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A DISPROOF OF KAHN-HEHRE'S PROPOSAL ON THE GROUND STATE CONFORMATIONS AND THE STERIC COURSE OF THE DIELS-ALDER REACTION OF VINYL SULFOXIDES

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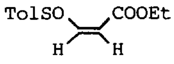
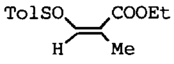
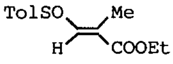
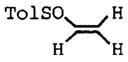
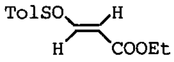
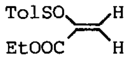
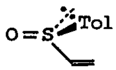
Summary---X ray analysis and CD spectra of some optically active vinyl sulfoxides revealed that the conformation of vinyl sulfoxides is affected by the substituents at alpha or beta position. The results strongly support our previous suggestion that the most stable conformation(*s*-*trans* or *s*-*cis*) dictates the diastereoselectivity of the Diels-Alder reaction of vinyl sulfoxides.

High diastereofacial selectivity observed in the cycloaddition of chiral vinyl sulfoxides with various dienes has recently received considerable attention from synthetic view points$^{1)}$. Mechanistic aspect of this Diels-Alder(D-A) reaction has been discussed by us and other investigators$^{2,3,4)}$ in terms of steric factors : The diastereofacial differentiation has been explained by the preferred addition of the dienes to energetically favored *s*-*trans*(or *s*-*cis*)conformer of vinyl sulfoxides from the less crowded side of the vinyl group, i.e., *syn* to the lone pair on sulfur. Also, the conformational equilibrium of the vinyl sulfoxides is mainly imposed by the substituents at alpha or beta position due to the dipole-dipole repulsion$^{5)}$and/or steric hindrance. The previous results are summarized in Table 1. The vinyl sulfoxides **1a,b,c**$^{2)}$ in which the *s*-*trans* conformation is most favorable due to the dipole-dipole repulsion or the steric hindrance, exhibited high diastereoselectivity and the determined absolute configurations of the cycloadducts were most reasonably explained by the addition of the diene to the *s*-*trans* conformer *syn* to the sulfur lone pair. Furthermore, the dienophile **2**$^{3)}$ which is considered to be predominantly in *s*-*cis* conformation due to the dipole-dipole repulsion between C=O and S=O, showed high diastereoselectivity and provided the major cycloadducts by the attack of the diene *syn* to the sulfur lone pair. On the other hand, the compounds **1d** and **1e**$^{4)}$ which may exist both in the *s*-*trans* and in the *s*-*cis* conformations because of the absence of alpha or *Z*-beta substituents, exhibited low diastereoselectivity.

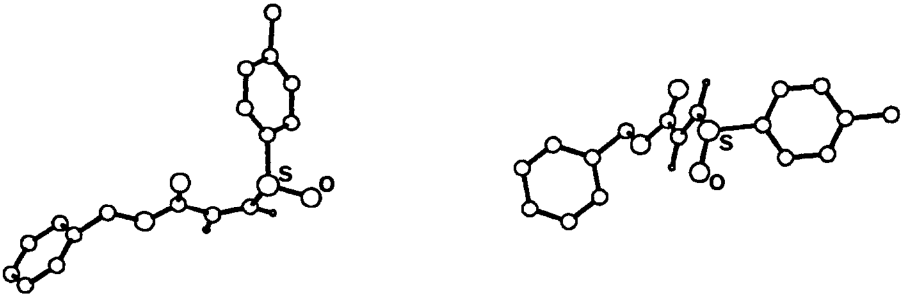
Very recently, Kahn and Hehre$^{6)}$ reported on the basis of FMO calculation that the conformational energy profile for methyl vinyl sulfoxide incorporated two potential minima, corresponding to structures in which the S=O bond or the sulfur lone pair is coplanar to C=C and the conformer in which the S=O and C=C are approximately *syn*(*s*-*cis*)is more stable.

Table 1. Ground State Conformations of Chiral Vinyl Sulfoxides and the Diastereoselectivity in Diels-Alder Reaction

Most stable Conformations and observed diastereoselectivity	Dienophiles		
s-trans high diastereoselectivity	 **1a**	 **1b**	 **1c**
s-trans + *s-cis* low diastereoselectivity	 **1d**	 **1e**	
s-cis high diastereoselectivity	 **2**	**chirality at S :** 	

They concluded that the former *s-cis* conformer will dictate eventual product distributions and the above D-A reactions should be explained by the addition of the diene to *s-cis* vinyl sulfoxides *anti* to the electron-rich sulfur lone pair(*syn* to bulky tolyl group). Their proposal is based on their belief that, under condition of kinetic control, Diels-Alder regio- and stereochemistry is not directed by steric factors but rather influenced primarily by electronic interactions between valence orbitals on diene and dienophilic fragment. Here, we would like to present a refutation of their proposal on the ground-state conformations and the steric course of the D-A reaction of vinyl sulfoxides on the basis of the X ray analysis and the CD spectra of some *p*-tolyl vinyl sulfoxides.

In order to carry out the X ray analysis of crystalline *p*-tolyl vinyl sulfoxides, we prepared benzyl (*Z*)- and (*E*)-3-*p*-tolylsulfinylacrylates[7]. Perspective views[8] of these compounds clearly revealed the former is in the conformation in which the S=O and C=C is approximately *anti* coplanar(*s-trans*)[9] and the latter is in the *s-cis* conformation. The results are very consistent with our previous suggestion that there are two possible conformations for the vinyl sulfoxides and the conformational preference is controlled by the substituents at alpha or beta position due to the dipole-dipole repulsion and the steric factor.



Perspective Structures of Benzyl (*Z*)- & (*E*)-3-*p*-Tolylsulfinylacrylates

Next, the circular dichroism (CD) spectra of these optically active vinyl sulfoxides were taken in methanol. As shown in Chart 1, there is a contrasting difference between **1a,b,c** and **2.** The opposite Cotton effect observed at about 240nm region should reflect the conformational difference of the vinyl sulfoxides: The dienophiles **1a,b,c** in which *s-trans* conformation was suggested to be predominant showed negative cotton effect(CE) and the compound **2** in *s-cis* conformation showed positive CE. The compounds **1d** and **1e** which were suggested to react in both *s-cis* and *s-trans* conformations showed positive CE. This fact is in good agreement with Kahn-Hehre's(K-H's) proposal that the *s-cis* conformer is most stable in alkyl vinyl sulfoxide10). The observed results strongly supported our previous suggestion that the ground state conformations of vinyl sulfoxides vary dramatically depending on the substituents at alpha and beta position and the most stable conformer dictates the product distributions(diastereoselectivity). Although further detailed chiroptical studies are needed to explain theoretically the opposite CE due to the conformational difference of the vinyl sulfoxides, the observations will provide an experimental tool for assigning the ground state conformation of vinyl sulfoxides by the CD spectral measurement.

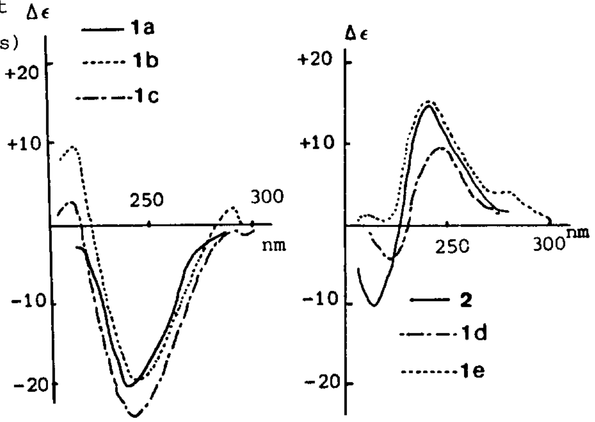


Chart 1. CD Spectra of Chiral Vinyl Sulfoxides **1a-e** and **2** in MeOH

Then, we would like to present a typical example in which K-H's proposal could not be applied. Let us consider the steric course of the D-A reaction of the dienophile **2** with cyclopentadiene. The absolute structure of the cycloadducts which was determined previously3) strongly indicates the addition of the diene occurs to the *s-cis* conformer not from the side of the bulky tolyl group but from the side of the lone pair on sulfur. If the diene should attack the vinyl sulfoxide **2** *syn* to the bulkyl tolyl group, as K-H suggested, the predominant *s-trans*(not *s-cis*) conformation should be assumed. This leads to a self-contradiction to the K-H's proposal. Furthermore, as we have already reported, the Lewis acid-catalyzed D-A reaction of the dienophile **2** showed the high diastereoselectivity and provided the cycloadducts with the completely opposite absolute structure3). The result is most reasonably explained by the change of the *s-cis* conformer to the *s-trans* conformer due to the chelation control.

Finally we would like to present the following comments: 1)K-H's calculation on the ground state conformations of alkyl vinyl sulfoxide is partly in accordance with our X ray analyses and CD spectral observation. 2) Unlike their proposal, substituents at alpha and beta position affect the ground state conformations dramatically. K-H's calcultation is based on the structurally simplest alkyl vinyl sulfoxide , whose D-A reaction is expected to show low diastereoselectivity[4a,b]. Thus, their calculation should be developed to the substituted vinyl sulfoxides, with which the high diastereoselectivity was observed. 3) The Diels-Alder stereochemistry is primarily influenced by the steric factor of the ground state conformers. Although the ground state conformer may most likely dictate the product distributions (diastereoselectivity), the detailed kinetic and theoretical study are required to find out the inherent dienophilic-reactivity of both *s-cis* and *s-trans* conformers.

Reference and Notes

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7) Benzyl (*Z*)-3-*p*-tolylsulfinylacrylate: mp.86-87°C(from benzene-hexane); $[\alpha]_D$ -119°(c=0.40, $CHCl_3$). Crystal data are: $C_{17}H_{16}O_3S$, M=300.4, monoclinic, space group $P2_1$, a=16.752(6),b=5.312(1), c=8.738(3) Å, β=98.79(3) , V=768.5(4) Å^3, Z=2, D_c=1.298g/cm^3,R=0.073 for 1371 reflections.

Benzyl (*E*)-3-*p*-tolylsulfinylacrylate: mp.76-78°C(from benzene-hexane); $[\alpha]_D$ +291°(c=1.10, $CHCl_3$). Crystal data are: $C_{17}H_{16}O_3S$, M=300.4, monoclinic, space group $P2_1$, a=15.675(6), b=5.474(2), c=9.518(3) Å, β=104.61(3) ,V=790.3(4) Å^3, Z=2, D_c=1.262g/cm^3, R=0.121 for 1446 reflections. Atomic coordinates for these structures have been deposited with the Cambridge Crystallographic Data Centre.

8) W.D.S. Motherwell and W. Clegg, PLUTO. Program for Plotting Molecular and Crystal Structures. Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, England.

9) X ray crystallography of menthyl 3-(2-pyridylsulfinyl)acrylate whose preparation has been reported in *Chem. Commun.*, **1986**, 771 shows that , in this case, the sulfur lone pair and C=C are *syn* coplanar. The results will be reported elsewhere.

10) Variable temperature experiments using EPA as a solvent revealed that the free energy difference(ΔG) between two conformers of these vinyl sulfoxides is in the range of 0.70-2.1 Kcal/mol, which agrees with K-H's calculation.

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