

AN ANALYSIS OF THE DIASTEREOMERIC TRANSITION STATE INTERACTIONS FOR STEREOSELECTIVE
EPOXIDATION OF ACYCLIC ALLYLIC ALCOHOLS WITH PEROXY-ACIDS*

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SUMMARY: Consideration of the magnitude of $A^{(1,2)}$ and $A^{(1,3)}$ -strain in the transition state of the epoxidation of acyclic allylic alcohols, has powerful predictive value.

Among the reactions¹ which are useful for controlling stereo-, regio-, and chemo-selectivity in acyclic systems, epoxidation of acyclic allylic alcohols, using either organic per-acids or more recently V^{5+} catalyzed tert-butyl hydroperoxide has had phenomenal success.^{2,3} While Sharpless and co-workers³ have recently provided a sound rationale for the observed selectivity of V^{5+} catalyzed tert-butyl hydroperoxide epoxidations, no parallel treatment has been advanced for per-acid epoxidations. This letter is concerned with evaluating the diastereomeric transition state interactions for the epoxidation of acyclic allylic alcohols using peroxy-acids.

Inspired by the remarkable observation of Henbest and Wilson⁴ that hydrogen bonding of the hydroxy group with a per-acid has a strong directive influence in the epoxidation of cyclohex-2-en-1-ol, Sassiver and English⁵ were the first to observe the threo-selectivity (Threo: erythro \approx 1.5) in the epoxidation of acyclic allylic alcohols (1, X = R¹ = R² = H, R may be Me, Et, i-Pr and t-butyl). Tables 1-3 provide a reflection of its current status and one would note that the chiral allylic centre is either on the left or right appendage of C=C.

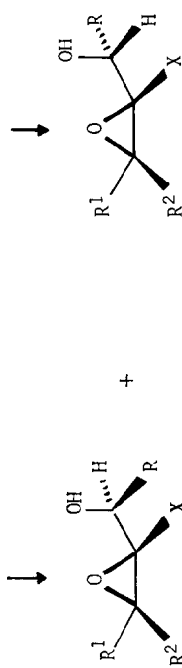
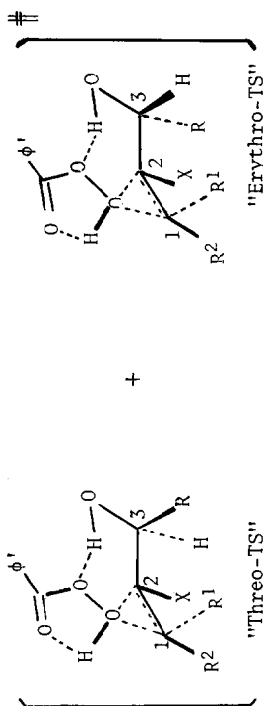
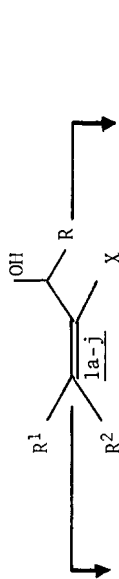
Transition State Model: The geometry of threo- and erythro-transition states shown in Tables 1-3, are in accord with those suggested by Henbest⁴ and Whitham⁹ respectively and draw support from the observed high negative entropy of activation ($\Delta S^\ddagger = -41$ eu) for the epoxidation of cyclohex-2-en-1-ol with peroxybenzoic acid, suggesting a highly chelated and oriented transition state. Recently Mihelich⁸ and Teranishi¹³ have also independently supported this model.

Evaluation of Diastereomeric Transition State Interactions for Epoxidation of Acyclic Allylic Alcohols: Before embarking on the steric aspects of the observed selectivity given in Tables 1-3, a proper understanding of $A^{(1,2)}$ and $A^{(1,3)}$ -strain as described by Johnson¹⁴ is essential. Although these concepts were originally proposed to rationalize the stereochemical behavior of enamines, enolate ions and imines in six membered rings, they have enormous predictive value in other systems as well, if the required geometric constraints are in order.

$A^{(1,2)}$ -Strain: For conformationally equilibrating conformers (4a \leftrightarrow 4b), 4a is the preferred conformer when R and R¹ are small, but as R and R¹ becomes moderately larger, 4b having the axial substituent becomes the dominant conformer. This is due to a small dihedral

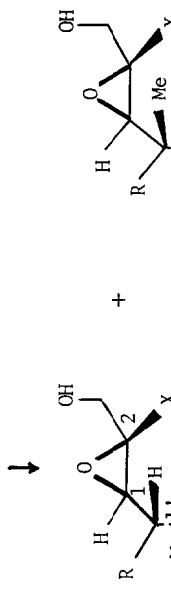
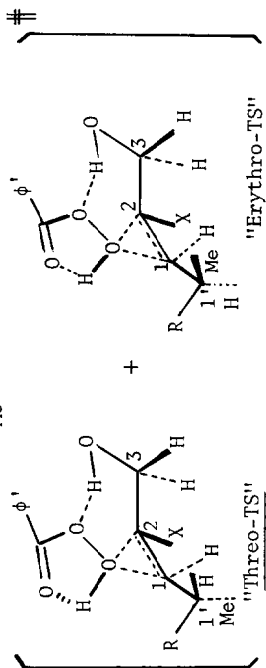
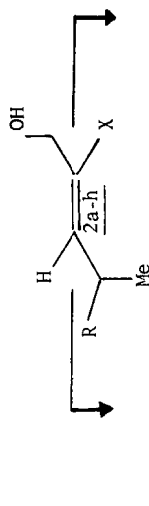
* Dedicated to Professor Arthur J. Birch on the occasion of his 65th birthday.

Table 1. Stereoselectivity in the Epoxidation of Acyclic Allylic Alcohols (1a-j)



Entry	X	R	R ¹	R ²	Erythro-epoxides (1a-j)	Threo-epoxides (1a-j)	(Threo: Erythro ratio)	Ref
a	Me	Me	H	H			(45:55) ²	
b	Me	n-C ₄ H ₉	H	H			(41:59) ²	
c	SiMe ₃	φ	H	H			(0:100) ⁶	
d	H	Me	H	H			(61:39) ⁵ ; (60:40) ²	
e	H	t-C ₄ H ₉	H	H			(56:44) ⁵ ; (54:46) ⁷	
f	H	t-C ₄ H ₉	H	Me			(60:40) ⁸	
g	H	Me	H	Me			(64:36) ² ; (67:31) ⁸	
h	H	φ	H	H			(64.9:34.1) ⁹	
i	H	Me	Me	H			(95:5) ² ; (98:2) ⁷	
j	H	Me	Me	Me			(95:5) ² ; (96.4) ⁷	

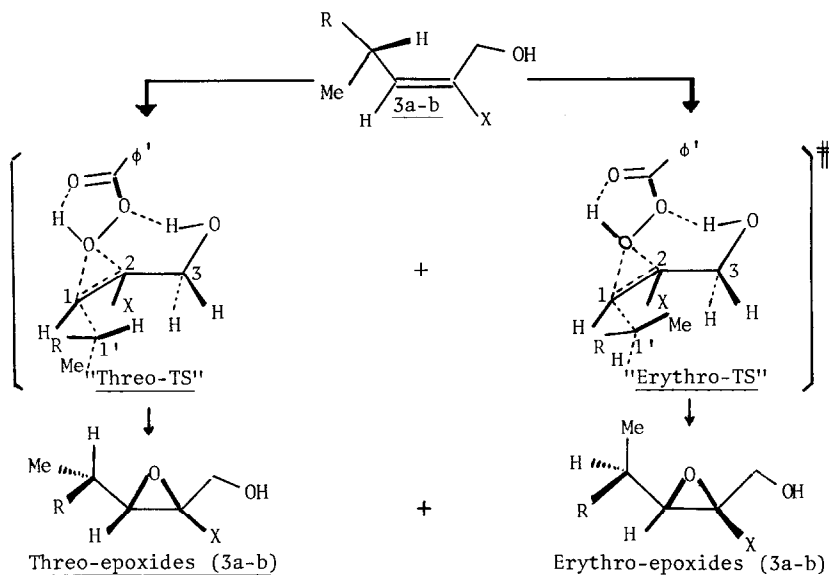
Table 2. Stereoselectivity in the Epoxidation of Acyclic Allylic Alcohols (2a-h)



Entry	X	R	Erythro-epoxides (2a-h)	Threo-epoxides (2a-h)	(Threo: Erythro ratio)	Ref
a	Me	-CH ₂ OH			> (96:4) ¹⁰	
b	Me	-CH ₂ OCH ₂ φ			> (96:4) ¹⁰	
c*	SiMe ₃	-CH ₂ OCH ₂ φ			≈ (100:0) ¹¹	
d	SiMe ₃	-OH			> (96:4) ¹¹	
e	SiMe ₃	-OCH ₂ φ			(75:25) ¹¹	
f	H	-CH ₂ OCH ₂ φ			(60:40) ¹²	
g	H	OH			(50:50) ¹¹	
h	H	-OCH ₂ φ			(50:50) ¹¹	

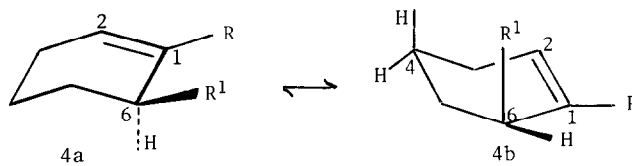
*For a discussion on the epoxidation of vinyl silanes, see: J.J. Eisch and J.T. Trainor, *J. Org. Chem.* **28**, 487 (1963); H. Sakura, N. Hayashi and M. Kumada, *J. Organometal. Chem.* **18**, 351 (1969).

Table 3. Stereoselectivity in the Epoxidation of Acyclic Allylic Alcohols (3a-b)



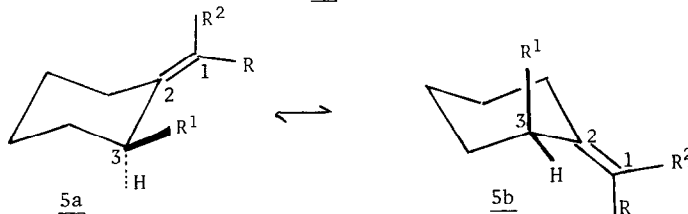
Entry	X	R	(Threo: Erythro ratio)
a	H	-CH ₂ OCH ₂ φ	≈ (100:0) ¹²
b	Me	-CH ₂ -OCH ₂ φ	(93:7) ¹⁰

angle ($\sim 35^\circ$) between R¹-(C-6)-(C-1)-R in conformer 4a and consequently the energy of



interaction between R and R¹ is greater than that of R¹ with the axial hydrogen at C-4, plus the C-6 pseudo-equatorial hydrogen and R in 4b.

A^(1,3)-Strain: For methylenecyclohexane such as 5a where R and R¹ are moderate in size, they interfere with each other drastically, in fact more so than if they were 1,3-diaxial in a cyclohexane ring. Thus conformer 5b having an axial substituent can be



expected to be favored at equilibrium. Conversely if R and R¹ are small, 5a is the preferred conformer. The strain experienced by 5a is due to an ideal near-planar and syn relationship between groups R and R¹ at C-1 and C-3.

With the above considerations in mind, a careful analysis of the transition states shown in Table 1, reveals that while the threo-transition state is destabilised due to a 1,2-eclipsing interaction (cf. $A^{(1,2)}$ -strain) between (C-2)-X and (C-3)-R (dihedral angle $\approx 15^\circ$, entry 1a-c), the erythro-transition state is destabilized as a consequence of $A^{(1,3)}$ -strain between the syn-substituents R^1 and R at C-1 and C-3 (entry 1d-j). The magnitudes of these interactions are clearly reflected in the observed selectivity (Table 1). Despite 100% stereo-selectivity for entry 1c, it is surprising that it did not appear in a recent report.¹ The observed threo-selectivity as seen in Table 2 (entry 2a-e) is a direct measure of $A^{(1,2)}$ -strain experienced by the erythro-transition state (notice the severe van der Waals repulsive interactions between the Me group at C-1' and group X at C-2). For threo-selectivity of Table 3, the $A^{(1,3)}$ -strain between Me at C-1' and axial H at C-3 in the erythro-transition state plays the dominant role. This results because of a shorter distance ≈ 2.0 Å between the 1,3-diaxially oriented hydrogen atoms at C-1 and C-3.

In conclusion, the discussion presented above¹⁵ relates the observed kinetic selectivity in the epoxidation of acyclic allylic alcohols to the relative energies of the diastereomeric transition states, which is in accord with the Curtin-Hammett principle,^{16,17} and differs from that of others^{6,7,11} who have relied upon the preferred conformation of the allylic alcohol. The merit of the latter argument probably has its origin in the principle of least conformational distortion,¹⁸ but strictly speaking is not valid here because of the strong influence of the hydroxy group on the approach of the per-acid.

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