

Chapter 6

Principles and New Approaches in Selective Catalytic Homogeneous Oxidation

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Goals and five limitations in conjunction with the development of selective catalytic homogeneous oxidation systems are evaluated. Systems are presented that address several of the problems or goals. One involves oxidation of alkenes by hypochlorite catalyzed by oxidatively resistant d-electron-transition-metal-substituted (TMSP) complexes. A second involves oxidation of alkenes by H_2O_2 catalyzed by specific TMSP complexes, and a third addresses functionalization of redox active polyoxometalate complexes with organic groups.

The focus of this chapter is on aspects, particularly mechanistic considerations and limitations, of transition metal-catalyzed controlled delivery of oxygen to hydrocarbon substrates. The points addressed here are pertinent to heterogeneous and homogeneous systems alike but are more defensible and applicable to homogeneous systems as the detailed molecular knowledge of the latter is at a higher level. General methodologies and practical, largely nonmechanistic, considerations in transition metal-catalyzed oxidation are given in several recent books and reviews (1-6). The selective catalytic oxidation of organic substrates or reactants, R, by O_2 and to a lesser extent, by more expensive and less desirable oxidants, OX, equation 1, offers great opportunities for modifications or innovations with both substantive scientific and economic import (1-6). The general goal at present is to develop catalytic



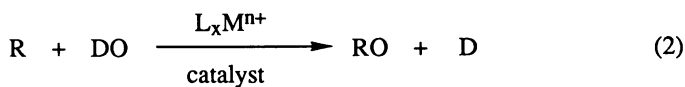
processes that are selective (chemo-, regio-, and stereoselective) at high conversion of substrate, stable, minimally expensive, and environmentally friendly (green).

General Thermodynamic and Mechanistic Features of Catalytic Homogeneous Oxidations

Unlike many of the other major types of catalytic processes involving the transformation of organic materials, oxidations are usually strongly exothermic which

dictates two limitations with respect to selectivity. The first derives from the fact that the more negative the ΔG° , the smaller the separation in the activation energies (or the differences in the free energies of activation, $\Delta\Delta G^\ddagger$) tends to be for the process generating the desired product (RO), ΔG^\ddagger , versus the other products (e.g. RO'), ΔG^\ddagger . Increasing the temperature to capitalize on the difference in the enthalpies of activation for the derived processes, $\Delta\Delta H^\ddagger$, may or may not help. Although selectivity will increase with temperature if ΔH^\ddagger and ΔH^\ddagger are substantially different, higher temperatures often lead to a loss in selectivity as side processes generating by-products with higher enthalpies of activation than ΔH^\ddagger become more operative. These often include destruction of the catalyst or even the components of the catalytic reactor. Second, the selectivity of oxidation processes is usually such that the activation energy (ΔG^\ddagger or E_a) for formation of an initial product, often the desired product, RO, is less favorable than for formation of a subsequent product(s), RO' or RO'', etc. If this situation pertains, high selectivity at high conversion of substrate can only be achieved by chemical or physical separation of RO from the reaction at a rate significantly higher than the rate at which it is formed. Physical separation of RO is not uncommon in heterogeneous catalytic oxidation systems engineered with recycling capabilities. Physical or chemical separation of a desired product from a catalytic oxidation reaction is usually more difficult and less practical in moderate-to-large scale homogeneous processes than in heterogeneous processes.

A major subset of equation 1, and the focus of much recent research for intellectual and practical reasons, is transition metal-catalyzed transfer of oxygen from oxygen donors (Table I) to organic substrates, equation 2, commonly referred to as oxo transfer oxidation or "oxygenation" in much of the recent literature. Equation 2 can proceed by one or more of several possible mechanisms. Two types of mechanism for equation 2 are predominant in the absence of autoxidation, however. The first type involves heterolytic (nonradical) activation and transfer of activated oxygen, usually from an alkylhydroperoxide, to a substrate by a metal center. The



DO = oxygen donor oxidants (see Table I);
 L_xM^{n+} = d-electron transition metal center.

catalyst in these cases is usually an early transition metal ion in the d^0 electronic state and the substrate is usually ligated to the transition metal during the process. This type of mechanism is characterized by the metal center functioning in an electrophilic and nonredox role. It is operable in two of the most commercially significant homogeneous catalytic oxygenation processes today, the Halcon epoxidation process (4,6) and the Sharpless chiral epoxidation technology (7-9) (R in equation 2 is alkene). The second common type of mechanism for oxygen transfer involves the formation of high-valent oxometal intermediates which then transfer oxygen to the substrate. This type of mechanism involves redox changes in the metal center, may or may not involve preequilibrium association of substrate with the metal center, and in most if not all cases, involves a solvent caged radical pair intermediate. The degree of escape of the radical from the solvent cage and/or oxidation of the intermediate caged radicals in these "oxygen atom rebound" processes (10) varies with the metal and the particular organic radical intermediate involved (11). This second type of mechanism is involved in hydrocarbon oxygenation (alkene epoxidation and alkane

C-H bond hydroxylation) catalyzed by cytochrome P-450. This class of enzymes is the dominant vehicle for oxidation and modification of hydrocarbons and other xenobiotics of low reactivity in the biosphere and remains one of the most studied of all enzymes (12).

Oxidants

In the development of effective catalytic oxidation systems, there is a qualitative correlation between the desirability of the net or terminal oxidant, (OX in equation 1 and DO in equation 2) and the complexity of its chemistry and the difficulty of its use. The desirability of an oxidant is inversely proportional to its cost and directly proportional to the selectivity, rate, and stability of the associated oxidation reaction. The weight % of active oxygen, ease of deployment, and environmental friendliness of the oxidant are also key issues. Pertinent data for representative oxidants are summarized in Table I (4). The most desirable oxidant, in principle, but the one with the most complex chemistry, is O₂. The radical chain or autoxidation chemistry inherent in O₂-based organic oxidations, whether it is mediated by redox active transition metal ions, nonmetal species, metal oxide surfaces, or other species, is fascinatingly complex and represents nearly a field unto itself (1,13). Although initiation, termination, hydroperoxide breakdown, concentration dependent inhibition

Table I. Oxygen Donor Oxidants, DO

DO	% Active oxygen	By-product and comments
O ₂	100	None, provided reducing agent-free non-radical-chain aerobic oxygenation can be achieved -- no commercially successful system yet exists.
H ₂ O ₂	47	H ₂ O. Environmentally attractive.
O ₃	33	O ₂ . Potentially environmentally attractive.
NaClO	21.6	NaCl. Although nontoxic, inorganic salt by-products are to be avoided in general. ClO ⁻ can produce toxic and carcinogenic chlorocarbon by-products in some cases.
<i>t</i> -BuOOH	17.8	<i>t</i> -BuOH. Commercially important in catalyzed oxygenations.
C ₅ H ₁₁ NO ₂ ^a	13.7	C ₅ H ₁₁ NO.
KHSO ₅	10.5	KHSO ₄ . Water compatible but generates marginally toxic salt.
C ₆ H ₅ IO	7.3	C ₆ H ₅ I. Metal catalyzed oxidations are often quite selective but cost is prohibitive.

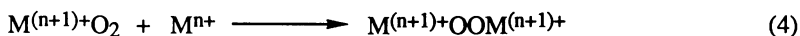
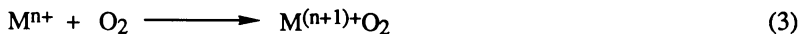
^a *N*-methylmorpholine *N*-oxide (MMNO).

by initiators and other kinetic aspects of metal-mediated autoxidation processes are relatively well delineated, other aspects of these reactions are not.

After O_2 , the next most desirable oxidant is H_2O_2 . It is relatively inexpensive, has a high weight % of active oxygen, and, by virtue of producing H_2O in formal oxo transfer or oxygenation processes (equation 2), is more environmentally friendly than other oxidants that produce either organic compounds or inorganic salt by-products. At the same time, metal-mediated oxidations by H_2O_2 are second in complexity to those by O_2 . Organic hydroperoxides such as *t*-butylhydroperoxide (TBHP), cumylhydroperoxide (CHP), and ethylbenzene hydroperoxide (EBHP), and various other peroxygen compounds, such as the perborates, come next in complexity. One principal difference between oxidations by H_2O_2 and these latter peroxygen oxidants derives from the difference in the richness of the chemistry between the actual metal complex and the oxidant. H_2O_2 forms more structurally characterized types of complexes with both mononuclear or polynuclear d-electron-transition metal systems than do the organo hydroperoxides. Although some *N*-oxides such as *N*-methylmorpholine *N*-oxide are commercially attractive oxidants in some catalyzed organic oxidations, the other oxidants below the peroxy compounds in Table I are primarily of academic interest. As some expensive and complex oxo donor compounds such as oxaziridines, some *N*-oxides, and to a lesser extent iodosylbenzenes, react cleanly with transition metal complex catalysts, they have been involved in elucidating many key features of both biological and abiological organic oxidations catalyzed by these transition metal centers. These oxidants will doubtless remain of value for seminal mechanistic studies of metal-catalyzed oxidations for a time.

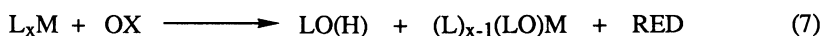
Catalytic Aerobic Oxygenation

One major goal in selective catalytic oxidation is embodied in equations 3-6 (the ligands in these equations have been omitted for clarity). This chemistry can be conveniently termed as aerobic oxygenation as oxygen atoms are formally being transferred in the substrate oxidation process and radical chain autoxidation is absent. Although the chemistry discussed here and below is applicable, in principle, to either heterogeneous or homogeneous catalytic oxidation systems, it is likely that homogeneous ones will be developed first since more electronic, structural, and other molecular features of the catalyst itself can be adequately evaluated and systematically modified. When systems are developed in which equations 3-6 dominate the observed reaction chemistry, the substrate oxygenation process, equation 6, is selective, and the general goals of catalytic processes cited above are met (high selectivity at high conversion of substrate, stability, environmental friendliness and economic feasibility), a new era in selective oxidation will have begun. These equations facilitate selective oxidation by using both atoms of dioxygen without consuming any reducing agent. Although various systems reported thus far have facilitated some aspects of this chemistry (equations 3-6) there have been a number of demonstrable limitations with even the most promising and provocative. In the next section, we outline 5 significant classes of problems that conspire to prevent development of effective and selective catalytic oxygenation systems.

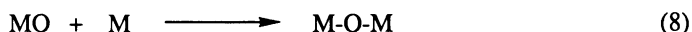


Problems and Limitations

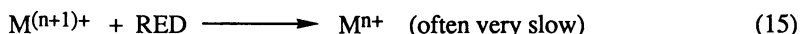
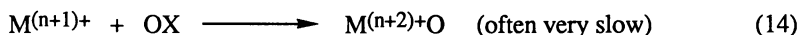
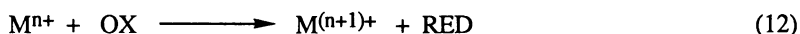
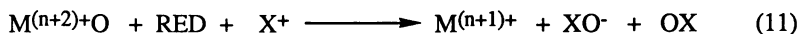
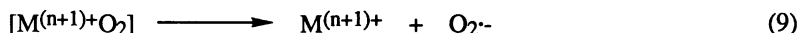
Instability of Catalyst Under Turnover Conditions. There is substantial literature on the use of transition metal complexes with organic ligands as catalysts for oxidation, including oxygenation, of organic substrates. These studies have collectively contributed greatly to our understanding of the energetic and mechanistic features of these processes. At the same time, only a handful of these systems offer the potential to be practically useful for the simple reason that organic structure, including organic ligands, is thermodynamically unstable with respect to CO₂ and H₂O. As a consequence the ligands of the catalyst, L in equation 7, are inevitably oxidized (to LO in equation 7) and/or degraded extensively at some point and the catalyst is inactivated. Alternatively, another situation can arise that can be just as deleterious: the metal center with altered ligands, (L)_{x-1}(LO)M, retains some catalytic activity but it is no longer selective.



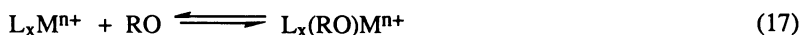
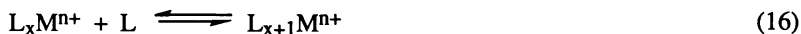
Formation of Oxo-bridged Dimers and Oligomers. A facile and pervasive type of process, and one that often leads to inactivation or significant attenuation in activity of the oxygenation catalysts, particularly under mild operating conditions, involves the trapping of oxometal intermediates by some form of the catalyst to generate bridging species, often μ-oxo dimers, equation 8. In some cases this type of dehydration condensation can proceed to oligomerized or polymerized transition metal species that are marginally active. Fortunately this type of process can often be controlled by the reaction conditions (for example, it is often quite pH dependent), it is often reversible, and it can be avoided altogether by using ligands that sterically preclude formation of such units.



Formation of Dead-end Intermediate Oxidation States, Particularly M⁽ⁿ⁺¹⁾⁺. For oxygenation involving oxometal species, M⁽ⁿ⁺²⁾⁺O, the regeneration mode in the catalytic cycle is substrate oxidation via equation 6. Occasional side reactions with M-based or other redox active species can lead to the intermediate oxidation state of the catalyst, M⁽ⁿ⁺¹⁾⁺. Equations 9-12 are routes to M⁽ⁿ⁺¹⁾⁺ in the presence of O₂ as the terminal oxidant. Although the relative likelihood of equations 9-12 will depend on the particular metal complex, M, these equations are given in approximate descending probability. Since M⁽ⁿ⁺¹⁾⁺ is often incapable of reentering the catalytic cycle, equations 13-15, its generation can constitute an effective termination of the catalysis.



Inhibition by One or More Species in the Catalytic Cycle. Inhibition of the catalyst can be manifested through binding of some reactant species to the catalytic active site, such as favorable ligand binding equilibria, equation 16, leading to coordinatively saturated species, $L_{x+1}M^{n+}$. A similar binding of some intermediates to the catalyst could also have kinetically significant consequences. The most likely form of inhibition, however, is by interaction of one of the forms of the catalyst, often the resting form, L_xM^{n+} , with one or more of the products, sometimes the principal or desired product, RO (equation 17). The resulting adduct complexes, $L_x(RO)M^{n+}$, are unreactive under the reaction conditions.



Diffusional Problems. The likelihood of diffusional problems will be increased as the active site of the catalyst becomes more sterically hindered and physically buried. These diffusional problems can derive simply from greatly inhibited mobility of reactants and products into and out of the active site, but they can also derive exclusively from diffusional escape of the products whose sizes or other properties affecting mobility are appreciably different from those of the reactant.

Approaches/New Systems

Sterically Hindered Metalloporphyrins Capable of Direct Aerobic Oxygenation. The catalytic aerobic olefin epoxidation system of Quinn and Groves, (tetramesitylporphyrinato)Ru/O₂/olefin substrate, effects equations 3-6, that is, the direct oxygenation of substrate using O₂ as the oxidant without consumption of reducing agent (14). The (tetramesitylporphyrinato)Ru complex sterically precludes formation of μ -oxo dimer and exhibits the appropriate redox potentials to facilitate the processes in the equations. This system and related sterically hindered metalloporphyrin systems, however, are rapidly inactivated by inhibition and by forming a kinetic dead-end intermediate oxidation state, Ru^{III}. Alcohols such as methanol and other oxygenated organic species can bind to and inactivate or decrease the activity of the Ru center. The inherent kinetic oxidative instability of the porphyrin ligand itself has not been addressed as the system does not last long enough to assess this issue.

Polyhalogenated Metalloporphyrin Oxygenation Catalysts. Recently tetraarylporphyrins and metallotetraarylporphyrins, some of the most oxidatively resistant of organic moieties, have been polyhalogenated by several research groups, and particularly by those of Traylor and Tsuchiya, to make them more resistant to oxidation (15-18). Indeed, a "teflon porphyrin", one with all C-H bonds replaced by C-F bonds, has been made. Although such metalloporphyrins have been shown to be remarkably stable in strongly oxidizing media, one concern with these systems is that the more electron withdrawing the porphyrin ligand becomes, the higher the redox potential of the central transition metal ion and the less likely it will be to bind and reduce O₂ or oxygen donors which is a requisite for effective catalytic oxygenation. Many of these complexes may be thermodynamically incapable of binding O₂. Furthermore, no highly halogenated metalloporphyrins that also are sterically hindered to prevent μ -oxo dimer formation have been made and shown to interact with O₂. In any event, the cost and effort required to obtain these elegant oxidatively robust complexes is prohibitive on all but the smallest of potential

applications. Despite the inherent limitations of metalloporphyrins as catalysts for sustained selective oxidation, these are fascinating materials and the approach continues to show promise. Recently some halogenated metalloporphyrins have exhibited reasonable levels of oxidative stability in some autoxidation processes despite the fact that the ligands are still thermodynamically unstable to oxidation (18). It should be noted that even perfluorocarbons are thermodynamically unstable to oxidation and are documented to combust in some cases (19).

Redox Active Zeolites. Metallophthalocyanines and other forms of d-electron redox active transition metals included within zeolites are totally inorganic systems capable of catalyzing the oxygenation of hydrocarbons including alkanes under mild conditions in solution (13). These systems effectively counter several of the five general limitations elaborated in the previous section. Under the modest thermal conditions of the reactions, however, diffusion of the more sterically encumbered alcohols versus the substrate alkanes in alkane oxygenation by such transition metal complex-encapsulated zeolite catalysts is a major problem (13). At the same time, titanium silicalite, TS-1, is a Ti-containing zeolite that has impressive catalytic properties with respect to oxidizing hydrocarbon substrates with H_2O_2 . TS-1 is already in commercial operation (20-21). There is little additional work in this area but the potential of such systems warrants serious investigation in our view.

d-Electron-transition-metal-substituted Polyoxometalate (TMSP) Catalysts. TMSP complexes are, as the name indicates, compounds formed by substituting one or more of the d^0 early-transition-metal ions that make up the inorganic skeleton of a polyoxometalate such as $\text{PW}_{12}\text{O}_{40}^{3-}$ (22-29) with d^n , $n \neq 0$, transition metal ion(s). The latter is(are) chosen with electronic and structural features requisite for the catalysis of interest. Catalytic hydrocarbon oxygenation is the focus of this article. Distinct coordination environments for the d-electron-containing "active sites" are exhibited in different classes of TMSP complexes. These complexes, by virtue of their composition, are stable to oxidative degradation. Catalytic oxidation based on TMSP-type complexes can be conducted in a homogeneous mode (dissolved in solution) or in a heterogeneous mode. In the homogeneous mode, TMSP-based catalysts combine the stability advantages of inorganic metal oxide systems, which include zeolites (both are entirely inorganic and hence thermodynamically resistant to oxidative degradation under catalytic reaction conditions), with the tractability advantages of homogeneous catalysis. Since our first paper and the initial patent on this subject (30-34), several other groups have published a number of papers exploring hydrocarbon oxygenation with a range of oxygen donors, equation 2, catalyzed by TMSP complexes (35-42).

The robustness of TMSP-type catalysts allows one to address many of the limitations regarding the development of optimal catalysts for homogeneous selective oxidation, including the five general limitations articulated above: (1) inadequate stability, particularly oxidative stability, (2) μ -oxo dimer formation, (3) deadend oxidation states, (4) inhibition by H_2O and products, and (5) diffusional problems. Points 2, 3, 4, and 5, are often not significant problems in heterogeneous catalytic oxidations as operation at high temperatures and other extreme conditions can eliminate several or all these considerations. Many TMSP catalysts are likely to be stable and operational at high temperature and under extreme conditions even in the homogeneous mode thus considerably reducing the impact of these limitations. I say "likely" as few such reactions have yet to be actually examined experimentally. In addition, however, TMSP compounds are available that preclude point 2, μ -oxo dimer formation, under very mild conditions where such processes might be a serious problem. One exemplary class of TMSP complexes where μ -oxo dimer formation is

sterically precluded is the d-electron-containing transition metal complexes of the polychelating HPA-23 d⁰ heteropolytungstate complex ($[\text{NaSb}_9\text{W}_{21}\text{O}_{86}]^{18-}$). The latter complex has six potential binding sites (43).


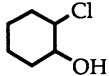
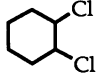
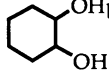



We report here three studies that address three separate but significant issues in the emerging area of selective catalytic oxidation by TMSP-type complexes. The first study establishes for the first time that some TMSP complexes are compatible with basic oxidants and basic conditions. The second study reports the first oxidation, in this case selective alkene epoxidation, by the economically and environmentally desirable oxidant, aqueous hydrogen peroxide, catalyzed by TMSP complexes. The third study demonstrates that redox active polyoxometalates can be derivatized with alcohols in a manner that should prove useful for fabricating future generations of more sophisticated and selective TMSP catalysts.

Results

Sustained Oxygenation of Alkenes by OCl^- Catalyzed by TMSP Complexes. None of the studies on TMSP-catalyzed homogeneous oxidation reactions reported to date involve basic media. The simple reason for this is that the families of TMSP complexes most accessible and amenable to rigorous characterization, principally those derived from the common Keggin structural family of polyoxometalates, $\text{X}^n\text{M}_{12}\text{O}_{40}^{(8-n)-}$, are not hydrolytically stable in basic media. Unfortunately, some terminal oxidants of interest are compatible only with basic media. One test case addressed here is hypochlorite, OCl^- an inexpensive although not environmentally optimal oxidant. We have found that by using two-phase conditions, keeping the TMSP complexes in the organic phase, and using complexes of reasonable stability in neutral or basic media that successful oxidation of organic substrates by OCl^- catalyzed by TMSP complexes can be realized. Table II summarizes the time dependence of the distribution of organic oxidation products generated by OCl^- oxidation of an exemplary alkene, cyclohexene, in a $\text{CH}_2\text{Cl}_2/\text{H}_2\text{O}$ two-phase system under low turnover conditions catalyzed by two TMSP complexes, ${}^6\text{Q}8[\text{Cu}(\text{II})\text{P}_2\text{W}_{17}\text{O}_{61}]$ and ${}^6\text{Q}_{16}[(\text{Ni}(\text{II}))_4(\text{P}_2\text{W}_{15}\text{O}_{56})_2]$, where ${}^6\text{Q} = (n\text{-C}_6\text{H}_{13})_4\text{N}^+$. Although it is possible to obtain up to 40% cyclohexene conversion or under different conditions 100% selectivity to cyclohexene oxide (Khenkin, A. M.; Weeks, M. S., unpublished results), the selectivity for epoxide is generally poor principally because of the facile further reaction of initial oxidation products under these particular reaction conditions. Little effort has been made thus far, however, to optimize this chemistry. The careful control of pH, removal of products and other techniques would doubtless improve the observed selectivities. The data available at present suggest that hypochlorite exhibits less selective olefin oxidation reactions in TMSP-catalyzed reactions than some other nonbasic oxygen donor oxidants (30-42).

A central issue in this exercise was to address the compatibility of TMSP catalysis with basic oxidants. A pertinent experiment involved the epoxidation of cyclohexene by hypochlorite under high turnover conditions. The spectroscopic properties of ${}^6\text{Q}_{16}[(\text{Ni}(\text{II}))_4(\text{P}_2\text{W}_{15}\text{O}_{56})_2]$, before and after reaction indicated minimal decomposition of this particular TMSP after 1,400 turnovers. The preliminary dynamic product data, the negligible amount of oxidation in the absence of the TMSP complex, and the stability of the catalyst under turnover conditions defines TMSP complexes to be capable, in principle, of sustained catalytic oxygenation of organic substrates by OCl^- and perhaps other basic oxidants. Given that several parameters could, in principle, be adjusted to further stabilize the TMSP complexes in basic conditions including the inclusion of one or more Nb or Ta atoms at key locations in the complexes, these systems are of some interest.

Table II. Oxidation of Cyclohexane by Hypochlorite Catalyzed by Two TMSP Complexes

Products	Yields ^a					
	${}^6\text{Q}_8[(\text{Cu}^{\text{II}})\text{P}_2\text{W}_{17}\text{O}_{61}]$			${}^6\text{Q}_{16}[(\text{Ni}^{\text{II}})_4(\text{P}_2\text{W}_{15}\text{O}_{56})_2]$		
	40 min	100 min	5 h	30 min	90 min	7 hr
	3.3	4.9	6.8	18.7	18.1	25.7
	3.9	7.8	11.1	3.7	2.8	8.0
	10.7	12.7	20.2	15.0	8.3	6.4
	c	c	c	c	c	c
	c	c	1.3	1.2	1.2	1.2
	1.3	3.3	2.3	0.9	1.8	0.9
	c	2.6	3.6	3.7	4.6	3.4

^aYields (%) based on hypochlorite after the elapsed reaction times indicated.^bPartitions principally into the aqueous phase. ^cNot detectable by GC (<< 1 mol %).

Another point about these hypochlorite oxidations concerns the fate of the oxidizing equivalents unaccounted for in the organic product distributions at the time of GC and GC/MS analysis. Despite the number of papers on biomimetic and other homogeneous catalyzed oxidations of hydrocarbon substrates by hypochlorite, the product balance with respect to this oxidant is rarely satisfactory. More telling, however, is that there may be no report addressing the fate of the equivalents of active oxygen that are not accounted for in the organic products. In the case of the oxidations studied here, perchlorate is generated in sufficient quantities to account for most of the missing active oxygen, a result implicating that the TMSP, and by inference, a host of conventional transition metal complexes with oxidizable organic ligands, may be capable of catalyzing disproportionation of hypochlorite.

The use of benzene as a solvent eliminates the chlorinated organic products in Table II. This point and the products in the table are consistent with radical abstraction (hydrogen atom transfer) from the substrate, cyclohexene, by the high valent (and likely oxometal) intermediate form of the TMSP complexes, followed by chlorine abstraction from the solvent by intermediate organic radicals. Separation and analysis of the two phases after the reaction reveals that the polyoxometalate is intact,

but resides in the aqueous phase. This probably results from one or more of four time-dependent phenomena: (1) the increasing concentration of polar organic products (largely diol) in the aqueous phase (shifting the partitioning coefficient of the TMSP anions further toward the aqueous phase), (2) the generation of protons from allylic hydroxylation and possibly other oxidations resulting in replacement of H^+ for Q^+ as the counterions of the TMSP complexes (the free acid forms of polyoxometalates are much more soluble in water than the Q forms), (3) the generation of chloride, both from the oxidation reactions and from hypochlorite disproportionation (this could favor a shifting to the right of the following metathetic equilibrium: $Q^+TMSP^-(CH_2Cl_2 \text{ phase}) + Na^+(aq \text{ phase}) + Cl^-(aqueous \text{ phase}) \rightleftharpoons Q^+Cl^-(CH_2Cl_2 \text{ phase}) + Na^+(aq \text{ phase}) + TMSP^-(aqueous \text{ phase})$), and (4) the partial oxidative destruction of the hydrophobic CH_2Cl_2 -solubilizing Q counter ions. The latter is unlikely as there is no evidence for Q destruction. The oxygenation and other oxidation chemistry going on in the aqueous phase at later reaction times has not been investigated but would be of much interest given the long term desirability of water-compatible catalysts and catalytic processes. The efficiency and selectivity in cyclohexene oxidation is dependent on the nature of the transition metal, the polyoxometalate and the solvent.

Alkene Epoxidation by H_2O_2 Catalyzed by TMSP Complexes. The principal chemistry on epoxidation of alkenes by H_2O_2 involving polyoxometalates is that of Venturello ($WO_4^{2-}/PO_4^{3-}/H_2O_2$ /chlorocarbon solvent + PTC) (44-48) and Ishii ($PW_{12}O_{40}^{3-}/H_2O_2$ /chlorocarbon solvent + PTC) (49-51), where PTC = phase transfer catalyst. Although definitive mechanistic work is lacking on these systems, it is clear that they are related and involve common epoxidizing intermediates. A dominant feature of this chemistry is that breakdown of the Keggin heteropolytungstate, $PW_{12}O_{40}^{3-}$, is facile in the presence of the commercially available aqueous H_2O_2 . For this reason, the conventional wisdom has been that polyoxometalates, in general, would be too susceptible to hydrolytic and peroxolytic degradation to be of interest as catalysts for H_2O_2 reactions other than to function as the precursor of the active epoxidizing species in the Venturello/Ishii chemistry. This study shows this is unlikely to be the case. Table III summarizes preliminary results on H_2O_2 oxidation of cyclohexene in CH_3CN catalyzed by three TMSP complexes with reasonable hydrolytic stability. The reactions catalyzed by the first two complexes are quite attractive and rival those seen in the toxic chlorocarbon containing Venturello/Ishii systems. Most interestingly, examination of the $[(Fe^{II})_4(B-PW_9O_{34})_2]^{10-}$ catalyst by ^{31}P NMR and other spectral methods before, during, and after 2087 turnovers indicates part of the catalyst had been degraded after this considerable chemistry. These data coupled with evaluation of initial reaction rates of cyclohexene epoxidation by the TMSP complexes in Table III and authentic species from the Venturello system argue strongly that different epoxidizing species are involved in these different systems. Given all the desirable attributes of H_2O_2 , this chemistry warrants rigorous investigation.

Modification of Catalytically Active Polyoxometalates with Organic Groups. The covalent attachment of organic groups to polyoxometalates would introduce organic structure and hence potential oxidative instability. At the same time, however, such groups could be used not only to change solubilities, partition coefficients and other bulk properties of relevance in catalysis but also to render catalytically active polyoxometalates capable of molecular recognition and highly selective catalysis. One example of the latter is chiral groups to make derivatized polyoxometalate catalysts for sustained catalyzed asymmetric oxygenation and other oxidation reactions. Our initial experiments have sought to assess the feasibility of

attaching polyfunctional organic groups to the surfaces of polyoxometalates. Several sites of attachment between organic groups and the polyoxometalate would enhance not only the stability but also molecular recognition capabilities of the adduct, the organic derivatized complex.

Table III. Oxidation of Cyclohexene by H₂O₂ Catalyzed by TMSP Complexes

TMSP ^a	[H ₂ O ₂] ₀ / [H ₂ O ₂] _f (M)	Time, h	Products, (Yield %) ^b	Sc %	T ^d
⁶ Q ₁₀ [(Ni ^{II}) ₄ (B-PW ₉ O ₃₄) ₂] ^c	1.0/0.3	16	oxide (30.4) enol (0.2) enone (0.2)	99	216
⁴ Q ₁₀ [(Fe ^{II}) ₄ (B-PW ₉ O ₃₄) ₂]	0.2/0.02	3	oxide (30.7) enol (0.8) enone (2.0)	95	15
⁴ Q ₄ [(Fe ^{II})PW ₁₁ O ₃₉]	0.2/0.16	27	oxide (3.7) enone (45)	15	2.5

^a⁶Q = (n-C₆H₁₃)₄N⁺; ⁴Q = (n-C₄H₉)₄N⁺. ^bYield on ΔH₂O₂; ^cSelectivity of cyclohexene oxide formation = mol of cyclohexene oxide/mol of all products. ^dTurnover number = mol of all products/mol catalyst. ^e[TMSP] = 1 mM.

The condensation of 1,1,1-tris(hydroxymethyl)ethane with [(n-C₄H₉)₄N]₅H₄[P₂V₃W₁₅O₆₂] proceeds to give the complex with the tris unit covalently attached to the three oxygens that bridge the three V atoms residing on one end of the polyoxometalate (the "cap" position of the Wells-Dawson structural family of polyoxometalates), [(n-C₄H₉)₄N]₅H[CH₃C(CH₂)₃P₂V₃W₁₅O₆₂]. Preliminary experiments have indicated that this C_{3v} complex with a tri-linked "hat" is quite stable to hydrolysis and capable of catalyzing the oxidation of tetrahydrothiophene (THT) to the corresponding sulfoxide, (THTO) by *t*-butylhydroperoxide (TBHP) for 30 turnovers without apparent hydrolytic or oxidative degradation of the capping organic group (Hou, Y.; Hill, C. L. unpublished work).

Some TMSP systems that preclude μ-oxo dimer formation and exhibit the right proton-linked redox potentials should facilitate selective catalytic aerobic oxidation such as that defined in equations 3-6. Selective catalytic aerobic oxidation has yet to be achieved, however. The few TMSP systems examined thus far in conjunction with O₂-based oxidations function as redox initiators of autoxidation.

Experimental Section

Materials and Methods. The lacunary heteropolytungstates Na₁₂P₂W₁₅O₅₆·18H₂O (52) and K₁₀P₂W₁₇O₆₁·22H₂O (52); and their transition metal substituted polyoxotungstate derivatives Na₁₆[(Ni^{II})₄(P₂W₁₅O₅₆)₂]·22H₂O (52), K₈[(Cu^{II})₂P₂W₁₇O₆₁] (53), K₁₀[(Fe^{II})₄(B-PW₉O₃₄)₂] (54-55), K₁₀[(Ni^{II})₄(B-PW₉O₃₄)₂] (54-55), and Na₅[(Fe^{II})PW₁₁O₃₉] (54-55), were prepared and purified

by literature methods. Purity of the complexes in all cases was judged to be satisfactory by ^{31}P NMR, FTIR, and elemental analysis. Stock solutions of the tetra-*n*-alkylammonium salts, either tetra-*n*-hexyl (^6Q) or tetra-*n*-butyl (^4Q) ammonium salts were prepared by direct extraction or by precipitation from water (56,57). All catalysts for the hypochlorite reactions were used as volumetric stock solutions in dichloromethane. Both the sodium hypochlorite (5.25%, Clorox) and the 30% aqueous H_2O_2 (Fisher) were commercial samples and titrated iodometrically using a standard literature procedure (58). The cyclohexene was reagent grade from Fluka and had a purity greater than 99% by gas chromatography (GC).

The distributions of organic oxidation products were unambiguously identified through the use of GC (Hewlett-Packard 5890 instrument; 5% phenyl methyl silicone fused-silica capillary column; nitrogen carrier gas, temperature programming; FID detection) and by gas chromatography-mass spectrometry (GC-MS, Hewlett-Packard 5971 A MSD instrument). The electronic absorption spectra were recorded on a Hewlett-Packard (H/P) Model 8451A diode-array UV-visible spectrometer. ^{31}P broad-band proton-decoupled NMR spectra were measured on an IBM WP-200-SY spectrometer, operating at a frequency of 81 MHz and reported relative to 0.1% trimethyl phosphate in CD_3CN as the external reference.

Catalytic OCl^- oxidations. In a typical reaction with TMSP (either $^6\text{Q}_{16}[(\text{Ni}^{\text{II}})_4(\text{P}_2\text{W}_{15}\text{O}_{56})_2]$ or $^6\text{Q}_8[(\text{Cu}^{\text{II}})\text{P}_2\text{W}_{17}\text{O}_{61}]$), aqueous hypochlorite and alkene, 4 mL of dichloromethane, and 1.7×10^{-5} mol of the phase transfer catalyst tetra-*n*-hexylammonium chloride (^6QCl) were placed in a 25-mL round-bottom schlenk flask. The solution was thoroughly degassed and then left under Ar. The reaction was initiated by addition of 1.70 mmol of cyclohexene, 0.01 mmol of the TMSP, and 0.17 mmol of hypochlorite in 1.0 mL of water (pH 10.8). Two homogeneous phases were exhibited throughout the duration of each of these reactions. The products in the organic layers were analyzed GC and GC/MS as indicated above while the reactions were stirred at room temperature for 7 h.

Catalytic H_2O_2 Oxidations. The reactions were carried out in 10-mL tubes equipped with serum cap and a stirring bar. The catalyst, hydrogen peroxide, and substrate were dissolved in of CH_3CN . Trimethylacetoneitrile was added to the reaction as an internal standard. All reactions were done under argon, each was purged by three freeze-thaw cycles and GC analysis was performed on aliquots withdrawn directly from the reaction mixture. Typically, alkene (1 mmol) was added to the solution of the TMSP (0.004 mmol) in 1 mL of CH_3CN then 25 μL of 30% aqueous H_2O_2 was added and reaction mixture was stirred at 20 $^\circ\text{C}$.

Synthesis of $[(n\text{-C}_4\text{H}_9)_4\text{N}]_5\text{H}[\text{CH}_3\text{C}(\text{CH}_2)_3\text{P}_2\text{V}_3\text{W}_{15}\text{O}_{62}]$. This compound was made by condensing a slight molar excess of 1,1,1-tris(hydroxymethyl)ethane with $[(n\text{-C}_4\text{H}_9)_4\text{N}]_5\text{H}_4[\text{P}_2\text{V}_3\text{W}_{15}\text{O}_{62}]$. Elemental analysis, ^1H , ^{31}P , ^{51}V , and ^{183}W NMR established the identity and purity of the compound. The hydrolytic stability of the complex was assessed using the ^1H and ^{31}P NMR. The stability of the complex during oxidation of tetrahydrothiophene (THT) to the corresponding sulfoxide, (THTO) by *t*-butylhydroperoxide (TBHP) was assessed using ^{51}V and ^{31}P NMR.

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