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DIASTEREOFACIAL SELECTIVITY IN DIELS-ALDER CYCLOADDITIONS INVOLVING VINYL SULFOXIDES

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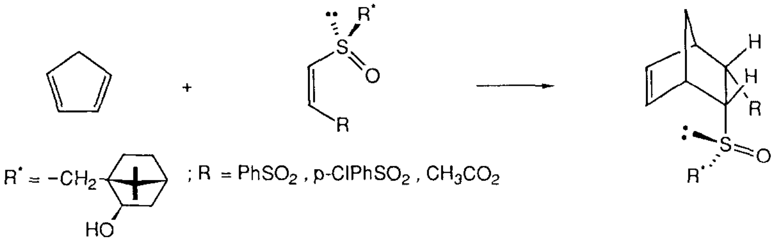
Abstract: Diastereofacial selectivities observed for Diels-Alder cycloadditions of achiral dienes with chiral vinyl sulfoxides are rationalized in terms of electrostatics. The "nucleophilic" diene adds to the electron-poor face of the "electrophilic" dienophile.

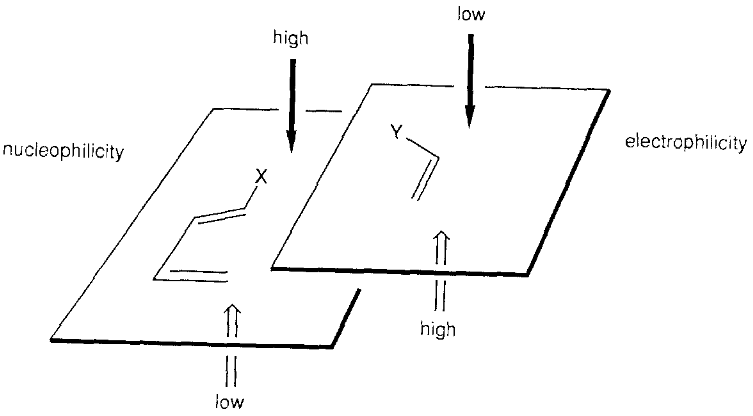
Stereoselective pericyclic transformations have emerged as a practical and efficient means of inducing reaction asymmetry [1]. For example, four contiguous chiral centers may be set in a single Diels-Alder reaction. The synthetic importance of Diels-Alder and related cycloadditions, has prompted a theoretical study aimed at elucidating the origins of stereofacial preferences [2]. The results reported herein, focus on diastereofacially selective reactions involving chiral vinyl sulfoxides as asymmetric dienophiles.

Several investigators have reported significant diastereofacial selectivity upon condensation of substituted vinyl sulfoxides with cyclic and methylated dienes [3-7]. For example, De Lucchi _et al_. [3] have shown that the cycloaddition of cyclopentadiene and _S_-isoborneol vinyl sulfoxides occurs with complete diastereofacial control, i.e.,



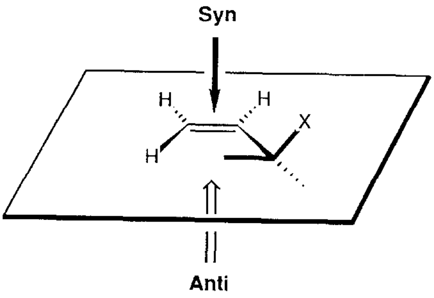
In the case of R′= $PhSO_2$, the sole product characterized by X-ray crystallography corresponds to addition of cyclopentadiene to the _S-cis_ vinyl sulfoxide [11a,12] _syn_ to the bulky chiral auxiliary (_anti_ to the lone pair on sulfur). Replacement of the sulfoxide group by sulfone functionality renders the dienophile totally non selective, a result which strongly implicates the asymmetry at sulfur as the origin of stereodifferentiation, rather than the asymmetry of the chiral auxiliary, as in the elegant work of Oppolzer [8]. Such an interpretation is also consistent with the noted insensitivity of product distributions to solvent. Were stereodirection due primarily to conformational restrictions imposed by hydrogen bonding between the hydroxyl group in the chiral auxiliary and the sulfoxide oxygen, solvents such as methanol would be expected to lead to a change in selectivity. To the contrary, similar stereoselectivities are observed for reactions in both hydrogen-bonding and non-hydrogen-bonding solvents [3].

Diastereofacial selectivity in Diels-Alder cycloadditions involving strained polycyclic systems has prevously been rationalized in terms of presumed distortions in frontier orbital topologies [9]. It has also been discussed in the context of an electrostatic model [2], whereby the more electron-rich face of the diene, which acts as a nucleophile, is paired with the more electron-poor face of the dienophile, which acts as an electrophile, i.e.,



X = electron-donating group
Y = electron-withdrawing group

Assignment of relative nucleophilicity and electrophilicity of diene and dienophile faces, respectively, follows from rules previously established for additions to chiral olefins [10,11], i.e.,



	Nucleophiles	Electrophiles
X = electron rich	**Anti**	**Syn**
X = electron poor	**Syn**	**Anti**

Their application to Diels-Alder cycloadditions involving chiral vinyl sulfoxides as dienophiles is straightforward, once the inherent reactivities of available conformations, as well as their stereochemical biases have been established. Previous experimental [12] and theoretical [11a] work suggests that vinyl sulfoxides react from an S-cis conformer. Here, one olefin face is rendered relatively electron rich due to the lone pair on sulfur, while the remaining face is left relatively electron poor, but sterically encumbered by a bulky substituent. Thus, a balance between steric dictates and the inherent electrostatic bias for addition of a nucleophile (the diene) anti to the electron-rich sulfur lone pair on the dienophile needs to be struck. Experimental results both on Michael additions [13] and on cycloadditions [3-7] involving vinyl sulfoxides suggest the dominance of electrostatic effects in reactions of such substrates.

In summary, diastereofacial selectivity in cycloaddition reactions involving achiral dienes and chiral vinyl sulfoxides arises from the electrostatic preference for a "nucleophilic" diene to avoid the electron-rich lone pair on sulfur, even at the expense of encountering a sterically bulky substituent. Further work, aimed at extending these concepts to selectivity in 1,3 dipolar cycloadditions, is currently underway.

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