STEREOSELECTIVE INTRODUCTION OF CHIRAL CENTRES IN ACYCLIC PRECURSORS: A PROBE INTO THE TRANSITION STATE OF V⁵⁺-CATALYZED t-BUTYLHYDROPEROXIDE (TBHP) EPOXIDATION OF ACYCLIC ALLYLIC ALCOHOLS AND ITS SYNTHETIC IMPLICATIONS.

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Utility of the (Me) 3Si-group for manipulating the relative energies of Summary: the diastereometric transition states for V^{5+} -catalyzed TBHP epoxidations of acyclic allylic alcohols is presented.

Among the challenging problems which a synthetic organic chemist faces in this decade, stereo-, regio-, chemo-, and enantio-selective introduction of chiral centres in acyclic precursors is undoubtedly at the top.¹ Several ingenious solutions pertaining to this objective are emerging.^{2,3} In particular the selectivities which have been recently witnessed in the epoxidations of acyclic allylic alcohols using (i) organic per-acids.⁴ (ii) ∇^{5+} -catalyzed TBHP^{5,6} and more recently (iii) (*i*-C₃H₇O)₄Ti, TBHP and (+) or (-) diethyl or diiosopropyl tartrate^{7,8} are indeed phenomenal

In a recent communication from this laboratory⁴, we presented an analysis of the diastereomeric transition state interactions for the stereoselective epoxidation of acyclic allylic alcohols using peroxy-acids. In this Letter we present results on our experiments which were aimed at probing the transition state of V⁵⁺-catalyzed TBHP-epoxidation of acyclic allylic alcohols.

On the Mechanism of Epoxidation of Allylic Alcohols with V⁵⁺-Catalyst and TBHP: In their pioneering study on the mechanism of molybdenum and vanadium catalyzed epoxidations of allylic alcohols with TBHP, Chong and Sharpless⁹ stated, "Epoxidations carried out in the presence of 18 O-enriched water provide evidence that the intact alkyl hydroperoxide is present in the activated complex responsible for oxygen transfer to the olefin. The literature mechanisms for these epoxidations are criticized, and a new mechanistic approach is presented".

Such a mechanism⁵ is presented in Scheme 1. It is argued that VO(acac)₂ upon reaction



5580

with TBHP undergoes oxidation to an oxo-alkoxide (<u>1</u>). Such V^{5+} -tetrahedral, d°, species then can undergo exchange reactions^{10,11} resulting in the formation of neutral, roughly trigonal bipyramidal complex (<u>2</u>). Intramolecular oxygen transfer from the metal bound peroxide linkage to C=C of allyloxy unit in (<u>2</u>), then proceeds under strict stereo-electronic control (displacement of the peroxide bond should occur from the back side and along the axis of the O-O bond being broken), leading to transition state structure (<u>3</u>). This oxygen transfer step is also probably the slow step of the catalytic cycle (Scheme 1).

Evaluation of Diastereomeric Transition State Interactions for V^{5+} -Catalyzed TBHP Epoxidation of Acyclic Allylic Alcohols. A quick perusal of Table 1 reveals that for entry 1, the threo-[TS][#] is destabilized in comparison to erythro-[TS][#] by a factor of $\sqrt{2.5}$. The main

Table 1: V⁺⁵ Catalyzed TBHP Epoxidations of Allylic Alcohols⁵



destabilizing interaction for threo-transition state is 1,2-eclipsing interaction (*Cf*. $A^{(1,2)}$ -strain⁴) between (C-1)-Me and (C-2)-H (dihedral angle $\sqrt{0}$ 0°, while erythro-transition state experiences a 1,3-diaxial interaction between (C-1)-Me and (C-3)-H.



A Probe into the Transition State of V^{5+} -Catalyzed TBHP Epoxidation of Acyclic Allylic Alcohols: With the above simplified analysis in mind, we thought that by a strategic positioning of a Me₃Si-group at C-2 or C-3 of the parent allylic alcohol, one would dramatically increase $A^{(1,2)}$ -strain for threo-[TS][#] and 1,3-diaxial interaction for erythro-[TS][#] shown above. Thus by replacing the hydrogen atom at C-2 with $(CH_3)_3Si$ -group in entry 4, Table 1, erythro selectivity must increase. Likewise, by substituting methyl group at C-3 with $(CH_3)_3Si$ -group in entry 2, Table 1, threo selectivity must increase.

In order to test the likelihood of our hypothesis, several representative allylic alcohols have been prepared,¹² and epoxidized according to the procedure of Sharpless and Coworkers.⁵ In accord with our expectations diastereomerically pure α , β -epoxysilyl-alcohols of indicated stereo-structures (based on spectroscopic data: ¹H and ¹³C-NMR, Mass and IR) were formed (see: Table 2) in 70-90% overall yields, and these selectivitics are indeed gratifying.

Table 2:	<u>Stereochem</u> Acyclic Al	istry of V ⁵⁺ -Cataly lylic Alcohols.	zed TBHP Epoxidations	of Silylsubstituted
	Entry	<u>Substrate</u>	Erythro-epoxide	Threo-epoxide
	I	Me 3Si OH	Me ₃ Si - 0 R	Me ₃ Si OHR
	2	$R = Me$ $R = i-C_{3}H_{7}$ $H \xrightarrow{H} R$ R R R R R R R R R	»99.0 100.0 H - 0 H - R SiMe ₃	H - OH H - SiMe ₃
	3	$R = Me$ $R = i-C_3H_7$ $R = Ø$ Me_3Si $Me + R$ R	~ 4.0 $=$ Me ₃ Si 0 0H Me R H	$\begin{array}{c} \sim 96.0 \\ 100.0 \\ 100.0 \end{array}$ $\begin{array}{c} \text{OH} \\ \text{Me}_{3}\text{Si} \\ \text{Me} \\ \text{H} \end{array}$
	4	$R = Me$ $R = i-C_3H_7$ H Me Me $SiMe_3$	≫ 99.0 100.0 H - O Me SiMe ₃	$Me \xrightarrow{H} 0 \xrightarrow{OH} Me$ $SiMe_3 \xrightarrow{99.0}$

Synthetic utility of these results is evident from the fact that desilylation (replacement of $(CH_3)_3Si$ -group with H) in related substrates is known to proceed with complete retention of configuration at the oxiranyl carbon.¹³ We have readily achieved this by simply stirring the epoxysilyl-alcohols with excess cesium fluoride¹⁴ (5-6 equ.) in DMSO at room temperature.

Extensions of these studies to include:

- (i) homo and bishomo allylic alcohols strategically substituted with (Me) $_3$ Si- or $(i-C_3H_7)_3$ Si-group.
- (ii) kinetic resolution and asymmetric epoxidations according to the procedure of Sharpless and Coworkers⁷; epoxidations using m-chloroperbenzoic acid.
- (iii) Simmon-Smith cycloproponations of silyl substituted acyclic allylic alcohols are envisaged and we hope to report on these aspects of our work in future.

In conclusion, of the various transition state models (e.g. see: preferred angle proposal⁵, tetrahedral vanadate ester open chain model⁶, and vanadium trigonal bipyramid model⁵), which have been invoked for V^{5^+} -catalyzed TBHP epoxidations, our total selectivities reported in this communication admirably support vanadium trigonal bipyramid model⁵, and is to be preferred.

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