Regio- and Diastereoselective Catalytic Epoxidation of Acyclic Allylic Alcohols with Methyltrioxorhenium: A Mechanistic Comparison with Metal (Peroxy and Peroxo Complexes) and Nonmetal (Peracids and Dioxirane) Oxidants

Waldemar Adam,* Catherine M. Mitchell, and Chantu R. Saha-Möller

Institute of Organic Chemistry, University of Würzburg, Am Hubland, D-97074 Würzburg, Germany

Received February 8, 1999

Geraniol and its 1-methyl derivative (regiochemical probes) and a set of methyl- and *tert*-butyl-substituted chiral allylic alcohols (stereochemical probes) have been used to elucidate the mechanism of the MTO-catalyzed epoxidation of allylic alcohols. The regiochemical probes are preferentially epoxidized at the unfunctionalized double bond by these MTO-based oxidants, which establishes that MTO/UHP and MTO/H_2O_2/pyridine mainly operate through hydrogen bonding. Metal-alcoholate binding does not apply, which is in contrast to the transition-metal oxidants $VO(acac)_2$/*t*-BuOOH, $Mo(CO)_6$/*t*-BuOOH, $MoO_2[PhCON(Ph)O]_2$/*t*-BuOOH, $MoO(O_2)[PhCON(Ph)O]_2$, and H_2WO_4/H_2O_2. For the stereochemical probes, the diastereoselectivity data show a good correspondence between the MTO-catalyzed systems (MTO/UHP and MTO/H_2O_2/pyridine) and the perhydrate-type oxidant Ti-β/H_2O_2 and the peracid *m*-CPBA. Conformational control through 1,3-allylic strain results in a high threo diastereoselectivity, in which hydrogen bonding between the hydroxy functionality and the rhenium catalyst is the decisive electronic feature. All these selectivity data are consistent with the rhenium peroxo complex as the active oxidant.

Introduction

Methyltrioxorhenium (MTO) has been the focus of much interest as oxidation catalyst in recent years.[1] Numerous such transformations have been reported for this versatile, selective, and highly active catalyst. The rapidly increasing number of applications of MTO in organic synthesis has been accompanied by intensive mechanistic investigations of these oxygen-transfer processes.[1c]

The catalytic cycle for oxidations with MTO/H_2O_2 is depicted in Scheme 1, in which the peroxo species **B** and **D** have been accepted as the catalytically active species.[1b−e] The diperoxo rhenium complex $CH_3ReO(O_2)_2 \cdot H_2O$ (**D**) has been isolated, characterized by X-ray crystallography, and shown to be catalytically active;[2] however, it should be added that the relative reactivity of complex **D** and its monoperoxo analogue $CH_3ReO_2(O_2)$ (**B**) has been a matter of controversial debate.[2,3] A recent computational study (DFT method) comes to the conclusion that the stability of the mono- and diperoxo complexes is similar and, thus, both should be capable of transferring oxygen.[4] Kinetic studies have shown that the H_2O_2 nucleophilically adds to MTO and the hydroperoxy species **A** is first formed,[5] which subsequently rearranges to yield the monoperoxo rhenium complex **B**. By an analogous sequence of events, the diperoxo complex **D** results through the intervention of the hydroperoxy complex **C**. O-17 labeling experiments[2] suggest that the formation of the peroxo complexes **B** and **D** from the hydroperoxy species **A** and **C** is reversible.[6] Although to date no catalytic data have been reported for the hydroperoxy complexes **A** and **C**, the question as to their catalytic activity and efficacy must, nevertheless, be posed.

The hydroxy-group directivity of chiral allylic alcohols is a useful tool for the investigation of the transition-state geometry in stereoselective epoxidation reactions.[7] In these transformations, the two π faces of the allylic double bond are differentiated by a hydroxy-directing effect of the allylic alcohol group, with either the threo or the erythro epoxide formed preferentially. The stereodifferentiation by this hydroxy-group directivity depends on the type of bonding between the substrate and the oxidizing species, which is expressed in the dihedral angle

* To whom correspondence should be addressed. Fax: +49(0)931/8884756. E-mail: adam@chemie.uni-wuerzburg.de.

(1) (a) Herrmann, W. A. *J. Organomet. Chem.* **1995**, *500*, 149−174. (b) Espenson, J. H.; Abu-Omar, M. M. *Adv. Chem. Ser.* **1997**, *253*, 99−134. (c) Gable, K. P. *Adv. Organomet. Chem.* **1997**, *41*, 127−161. (d) Herrmann, W. A.; Kühn, F. E. *Acc. Chem. Res.* **1997**, *30*, 169−180. (e) Romão, C. C.; Kühn, F. E.; Herrmann, W. A. *Chem. Rev.* **1997**, *97*, 3197−3246.

(2) Herrmann, W. A.; Fischer, R. W.; Scherer, W.; Rauch, M. U. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1157−1160.

(3) (a) Fischer, R. W. Ph.D. Thesis, T. U. München, 1994. (b) Al-Ajlouni, A. M.; Espenson, J. H. *J. Am. Chem. Soc.* **1995**, *117*, 9243−9250.

(4) Gisdakis, P.; Antonczak, S.; Köstlmeier, S.; Herrmann, W. A.; Rösch, N. *Angew. Chem., Int. Ed. Engl.* **1998**, *37*, 2333−2336.

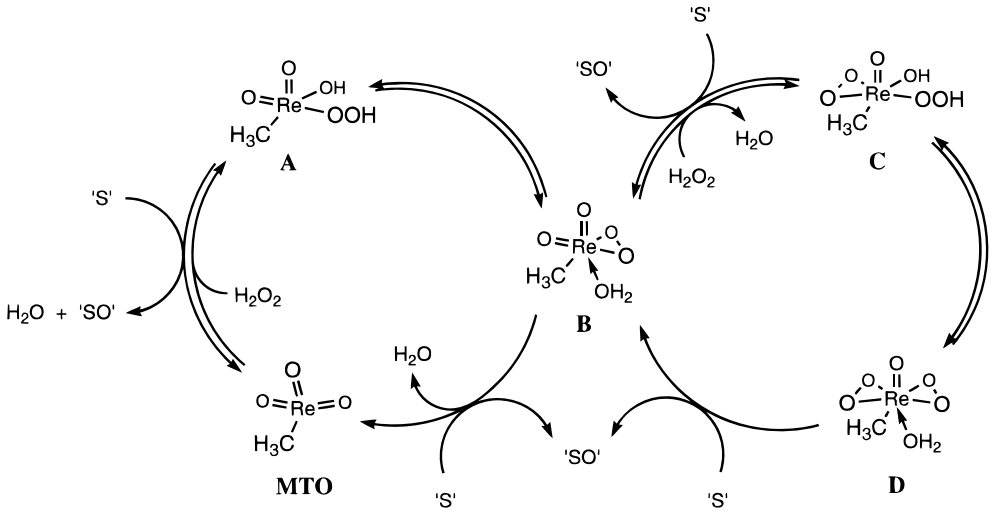
(5) Pestovsky, O.; van Eldik, R.; Huston, P.; Espenson, J. H. *J. Chem. Soc., Dalton Trans.* **1995**, 133−137.

(6) In an isotope exchange process the terminal oxo ligand of the rhenium diperoxo complex $CH_3ReO(O_2)_2 \cdot H_2O$ (**D**) can be rapidly exchanged to ^{17}O with $H_2{}^{17}O$. It is proposed that the isotopically labeled oxo ligand results from the initial addition of $H_2{}^{17}O$ to a peroxo group (formation of labeled **A** and **C**!). Subsequent rearrangement within the ligand sphere and the elimination of $H_2{}^{16}O$ gives the labeled peroxo species **B** and **D**.

(7) (a) Hoffmann, R. W. *Chem. Rev.* **1989**, *89*, 1841−1860. (b) Adam, W.; Nestler, B. *Tetrahedron Lett.* **1993**, *34*, 611−614. (c) Adam, W.; Mitchell, C. M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 533−535. (d) Adam, W.; Kumar, R.; Reddy, T. I.; Renz, M. *Angew. Chem., Int. Ed. Engl.* **1996**, *35*, 880−882. (e) Adam, W.; Smerz, A. K. *J. Org. Chem.* **1996**, *61*, 3506−3510. (f) Smerz, A. K. Ph.D. Thesis, Universität Würzburg, 1996. (g) Adam, W.; Corma, A.; Reddy, T. I.; Renz, M. *J. Org. Chem.* **1997**, *62*, 3631−3637.

10.1021/jo9902289 CCC: $18.00
Published on Web 04/30/1999

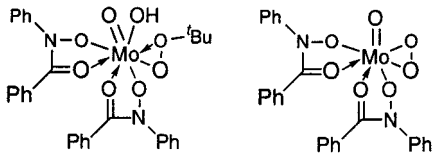
Scheme 1. Catalytic Cycle of MTO-Catalyzed Oxidations



(C=C−C−O) of the allylic alcohol and by the conformational control by 1,2- and 1,3-allylic (^{1,2}A and ^{1,3}A) strain.[7c−g] The synergism between the hydroxy-directing effect and the steric interactions caused by allylic strain are reflected in the diastereoselectivities of the oxygen transfer to the stereochemical probes (methyl- and *tert*-butyl-substituted allylic alcohols). Valuable structural information may be obtained on the transition state in both catalytic and stoichiometric epoxidations, e.g., as previously demonstrated for dioxiranes, peracids, and vanadium and titanium complexes.[7b,d−g,8] On the basis of the diastereoselectivity data, the dihedral angles (α) of these oxidation systems have been reported to lie in a range from as acute as 50° for $VO(acac)_2$, to 120° for *m*-CPBA, and to as obtuse as 130° for DMD.[7g]

By the use of regiochemical probes with allylic and unfunctionalized double bonds, e.g., geraniol (**1r**), the electronic nature of the association between the oxidant and the allylic alcohol may be assessed, i.e., hydrogen bonding versus metal-alcoholate binding. For the stoichiometric oxidants *m*-CPBA, DMD, and some molybdenum and tungsten peroxo complexes, hydrogen bonding has been documented,[7e,9] while metal-alcoholate binding applies in the catalytic systems $VO(acac)_2$/*t*-BuOOH, $Mo(CO)_6$/*t*-BuOOH, and H_2WO_4/H_2O_2.[10]

Herein we present the full details of the MTO-catalyzed regio- and diastereoselective epoxidation of acyclic allylic alcohols with UHP (urea/hydrogen peroxide adduct) and H_2O_2 (30%)/pyridine as oxygen sources. Besides the chiral allylic substrates **1**, derivatives have been employed in which the allylic hydroxy group is either capped by methylation or acetylation or is replaced by other functionalities not capable of donating hydrogen bonds. The observed regio- and diastereoselectivities are compared with those of the reported catalytic oxidation systems Ti-β/H_2O_2, $VO(acac)_2$/*t*-BuOOH, $Mo(CO)_6$/*t*-BuOOH, MoO_2-$[PhCON(Ph)O]_2$/*t*-BuOOH (**E**), and H_2WO_4/H_2O_2 and the stoichiometric oxidants *m*-CPBA, DMD, and $MoO(O_2)$-$[PhCON(Ph)O]_2$ (**F**) to deduce a likely transition-state geometry for the MTO oxidants.



E **F**

Results

The oxidation of the allylic alcohols **1** with MTO as catalyst led exclusively to the corresponding epoxy alcohols **2**; in most cases, no α,β-unsaturated ketones were obtained and cis−trans isomerization was not observed (Scheme 2). The usual secondary reactions that occur in epoxidations, i.e., hydrolysis, cleavage, and rearrangement, could be successfully avoided with the oxidants MTO/UHP and MTO/30% H_2O_2/pyridine.[11] The results of the product studies are given in Table 1.

With the homogeneous oxidizing system MTO/H_2O_2 (30%)/pyridine, the conversions were good to excellent for all allylic alcohols **1**; however, for the heterogeneous oxidant MTO/UHP, a pronounced substrate dependence was observed. The conversions of the methyl-substituted allylic alcohols **1b**−**i** (60−95%) and the *tert*-butyl-substituted derivatives **1j**−**l** (61−74%), which have the *tert*-butyl group at the stereogenic center, were good to excellent with MTO/UHP. In contrast, lower conversions were observed for substrates **1m**−**o** (12−56%) with the *tert*-butyl substituent at the double bond.

Quite generally and expectedly, substrates **1b**,**d** (Table 1, entries 1 and 3) without allylic strain are epoxidized in low threo diastereoselectivity. The substrates **1e**,**h**,**i** (entries 4, 7, and 8) with 1,3-allylic strain display threo selectivity, whereas the derivatives **1c**,**f** (Table 1, entries 2 and 5) with 1,2-allylic strain are oxidized unselectively with both catalytic oxidants MTO/UHP and MTO/30% H_2O_2/pyridine. For the stereochemical probe **1g** (Table 1, entry 6) with both 1,2- and 1,3-allylic strain, the threo-epoxide prevails.

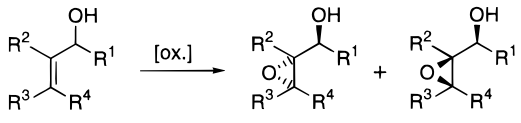
(8) Rossiter, B. E.; Verhoeven, T. R.; Sharpless, K. B. *Tetrahedron Lett.* **1979**, 4733−4736.

(9) (a) Sharpless, K. B.; Verhoeven, T. R. *Aldrichim. Acta* **1979**, *12*, 63−74. (b) Arcoria, A.; Ballistreri, F. P.; Tomaselli, G. A.; Di Furia, F.; Modena, G. *J. Org. Chem.* **1986**, *51*, 2374−2376.

(10) (a) Sharpless, K. B.; Michaelson, R. C. *J. Am. Chem. Soc.* **1973**, *95*, 6136−6137. (b) Prat, D.; Lett, R. *Tetrahedron Lett.* **1986**, *27*, 707−710.

(11) (a) Copéret, C.; Adolfsson, H.; Sharpless, K. B. *J. Chem. Soc., Chem. Commun.* **1997**, 1565−1566. (b) Rudolph, J.; Reddy, K. L.; Chiang, J. P.; Sharpless, K. B. *J. Am. Chem. Soc.* **1997**, *119*, 6189−6190.

Scheme 2. MTO-Catalyzed Epoxidation of Allylic Alcohols



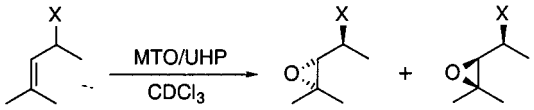
1 *threo*-**2** *erythro*-**2**

1,2	R^1	R^2	R^3	R^4
a	H	Me	H	H
b	Me	H	H	H
c	Me	Me	H	H
d	Me	H	Me	H
e	Me	H	H	Me
f	Me	Me	Me	H
g	Me	Me	H	Me
h	Me	H	Me	Me
i	Me	Me	Me	Me
j	*t*-Bu	Me	H	H
k	*t*-Bu	H	Me	H
l	*t*-Bu	H	H	Me
m	Me	*t*-Bu	H	H
n	Me	H	*t*-Bu	H
o	Me	H	H	*t*-Bu
p	Me	H	H	*n*-Bu
q	*i*-Pr	H	Me	H

More subtle differences in the diastereoselectivities for MTO/UHP were observed for the *tert*-butyl-substituted allylic alcohols **1j**−**o** (Table 1, entries 9−14). The two allylic alcohols **1k** and **1n** (Table 1, entries 10 and 13), which have a substituent in the trans position of the double bond, showed only moderate threo selectivity, as did substrate **1o** (Table 1, entry 14), despite the fact that it possesses 1,3-allylic strain due to the *tert*-butyl group in the cis position. It is significant to note that for the corresponding *n*-butyl-substituted allylic alcohol **1p** (data not shown in Table 1), the threo selectivity (89:11) is much higher. In the case of the allylic alcohol **1l** (Table 1, entry 11) with 1,3-allylic strain, the *threo*-epoxy alcohol **2l** was obtained essentially exclusively. For the two *geminally* substituted allylic alcohols **1j**,**m**, threo selectivity was observed for **1j** (Table 1, entry 9), but erythro selectivity for **1m** (Table 1, entry 12). The diastereoselectivities obtained in the epoxidation of the *tert*-butyl-substituted allylic alcohols **1j**,**l**,**m**,**n** with the oxidant MTO/30% H_2O_2/pyridine are similar to those for the MTO/UHP combination. However, substrate **1k** (Table 1, entry 10) gave the corresponding epoxy alcohols **2k** as a ca. 50:50 mixture of threo and erythro diastereomers with MTO/30% H_2O_2/pyridine, while allylic alcohol **1o** (Table 1, entry 14) was epoxidized exclusively to *threo*-**2o**.

A substantial solvent effect was observed on the threo/erythro ratio of the epoxides **2g** (Table 1, entry 6) and epoxide **2q** (data not shown). While high threo selectivity (91:9) was observed for allylic alcohol **1g** in deuteriochloroform, the ratio dropped to 39:61 in methanol-d_4. Similarly, for substrate **1q** the threo/erythro diastereoselectivity decreased from 72:28 to 55:45 in $CDCl_3$ versus CD_3OD.

Scheme 3. Diastereoselectivities (Threo/Erythro) for the MTO-Catalyzed Epoxidation of the Allylic Derivatives 3h−6h



1h,3h-6h	**2h,7h-10h** *threo*		*erythro*
1h: X = OH	83	:	17
3h: X = OMe	77	:	23
4h: X = OAc	34	:	66
5h: X = SO_2Ph	≤5	:	95
6h: X = $NBoc_2$	31	:	69

For the allylic derivatives **3h**−**6h** (Scheme 3), the diastereoselectivities with MTO/UHP were lower or even reversed compared to the alcohol **1h** (Table 1, entry 7). Most notably, for the sulfone **5h** the corresponding *erythro*-epoxide was obtained exclusively (≤5:95). While the parent allylic amine was not epoxidized at all by the MTO/UHP oxidant even in the coordinating solvent methanol-d_4 (possibly due to coordination of the substrate to the catalyst), a moderate erythro selectivity was observed for the diBoc-protected amine **6h** (31:69).

The regioselectivity in the epoxidation with MTO/UHP was tested with geraniol (**1r**) and its methyl derivative **1s** (Scheme 4). The remote olefinic double bond is epoxidized preferentially over the allylic one for both substrates **1r**,**s**. In the epoxidation of geraniol (**1r**) in $CDCl_3$ the regioselectivity with the oxidant MTO/30% H_2O_2/pyridine (18:82) is similar to that obtained with the system MTO/UHP (22:78). In the hydrogen-bonding methanol, the regioselectivity is shifted even further toward the remote double bond. As expected, 1-methylgeraniol (**1s**) showed no diastereoselectivity (dr 50:50) for the remote double bond, while the threo isomer is favored for the allylic double bond; as expected, the threo/erythro ratio is lower in methanol than in $CDCl_3$.[12]

The reactivities of allylic versus homoallylic alcohols were tested for the substrates **1a** and **1a′** (Scheme 5). A competition experiment showed that the relative conversions to the corresponding epoxides **2a** and **2a′** was 42:58. Thus, the homoallylic alcohol is only marginally more reactive than the allylic one.

For comparison purposes with the MTO results, the oxidation of the allylic alcohols **1** with other transition-metal catalysts was examined. To this end, the already thoroughly investigated catalytic epoxidations by $Mo(CO)_6$/*t*-BuOOH and H_2WO_4/H_2O_2 were employed.[8−10,13,14] MoO_2[PhCON(Ph)O]$_2$/*t*-BuOOH (**E**) and $MoO(O_2)$[PhCON(Ph)O]$_2$ (**F**) were selected to compare alkylperoxy versus peroxo complexes as oxidants.

$Mo(CO)_6$/*t*-BuOOH and H_2WO_4/H_2O_2 showed a similar reactivity at ambient temperature as MTO/UHP (data are given as Supporting Information); small amounts (<10%) of the enone side product were observed for **1f** with $Mo(CO)_6$/*t*-BuOOH and for **1c**,**f** with H_2WO_4/H_2O_2.

(12) Adam, W.; Mitchell, C. M.; Paredes, R.; Smerz, A. K.; Veloza, L. A. *Liebigs Ann./Recueil* **1997**, 1365−1369.

Table 1. Conversions, Mass Balances, and Diastereoselectivities (Threo/Erythro) in the Epoxidation of Methyl- and *tert*-Butyl-Substituted Allylic Alcohols with MTO as Catalyst

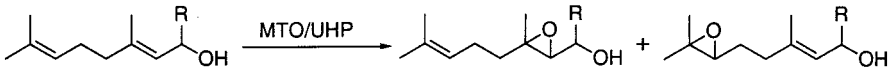
entry		R^1	R^2	R^3	R^4	[a]	MTO/ UHP [b]	MTO/ H_2O_2 (30%) [c]
1	**1b**	Me	H	H	H	convn m.b. d.r.	60 ≥95 60 : 40	
2	**1c**	Me	Me	H	H	convn m.b. d.r.	89 ≥95 50 : 50	≥95 63 41 : 59
3	**1d**	Me	H	Me	H	convn m.b. d.r.	82 ≥95 67 : 33	
4	**1e**	Me	H	H	Me	convn m.b. d.r.	90 ≥95 82 : 18	≥95 50 86 : 14
5	**1f**	Me	Me	Me	H	convn m.b. d.r.	84 ≥95 55 : 45	≥95 69 50 : 50
6	**1g**	Me	Me	H	Me	convn m.b. d.r.	95 ≥95 91 : 09 (39 : 61 [d])	≥95 61 80 : 20
7	**1h**	Me	H	Me	Me	convn m.b. d.r.	91 ≥95 83 : 17	≥95 64 81 : 19
8	**1i**	Me	Me	Me	Me	convn m.b. d.r.	≥95 ≥95 95 : 05	≥95 79 ≥95 : 05
9	**1j**	*t*-Bu	Me	H	H	convn m.b. d.r.	73 ≥95 64 : 36	92 ≥95 68 : 32
10	**1k**	*t*-Bu	H	Me	H	convn m.b. d.r.	61 ≥95 67 : 33	≥95 ≥95 44 : 56
11	**1l**	*t*-Bu	H	H	Me	convn m.b. d.r.	74 ≥95 ≥95 : 05	≥95 ≥95 92 : 08
12	**1m**	Me	*t*-Bu	H	H	convn m.b. d.r.	43 ≥95 23 : 77	67 ≥95 08 : 92
13	**1n**	Me	H	*t*-Bu	H	convn m.b. d.r.	56 ≥95 74 : 26	84 ≥95 81 : 19
14	**1o**	Me	H	H	*t*-Bu	convn m.b. d.r.	12 ≥95 69 : 31	95 ≥95 ≥95 : 05

[a] Conversions, mass balances, and diastereomeric ratios (*threo/erythro*) are given in %; error ca. ±5% of the stated values. [b] For entries 2-4 and 6-8 see ref 7c. [c] In the presence of 12 mol% pyridine; in the case of **1j** the corresponding enone (20%) was formed; **1n** led to 10% *cis-trans* isomerization products. [d] In methanol-d_4, all others in $CDCl_3$.

The oxidants MoO_2[PhCON(Ph)O]$_2$/*t*-BuOOH (**E**) and $MoO(O_2)$[PhCON(Ph)O]$_2$ (**F**) showed moderate to excellent reactivity (data are given in the Supporting Information), and high epoxide yields were obtained for most allylic alcohols within 2.5−5 h at 60 °C, with only traces of enone.

The diastereoselectivity data in Table 2 show that for the allylic alcohols **1c**,**f** without a *cis*-methyl substituent (no 1,3-allylic strain), but with a geminal methyl group (1,2-allylic strain), the molybdenum- and tungsten-based oxidation systems preferentially gave the corresponding *erythro*-epoxides in moderate to high diastereoselectivities (Table 2, entries 2 and 5). For substrate **1d** with a *trans*-methyl substituent (no 1,2- or 1,3-allylic strain), low threo selectivity was observed for $Mo(CO)_6$/*t*-BuOOH and MoO_2[PhCON(Ph)O]$_2$/*t*-BuOOH (**E**), while low erythro selectivity was obtained with $MoO(O_2)$[PhCON(Ph)O]$_2$ (**F**) and H_2WO_4/H_2O_2 (Table 2, entry 3). For the derivatives **1e**,**h** with a cis substituent (1,3-allylic strain and no 1,2-allylic strain), the threo selectivity was good to excellent for the catalytic oxidants $Mo(CO)_6$/*t*-BuOOH, MoO_2[PhCON(Ph)O]$_2$/*t*-BuOOH (**E**), and H_2WO_4/H_2O_2

Scheme 4. MTO-Catalyzed Epoxidation of Geraniol (1r) and Its Methyl Derivative 1s



		2,3-**2r**		*6,7*-**2r**
1r (R = H)	$CDCl_3$	22	:	78
	CD_3OD	14	:	86
		threo/erythro-3,4-**2s**		*threo/erythro-7,8*-**2s**
1s (R = Me)	CCl_4	24	:	76
		(d.r. 88 : 12)		(d.r. 50 : 50)
	CH_3OH/acetone (9:1)	19	:	81
		(d.r. 75 : 25)		(d.r. 50 : 50)

Table 2. Diastereoselectivities (Threo/Erythro) in the Epoxidation of Methyl-Substituted Allylic Alcohols 1 by Mo and W Complexes

		threo/erythro diastereoselectivities [a]			
entry	allylic alcohol	$Mo(CO)_6$/ *t*-BuOOH [b]	$MoO_2[PhCON(Ph)O]_2$/ *t*-BuOOH (**E**) [c]	$MoO(O_2)[PhCON(Ph)O]_2$ (**F**),(stoich.) [c]	H_2WO_4/ H_2O_2 (30%) [d]
1	 **1b**	44 : 56	35 : 65	07 : 93	15 : 85
2	 **1c**	16 : 84	*24 : 76*	*≤05 : 95*	*≤05 : 95*
3	 **1d**	62 : 38	71 : 29	27 : 73	40 : 60
4	 **1e**	84 : 16	*91 : 09*	*55 : 45*	*79 : 21*
5	 **1f**	*29 : 71*	*38 : 62*	*14 : 86*	*12 : 88*
6	 **1g**	*77 : 23*	*74 : 26*	*20 : 80*	*56 : 44*
7	 **1h**	95 : 05	94 : 06	70 : 30	90 : 10

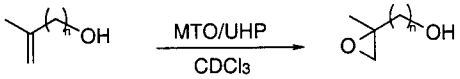
[a] Diastereoselectivities given in italics are this work; error ca. ±5% of the stated values. [b] For entries 1-4 and 7 see ref 8. [c] For entries 1,3, and 7 see ref 15. [d] For entries 1,3, and 7 see ref 14c.

(Table 2, entries 4 and 7). In contrast, the stoichiometric oxidant $MoO(O_2)[PhCON(Ph)O]_2$ (**F**) showed only a moderate (70:30) threo selectivity for **1h**, while **1e** was epoxidized unselectively (55:45). In the case of the stereochemical probe **1g** (Table 2, entry 6), which contains both *geminal* (1,2-allylic strain) and cis (1,3-allylic strain) substituents, threo diastereoselectivity was found for the catalytic oxidants $Mo(CO)_6$/*t*-BuOOH and MoO_2-$[PhCON(Ph)O]_2$/*t*-BuOOH (**E**). With the stoichiometric $MoO(O_2)[PhCON(Ph)O]_2$ (**F**), the *erythro*-epoxide was formed preferentially, while the catalytic H_2WO_4/H_2O_2 gave a ca. 50:50 mixture of the threo and erythro diastereomers.

Discussion

The present regio- and stereochemical data clearly establish a hydroxy-directing effect in the MTO-catalyzed

Scheme 5. MTO-Catalyzed Epoxidation of the Allylic Alcohol 1a and the Homoallylic Alcohol 1a′



1 **2**

a: n = 1;
a': n = 2

epoxidation of the chiral allylic alcohols **1**. The fact that in protic solvents such as methanol the regio- and diastereoselectivities are noticeably affected substantiates the hydrogen-bonding mechanism. In particular, the regioselectivity (Scheme 4) is enhanced in methanol in favor of the epoxidation of the unfunctionalized double bond to afford more of the *6,7*-**2r** (from **1r**) and *7,8*-**2s** (from **1s**) epoxides, while the threo diastereoselectivity is lowered for the substrate **1g** (Table 1, entry 6) in methanol-d_4 versus $CDCl_3$. This convincingly demonstrates that the intramolecular hydrogen bonding between the metal catalyst and the allylic alcohol in the transition-state complex is interfered with by intermolecular association with the protic solvent.

The question arises what the electronic nature of the interaction between the substrate and the metal catalyst is, e.g., hydrogen bonding or metal-alcoholate binding, to account for the observed directivity. For a variety of transition-metal oxidants, most prominently vanadium,[8,16] but also titanium[17] and molybdenum,[18] metal-alcoholate binding has been established, but this template effect does not operate in the present rhenium case. This becomes most evident on inspection of the regioselectivities obtained for geraniol (**1r**) and its methyl derivative **1s** as substrates (Scheme 4). Thus, with $VO(acac)_2$/*t*-BuOOH,[10a] Ti(O*i*-Pr)$_4$/*L*-DET/*t*-BuOOH,[19] $Mo(CO)_6$/*t*-BuOOH,[10a] and H_2WO_4/H_2O_2 (30%),[10b] geraniol (**1r**) is exclusively epoxidized at the functionalized allylic double bond to give *2,3*-**2r**; 1-methylgeraniol (**1s**) also affords the allylic epoxide *3,4*-**2s** in high regioselectivity with Ti(O*i*-Pr)$_4$/*t*-BuOOH and $VO(acac)_2$/*t*-BuOOH.[12] In contrast, in the epoxidation of 1-methylgeraniol (**1s**) with the titanium-doped zeolite oxidants TS-1/UHP and Ti-β/H_2O_2, for which hydrogen-bonded transition states have been proposed,[7g] the *7,8*-**2s** regioisomer is formed preferentially.[12] Consequently, since the MTO-catalyzed oxidants MTO/UHP[12] and MTO/H_2O_2 (30%)/pyridine also prefer to transfer the oxygen atom to the unfunctionalized double bond (Scheme 4), the rhenium catalyst associates with the allylic hydroxy functionality through hydrogen bonding. This interaction is relatively weak and the more nucleophilic remote double bond wins out to form predominantly the *6,7*-**2r** regioisomer for geraniol (**1r**) and the epoxide *7,8*-**2s** for 1-methylgeraniol (**1s**). The fact that in methanol the regioselectivity with MTO/UHP shifts further in favor of the isolated double bond for both **1r** and **1s** substantiates the hydrogen-bonding mechanism. Also the high threo selectivity observed for the *3,4*-**2s** regioisomer (Scheme 4), but not for the *7,8*-**2s** one, in the epoxidation of the chiral methyl derivative **1s** speaks for hydrogen bonding, as does the lower diastereoselectivity in methanol compared to CCl_4.

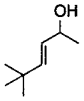
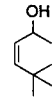
Diastereoselectivity, as we have amply demonstrated by comparison with established cases,[7b-g] allows the hydrogen-bonding mechanism to be refined and pertinent structural details of the transition state for the oxygen-transfer process to be elucidated. To facilitate such a comparison for the MTO catalyst, the relevant diastereoselectivity data are listed in Table 3. Besides MTO/UHP and MTO/H_2O_2 (30%)/pyridine, for which the geometry of the hydrogen bonding is to be assessed, the stoichiometric oxidants *m*-chloroperbenzoic acid (*m*-CPBA) and dimethyldioxirane (DMD) were chosen, as well as the heterogeneous metal-catalyzed system Ti-β/H_2O_2 (85%) and the homogeneous one $VO(acac)_2$/*t*-BuOOH. The large variety of methyl- and *tert*-butyl-substituted chiral allylic alcohols **1b**−**o** have been selected to allow a detailed "fingerprinting" of the transition-state geometry through the observed threo/erythro selectivities; the latter reflect the effects of 1,2- and 1,3-allylic strain (^{1,2}A and ^{1,3}A strain) on the operating hydrogen-bonding mechanism.

Inspection of the diastereoselectivities in Table 3 for the methyl-substituted substrates **1b**−**i** discloses that the data for the MTO systems fit with both the *m*-CPBA and DMD values in that the threo diastereomer is favored for the substrates **1e**,**g**,**h**,**i** (Table 3, entries 4 and 7) with ^{1,3}A strain. That ^{1,2}A strain is ineffective is displayed by the stereochemical probe, the chiral allylic alcohol **1g**, in which both ^{1,2}A and ^{1,3}A strain are competing for conformational control (entry 6). Clearly, the high threo selectivity for both MTO oxidants indicates the dominance of ^{1,3}A strain. This is to be contrasted with the $VO(acac)_2$/*t*-BuOOH system, earlier disposed of on account of the regioselectivities (Scheme 4), for which the observed erythro selectivity expresses the effectiveness of ^{1,2}A strain. The catalytic oxidants $Mo(CO)_6$/*t*-BuOOH, $MoO_2[PhCON(Ph)O]_2$/*t*-BuOOH (**E**), and H_2WO_4/H_2O_2 and the stoichiometric peroxo complex $MoO(O_2)[PhCON(Ph)O]_2$ (**F**) show similar behavior (Table 2) to $VO(acac)_2$/*t*-BuOOH (Table 3). They are all sensitive to ^{1,2}A strain and experience metal-alcoholate binding with the allylic substrates. Transition states analogous to $VO(acac)_2$/*t*-BuOOH (**VII**) are postulated (Figure 1) for these molybdenum- and tungsten-based oxidation systems.[18,22]

The diastereoselectivities of the methyl-substituted allylic alcohols **1b**−**i** (Table 3, entries 1−8) for the oxidants MTO/UHP and MTO/H_2O_2 (30%)/pyridine are consistent with the transition states **I**−**III**, of which the peracid-like structure **I** and the perhydrate one **II** are related to the structures **IV** and **V** for *m*-CPBA[23] and Ti-β/H_2O_2,[7g] while the peroxo-like transition state **III** is

(13) Tanaka, S.; Yamamoto, H.; Nozaki, H.; Sharpless, K. B.; Michaelson, R. C.; Cutting, J. D. *J. Am. Chem. Soc.* **1974**, *96*, 5254−5455.
(14) (a) Raciszewski, Z. *J. Am. Chem. Soc.* **1960**, *82*, 1267−1277. (b) Stevens, H. C.; Kaman, A. J. *J. Am. Chem. Soc.* **1965**, *87*, 734−737. (c) Prat, D.; Delpech, B.; Lett, R. *Tetrahedron Lett.* **1986**, *27*, 711−714.
(15) Tomioka, H.; Takai, K.; Oshima, K.; Nozaki, H.; Toriumi, K. *Tetrahedron Lett.* **1980**, *21*, 4843−4846.
(16) Mihelich, E. D. *Tetrahedron Lett.* **1979**, 4729−4732.
(17) Finn, M. G.; Sharpless, K. B. In *Asymmetric Synthesis*; Morrison, J. D., Ed.; Academic Press: Orlando, FL, 1985; Vol. 5, p 247.
(18) Chaumette, P.; Mimoun, H.; Saussine, L.; Fischer, J.; Mitschler, A. *J. Organomet. Chem.* **1983**, *250*, 291−310.
(19) Katsuki, T.; Sharpless, K. B. *J. Am. Chem. Soc.* **1980**, *102*, 5974−5976.
(20) Adam, W.; Braun, M.; Griesbeck, A.; Lucchini, V.; Staab, E.; Will, B. *J. Am. Chem. Soc.* **1989**, *111*, 203-212.
(21) Chautemps, P.; Pierre, J.-L. *Tetrahedron* **1976**, *32*, 549−557.
(22) Michaelson, R. C.; Palermo, R. E.; Sharpless, K. B. *J. Am. Chem. Soc.* **1977**, *99*, 1990−1992.
(23) Narula, A. S. *Tetrahedron Lett.* **1981**, *22*, 2017−2020.

Table 3. Diastereoselectivities (Threo/Erythro) in the Epoxidation of Methyl- and *tert*-Butyl-Substituted Allylic Alcohols 1 by Various Catalytic and Stoichiometric Oxidants

			threo/erythro diastereoselectivities [a]					
entry	allylic alcohol		MTO/ UHP [b]	MTO/ H_2O_2 (30%) [c]	*m*-CPBA [d]	DMD [e]	Ti-beta/ H_2O_2 (85%) [f]	$VO(acac)_2$/ *t*-BuOOH [g]
1		**1b**	*60 : 40*		60 : 40	50 : 50	62 : 38	20 : 80
2		**1c**	50 : 50	*41 : 59*	45 : 55	60 : 40	56 : 44	05 : 95
3		**1d**	66 : 34		64 : 36	53 : 47	64 : 36	29 : 71
4		**1e**	82 : 18	*86 : 14*	95 : 05	67 : 33	91 : 09	71 : 29
5		**1f**	*56 : 44*	*50 : 50*	*48 : 52*	*51 : 49*		*10 : 90*
6		**1g**	91 : 09	*80 : 20*	90 : 10	87 : 13	89 : 11	33 : 67
7		**1h**	83 : 17	*81 : 19*	95: 05	76 : 24	95 : 05	86 : 14
8		**1i**	95 : 05	*≥95 : 05*		≥95 : 05		
9		**1j**	*64 : 36*	*68 : 32*	44 : 56	24 : 76	70 : 30	05 : 95
10		**1k**	*67 : 33*	*44 : 56*	53 : 47	52 : 48	70 : 30	18 : 82
11		**1l**	*≥95 : 05*	*92 : 08*	95 : 05	95 : 05	88 : 12	84 : 16
12		**1m**	*23 : 77*	*08 : 92*	10 : 90	50 : 50	15 : 85	05 : 95
13		**1n**	*74 : 26*	*81 : 19*	60 : 40	[h]	58 : 42	30 : 70
14		**1o**	*69 : 31*	*≥95 : 05*	95 : 05	73 : 27	95 : 05	72 : 28

[a] Diastereoselectivities given in italics are this work. [b] For entries 2-4 and 6-8 see ref 7c. [c] In the presence of 12 mol% pyridine. [d] For entries 1-4 and 7 see ref 8; for entry 6 see ref 7b; for entries 10-12 see ref 7g; for entry 9 see ref 20; for entries 13 and 14 see ref 21. [e] For entries 1-4 and 6-8 see ref 7e; for entries 9-14 see ref 7f. [f] For entries 1-4 and 6-14 see ref 7g. [g] For entries 1-4 and 7 see ref 8; for entry 6 see ref 7b; for entries 9-14 see ref 7g. [h] Only enone formation.

analogous to the dimethyldioxirane (DMD) one **VI** (Figure 1). Both *m*-CPBA and Ti-β/H_2O_2 associate with the substrate by hydrogen bonding with an optimal dihedral angle (O−C−C=C) of ca. 120°,[8,24] while DMD prefers ≥130°.[7g] Unfortunately, the methyl derivatives **1b**−**i** do not allow a differentiation between these two dihedral arrangements for the rhenium oxidants; presumably the steric interactions are not sufficiently severe. For this reason, the *tert*-butyl-substituted substrates **1j**−**o** (Table 3, entries 9−14) were employed because such a massive substituent should be more effective in displaying steric effects. Indeed, a clear-cut distinction can be made between DMD versus *m*-CPBA and Ti-β/H_2O_2. In view of the good match in the observed diastereoselectivities of the latter two oxidants with MTO/UHP and especially

(24) In a recent theoretical paper (Bach, R. D.; Estévez, C. M.; Winter, J. E.; Glukhovtsev, M. N. *J. Am. Chem. Soc.* **1998**, *120*, 680−685) on the epoxidation of the parent allylic alcohol by performic acid, a dihedral angle (α) of ca. 134° was computed for the minimum-energy transition state of the oxygen-atom transfer, with preferential hydrogen bonding between the allylic hydroxy group and the carbonyl group. Thus, the dihedral angle may be significantly larger than the ca. 120° estimated in ref 8 from experimental diastereoselectivity data; however, the effect of 1,3-allylic strain was not assessed in the computational work, and for the time being we adhere to the 120° angle.

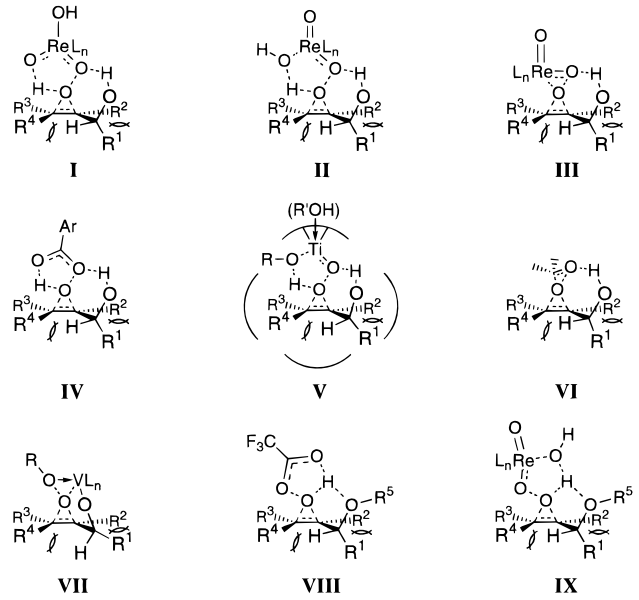
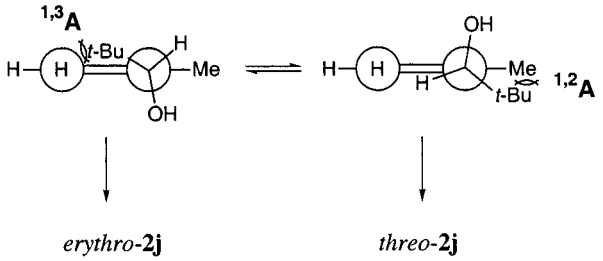


Figure 1. Proposed peracid-, peroxy-, and peroxo-type transition states **I**−**IX** for the epoxidations with the oxidation systems MTO/UHP and MTO/30% H_2O_2/pyridine (**I**, **II**, **III**, and **IX**), *m*-CPBA (**IV**), Ti-β/H_2O_2 (**V**), DMD (**VI**), VO(acac)$_2$/*t*-BuOOH (**VII**), and CF_3CO_3H (**VIII**).

the MTO/H_2O_2 (30%)/pyridine oxidant, a similar dihedral angle is preferred for the two MTO oxidants. Substrates **1m** (^{1,2}A strain) and **1o** (^{1,3}A strain) are most definitive for this purpose. While with DMD no selectivity is observed for **1m** (Table 3, entry 12) and there is a low threo preference for **1o** (Table 3, entry 14), the oxidants *m*-CPBA, Ti-β/H_2O_2, and MTO/H_2O_2 (30%)/pyridine display very high and opposite stereodifferentiation, i.e., erythro for **1m** and threo for **1o**, as expected from ^{1,2}A versus ^{1,3}A strain. Substrates **1k** (Table 3, entry 10) and **1n** (Table 3, entry 13) are uninformative because they possess no appreciable allylic strain, as is borne out by the very similar diastereoselectivities for all the oxidants in Table 3, except VO(acac)$_2$/*t*-BuOOH, for which metal-alcoholate binding and not hydrogen-bonding operates. Also instructive is the **1j** and **1l** pair (Table 3, entries 9 and 11), for which the *tert*-butyl group is located at the chirality center, in contrast to the **1m** and **1o** pair (Table 3, entries 12 and 14) with the *tert*-butyl group at the double bond. The very high threo selectivity for substrate **1l** (^{1,3}A strain) for all oxidants is not surprising, but the appreciable amount of threo epoxide that is formed (except for DMD and, of course, VO(acac)$_2$/*t*-BuOOH) for **1j** (^{1,2}A strain) seems quite puzzling. Presumably, to avoid the strong Me/*t*-Bu steric interaction due to ^{1,2}A strain, the *tert*-butyl group rotates away but encounters the olefinic hydrogen atom and experiences appreciable H/*t*-Bu repulsion from ^{1,3}A strain (Scheme 6). The balance between ^{1,2}A and ^{1,3}A strain in the corresponding transition states for the epoxidation is expressed in terms of the threo/erythro selectivities. As expected for such effective competition, the stereoselection is quite low, except for the vanadium catalyst (Table 3, entry 9); but for the latter, the strong ^{1,2}A strain due to the metal-alcoholate binding in the template (Figure 1, structure **VII**) dominates over ^{1,3}A strain compared to the other oxidants that operate through relatively weak hydrogen bonds (structures **I**−**VI**). The trends in the selectivities

Scheme 6. 1,2- and 1,3-Allylic Strain in the MTO-Catalyzed Epoxidation of Allylic Alcohol 1j



for the MTO/UHP oxidant fit quite well with those of MTO/H_2O_2 (30%)/pyridine in that the same sense is observed in most cases (Table 3); but quantitative discrepancies are evident, most notably for substrate **1o** (Table 3, entry 14). It is proposed that the cause for this divergence between the two MTO catalytic systems is due to the heterogeneous nature of the system MTO/UHP (the urea serves as host for the reaction[25]), while the oxidant MTO/H_2O_2 (30%)/pyridine is homogeneous. Thus, the restricted environment of the urea channels in the MTO/UHP combination may lead to additional steric interactions or hydrogen-bonding between the allylic alcohol as guest and the urea as host such that a quantitative correspondence between the heterogeneous MTO/UHP and the homogeneous MTO/H_2O_2 (30%)/pyridine systems should not be expected. This difference in behavior between the two rhenium oxidants is manifested particularly well for the sterically more bulky *tert*-butyl- versus methyl-substituted allylic alcohols (Table 3).

An instructive mechanistic test to assess the synergistic efficacy between conformational control through allylic strain and hydrogen bonding in the oxidation of acyclic chiral allylic alcohols is to determine the diastereoselectivities for derivatives in which the hydroxy functionality is either capped by methylation or acetylation or is replaced by other groups not capable of donating hydrogen bonds. For this purpose, we have employed the methyl ether **3h** and acetate **4h** of the allylic alcohol **1h**, as well as the sulfone **5h** and the diBoc-protected allylic amine **6h** (Scheme 3). As expected,[26] for the latter two substrates the erythro diastereoselectivity applies (Scheme 3) when MTO/UHP is used as oxidant. Since for these functionalities no hydrogen bonding is possible, their steric bulk operates and shields the π face that carries the SO_2Ph or $NBoc_2$ substituents (conformationally controlled through ^{1,3}A strain), and the *erythro*-epoxides **9h** and **10h** are favored. The acetate **4h** gives no or even slight erythro selectivity for MTO (34:66), as well as *m*-CPBA (**4h**: 28:72)[7f] and DMD (**4h**: 58:42).[7e] Surprisingly, a moderate threo selectivity (Scheme 3) has been obtained in the MTO-catalyzed epoxidation of the methyl ether **3h** (77:23). This is to be contrasted with no or slight erythro selectivity that is observed for *m*-CPBA (**3h**: 52:48)[7f] and DMD (**3h**: 38:62).[7e] Therefore, a small directing effect still operates for the capped derivative **3h** in the case of MTO/UHP versus *m*-CPBA and DMD.

Mechanistically significant in this context is Ganem's report[27] that the epoxidation of cyclic allylic silyl ethers with CF_3CO_3H is syn but with *m*-CPBA anti stereose-

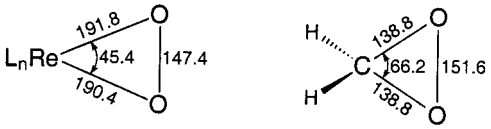
(25) Adam, W.; Mitchell, C. M.; Saha-Möller, C. R.; Weichold, O. *J. Am. Chem. Soc.* **1999**, *121*, 2097−2103.

(26) Adam, W.; Brünker, H.-G.; Kumar, A. S.; Peters, E.-M.; Peters, K.; Schneider, U.; von Schnering, H. G. *J. Am. Chem. Soc.* **1996**, *118*, 1899−1905.

lective. The hydrogen-bonded structure **VIII** (Figure 1) was suggested for the much more acidic trifluoroperacetic acid to account for the discrepancies in these diastereoselectivities. In analogy, for the MTO/UHP oxidant the related structure **IX** (Figure 1) is suggested in the epoxidation of derivative **3h** to rationalize the moderate but significant threo selectivity. The acidity of rhenium-based oxidants is well established,[2] such that hydrogen bonding to ether and acetoxy functionalities seems reasonable. The fact that the selectivity is reversed for the acetate **4h** compared to the ether **3h** (Scheme 3) is expected since the former oxygen functionality is less basic, and thus, hydrogen bonding is not as effective.

With all the experimental facts mechanistically interpreted, the active oxygen-transferring species in the complex catalytic oxidation cycle in Scheme 1 remains to be defined and its electronic structure assigned. The four peroxide species **A**−**D** qualify in principle for the oxidizing species, of which the monoperoxo (**B**) and diperoxo (**D**) complexes have been documented in a variety of oxygen-transfer processes.[1] To date, no experimental evidence for the peracid-type structures **A** and **C** is available. Nonetheless, the threo-selective hydroxy-group directivity in the epoxidation of the chiral allylic alcohols **1** (Table 3), controlled by hydrogen bonding and allylic strain, suggest the peracid- and perhydrate-type transition-state structures **I** and **II** in favor of the dioxirane-like one **III**. Thus, our diastereoselectivity data in Table 3 convey that the dihedral angle (α) for the MTO oxidants complies better with the peracid geometry (ca. 120°)[24] than the dioxirane one (≥130°). However, in the absence of other experimental clues, this geometrical preference must not necessarily be construed to mean that also the electronic structure of the epoxidizing species is akin to that of a peracid (structure **I**) or perhydrate (structure **II**) rather than dioxirane (structure **III**). The structural parameters (bond angles and lengths) of a rhenium peroxo functionality (X-ray data)[2] are distinct from those of a dioxirane (microwave data),[28] such that the optimal dihedral angle (α) for effective hydrogen bonding should not be expected to be the same (Scheme 7).[29] Therefore, for the time being until other experimental data become available, we adhere to the generally accepted rhenium peroxo complexes **B** and **D** as the active epoxidants,[2,3b,30] with the electronic structure **III** (Figure 1) as likely transition state for the oxygen transfer, which is also supported by recent computational work.[4]

Scheme 7. Structural Parameters [Bond Angles (deg) and Lengths (pm)] of a Rhenium Peroxo Funtionality and of a Dioxirane



Acknowledgment. The generous financial support of the Deutsche Forschungsgemeinschaft (SFB 347 "Selektive Reaktionen Metall-aktivierter Moleküle"), the Bayerische Forschungsstiftung (Bayerischer Forschungsverbund Katalyse−FORKAT), and the Fonds der Chemischen Industrie is gratefully appreciated.

Supporting Information Available: Experimental Section and structure matrix. This material is available free of charge via the Internet at http://pubs.acs.org.

JO9902289

(27) McKittrick, B. A.; Ganem, B. *Tetrahedron Lett.* **1985**, *26*, 4895−4898.

(28) Suenram, R. D.; Lovas, F. J. *J. Am. Chem. Soc.* **1978**, *100*, 5117−5122.

(29) The two Re−O bonds do not have identical bond lengths as one oxygen atom in the peroxo group is adjacent to the methyl group while the other is next to the second peroxo group.

(30) (a) Al-Ajlouni, A. M.; Espenson, J. H. *J. Org. Chem.* **1996**, *61*, 3969−3976. (b) Boehlow, T. R.; Spilling, C. D. *Tetrahedron Lett.* **1996**, *37*, 2717−2720. (c) Tan, H.; Espenson, J. H. *Inorg. Chem.* **1998**, *37*, 467−472.