

Molecular oxygen and oxidation catalysis by phosphovanadomolybdates

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The history of aerobic catalytic oxidation mediated by a subclass of polyoxometalates, the phosphovanadomolybdates of the Keggin structure, $[\text{PV}_x\text{Mo}_{12-x}\text{O}_{40}]^{(3+x)-}$, is described. In the earlier research it was shown that phosphovanadomolybdates catalyze oxydehydrogenation reactions through an electron-transfer oxidation of a substrate by the polyoxometalate that is then reoxidized by oxygen. These aerobic oxidations are selective and synthetically useful in various transformations, notably diene aromatization, phenol dimerization and alcohol oxidation. Oxygen transfer from the polyoxometalate to arenes and alkylarenes was also discussed as a homogeneous analog of a Mars–van Krevelen oxidation. “Second generation” catalysts include binary complexes of the polyoxometalate and a organometallic compound useful, for example, for methane oxidation and nanoparticles stabilized by polyoxometalates effective for aerobic alkene epoxidation.

Organic chemistry as the science of synthesis of organic matter has historically been dominated by a stoichiometric substrate–reagent approach. Useful products are formed by a series of modifications of a reactive substrate often using expensive and toxic reagents that also yield very copious amounts of waste. It has become apparent that this synthetic approach is less and less sustainable because of the high negative environmental load of such syntheses and the related high economic cost. Therefore, the challenges confronting organic chemists are significantly changing. Future synthetic organic chemistry will require (a) highly selective transformations of relatively inert chemical substrates, (b) process mediation *via* activation of chemical bonds by specifically designed catalysts, and (c) a shift towards high product selectivity *via* ligand control and design. In order to meet the goals of this future synthetic organic chemistry, new basic, fundamental research is required and new knowledge bases need to be established in various

areas. Specifically and quite obviously in the area of catalytic oxygen transfer and catalytic oxidation, an important goal is the activation of molecular oxygen (abundant, inexpensive and environmentally benign) towards selective oxidation reactions.

Most of the existing known pathways for the activation of mono-oxygen donors (DO), hydroperoxides (ROOH; R = H, alkyl, acyl), and molecular oxygen can be summarized by the pictorial representation, Scheme 1, below.

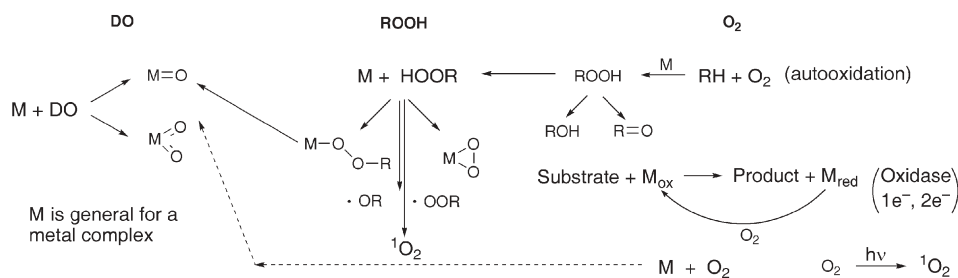
A careful examination of Scheme 1 can summarize much of the present research interest, activity and applications of catalytic oxidation and catalytic oxygen transfer. Some points for emphasis are the following. Mono-oxygen donors, for example hypochlorite, iodosobenzene, periodate, sulfoxides, nitrous oxide and many others can be used to form higher valent metal–oxo and metal–dioxo species that can be excellent active oxygen transfer intermediates for oxidation of alkenes, alkanes and also functionalized hydrocarbons (amines, sulfides, alcohols). Major examples include iron,¹ manganese,² and also ruthenium oxo species,³ and osmium and ruthenium dioxo species.⁴

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Ronny Neumann, born in New York, received his undergraduate and graduate education at the Hebrew University of Jerusalem, Israel, completing his PhD in 1985 on the subject of phase-transfer catalysis. He then was a postdoctoral fellow at Princeton University with John T. Groves working on metalloporphyrins in synthetic membrane assemblies. In 1988 Ronny returned the Hebrew University where took up a lectureship and in 1995 was promoted to associate professor. In 1999 Ronny moved to the Weizmann Institute of Science where he is now the Rebecca and Israel Sieff Professor of Organic chemistry and head of the department. His research interests lie in the areas of oxidation chemistry related to development of new synthetic organic chemistry using benign oxidants. Much of the research entails use of polyoxometalates as catalysts, which is now evolving into more complex catalytic systems requiring higher-level organization of catalytic entities. An important aspect the research is also

related to mechanistic questions especially concerning modes of oxygen activation.

Alex Khenkin completed his MSc at the Moscow Institute of Fine Chemical Technology and PhD at the Institute of Chemical Physics, Soviet Academy of Sciences in 1982 under the supervision of Professor Alexander E. Shilov. He then continued to work at the Institute of Chemical Physics as group leader in biomimetic oxidation. In 1991 Alex moved to the US and was a research associate with Craig Hill at Emory University. After two years he immigrated to Israel and took up a position in the laboratory of Ronny Neumann at the Hebrew University and then moved to the Weizmann Institute of Science in 1999, where he is currently senior staff scientist. Alex's research interests are in oxidation chemistry with emphasis on mechanistic research using kinetic tools, isotope labeling and spectroscopic techniques.



Scheme 1 Pathways for activation of oxygen donors, hydroperoxides and molecular oxygen.

Hydroperoxides, especially in the presence of d^0 metal compounds, typically Ti^{IV} , V^V , W^{VI} , Mo^{VI} , and Re^{VII} based compounds, can form metal-alkyl (hydro, acyl) peroxide species and side-on metal peroxides capable of oxygen transfer to nucleophilic substrates such as amines, sulfides and alkenes.⁵ However, hydroperoxides in the presence of metals with higher oxidation potentials often lead to considerable dismutation of the hydroperoxide and formation of highly reactive radicals such as hydroxy, alkyloxy and acyloxy species.⁶ These radicals, often unselectively, can abstract hydrogen from carbon-hydrogen bonds in hydrocarbons leading to alkyl radicals, propagation of radical chain reactions and non-selective product formation. In certain cases, usually using iron and manganese based complexes, the formation of metal-oxo intermediates from metal hydroperoxide has been suggested, although some of this research has stirred controversy and disagreement. Under certain conditions hydrogen peroxide in the presence of metal complexes can lead to the “dark” formation⁷ of singlet oxygen that is commonly formed photochemically from ground-state triplet oxygen in the presence of a suitable photosensitizer.⁸ Singlet oxygen can react with unsaturated substrates to form hydroperoxides (ene reaction), oxetanes and endoperoxides.

The chemistry of ground-state molecular oxygen is even much more complicated.⁹ Molecular oxygen ubiquitously reacts with hydrocarbons by a free radical autooxidation mechanism.¹⁰ The initial product of these autooxidation reactions is formation of a hydroperoxide, however, the common use of high oxidation potential metal complexes for initiation of the autooxidation sequence, leads to decomposition of the hydroperoxide to form alcohols and carbonyl products, but also radicals, and thus, often non-selective product formation as described above. The activation of molecular oxygen in the “biological world” for hydrocarbon (alkane, alkene) oxidation is attained through use of monooxygenase type enzymes such as cytochrome P-450 or methane monooxygenase where reducing agents and protons (*co-reactants*) supply the energy for the cleavage of the oxygen-oxygen bond.¹¹ The cleavage of the oxygen-oxygen bond leads to formation of water and high-valent metal (iron)-oxo species capable of alkane hydroxylation and alkene epoxidation under ambient conditions. During the last 25 years there has been intense and continuing interest in the development of biomimetic systems to understand the function and mechanism of these enzymes. There are also enzymes such as galactose oxidase and catechol dioxygenase,¹² that oxidize substrates without requiring reducing agents, however, their reactivity

and those of their mimics is limited to relatively reactive substrates; they are ineffective for alkane and alkene oxidation. There has also been much activity in the area of organic synthesis with molecular oxygen by synthetic, and not necessarily bio-inspired, catalysts in the presence of reducing agents that range (the list here is limited) from the rather innocuous molecular hydrogen and carbon monoxide,¹³ to popular use of aldehydes and alcohols as co-reagents,¹⁴ as well as application of more esoteric agents such as flavins and hydrazine.¹⁵

Certain metal complexes can mediate the one- or two-electron oxidation of organic substrates. These reactions, termed also catalytic oxidase type reactions are typified by two-electron oxidation with palladium based catalysts,¹⁶ for example the Wacker reaction. Oxidase type catalysis can also be mediated by polyoxometalates.¹⁷ Common to oxidase catalysis is the reoxidation of the oxidase catalyst with molecular oxygen as the primary oxidant.

Our interest in the possible use of polyoxometalates as oxidase catalysts was piqued about fifteen years ago by earlier research carried out by the Russian group at Novosibirsk headed by Matveev and Kozhevnikov who described the use of the phosphovanadomolybdate compounds, $H_{3+x}PV_xMo_{12-x}O_{40}$ ($x = 1-6$, but especially 2) as cocatalysts in place of copper salts in palladium-catalyzed oxidations.¹⁸ They described the $H_{3+x}PV_xMo_{12-x}O_{40}$ compounds as essentially redox oxidants of high potential that in turn could be easily reoxidized by molecular oxygen. Grate and co-workers at Catalytica refined this use of phosphovanadomolybdates and demonstrated the oxidation of ethylene to acetaldehyde at the pilot plant level.^{19a†} In parallel, research in France led by Tézé, Hervé and their co-workers showed that the same compounds were also effective for high-temperature gas-phase oxidation reactions, such as the oxydehydrogenation of isobutyric acid or methacrolein to methacrylic acid.²⁰ This work showed that the $H_{3+x}PV_xMo_{12-x}O_{40}$ compounds showed relatively high thermal stability and pointed to us the opportunity of carrying out oxydehydrogenation reactions in the liquid phase.

Before delving into the catalytic activity of the $H_{3+x}PV_xMo_{12-x}O_{40}$ polyoxometalates and its development in our group over the years some background should be given as to the compound itself. In the majority of the research the

† The use of Pd(II) salts and phosphovanadomolybdates has been extended over the years. One interesting recent application is the oxidative coupling of benzene with acrylates, *cf.* ref. 19b.

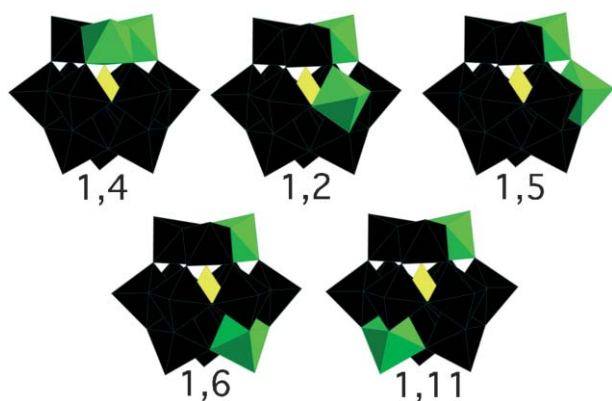
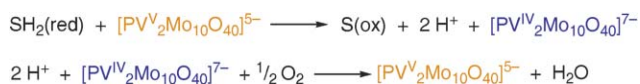
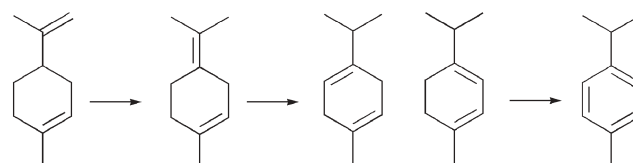


Fig. 1 Polyhedral representation of the five isomers of [PV₂Mo₁₀O₄₀]⁵⁻ (P – yellow; Mo – black; V – green).

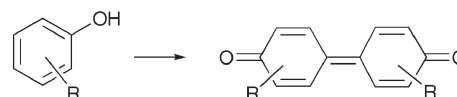
catalyst used has been based on the polyanion containing two vanadium atoms, [PV₂Mo₁₀O₄₀]⁵⁻. The polyanions in fully oxidized state are orange and have the well-known α -Keggin structure.²¹ A central phosphate moiety is surrounded by twelve molybdenum and vanadium addenda that are arranged as four M₃O₉ triads loosely connected to the four corners of the tetrahedral phosphate. In its oxidized form, all the addenda metals have empty d orbitals. Each addenda atom has a tetragonally distorted octahedral coordination sphere with short (~1.74 Å) M=O terminal bonds and longer (~2.45 Å) *trans* P–O–M bonds. The other equatorial M–O bonds lengths are in the 1.92–1.94 Å range. Upon reduction the polyanion becomes “blue” with up to one-electron localized at each of the vanadium atoms. Colors vary from green to blue depending on the degree of reduction; the bluer, the more reduced. There is considerable uncertainty as to the position of the vanadium addenda upon reduction, but it is generally accepted that the tetragonal distortion around the vanadium atoms is increased, *i.e.* the *trans* P–O–M bond length is longer in the reduced polyanion. As shown in the polyhedral models pictured in Fig. 1, there are five positional isomers of this compound that have not and probably cannot be separated due to interchange of the isomers in solution. It is likely as deduced from ³¹P NMR and ⁵¹V NMR studies that the specific isomer distribution is a function of the solvent used.²² There is no clear-cut evidence as to differences in activity between the isomers, however, some evidence seems to indicate that the isomers with nearest neighbor vanadium atoms (1,2, 1,4 and 1,5) are more reactive than the isomers with more separated vanadium atoms (1,6 and 1,11).^{22a} In most polyanion preparations it is likely that some, <5%, [PVMo₁₁O₄₀]⁴⁻ and [PV₃Mo₉O₄₀]⁶⁻ are present, however the differences in catalytic activity are too small for these impurities to have any significant effect on the interpretation of the results.



Scheme 2 The redox transformation of substrates by H₅PV₂Mo₁₀O₄₀.



Scheme 3 Aerobic isomerization and aromatization of limonene catalyzed by [PV₂Mo₁₀O₄₀]⁵⁻.



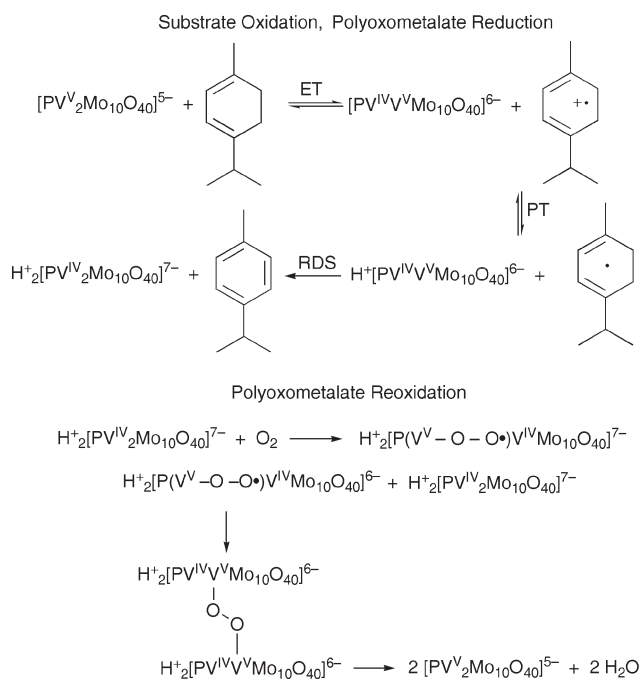
Scheme 4 Aerobic oxidative dimerization of phenols to diphenoquinones catalyzed by [PV₂Mo₁₀O₄₀]⁵⁻.

At first the paradigm that we thought of using can be simply stated as a two-step redox reaction as presented in Scheme 2. For example, a substrate, SH₂, reacts with the oxidized polyoxometalate, [PV₂Mo₁₀O₄₀]⁵⁻ through transfer of two electrons and two protons from the organic substrate to the catalyst to yield the oxidized product and reduced polyoxometalate. The catalyst is reoxidized by molecular oxygen to yield water and completes the catalytic cycle.

This type of reactivity was originally observed around fifteen years ago for several types of oxydehydrogenation reactions such as the aromatization of cyclic dienes²³ and the dimerization of activated phenol to diphenoquinones.²⁴ For example dienes such as 9,10-dihydroanthracene, 9,10-dihydrophenanthrene and α -terpinene were quantitatively oxidized to the corresponding aromatic products. The oxidation of limonene was preceded by the isomerization of the exocyclic double bond to yield α - and γ -terpinene (Scheme 3).

Importantly, the reactivity of several phenols, 2,6-di-*tert*-butylphenol > 2,6-dimethylphenol > 2,5-dimethylphenol > 2,6-dimethylphenol to yield the respective diphenoquinones, Scheme 4, was linearly correlated with the oxidation potential of the substrate pointing to an electron-transfer rate determining step in the reaction.

Based on further kinetic and UV-vis, EPR, ³¹P NMR and IR spectroscopic studies on the oxydehydrogenation of α -terpinene to *p*-cymene as a model reaction the following reaction mechanism was formulated, Scheme 5.²⁵ The substrate oxidation step was concluded to involve an electron transfer (ET) from α -terpinene to [PV₂Mo₁₀O₄₀]⁵⁻ and formation of α -terpinene cation radical–[PV^{IV}V^VMo₁₀O₄₀]⁶⁻ ion pair followed by a coupled proton transfer (PT) to yield a α -terpinene radical–H⁺[PV^{IV}V^VMo₁₀O₄₀]⁶⁻ complex as an EPR observable intermediate. A further proton coupled electron transfer (rate determining step, RDS) yields the *p*-cymene product and reduced H⁺₂[PV^{IV}₂Mo₁₀O₄₀]⁷⁻. For the catalyst reoxidation step, the kinetic measurements indicated (the reaction was second order in [PV₂Mo₁₀O₄₀]⁵⁻ and first order in dioxygen) that one molecule of oxygen reacted with two molecules of reduced H⁺₂[PV^{IV}₂Mo₁₀O₄₀]⁷⁻ to yield two molecules of water and the reoxidized catalyst, [PV₂Mo₁₀O₄₀]⁵⁻ in a *four*-electron oxidation. There was no evidence of formation of hydrogen peroxide from oxygen in a possible two-electron oxidation. It was hypothesized that

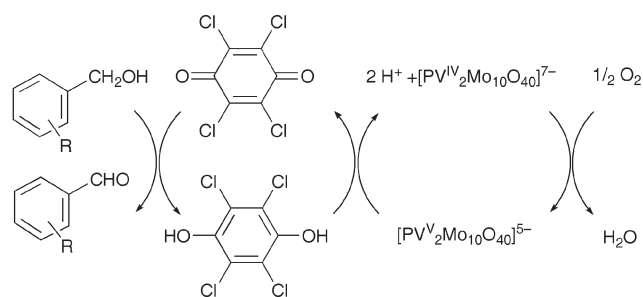


Scheme 5 Mechanism for the aerobic oxydehydrogenation of α -terpinene catalyzed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.

oxygen reduction was *via* a inner-sphere process possibly through formation of a μ -peroxo intermediate. It should be noted that for oxidation of reduced polyoxotungstates as opposed to polyoxovanadomolybdates a two-electron outer-sphere mechanism for the reoxidation step has been proposed.²⁶

The selective aerobic oxidation of alcohol substrates, especially primary alcohols to aldehydes is also an important synthetic objective. Indeed, $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ also catalyzes the oxidation of benzylic alcohols to aldehydes, however, in most polar solvents (except DMSO, see below) the acidity of the polyoxometalate leads to formation of significant amounts of dibenzyl ethers as acid-catalyzed reaction products. $[(\text{C}_4\text{H}_9)_4\text{N}]_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, a neutralized catalyst, was completely inactive presumably because the oxidation potential of $[(\text{C}_4\text{H}_9)_4\text{N}]_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, as measured by cyclic voltammetry, is only about 0.3 V *vs.* a oxidation potential of 0.7 V for $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. However, a neutral catalyst, $\text{Na}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$, supported on activated carbon was shown to be effective heterogeneous catalyst for the oxidation of benzylic alcohols to the corresponding aldehydes in apolar solvents such as toluene.²⁷ Secondary aliphatic alcohols were only slightly reactive, while primary alcohols did not react. Ishii and co-workers extended the application of such supported polyoxometalates to aerobic oxidation of a few allylic alcohols.²⁸

Almost a decade later, the use of the supported catalyst, $\text{Na}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}/\text{C}$ was reconsidered in light of the observation that only the use of active carbon as a support led to an active catalyst; silica, alumina and other matrices did not yield active catalysts. It was thus hypothesized that oxidants present or formed under reaction conditions on active carbon surface such as quinones may be the immediate oxidant of the benzylic

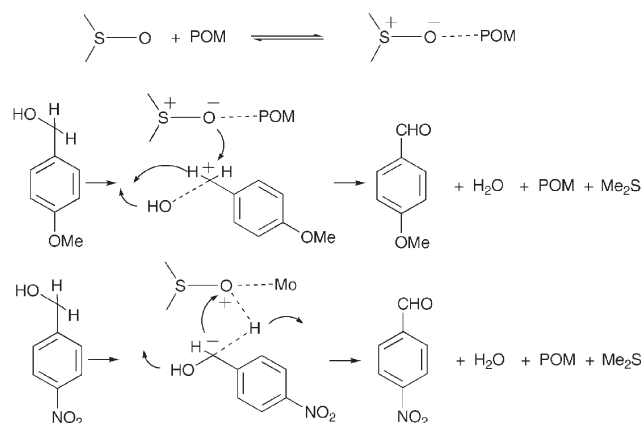


Scheme 6 Depiction of a generalized catalytic cycle for the aerobic oxidation of benzylic alcohols.

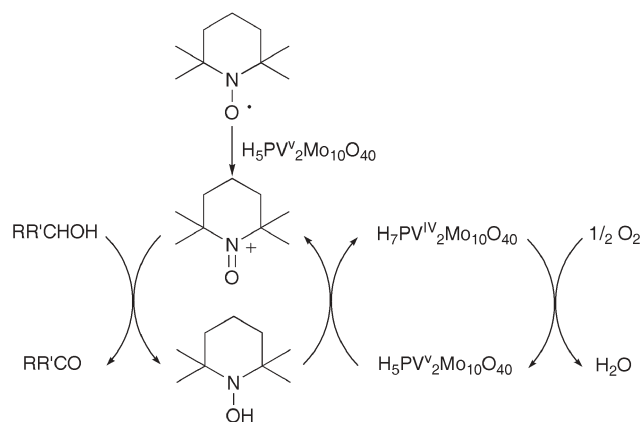
alcohols. In such a scenario the polyoxometalate functions to form and/or regenerate the oxidant on the carbon surface. In order to examine the possibility of such a reaction pathway, benzylic alcohols were effectively aerobically oxidized in the combined presence of quinones, preferably 2,3,5,6-tetrachloro-1,4-benzoquinone (*p*-chloranil) and $\text{Na}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in water (biphasic system) or $[(\text{C}_4\text{H}_9)_4\text{N}]_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in an organic solvent (monophasic system) as outlined in Scheme 6.²⁹

Kinetic experiments supported by EPR and UV measurements coupled with some probe reactions showed that in reality, the benzylic alcohols were not oxidized directly by benzoquinone derivatives but rather by a semiquinone- $\text{PV}^{\text{IV}}\text{V}\text{Mo}_{10}\text{O}_{40}$ intermediate, which was shown to be a more potent oxidizing species than the benzoquinone compound alone. This may also explain why indeed $\text{Na}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}/\text{C}$ is active for benzylic alcohol oxidation whereas the active carbon alone showed little reactivity.

It is valuable to note that the aerobic oxidation of benzyl alcohol catalyzed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ in DMSO as solvent was selective to benzaldehyde although reactions carried out in other solvents, such as acetonitrile, nitromethane and so forth, yielded mostly dibenzyl ether as primary product. This raised the possibility that the DMSO solvent was in fact an oxidant in reactions catalyzed by polyoxovanadomolybdates.³⁰ Postulated reaction steps as determined from isotope labelling experiments, kinetic isotope effects and Hammett plots include (a) sulfoxide activation by complexation to the polyoxometalate and (b) oxygen transfer from the activated



Scheme 7 Oxidation of benzylic alcohols with DMSO catalyzed by phospho(vanado)molybdates (POMs).



Scheme 8 Catalytic cycle for the aerobic oxidation of alcohols to aldehydes/ketones using TEMPO/ $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ co-catalysis.

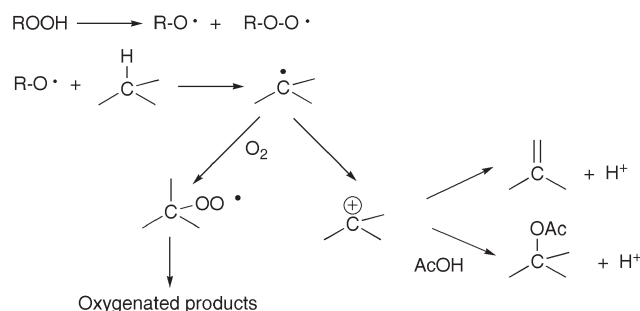
sulfoxide and elimination of water from the alcohol. The Hammett plot indicated a change of mechanism when going from electron donating to electron withdrawing substituents, Scheme 7.

It should be noted that the sulfoxide–polyoxometalate combination was also an efficient oxidizing system for alkylarene substrates. The reaction scope showed that for secondary alkylarene substrates without hydrogen α to the benzylic position, there was oxygenation at the benzylic position and selective formation of the diaryl ketone. For other substrates, 9,10-dihydroanthracene, 9,10-dihydrophenanthrene and 1,2-diphenylethane, the possibility of hydrogen elimination led mostly to oxydehydrogenation.³¹ The experimental evidence (kinetic and labelling studies) indicates that a polyoxometalate–sulfoxide complex catalyses hydride abstraction from the alkylarene substrate yielding a carbocation intermediate and a reduced polyoxometalate. Then the carbocation is oxygenated by the sulfoxide to give the oxygenated product and a proton is released. The reduced polyoxometalate is re-oxidized quickly by an additional equivalent of sulfoxide to yield the oxidized polyoxometalate, sulfide and water. The quantitative formation of the latter (GC-MS) was verified using ^{18}O labelled PMSO.

The catalytic oxidation of alcohols described above had a distinct disadvantage in that they showed limited synthetic utility because only the transformation of benzylic alcohols to the respective benzaldehyde derivatives was proceeded in high yields. Therefore, noting that $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ successfully supplanted copper(II) salts in the Wacker reaction, we tested the use of a $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ /nitroxide (TEMPO) catalyst combination for the aerobic oxidation of alcohols, Scheme 8,^{32a‡} since Cu(II)/nitroxide had been shown to be an effective combination for aerobic alcohol oxidation.³³

The TEMPO/ $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ catalyst combination proved to be highly efficient, that is significantly more active than the

‡ At the time of our publication others^{32b} published on a similar oxidation using a combination of Mn/Cu and Co/Cu nitrate salts as catalysts. Our analysis of that work showed that the nitrate anion was an *essential* component of the catalyst combination. This combination led to the significant formation of carcinogenic suspect *N*-nitrosoamine compounds.



Scheme 9 Mechanism for formation of alkenes and acetates by electron oxidation of intermediate alkyl radicals.

previously disclosed Cu/TEMPO catalyst. Nearly quantitative yields were obtained for the oxidation of primary aliphatic, allylic and benzylic alcohols to the corresponding aldehydes *only* at 1–5 mol% catalyst levels. Where pertinent, the oxidation proceeded without loss of stereogenic centers, for example *cis*-2-hexen-1-ol yields *cis*-2-hexen-1-al and *trans*-2-hexen-1-ol yields *trans*-2-hexen-1-al quantitatively. The TEMPO/ $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ catalyst combination also quantitatively yielded ketones from secondary alcohols, a reaction that was largely unsuccessful with previously known Cu(II)/TEMPO catalytic systems.

If one further looks at the aerobic reactions catalyzed by phosphovanadomolybdates described above, one common feature appears to be that autooxidation pathways, that is reactions where intermediate radical species could react with the molecular oxygen present in the reaction mixture, appear to be significantly absent. This is an unusual trait not often observed in aerobic metal-catalyzed liquid phase reactions. We were able to use the characteristic in a unique way whereby, oxidation of alkanes could be directed to formation of alkenes rather than to oxygenated species, Scheme 9.³⁴ Thus, *tert*-butylhydroperoxide was used as a source of *tert*-butylalkoxy radical, formed by a Haber–Weiss type redox reaction. The formation of the *tert*-butylalkoxy radical was verified by its capture with 5,5-dimethyl-1-pyrroline *N*-oxide (DMPO) and *N*-*tert*-butyl- α -phenylnitron (PBN) spin traps and then their observation by EPR spectroscopy. The very potent *tert*-butylalkoxy radical, reacted with the alkane substrate to yield an alkyl radical intermediate. Unusually, however, instead of reacting with molecular oxygen to give oxygen containing products, the intermediate alkyl radical underwent oxidative electron transfer to yield a carbocation. Through further loss of a proton and alkene was formed (major pathway). Alternatively, the carbocation reacted with acetic acid (the solvent) to yield the acetate ester.

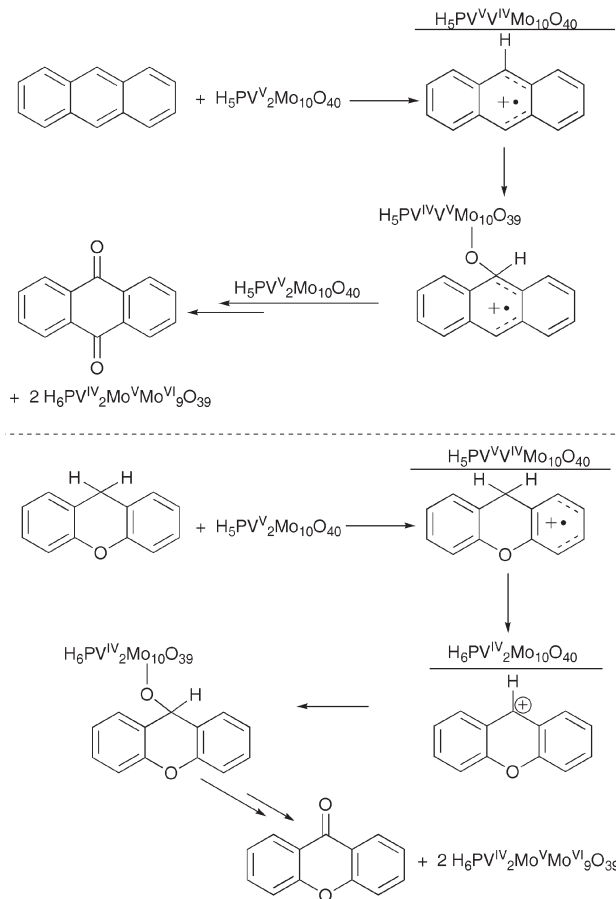
An important feature of these reactions is that the less substituted alkenes (kinetic product) were preferentially formed relative to the more substituted alkene (thermodynamic product). This is manifested, for example, by the observation that 2,2,4-trimethylpentane yielded 79% 2,2,4-trimethyl-4-pentene and 21% 2,2,4-trimethyl-3-pentene and methylcyclohexane yielded 83% 3- and 4-methylcyclohexene and only 11% 1-methylcyclohexene. Since in a competitive oxidation of $\text{C}_6\text{H}_{12}/\text{C}_6\text{D}_{12}$ an isotope effect of $k_{\text{H}}/k_{\text{D}} = 3.5 \pm 0.3$ was measured, it can be deduced that the rate-determining

step of the reaction is hydrogen abstraction of the alkane by the *tert*-butyloxy radical. In a substrate with tertiary, secondary and/or primary atoms, radical formation at the more substituted carbon is preferred, but perhaps not exclusive. Using 2,2,4-trimethylpentane as an example, a carbocation at the 4- position would lead to a 3:1 mixture of 2,2,4-trimethyl-4-pentene and 2,2,4-trimethyl-3-pentene from strictly statistical considerations. In addition, results are skewed in consideration of the likelihood of formation of other carbocations.

The examples presented above all demonstrate the activity of the phosphovanadomolybdates as oxidants that oxidize substrates by electron transfer. The subsequent aerobic oxidation is in essence an oxidative dehydrogenation reaction, without oxygenation of the substrate. In this context, two issues arise: (i) can the phosphovanadomolybdates elicit oxygenation utilizing only molecular oxygen as terminal or primary oxygen donor and (ii) by what process does the electron transfer occur, in particular, can we distinguish between outer-sphere and inner-sphere-type electron-transfer reactions.

If we wish to take our inspiration from biological systems that activate and use molecular oxygen as primary oxidant then one realizes that for hydrocarbon oxygenation, activation of molecular oxygen involves the use of reducing agents to attain the active high-valent metal-oxo species that are the true oxygen donors in the catalytic cycle.^{11,12} Since we are interested in activation or use of molecular oxygen in the absence of sacrificial co-reagents (reducing agents), taking our inspiration from biological systems is insufficient – we need to find abiotic or superbionic catalysts. On the other hand it is known from the field of heterogeneous catalysis that transition metal oxides, especially non-stoichiometric mixed metal oxide compounds are effective oxygenation catalysts at high temperature, generally >350–400 °C. Generically these catalysts appear to operate by the so-called Mars–van Krevelen mechanism whereby the substrate reacts with a metal oxide both *via* proton coupled electron transfer from the hydrocarbon to the metal oxide and *via* oxygen transfer from the metal oxide to the substrate.³⁵ The net result of this reaction is the oxygenation of the hydrocarbon and formation of a reduced metal oxide with an “oxygen hole”. Further reaction of the reduced lacunary metal oxide with molecular oxygen completes the catalytic cycle by reformation of the fully oxidized metal oxide coupled with formation of water.

Since $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ already showed a good propensity for proton coupled electron-transfer interactions with (functionalized) hydrocarbons and can also be visualized as a soluble analogue with discrete structure of non-stoichiometric mixed metal oxides, it seemed relevant to test the possibility that $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ could act as a Mars–van Krevelen type *homogeneous* catalyst.³⁶ The oxidation of anthracene to anthraquinone, involving the activation of an aromatic C–H bond (>100 kcal mol⁻¹) and the oxidation of xanthene to xanthone involving activation of benzylic C–H bonds (~75–80 kcal mol⁻¹) were investigated as model reactions. Using a combination of kinetic measurements, rate correlation measurements, probe reactions, oxygen and deuterium isotope labelling experiments and identification of reaction



Scheme 10 Mechanisms for aerobic oxygenation of anthracene (top) and xanthene (bottom) catalysed by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.

intermediates by magnetic resonance techniques we were able to suggest the following mechanisms for the oxidation of anthracene, Scheme 10 (top) and xanthene, Scheme 10 (bottom).

Some key points for emphasis are: (i) there is abundant kinetic evidence for the electron transfer for both substrates as the original reaction step. (ii) In the case of anthracene coupled proton transfer step is slow so that the ion pair, $\text{H}_5\text{PV}^{\text{V}}\text{V}^{\text{IV}}\text{Mo}_{10}\text{O}_{40}$ –anthracene cation radical, may be observed directly by EPR spectrometry including simulation of the spectrum of the anthracene cation radical. (iii) In the case xanthene the initial electron transfer is coupled to a further fast proton transfer and additional fast electron transfer to yield a $\text{H}_5\text{PV}^{\text{IV}}\text{Mo}_{10}\text{O}_{40}$ –xanthenyl cation ion pair, which was directly observed by ¹H NMR spectroscopy, presumably due to the stabilization of the xanthenyl cation by the lone pairs of the oxygen in xanthene. (iv) There is direct infra red and mass spectral evidence for the oxygen transfer step through use of ¹⁸O labelled $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$; there is also evidence against autooxidation from experiments with ¹⁸O labelled O_2 . (v) The rate determining steps for both substrates is the oxygen transfer step; this conclusion is also supported by deuterium isotope labelling experiments. (vi) The initial oxidation products are anthrone and xanthenol, respectively (not shown), which however are not accumulated in significant amounts because they are two magnitudes more reactive than

the starting substrate. Finally (vii) the reoxidation (not shown) of the proposed reduced lacunary $\text{H}_6\text{PV}_2\text{Mo}^{\text{IV}}\text{Mo}^{\text{VI}}\text{O}_{39}$ is fast on the reaction time scale; the mechanism of the reoxidation reaction is unknown at this time.

In this research we also investigated more thoroughly the electron-transfer reaction of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ with several hydrocarbons. A priori, the oxidation potential of 0.69 V for $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ precludes the possibility of an inner-sphere electron transfer since the oxidation potential of typical hydrocarbon substrates investigated is about 1.35–1.45 V. Correction of the free energy, ΔG° , under prevailing reaction conditions using Marcus theory³⁷ can give the corrected free energy value, $\Delta G^{\circ'}$,

$$\Delta G^{\circ'} = \Delta G^\circ + \frac{331.2B}{r_{12}D}(Z_1 - Z_2 - 1)$$

$$\text{where } B = 10^{-\left(21.9r_{12}\sqrt{\mu/DT}\right)}$$

$B = 1$ assuming an ion strength, $\mu = 0$ and $Z_1 = -5$; $Z_2 = 0$; $D = 35$ (acetonitrile); $r_{12} = r_1 + r_2 = 5.6 \text{ \AA}$ ($\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$) + 1.7 \AA (assuming side-on interaction between the polyoxometalate and the aromatic ring) = 7.3 \AA . It is important to note the strong influence of the negative charge of the polyoxometalate as electron acceptor (Z_1). The innate anionic nature of the polyoxometalates is advantageous to their activity as electron-transfer oxidants.

In general, the free energy values, both ΔG° and $\Delta G^{\circ'}$ vs. ΔG^\ddagger appear to support an outer-sphere electron transfer as opposed to an inner-sphere process for activation of hydrocarbons by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. It should be pointed that the kinetic analysis of the reaction of polyoxometalates with electron donors may be complicated by effects of ionic strength, ion pairing between the polyoxometalate and any cations in the solution, and formation of stable complexes between the polyoxometalate and the electron donor (hydrocarbon). In fact, further analysis based on the Marcus theory would indicate that there is pre-association between the polyoxometalate and the hydrocarbon substrate prior to electron transfer.

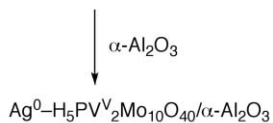
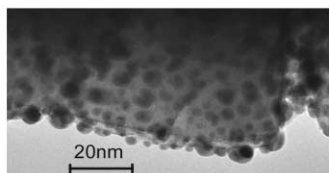
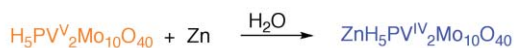
In line with the observations delineated above that $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ catalyses oxidation by electron transfer is the observation that in a series of alkylated anisole substrates the observed reactivity was 4-ethylanisole > 4-isopropylanisole > 4-methylanisole. For electron-transfer reactions the relative rates are $2^\circ > 1^\circ > 3^\circ$ or $2^\circ > 3^\circ > 1^\circ$ whereas for hydrogen atom transfer reactions, it is always found that $3^\circ > 2^\circ > 1^\circ$.³⁸ Substrates with higher oxidation potentials such as toluene were expectedly unreactive. Thus, it was unanticipated that 2- and 4-nitrotoluene with significantly higher oxidation potentials did form the corresponding 2- and 4-nitrobenzaldehyde under aerobic oxidation in the presence of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$. Clearly there is a change in the reaction mechanism that may be related to the high acidity of the hydrogen atoms on the methyl substituent. However, more startling was the recent finding that nitrobenzene was selectively (>99%) oxidized to 2-nitrophenol by molecular oxygen in the presence of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$.³⁹ The results indicate that $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ protonates the nitro substituent of the reactant, which allows *intramolecular* hydrogen abstraction at the *ortho* position followed by oxygenation of the incipient radical

with molecular oxygen to form a peroxo intermediate that was captured by a spin trap and then observed by EPR spectroscopy.

An intermediate summary of the research that emanated from our group as described above shows mostly the activity of the phosphovanadomolybdate compounds as catalysts for oxidation by electron transfer wherein the polyoxometalate directly oxidizes the organic substrate. A question that we asked ourselves was can we utilize the unique properties of polyoxometalates in general and the phosphovanadomolybdates in particular to create new binary catalytic systems that will be effective for the selective aerobic oxidation of basic hydrocarbons such as alkenes and alkanes?

From work over the last decade by Finke and co-workers,⁴⁰ it was clear that polyoxometalates taken as polyanions were highly effective in the stabilization of nanoparticles of rhodium and iridium and presumably other metals in solution. Our hypothesis was that it is therefore conceivable that polyoxometalates may modulate the intrinsic catalytic activity of the metal nanoparticles. An early hint that polyoxometalates may indeed modify the selectivity of “classic” catalytic activity was in a reaction where $\text{K}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and $\text{K}_4\text{SiW}_{12}\text{O}_{40}$ supported on γ -alumina catalyzed the deoxygenation of ketones and aldehydes using molecular hydrogen.⁴¹ This is a considerable change in reactivity from the typical hydrogenation pathway wherein carbonyl compounds are reduced to alcohols. Later on we indeed showed that palladium nanoparticles stabilized by polyoxometalates formed *in situ* by reduction of $\text{K}_5\text{PPd}(\text{H}_2\text{O})\text{W}_{11}\text{O}_{39}$ in a hydrogen environment led to an improved catalyst for carbon–carbon coupling reactions,⁴² but perhaps more importantly in the context of this article allowed the preferential hydrogenation of an arene in the presence of a ketone.⁴³ The unique selectivity could be observed both in a single substrate, for example, the reduction of 4-phenyl-2-butanone yielded 4-cyclohexyl-2-butanone rather than 4-phenyl-2-butanol, and a mixture of substrates, for example, co-reduction of toluene and 2-octanone yielded methylcyclohexane and left 2-octanone unchanged; typical Pd/C yielded 2-octanol and left toluene unchanged.

A commercially very interesting oxidation reaction is the transformation of alkenes by molecular oxygen to epoxides. Silver supported on α -alumina has been shown to be uniquely active for this transformation and well-established processes exist for the oxidation of ethylene to ethylene oxide.⁴⁴ However, this aerobic epoxidation has been largely unsuccessful for many other interesting alkenes due to low selectivity to epoxidation that is often associated with reaction at allylic C–H moieties, which easily undergo homolytic C–H bond cleavage. We reasoned that nanoparticles stabilized by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ should be promising catalyst candidates for aerobic epoxidation of alkenes since it generally does not homolytically cleave C–H bonds and therefore tends to inhibit free radical autooxidation reactions. We, thus, prepared novel silver and ruthenium nanoparticles stabilized by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ using a redox reaction sequence. The Ag/ $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and Ru/ $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ nanoparticle combinations were then supported on α - Al_2O_3 , characterized by transmission electron microscopy and then used as catalysts for alkene epoxidation, Scheme 11.⁴⁵

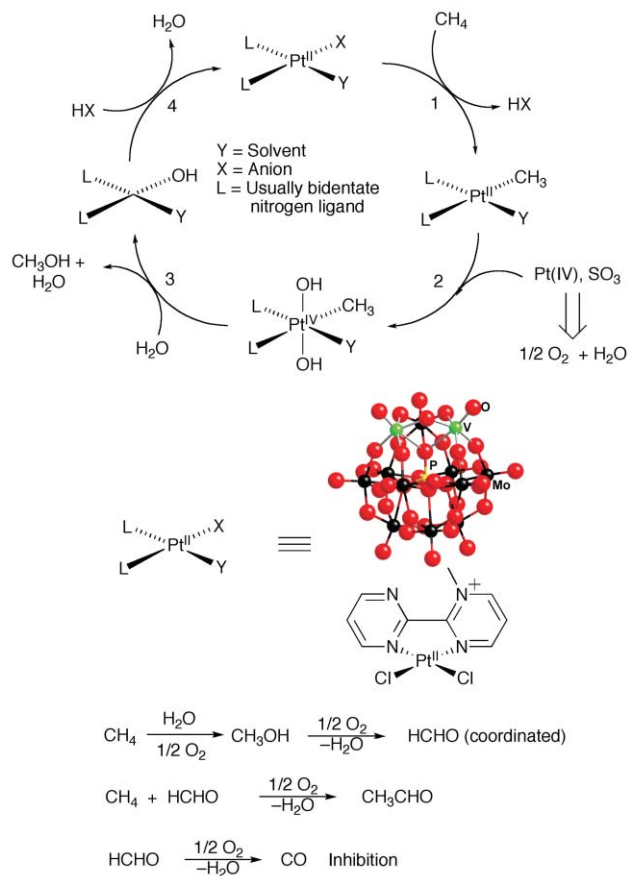


Scheme 11 Outline of the preparation of silver particles stabilized by $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and then supported on $\alpha\text{-Al}_2\text{O}_3$, including a TEM image of the obtained catalyst.

In alkene epoxidation reactions we obtained promising results for the alkenes, cyclohexene (50% selectivity) and 1-methylcyclohexene (90% selectivity). For a series of terminal alkenes such as 1-octene, epoxidation reactions catalyzed by both $\text{Ag}^0\text{-H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ and $\text{Ru}^0\text{-H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ on $\alpha\text{-Al}_2\text{O}_3$ yielded at 10–15% conversion (0.5–1 h) approximately 90% epoxide; there were *no* additional volatile products. After longer reaction times, the conversion continued to increase linearly, however, the selectivity decreased eventually to about 50%. The superior results found for these nanoparticle-polyoxometalate combinations hopefully can be improved in order to achieve higher yields. On the other hand, the principles outlined above can also be applied to additional targets for selective oxidation by molecular oxygen.

Another class of binary catalyst systems are those based on a metallorganic complex modified by a polyoxometalate. The reasoning behind the preparation of these binary or conjugate systems is that the electron accepting properties and steric bulk of the polyoxometalates may significantly affect the catalytic properties of a conjugate metallorganic center. Modification of polyoxometalates by organic entities has been known for quite some time and there have been also numerous reports of metallorganic–polyoxometalate binary systems.⁴⁶ However, until recently, the investigations have been limited to the development of the synthetic aspects of such binary systems. A few years ago we started our research in this area.⁴⁷ We synthesized a binary system comprised of a metallo-salen center attached covalently to a polyoxometalate *via* two dual propyl spacers. Importantly, NMR, EPR, UV-vis and other measurements clearly showed that the metallosalen was in an oxidized state relative to the control, non-modified metallosalen analog. Thus, for example, instead of obtaining a usual Mn(III) salen species, modification of the metallosalen with the polyoxometalate led to formation of a more oxidized Mn(IV) salen–POM or Mn(III) salen cation radical–POM compound.

After having demonstrated the modification of the electronic properties of a metalloorganic center *via* formation of a binary system, we applied the principle to the aerobic oxidation of methane in water catalyzed by platinum(II) bipyrimidinium– $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ complex. The catalytic oxidation of methane by platinum(II) species had been known for some time. A key step in the catalytic cycle, oxidation of a platinum(II) intermediate to a platinum(IV) intermediate, which has also been intensively studied,⁴⁸ could only be



Scheme 12 Aerobic methane oxidation catalyzed by a platinum(II) bipyrimidinium– $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ binary complex.

effected by strong oxidants, originally Pt(IV) and latter on SO_3 as fuming sulfuric acid (oleum).⁴⁹ We thought that conjugation of $\text{H}_5\text{PV}_2\text{Mo}_{10}\text{O}_{40}$ to a known platinum(II)–bipyrimidine complex, in this case by electrostatic interaction could facilitate the oxidation of the platinum(II) intermediate to a platinum(IV) intermediate by molecular oxygen, Scheme 12.⁵⁰ In fact, the binary complex supported on silica did in fact allow the catalytic aerobic oxidation in water of methane to methanol and then surprisingly further to acetaldehyde *via* a carbon–carbon coupling reaction. Use of isotope labelling techniques showed that the catalytic cycle is consistent with an oxidative nucleophilic substitution of a platinum(IV) methyl intermediate as shown in Scheme 12. The study also indicated that the acetaldehyde formation is *via* the reaction sequence presented in Scheme 12 (bottom).

Conclusions and future perspectives

The catalytic activity of phosphovanadomolybdates as aerobic oxidation catalysts has been surveyed. In most cases the compounds act as electron-transfer oxidants leading to oxydehydrogenation reactions. Oxygen transfer reactions *via* a homogeneous analogue of a Mars–van Krevelen process has also been demonstrated. Binary catalyst systems involving nanoparticles stabilized by polyoxometalates and metallorganic–polyoxometalate hybrid compounds significantly increase the scope of catalyst activity to areas such as direct

epoxidation of alkenes with molecular oxygen and catalytic oxidation of alkanes. We are presently interested in additional applications of phosphovandomolybdates as stand-alone catalysts for oxidation§ and we expect that the use of binary catalyst systems and more higher-level organization control will greatly extend our ability to use molecular oxygen for selective oxidation. This is certainly a worthy objective in our search and society's demand for environmentally benign and sustainable chemical synthesis.

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References

- (a) M. Costas, M. P. Mehn, M. P. Jensen and L. Que, Jr., *Chem. Rev.*, 2004, **104**, 939–986; (b) E. Y. Tshuva and S. J. Lippard, *Chem. Rev.*, 2004, **104**, 987–1012; (c) L. Que, Jr. and W. B. Tolman, *Angew. Chem., Int. Ed.*, 2002, **41**, 1114–1137.
- (a) T. J. Collins and S. W. Gordon-Wylie, *J. Am. Chem. Soc.*, 1989, **111**, 4511–4513; (b) C. L. Hill and R. B. Brown Jr., *J. Am. Chem. Soc.*, 1986, **108**, 536–538; (c) J. T. Groves, J. Lee and S. S. Marla, *J. Am. Chem. Soc.*, 1997, **119**, 6269–6273.
- (a) I. W. C. E. Arends, T. Kodama and R. A. Sheldon, *Top. Organomet. Chem.*, 2004, **11**, 277–320; (b) C.-M. Che and W.-Y. Yu, *Pure Appl. Chem.*, 1999, **71**, 281–288; (c) J. T. Groves, M. Bonchio, T. Carofiglio and K. Shalyaev, *J. Am. Chem. Soc.*, 1996, **118**, 8961–8962.
- (a) W. P. Griffith, *Chem. Soc. Rev.*, 1992, **21**, 179–185; (b) S. -I. Murahashi and N. Kamiya, in *Modern Oxidation Methods*, ed. J. E. Backvall, Wiley-VCH, Weinheim, Germany, 2004, pp. 165–191; (c) D. Sica, *Recent Res. Dev. Org. Chem.*, 2003, **7**, 105–127; (d) J. L. Courtney, in *Organic Synthetic Oxidation with Metal Compounds*, ed. W. J. Mijs and R. H. I. C. De Jonge, Plenum Press, New York, USA, 1986, pp. 445–467; (e) M Schröder, *Chem. Rev.*, 1980, **80**, 187–213.
- (a) R. A. Sheldon, in *Applied Homogeneous Catalysis with Organometallic Compounds*, ed. B. Cornils and W. A. Herrmann, Wiley-VCH, Weinheim, 2nd edn, 2002, pp. 412–427; (b) R. Landau, G. A. Sullivan and D. Brown, *Chemtech*, 1979, **9**, 602–607; (c) Titanium Silicate: A New Selective Oxidation Catalyst: B. Notari, *Stud. Surf. Sci. Catal.*, 1991, **67**, 243–256; (d) Metal-Catalyzed Epoxidations of Alkenes with Hydrogen Peroxide: B. S. Lane and K. Burgess, *Chem. Rev.*, 2003, **103**, 2457–2473.
- Metal Catalyzed Oxidation of Organic Compounds*, ed. R. A. Sheldon and J. K. Kochi, Academic Press, New York, USA, 1981.
- (a) J. Wahlen, D. E. De Vos, P. A. Jacobs and P. L. Alsters, *Adv. Synth. Catal.*, 2004, **346**, 152–164; (b) V. Nardello, L. Caron, J. M. Aubry, S. Bouttemy, T. Wirth, C. Saha-Müller and W. Adam, *J. Am. Chem. Soc.*, 2004, **126**, 10692–10700.
- E. L. Clennan and A. Pace, *Tetrahedron*, 2005, **61**, 6665–6691.
- (a) *Modern Oxidation Methods*, ed. J. E. Backvall, Wiley-VCH, Weinheim, Germany, 2004; (b) *Advances in Catalytic Activation of Dioxygen by Metal Complexes*, ed. L. I. Simandi, Kluwer Academic, Boston, USA, 2003; (c) *Oxygen Chemistry*, ed. D. T. Sawyer, Oxford University Press, New York, 1991.
- (a) C. Walling, *Struct. Energ. React. Chem. Ser.*, 1995, **2**, 24–65; (b) W. Partenheimer, *Catal. Today*, 1995, **23**, 69–127; (c) F. R. Mayo, *Acc. Chem. Res.*, 1968, **1**, 193–201.
- (a) *Cytochrome P-450*, ed. P. Ortiz de Montellano, Marcel Dekker, New York, 2nd edn, 1995; (b) M. Sono, M. P. Roach, E. D. Coulter and J. H. Dawson, *Chem. Rev.*, 1996, **96**, 2841–2887; (c) B. J. Wallar and J. D. Lipscomb, *Chem. Rev.*, 1996, **96**, 2625–2657; (d) A. L. Feig and S. J. Lippard, *Chem. Rev.*, 1994, **94**, 759–781; (e) E. I. Solomon, U. M. Sundaram and T. E. Machonkin, *Chem. Rev.*, 1996, **96**, 2563–2605; (f) E. I. Solomon, T. C. Brunold, M. I. Davis, J. N. Kemsley, S. K. Lee, N. Lehnert, F. Neese, A. J. Skulan, Y. S. Yang and J. Zhou, *Chem. Rev.*, 2000, **100**, 235–349; (g) M. Merckx, D. A. Kopp, M. H. Sazinsky, J. L. Blazyk, J. Müller and S. J. Lippard, *Angew. Chem., Int. Ed.*, 2001, **40**, 2782–2807; (h) L. Que, Jr. and R. Y. N. Ho, *Chem. Rev.*, 1996, **96**, 2607–2624.
- (a) M. Fontecave, S. Ollangier de Choudens and E. Mulliez, *Chem. Rev.*, 2003, **103**, 2149–2166; (b) J. W. Whittaker, *Adv. Protein Chem.*, 2002, **60**, 1–49; (c) J. B. Broderick, *Essays Biochem.*, 1999, **34**, 173–189.
- (a) A. K. Sinha, S. Seelan, S. Tsubota and M. Haruta, *Top. Catal.*, 2004, **29**, 95–102; (b) M. Haruta, *CATTECH*, 2002, **6**, 102–115, and references therein.
- T. Mukaiyama and T. Yamada, *Bull. Chem. Soc. Jpn.*, 1995, **68**, 17–35.
- Y. Imada, H. Iida, S. Ono and S. -I. Murahashi, *J. Am. Chem. Soc.*, 2003, **125**, 2868–2869.
- (a) S. S. Stahl, *Angew. Chem., Int. Ed.*, 2004, **43**, 3400–3420; (b) B. L. Feringa, in *Transition Metals for Organic Chemistry*, ed. M. Beller and C. Bolm, Wiley-VCH, 1998, vol. 2, pp. 307–315.
- (a) T. Okuhara, N. Mizuno and M. Misono, *Adv. Catal.*, 1996, **41**, 113–174; (b) C. L. Hill and C. M. Prosser-McCartha, *Coord. Chem. Rev.*, 1995, **143**, 407–451; (c) R. Neumann, *Prog. Inorg. Chem.*, 1998, **47**, 317–370; (d) *Catalysts for Fine Chemical Synthesis, Volume 2, Catalysis by Polyoxometalates*, ed. I. V. Kozhevnikov, Wiley, Weinheim, Germany, 2002.
- I. V. Kozhevnikov and K. I. Matveev, *Appl. Catal.*, 1983, **5**, 135–50.
- (a) J. H. Grate, D. R. Hamm and S. Mahajan, *Mol. Eng.*, 1993, **3**, 205–229; (b) T. Yokota, M. Tani, S. Sakaguchi and Y. Ishii, *J. Am. Chem. Soc.*, 2003, **125**, 1476–1477.
- C. Marchal-Roch, R. Bayer, J. F. Moisan, A. Tezé and G. Hervé, *Top. Catal.*, 1996, **3**, 407–419.
- J. F. Keggin, *Proc. R. Soc. London, Ser. A*, 1934, **144**, 75–100.
- (a) L. Pettersson, I. Andersson, A. Selling and J. H. Grate, *Inorg. Chem.*, 1994, **33**, 982–992; (b) A. Selling, I. Andersson, J. H. Grate and L. Pettersson, *Eur. J. Inorg. Chem.*, 2000, 1509–1521; (c) A. M. Khenkin, A. Rosenberger and R. Neumann, *J. Catal.*, 1999, **182**, 82–91.
- R. Neumann and M. Lissel, *J. Org. Chem.*, 1989, **54**, 4607–4610.
- M. Lissel, H. Jansen van de Wal and R. Neumann, *Tetrahedron Lett.*, 1992, **33**, 1795–1798.
- R. Neumann and M. Levin, *J. Am. Chem. Soc.*, 1992, **114**, 7278–7286.
- D. C. Duncan and C. L. Hill, *J. Am. Chem. Soc.*, 1997, **119**, 243–244.
- R. Neumann and M. Levin, *J. Org. Chem.*, 1991, **56**, 5707–5710.
- S. Fujibayashi, K. Nakayama, M. Hamamoto, S. Sakaguchi, Y. Nishiyama and Y. Ishii, *J. Mol. Catal.*, 1996, **110**, 105–117.
- A. M. Khenkin, I. Vigdergauz and R. Neumann, *Chem. Eur. J.*, 2000, **6**, 875–882.
- A. M. Khenkin and R. Neumann, *J. Org. Chem.*, 2002, **67**, 7075–7079.
- A. M. Khenkin and R. Neumann, *J. Am. Chem. Soc.*, 2002, **124**, 4198–4199.
- (a) R. Ben-Daniel, P. Alsters and R. Neumann, *J. Org. Chem.*, 2001, **66**, 8650–8653; (b) A. Cecchetto, F. Fontana, F. Minisci and F. Recupero, *Tetrahedron Lett.*, 2001, **42**, 6651–6653.
- M. F. Semmelhack, C. R. Schmid, D. A. Cortés and C. S. Chou, *J. Am. Chem. Soc.*, 1984, **106**, 3374–3376.
- A. M. Khenkin and R. Neumann, *J. Am. Chem. Soc.*, 2001, **123**, 6437–6438.

§ An interesting finding is that carbon monoxide and molecular oxygen together in the presence of H₅PV₂Mo₁₀O₄₀ appear to form hydroxyl radicals leading to oxidation of methane and benzene, cf. ref. 51.

- 35 (a) P. Mars and D. W. van Krevelen, *Chem. Eng. Sci.*, 1954, **3**, 41–59; (b) C. N. Satterfield, *Heterogeneous Catalysis in Practice*, McGraw-Hill, New York, 1980.
- 36 (a) A. M. Khenkin and R. Neumann, *Angew. Chem., Int. Ed.*, 2000, **39**, 4088–4090; (b) A. M. Khenkin, L. Weiner, Y. Wang and R. Neumann, *J. Am. Chem. Soc.*, 2001, **123**, 8531–8542.
- 37 L. Ebersson, *Adv. Phys. Org. Chem.*, 1982, **18**, 79.
- 38 E. Baciocchi, F. D'Acunzo, C. Galli and O. Lanzalunga, *J. Chem. Soc., Perkin Trans. 2*, 1996, 133.
- 39 A. M. Khenkin, L. Weiner and R. Neumann, *J. Am. Chem. Soc.*, 2005, **127**, 9988–9989.
- 40 (a) R. G. Finke and S. Oezkar, *Coord. Chem. Rev.*, 2004, **248**, 135–146; (b) S. Oezkar and R. G. Finke, *J. Am. Chem. Soc.*, 2002, **124**, 5796–5810; (c) R. G. Finke, *Met. Nanoparticles*, 2002, 17–54.
- 41 V. Kogan, Z. Aizenshtat and R. Neumann, *Angew. Chem., Int. Ed.*, 1999, **38**, 3331–3334.
- 42 V. Kogan, Z. Aizenshtat, R. Popovitz-Biro and R. Neumann, *Org. Lett.*, 2002, **4**, 3529–3532.
- 43 V. Kogan, Z. Aizenshtat and R. Neumann, *New J. Chem.*, 2002, **26**, 272–274.
- 44 (a) P. A. Kilty and W. M. H. Sachtler, *Catal. Rev.-Sci. Eng.*, 1974, **10**, 1–16; (b) M. A. Barteau, *Top. Catal.*, 2003, **22**, 3–8.
- 45 G. Maayan and R. Neumann, *Chem. Commun.*, 2005, 4595–4597.
- 46 (a) P. Gouzerh and A. Proust, *Chem. Rev.*, 1998, **98**, 77–111; (b) R. Villanneau, R. Delmont, A. Proust and P. Gouzerh, *Chem. Eur. J.*, 2000, **6**, 1184–1192; (c) C. Sanchez, G. J. de A. A. Soler-Illia, F. Ribot, T. Lalot, C. J. Mayer and V. Cabuil, *Chem. Mater.*, 2001, **13**, 3061–3083.
- 47 (a) I. Bar-Nahum, H. Cohen and R. Neumann, *Inorg. Chem.*, 2003, **42**, 3677–3684; (b) I. Bar-Nahum and R. Neumann, *Chem. Commun.*, 2003, 2690–2691; (c) I. Bar-Nahum, K. V. Narasimhulu, L. Weiner and R. Neumann, *Inorg. Chem.*, 2005, **44**, 4900–4902.
- 48 J. A. Labinger and J. E. Bercaw, *Nature*, 2002, **417**, 507–514.
- 49 (a) A. E. Shilov and G. B. Shulpin, *Russ. Chem. Rev.*, 1987, **56**, 442–464; (b) R. A. Periana, D. J. Taube, S. Gamble, H. Taube, T. Satoh and H. Fujii, *Science*, 1998, **280**, 560–564.
- 50 I. Bar-Nahum, A. M. Khenkin and R. Neumann, *J. Am. Chem. Soc.*, 2004, **126**, 10236–10237.
- 51 (a) G. V. Nizova, G. B. Shulpin, G. Süß-Fink and S. Stanislas, *Chem. Commun.*, 1998, 1885–1886; (b) M. Tani, T. Sakamoto, S. Mita, S. Sakaguchi and Y. Ishii, *Angew. Chem., Int. Ed.*, 2005, **44**, 2586–2588.



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