Chemistry of Oxaziridines. 7.[1] Kinetics and Mechanism of the Oxidation of Sulfoxides and Alkenes by 2-Sulfonyloxaziridines. Relationship to the Oxygen-Transfer Reactions of Metal Peroxides

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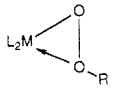
A kinetic investigation of the oxidation of sulfoxides to sulfones and the epoxidation of 1-methylcyclohexene by a series of aryl-substituted 2-sulfonyloxaziridines, **5** and **9**, is described. On the basis of linear free energy relationships and a qualitative frontier molecular orbital analysis, an S_N2-type mechanism is proposed that involves displacement of a substituted sulfonylimine from the oxaziridine functional group by the lone pair on the sulfur or the π-bond of the alkene. The reaction rates are subject to both steric and electronic effects with only a minor amount of negative charge residing on the leaving group. The relationship and similarity of oxygen-transfer mechanisms for 2-sulfonyloxaziridines, metal peroxides such as the Sharpless reagent, dioxiranes, and peracids is discussed.

The transfer of an oxygen atom from compounds containing the peroxide moiety transcends many different fields of organic chemistry, inorganic chemistry, and biochemistry.[2] Although the mechanisms of oxidations by these species have been extensively investigated, many details of the oxygen-transfer step remain obscure. This is particularly true of the oxygen transfer from structures where the active-site oxygen is part of a three-membered ring. These oxidizing reagents include metal (Cr, Mo, W) peroxides and hydroperoxides catalyzed by high-valent d^0 transition-metal complexes (Mo, V, Ti) **1**, dioxiranes **2**, and oxaziridines **3**. The metal peroxides, **1**,[3] are of commercial



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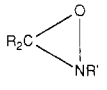

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importance in the production of propylene oxide,[4] in organic synthesis,[5] in the asymmetric epoxidation of allylic alcohols (Sharpless reagent),[6,7] the asymmetric oxidation of sulfides to sulfoxides,[8] and as intermediates in biological oxidations.[9] Molybdenum diperoxo compounds have been used in the oxidation of carbanions to alcohols[10a] and the oxidation of enolates to α-hydroxy carbonyl compounds.[10b] Dioxiranes **2** also appear to be powerful oxidizing reagents capable of oxidizing arenes to arene oxides, sulfides to sulfoxides, and alkenes to their corresponding epoxides.[11]

Stable oxaziridines **3** (R′ = alkyl, aryl, H) are active oxygen compounds capable of oxidizing I^- to I_2 and phosphines to phosphine oxides.[12,13] However, they are not sufficiently reactive to oxidize sulfides to sulfoxides or to epoxidize alkenes.[14] 2-Sulfonyloxaziridines **4** are aprotic, neutral oxidizing reagents that exhibit reactivity similar to peroxy acids but are more selective (Figure 1).[1,15-22] Like the metal peroxides 2-sulfonyloxaziridines have found applications in the oxidation of carbanions to alcohols and phenols[20] and in the synthesis of α-hydroxy carbonyl compounds by oxidation of enolates.[21,22] Chiral 2-sulfonyloxaziridines **4**[23] are asymmetric oxidizing reag-

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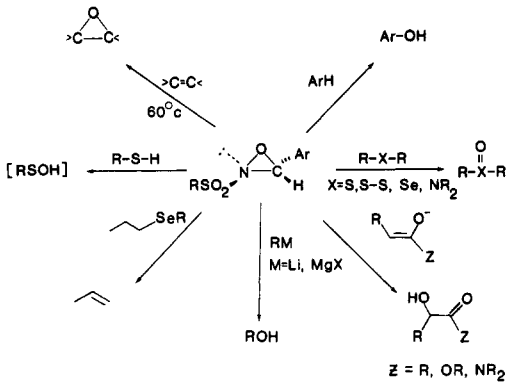
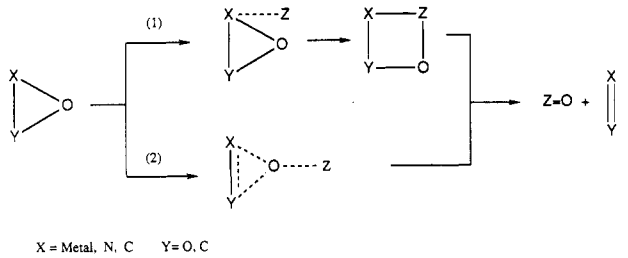


Figure 1. Oxygen-transfer reactions of 2-sulfonyloxaziridines 4.

ents for the epoxidation of alkenes (11–65% ee)[24] and the oxidation of sulfides to sulfoxides (11–83% ee),[25] selenides to selenoxides (8–9% ee)[26] and enolates to α-hydroxycarbonyl compounds (50–95% ee).[27]

The similarities in the active-site structures for 1–4 suggest that they may have a common mechanism of oxygen transfer. Indeed, Mimoun was the first to propose this possibility for 1–4 as well as for peracids.[28] For the metal peroxides a pseudocyclic peroxy metalation mechanism has been suggested which first involves coordination of the substrate (Z) with the metal atom, followed by its insertion into the metal oxygen bond to form a pseudocyclic intermediate (eq 1).[29]



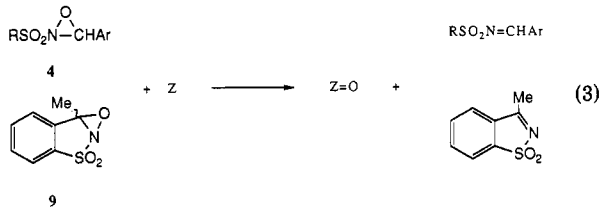
An alternative view of this mechanism involves an S_N2-type displacement by the nucleophilic substrate (Z) on the electrophilic oxygen atom of 1–4 or the peracid (eq 2).[2,5,30] Sharpless[7a] and Bach[30,31a] have argued that the mechanism suggested by Mimoun is not important for the d^0 early transition metals of groups 4, 5, and 6. Indeed studies by Sharpless,[5,7] Curci,[3] and others[8] have shown that there is similarity between the mechanisms of oxidation by the peracids and the metal peroxides. The metal peroxides, like peracids, appear to behave as electrophiles in the sense that they readily react with nucleophilic reagents such as alkenes, sulfides, etc. Kinetic studies of the deoxygenation of oxaziridine 3 (R′ = CMe_3)[13] and sulfonyloxaziridine 4[12] are also in accord with the S_N2 mechanism (eq 2) as are ab initio MO calculations on the transfer of oxygen from oxaziridines to ethylene.[31b]

If a common mechanism of oxygen transfer could be demonstrated for 1–4 it would be of considerable significance, not only in enhancing our understanding of the mechanism of oxidation by these reagents but also in providing insights that result in the development of more effective asymmetric oxidizing reagents. This is particulary important considering the fact that in solution the nature of the active site for the metal peroxides has not been clearly established.

In this paper we describe a kinetic and mechanistic study of the oxidation of sulfoxides to sulfones and the epoxidation of alkenes by 2-sulfonyloxaziridines 4 which supports the S_N2 mechanism (eq 2). Comparisons of the structural reactivity trends for the metal peroxides 1 and peracids with 4 suggest that there is a surprising similarity.

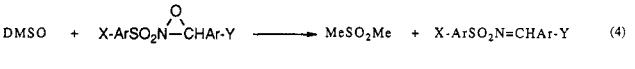
Results

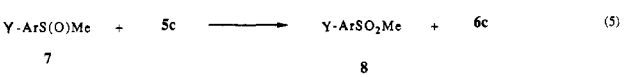
2-Sulfonyloxaziridines 4 oxidize a variety of substrates (Z, Figure 1) according to the stoichiometry shown in reaction 3.[16,18] The rate of oxidation may be conveniently



monitored by proton NMR since the oxaziridine 3-proton at the benzylic carbon and the imino proton of the sulfonimine appear as sharp singlets at about δ 5.5 and 9.0, respectively. We have been less successful in our attempts to follow the rates of these reactions by UV or GLC. Oxaziridines and sulfonimines have few characteristic UV absorptions and the former decompose when subjected to the high temperatures of GLC.

The oxidation of a sulfide to a sulfoxide by 4 is too fast to be easily measured by proton NMR. For example, the oxidation of methyl phenyl sulfide by 4 (R = Ar = Ph) is complete in less than a minute at 25 °C.[16] The oxidation of a sulfoxide to a sulfone is a much slower reaction and we were able to conveniently measure the rate of the oxidation of dimethyl sulfoxide (Me_2SO) and a series of aryl methyl sulfoxides 7 utilizing oxaziridine 5 and 3-methyl-1,2-benzisothiazole-1,1-dioxide oxide (9) as oxidants (eq 4 and 5). Under neutral conditions, there is good reason to believe that the mechanisms of oxidation of sulfides to sulfoxides and sulfoxides to sulfones by peracids are similar in respect to the ones described herein.[32]





a,	X = H; Y = 4-Me	g,	X = H; Y = 4-NO_2
b,	X = H = Y = H	h,	X = 4-Me; Y = H
c,	X = H; Y = 4-Cl	i,	X = 4-Cl; Y = H
d,	X = H; Y = 2-Cl, 6-Cl	j,	X = 3-NO_2; Y = H
e,	X = H; Y = 2-NO_2	k,	X = 4-NO_2; Y = H
f,	X = H; Y = 3-NO_2		

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Table I. Second-Order Rate Constants for the Oxidation of Me_2SO by 5 and 9 at 25.0 °C in $CDCl_3$

entry	oxaziridine[a] (X, Y)	k (L/mol·s) X 10^5	corr coeff (r)	rel rate
1	**5a** (X = H, Y = 4-Me)	2.49 ± 0.15	0.991	0.54
2	**5b** (X = Y = H)	4.59 ± 0.36	0.985	1.00
3	**5b** (CD_3CN)[b]	19.91 ± 2.36	0.973	
4	**5c** (X = H, Y = 4-Cl)[c]	4.55 ± 0.18	0.992	1.99
5	**5c** 0.0 °C	2.47 ± 0.24	0.991	
6	**5c** 60.0 °C	35.87 ± 6.82	0.996	
7	**5f** (X = H, Y = 3-NO_2)	23.88 ± 0.62	0.997	5.20
8	**5g** (X = H, Y = 4-NO_2)[d]	21.85 ± 0.28	0.996	4.76
9	**5g** 40.0 °C	44.28 ± 0.68	0.996	
10	**5g** 60.0 °C	96.17 ± 1.48	0.997	
11	**5a** (X = 4-Me, Y = H)	2.88 ± 0.08	0.997	0.63
12	**5i** (X = 4-Cl, Y = H)	5.13 ± 0.34	0.987	1.11
13	**5j** (X = 4-NO_2, Y = H)	9.56 ± 0.47	0.992	2.08
14	**9**	9.08 ± 0.35	0.993	1.98

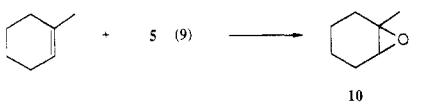
[a] $\rho_Y = 1.03 \pm 0.13$ ($r = 0.976$); $\rho_X = 0.505 \pm 0.0825$ ($r = 0.974$). [b] Solvent. [c] Thermodynamic parameters for oxaziridine **5c**: $\Delta E_a^\ddagger = 8.15$ kcal/mol; $\Delta H^\ddagger = 7.61$ kcal/mol; $\Delta G^\ddagger = 23.30$ kcal/mol; $\Delta S^\ddagger = -52.2$ eu. [d] Thermodynamic parameters for oxaziridine **5g**: $\Delta E_a^\ddagger = 8.34$ kcal/mol; $\Delta H^\ddagger = 7.72$ kcal/mol; $\Delta G^\ddagger = 23.26$ kcal/mol; $\Delta S^\ddagger = -49.36$ eu.

Table II. Second-Order Rate Constants for the Oxidation of Aryl Methyl Sulfoxides 7 by 2-(Phenylsulfonyl)-3-(4-chlorophenyl)oxaziridine (5c) at 25.0 °C in $CDCl_3$

entry	sulfoxide[a] (X, Y)	k (L/mol·s) × 10^5	corr coeff (r)	rel rate
1	**7a** (Y = 4-Me)	15.48 ± 0.15	0.997	2.64
2	**7b** (Y = H)	5.56 ± 0.36	0.994	1.00
3	**7c** (Y = 4-Cl)	2.26 ± 0.17	0.991	0.39
4	**7f** (Y = 3-NO_2)	0.68 ± 0.054	0.994	0.12

[a] $\rho = -1.49 \pm 0.20$ ($r = 0.982$).

In a typical experiment, equimolar amounts (1.69–3.39 × 10^{-4} M) of the sulfoxide, oxaziridine **5**, and an internal standard (diphenylmethane) were dissolved in $CDCl_3$ in an NMR tube. The course of the reaction was monitored by NMR as a function of time by comparison of the integrated peak areas of the protons of the sulfone and the diphenylmethane standard. The epoxidation of methylcyclohexene to methylcyclohexene oxide (**10**) by **5** and **9** was also explored (eq 6). Equimolar amounts of the alkene, oxaziridine (7.7×10^{-4} M), and diphenylmethane standard were thermostated at 30.0 °C in $CDCl_3$. The amount of **10** present at anyone time was determined by monitoring the oxirane three-membered ring proton at δ 4.0 vs. the internal standard.



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In all cases second-order kinetics were observed. This was ascertained by plotting the reciprocal of the concentration ($1/c$) vs. time (t). The rate constants were determined from the slopes of those lines that exhibit correlation coefficients of $r = 0.997$–0.973 for each rate determination (Tables I–III). The second-order rate constants proved to be invariant at several different concentrations of Me_2SO, methylcyclohexene and **5** (Tables I and III). Activation parameters were calculated from the slope of the Arrhenius plot of ln k vs. $1/T$ for the oxidation of Me_2SO and methylcyclohexene by oxaziridine **5b** and **5g**, respectively. Since errors using NMR are likely to be larger than those obtained by some other analytical methods, care should be exercised in interpreting the absolute magnitudes of the entropies.[35]

Substituent electronic effects were determined by correlation with Hammett substituent constants (Tables I–III) and are summarized in Table IV.

Discussion

The reaction of nucleophiles with three-membered heterocyclic compounds has been extensively explored.[14] Oxiranes and aziridines give ring-opened products resulting from attack of the nucleophile at the carbon atom adjacent to the heteroatom.[36,37] In thiiranes nucleophilic attack at both carbon and sulfur has been reported.[38] All of the various combinations of nucleophilic attack at the ring atoms of the oxaziridine three-membered ring have been observed.[14] Hata and Watanabe have reported a detailed study of the reaction of nucleophilies with oxaziridines.[39] When the nitrogen substituents are small (**3**, R′ = H, Me, Et, etc.), the favored site of attack is at nitrogen. As the bulk of R′ increases the site of attack shifts to oxygen.

Products resulting from attack at the ring carbon or nitrogen atoms in 2-sulfonyloxaziridines **4** have not been detected in our studies.[40] Reaction of Z at the carbon atom of the oxaziridine ring in **4** seems most unlikely because the rate of oxidation of Me_2SO by **5** and **9** are similar (Table I). The ring carbon atom in **9** is very hindered and a significant decrease in the rate of oxidation would be expected if the site of attack were to occur at this tertiary position. Nucleophilic attack at the oxaziridine nitrogen in **5** to give **11** should be inhibited by the large sulfonyl group and accelerated by polar solvents. Solvent effects are relatively small (Table I, entries 2 and 3, and Table III, entries 7 and 8). Attack at nitrogen also seems to be incompatible with the high enantioselectivities and the

(32) Two mechansims of oxidation of sulfoxides to sulfones have been suggested for peracids.[38] At high pH a nucleophilic mechanisms where RCO_3^- attacks the polar S–O bond and at neural or low pH an electrophilic mechanism similar to the oxidation of sulfides to sulfoxides is believed to be operating.[34] Since 2-sulfonyloxaziridines are neutral and aprotic oxidizing reagents it is reasonable to assume that the latter mechanism will be operating.

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Table III. Second-Order Rate Constants for the Epoxidation of 1-Methylcyclohexene by Oxaziridines 5 and 9 at 30.0 °C in $CDCl_3$

entry	oxaziridine[a] (X, Y)	k (L/mol·s) × 10^4	corr coeff (r)	rel rate
1	**5a** (X = H, Y = 4-Me)	4.22 ± 0.24	0.995	1.28
2	**5b** (X = Y = H)	3.29 ± 0.27	0.979	1.00
3	**5c** (X = H, Y = 4-Cl)	12.97 ± 0.81	0.991	3.95
4	**5d** (X = H, Y = 2,6-Cl)	3.72 ± 0.16	0.996	1.13
5	**5e** (X = H, Y = 2-NO_2)	4.89 ± 0.24	0.993	1.49
6	**5f** (X = H, Y = 3-NO_2)	35.73 ± 1.55	0.997	10.87
7	**5g** (X = H, Y = 4-NO_2)[b]	31.28 ± 1.35	0.997	9.52
8	**5g** (CD_3CN)[c]	46.39 ± 4.22	0.992	14.11
9	**5g** 40.0 °C	75.65 ± 3.82	0.996	23.02
10	**5g** 50.0 °C	100.4 ± 5.52	0.993	30.55
11	**5h** (X = 4-Me, Y = H)	3.35 ± 0.23	0.987	1.02
12	**5i** (X = 4-Cl, Y = H)	8.77 ± 0.52	0.990	2.67
13	**5j** (X = 4-NO_2, Y = H)	29.34 ± 5.99	0.960	8.93
14	**9**	1.07 ± 0.043	0.987	0.33

[a] ρ_Y = 1.09 ± 0.19 (r = 0.956), ρ_X = 1.07 ± 0.15, (r = 0.981). [b] Thermodynamic parameters for oxaziridine **5g**: $\Delta E_a^{\ddagger}$ = 11.43 kcal/mol; $\Delta H^{\ddagger}$ = 10.83 kcal/mol; $\Delta G^{\ddagger}$ = 21.23 kcal/mol; $\Delta S^{\ddagger}$ = −34.20 eu. [c] Solvent.

Table IV. Thermodynamic Parameters and Values for Substrate Oxidation by Oxaziridines, Metal Peroxides, and Peroxyacids

entry	oxidizing reagent	substrate	$\Delta F_a^{\ddagger}$ (kcal/mol)	$\Delta S^{\ddagger}$ (eu)	ρ
1	**5**	Me_2SO[a]	8.25	−52.2, −49.36	
	X				0.51
	Y				1.03
2	**5c**	XPhS(O)Me[a]			−1.48
3	**5**	methylcyclohexene[a]	11.4	−34.2	
	X				1.09
	Y				1.07
4	**5**	I^-[b]			
	X				0.81
	Y				0.99
5	**3** (R = Me_3C)	(n-Bu)$_3$P[c]	12.1	−29.2	1.06, 1.12
4	$CrO(O)_2$HPMT	XPhSMe[d]			−1.0
5	Ti(O-i-Pr)$_4$DET (TBHP) (H_2O)	XPhSMe[e]			−1.02
6	H_2O_2	XPhSMe[f]			−1.17
7	$(PhC(O)O)_2$	XPhSMe[f]			−1.30
8	$XPhCO_3H$	Ar_2S[g]		−34.3	+0.75, −1.05
9	$XPhCO_3H$	PhCH=CHPh[h]		−22.8	0.9

[a] This work. [b] Reference 12. [c] Reference 13. [d] Reference 3. [e] Reference 8. [f] Mondena, G.; Maioli, L. *Gazz. Chim. Ital.* **1957**, *87*, 1306. Pryor, W. A.; Hendrickson, W. H., Jr. *J. Am. Chem. Soc.* **1983**, *105*, 7114. [g] Curci, R.; Giovine, A.; Modena, G. *Tetrahedron* **1966**, *22*, 1235. Overberger, C. G.; Cummins, R. W. *J. Am. Chem. Soc.* **1953**, *75*, 4250. [h] Reference 2b.

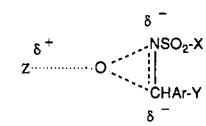
correlation of product stereochemistry with the configuration of the oxaziridine three-membered ring observed with chiral 2-sulfonyloxaziridines.[24-27] Finally, detailed analyses of the NMR spectra during the course of oxidations (eq 4–6) failed to show any new absorptions which might be attributed to the formation of long-lived zwitterionic intermediates or side products that would we required of the Mimoun mechanism (eq 1).

11

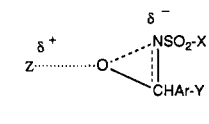
The second-order kinetics observed for the oxidation of sulfoxides to sulfones (eq 4 and 5) and the epoxidation of alkenes (eq 6) by **5** are consistent with a rate-limiting S_N2-type attack of the nucleophile Z on the oxaziridine oxygen atom. The more nucleophilic the substrate Z, the faster the rate as evidence by the negative ρ value of −1.48 for oxidation of a series of aryl methyl sulfoxides **7** (Table II).

As expected of an S_N2-type displacement reaction steric effects are more pronounced for epoxidations of alkenes than sulfoxide oxidation. The rate of epoxidation of methylcyclohexene by bicyclic oxaziridine **9** is three times slower than for **5b** (Table III, compare entry 2 with 14). A two-fold increase in the rate is observed for oxidation of Me_2SO by **9** compared to **5b** (table I, compare entries 2 and 14). While electron-withdrawing nitro groups at the 3 and 4 positions of the aryl moiety (Ar_Y) increased the rate of epoxidation, a 2-NO_2 group sterically decreased the rate by a factor of 7 (Table III, compare entries 5–7). A similar sterically induced rate decrease is observed for **5d** (2,6–dichloro) compared to **5c** (4-chloro) (Table III, entries 3 and 4).

For oxidations of Me_2SO and methylcyclohexene by 2-sulfonyloxaziridine **5**, the small positive values ($\rho(Ar_X)$ = 0.51–1.06; $\rho(Ar_Y)$ = 0.91–1.05), the large negative entropy values ($\Delta S^{\ddagger}$ −51.2, −34.3 eu), and the lack of solvent effects is consistent with an early, highly ordered, nonpolar transition state (Table IV). The fact that both ρ values for Ar_X and Ar_Y in **5** are positive suggests a transition state in which a relatively small amount of negative charge is developing on both the oxaziridine carbon and nitrogen atoms **12**. A similar transition state has been proposed for oxidation of phosphines by **3** (R′ = CMe_3).[13]



12



13

For oxidation of I^- by **5** Knipe and co-workers suggested a transition state where N–O bond breaking precedes C–O bond breaking.[12] This transition state, **13**, would require that all of the effect of the substituents in Ar_Y (ρ = 0.99) must be transmitted through the oxaziridine carbon to the nitrogen. While there is some evidence to suggest that electronic effects may be more efficiently transmitted through an sp^3 carbon than a sulfonyl sulfur, the difference is quite small.[42] The major influence of Ar_Y would be to exert its influence on N–O bond cleavage. Furthermore, a more pronounced solvent effect should have been observed. On the other hand, recent studies of the oxidation of carbanions and enolates by **5** suggest that a relatively stable intermediate, similar to **13**, may be formed when the nucleophile is anionic in nature.[43]

We feel, however, that transition state **12** satisfactorily explains the results in this as well as other studies of oxidations by oxaziridines.[12-14] A concerted transition state, **12**, for oxygen transfer to alkenes is also predicted by the calculations of Bach and Wolber.[31b] The high enantioselectivities for epoxidations (up to 65% ee),[24] the asymmetric oxidation of sulfides to sulfoxides (up to 83% ee),[25] and the asymmetric oxidation of enolates (up to 95% ee)[27] by chiral 2-sulfonyloxaziridines also seem to be more consistent with a highly ordered transitions state such as **12**.

The driving force for oxygen transfer by the three-membered peroxides **1–2** and oxaziridines **3** encompasses the relief of ring strain and the enthalpy associated with formation of strong multiple X=Y bonds (eq 2). The high reactivity of 2-sulfonyloxaziridines **4** and the exclusive attack of nucleophilies at the oxygen atom is probably a consequence of several factors. The large N-sulfonyl group (*A* value 2.5)[44] undoubtedly shields the oxaziridine nitrogen atom from attack and stabilizes any incipient charge in the transition state for sulfonimine displacement, **12**.

We may also glean some information about the nature of the transition state from a qualitative frontier molecular orbital analysis of the oxygen-transfer step. First we need to describe the molecular orbitals of the sulfoxide that identify it as the nucleophilic component of the reaction. The significant orbital interaction of the sulfoxide itself that is involved is the orbital mixing between the lone pair on sulfur and one of the lone pairs on the oxygen. The HOMO Ψ_{13}) is largely comprised on a long pair on oxygen with a small antibonding contribution from the sulfur lone pair. The fourth highest occupied orbital (Ψ_{10}) is the bonding combination of that four-electron interaction that has a high contribution from the sulfur atom. Thus, the occupied "nucleophilic" MO that is principally involved in displacing an oxygen atom from the oxaziridine constitutes a pair of electrons that has its electron cloud *delocalized over both the sulfur and oxygen atoms* (Figure 2). The second and third HOMOs are a lone pair on oxygen and the σ S–O bond, respectively, and these orbitals do not exert a direct electronic influence on the reaction.

The pertinent frontier molecular orbitals of the oxaziridine that are participating in this S_N2 type of displacement have been discussed previously.[31b] The in-plane σ-type electron pair on the oxygen atom of the oxaziridine that is involved resides in one of the Walsh type orbitals (Ψ_{11}) that describes the three-membered ring. The other p-type of oxygen lone pair (ψ_{12}) is orthogonal to the plane

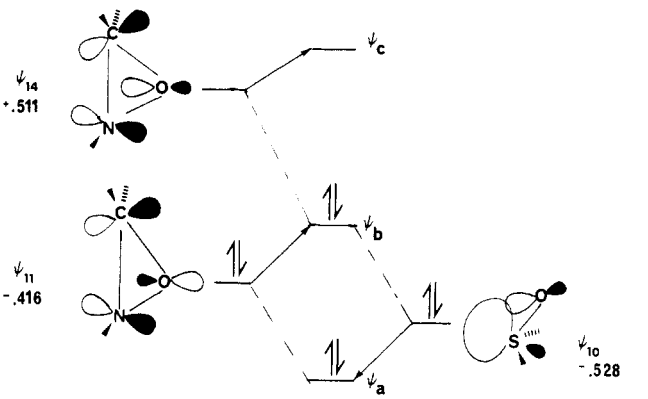
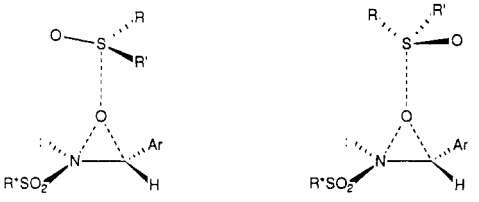


Figure 2. Molecular orbital four-electron interactions involved in the transfer of an oxygen from an oxaziridine to a sulfoxide (energies in au).

of the ring and is the HOMO. As the two reactants approach each other, the initial electronic interaction is between the nucleophilic orbital on sulfur (Ψ_{10}) and the in-plane filled one pair (Ψ_{11}) on oxygen. This close shell repulsion elevates the filled antibonding combination of this four-electron interaction (Ψ_{10}–Ψ_{11}) affording Ψ_b (Figure 2) and facilitates the attendant two-electron interaction of this "effective" HOMO with an empty antibonding orbital (Ψ_{14}) on the oxaziridine ring. As we have advocated previously, the nucleophile must interact with both the bonding and antibonding orbitals of the atom being displaced. By analogy to our previous study on the comparable transfer of an oxygen atom to ethylene,[31b] we anticipate that the sulfur atom can attack the oxygen approximately in the plane of the oxaziridine ring with a slight bias toward the axis of the carbon–oxygen bond in a typical S_N2 fashion. We do not anticipate that the planar transition state **14**, where the sulfur–oxygen bond shares a common plane with the ring, will be significantly lower in energy than a spiro orientation, **15**, where the S–O bond is at right angles to the three-membered ring.



Finally, the results summarized in Table IV suggest that there is indeed similarity between the oxidation structure–reactivity trends for metal peroxides **1**, peracids, and 2-sulfonyloxaziridines **4**. Thus there seems good reason to believe that the oxygen transfer from **1–4** and peracids, as previously proposed by Mimoun, share a common mechanism. This mechanism of oxidation involves an S_N2-type attack by the nucleophilic substrate, Z, on the electrophilic oxygen of the reagent (eq 2). 2-Sulfonyloxaziridines **4** would appear to be particularly useful model systems for studying the oxygen-transfer reactions of the metal peroxides because they are stable, have a well-defined active site, and may be readily manipulated.

Experimental Section

Melting points were determined on a Mel-Temp apparatus and are uncorrected. ^1H NMR spectra were measured on a Varian A-60A or JOEL FX 90Q (90 MHz) NMR spectrometer using Me_4Si as the internal reference.

Solvents were purified by standard methods. 2-Sulfonyloxaziridines **5** and **9** were prepared as previously described.[15]

(42) The difference in ρ values for transmissiosn of electronic effects through an sp^3 carbon (ρ = 1.05) vs. a sulfonyl sulfur (ρ = 0.88) is only 0.17. See ref 11 for a discussion of this point.

(43) Gubernick, S., unpublished results from these laboratories. See also ref 24 and 26.

(44) Eliel, E. L.; Kandasamy, D. *J. Org. Chem.* 1976, *41*, 3899.

2-(Phenylsulfonyl)-3-(2,6-dichlorophenyl)oxaziridines (**5d**): 86% yield; mp 97–8 °C dec; NMR ($CDCl_3$) 5.75 (s, 1 H), 7.2–8.3 (m, 8 H, Ar).

Anal. Calcd for $C_{13}H_9Cl_2NO_3S$: C, 47.28; H, 2.75. Found: C, 47.42; H, 2.80.

Aryl methyl sulfoxides **7** were purchased from Parish Chem. Co. or were prepared by oxidation of the corresponding sulfides[45] using (*E*)-2-(phenylsulfonyl)-3-phenyloxaziridine (**5b**) as previously described.[20]

Kinetic Study of the Oxidation of Me_2SO to Dimethyl Sulfone. In a 1.0-mL volumetric flask, 0.38 mmol of the appropriate oxaziridine **5** and an equilmolar amount of Me_2SO, 0.0296 g (0.38 mmol), was combined with 0.0346 g (0.019 mmol) of the diphenylmethane standard and diluted to 1.0 mL with $CDCl_3$. The solution was transferred to an NMR tube, thermostated in an oil bath at the desired temperature or in the NMR probe using an NMR variable-temperature controller. For kinetics the course of the oxidation was determined by NMR initially at 0.5 h and than at 1-h intervals at which time the reaction was quenched by cooling the NMR tube in an ice bath. The amount of dimethyl sulfone present at anyone time was determined by comparison of the integrated peak areas of the sulfone (s, 2.9 ppm) and the methylene protons of the diphenylmethane standard (s, 4.0 ppm).

The reactions were followed beyond 75% completion and the individual integrations were repeated at least four times and the results averaged. Errors in the NMR technique are estimated to be between 1–2% by Kesler.[35] All kinetic determinations were performed at least twice and the results averaged.

The second-order rate constants (k) were calculated from the slope of the line obtained by plotting the reciprocal of the concentration ($1/c$) vs. the time (t) by using a least-squares program. Errors reported are standard deviations. These results are summarized in Table I.

Kinetic Study of the Oxidation of Aryl Methyl Sulfoxides 7 to Aryl Methyl Sulfones. This studies were carried out as described above. The amount of aryl methyl sulfone **8** present at anyone time was determined by comparison of the integrated peak areas of the sulfone (s, 3.6 ppm) and the methylene protons of the diphenylmethane standard (s, 4.0 ppm). These results are summarized in Table II.

Kinetic Study of the Oxidation of Methylcyclohexene to Methylcyclohexene Oxide (10). In a 1-mL volumetric were placed 0.074 g (0.077 mmol) of 1-methylcyclohexene, an equivalent molar amount of the appropriate 2-sulfonyloxaziridine **5** or **9**, and 0.129 g (0.077 mmol) of the diphenylmethane standard. The mixture was dissolved in $CDCl_3$ and transferred to an NMR tube. In the case of oxaziridines **5e,f**, it was necessary to use 1.5 mL of $CDCl_3$ for complete solubility. The NMR tubes were heated in an oil bath at 30 °C. After the reaction mixture was heated in the NMR tube for the prescribed period of time, the reaction was quenched by cooling in an ice bath. The amount of 1-methylcyclohexene oxide (**10**) at any one time was determined by comparison of the integrated peak areas of **10** (2.8–3.0 ppm) and the methylene protons of the diphenylmethane standard (s, 4.0 ppm). These results are summarized in Table IV.

Acknowledgment. This work was supported by the donors of the Petroleum Research Fund, administered by the American Chemical Society, and the National Science Foundation.

Registry No. **5a**, 104393-73-9; **5b**, 63160-13-4; **5c**, 104393-74-0; **5f**, 104393-75-1; **5g**, 86428-23-1; **5i**, 63160-14-5; **5j**, 63160-15-6; **7a**, 934-72-5; **7b**, 1193-82-4; **7c**, 934-73-6; **7f**, 940-12-5; **9**, 73845-10-0; Me_2SO, 67-68-5; 1-methylcyclohexane, 591-49-1.

(45) Baliah, V.; Uma, M. *Tetrahedron* **1963**, *19*, 455.

An Efficient, Fully Stereocontrolled Total Synthesis of *N*-Benzoyl-L-daunosamine

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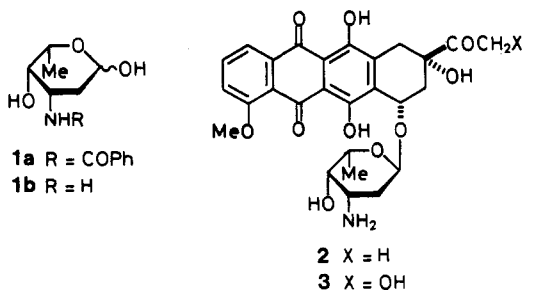
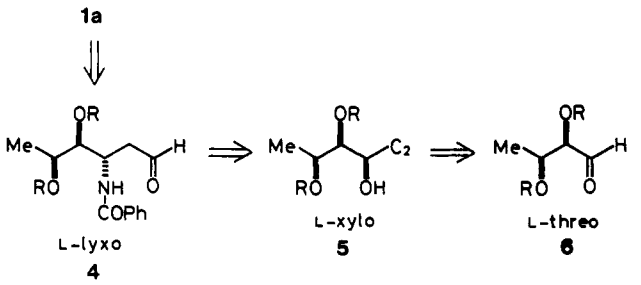
Completely stereocontrolled synthesis of *N*-benzoyl-L-daunosamine (**1a**) is described. The synthesis starts with 4-*O*-benzyl-2,3-*O*-bis(methoxymethyl)-L-threose (**12**), readily accessible from L-tartaric acid, and proceeds via the xylo alcohol **14** which is formed by an extremely high degree of chelation controlled addition of the acetal-containing Grignard reagent to **12**. The Mitsunobu reaction of **14** gives the phthalimide **15** which undergoes debenzylation followed by tosylation, iodination, and deiodination. The resulting 6-deoxyphthalimide **19** is converted to the *N*-benzoyl derivative **20**. Deprotection of **20** by treatment with BF_3·Et_2O–EtSH followed by $HgCl_2$–HgO provides *N*-benzoyl-L-daunosamine (**1a**).

L-Daunosamine (**1b**),[1] which is important as the amino sugar moiety of anthracycline antitumor agents daunorubicin (**2**) and adriamycin (**3**), has been the object of intense synthetic study because it contributes significantly to reduce its toxity and to improve upon its potency and efficiency, and several successful syntheses of optically active L-daunosamine have been described.[2,3] Traditionary, most



Scheme I



(1) Arcamone, F.; Cassinelli, G.; Orzezzi, P.; Franceschi, G.; Mondelli, R. *J. Am. Chem. Soc.* **1964**, *86*, 5335.

0022-3263/86/1951-4245$01.50/0