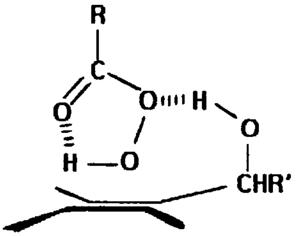
Tetrahedron Letters,Vol.26,No.40,pp 4895-4898,1985 0040-4039/85 \$3.00 + .00
Printed in Great Britain

SYN-STEREOSELECTIVE EPOXIDATION OF ALLYLIC ETHERS USING CF_3CO_3H.

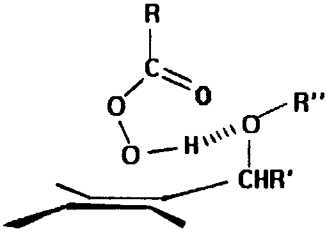
Brian A. McKittrick and Bruce Ganem*
Department of Chemistry
Baker Laboratory
Cornell University
Ithaca, NY 14853, USA

Summary: Good *syn*-stereoselectivity is observed in the epoxidation of allylic silyl ethers with CF_3CO_3H, indicating a new type of hydrogen-bonded transition state.

The well-known *syn*-epoxidation of allylic and homoallylic alcohols by organic peracids has been attributed to hydrogen bonding between the alkene's OH group and an acceptor oxygen on the peracid, as depicted in 1 below.$^{1-5}$ Consistent with the alcohol serving as an H-bond donor, allylic ethers and acetates are epoxidized at diminished rates and afford mostly the *anti* isomer as a result of steric interactions. Recently, Chavdarian and Heathcock^{6} and others^{7} reported that trimethylsilyl ethers exerted the most pronounced *anti* directive effect: with *m*-chloroperoxybenzoic acid (MCPBA), cyclohexenyl TMS ether afforded a 9:1 ratio of *anti*:*syn* epoxides. In the course of synthetic studies on the antileukemic agent quasimarin,^{8} we attempted the epoxidation of a sterically hindered allylic *t*-butyldimethylsilyl (TBDMS) ether using CF_3CO_3H. The predominance of *syn*-product we observed suggested that highly acidic peracids might direct the epoxidation of certain alkenes bearing allylic H-bond acceptor substituents via alternative complex 2.^{9} Here we describe studies comparing the reactivity of MCPBA and CF_3CO_3H which lend support to this idea.



1

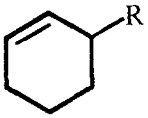


2

Table I presents the peracid oxidation of several allylically substituted cyclohexenes. Note that the CF_3CO_3H epoxidation of 2-cyclohexenol itself (which has apparently not been reported before) was considerably more *syn*-stereoselective than with MCPBA. Moreover in each case studied, reaction with CF_3CO_3H in CH_2Cl_2 afforded a higher proportion of *syn*-product than with MCPBA in CH_2Cl_2. When CF_3CO_3H oxidations were run in tetrahydrofuran (THF, to disrupt hydrogen-bonding), predominantly *anti*-products were obtained. Competition experiments revealed the expected relative reactivity 3 > 4 > 7.

The *syn*-directive effect was most striking with TBDMS ether 4, where almost a complete stereochemical reversal was achieved merely by switching peracids. Preparatively useful yields of the cis-epoxyether could thus be obtained. *Syn*-selectivity was lower with triethylsilyl or diphenylmethylsilyl ethers, and also with benzyl ethers. Trimethylsilyl ethers were unstable to CF_3CO_3H.

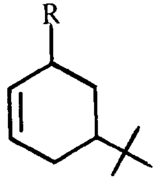
TABLE I

ALKENE		EPOXIDE SYN:ANTI RATIO[a,b]	
		$CF_3CO_3H/CH_2Cl_2/-40^oC$[c]	$MCPBA/CH_2Cl_2/0^oC$
3	R= OH	50:1 (76%)	24:1
4	= OTBDMS	4.5:1 (82%) (1:7.5 in THF)	1:6.7
5	= OBn	1.4:1 (78%) (1:5 in THF)	1:2.7
6	= OCH_3	1:1.3	1:2.3
7	= OAc	1:1.1 (1:3 in THF)	1:1.5
8	= SO_2Ph	1:1.3 (78%)	1:4.3

(a) Yields in parentheses are for isolated, pure products.
(b) Ratios were determined by capillary GLC on a 25m Quadrex column packed with 0.5μ SE-30 methyl silicone.
(c) Buffered with 5-10 equiv Na_2HPO_4.

It was also of interest to determine whether the pseudoaxial or pseudoequatorial allylic isomers exhibited greater syn-stereoselectivity in CF_3CO_3H epoxidations. In published studies on conformationally biased allylic alcohol pairs like 9 and 10, common peracids such as MCPBA or perbenzoic acid generally reacted faster and gave more syn product with the pseudoequatorial epimer.[2] Table II summarizes several oxidations of 5-t-butyl-2-cyclohexenol derivatives using both MCPBA and CF_3CO_3H. Besides confirming the known behavior of MCPBA, Table II indicates that the pseudoaxial ethers 11 and 13 afforded the highest syn-selectivity with CF_3CO_3H in CH_2Cl_2. There was, as anticipated, a dramatic solvent effect: when 11 was treated with CF_3CO_3H in THF, a 1:12 syn:anti ratio of epoxides was obtained. Anti products also predominated in oxidations of 12 and 14, suggesting that the oxygen in these equatorial epimers is incorrectly disposed to participate in the hydrogen bonding depicted in 2. The fact that CF_3CO_3H, unlike MCPBA, highly selectively oxidized both 9 and 10 to the corresponding syn-epoxyols is further evidence that the more acidic peracid may hydrogen bond to an allylic hydroxyl group in either of the two favorable orientations 1 and 2.[9]

TABLE II

		EPOXIDE SYN:ANTI RATIO[a,b]	
ALKENE		$CF_3CO_3H/CH_2Cl_2/-40^oC$[c]	$MCPBA/CH_2Cl_2/0^o$
9	R= α-OH	100:1	5.2:1
10	R= β-OH	100:1	24:1
11	R= α-OTBDMS	12.4:1 (89%)	1:7.6
12	R= β-OTBDMS	1:5.5 (60%)	1:3.8
13	R= α-OBn	5:1	1:4.5
14	R= β-OBn	1:2.4	1:2.5

(a) Yields in parentheses are for isolated, pure products.

(b) Ratios were determined by capillary GLC on a 25m Quadrex column packed with 0.5μ SE-30 methyl silicone.

(c) Buffered with 5-10 equiv Na_2HPO_4.

ACKNOWLEDGMENT: We thank the National Institutes of Health (GM 30050) for generous financial assistance. Support of the Cornell Nuclear Magnetic Resonance Facility by NSF (CHE 7904825, PCM 8018643) and NIH (RR02002) is gratefully acknowledged.

REFERENCES AND FOOTNOTES

1. Henbest, H.B.; Wilson, R.A.L. J. Chem. Soc. 1957, 1958.
2. (a) Chamberlain, P.; Roberts, M.L.; Whitham, G.H. J. Chem. Soc. (B), 1970, 1374.
   (b) Dehnel, R.B.; Whitham, G.H. J. Chem. Soc. Perkin I, 1979, 953.
3. Narula, A.S. Tetrahedron Lett., 1981, 22, 2017.
4. Itoh, T.; Jitsukawa, K.; Kaneda, K.; Teranishi, S. J. Am. Chem. Soc., 1979, 101, 159.
5. For a comprehensive review, see Berti, G. Topics in Stereochemistry, 1973, 7, 93.
6. Chavdarian, C.G.; Heathcock, C.H. Syn. Commun., 1976, 6, 277.
7. Schlessinger, R.H.; Lopes, A. J. Org. Chem., 1981, 46, 5252.
8. Batt, D.G.; Takamura, N.; Ganem, B. J. Am. Chem. Soc., 1984, 106, 3353.
9. This effect may also explain the following observations: (a) epoxidation of trans, trans-3,4,5-tribenzoyloxycyclopentene using CF_3CO_3H in sulfolane occurs syn to the two allylic benzoates: Sinnott, M.L.; Widdows, D. J. Chem. Soc. Perkin I., 1981, 401; (b) epoxidation of (2-cyclohexenyl)acetate 7 with 2-hydroperoxy-hexafluoro-2-propanol affords a 4:1 syn:anti ratio: Heggs, R.P.; Ganem, B. J. Am. Chem. Soc., 1979, 101, 2484.

(Received in USA 8 July 1985)