Practical Heterogeneous Catalysts for Epoxide Production

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Abstract: An overview of heterogeneous epoxidation catalysts is given, with an emphasis on practical parameters such as catalyst productivity, turnover numbers and stereoselectivity. Special focus is directed towards catalysts that have resulted from research in the authors' group.

Keywords: alkenes; allylic alcohols; epoxidation; heterogeneous catalysis; manganese; peroxides; titanium; tungsten

1 Introduction

Epoxide formation is a central reaction in the oxyfunctionalization of many molecules. Despite successes in homogeneous catalysis, there is a clear demand for solid materials that catalyze epoxidations with easily available oxidants such as H_2O_2 and organic peroxides. In response to this, heterogeneous epoxidation remains a very active field of research, with wholly new and improved materials being proposed over the last few years.

In the present account, the existing heterogeneous epoxidation catalysts are reviewed and compared on a practical basis, i.e., considering substrate scope, activity and selectivity. Special attention goes to several W-, V- or Mn-based systems that we have developed in our own laboratories. In some cases, the use of the heterogenized catalyst brings about differences in substrate scope or stereochemistry with the corresponding homogeneous catalyst, and such examples are highlighted. Apart from simple olefins, two classes of functionalized olefins are discussed, *viz.* unsaturated alcohols and unsaturated ketones.

Quantitative comparison of catalysts from different research groups may not be easy, since reactant concentrations, temperature and analytics often vary. However, we believe that the following parameters give a sound idea of the practical value of a catalyst:

- turnover number (TON) = (moles of epoxide product)/(moles of metal),
- productivity = (mass of epoxide product)/(mass of catalyst).

The productivity may be calculated for a continuous experiment, or more commonly, for a batch reaction. For both values, we have systematically mentioned the time needed to reach this turnover number or productivity. Normalizing these data to equal times, as is often done with the *turnover frequency (TOF)*, somehow obscures the stability of the catalytic material as a function of time. While performing experiments in a continuous reactor would be most appropriate to evaluate the long-term stability of a catalyst, such data are unfortunately almost unavailable. Therefore, parameters such as turnover number (TON) and productivity, coupled to time, are the best approximation of catalyst stability one may obtain. Clearly, in several cases, scientists have rather concentrated on the novelty of the catalyst and its characterization, rather than on the lifetime of the new material. Nevertheless, the stability of the catalytic activity will eventually be decisive for a future application.

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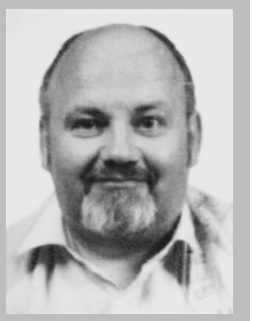
Dirk E. De Vos was born in Mechelen, Belgium, in 1967. After Ph. D. research with Pierre Jacobs in Leuven, he was a post-doc with Thomas Bein at Purdue University. After returning to Leuven, he became an Associate Professor and teaches Phytopharmaceutical Chemistry and Colloid Chemistry. His research focuses on solid catalysts for organic transformations. Awards include the Breck award (1998), the Award of the Royal Academy of Sciences (1999), the Deruyttere Award, and the BASF award for Catalysis (2001).

Bert F. Sels was born in Mol, Belgium, in 1972. He graduated from the University of Leuven and stayed for doctoral and post-doctoral work in the group of Pierre Jacobs. His Ph. D. thesis focused on organic reactions with LDH-derived catalysts. For his work, he was awarded several prizes, including the DSM award for Chemistry and Technology (1999).



Pierre A. Jacobs is the head of the Department Interphase Chemistry of the K. U. Leuven, Belgium. His research started in physical chemistry of zeolite catalysts, under the direction of Jan Uytterhoeven. He pioneered hydrocarbon reactions with zeolites, and then gradually took an interest in heterogeneous catalysis applied to the synthesis of fine chemicals. He is a former president of the International Zeolite Association, and received numerous awards, including the P. H. Emmett award in Fundamental Catalysis of the ACS (1981), the Donald W. Breck award of the International Zeolite Association (1998) and the Blechner award (2001). He teaches Organic Chemistry, Chemistry of Natural Products, Chromatography and Heterogeneous Catalysis.

The aim of the present paper is not to give a comprehensive overview of all catalysts that have ever been used in heterogeneous epoxidation; neither do we consider immobilized Ti or Mn catalysts for asymmetric epoxidation. For more information, e.g., concerning mechanistic aspects, immobilization methods, etc. the reader is referred to more or less recent literature.[1,2]

2 Epoxidation of Non-Functionalized Olefins

2.1 Ti-Catalyzed Epoxidation with H_2O_2

The scope of the TS-1-catalyzed epoxidation of olefins with H_2O_2 is accurately known.[3] Some data on turnover numbers and productivity are given in Table 1 (entries 1–4). Preferred substrates are small α-olefins and *cis*-disubstituted olefins. *trans*-Disubstituted and 1,1-disubstituted olefins react more slowly. This shows that even for molecules with equal access to the zeolite 10-MR pores, the position of the substituents influences the reactivity, proving that there are steric constraints to the approach of the olefin to the active site. Methanol is a preferred solvent, because it specifically coordinates to the Ti site, and since it causes a strong accumulation of the apolar olefin substrate inside the pores of the hydrophobic zeolite.[4,5] However, not only the olefin but also the epoxide product remains adsorbed inside the pores, and therefore deactivation of TS-1 is more rapid in methanol than in other solvents, particularly for long olefins. For the latter, it might be preferable to work in acetone. There are several known methods to regenerate deactivated TS-1 catalysts, e.g., calcination, or refluxing with dilute H_2O_2.[3,6] Work-up of TS-1 reaction mixtures is a delicate operation, since small amounts of α-hydroperoxy alcohols may be formed by attack of H_2O_2 on the epoxide product. These α-hydroperoxy alcohols may be removed by catalytic hydrogenation; or they may be separated from the epoxide product in a distillation.[3d]

It is well known that in contact with aqueous dilute H_2O_2, the TS-1 catalyst possesses a mild Brönsted acidity,[4] and in some cases, like the styrene epoxidation, this gives rise to extensive epoxide secondary reaction.[7] Epoxide selectivities can be increased in various ways. For propylene epoxidation, controlled trimethylsilylation of TS-1 increases the selectivity up to 97%.[3b] In the styrene case, the urea-H_2O_2 adduct has been used as an oxidant in acetone, and this resulted in a selectivity of 87%.[8]

Molecules with a kinetic diameter equal to or larger than that of cyclohexene are practically excluded from epoxidation with TS-1, and alternative Ti-containing zeolites with larger pores have been explored. The Ti-containing zeolite Beta seemed the best candidate, but it

was not until Al-free methods were developed for the synthesis of zeolite Beta that this work resulted in highly selective epoxidation catalysts. Al-free Ti-Beta may be prepared in a fluoride medium, or by seeding with dealuminated zeolite Beta seeds, or by using a special template such as di(cyclohexylmethyl)dimethylammonium hydroxide.[9–11] With Al-free Ti-Beta, epoxides can be obtained even from rather large olefins with selectivities that often exceed 90% (Table 1, entries 6–11). Note, however, that the structure still contains too much Lewis acidity to permit accumulation of acid-sensitive epoxides such as α-pinene epoxide. Suitable substrates are norbornene, limonene, or methyl-substituted cyclohexenes. In the latter group, the trisubstituted 1-methyl-1-cyclohexene is clearly less reactive than the 1,1-disubstituted methylenecyclohexane (Table 1, entries 9 and 10).[11] This proves that also for Ti-Beta, steric effects control the approach of the substrate to the active site or the formation of the transition state. The epoxidation of methyl oleate with aqueous H_2O_2 in acetonitrile shows that the highly hydrophobic Ti-Beta can successfully adsorb this apolar substrate, allowing its epoxidation with H_2O_2 (Table 1, entry 11).[12]

A few other Ti-zeolites have been proposed for epoxidation with H_2O_2, but the activities are not superior to those of Ti-Beta. Ti-substituted ferrierite has a low activity, but better activity is obtained with Ti-ITQ-6.[13] This zeolite is obtained by delamination of a layered, Ti-containing precursor of ferrierite, and calcination. This delamination strategy is very useful for increasing the accessibility of zeolite frameworks. Finally, a Ti-substituted ITQ-7 zeolite has been prepared; ITQ-7 is a three-dimensional large pore zeolite.[14] Data for the activity of Ti-ITQ-6 and Ti-ITQ-7 are included in Table 1 (entries 12, 13).

Ti has also been incorporated in mesoporous molecular sieves or amorphous SiO_2-based materials, and the properties of these materials as epoxidation catalysts with H_2O_2 have been studied. From the various studies, it emerges that the incorporation of organic groups in the siliceous surface, either during the formation of the material, or by post-synthesis modification, increases the epoxide selectivity.[15] Indeed, desorption of the epoxide is easier when there are fewer silanol groups on the material, and this reduces the amount of secondary reactions. The turnover number and productivity are generally lower than for Ti-zeolites (Table 1, entry 14). For cyclohexene, for instance, epoxide selectivities are generally not higher than 65%.[15] Therefore, use of such Ti-containing molecular sieves should only be preferred over use of TS-1 when truly bulky olefins are to be epoxidized, or when different stereoselectivities are expected.

2.2 Ti-Catalyzed Epoxidations with Organic Peroxides

The classical Ti-SiO_2 catalyst for epoxidation with organic peroxides was developed over 30 years ago. It is prepared by reaction of pyrogenic SiO_2 with $TiCl_4$.[16] Its excellent properties can be evaluated from data of batch experiments (Table 2, entries 1 and 2) or from

Table 1. Epoxidation of olefins with H_2O_2 catalyzed by Ti-zeolites or Ti-molecular sieves.

	Catalyst	Ti content [mmol · g^{-1}]	Substrate	T	Solvent	TON	Time	Productivity [(g product) · (g catalyst)]$^{-1}$	Time	Epoxide sel. [%]	Ref.
1	TS-1	0.33	propylene	40 °C	MeOH	610	1 h	11.5	1 h	95	[3a]
2	TS-1[a]	nm	propylene	40 °C	MeOH	nm		3.8	1 h	97	[6]
3	TS-1	0.35	1-hexene	25 °C	MeOH	37	0.13 h	1.3	0.13 h	>95	[3c]
4	TS-1	0.35	1-octene	45 °C	MeOH	35	0.08 h	1.6	0.08 h	>95	[3c]
5	TS-1	0.52	styrene[b]	40 °C	acetone	57	12 h	3.6	12 h	87	[8]
6	Ti-Beta[c]	0.36	1-hexene	50 °C	CH_3CN	47	2 h	1.7	2 h	100	[10b]
7	Ti-Beta[d]	0.24	1-hexene	70 °C	CH_3CN	182	3 h	4.4	3 h	93	[11]
8	Ti-Beta[d]	0.24	5-decene	70 °C	CH_3CN	166	3 h	6.2	3 h	90	[11]
9	Ti-Beta[d]	0.24	1-CH_3-cyclohexene	70 °C	CH_3CN	182	3 h	4.9	3 h	88	[11]
10	Ti-Beta[d]	0.24	methylene-cyclohexane	70 °C	CH_3CN	456	3 h	12.2	3 h	98	[11]
11	Ti-Beta[c]	0.49	methyl oleate	50 °C	CH_3CN	7.6	8 h	1.1	8 h	97	[12]
12	Ti-ITQ-6	0.13	1-hexene	50 °C	CH_3CN	23	5 h	0.3	5 h	96	[13a]
13	Ti-ITQ-7	0.14	1-hexene	50 °C	CH_3CN	78	7 h	1.1	7 h	100	[14]
14	Ti-MCM-41	0.4	1-octene	60 °C	MeOH	11	5 h	0.56	5 h	76	[11]

[a] Continuous experiment; data were evaluated after 3 h on stream. nm = not mentioned.
[b] Urea-H_2O_2 was used.
[c] Catalyst synthesized in an F medium.
[d] Synthesized with $(C_6H_{11}CH_2)_2(CH_3)_2NOH$.

continuous experiments. Most remarkably, in a continuous propylene epoxidation, the productivity of the Ti-SiO_2 catalyst hardly decreases with time on stream; over 380 h, a constant ethylbenzene hydroperoxide conversion was observed in the propylene epoxidation. In spite of the high temperatures (85–110 °C), acceptable epoxide selectivities are obtained.

Numerous modified preparation processes have been proposed, and catalytic results for these materials are gathered in Table 2. Maier and coworkers prepared microporous silica glasses containing Ti, starting from various Ti-cyclopentadienyl complexes, activated with *t*-BuOOH or H_2O_2.[17] *Via* a sol-gel process with TEOS, a xerogel was obtained which was calcined (Table 2, entries 3 and 4). Baiker and coworkers produced highly active aerogels. In the sol-gel process, acetylacetone modified Ti(O-*i*-Pr)$_4$ and TMOS were employed; the aerogel was obtained after semi-continuous extraction with supercritical CO_2 (Table 2, entries 5 and 6).[18,19]

On the other hand, a series of catalysts has been prepared based on the mesoporous siliceous sieve MCM-41, or on related mesoporous structures such as TUD-1.[20–22] Ti may be incorporated during the synthesis of MCM-41, or it may afterwards be grafted as $TiCp_2Cl_2$ on the calcined structure. The latter grafting method seems to result in more active catalysts (Table 2, entries 7 and 8).[20] As an alternative Ti-precursor, the compound (O-*i*-Pr)Ti[OSi(O-*t*-Bu)$_3$]$_3$ was recently used on SBA-15, a hexagonal, highly stable SiO_2 polymorph (Table 2, entry 9).[23] Another strategy to improve the activity of Ti-MCM-41 type catalysts is *via* controlled silylation.[21] An optimum was reached when about 80% of the surface was covered with trimethylsilyl groups (Table 2, entry 10). As a high-surface siliceous support, the delaminated zeolite ITQ-2 has also been used (Table 2, entry 11).[24]

From the data in Table 2, it is clear that using materials with well-defined mesoporosity, or special Ti precursors, very active materials may be obtained. An excellent example is the Ti-doped SBA-15 material: both the productivity and the number of Ti turnovers are very high.[23] Extremely high turnover numbers were observed for Ti-ITQ-2 (0.015 mmol Ti per g), but TON decreases as the Ti content increases, resulting in a more or less constant productivity.[24] In the class of the mixed oxides, the TiO_2-SiO_2 aerogels are still among the most active materials known.[18]

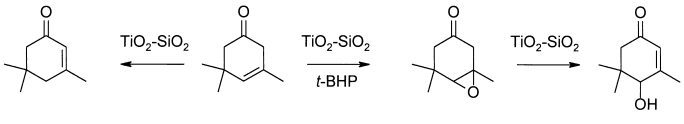
In many cases the scope of these materials has not yet been documented in detail, and only standard reactions with cycloalkenes or α-olefins have been performed. However, in case other substrates are used, some of the limitations of these catalysts may surface. For instance, because of Brönsted or Lewis acid sites in TiO_2-SiO_2, this material can also catalyze alkene isomerization, epoxide opening or alcohol dehydration.[18e] The presence of *t*-BHP appeared to even enhance the activity of the TiO_2-SiO_2 mixed oxide in the side reactions. To fine tune selectivities in epoxidation, weak bases may be useful, as in the case of β-isophorone: this molecule is

Table 2. Epoxidation of olefins with *t*-BHP catalyzed by Ti catalysts.[a]

	Catalyst	Ti content [mmol · g^{-1}]	Ti precursor	Substrate	*T*	TON	Time	Productivity [(g product) · (g catalyst)]$^{-1}$	Time	Epoxide sel. [%]	Ref.
1	Ti-SiO_2	0.083	$TiCl_4$	1-octene	107 °C	120	1 h	1.28	4 h	97.3	[16]
2	Ti-SiO_2	0.83	$TiCl_4$	1-octene	107 °C	47	1 h	5.5	1 h	90	[16]
3	Ti-SiO_2 glass	0.17	$(CpTiCl_2)O$	1-octene	80 °C	176	10 h	3.8	10 h	*nm*	[17a]
4	Ti-SiO_2 glass	0.083	$TiCp_2Cl_2$	cyclo-hexene	80 °C	340	10 h	2.8	10 h	*nm*	[17a]
5	TiO_2-SiO_2 aerogel[a]	2.5	Ti(O-*i*-Pr)$_4$ + acac	1-hexene	90 °C	25	1.3 h	6.4	1.3 h	95	[18b]
6	TiO_2-SiO_2 aerogel[a]	2.5	Ti(O-*i*-Pr)$_4$ + acac	cyclo-hexene	90 °C	27	0.06 h	6.6	0.06 h	100	[18b]
7	Ti-grafted MCM-41	0.37	$TiCp_2Cl_2$	cyclo-hexene	40 °C	140	6 h	6.3	6 h	*nm*	[20b]
8	Ti-grafted TUD-1	0.39	$TiCp_2Cl_2$	cyclo-hexene	40 °C	166	6 h	5.1	6 h	*nm*	[20b]
9	Ti on SBA-15	0.23	(O-*i*-Pr)Ti[O-Si(O-*t*-Bu)$_3$]$_3$	cyclo-hexene	65 °C	560	0.5 h	12.7	0.5 h	*nm*	[23]
10	Ti-MCM-41, silyl.	0.26	Ti(OEt)$_4$	cyclo-hexene	60 °C	160	0.5 h	4.1	0.5 h	98	[21]
11	Ti-ITQ-2	0.015	$TiCp_2Cl_2$	cyclo-hexene	60 °C	2300	2 h	3.5	2 h	98	[24]

[a] CumylOOH was used as the oxidant in entries 5 and 6. Mostly no solvent was used, except a dilutent for the oxidant, e.g., isooctane in entries 3 and 4. *nm* = not mentioned.

easily isomerized to α-isophorone; and β-isophorone oxide can be rearranged to 4-hydroxyisophorone (Equation 1).



(1)

By pretreating the aerogel TiO_2-SiO_2 catalyst with NaOAc, the overall epoxide yield of the reaction was increased from 70% to 85% based on peroxide.

2.3 W-Catalyzed Epoxidations

Tungsten-based epoxidation catalysts are generally anionic in the presence of aqueous H_2O_2. At least two general strategies have proven successful for the immobilization of W epoxidation catalysts. First, electrostatic interactions can be used, whether in an ion exchanger, or in a precipitated ionic compound. Secondly, peroxotungstates form heteronuclear associations with As, S or P oxyanions, and especially P-O-W associations are sufficiently stable in catalytic conditions to permit immobilization.

Tungstate can be easily exchanged on a layered double hydroxide;[25] usually only a fraction of the anion exchange capacity is used. The remainder can be occupied by small inorganic anions, which results in a highly hydrophilic catalyst; alternatively, tungstate can be co-exchanged with organic anions such as dodecyl sulfate or tosylate (Table 3, entries 1 and 2). These expand the interlayer galleries of the LDH structure and render the material highly hydrophobic. Alternatively, W polyoxoanions such as $[W_{12}O_{41}]^{10-}$ or $[SiW_{11}O_{39}]^{8-}$ can be used as intercalating anions to obtain expanded LDH structures. In such cases, the positive charge of the LDH is completely balanced by the W oxoanions alone (Table 3, entry 3). However, the polyoxoanions are not always completely stable in reactions with aqueous H_2O_2. In terms of stability, $[SiW_{11}O_{39}]^{8-}$ appeared a better choice than, e.g., $[W_{12}O_{41}]^{10-}$, and therefore the discussion will further focus on the former species.[26]

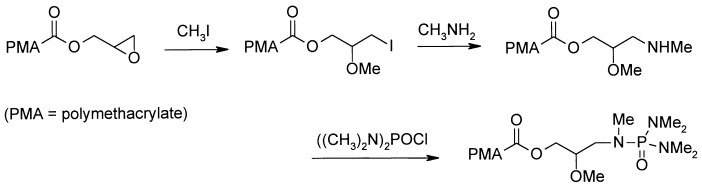
Another class of materials contains heterogenized quaternary ammonium functions, with charge-balancing anionic W catalysts. Examples are

- Amberlite IRA-900, a strong basic anion exchanger, partially exchanged with $[PW_4O_{24}]^{3-}$ (Table 3, entry 4);[27–30]
- an SiO_2 gel with phenyl and quaternary ammonium groups, exchanged with $[PW_4O_{24}]^{3-}$ or Neumann's sandwich compound $[WZnMn_2(ZnW_9O_{34})_2]^{12-}$; alternatively, an MCM-41 with quaternary ammonium groups can be used (Table 3, entries 5 and 6);[30,31]
- a polymeric organosiloxane containing quaternary ammonium groups, exchanged with $[WO_4]^{2-}$ or $[W_2O_{11}]^{2-}$.[32]

The stability of the W oxoanion in catalytic conditions is not always easily predicted. For instance, using the same quaternized MCM-41 support, we found that the use of $[WO_4]^{2-}$ or $[W_2O_{11}]^{2-}$ catalyst precursors led to small but detectable leaching (6–7%); by contrast, with the same support and $[PW_4O_{24}]^{3-}$, no leaching could be detected at all.[30]

For immobilization of W through P-O-W groups, immobilization of a P-containing group is first required. Some examples are:

- polyglycidyl methacrylate (PGMA) was functionalized with secondary amine groups (CH_2-NH-CH_3); these reacted with tetramethylphosphorodiamidic chloride to form an immobilized analogue of hexamethylphosphoric triamide, known to be a good ligand for peroxo W units (Equation 2 and Table 3, entry 8);[33]



(2)

- SiO_2 or MCM-41 were first functionalized with primary or secondary amines; these reacted with $OPCl_3$, $Cl_2PO(NMe_2)$ or $ClPO(NMe_2)_2$ to form immobilized phosphoramides as ligands for peroxo W (Table 3, entries 7 and 9).[29,30,34]

With the MCM-41-based catalyst, no leaching could be detected at all; with the catalysts containing phosphotriamides, W leaching levels were typically below 5%.[30,34]

Finally, two groups reported on immobilization of W oxidation catalysts by hydrophobic interactions. In this case, the countercation of the polyoxometallate is an organic ammonium compound, which favorably interacts with a support with an adjusted polarity. Examples are:

- a polyether modified silica, with adsorbed (tetrahexylammonium)$_3$(PW_4O_{24}),[35]
- an SiO_2, modified with Ph_3SiOEt and a benzylating agent, was used as an adsorbent for (cetylpyridinium)$_3$($PW_{12}O_{40}$).[36]

Silicates with embedded W have also been proposed, but the stability of the W in these structures has not always been unequivocally established.[37]

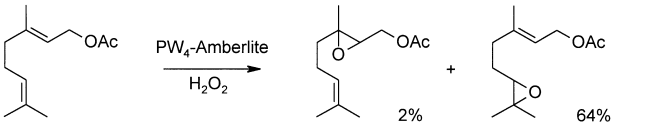
Most of the heterogenized W catalysts have been tested with reactive olefins such as cyclohexene or

cyclooctene. Data for cyclohexene epoxidation are compiled in Table 3. The turnover numbers, turnover frequencies and the productivity of the catalysts vary widely. The productivity variations to some extent parallel the W content of the materials: for instance, PW_4-Amberlite can easily contain up to 2.1 mmol W per g catalyst, and this positively influences the productivity (entry 4). In the case of $[SiW_9O_{34}]^{9-}$ intercalated in an LDH, it is unlikely that all the W in the interlayer space is available for the reaction, and this is reflected in rather moderate productivity and TON (entry 3).[26]

In cyclohexene epoxidation, both allylic oxidation and epoxide hydrolysis may decrease the epoxide selectivity. Interestingly, a large selectivity difference is observed in cyclohexene epoxidation with hydrophilic and hydrophobic LDH-based catalysts: in the apolar environment of the tosylate and $[WO_4]^{2-}$-exchanged LDH, both epoxide hydrolysis and aselective reactions are prevented (entry 2 *vs.* 1).[25] High epoxide selectivity is also observed for the catalyst containing an ammonium-polyoxometallate embedded in a hydrophobized SiO_2 (entry 10),[36] and for the phosphotriamide-functionalized polymer loaded with peroxoW (entry 8).[33] Moreover, the excellent selectivity is accompanied by high epoxide productivities; it should be remarked, though, that these catalysts were used in very concentrated conditions, e.g., 4.8 M olefin.

Only a few of the proposed heterogeneous W catalysts were also effective for the epoxidation of the poorly reactive α-olefins, and in all these catalysts, W occurs in a heteronuclear association with P (Table 3, entries 12–14).[27,31,36] Again, the PW_4-Amberlite catalyst is clearly most productive: it yields 0.7 g epoxyoctane per g catalyst per h.[27]

Obviously, a wide range of even bulky olefins are smoothly epoxidized by the PW_4-Amberlite, or by the heterogeneous W-phosphoramide catalysts, and a few examples are shown in Table 3 (entries 15–19).[28,29,34] The selectivity in the epoxidation of dienes is directed by electronic factors: thus limonene yields mainly the 1,2-epoxide, and geranyl acetate gives the 6,7-epoxide (Equation 3):



(3)

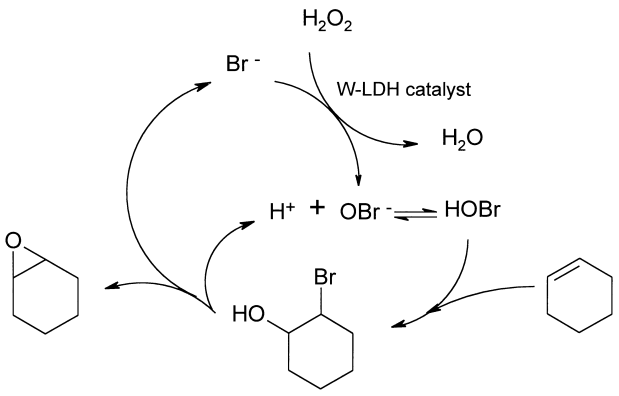
Other successful reactions are those with indene and 3-carene (Table 3, entries 17 and 19).

In our search toward new synthetic analogues of haloperoxidases, we accidentally encountered an extremely high epoxidation activity of W-LDH type catalysts.[38,39] Although the W-LDH catalyst previously showed moderate epoxidation activity, the epoxidation rate was drastically improved when the reaction was carried out in the presence of NH_4Br (entries 20 and 21 in Table 3). Only after careful mechanistic investigation, did it become clear that the epoxidation mechanism was completely different from that of the classical metal-catalyzed epoxidation. The proposed mechanistic cycle closely resembles that of the haloperoxidase activity (Scheme 1).

So, instead of directly forming the epoxide at the peroxometal, W catalyzes the oxidation of the bromide ions. The *in situ* oxidized bromide species, e.g., HOBr and Br_2, immediately react with the olefin in the aqueous conditions yielding a bromohydrin intermediate which is converted into the epoxide with a recycle of the bromide. Bromohydrin formation, for instance, was evidenced by performing the reaction in a biphasic protocol in which the bromohydrin is protected from further cyclization. According to the catalytic cycle, the oxirane oxygen appears to originate from water and not from the oxidant H_2O_2. Labeling experiments with isotopic $H_2{}^{18}O$ have indeed proved this unusual pathway.[38]

As an example, the reaction of α-methylstyrene with H_2O_2 in the presence of NH_4Br at 40 °C produces almost 50 g epoxide per g $[WO_4]^{2-}$-LDH catalyst within 5 hours with an epoxide selectivity of at least 95%. The activity corresponds to 380 catalytic cycles in one hour. Note that in the absence of the bromide source, values of TOF seldom exceed 5 h^{-1} for $[WO_4]^{2-}$-LDH based catalysts.[39]

Besides the high activity obtained, this new epoxidation strategy also leads to unique selectivities, totally different from those obtained *via* the classic route of metal-catalyzed epoxidation. For instance, in the epoxidation of 3-carene, the α-epoxide was exclusively formed when the reaction procedure was carried out in traditional fashion with metal and oxidant or with peracids, whereas the bromide-assisted epoxidation paves the way for the selective production of the more sterically hindered β-epoxide isomer (Equation 4).

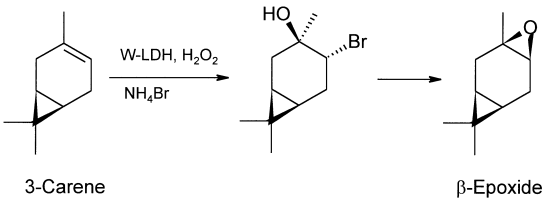


Scheme 1.

Table 3. Olefin oxidation over heterogenized W catalysts.

	Catalyst	W content [mmol · g^{-1}]	Substrate	*T*	Solvent	TON	Time	Productivity [(g product) · (g catalyst)]$^{-1}$	Time	Epoxide sel. [%]	Ref.
1	$[WO_4]^{2-}$-LDH, hydrophilic	0.16	cyclohexene	25 °C	methanol	93	90 h	1.4	90 h	65	[25a]
2	$[WO_4]^{2-}$-LDH, hydrophobic	0.13	cyclohexene	25 °C	methanol	132	90 h	1.64	90 h	91	[25a]
3	$[SiW_9O_{34}]^{9-}$-LDH, intercalated	3.3	cyclohexene	70 °C	$(BuO)_3PO$	8.1	3 h	2.59	3 h	59	[26c]
4	PW_4-Amberlite	2.1	cyclohexene	32 °C	acetone	42	24 h	5.0	24 h	57	[29]
5	PW_4-quat. MCM-41	0.66	cyclooctene	50 °C	CH_3CN	20	16 h	1.6	16 h	>95	[30]
6	$[WZnMn_2(ZnW_9O_{34})_2]$-quat. SiO_2	0.12	cyclohexene	25 °C	*none*	38	24 h	0.44	24 h	72	[31]
7	W-phosphoramide-MCM-41	1.5	cyclohexene	50 °C	CH_3CN	20	20 h	2.9	20 h	85[a]	[30]
8	W-phosphotriamide-PGMA	0.7	cyclohexene	70 °C	dioxane	108	0.16 h	7.5	0.16 h	96	[33]
9	W-phosphotriamide-SiO_2[b]	0.18	cyclohexene	60 °C	dioxane	19	0.14 h	0.34	0.14 h	96	[34]
10	Phenyl $SiO_2 + Q_3PW_{12}O_{40}$[c]	0.93	cyclohexene	70 °C	*none*	16	3 h	1.5	3 h	97	[36]
11	Polyether SiO_2 + $Q'_3PW_4O_{24}$[d]	0.2	cyclooctene	23 °C	*none*	48	17 h	0.93	17 h	*nm*	[35]
12	PW_4-Amberlite	0.89	1-octene	70 °C	DCE[e]-water	12.2	2 h	1.4	2 h	*nm*	[27]
13	$[WZnMn_2(ZnW_9O_{34})_2]$-quat. SiO_2	0.12	1-octene	25 °C	*none*	1.3	24 h	0.02	24 h	*nm*	[31]
14	Phenyl $SiO_2 + Q_3PW_{12}O_{40}$[c]	0.93	1-octene	90 °C	*none*	16	10 h	1.9	10 h	97	[36]
15	PW_4-Amberlite	1.5	limonene	38 °C	CH_3CN	26	24 h	5.9	24 h	93	[28]
16	PW_4-Amberlite	1.5	geranyl acetate	38 °C		29	40 h	9.2	40 h	92	[28]
17	PW_4-Amberlite	1.5	3-carene	38 °C		18	24 h	4.1	24 h	97 (α)[f]	[28]
18	PW_4-Amberlite	2.1	cyclopentene	32 °C	acetone	39	24 h	7.0	24 h	99	[29]
19	W-phosphotriamide-SiO_2[b]	0.31	indene	60 °C	dioxane	14	6 h	0.58	6 h	99	[34]
20	$[WO_4]^{2-}$-LDH + NH_4Br	0.18	α-Me-styrene	40 °C	CH_3CN-water	1800	4.5 h	46.5	4.5 h	95	[39]
21	$[WO_4]^{2-}$-LDH + NH_4Br	0.18	3-carene	40 °C	CH_3CN-water	1400	3.5 h	33.5	3.5 h	88 (β)[f]	[39]

[a] Pyridine was added to enhance the selectivity.
[b] A micelle-templated ordered SiO_2 was used.
[c] $Q = C_5H_5N(C_{15}H_{31})^+$.
[d] $Q' = (C_6H_{13})_4N^+$.
[e] DCE = 1,2-dichloroethane. *nm* = not mentioned.
[f] Exclusively α-epoxide or β-epoxide.

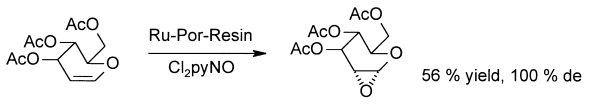


(4)

Considering the advantages of the bromide-assisted epoxidation method, the $[WO_4]^{2-}$-LDH/NH_4Br catalytic system is very simple to employ and cheap to apply. The substrate scope is limited to well-substituted olefins; for α-olefins the dehydrobromination is often incomplete, and the bromohydrin is the main product. Despite this limitation, this catalytic system can be applied to a whole list of geminal disubstituted, tri- and tetrasubstituted olefins.[38] Moreover, for obvious reasons, there is no restriction concerning the size of the organic reactant with this catalytic system. Only the additional need of a soluble bromide salt, albeit in understoichiometric amounts, may limit to a certain extent its large-scale application.

2.4 Ru catalysts

Che and coworkers have explored immobilized Ru epoxidation catalysts, with the Ru both in heme and non-heme environments. The Ru complex of *meso*-tetrakis(2,6-dichlorophenyl)porphyrin was immobilized *via* axial coordinative binding on an aminopropylated MCM-41 silica structure ('Ru-Por-MCM-41');[40] on the other hand, Ru^{II}(CO)-5,10,15-tris(4-Cl-phenyl)-20-(4-hydroxyphenyl)porphyrin was covalently bound to the Merrifield resin ('Ru-Por-Resin').[41] While the preparation of these complexes is not easy, and in spite of the use of 2,6-dichloropyridine *N*-oxide as the oxidant, these catalysts offer some interesting features, such as very high turnover numbers, and stereospecificity in the epoxidation of *cis*-alkenes (Table 4, entries 1–3). With Ru-Por-MCM-41 in the epoxidation of styrene, the catalyst is still very active after 11700 catalytic cycles.[40] Ru-Por-Resin seems even a more general olefin epoxidation catalyst. The scope also comprises aromatic olefins, such as *cis*-stilbene and *cis*-β-methylstyrene, which are oxidized stereospecifically.[41] The same heterogeneous catalyst also enables highly diastereoselective reactions, for instance, in the epoxidation of 3,4,6-tri-*O*-acetyl-D-glucal (Equation 5).



(5)

Apart from the porphyrins, Ru complexes based on the non-heme ligand 1,4,7-trimethyl-1,4,7-triazacyclononane (tmtacn) have also been studied.[42] In contrast to other covalent approaches to tmtacn immobilization (*vide infra*), in this case simple physisorption was used to deposit the complex on Kiesel gel. The reactions were run with S/C = 100, with *t*-BuOOH as the oxidant, and in CH_2Cl_2 as the solvent. In view of the very low complex loading of the support (17 μmol Ru g^{-1}), it is not surprising that the productivity of the catalyst is low (Table 4, entry 4). However, about 100 Ru turnovers are easily achieved in several consecutive runs with recycled catalysts.

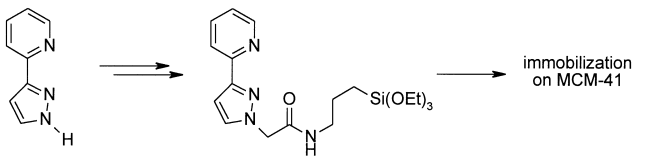
2.5 Mo on Polybenzimidazole and Other Supports

Many coordinating groups have been proposed for immobilization of Mo; however, the work on polybenzimidazoles by the Sherrington group stands out.[43] The catalyst is simply prepared by refluxing commercial polybenzimidazole with $MoO_2(acac)_2$ in toluene (Mo-PBI); its activity to some extent depends on whether the catalyst has been pre-exposed to the oxidant.

The productivity of this catalyst is remarkable: for cyclohexene epoxidation at 80 °C, the Mo turnover frequency is 200 h^{-1}, corresponding to 40 g product per g catalyst and h. Even for α-olefins such as 1-octene and propene, the TOFs amount to 40–160 h^{-1}. The substrate scope hence seems to encompass at least a series of cyclic and acyclic alkenes (Table 4, entries 5 and 6).

The catalyst is subject to gradual deactivation, but this seems not due to Mo loss. Rather, the access to the catalytic sites seems hindered by accumulation of oligomeric side products on the catalyst.

Many other immobilized ligands have been proposed for Mo immobilization, but often insufficient proof has been given for the stability of the Mo on the material. In a recent, conceptual approach, 2-(1-alkyl-3-pyrazolyl)-pyridine ligands were anchored to the inner pore walls of MCM-41, and this seems to ensure a zero-activity in the reaction filtrate (Equation 6 and Table 4, entry 7).[44]



(6)

2.6 Heterogeneous Mn Catalysts

When surrounded by the appropriate N ligands, particularly mononuclear Mn becomes an excellent epoxidation catalyst with H_2O_2.[45] Several methods are available to immobilize Mn-amine or Mn-diimine complexes, such as entrapment in zeolite cages,[46] or

Table 4. Epoxidation of olefins catalyzed by miscellaneous heterogenized metal catalysts or by solid base catalysts.

	Catalyst	Metal content [mmol · g^{-1}]	Substrate	Oxidant	*T*	Solvent	TON	Time	Productivity [(g product) · (g catalyst)]$^{-1}$	Time	Epoxide sel. [%]	Ref.
1	Ru-Por-MCM-41	0.004	*cis*-β-Me-styrene	Cl_2pyNO[a]	40 °C	CH_2Cl_2	4400	24 h	2.4	24 h	90	[40]
2	Ru-Por-Resin	0.088	1-octene	Cl_2pyNO [a]	25 °C	benzene	1270	24 h	14.3	24 h	100	[41]
3	Ru-Por-Resin	0.088	cyclohexene	Cl_2pyNO [a]	25 °C	benzene	920	24 h	8	24 h	67	[41]
4	Ru-tmtacn-SiO_2	0.017	cyclohexene	*t*-BHP	25 °C	CH_2Cl_2	59	24 h	0.1	14 h	75	[42]
5	Mo-PBI	1.8	1-octene	*t*-BHP	80 °C	none	54	0.33 h	12.6	0.33 h	100	[43]
6	Mo-PBI	1.8	cyclohexene	*t*-BHP	80 °C	none	76	0.33 h	13.5	0.33 h	99	[43]
7	Mo-MCM-41	0.34	cyclooctene	*t*-BHP	61 °C	$CHCl_3$	166	2 h	6.3	2 h	100	[44]
8	Mn-dmtacn-SiO_2	0.5	1-hexene	H_2O_2	0 °C	CH_3CN	220	3 h	11.1	3 h	92	[48]
9	Mn-dmtacn-SiO_2	0.5	styrene	H_2O_2	0 °C	CH_3CN	225	1 h	15.8	1 h	90	[48]
10	Mn-dmtacn-SiO_2	0.57	limonene	H_2O_2	0 °C	CH_3CN	73	1.1 h	6.5	1.1 h	86	[29]
11	Mn(bpy)$_2^{2+}$-NaX	0.6	cyclohexene	H_2O_2	20 °C	acetone	76	4 h	4.5	4 h	62	[46a]
12	Mg,Al-LDH, $[CO_3]^{2-}$	*na*	cyclooctene	H_2O_2	60 °C	PhCN	*na*	*na*	9.3	2 h	100	[50]
13	MgAl-LDH, *t*-BuO$^-$	*na*	cyclooctene	H_2O_2	60 °C	PhCN	*na*	*na*	50	0.25 h	100	[51]
14	Mg,Al-LDH, $[CO_3]^{2-}$	*na*	cyclooctene	H_2O_2	70 °C	isobutyramide/DCE[b]	*na*	*na*	10	6 h	100	[52]
15	Mg,Al-LDH, $[CO_3]^{2-}$	*na*	cyclohexene	H_2O_2	70 °C		*na*	*na*	7.8	8 h	99	[52]

[a] Cl_2pyNO = 2,6-dichloropyridine *N*-oxide.
[b] DCE = 1,2-dichloroethane. *na* = not applicable.

covalent immobilization on SiO_2 materials or polymer backbones.[47,48] An advantage of Mn catalysts is that they can use H_2O_2 at low temperatures, and still very high turnover numbers are achieved within short reaction times. Examples are Mn-bis-bipyridine complexes in faujasite zeolites (Table 4, entry 11), or Mn-triazacyclononane complexes attached to SiO_2. With the latter systems, high turnover numbers and productivity are reached within a few hours, for example, for aromatic olefins such as styrene (Table 4, entries 8–10). One disadvantage is that a mixed selectivity is often observed: apart from the main epoxide product, a small amount of diols is formed by direct, *cis*-dihydroxylation of the double bond.[48]

2.7 Base-Catalyzed Epoxidation with Co-Reagents

Basic catalysts such as LDHs can be used in combination with a nitrile and H_2O_2 to effect epoxidation. The original procedure, using dissolved base, was proposed by Payne.[49] The nitrile is in this process transformed to a peroxyimidic acid, which is the actual oxidant and is transformed to an amide. Even though this procedure yields a mole of amide per mole of epoxide, it is one of the most reliable epoxidation processes. In an exemplary procedure, a carbonate exchanged Mg,Al-LDH is used with benzonitrile in methanol.[50] Up to 5 g of product, e.g., 1,2-epoxycyclooctane, can be obtained per h and g catalyst (Table 4, entry 12).

Instead of simple LDHs, the *tert*-butoxide-exchanged forms may be used; this results in much higher productivities, e.g., 50 mg of 1,2-epoxycyclooctane per mg of catalyst per 15 minutes (Table 4, entry 13).[51]

Instead of nitriles, amides may be used as a co-reagent (Table 4, entries 14, 15).[52] It is thought that in this case the LDH-activated H_2O_2 reacts with the amide, e.g., isobutyramide, to form a peracid which is the actual oxidant. In this case, the reaction is best conducted in the triphasic mode, with a solid catalyst, the olefin and epoxide in an apolar solvent, and an aqueous peroxide phase. The addition of an anionic surfactant such as sodium dodecyl sulfate remarkably accelerates the reaction rate. Due to the buffered conditions, even labile epoxides such as 1,2-epoxycyclohexane can be obtained in very high yields. While the procedure applies to variously substituted olefins, less substituted olefins are less reactive: in order to enable smooth epoxidation of terminal olefins, 10 equivalents of the amide are needed.

3 Epoxidations of Unsaturated Alcohols

3.1 Ti Catalysis

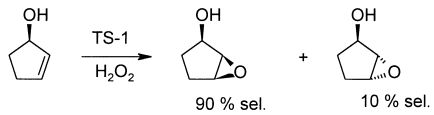
In well-defined conditions, allylic alcohols can be converted selectively to the corresponding epoxide over TS-1. Since TS-1-catalyzed epoxidations generally take place at lower temperature (-5 to 45 °C) than TS-1-catalyzed alcohol oxidations ($T \geq 45$ °C), one may generally expect that the double bond is more easily oxidized than the alcohol group.[3,53] Alcohol oxidation is more pronounced for secondary allylic alcohols than for primary alcohols; when the double bond is sterically encumbered, as for 1,1-disubstituted or trisubstituted double bonds, its epoxidation becomes slower, and the chemoselectivity for epoxidation again decreases.[54] These trends are consistent with the known reactivities of various olefins and aliphatic alcohols over TS-1.

The solvent is important in improving the epoxide chemoselectivity: in water or primary alcohols, there is a more pronounced epoxide solvolysis.[55,56] To some extent, this can be suppressed by base addition, as in the glycidol formation from allyl alcohol.[55] In acetone, for TS-1,[56,57] or in acetonitrile, for Al-free Ti-Beta,[11] the epoxy alcohol selectivity is increased. A final means to suppress acid-catalyzed side reactions with TS-1 is to work with highly concentrated, dried 85% H_2O_2, or with the urea-H_2O_2 adduct. For instance, with the acid-sensitive 3-methyl-2-buten-1-ol, this allowed one to achieve 95% epoxide yield.[58,59]

An important issue is whether an alcohol group in the allylic position has any rate- or selectivity-enhancing effect on the epoxidation of a double bond. With V catalysts for instance, this alcohol group is able to coordinate as an alcoholate; this increases the epoxidation rate and impacts on the stereoselectivity.[60] With heterogeneous Ti catalysts such as TS-1 and Ti-Beta, allylic alcohols with a terminal double bond are much less reactive than the corresponding α-olefins;[3a,11] this means that the electron-withdrawing effect of the -OH group is dominant over any other effects. In line with this observation, the electron-rich 6,7-bond in geraniol is preferentially epoxidized over the 2,3-bond with TS-1 and H_2O_2 in acetone (compare with Equation 3).[61] Note that previously, a conflicting result has been reported, with exclusive epoxidation at the 2,3-bond, also employing TS-1 and H_2O_2 in acetone.[57]

Even more detailed information on the interaction between the alcohol group and the active site comes from the diastereoselectivity studies with differently substituted allylic alcohols by Adam and coworkers, using both TS-1 and Al-free Ti-Beta.[59,62] Specifically, *threo:erythro* ratios were determined for epoxides produced from allylic alcohols with 1,3-strain, such as *cis*-3-methyl-3-penten-2-ol, or with 1,2-strain, such as 3-methyl-3-buten-2-ol. These ratios seem to argue against

direct attachment of the alcohol group as an alcoholate to the framework Ti species. In a proposal for a more plausible transition state, the alcohol group forms a hydrogen bond with the HOO-ligand on Ti. This transition state is strongly like that of a peracid epoxidation. This analogy would also explain the *syn* epoxidation of cyclic allylic alcohols such as 2-cyclohexen-1-ol and 2-cyclopenten-1-ol (Equation 7).[57]



(7)

Just as with mCPBA, TS-1 seems to form only the *syn* epoxide, which is rationalized by the directing effect of the hydroxyl group through hydrogen bonding.

Epoxidation of allylic alcohols has also been studied with organic peroxides and Ti on SiO_2 catalysts. With the original Shell catalyst, moderate to good epoxide selectivities were obtained with Ti/SiO_2 in the epoxidation of, e.g., allyl alcohol (71%) and 2-cyclohexen-1-ol (85%).[16] In a detailed study of *E*-2-hexen-1-ol epoxidation with *t*-BHP and TiO_2/SiO_2 aerogel catalysts, both activity and selectivity were optimized.[19a, b] For instance, careful removal of water from the aerogel increases the activity. Alternatively, zeolite 4A was used as an additive with a double effect: it efficiently traps adventitious water in the reaction mixture; the water may result from aldehyde formation or from homolytic peroxide decomposition. Moreover, zeolite 4A behaves as a base, suppressing side reactions that could be catalyzed by silanol groups formed under the effect of water. Thus 4A addition not only improves the selectivity, but also the activity, since the chances that oligomeric by-products block the pores become smaller. The productivity with this catalyst amounts to 6.1 g 2,3-epoxyhexan-1-ol per g aerogel per h; at 90% conversion, 86% selectivity for the epoxide is obtained.[19a] Similar conditions were applied for 3-methyl-2-buten-1-ol and many other cyclic or acyclic allylic alcohols.[19c] Unfortunately, chemoselectivities are variable, and sometimes only low epoxide selectivity is observed. In the epoxidation of 2-cyclohexen-1-ol, the *syn:anti* ratio of the epoxides is 70:30, indicating that there is a small but clear directing effect of the hydroxy group.

Varying epoxide selectivities were also observed for a catalyst obtained by reaction of $Ti(O\text{-}i\text{-}Pr)_4$ with silica gel, and activated at 140 °C. With *t*-BHP as the oxidant, secondary allylic alcohols are oxidized only to the ketones; but the catalyst is useful for epoxidation of primary allylic alcohols such as nerol, cinnamyl alcohol and crotyl alcohol, with selectivities between 68 and 100%.[63] A catalyst prepared by reaction of titanocene dichloride with SiO_2 and calcination was used in the *t*-BHP oxidation of the unsaturated primary alcohol menth-1-en-9-ol, resulting in a 63% epoxide selectivity at 72% conversion.[64]

3.2 W Catalysis

Tungsten, whether as tungstic acid, in homonuclear complexes such as $[W_2O_{11}]^{2-}$, or in heteronuclear complexes such as $[PW_{12}O_{40}]^{3-}$, is an effective catalyst for allylic alcohol epoxidation. The homogeneous epoxidation with H_2O_2 in a buffered monophasic or liquid biphasic system is often accelerated and directed by an allylic OH group. It is highly chemoselective for the epoxide with primary allylic alcohols; particularly with cyclic secondary alcohols, ketone formation is a frequent observation.[65]

Several of the heterogeneous W catalysts have also been applied in epoxidation of unsaturated alcohols, and an overview of some reaction parameters is given in Table 5. A few examples of homogeneously catalyzed reactions are included for reference. A new heterogeneous catalyst is the compound obtained by reaction of an amphiphilic polymer with an anionic tungstate compound. Specifically, a polyacrylamide with quaternary ammonium functions was precipitated with $[PW_{12}O_{40}]^{3-}$. The resulting solid proved insoluble in water and most organic solids, but featured a rather well-defined macroporosity. Since its structure contains hydrophilic and hydrophobic portions, it was used in liquid biphasic reactions, in the absence of an organic solvent.

Two highly productive heterogeneous catalysts are tungstate, anchored on MCM-41 immobilized phosphoramide, and the W-containing amphiphilic polymer: 20–40 g epoxygeraniol is obtained per g of catalyst (Table 5, entries 4 and 5). This high productivity is clearly linked to a high W content of the catalysts. Maximum turnover frequencies vary between 10 and 14 h^{-1} at temperatures between 25 and 50 °C. Clearly, productivities are lowest when monosubstituted bonds are epoxidized, as in allyl alcohol or 1-octen-3-ol (Table 5, entries 11 and 12).

The selectivity of W-catalyzed allylic alcohol epoxidation is to a serious extent influenced by the alcohol group, and this explains the very strong preference for epoxidation at the 2,3-double bond in geraniol, which is ascribed to coordination of the allylic alcohol on the tungstate center. However, the immobilization of the tungstate can modify such interactions, as is evident from the results with the hydrophobic $[WO_4]^{2-}$-LDH catalyst: the 6,7-epoxide is now the dominant product with 85% selectivity, against 99% selectivity for the 2,3-epoxide with dissolved tungstate (Table 5, entries 3 and 6).

The combination of $[WO_4]^{2-}$-exchanged LDH catalysts and NH_4Br provides a highly productive epoxidation of substituted allylic alcohols with H_2O_2 (Table 5,

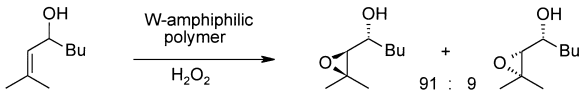
Table 5. Oxidation of unsaturated alcohols over heterogenized W catalysts.

	Catalyst	Substrate	*T*	TON	Time	Productivity [(g product) · (g catalyst)$^{-1}$]	Time	Epoxide sel. [%]	Epoxide distribution		Ref.
1	PW_4-Amberlite	geraniol	0 °C	15	24 h	5.9	24 h	94	2,3:6,7 =	91:9	[28]
2	$[WO_4]^{2-}$-LDH, hydrophilic	geraniol	25 °C	242	60 h	7.0	60 h	89		52:48	[25]
3	$[WO_4]^{2-}$-LDH, hydrophobic	geraniol	25 °C	294	60 h	6.6	60 h	99		15:85	[25]
4	W-phosphoramide-MCM-41	geraniol	50 °C	80	6 h	20.5	6 h	95		98:2	[30]
5	W-amphiphilic polymer	geraniol	25 °C	160	15 h	40	15 h	96[a]		98:2	[66]
6	H_2WO_4 + NaOAc	geraniol	0 °C	98	4 h	–	–	98		99:1	[65a]
7	PW_4-Amberlite	2-cyclohexen-1-ol	0 °C	7.3	40 h	2	40 h	76	*syn*:*anti* =	64:36	[28]
8	$[WO_4]^{2-}$-LDH, hydrophilic	2-cyclohexen-1-ol	25 °C	29	80 h	0.5	8 h	31		90:10	[25]
9	$[WO_4]^{2-}$-LDH, hydrophobic	2-cyclohexen-1-ol	25 °C	21	80 h	0.32	80 h	35		69:31	[25]
10	H_2WO_4 + NaOAc	2-cyclohexen-1-ol	25 °C	44	17 h	–	–	44		95:5	[65b]
11	$[WO_4]^{2-}$-LDH, hydrophilic	allyl alcohol	25 °C	38	24 h	0.55	24 h	91			[25]
12	$[WZnMn_2(ZnW_9O_{34})_2]$-quat. SiO_2	1-octen-3-ol	25 °C	10.5	24 h	0.18	24 h	80			[31]
13	$[WO_4]^{2-}$-LDH + NH_4Br	geraniol	40 °C	1380	4.5 h	41.1	4.5 h	98	2,3:6,7 =	2:98	[39]
14	$[WO_4]^{2-}$-LDH[b] + NH_4Br	3-Me-3-buten-1-ol	45 °C	1300	2.5 h	45.9	2.5 h	94			[39]

[a] Pyridine was added to enhance the selectivity.
[b] 0.36 mmol W instead of 0.18 mmol W per g catalyst; solvent = water

entry 13 and 14). The bromide-assisted reaction, for instance, is capable of converting 3-methyl-3-buten-1-ol almost quantitatively into the epoxide at extremely high rate. Taken into account typical activities of W-based catalysts, a TOF of 520 h^{-1} at 45 °C is indeed rather remarkable. Moreover, due to the unique halide-assisted epoxidation mechanism, the regioselectivity is totally switched. While geraniol is predominantly converted into the 2,3-epoxide for tungsten-based catalysts, the 6,7-epoxide is the dominant product when the $[WO_4]^{2-}$-LDH is used in combination with the bromide salt.

The diastereoselectivity of the allylic alcohol epoxidation has only been studied in a few cases; for 2-methyl-2-octen-4-ol, Ikegami et al. obtained the *threo* and *erythro* epoxides in a 91:9 ratio, using the W-containing amphiphilic polymer (Equation 8).[66]



(8)

This is a normal result for an allylic alcohol with a pronounced 1,3-allylic strain.

3.3 V Catalysis

Homogeneous V catalysts are particularly suitable for the epoxidation of allylic and homoallylic alcohols with *t*-BHP, but the active V species is not easily immobilized.[60] Apart from immobilized organic ligands, inorganic solids have been tested as a host for catalytic V. Early examples are the V-substituted aluminophosphates such as VAPO-5, or V-pillared montmorillonite (Table 6, entries 1 and 2).[67,68] There is little explicit evidence for the heterogeneity of these materials. We have ourselves explored the potential of decavanadate-pillared layered double hydroxides (V_{10}-LDH) as catalysts for allylic alcohol epoxidation.[69] A fundamental difference between this work and previous approaches is that in the $[V_{10}O_{28}]^{6-}$ pillars, all V is linked *via* at least five V-O-V bonds to the rest of the pillar. Apparently, this five-fold bonding sufficiently withstands the conditions of the epoxidation reaction, so that there is no leaching whatsoever of V. A series of allylic alcohols were smoothly epoxidized with V_{10}-LDH and *t*-BHP in toluene (Table 6, entries 3–5). With V_{10}-LDH, V turnover numbers are strikingly lower than with VAPO-5, but this is likely the price to be paid for true heterogeneity.

3.4 Base Catalysis

The epoxidation using bases, H_2O_2 and a nitrile co-reagent can easily be applied to allylic alcohols. With a carbonate-exchanged Mg,Al-LDH as the catalyst, the

Table 6. Oxidation of unsaturated alcohols over heterogenized V catalysts.

	Catalyst	Metal content [mmol · g^{-1}]	Substrate	*T*	Solvent	TON	Time	Productivity [(g product) · (g catalyst)]$^{-1}$	Time	Epoxide sel. [%]	Ref.
1	VAPO-5	0.071	geraniol	70 °C	PhCl	1400	1 h	16.5	1 h	97	[67]
2	V-PILC	2.4	geraniol	25 °C	PhH	61	7.5 h	24.9	7.5h	ng	[68]
3	V_{10}-LDH	4.1	geraniol	20 °C	$PhCH_3$	16	4 h	9.1	4 h	97	[69]
4	V_{10}-LDH	4.1	*trans*-pinocarveol	20 °C	$PhCH_3$	16	10 h	11	10 h	87	[69]
5	V_{10}-LDH	4.1	perillyl alcohol	20 °C	$PhCH_3$	20.1	14 h	13.9	14 h	99	[69]

epoxide of 2-cyclohexen-1-ol was obtained in 89% yield, with a *syn:anti* ratio of 80:20. 8 g of product were obtained per g of LDH after 24 h.[50]

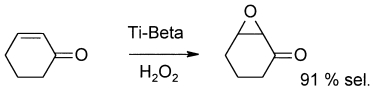
4 Epoxidation of α,β-Unsaturated Carbonyl Compounds

4.1 Transition Metal-Catalyzed Reactions

The presence of a carbonyl group in the α-position of a double bond decreases the electron density in this bond, and therefore epoxidation of such bonds with electrophilic agents is rarely attempted. For instance, with the highly electrophilic oxidant generated from Mn-tmtacn in the presence of H_2O_2 and oxalate, methyl vinyl ketone could be epoxidized in 66% yield, with a turnover number of 450;[45] but such cases are rare.

Two teams have also reported on the application of heterogeneous Ti catalysts to the epoxidation of enones. For the epoxidation of α-isophorone, a TiO_2-SiO_2 aerogel was applied, using *t*-BHP as the oxidant. The initial productivity of a 20 wt. % TiO_2 catalyst was 1.5 g epoxide (g catalyst)$^{-1}$ h^{-1}, which is obviously less than with the same catalyst and regular olefins.[18c]

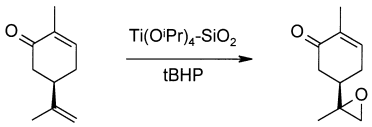
Alternatively, a wide range of catalysts and conditions was screened in order to use dilute H_2O_2 for epoxidation of enones. For 2-cyclohexen-1-one, the best result was obtained with a hydrophobic, Al-free Ti-Beta catalyst, which was superior over TS-1, Ti-MCM-22 and other Ti-Beta samples; at 70 °C and in acetonitrile, a 61% conversion combined with a 91% selectivity for the epoxide was obtained (Equation 9).[70] No products of a Baeyer – Villiger side reaction were reported.



(9)

When the reaction is conducted in a triphasic mixture, with water as the solvent, the reaction largely proceeds to the diol, *trans*-2,3-dihydroxycyclohexanone, which can be obtained in 75% yield. Unfortunately, these reactions are not easily extrapolated from 2-cyclohexen-1-one. β-Alkyl-substituted substrates such as 3-methyl-2-cyclohexen-1-one or isophorone are hardly reactive, which indicates that steric effects influence the active site. Low reactivities were obtained with open-chain α,β-unsaturated ketones. When unsaturated aldehydes such as *trans*-2-hexenal were employed, the carboxylic acid was the main product, and epoxidation was only a minor reaction.

The lack of reactivity of electron-poor double bonds with most Ti catalysts can also be useful in obtaining chemoselectivity: for instance, in carvone, the exocyclic double bond can be oxidized chemoselectively (Equation 10).[63]

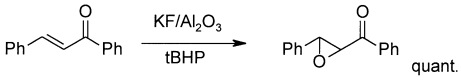


(10)

Immobilized Ru-porphyrins are also potential catalysts for epoxidation of unsaturated ketones. With a Ru-porphyrin, covalently linked to the Merrifield resin, and Cl_2pyNO as the oxidant, 4-phenyl-3-buten-2-one was epoxidized in 89% yield.[41]

4.2 Base Catalysis

In another, more generally applicable approach, solid base catalysts are used in combination with a hydroperoxide to effect epoxidation of electron-deficient double bonds such as in enones. The base deprotonates the hydroperoxide, which attacks on the carbon atom β of the carbonyl group to form a stabilized carbanion intermediate; by rearrangement of the latter, the epoxide product is obtained. In early procedures, the use of the KF/Al_2O_3 catalyst in combination with *t*-BHP was proposed, in acetonitrile-dichloroethane solvent.[71] With molecules such as chalcone, methyl vinyl ketone and 2-cyclohexen-1-one, this procedure gives excellent chemical yields (Equation 11).

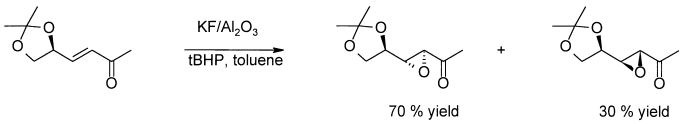


(11)

However, alkyl substitution β of the carbonyl group slows down the reaction, and α-isophorone seems unreactive. Relatively large amounts of the basic reagent are used, e.g., 5 g of catalyst per g of product, and based on stoichiometry, the KF should be regarded as a reagent rather than as a catalyst.

Cativiela et al. later proposed to use hydrotalcites or layered double hydroxides as catalysts in combination with H_2O_2.[72] A calcined carbonate Mg,Al-LDH was used in methanol. While this procedure works well for a number of substrates, it gives rise to the formation of 3-hydroxy-1,2-dioxolane by-products in the reaction of most open-chain aliphatic enones, and possibly to adducts with methoxide anions. Methoxide adducts were also formed as by-products when a silica-anchored strong base, 1,5,7-triazabicyclodecene, was used as a catalyst with H_2O_2 in methanol.[73]

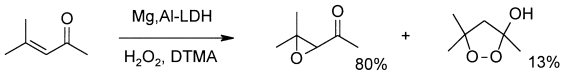
For open-chain aliphatic enones, KF/Al_2O_3 with *t*-BHP results in much higher selectivity than H_2O_2-LDH. This is exemplified in the epoxidation of a chiral glyceraldehyde-derived enone (Equation 12).



(12)

In this reaction, a substantial diastereomeric excess was achieved, which is not found for H_2O_2-LDH. The functional group compatibility of the H_2O_2-LDH procedure is limited: nitriles as in cinnamonitrile are hydrolyzed to amides, and esters form carboxylates.[74] On the other hand, a potential advantage of the H_2O_2-LDH procedure is an easier work-up, and in some cases better stereoselectivity is obtained. With cinnamaldehyde, only the *trans* epoxide is formed, while *t*-BHP-KF/Al_2O_3 gives a mixture of both epoxides.

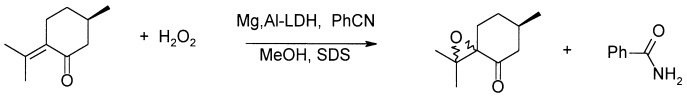
The H_2O_2-LDH procedure was further refined by Kaneda and coworkers.[75] When a liquid biphasic reaction mixture is used, containing heptane, water and a long-chain alkyl quaternary ammonium detergent, even aliphatic enones such as mesityl oxide can be epoxidized in high yield (Equation 13); the formation of the 1,2-dioxolane is largely avoided (DTMA = dodecyltrimethylammonium bromide).



(13)

In some cases, e.g., with 2-cyclopenten-1-one, the reaction can even be conducted without a solvent; 1.4 g epoxycyclohexanone is obtained per g and h. Parameters such as the elemental LDH composition, or the calcination pretreatment have various effects on the epoxidation: the activity of the catalysts increases with an increasing Mg content or basicity, and with calcination. However, calcination not only creates strong base sites, but also acid sites, which might lead to side reactions. In order to obtain strong basic sites without performing a calcination, LDHs exchanged with *tert*-butoxide anions were used.[51] Reactions were conducted in MeOH with aqueous H_2O_2. For 2,3-epoxycyclohexanone, 20 mg of product were obtained per mg of catalyst within 5 minutes. It is unclear though, whether the butoxide anions are stable, since both water and methanol are stronger acids than *tert*-butyl alcohol.

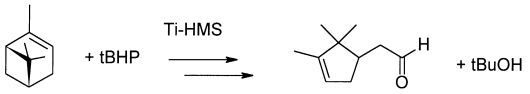
In some cases, Payne's base-catalyzed procedure is to be preferred over the simple base-catalyzed epoxidation with H_2O_2, even for unsaturated ketones. This is illustrated by pulegone, which hardly reacts without a nitrile solvent, but in benzonitrile, under Payne conditions, 93% of the epoxide is obtained (Equation 14).



(14)

5 Heterogeneously Catalyzed Two-Step Reactions Comprising an Epoxidation

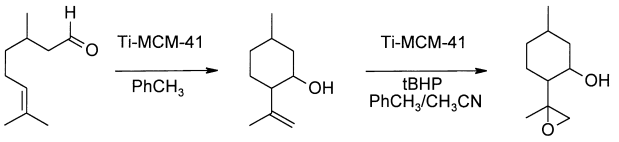
α-Pinene oxide is an important intermediate for the preparation of the fragrance campholenic aldehyde. High yield isomerization of α-pinene oxide to campholenic aldehyde can be achieved with well-chosen Lewis acid catalysts, e.g., dealuminated zeolites.[76a] Other excellent catalysts are SiO_2-immobilized Zn triflate, with 80% selectivity at 50% conversion, or Ti-Beta, with selectivities at high conversion of 89 and 94% in the liquid and gas phase respectively.[76b, c] α-Pinene oxide is a very labile compound, which is now produced in a buffered peracid process. Catalytic epoxidation of α-pinene over a solid has till now not been achieved: Ti catalysts are intrinsic Lewis acids, and even W catalysts operate in slightly too acid conditions to permit high-yield isolation of the epoxide. However, one may also envisage to use the same Lewis acid as an epoxidation and isomerization catalyst. Rhee and coworkers used a Ti-containing hexagonal mesoporous sieve (Ti-HMS), with strictly anhydrous *t*-BHP in acetonitrile and under N_2, and obtained campholenic aldehyde in 82% selectivity at 32% conversion, or 2.0 g product per g catalyst in 24 h (Equation 15).[77]



(15)

If some water is present, verbenone is the dominant product.

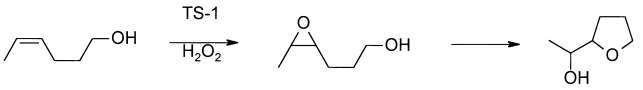
The inverse sequence, with an acid-catalyzed rearrangement followed by an epoxidation is found in the conversion of citronellal to isopulegol epoxide.[78] Again a mesoporous material proved useful; $TiCp_2Cl_2$ was grafted on MCM-41, which was then calcined. For the rearrangement, toluene was used; later, tBHP in acetonitrile was added. After the second step, isopulegol and isopulegol epoxide were obtained in 24 and 67% yields (Equation 16).



(16)

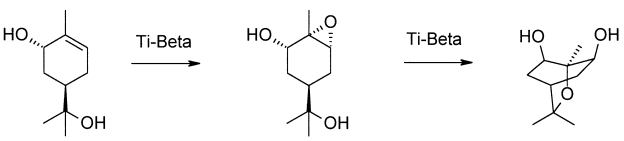
The one-step conversion of olefins to (*trans*)-diols over Ti zeolites has been studied in much detail. A preferred catalyst is Al-free Ti-Beta, in water as the solvent.[79] For instance, pinacol is formed in 93% selectivity from 2,3-dimethyl-2-butene using H_2O_2 at 60 °C. Upon increasing the bulkiness of the substituents around the double bond, the reaction rate decreases, which indicates that the approach of the alkene to the zeolite-embedded Ti site is subject to steric factors.

A common reaction is the epoxidation of an unsaturated alcohol, which is followed by intramolecular attack of the alcohol group on the epoxide ring. Starting from TS-1, *cis*-4-hexen-1-ol and H_2O_2, alcohol attack on the intermediate epoxide may lead to the tetrahydrofuran or to the tetrahydropyran.[80] However, only the tetrahydrofuran is formed, with 100% selectivity at 92% conversion, without any 6-ring formation (Equation 17).



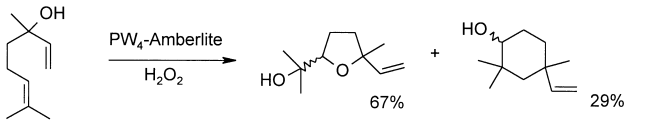
(17)

Water or acetone are preferred solvents. This preference for 5-ring formation was ascribed to the steric constraints inside the TS-1 pores. In the more spacious pores of Ti-Beta, even cyclic unsaturated alcohols may undergo similar reactions. For instance, *trans-p*-menth-6-ene-2,8-diol was claimed to form a tricyclic compound at 90% conversion and 95% selectivity (Equation 18).



(18)

Steric constraints have less influence on the product distribution in Ti-MCM-41 type structures than in zeolites such as Ti-Beta and TS-1;[81] for the rearrangement of several epoxyalcohols, it has been observed that the tetrahydropyran over tetrahydrofuran ratio is larger in, e.g., an organically modified Ti-MCM-41, than in Ti-Beta. A well-studied reaction is the epoxidation of linalool, followed by intramolecular cyclization to a mixture of tetrahydrofurans and tetrahydropyrans. This reaction may be catalyzed by Ti-containing, slightly acidic molecular sieve;[82] but even in a reaction with a PW_4-amberlite and H_2O_2 there is sufficient acidity to obtain the mixture of cyclic ethers in 96% yield (Equation 19).[28]



(19)

In a final example, Ti,Al-Beta zeolites were used as bifunctional catalysts for the formation of pinacolone from 2,3-dimethyl-2-butene.[83] The diol pinacol was obtained in 90% yield in dioxane, after which dichloroethane was added to promote the pinacol rearrangement. However, the latter step was slow, and eventually only 25% yield of pinacolone was obtained.

6 Conclusion

In spite of a considerable body of research, many challenges still remain in the field of heterogeneous liquid phase epoxidation. Firstly, there is a clear need to test the most productive epoxidation catalysts in a continuous set-up. Only such experiments will provide adequate comparisons between the different catalytic materials, and will point the way to new improvements of catalyst stability. Up to now, such data are only available for some Ti catalysts.

Secondly, the trend is clearly towards liquid biphasic or even solvent-free systems, and new catalysts should be designed to operate in such conditions. Thirdly, there has been no satisfactory heterogenization for some very efficient homogeneous catalysts, notably CH_3ReO_3, and new concepts are really needed here. Next, stereoselectivity in the epoxidation of complex molecules deserves continuous attention. As illustrated by the case of 3-carene, different catalysts or operation modes can lead to complementary selectivity patterns.[28,39] In this respect, it is worthwhile to explore new pathways, such as the W-catalyzed, bromide-assisted epoxidation; meanwhile, embedding active centers in hosts of varying topology, such as zeolites, has also proved to be a rewarding approach.[82] Finally, real breakthroughs in

terms of productivity and turnover numbers can be expected if new epoxidation pathways and novel, well-organized materials are explored.

Acknowledgements

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