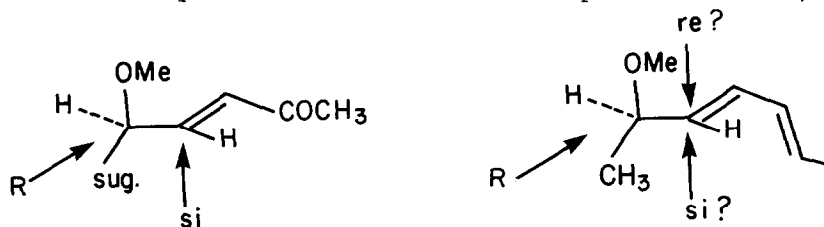


## The Face Selectivity Directed by an Allylic Group of a Diene in the Diels-Alder Reaction Is Reversed from that of a Dienophile

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**Abstract** The Diels-Alder reaction of 2-alkoxy hepta-3,5-dienes with N-phenylmaleimide gives good diastereofacelectivity; and a face selectivity rule is formulated.

Several years ago we demonstrated that a chiral allylic substituent adjacent to a dienophilic double bond directed intermolecular Diels-Alder cycloaddition with some selectivity to one face.<sup>1</sup> In the example illustrated, the allylic



center derived from an "R" carbon in a sugar directed attack on the si face of the dienophile. Subsequent work<sup>2,3,4</sup> (with one exception)<sup>5</sup> on intermolecular Diels-Alder reactions and dipolar cycloadditions to acyclic dienophiles and dipolarophiles confirmed this pattern of selectivity viz. an "R" derived group favors si face approach whereas an "S" derived group favors re face attack.<sup>6</sup>

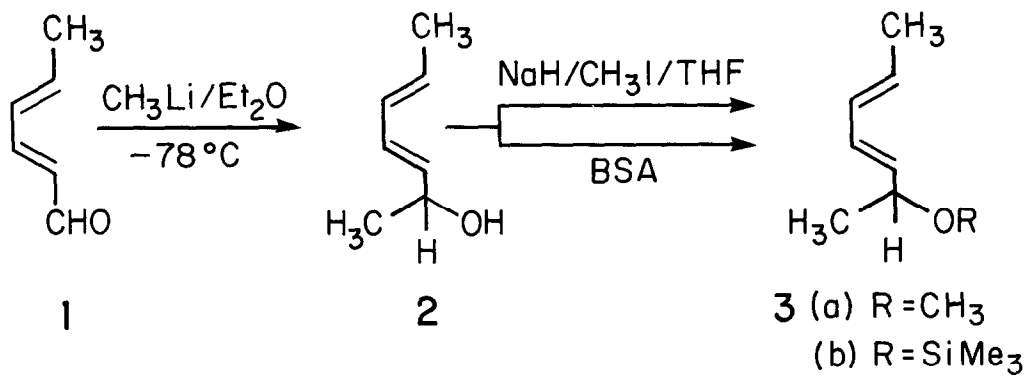
The selectivity has been rationalized in two ways by invoking two different preferred conformations of the allylic group with different interactions between the allylic functions and the developing transition state. Of course both rationales are in accord with the same face selectivity outcome.<sup>1,2,3</sup> A very recent report<sup>7</sup> on face selectivity in an allylic substituted diene prompts us to report our similar results which shows that the face selectivity observed is opposite to that in the dienophile case. Here an "R" derived group induces re face selectivity and "S" induces si face selectivity.<sup>8</sup> Recently, two related rationales have been published to explain allylic effects on face selectivity in the reactions of alkenes. Both Fleming<sup>9</sup> and McGarvey<sup>10</sup> suggest that there are two controlling conformations of the allylic group, one rotamer for an adjacent  $\pi$  system that is being subjected to nucleophilic attack and a second rotamer when the  $\pi$  system is undergoing electrophilic attack. McGarvey explicitly invokes a  $\sigma^*$ ,  $\pi^*$  interaction between the allylic group and the LUMO of the allylically perturbed system being attacked by a nucleophile; and he calls into play a  $\sigma$ ,  $\pi$  interaction for the allylic effect on the HOMO of the system being attacked by an electrophile. These two different effects serve to increase the reactivity of opposite faces in the

two systems. McGarvey's arguments,<sup>11</sup> translated to the Diels-Alder reaction, where the dienophile reactivity is LUMO-controlled while the diene is HOMO-controlled, would rationalize our observations. Without recourse to conformational or FMO arguments, an empirical rule for allylic group effects can be formulated:<sup>11</sup>

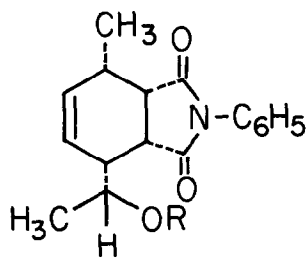
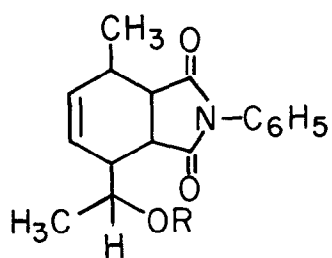
| chirality of allylic group | face selected dienophile diene |    |
|----------------------------|--------------------------------|----|
|                            | R                              | si |
| S                          | re                             | si |

The test dienes were prepared by reacting sorbic aldehyde **1** with methyl lithium in ether at  $-78^{\circ}\text{C}$  to give the allylic alcohol **2** (b.p.  $86^{\circ}\text{C}/15\text{ mm}$ ) in 90% yield. The alcohol **2** was treated with sodium hydride-methyl iodide in THF to afford the methyl ether (**3a**) (b.p.  $57^{\circ}\text{C}/15\text{ mm}$ ) in 68% yield and with BSA to form **3b**. The methyl ether **3a** was allowed to react with N-phenylmaleimide in benzene at  $55^{\circ}\text{C}$  for three days to give a mixture of diastereoisomers **4a** and **5a** in a ratio of 5:1 based on NMR. A benzene solution of N-phenylmaleimide was added to the crude silyl ether **3b** and the mixture stirred at room temperature for ten days. Once again a mixture of diastereoisomers **4b** and **5b** were obtained in a ratio of 7.3:1 based on isolation of the two isomers. Both major products **4a** and **4b** exhibit very similar NMR spectra, as do the minor pair **5a** and **5b**. In order to determine the stereochemistry of the two isomers and hence the face of attack that predominates in the Diels-Alder reaction the mixture of silyl ether isomers were separated by preparative chromatography to obtain **4b** (m.p.  $130^{\circ}\text{C}$ ) in 88% and **5b** in 12% yields. The two silyl ethers **4b** and **5b** were treated with a solution of tetrabutylammonium fluoride in THF at room temperature for 24 hours to afford a mixture of lactones **6** and **7** along with the corresponding alcohols **4c** and **5c**. While the major isomer **4b** gave a greater amount of the lactone **6** the minor isomer **5b** gave a greater proportion of the alcohol **5c**. The two lactones **6** and **7** were separated from their respective alcohols by preparative chromatography and analysed by NMR to determine the stereochemistry of the two lactone isomers. However, the coupling constants of the protons  $\text{H}_a$  and  $\text{H}_b$  in the two lactone isomers were found to be 7.3 Hz for the major lactone **6** and 6.72 Hz for the minor lactone **7**. These values are too close for us to assign the stereochemistry. Therefore the stereochemistry was determined by NOEds experiments. Our NOEds results are shown on the structural diagrams of **6** and **7**. Further the silyl ether **4b** and the methyl ether **4a** were converted to the same iodo compound **5d**.<sup>12</sup> This shows that the two major Diels-Alder adducts **4a** and **4b** belong to the same stereochemical series, therefore **5a** and **5b** must belong to the isomeric series.

It appears to follow from our complementary results with dienophiles and

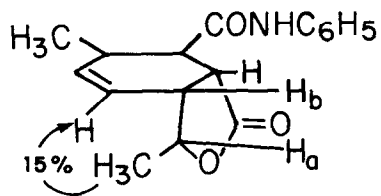
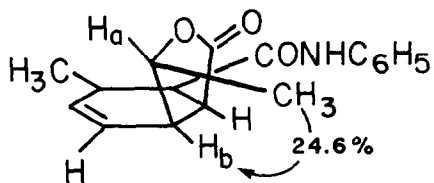


N-Phenylmaleimide  
Benzene



Bu<sub>4</sub>N<sup>+</sup> F<sup>-</sup>

Bu<sub>4</sub>N<sup>+</sup> F<sup>-</sup>

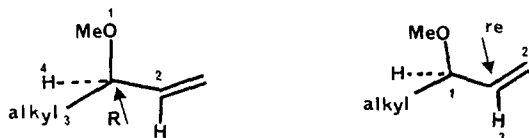


dienes that the face selectivity in the intermolecular Diels-Alder reaction is a predictable function of the configuration of the adjacent chiral center.

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### References and Notes

1. Franck, R.W.; John, T.V.; Olejniczak, K.; and Blount, J.F.; *J. Am. Chem. Soc.*, 1982, **104**, 1106.
2. Schmidlin, T.; Burckhardt, P.E.; Waespe-Sarevic, N.; and Tamm, C.; *Helv. Chim. Acta.*, 1983, **66**, 450.
3. Houk, K.N.; Moses, S.R.; Yun-Dong Wu; Rondan, N.G.; Jager, V.; Schohe, R.; and Fronczeck, F.R.; *J. Am. Chem. Soc.*, 1984, **106**, 3880. This paper rationalizes the face selection of dienophiles and dipolarophiles. It does not agree with the diene results.
4. Kozikowski, A.P.; and Ghosh, A.K.; *J. Org. Chem.*, 1984 **49**, 2762.
5. Horton, D.; Machinami, T.; and Takagi, Y.; *Carbohydrate Res.*, 1983, **121**, 135.
6. Roush, W.R.; Gillis, H.R.; and Essinfeld, A.P.; *J. Org. Chem.*, 1984, **49**, 4674. The article reviews the status of chiral auxiliaries in the Diels-Alder, which is related to, but different from our work.
7. Rene, G.; Jilali, K.; Mosset, P.; Martelli, J.; and Carrie, R.; *Tetrahedron Lett.*, 1984, 3697.
8. DeShong, P.; and Legnius, J.M.; *J. Am. Chem. Soc.*, 1983, **105**, 1686. This work includes a dipolar addition where a nitron with an adjacent "R" chiral center is attacked on its re face.
9. Fleming, I.; Lewis, J.L.; *J.C.S. Chem. Com.*, 1985, 149. Opposite face selectivities are described for electrophilic and nucleophilic additions to double bonds.
10. McGarvey, G.J.; Williams, J.M., *J. Am. Chem. Soc.*, 1985, **107**, 1435.
11. (a) To define the chirality of the allylic carbon, we modify the rules so that the  $sp^2$  carbon is always #2, even if the side-chain has hetero atoms.  
(b) To define the face selected, priorities are set so that the allylic carbon is #1 and the alkene carbon is #2.



12. The stereochemistry of 5d is assigned as drawn because its nmr spectrum closely resembles those of 5a and 5b.

