

# Olefin Epoxidation with Inorganic Peroxides. Solutions to Four Long-Standing Controversies on the Mechanism of Oxygen Transfer

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## ABSTRACT

Four controversies on the mechanism of the olefin epoxidation with Mimoun-type complexes,  $[\text{MoO}(\text{O}_2)_2(\text{OPR}_3)]$ , Herrmann-type complexes,  $[\text{ReO}(\text{O}_2)_2\text{Me}]$ , and related inorganic peroxides have inspired industrial and academic researchers in the last three decades. First, is the oxygen transfer from the peroxo complex to the olefin concerted or stepwise? Second, does the oxidant act as an electrophile or a nucleophile? Third, is the mechanism of the stoichiometric reaction also valid for catalytic protocols? Fourth, how can stereochemical information be transferred between oxidant and substrate? In this Account, we discuss answers to the long-standing questions, focusing on recent contributions from quantum chemical calculations.

## Introduction

Propylene oxide is a key intermediate in the chemical industry with an annual production capacity of approximately 4 million tons.<sup>2</sup> The oxirane is particularly important in the large-scale synthesis of propylene glycol, polyurethanes, and resins (Figure 1). A considerable

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amount of propylene oxide is still produced via the chlorohydrin route despite a large consumption of  $\text{Cl}_2$  and the environmental impact of this method.<sup>2</sup> Therefore, tremendous research efforts have focused on the development of homogeneous and heterogeneous catalysis for the epoxidation of olefins.<sup>3–5</sup>

Since the development of the Halcon–Arco process, peroxides of group 4–7 metals have been employed for olefin epoxidation.<sup>6</sup> Methods that use the green oxidant hydrogen peroxide are of particular interest, because water is the only waste product.<sup>4,7,8</sup> Based on Mimoun's pioneering work on the stoichiometric olefin epoxidation with  $[\text{MoO}(\text{O}_2)_2(\text{OP}(\text{NMe}_2)_3)]$ ,<sup>9,10</sup> several catalytic protocols have been designed that use hydrogen peroxide as the terminal oxidant. Venturello and co-workers reported a method for the olefin epoxidation with peroxotungstates as active catalysts under phase-transfer conditions.<sup>11</sup> Wahl et al.<sup>12</sup> developed a surfactant-mediated biphasic olefin epoxidation with  $[\text{MoO}(\text{O}_2)_2(\text{OE}(\text{alkyl})_3)]$  complexes (E = N, P, As, see Figure 2). Herrmann and co-workers<sup>13,14</sup> developed earlier a method using methyloxodiperoxorhenium(VII) as a catalytically active species. Further investigations and

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Philip Gisdakis was born in Munich, Germany, in 1970. He graduated in chemistry and received his doctoral degree, Ph.D., in Theoretical Chemistry *summa cum laude* from the Technische Universität München. In addition, he studied Mathematical Finance at the University of Oxford. His current research interests are mathematical methods for measuring and managing market and credit risk in capital markets. Currently he is Senior Consultant at d-fine GmbH.

Wolfgang A. Herrmann was born in Kelheim, Bavaria, Germany, in 1948. He received his M.Sc. in chemistry in 1971 from the Technische Hochschule München, where he worked with Nobel laureate Prof. Ernst Otto Fischer. Then he moved to the Universität of Regensburg, where he worked with Prof. Henri Brunner, and received his Ph.D. in 1973. After postdoctoral work with Prof. P. S. Skell at the Pennsylvania State University, he returned to Germany to complete his *Habilitation* at the Universität of Regensburg in 1977. In 1979, he became Associate Professor of Inorganic Chemistry, and in 1982, he was appointed Full Professor at the Universität of Frankfurt, Germany. In 1985, he moved to the Technische Universität of München, where he has been the President since 1995. He has received various awards, including seven honorary doctorates, the Leibnitz price of the Deutsche Forschungsgemeinschaft (1986), the Humboldt prize (1989), the Max-Planck research prize (1991), the Federal Cross of Merit (1997), and the American Chemical Society award in Organometallic Chemistry (2004). Major topics of his research are the discovery of novel organometallic species and the development of industrial catalysis.

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Jörg Sundermeyer earned his Ph.D. in Chemistry at the University of Göttingen, Germany, where he worked with Prof. H. W. Roesky. After postdoctoral work at the University of Natal, South Africa, with Prof. R. J. Haines, he moved to Würzburg, Germany, where he took the *Habilitation* at the chair of Prof. H. Werner. Currently he is Professor for Inorganic Chemistry at the University of Marburg. His research interests include the metal activation of hydrogen peroxide and oxygen and the design of Lewis acid catalysts for polymerization reactions and other organic transformations.

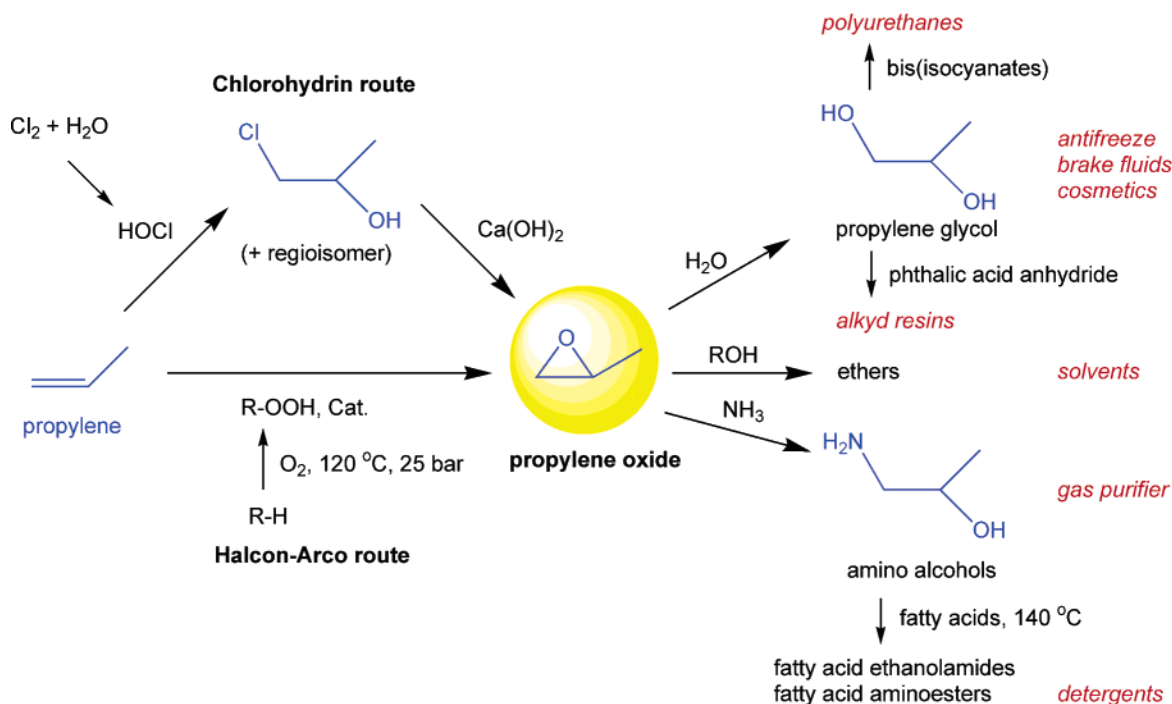


FIGURE 1. Industrial chemistry of propylene oxide. Data compiled from ref 2.

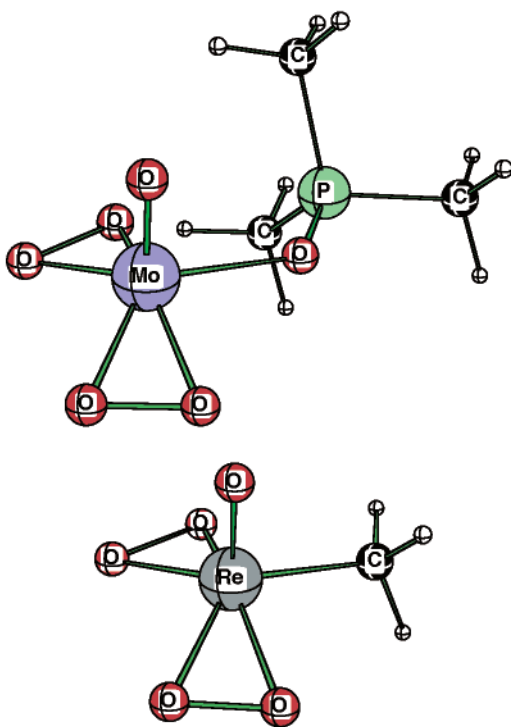


FIGURE 2. Mimoun-type complexes [MoO(O<sub>2</sub>)<sub>2</sub>(OPR<sub>3</sub>)<sub>2</sub>] and Herrmann-type complexes [ReO(O<sub>2</sub>)<sub>2</sub>Me] as olefin epoxidation catalysts, showing the characteristic "butterfly" geometry. R = N(CH<sub>3</sub>)<sub>2</sub> (ref 9) or alkyl (ref 12). An additional ligand may bind trans to the oxo group.

new catalytic protocols illustrate the current scope.<sup>15</sup> A highlight is the reaction-controlled phase-transfer catalysis developed by Xi and co-workers.<sup>16</sup> The reaction of an active tungsten peroxo complex with the olefin generates an insoluble inactive form of the catalyst, which can be recycled by reoxidation.<sup>16</sup>

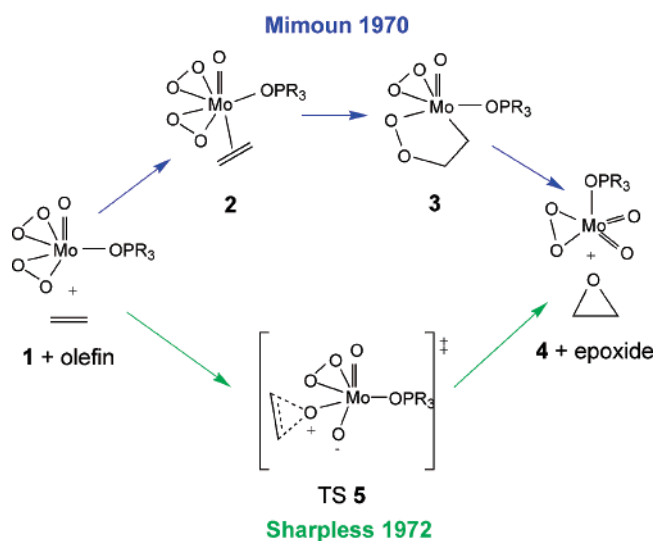


FIGURE 3. Olefin epoxidation with molybdenum diperoxo complexes—stepwise (top) or concerted (bottom)?

To provide a rational base for developing new reactions, the clarification of the molecular oxygen-transfer mechanism was an important research goal. Two seminal studies<sup>10,17</sup> in the early 1970s were contradictory and caused a long-lasting debate<sup>18</sup> that has concentrated on four central themes: (i) Stepwise versus concerted oxygen transfer. Mimoun and co-workers<sup>10</sup> suggested in 1970 a stepwise pathway (Figure 3, top), whereas Sharpless and co-workers<sup>17</sup> suggested in 1972 a concerted pathway (Figure 3, bottom). (ii) Electronic character of oxygen transfer. Whereas early studies of substituent effects indicated the electronic character of inorganic peroxides to be electrophilic, it was unclear whether these oxidants may also act as nucleophiles. Furthermore, quantum

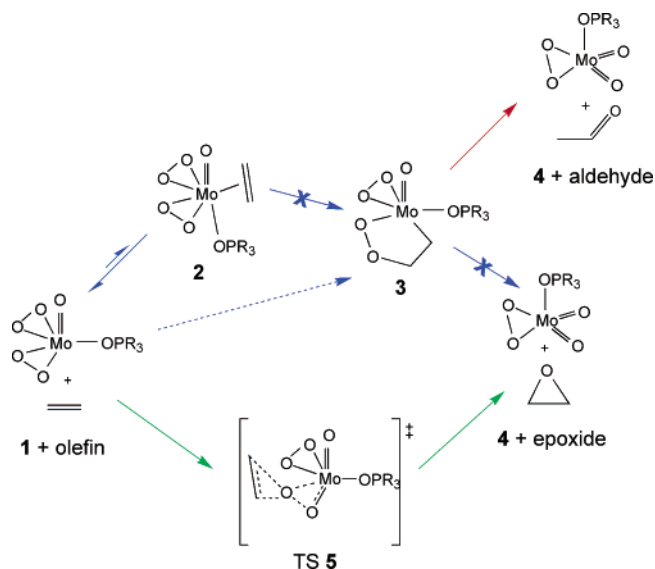
chemical studies have demonstrated that the nature of the transition state differs from what was originally proposed to support the suggested reaction mechanism. (iii) Stoichiometric versus catalytic oxygen transfer. Is the mechanism of the stoichiometric reaction valid for catalytic protocols as well? (iv) Stereoselective oxygen transfer. Asymmetric olefin epoxidations mediated by inorganic peroxides are of fundamental importance in chemical synthesis.<sup>19,20</sup> Several models were proposed to elucidate how stereochemical information is transferred between oxidant and substrate. In this Account, we present solutions to the four controversies, emphasizing recent contributions from quantum chemical calculations.

## Stoichiometric Oxygen Transfer

In 1970, Mimoun and co-workers<sup>10</sup> reported a kinetic study of the olefin epoxidation with molybdenum diperoxo complexes of the type  $[\text{MoO}(\text{O}_2)_2(\text{OP}(\text{NMe}_2)_3)]$  as stoichiometric oxidants and suggested a three-step mechanism for this reaction (Figure 3, top): First, the olefin coordinates at the metal ( $1 \rightarrow 2$ ). The observation that a higher concentration of additional donor ligands inhibits epoxidation<sup>10</sup> seemed to support the mechanistic proposal of the initial coordination of the olefin, because other donor ligands can block a free coordination site that would be required for the olefin. Second, a five-membered metallacycle (metalla-2,3-dioxolane) is formed by cycloinsertion of the coordinated olefin into a Mo–O(peroxo) bond ( $2 \rightarrow 3$ ). “Organometallacycles” like **3** are known for late transition metals.<sup>21,22</sup> Third, the epoxide is formed by cycloreversion of the metallacycle ( $3 \rightarrow 4$ ).

The mechanism of the reaction was further studied in the Sharpless laboratories.<sup>17</sup> Reaction of  $[\text{Mo}(\text{O}_2)_2(\text{OP}(\text{NMe}_2)_3)]$  with *trans*-cyclododecene yielded *trans*-cyclododecene oxide without incorporation of the <sup>18</sup>O isotope, confirming the oxygen transfer from a peroxo moiety rather than from the oxo moiety. However, a comparison of substituent effects on the relative rates in various oxygen-transfer reactions indicated two classes of reactions, one proceeding via a five-membered transition state (e.g., the addition of  $\text{OsO}_4$  across C=C bonds)<sup>23</sup> and the other proceeding via a three-membered transition state (e.g., the olefin epoxidation with *m*-chloroperbenzoic acid). Substituent effects in the olefin epoxidation with  $[\text{MoO}(\text{O}_2)_2(\text{OP}(\text{NMe}_2)_3)]$  fit in the latter category, whereas the assumption of a rate-determining formation of a metalla-2,3-dioxolane ( $2 \rightarrow 3$  in Figure 3) had implied that the reaction belongs to the former category. Based upon this evaluation, Sharpless and co-workers suggested a concerted oxygen-transfer pathway ( $1 \rightarrow 4$ ). Figure 3 displays the original model of the three-membered transition state, TS 5, for the concerted reaction course.<sup>17</sup> The two contradicting studies by the Mimoun<sup>10</sup> and Sharpless<sup>17</sup> laboratories led to a long-standing debate.<sup>18</sup>

The mechanism of the olefin epoxidation with molybdenum diperoxo complexes was finally clarified with the help of modern quantum chemistry.<sup>24,25</sup> Density functional theory (DFT) calculations at the B3LYP level were initially



**FIGURE 4.** Quantum chemical calculations support the concerted mechanism, whereas the stepwise mechanism would give the wrong product.

performed using ethylene and  $[\text{MoO}(\text{O}_2)_2\text{L}]$  ( $\text{L} = \text{OPH}_3$ ) complexes as models; additional studies with different ligands *L* corroborated the conclusions. Figure 4 summarizes the results of the DFT calculations. The investigation of the stepwise mechanism suggested by Mimoun is given at the top of the Figure. The  $\eta^2$  coordination of ethylene with the metal ( $1 \rightarrow 2$ ) is a 5 kcal/mol endothermic process. The calculations indicate that there is neither a subsequent reaction channel from the olefin complex to the metallacycle nor to the product. Can the metallacycle be formed directly from the reactants ( $1 \rightarrow 3$ )? The calculations predict a relative high activation energy of 25 kcal/mol for this reaction step.<sup>25</sup>

The clue of the quantum chemical investigations is the last step of the Mimoun mechanism. The calculations show that, if the metallacycle was formed, its decomposition would give the aldehyde via sigmatropic cycloreversion rather than the epoxide (Figure 4).<sup>26</sup> Hence, the stepwise mechanism would lead to the wrong product. This result is interesting in light of recent experiments by Gal and co-workers,<sup>27</sup> who synthesized a rhoda-2,3-dioxolane by activating dioxygen with a rhodium(I) olefin complex. The proton or photon-assisted decomposition of this metallacycle gives a rhodium(III) formylmethyl hydroxo complex, demonstrating again the contrast between the oxygen-transfer chemistry of early and late transition metal complexes.<sup>27</sup>

For the olefin epoxidation with  $[\text{MoO}(\text{O}_2)_2(\text{OPR}_3)]$ , the concerted reaction course remains as the alternative. Density functional theory (DFT) calculations predict an activation energy of 15 kcal/mol ( $1 \rightarrow \text{TS 5} \rightarrow 4$ ).<sup>25</sup> Is this mechanism also valid for peroxo complexes of other metals? Gisdakis et al.<sup>28</sup> reported a DFT study on the ethylene epoxidation with  $[\text{ReO}(\text{O}_2)_2\text{Me}]$ . The calculations show that (i) there is no olefin complex similar to **2** and (ii) the activation energy for the direct formation of the metallacycle is significantly higher than that of the con-

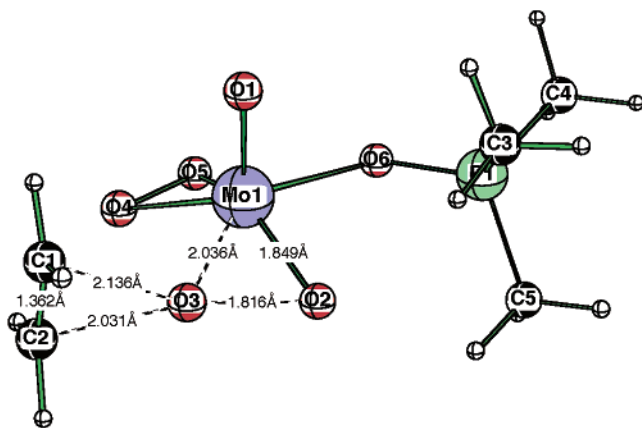


FIGURE 5. Calculated transition structure for the ethylene epoxidation with  $[\text{MoO}(\text{O}_2)_2(\text{OPMe}_3)]$ . The oxygen atom O3 (*distal* to the phosphane oxide) rather than O2 (*proximal* to the phosphane oxide) is transferred.

certed oxygen transfer. A concerted oxygen transfer mechanism was also demonstrated for the olefin epoxidation with peroxy complexes of the entire Cr–Mo–W triad<sup>24</sup> and with  $[\text{VO}(\text{O}_2)_2(\text{imidazole})]^-$ , which may represent the active site of vanadium-dependent haloperoxidases.<sup>29</sup> The oxygen transfer from an intact peroxy functionality of group VI and rhenium(VII) diperoxy complexes to olefins is a concerted process as postulated by Sharpless.<sup>17</sup>

## Electronic Character of Oxygen Transfer

When the mechanism of a reaction is known, one can explore the electronic structure of the transition state to develop strategies for a rational control of reactivity. The original model of the concerted mechanism,<sup>17</sup> TS 5 in Figure 3, implies (i) a three-membered transition state that involves the two carbon atoms of the olefin and the transferred oxygen and (ii) an electrophilic attack of the oxidant on the olefin. This model can now be critically evaluated by a quantum chemical analysis of the calculated transition structure.

The geometric structure of the transition state given in Figure 5 shows that the distal oxygen O3 is transferred and that the environment at O3 is *spiro* rather than planar. Pioneering DFT studies by Wu and Sun<sup>30</sup> and by Gisdakis et al.<sup>28</sup> revealed a similar TS in the ethylene epoxidation with  $[\text{ReO}(\text{O}_2)_2\text{Me}]$ . A *spiro* transition state is now well-accepted in the olefin epoxidation with organic peracids and dioxiranes, which was extensively studied by the Bach and Houk groups and others,<sup>31,32</sup> so the olefin epoxidation with peroxy complexes can be considered a metalla-analogue of the olefin epoxidation with dioxiranes. The oxygen-transfer event from  $[\text{ReO}(\text{O}_2)_2\text{Me}]$  and  $[\text{MoO}(\text{O}_2)_2(\text{OPR}_3)]$  involves a metalladioxirane moiety (Mo, O2, O3) rather than only the oxygen atom O3, which is transferred. The O2–O3 bond in the transition state shown in Figure 5 is elongated but not entirely cleaved. The Mo–O2 bond in the TS is significantly shortened in comparison with that in the reactant.<sup>33</sup> Following the topological classification of chemical reactions by Herges,<sup>34</sup> the transition state is five-membered and coarctate,

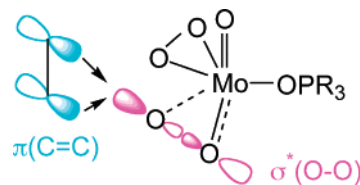


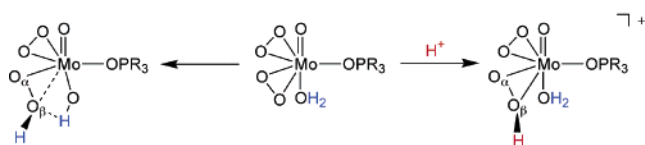
FIGURE 6. Predominant orbital interactions in the transition state.

because two bonds to O3 are formed and cleaved at a time (see TS 5 in Figure 4).

The electronic character of oxygen transfer, that is, whether the oxidant acts as an electrophile or a nucleophile, was studied using charge decomposition analysis (CDA).<sup>35,36</sup> CDA is a quantitative interpretation of the Dewar–Chatt–Duncanson model and evaluates the relative importance of the orbital interactions between the olefin (donor) and the oxidant (acceptor) and vice versa. The analysis shows an electrophilic attack of the oxidant on the substrate.<sup>25</sup> Rate enhancement by alkyl substituents on the olefinic double bond<sup>10,37</sup> and a  $\rho$  value of  $-0.93$  (versus  $\sigma^+$ ) in a Hammett study of the epoxidation of substituted styrenes with  $[\text{ReO}(\text{O}_2)_2\text{Me}]$  reported by Al-Ajlouni and Espenson<sup>38</sup> agree with the CDA results. Thianthrene 5-oxide (SSO)<sup>39,40</sup> was designed by Adam and co-workers as a probe for the electronic character of oxygen transfer, because it contains both a sulfide and a sulfoxide moiety. Inorganic peroxides oxidize SSO at the sulfide site and are thus identified as electrophiles,<sup>41,42</sup> whereas nucleophilic oxidants react with SSO at the sulfoxide moiety.

The electronic character of oxygen transfer is particularly important to an understanding of the reaction mechanism. Mimoun et al.<sup>10</sup> observed the inhibition of the olefin epoxidation with  $[\text{MoO}(\text{O}_2)_2\text{L}]$  in case of a high concentration of the phosphine oxide L. The equilibrium between  $[\text{MoO}(\text{O}_2)_2\text{L}]$  and  $[\text{MoO}(\text{O}_2)_2\text{L}_2]$  is shifted to the latter compound when much L is present. The observed inhibition of epoxidation could have suggested that the second ligand L occupies a free coordination site at the metal that would be required for the olefin. However, the electrophilic nature of the oxidant provides a different explanation. An additional ligand at the metal makes the peroxy complex less electrophilic and thus less reactive.<sup>43</sup>

Charge decomposition analysis of the transition state also reveals the orbital interactions involved in the oxygen-transfer event.<sup>44</sup> Electron donation from the  $\pi$  orbital of the olefin into the  $\sigma^*$  orbital of the O–O bond is found to be predominant in the transition state (Figure 6).<sup>25</sup> Edwards<sup>45</sup> and Bach<sup>46</sup> suggested this interaction to be most important in the olefin epoxidation with peroxides. The energy levels of the  $\sigma^*(\text{O}–\text{O})$  orbitals in diperoxy complexes of group 6 metals were used to elucidate the greater reactivity of tungsten diperoxy complexes compared to that of the Mo congeners. The lower the  $\sigma^*(\text{O}–\text{O})$  orbital energy level, the smaller is the activation energy of ethylene epoxidation.<sup>24</sup> A refined analysis shows relativistic effects to be a crucial factor in the reactivity of the peroxy complexes. The relativistic stabilization of the tungsten–O(peroxy) bonds leads to a destabilization of the remain-



**FIGURE 7.** Tautomerism (left) and intermolecular proton transfer (right) lead to  $\eta^1$ - and  $\eta^2$ -hydroperoxo species that are potentially more active than the parent  $\eta^2$ -diperoxo complex (middle, here shown with an aqua ligand).

ing O–O bond in the W(O<sub>2</sub>) moiety, thus activating the tungsten complexes for olefin epoxidation.<sup>47</sup>

Relatively recent theoretical and experimental studies, however, indicated organic and inorganic peroxides to be potential nucleophiles. For instance, CDA identifies dioxiranes as chameleon oxidants that can be either electrophilic or nucleophilic, depending on substrate. Acrolein and acrylonitrile are attacked by dioxirane in a *nucleophilic* manner.<sup>32</sup> Ligands at the metal of peroxo complexes may provide a tool for controlling the electronic character of inorganic peroxides. A study of Selke and Valentine<sup>48</sup> indicated the opening of the intact  $\eta^2$ -peroxo functionality of a peroxo porphyrin iron(III) complex upon coordination of dimethyl sulfoxide with the metal, giving a nucleophilic  $\eta^1$ -peroxo complex that epoxidizes the electron-deficient C=C bond of 2-methyl-1,4-naphthaquinone.

## Catalytic Oxygen Transfer

The development of a catalytic protocol from a known stoichiometric reaction may be based on the assumption that the elementary mechanism is identical in the two systems. However, if other more reactive species are formed under catalytic conditions, other mechanisms may take place. In the biphasic protocol reported by Wahl et al.,<sup>12</sup> molybdenum trioxide was anticipated to be perhydrolyzed in the aqueous phase, giving peroxo species. These peroxo species can be trapped at the interphase by amphiphilic phosphane oxides and be transferred into the chloroform phase, where the olefin is epoxidized. A quantum chemical screening of monoperoxo, diperoxo, and triperoxo species of the type [Mo(O)<sub>3-n</sub>(O<sub>2</sub>)<sub>n</sub>L<sub>m</sub>] indicated a greater relative stability and reactivity of the diperoxo complexes ( $n = 2$ ).<sup>49,50</sup> Herrmann and co-workers<sup>51</sup> also suggested rhenium diperoxo complexes to be active species in the methyltrioxorhenium-catalyzed olefin epoxidation.

The results from quantum chemical studies on the control of reactivity by substituents are in line with an electrophilic character of the oxidant.<sup>43</sup> The more electrophilic the inorganic peroxide, the faster is the epoxidation of electron-rich, alkyl-substituted olefins. The fact that the proton is one of the strongest electrophiles points toward the potential role of protonated peroxo ligands in the catalytic olefin epoxidation with inorganic peroxides. The peroxo functionality of the metal complexes may be activated via *intramolecular* proton transfer, for example, from an aqua ligand to the peroxo ligand: [Mo( $\eta^2$ -O<sub>2</sub>)<sub>2</sub>(H<sub>2</sub>O)L] → [Mo( $\eta^2$ -O<sub>2</sub>)( $\eta^1$ -OOH)(OH)L] (Figure 7, left). Quantum chemical calculations<sup>52</sup> predict the peroxo

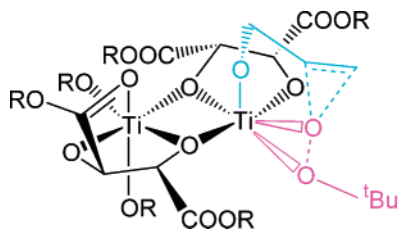
functionality to open upon this tautomerism, giving an  $\eta^1$ -OOH hydroperoxo species. Intramolecular proton transfer is predicted to be endothermic in case of the rhenium-(VII) peroxides. In contrast, the reaction is predicted to be exothermic in case of molybdenum(VI) peroxides, and the activation energies for the ethylene epoxidation with hydroperoxo species are only slightly higher than those with the parent diperoxo species. The calculations indicate multiple competing epoxidation mechanisms with an oxygen transfer from  $\eta^2$ -O<sub>2</sub> or  $\eta^1$ -OOH ligands. The attack of the  $\alpha$  oxygen atom of the hydroperoxo moiety (Figure 7, left) on the substrate is preferred to that of the  $\beta$  oxygen atom.<sup>52</sup> In conclusion, hydroperoxo mechanisms are less important in the catalytic epoxidation with Re(VII) peroxides, whereas they are competitive to peroxo mechanisms in case of molybdenum(VI) catalysts. Hydroperoxo mechanisms are superior to peroxo mechanisms in the olefin epoxidation with titanium(IV) species.<sup>53,54</sup>

When Brønsted acids are available in catalytic methods, hydroperoxo species may be generated by *intermolecular* proton transfer as well. Note that the largest turnover rate in the biphasic protocol reported by Wahl et al.<sup>12</sup> was obtained at pH 2 of the aqueous phase. A quantum chemical study considered the potential formation of cationic hydroperoxo complexes upon protonation of a peroxo functionality (Figure 7, right).<sup>55</sup> The calculations predict a negligible activation energy for ethylene epoxidation with the cationic species, leaving a purely entropic barrier.<sup>55</sup> Although additional investigations that include environmental effects<sup>56</sup> more accurately are still in progress, the olefin epoxidation with protonated species is anticipated to be very fast.

Oxygen transfer from an hydroperoxo functionality resembles the Ti(IV)-, V(V)-, and Mo(VI)-mediated olefin epoxidation with alkylhydroperoxides. In the Halcon–Arco process, alkylhydroperoxides generated from alkanes and dioxygen under extreme conditions are employed for olefin epoxidation in the presence of d<sup>0</sup>-metal catalysts. Due to the industrial importance, the reaction mechanism was studied by several groups.<sup>57</sup> For example, Thiel and Priermeier<sup>58</sup> incorporated the *cis*-cyclooctene substrate into a bidentate 2-(pyrazol-3-yl)-pyridine ligand (L–L') of an oxidiperoxo molybdenum(VI) complex, [Mo(O<sub>2</sub>)<sub>2</sub>(L–L')], and demonstrated that epoxidation does not occur before adding *tert*-butylhydroperoxide. These studies provide strong evidence for a direct oxygen transfer from coordinated alkylhydroperoxide to the olefin, as suggested by Chong and Sharpless.<sup>57b</sup>

## Stereoselective Oxygen Transfer

The 2001 Nobel prize was awarded for the development of asymmetric oxidation reactions,<sup>19</sup> and we wish to conclude this Account with two pioneering examples in this field. The rigid “butterfly” geometry of the {Mo(O<sub>2</sub>)<sub>2</sub>} core<sup>49</sup> in Mimoun-type diperoxo complexes indicates a potential for storing stereochemical information in the presence chiral ligands. In 1979, Schurig and co-workers<sup>59</sup> achieved the enantioselective epoxidation of prochiral



**FIGURE 8.** Dinuclear transition state model for the Katsuki–Sharpless epoxidation of prochiral allylic alcohols on the *Re* enantiotopic face in the presence of (*R,R*)-tartrate. See ref 69.

alkyl-substituted olefins with a Mimoun-type complex bearing a chiral ligand, but the enantioface selectivity was moderate. Polar groups adjacent to the olefinic C=C bond render a stereochemical recognition of the substrate by the oxidant much more efficient, for instance, via coordination of the functional group at the metal or via hydrogen-bond directivity.<sup>60–62</sup> A prominent example is the titanium(IV)-mediated Katsuki–Sharpless asymmetric epoxidation<sup>63</sup> of allylic alcohols using *tert*-butylhydroperoxide as the terminal oxidant and (+)-(*R,R*)- or (–)-(*S,S*)-tartrate as a chiral ligand. A very high enantioselectivity was achieved, and the catalyst–substrate ratio was later reduced to 5–10%.

In search of the active species in the Katsuki–Sharpless epoxidation, Sharpless, Lippard, and co-workers reported a crystal structure of a dinuclear bis[( $\mu_2$ -O)( $\mu_1$ -O)-diolato] complex with one oxygen atom of the diolato moiety of each tartrate bridging the two Ti centers.<sup>64</sup> An alternative ion-pair model<sup>65</sup> does not obey the observed kinetic rate expression of the olefin epoxidation.<sup>66</sup> Semiempirical calculations of Jørgensen et al.<sup>67</sup> suggested a *spiro* structure of the transition state, which was later confirmed by DFT studies of Wu and Lai.<sup>68</sup> The latter researchers also indicated conformational preferences in the transition state.<sup>69</sup> The synergy of experiment and theory led to a transition state model shown in Figure 8, where both the substrate and the oxidant are coordinated at one of the metals. Boche et al.<sup>70</sup> supported the computationally predicted<sup>68</sup>  $\eta^2$  coordination of the alkylperoxide by a crystal structure. We believe that our ongoing Car–Parrinello simulations<sup>71</sup> of the reaction (including a large number of explicit solvent molecules) will provide further insights into the dynamic mechanism and origin of stereoselectivity in the Katsuki–Sharpless epoxidation.

## Conclusions

Many developments in modern oxygen-transfer catalysis are based on the pioneering work of Mimoun, Sharpless, and others on the olefin epoxidation with inorganic peroxides. Research efforts have particularly focused on the activation of green terminal oxidants such as hydrogen peroxide. Four controversies on the molecular mechanism of oxygen transfer have been solved recently with the help of quantum chemical calculations:

**(i) Concerted versus Stepwise Oxygen Transfer.** The stoichiometric olefin epoxidation with Mimoun-type complexes [MoO( $\eta^2$ -O<sub>2</sub>)<sub>2</sub>(OPR<sub>3</sub>)] and Herrmann-type com-

plexes [ReO( $\eta^2$ -O<sub>2</sub>)<sub>2</sub>Me] proceeds via a concerted oxygen-transfer mechanism postulated by Sharpless rather than via a stepwise mechanism postulated by Mimoun. The formation of a metalla-2,3-dioxolane as an organometallic intermediate is not favorable, and its decomposition would give aldehydes rather than epoxides.

**(ii) Electronic Character of Oxygen Transfer.** In the transition state of the concerted mechanism, the olefin is attacked by the diperoxo complex in an electrophilic manner with electron donation from the ethylene HOMO into the  $\sigma^*(\text{O}-\text{O})$  orbital representing the predominant orbital interaction. The transition state is five-membered and coarctate rather than three-membered as originally suggested. Furthermore, certain peroxides may also act as nucleophiles toward electron-deficient C=C bonds.

**(iii) Stoichiometric versus Catalytic Oxygen Transfer.** The mechanism of Mo(VI)-catalyzed olefin epoxidation with hydrogen peroxide as the terminal oxidant differs from that of the stoichiometric olefin epoxidation with  $\eta^2$ -peroxo species.  $\eta^1$ -Hydroperoxo species formed upon intra- or intermolecular proton transfer are predicted to be more stable than the  $\eta^2$ -peroxo species but competitive or superior in epoxidation. Hydroperoxo species are less important in the Re(VII)-catalyzed olefin epoxidation with hydrogen peroxide.

**(iv) Stereoselective Oxygen Transfer.** Transferring stereochemical information between peroxo complexes and C=C bonds can be particularly efficient if the substrate contains an additional functional group. A prominent example is the titanium(IV)-catalyzed asymmetric epoxidation of allylic alcohols with *tert*-butylhydroperoxide, known as Katsuki–Sharpless epoxidation. The synergy of experiment and theory led to a conformationally constrained transition state model where both the substrate and the oxidant are coordinated to the same metal center of a dinuclear complex.

The enormous potential of quantum chemical calculations in the current development of novel group-transfer reactions may be demonstrated by one of the most recent studies.<sup>72</sup> An isoelectronic replacement of the peroxo ligand (O–O)<sup>2–</sup> in the monoperoxo complex [Re(O)<sub>2</sub>(O<sub>2</sub>)-Me] by the hydroxylamine derivative (O–NH)<sup>2–</sup> leads to an entirely different mechanism. More than three decades after Mimoun’s pioneering work, theory predicts favorable pathways to five-membered organometallacycles of d<sup>0</sup>-metal complexes in the nitrogen-analogue chemistry of the methyltrioxorhenium-catalyzed olefin epoxidation.<sup>72</sup>

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