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Significant Orbital Interactions in π-Facial Stereoselection of Electrophilic Addition Reactions to Vinylic Sulfoxides

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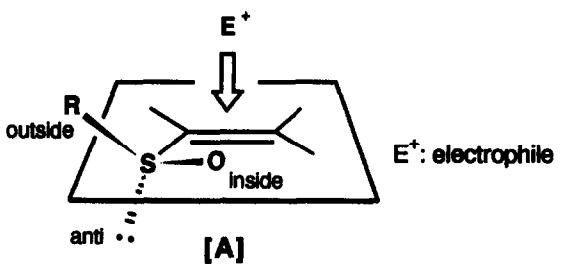
Both theoretical and experimental studies demonstrated that the π-facial stereoselection of the electrophilic addition reactions to vinylic sulfoxides is ascribed to a transition-state model in which the lone pair and the oxygen atom are oriented at the anti and inside positions, respectively, to the incipient bond.

Described here is a remarkable orbital control in the stereoselection of electrophilic addition reactions to vinylic sulfoxides. Against many empirical interpretations,[1] both experimental and theoretical studies demonstrated that *the π-facial stereoselectivity of these reactions are ascribed to an electronic model [A].*

The electronic control of the π-facial stereoselection in the addition reactions to stereogenic allylic bonds has been recently explained by the Houk's model.[2] In this model the most electron-donating group is oriented at the anti position to maximize σ - π overlap that increases the energy level of the alkene HOMO. On the other hand, the most electron-withdrawing group occupies the inside position to minimize σ* - π overlap that decreases the HOMO energy level. The model [A] is closely associated with this model in electronic effects because the lone pair and the oxygen atom on the sulfur atom behave as the most electron-donating and the most electron-withdrawing groups, respectively.



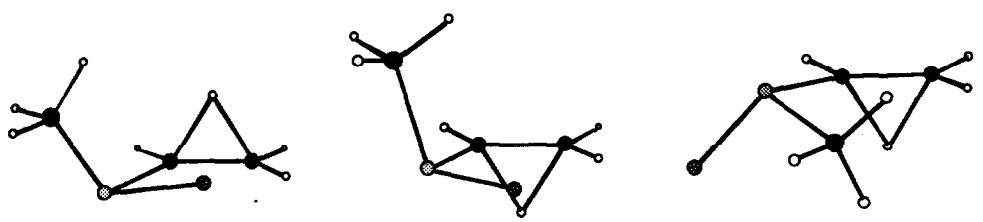
[A]

The model [A] was strongly supported by quantum chemical calculations. The transition-state structures of the addition of a proton (a test electrophile) to methyl vinyl sulfoxide were examined by semi-empirical (MNDO/PM3)[3] and ab initio[4] molecular orbital methods.[5] When a proton approaches to methyl vinyl sulfoxide of *S* form from the *si* face, only one energy minimum ([I]) was found for the transition-state structure (Figure 1).[6] For the attack of a proton from the *re* face, in contrast, two energy minima ([II] and [III]) were found. The calculations showed that the transition-state structure with the lowest total energy was [I] that predicted the preferable attack of the electrophile from the *si* face. Worthy of note is that the structure [I] has an anti lone pair and an inside oxygen atom, both of which should cooperatively stabilize this structure.

Experimental results also agreed with the model [A]. High stereoselectivities in the predicted mode were achieved in the alkylation of enolates bearing a sulfinyl group on the enolate carbon.[9] For example, treatment of the sodium enolate of 3-(*p*-tolylsulfinyl)-2-butanone with allyl bromide in DMF (-20 °C) gave the allylated product of *R*,R** configuration with 95% diastereoselectivity (Table I, run 1).[10] The substituent effect on the sulfur atom is remarkable: displacement of the *p*-tolyl group with alkyl groups significantly increased the selectivity up to >99% (runs 4 and 5). In addition, other electrophilic additions such as hydroboration,[11] bromination,[2] and bromohydroxylation[12] are also explained by the model [A] (Table I, runs 6-10).

Steric control does not work significantly in these reactions. Indeed, the bulkiness of the substituent on the sulfur atom was not a dominant factor in the alkylation and bromination, and the electrophiles are predicted to approach from the more crwoded face in the model [A]. The unimportance of the steric control can be explained by the small steric demands of the sulfinyl group as recognized by its low *A* value (1.9 kcal mol^{-1} for S(O)Ph)[13] and low rotation barrier around the C-S bond (0.9 kcal mol^{-1} for CH_3-S(O)CH_3 by MNDO/PM3).

In marked contrast, electronic control is very significant as supported by the MO calculations. Particularly interesting is that the selectivity in the enolate allylation

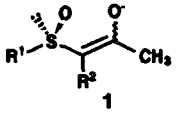
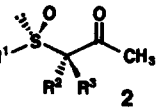
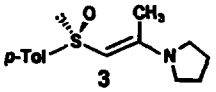
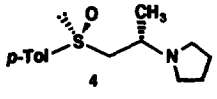
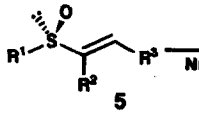
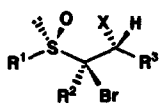


[I] [II] [III]

0.0, 0.0, 0.0, 0.0 3.0, 1.2, 0.9, 1.0 3.6, 11.7, 10.4, 9.1

Figure 1. The transition-state structures for protonation to (*S*)-(methyl vinyl sulfoxide). Relative energies (kcal mol^{-1}) were calcurated at MNDO/PM3, 6-21G, 3-21G*, and MP2/3-21G*//3-21G*, and shown in this order below each structure.

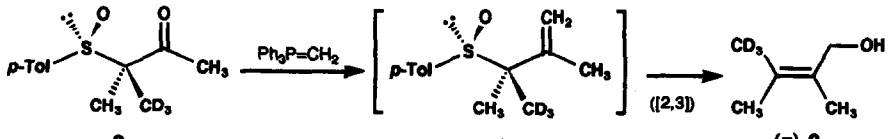
Table I. Stereoselective Addition of Electrophiles to Vinylic Sulfoxides

run	substrate	electrophile	product	yield,%	select
	 1	R^3-X	 2	a: R^1 = *p*-Tol, R^2 = CH_3 b: R^1 = *p*-Tol, R^2 = allyl c: R^1 = *n*-Bu, R^2 = CH_3 d: R^1 = *t*-Bu, R^2 = CH_3	
1[a]	1a	CH_2=$CHCH_2Br$	2a (R^3 = allyl)	74	95 : 5
2[a]	1a	CD_3I	2a (R^3 = CD_3)	80	93 : 7
3[a]	1b	CH_3I	2b (R^3 = CH_3)	63	95 : 5
4[a]	1c	CH_2=$CHCH_2Br$	2c (R^3 = allyl)	41	98 : 2
5[a]	1d	CH_2=$CHCH_2Br$	2d (R^3 = allyl)	56	>99 : 1
	 3	HBR_2	 4		
6[b]	3	BH_3•$S(CH_3)_2$	4	95	87 : 13
7[a]	3	$(sia)_2BH^{\ominus}$	4	11	59 : 41
	 5	Br_2 or NBS/CH_3OH	 6	a: R^1 = *p*-Tol, R^2 = CH_3, R^3 = H b: R^1 = *c*-Hexyl, R^2 = CH_3, R^3 = H c: R^1 = *p*-Tol, R^2 = H, R^3 = Ph	
8[a,c]	5a	Br_2/CH_2Cl_2	6a (X = Br)	68	83 : 17
9[a]	5b	Br_2/CH_2Cl_2	6b (X = Br)	79	86 : 14
10[d]	5c	NBS/CH_3OH	6c (X = OCH_3)	72	95 : 5

[a]This work. [b]Ref 11. [c]In AcOH, the selectivity reported is ca. 7 : 3 (ref 2a). [d]Ref 12. [e]Sia = siamyl (1,2-dimethylpropyl).

was enhanced with the increasing ability of electron-donation (*p*-Tol < *n*-Bu < *t*-Bu, runs 1, 4, 5) (not with the increasing steric bulkiness!). This order is consistent with the increasing energy level of the n_S orbital leading to easier mixing with the π orbital.

The electrophilic additions to vinyl sulfoxides have obvious synthetic potential. For example, treatment of 2a (R^3 = CD_3) with Ph_3P=CH_2 (2 equiv) in dimethyl sulfoxide at 0 °C - room temperature gave an allylic sulfoxide 7[15] that immediately rearranged to (*Z*)-8[16] with high stereospecificity of 82%.[17] This reaction opens a way to stereoselective construction of tetrasubstituted olefins.



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(14) Only if the electrophile is large enough, the steric interaction appeared: while BH_3 showed high selectivity in the hydroboration (run 6), employment of a bulky borane reduced the selectivity (run 7).

(15) The allyl sulfoxide 2 rearranged too rapidly to be detected during the reaction. Since 2 mol of $Ph_3P{=}CH_2$ was required, it seems to trap rapidly the rearranged sulfenyl ester preventing the reversibility of the rearrangement.

(16) The stereochemistry was tentatively assigned on the basis of an empirical rule $|^5J_{HH}|_{trans} > |^5J_{HH}|_{cis}$ in homoallylic coupling: Pretsch, E.; Clerc, T.; Seibl, J.; Simon, W. *Tabellen zur Structuraufklärung organischer Verbindungen mit spektroskopischen Methoden*; Springer-Verlag, 1981, H210.

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