

Diastereoselective Catalytic Epoxidation of Chiral Allylic Alcohols by the TS-1 and Ti- β Zeolites: Evidence for a Hydrogen-Bonded, Peroxy-Type Loaded Complex as Oxidizing Species

Waldemar Adam,^{*,†} Avelino Corma,[‡] T. Indrasena Reddy,[†] and Michael Renz[†]

Institute of Organic Chemistry, University of Würzburg, Am Hubland, D-97074 Würzburg, Germany, and Instituto Tecnología Química, UPV-CSIC, Avd. de los Naranjos s/n, E-46022 Valencia, Spain

Received February 26, 1997[®]

The similar diastereoselectivities as for peracids implicate a pentacoordinated metal peroxy species in the epoxidation of chiral allylic alcohols by the titanium-containing zeolites TS-1 and Ti- β . In the loaded complex, the allylic alcohol substrate is fixed through hydrogen bonding to the metal center, with A^{1,3} strain as the dominant conformational feature. By comparison of the diastereoselectivities to those for VO(acac)₂/*t*-BuOOH, we exclude a peroxy-type complex with direct coordination of the allylic alcohol to the titanium center by means of metal–alcoholate bonding. Neither does a peroxo-type titanium complex apply, as confirmed by comparing the diastereoselectivities with those observed for dioxiranes. With the help of *tert*-butyl-substituted allylic alcohols as substrates, which are not epoxidized by the TS-1 but by the Ti- β catalyst, it was unequivocally confirmed that the oxidation occurs inside of the zeolite and not on the outer surface.

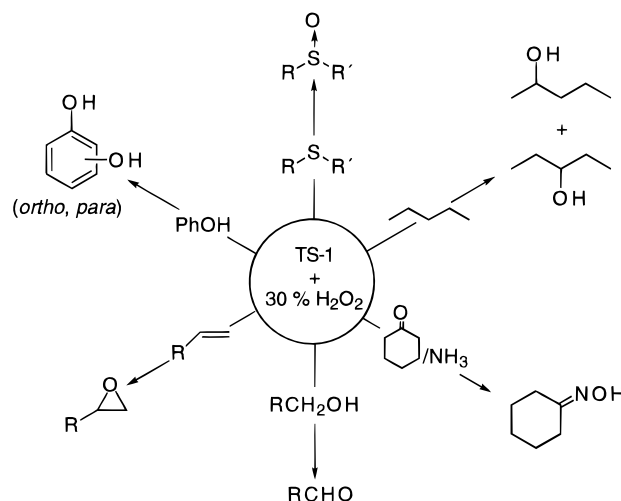
Introduction

Titanium silicalite 1 (TS-1) is known to be a powerful and selective redox molecular sieve. It has been found to catalyze many useful oxidations with hydrogen peroxide under mild conditions, which include alkene epoxidation and alkane and arene hydroxylations (Scheme 1).¹ The problem of entry into the TS-1 cavity was solved by the synthesis of the large-pore-sized zeolite Ti- β ² or the mesoporous material Ti-MCM-41.³

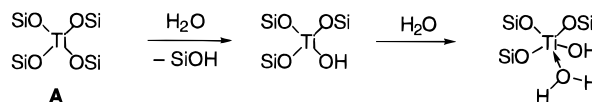
The catalytic activity of these zeolites derives from the titanium atom that substitutes isomorphously a silicon atom in the lattice. From the EXAFS analysis of non-calcined and of calcined TS-1⁴ and Ti- β ⁵ samples, valuable structural information on the titanium environment in the zeolite lattice has become available. It was shown that calcination decreases the coordination number from 5 or 6 to 4 (structure **A** in Scheme 2). On addition of water, one Ti–O–Si bond is hydrolyzed, but the tetra-coordination is kept intact. Subsequent addition of another water molecule generates a pentacoordinated titanium species (Scheme 2).

The same coordination sphere as for water applies also to hydrogen peroxide. For the latter, the pentacoordinated structure **B** (Scheme 3) with a hydrogen-bonded cyclic structure was proposed as the most favored active species for the epoxidation, formed by exchange of a silyloxy group through Ti–O covalent bonding with a

Scheme 1. Catalytic Oxidations with Titanium Silicate 1 (TS-1) and Aqueous Hydrogen Peroxide as Oxygen Donor



Scheme 2. Postulated Titanium Species of the Calcined Form A and Its Hydrolysis and Hydration



hydrogen peroxide molecule and a water or alcohol molecule without deprotonation.⁶ The hydroperoxy **B** structure was preferred over the alternative peroxy-type **C** (Scheme 3) one on the basis of indirect, in our opinion unconvincing, evidence. The Brønsted acid-catalyzed hydrolysis of *cis*- and *trans*-butene oxides was chosen as the model reaction, rather than an oxygen-transfer process. For the former it was found that, in methanol, the epoxide opening of *trans*-2,3-butene oxide was very slow, greatly enhanced by hydrogen peroxide, but inhib-

* To whom correspondence should be addressed. Tel.: Int + 931 888 5340. Fax: Int + 931 888 4756. E-mail: adam@chemie.uni-wuerzburg.de.

[†] University of Würzburg.

[‡] Instituto Tecnología Química.

[®] Abstract published in *Advance ACS Abstracts*, May 1, 1997.

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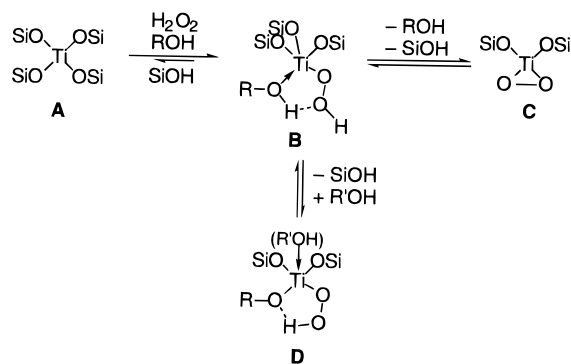
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Scheme 3. Postulated Structures of the Oxidizing Species B–D Derived from the Reaction of the Titanium Species A with Hydrogen Peroxide



ited by sodium hydroxide. The rate of the hydrolysis was also solvent dependent and decreased in the following order: MeOH > EtOH > H₂O. On the basis of these observations, an active species was postulated in which a hydrogen peroxide and a solvent molecule are coordinated to the titanium atom. Steric and electronic effects of the ligated solvent molecule in the active species were made responsible for the solvent dependence, while for the Brønsted-acid catalysis the peroxy proton was proposed, which is neutralized by sodium hydroxide. It is difficult to reconcile these epoxide hydrolysis results with the oxidation process in question.

Another feature not taken into account is the ease of substrate diffusion within the zeolite, which is affected by the size and polarity of the solvent and should determine the reactivity. Also neglected are the well-known Lewis-acid-catalyzed epoxide opening⁷ by titanium compounds and the recently reported perhydrolysis of epoxides by hydrogen peroxide with titanium-containing zeolites.⁸ In view of these facts, it is our own contention that alternative active species, e.g., the peroxy structure **C**, formed from the postulated **B** species by desilanolation and alcohol loss, are still viable oxidants in Ti-containing zeolites, a conflictive situation that demands mechanistic scrutiny.

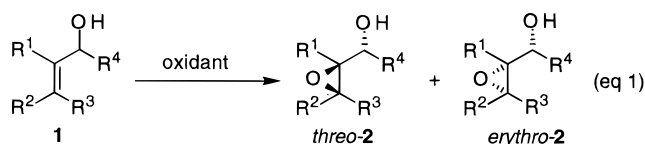
Recently, we have reported that chiral, acyclic allylic alcohols serve as a valuable stereochemical probe to gain mechanistic insight into the epoxidation by metal-activated and nonmetal oxidants.⁹ When such oxygen acceptors are stereolabeled to possess allylic strain, high diastereoselectivities may be observed, which derive from the synergistic interaction between the oxidizing species and the hydroxy group of the allylic substrate in the transition state for oxygen transfer. The advantage of this stereochemical approach is that it affords detailed mechanistic information directly on the active species in the catalyzed oxidation process.

The purpose of the present study was to employ our stereochemical probe for assessing the plausible structure of the oxidizing entity in the catalytic, heterogeneous epoxidation by the Ti-containing zeolites TS-1 and Ti-β with hydrogen peroxide as oxygen donor. Besides the

already mentioned active species **B** (peroxy-type) and **C** (peroxo-type), we additionally propose structure **D** (Scheme 3), in which unlike species **B**, the water or alcohol molecule is directly bonded (Si–OR) to the titanium atom rather than coordinated. In contrast to the species **B**, the alternative active species **C** and **D** (Scheme 3) may coordinate the allylic alcohol substrate by hydrogen bonding, i.e., peroxy for **C** versus hydroperoxy in **D**, differences in the diastereomeric ratios are expected. By comparison of the observed diastereoselectivities for the heterogeneous TS-1 and Ti-β catalysts with literature data obtained for structurally similar, already established oxidants, valuable structural information on the active species should be obtained. For this purpose, on one hand, the peroxy-type oxidants such as the catalytic, homogeneous Ti(O-*i*-Pr)₄/TBHP,^{9a} VO(acac)₂/TBHP¹⁰ and the stoichiometric *m*-chloroperbenzoic acid (*m*-CPBA)¹⁰ shall be employed; on the other hand, the peroxo-type catalytic, homogeneous methyltrioxorhenium (MTO)/H₂O₂ oxidant¹¹ and the stoichiometric dimethyldioxirane (DMD)¹² should offer valuable mechanistic comparison. Indeed, as the results presented here verify, this anticipation has been substantiated with the help of the chiral allylic alcohols **1a–m** (cf. Table 1 for the structures) as stereolabeled substrates with 1,2- and 1,3-allylic strain.

Results

In the epoxidation of the chiral, acyclic allylic alcohols **1** by the urea hydrogen peroxide (UHP)/TS-1 or by the 85% aqueous hydrogen peroxide/Ti-β catalytic systems, the corresponding epoxy alcohols **2** were obtained quantitatively (eq 1). For the derivatives **1a–f**, the diaste-



reoselectivities are the same within the error limit for both catalysts (Table 1, entries 1–6). For the derivatives **1a–c** without a *cis*-methyl group (1,3-allylic strain absent) next to the stereogenic center, the epoxy alcohols **2a–c** were obtained as a 50:50 mixture of *threo* and *erythro* diastereomers. In contrast, for the substrates **1d–f** with a *cis*-methyl group (1,3-allylic strain present), a high *threo* preference was observed (Table 1, entries 4–6). The same trend was found for the *n*-butyl-substituted (R³ = *n*-Bu) allylic alcohol **1g** (Table 1, entry 7); however, whereas for the Ti-β-catalyzed oxidation the *threo*-epoxy alcohol **2g** was obtained essentially exclusively, for TS-1 the diastereomeric ratio is only 80:20 (Table 1, entry 7).

The *tert*-butyl-substituted derivatives **1h–m** are not epoxidized by TS-1 (Table 1, entries 8–13), but for the (*E*)-configured **1h**, 8% oxidation to the enone took place

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












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Table 1. Diastereomeric Ratios (dr) for the Epoxidation of the Chiral Allylic Alcohols 1 with TS-1/UHP, Ti- β /H₂O₂, Ti(O-*i*-Pr)₄/TBHP, VO(acac)₂/TBHP, *m*-Chloroperbenzoic Acid (*m*-CPBA), and Dimethyldioxirane (DMD)

entry	substrate	diastereomeric ratios (<i>threo</i> : <i>erythro</i>) ^d						
		catalyst: donor: solvent:	TS-1 UHP CH ₃ COCH ₃	Ti- β H ₂ O ₂ (85%) CH ₃ CN	Ti(O- <i>i</i> -Pr) ₄ ^a TBHP CDCl ₃	VO(acac) ₂ ^b TBHP C ₆ H ₆	<i>m</i> -CPBA ^b CH ₂ Cl ₂	DMD ^c CH ₃ COCH ₃
1	 1a	64 : 36	62 : 38	71 : 29	20 : 80	60 : 40	50 : 50	
2	 1b	55 : 45	56 : 44	22 : 78	05 : 95	45 : 55	60 : 40	
3	 1c	65 : 35	64 : 36	66 : 34	29 : 71	64 : 36	53 : 47	
4	 1d	87 : 13	91 : 09	91 : 09	71 : 29	95 : 05	67 : 33	
5	 1e	81 : 19	89 : 11	83 : 17	33 : 67	90 : 10	87 : 13	
6	 1f	95 : 05	95 : 05	95 : 05	86 : 14	95 : 05	76 : 24	
7	 1g	80 : 20	93 : 07	95 : 05	78 : 22	90 : 10	80 : 20	
8	 1h	--- ^e	58 : 42	61 : 39	30 : 70	60 : 40 ^f	--- ^g	
9	 1i	--- ^h	95 : 05	95 : 05	95 : 05	95 : 05 ^f	73 : 27	
10	 1j	--- ^h	70 : 30	57 : 43	18 : 82	53 : 47	52 : 48	
11	 1k	--- ^h	88 : 12	94 : 06	84 : 16	95 : 05	95 : 05	
12	 1l	--- ^h	15 : 85	05 : 95	05 : 95	10 : 90	50 : 50	
13	 1m	--- ^h	70 : 30	05 : 95	05 : 95	56 : 44 ⁱ	24 : 76	

^a 0.05 equiv of Ti(O-*i*-Pr)₄ was used in the presence of molecular sieves (4 Å) in CDCl₃; conversion was always complete. ^b For substrates **1a–d,f** see ref 10; for substrate **1e** see ref 13. ^c For entries 1–6 see ref 12a; for entries 7–13 see ref 12b. Also, some enone formation was observed. ^d Diastereomeric ratios (dr), determined by ¹H NMR analysis of the characteristic signals of the epoxides in the crude reaction mixture, error $\pm 5\%$ of the stated values. ^e 8% ketone was detected. ^f See ref 14. ^g Only ketone formation. ^h No conversion was observed. ⁱ See ref 15.

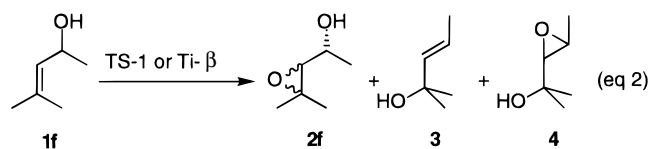
(Table 1, entry 8).¹⁶ Fortunately, the Ti- β zeolite with the larger pores was effective for the epoxidation of these sterically more demanding substrates. The observed diastereomeric ratios are similar to those obtained for the methyl-substituted allylic alcohols. Only for derivative **1l** with a *geminal tert*-butyl group a pronounced *erythro* diastereoselectivity was found (Table 1, entry 12).

For comparison, the homogeneous titanium oxidant system Ti(O-*i*-Pr)₄/TBHP is also sensitive to methyl or *tert*-butyl substitution (R³ = Me, *t*-Bu). Thus, the derivatives **1d–g,i,k** afforded the corresponding epoxy alcohols

2 with a very high preference for the *threo* diastereomer (Table 1, entries 4–7, 9, and 11); however, in contrast to the heterogeneous titanium catalysts TS-1 and Ti- β , a methyl substituent *geminal* to the stereogenic center provides high *erythro* selectivity (Table 1, entry 2). The exchange of one of the two methyl groups (R¹ or R⁴) by a *tert*-butyl substituent as in the substrates **1l** and **1m** yields the respective *erythro*-epoxy alcohols essentially as only diastereomers (Table 1, entries 12 and 13).

In the epoxidation of allylic alcohol **1f**, two side products were found, i.e., the rearranged alcohol **3** and its corresponding epoxy alcohol **4** (eq 2, Table 2). For the TS-1-catalyzed epoxidation with 35% aqueous hydrogen peroxide, 38% of these side products was observed

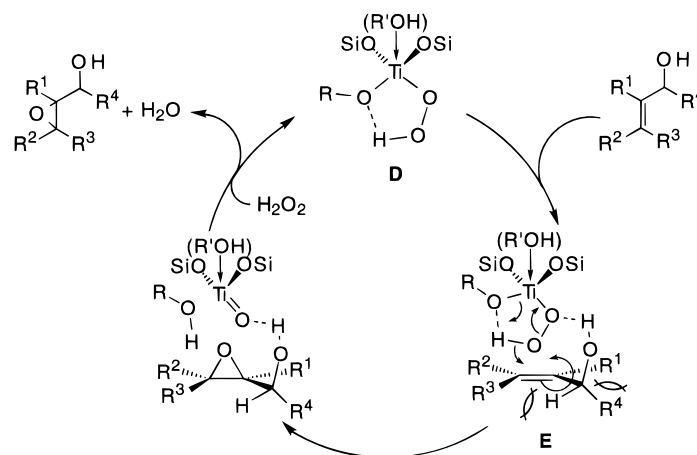
(16) The oxidation to the enone is a well-established substrate-dependent process.¹² For sterically encumbered double bonds, alcohol oxidation is preferred over epoxidation.

Table 2. Reaction Conditions and Product Distribution for the Epoxidation of the Allylic Alcohol **1f Catalyzed by Titanium-Containing Zeolites**

entry ^c	cat.	medium ^d	T (°C)	mb ^a (%)	convn ^a (%)	yield ^a (%)	product distr ^b		
							2f ^e	3	4
1	TS-1	H ₂ O ₂ (35%), CD ₃ COCD ₃	50	67	95	67	63	25	12
2	TS-1	H ₂ O ₂ ·urea, CD ₃ COCD ₃	50	81	71	52	100	0	0
3	TS-1	H ₂ O ₂ (85%), CH ₃ COCH ₃	50	95	90	95	100	0	0
4	TS-1	CD ₃ COCD ₃	50	86	26	12	0	100	0
5	Ti-β	CD ₃ CN	20	85	56	41	0	100	0
6	Ti-β	H ₂ O ₂ (85%), CH ₃ CN	20	81	95	81	78	12	10
7	Ti-β ^f	H ₂ O ₂ (85%), CH ₃ CN	20	93	96	89	93	7	0

^a Determined by quantitative ¹H NMR analysis (for details see Experimental Section); mass balance based on naphthalene as standard for entries 1, 2, 4, and 5; for entries 3, 6, and 7 it is the yield of isolated material. ^b Product distribution, normalized to 100%. ^c For entries 1, 2, 4, and 5 the general procedures III (TS-1) and IV (Ti-β) were used and 25.0 mg (250 μmol) allylic alcohol **1f** and 25.0 mg catalyst. ^d For entries 1 and 2, 1.5 equiv of oxygen donor was employed. ^e Diastereomeric ratios were in all cases ca. 95:05 within the error limits. ^f Ti-β sample with a low Al content.

Scheme 4. Catalytic Cycle for the Proposed Structures of the Active Species **D** and the Transition State **E** for the Oxygen Transfer in the Titanium-Containing Zeolites



(Table 2, entry 1). When the water-free, crystalline urea adduct of hydrogen peroxide (UHP) or a highly concentrated (85%) aqueous hydrogen peroxide solution was employed, the desired product **2f** was obtained as the only product (Table 2, entries 2 and 3). Temperature (20 and 50 °C) had no effect on the product distribution. In the presence of the zeolite without oxidant, the substrate **1f** was rearranged partly to alcohol **3** (Table 2, entry 4). The rearrangement was also observed (Table 2, entry 5) for Ti-β, and under oxidative conditions, the rearrangement epoxide **4** was also formed (Table 2, entry 6). For this zeolite, which normally contains Brønsted-acidic Al–OH–Si sites, these side products cannot be completely suppressed. Minimal rearrangement (only 7%) was achieved for a Ti-β sample with a low Al content by avoiding Brønsted-acid catalysis (Table 2, entry 7).¹⁷

Discussion

A detailed comparison of the stereochemical data in Table 1 leads to the conclusion that the peracid-type structure **D** operates as the active species in the zeolite-catalyzed epoxidation of the chiral allylic alcohols **1**, as

portrayed in Scheme 4. Analogous to the peracids, in the peroxy-type **D** complex the hydrogen peroxide and a small molecule (alcohol or water) are coordinated to the titanium site with deprotonation to establish a hydrogen-bonded five-membered ring. Additionally, a small molecule (alcohol or water) is coordinatively ligated to the titanium atom without deprotonation, to achieve a pentacoordinated ligand sphere for the oxidatively active **D** complex. The electronic changes during the oxygen transfer process are similar to the peracid epoxidation, with the allylic alcohol also associated to the active species by hydrogen bonding to form the loaded complex **E** (Scheme 4). The Ti=O functionality that results from the oxygen transfer in the complex **E** will rapidly be trapped by the temporarily released ROH molecule. Subsequent substitution of the titanium hydroxyl group by a fresh hydrogen peroxide molecule and displacement of the epoxy alcohol product regenerates the oxidizing species **D** to complete the catalytic cycle. Thus, we postulate that the transition state **E** applies in the epoxidation of allylic alcohols, which is akin to the structure **H** established for peracids (Figure 1).

Other viable alternatives are the transition-state structures **F** and **G** (Figure 1); however, on the basis of the present diastereoselectivity data (Table 1), we will show that these do not apply. The former also engages

(17) For TS-1 without Brønsted-acidic Al–OH–Si sites, these complicating acid-catalyzed side reactions are presumably caused by the inherent Lewis acidity of the titanium metal.

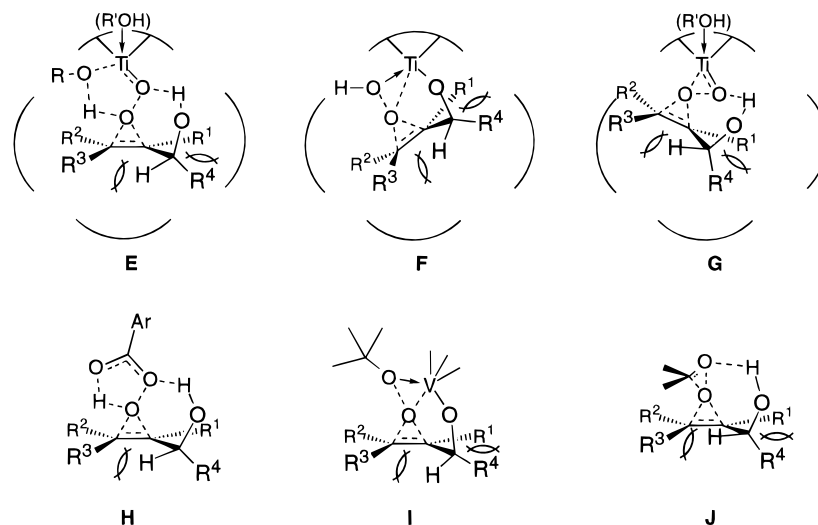


Figure 1. Proposed transition-state structures **E–J** for the epoxidations catalyzed by the heterogeneous titanium-containing zeolites TS-1 and Ti- β , the homogeneous vanadium-catalyzed oxidant VO(acac)₂/TBHP, and the stoichiometric, nonmetal-activated oxygen transfer agents *m*-CPBA and DMD.

a peroxy-type titanium species, but instead of the hydrogen-bonded association of the allylic alcohol to the titanium center as in **E**, the substrate is attached through a metal–alcoholate bond. Structure **I** serves as a prototype for this transition state of the homogeneous titanium- and vanadium-catalyzed epoxidations and *tert*-butyl hydroperoxide as oxygen source.¹⁸ The peroxy-type structure **G**, derived from the titanium peroxy species **C** (Scheme 3), analogous to **E** also has the allylic alcohol associated by hydrogen bonding in the loaded complex. This geometry is exemplified by the transition state for the epoxidation of allylic alcohols by dimethyldioxirane (DMD),¹² which constitutes a useful analogy. Since transition-metal-catalyzed reactions are involved, a more genuine model for comparison would be epoxidations with the diperoxo complex of methyltrioxorhenium (MTO).¹¹ Unfortunately, for the set of allylic alcohols **1** examined as substrates herein, the data are rather incomplete and the few available cases are not in the same solvent. However, in solvents of comparable polarity, essentially identical diastereoselectivities were observed for the epoxidation of chiral allylic alcohols by the rhenium diperoxo complex and the DMD,^{9b} so that the latter comprises a legitimate model for the metal-type dioxirane structure contained in the transition state **G**.

With this mechanistic preamble, we are now ready to rationalize the diastereoselectivity data in Table 1. We shall show that the transition-state structure **E** applies for the titanium-catalyzed epoxidation of the chiral allylic alcohols **1** in zeolites rather than **F** and **G** (Figure 1) and propose the catalytic cycle in Scheme 4.

Transition state E is supported by the good correspondence between the diastereoselectivities of the zeolite-catalyzed and the stoichiometric peracid epoxidations!

First, we shall consider the chiral, methyl-substituted substrates **1a–f** as stereochemical probes. Analogous to the peracids, for the Ti-containing zeolites and the allylic alcohols with A^{1,3} strain, i.e., the derivatives **1d** and **1f**, the *threo*-epoxy alcohols **2d** and **2f** are obtained essentially exclusively (Table 1, entries 4 and 6). When

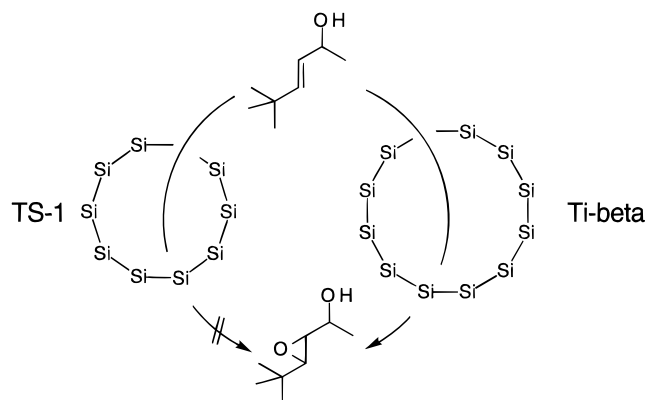
A^{1,3} strain is relaxed as in the (*E*)-derivative **1c**, diastereoselective control is essentially lost for both the zeolites and the peracid (Table 1, entry 3). A^{1,2} strain, as in substrate **1b**, does not manifest itself both for the zeolites as well as peracid (Table 1, entry 2). Additionally, for the stereochemical probe **1e** with A^{1,3} and A^{1,2} strain in competition,¹³ the epoxy alcohol **2e** is obtained highly *threo*-selectively (Table 1, entry 5), which emphasizes the dominance of A^{1,3} strain. Thus, the diastereomeric ratios for the five mechanistically informative, stereolabeled allylic alcohols **1b–f** (Table 1) show that the transition-state geometries for the oxygen transfer by titanium-containing zeolites and *m*-CPBA are very close to each other (structures **E** and **H**, Figure 1). The peracid associates with the substrate by hydrogen bonding with an optimal dihedral angle (O–C–C=C) of 120° in the allylic alcohol. Consequently, the *threo*-epoxy alcohols **2** are obtained preferentially since A^{1,3} strain dominates the transition-state geometry, whereas A^{1,2} strain is essentially negligible.

To generate the transition state **E** (Figure 1), it should be evident that the oxidizing species **D** rather than the popularized structure **B**⁶ (Scheme 3) qualifies. The latter cannot associate with the allylic alcohol substrate through hydrogen bonding to form the loaded complex **E** because the proton of the hydroperoxy functionality obstructs sterically and deactivates electronically. Consequently, activation is necessary by displacing a framework SiOH ligand in form of SiOH by the coordinated ROH molecule to afford the oxidizing species **D**; pentacoordination is reestablished by association with another R'OH molecule.

The diastereoselectivities of the methyl-substituted allylic alcohols **1a–f** are within the experimental error identical (except for derivative **1e**) for the TS-1 compared to Ti- β catalyst (Table 1, entries 1–6). Nevertheless, a significant difference is noticeable for the *n*-butyl-substituted substrate **1g** (Table 1, entry 7), which expresses influences of the different zeolite frameworks on the transition-state geometry. For the longer *n*-butyl substituent at the double bond, apparently steric reasons prevent an optimal arrangement in the zeolite channels of TS-1, a problem not displayed by the larger pored Ti- β network. Consequently, the diastereomeric ratio drops from 93:07 for the Ti- β to 80:20 for TS-1 (Table 1, entry

(18) (a) Woodard, S. S.; Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 106–113. (b) Finn, M. G.; Sharpless, K. B. *J. Am. Chem. Soc.* **1991**, *113*, 113–126. (c) Hoveyda, A. H.; Evans, D. A.; Fu, G. C. *Chem. Rev.* **1993**, *93*, 1307–1370.

Scheme 5. Sterically More Demanding Substrates Are Able To Enter the Ti- β Channels^a But Not the Smaller Ones of TS-1^b



^a Right hand side, each Si represents a SiO₄ tetrahedron. ^b Left hand side.

7). Steric effects become particularly acute for the more demanding *tert*-butyl-substituted substrates **1h–m** since these no longer penetrate into the TS-1 interior and, hence, are not epoxidized (Table 1, entries 8–13). In contrast, for the Ti- β catalyst with its larger cavities (12 Si tetrahedra, Scheme 5) compared to TS-1 (10 Si tetrahedra), oxidation takes place readily (Table 1, entries 8–13). These facts demonstrate unequivocally that all the epoxidations in Table 1 take place inside of the zeolites and not on the outer surface. The diastereoselectivities for these *tert*-butyl substrates with Ti- β coincide well with those observed for the simple methyl-substituted allylic alcohols **1b–d**. Thus, for substrates with A^{1,3} strain, i.e., allylic alcohols **1i** and **1k**, the epoxy alcohols are again obtained highly *threo*-selectively (Table 1, entries 9 and 11). For derivative **1l**, the increased A^{1,2} strain becomes evident since now the *erythro*-epoxy alcohol **2l** is formed preferentially analogous to the *m*-CPBA (Table 1, entry 12). Again, these data corroborate that the transition state **E** operates in the zeolite-catalyzed epoxidations.

The question whether steric demands exerted by the zeolite framework influence the stereoselectivity is definitively negated by our results. Comparison of the Ti- β -catalyzed epoxidations of the *cis*-substituted substrates **1d** (R³ = Me), **1h** (R³ = *n*-Bu), and **1i** (R³ = *t*-Bu) reveals the same *threo* selectivities (93 ± 2:7 ± 2) within the experimental error (Table 1, entries 4, 7, and 9). Clearly, if the zeolite framework were to exert a significant steric effect on the chiral substrate, for such a sterically widely varied set of derivatives (R³ = Me, *n*-Bu, *t*-Bu) dramatically different diastereoselectivities would have been observed. Such steric effects would be expected to change the preferred conformation of the chiral allylic alcohols, which would affect the optimal C=C–C–O dihedral angle, therewith the degree of hydrogen bonding, and in turn the π -facial selectivity. That the *threo*-diastereoselectivity is very high and constant within the experimental error, and the same for the heterogeneous and homogeneous Ti-catalyzed and *m*-CPBA epoxidations (Table 1, entries 4, 7, and 9), demonstrates unequivocally that there is no influence of the zeolite framework on the diastereoselectivity. The only role the zeolite displays is that of a molecular sieve, i.e., whether the substrate can enter the channel and reach the active site or not.

An exception is the *n*-butyl-substituted substrate **1g** (entry 7), for which in the TS-1 catalyst the longer alkyl chain does restrict conformational preferences.

Transition state **F** is excluded by the lack of correspondence between the diastereoselectivities of the zeolite and the VO(acac)₂/TBHP or Ti(*O-i-Pr*)₄/TBHP catalytic epoxidations!

For the metal-catalyzed epoxidation by the homogeneous VO(acac)₂/TBHP oxidant, the allylic alcohol **1** is bound by a metal–alcoholate bond to the vanadium and the oxygen atom is transferred at an optimal dihedral angle (O–C–C=C) of 40–50°. In terms of diastereoselectivity, this is expressed in a high preference of the *erythro* isomer for substrates **1b**, **1l**, and **1m** with A^{1,2} strain (Table 1, entries 2, 12, and 13). Comparison of these diastereoselectivities with the heterogeneous zeolite-catalyzed epoxidations brings out clear differences (Table 1). Thus, while for substrate **1b** (entry 2) no preference between *erythro* and *threo* isomers is noted, for derivative **1l** (entry 12) *erythro* selectivity is observed, yet for **1m** (entry 13) the *threo* isomer is preferred. Clearly, although all these allylic alcohols possess A^{1,2} strain, all possible diastereoselectivities are displayed, in complete contrast to the homogeneous vanadium-catalyzed epoxidation that is consistently *erythro*-selective. Unquestionably, metal–alcoholate bonding of the substrate as in the loaded complex **F** for the homogeneous vanadium-catalyzed epoxidation cannot apply to the heterogeneous zeolite catalytic process.

This conclusion may be challenged in the sense that the vanadium-centered complex does not genuinely serve as model for the heterogeneous titanium-containing zeolites. That this objection is unfounded makes evident a comparison of the diastereoselectivities for the homogeneous Ti(*O-i-Pr*)₄/TBHP oxidant (Table 1), in which the loaded complex similar to structure **I** is of the peroxy type and the allylic alcohol attached through a metal–alcoholate bond. Despite the close resemblance in the diastereoselectivities for the homogeneous Ti(*O-i-Pr*)₄ and the heterogeneous TS-1 catalysts with the A^{1,3}-controlled substrates **1d–f** (Table 1, entries 4–6), the derivatives **1b** (Table 1, entry 2) with A^{1,2} strain and **1g** (Table 1, entry 7) with A^{1,3} strain definitely fall out of line. Similar discrepancies are observed for the Ti- β catalyst, especially with the *tert*-butyl derivatives **1l** and **1m** (Table 1, entries 12 and 13). The larger dihedral angle (O–C–C=C) for the homogeneous titanium- versus vanadium-catalyzed epoxidations is responsible for the less definitive trends of the former because the distinction between A^{1,3} and A^{1,2} strain is less clear-cut in the transition state **I** for the oxygen transfer.

Additionally, for steric reasons, we speculate that the space around the titanium site in the zeolite lattice is too crowded to accommodate the oxygen acceptor (allylic alcohol) through direct Ti–O bonding as well as the activated oxygen donor (H₂O₂) to generate the loaded complex **F** (Figure 1) for the oxygen transfer. Inspection of models for the transition state **F** implies severe steric congestion in an attempt to align the double bond of the bound allylic alcohol and the activated peroxide bond for the stereoelectronically controlled S_N2 attack, i.e., along the required linear (180°) coordinate.^{18c} Be this as it may, the loaded complex **F** with bonding of the allylic alcohol substrate through a titanium–alcoholate bond does not allow us to rationalize consistently the set of diastereoselectivity data in Table 1.

Transition state G is excluded by the lack of correspondence between the diastereoselectivities of the zeolite-catalyzed and the stoichiometric DMD epoxidations!

For DMD it has been established with conformationally fixed cyclic substrates that the optimal dihedral angle in the allylic alcohol lies between 130 and 140°. ¹² Since the hydroxy group is now further away from the oxygen-transferring site in the loaded complex **G**, hydrogen bonding is expectedly weaker and the diastereoselectivity for the A^{1,3}-strained substrates **1d**, **1f**, and **1i** drops substantially for DMD compared to Ti-β and TS-1 (Table 1, entries 4, 6, and 9). Also for the allylic alcohols with large A^{1,2} strain, as the *tert*-butyl derivative **1l**, a significant discrepancy between the zeolites and DMD is observed. The *erythro*-epoxy alcohol **2l** is obtained preferentially in the Ti-β-catalyzed epoxidation, whereas with DMD the two diastereomers are formed in equal amounts (Table 1, entry 12). A more dramatic difference is noted for substrate **1m** (Table 1, entry 13), for which the *threo* isomer of the epoxy alcohol **2m** is formed preferentially in the zeolite-catalyzed process, but the *erythro* isomer for DMD. From these differences in the diastereoselectivities we suggest that a peroxy-type transition state **G**, analogous to the DMD-based structure **J** (Figure 1), does not apply for the epoxidation by the titanium-containing zeolite.

Conclusions

Through the use of chiral allylic alcohols with A^{1,2} and A^{1,3} strain as a stereochemical probe, a peroxy metal species has been identified as the oxygen-transferring species, in which the substrate is bound in the loaded

complex by hydrogen bridging. Direct attachment of the allylic alcohol substrate by metal–alcoholate bonding to the peroxy-type species was excluded, as well as a peroxy-type titanium complex. For the first time, valuable mechanistic insight has been directly acquired on the structural nature of the oxidizing species in the epoxidation by titanium-containing zeolites.

Although there is good correspondence between the diastereomeric ratios of the homogeneous and heterogeneous catalytic processes, which allow us to conclude what transition-state geometry likely operates for the oxygen transfer of the zeolite-catalyzed epoxidations, it should be cautioned that this may not apply generally. Mechanistic comparison should be valid, however, for small substrates that are not severely encumbered by the zeolite framework.

Acknowledgment. The generous financial support of the *Deutsche Forschungsgemeinschaft* (SFB 347 “Selektive Reaktionen Metall-aktivierter Moleküle”), the *Bayerische Forschungsförderung* (Bayerischer Forschungsvorhaben Katalyse - FORKAT), and the *Fonds der Chemischen Industrie* is gratefully appreciated. M.R. thanks the DAAD for a six-month doctoral fellowship to initiate the cooperation with the Valencia group.

Supporting Information Available: All experimental details (13 pages). This material is contained in libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

JO970364I