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Possible mechanism of oxygen atom transfer from enantiopure 3-substituted 2,3-epoxy-2,3-dihydro-1,2-benzisothiazole 1,1-dioxides to 2-phenyl-1,3-dithiane

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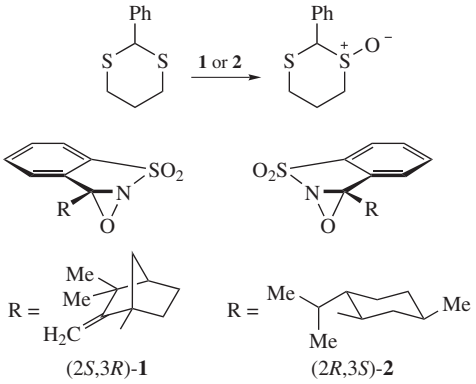
A possible mechanism of oxygen atom transfer from enantiopure oxaziridines **1** and **2** to 2-phenyl-1,3-dithiane is described.

N-Sulfonyloxaziridines are versatile reagents for the electrophilic oxygenation of a variety of organic functional groups.[1] The fact that such oxygenations can be performed with a high degree of asymmetric induction has created considerable interest in the mechanism of the overall oxygen atom transfer process.[2] Theoretical studies have led to the conclusion that the oxygenation process is a dipolar S_N2-like reaction, in which the sulfide acts as a nucleophile and the *N*-sulfonylimine acts as a leaving group.[3–6]

We have reported the use of mediators for sulfur oxidation based upon 3-substituted 2,3-epoxy-2,3-dihydro-1,2-benzisothiazole 1,1-dioxides as the oxidants (Scheme 1).[7] High *ee* values in the oxidation of 2-phenyl-1,3-dithiane were obtained (Table 1). Here, we describe the mechanism of oxygen atom transfer from **1** and **2** to 2-phenyl-1,3-dithiane (Scheme 1).



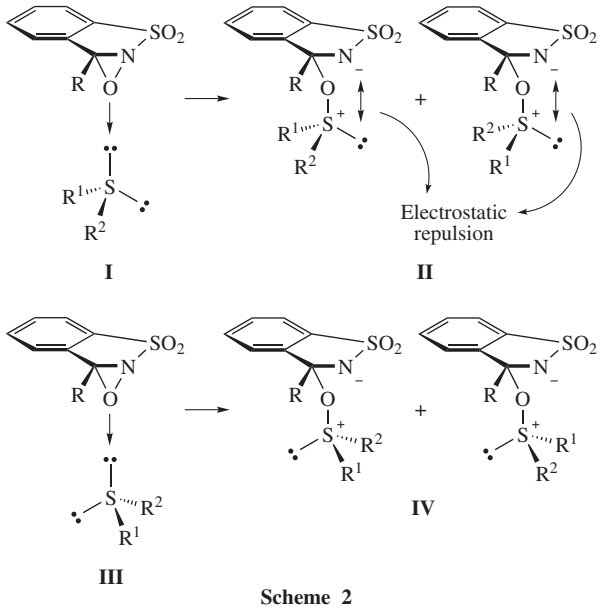
Scheme 1 Oxaziridines **1** and **2**.

For the oxidation of sulfides to sulfoxides, the molecular recognition is largely steric in origin dictated by the substituents on the oxaziridine and the substrate.[8,9] Therefore, the step in which the sulfide approaches the active-site oxygen of the oxaziridine three-membered ring should determine the enantioselectivity in generation of sulfoxides, and thus two transition state structures (**I** and **III**) for the oxidation of sulfides to sulfoxides by oxaziridines would be expected (Scheme 2). Note that the symmetry of the product at sulfur, and the σ* orbital of the O–N bond in the oxaziridine with respect to the direction of approach, allow sulfide rotation to minimise the transition state energy. The actual conformation in the transition state will be a trade-off between electrostatic repulsion and steric interaction. The inspection of intermediates **II** and **IV**, produced from transition states **I** and **III**, reveals that **IV** is likely more favourable than **II** because of an unfavourable electrostatic repulsive interaction between the negative charge at the nitrogen atom and the lone pair on the sulfur in intermediates **II**.

Table 1 Oxidation of 2-phenyl-1,3-dithiane to *trans*-phenyl-1,3-dithiane 1-oxide using oxaziridine **1** or **2**.[7]

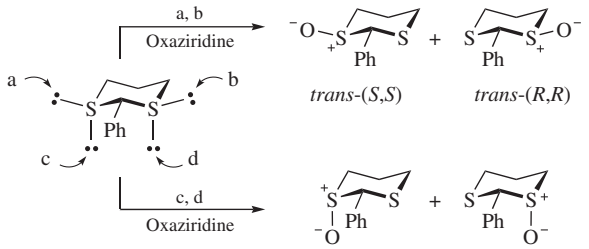
Entry	Oxaziridine	Temperature/°C	Time/min	Yield (%)	*ee* (%)	Configuration at the sulfur atom
1	**1**	0	45	100[a]	82	*S*
2	**1**	–20	80	100[a]	83	*S*
3	**1**	0	30	100[a]	60	*S*
4	**2**	20	60	100[a]	44	*R*
5	**2**	–14	60	99[a]	54	*R*
6	**2**	–25	80	100[a]	62	*R*

[a]*Anti*.



Scheme 2

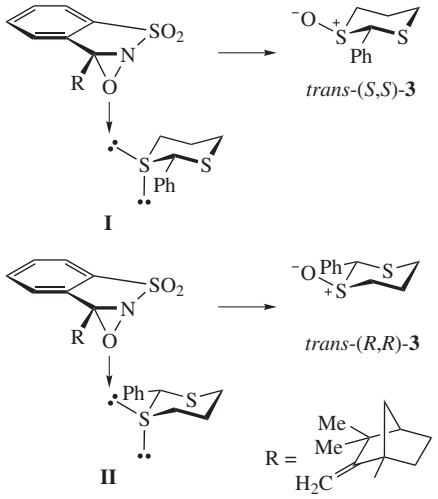
Oxidation of 2-phenyl-1,3-dithiane using oxaziridines (+)-(2*S*,3*R*)-3-[(1′*R*,4′*R*)-1′-(3′,3′-dimethyl-2′-methylidenebicyclo[2.2.1]hept-1-yl)]-2,3-epoxy-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide **1** or (+)-(2*R*,3*S*)-3-[(1′*R*)-1′-menthyl]-2,3-epoxy-2,3-dihydro-1,2-benzisothiazole 1,1-dioxide **2** produces only *trans*-2-phenyl-1,3-dithiane 1-oxide. The fact that *cis* sulfoxide is not observed in these reactions suggests that the *p*-type orbitals in the sulfide do not approach the active-site oxygen in oxaziridine from the directions c and d (Scheme 3).



Scheme 3

The assignment of the absolute configurations of the oxaziridine rings of compounds **1** and **2** as (2*S*,3*R*) and (2*R*,3*S*), respectively, on the basis of X-ray diffraction analysis was previously reported.[7]

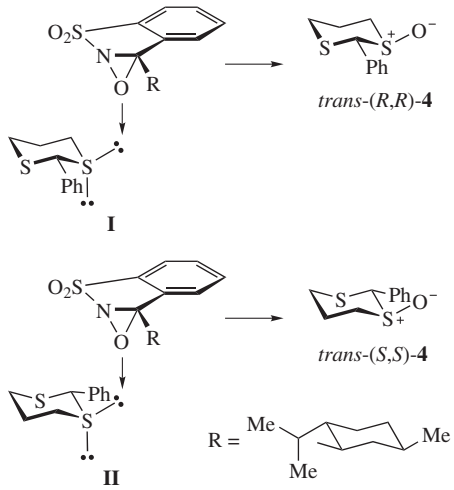
For the oxidation of 2-phenyl-1,3-dithiane by oxaziridine **1**, two possible transition states are shown in Scheme 4. The fact that the product has the *S* configuration at sulfur reveals that **I** is more favourable than **II**. In this regard, one can consider that repulsion forces between the chiral group R* and the substrate, including those between SO_2 and the non-bonded electrons of the other dithiane sulfur, make transition state **II** unfavourable. Thus, the phenyl group of the sulfide prefers to locate itself in the region where there are the fewest non-bonded interactions and also the least unfavourable repulsive interaction between the π-system of the oxaziridine and the π-aryl system of the sulfide, as reported by Davis *et al.*;[10] *i.e.*, transition state **I** is favoured (Scheme 4).



Scheme 4

More favourable transition state **I** (Scheme 4) leads to *trans*-2-(*S*)-phenyl-1,3-dithiane 1-(*S*)-oxide **3**, which is in agreement with the configuration resulting from the reaction of oxaziridine (2*S*,3*R*)-(+)-**1** and the sulfide substrate (Table 1, entries 1–3).

Oxaziridine **2** oxidises 2-phenyl-1,3-dithiane to give *trans*-2-(*R*)-phenyl-1,3-dithiane 1-(*R*)-oxide **4** with no *cis* sulfoxide being observed (Table 1). Using oxaziridine **2** in the oxidation of 2-phenyl-1,3-dithiane, the opposite sense of asymmetric induction was observed in the corresponding sulfoxide from that obtained under similar conditions using oxaziridine **1** (Table 1, entries 4–6). This is not surprising since the oxaziridine ring in **1** has the opposite configuration to that in **2**. The fact that the sulfoxide with *R*,*R* configuration was generated, reveals that transition state **I** (Scheme 5) is more stable than **II**. The instability of transition state **II**, leading to the *S*,*S*-product, is attributed to unfavourable repulsion, particularly, between the π-system of the oxaziridine and the π-aryl system of the sulfide.



Scheme 5

Therefore, a possible mechanism of oxygen atom transfer from enantiopure 3-substituted 2,3-epoxy-2,3-dihydro-1,2-benzisothiazole 1,1-dioxides **1** and **2** to 2-phenyl-1,3-dithiane has been suggested.

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