Chromium – Salen-Mediated Alkene Epoxidation: A Theoretical and Experimental Study Indicates the Importance of Spin-Surface Crossing and the Presence of a Discrete Intermediate

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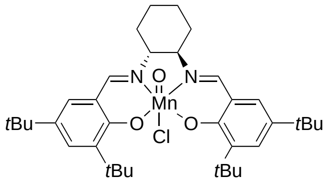
Abstract: The mechanism of alkene epoxidation by chromium(v) oxo salen complexes has been studied by DFT and experimental methods. The reaction is compared to the closely related Mn-catalyzed process in an attempt to understand the dramatic difference in selectivity between the two systems. Overall, the studies show that the reactions have many similarities, but also a few critical differences. In agreement with experiment, the chromium system requires a change from low- to high-spin in the catalytic cycle, whereas the manganese system can proceed either with spin inversion or entirely on the high-spin surface. The low-spin addition of metal oxo species to an alkene leads to an intermediate which forms epoxide either with a barrier on the low-spin surface or without a barrier after spin inversion. Supporting evidence for this intermediate was obtained by using vinylcyclopropane traps. The chromium(v) oxo complexes can adopt a stepped shape or form a more concave surface, analogous to previous results on manganese salen complexes.

Keywords: chromium · density functional calculations · epoxidation · manganese · N,O ligands

Introduction

Chiral, nonracemic manganese[1] and chromium[2] oxo salen complexes such as **1** and **2** have been used successfully for asymmetric epoxidation. Complex **1** (with or without chloride counterion, vide infra) is now the accepted reactive intermediate in epoxidation with Jacobsen's catalyst[1] and has been studied by combined mass spectrometric and theoretical methods,[3] EPR spectroscopy, and other techniques.[4] Complex **2** is the best reagent within the chromium – salen series.[2e]



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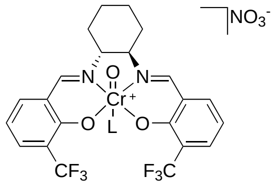

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Although they share many similarities, there are also some substantial differences in the characteristics of the two reagents. The manganese-based system shows a wider spectrum of reactivity[5] and therefore has generally been found to be more useful. On the other hand, the stoichiometric variant of the chromium system is easily studied since the oxo complex **2** is isolable,[5a] whereas **1** is only a fleetingly observed intermediate.[4] However, the major difference between **1** and **2** is in their different substrate selectivity in asymmetric epoxidation. Manganese salen complexes show high enantioselectivities in the epoxidation of *Z* alkenes, but *E* alkenes are poor substrates. Chromium – salen complexes show the opposite characteristics (Table 1). Other minor differences include[1, 2b, 5] the greater effect of O-donor ligand additives in the chromium series; the type of oxidant, which is more variable in the manganese series; and the nature of the substituents on the salen rings: chromium requires electron-withdrawing substituents for reasonable rates, but these need not be bulky, in contrast to the manganese case.

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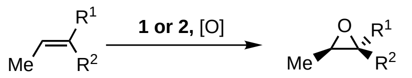
Table 1. Reported enantioselectivities in epoxidation of *E*- and *Z*-β-methylstyrene with **1**[2h, 6] and **2**.[2e]



R^1	R^2	Reagent	*ee* [%]
H	Ph	**1**	92
H	Ph	**2**[a]	– 27
Ph	H	**1**	22
Ph	H	**2**[a]	92

[a] L = triphenylphosphine oxide.

The success of these metal–salen systems has led to considerable discussion of the mechanism of oxo transfer[1, 2b, 7–11] and the origin of enantioselectivity.[1, 2b, 12] Recently, some agreement has been reached on the mechanism of oxo transfer in the manganese series. The crucial breakthrough was recognition of the importance of the spin state of the manganese–oxo moiety in determining the reaction pathway.[7–10] Both theoretical and experimental studies agree that the most stable spin state for the $\mathrm{Mn^{III}}$ stage of the catalytic cycle is the quintet ($S = 2$).[4, 7–10, 12, 13] However, there is disagreement about the preferred spin state of the actual epoxidizing species, the $\mathrm{Mn^{V}{=}O}$ complex. Observable $\mathrm{Mn^{V}{=}X}$ species (X = O, N; always neutral or anionic complexes) are generally diamagnetic singlets ($S = 0$),[4, 13] and some theoretical studies also identify this as the most stable state of the [(salen)Mn=O] species.[8, 10] However, the energetic differences between available spin states are small and strongly dependent both on the exact model used (naked cationic,[3b, 7, 8] with neutral ligand,[3d] or with anionic chloride ligand[8, 9, 10]) and the level of theory employed. For the related Mn–porphyrin series, it was suggested that the singlet complexes are observable because they are less reactive than the corresponding catalytically active complexes.[13b] There is consensus on some important points in the available theoretical studies. Most importantly, all spin states for Mn=O are energetically accessible, so that if spin change in these systems is slow,[14] the reaction can proceed completely on the quintet surface. Indeed, in a recent EPR study, signals which could arise from a triplet or quintet $\mathrm{Mn^{V}{=}O}$ species were observed.[4a] Furthermore, all comparative studies of transition states have shown that the addition on the triplet surface ($S = 1$) is lower in energy than that on the singlet surface ($S = 0$),[7, 10] and experimental evidence also indicates that addition on the singlet surface is a slow process.[13b] Thus, if spin change does occur, the addition will proceed on the triplet surface to give a radical intermediate with subsequent formation of product either on the triplet or quintet surface. For this reason, the singlet state, although preferred for less reactive, isolable complexes, can be neglected for the catalytic process. Finally, the quintet potential energy surface (PES) seems very responsive to the charge of the axial ligand. In the presence of chloride ligand, the quintet PES is very similar to the triplet PES and proceeds through a radical intermediate.[9, 10] For the cationic quintet complex, the addition is still strongly asynchronous, but now formation of epoxide is a concerted process.[7] Thus, the recent observation by Adam et al.[15] that isomerization in a radical intermediate is much more pronounced in the presence of chloride can be rationalized by the qualitative PES differences on the quintet surface, although they also suggested that two different oxidizing species offer competing pathways.[15b] The relevant spin surfaces are depicted in Figure 1. By postulating that the reaction can proceed in parallel on at least two different spin surfaces, whereby the preference for and rate of transfer between the spin surfaces can be affected by the reaction conditions and mode of production of the $\mathrm{Mn^{V}{=}O}$ complex, various contrasting experimental observations, such as the survival of vinylcyclopropane radical traps[16] and the observed isomerization of *Z* alkenes to *trans* epoxides,[17] can be rationalized. Recently, Linde et al. provided further experimental evidence for competing oxidation pathways by studying the electronic effects of the substrate on the diastereoselectivity and enantioselectivity in the catalytic epoxidation by iodosylbenzene of *para*-substituted *cis*-stilbenes with Jacobsen's catalyst (**1**).[11]

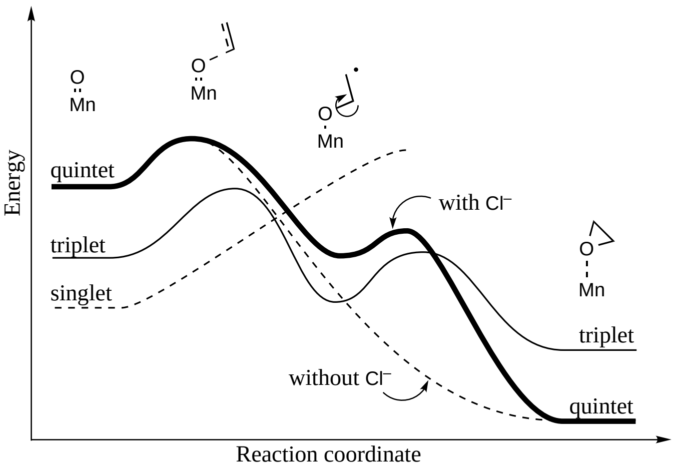


Figure 1. Qualitative consensus PES for the reaction of (salen)Mn=O species with alkene, collected from literature sources.[7, 9, 10]

With regard to the origin of stereoselectivity in the manganese system, there is still substantial disagreement. Most fundamentally, there is no agreement as to the shape of the active complex. In addition, although nearly all workers use the concept that the alkene approaches side-on[18] to the oxygen atom, essentially all possible trajectories of approach to the metal oxo moiety have been used as a basis for an explanation. For example, Jacobsen et al. assumed a planar salen ligand framework and explained enantioselection by approach of alkene over the cyclohexyl ring of the complex.[19] They also invoked side-on approach to rationalize the better selectivity for *Z* alkenes than for *E* alkenes. Katsuki et al. suggested a nonplanar structure and accumulated much experimental evidence for this.[12b] They suggest that the alkene approaches along the metal–nitrogen bond axis. Houk et al. independently suggested a similar nonplanar structure but suggested approach of alkene between the 3,3′-positions of the salen ligand.[12a] This is similar to our explanation for the selectivity in the chromium series.[2b, 2f, 20] We also had to postulate[2b, 20] a nonplanar salen structure for the chromium complex to retain the side-on approach model for its epoxidation reactions. Recently, Wiest et al. performed calculations on a complete salen ligand and, significantly, they showed that the catalyst could adopt two different conformations with a stepped or a concave catalyst/substrate interface.[3c,d] None of this work provides an explanation for the contrasting selectivity behavior of chromium salen complexes in asymmetric epoxidation. Therefore, we felt that a detailed study of the chromium system would shed light on these differences and in turn give insight into the manganese system.

In recent years, quantum chemical methods have been successfully employed in the evaluation of mechanistic alternatives in transition-metal-catalyzed reactions.[21] In particular, density functional theory has been extensively used, the most popular methods being B3LYP and BP. While our study on the chromium system was in progress, several papers, including theoretical studies into the Mn system, appeared.[3b–d, 7–10] Our results, in combination with the literature reports, could therefore be used to compare the two systems and rationalize some of the differences.

The spin states of Cr^{III} and $Cr^{V}{=}O$ in salen complexes **13** and **14** were established by Kochi et al.[5] by measurement of the magnetic moment, and those of Cr^{III} by Bryliakov et al.[22] by EPR measurements. These provide a useful check on the calculations reported here, something that is presently unavailable for the manganese series. We used the B3LYP method, which has been criticized as unsuitable for spin-state determinations in the Mn system.[10] However, the results of the present calculations are in agreement with the experimental determinations, the best measure of their validity.

We now report details of our theoretical and experimental study, which has led to insight into the mechanism of oxygen transfer in the chromium system. Results of our studies into the mode of enantioselection will be the subject of a future paper. We are aware of one other recent theoretical study of a (non-salen)chromium(V) oxo system.[23]

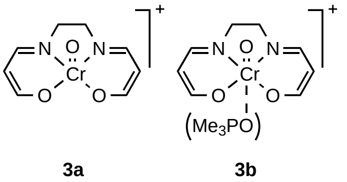
Methods of Calculation

All calculations were performed with the Gaussian 98 program package[24] using the B3LYP hybrid functional.[25] Geometry optimizations were performed with d95v for C, N, O, and H; d95 for P; and a (14s,11p,6d) primitive basis from Wachters,[26] augmented by two p and one diffuse d function contracted to [6s,5p,3d], for Cr (see Supporting Information). This basis set is referred to as BS I in the following. Final energies were determined by using 6-311 + G* for Cr, 6-31 + G* for N and O, and 6-31G* for P, C, and H (BS II).

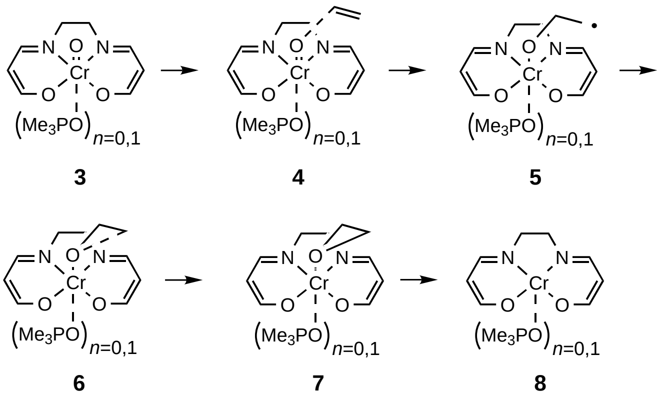
A reduced model system was used to mimic the full chromium salen complex and the donor ligand used experimentally (Scheme 1). This truncated ligand proved to be very similar to the real salen ligand for the related Mn(salen)(Cl)-catalyzed reaction.[9] Ethene was used as the model alkene.

Results

The potential energy surface: The energies of the twelve species **3a,b – 8a,b** (Scheme 2) on a nonconcerted PES were evaluated. Calculated energies are tabulated in Table 2; those of **3b – 8b** are given at both BS I and BS II levels. Figure 2 shows these energies graphically for systems **b** (with axial ligand).



Scheme 1. Truncated molecules used in the calculations. Species without donor ligand are denoted **a**; with donor **b**.

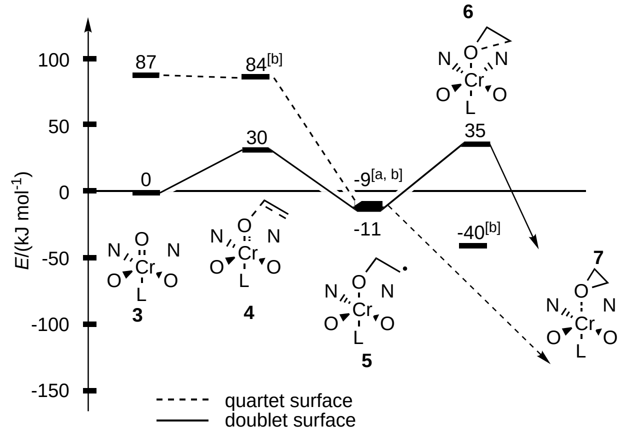


Scheme 2. Species evaluated in the quantum chemical study (**a**: $n = 0$; **b**: $n = 1$).

Table 2. Potential energy surfaces (B3LYP/BS I) of the reactions of ethylene with complexes **3a** and **3b** [$kJ\,mol^{-1}$].

	a: No donor ligand		**b**: Axial Me_3PO[a]	
	doublet	quartet	doublet	quartet
3 + ethylene	0	102	0 (0)	73 (87)
4	64	–	14 (30)	71 (84)[b]
5	12	–	– 23 (– 11)	– 19 (– 9)[b]
6	64	–	17 (35)	– 50 (– 40)[b]
7	14	– 77	– 69	– 162
8 + epoxide	–	55	41	– 49

[a] Values in parenthesis from B3LYP/BS II//B3LYP/BS I. [b] Vertical excitation.

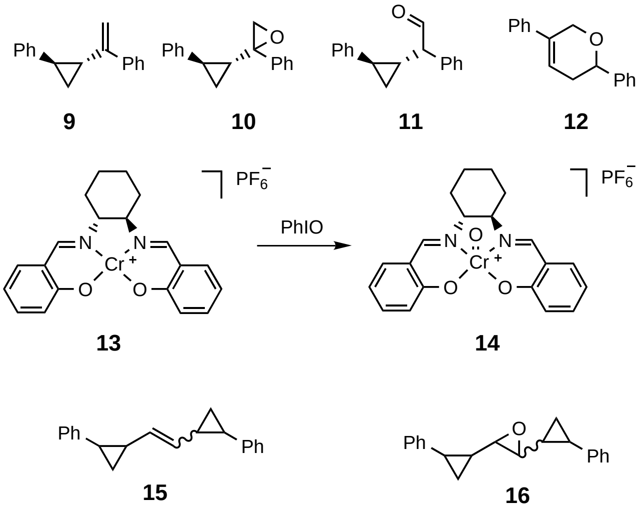


[a] This quartet ring-closes without barrier.

[b] Vertical excitation from the doublet surface.

Figure 2. The PES at the B3LYP/BS II//B3LYP/BS I level for systems **b**.

Radical-trap experiments: Radical traps **9** and **15** were prepared and treated with chromium and manganese salen complexes **13** and **14** (Scheme 3). The results are listed in Table 3 and Table 4.



Scheme 3.

Table 3. Results of investigations with radical probe **9** and derivatives.

Entry	Substrate	Reactant	Cr complex [mol%]	**11**:**12**	Total yield [%]
1	**9**	**14**	100	>20:1	7[a]
2	**9**	**13** + PhIO	10	4:1	50[a]
3	**10**	**13**	100	3:2	90
4	**10**	**13**	50	2:1	93
5	**10**	**13**	10	10:1	87
6	**10**	**14**	100	10:1	83
7	**10**	**14**	50	10:1	86
8	**10**	**14**	10	1:1	85
9	**10**	PhIO	-	n.d.[b]	96
10	**10**	none	-	n.d.	96
11	**11**	**13**	100	n.d.	90
12	**11**	**14**	100	n.d.	86
13	**12**	**13**	100	n.d.	86
14	**12**	**14**	100	n.d.	95

[a] Reduced yield accounted for by unconsumed alkene. [b] n.d. = no decomposition.

Table 4. Epoxidation of alkene **15** (mixture of isomers) with various complexes and oxidants.

Entry	Complex	mol%	Oxidant	Yield of **16** [%]		Unconsumed **15** [%]	
				cis	*trans*	*Z*	*E*
1	**13**	10	PhIO	0	0	30	30
2	**14**	100	none	0	0	11	0
3	deoxy-**1**	2.5	NaOCl	33	12	11	39
4	deoxy-**1**	2.5	PhIO	20	2	21	47

Discussion

Calculations on intermediates and the PES: Chromium has one less d electron than manganese, and analogously to the spin states of manganese salen complexes, the chromium complexes studied here can be in a doublet or quartet state.

*Chromium–oxo complexes **3a** and **3b***: The chromium-catalyzed epoxidation of alkenes differs from its Mn-catalyzed counterpart in that the oxidized form of the catalyst has been isolated and characterized.[5a] This is possibly due to its lower reactivity compared to the better known Mn analogue. This trend is not unexpected given the lower M=O bond strength to the right of the periodic table.[27]

The chromium—salen–oxo complexes studied here (Figure 3) show a doublet ground state with the spin density centered on chromium ($s = 1.42$ for **3b**) and on the oxo oxygen atom ($s = -0.39$ for **3b**). This agrees with experimental measurement of $\mu_{\text{eff}} = 1.9\ \mu_B$ for [(salen)Cr^V=O] complex **14**.[5a] In the quartet state, an electron has been promoted from the π system of one half of salen into an antibonding Cr=O orbital (ligand-to-metal charge transfer, LMCT). This excitation (87 kJ mol^{-1}) causes elongation of the Cr=O bond from 1.594 to 1.680 Å and a slight conformational change in the complex.[28] The high excitation energy makes involvement of the quartet state in the initial part of the reaction less likely. Therefore, no attempts were made to locate transition states on this PES.

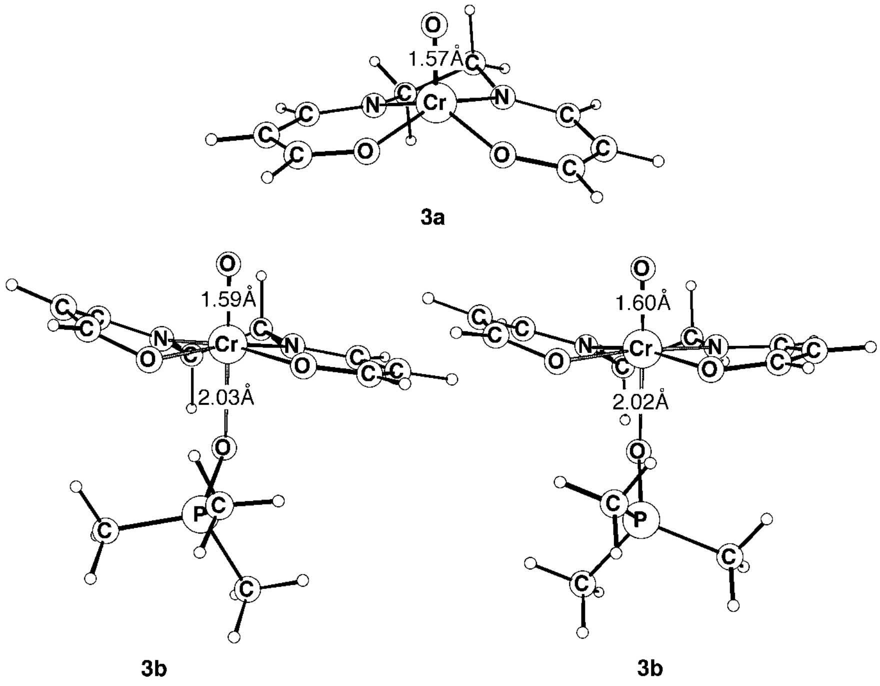


Figure 3. Structures of the doublet Cr oxo complexes **3a** and **3b**.

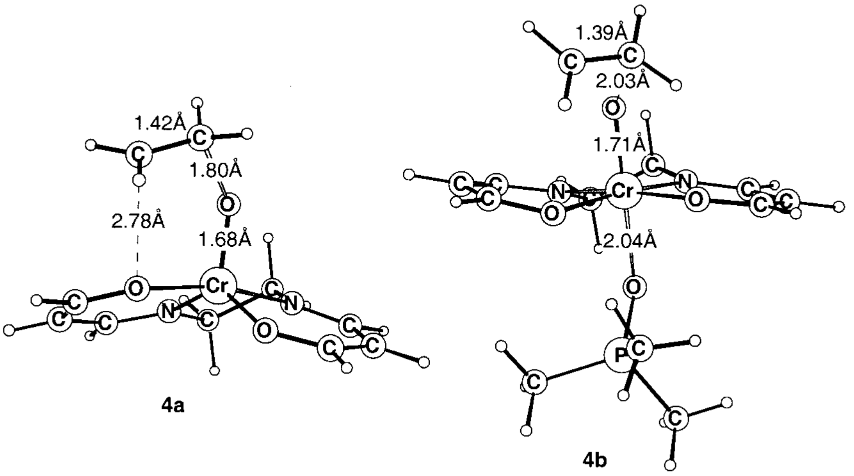


Figure 4. Transition states **4a** and **4b** in the doublet states.

Another notable feature in Figure 3 is that coordination of a donor-ligand *trans* to the oxo group results in a dramatic conformational change in which salen is pushed towards the oxo ligand and a stepped conformation is generated. This is in agreement with the crystal structures of [(salen)Cr^{V}=O] obtained by Kochi et al.[29]

An interesting discovery by Wiest et al.[3b,d] is that [(salen)Mn=O] with an axial Me$_3$NO ligand can also adopt different conformations; stepped and bowl-shaped conformations are energetically accessible. For the Cr catalysts examined here two analogous conformations were located that differ by only 3 kJ mol^{-1} in relative energy. In terms of substrate compatibilty, conformational differences between the two catalysts might explain why Mn–salen complexes are better suited for the epoxidation of *Z* alkenes, whereas Cr–salen complexes perform better with *E* alkenes (Table 1). This rationale is particularly attractive to explore because of the different requirements of the 3,3′-substituents for the Mn versus the Cr system. Bulky substituents at these positions and partially charged groups will be within van der Waals interaction distance and could thus affect the conformational behavior of the catalysts.

*Transition states **4a** and **4b** for the addition of ethylene to oxo complexes **3a** and **3b***: Experimentally, the reaction rate and yield is improved by the addition of various donor ligands to the reaction.[2a,c,g] Among the ligands experimentally evaluated were various *N*-oxides, phosphane oxides, DMSO, and DMF, but triphenylphosphane oxide is usually the most effective.[2a,e,g] The activation energy for the addition of ethylene to **3** is 64 kJ mol^{-1} without an axial ligand, but this value drops to 14 kJ mol^{-1} when Me$_3$PO is coordinated. This is in agreement with the experimentally observed ligand acceleration. The effect of donor ligand on the salen conformation can be seen in Figure 4. The salen ligand is brought closer to the active site by axial coordination. This could be interpreted as a cause of improved enantioselectivity.

*Intermediate ethyl radicals **5a** and **5b***: Both TSs **4a** and **4b** lead to stable intermediates with a carbon-centered radical (**5a** and **5b**). The doublet ethyl radical **5b** has a Mulliken spin density of 2.28 at Cr and −1.03 at the ethyl terminus. Thus, the stepwise mechanism suggested by Kochi et al.[5a] is confirmed, although our results suggest that the intermediate may be a radical rather than a cation. Most significant is that when an axial ligand is present an energy difference of only 2 kJ mol^{-1} separates the doublet and quartet states of **5b**. Excitation from doublet to quartet state results in direct collapse to the corresponding epoxide. Once again the effect of the donor ligand on complex conformation can be seen when the structures of **5a** and **5b** are compared (Figure 5).

*Transition states **6** for ring closure*: Ring closure of the ethyl radical intermediate on the doublet spin surface (Figure 6) is calculated to be slightly higher in energy than the reverse reaction leading back to the alkene (35 versus 30 kJ mol^{-1}). The energy difference of only 5 kJ mol^{-1} is, however, beyond the accuracy of the computational method. The experimental observation of no isomerization of *Z*-β-methylstyrene implies that ring closure is faster than the back-reaction. As discussed previously,[7] vertical excitation from the doublet to the quartet of **5b** requires not more than 2 kJ mol^{-1}. A small energy difference offers the possibility of a fast spin inversion, and ring closure can then take place without barrier on the quartet PES. Thus, two alternative pathways exist for this step.

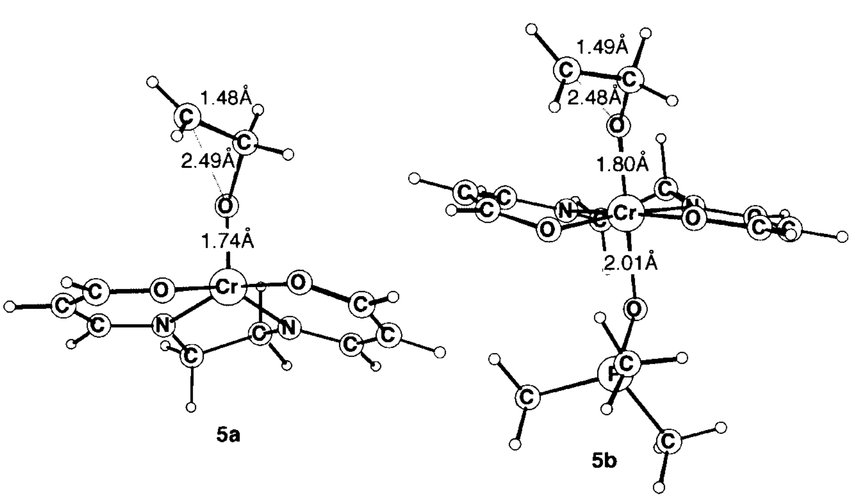


Figure 5. Intermediate ethyl radicals **5a** and **5b**.

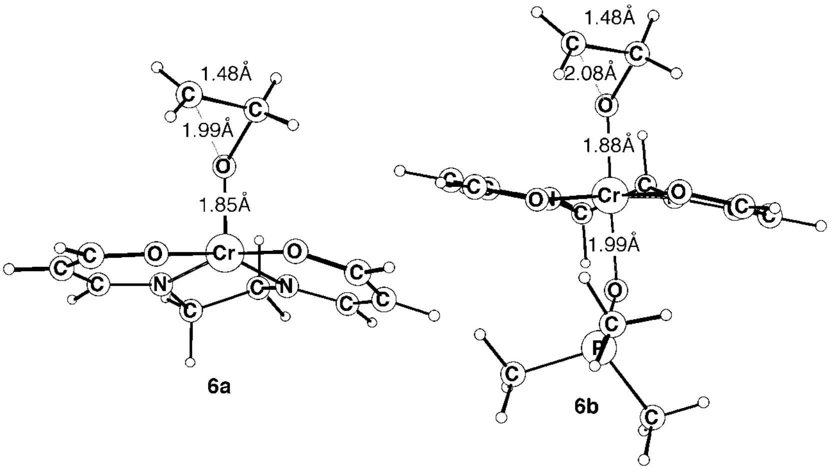


Figure 6. Transition states **6a** and **6b** for ring closure of the intermediate ethyl radicals (doublets).

Chromium-coordinated epoxide: The structures of the species produced on ring closure (**7a**, **7b**) in both the doublet excited states and quartet ground states are shown in Figure 7. The prediction of a quartet ground state for Cr^{III} salen complexes agrees with an experimental measurement of $\mu_{eff} = 3.5\ \mu_B$ for complex **13** and with EPR measurements on the (salen)Cr^{III} spin state.[22]

Recall that Kochi et al. found strong indications of a cationic mechanism.[5a] Byproducts found in the reaction mixture were characteristic of a cation rearrangement. Our failure to identify carbocationic intermediates in the theoretical investigations suggests that byproducts in the reaction arise from Lewis-acid-catalyzed reactions mediated by Cr^{III} or Cr^{V} complexes. The observed rearrangement of epoxide **10** to aldehyde **11** (see below) is evidence for this.

Diastereoselectivity: investigation of [(salen)Cr^{IV}=O]: We recently discovered an unusual experimental effect. Replacement of the NO_3^- counterion in **2** with BARF[30] led to a clean conversion of *E*-olefins to a 1:1 mixture of *cis* and *trans* epoxides.[2e] We suggested that this was due to the formation of a [(salen)Cr^{IV}=O] species by one-electron reduction of the chromium complex in the presence of a tetraarylborate. We have investigated such a species theoretically. In short, [(salen)Cr^{IV}=O] has a triplet ground state, and the singlet and quintet states are 38 and 59 kJ mol^{-1} higher in energy (BSI). Thus, the initial reaction takes place on the triplet PES and leads to a radical intermediate, which is stable both as a triplet and a quintet. This stability allows time for rotation about the C–C bond to give a mixture of products, which approaches a thermodynamic distribution of *cis* and *trans* epoxides.

Summary: The above theoretical investigation suggests that the epoxidation reaction proceeds through an intermediate **5** with a doublet ground state of the starting [(salen)Cr^{V}=O] (**3**) and formation of a quartet [(salen)Cr^{III}] product **8**. It seems most likely that the necessary spin change occurs after the formation of the intermediate **5** and prior to ring closure of epoxide. The spin crossing probability p_{SI} will therefore determine the lifetime of the intermediate.[31] The experimental observation of small amounts of isomerized epoxide from

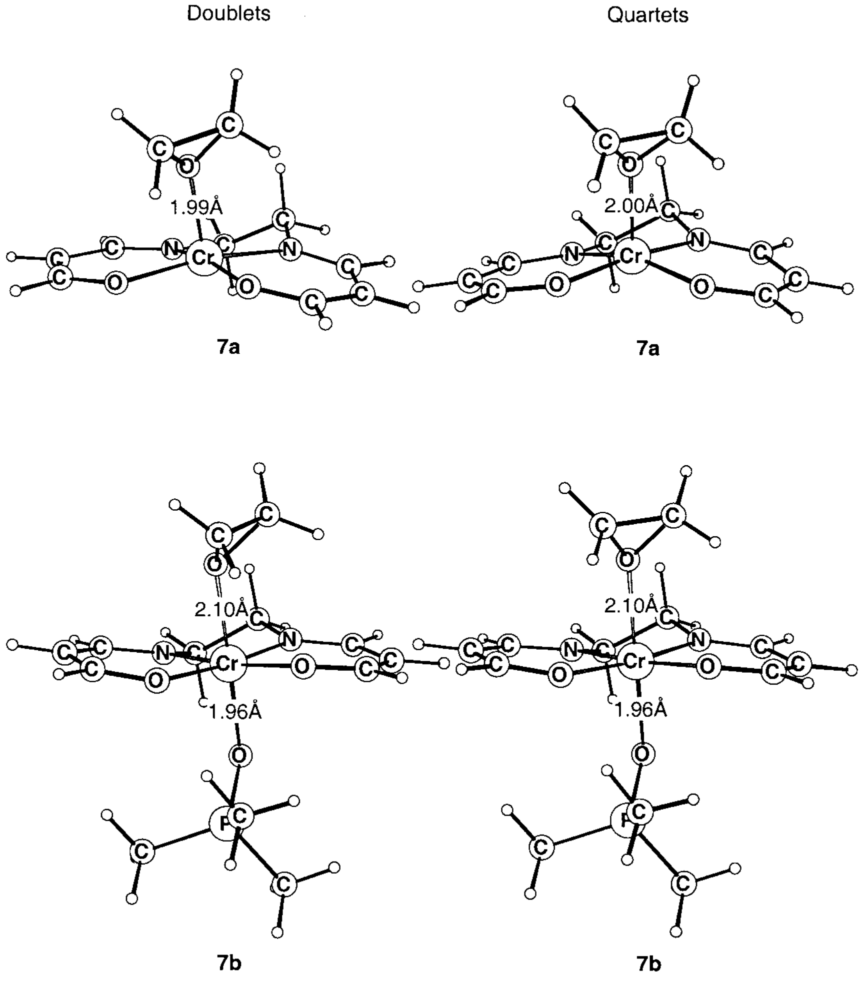


Figure 7. Product complexes **7a** and **7b**.

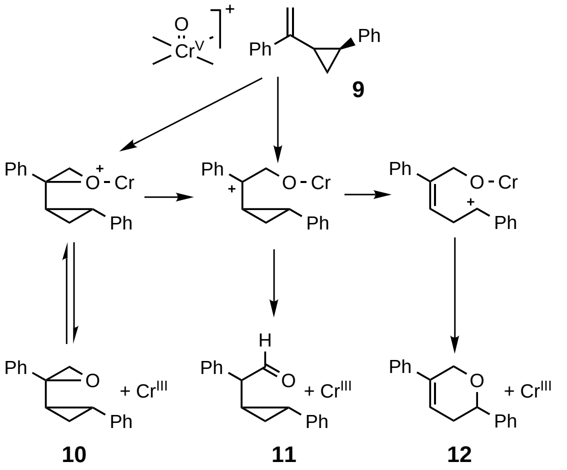
Z-β-methylstyrene suggests that the spin crossing is relatively facile. Only in a small number of cases does the intermediate live long enough to undergo C–C bond rotation prior to ring closure, and therefore only a small amount of *trans*-β-methylstyrene oxide (ca. 10%) is produced from *Z*-β-methylstyrene.

Terminal oxidants: We have previously noted the failure of terminal oxidants other than iodosylbenzene.[2e] In light of these calculations, a possible interpretation of those results becomes apparent. To oxidize Cr^{III} to $Cr^{V}{=}O$, a spin change from quartet to doublet must take place. Oxidants containing a heavy atom could facilitate this spin change, hence the success of PhIO, but the failure of the other oxidants that we have tried.[32]

Radical/cation-trap experiments: On the basis of these theoretical results we sought an experimental method to confirm the presence of an intermediate in the reaction of a chromium oxo species with alkenes. We chose vinylcyclopropanes, which have been used extensively in recent mechanistic investigations.[33] A disadvantage of this approach is that distinction between radical and cationic intermediates would not be possible. More seriously, the relatively limited substrate scope of the chromium system[2b, 5a] limits the number of potential test compounds. A radical/cation trap only produces irrefutable results when the cyclopropyl ring remains intact. Ring opening strongly suggests an intermediate but does not prove it conclusively.

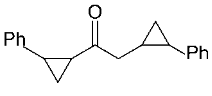
Styrene-like trap. Substituted styrenes are good substrates for epoxidation with the chromium system,[2, 5a] because the incipient cation/radical is stabilized at the benzylic position that bears the cyclopropyl group. 1-Phenyl-1-(*trans*-2-phenylcyclopropyl)ethene (**9**) and derivatives thereof were used to good effect in the manganese system by Linde et al., who found that formation of *cis* epoxide from *Z* alkene and of *trans* epoxide from *E* alkene did not involve a radical intermediate.[16b, 34]

Unfortunately 1,1-disubstituted alkenes of this type are not ideal for the chromium system,[35] and when **9** was treated with **13** as catalyst and PhIO as oxidant, or with a stoichiometric amount of **14**, none of the corresponding epoxide **10** was generated. Instead, we obtained the dihydropyran **12** and the aldehyde **11** in a ratio that depended on the amount of chromium complex used in the reaction (Table 3, entries 1 and 2). This, in itself, suggests the intervention of a reaction intermediate. However, we also found that, under the reaction conditions, epoxide **10** reacts with **13** and **14** to give **11** and **12** in various ratios (Table 3, entries 3–8). Linde et al. also found aldehyde **11** and pyran **12** in the manganese system in cases when epoxide yield was not quantitative.[16b] The varying ratios of **11** and **12** in the control reactions strongly suggests their formation by a combination of the two routes outlined in Scheme 4. A possible caveat is that spin-change factors might influence the product distribution in the attempted epoxidation experiment, whereas in the control reactions they would not come into play. In any event, the fact that ring-opened products are observed is overwhelming evidence for an intermediate in the reaction of this Cr oxo species with alkene **9**. Whether this same intermediate can also lead to epoxide **10** is, of course, unproven.



Scheme 4. Possible pathways for the formation of **10**–**12**.

Hexene-like trap: In an attempt to resolve the issue we designed an alternative cyclopropylalkene, namely, 1,2-bis-(*trans*-2-phenylcylopropyl)ethene (**15**), which bears a greater resemblance to substrates that were successfully epoxidized, albeit poorly, by the chromium system.[36–38] We first confirmed the stability of the bis(cyclopropyl) epoxide **16** to the reaction conditions. In the presence of **13** or **14** monitoring by TLC showed that it remained stable for up to 10 h. The decomposition products which formed after this time, a set of isomers, had mass spectrometric and ^{1}H NMR data consistent with the expected[39] rearrangement product, ketone **17**. Alkene **15** was then subjected to both stoichiometric and catalytic epoxidation with [(salen)Cr] (Table 4, entries 1 and 2). In neither case was epoxide **16** or its isomer **17** produced.[40] In both cases just one product was detected by TLC, but it proved impossible to isolate.[41]



17

The failure to observe epoxide **16**, known to be stable under the reaction conditions, as a product of this reaction would suggest that a radical or cationic intermediate intervened along the reaction path leading to cyclopropane ring opening. This strongly supports the existence of a discrete intermediate in the epoxidation of alkenes by chromium–salen complexes.

We confirmed that **15** was indeed epoxidizable by a metal oxo species by examining its behavior in the manganese system, with hypochlorite and PhIO as oxidants (Table 4, entries 3 and 4). The results were as expected, in that the *Z* isomer reacted faster in this case. With hypochlorite (entry 3) there is a slight discrepancy between the amount of *Z* alkene consumed and the yield of *cis* epoxide, a result similar to those obtained by Jacobsen et al.[16a] for this type of nonconjugated alkene substrate. With PhIO (entry 4), there is a somewhat larger discrepancy, in good agreement with the results of Linde et al.[16b]

Conclusion

We have thoroughly investigated the mechanism of [(salen)Cr]-mediated epoxidation. Both theoretical and experimental results indicate the existence of an intermediate along the reaction path. The B3LYP calculations identified this intermediate as a β-alkoxy radical bound to chromium. The calculations suggest almost complete degeneracy between the low- and high-spin state at this point, and this facilitates spin-surface crossing. Considering the accuracy of the B3LYP functional, we correctly predicted a low-spin state for the $Cr^{V}{=}O$ reactant and a high-spin state for the Cr^{III} product. The fact that the catalyst must change between high- and low-spin during the catalytic cycle could affect both the diastereoselectivity and the rate of reoxidation of the catalyst.

Axial donor ligands significantly lower the barrier of the reaction and dramatically change the conformation of the catalyst. This conformational change brings the salen ligand closer to the substrate in the selectivity-determining transition state and thereby increases the enantioselectivity. In close analogy to the [Mn(salen)] catalyst the model [Cr(salen)] complex could adopt two different conformations with a stepped or a concave catalyst/substrate interface. We speculate that a difference in conformational preference is the cause of differences in substrate selectivity between [Mn(salen)] and [Cr(salen)] catalysts.

In addition, our calculations assigned the increased tendency of formation of *trans* epoxides from *cis* alkenes with a BARF counterion to a decreased rate of ring closure of the β-alkoxy radical formed from the reaction between the alkene and a Cr^{IV} species.

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[35] For example, we previously found that α-methylstyrene gave poor epoxide yields and low *ee* with complex **14**: C. Bousquet, D. G. Gilheany, unpublished results.

[36] It may be compared to *E*-3-hexene, which gave 10% yield and 33% *ee* in the reaction with **2** ($L = Ph_3PO$),[2e] and *E*-2-hexene, which gave 20% yield in achiral epoxidation.[5a]

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[38] A complication with alkene **15** is the presence of four chiral centers. The two *E* isomers were distinguishable from the two *Z* isomers by NMR spectroscopy, and all four were distinguishable by GC. Due to a lack of a large-scale method of separation, **15** was used as the 1:1 mixture of *E* and *Z* isomers obtained from the Wittig reaction used for its synthesis.

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[40] The catalytic reaction was slow, and substantial residual starting material remained. In the stoichiometric case, ^1H NMR spectroscopy of the crude reaction mixtures showed that the *E* alkene reacted somewhat faster, since when the *E* alkene had been consumed, 11% of the *Z* isomer remained.

[41] In the ^1H NMR spectrum of the crude product the only new signals identifiable were in the methylene (broad multiplet: $\delta = 1.6$) and aldehyde (singlet: $\delta = 10.0$) regions.

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