex, as is typical of chromyl chloride reactions.[8,16,17] At the end of the reaction the solution contains two oxidized cyclohexane products, chlorocyclohexane, 10.0(4)%, and a small amount of cyclohexene, ca. 0.3%, which can be removed from the precipitate either by filtration or by vacuum transfer. The precipitate rapidly dissolves upon addition of aqueous $Na_2S_2O_3$, forming a clear green solution containing two other oxidation products, cyclohexanone and 2-chlorocyclohexanone, in 8.0(3)% and 2.5(2)% yields vs CrO_2Cl_2[26] (Scheme 1; Table 1). Products were identified and quantified by GC/FID and GC/MS analysis. Trace amounts of cyclohexanol and 2-chlorocyclohexanols were observed, and a tiny amount of 2-hydroxy-cyclohexanone was occasionally observed in reactions containing large amounts of CrO_2Cl_2.

Our studies of this reaction are presented here in three sections, concerning (I) the nature of the Étard complex, (II) the nature of the initial activation of the alkane substrate, and (III) the pathway by which the isolated products are formed from initial intermediates.

I. The Étard Complex. The Étard complex is formed as a highly hygroscopic brown powder. The cyclohexanone and chlorocyclohexanone products are bound in the complex but may be displaced by addition of coordinating solvents such as acetonitrile, acetone, or water.[27] Hydrolysis of the complex with D_2O does not lead to deuterium incorporation into the isolated products. These data suggest that the ketone products are present intact in the complex as ligands to the chromium.

The IR spectrum of the complex in either Nujol or KBr shows strong bands at 3295, 1636, 1520, and 1426 cm^{-1}. In spectra of complex prepared from reaction of cyclohexane-d_{12}, only the broad high frequency band shifts, appearing at 2456 cm^{-1}, consistent with its assignment as due to O–H (O–D) stretches. Dissolving the complex in water and removing the volatiles leaves a green solid whose IR spectrum does not contain the 1636-cm^{-1} band, but the 1520- and 1426-cm^{-1} modes are still present. The 1636-cm^{-1} band is assigned as the C=O stretching modes of η^1-bound cyclohexanone and chlorocyclohexanone, by comparison with other ketone adducts[28] and aromatic aldehyde adducts of $CrCl_3$.[29] The two strong peaks at 1520 and 1426 cm^{-1} are tentatively assigned to bidentate carboxylate ligands, which typically show $\nu(OCO)_{asym}$ and $\nu(OCO)_{sys}$ in the ranges 1490–1540 and 1400–1470 cm^{-1}.[30] While carboxylic acid products are not observed

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[26] Yields throughout this report are moles of product per mole of CrO_2Cl_2 unless otherwise noted; errors given in parentheses are one standard deviation (in the last decimal place) of the values obtained in repeated experiments.

[27] Studies on methylcyclohexane and propylbenzene oxidation by CrO_2Cl_2 have previously concluded that ketone products were bound in the Étard complex.[18b]

[28] Collman, J. P.; Hegadus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; p 155. See also: Méndez, N. Q.; Seyler, J. W.; Arif, A. M.; Gladysz, J. A. *J. Am. Chem. Soc.* **1993**, *115*, 2323–2334 and references therein.

[29] Duffin, H. C.; Tucker, R. B. *Tetrahedron* **1968**, *24*, 6999.

[30] Robinson, S. D.; Uttley, M. F. *J. Chem. Soc., Dalton Trans.* **1973**, 1912. Nakamoto, K. *Infrared and Raman Spectra of Inorganic and Coordination Compounds*, 3rd ed.; Wiley-Interscience: New York, 1978; pp 230–233.

in the reaction (except under forcing conditions, see below), this is at least consistent with the observation that these bands do not disappear on hydrolysis—the carboxylate ligands are not displaced from the chromium.

Iodometric titration of isolated complex from reactions run at 80 °C shows that the average oxidation state of the chromium atoms in the complex is +3.41(2). As shown in Table 1, slightly different values are obtained under different reaction conditions. The value of 3.41 indicates that at least 59% of the chromium in the complex is in a +3 oxidation state (at most 86%, if the remainder is all Cr^{VI}). As chromium starts in the +6 oxidation state, 86(1)% of the total oxidizing equivalents of the CrO_2Cl_2 reacted are used in the oxidation of the organic substrate.

These data taken together show that the Étard complex is a complicated, heterogeneous material, in contrast with previous suggestions of a stoichiometric material with a well-defined structure.[31] It is mixed-valence and contains a mixture of ligands. The cyclohexanone and chlorocyclohexanone products are present intact in the complex, as indicated by IR spectra and by their displacement. The tight binding of the ketones to the chromium product is not surprising given the limited number of ligands available. Chromium starts with only four ligands in CrO_2Cl_2, some of which are lost in the formation of oxidized organic products, while reduction of the chromium center yields primarily Cr(III), with a preferred octahedral geometry. The higher coordination number is mostly likely achieved by bridging oxide and chloride ligands, those of CrO_2Cl_2 that are not used to form organic products.

II. C–H **Bond Activation. A. Kinetics.** The progress of the reaction has been followed by UV–vis spectroscopy, monitoring the disappearance of red CrO_2Cl_2. The formation of the Étard complex on the walls of the cuvette prevents the use of solution-phase spectroscopy. However, the volatility of CrO_2Cl_2 allows monitoring of its concentration in the vapor phase above the solution. As described in the Experimental Section, a special cell holder was built to keep the entire sealed reaction vessel at a constant temperature and reactions were run under vacuum and vigorously stirred to ensure rapid mass transfer. Under these conditions, the concentration of CrO_2Cl_2 in the gas phase is proportional to the solution concentration. This method does not completely avoid interference by the formation of a precipitate because a thin film of reaction solution is typically present on the cell faces during reaction and a small amount of complex is formed in the light path. The absorbance due to the precipitate (predominantly scattering) behaves as if it obeys Beer's law, as evidenced by the presence of isosbestic points in the series of spectra over the course of the reaction (Figure 1).

Reactions of CrO_2Cl_2 with cyclohexane and cyclohexane-d_{12} were monitored at various temperatures using the above technique. The concentration of CrO_2Cl_2 decays monotonically over the course of the reaction and plots of $\ln[CrO_2Cl_2]$ vs time are linear to over 4 half-lives (Figure 2). The initial rates of reaction are proportional to the initial chromyl chloride concentration: for $[CrO_2Cl_2]_{in} = 0.0617$ and 0.123 M (entries 1 and 2 in Table 2), $R_{initial} = 3.69$ and 7.39×10^{-6} M^{-1} s^{-1}, respectively. These data show that the reaction is first order in CrO_2Cl_2 over the temperature range studied, 75.0–91.2 °C. Rate constants were derived from the spectra by comparison of the absorbances at two different wavelengths in a standard two-component model, assuming Beer's law behavior for the precipitate (see Experimental Section). In order to minimize any errors due to this assumption, the spectra for each reaction were analyzed using four different pairs of wavelengths to give four different apparent rate constants (see Experimental Section); the average of these four is taken as k_{obs} for the reaction (Table 2). As can be seen by entries 1 and 2 in Table 2 and by the linearity of the Eyring plot (Figure 3), the reproducibility of the average value is excellent.

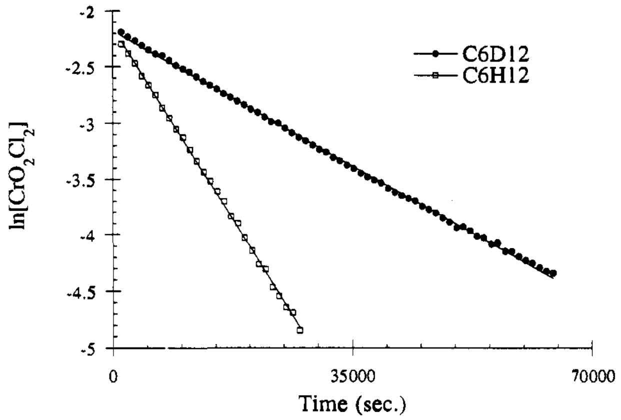

Figure 2. A plot of $\ln[CrO_2Cl_2]$ vs time for the reaction of CrO_2Cl_2 with cyclohexane (open squares) and cyclohexane-d_{12} (filled circles) at 75.0 °C.

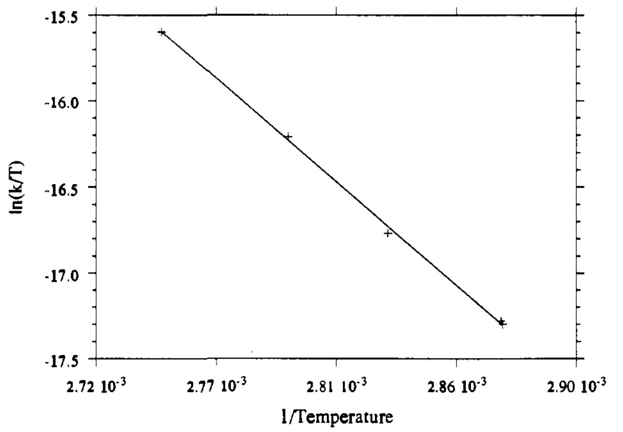

Figure 3. An Eyring plot, $\ln(k/T)$ vs $1/T$, of second-order rate constants for the reaction of CrO_2Cl_2 with cyclohexane.

The reaction is most likely first order in both CrO_2Cl_2 and cyclohexane, although the lack of an inert solvent prevents a direct test of the cyclohexane dependence. First-order dependence has been reported for the CrO_2Cl_2 oxidation of toluene[13] and is observed in our preliminary kinetic studies on the CrO_2Cl_2 oxidation of cyclooctane in cyclohexane.[32] There is clearly a dependence on the nature of the alkane, as methylcyclohexane reacts much more rapidly than cyclohexane and cyclohexane-d_{12} reacts more slowly than C_6H_{12} (Figure 2). The kinetic deuterium isotope effect on k_{obs}, $k_{C_6H_{12}}/k_{C_6D_{12}}$, is 2.5(2) at 75.0 °C. The second-order rate constants k in Table 2 (eq 3) are derived from the k_{obs} by dividing by the concentration of cyclohexane solvent (from 8.629 M at 75.0 °C to 8.436 M at 91.2 °C[33]).

$$\frac{d[CrO_2Cl_2]}{dt} = k[CrO_2Cl_2][C_6H_{12}]; \quad k = k_{obs}/[C_6H_{12}] \tag{3}$$

An Eyring plot of the second-order rate constants is linear (Figure 3) and gives the activation parameters $\Delta H^{\ddagger} = 26.6(8)$ kcal/mol and $\Delta S^{\ddagger} = -5(2)$ eu. It should be noted that these values refer

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[31] The Étard complex derived from toluene has been suggested to contain only Cr(IV), on the basis of the ambient temperature magnetic susceptibility by the Gouy method, $\mu = 3.16\ \mu_B$,[15b] or half Cr(VI) and half Cr(IV),[18a] on the basis of integrated esr peak intensities (although a reinterpretation[10] suggested all Cr(IV)). Neither technique would today be considered reliable for detemining the average oxidation state in such a complicated, oligomeric material (Drago, R. S. *Physical Methods in Chemistry*; Sanders: Philadelphia, 1977. Ebsworth, E. A. V.; Rankin, D. W. H.; Cradock, S. *Structural Methods in Inorganic Chemistry*; Blackwell: Brookline Village, MA, 1987). Further work is required to determine whether our conclusions are general for all Étard complexes or are specific to the oxidation of cyclohexane.

[32] Cook, G. K.; Mayer, J. M. Unpublished results.

[33] *Thermodynamic Tables (Hydrocarbons)*; Thermodynamic Research Center, Texas A&M University, College Station, Texas, 1986–1991.

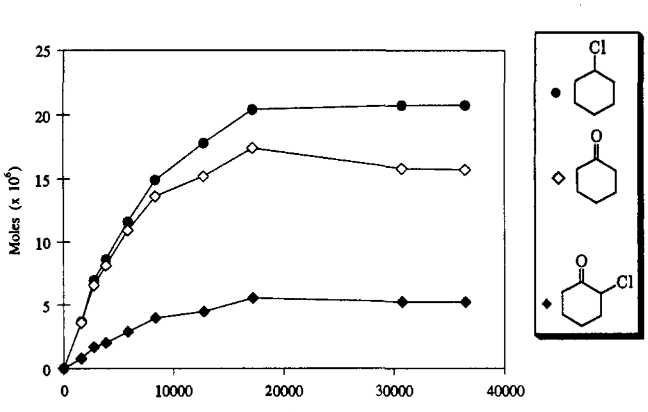


Figure 4. The appearance of the major organic products of the reaction of CrO_2Cl_2 and cyclohexane as a function of time. Nine identical reaction mixtures were heated together in a water bath at 79.5 ± 0.5 °C; each column of three data points is the yields from one of these reactions, quenched at the time shown.

to the rate of disappearance of CrO_2Cl_2, not specifically to the rate of initial cyclohexane activation (see below).

The reaction has also been monitored by following the formation of the major organic products over time. This cannot be done by simply removing an aliquot from a reaction mixture, as the ketone products are present in the precipitate. Instead, identical solutions of CrO_2Cl_2 in cyclohexane were prepared in nine similar reaction vessels, each sealable with a Teflon needle valve, and simultaneously heated to 80 °C in a water bath. At regular intervals a flask was removed from the bath, the reaction quenched, and the products analyzed; the results are summarized in Figure 4. The three major products—chlorocyclohexane, cyclohexanone, and chlorocyclohexanone—grow in fairly smoothly over the course of the reaction, indicating that they are formed independently rather than sequentially. (Cyclohexene cannot be monitored by this procedure because it is reactive with CrO_2Cl_2 at ambient temperatures so that its concentration changes during the quenching procedure.) The formation of each of the major products appears to be first order as plots of $\ln(x_f - x)$ vs time are all reasonably linear. The rate constants for formation of chlorocyclohexane and 2-chlorocyclohexanone are the same as the rate constant for disappearance of CrO_2Cl_2 at the same temperature, within the experimental error.

The formation of cyclohexanone obeys first-order kinetics through most of the reaction, but toward the end the cyclohexanone concentration decreases (Figure 4). There is thus a pathway for further reaction of the cyclohexanone. Quantitatively, the molar ratio of cyclohexanone to chlorocyclohexane begins at almost 1:1 early in the reaction but decreases to 1:0.76 by the end, indicating that approximately 20% of the total cyclohexanone formed undergoes further oxidation.

B. Reaction in the Gas Phase. Because of the volatility of both CrO_2Cl_2 and cyclohexane, their reaction can also be run in the gas phase. At ~100 °C in a 205-mL vessel, 0.370 mmol of CrO_2Cl_2 and 9.26 mmol of cyclohexane reacted to completion within 164 h, as evidenced by colorless headspace (no more red CrO_2Cl_2 vapor). Under these conditions, the reactants are completely in the gas phase, at 42 and 1050 Torr, respectively. As in the solution-phase experiments, a brown precipitate is formed along the sides and bottom of the reaction vessel. Standard aqueous workup showed chlorocyclohexane (3.8%), cyclohexanone (3.5%), 2-chlorocyclohexanone (1.0%), and cyclohexene (2.1%) (Table 1, entry 3). The products and product ratios are very similar to those in the solution-phase reactions, except for the high yield of cyclohexene. Even the rate of reaction is similar to that predicted from solution data: extrapolation of the Eyring plot to 100 °C and correcting for the lower concentration of cyclohexane in the gas phase gives a calculated half-life of 28 h, in excellent agreement with the observed complete reaction in 164 h (5.9 calculated half lives).

The formation of a higher amount of cyclohexene at higher temperatures is consistent with a steady-state approximation for cyclohexene in which the concentration depends on the rates at which it is formed and consumed. Since cyclohexene is much more reactive toward oxidation by CrO_2Cl_2 than cyclohexane (see below), there is likely a smaller $\Delta H^{\ddagger}$ for reaction of the alkene. Thus the formation of cyclohexene from cyclohexane + CrO_2Cl_2 should show a much greater rate dependence with temperature than the rate at which the cyclohexene is consumed, leading to higher observed yields at higher temperatures.

C. Radical Trapping Experiments. To test for the possible intermediacy of cyclohexyl radicals, the reaction of CrO_2Cl_2 with cyclohexane was run in the presence of bromotrichloromethane, $CBrCl_3$. $CBrCl_3$ is a reactive radical trap[34] which is stable to strong oxidants. It is, however, sensitive to light and heat, and commercial samples contained impurities that acted as free radical initiators. It was therefore stored in the glovebox in the dark and filtered through a short column of activated alumina prior to use. All reactions employing $CBrCl_3$ were prepared, run, and analyzed in the dark. Only after application of the above procedures did we find the $CBrCl_3$ to be stable toward cyclohexane.

Reactions of CrO_2Cl_2 with a solution of $CBrCl_3$ in cyclohexane (10.5 mol %, 1.09 M) at 80 °C for 4.3 h yield detectable amounts of bromocyclohexane, the expected product resulting from trapping of cyclohexyl radicals by $CBrCl_3$. Under identical reaction and workup conditions (see Experimental Section) no measurable bromocyclohexane is produced in the absence of CrO_2Cl_2, nor from quenching of unreacted CrO_2Cl_2 or workup of the complex. Thus formation of $C_6H_{11}Br$ occurs only under conditions when CrO_2Cl_2 reacts with cyclohexane. This is strong evidence for the intermediacy of cyclohexyl radicals.

At high initial concentrations of CrO_2Cl_2, the amount of bromocyclohexane formed is quite small (<3%) and the bulk of the CrO_2Cl_2/cyclohexane reaction is unaffected, as revealed in the percentage yields of cyclohexanone, chlorocyclohexanone, and chlorocyclohexane (entries 1 and 2 of Table 3). However, the percentage yields of bromocyclohexane—yields vs CrO_2Cl_2—are inversely proportional to the amount of CrO_2Cl_2 reacted (Table 3). In fact, the *absolute* yields of bromocyclohexane from the two reactions run at higher initial $[CrO_2Cl_2]$ are virtually identical even though the amount of CrO_2Cl_2 varied by 50%.

The yields of bromocyclohexane can be understood on the basis of the radical trapping mechanism proposed in Scheme 2. Applying the steady-state approximation to the concentrations of $^{\bullet}CCl_3$ (eq 4) and cyclohexyl radical ($R^{\bullet}$, eq 5), one obtains the expression in eq 6 for the concentration of cyclohexyl radical.

$$\frac{d[^{\bullet}CCl_3]}{dt} = k_3[CBrCl_3][R^{\bullet}] - k_4[^{\bullet}CCl_3][CrO_2Cl_2] - k_5[^{\bullet}CCl_3][C_6H_{12}] = 0 \quad (4)$$

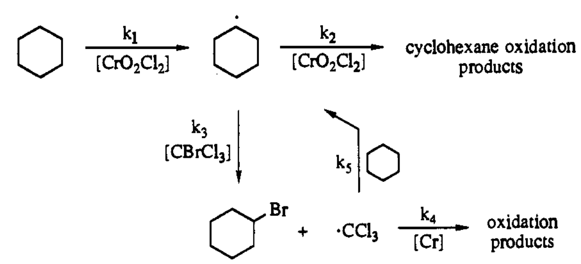
$$\frac{d[R^{\bullet}]}{dt} = k_1[CrO_2Cl_2][C_6H_{12}] - k_2[R^{\bullet}][CrO_2Cl_2] - k_3[R^{\bullet}][CBrCl_3] + k_5[^{\bullet}CCl_3][C_6H_{12}] = 0 \quad (5)$$

$$[R^{\bullet}] = \frac{k_1[CrO_2Cl_2][C_6H_{12}]}{k_2[CrO_2Cl_2] + ak_3[CBrCl_3]} \quad (6)$$

$$\text{where } a = 1 - \frac{1}{1 + k_4[CrO_2Cl_2]/k_5[C_6H_{12}]}$$

Equation 6 simplifies with the assumption that $k_2[CrO_2Cl_2] \gg k_3[CBrCl_3]$ (note that $a \leq 1$), in other words that most of the radicals formed are trapped by CrO_2Cl_2 rather than $CBrCl_3$.

Scheme 2. CrO_2Cl_2 Oxidation of Cyclohexane in the Presence of $CBrCl_3$



This is reasonable under conditions where only a few percent of bromocyclohexane is formed and when added $CBrCl_3$ does not affect the yield of the cyclohexane oxidation products. (The conclusion that CrO_2Cl_2 is the predominant chromium species responsible for trapping of $R^\bullet$ is discussed below.) It is not surprising that CrO_2Cl_2 is a much better radical trap than $CBrCl_3$, as aqueous chromium(VI) is known to trap alkyl radicals at close to diffusion limited rates[35] while trapping of cyclohexyl radicals by $CBrCl_3$ occurs at a rate of 2×10^7 M^{-1} s^{-1}.[36] Under these conditions, when $k_2[CrO_2Cl_2] \gg ak_3[CBrCl_3]$, the concentration of cyclohexyl radical (eq 6) reduces to $[R^\bullet] \simeq k_1[C_6H_{12}]/k_2$. Thus at high chromium concentrations, the mechanism in Scheme 2 predicts that the amount of bromocyclohexane (RBr) formed should be roughly independent of the chromium concentration (eq 7), as observed in entries 1 and 2 in Table 3.

$$\frac{d[RBr]}{dt} = k_3[CBrCl_3][R^\bullet] \simeq \frac{k_1k_3}{k_2}[C_6H_{12}][CBrCl_3] \quad (7)$$

The fact that this scheme predicts the unusual dependance of the bromocyclohexane yield on the initial CrO_2Cl_2 concentration is strong evidence for the presence of cyclohexyl radicals in the reaction. An alternative pathway to bromocyclohexane that is independent of the CrO_2Cl_2 + cyclohexane pathway, perhaps initiated by CrO_2Cl_2, should show a very different dependence of bromocyclohexane yield on $[CrO_2Cl_2]$. At lower chromium concentrations, when $k_2[CrO_2Cl_2] \gg k_3[CBrCl_3]$ is less valid, the formation of RBr should begin to depend on $[CrO_2Cl_2]$, as observed in entry 3 of Table 3. The observation that all three major products appear to decrease proportionately when substantial bromocyclohexane is formed suggests that cyclohexyl radicals are on the pathway to all these products.

III. Product Cascade

The organic products observed on reaction of CrO_2Cl_2 with cyclohexane at 80 °C (Scheme 1, Table 1) account for only 26% of the chromium oxidizing equivalents used. Analysis of gaseous products resulting from the reaction by IR analysis showed no detectable HCl or CO and only a small amount of CO_2, $\leq 0.4\%$. Reaction of cyclohexane-d_{12} gives the same major products, in significantly higher yields (Table 1) except that no cyclohexene-d_{10} is observed ($\leq 0.1\%$ versus CrO_2Cl_2 based on the analytical detection limits). In the deuterium case, the observed products account for 47% of the chromium oxidative equivalents used.

The remaining oxidative equivalents are most likely used in formation of ring-opened products, primarily adipic acid. This is based (i) on the carboxylate stretches seen in the IR of the Étard complex, (ii) by analogy with chromic acid oxidation of cyclohexane which gives adipic acid as the major organic product,[37] and (iii) on the basis of mass balance considerations (see below). A potentially chelating and bridging ligand such as adipic acid would not be displaced from a substitution inert Cr(III) metal center by the workup procedure used (aqueous $Na_2S_2O_3$). Under more forcing conditions—refluxing for days in concentrated HCl or aqueous Na_2H_2EDTA—small amounts of dimethyl adipate are observed after esterification with diazomethane (2% and 0.7% in the two procedures, see Experimental Section). Note that the maximum yield of adipic acid, based on the "missing" oxidizing equivalents, is only 19% vs CrO_2Cl_2, because the adipic acid is a 10-electron oxidation of cyclohexane. No other new products were detected in these experiments.

The plot of the formation of organic products as a function of time (Figure 4) shows that chlorocyclohexane, cyclohexanone, and 2-chlorocyclohexanone grow in concurrently over the course of the reaction. This implies that these products are formed independently of one another rather than sequentially: i.e., the chlorocyclohexanone cannot derive from further oxidation of either the chlorocyclohexane or cyclohexanone. Consistent with this conclusion, added chlorocyclohexane is not oxidized during a CrO_2Cl_2/cyclohexane reaction (Table 1, entry 4). 2-Chlorocyclohexanone is therefore also not oxidized further, as it is formed in a constant ratio with chlorocyclohexane (Figure 4). Free 2-chlorocyclohexanone and cyclohexanone in solution—which are not present in the CrO_2Cl_2/cyclohexane reaction (see above)—are roughly 30 and 400 times more reactive than cyclohexane toward attack by CrO_2Cl_2 (as observed in chromic acid oxidations[37a]). As shown in Table 1 (entries 5 and 6), the oxidation products from chlorocyclohexanone were not detected but cyclohexanone yields small amounts of 2-chloro-cyclohexanone and 2-hydroxycyclohexanone, in addition to unobserved, presumably ring-opened products, probably formed via 2-hydroxycyclohexanone through oxidation to the 1,2-dione.

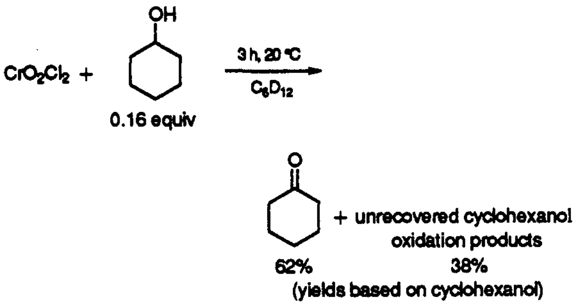
Since the ketone products are present bound to chromium and not free in solution, the reactions of added cyclohexanone and 2-chlorocyclohexanone are suggestive but not directly relevant. This illustrates the difficulty in reproducing the exact reaction conditions to determine the reactivity of products or intermediates to further oxidation. A better way to test the reactivity of cyclohexanone formed in the cyclohexane/CrO_2Cl_2 reaction is to prepare chromium-bound ketone *in situ*. Reaction of 0.16 equiv of cyclohexanol with CrO_2Cl_2 in cyclohexane-d_{12} at ambient temperatures (where alkane oxidation is slow) gives a 62% yield of cyclohexanone (eq 8) after hydrolytic workup of the brown precipitate. A similar reaction mixture was stirred at ambient temperature to form the bound cyclohexanone, then heated at 80 °C to consume all of the remaining CrO_2Cl_2. This resulted in a 31% yield of protiocyclohexanone, plus the expected cyclohexane-d_{12} oxidation products (eq 9 and Table 1, entry 7). Thus bound cyclohexanone is susceptible to further attack, apparently leading to ring-opened products. Consumption of roughly half of the cyclohexanone-h_{10} on reaction in cyclohexane-d_{12} (eq 9) is qualitatively consistent with the conclusion, from the appearance of products over time (Figure 4), that roughly 20% of the cyclohexanone formed in the reaction of CrO_2Cl_2 in protiocy-

Table 3. Product Yields from the Reaction of CrO_2Cl_2 with Cyclohexane and $CBrCl_3$[a]

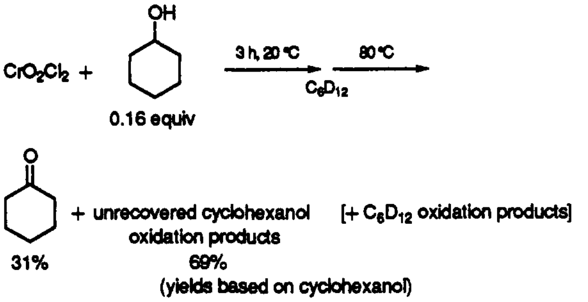
			% yields[b] [yield in mol[c]]			
	CrO_2Cl_2 added (mol)	initial $[CrO_2Cl_2]$ (M)	chlorocyclohexane	cyclohexanone	2-chlorocyclohexanone	bromocyclohexane
1.	3.70×10^{-4}	0.36	10.0(4)	8.5(3)	2.4(2)	1.5(1) [5.6×10^{-6}]
2.	2.47×10^{-4}	0.24	10.2(4)	8.8(3)	2.2(2)	2.2(1) [5.3×10^{-6}]
3.	0.6×10^{-4}	0.06	7(2)	4(1)	2.0(5)	7(2) [3.9×10^{-6}]

[a] Conditions: CrO_2Cl_2 + 1 mL of 10.5% (1.09 M) $CBrCl_3$ in C_6H_{12} for 4 h at 80 °C. [b] Values in parentheses are estimated 1σ errors. Values for the last entry are less accurate due to experimental difficulties. [c] Total amount of bromocyclohexane formed.

clohexane undergoes further oxidation, given that C_6D_{12} is 2.5 times less reactive than C_6H_{12}.



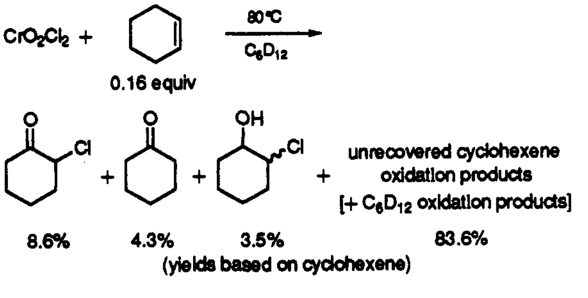
(8)



(9)

No protio-2-chlorocyclohexanone was detected from the further oxidation of bound cyclohexanone, again indicating that cyclohexanone is not on the pathway to chlorocyclohexanone. As the final yield of cyclohexanone in the cyclohexane/CrO_2Cl_2 reaction is only 8%, its further oxidation accounts for only a 2% yield of ring-opened products vs CrO_2Cl_2. Therefore cyclohexanone is not a significant intermediate in the pathway to ring-opened products.

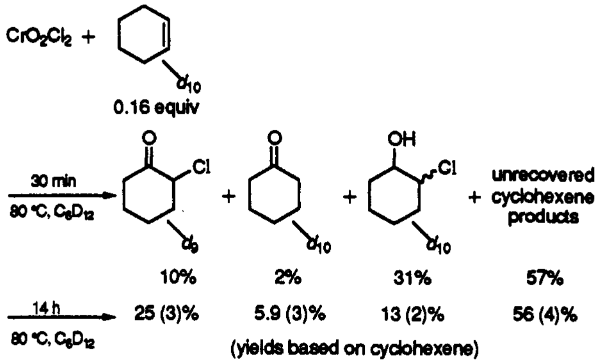
The reaction of cyclohexene with CrO_2Cl_2 has also been explored, as cyclohexene is observed as a product of cyclohexane oxidation. Cyclohexene reacts rapidly with CrO_2Cl_2 at room temperature, virtually within the time of mixing. In order to mimic the cyclohexane/CrO_2Cl_2 reaction conditions, mixing was accomplished at elevated temperatures by rupturing a breakseal vial containing cyclohexene in C_6D_{12} within a solution of CrO_2Cl_2 in C_6D_{12} cyclohexane-d_{12}. Following this procedure, reaction of 0.16 equiv of cyclohexene with CrO_2Cl_2 in C_6D_{12} at 80 °C gave small amounts of 2-chlorocyclohexanone, cyclohexanone, and *cis*- and *trans*-chlorohydrin, as well as the expected products of C_6D_{12} oxidation (eq 10, Table 1). Most of the cyclohexene (83.6%) reacted to form undetected products.



(10)

It has been shown previously that neither chlorocyclohexane nor cyclohexanone are significant precursors to chlorocyclohexanone or to ring-opened (undetected) products. Reaction 10 shows that cyclohexene is competent to be a precursor to both products. The first-order appearance of chlorocyclohexanone is consistent with cyclohexene as an intermediate assuming the steady-state approximation for cyclohexene concentration. This is reasonable given the high reactivity of cyclohexene with CrO_2Cl_2. Conversely, cyclohexene cannot be the major precursor to cyclohexanone formation, as much more chlorocyclohexanone than cyclohexanone is formed from cyclohexene, while the reaction of cyclohexane favors cyclohexanone.

Reaction of cyclohexene also forms chlorohydrin products (eq 10), which are observed in only trace quantities in the cyclohexane reaction. Chlorohydrins are common products in alkene oxidations by CrO_2Cl_2, and Sharpless has discussed their formation from cyclohexene, decene, and cyclododecene in some detail.[38] In our cyclohexene reaction, rapid precipitation occurs upon mixing the reagents, which may allow larger quantities of chlorohydrins to be trapped out as chromium-bound alkoxides. Under standard cyclohexane/CrO_2Cl_2 reaction conditions, formation of the Étard complex is slow and further oxidation of a chromium-bound alkoxy species yields 2-chlorocyclohexanone. This further oxidation is evident in reactions of cyclohexene-d_{10} with CrO_2Cl_2 in C_6H_{12}: the chlorohydrin yield is higher when the reaction is quenched soon after mixing while running the reaction to completion causes conversion of chlorohydrin predominantly to chlorocyclohexanone (eq 11, Table 2, entries 9a,b; cyclohexane oxidation products not shown).



(11)

In reaction with CrO_2Cl_2, 83% of the protiocyclohexene (57% of the deuteriocyclohexene) is converted to undetected products. The results of these experiments enable us to calculate, on mass balance considerations, the number of oxidative equivalents used per mole of undetected product—in other words, the average amount each cyclohexene becomes oxidized. The total number of chromium oxidative equivalents used in the reaction is determined from the amount of chromium(VI) added and the average chromium oxidation state in the Étard complex (the latter by iodometric titration). Some of these oxidizing equivalents are used in the formation of observed cyclohexene oxidation products (2-chlorocyclohexanone, cyclohexanone, and chlorohydrin) and

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(34) Danen, W. C. In *Methods in Free Radical Chemistry*, 5th ed.; Huyser, E. S., Ed.; M. Dekker: New York, 1974; pp 1–99, especially p 23ff. See also ref 23.

(35) (a) Al-Sheikhly, M.; McLaughlin, W. L. *Radiat. Phys. Chem.* **1991**, *38*, 203–211. (b) Diffusion limited trapping of alkyl radicals by permanganate: Steenken, S.; Neta, P. *J. Am. Chem. Soc.* **1982**, *104*, 1244–8.

(36) (a) The cyclohexyl radical reacts 1300 times faster with $CBrCl_3$ than with CCl_4 at 70 °C[36c] and the rate of the reactions of the cyclo*pentyl* radical plus CCl_4 at 70 °C is 1.5×10^4 M^{-1} s^{-1} (calculated from the Arrhenius parameters in ref 36d), suggesting a rate constant for $\cdot C_6H_{11} + CBrCl_3$ of 2×10^7 M^{-1} s^{-1}. The rate constant for cyclopentyl radical should be quite close to that for cyclohexyl as the nature of the alkyl does not have a large effect on the rate: $k(R^\cdot + CCl_4) = 1.5 \times 10^4$, 1.5×10^4, and 3.8×10^4 M^{-1} s^{-1} for $R^\cdot = C_6H_{11}{}^\cdot$, ${}^nBu^\cdot$, and ${}^tBu^\cdot$, respectively.[36d] (b) The rate of reaction of cyclohexane with $\cdot CCl_3$, k_5 in Scheme 2, is slow (49 M^{-1} s^{-1})[36d] so the constant a in eq 6 is likely to be close to 1. (c) Reference 24b, p 100. (d) Hawari, J. A.; Davis, S.; Engel, P. S.; Gilbert, B. C.; Griller, D. *J. Am. Chem. Soc.* **1985**, *107*, 4721–4.

(37) (a) Mareš, R.; Roček, J.; Sicher, J. *Collect. Czech. Chem. Commun.* **1961**, *26*, 2355–2368. (b) For other papers dealing with chromic acid oxidation of alkanes, see refs 10, 16, 17, 18d, 44, and the following: Roček, J. *Collect. Czech. Chem. Commun.* **1957**, *22*, 1519; Mareš, R.; Roček, J. *Collect. Czech. Chem. Commun.* **1961**, *26*, 2370–2388. Foster, G.; Hickinbottom, W. J. *J. Chem. Soc.* **1960**, 680–683. Sager, W. F.; Bradley, A. *J. Am. Chem. Soc.* **1956**, *78*, 1187–1190.

(38) (a) Sharpless, K. B.; Teranishi, A. Y.; Backvall, Jan-E. *J. Am. Chem. Soc.* **1977**, *99*, 3120–3128. (b) For other studies of CrO_2Cl_2 oxidations of alkenes, see: Miyaura, N.; Kochi, J. K. *J. Am. Chem. Soc.* **1983**, *105*, 2368–2378 and refs 12a, 14, and 16–18.

some are used in oxidation of the cyclohexane solvent. Since the ratios of the cyclohexane oxidation products are unaffected by the presence of added cyclohexene (Table 1), we assume that the total oxidative equivalents used per detected cyclohexane products is the same as found in cyclohexane/CrO_2Cl_2 reactions run in the absence of added alkene. This calculation indicates that the net number of oxidative equivalents used in the reaction per mole of unobserved protiocyclohexene product is 8.1(10). For the deuterioalkene, a value of 7.5(10) is obtained. As formation of adipic acid from cyclohexene requires 8 oxidative equivalents, these values are strong evidence that adipic acid is the primary unobserved product.

In conclusion, the oxidation of cyclohexane proceeds in part through cyclohexene as an intermediate, leading to chlorocyclohexanone and (mostly) unobserved products. A variety of evidence points to adipic acid as the primary unobserved product, which remains bound to the substitution inert Cr(III) product. There must also be separate pathways from cyclohexane to chlorocyclohexane and cyclohexanone since chlorocyclohexane is not formed at all from cyclohexene and cyclohexanone is only a minor product of cyclohexene reaction relative to chlorocyclohexanone. Under the reaction conditions, the three major observed products are not substantially oxidized further.

Discussion

The results provide a comprehensive picture of the reaction of cyclohexane with chromyl chloride, both qualitative and quantitative. We begin with a discussion of the first step, the activation of the alkane substrate. The next section describes the "product cascade", putting together the results into a single picture that describes the mass balance, the nature of the different pathways to products, and the observed yields. We conclude, perhaps most importantly, with a discussion of how and why chromyl chloride can react with a substrate like cyclohexane.

Initial Activation of Cyclohexane. The reaction of CrO_2Cl_2 with cyclohexane is first order in CrO_2Cl_2 and has a primary isotope effect. Hydrocarbon oxidation by CrO_2Cl_2 is in general quite sensitive to the nature of the substrate, with much faster reactions for compounds with benzylic or tertiary C–H bonds.[16] These data prove that chlorine atoms are not the reactive species. Rate-limiting Cr–Cl bond homolysis is not consistent with the observed substrate dependence and pre-equilibrium loss of $Cl^\bullet$ is not possible because this requires that the recombination of $Cl^\bullet$ and $[CrO_2Cl]$ be faster than the reaction of $Cl^\bullet$ with the cyclohexane solvent. $Cl^\bullet$ reacts with alkanes at close to diffusion-limited rates,[39] making it impossible for recombination with a low concentration chromium species to be faster than reaction with the solvent. In addition, CrO_2Cl_2 does not readily lose $Cl^\bullet$ thermally, as it is stable to liquid mercury, an excellent chlorine atom trap. Furthermore, hydrocarbon oxidation is a general property of chromyl compounds, including those without halogen ligands such as $CrO_2(NO_3)_2$ and $CrO_2[OC(O)CF_3]_2$.[8,9,16,17]

The C–H bond activation step is indicated to be direct attack by CrO_2Cl_2 at cyclohexane, by the simple first-order kinetics, the reproducible rates, the lack of any induction period, and the bromocyclohexane yields in the presence of $CBrCl_3$. A chain mechanism is very hard to rationalize with the data, especially the almost diffusion limited trapping of cyclohexyl radical by CrO_2Cl_2 (see below). While an early report suggested that an alkene initiator was required for CrO_2Cl_2 to react with methylcyclohexane,[40] under our more careful conditions these reactions proceed without initiation. We find that addition of a small amount of alkene to a reaction mixture results in rapid alkene oxidation, but once the alkene is consumed, the alkane oxidation proceeds at a similar rate and to similar product ratios as in the absence of alkene (see Table 1, entries 8 and 9, and Table 2, entry 8).

Formation of bromocyclohexane in the presence of $CBrCl_3$ shows the intermediacy of cyclohexyl radicals. The unusual variation in the yield of bromocyclohexane is consistent with cyclohexyl radical being both formed and consumed by CrO_2Cl_2 (Scheme 2, Table 3, eqs 4–7) and indicates that the radical is an intermediate rather than a side product. Alternative mechanisms involving initial electron transfer or hydride transfer from cyclohexane are very unlikely. Alkanes are extremely difficult to oxidize by outer-sphere electron transfer, with potentials estimated at +3 V,[41] and CrO_2Cl_2 is not a powerful outer-sphere oxidant.[42] Electron or hydride transfer would form charged species in cyclohexane which is quite difficult because of the low dielectric constant. That fact that the reaction runs so similarly in the gas phase—both in rate and product yields—virtually precludes the possibility of formation of charged intermediates. Concerted mechanisms, such as C—H addition across a Cr=O bond (suggested on the basis of *ab initio* calculations[20]) or simultaneous transfer of two hydrogens from cyclohexane to CrO_2Cl_2,[43] are difficult to rationalize with the radical trapping study, the low $\Delta S^\ddagger$ (–5 eu), the variety of products, and results on other systems.[16]

The intermediacy of cyclohexyl radicals and the conclusion that CrO_2Cl_2 is the reactive species indicate that alkane activation occurs by hydrogen atom transfer from cyclohexane to CrO_2Cl_2. While a variety of mechanisms have been suggested for related chromium oxidations,[10–20] the mechanism implicated here is similar to one of the pathways for CrO_2Cl_2 oxidation of arylalkanes advocated by Wiberg in 1965.[16] For arylalkanes, Wiberg could not distinguish between this path ($H^\bullet$ transfer to CrO_2Cl_2) and a radical chain pathway involving Cr^V as the abstracting reagent; the chain was the only favored mechanism for alkane oxidation by CrO_2Cl_2.[16] The partial retention of configuration in chromium oxidations, of (–)-α-deuteriopropylbenzene by CrO_2Cl_2 and of (+)-3-methylheptane by chromic acid, has been attributed to initial hydrogen atom transfer followed by significant cage recombination.[19,44]

Product Cascade. The cyclohexyl radical generated in the oxidation of cyclohexane by CrO_2Cl_2 is rapidly trapped by an oxidizing chromium species (predominantly chromyl chloride, see below). The trapping occurs by one of three possible pathways, which lead to formation of the observed cyclohexane oxidation products (Scheme 3). (1) The cyclohexyl radical may abstract a chlorine atom from chromium, resulting in formation of chlorocyclohexane. This step is proposed in the (–)-α-deuteriopropylbenzene oxidation mentioned above[19] and, in general, it is well established that oxidizing metal halides are very facile halogen atom donors.[45] (2) The cyclohexyl radical may instead attack at oxygen leading eventually to formation of cyclohexanone. Chromate and permanganate, as noted above, trap organic radicals at close to diffusion-controlled rates, and the trapping reaction is thought to be formation of a C–O bond.[35] (3) The cyclohexyl radical can also transfer a second hydrogen atom to give

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[39] Bunce, N. J.; Ingold, K. U.; Landers, J. P.; Lusztyk, J.; Scaiano, J. C. *J. Am. Chem. Soc.* **1985**, *107*, 5464–5472. Also see: Ingold, K. U.; Lusztyk, J.; Raner, K. D. *Acc. Chem. Res.* **1990**, *23*, 219–225 and references therein.

[40] Reference 12b. A later paper[12c] suggested that trace amounts of alkene present in the alkanes available at that time could be initiators.

[41] Kochi, J. K. in ref 7a, pp 849–890. Ross, S. D.; Finkelstein, M.; Rudd, E. J. *Anodic Oxidation*; Academic Press: New York, 1975; p 117ff.

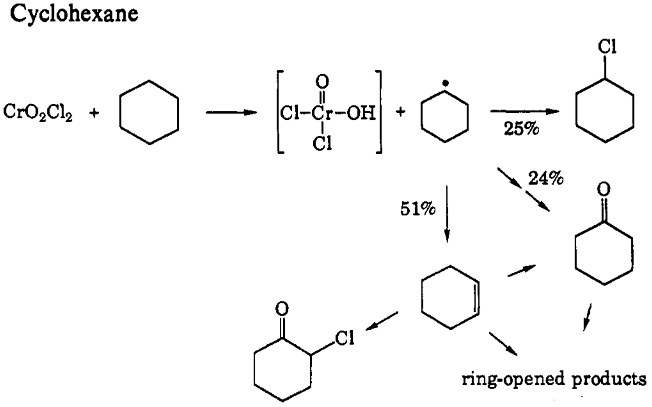
[42] Nyasulu, F.; Lachgar, A.; Mayer, J. M. Unpublished results based on electrochemistry in CH_2Cl_2.

[43] This was suggested by a reviewer as a pathway to cyclohexene, possibly in addition to the radical pathway advocated here. This pathway seems inconsistent with the small entropy of activation and with prior work on the oxidation of *cis*- and *trans*-decalin (which both proceed through the tetrasubstituted alkene[18c]). While we cannot rule out the possibility of multiple pathways, it would be remarkable if CrO_2Cl_2 had two ways of activating cyclohexane that occurred at close to the same rate.

[44] Oxidation of (+)-3-methylheptane by chromic acid in 91% acetic acid gave the corresponding tertiary alcohol with 70–85% retention of configuration: Wiberg, K. B.; Foster, G. *J. Am. Chem. Soc.* **1961**, *83*, 424.

[45] For instance, oxidation of the 5-hexenyl radical by $CuCl_2$ occurs at a rate grater than 2×10^8 M^{-1} s^{-1}: see ref 24b, p 9, and Kochi, J. K. *Acc. Chem. Res.* **1974**, *7*, 351.

Scheme 3. Mechanism of Chromyl Chloride Oxidation of Cyclohexane



cyclohexene. Such a second abstraction is very facile in radicals because the α-C–H bond is so weak, only ca. 35 kcal/mol.[46] So if chromium species are reactive enough to remove a hydrogen atom from the 95.5($\pm$1.0)-kcal/mol C–H bond in cyclohexane,[47] removal of a second hydrogen should be very rapid.

These three pathways are intuitively the three most likely fates for the cyclohexyl radical. They also essentially completely describe the cyclohexane/CrO_2Cl_2 reaction, based on mass balance considerations. Carbon–chlorine bond formation to make chlorocyclohexane is a reaction "dead end" so the amount of $C_6H_{11}Cl$ directly reflects the percentage of this pathway. Chlorocyclohexanone appears to be formed solely via the cyclohexene path (in 15(2)% yield[48]) and is not further oxidized. Therefore, the chlorocyclohexanone yield reflects the total path through cyclohexene. Cyclohexanone is formed both directly from cyclohexyl radicals (the major source) and via cyclohexene (4% of the cyclohexene pathway), and a small amount is consumed by further oxidation (roughly 20% of the amount formed, as described above). These pathways are summarized in the arrows of Scheme 3.

This mechanism can be checked because it implies a certain mass balance for the entire reaction. Calculating the amount of the cyclohexene pathway from the chlorocyclohexanone yield, and using the oxidative equivalents per undetected cyclohexene oxidation product as calculated above, the oxidative equivalents used in the cyclohexene pathway can be determined. The total oxidative equivalents used through the cyclohexene, chlorocyclohexane, and cyclohexanone pathways account for 88(10)% of the chromium oxidizing equivalents expended in the reaction.[49] Thus *the three pathways in Scheme 3 represent essentially the entire reaction.* This analysis assumes that the product distribution from the cyclohexene in the alkane oxidation is accurately modeled by the experiments with added cyclohexene, a good but not perfect assumption (see above).

The cyclohexyl radical reacts fairly indiscriminately with chromium oxidant(s): 25% reacting by chlorine atom transfer, 24% reacting via C–O bond formation, and 51% reacting by a second hydrogen atom transfer to give cyclohexene.[50] For each cyclohexyl radical formed in the reaction, an average of 2.5 CrO_2Cl_2 molecules are consumed. This is because a large fraction of the cyclohexane oxidized is converted to ring-opened products such as adipic acid, which requires 10 oxidizing equivalents—roughly 4 equiv of CrO_2Cl_2—to be made from cyclohexane. Thus one mole of CrO_2Cl_2 yields a total of only 0.4 mol of oxidized cyclohexane products. For this reason, the yields per mole of CrO_2Cl_2 we observe in the reaction—10.0% chlorocyclohexane, 8.0% cyclohexanone, and 2.5% chlorocyclohexane—actually represent slightly more than half of the cyclohexane oxidized.

The relatively indiscriminate trapping of the cyclohexyl radical via the three pathways is due to all the rates being close to the diffusion limit. Data from the radical trapping experiments (Table 3) can be used to estimate the overall rate of trapping of the cyclohexyl radical by chromium, k_2 in Scheme 2. The fraction of the cyclohexyl radicals trapped by bromine atom transfer from $CBrCl_3$ (F_{Br}) is given by eq 12, which rearranges to solve for $k_2[CrO_2Cl_2]$ as eq 13.[51]

$$F_{Br} = \frac{k_3[CBrCl_3]}{k_2[CrO_2Cl_2] + k_3[CBrCl_3]} \qquad (12)$$

$$k_2[CrO_2Cl_2] = k_3[CBrCl_3]\left\{\frac{1}{F_{Br}} - 1\right\} \qquad (13)$$

From entry 1 in Table 3, 370 μmol of CrO_2Cl_2, which should form 0.4 equiv or 150 μmol of cyclohexyl radical, gave 5.6 μmol of cyclohexyl bromide, so $F_{Br} = 0.038$. Using $[CBrCl_3] = 1.09$ M, $k_3 \cong 2 \times 10^7$ M^{-1} s^{-1},[36] and the average $[Cr] \cong 0.5[Cr]_i = 0.18$ M, k_2 is calculated to be roughly 3×10^9 M^{-1} s^{-1}. (The same value is obtained using reaction 2 in Table 3.) This estimate is consistent with the report of radical trapping by chromate in aqueous media being close to the diffusion limit, as mentioned above.[35a]

The radical trapping experiments also show that the cyclohexyl radicals are trapped predominantly by CrO_2Cl_2. Some trapping of $C_6H_{11}\cdot$ by $Cr(O)(OH)Cl_2$ within a solvent cage is possible, as suggested in related systems,[19,44] but is unlikely to be a major part of the reaction based on the similarity of the reaction in solution and in the gas phase (where there is no solvent cage). The analysis also rules out bimolecular trapping of the cyclohexyl radical by a chromium species other than CrO_2Cl_2 outside the solvent cage: k_2 is almost at the diffusion limit with CrO_2Cl_2 as the reactive species and it would have to be greater than this limit if trapping were to involve a low-concentration species such as a Cr(V) or Cr(IV) intermediate.

The mechanism for chromyl chloride oxidation of cyclohexane shown in Scheme 3 is thus quite similar to that proposed for alkane oxidation by cytochrome P-450 and model systems.[4a,b,52] Initial hydrogen atom transfer from the alkane to the metal–oxo group gives an alkyl radical and the metal hydroxide. The alkyl radical is then very rapidly trapped by the oxidizing metal center.[52]

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(46) For instance, $\Delta H°$ for $CH_3\cdot CHCH_2CH_3 \rightarrow$ *cis*-$CH_3CH{=}CHCH_3$ + H· is 34 kcal/mol based on data from: (a) Colussi, A. J. In *Chemical Kinetics of Small Organic Radicals*; Alfassi, Z. B., Ed.; CRC Press: Boca Raton, FL, 1988; p 33. (b) *JANAF Thermochemical Tables*, 3rd Ed. *J. Phys. Chem. Ref. Data* **1985**, *14*, Suppl. #1. (c) Stull, D. R.; Westrum, E. F., Jr.; Sinke, G. C. *The Chemical Thermodynamics of Organic Compounds*; Wiley: New York, 1969. (d) Reference 33. (e) See also: Gibian, M. J.; Corley, R. C. *Chem. Rev.* **1973**, *73*, 441–464.

(47) (a) McMillen, D. F.; Golden, D. M. *Annu. Rev. Phys. Chem.* **1982**, *33*, 493–532. (b) Recent reports of the heat of formation of isopropyl radical give the ^iPr–H bond strength as 96–98 kcal/mol: ref 47a and Luo, Y.-R.; Benson, S. W. *J. Phys. Chem.* **1989**, *93*, 3304–6; Seetula, J. A.; Russell, J. J.; Gutman, D. *J. Am. Chem. Soc.* **1990**, *112*, 1347–1353.

(48) The yields from cyclohexene are based on a reaction quenched at early times to avoid further oxidation of the products and assumes that 84% of the chlorohydrin is converted to chloro ketone, as found for cyclohexene-d_{10}.

(49) The 22% further oxidation of cyclohexanone has been included in this calculation (although it is a very small piece of overall mass balance), assuming that 6.1 ± 1.0 oxidative equivalents are used to oxidize each mole of cyclohexanone that reacts further. This is by analogy with the 8.1 ± 1.0 oxidative equivalents found for cyclohexene and is equivalent to assuming that the dominant unobserved oxidation product is adipic acid.

(50) These values are calculated assuming that Scheme 3 represents the entire reaction. On the basis of this assumption, the total yield of ring-opened products is 19%: 17% via the cyclohexene intermediate and 2% via further oxidation of cyclohexanone.

(51) The formation of cyclohexyl radicals from $\cdot CCl_3$ plus cyclohexane (k_5 in Scheme 2) can be neglected because so little $\cdot CCl_3$ is formed and because k_5 is relatively small (49 M^{-1} s^{-1} [36d]) while the trapping of $\cdot CCl_3$ by chromium, k_4[Cr], is probably much faster. This argument, that $k_5[C_6H_{12}] \ll k_4[Cr]$ also indicates that the constant *a* in eq 6 is close to 1.

(52) (a) Ortiz de Montellano, P. R.; Stearns, R. A. *J. Am. Chem. Soc.* **1987**, *109*, 3415–3420. (b) Bowry, V. W.; Lusztyk, J.; Ingold, K. U. *J. Am. Chem. Soc.* **1989**, *111*, 1927–1928. (c) Newcomb, M.; Manek, M. B.; Glenn, A. G. *J. Am. Chem. Soc.* **1991**, *113*, 949–958 and references therein and refs 4a,b.

Within the enzyme pocket trapping occurs stereospecifically, but in model systems the radical diffuses into solution and can be trapped by $CBrCl_3$.[4a,b]

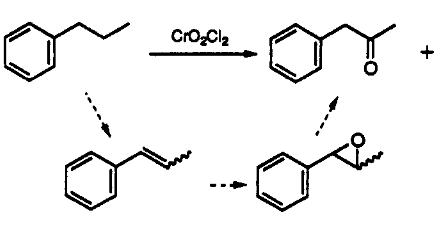
Further support for the mechanism in Scheme 3 comes from the product distribution in the reaction of cyclohexane-d_{12} (Table I, entry 2). The yields of observed products are higher for C_6D_{12} than for C_6H_{12}, increasing from 10.0% to 14.2% for chlorocyclohexane and from 8.0% to 13.6% for cyclohexanone. This reflects a different partitioning of the cyclohexyl-d_{11} radical among the three pathways, due to a primary deuterium isotope effect for pathway 3, hydrogen atom abstraction from cyclohexyl radical to give cyclohexene (Scheme 3). The isotope effect reduces the rate of cyclohexene formation while the rates of the other two pathways, radical attack at chlorine and oxygen, should not be significantly affected by deuteration. Thus a greater fraction of the reaction proceeds by the chlorocyclohexane and cyclohexanone pathways, which increase in roughly the same proportion (from 25% to 31% and from 24% to 27%).[53] The data indicate an isotope effect of 1.5 for hydrogen atom abstraction from C_6H_{11} vs $C_6D_{11}{}^{\bullet}$.

The yield of 2-chlorocyclohexanone is also larger from C_6D_{12} than from C_6H_{12}, which at first seems inconsistent with the analysis, since chlorocyclohexanone results from the cyclohexene pathway. It is consistent only if the yield of chlorocyclohexanone is much larger from cyclohexene-d_{10} than from protiocyclohexene. Quantitatively, the mechanism in Scheme 3 requires that the yield of chlorocyclohexanone vs adipic acid must be 3.0 times greater for C_6D_{10} than for C_6H_{10} (assuming that all of the oxidative equivalents unaccounted for in the isolated products go to formation of adipic acid or products requiring a similar number of oxidative equivalents). The independent cyclohexene oxidation experiments show the yield of chlorocyclohexanone vs undetected products (reacted cyclohexene which was not recovered in any form) is 3.3 times greater for C_6D_{10} than for C_6H_{10}.[54] The close agreement between the two independent calculations strongly supports the proposed mechanism.

An important corollary of the mechanism, as mentioned above, is that each oxidized cyclohexane consumes, on average, 2.5 molecules of CrO_2Cl_2. The second-order rate constants k in Table 2 are therefore 2.5 times the rate of hydrogen atom transfer from cyclohexane to CrO_2Cl_2, k_1 in Scheme 2 (this factor is assumed not to change very much over the temperature range studied, 75.0–91.2 °C, because there is little change in product yields). Taking this scale factor into account gives a $\Delta S^{\ddagger}$ for the hydrogen atom abstraction step as −7(2) eu, slightly lower than the value derived from the Eyring plot above using the second-order rate constants from Table 2. ($\Delta H^{\ddagger} = 26.6(8)$ kcal/mol is unaffected.) From an Arrhenius plot, $A = 6(5) \times 10^{11}$ and $E_a = 27.3(8)$ kcal/mol for the hydrogen atom abstraction step.

The different branch ratios for protio- vs deuteriocyclohexane result in a change in the reaction stoichiometries as well. For the reaction of cyclohexane-d_{12} with CrO_2Cl_2, an average of only 2.2 CrO_2Cl_2 molecules are used per C_6D_{12} activated. Thus the isotope effect for the hydrogen atom transfer step is not simply the ratio of rates of CrO_2Cl_2 disappearance but must take into account the reaction stoichiometries. The corrected isotope effect for hydrogen transfer (k_1) is $k_1(C_6H_{12})/k_1(C_6D_{12}) = 2.2(2)$ at 75.0 °C.

The cyclohexene pathway accounts for about half of the cyclohexane oxidized by CrO_2Cl_2 (Scheme 3). This perhaps surprising result has precedent in other reactions of CrO_2Cl_2, for instance the oxidation of *n*-propylbenzene in large part to benzyl methyl ketone (eq 14).[11] The product would appear to suggest

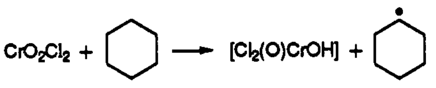


(14)

activation at the β carbon but the likely mechanism, based on labeling studies, is initial hydrogen abstraction to form the benzylic radical followed by a second hydrogen atom transfer to give 1-phenyl-1-propene (observed as a minor product[11]). Epoxidation, electrophilic ring opening of the epoxide to the benzylic carbocation, and a hydride shift yield the product. Independent reactions of the alkene and the epoxide with CrO_2Cl_2 give the same detected products in similar yields, including benzyl methyl ketone, chloro ketone products, and the C–C bond cleavage product, benzaldehyde.[18b] Other studies of alkene oxidation by CrO_2Cl_2 are consistent with this path.[38] The route to products from propylbenzene (eq 14) is closely related to the cyclohexane product cascade in Scheme 3, where some of the cyclohexanone and all of the 2-chlorocyclohexanone and ring-opened products are derived from oxidation of the cyclohexene intermediate.

We have neglected, up to this point, the involvement of chromium-containing intermediates. Hydrogen atom transfer to CrO_2Cl_2 generates a chromium(V) species, and a second hydrogen atom transfer to that would make a chromium(IV) species. Similarly, epoxidation of cyclohexene by CrO_2Cl_2 would form a chromium(IV) complex. The nature and the chemistry of such intermediate chromium species is perhaps the most difficult aspect of these reactions to unravel, and it has received significant attention in discussions of chromium(VI) oxidations.[55] In the oxidation of cyclohexane by CrO_2Cl_2, the disappearance of reactant (CrO_2Cl_2) and the formation of products both obey simple pseudo-first-order kinetics without an induction period which indicates that intermediate oxidation states are not kinetically important (note that some species with intermediate oxidation states are removed from the reaction by precipitation of the Étard complex). Moreover, the addition of other substrates (cyclohexanone, cyclohexanol, or cyclohexene), which should influence the concentrations of intermediate oxidation states, has little effect on the product distribution of concurrent cyclohexane oxidation. Thus a detailed description of the role of Cr(V) and Cr(IV) species—about which we have little information—does not appear necessary for a basic understanding of this reaction.

Understanding the Hydrogen Atom Transfer from Cyclohexane to CrO_2Cl_2. Why is chromyl chloride able to abstract a hydrogen atom from cyclohexane (eq 15)?



(15)

The classic reagents that abstract hydrogen atoms from alkanes are main group radicals such as $OH^{\bullet}$, $Br^{\bullet}$, and $ROO^{\bullet}$. In cytochrome P-450 and related enzymes and model systems that oxidize alkanes by initial hydrogen atom abstraction, the remarkable reactivity of the ferryl unit (FeO) is often rationalized by describing it as an oxygen radical.[4a–c] But chromyl chloride is diamagnetic, with no unpaired spins and cannot be described as a radical. There is no evidence for a $[Cr^{V}(O^{\bullet -})]$ resonance structure based on spectroscopic or theoretical studies.[56] *We suggest that radical character is not relevant to the ability to abstract a hydrogen atom from a substrate.* Radical character is not a key issue in the very extensive literature on rates of organic radical reactions.[23b] Rather, it has long been known that rates

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(53) The isotope effect on the partitioning of the cyclohexyl radicals also rules out an alternative pathway to cyclohexene, by elimination in a chromium alkoxide species (which has long been the favored path to alkenes[16–18]). This alternative would not result in an increase in the chlorocyclohexane yield on deuteration, only a change in the cyclohexanone/cyclohexene path ratio.

(54) Calculated from the data in entries 8b and 9a in Table 1 assuming that 84% of the chlorohydrin is converted to chlorocyclohexanone.

Scheme 4 Calculation of ΔH° for the Addition of $H^\bullet$ to Permanganate

$$\begin{array}{rcll}
\mathrm{MnO_4^-} + e^- & \longrightarrow & \mathrm{MnO_4^{2-}} & E^\circ = +0.564\ \mathrm{V}^{60} \\
{}^1/_2\mathrm{H_2} & \longrightarrow & \mathrm{H^+} + e^- & \\
\mathrm{MnO_4^{2-}} + \mathrm{H^+} & \longrightarrow & \mathrm{HMnO_4^-} & \mathrm{p}K_a = 10.5^{61} \\
\mathrm{H^\bullet} & \longrightarrow & {}^1/_2\mathrm{H_2} & \Delta G^\circ = -52\ \mathrm{kcal/mol}^{62} \\
\hline
\mathrm{MnO_4^-} + \mathrm{H^\bullet} & \longrightarrow & \mathrm{HMnO_4^-} & \Delta G^\circ = -79\ \mathrm{kcal/mol} \\
 & & & \Delta H^\circ = -80\ \mathrm{kcal/mol}
\end{array}$$

of hydrogen atom transfer reactions are directly related to the thermodynamic driving force.[57] For instance, $OH^\bullet$ abstracts hydrogen atoms from organic molecules much faster than ${}^tBuO^\bullet$ because the O–H bond formed by the hydroxyl radical is 14 kcal/mol stronger then ${}^tBuO$–H,[58] not because of any difference in the radical character. The relationship between activation energy (E_a) and exo- or endothermicity (ΔH) is summarized in the Polanyi equation[57] in which α and β are constants (eq 16).

$$E_a = \beta + \alpha(\Delta H) \qquad (16)$$

For the hydrogen atom transfer reaction $A–H + B \rightarrow A + H–B$, ΔH is simply the difference in the AH and BH bond strengths. For this reason, the extensive physical–organic literature on radical reactions is permeated by discussions of bond strengths.

We propose that hydrogen atom transfer to CrO_2Cl_2 behaves just like organic hydrogen atom transfer reactions, for instance following the Polanyi equation. *The key feature of chromyl chloride is its ability to make a strong O–H bond because the rate of hydrogen atom transfer is directly related to the strength of this O–H bond.* If the O–H bond in the chromium(V) species shown in eq 15 is strong enough, hydrogen atom transfer will occur, regardless of the radical character at the oxo groups.

The strength of the O–H bond in $[Cl_2(O)CrOH]$ is not known, but the strength of the analogous O–H bond formed by permanganate can be calculated (Scheme 4). The O–H bond strength in $[O_3MnOH]^-$ (normally written $HMnO_4^-$) is by definition $-\Delta H$ for addition of a hydrogen atom to permanganate. Addition of $H^\bullet$ is thermodynamically equivalent to addition of a proton and an electron so it can be calculated from redox potentials and pK_a values. This ability to calculate X–H bond strengths from redox potentials and pK_a values has been developed for organic compounds and its accuracy is now well established.[59] Converting the E° and pK_a values to free energies ($\Delta G^\circ = -nFE^\circ$ and $\Delta G^\circ = -RT \ln K$) gives a ΔG° of −79 kcal/mol for the addition of $H^\bullet$. This value can be converted to an enthalpy using $\Delta S^\circ(H^\bullet, aq)$ of 1.9 eu[63] and making the well-documented assumption[59] that the entropy of MnO_4^- is the same as that of $HMnO_4^-$. The value obtained for the $[O_3MnO–H]^-$ bond strength is 80 kcal/mol.

This simple calculation provides new intuition for hydrogen atom transfer processes involving metal–oxo species. The 80-kcal/mol bond permanganate makes with $H^\bullet$ is comparable to the bonds made by ${}^tBuOO^\bullet$, $Br^\bullet$, and $I^\cdot$ (89, 87, and 71 kcal/mol, respectively).[58] It is remarkable that permanganate, a stable species one can purchase, has a bond strength to a hydrogen atom comparable to fleeting main group radical intermediates. This perspective, that permanganate is like a weak bromine atom, provides an explanation for how and why permanganate—and, by analogy, chromyl chloride—can oxidize alkanes: the strong O–H bond formed allows them to remove a hydrogen atom, just as a bromine atom can abstract hydrogen to form HBr. A related thermodynamic cycle was used by Wiberg and Foster in 1961 to crudely estimate ΔG for (and thus rationalize) hydrogen abstraction by chromic acid.[44]

If chromyl chloride really behaves like a main group oxygen radical with a roughly 80 kcal/mol O–H bond strength, there should be a strong connection between its reactivity and that of $HO^\bullet$, $RO^\bullet$, and $ROO^\bullet$. The rates of oxygen radicals abstracting a hydrogen atom from a particular substrate are directly related to the strength of the O–H bond being formed, following the Polanyi equation.[57] *The correlation of O–H bond strength with hydrogen atom transfer rate also appears to hold for chromyl chloride*: Figure 5 plots the rates of hydrogen atom abstraction from cyclohexane at 25–30 °C by $OH^\bullet$, ${}^tBuO^\bullet$, ${}^tBuOO^\bullet$, and CrO_2Cl_2.[64] The rate for chromyl chloride is extrapolated from higher temperature data and the bond strength made by chromyl chloride is taken as that of permanganate.[65] It is remarkable that chromyl chloride can be put on a graph of this kind with oxygen radicals. It is also remarkable that the plot is reasonably

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(55) See, for instance: (a) Westheimer, F. H. *Chem. Rev.* **1949**, *45*, 419. (b) Watanabe, W.; Westheimer, F. H. *J. Chem. Phys.* **1949**, *17*, 61. (c) Wiberg, K. B.; Richardson, W. H. *J. Am. Chem. Soc.* **1962**, *84*, 2800. (d) Freeman, F.; Armstead, C. R.; Essig, M. G.; Karchefski, E. M.; Kojima, C. J.; Manopoli, V. C.; Wickman, A. H. *J. Chem. Soc., Chem. Commun.* **1980**, 65–6. (e) Scott, S. L.; Bakac, A.; Espenson, J. H. *J. Am. Chem. Soc.* **1992**, *114*, 4205–4213 and refrences therein. (f) Reference 16. (g) Beattie, J. K.; Haight, G. P., Jr. *Prog. Inorg. Chem.* **1972**, *17*, 93–145. (h) Recent estimates of $Cr^{V/IV}$ and $Cr^{IV/III}$ redox potentials for complexes of 2-hydroxyl-2-ethylbutyric acid suggest that these oxidation states are at least as strong oxidants as Cr^{VI}: Ghosh, M. C.; Gould, E. S. *J. Am. Chem. Soc.* **1993**, *115*, 3167–3173.

(56) Cieślak-Golonka, M. *Coord. Chem. Rev.* **1991**, *109*, 223–249, especially 233–237.

(57) (a) Ingold, K. U. Chapter 2 in Vol 1 of ref 23b, pp 69ff. (b) Russell, G. A Chapter 7, Vol. 1 of ref 23b, pp 283–293. (c) The correlation of rates with driving force holds for similar kinds of radicals, when polar effects are not significant.[57b,d] (d) Tedder, J. M. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 401–410. (e) 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. (f) The Polanyi equation relates the driving force (ΔH) to the activation energy or enthalpy (E_a or $\Delta H^\ddagger$) but we have chosen here to relate it to log k, which is proportional to $\Delta G^\ddagger$. Linear free energy relationships like the Polanyi equation are at least as valid with free energies as with enthaplies: Exner, O. *Prog. Phys. Org. Chem.* **1973**, *10*, 411–482, especially pp 466ff.

(58) Bond strengths in kcal/mol: HO–H, 119; ${}^tBuO$–H, 105; H–Cl, 104; ${}^tBuOO$–H, 89; H–Br, 87; H–I, 71. Values from ref 46b for H_2O and HX; for ${}^tBuO^\cdot$ and ${}^tBuOO^\cdot$ from ref 46a. A lower value for ${}^tBuOO$–H is suggested in: Holmes, J. L.; Lossing, F. P.; Mayer, P. M. *J. Am. Chem. Soc.* **1991**, *113*, 9723–8. The C–H bond strength in cyclohexane is 95.5 kcal/mol.[46a,47a]

(59) For leading references, see: (a) Bordwell, F. G.; Cheng, J.-P.; Harrelson, J. A., Jr. *J. Am. Chem. Soc.* **1988**, *110*, 1229–1231. Zhang, X.-M.; Bordwell, F. G. *J. Am. Chem. Soc.* **1992**, *114*, 9787–9792. (b) Parker, V. D. *J. Am. Chem. Soc.* **1992**, *114*, 7458; and correction: Parker, V. D. *J. Am. Chem. Soc.* **1993**, *115*, 1201. (c) For application to the calculation of metal hydride bond strengths see: Tilset, M.; Parker, V. D. *J. Am. Chem. Soc.* **1989**, *111*, 6711–6717; and correction: Tilset, M.; Parker, V. D. *J. Am. Chem. Soc.* **1990**, *112*, 2843. (d) Bordwell and co-workers have calculated bond strengths in DMSO as $\mathrm{BDE} = 23.1E^\circ + 1.37\mathrm{p}K_a + C$, where the constant C (solvent dependent) is viewed as semiempirical.[59a] The values of C derived here (52 kcal/mol to give ΔG, 53 kcal/mol including the entopy term, to give ΔH) agree well with $E^\circ(H^+/H^\cdot) = -2.29$ (53 kcal/mol) derived in ref 59c.

(60) Latimer, W. M. *The Oxidation States of the Elements and Their Potentials in Aqueous Solution*, 2nd ed.; Prentis Hall: New York, 1952.

(61) The following report pK_a values of 10.8 and 10.2: Lister, M. W.; Yoshino, Y. *Can. J. Chem.* **1960**, *38*, 2342–2348. Heckner, K.-H.; Landsberg, R. *J. Inorg. Nucl. Chem.* **1967**, *19*, 423–430.

(62) (a) In the gas phase, $\Delta G^\circ(H^\cdot \rightarrow {}^1/_2 H_2)_g$ is −48.6 kcal/mol.[46b] Solvation of H_2 is typically taken as a good model for the solvation of $H^\cdot$ (see extensive discussions in ref 59, including ref 59b correction). $\Delta G^\circ_{\mathrm{solvation}}(H_2) = +6.6$ kcal/mol,[62b] so $\Delta G^\circ(H^\cdot \rightarrow {}^1/_2 H_2)_{H_2O} = -48.6 - 6.6 + 3.3 = -51.9$ kcal/mol. (b) *Solubility Data Series*; Young, C. L., Ed., Pergamon: New York, 1981; Vol. 5/6, p 2.

(63) Using the approximation that H_2 is a good model for the solvation of $H^\cdot$[59] $\Delta S^\circ(H^\cdot,aq) \cong \Delta S^\circ(H^\cdot,g)^{46b} + \Delta S(H_2,aq)_{\mathrm{solvation}}{}^{62b} = 27.4 - 25.5 = 1.9$ eu.

(64) Rate constants for hydrogen abstraction by ${}^tBuO^\cdot$ and ${}^tBuOO^\cdot$ [64a] and by $OH^\cdot$ [64b] are from the references indicated. (a) Howard, J. A.; Scaiano, J. C. Oxyl-, Peroxyl- and Related Radicals. In *Radical Reaction Rates in Liquids*; Landolt-Börnstein New Series; Fischer, H., Ed.; Springer Verlag: New York, 1984; Vol. 13, subvol. d. (b) Buxton, G. V.; Greenstock, C. L.; Helman, W. P.; Ross, A. B. *J. Chem. Phys. Ref. Data* **1988**, *17*, 513. (c) Bond strengths: see ref 58. These bond strengths are likely to be accurate for solution studies as well: see ref 23b; Bordwell, F. G.; Cheng, J.-P.; Ji, G.-Z.; Satich, A. V.; Zhang, X. *J. Am. Chem. Soc.* **1991**, *113*, 9790–9795; Kanabus-Kaminska, J. M.; Gilbert, B. C.; Griller, D. *J. Am. Chem. Soc.* **1989**, *111*, 3311–4.

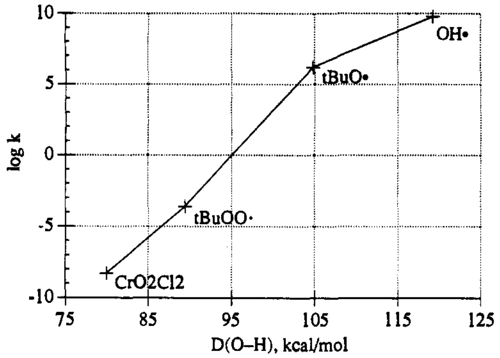

Figure 5. Rates of hydrogen atom abstraction from cyclohexane by OH•, ᵗBuO•, ᵗBuOO•, and CrO_2Cl_2 at 25–28 °C vs the O–H bond strength formed. Kinetic and bond strength data are from ref 64 exept for CrO_2Cl_2, for which the rate was extrapolated from higher temperature data and the bond strength was taken as that of permanganate, 80 kcal/mol (Scheme 4).

linear, covering an almost 40-kcal/mol range of driving force and a 10^{19} range of rates! The plot may be leveling out at high driving force because the reaction of OH• is essentially at the diffusion limit. A similar correlation of rate with driving force is seen in the oxidation of toluene by HO•, RO•, ROO•, and CrO_2Cl_2, using either the literature[13] or our own preliminary values[66] for the CrO_2Cl_2 oxidation (although it is not clear that this reaction proceeds via hydrogen atom transfer).

The observed correlation of rate with driving force provides strong evidence that diamagnetic CrO_2Cl_2, a stable molecular species and not a radical, behaves just like a fleeting oxygen radical based solely on the strength of the O–H bond that is formed. We believe that this type of analysis will prove to be very powerful in the understanding, both qualitative and quantitative, of hydrogen atom transfer reactions by metal–oxo complexes (and perhaps other inorganic compounds).

The calculation in Scheme 4 and the analogy between permanganate and chromyl chloride suggest that hydrogen atom transfer from cyclohexane to CrO_2Cl_2 is endothermic by ca. 16 kcal/mol. This is likely a reason for the high activation barrier ($\Delta H^\ddagger$ = 26.6(8) kcal/mol). Hydrogen atom abstraction from cyclohexane by ᵗBuOO• is endothermic by 7 kcal/mol[58] and proceeds with $\Delta H^\ddagger$ = 18.9 kcal/mol, $\Delta S^\ddagger$ = −13 eu (log A = 10.4 and E_a = 19.5 kcal/mol).[67] The high endothermicity suggests a late transition state for hydrogen atom transfer, with considerable CrO–H bond formation and C–H bond cleavage. The late transition state provides a rationale for the low isotope effect for hydrogen atom transfer and may account for the small $\Delta S^\ddagger$ and the rather large Arrhenius pre-exponential factor (log A = 11.8).

Conclusions

Chromyl chloride oxidizes cyclohexane by initial hydrogen atom transfer. The cyclohexyl radical is then trapped by high oxidation state chromium by one of three pathways: by chlorine atom transfer to give chlorocyclohexane; by formation of a carbon–oxygen bond, leading to cyclohexanone; or by transfer of a second hydrogen atom to give cyclohexene. Cyclohexene is further oxidized to chlorocyclohexanone and cyclohexanone, which are observed, and ring-opened products which are not directly observed. From mass balance considerations and IR spectra, the ring-opened products are thought to be primarily adipic acid. This mechanism, summarized in Scheme 3, accounts for 88(±10)% of the mass balance in the reaction. The reaction of cyclohexane-d_{12} proceeds similarly although the partitioning of the cyclohexyl-d_{11} radical is different because of an isotope effect on the second hydrogen atom transfer step. There is also a significant isotope effect on the pathways for cyclohexene oxidation.

Initial hydrogen atom transfer from cyclohexane to CrO_2Cl_2, to give cyclohexyl radical and $[Cr(O)(OH)Cl_2]$, occurs at a rate of 4.3×10^{-6} M^{-1} s^{-1} at 75 °C, with the activation parameters $\Delta H^\ddagger$ = 26.6(8) kcal/mol and $\Delta S^\ddagger$ = −7(2) eu. There is a primary isotope effect on the hydrogen atom transfer step of 2.2(2). It is suggested that chromyl chloride is able to abstract a hydrogen atom primarily because of the strength of the O–H bond formed in $[Cr(O)(OH)Cl_2]$, *not* because of any radical character at the abstracting oxygen in diamagnetic CrO_2Cl_2. The strength of this O–H bond is estimated by analogy with permanganate, whose ability to abstract a hydrogen atom appears to be similar. The O–H bond formed by H• addition to permanganate, giving $[O_3MnO–H]^-$, is calculated to be 80 kcal/mol from redox potential and pK_a values (Scheme 4). Assuming this value for chromyl chloride, the rate of hydrogen atom transfer is consistent with the rates of hydrogen atom abstraction from cyclohexane by peroxy, alkoxy, and hydroxy radicals (Figure 5). This suggests a close analogy between the reactivity of metal–oxo species and oxygen radicals, based solely on the strength of the O–H bond they form.

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(65) (a) A crude estimate can be made for the addition of H• to $HCrO_4^{2-}$, which appears to be the active species in many organic oxidations by Cr^{VI} (refs 55a and 65b,c). $E°$ for the $Cr^{VI/V}$ redox couple was estimated by Westheimer to be ≤0.62 V[55a] (see also ref 55h). The pK_a value for d^1 $H_2CrO_4^-$ is not known but it should be larger than that of the d^0 vanadium analog (8[65d]), since the pK_a of d^1 $HMnO_4^-$ is ~4 units larger than that of d^0 $HCrO_4^-$.[61,65d] Using $E°$ = 0.62 V and pK_a = 8, following Scheme 4, an estimate of $D(HO_3CrO–H)$ = 77 kcal/mol is obtained. (b) Beattie, J. K.; Haight, G. P., Jr. *Prog. Inorg. Chem.* **1972**, *17*, 93–145. (c) Lee, D. G.; Spitzer, U. A. *Can. J. Chem.* **1971**, *49*, 2763–9. (d) Baes, C. F., *Jr.*; Mesmer, R. E. *The Hydrolysis of Cations*; Wiley-Interscience: New York, 1976.

(66) Cook. G. K.; Mayer, J. M.—work in progress: $k(C_7H_8+CrO_2Cl_2) \cong 9 \times 10^{-4}$ M^{-1} s^{-1} at 40 °C, which compares well to the values of ca. 10^{-4} M^{-1} s^{-1} reported on the basis of initial rates for the oxidation of toluene by CrO_2Cl_2 in chlorinated solvents at 25 °C.[13b]

(67) Reference 64a, p 257.