

Inorganic compounds and materials as catalysts for oxidations with aqueous hydrogen peroxide

Véronique Nardello^a, Jean-Marie Aubry^a, Dirk E. De Vos^b, Ronny Neumann^c, Waldemar Adam^d, Rui Zhang^e, Johan E. ten Elshof^f, Peter T. Witte^g, Paul L. Alsters^{h,*}

^a LCOM, Equipe de Recherches "Oxydation et Formulation", UMR CNRS 8009, ENSCL BP 90108, F-59652 Villeneuve d'Ascq Cedex, France

^b Centre for Surface Chemistry and Catalysis, K.U. Leuven, Kasteelpark Arenberg 23, 3001 Leuven, Belgium

^c Department of Organic Chemistry, Weizmann Institute of Science, Rehovot 76100, Israel

^d Department of Chemistry, Facundo Bueso 110, University of Puerto Rico, Rio Piedras 00931, Puerto Rico

^e Institute of Organic Chemistry, University of Würzburg, Am Hubland, 97074 Würzburg, Germany

^f University of Twente, Inorganic Materials Science, MESA⁺ Institute of Nanotechnology and Faculty of Science and Technology, P.O. Box 217, 7500 AE Enschede, The Netherlands

^g Engelhard De Meern B.V., Strijkviertel 67, P.O. Box 19, 3454 ZG De Meern, The Netherlands

^h DSM Pharma Chemicals, Advanced Synthesis, Catalysis, and Development, P.O. Box 18, NL-6160 MD Geleen, The Netherlands

Available online 3 April 2006

Abstract

This paper reviews our work on oxidations with aqueous hydrogen peroxide catalyzed by inorganic catalysts devoid of organic ligands. In the first part of the review, the use of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ "sandwich" polyoxometalate as a multi-purpose oxidation catalyst is described. Attention is paid to practical aspects that are of relevance for large-scale, industrial use of this catalyst, such as catalyst preparation, handling, and recycling. Its activity in cyclooctene epoxidation compared to other W-based catalyst systems has been determined under ceteris paribus conditions. The second part of the review deals with homogeneous and heterogeneous inorganic catalysts for "dark" singlet oxygenation, i.e., singlet oxygenation by catalytic disproportionation of hydrogen peroxide into singlet oxygen and water. The industrial advantages of "dark" singlet oxygenation compared to conventional photo-oxidation are described. It is pointed out that the reaction medium and nature of the catalyst strongly influence the selectivity and scope of the method.

© 2006 Elsevier B.V. All rights reserved.

Keywords: Hydrogen peroxide; Epoxidation; Singlet oxygen

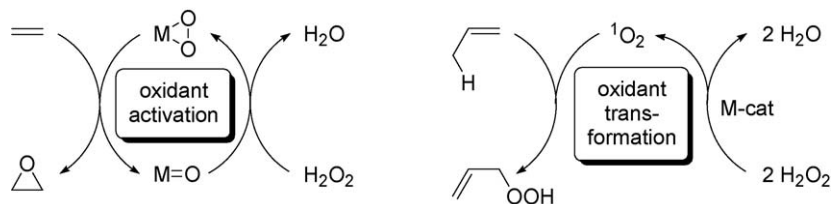
1. Introduction

The industrial, large-scale application of catalysts makes high demands upon these catalysts in order to meet technical, economical, and environmental requirements. Thus, the catalyst should be cost-efficient in term of catalyst costs per kilogram product. Catalyst separation from the product should be facile in order to avoid contamination of the latter with catalyst residues. In the down-stream processing, the catalyst should not interfere negatively with the waste-water treatment or affect the waste-water quality in a negative way that conflicts with environmental legislation.

In the area of liquid-phase oxidation catalysis, it is often particularly hard to meet industrial demands. One of the underlying reasons for this is that liquid-phase oxidation catalysts often display a relatively low catalyst activity when compared to, for example, typical reduction catalysts used for hydrogenations. Accordingly, typical catalyst loadings used in oxidative transformations are relatively high in order to compensate for the lack of catalyst activity. In contrast to catalytic reductions, catalytic oxidations usually suffer from an intrinsic instability of the catalyst under the reaction conditions, since most catalysts contain organic ligands that are inherently susceptible to oxidative degradation [1]. This catalyst instability is another cause for the high catalyst loadings commonly employed in oxidation catalysis. In addition, it negatively affects the overall process robustness.

In this article, we will review our work on inorganic oxidation catalysts devoid of any organic ligands for affecting

* Corresponding author. Tel.: +31 46 476 13 48; fax: +31 46 476 76 04.
E-mail address: paul.alsters@dsm.com (P.L. Alsters).



Scheme 1.

liquid-phase oxidative transformations with aqueous hydrogen peroxide of relevance for chemical manufacturing. Because of their inorganic nature, these catalysts do not suffer from oxidative degradation. In addition, they do not require a costly and lengthy organic synthesis of ligands, but instead they are readily available from inexpensive salts. Since the physical properties of such inorganic catalysts differ widely from those of the organic product, their separation of the latter is straightforward. All these aspects evidently contribute positively to their industrial application.

The inorganic catalysts dealt with in the following might be homogeneous catalysts based on well-defined molecular compounds or heterogeneous catalysts based on inorganic materials. We will demonstrate the usefulness of polyoxometalates and simple inorganic salts as homogeneous inorganic oxidation catalysts suitable for liquid-phase oxidations with aqueous hydrogen peroxide. Inorganic materials suitable as catalysts for this purpose are obtained by ion exchange on layered double hydroxides, metal exchange in zeolites, or by precipitation on pH adjustment of soluble salts.

Two different mechanistic roles can be distinguished for these catalysts. A very common role for oxidation catalysts with hydrogen peroxide as the terminal oxidant is to activate the latter by formation of peroxo metal species. In this case, the substrate oxidation occurs via an intimate contact between the catalyst and the substrate. Many useful oxidative transformations proceed via such a mechanism, including alkene epoxidation, alcohol dehydrogenation, and heteroatom oxidation. Besides oxidant activation, a rarer role of the catalyst is that of oxidant transformation. In this case, the catalyst interacts with hydrogen peroxide to generate another active oxidizing species that reacts with the substrate outside the coordination sphere of the catalyst. As an example of this type of mechanism, we will discuss “dark” singlet oxygenation by catalytic disproportionation of hydrogen peroxide into water and singlet oxygen [2,3]. Scheme 1 summarizes the general characteristics of oxidations proceeding via oxidant activation and oxidant transformation.

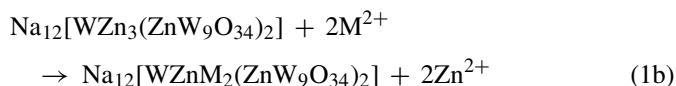
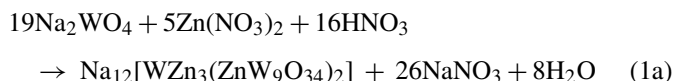
2. Oxidations with “sandwich” polyoxometalates

2.1. Catalyst availability and stability

There are many reports on the use of polyoxometalates (POMs) as oxidation catalysts [4–7]. Because of their inorganic nature, these species are usually very tolerant towards high temperatures and strongly oxidizing conditions. In contrast, many

Keggin and Wells-Dawson type POMs are prone to hydrolytic degradation. This is an obvious disadvantage when it comes to their use as catalysts for oxidations with aqueous hydrogen peroxide. In this respect, we were intrigued by the hydrolytic stability of polytungstozincate species reported by Tourné et al., who noted that various concentrated aqueous solutions of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ anion could be kept unaltered for twenty years at room temperature [8]. Fig. 1 illustrates the structure of this polytungstozincate anion, which is reminiscent of a “sandwich”.

Another attractive feature of this “sandwich” POM is its ease of preparation by “self-assembly” from inexpensive, readily available chemicals [9]. Near quantitative formation of this species in just one step simply requires the gradual addition of aqueous $\text{Zn}(\text{NO}_3)_2$ to an aqueous solution of Na_2WO_4 and nitric acid, with all the reagents being used in the amounts requires according to the stoichiometry dictated by Eq. (1a) [8]:



Despite these obvious advantages, and in spite of the large variety of tungsten-based catalysts reported for oxidations with hydrogen peroxide, the use of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$

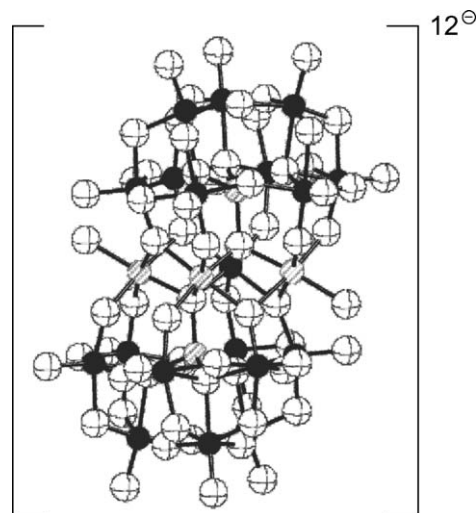


Fig. 1. Structure of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ “sandwich” polyoxometalate anion.

species as an oxidation catalyst was not known prior to our studies.

When required, one of the Zn atoms in the “sandwich interlayer” can be exchanged for other metal atoms, such as Mn or V (Eq. (1b)). This allows further fine tuning of the chemical properties of the “sandwich” POM to match the desired catalytic activity. Anionic species obtained in this way [8] are $[\text{WZnMn}_2(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ [10] and $[\text{WZn}(\text{VO})_2\text{Zn}_2(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ [11]. By simply exchanging the sodium counter cations for more lipophilic quaternary ammonium ions, the solubility of these “sandwich” POMs is readily adjusted. The “sandwich” anions can be dissolved into highly apolar media such as toluene with, for example, methyltri-*n*-octylammonium chloride.

2.2. Catalytic behavior

The nature of the species obtained on addition of aqueous H_2O_2 (2000 M equivalents) to aqueous $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ has been studied by ^{183}W NMR spectroscopy [12]. These measurements indicate the presence of two distinct monoperoxo tungsten species, since two new peaks appear around -700 ppm. No evidence for any degradation of the POM structure into a mononuclear tungsten species was obtained. Thus, these measurements underline the robust nature of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ “sandwich” POM anion under oxidative, hydrolytic conditions.

For industrial applications of catalytic oxidations with H_2O_2 , it is very undesirable to be dependent on catalysts that suffer from unproductive H_2O_2 decomposition. Not only poses the evolution of large amounts of gaseous dioxygen implementation problems with respect to process safety, but it also negatively affects the process economics, since a large excess of diluted H_2O_2 has to be added to reach full conversion. This increases the variable costs of the process and decreases the space-time yield, thus also increasing the fixed costs. Fortunately, the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ species has a very low activity for H_2O_2 decomposition, even at elevated temperatures [12].

We have conducted a detailed study to determine the epoxidation activity of the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ “sandwich” POM relative to other W-based epoxidation catalysts [13]. These catalysts vary greatly with respect to their structure and W source, from simple mononuclear H_2WO_4 to the $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ species with 19 W atoms. From an industrial point of view, it is much more relevant to measure the activity on a “per W atom” basis rather than on a “per catalyst molecule” basis, since the molecular weights of these catalysts are largely determined by the number of W atoms in the molecular formula, and in industrial practice catalyst loadings are usually expressed in wt.%. In this comparative study, the various catalysts were either added as an isolated tungsten compound or prepared in situ without isolation. The eleven catalyst systems used for these experiments are listed below:

- $12[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl} + \text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$, i.e., in situ “sandwich” POM;

- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$, i.e., isolated “sandwich” POM;
- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]_{12}[\text{WZnMn}_2(\text{ZnW}_9\text{O}_{34})_2]$, i.e., isolated Mn “sandwich” POM [10];
- $3[N\text{-}(n\text{-C}_{16}\text{H}_{31})\text{pyridinium}]\text{Cl} + \text{H}_3[\text{PO}_4(\text{WO}_3)_{12}]$, i.e., in situ Ishii et al. [14];
- $[N\text{-}(n\text{-C}_{16}\text{H}_{31})\text{pyridinium}]_3[\text{PO}_4(\text{WO}_3)_{12}]$, i.e., isolated Ishii;
- $3[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl} + \text{H}_3\text{PO}_4 + 4\text{H}_2\text{WO}_4$ i.e., in situ Venturello et al. [15];
- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]_3[\text{PO}_4\{\text{WO}(\text{O}_2)_2\}_4]$ i.e., isolated Venturello;
- $2[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl} + 2\text{H}_2\text{WO}_4$ i.e., in situ Prandi et al. [16];
- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]_2[\{\text{WO}(\text{O}_2)_2\}_2\text{O}]$ i.e., isolated Prandi;
- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{HSO}_4 + \text{PO}(\text{OH})_2\text{CH}_2\text{NH}_2 + 2\text{Na}_2\text{WO}_4$ i.e., in situ Noyori [17];
- $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{HSO}_4 + \text{PO}(\text{OH})_2\text{CH}_2\text{NH}_2 + 2\text{H}_2\text{WO}_4$ i.e., in situ Noyori-plus.

This comparative study was carried out using the catalytic epoxidation of cyclooctene as a representative transformation by measuring conversion-time profiles for each catalyst system under identical conditions. The results are shown in Fig. 2. These experiments were carried out in toluene as solvent at 60°C with 1.5 M equivalent 50% H_2O_2 using a constant catalyst loading corresponding to 0.1 mol% W.

The main conclusions from this study and additional experiments on “sandwich” POM catalyzed epoxidations are listed below:

1. The three most active systems are all acidic in nature because they are based on in situ catalyst formation from H_2WO_4 . On reaction of the latter with H_2O_2 to form the catalytically active peroxo tungsten species, mineral acid is liberated, as shown in Eqs. (2) and (3) for the in situ Venturello and Prandi

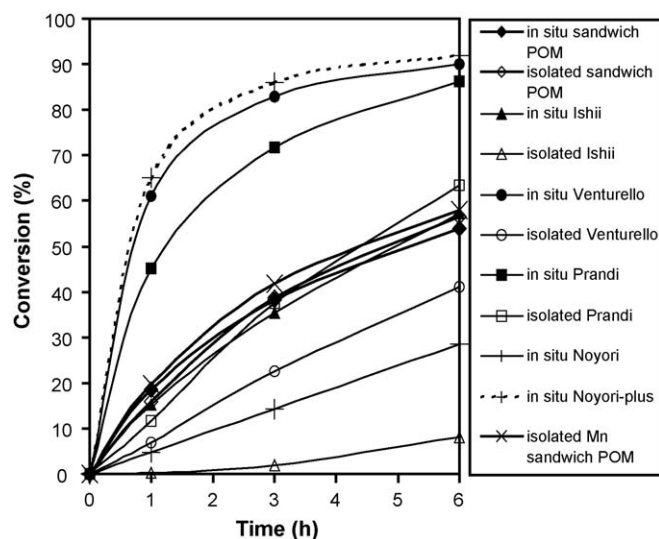


Fig. 2. Conversion/time profiles for the epoxidation of cyclooctene with 1.5 equivalent 50% H_2O_2 catalyzed by various W-based catalyst systems (0.1 mol% W) at 60°C in toluene.

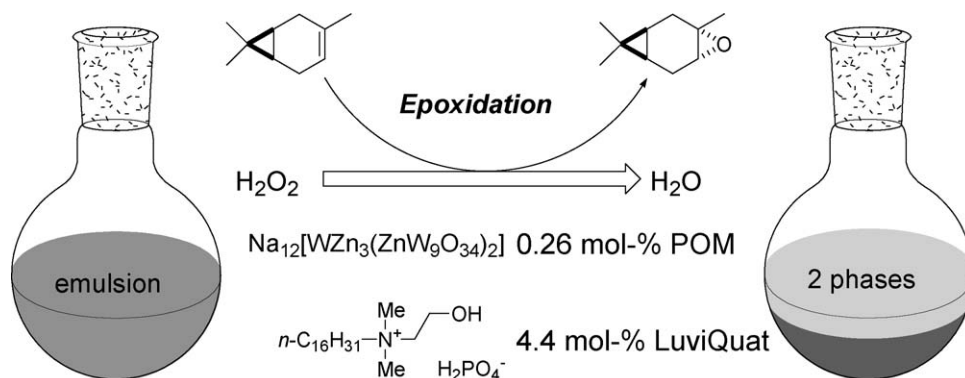
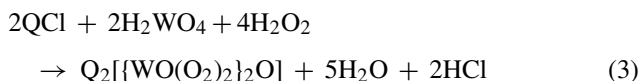
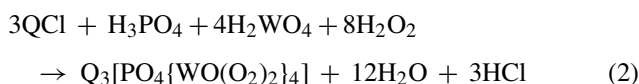


Fig. 3. Epoxidation of 3-carene with H_2O_2 catalyzed by the mixed in situ $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ /Luviquat mono CP system, accelerating the reaction by formation of a stable emulsion that separates into an aqueous and organic phase at full conversion.

systems (Q = quaternary ammonium cation):



When H_2WO_4 is replaced by Na_2WO_4 in the in situ Venturello and Prandi systems, the activity drops to insignificant levels. Remarkably, this loss of activity cannot be restored by using $\text{Na}_2\text{WO}_4 + 2\text{HCl}$ instead of H_2WO_4 . The higher activity of the in situ Ishii, Venturello, and Prandi systems compared to their *isolated* analogues can be attributed to a higher acidity of the former catalysts systems. The importance of the nature of the W source (Na_2WO_4 or H_2WO_4) is stressed further by the strong activity increase of the well known Na_2WO_4 -based Noyori system when Na_2WO_4 is replaced by H_2WO_4 to generate the “Noyori-plus” system. Clearly, this W source effect is largely overlooked in the literature.

- Whereas a high acidity of the catalyst system can be tolerated for acid resistant epoxides such as cyclooctene oxide, most epoxidations will not be compatible with a high acidity. In this respect, it should be noted that the “sandwich” POM catalyzed epoxidations with either the in situ or the *isolated* catalyst are among the fastest of the neutral catalyst systems without additional acidity imparted on the system by the catalyst. The pH neutral nature of the “sandwich” POM compared to the more acidic in situ Venturello, Prandi, and Noyori-plus systems broadens the synthetic scope relative to the latter catalyst systems. Selectivity in case of acid sensitive epoxides with the quaternary ammonium salt + “sandwich” POM catalyst system can be increased further by using $[(n\text{-C}_{16}\text{H}_{31}(\text{HOCH}_2\text{CH}_2)\text{NMe}_2)\text{H}_2\text{PO}_4]$ instead of $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl}$ as the quaternary ammonium cocatalyst [13]. The former is an inexpensive quaternary ammonium compound with the trade name “Luviquat mono CP”. The unusual dihydrogenphosphate anion provides pH buffering capacity to the reaction mixture, whereas the quaternary ammonium cation serves as an emulsifier of the two-phase system (Fig. 3).

- Epoxidations catalyzed by the “sandwich” POMs start immediately on addition of H_2O_2 , i.e., no induction period is noted for these catalysts and apparently the active epoxidizing peroxy tungsten species is formed rapidly from the “sandwich” POM precursor on contact with H_2O_2 . Except for the *isolated* Venturello system, considerable induction periods are observed for the other catalysts. In particular, in situ systems based on H_2WO_4 require a catalyst activation step in order to avoid such an induction period [18], since formation of peroxy tungsten species from poorly soluble H_2WO_4 proceeds only slowly even in hot concentrated H_2O_2 . The lack of induction period when employing the “sandwich” POM facilitates large-scale processing of such exothermic reactions like epoxidations, since the risk of nonisothermal processing conditions is increased in case of a slow start of the reaction caused by an appreciable induction period. From a large-scale processing point of view, another highly attractive feature of epoxidations catalyzed by the $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ “sandwich” POM is that these can be carried out by simply using a self-assembled solution prepared according to Eq. (1a). This increases the cost efficiency because catalyst isolation and purification are not required.
- The optimum ratio of $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl}$ to $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ may differ from the expected stoichiometrical ratio of 12 and depends on the nature of the alkene to be epoxidized. For the epoxidation of cyclooctene under two-phase toluene/water conditions, a maximum epoxidation rate was obtained with only half of the theoretical amount of quaternary ammonium salt. Epoxidations with the “sandwich” POM catalyst system do not necessarily require solvents to proceed efficiently, and in case of substrates that are liquid at the reaction temperature, the epoxidations can be run without any solvent. High process efficiencies can often be achieved, in particular in case of epoxidations of allylic alcohols, for which the “sandwich” POM is an extremely efficient catalyst. For example, 1 kg of $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ is enough to convert 6 m³ of geraniol into 2,3-geranyl oxide within 4 h. This corresponds to a TOF of 43 385 h⁻¹, a TON of 173 538, and a space-time yield of 95 kg m³ h⁻¹.

Besides alkene epoxidation [19], the “sandwich” POM catalyzes a variety of other useful oxidations with aqueous H_2O_2 .

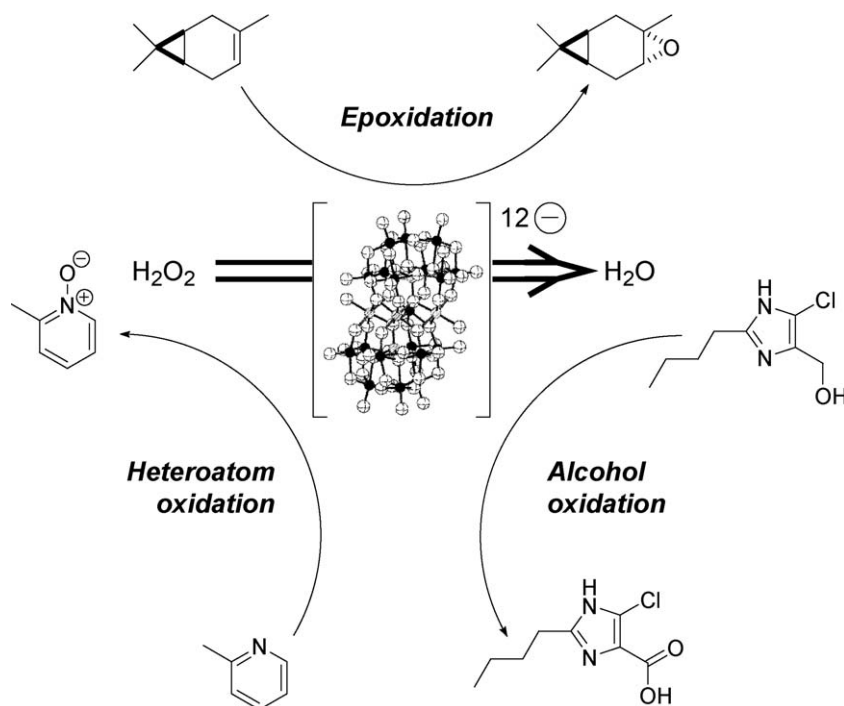


Fig. 4. Various oxidations with aqueous H_2O_2 catalyzed by the “sandwich” POM.

Some of these can be run under aqueous biphasic conditions using only $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ as the catalyst without additional quaternary ammonium cocatalyst [12]. A prerequisite for this is that the substrate is polar enough to have some water-solubility. The variety of oxidative transformations with H_2O_2 accessible through “sandwich” POM catalysis is illustrated in Fig. 4.

From the foregoing, it is evident that (self-assembled) $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$, either as such or in combination with a (quaternary ammonium) phase-transfer cocatalyst, can be considered as a multi-purpose oxidation catalyst for oxidations with aqueous H_2O_2 .

2.3. Catalyst recycling

Under the aqueous biphasic conditions with only $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ as the catalyst without additional phase-transfer cocatalyst, the catalyst simply resides in the aqueous phase, and catalyst separation from the water-insoluble product is simply achieved by phase separation. Catalyst recycling additionally requires that the catalyst remains intact after each run. Efficient recycling by simple phase separation under aqueous biphasic conditions has been demonstrated for the oxidation of 2-pentanol to 2-pentanone [9]. No significant loss in activity or selectivity was observed over three reaction cycles, repetition being simply achieved by adding fresh substrate and H_2O_2 to the aqueous catalyst solution separated from the organic phase.

Obviously, the above phase separation method for catalyst recycling cannot be applied when the product and catalyst reside in the same phase. This is the case for substrates with a low polarity such as most alkenes, which require a phase-transfer

cocatalyst in order for the oxidation with aqueous H_2O_2 under $\text{Na}_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ catalysis to proceed. We reasoned that the polyoxometalate anions might be efficiently retained by nanofiltration, not only because polyoxometalate anions are large and highly charged, but also because they have a highly rigid, shape-persistent structure. The latter is a prerequisite for obtaining very high retentions through nanofiltration techniques [20]. In particular under continuous rather than batch-wise processing conditions, it is important to achieve near quantitative catalyst retentions in order to minimize gradual catalyst supply over time to compensate for the loss of catalyst caused by a low retention. Because of their robustness towards elevated temperatures, organic solvents, and oxidizing conditions, we investigated the use of ceramic membranes for “sandwich” POM recycling through nanofiltration (Fig. 5). We were pleased that indeed near quantitative retentions (>99.9%) were obtained in

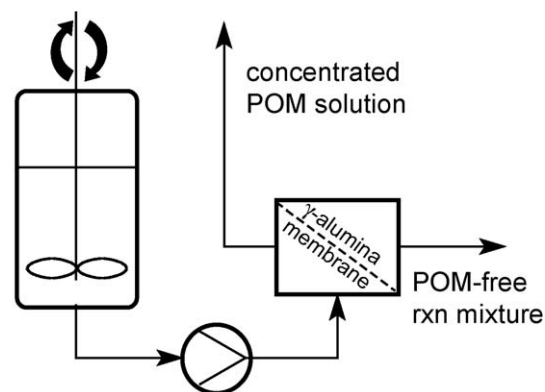


Fig. 5. Recycling of the “sandwich” POM catalyst by nanofiltration based on an inorganic membrane.

toluene as the solvent with a α -alumina supported γ -alumina membrane [21].

Using the epoxidation of cyclooctene under $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]_{12}[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]$ catalysis as a model reaction, it was demonstrated that the catalyst could be recycled efficiently over six runs without loss in activity.

3. “Dark” singlet oxygenation with homogeneous and heterogeneous catalysts

3.1. General process characteristics of Na_2MoO_4 -catalyzed “dark” singlet oxygenation

Singlet oxygenations are commonly carried out using classical photo-oxidation based on excitation of triplet dioxygen to singlet oxygen by photons in the presence of a sensitizer. From an industrial manufacture point of view, this technology has a number of disadvantages. Firstly, it is not suitable for implementation in ordinary multi-purpose plant stirred tank reactors, but instead requires dedicated bubble column photo-reactors. Secondly, in contrast to stirred tank reactors, such photo-reactors do not profit from economy of scale, i.e., capacity expansion can only be achieved by multiplying photo-reactor units. Thirdly, photo-oxidation processing conditions involve safety hazards that result from the combination of dioxygen, light, and organic compounds.

We were intrigued by the simplicity of “dark” singlet oxygenation from an industrial processing point of view, and it appeared to us that “dark” singlet oxygenation is, ideally, more suitable for large-scale manufacture than photo-oxidation. This simplicity also holds for the nature of typical catalysts for “dark” singlet oxygenation. In fact, simple sodium molybdate is a highly efficient catalyst for H_2O_2 disproportionation into singlet oxygen and water. The latter is unavoidably present under “dark” singlet oxygenation conditions. This might be disadvantageous in case of poorly reactive substrates, since the lifetime of singlet oxygen is low in aqueous solvent systems. As a result, a large excess of aqueous H_2O_2 has to be added in order to reach high conversions of poorly reactive substrates. Using more H_2O_2 has a negative impact on the cost efficiency, since variable costs increase and reactor yields decrease because of dilution that occurs on adding aqueous H_2O_2 . For such poorly reactive substrates, photo-oxidation is preferred, since it can be carried out in solvents in which singlet oxygen has a high lifetime, and no dilution occurs on bubbling of an excess of oxygen through a solution. For sufficiently reactive substrates, however, “dark” singlet oxygenation is an attractive and very practical method.

Fig. 6 illustrates how the “dark” singlet oxygenation of sodium tiglate is carried out using ordinary laboratory equipment [22].

This conversion proceeds efficiently in methanol as the solvent with Na_2MoO_4 as the catalyst. At the onset of the reaction, when no H_2O_2 has been added yet (Fig. 6; left), most of the catalyst is present as a solid, since Na_2MoO_4 is only poorly soluble in methanol. On gradual addition of H_2O_2 (Fig. 6; middle), more soluble peroxo molybdate species are formed, and a homogeneous reaction mixture is obtained. The rate of H_2O_2 addition

has to be such that the concentration of triperoxo molybdate, i.e., $\text{MoO}(\text{O}_2)_2^{2-}$, is maximum, since this species decomposes much more rapidly under generation of singlet oxygen than either lower or higher peroxidized molybdate species. When all H_2O_2 has been disproportionated and conversion is complete (Fig. 6; right), Na_2MoO_4 is regenerated and most of it precipitates from the reaction mixture. Thus, most of the molybdate is easily recovered by simple filtration.

The above procedure is generally applicable to substrates that are soluble in polar solvents that are miscible with water, such as MeOH and DMF. It cannot be applied to the “dark” singlet oxygenation of strongly lipophilic substrates that would create two-phase systems because of their hydrophobic nature. The formation of singlet oxygen from the triperoxo molybdate species needs a polar medium to proceed efficiently, and under two-phase conditions where this species resides in the polar (aqueous) phase whereas the substrate resides in the apolar phase, the singlet oxygen would have to travel from the polar to the apolar phase for substrate peroxidation to occur. The microsecond lifetime of singlet oxygen in aqueous media prevents this phase transition: the mean travel distance of singlet oxygen before it decays to triplet oxygen is far smaller than the distance to be traveled to go from the bulk polar phase to the apolar phase. The solution to this dilemma is provided by micro-emulsions [23]. For a water-in-oil micro-emulsion, the molybdate catalyst and H_2O_2 reside in extremely small aqueous droplets. Singlet oxygen is generated very efficiently in this aqueous environment by molybdate, and since the radius of these micro-droplets is much smaller than the mean $^1\text{O}_2$ travel distance, singlet oxygen easily reached the continuous organic phase where it peroxidizes the lipophilic substrate. Ethyl acetate turns out to be a suitable non-chlorinated organic solvent for such micro-emulsions [24]. For certain liquid substrates such as β -citronellol, even solvent-free micro-emulsions that allow efficient “dark” singlet oxygenation can be developed. Such solvent-free micro-emulsions allow very high reactor yields to be achieved with very small catalyst loadings. The overall mass-composition of the reaction medium required for the peroxidation of β -citronellol under solvent-free micro-emulsion conditions is shown in Fig. 7. As can be judged from Fig. 7, the SDS surfactant and *n*-BuOH cosurfactant are used in only small amounts relative to the substrate under such solvent-free conditions.

3.2. Other catalyst systems to overcome limitations of the Na_2MoO_4 system

Synthetic organic chemists often consider singlet oxygen as a rather indiscriminate species when it comes to its regio- and stereoselectivity in alkene peroxidations, in particular in the case of the singlet oxygen “ene”-reaction. Thus, all six expected hydroperoxides are formed from attack on the triply-substituted double bond of limonene. Under photo-oxidation conditions, however, it has been shown that singlet oxygen can exert a high regio- and stereoselectivity when the substrate contains *O*- or *N*-heteroatoms at the allylic position of the double bond to be attacked by singlet oxygen [25,26]. The double bond in allylic alcohols, for example, is usually attacked by singlet oxygen

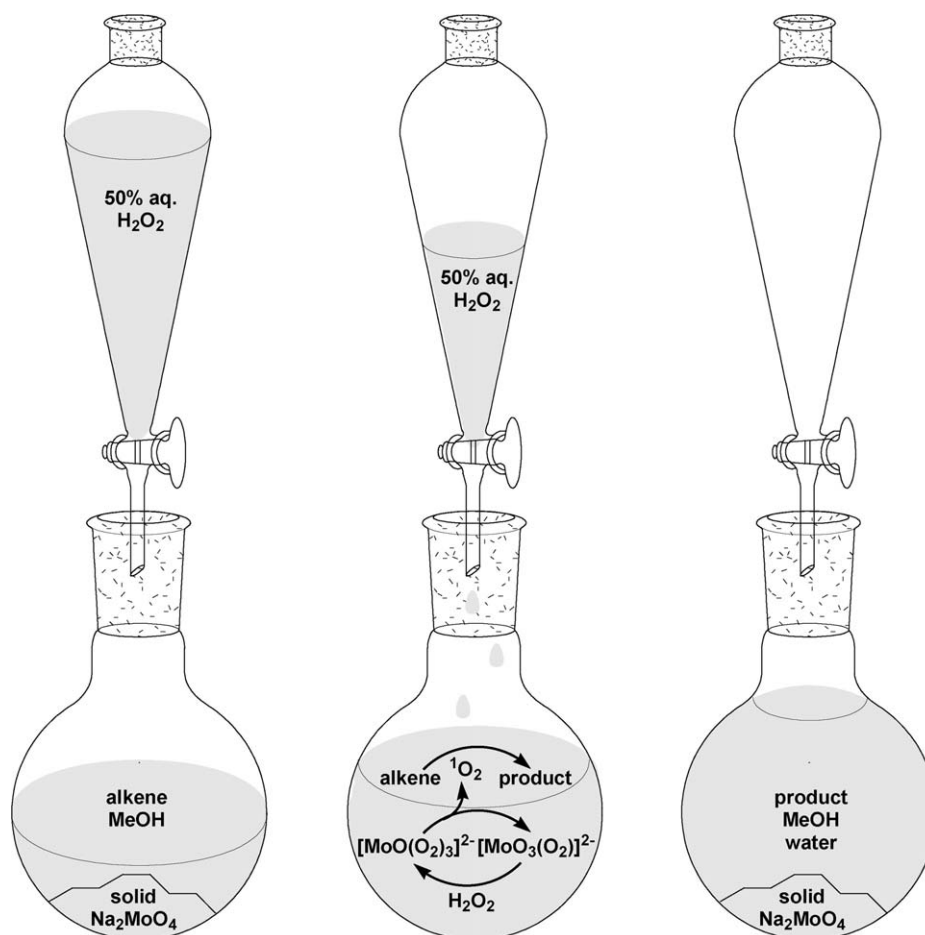


Fig. 6. How to carry out “dark” singlet oxygenation with Na_2MoO_4 as catalyst in MeOH as solvent.

in such a way that vicinal diols and not 1,3-diols are obtained after reduction of the hydroperoxide, and when the OH-group is linked to a chiral C-atom, such vicinal diol products can be obtained with a high *threo/erythro*-selectivity, depending on the nature of the substrate and the reaction conditions. Unfortunately, under the conditions as shown in Fig. 6, allylic alcohols are epoxidized instead of peroxidized by the $\text{Na}_2\text{MoO}_4/\text{H}_2\text{O}_2$ system. The reason for this is that epoxidation is greatly accelerated by coordination of the allylic alcohol O-atom to the strongly

Lewis-acidic Mo(VI) peroxy species, thus bringing the alkene double bond in an ideal position with respect to a peroxy group to induce rapid epoxidation.

In order to avoid undesirable epoxidation that results from an intimate contact between the metal catalyst and the substrate, one can devise strategies that are based on the “oxidant transformation” mechanism of “dark” singlet oxygenation. Since the actual peroxidation step proceeds by attack of singlet oxygen on the substrate without involvement of the metal catalyst, whereas

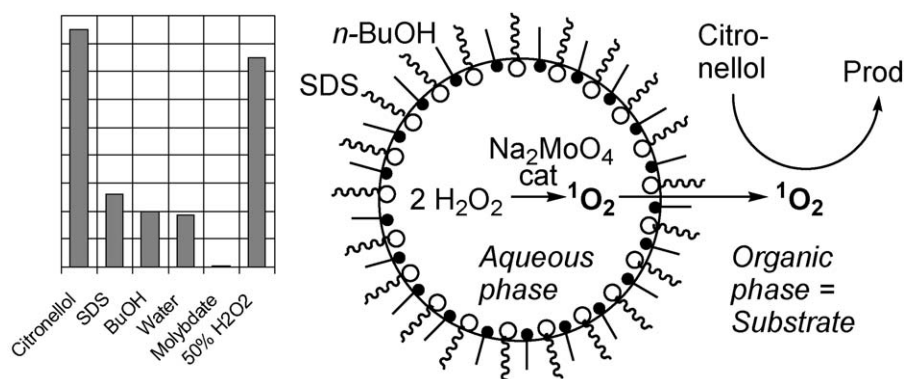


Fig. 7. “Dark” singlet oxygenation of citronellol in a solvent-free micro-emulsion showing the mass-composition of the system (left) and a catalyst-containing water droplet in the organic continuous phase (right).

the epoxidation does require an intimate contact between the substrate and the catalyst, peroxidation should be favored over epoxidation when the catalyst and the substrate are in different phases and singlet oxygen is capable to diffuse to the substrate-containing phase before decaying to its ground-state. Alternatively, one could design another “dark” singlet oxygenation catalyst that has very little epoxidation activity, but is very active for H_2O_2 disproportionation. In the latter case, the catalyst might be in the same phase as the substrate. Three different systems that allow the peroxidation of substrates that cannot be successfully peroxidated with Na_2MoO_4 are discussed below:

1. Based on the foregoing reasoning, it should not come as a surprise that water-in-oil micro-emulsions are perfect media to avoid unfavorable catalyst–substrate interactions that lead to side-reactions such as epoxidation. Indeed, it has recently been demonstrated by Aubry et al. that even allylic alcohols are peroxidated rather than epoxidated when Na_2MoO_4 is trapped in the tiny aqueous droplets in a micro-emulsion [27]. Since the continuous phase in this case usually consists of apolar, non-protic solvents (e.g., CH_2Cl_2), there is even a good control of diastereoselectivity in the case of chiral allylic alcohols. Such a high degree of diastereoselectivity cannot be obtained in water-miscible media because water prevents singlet oxygen to interact with the allylic OH group through hydrogen bonding, which is thought to be responsible for control of the *threo/erythro* selectivity. Thus, of all “dark” singlet oxygenation systems, “dark” singlet oxygenation in micro-emulsion media has the broadest synthetic scope, which actually most closely resembles that of photo-oxidation.
2. Immobilization of molybdate by anion exchange on layered double hydroxides (LDHs) provides another method for creating a phase separation between the catalyst and the substrate [28]. Evidently, in this case the catalyst is trapped in a heterogeneous, solid environment. Molybdate/LDH is a very efficient H_2O_2 disproportionation catalyst that allows the use of organic solvents (such as dioxane) which are not suitable for “dark” singlet oxygenation with homogeneous Na_2MoO_4 . Singlet oxygen is generated at the surface of the solid cat-

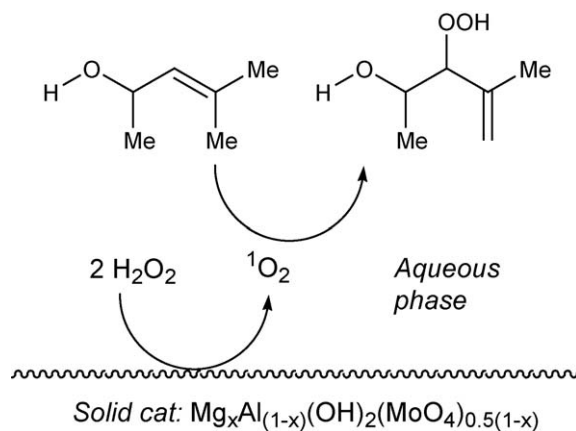


Fig. 8. “Dark” singlet oxygenation of allylic alcohols with molybdate immobilized on a layered double hydroxide as catalyst.

alyst, and diffuses from there into the bulk organic phase to effect substrate peroxidation. Accordingly, allylic alcohols can be peroxidated without epoxidation (Fig. 8). Apart from an increased synthetic scope compared to homogeneous Na_2MoO_4 , the added value of molybdate/LDH also lies in the fact that the LDH matrix retains the molybdate anions very tightly. This prevents product contamination by traces of molybdenum, and it allows the catalyst to be reused many times after simple catalyst isolation by filtration.

3. Besides molybdenum, a variety of other metals is capable of catalyzing H_2O_2 disproportionation into $^1\text{O}_2$ and water [29]. We were intrigued by lanthanum, since it is readily available, inexpensive, and non-toxic. An active La-based catalyst was obtained from aqueous H_2O_2 solutions of $\text{La}(\text{NO}_3)_3$ or LaCl_3 by precipitation through addition of NaOH at pH 9 [30]. When generated in this way, the catalyst is actually present in the form of a milky gel. Even although this La-catalyst is a less efficient singlet oxygen generator than molybdate, it allows the peroxidation of certain alkenes for which NaMoO_4 is not suitable. Besides allylic alcohols, it even enables the peroxidation of alkenyl amines. Thus, whereas geranylamine is converted into a complex mixture on attempted “dark” singlet oxygenation with molybdate, this lanthanum cata-

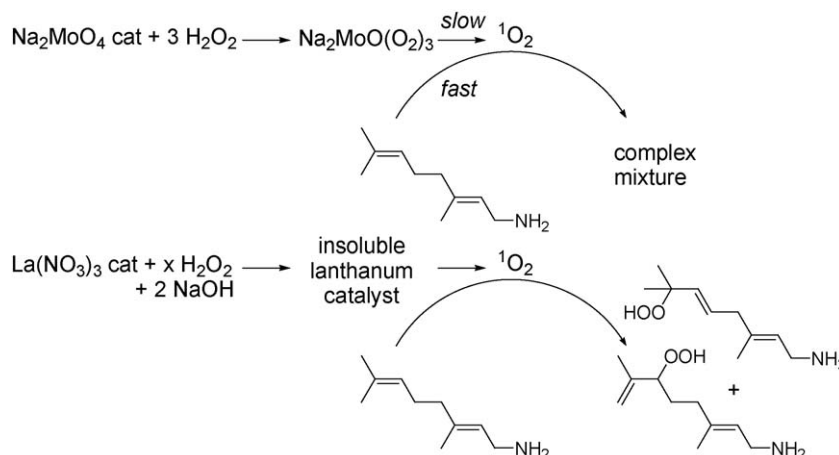


Fig. 9. “Dark” singlet oxygenation of geranyl amine with molybdate as catalyst (top) and with a heterogeneous lanthanum catalyst (bottom).

lyst cleanly converts it into the two expected hydroperoxides derived from attack of $^1\text{O}_2$ on the terminal $\text{Me}_2\text{C}=\text{C}$ bond, while leaving the double bond adjacent to the amine group intact (Fig. 9). The enhanced selectivity obtained with this La-catalyst compared to molybdate is not only ascribed to its heterogeneous nature, which reduces selectivity-lowering substrate–catalyst interactions. It also results from the fact that the heterogeneous La-catalyst is capable of generating singlet oxygen from H_2O_2 under acidic conditions ($\text{pH} > 5$), whereas molybdate only works under alkaline conditions. Under such acidic conditions, the amine group is fully protonated. This prevents electrophilic attack on the nitrogen lone-pair by oxidizing species, and it also deactivates the nearby $\text{C}=\text{C}$ bond for attack by electrophilic $^1\text{O}_2$, which instead prefers attack of the more electron-rich terminal $\text{Me}_2\text{C}=\text{C}$ bond. An additional factor that might contribute to the higher selectivity of the La-catalyst is the lower oxygen-transfer power of lanthanum peroxo species compared to peroxo molybdates. Finally, it is noted that by incorporating La into a zeolite framework (Beta; USY), a “dark” singlet oxygenation catalyst is obtained with a superior performance in terms of rate and selectivity of the H_2O_2 disproportionation compared to the gel-type La-catalyst described above [31]. Accordingly, the La-zeolite catalyst allows high substrate conversions to be achieved with less excess of H_2O_2 and within a shorter period of time.

4. Conclusions

The $[\text{WZn}_3(\text{ZnW}_9\text{O}_{34})_2]^{12-}$ “sandwich” polyoxometalate is a useful multi-purpose oxidation catalyst for oxidations with aqueous hydrogen peroxide. It is easily prepared by “self-assembly” from readily available inorganic materials. Catalyst recycling can be achieved with very high efficiency through nanofiltration using ceramic membranes. “Dark” singlet oxygenation through disproportionation of aqueous hydrogen peroxide is catalyzed efficiently by molybdate, either in homogeneous form or immobilized on a layered double hydroxide support. Besides these molybdate-based catalysts, also heterogeneous lanthanum catalysts have been developed that allow peroxidations which proceed with low selectivity in the case of molybdate, such as peroxidation of allylic alcohols or alkenyl amines. Microemulsions are very efficient media for “dark” singlet oxygenations and allow to obtain both a high selectivity and high productivity.

Acknowledgement

We thank the European Commission (SUSTOX grant, G1RD-CT-2000-00347) for generous financial support.

References

- [1] T.J. Collins, *Acc. Chem. Res.* 27 (1994) 279.
- [2] The Fenton and Udenfried systems provide other examples of catalysis by oxidant transformation.
- [3] Unambiguous proof for the formation of singlet oxygen in the “dark” singlet oxygenations referred to in this paper has been obtained by IR luminescence at 1270 nm, see for example Refs. [22,30,31].
- [4] N. Mizuno, M. Misono, *Chem. Rev.* 98 (1998) 199.
- [5] C.L. Hill, C.M. Prosser-McCartha, *Coord. Chem. Rev.* 143 (1995) 407.
- [6] I.V. Kozhevnikov, *Chem. Rev.* 98 (1998) 171.
- [7] R. Neumann, *Prog. Inorg. Chem.* 47 (1998) 317.
- [8] C.M. Tourné, G.F. Tourné, F. Zonnevijlle, *J. Chem. Soc., Dalton Trans.* (1991) 143.
- [9] D. Sloboda-Rozner, P.L. Alsters, R. Neumann, *J. Am. Chem. Soc.* 125 (2003) 5280.
- [10] R. Neumann, M. Gara, *J. Am. Chem. Soc.* 117 (1995) 5066.
- [11] W. Adam, P.L. Alsters, R. Neumann, C.R. Saha-Möller, D. Seebach, A.K. Beck, R. Zhang, *J. Org. Chem.* 68 (2003) 8222.
- [12] D. Sloboda-Rozner, P. Witte, P.L. Alsters, R. Neumann, *Adv. Synth. Catal.* 346 (2004) 339.
- [13] P.T. Witte, P.L. Alsters, W. Jary, R. Müllner, P. Pöchlauer, D. Sloboda-Rozner, R. Neumann, *Org. Process. Res. Dev.* 8 (2004) 524.
- [14] Y. Ishii, K. Yamawaki, T. Ura, H. Yamada, T. Yoshida, M. Ogawa, *J. Org. Chem.* 53 (1988) 3587.
- [15] C. Venturello, R.D. Aloisio, *J. Org. Chem.* 53 (1988) 1553.
- [16] J. Prandi, H.B. Kagan, H. Mimoun, *Tetrahedron Lett.* 27 (1986) 2617 (originally, $[\text{Ph}_3\text{PB}_n]\text{Cl}$ instead of $[(n\text{-C}_8\text{H}_{17})_3\text{NMe}]\text{Cl}$ was used as phase-transfer catalyst).
- [17] K. Satu, M. Aoki, M. Ogawa, T. Hashimoto, R. Noyori, *J. Org. Chem.* 61 (1996) 8310.
- [18] This catalyst activation step is not included in Fig. 2.
- [19] W. Adam, P.L. Alsters, R. Neumann, C.R. Saha-Möller, D. Sloboda-Rozner, R. Zhang, *J. Org. Chem.* 68 (2003) 1721.
- [20] H.P. Dijkstra, G.P.M. van Klink, G. van Koten, *Acc. Chem. Res.* 35 (2002) 798.
- [21] P.T. Witte, S.R. Chowdhury, J.E. ten Elshof, D. Sloboda-Rozner, R. Neumann, P.L. Alsters, *Chem. Commun.* (2005) 1206.
- [22] V. Nardello, S. Bogaert, P.L. Alsters, J.M. Aubry, *Tetrahedron Lett.* 43 (2002) 8731.
- [23] J.M. Aubry, S. Bouttemy, *J. Am. Chem. Soc.* 23 (1997) 5286.
- [24] V. Nardello, M. Herve, P.L. Alsters, J.M. Aubry, *Adv. Synth. Catal.* 344 (2002) 184.
- [25] W. Adam, B. Nestler, *J. Am. Chem. Soc.* 114 (1992) 6549.
- [26] W. Adam, H.G. Bruenker, *J. Am. Chem. Soc.* 115 (1993) 3008.
- [27] V. Nardello, L. Caron, J.M. Aubry, S. Bouttemy, T. Wirth, C.R. Saha-Möller, W. Adam, *J. Am. Chem. Soc.* 126 (2004) 10692.
- [28] J. Wahlen, D.E. De Vos, P.A. Jacobs, P.L. Alsters, *Adv. Synth. Catal.* 346 (2004) 152.
- [29] J.M. Aubry, in: C. Vigo-Pelfrey (Ed.), *Membrane Lipid Oxidation*, vol. 2, CRC Press, Boca Raton, FL, 1991, pp. 65–102.
- [30] V. Nardello, J. Barbillat, J. Marko, P.T. Witte, P.L. Alsters, J.M. Aubry, *Chemistry* 9 (2003) 435.
- [31] J. Wahlen, D.E. De Vos, S. De Hertogh, V. Nardello, J.M. Aubry, P.L. Alsters, P.A. Jacobs, *Chem. Commun.* (2005) 927.