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A Highly Chemoselective, Diastereoselective, and Regioselective Epoxidation of Chiral Allylic Alcohols with Hydrogen Peroxide, Catalyzed by Sandwich-Type Polyoxometalates: Enhancement of Reactivity and Control of Selectivity by the Hydroxy Group through Metal−Alcoholate Bonding

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Sandwich-type polyoxometalates (POMs), namely $[WZnM_2(ZnW_9O_{34})_2]^{q-}$ [M = Mn(II), Ru(III), Fe(III), Pd(II), Pt(II), Zn(II); $q = 10-12$], are shown to catalyze selectively the epoxidation of chiral allylic alcohols with 30% hydrogen peroxide under mild conditions (ca. 20 °C) in an aqueous/organic biphasic system. The transition metals M in the central ring of polyoxometalate do not affect the reactivity, chemoselectivity, or stereoselectivity of the allylic alcohol epoxidation by hydrogen peroxide. Similar selectivities, albeit in significantly lower product yields, are observed for the lacunary Keggin POM $[PW_{11}O_{39}]^{7-}$, in which a peroxotungstate complex has been shown to be the active oxidizing species. All these features support a tungsten peroxo complex rather than a high-valent transition-metal oxo species operates as the key intermediate in the sandwich-type POM-catalyzed epoxidations. On capping of the hydroxy functionality through acetylation or methylation, no reactivity of these hydroxy-protected substrates [**1a(Ac)** and **1a(Me)**] is observed by these POMs. A template is proposed to account for the marked enhancement of reactivity and selectivity, in which the allylic alcohol is ligated through metal−alcoholate bonding, and the H_2O_2 oxygen source is activated in the form of a peroxotungsten complex. 1,3-Allylic strain promotes a high preference for the *threo* diastereomer and 1,2-allylic strain a high preference for the *erythro* diastereomer, whereas tungsten−alcoholate bonding furnishes high regioselectivity for the epoxidation of the allylic double bond. The estimated dihedral angle α of 50−70° for the metal−alcoholate-bonded template of the POM/H_2O_2 system provides the best compromise between ^{1,2}A and ^{1,3}A strain during the oxygen transfer. In contrast to acyclic allylic alcohols **1**, the M-POM-catalyzed oxidation of the cyclic allylic alcohols **4** by H_2O_2 gives significant amounts of enone.

Introduction

The fine chemical industry is facing increased pressure to develop sustainable alternatives for classical processes that no longer meet current environmental constraints. With respect to oxidative transformations, there is a need for the development of effective catalytic systems that enable the selective manufacture of oxygen-functionalized fine chemicals based on cheap, readily available, and environmentally benign oxidants such as hydrogen peroxide and nontoxic metal catalysts.[1] In this context, recently polyoxometalates (POMs), in particular their transition-metal-substituted derivatives, have gained importance as homogeneous and heterogeneous oxidation catalysts due to their oxidative and hydrolytic stability, ease of preparation and facile modification.[2] For this purpose, a variety of oxygen sources may be employed, which include iodosobenzene,[3] *N*-oxide,[4] nitrous oxide,[5] periodate,[6] ozone,[7] dioxygen,[8] hydrogen peroxide,[9] and *tert*-butyl hydroperoxide.[10]

Initially, the tungsten-based polyoxometalates $[PW_{12}O_{40}]^{3-}$ and $\{PO_4[W(O)(O_2)_2]_4\}^{3-}$ were used to cata-

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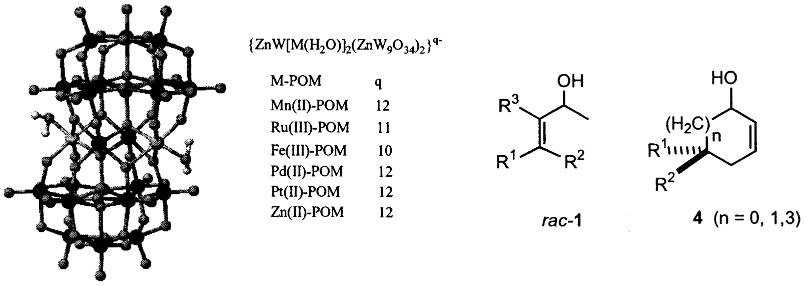

FIGURE 1. Structures of the sandwich-type polyoxometalate M-POM catalysts and allylic alcohols.

lyze the oxidation of organic substances by hydrogen peroxide under phase-transfer conditions.[11,12] The resulting tungsten peroxo complexes, derived from these polyoxometalate catalysts, serve as the active oxygen-transfer agent.[13] With regard to the commonly used α-Keggin and Wells−Dawson POMs, their unfortunate property is that they do not persist against solvolytic and oxidative decomposition, especially in the presence of H_2O_2, as has been proved by kinetic and spectral studies.[2b,13]

Recently, the so-called sandwich-type polytungstometalates $[WXM_2(H_2O)_2(XW_9O_{34})_2]^{12-}$ with X = Zn(II) or Co(II) (Figure 1), initially prepared by Tourné,[14] have received attention as promising oxidation catalysts.[7,8a−c,9b−f,10b] These anions contain two B-$[XW_9O_{34}]^{12-}$ truncated Keggin fragments, linked by four coplanar octahedrally coordinated and close-packed d transition-metal atoms. Both the heteroatoms in the trivacant Keggin fragments and the four transition-metal ions in the central ring may be varied extensively,[14] which provides still unexplored opportunities for the design of new oxidation catalysts. A definite advantage of the sandwich-type POMs is their higher resistance toward hydrolysis as well as oxidative degradation by H_2O_2[9c] than those of most common Keggin and Wells−Dawson structures.

A good example of uniquely high catalytic activity in hydrogen peroxide-mediated oxidations is the Mn(II)-disubstituted POM, namely $[WZnMn^{II}_2(ZnW_9O_{34})_2]^{12-}$, which displays high selectivity for the epoxidation of alkenes and the oxidation of alcohols by 30% H_2O_2 in a biphasic system; indeed, hundreds to thousands of catalytic turnovers have been achieved.[9b,c] Other isostructural noble-metal [Rh(III), Pd(II), Pt(II), and Ru(III)] disubstituted analogues have also been shown to exhibit activity in alkene and alkane oxidations with H_2O_2 and ^{t}BuOOH.[9d,10b] In fact, the ruthenium derivative was found to be effective in the oxidation of adamantane even by molecular oxygen.[8a−c]

Despite this success, conspicuous is the fact that sandwich-type POMs have not been employed for the epoxidation of chiral allylic alcohols.[15] The chiral allylic alcohols not only are valuable stereochemical probes for the elucidation of oxygen-transfer transition structures,[16] but also offer the opportunity to test the chemoselectivity of the oxidation in terms of epoxide versus enone formation, that is, oxygen transfer to the double bond or oxygen insertion into the allylic CH bond. In this context, catalytic systems such as $Ti(O^iPr)_4$/TBHP,[17] $VO(acac)_2$/TBHP,[18] H_2WO_4/H_2O_2,[19] methyltrioxorhenium (MTO)/UHP,[20] manganese(salen)/PhIO,[21] and iron(porphyrin)/PhIO,[21] and the stoichiometric oxidants DMD[22] and *m*-CPBA[18] have been used in the epoxidation of allylic

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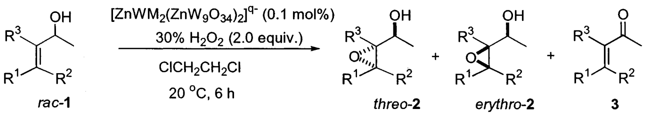
SCHEME 1. Catalytic Epoxidation of Chiral Allylic Alcohols Catalyzed by Sandwich-Type POMs with H_2O_2



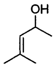
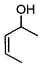
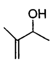
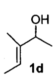
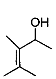
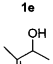
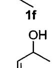
alcohols and have furnished relevant information on the transition structures of the oxygen-transfer process. Indeed, a very recent preliminary report[23] demonstrated the efficacy of the oxidatively and solvolytically persistent sandwich-type polyoxometalates for the epoxidation of the chiral allylic alcohols **1** by hydrogen peroxide. High (>95%) chemo-, regio-, and diastereoselectivities have been achieved in the epoxidation of 1,3- or 1,2-allylically strained alcohols.

Herein, we present our detailed study on the epoxidation of chiral allylic alcohols **1** with aqueous hydrogen peroxide as the oxygen source, catalyzed by the sandwich-type polyoxometalates, in particular $\{WZn[M(H_2O)]_2(ZnW_9O_{34})_2\}^{q-}$ [M-POM; M = Mn(II), Ru(III), Fe(III), Pd(II), Pt(II), and Zn(II); Figure 1]. Besides chemoselectivity and stereoselectivity, also the regioselectivity was assessed with the help of 1-methylgeraniol (**1h**) and geraniol (**1i**) as substrates. For mechanistic comparison, the catalytic epoxidation of the same set of chiral allylic alcohols **1** was also conducted with the lacunary Keggin-type POM $[PW_{11}O_{39}]^{7-}$ as catalyst. To acquire structural information on the transition-state geometry in the M-POM-catalyzed epoxidation, a set of cyclic allylic alcohols **4** with varying ring size and defined dihedral angles α (C=C—C—OH) were selected as substrates in this work.

Results

The polyoxometalates used in the present studies and their corresponding hydrophobic methyltricaprylammonium salts,[24] as well as the racemic allylic alcohols **1**, were synthesized according to literature procedures (see the Experimental Section). The epoxidations (Scheme 1) were conducted at ca. 20 °C with an M-POM:allylic alcohol:H_2O_2 (30%) ratio of 1:1000:2000 in a biphasic system of water and 1,2-dichloroethane (Table 1); similar results have been obtained in toluene (data not shown). The results in Table 1 reveal that these sandwich-type POMs effectively catalyze the epoxidation of the allylic alcohols **1** to the epoxy alcohols **2**, most of them in excellent conversions (>95%). A comparatively low reactivity (30—50% conversion) was observed for the 1,2-allylically strained substrate **1c** (entries 11—13), which is due to the poorer nucleophilicity of the terminal double bond. Allylic oxidation (CH insertion) to the α,β-unsaturated enone **3** was observed to a minor extent (ca. 5—17%) only for derivative **1g** (Table 1, entries 23—25). Thus, the epoxidation of allylic alcohols by M-POM is highly chemoselective. Fortunately, the usual undesirable secondary reactions of the epoxides, i.e., hydrolysis, cleavage, and rearrangement, were not observed under the present reaction conditions.[25]

TABLE 1. Reactivity, Chemoselectivity, and Diastereoselectivity for the Catalytic Epoxidation of Chiral Allylic Alcohols 1 by 30% H_2O_2 and the Sandwich-Type Polyoxometalates in 1,2-Dichloroethane[a]

entry	substrate	M-POM	convn [%][b]	yield **2** [%][b]	selectivity[b]	
					chemo **2 : 3**	diastereo (*threo:erythro*)
1	 **1a**	Mn(II)	> 95	88 (80)	> 95: 5	92: 8
2		Ru(III)	> 95	95	> 95: 5	92: 8
3		Fe(III)	> 95	90	> 95: 5	95: 5
4		Pd(II)	> 95	92	> 95: 5	93: 7
5		Pt(II)	> 95	89	> 95: 5	93: 7
6		Zn(II)	> 95	85	> 95: 5	95: 5
7	 **1b**	Mn(II)	90	95 (84)	> 95: 5	90:10
8		Ru(III)	82	80	> 95: 5	88:12
9		Fe(III)	80	95	> 95: 5	89:11
10		Zn(II)	90	> 95	> 95: 5	88:12
11	 **1c**	Mn(II)	50	95	> 95: 5	8:92
12		Ru(III)	47	94	> 95: 5	7:93
13		Fe(III)	30	95	> 95: 5	5:95
14	 **1d**	Mn(II)	80	77	> 95: 5	13:87
15		Ru(III)	71	92	> 95: 5	14:86
16		Fe(III)	65	75	> 95: 5	14:86
17	 **1e**	Mn(II)	95	80	> 95: 5	78:22
18		Ru(III)	95	80	> 95: 5	76:24
19		Fe(III)	90	82	> 95: 5	78:22
20[c]	 **1f**	Mn(II)	95	95 (86)	> 95: 5	45:55
21[c]		Ru(III)	90	85	> 95: 5	44:56
22[c]		Fe(III)	82	90	> 95: 5	46:54
23	 **1g**	Mn(II)	81	83	95: 5	55:45
24		Ru(III)	60	90	83:17	60:40
25		Fe(III)	70	90	95: 5	57:43

[a] All reactions were carried out at ca. 20 °C for 6 h with allylic alcohol **1** (0.50 mmol), M-POM (0.1 mol %), and 2 equiv of 30% H_2O_2. [b] Conversions (allylic alcohol), yields of epoxy alcohol **2** (adjusted to 100% conversion), and product ratios were determined by ^1H NMR analysis on the crude reaction mixture with dimethyl isophthalate as internal standard, ca. 5% error of the stated value. For ratios >95%, only one product was observed in the ^1H NMR analysis. In parentheses are given the yields of isolated material after silica gel chromatography. [c] About 10—12% isomerized epoxide (*E*)-**2f** was observed in a *threo:erythro* ratio of ca. 12:88.

The M-POM-catalyzed epoxidation of allylic alcohols is not only chemoselective, but also highly diastereoselective. The alcohols **1a,b** with 1,3-allylic strain were exclusively epoxidized by Mn(II)-POM predominately to the *threo*-epoxy alcohols **2a**,**b** in excellent chemoselectivity (no enone formation) and high reactivity (>90% conversion) within 6 h (entries 1 and 7). It should be noted that the substituting transition metal in the sandwich POM displays little effect on the catalytic activity and selectivity. This indicates that redox-type transition metals are not directly involved in the M-POM-catalyzed epoxidation of allylic alcohols by H_2O_2.

The allylic alcohols **1c**,**d** with 1,2-allylic strain were epoxidized less efficiently by these POM catalysts; mechanistically more significant, the *erythro*-epoxides **2c**,**d** were

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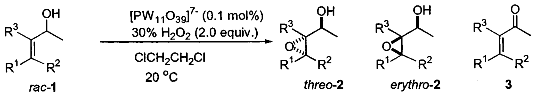
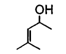
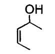
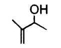
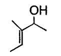
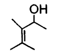
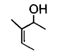
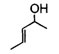
(24) Catalysis with polyoxometalates is commonly conducted by transferring the polyoxoanion into an organic solvent by means of a quaternary ammonium cation. Upon extraction into the organic solvent, the labile H_2O ligand, initially coordinated to the transition metal, is displaced, to afford the preferred salt $Q_q[ZnWM_2(ZnW_9O_{34})_2]$ $[Q = (n\text{-}C_8H_{17})_3CH_3N^+]$; see ref 9c.

(25) In this study, no buffer was used in the epoxidation, despite the relatively high acidity (pH ca. 2) of the aqueous phase of the biphasic system. Fortunately, for the substrates reported herein, the acid-catalyzed decomposition of both the allyl alcohols and their epoxides was not appreciable during the relatively short reaction time. The material balance was good to excellent under the present reaction conditions.

TABLE 2. Reactivity, Chemoselectivity, and Diastereoselectivity for the Catalytic Epoxidation of Chiral Allylic Alcohols 1 by 30% H_2O_2 and the Lacunary Keggin-Type Polyoxometalate[a]



entry	substrate	time [h]	convn [%][b]	yield **2** [%][b]	selectivity[b] chemo **2:3**	selectivity[b] diastereo (*threo:erythro*)
1	 **1a**	1	50	70	> 95: 5	95: 5
2		6	86	< 5[c]	–	–
3[d]		6	> 95	90	> 95: 5	89:11
4	 **1b**	6	64	40	> 95: 5	90:10
5	 **1c**	6	66	50	> 95: 5	4:96
6	 **1d**	6	65	75	> 95: 5	10:90
7	 **1e**	6	87	30	> 95: 5	76:24
8	 **1f**	6	90	45	> 95: 5	48:52
9	 **1g**	6	84	40	95: 5	54:46

[a,b] For details see Table 1. [c] Only a trace of epoxide **2a** was observed. [d] In the presence of pyridine (1.0 mol %).

produced in excellent diastereoselectivity (entries 11−16). This reveals that both 1,2- and 1,3-allylic strains dominate in the stereocontrol of the oxygen transfer to chiral allylic alcohols in the M-POM-catalyzed epoxidation. Consequently, substrates **1e**,**f** (entries 17−22) with both 1,2- and 1,3-allylic strain were epoxidized in low diastereoselectivity because of the opposing sense in the stereodifferentiation displayed by these two types of allylic strain. Expectedly, poorer diastereoselectivity was also observed for the alcohol **1g** (entries 23−25) with no allylic strain.

To gain mechanistic insight, the catalytic epoxidation of the same set of chiral allylic alcohols **1** has also been conducted with the lacunary Keggin-type POM $[PW_{11}O_{39}]^{7-}$ as catalyst under identical reaction conditions, in which the peroxotungstate complex $\{PO_4[W(O)(O_2)_2]_4\}^{3-}$ has been shown to serve as the active oxidizing species.[13] Although this POM does not contain a redox-active transition metal, chemoselectivities and diastereoselectivies (Table 2) similar to those of the transition-metal-substituted M-POMs were observed (Table 1). However, compared to the M-POM-catalyzed epoxidations, significantly lower product yields were obtained for the lacunary Keggin POM, especially in the case of the substrate **1a**, for which only traces of epoxide were observed upon 86% conversion (Table 2, entry 2). Control experiments showed that acid-sensitive allylic alcohols and their epoxides do not persist under these reaction conditions. Presumably, appreciable acidity of this catalytic system led to the decomposition of both the substrate and the epoxide, which is responsible for the low yields in these epoxidations. Indeed, the use of pyridine as buffer dramatically increased the product yields in the epoxidation of allylic alcohol **1a** by the lacunary Keggin POM (Table 2; cf. entries 2 and 3). These results demonstrate that sandwich-type POMs are more advantageous than lacunary Keggin-type POMs for the selective catalytic epoxidation of chiral allylic alcohols.[26]

To assess the regioselectivity of the M-POM-catalyzed epoxidation by H_2O_2 as the oxygen source, 1-methylgeraniol **1h** and geraniol **1i** were employed as substrates; the former also permits one to probe the diastereoselectivity (Table 3).[27] Both substrates were epoxidized exclusively at the allylic alcohol site by the sandwich-type POMs (entries 1−9, 11, and 12). Essentially the same regioselectivity was observed in the epoxidation of substrate **1h** by the Keggin-type POM $[PW_{11}O_{39}]^{7-}$ (entry 10). As expected, analogous to the related 1,3-allylically strained alcohols **1a**,**b**, also a very high *threo* selectivity was obtained for the 3,4-epoxide in the epoxidation of **1h** by the M-POMs (entries 1−9) and with the lacunary Keggin-type POM (entry 10). In toluene (entry 2), the results are essentially the same as in 1,2-dichloroethane (entry 1), whereas in methanol (entry 3), the selectivities are the same as those in the nonprotic solvents, yet the reactivity dropped considerably, i.e., to only 20% conversion from 95%. Significantly, similar catalytic activity and identical selectivities were observed when 0.01 mol % instead of 0.1 mol % Mn(II)-POM and only 1.0 equiv of H_2O_2 were employed in the catalytic epoxidation of substrate **1h** (entry 4). These findings illustrate the very high catalytic efficiency (ca. 8000 TON) of the sandwich-type POMs in the selective epoxidation of allylic alcohols. Again, the type of transition metal in the polyoxometalate does not affect the reactivity, chemoselectivity, or stereoselectivity of the allylic alcohol oxidation by hydrogen peroxide (entries 1 and 5−9).

To acquire structural information on the transition-state geometry in the M-POM-catalyzed epoxidation, a set of chiral cyclic allylic alcohols **4** with varying ring size and defined dihedral angles α (C=C−C−OH) in their favored ground-state conformations were oxidized by Mn(II)-POM with H_2O_2 as the oxygen source (Table 4). In contrast to acyclic allylic alcohols **1**, for which only small amounts, if at all, of the α,*β*-unsaturated enones were observed (cf. Table 1), the M-POM-catalyzed oxidation of the cyclic allylic alcohols **4** by H_2O_2 gave significant amounts of enone. In the case of the cyclopentenol **4a**, the epoxide **5a** was obtained as the major product with exclusive *cis* diastereoselectivity, but as much as 12% enone was also formed (entry 1). However, in the oxidation of 2-cyclohexen-1-ol (**4b**) by Mn(II)-POM, the enone **6b** was produced as the major product, albeit the *cis*-epoxy alcohol **5b** was obtained in a high diastereoselectivity (entry 2). This product selectivity and stereochemical course is independent of the transition metal in the M-POM catalyst, since nearly the same results were obtained with the Zn(II)-POM catalyst (entry 3). In the oxidation of the conformationally rigid *cis*- and *trans*-5-*tert*-butyl-2-cyclohexenols (*cis*-**4c** and *trans*-**4c**), more enone is formed from the *cis* isomer (OH *pseudo equatorial*, α = 140°) than the *trans* one (OH *pseudo axial*, α = 110°), although very high diastereoselectivities were

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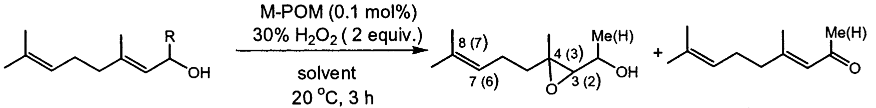
(26) A full comparison of the catalytic activity of the sandwich-type POMs with the simple α-Keggin POMs and tungstic acid (H_2WO_4) is beyond the scope of this paper. It is certainly an advantage, however, that the sandwich POMs catalyze the epoxidation of the allylic alcohols in up to 10000 turnovers compared to the α-Keggin POMs, which are irreversibly inactivated already after several hundred turnovers.

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

TABLE 3. Catalytic Epoxidation of 1h and 1i by 30% H_2O_2 and the Sandwich-Type Polyoxometalate M-POM[a]

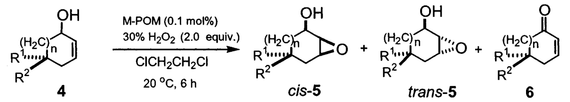


R = Me, **1h**
R = H, **1i**
3,4-**2h**
2,3-**2i**
3h
3i

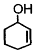
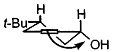
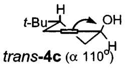
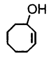
entry	R	catalyst	solvent	convn (%)	yield[b] (%)	selectivity regio[c]	chemo (2:3)	diastereo (*threo*:*erythro*)
1	Me	Mn(II)-POM	$ClCH_2CH_2Cl$	>95	95 (86)	>95:5	>95:5	93:7
2			$C_6D_5CD_3$	95	95	>95:5	>95:5	90:10
3			CD_3OD	20	95	>95:5	>95:5	95:5
4[d]	Me	Mn(II)-POM	$ClCH_2CH_2Cl$	85	92	>95:5	>95:5	93:7
5	Me	Ru(III)-POM	$ClCH_2CH_2Cl$	>95	90	>95:5	95:5	92:8
6	Me	Fe(III)-POM	$ClCH_2CH_2Cl$	>95	95 (93)	>95:5	>95:5	94:6
7	Me	Zn(II)-POM	$ClCH_2CH_2Cl$	95	95	>95:5	>95:5	94:6
8	Me	Pd(II)-POM	$ClCH_2CH_2Cl$	>95	95	>95:5	>95:5	94:6
9	Me	Pt(II)-POM	$ClCH_2CH_2Cl$	>95	95	>95:5	>95:5	94:6
10	Me	$[PW_{11}O_{39}]^{7-}$	$ClCH_2CH_2Cl$	76	90	>95:5	>95:5	93:7
11	H	Mn(II)-POM	$ClCH_2CH_2Cl$	>95	95 (90)	>95:5	>95:5	
12	H	Zn(II)-POM	$ClCH_2CH_2Cl$	>95	>95	>95:5	>95:5	

[a,b] For details see Table 1, except that the reaction time was 3 h. [c] Entries 1–10 for **2h** (3,4:7,8 ratio) and entries 11 and 12 for **2i** (2,3:6,7 ratio). [d] The reaction was run with 0.01 mol % catalyst and 1.0 equiv of 30% H_2O_2 for 6 h.

TABLE 4. Catalytic Epoxidation of Cyclic Allylic Alcohols 4 by 30% H_2O_2 and the Sandwich-Type Polyoxometalate M-POM[a]



4 *cis*-**5** *trans*-**5** **6**

entry	substrate (α)[c]	M-POM	convn [%][b]	yield 5 [%][b]	selectivity[b] chemo (5 : 6)	diastereo (*cis:trans*)[d]
1	 **4a** (α 120°)	Mn(II)-POM	88	66	88:12	> 95:05
2	 **4b** (α 139°)	Mn(II)-POM	66	36	42:58	93:07
3		Zn(II)-POM	65	38	45:55	90:10
4	 *cis*-**4c** (α 140°)	Mn(II)-POM	88	43	45:55	93:07
5	 *trans*-**4c** (α 110°)	Mn(II)-POM	46	70	71:29	96:04
6	 **4d** (α 199°)	Mn(II)-POM	> 95	88	92:08	< 05:95

[a,b] For details see Table 1. [c] Dihedral angle of C=C–C–OH. [d] The descriptors *cis* and *trans* pertain to the configuration of the epoxide functionality relative to the allylic hydroxy group.

observed in both cases, again in favor of the *cis*-epoxides (entries 4 and 5). The exclusive *trans* selectivity for the cyclooctenol **4d** (entry 6) speaks for purely steric interactions in the conformer of minimal transannular strain, as reported for other oxidants.[28]

Discussion

The present results (Tables 1 and 3) conspicuously demonstrate that chiral allylic alcohols may be epoxidized in high selectivities with the environmentally benign oxygen source 30% H_2O_2, catalyzed by the oxidatively and solvolytically persistent sandwich-type polyoxometalates. As for the mechanism of the oxygen transfer, in view of the structural composition of these sandwich-type POMs, the reaction may occur at either the substituting metal center or the framework tungsten site of the intactcatalyst;[9c] however, possibly also W-containing fragments derived from the sandwich-type POM may function as the active oxidant.[9k] The following facts constitute evidence that a tungsten peroxo complex serves as the likely oxidant rather than a high-valent transition-metal oxo species:[29] The transition metal in the central ring of these sandwich-type POMs (Mn, Ru, Fe, Pd, Pt) does not notably affect the reactivity and selectivity of these catalysts (Tables 1 and 3); the oxidatively inactive Zn metal (Tables 1 and 3) performs just as effectively in this epoxidation as the former redox metals; the purely tungsten containing lacunary Keggin POM $[PW_{11}O_{39}]^{7-}$ epoxidizes the same set of chiral allylic alcohols in similar selectivities (Table 2). The advantage of epoxidations catalyzed by the sandwich-type POMs compared to the phospho-Keggin POMs is the higher persistence of the former against degradation, such that very high catalytic activity (ca. 8000 TON) may be achieved. Moreover, the lower Lewis acidity of the sandwich POMs circumvents the need of adding a basic buffer (e.g., pyridine), as is required for tungstic acid-catalyzed epoxidations of allylic alcohols.[19] Be this as it may, it must be emphasized that, irrespective of these mechanistic options, the preparative value of this expoxidation methodology should be evident.

The present stereochemical (Table 1) and regiochemical data (Table 3) shall now be analyzed to propose a catalytic cycle for the sandwich-type POM-catalyzed epoxidation of the chiral allylic alcohols. First, the question arises about the electronic nature of the interaction between the substrate and the POM catalyst, that is, hydrogen bonding versus metal–alcoholate binding,

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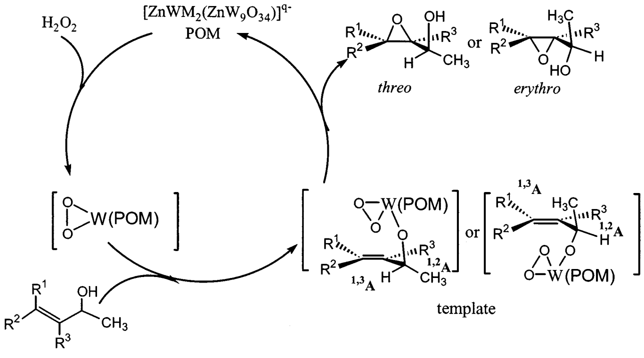
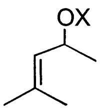
(28) Adam, W.; Mitchell, C. M.; Saha-Möller, C. R. *Eur. J. Org. Chem.* **1999**, 785–790.

(29) A tungsten hydroperoxy species $[W(OOH)^+]$ may not be excluded as oxidant, since the present catalytic system is strongly acidic.

SCHEME 2. Proposed Catalytic Cycle for the M-POM-Catalyzed Epoxidation of Chiral Allylic Alcohols by Hydrogen Peroxide



to account for the observed high selectivities. The need of the hydroxy functionality is demonstrated by the total lack of epoxidation reactivity of the ester and ether derivatives **1a(Ac)** and **1a(Me)** under the present reaction conditions.



X = Ac: **1a(Ac)**
X = Me: **1a(Me)**

Furthermore, the finding that in protic solvents such as methanol the regioselectivity and diastereoselectivity are not affected, although the reactivity drops considerably (Table 3, entry 3), indicates that the hydrogen-bonding mechanism does not operate in the present POM system.[16] As for the low reactivity in the methanol, it is known that the epoxidation activity of the peroxo species of tungsten or molybdenum is inhibited by strongly coordinating solvents.[30]

The high regioselective preference for the allylic alcohol double bond in the 1-methylgeraniol and geraniol (Table 3) substantiates the fact that the allylic hydroxy group is ligated to the catalytic species by means of a metal–alkoxide bond to give the 3,4 or 2,3 regioisomer as the epoxide product. Such binding favors the oxygen transfer to the proximate allylic double bond rather than to the remote unfunctionalized double bond. This is analogous to the known catalytic oxidants $Ti(O^iPr)_4$/TBHP and $VO(acac)_2$/TBHP, typical for metal–alcoholate binding, which also afford the 3,4 epoxide in high preference (95:5) in the epoxidation of **1h** or **1i**; in contrast, the characteristic hydrogen-bonding systems *m*-CPBA and DMD favor the 7,8 regioisomer.[27]

Clearly, a template effect operates, in which metal–alkoxide bonding of the allylic substrate and metal activation of the oxygen donor H_2O_2 through a tungsten peroxo species assist the oxygen-transfer process [a peroxy-type structure ($WOOH^+$) would also qualify]. This accounts for the remarkable enhancement of reactivity and selectivity in the M-POM-catalyzed epoxidation of allylic alcohols, as displayed in the proposed catalytic cycle in Scheme 2.

The transition-state geometry of this oxygen-transfer process shall now be considered in terms of the dependence of the diastereoselectivity on the dihedral angle O–C–C=C (α) between the π plane of the double bond and the hydroxy group of the allylic alcohols. The α angles assume characteristic values for catalytic and stoichiometric epoxidations of chiral allylic alcohols with allylic strain. Typical dihedral angles for some pertinent established oxidants and their *threo*/*erythro* diastereoselectivities are listed in Table 5, with which the data for the POM catalysts in Tables 1 and 2 shall be compared.

For the POM/H_2O_2 catalytic system, the *threo* diastereomer is highly preferred in the epoxidation of substrates **1a** and **1b** with 1,3-allylic strain (entries 1 and 2). Mechanistically significant, for the substrates **1c** and **1d** with only 1,2-allylic strain, also excellent diastereoselectivity is expressed, but the *erythro* diastereomer is now favored (entries 3 and 4). When 1,2- and 1,3-allylic strains are both competing in the same molecule, as in the stereochemical probe **1f**, the epoxidation is nondiastereoselective (entry 5) because of the opposing sense in the stereodifferentiation displayed by these two types of allylic strain. Comparison of these POM diastereoselectivities with the ones of established oxidants in Table 5 discloses that the POM data fit qualitatively well with both the $Ti(O^iPr)_4$/TBHP and $VO(acac)_2$/TBHP oxidants, for which also a template with metal–alcoholate bonding applies. Therefore, this stereochemical comparison suggests that the dihedral angle in the transition structure with the POM oxidants lies between those for $VO(acac)_2$/TBHP (40–50°) and $Ti(O^iPr)_4$/TBHP (70–90°), and may be estimated to be 50–70° (Figure 2). Evidently, the intermediate α angle for the metal–alcoholate-bonded structure **III** [a peroxy-type structure ($WOOH^+$) would also qualify] in the case of the POM/H_2O_2 system provides the best compromise between $^{1,2}A$ and $^{1,3}A$ strain during the oxygen transfer.

The α angle of 50–70° estimated for the POM-catalyzed epoxidation of the acyclic allylic alcohols (Figure 2) also provides a clue to why so much enone is formed with the cyclohexenol substrates **4b**,**c** (Table 4). The fact that about twice as much enone is formed for the *cis*-**4c** (OH *pseudo equatorial*) than for the *trans*-**4c** (OH *pseudo axial*) demonstrates that the product selectivity depends on the dihedral angle α (Table 4, entries 4 and 5). Clearly, the larger the deviation from this optimal α angle of 50–70° in the metal–alcoholate template, the more competitive the allylic oxidation. Thus, more enone is expected to be formed from the *cis*-**4c** (α 140°) than from the *trans*-**4c** (α 110°) cyclic allylic alcohols (Table 4, entries 4 and 5). The high *cis* diastereoselectivity for the epoxidation of these cyclic substrates is independent of the α angle, because the conformationally fixed geometry and metal–alcoholate bonding oblige that the oxygen atom is transferred to the double bond from the side at which the allylic hydroxy functionality is located.

Conclusion

From our work on the sandwich-type POM-catalyzed epoxidation of allylically strained chiral alcohols **1**, a highly efficient, selective and mild oxyfunctionalization

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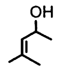
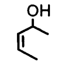
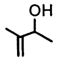
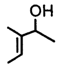
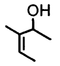
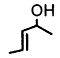
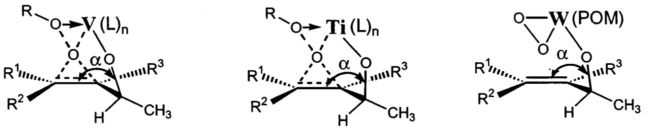
(30) (a) Mimoun, H.; De Roch, I. S.; Sajus, L. *Tetrahedron* **1970**, *26*, 37–50. (b) Mimoun, H. *Angew. Chem., Int. Ed. Engl.* **1982**, *21*, 734–750.

TABLE 5. Diastereoselectivities (*threo*:*erythro*) for the Epoxidation of Allylic Alcohols 1 by Polyoxometalates and Other Pertinent Catalytic and Stoichiometric Oxidants

entry (α)[e]	substrate	$[ZnWMn_2(II)(ZnW_9O_{34})_2]^{12-}$/ H_2O_2 (30%)[a]	$[PW_{11}O_{39}]^{7-}$/ H_2O_2 (30%)[a]	$VO(acac)_2$/ *t*-BuOOH[b] (α ca. 40-50°)	$Ti(O^iPr)_4$/ *t*-BuOOH[c] (α ca. 70-90°)	*m*-CPBA[c] CH_2Cl_2 (α ca. 120°)	DMD[d] acetone (α ca. 130°)
1	 **1a**	92: 8	95: 5	86:14	95: 5	95: 5	76:24
2	 **1b**	90:10	90:10	71:29	91:09	95: 5	67:33
3	 **1c**	8:92	4:96	05:95	–	45:55	56:44
4	 **1d**	13:87	10:90	10:90	24:76	48:52	51:49
5	 **1f**	45:55	48:52	33:67	83:17	90:10	87:13
6	 **1g**	55:45	54:46	29:71	66:34	64:36	64:36

[a] Data from this work; see Tables 1 and 2. [b] See ref 18. [c] See ref 17. [d] See ref 22. [e] Dihedral angle of C=C—C—OH.



I (40°< α < 50°) **II** (70°< α < 90°) **III** (50°< α < 70°)

FIGURE 2. Proposed transition structures with the optimal dihedral angles for the epoxidation of the chiral allylic alcohols by $VO(acac)_2$/TBHP (**I**), $Ti(O^iPr)_4$/TBHP (**II**), and POM/H_2O_2 (**III**).

has become available, in which the reactivity and selectivity derive from template formation with the tungstate metal. In this template, the allylic alcohol is ligated through metal—alcoholate bonding and the hydrogen peroxide oxygen source is activated in the form of a peroxotungsten complex. 1,3-Allylic strain expresses a high preference for the *threo* diastereomer and 1,2-allylic strain a high preference for the *erythro* diastereomer, whereas tungsten—alcoholate bonding accelerates the reaction rate and furnishes high regioselectivity for the epoxidation of the allylic double bond. Evidently, the catalysis by the readily available sandwich-type polyoxometalates provides a valuable synthetic method for the selective catalytic epoxidation of allylic alcohols by H_2O_2 as the oxygen source.

Experimental Section

General Aspects. The conversions, yields, and product ratios were determined by ^1H NMR spectroscopy with dimethyl isophthalate as internal standard. TLC analysis was conducted on precoated silica gel foils 60 F_{254} (20 × 20 cm). Spots were visualized by treatment with polymolybdic acid (5% solution in ethanol) test spray. Silica gel (32—63 μm) was used for flash chromatography. For peroxide tests, potassium iodide/starch indicator paper was used. Solvents were dried by standard methods and purified by distillation before use. Commercially available chemicals were used without further purification, unless otherwise stated.

Starting Materials. The sandwich-type polyoxometalate $Na_{12}\{ZnW[Zn(H_2O)]_2[ZnW_9O_{34}]_2\}\cdot 44H_2O$, and other isostructral disubstituted transition-metal derivatives with the Mn(II), Fe(III), Pd(II), and Pt(II) metals were synthesized and characterized by a literature procedure.[14] The ruthenium(III) analogue $Na_{11}\{ZnW[Ru_2(H_2O)(OH)](ZnW_9O_{34})_2\}\cdot 42H_2O$ was likewise prepared by a known procedure.[10b] The lacunary α-Keggin $Na_7[PW_{11}O_{39}]$ was obtained according to a procedure as reported.[31] The known and fully characterized allylic alcohols **1a**,[32] **1a(Ac)**,[33] **1a(Me)**,[34] **1b**,[35] **1c**,[36] **1d**,[37] **1e**,[32] **1f**,[37] **1g**,[38] and **1h**[27] and the conformationally fixed *cis*- and *trans*-5-*tert*-butyl-2-cyclohexenols (**4c**)[39] were synthesized according to known methods. The 2-cyclopentenol (**4a**) and 2-cyclooctenol (**4d**) were prepared by photooxygenation of the corresponding cycloalkenes and subsequent reduction with triphenylphosphine according to a literature procedure.[40] Geraniol (**1i**) and 2-cyclohexenol (**4b**) were commercially available. Hydrogen peroxide was employed as a 30% aqueous solution, whose concentration was determined by iodometry.[41]

Preparation of Stock Solutions of Hydrophobic POM Catalysts. The catalytic reactions with the polyoxometalates were performed by transferring the polyoxoanion into the organic solvents with a quaternary ammonium cation. For this purpose, the alkali metals of all transition-metal-substituted

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POMs were exchanged with hydrophobic quaternary ammonium salts (Aliquot 336), analogous to literature protocol.[9b−f] Thus, the stock solution (1.0 mM) was prepared by dissolving the particular sandwich M-POM (0.1 mmol), namely $Na_{12}\{ZnW[Zn(H_2O)]_2(ZnW_9O_{34})_2\}\cdot 44H_2O$ [Zn(II)-POM], $Na_{12}\{ZnW[Mn(H_2O)]_2(ZnW_9O_{34})_2\}\cdot 46H_2O$ [Mn(II)-POM], $Na_{10}\{ZnW[Fe(H_2O)]_2(ZnW_9O_{34})_2\}\cdot 46H_2O$ [Fe(III)-POM], $Na_{11}\{ZnW[Ru_2(H_2O)(OH)](ZnW_9O_{34})_2\}\cdot 42H_2O$ [Ru(III)-POM], $K_{12}\{ZnW[Pd(H_2O)]_2(ZnW_9O_{34})_2\}\cdot 38H_2O$ [Pd(II)-POM], or $K_{12}\{ZnW[Pt(H_2O)]_2(ZnW_9O_{34})_2\}\cdot 36H_2O$ [Pt(II)-POM] or the lacunary Keggin POM $Na_7(PW_{11}O_{39})$ (0.1 mmol) and methyltricaprylammonium chloride (1.25 mmol) in a 1:1 mixture of water and 1,2-dichloroethane (200 mL). Under gentle heating at 40 °C and magnetic stirring, the color of the organic phase turned yellow [except for Zn(II)-POM and lacunary Keggin POM], whereas the aqueous phase was decolorized. The organic layer was separated, dried over anhydrous Na_2SO_4, and used as such.

General Procedure for the Catalytic Epoxidation of Chiral Allylic Alcohols 1 by POM Catalysts. For the epoxidation of the allylic alcohols **1** with 30% H_2O_2, the reactions were carried out in a 5 mL flask, equipped with a magnetic stirring bar. In a typical reaction, the specific substrate **1** (0.50 mmol) and dimethyl isophthalate (0.20 mmol), as internal standard, were dissolved in the stock solution of the particular M-POM catalyst (0.50 mL, 1.0 mM). The reaction was initiated by addition of 30% hydrogen peroxide (110 μL, 1.0 mmol) to the solution at ca. 20 °C with magnetic stirring. The resulting biphasic mixture was stirred at a constant rate (ca. 1000 rpm) for all runs. The reaction progress was monitored by ^1H NMR spectroscopy or TLC, and after the required reaction time, the organic phase of the reaction medium was separated and dried over Na_2SO_4, and the solvent was removed (20 °C, 50 mbar). The conversions, yields, and product ratios were determined by ^1H NMR analysis directly on the crude mixture and are given in Tables 1−4. In some cases, the epoxides **2** were purified by silica gel chromatography with a 1:1 mixture of ethyl ether and petroleum ether (30−50 °C) as eluent. The epoxides **2**[27,42−47] and **5**[22,39] are both known and have been identified by comparison of their characteristic NMR signals with the literature reported data.

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