On the Trail of CrO_2Cl_2 in Its Reactions with Organic Compounds

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Abstract: The simple metal oxo compound chromyl chloride, CrO_2Cl_2, displays a very complex reactivity with respect to alkanes, olefins, alcohols, and epoxides. Synergetic investigations applying various techniques and methods have only recently led to an understanding of the key steps in the corresponding mechanisms, which are representative for more complex systems. Product formation seems to be largely determined by radical reactions initiated by this d^0-metal compound.

Keywords: chromium · epoxides · oxidations · radicals · reaction mechanisms

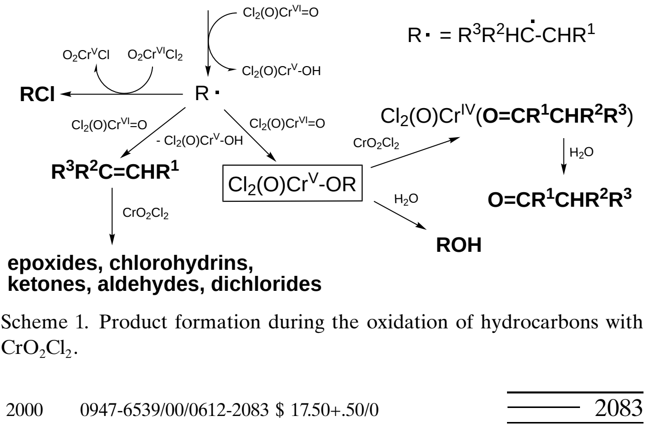
Introduction

Transition metal oxides and their complexes play pivotal roles in numerous important biological and nonbiological stoichiometric and catalytic processes by which oxo functionalities are transferred to organic substrates.[1–4] For instance, simple metal oxo compounds and oxometal halides such as CrO_2Cl_2,[5–7] OsO_4,[8, 9] MnO_4^-[10–12] are applied extensively in conversions where oxygen is inserted into a C–H linkage or added to an olefin double bond. The widespread practical use of such reagents has spurred considerable interest into the underlying activation mechanisms,[1–4, 8, 13–16] with kinetic studies dating back to the 1940s. However, although intense research in this area has provided a broad synthetic, structural, and mechanistic basis, many of the key steps remained unknown, some of the reasons being high and complex reactivities, diverse reaction pathways, and the heterogeneity of the inorganic reduction products, which therefore elude characterization. In the past 4–5 years investigations concerning the reaction mechanisms of simple metal oxides and oxometal halides have been reintensified,[17–29] as it was recognized that the combination of methods available today (elaborate quantum-mechanical calculations, matrix-isolation and gas-phase techniques, and sophisticated kinetic studies) allows deeper insights into these systems, which in turn can be regarded as models[21] for more complex metal–oxo moieties such as those occurring in enzymes.

This concept highlights the progress that has been made within the past few years in understanding the reactivity principles of a representative, classical oxidising agent, chromyl chloride, as well as the conceptional and methodological approaches which made this progression possible, leading to a new way of thinking about d^0-metal oxo compounds in general.

Discussion

C–H bond activation: The oxidation of hydrocarbons by chromyl chloride, CrO_2Cl_2, is known as the Etard reaction[30] and was developed as early as 1877. Despite the recognition this reaction has achieved in the meantime, its course and the nature of its intermediates remained unknown until more than 100 years later J. M. Mayer et al. provided strong evidence—mainly by kinetic studies and trapping experiments—that in reactions of alkanes with CrO_2Cl_2 the first step consists of a proton-coupled electron transfer: the addition of an electron to the Cr=O π* orbital significantly increases the basicity of the oxo group and—conversely—protonation of the oxo ligand makes the complex a much stronger electron acceptor. Consequently the Cr=O functions of CrO_2Cl_2[18] are capable of abstracting alkylic H atoms (as had previously been suggested by K. B. Wiberg[5]) thereby generating organic radicals, which then give rise to the various organic oxidation products in subsequent reaction with CrO_2Cl_2 (Scheme 1).



Scheme 1. Product formation during the oxidation of hydrocarbons with CrO_2Cl_2.

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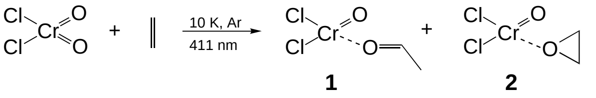
The finding of simple alcohols among the products required the assumption of an additional important step: radicals resulting from the primary hydrogen abstraction were proposed[20] to add to Cr=O groups of excessive CrO_2Cl_2 to yield Cr^V alkoxides (framed in Scheme 1), which should then release the alcohols during aqueous work-up.[18] Only recently we have achieved the isolation and characterization of such a species for the first time (vide infra).[31]

Traditionally H-atom transfer onto oxometal species had been rationalized in terms of assumptions based on an analogy with organic radical chemistry, that is unpaired electron density was thought to be transferred to the oxygen atoms of the metal compounds, which are then ready to enter into radical reactions.[8] The studies mentioned, however, established that CrO_2Cl_2—a d^0 system without unpaired spin density—can in fact abstract hydrogen *atoms* from saturated organic systems, primarily because of the strength of the OH bond formed in $[Cl_2(O)CrOH]$. Its reactivity is therefore reminiscent of oxygen radicals, even though it is not a radical, and a progression has occurred from thinking about radicals and spin density to an approach based on the thermochemistry of the H-atom transfer step.[20] More work is needed to test the generality and the predictive power of this "bond strength approach" to metal-mediated hydrogen atom abstraction reactions.

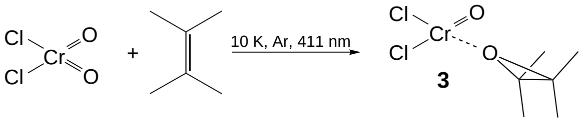
Oxidation of unsaturated systems: For the *olefin oxidation* by CrO_2Cl_2 complex mechanisms have been put forward in the past[13, 32] that attempted to explain the great variety of products obtained (like dichlorides, chlorohydrins and epoxides) on the basis of intermediates such as chromaoxetanes, chromium alkoxides, and epoxide complexes. However, due to the aggregation of the actual intermediates (forming the heterogeneous "Etard complex") none of the proposed species was ever really identified as such in the reaction mixtures and they also eluded synthesis by alternative routes. On the other hand, it was neither possible to show that they are *not* formed or existent, so that the reaction mechanism was left to discussion for quite some time. In addition to the aforementioned products carbonyl compounds were often obtained, too, but these were considered as secondary rather than primary products and proposed to follow from subsequent reactions of the epoxides or chlorohydrins during workup.[32, 33] However, recently a hint to the relevance of intermediate chromium complexes *also* for the formation of the carbonyl products was provided: H. Schwarz, D. Schröder et al. showed that the CrO_2^+ ion—that is a Cr^V oxide—reacts with ethylene in the gas phase to yield $O{=}Cr^+\cdots O{=}CH\text{-}CH_3$[34a] and (more relevant to the present problem as a d^0 system is considered) VO_2^+ oxidizes ethylene to form $O{=}V^+\cdots O{=}CHCH_3$.[34b]

In an attempt to investigate the ethylene oxidation by CrO_2Cl_2 at an early stage at very low temperatures and to thereby obtain direct information about occurring primary and secondary intermediates we have successfully employed matrix isolation techniques: if the activation energy necessary to trigger the reaction in argon at 10 K is provided by means of irradiation, the species $O{=}CrCl_2\cdots O{=}CHCH_3$ (**1**) and $O{=}CrCl_2\cdots \overline{OCH_2CH_2}$ (**2**) [Eq. (1)] are formed.[22, 23]



(1)

The extension of this matrix study to substituted olefins[23] yielded additional mechanistic information: i) epoxidation proceeds stereoselectively as a *cis*-addition reaction and ii) carbonylation occurs regioselectively at the least substituted C atom. Furthermore an increase of the degree of methylation at the olefinic bond appeared to decrease the yield of the corresponding carbonyl compound relative to the epoxide, and hence the oxidation of tetramethylethylene yields selectively the epoxide complex **3** [Eq. (2)].[23] The fact that the epoxide complexes were found to be photolytically stable excludes that the complexes of the carbonyl compounds were generated by rearrangement of the former, that is both types of species are generated by independent routes. In principle, they can be envisaged to form via a common primary product such as a cycloadduct. Recent results by T. Ziegler et al.,[24] who studied the thermally activated reaction of ethylene with chromyl chloride independently by means of density functional theory (DFT) calculations, showed, that—analogously to the $OsO_4/H_2C{=}CH_2$ system[26]—the [2+3] addition of ethylene to the metal–oxygen bonds in chromyl chloride is favored over the [2+2] cycloaddition both kinetically and thermodynamically (Scheme 2). However, since the [2+3] cycloadduct **4** is more stable[25] than **2**, **4** cannot represent an essential intermediate in the matrix reaction without being observed itself and there was not hint to it in the IR spectra.[23] Alternative reaction routes therefore have to be considered. One possibility certainly is a direct oxo transfer from a Cr=O function onto the olefinic bond as shown in Scheme 2 (Route (i)), explaining the retention of stereochemistry observed for the epoxidation. In a competing reaction route ((ii) in Scheme 2) chromyl chloride could be imagined to react with olefins under homolysis of the π bond (that is, in a fashion comparable to the one found for the thermal alkane



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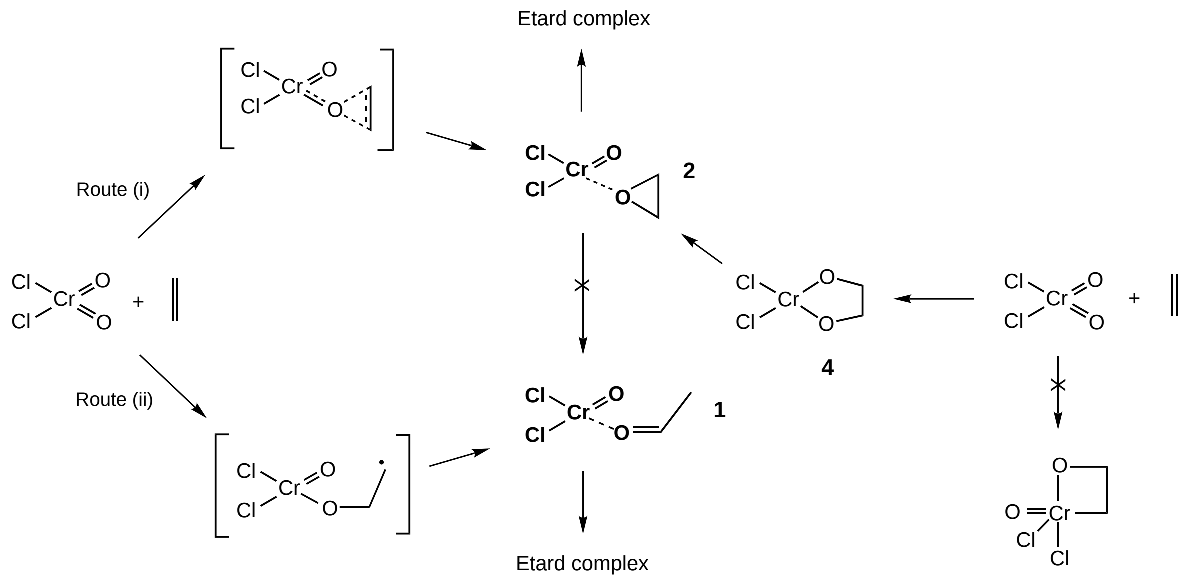
Abstract in German: *Die einfache Oxometall-Verbindung Chromylchlorid, CrO_2Cl_2, zeigt eine sehr komplexe Reaktivität in Bezug auf Alkane, Olefine, Alkohole und Epoxide. In jünster Vergangenheit konnten durch synergetische Studien unter Einsatz verschiedenster Arbeitstechniken und Methoden große Fortschritte in Bezug auf das Verständnis der jeweiligen Schlüsselschritte gemacht werden, die wiederum repräsentativ für komplexere Oxometall-Verbindungen sein sollten. Die Produktbildung scheint zu einem großen Anteil von Radikalreaktionen bestimmt zu werden, die erstaunlicherweise von der d^0-Metall-Verbindung CrO_2Cl_2 ausgelöst werden.*



Photochemistry at 10 K in Argon
C. Limberg et al.[22, 23]

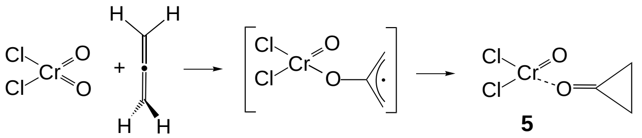
Thermochemistry according to calc. by
T. Ziegler et al.[24, 25]

Scheme 2. Mechanisms for the thermal and photolytical reaction of CrO_2Cl_2 with ethylene.

oxidation where it homolytically splits C–H σ bonds (vide supra)) leading to radical intermediates or transition states as shown in Scheme 2. These are reminiscent of the species discussed as intermediates for olefin oxidations with O=M(salen) (salen = *N*,*N*′-bis(salicylidene)ehtylenediamine dianion and O=M(porphyrin) (M = Mn, Fe) complexes,[35] and they should yield the observed complexes of carbonyl compounds after a 1,2-H migration (the activation barriers for this process can be easily crossed under the photolytic conditions). On employment of higher olefins, the most stable radicals should be formed initially, explaining the regioselectivity found for the carbonylations.[23] The kinetics calculated by Ziegler et al.[25] are not valid for the matrix experiments as they involve CrO_2Cl_2 in its excited states and consequently under these conditions the formation of chromaoxetanes in the first step cannot be excluded. The necessary condition would be a completely kinetically controlled reaction in this direction (the barriers to the [2+3] cycloadducts would have to be very high) and making several additional assumptions concerning their photolytic decomposition, which are difficult to ascertain, formation of **1** and/or **2** in the matrices could in principle be explained starting from such chromaoxetanes, too.

The discussion in the preceeding paragraph shows already that the photochemical process investigated in the matrix studies has to be distinguished from the thermal process considered in the calculations. However, the potential energy surfaces of both systems may have common areas and it can be claimed that the species isolated in the matrix experiments are minima within these regions. This hypothesis is very nicely supported by most recent results of T. Ziegler et al. who performed calculations concerning the progress of the thermally activated reaction *after* the formation of **4**. This investigation was inspired by the fact that the hydrolysis products of $\overline{[\mathrm{Cr}]\mathrm{OCR_2CR_2O}}$ moieties, diols, are *not* isolated after aqueous work-up of olefin oxidations with CrO_2Cl_2, so that the diolate intermediates (like **4**) must undergo further transformations. The calculations showed[25] that **4** is indeed sufficiently flexible to allow a facile rearrangement to yield **2** via a modest barrier. Compound **2** and its methylated derivatives, which had been suggested as short-lived species during olefin oxidations with CrO_2Cl_2 for the first time by K. B. Sharpless[13] and which we have been able to isolate and characterize in the course of the above studies, therefore seem to represent intermediates of the processes under thermal conditions, indeed (Scheme 2). This on the other hand suggests that the same is true for the $O{=}CrCl_2$ complexes of the carbonyl compounds (e.g. **1**, Scheme 2) which form simultaneously to the epoxide complexes in the matrix experiments and which could nicely serve to explain why many authors reported the occurrence of carbonyl compounds among the products of olefin oxidations with CrO_2Cl_2 in the past.[5, 6, 32] While no chlorinated products are generated under photolytic matrix conditions, further products of *thermally* activated oxidations are, as mentioned above, chlorohydrins and dichlorides, which were observed to principally form in the course of formal *cis*-additions of HOCl and Cl_2 to olefins.[13] According to the DFT results of Ziegler et al. this can be rationalized by [2+3] additions of the olefin to the O=Cr–Cl and Cl–Cr–Cl moieties of CrO_2Cl_2, respectively.[25] Dichlorination was computed to be thermodynamically far less favourable than either epoxidation or oxychlorination, explaining why the yields for the dichlorides are always comparatively low.[13] Sharpless's observation that a small fraction of the chlorohydrins obtained had formed in the course of a formal *trans*-addition of HOCl remains to be explained, and an attempt is made below (see Epoxide cleavage).

The mechanism shown in Scheme 2 is further supported by the results obtained in experiments where alkynes and allene were used as substrates: photolytically activated, matrix-isolated CrO_2Cl_2 reacts with alkynes to yield complexes of the type $O{=}CrCl_2(\eta^1\text{-}O{=}C{=}CR_2)$ ($R = H$, Me) featuring ketene ligands in a hitherto (in structurally characterised compounds) unprecedented η^1-coordination mode,[36] and the oxidation of allene yields a corresponding cyclopropanone complex $O{=}CrCl_2(\eta^1\text{-}O{=}\overline{CCH_2CH_2})$ (**5**, in Scheme 3).[36] The formation of **5** supports the hypothesis of a π-bond homolysis initiated by the attack of CrO_2Cl_2 at the unsaturated bond leading to radical intermediates or transition states in the matrices. A similar type of reaction under thermal conditions is, however, not likely as it would lead to a significant loss of stereoselectivity.

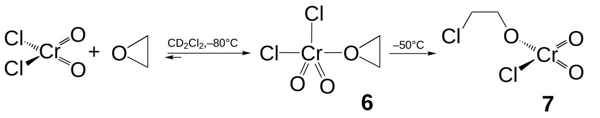


Scheme 3. Photoreaction of CrO_2Cl_2 with allene at 10 K.

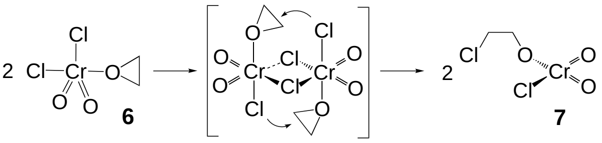
Although a giant step forward has been made in understanding the reactions of chromyl chloride with olefins, several questions remain to be answered. For instance, the role of the solvent (in acetone α-chloro carbonyl compounds become mayor products)[33] remains unclear and more importantly the present investigations do not explain why diols are absent as products in the reactions between CrO_2Cl_2 and olefins, whereas the corresponding reactions between OsO_4 and olefins generate exclusively diols with little epoxide as a product.[9] To answer this question one would have to consider the diolates formed from the [2+3] addition of ethylene to CrO_2Cl_2 and OsO_4, respectively, and compare their rate of hydroxylation with water to their rate of rearrangements to epoxides. The exothermic character of the [2+3] cycloaddition of ethylene to CrO_2Cl_2 to give **4** ($-13\ \text{kcal mol}^{-1}$)[24, 25] further raises the question whether such a diolate can be isolated and studied under certain conditions—the corresponding esters of OsO_4 are well known.[9]

Only if all these points are understood will it be possible to predict the mechanism of oxidation for a given substrate.

Epoxide cleavage and alcohol oxidation: Epoxides are very reactive synthons and after their formation during olefin oxidations with CrO_2Cl_2 subsequent reactions, for example with unreacted CrO_2Cl_2, can be expected. The investigation of the behaviour of epoxides in the presence of CrO_2Cl_2 by means of low-temperature NMR spectroscopy allowed us to observe ring-opening reactions leading to thermally labile Cr^{VI} alkoxides such as **7** (Scheme 4).[37] Starting from the epoxide complex **6**, which is produced initially in the reaction of CrO_2Cl_2 with oxirane, various mechanistic possibilities can be envisaged for the formation of **7**, which became the subject of further investigations: the consumption of **6** was determined to obey a second-order rate law, suggesting a bimolecular rate-determining step in which two of those molecules collide forming a energetically high-lying complex weakly stabilised by μ-Cl bridges (Scheme 5).[38] Subsequently one Cl ligand at the first Cr center could attack the backside of an epoxide molecule complexed at the second Cr center and the resulting dinuclear alkoxide dissociates thereby re-establishing low coordination numbers at the small Cr^{VI} centers. The hypothesis of formation of a dimeric complex in the rate-determining step, where all of the epoxide bonds are still basically intact, is supported by the lack of regioselectivity observed when unsymmetrical epoxides are reacted[37, 38] and the *trans*-opening of the epoxides was proved by determining the configuration of the alkoxide ligands in the products obtained from *cis*- and *trans*-dimethyloxirane.[38]

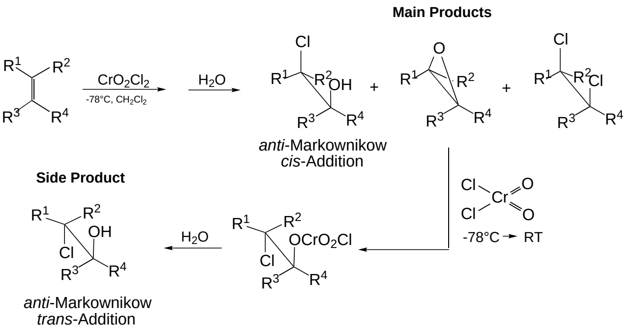


Scheme 4. Oxirane cleavage with CrO_2Cl_2.



Scheme 5. Possible mechanism for the formation of **7**.

These results may have an impact on the finding of K. B. Sharpless et al. (vide supra) that in olefin oxidations with chromyl chloride, chlorohydrins are not exclusively formed in formal *cis*-additions of HOCl but also—to a minor extent—in *trans*-additions (Scheme 6).[13] Sharpless “felt that [under the conditions of these reactions] epoxides [formed initially] undergo sufficient *trans* opening [by chloride] to chlorohydrins to completely account for the *trans* addition of HOCl observed in olefin oxidations” leaving open how this epoxide opening is supposed to proceed.[13] As he also found that “epoxides are completely stable to the reagent [CrO_2Cl_2] itself under the reaction conditions [$-80\,^\circ C$]”, he coupled the epoxide cleavage to a simultaneously proceeding olefin oxidation process, that is to HCl or reduced chromium species generated thereby. Our results show that indeed no reactions involving epoxides (apart from complexation) occur at $-80\,^\circ C$, but on quenching with water the olefin oxidation

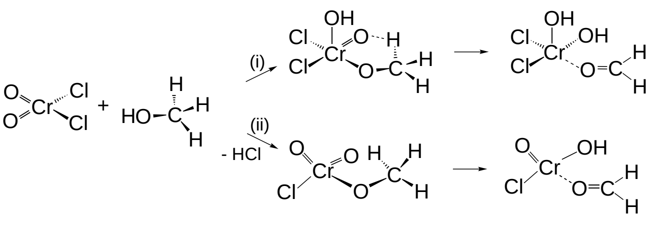


Scheme 6. Mechanisms calculated for the MeOH oxidation with CrO_2Cl_2.[27]

mixtures will eventually reach temperatures where *trans*-cleavages of epoxides by CrO_2Cl_2 are triggered, which can then proceed until hydrolysis becomes effective.

The epoxide cleavage studies described are important also in so far as they allowed the characterisation of the first representatives of chromate esters bearing α-hydrogen atoms[37, 38] (e. g. **7**, Scheme 5) closely resembling those species which were proved later on to occur intermediately during alcohol oxidations with CrO_2Cl_2.

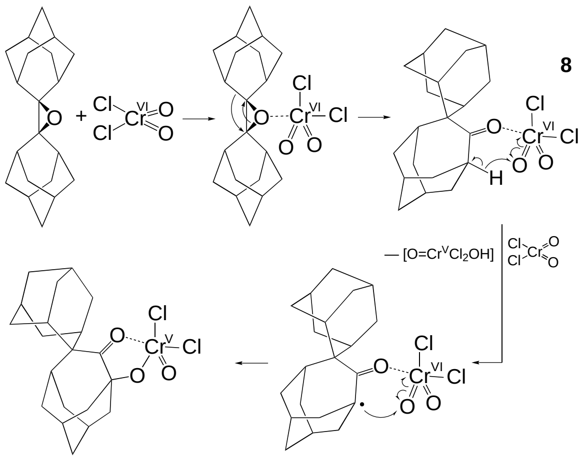
In organic text books the oxidation of primary and secondary alcohols by Cr^{VI} oxo compounds is offered as one method for the synthesis of carbonyl compounds but the secret of its success remained speculative. A series of intermediates had been suggested over the years to explain, for instance, the role of CrO_2Cl_2 in the oxidation of CH_3OH leading to $CH_2{=}O$. Calculations by W. A. Goddard et al.[39] as well as more recent calculations by T. Ziegler et al.[27] both identified $Cl_2CrO(OH)(OCH_3)$ and $ClCrO_2(OCH_3)$ as potential intermediates (Scheme 7). Ziegler et al. concluded[27a] that $ClCrO_2(OCH_3)$ (Route (ii)), while lower in energy, was *not* an active intermediate on the basis of the substantial endothermicity they calculated for its dissociation into CH_2O, HCl, and CrO_2. However, in 1998 B. Ault showed that this species is not only formed if CrO_2Cl_2 and MeOH are photolysed in noble gas matrixes, but was also able to trap it from the room-temperature gas-phase reaction with the aid of a matrix apparatus;[28] thus, this is another example of a reaction where the thermal and photochemical potential energy surfaces have common minima as suggested above for the olefin oxidation. $ClCrO_2(OCH_3)$ must therefore definitely be part of the methanol oxidation with chromyl chloride, but the experiments of Ault supported the endothermicity calculated for its decomposition to give CH_2O[27a] (temperatures of ca. 150 °C were reported to be required in the gas phase) posing the question, why then do the carbonyl products of CrO_2Cl_2 reactions with primary and secondary alcohols form already at ambient temperatures.



Scheme 7. Products of olefin oxidation with CrO_2Cl_2.

In contrast to these findings the alkoxide $ClCrO_2(OCH_2CH_2Cl)$ (**7**, Scheme 5), being closely related to $ClCrO_2(OCH_3)$, had proved to be very sensitive, decomposing at temperatures above −30 °C to give paramagnetic complexes, whose aqueous work-up provided the desired carbonyl compounds.[37, 38] This fact supports the idea that—even if they are relatively stable in the gas phase—alkoxides of the type $ClCrO_2(OR)$ are indeed the intermediates, which lead to the ketones and aldehydes formed in alcohol oxidations with CrO_2Cl_2 and the apparent contradiction with regard to the stabilities of these species in different states of aggregation is resolved if bimolecular decomposition pathways are assumed. Theoretical work in this direction or kinetic studies might provide deeper insights. Further research aimed at synthesizing isolable $ClCrO_2(OR)$ derivatives appears promising as such species can be expected to be more selective oxidants than CrO_2Cl_2.

Radical trapping: The employment of tetraalkyl- or tetraaryl-substituted epoxides in reactions with CrO_2Cl_2 results in the Cr^{VI}-catalyzed isomerization of the former to give the corresponding ketones. Analogously bisadamantylidene epoxide rearranges after its complexation to CrO_2Cl_2 to give the spiro-ketone complex **8** (Scheme 8).[31] However, in this very special case the rigid framework of the ketone forces the complex to adopt an arrangement in which a Cr=O group of CrO_2Cl_2 comes to lie in close proximity to a comparatively weak α-keto C−H bond, as can be seen in a DFT-optimised structure for **8** (Figure 1). This enables—already at very low temperatures—a facile chelation-assisted intracomplex H-atom transfer resulting in a radical coordinated at the reduced metal species $HOCr^V(O)Cl_2$. As the latter is inefficient as a radical trap[18] it must be quickly exchanged (maybe only formally in a redox reaction) by CrO_2Cl_2, and the reaction proceeds with the addition of the radical to a $Cr^{VI}{=}O$ function of excessive CrO_2Cl_2 yielding a stable Cr^V alkoxide which could be isolated and investigated by X-ray analysis.[31] Its identification, which became possible owing to the special



Scheme 8. Trapping of an organic radical with CrO_2Cl_2.

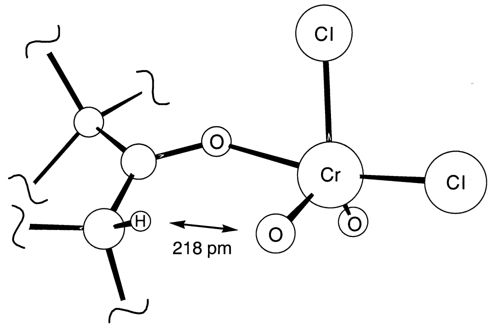
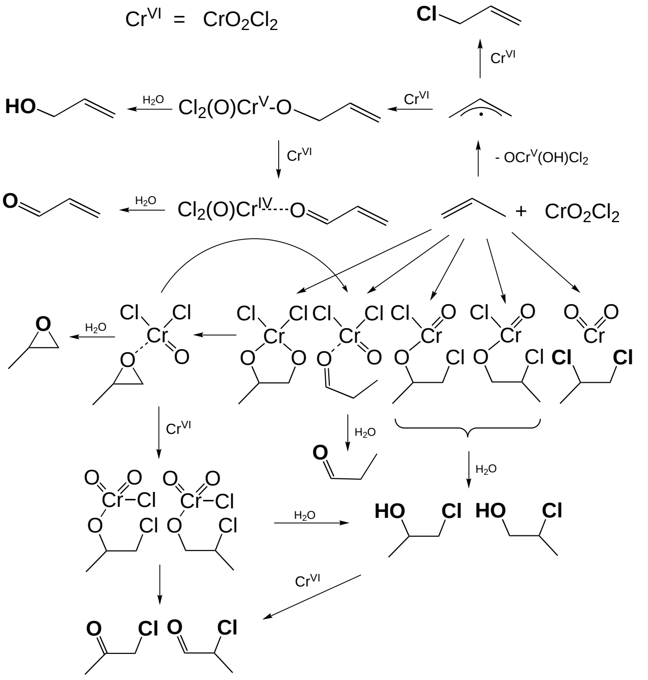


Figure 1. Segment of the structure of **8** as optimized by DFT methods (B3LYP, LANL2DZ).

advantageous electronic and geometric conditions of the substrate, provides forthright evidence on a molecular level for a fundamental type of reaction, which had frequently been proposed to rationalize experimental findings in alkane oxidations with oxo metal compounds (including CrO_2Cl_2 itself; see above section on C–H bond activation): The trapping of organic radicals by terminal d^0-metal oxo bonds. According to the results of Wiberg et al.[5] and Stephenson et al.[40], who found predominant retention of stereochemistry on oxidation of chiral tertiary C–H bonds, the rate of radical trapping must be very high (close to the diffusion limit[18]). The mechanism of such CrO_2Cl_2 oxidations is therefore in principle comparable to that proposed for cytochrome P-450 oxidations of C–H bonds, the "oxygen rebound" path of hydrogen atom abstraction followed by rapid trapping of the carbon radical,[5, 7b, 8, 20] which is considered in most recent mechanistic descriptions as part of a complex multistate reactivity paradigm.[21] The findings summarized in Scheme 8 demonstrate that even for a reagent as reactive as CrO_2Cl_2 the selectivity can be significantly enhanced if the substrate is preorganized in close proximity. This principle, which is also the basis of enzyme reactivity, suggests further research should be aimed towards incorporating high-valent oxo metal centers into a ligand environment that can direct incoming substrates. Such ligand spheres might also help to prevent the aggregation of the reduced metal species after the oxidation step, thereby setting a basis for the establishment of catalytic cycles.



Scheme 9. Proposal for the product formation in the propene oxidation with CrO_2Cl_2 (propylene oxide is only formed in insignificant amounts).

Conclusions

The results presented suggest that the reactions of chromyl chloride—alkane, olefin, and alcohol oxidation as well as epoxide cleavage—are closely interconnected, which explains the products obtained especially when olefins and hydrocarbons are oxidized. If, for instance, propylene is treated with this reagent, all these processes occur in one and the same experiment leading to ten products,[23] which are all accounted for by the results given in this article (summarized in Scheme 9). An improvement in the understanding of the mechanism of one of these reactions automatically leads to an increased knowledge about the others, and this is precisely what has occurred for chromyl chloride in a very pronounced fashion over the past few years, as several researchers set out at the same time to reinvestigate its reactivity from diverse viewpoints applying different methodologies.

It becomes apparent that the synergetic application of all the current knowledge and of all methods available to study details of oxidation reactions will ultimately lead to a situation where the reactivity of high-valent metal oxo compounds does not appear strange anymore.

Acknowledgement

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