

Strategies for oxidation catalyzed by polyoxometalates at the interface of homogeneous and heterogeneous catalysis

Maxym Vazylyev, Dorit Sloboda-Rozner, Adina Haimov, Galia Maayan, and Ronny Neumann*

Department of Chemistry, Weizmann Institute of Science, Rehovot, Israel 76100

A basic premise behind the use of polyoxometalates in oxidation chemistry is the fact that polyoxometalates are oxidatively stable. This, *a priori*, leads to the conclusion that for practical purposes polyoxometalates would have distinct advantages over widely investigated organometallic compounds that are vulnerable to decomposition due to oxidation of the ligand bound to the metal center. Since polyoxometalate synthesis is normally carried out in water by mixing the stoichiometrically required amounts of monomeric metal salts and adjusting the pH to a specific acidic value many structure types are accessible by variation of the reaction stoichiometry, replacement of one or more addenda atoms with other transition or main group metals, and pH control. The structural variety available has enabled the use of polyoxometalates as catalysts for oxidation of hydrocarbons and functionalized organic substrates (alcohols, amines, sulfides, etc.) with a wide range of oxygen donors ranging from molecular oxygen, hydrogen peroxide, nitrous oxide, ozone, alkyl hydroperoxides, periodate, sulfoxide and others. The wide purview of oxidation reactions is enabled because the structural variety leads to oxidation through a number of different mechanistic motifs.

From a synthetic organic point of view, the most applicable uses of polyoxometalates as catalysts involve the “green” oxygen donors – hydrogen peroxide and molecular oxygen. Since practical applications are in hand in this area, practical considerations concerned with catalyst recycle and/or recovery and the elimination of environmentally problematic solvents are also coming to the forefront. In this paper, we will present some of our activities in the area of “catalyst engineering” for catalytic synthetic applications by polyoxometalates including: (a) catalytic mesoporous solids from organic-polyoxometalate hybrid materials, (b) fluoros phase polyoxometalates with and without fluoros solvents and (c) the use of aqueous biphasic media for oxidation with hydrogen peroxide.

KEY WORDS: aqueous biphasic; hydrogen peroxide; mesoporous; oxidation; oxygen; polyoxometalates.

1. Introduction

A societal dictated push towards chemical processing free of dangerous waste that requires reactions of high atom economy and use of environmentally friendly solvents has led to the introduction of mainly homogeneous liquid phase catalysis into the arena of organic chemistry. Thus, catalytic metal-based oxidation, especially using molecular oxygen and hydrogen peroxide as intrinsically non-waste producing terminal oxidants, is becoming an important alternative to classic stoichiometric procedures. Research published since *circa* 1980 has established the potential of polyoxometalates as homogeneous oxidation catalysts especially in the context of the use of molecular oxygen and hydrogen peroxide as oxidants [1]. Although many examples of the use of polyoxometalates in oxidation catalysis exist we will confine this discussion to two important cases. First, for oxidation with molecular oxygen, the mixed addenda phosphovanadomolybdates, $[\text{PV}_x\text{Mo}_{10-x}\text{O}_{40}]^{-(3+x)}$ (especially for $x = 2$), has been shown to be a good/excellent oxidation catalyst for numerous transformations such as oxydehydrogenation of dienes, alcohols, amines, and phenols, and the oxidation of

sulfur containing compounds and halides[1]. Second for oxidation with hydrogen peroxide, polyoxotungstates in general and more specifically the “sandwich” type polyoxometalates, such as $\{\text{WZnM}_2(\text{H}_2\text{O})_2[\text{Zn}-\text{W}_9\text{O}_{34}]_2\}^{12-}$ (notably for $\text{M} = \text{Zn}^{\text{II}}, \text{Mn}^{\text{II}}$), and the so-called Venturello compound $\{\text{PO}_4[\text{WO}(\text{O}_2)_2]_4\}^{3-}$ have been shown to have excellent catalytic activity especially in the oxidation of alkenes, alcohols, amines and sulfides [1].

Since in research involving catalysis questions of catalyst integrity, recovery and recycling are vital issues for eventual larger-scale application, strategies for converting homogeneous catalytic methods to heterogeneous ones are of primary interest. Thus, in this paper we discuss various systems for catalyst “engineering” designed to aid in polyoxometalate catalyst recovery and recycling. In general one can discern between two broad approaches. The first basic approach is to immobilize a catalyst with proven catalytic properties onto a solid support leading to catalytic system that may be filtered and reused. Such approaches include concepts such as simple use of catalysts as insoluble bulk material, impregnation of a catalyst onto a solid and usually inert matrix, attachment through covalent or ionic bonds of a catalyst to a support, inclusion of a catalyst in a membrane or other porous material and

*To whom correspondence should be addressed.

E-mail: Ronny.Neumann@weizmann.ac.il

several others. The second basic approach is to use biphasic liquid–liquid systems, such that at separation temperatures, which are usually ambient, the catalyst and product phases may be separated by phase separation; the catalysts phase is reused and the product is worked up in the usual manner. Numerous biphasic media have been discussed in the literature that include using catalysts in aqueous, fluoruous, ionic liquid, super critical fluid and other liquid phases.

2. Previous research

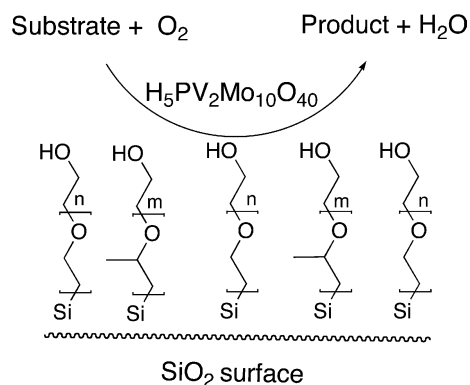
In the area of solid–liquid reactions, liquid phase oxidation by heterogenization of the homogeneous catalyst was initially applied by classic wet impregnation of the polyoxometalate onto a solid support. In this way phosphovanadomolybdate catalysts such as $\text{Na}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and $(\text{NH}_4)_9\text{PV}_6\text{Mo}_6\text{O}_{40}$ were supported on active carbon, which was observed to lead to the high activity for aerobic oxidation with these catalysts. Reactions that were especially efficient included the oxidation of (i) benzylic alcohols to the corresponding benzylic aldehydes (>95% conversion, ~100 selectivity) (ii) benzylic amines to the corresponding imines that in the presence of traces of water led to the formation of Schiff bases and then benzylic aldehydes (>95% conversion, ~100 selectivity) and (iii) phenols to quinines [2]. More recently, a ruthenium containing polyoxometalate has expanded the possibility of aerobic alcohol oxidation to additional less reactive substrates [3]. Hydrophobic solvents such as toluene are good solvents for many of these reactions and do not lead to measurable leaching. It was originally assumed that the catalyst support was inert and was simply useful for increasing the surface area for the heterogeneous reaction. However, comparison of active carbon with other supports, such as silica or alumina, for the oxidation of alcohols, amines and phenols showed that carbon supports were in fact far superior. This led to the suggestion that the support may be actively involved in the catalysis. A subsequent study led to the formulation that quinones, likely formed on the active carbon surface through the presence of the polyoxometalate and oxygen, might play a role as an intermediate oxidant [4]. Thus, a catalytic cycle may be considered, whereby a surface quinone oxidizes the alcohol to the aldehyde and is reduced to a hydroquinone, which is reoxidized in the presence of the catalyst and molecular oxygen.

The use of phosphovanadomolybdates, in this case $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, as catalysts was expanded by either their adsorption onto a mesoporous molecular sieve such as MCM-41 or by electrostatic binding to MCM-41 modified with amino groups. These catalytic systems were active in the aerobic oxidation of alkenes and alkanes in the presence of isobutyraldehyde as sacrificial reagent [5]. Further research, whose impetus was not

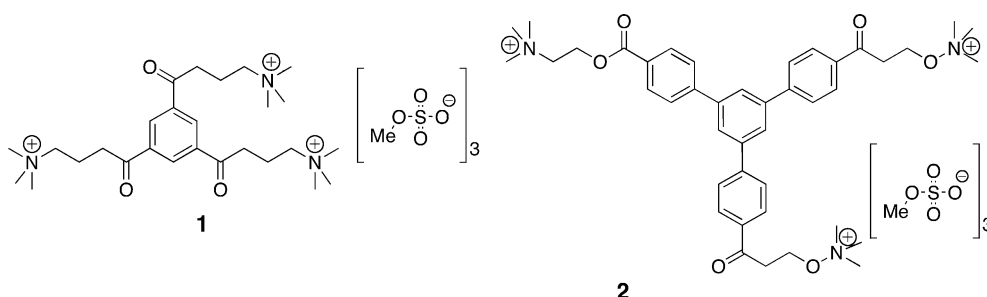
synthetically oriented but rather designed to effect deodorization of air, showed that $[\text{PV}_2\text{Mo}_{10}\text{O}_{40}]^{5-}$ on several supports, such as carbon or textile fibers was active for oxidation of various odorous volatile organics such as acetaldehyde, 1-propanethiol and thiolane [6]. More recently, an iron substituted polyoxometalate supported on cationic silica was also found to be active for similar oxidation of sulfides and aldehydes at ambient conditions [7].

Catalysts useful for reactions with hydrogen peroxide have also been heterogenized on a solid support. Since polyoxometalates are anionic, preparation of silica particles with quaternary ammonium moieties on the surface led to a useful catalytic assembly with $\{[(\text{WZnMn}_2(\text{H}_2\text{O})_2)[(\text{ZnW}_9\text{O}_{34})_2]\}^{12-}$ as active species. Importantly, using the sol-gel synthesis for the preparation of silica the surface hydrophobicity could be controlled by choice of the organocilicate precursors, $\text{RSi}(\text{OEt})_3$ where $\text{R} = \text{Ph}$, alkyl [8]. This control of surface hydrophobicity led to the tuning of the catalytic activity and gave essentially the same reactivity as in the previously reported biphasic liquid–liquid reaction medium where the catalyst is dissolved in a chlorohydrocarbon organic phase.

Since heteropoly acids can form complexes with crown ether type complexes [9], an interesting twist useful especially useful for oxidation with the acidic $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ was use the inexpensive polyethylene glycol as solvent [10]. Upon cooling the reaction mixture the $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ -polyethylene glycol phases separates from the product. In this way, previously known reactions with $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ as catalyst, such as aerobic oxidation of alcohols, dienes and sulfides, and Wacker type oxidations were demonstrated. Beyond the simple use of polyethylene glycol as solvent, the attachment of both hydrophilic polyethylene glycol and hydrophobic polypropylene glycol to silica by the sol-gel synthesis leads to solid particles that upon dispersion in organic solvents lead to liquid-like phases, Scheme 1. Addition of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ leads to what we have termed solvent anchored supported liquid phase catalysis and reactivity typical for this catalyst [11]. The



Scheme 1. Solvent anchored supported liquid phase catalysis-Silica-PEG/PPG- $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.



Scheme 2. The tripodal polyammonium cations.

balance of hydrophilicity–hydrophobicity of the surface is important for tweaking the catalytic activity.

3. Mesoporous polyoxometalate based materials

Polyoxometalate based hybrid compounds[12] have been constructed either by formation of covalent bonds between organic and inorganic moieties or by creation of electrostatic interactions[13] between the inorganic and organic components. Polyoxometalates are also important as building units of supramolecular complexes since they can exhibit diverse self-assembly properties for such supramolecular materials, thus controlling the formation of n -dimensional organic–inorganic hybrid networks in self-organization processes. Previously such an approach was used to prepare well-defined polyoxometalate containing films[14]. In order to realize the potential self-assembly properties it is important to correctly design an organic component for the hybrid material synthesis.

Now, we can show that by the synthesis of tripodal polyammonium cations and their utilization as building blocks together with a “sandwich” type polyoxometalate, $[(WZnZn_2(H_2O)_2)[(ZnW_9O_{34})_2]]^{12-}$, a mesoporous material of moderate surface area can be obtained[15]. The hybrid material is an active and recyclable catalyst for the oxidation of allylic alcohols and alcohols with hydrogen peroxide. The tripodal polyammonium cations, benzene-1,3,5-tricarboxylic acid tris-(2-trimethylammonium ethyl)ester, **1**, and benzene-1,3,5-[tri(phenyl-4-carboxylic acid)] tris-(2-trimethylammonium ethyl)ester, **2**, Scheme 2, were synthesized relatively simple procedures. The tripodal cation, **1**, was prepared by acylation of N,N -dimethylaminoethanol with 1,3,5-benzenetricarbonyl trichloride followed by quaternization with dimethylsulfate to yield the methylsulfate salt of **1**. The tripodal cation, **2**, was prepared by the following sequence (a) self-condensation of 4-bromacetophenone to yield 1,3,5-tri(4-bromophenyl)benzene, (b) lithiation followed by (c) carboxylation with carbon dioxide yielded 1,3,5-tri(4-carboxyphenyl)benzene, (d) preparation of the acyl chloride derivative with oxalyl chloride, (e) esterification with N,N -dimethylaminoethanol and (f) quaternization by dimethyl sulfate to yield the methylsulfate salt of **2**.

By mixing DMSO solutions of one equivalent of $Q_7Na_5[(WZnZn_2(H_2O)_2)[(ZnW_9O_{34})_2]]$ (Q = tetrabutylammonium) and four equivalents of methylsulfate salts of **1** or **2**, white, insoluble, amorphous solids, termed **1-POM** and **2-POM**, respectively, were obtained almost immediately. Both materials showed the requisite IR. Transmission electron microscope (TEM) images, Figure 1, showed a granular material with small highly contrasting dots situated within a more poorly contrasting substance. The diameter average found for the black dots is c.a. 1.8 nm which is approximately the cross-section diameter of the $\{[(WZnZn_2(H_2O)_2)[(ZnW_9O_{34})_2]]^{12-}$ polyanion (dimensions of ~ 1.0 to ~ 1.5 nm for the X-ray crystal structure of $\{[(WZnZn_2(H_2O)_2)[(ZnW_9O_{34})_2]]^{12-}$ [16]. We believe that the poorly contrasting substance are the organic polycations surrounding polyoxometalate anions.

N_2 sorption analyses showed isotherms and adsorption–desorption curves that are typical for mesoporous materials. BET surface areas of 51 and 27 $m^2 g^{-1}$ were calculated for **1-POM** and **2-POM**, respectively. Pore size distribution curves calculated by Barret–Joyner–Halenda (BJH) method indicated an average pore size of 36 ± 6 Å for both hybrid materials.

The mesoporous hybrid materials were tested as heterogeneous catalysts for oxidation reaction with

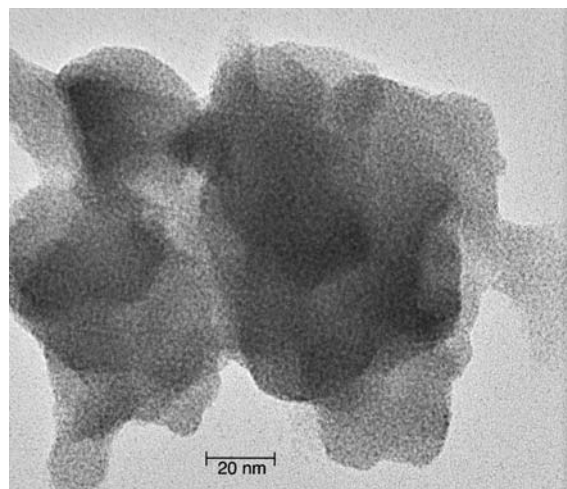
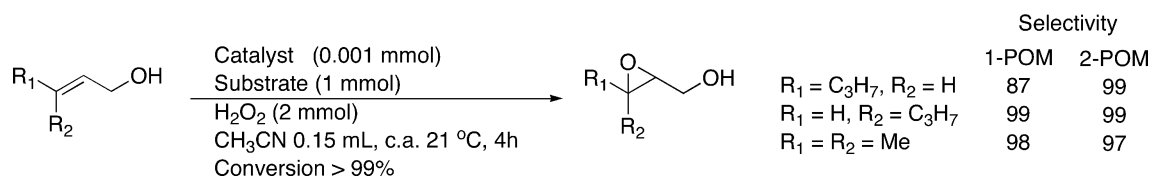


Figure 1. TEM images of a typical mesoporous material.

Scheme 3. Epoxidation of primary allylic alcohols with H_2O_2 .

hydrogen peroxide. In the epoxidation of primary allylic alcohols, Scheme 3, quantitative conversions with generally very high chemoselectivity to the epoxide product (>90%) was observed.

In order to probe the diastereo- and chemoselectivity of epoxidation reactions catalyzed by the mesoporous materials, the epoxidation of chiral allylic alcohols was further studied, Scheme 4. The results reveal that these chiral allylic alcohols were oxidized with the heterogeneous catalysts with diastereoselectivities comparable to reactions carried out with the $\{[(WZnZn_2(H_2O)_2)[(Zn-W_9O_{34})_2]\}^{12-}$ polyoxometalate dissolved in 1,2-dichloroethane. Chemoselectivity towards epoxidation was somewhat lower than in the biphasic system possibly because the formation of the proposed template intermediate[15] that leads to epoxidation *versus* alcohol oxidation is hindered in a heterogeneous catalyst.

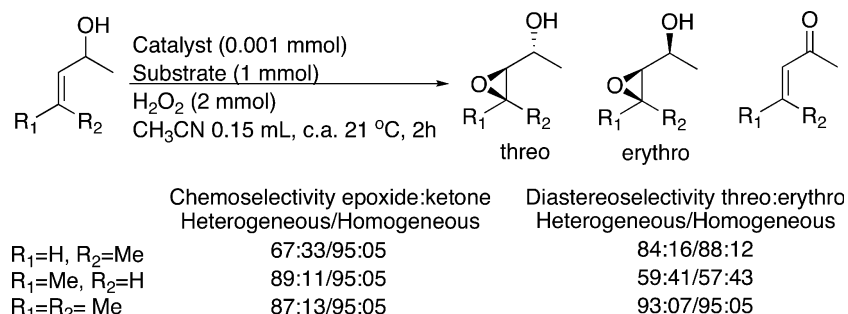
Finally, hydrogen peroxide mediated oxidation catalyzed by **1-POM** and **2-POM** of aliphatic secondary alcohols were tested as well. The results showed high conversion, especially with **2-POM** based on the more extended tripod cation, and full selectivity to the ketone product. Notably, also there appear to be no shape constraints on catalytic activity, since it was observed that the linear 2-pentanol and cyclic cyclooctanol reacted at the same rates with essentially identical kinetic profiles. Recycle-recovery experiments using cyclooctanol showed that both **1-POM** and **2-POM** showed nearly quantitative conversion and selectivity to cyclooctanone over five reaction cycles. The catalyst was recovered after each cycle by filtration. After the fifth catalytic cycle the IR spectra and adsorption isotherms showed no significant structural changes for **1-POM** or **2-POM**. Furthermore, filtered solutions of acetonitrile and hydrogen peroxide heated for 5 h at 60 °C in the

presence **1-POM** or **2-POM** showed no catalytic activity or evidence of zinc or tungsten metals.

4. Fluorous phase catalysts

One liquid phase method that has quite recently attracted significant attention as a separation/recovery method is fluorous biphasic catalysis[17]. The concept is based on modifying known catalytic entities with fluorous “ponytails” yielding catalysts soluble in very hydrophobic perfluorohydrocarbon solvents. Commonly, there are very temperature dependent organic substrate/fluorous solvent–liquid/liquid phase miscibilities that allow single phase reactions at elevated reaction temperature and biphasic separation of the organic product from the fluorous solvent containing the catalyst at ambient or sub-ambient temperatures. Because of the unknown environmental impact and degradability of perfluorinated solvents and their high cost the concept of fluorous phase catalysis without fluorous solvents has also been introduced[18]. In such systems, polyfluorinated thermomorphic catalysts are soluble in normal hydrocarbons at elevated temperatures but are immiscible in the solvent at decreased temperatures allowing the separation by precipitation of the fluorous catalyst from the product and solvent phase by cooling the reaction mixture.

We have found that thermomorphic fluorous polyoxometalates may be prepared and used in fluorous biphasic catalysis despite the polyanionic nature of the polyoxometalates by use of perfluorinated quaternary ammonium cations, $[CF_3(CF_2)_7(CH_2)_3]_3CH_3N^+$ or (R_FN^+) , as counter-cations[19]. Consequently, effective catalytic oxidation reactions of alkenes, alkenols and

Scheme 4. Oxidation of chiral allylic alcohols with H_2O_2 in homogeneous and **2-POM** catalyzed reactions.

alcohols can be carried out using “sandwich” type polyoxometalates, $(R_F N^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ with aqueous hydrogen peroxide as oxidant with or without fluoruous solvents. The fluoruous quaternary ammonium salt $\{[CF_3(CF_2)_7(CH_2)_3]_3 CH_3 N^+\} CH_3 O-SO_3^-$ was prepared by quaternization of the known fluoruous tertiary aliphatic amine[20], by dimethylsulfate. The fluoruous polyoxometalates, $(R_F N^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$, were then prepared by mixing 12 equivalents of $\{[CF_3(CF_2)_7(CH_2)_3]_3 CH_3 N^+\} CH_3 O-SO_3^-$ with one equivalent of $Na_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ polyoxometalate. The fluorine content by weight of the fluoruous catalyst, $(R_F N^+)_{12}[WZnM_2(H_2O)_2(ZnW_9O_{34})_2]$ is 51.5 leading to a freely soluble catalyst in perfluorohydrocarbons at room temperature. In other common solvents such as ethylacetate the fluoruous catalysts is insoluble at room temperature, but dissolves upon heating to 60–80 °C. This property leads to two different reaction protocols for the fluoruous biphasic catalysis: (a) with a perfluorohydrocarbon (perfluorodecalin) solvent and (b) without a fluoruous solvent, in this case EtOAc. Results using the two catalytic reaction protocols for the oxidation of alcohols is presented in Scheme 5.

One may observe that secondary aliphatic alcohols were rather effectively oxidized to the expected ketones with without formation of by-products. There was an interesting trend of reactivity as a function of the length of the aliphatic chain. Fairly water soluble 2-butanol hardly reacts due to its limited solubility in EtOAc and perfluorodecalin in the presence of aqueous H_2O_2 . For the shorter chain alcohols e.g. 2-pentanol, 2-hexanol probably better solubility in EtOAc *versus* perfluorodecalin leads to higher conversion in the non-fluoruous solvent. As the aliphatic chain is lengthened, the relative activity EtOAc/perfluorodecalin is inverted.

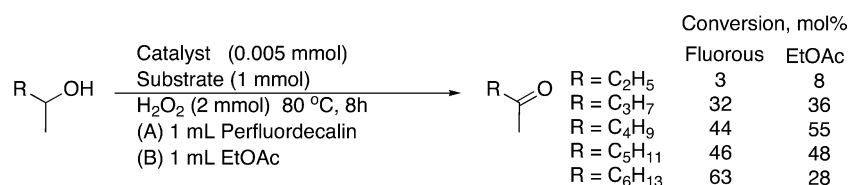
The reactivity of alkenes towards epoxidation was also tested. Weakly nucleophilic alkenes such as 1-octene and 2-octene were unreactive (0–3% yield) using the fluoruous polyoxometalate catalyst, however, more reactive cyclohexene derivatives such as cyclohexene, 4-methylcyclohexene, and 1-methylcyclohexene reacted almost quantitatively with the fluoruous catalyst with no evidence of acid catalyzed epoxide ring opening and diol formation, which is unusual for such acid sensitive epoxides in the absence of a buffer. Catalyst recovery protocols were also tested using both perfluorodecalin and EtOAc as solvents and the oxidation of 1-cyclohex-

en-3-ol to 1-cyclohexen-3-one as a probe reaction. In both cases three repetitive cycles showed good catalyst recovery and minimal loss of activity. ^{19}F NMR of the organic product phases showed no measurable (by NMR) presence of the catalyst in the product phase.

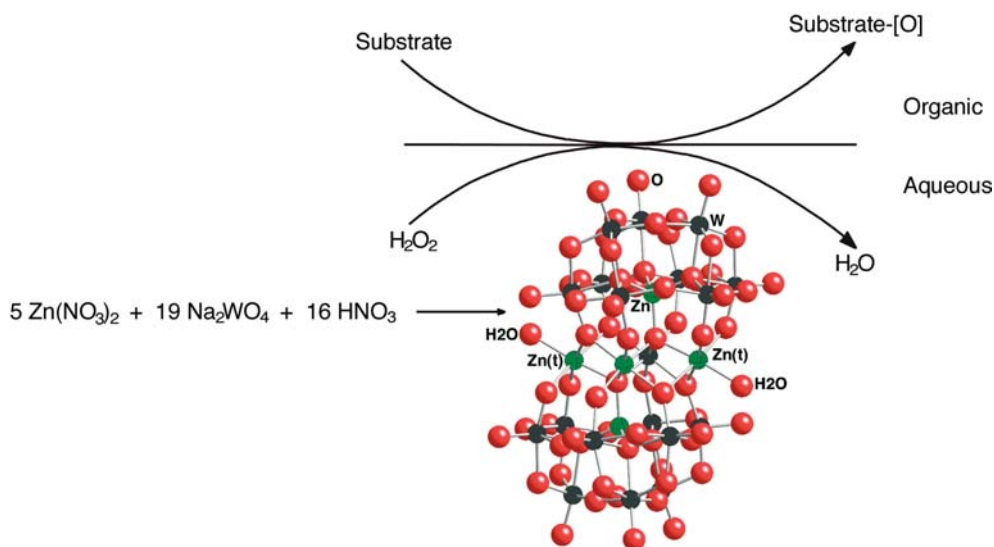
5. Aqueous biphasic catalysts

Although polyoxometalates are commonly synthesized as water soluble alkali salts, the idea of carrying out reactions in biphasic media polyoxometalate-water/organic substrate has not been realized until recently. We have observed that the catalytically active polyoxometalate catalyst $\{[(WZn_3(H_2O)_2)[(ZnW_9O_{34})_2]]^{12-}$, can (a) be assembled *in situ* in water by mixing zinc nitrate, sodium tungstate and nitric acid as shown by ^{183}W NMR spectroscopy and (b) that this assembled polyoxometalate in water catalyzes the aqueous biphasic oxidation of alcohols, diols, amines, and pyridine derivatives with hydrogen peroxide, Scheme 6[21].

The oxidation of various secondary alcohols including 2-butanol, 2-pentanol, 2-octanol, 2, 5-hexanediol, 1-phenylethanol, cyclohexanol, cyclooctanol, and 2-ethyl-1, 3-hexanediol under the following reaction conditions: 1 mmol substrate, 5 mmol (~17% wt) H_2O_2 , 4 μ mol $Na_{12}[WZnZn_2(H_2O)_2(ZnW_9O_{34})_2]$, 1 ml water, 75 °C, 7 h, yielded the corresponding ketones in very high yields, >90% in all cases and high selectivity (only ketones were formed). Thus, the method was highly successful for oxidation of simple acyclic, cyclic and benzylic secondary alcohols to the corresponding ketones. The presence of two non-vicinal alcohol moieties, e.g. in 2,5-hexanediol, led to the formation of the corresponding diketone, 2,5-hexanedione. There is very high chemoselectivity in this reaction in reference to oxidation at a secondary alcohol in the presence of a primary alcohol as is evident in the oxidation of 2-ethyl-1,3-hexanediol to 2-ethyl-3-oxo-1-hexanol. However, primary alcohols can be oxidized cleanly to the corresponding carboxylic acids in nearly quantitative yields in the absence of a secondary alcohol moiety. Thus, 1-pentanol, benzyl alcohol and 4-hydroxymethyl imidazole were oxidized to the corresponding pentanoic acid, benzoic acid and imidazole-4-carboxylic acid, respectively, in upwards of 95% yields under the conditions noted above. Similarly, 1,6-hexanediol was oxidized to the corresponding adipic acid in essentially quantitative yields.



Scheme 5. Oxidation of aliphatic alcohols catalyzed by $(R_F N^+)_{12}[WZn_3(H_2O)_2(ZnW_9O_{34})_2]$.



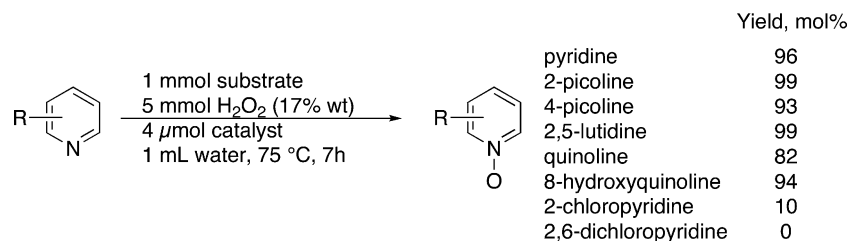
Scheme 6. The assembly the $\text{Na}_{12}[(\text{WZn}_3(\text{H}_2\text{O})_2)(\text{ZnW}_9\text{O}_{34})_2]$ polyoxometalate catalyst and a representation of aqueous biphasic oxidation.

The oxidation of vicinal diols was also probed. Under the following reaction conditions: 1 mmol diol, 5 mmol (~17% wt) H_2O_2 , 4 μmol $\text{Na}_{12}[\text{WZnZn}_2(\text{H}_2\text{O})_2(\text{ZnW}_9\text{O}_{34})_2]$, 1 ml water, 75 °C, 7 h, carbon-carbon bond cleavage products were obtained in high yields. Thus, 1-phenyl-1,2-ethanediol, *cis*-1,2-cyclooctanediol, *cis*-1,2-cyclopentanediol and *cis*- and *trans*-cyclohexanediol yielded benzoic acid, suberic acid, glutaric acid and adipic acid in nearly quantitative yields. The efficiency of H_2O_2 utilization was >85%. *Cis*- and *trans*-cyclohexanediol were oxidized with similar efficiency. For the more hydrophobic 1,2-octanediol, some 2-oxo-1-octanol was also formed. In fact it would appear that the α -hydroxyketones are the initial oxidation products in these reactions. For example, oxidation of 1-phenyl-1,2-ethanediol at room temperature (1 mmol 1-phenyl-1,2-ethanediol, 5 mmol (~17% wt) H_2O_2 , 4 μmol $\text{Na}_{12}[\text{WZnZn}_2(\text{H}_2\text{O})_2(\text{ZnW}_9\text{O}_{34})_2]$, 1 ml water, 22 °C, 7 h) yielded, 2-oxo-2-phenylethanol, benzaldehyde and benzoic acid in an approximately 1:3:3 ratio after 27% conversion.

Oxidation of aliphatic tertiary amines has been reported with hydrogen peroxide, but oxidation of aromatic tertiary amines, i.e. pyridine derivatives, usually requires use of peracids. For the latter, some

catalytic systems are known using, for example, methylrhodium oxide[22] or perfluorinated ketones[23] as catalysts in organic media. Our results for the oxidation of pyridine derivatives in the aqueous biphasic reaction medium are summarized in Scheme 7. From the results, one may observe that in general electron rich pyridine derivatives reacted to yield the expected N-oxides cleanly, whereas electron deficient compounds 2-chloropyridine and especially 2,6-dichloropyridine were hardly reactive.

In this case recovery and reuse of the catalyst can be carried out by simple phase separation after the reaction and addition of more organic substrate. Here since water is a product of the reaction its accumulation in the system will need to be rectified by evaporation after several reaction cycles. An illustration of the effectiveness of the aqueous catalysts phase was carried out using 2-pentanol as model substrate. Thus reaction of 10 mmol 2-pentanol, 50 mmol H_2O_2 , 40 μmol $\text{Na}_{12}[\text{WZnZn}_2(\text{H}_2\text{O})_2(\text{ZnW}_9\text{O}_{34})_2]$, 10 ml water, 75 °C, 7 h followed by phase out separation of the organic phase and re-addition of 2-pentanol (10 mmol) and hydrogen peroxide (50 mmol) showed 95, 90, and 96% conversions over three reaction cycles with 2-pentanone as only product. There was no discernible loss in activity or selectivity.



Scheme 7. Oxidation of pyridine derivatives catalyzed by $\text{Na}_{12}[\text{WZnZn}_2(\text{H}_2\text{O})_2(\text{ZnW}_9\text{O}_{34})_2]$.

Above, we have discussed the oxidation of alcohol moieties in the aqueous biphasic media. In efforts to extend this methodology we attempted to oxidize simple reactive alkenes such as cyclooctene. Unfortunately, they did not react. Since “sandwich” type polyoxometalates, e.g. $[\text{WZnMn}_2(\text{H}_2\text{O})_2(\text{ZnW}_9\text{O}_{34})_2]^{12-}$, are known catalysts for these epoxidations when dissolved in organic media, the lack of reactivity in the biphasic aqueous system was attributed to lack of miscibility at the interface. In order to overcome this problem we have just recently shown water-soluble alkylated polyethylenimines can electrostatically bind polyoxometalates to quaternary ammonium sites of the alkylated polyethylenimine. These new alkylated polyethyleneimine/polyoxometalate (Alk-PEI/POM) systems also have hydrophobic regions enabling the solubilization or binding of hydrophobic substrates and therefore are active catalysts for the selective oxidation of such substrates in water. Thus, while cyclooctene, styrene, diphenylsulfide and methyloleate are not oxidized in simple biphasic media, the addition of alkylated polyethyleneimine leads to efficient and selective oxidation [24].

6. Conclusion

In this paper, we have demonstrated some of our recent activities in the area of “catalyst engineering” for catalytic synthetic applications by polyoxometalates including: (a) catalytic mesoporous solids from organic-polyoxometalate hybrid materials, (b) fluorine phase polyoxometalates with and without fluorine solvents and (c) the use of aqueous biphasic media for oxidation with hydrogen peroxide. The results show that given good catalytic activity of the polyoxometalates themselves, there are a significant variety of possibilities to further apply these catalysts in practical catalytic systems.

Acknowledgements

The research was supported by the European Commission (G1RD-CT-2000-00347), the Israel Science Foundation, and the Helen and Martin Kimmel Center for Molecular Design. R. N. is the Rebecca and Israel Sieff Professor of Organic Chemistry.

References

[1] (a) M.T. Pope, *Isopoly and Heteropoly Anions* (Springer, Berlin, Germany, 1983). (b) A. Müller, *Polyoxometalate Chemistry* (Kluwer Academic, Dordrecht, The Netherlands, 2001). (c) I.V.

Kozhevnikov, *Catalysis by Polyoxometalates* (Wiley, Chichester, England, 2002). (d) C.L. Hill and C.M. Prosser-McCartha, *Coord. Chem. Rev.* 143 (1985) 407. (e) N. Mizuno and M. Misono, *Chem. Rev.* 98 (1998) 171. (f) R. Neumann, *Prog. Inorg. Chem.* 47 (1998) 317.

[2] (a) R. Neumann and M. Levin, *J. Org. Chem.* 56 (1991) 5707. (b) S. Fujibayashi, K. Nakayama, M. Hamamoto, S. Sakaguchi, Y. Nishiyama and Y. Ishii, *J. Mol. Catal. A* 110 (1996) 105. (c) K. Nakayama, M. Hamamoto, Y. Nishiyama and Y. Ishii, *Chem. Lett.* (1993) 1699.

[3] K. Yamaguchia and N. Mizuno, *New J. Chem.* 26 (2002) 972.

[4] A.M. Khenkin, I. Vigdergauz and R. Neumann, *Chem. Eur. J.* 6 (2000) 875.

[5] A.M. Khenkin, R. Neumann, A.B. Sorokin and A. Tuel, *Catal. Lett.* 63 (1999) 189.

[6] L. Xu, E. Boring and C.L. Hill, *J. Catal.* 195 (2000) 394.

[7] (a) N.M. Okun, T.M. Anderson and C.L. Hill, *J. Am. Chem. Soc.* 125 (2003) 3194. (b) N.M. Okun, T.M. Anderson and C.L. Hill, *J. Mol. Catal. A* 197 (2003) 283.

[8] R. Neumann and H. Miller, *J. Chem. Soc., Chem. Commun.* (1995) 2277.

[9] R. Neumann and I. Assael, *J. Chem. Soc., Chem. Commun.* (1989) 547.

[10] A. Haimov and R. Neumann, *Chem. Commun.* (2002) 876.

[11] (a) R. Neumann and M. Cohen, *Angew. Chem. Int. Ed.* 36 (1997) 1738. (b) M. Cohen and R. Neumann, *J. Mol. Catal. A* 146 (1999) 293.

[12] (a) P. Gouzerh and A. Proust, *Chem. Rev.* 98 (1998) 77. (b) R. Villanneau, R. Delmont, A. Proust and P. Gouzerh, *Chem. Eur. J.* 6 (2000) 1184. (c) C. Sanchez, G.J. de A.A. Soler-Illia, F. Ribot, T. Lalot, C.J. Mayer and V. Cabuil, *Chem. Mater.* 13 (2001) 3061.

[13] E. Coronado and C.J. Gomez-García, *Chem. Rev.* 98 (1998) 273.

[14] (a) M. Clemente-León, C. Mingotaud, B. Agricole, C.J. Gómez-García, E. Coronado, P. Delhaes and P. Angew. Chem. Int. Ed. Eng. 36 (1997) 1114. (b) M. Clemente-León, E. Coronado, P. Delhaes, C.J. Gómez-García and C. Mingotaud, *Adv. Mater.* 13 (2001) 574. (c) F. Caruso, D.G. Kurth, D. Volkmer, M.J. Koop and A. Müller, *Langmuir*, 14 (1998) 3462. (d) D.G. Kurth, D. Volkmer, M. Kuttorf and A. Müller, *Chem. Mater.* 12 (2000) 2829.

[15] M.V. Vasylyev and R. Neumann, *J. Am. Chem. Soc.* 126 (2004) 884.

[16] C.M. Tourne, G.F. Tourne and F. Zonneville, *J. Chem. Soc., Dalton Trans.* (1991) 143.

[17] (a) I.T. Horváth, *Acc. Chem. Res.* 31 (1998) 641. (b) M. Cavazzini, F. Montanari, G. Pozzi and S. Quici, *J. Fluorine Chem.* 94 (1999) 183. (c) P. Bhattacharyya, B. Croxtall, J. Fawcett, J. Fawcett, D. Gudmunsen, E.G. Hope, R.D. W. Kemmitt, D.R. Paige, D.R. Russell, A.M. Stuart and D.R. W. Wood, *J. Fluorine Chem.* 101 (2000) 247. (d) R.H. Fish, *Chem. Eur. J.* 5 (1999) 1677. (e) L.P. Barthel-Rosa and J.A. Gladysz, *Coord. Chem. Rev.* 190–192 (1999) 587.

[18] (a) M. Wende, R. Meier and J.A. Gladysz, *J. Am. Chem. Soc.* 123 (2001) 11490. (b) M. Wende, and J.A. Gladysz, *J. Am. Chem. Soc.* 125 (2003) 5861.

[19] G. Maayan, R.H. Fish and R. Neumann, *Org. Lett.*, 5 (2003) 3547.

[20] C. Rocoboy, W. Bauer and J.A. Gladysz, *Eur. J. Chem.* (2000) 2621.

[21] (a) D. Sloboda-Rozner, P.L. Alsters and R. Neumann *J. Am. Chem. Soc.* 125 (2003) 5280. (b) D. Sloboda-Rozner, P. Witte, P.L. Alsters and R. Neumann, *Adv. Synth. Catal.* 346 (2004) 339.

[22] K. Neimann and R. Neumann, *Chem. Commun.* (2001) 487.

[23] C. Copéret, H. Adolphsson, T.-A.V. Khoung, A.K. Yudin and K.B. Sharpless, *J. Org. Chem.* 63 (1998) 1740.

[24] A. Haimov, H. Cohen and R. Neumann, *J. Am. Chem. Soc.* 126 (2004) 11762.