J. Org. Chem. 1992, 57, 2861-2864

An ab Initio Study of the Mechanism of Oxidation of Sulfides and Sulfoxides by Dioxirane

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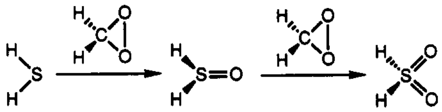
Received September 24, 1991

The oxidation of sulfides and sulfoxides by dioxirane is investigated using ab initio molecular orbital theory. Some discussion is given to the choice of an appropriate theoretical model for studying these reactions. The gas-phase results suggest that the oxidation of sulfoxides is energetically preferred over the oxidation of sulfides. Using a simple electrostatic model of the effect of solvent (Kirkwood–Onsager equation), it is shown that the gas-phase trend may be inverted in solution.

Introduction

Dioxirane chemistry is currently the subject of much experimental and theoretical interest, and several reviews of various aspects of dioxirane reactivity have recently appeared.[1,2] The property of greatest interest and utility associated with dioxiranes is the ability to transfer an oxygen atom to a wide variety of reagents. Examples of such transformations include epoxidation, insertion of oxygen into carbon–hydrogen bonds, and the oxidation of atoms containing lone pairs. In addition to experimental interest, there has been much theoretical work directed at understanding the relative stability of dioxiranes and their isomeric forms, the carbonyl oxides.[3-13]

This paper attempts to address the question of the mechanism of oxidation of atoms bearing lone pairs of electrons; specifically, the oxidation of sulfides to sulfoxides followed by further oxidation to sulfones in the model reaction sequence



It is appropriate to emphasize that this scheme represents a first approximation to the modeling of dioxirane, since the experimental work is invariably carried out using dialkyl dioxiranes. *gem*-Dialkyl substitution appears to give increased kinetic stability to dioxirane. Hence it should be borne in mind that the dialkyldioxiranes may possess a different reactivity to the parent species.

Using dimethyldioxirane, Murray et al.[14] have oxidized a series of aryl methyl sulfides to the corresponding sulfoxides, and in a separate series of reactions have oxidized the sulfoxides to the corresponding sulfones. Treating the relative rates of oxidation in both series with the Hammett equation, they obtained ρ values of -0.77 and -0.78 for the sulfide and sulfoxide oxidations, respectively. These results suggested that electron-donating substituents increased the rate of reaction, and hence the oxidizing agent should be electrophilic in character.

In an earlier study, Adam[15] et al. had designed a mechanistic probe, thianthrene 5-oxide, containing both a nucleophilic sulfide and an electrophilic sulfoxide site to investigate the relative degree of nucleophilic attack in oxygen-transfer reactions. They argued that reaction at the sulfide indicated electrophilic character, while reaction at the sulfoxide implied nucleophilic character. Using a variety of solvents,[16] it was found that oxygen transfer by dioxirane to thianthrene 5-oxide occurred predominantly at the sulfoxide sulfur, implying a nucleophilic character. This was a surprising result since the overall chemistry of dioxirane suggested it to be an electrophile. Murray[2,14] has suggested that this conflict may be attributable to a change in the character of the sulfide and sulfoxide groups brought about through resonance interaction in thianthrene 5-oxide or alternatively than an electrophilic attack on the sulfoxide group may take place via the negatively charged oxygen. More recently, Baumstark and Vasquez[17] have concluded that dioxirane is essentially electrophilic in character but highly sensitive to the nature of the solvent used. These findings will be returned to and discussed in the context of the results obtained in this ab initio study. While these calculations were performed without any consideration of the influence of solvent, a qualitative discussion of the effects of solvation is presented at the end.

Computational Methods

All calculations were carried out with the GAUSSIAN 90 suite of programs.[18] The 6-31G* basis set[19] was used throughout. Equilibrium and transition-state geometries were fully optimized at the restricted Hartree–Fock (HF) level and subsequently refined using Møller–Plesset perturbation theory at second order[20] (MP2). In the following

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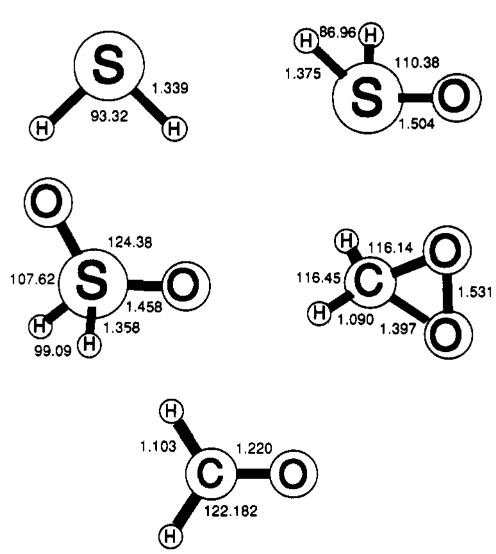

Figure 1. Optimized MP2/6-31G* geometries of reactants and products. Bond lengths in angstroms, angles in degrees.

section only the structures obtained at the correlated level of theory are reported since the HF geometries for these species differ by as much as 0.5 Å from the MP2, indicating that the single determinant spin-restricted description of these reactions is quite invalid. All transition states were characterized by a frequency analysis at the MP2/6-31G* level and found to be first-order saddle points. The geometries obtained at the MP2 level are in reasonable agreement with more sophisticated calculations to be found in refs 3–13. Hence, MP2/6-31G* is the lowest level of theory that may be applied to the study of the geometries of these systems.

The stability of the HF wave function was tested for all species. At the transition-state geometries, real-RHF → real-UHF instabilities[21] were found, confirming that a more flexible wave function was necessary to describe these structures. Dioxirane at its equilibrium geometry also showed a similar instability, inspection of the natural orbital occupation numbers showed this to be attributable to a significant population (0.16) of the antibonding orbital corresponding to the O–O bond. However it should be noted that the RHF wave functions are all internally stable. To correctly describe the O–O bond requires a $\sigma^2_{O-O} - \lambda\sigma^{*2}_{O-O}$ type mixing which will allow the bond to break yielding either a diradical structure ($\lambda = 1$) or a zwitterionic structure ($\lambda \ll 1$). The MP2 wave function contains all double excitations out of the occupied orbitals and so includes the excitations necessary to describe both types of situation.

The effects of higher-order dynamic correlation were estimated using full fourth-order perturbation theory[22,23] (MP4(STDQ)) and also quadratic configuration interaction in the space of single and double excitations including a perturbative treatment of the effect of triple excitations[24] (QCISD(T)). All correlation calculations used the full orbital space.

Results and Discussion

The optimized geometries of the reactants and products may be found in Figure 1. The transition states for oxygen transfer from dioxirane to hydrogen sulfide (TS-1) and sulfoxide (TS-2) are shown in Figure 2, full Cartesian specification of the transition states may be found in the Appendix. In TS-1 the C–O bond being cleaved in dioxirane has undergone an 8% elongation while the O–O is elongated by 30%. Similarly in TS-2, the C–O bond in dioxirane is much less perturbed (4%) than the O–O bond (28%). This suggests that in approaching the transition state, the reaction coordinate is dominated by the opening of the dioxirane ring rather than by the loss of the leaving oxygen atom. At the same time, the forming S–O bonds

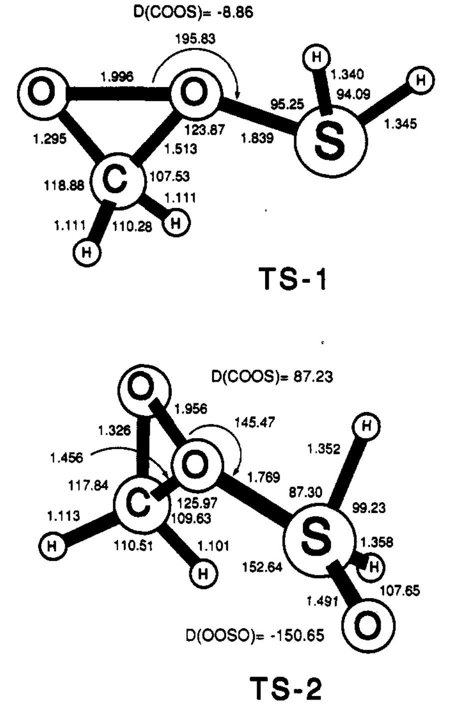

Figure 2. Optimized MP2/6-31G* geometries of TS-1 and TS-2. Bond lengths in angstroms, angles in degrees.

atom	X	Y	Z
		TS-1	
C	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.295198
O	1.513172	0.000000	−0.006810
S	2.531003	−0.077187	−1.536138
H	3.216628	1.079443	−1.509084
H	3.523778	−0.789694	−0.986768
H	−0.337070	−0.911546	−0.538395
H	−0.339249	0.911877	−0.536757
		TS-2	
C	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.325474
O	1.455489	0.000000	0.018384
S	2.507221	1.001373	−0.991273
H	1.639071	2.038480	−0.873194
H	3.255243	1.217657	0.114050
H	−0.363347	−0.905505	−0.509836
H	−0.365671	0.913312	−0.519661
O	3.338120	1.243254	−2.205132

Table II. Relative Energies (kcal mol^{-1}) Using the 6-31G* Basis (All Geometries Correspond to the MP2/6-31G* Level)

molecule	MP2	MP4(SDTQ)	QCISD(T)
H_2S + dioxirane	0.0	0.0	0.0
TS-1	26.8	23.7	24.4
H_2SO + H_2CO	−18.7	−17.9	−17.2
H_2SO + dioxirane	0.0	0.0	0.0
TS-2	11.7	9.6	–
H_2SO_2 + H_2CO	−63.3	−59.1	−57.7

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[24] Pople, J. A.; Head-Gordon, M.; Krishnan, R. *J. Chem. Phys.* **1987**, *87*, 5968.

are only ≈22% longer than in the final products for both reactions, indicating that a significant level of bond formation has taken place.

Table I shows the total energies for all species at various levels of theory. Reaction barriers and exothermicities may be found in Table II. In this gas-phase study it was found that the activation barrier for the reaction of dioxirane with hydrogen sulfide (24.4 kcal mol^{-1}) is significantly higher than that for reaction with sulfoxide (9.6 kcal mol^{-1}). This is in broad agreement with the findings of Adam[16] et al. who showed that in reaction with thianthrene 5-oxide, oxidation occurred mainly at the sulfoxide sulfur. However, this stands in contrast to the results of Murray[14] et al. who found that in oxidizing a series of aryl methyl sulfides, the products were exclusively the corresponding sulfoxides, indicating a preferred reaction at the sulfide sulfur. It should be noted that in Murray's experiments the total amount of sulfide was 3 times greater than the amount of dimethyldioxirane present. (I am grateful to the anonymous reviewer for pointing this out.) In the gas phase these reactions have very different activation requirements, but if in solvent the two competing reactions had similar activation requirements this would bias the product toward the sulfoxide and provide a rationalization of Murray's observations. The effects of solvent on the activation barriers are considered below.

Given the much greater exothermicity of the sulfoxide → sulfone reaction in the gas phase (−57.7 kcal mol^{-1}) relative to that of the sulfide → sulfoxide reaction (−17.2 kcal mol^{-1}), the present results are in general agreement with the Hammond postulate and appear to be consistent.

The question of nucleophilicity versus electrophilicity of dioxirane has been the center of much debate, and it is appropriate to give some discussion to this in the light of the current results. Parts a and b of Figure 3 show a schematic depiction of dioxirane attacking the sulfide and sulfoxide sulfur atoms, respectively. This should be compared with the more precise plots in Figure 2. Figure 3a shows the two lone pairs of hydrogen sulfide and the approach of the transferring oxygen of dioxirane approximately along the line of the out-of-plane lone pair. From this it can be seen that dioxirane transfers an oxygen atom to hydrogen sulfide by pushing it onto the lone pair and hence may be said to be behaving as an electrophile. The situation is a little more complicated in the case of oxygen transfer to sulfoxide. Figure 3b shows a schematic of the lone pair in the pyramidal sulphoxide. As can be seen from Figure 2 (TS-2), the oxygen atom of dioxirane approaches at a considerable angle to the lone pair. In this case, the dioxirane appears to be behaving as a nucleophile, approaching the positive sulfur while avoiding the lone pair. This shows a marked similarity to an S_N2-like backside attack. The suggestion by Murray[2] that an electrophilic attack on the sulfoxide group may take place via the negatively charged oxygen does not appear to be consistent with the transition structures located here. This supposition was tested further by bringing in the dioxirane along the oxygen of the sulfoxide, this resulted in a large force on the sulfoxide oxygen which when allowed to relax "rotated" back to the structure in Figure 2.

Given the conflict between different experiments and also between theory and some experiments, it is conventional to rationalize discrepancies by suggesting that some unknown solvent or aggregation effects may influence the mechanisms of these reactions. While this is quite valid, since a notable sensitivity to solvent has been detected,[17] it is less than satisfying from a "modeling" point of view. The most satisfactory resolution of such questions may be brought about through molecular dynamics simulations or by incorporating solvent molecules directly into the electronic structure calculations. Both of these approaches are computationally very demanding and, given the level of electronic structure theory required to obtain reliable results for these species, somewhat intractable. However, a qualitative discussion of solvation may be formulated in terms of various empirical solvation indices derived from the macroscopic physical properties of the solute and solvent. Perhaps the most simple of these is the Kirkwood–Onsager equation[25-27]

$$\Delta G = -\frac{\mu^2(\epsilon - 1)}{r^3(2\epsilon + 1)}$$

which gives the electrostatic contribution to ΔG for transfer of an isolated spherical dipole (of dipole moment μ and radius r) to a medium of dielectric constant ϵ from one for which $\epsilon = 1$. Hence, the solute is pictured as a dipole in a spherical cavity surrounded by a solvent which acts as a continuous isotropic dielectric medium. In developing a discussion based on the Kirkwood–Onsager equation it is necessary to know the dipole moment of the solute, the bulk dielectric constant of the solvent and the radius of the solute cavity. The dipole moments were taken from MP2 calculations and are given in Table III. The diameter of the solute cavity was chosen to be the distance between the two atoms furthest apart plus their van der Waals radii. Two solvents were chosen, acetone ($\epsilon = 20.70$) and chloromethane ($\epsilon = 9.08$). This seemed an appropriate choice given the experiments of Adam[16] et al. in these solvents.

The Kirkwood–Onsager model is purely electrostatic and so governed very much by the dipole moment of the solute, no account of the microscopic structure of the solvent is taken into account. Hence the absolute magnitudes of ΔG predicted must be viewed with some caution. The third column of Table III shows the values of ΔG obtained. The two solvents show very similar solvation effects, and the discussion below is based on the acetone results alone.

The sulfide → sulfoxide transition state is stabilized by 7.7 kcal mol^{-1}, while the reactants are stabilized by only 5 kcal mol^{-1} yielding an overall stabilization of 2.7 kcal mol^{-1}. For the sulfoxide → sulfone transition state a much smaller stabilization of 0.5 kcal mol^{-1} is predicted, while the reactants are stabilized by 9.1 kcal mol^{-1} giving a total destabilization of 8.6 kcal mol^{-1}. These predictions are easily rationalized in terms of the dipole moments of the various species. In TS-1, the very large dipole stabilizes the transition state more significantly than the reactants leading to a decrease in ΔG. The origin of the large dipole moment can be understood on the basis of the products being formed (i.e. sulfoxide and formaldehyde). Both products possess very large dipole moments and at the transition-state geometry are sufficiently separated that the two components of the dipole simply add together, yielding a very large moment. In TS-2, a much smaller dipole moment is distributed over a larger cavity and gives very little stabilization, yet both reactants carry large dipoles leading to a stronger stabilization and consequently the reaction shows a net increase in ΔG. It should be noted that these trends may be significantly changed on going

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[25] Kirkwood, J. G. *J. Chem. Phys.* **1934**, *2*, 351.

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[27] A good pedagogical exposition may be found in the following: Isaacs, N. S. In *Physical Organic Chemistry*; Longman (UK): Essex; Wiley (USA): New York, 1987; Chapter 5.

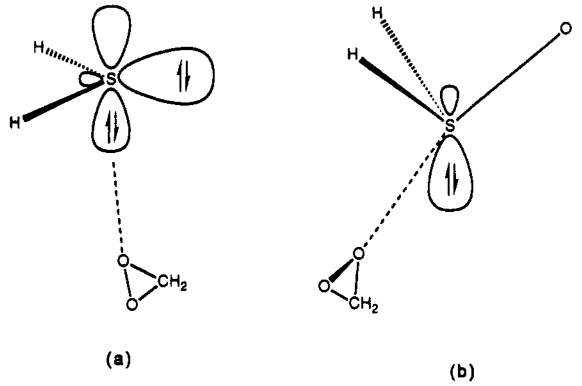

Figure 3. Schematic depiction of (a) electrophilic and (b) nucleophilic attack of dioxirane on sulfide and sulfoxide.

Table III. Dipole Moments (Debye) Calculated at the MP2/6-31G* Level and Corresponding ΔG Values Obtained from the Kirkwood–Onsager Equation[a]

		ΔG/kcal mol^{-1}	
molecule	μ/D	acetone	chloromethane
H_2S	1.48	-1.4	-1.3
H_2SO	3.56	-5.5	-5.0
H_2SO_2	3.44	-	-
H_2CO	2.27	-	-
dioxirane	2.66	-3.6	-3.3
TS-1	7.01	-7.7	-7.0
TS-2	2.20	-0.5	-0.5

[a] See text for the equation. 1 au of dipole moment = 2.5418 D.

from a polar to a nonpolar solvent.

In conclusion, this study suggests that the oxidation of sulfoxide to sulfone by dioxirane ($\Delta E^{\ddagger}$ = 9.6 kcal mol^{-1}) in the gas phase is greatly favored over the oxidation of hydrogen sulfide to sulfoxide ($\Delta E^{\ddagger}$ = 24.4 kcal mol^{-1}). In acetone solvent, these barriers are modified to 18.3 and 21.7 kcal mol^{-1} for sulfone and sulfoxide formation, respectively. The gas-phase results are in general agreement with the results of Adam[16] et al. who found that dioxirane, in reaction with thianthrene 5-oxide, preferentially oxidized the sulfoxide sulfur. However, using a simple electrostatic model with acetone as a typical solvent, the sulfide → sulfoxide reaction is shown to be stabilized by the presence of solvent while the sulfoxide → sulfone reaction is destabilized, leading to a difference in the activation barriers of only 3.4 kcal mol^{-1}. Hence the difference in the predicted reactivity of dioxirane with sulfides and sulfoxides in solution may be quite small and the relative stabilization/destabilization of these competing processes will clearly be highly sensitive to the nature of the solute–solvent interactions. To investigate such effects it is necessary to use a more subtle model of the effect of solvent than that used here.

Acknowledgment. I thank the University of Manchester Regional Computing Centre for the allocation of time on the Amdahl VP1100, on which the majority of calculations reported here were carried out. This work was also partially supported by the Science and Engineering Research Council (U.K.) under grant no. GR/H01717.

Appendix

The Cartesian coordinates of TS-1 and TS-2 (Figure 2) are given below in angstroms.

atom	*X*	*Y*	*Z*
		TS-1	
C	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.295198
O	1.513172	0.000000	-0.006810
S	2.531003	-0.077187	-1.536138
H	3.216628	1.079443	-1.509084
H	3.523778	-0.789694	-0.986768
H	-0.337070	-0.911546	-0.538395
H	-0.339249	0.911877	-0.536757
		TS-2	
C	0.000000	0.000000	0.000000
O	0.000000	0.000000	1.325474
O	1.455489	0.000000	0.018384
S	2.507221	1.001373	-0.991273
H	1.639071	2.038480	-0.873194
H	3.255243	1.217657	0.114050
H	-0.363347	-0.905505	-0.509836
H	-0.365671	0.913312	-0.519661
O	3.338120	1.243254	-2.205132

Registry No. H_2S, 7783-06-4; $H_2(SO)$, 25540-60-7; $H_2(SO_2)$, 81824-08-0; formaldehyde, 50-00-0; dioxirane, 157-26-6.