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STEREOSELECTIVE INTRODUCTION OF CHIRAL CENTRES IN ACYCLIC PRECURSORS : A PROBE INTO THE TRANSITION STATE OF m-CHLOROPERBENZOIC (m-CPBA) ACID EPOXIDATION OF ACYCLIC ALLYLIC ALCOHOLS AND ITS SYNTHETIC IMPLICATIONS.*

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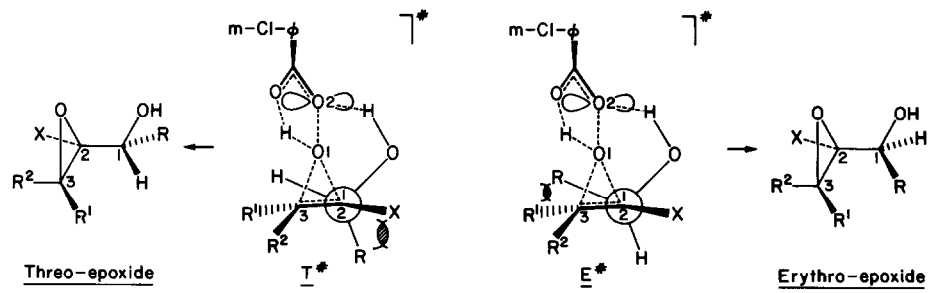
Summary: The magnitude of $A^{(1,3)}$-interaction far exceeds that of $A^{(1,2)}$-interaction in the transition state for the organic per-acid epoxidation of acyclic allylic alcohols.

Theoretical considerations have established that an energy difference of ∿3 Kcal mol^{-1} at 27°C between the competing diastereomeric transition states is sufficient to achieve >99% stereoselectivity for kinetically controlled reactions.[1] With this in mind we have analysed the interactions within the diastereomeric transition states for the stereoselective epoxidation of acyclic allylic alcohols using (i) organic peroxy-acids,[2] (ii) V^{+5}-catalyst and t-butylhydroperoxide (TBHP),[3] and (iii) for the kinetic deprotonation of acyclic carbonyl derivatives.[4] Along with the spectacular achievements of Sharpless and Coworkers[5] for asymmetric epoxidation of acyclic allylic alcohols, the above three reactions have been widely exploited in recent years for achieving regio-, stereo-, chemo- and enantio-selectivity in acyclic precursors.[6]

In a recent communication[3] from this laboratory, we have reported on our work which has provided vital information regarding the possible transition state model for V^{+5}-catalyzed TBHP epoxidation of acyclic allylic alcohols. In this Letter, we present results of our experiments which were aimed at probing the transition state of m-CBPA epoxidation of acyclic allylic alcohols.

Transition State Model: The working model[7] for the threo-transition state ($T^{\#}$) and erythro-transition state ($E^{\#}$) that we have established for the observed (see Table 2) π-facial selectivity in the epoxidation[8] of acyclic allylic alcohols is illustrated below. In both $T^{\#}$ and $E^{\#}$, we assume[8] substantially more pyramidization at C-3 as compared with C-2.

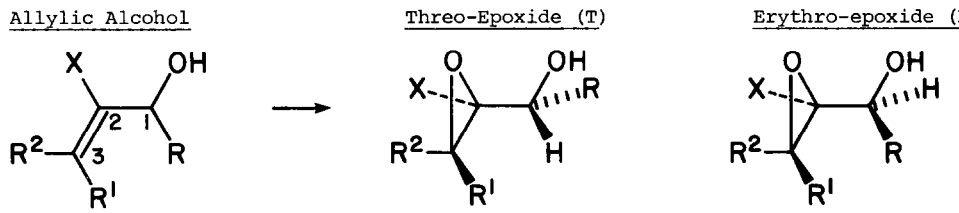


* Dedicated to Dr Sukh Dev on the occasion of his 60th birthday.

The indicated preferred conformation of the allylic OH-group in both $T^{\#}$ and $E^{\#}$ arises as a consequence of its ability[9] to hydrogen bond with the p-type lone pair (HOMO) on oxygen-2 [(O-2)--H—O distance, $\tilde{-}$ 3.1A°] of the per-acid, while the other substituent at C-1 is oriented periplanar to the partially formed (O-1)-(C-2) bond. This is in line with the recent theoretical work of Houk and Coworkers[10] on the staggered models for 1,2-asymmetric induction. Such a conformation also provides for the centre of the C=Cπ orbital (HOMO) to attack oxygen-1 from a distance of ∿2.0A°, backside to and colinear with the peroxide bond being broken.[11]

Evaluation of Diastereomeric Transition State Interactions for m-CPBA Epoxidation of Acyclic Allylic Alcohols: A quick perusal of the Table 1 reveals that while for entry 1-4, threo-epoxides predominate, reaching a zenith value for entry 3 and 4, the erythro-epoxide is the sole product for entry 6. A careful analysis of the diastereomeric transition state $T^{\#}$ and $E^{\#}$ shown above suggests that while $E^{\#}$ is destabilized as a consequence of $A^{(1,3)}$-interactions[2] between the syn-substituents R and R^1 at C-1 and C-3 (entry 1-4) the $T^{\#}$ suffers from a mild

Table 1 Stereoselectivity in the Epoxidation of Acyclic Allylic Alcohols with m-CPBA.[2]



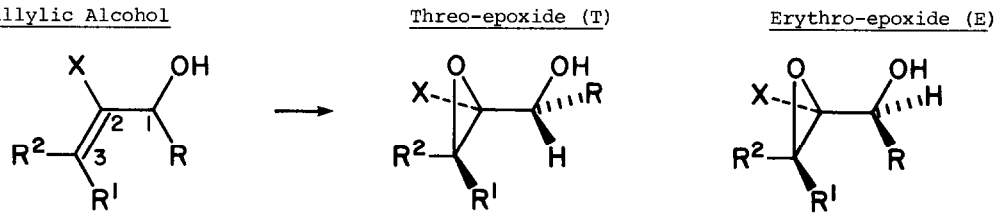
Entry:	X	R	R^1	R^2	(T:E Ratio)
1	H	Me	H	Me	67:31
2	H	Me	H	H	60:40
3	H	Me	Me	H	95:5
4	H	Me	Me	Me	95:5
5	Me	Me	H	H	45:55
6	$-SiMe_3$	ϕ	H	H	0:100

$A^{(1,2)}$-strain, the magnitude of which being highly dependent on the steric bulk and torsional angle of the 1,2-substitutes which relate them (e.g., (C-1)-R and (C-2)-X, torsional angle ∿ 50°-60°, entry 5 and 6).

A Probe into the Transition State of m-CPBA Epoxidation of Acyclic Allylic Alcohols: Taking into account the above postulated interactions, we thought that by a strategic positioning of a Me_3Si-group (A value[12]: 2.4-2.6) at C-2 or C-3 of the parent allylic alcohol, one could substantially increase $A^{(1,2)}$-interaction for $T^{\#}$ and dramatically increase 1,3-syn-interaction (Cf. $A^{1,3}$-strain) for $E^{\#}$ illustrated above. Thus by replacing R^1=H at C-3 with Me_3Si-group in entry 2, Table 1, threo selectivity must increase dramatically. Likewise, by substituting X=H at C-2 with Me_3Si-group in entry 1 and 2, Table 1, erythro selectivity should increase, although not dramatically.

In order to test the likelihood of our hypothesis, m-CPBA epoxidations of several representative silyl-substituted acyclic allylic alcohols[13] were performed in dry dichloromethane initially at 0°C leading to ambient temperature (∿20°C). The indicated 2,3-epoxysilyl-alcohols (Table 2) were produced in 65-92% yields and the assigned stereo-structures are in full accord with their spectroscopic data (^{1}H and ^{13}C NMR, Mass and IR).

Table 2: Stereochemistry of Epoxidation of Silyl substituted Acyclic Allylic Alcohols with m-CPBA.



Entry	X	R	R^1	R^2	(T:E Ratio)
1	$SiMe_3$	Me	H	H	40:60
2	$SiMe_3$	$i\text{-}C_3H_7$	H	H	24:76
3	$SiMe_3$	Me	H	Me	12:88
4	$SiMe_3$	ϕ	H	H	0:100
5	$SiMe_3$	Me	Me	H	80:20
6	H	Me	$SiMe_3$	H	99:1
7	H	$i\text{-}C_3H_7$	$SiMe_3$	H	100:0
8	H	Me	$SiMe_3$	Me	99:1

From the observed ratio of the diastereomeric 2,3-epoxysilyl-alcohols in Table 2, it can be seen that in accord with our expectation, the erythro-epoxides are the dominant products when a Me_3Si-group is placed at C-2 (entry 1 to 4). Interestingly, the Me group at C-3 (R^2= Me, entry 3) also enhances the erythro-selectivity (Cf., entry 1 & 2 with entry 3), presumably due to the steric strain in $T^{\#}$, arising because of the cumulative interaction between the Me at C-1, Me_3Si at C-2 and Me at C-3, relative to $E^{\#}$. Notice that the cis-substituent i.e. R^1 at C-3 (entry 1 to 4) is not an alkyl group, in the presence of which (entry 5) $A^{(1,3)}$-strain overrides the $A^{(1,2)}$-interaction, thereby leading to threo-selectivity. In the absence of a bulky substituent at C-2 and presence of a syn-Me_3Si group at C-3 (entry 6,7 and 8), total threo-selectivities were expected, and are observed, which is indeed gratifying.

Synthetic utility of these results is evident from the fact that desilylation (replacement of Me_3Si with hydrogen atom) of such substrates[3,14] is known to proceed with complete retention of configuration at the oxiranyl carbon. Fundamental chemistry associated with our 2,3-epoxysilyl-alcohols has not yet been investigated, but in view of the growing importance of 2,3-epoxy alcohols in the synthesis of complex natural products,[15,16] such a study should prove rewarding.

In conclusion, the discussion presented above provides a vivid demonstration of the viability of our analysis which is in accord with the Curtin-Hammett Principle[17] and differs from that of Kishi and Coworkers[16] who have relied upon the preferred conformation of the Sp^3-Sp^2 carbon-carbon single bond of the allylic alcohol. The merit of the latter argument was assumed to rest on the principle of least conformational distortion,[18] but strictly speaking it is not valid here because of the strong direct influence of the hydroxyl group on the approach of the per-acid.

ACKNOWLEDGMENT

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