Mechanistic Study of the Oxidation of Sulfides to Sulfoxides and Asymmetric Sulfoxides Catalysed by Transition Metal Peroxide Complexes

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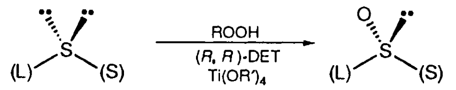
The mechanism for the oxidation and asymmetric oxidation of sulfides by transition metal peroxide complexes is studied using a theoretical approach. First, the oxygen transfer from a lithium peroxide complex to H_2S is investigated, with η^2-Li as a model for a bidentate-coordinated peroxide to a transition metal. Then, oxygen transfer is investigated for a titanium peroxide complex, η^2-$(O_2H)Ti(X)_3$, to H_2S. These calculations show that the sulfur atom of the sulfide coordinates first to the metal, followed by a slipping motion towards the peroxygen which is going to be transferred to the sulfur atom, leading to the transition state for the reaction. The pre-coordination of the sulfide to the metal and the transition state for the reaction are described using a frontier-orbital approach and total-energy considerations. The lithium and titanium peroxide systems give nearly similar results for the oxygen-transfer step to the sulfide. The results obtained are discussed in relation to the experimental data for the oxidation of sulfides to sulfoxides by different oxidation systems containing peroxygen–peroxygen bonds. The transition state geometry for the oxygen transfer from the titanium peroxide complex to the sulfide, and the pre-coordination of the sulfide to the metal, are then used to study the asymmetric oxidation of sulfides to sulfoxides catalysed by titanium tartrate complexes. These considerations lead to a model for the oxygen-transfer step with an enantioselectivity for the oxidation of the prochiral sulfide in accordance to the experimental data.

The titanium tartrates show unique properties in catalytic oxidation chemistry as these complexes can catalyse both the asymmetric epoxidation of allylic alcohols[1] and the asymmetric oxidation of sulfides to sulfoxides.[2]

The asymmetric oxidation of allylic alcohols catalysed by the titanium tartrate complexes using an alkyl peroxide as oxygen donor (known as the Sharpless epoxidation) produces the corresponding allylic epoxides in high yield and with a high enantiomeric excess (ee).[1] This reaction has already shown its great usefulness in the synthesis of a variety of compounds where chiral centres are of utmost importance.[1c] With regard to the active catalyst and the mechanism for the oxygen-transfer step to one of the enantiofaces of the allylic alcohol, there are now results that enable one to begin to understand this reaction.[3]



L = Large group
S = Small group

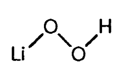
Scheme 1

The asymmetric oxidation of sulfides to sulfoxides catalysed by titanium tartrate complexes and with an alkyl peroxide as oxygen donor (Scheme 1) has also found great applicability for the synthesis of compounds with asymmetric sulfoxide functionalities.[2,4] In contrast to the mechanism for the asymmetric epoxidation of allylic alcohols catalysed by titanium tartrate complexes, the mechanism for the formation of asymmetric sulfoxides catalysed by titanium tartrate complexes is less well understood. To quote Kagan in a recent review: 'The mechanism of the oxidation reaction still remains a matter of debate.'[2h] A variety of other transition metal complexes, using either hydrogen peroxide or alkyl peroxides as oxygen donors, have also been used for the oxidation of sulfides to racemic sulfoxides.[5]

The present work is devoted to an investigation of the mechanism of the oxidation of sulfides to sulfoxides by transition metal peroxide complexes using a theoretical approach. The mechanism for the sulfide to sulfoxide oxidation will be presented as a 'three-step rocket': first, the oxygen transfer from a lithium peroxide model to H_2S will be put forward using *ab initio* calculations[6] and a relatively large basis set. The lithium peroxide system has been used previously to study the mechanism of metal-catalysed epoxidations.[7] This will be followed by a study of oxygen transfer from a titanium peroxide complex to H_2S also using *ab initio* calculations.[6] Moving from the first to the second step leads thus to a more realistic representation of the actual system. The third step combines the results obtained in the first two steps with models of the titanium tartrate catalyst using molecular mechanics calculations,[8] to account for the enantioselectivity in the oxygen-transfer step. The approach outlined here will cast some light over the general mechanism for the oxidation of sulfides to sulfoxides by transition metal peroxide complexes and how the titanium tartrate moiety induces the enantioselectivity in this oxidation reaction.

Results and Discussion

Oxidation of H_2S *to* H_2SO *by a* LiO_2H *Model.*—The structure of LiO_2H will be discussed as a starting point: a peroxide can bind in an η^1- or η^2-fashion to a metal,[9] shown as species **1** and **2**, respectively, for the lithium peroxide system.



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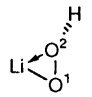

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Optimization of the structures of **1** and **2** using 4-31G* and 6-31G* basis sets gives η^2-$(O_2H)Li$, **2**, as the more stable. In the following, only the closed-shell singlet states for the systems studied are considered, as these are found to be considerably lower in energy than the open-shell states. The total energy, the Li–O^1, Li–O^2 and O^1–O^2 bond lengths, orbital populations and

Table 1 Some electronic parameters for the different lithium and titanium peroxide systems

				Bond length/Å			Orbital population (O^1)				Charge
Entry	Compound	Basis set	Energy/au	M–O^1	M–O^2	O^1–O^2	s	p_x	p_y	p_z	O^1
1	η^2-(O_2H)Li	4-31G*	−157.5355	1.712	1.804	1.472	3.906	0.844	1.797	1.915	−0.508
2	η^2-(O_2H)Li	6-31G*	−157.7208	1.706	1.793	1.462	3.965	0.837	1.761	1.926	−0.502
3	η^2-(O_2H)Li	CISD/6-31G*	−158.0635	1.706	1.793	1.462	3.944	0.851	1.776	1.921	−0.534
4	η^2-(O_2H)Ti(H)$_3$	*a*	−1000.5656	1.930	1.967	1.446	3.958	0.902	1.792	1.890	−0.484
5	3[10]	—	—	1.872	1.999	1.436	—	—	—	—	—

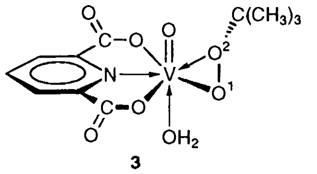
[a] See appendix.

Table 2 Some electronic parameters for hydrogen sulfide

			Bond length/Å	Bond angle/°	Orbital population (S)				Charge
Compound	Basis set	Energy/au	S–H	HSH	s	p_x	p_y	p_z	S
H_2S	CISD/6-31G*	−398.8043	1.326	94.4	5.827	3.999	2.953	3.329	−0 .222

charge at peroxygen-atom-1 for **2** obtained by the different basis sets are presented in Table 1.

It appears that the bond lengths do not vary significantly within the two basis sets. Experimentally there is evidence for an η^2-bound peroxide to a d^0 metal, as such a bidentate-binding mode of an alkyl peroxide has been characterized in the vanadium(v) dipicolato *tert*-butyl peroxide complex, **3**.[10]



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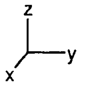
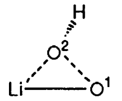
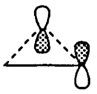
The bond lengths for the vanadium peroxide fragment in **3** are given as entry 5 in Table 1. Comparing the experimental results for the geometry of the vanadium peroxide fragment in **3**, with the theoretical results for η^2-(O_2H)Li, **2**, (entries 1–3) it is observed that the Li–O^1 and Li–O^2 bond lengths in **2** are about 0.2 Å shorter than the V–O^1 and V–O^2 bond lengths in **3**, whereas the O^1–O^2 bond lengths in **2** and **3** are more or less alike.

Activation of oxygen transfer from hydrogen peroxide or alkyl/aryl peroxides by transition metals to a substrate requires low-lying empty d-orbitals at the metal.[7a] Lithium does not generally belong to the metals that catalyse oxygen transfer from peroxides to a substrate.* However, by applying a relatively large basis set, including polarized d orbitals to describe the polarization of the valence sp orbitals, lithium becomes 'more transition metal like'. It is thus possible at this first stage to perform relatively reliable calculations on the oxygen transfer from η^2-(O_2H)Li, **2**, to H_2S. In the following, this transfer will be outlined, in an attempt to obtain information about oxygen transfer of this system. The geometries given in the remaining part of this section are obtained using a 6-31G* basis set and the electronic data at a CISD/6-31G* level of calculations.

The frontier orbitals of η^2-(O_2H)Li, **2** are (the orbitals are represented relative to the coordinate system shown as species **4**–**7**): The HOMO is found at −9.96 eV located at the peroxygens as π^*_{O-O} of mainly p_z character, mixed in with a small part of p_y, **4**; at −10.79 eV is the π^*_{O-O} of mainly p_y character mixed in with a small part of p_z, **5**, found. At −13.77 eV is the σ_{O-O}, **6**, located. The unoccupied orbitals of **2** are at the metal having some d-orbital character, and at 0.41 eV is the σ^*_{O-O}, **7**, found. The two peroxygens, O^1 and O^2 in **2** are different from an electronic point of view. The orbital populations and atomic charge for peroxygen-atom-1 are given in Table 1. Comparing the orbital population for the two peroxygens in **2** reveals that peroxygen-atom-1 (the orbital population and atomic charge for peroxygen-atom-2 are not presented here) is both more electrophilic and nucleophilic than peroxygen-atom-2, indicating that it is the former that is the most reactive of the two peroxygens. The acceptor properties of **2** are found in the Li–O^1–O^2-plane, either at the metal with its empty orbitals, or at peroxygen-atom-1 with its acceptor orbital outlined in **7**. The π^*_{O-O} orbitals, depicted in **4** and **5** can interact with acceptor orbitals, located either perpendicular to the metal–peroxo plane (interaction with the orbital shown in **4**), or parallel to the metal–peroxo plane (interaction with the orbital shown in **5**).







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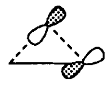

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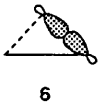

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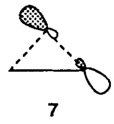

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In the first two sections H_2S has been chosen as the sulfide. The geometry of H_2S has been optimized with a 6-31G* basis set and the electronic data are obtained at a CISD/6-31G* level of calculations. Some geometrical and electronical data for H_2S are given in Table 2. The frontier orbitals of H_2S, species **8**–**11**, are presented relative to the coordinate systems shown. The HOMO is calculated to be −10.43 eV and is of p_x character at sulfur, **8**, and corresponds well with the ionization potential for H_2S.[11] At −13.55 eV is found the bonding combination of hydrogen s and the sulfur p_z orbitals, **9**. The sulfur p_y orbital mixed in with hydrogen s character, **10**, is located at −16.37 eV, while the corresponding antibonding orbital, **11**, is at 4.70 eV as

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* Oxygen transfer from Li peroxygen systems has not according to our knowledge been observed.

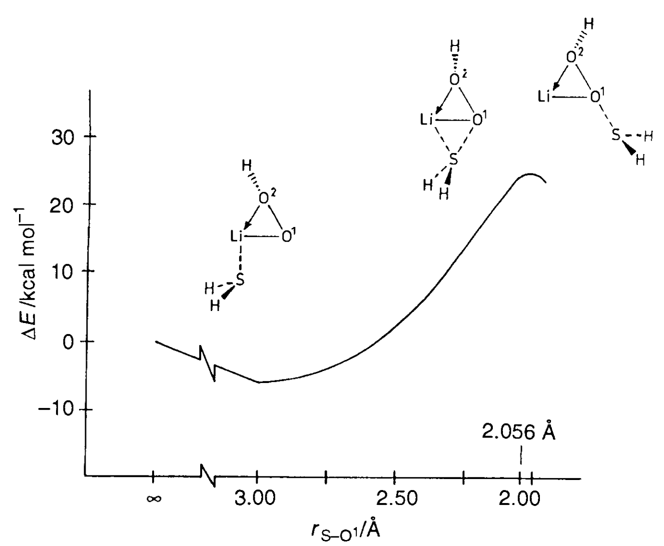
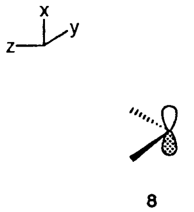


Fig. 1 The change in total energy and 'snap shots' of the geometrical structure of the H_2S–η^2-(O_2H)Li system as a function of the S–O^1 distance

the LUMO of H_2S. The orbital population for the sulfur atom in H_2S (Table 2) shows a high population in the p_x orbital, compared to the p_y and p_z orbitals.



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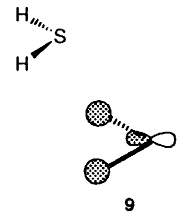

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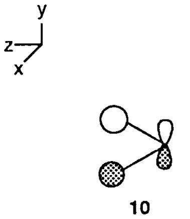

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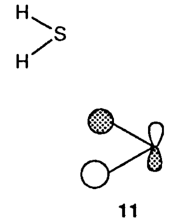
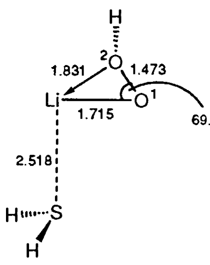


11

The reaction of H_2S with η^2-(O_2H)Li, **2**, has been studied. The following calculations have been performed with all parameters in the H_2S–η^2-(O_2H)Li system free, except the S–H bond length in H_2S (1.326 Å), the O–H bond length in **2** (0.946 Å) and the distance between the sulfur atom and the peroxygen-atom-1. The S–O^1 bond length is reduced from 3.00 Å until a maximum in energy is reached. From this energy maximum the transition state is then calculated. The total energy for the H_2S–η^2-(O_2H)Li system is calculated to be −556.8774 au for a S–O^1 distance of 3.00 Å. The change in energy for the H_2S-η^2-(O_2H)Li system as a function of the S–O^1 distance is depicted in Fig. 1. Along with the change in energy, three 'snap shots' of the geometry of the system are also shown. The 'snap shots' shown are at S–O^1 distances of 3.00, 2.25 and 2.056 Å—the last corresponding to the transition state for the reaction. The transition-state geometry is found to have one and only one imaginary frequency.

It appears from the curve in Fig. 1 that at a S–O^1 distance of 3.00 Å the H_2S–η^2-(O_2H)Li system is stabilised by 6 kcal mol^{-1}, relative to the separated molecules. The transition state energy for the reaction is calculated to be 25 kcal mol^{-1}, relative to the separated molecules, at a S–O^1 distance of 2.056 Å. More detailed drawings of the H_2S–η^2-(O_2H)Li system at a S–O^1 distance of 3.00 Å and at the transition state are shown in **12** and **13**.



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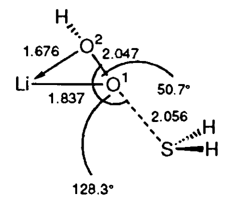

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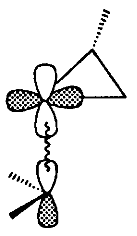
It can be seen from **12** that the sulfide approaches the metal at a S–O^1 distance of 3.00 Å, with a sulfur–lithium distance of 2.518 Å. Decreasing the S–O^1 distance leads to a change in the direction of the approach of the sulfide as it now moves from the metal to peroxygen-atom-1 as depicted in the 'snap shots' in Fig. 1 and **13**. These results point towards an initial coordination of the sulfide to the metal followed by a slipping motion to peroxygen-atom-1—the one to be transferred to the sulfide, as the S–O^1 distance decreases. At a S–O^1 distance of 3.00 Å the S–O^1–O^2 angle is 124.4°, whereas it is 179.0° in the transition state, showing that the sulfur atom has to approach peroxygen-atom-1 on the O^2–O^1 connecting line. The structure of η^2-(O_2H)Li is also changed in the transition state. The most remarkable change is found for the O^1–O^2 distance, which increases by 0.574 Å relative to its value in **2**. The Li–O^1 bond length increases by 0.122 Å, while the Li–O^2 bond length decreases by 0.155 Å, relative to the bond lengths in **2**. The H–S–H bond angle in H_2S is reduced to 89.6° in **13**, compared to 94.4° for the H_2S molecule. It should be noted that forcing the sulfur atom in H_2S out of the Li–O^1–O^2 plane causes an increase in energy; a 5° displacement leads to an increase in energy by 4 kcal mol^{-1}.

Recently the oxidation of sulfides to sulfoxides by dioxirane has been studied using *ab initio* calculations.[12] In the transition state for this reaction the sulfur–peroxygen and the peroxygen–peroxygen bond lengths were calculated to be 1.839 and 1.996 Å, respectively,[12] which are very similar to the sulfur–peroxygen and peroxygen–peroxygen distances obtained in the present work. The transition state energy obtained in the present study corresponds well to the transition state energy calculated for oxygen transfer from a dioxirane to a sulfide [26.8 kcal mol^{-1} (MP2/6-31G*)].[12]

Let us, in the following, discuss the electronic changes involved when moving from the isolated molecules to species **12** and to **13**. The initial interaction between H_2S and η^2-(O_2H)Li, **2**, at a S–O^1 distance of 3.00 Å, causes a transfer of electron density from H_2S to **2** as the charge on the sulfur atom decreases from −0.222 in H_2S to −0.047 in **12**. The interaction of the sulfur atom in H_2S with the metal in **12** can to a certain extent be traced to relatively weak orbital interactions, although one has to be cautious not to interpret too much from these weak interactions, as the interaction energy in **12** is calculated to be 6 kcal mol^{-1}. The orbital interaction leading to the stabilization of **12** takes place by an interaction of mainly the sulfur p_x orbital in H_2S interacting with an empty metal orbital having some $d_{x^2-y^2}$ orbital character, as outlined in **14**. By this interaction electron density is transferred from the sulfur p_x orbital to the metal, as the orbital population at the sulfur atom decreases from 3.999 to 3.602.

The interaction between H_2S and η^2-(O_2H)Li changes when moving from **12** to the transition state, **13**. Along the reaction



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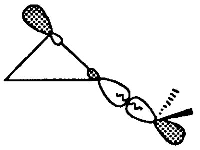
path from **12** to **13** (see the 'snap shot' at 2.25 Å in Fig. 1) the sulfur p_x orbital interacts with both the empty metal orbital and the peroxygen-σ^*_{O-O} orbital. The interaction for the reaction in the transition state can be traced to mainly two types of interaction. The sulfur p_x orbital interacts with the σ^*_{O-O} orbital, **7**, causing a reduction of the sulfur p_x orbital population from 3.999 in H_2S to 3.348 in **13**. There is also a less important interaction between the sulfur p_y orbital with the π^*_{O-O} orbital, **4**. These two interactions are shown in **15** and **16**.



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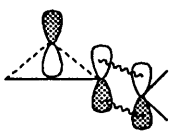
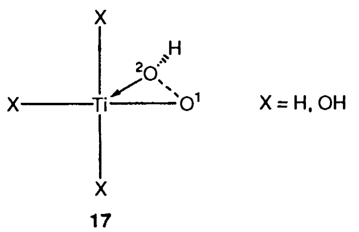


16

By the interaction outlined in **15** electron density is donated into the σ^*_{O-O} bond of η^2-$(O_2H)Li$, causing the increase of the O^1–O^2 bond length in the transition state, **13**, compared to η^2-$(O_2H)Li$. Due to the donation of electron density from the sulfur atom to the peroxygens the charge on the sulfur atom is reduced to 0.009 in the transition state, *i.e.* sulfur has depleted 0.231 electron to the η^2-$(O_2H)Li$ fragment.

Oxygen Transfer from $X_3Ti(O_2H)$ *to* H_2S.—The geometry of $X_3Ti(O_2H)$ (X = H, OH) has been optimized using the basis set described in the Appendix. The most stable form of $X_3Ti(O_2H)$ is with a bidentate-coordinated peroxide, **17**. It is found that both the electron and geometrical data for the peroxide part of **17** are more or less invariant upon changes in X and basis sets (only the results with the basis set described in the Appendix will be presented here). As the difference in both geometrical and electronic data between η^2-$(O_2H)Ti(H)_3$ and η^2-$(O_2H)Ti(OH)_3$ is minor, we have for the remaining part of this section used the former to save computer time. In Table 1, entry 4 some geometrical and electronic data for η^2-$(O_2H)Ti(H)_3$ are presented.



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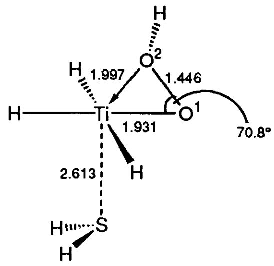
It appears from the results for η^2-$(O_2H)Ti(H)_3$ in Table 1 that the bond lengths for the titanium peroxide fragment are very similar to the experimental bond lengths found for the vanadium peroxide fragment in **3**.[10] It is also observed that the peroxygen-atom-1 orbital populations in η^2-$(O_2H)Ti(H)_3$ are similar to those found for peroxygen-atom-1 in η^2-$(O_2H)Li$, but that peroxygen-atom-1 in the former is slightly more electrophilic than the latter.

The frontier orbitals of **17** are very similar to those of **2**. The occupied MOs are similar to those shown in **4**–**6**, while the lowest unoccupied MOs are located at the titanium atom as d orbitals. Among the lowest unoccupied MOs the σ^*_{O-O}, similar to **7**, is found. The only major difference in the frontier orbitals of the η^2-$(O_2H)Li$ and η^2-$(O_2H)Ti(H)_3$ systems is the orbital energies, due to difference in the metal.

The reaction of H_2S with η^2-$(O_2H)Ti(H)_3$ as a function of the S–O^1 distance has been investigated, with the S–H and O^2–H distances held fixed. This approach corresponds to an intrinsic reaction coordinate for the reaction. Optimization of H_2S–η^2-$(O_2H)Ti(H)_3$ system with an S–O^1 distance of 3.00 Å leads to the structure shown in **18**.



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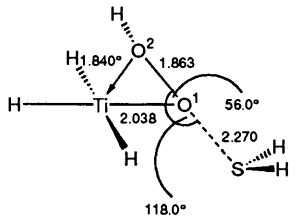


19

Ths sulfide also prefers in this case to coordinate to the metal, with an S–Ti bond distance of 2.613 Å, compared to an S–Li distance of 2.518 Å for the H_2S–η^2-$(O_2H)Li$ system. The total energy of **18** is calculated to be −1399.4678 au, corresponding to a decrease in energy of 6 kcal mol^{-1}, relative to the separated molecules. The geometry of the titanium peroxide part of the η^2-$(O_2H)Ti(H)_3$ fragment remains unchanged by the coordination of H_2S to the titanium atom. The interaction between H_2S and η^2-$(O_2H)Ti(H)_3$ in **18** is very similar to the one taking place in **12** outlined in **14**, as the HOMO of H_2S, the sulfur p_x orbital, interacts with the LUMO of η^2-$(O_2H)Ti(H)_3$, the titanium $d_{x^2-y^2}$ orbital. A small donation of electron density from H_2S to η^2-$(O_2H)Ti(H)_3$ takes place as the sulfide atom is depleted by 0.111 electrons. The H_2S–η^2-$(O_2H)Ti(H)_3$ system, has also been optimized to find the total-energy minimum structure. The optimized structure is not significantly different from the one shown in **18**, the only major differences are the S–Ti and S–O^1 bond lengths, which have been calculated to be 2.658 and 3.255 Å, respectively. The total energy for the H_2S–η^2-$(O_2H)Ti(H)_3$ system is calculated to be 2 kcal mol^{-1} lower in energy than **18**.

Decreasing the S–O^1 distance in **18** leads to a similar reaction path to that found for the H_2S–η^2-$(O_2H)Li$ system, as H_2S moves from the titanium atom towards peroxygen-atom-1. The transition state, with one and only one imaginary frequency, is found for a S–O^1 distance of 2.270 Å and this geometry is outlined in **19**. The transition state energy for **19** (−1399.4143 au) is calculated to be 28 kcal mol^{-1}, relative to the separated molecules, and compares thus well to the transition-state energy obtained for the oxygen transfer from η^2-$(O_2H)Li$ to H_2S. Comparing the transition state geometry for the reaction of H_2S with η^2-$(O_2H)Ti(H)_3$, **19**, with the H_2S–η^2-$(O_2H)Li$ transition state geometry, **13**, it appears that the former reaction occurs at an earlier stage of the reaction path than the latter (S–O^1 bond length in **19** is 2.270, relative to 2.056 Å in **13**). The S–O^1–O^2 bond angle is 174.0° in **19**, compared to 179.0° in **13**, while the O^1–O^2 bond length in **19** is elongated with only 0.417, compared with 0.574 Å in **13**. The Ti–O^1 and Ti–O^2 bond lengths have increased by 0.107 and decreased by 0.157 Å, respectively, in **19**. It has for **19** also been found that moving the sulfur atom of the H_2S molecule out of the Ti–O^1–O^2-plane leads to an increase in energy for the system.

Comparing the transition state geometry for **19** to the transition state geometry for oxygen-transfer from dioxirane to H_2S,[12] it appears that the peroxygen–peroxygen bond length in the two transition states is very similar, while the sulfur–peroxygen bond length in the $H_2S–\eta^2-(O_2H)Ti(H)_3$ transition state is 0.247 Å longer than in the H_2S–dioxirane transition state.

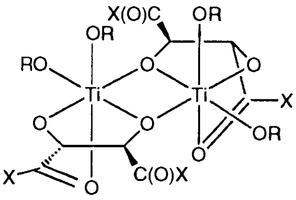
The orbital interactions between H_2S and $\eta^2-(O_2H)Ti(H)_3$ in the transition state, **19**, are very similar to those for the $H_2S–\eta^2-(O_2H)Li$ transition state, **13**, discussed above. The charge on the sulfur atom in **19** is calculated to be −0.078. The reason for the more negatively charged sulfur atom in **19**, compared to **13**, could be that the transition state for the former reaction is at an earlier stage of the reaction path, and that the sulfur atom not at this stage has donated as much electron density to the titanium peroxide fragment, compared to the sulfur atom in the latter reaction path. The population of the sulfur p_x orbital in **19** is also only depleted by 0.192, compared to 0.651 in **13**. The reduced donation of electron density from the sulfur atom in transition state **19** might account for the shorter peroxygen–peroxygen bond in **19**, compared to **13** as less electron density is donated into the σ^*_{O-O} orbital.

Let us, in the following, discuss these results in relation to the experimental data for the oxidation of sulfides to sulfoxides by transition metal peroxide complexes. The present results show that the sulfide to sulfoxide oxidation reaction using transition metal peroxide complexes as the oxygen-donor system can proceed *via* an initial weak coordination of the sulfide to the metal. This initial coordination is followed by a slipping-motion of the sulfide towards peroxygen-atom-1. The sulfide uses its HOMO for the coordination to the metal atom, as seen in **18** (**14**) where the two hydrogen atoms point away from peroxygen-atom-1. When the sulfide moves towards peroxygen-atom-1 and the transition state is reached, the HOMO of the sulfide is also used for interaction with peroxygen-atom-1. The hydrogen atoms of the sulfide now point away from the metal. Peroxygen-atom-1 can be considered as an electrophilic oxygen and it appears from the electronic data for the transition-state geometry that the sulfide acts as a nucleophile in these reactions, as it donates electron density into the peroxide part of the metal-peroxide fragment.

Oxidation of sulfides to sulfoxides by H_2O_2, benzoyl peroxide[13] or peroxides–titanium tartrates (for asymmetric oxidation)[2b] all show a negative Hammett ρ value (−1.02 to −1.30),[2b,13] indicating a nucleophilic attack of the sulfur atom on the electrophilic peroxygen. These results are in agreement with the present theoretical results. Coordination of H_2S to a metal as outlined here is not an unlikely process, especially for titanium(IV), as several titanium complexes with sulfide ligands have been identified.[14] But, the alike ρ values could be an indication of a common path for the sulfide to sulfoxide oxidation by these different systems, and that the weak coordination of the sulfide to the metal might not be the rate-determining step. If no vacant site at the metal is present a direct attack of the sulfide at the peroxygen might be a likely process. However, it should also here be noted that there is experimental evidence for that the sulfide does not coordinate to the metal prior to oxidation by anionic and coordinatively saturated oxodiperoxomolybdenum complexes.[5a]

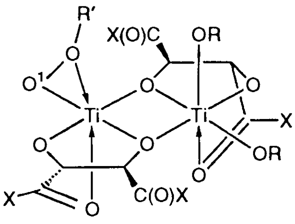
To account for the asymmetric induction in this reaction in the presence of a titanium tartrate catalyst, a requirement must then be that a preferred coordination of the sulfide to titanium (if titanium has a vacant site) and/or the interaction in the transition state with the peroxygen minimizes the steric repulsion between the sulfide and the tartrate ligand. In the following, attempts to explain the asymmetric oxidation of sulfides catalysed by titanium tartrates will be put forward.

The Oxygen-transfer Step in the Asymmetric Oxidation of Sulfides Catalysed by Titanium Tartrate Complexes.—Extensive studies of the titanium tartrate catalyst in solution show that it exists as a dimeric structure,[3c] very similar to the solid-state structure, **20**.[15]



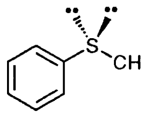
20

The first step in the asymmetric oxidation of sulfides to sulfoxides catalysed by titanium tartrate complexes is a binding of the alkyl peroxide to the metal. In this step two of the alkoxide ligands have, in the mechanistic studies of the titanium tartrate-catalysed epoxidation reaction of allylic alcohols, been assumed to be exchanged with a bidentate-bound alkyl peroxide,[3] giving **21**.



21

In the subsequent investigation **21** will be used as a model for the reactive intermediate, and the sulfide chosen for the oxygen transfer step from **21** to the pro-chiral sulfide is methyl phenyl sulfide, **22**.



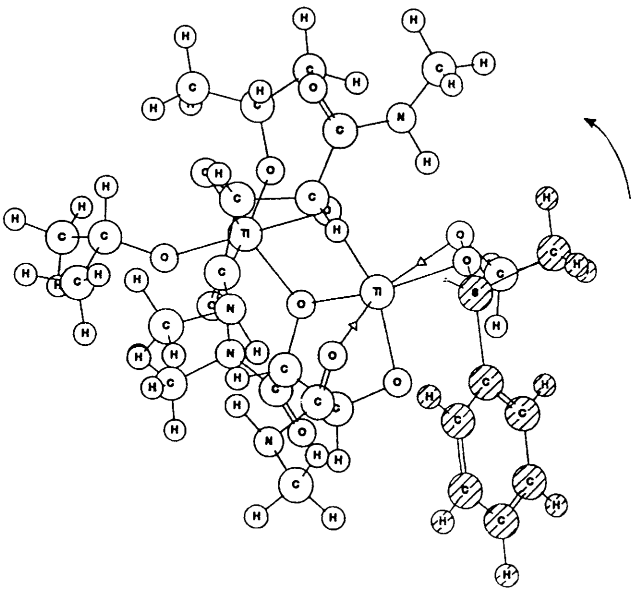
22

The geometry obtained for the pre-coordination of the sulfide to the metal and the subsequent transition state for oxygen transfer from the titanium peroxide complexes to the sulfide using the *ab initio* approach will be used. The tartrate moiety will then be added to the titanium peroxide system and models for the reactive intermediates are obtained. *Ab initio* calculations of the titanium tartrate–peroxide–sulfide system are at the present time not realistic. It has thus in the following been assumed that the transition state obtained for the oxygen transfer from the titanium peroxide to the sulfide, **19**, is similar to the transition state when the tartrate ligand is present. The geometry of the titanium peroxide–sulfide fragment is therefore kept fixed and MM2 calculations[8] are performed for the whole system (see Appendix). The use of MM2 calculations combined with quantum chemical calculations in relation to asymmetric oxidations has recently been found useful in the ligand-catalysed oxidation of alkenes to *cis*-diols by osmium tetroxide–ligand complexes,[16] as well as for several other reactions.[17] Four different possibilities in the approach of **22** to **21** are possible. First, the two different approaches of **22** to peroxygen-atom-1 in the titanium tartrate–peroxide complex—the transition state—will be studied, using in principle the two pro-chiral lone-pair electrons of the sulfide, or as discussed above, the two possible interactions of the HOMO of the sulfide with peroxygen-atom-1. Then the two modes of a pre-coordination of **22** to the metal in the titanium tartrate–peroxide complex will be investigated. The first approach takes place with the tartrate-carbonyl-oxygen atom axially coordinated to the titanium atom, while the second approach requires an unbound carbonyl, and that the sulfur atom of the sulfide coordinates to the titanium atom at the axial position in **21**. In the actual calculations the R, R' and X groups in **21** are: $-CH(CH_3)_2$, $-CH_3$ and $-NHCH_3$, respectively, in an attempt to obtain a realistic model for the titanium tartrate–peroxide complex. The geometries of the titanium peroxide–sulfide fragment used in the following are those obtained above. The geometry of **22** has been optimized and held fixed, and used to investigate the influence of the tartrate ligand on the enantioselectivity of the oxygen-transfer step to the pro-chiral sulfide. The calculations of the two approaching modes of **22** to peroxygen-atom-1 in **21** (the transition state for the reaction) and the two pre-coordination modes to the titanium atom in **21**, have been performed with geometrical variation and optimization of the substituents in the titanium tartrate ligand in order to minimize the steric repulsion between the methyl and phenyl substituents of the sulfide with the tartrate ligand.

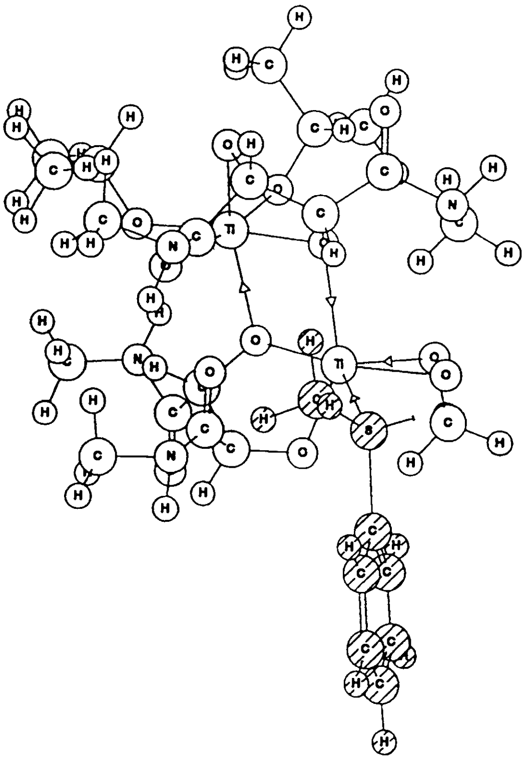
The experimental difference in transition state energies for the oxygen transfer from the reactive intermediate, **21** to the two enantiofaces of the pro-chiral sulfide, **22**, is of the magnitude of just a few kcal mol^{-1}. The present calculations on the four approaches of **22** to **21** are not reliable at that level. The complexity of the system does not allow us to give an overall description of the reaction. However, the present calculations give substantive clues about the influence of the tartrate moiety in the mechanism on the asymmetric oxidation of sulfides to sulfoxides.

The minimum-energy structure of the transition state for the oxygen transfer from the titanium tartrate–peroxide complex to **22** is shown in **23** (the methyl phenyl sulfide is hatched for clarity). The oxygen transfer leads to the *R*-form of the asymmetric sulfoxide, which is in accordance with the experimental results. The orientation of the sulfide in **23** is flexible within 20–30°, as a rotation around the O–O–S-connecting line (indicated by an arrow in **23**) only leads to a minor increase in energy (2–3 kcal mol^{-1}). The steric repulsion between the methyl phenyl sulfide and the tartrate ligand is most pronounced for the phenyl group interacting with the methyl group of the axially coordinated amide (the lower right corner in **23**). Exchanging the methyl group in **22** for more bulky substituents leads to an increased steric repulsion between these groups and the amide group, and might cause a decrease in the ee of the reaction. The transition state structure in **23** is calculated to be 5 kcal mol^{-1} lower in energy than the transition state for the approach of the other enantioface of the pro-chiral sulfide to peroxygen-atom-1.

The pre-coordination of methyl phenyl sulfide to the titanium atom by using the other lobe of the HOMO of the sulfide, or from an electronic point of view, the other lone-pair electrons, compared to those used for the interaction with peroxygen-atom-1 in the transition state, leads to the energy-minimum structure shown in **24** (the methyl phenyl sulfide has been hatched for clarity).



23



24

The preferred coordination site for the pro-chiral sulfide at the titanium atom is the *S*-form, as this is more than 20 kcal mol^{-1} lower in energy than coordination of the *R*-form of the sulfide at the metal. The preferred coordination for the methyl phenyl sulfide at the metal can be envisaged from **24**, as the methyl substituent is 'locked into a pocket' by this coordination mode. Comparing the energies for **23** and **24** it has been found that **23** is lower in energy than **24** by 42 kcal mol^{-1}. The reason for the instability of **24** compared to **23** is because the methyl phenyl sulfide, in the former case, is placed in a more sterically hindered environment, compared to the transition state. These results could indicate that the sulfide prefers to interact directly with the peroxygen leading to the sulfoxide, rather than a pre-coordination to the metal, followed by a slipping motion to the peroxygen. If the sulfide should pre-coordinate to the titanium atom it would require that the carbonyl group axially coordinated to titanium is replaced by the sulfide. Such a replacement has been found as one of the crucial steps in the asymmetric epoxidation of allylic alcohols catalysed by titanium tartrates.[3]

Let us finally discuss the mechanism presented here for the asymmetric oxidation of sulfides to sulfoxides catalysed by the titanium tartrate complexes with the experimental results, obtained especially by Kagan *et al.*[2b] Asymmetric oxidation of R–S–Ar has optimum in ee for R = Me and a significant decrease in ee is observed for R = butyl and benzyl substituents, whereas for Me–S–Ar, with different Ar substituents, the ee does not change significantly by variation of the Ar substituent.[2b] These results are in nice agreement with the prediction based on the transition state for the reaction outlined in **23**.

The model used in this section for the titanium tartrate complex is mainly based on the very extensive experimental studies on the mechanism for the asymmetric epoxidation of allylic alcohols. The reaction conditions for the asymmetric oxidation of sulfides takes place under slightly different experimental reaction conditions than for the asymmetric epoxidation and this difference could lead to a different structure for the active catalyst, although there are, according to our knowledge, no experimental results for the asymmetric oxidation of sulfides, which give a definite clue about the structure of the active catalyst. However, the present results account to a great extent for the observed reactivity of the sulfides with transition metal peroxide complexes and the mechanism for the asymmetric oxidation of sulfides catalysed by titanium tartrate complexes.

Conclusions

The mechanism for the oxidation and the asymmetric oxidation of sulfides by transition metal peroxide complexes has been studied using a theoretical approach. Two metal peroxide systems are considered: η^2-(O_2H)Li and η^2-(O_2H)Ti(X)$_3$, the first as a simple model for the reactive metal peroxide intermediate, while the latter is a more realistic representation of the 'real intermediate' in the transition metal catalysed oxidation of sulfides. *Ab initio* calculations give the bidentate-coordinated peroxide as the most stable, and calculated titanium–peroxygen and peroxygen–peroxygen bond lengths are similar to the vanadium–peroxygen and peroxygen–peroxygen bond lengths characterized in a vanadium(V)-*tert*-butyl peroxide complex. The metal peroxide complexes are characterized by having unoccupied MOs in the metal–peroxo-plane at the metal or at the peroxygens as $\sigma^*_{\text{O–O}}$ orbital. The highest occupied MOs are found at the peroxygens as $\pi^*_{\text{O–O}}$, either parallel, or perpendicular, to the metal–peroxo plane. Approach of H_2S to these metal–peroxide complexes leads to an initial pre-coordination to the metal, causing a stabilization of the system by 6–8 kcal mol^{-1}. This is followed by a slipping-motion of the sulfide towards the peroxygen and the transition state for the reaction is reached. The transition state energies are 25 and 28 kcal mol^{-1} for the η^2-(O_2H)Li and η^2-(O_2H)Ti(X)$_3$ complexes, respectively. The H_2S is located in a perpendicular orientation relative to the metal–peroxo plane, both at the coordination to the metal and by interaction with the peroxygen in the transition state. The electronic interactions in the transition state are characterized as mainly a donation of electron density from the sulfur atom to the metal-peroxo fragment causing a significant elongation of especially the peroxygen–peroxygen bond. The donation of electron density is mainly from the HOMO of the sulfide located in the metal-peroxo plane into the peroxygen $\sigma^*_{\text{O–O}}$ orbital. The sulfide acts as a nucleophile in these oxidation reactions with transition-metal peroxo and peroxide complexes, which fits the experimental results. The geometrical results obtained for the transition state for oxygen transfer from the titanium peroxide complex to the sulfide and the pre-coordination of the sulfide to the titanium atom, are assumed to be similar to the geometry in the asymmetric oxidation of sulfides when tartrate ligands are present. On the basis of the X-ray structure of the titanium tartrate catalyst, combined with the transition-state geometry a model for the asymmetric oxidation reaction is presented using MM2 calculations. In the model for both the transition state, as well as for the pre-coordination, the asymmetric oxidation of the sulfides leads to the (*R*)-configuration of the sulfoxide, in agreement with the experimental results. These calculations indicate that the asymmetric oxidation of the sulfide takes place by interaction with the peroxygen, but a pre-coordination of the sulfide to titanium atom can not be excluded.

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Appendix

The *ab initio* calculations were carried out using Gaussian 88 and Gaussian 92.[6] The calculations for the lithium peroxide system and H_2S were carried out with 4-31G* and 6-31G* basis sets, and for the latter followed by configuration interactions using single and double-substitutions (CISD). The sulfur–hydrogen and the peroxygen–hydrogen bond lengths were held fixed as 1.326 and 0.946 Å, respectively in the calculations leading to **12** and **13**. For the calculations involving titanium a combined basis set was used, where the basis set for titanium was: [62111111/5112/32][18] combined with a 6-31G* basis set for the remaining atoms. The calculations were also here followed by CISD. The titanium–hydrogen, sulfur–hydrogen and the peroxygen–hydrogen bond lengths were kept fixed as 1.680, 1.326 and 0.946 Å, respectively in the calculations leading to **18** and **19**. The transition state geometries were found to have one and only imaginary frequency. For the MM2 calculations[8] the X-ray structure of the titanium tartrate catalyst combined with the *ab initio* results were used.[15] The R, R^1 and X substituents used in the MM2 calculations of **21**, **23** and **24** are: $CH(CH_3)_2$, CH_3 and $NHCH_3$.