Biomimetic catalysis in a larger context. Correlation of structure and function with genesis

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Abstract

The relationships between the formation (serial synthesis, self assembly, etc.) of biological and man-made catalysts and their catalyzed reactions are discussed. A potentially utilitarian implication of a correlation between catalyst genesis and function is a more resilient catalyst can 'sense' certain kinds of damage (those involved in reversal of the catalyst into its synthetic components) and repair itself. A set of correlated reactions has been developed. The catalyst, $H_4PVMo_{11}O_{40}$, self assembles from several components and simultaneously catalyzes a new, fast and highly selective reaction, the oxidative dehydrogenation of α-terpinene to p-cymene by t-butyl hydroperoxide (TBHP).

Keywords: Biomimetics; Polyoxometalate; Self-Assembly; Catalysis; Dehydrogenations

1. Introduction

The correlation of structure with function is a paradigm implicit in all size regimes in the biosphere from the molecular (picoscopic) and nanoscopic (enzymes, membrane structures, ribosomes, etc.) to the microscopic (large viruses, cells, etc.) and macroscopic (large plants and animals). It has also been an underlying theme in the design of synthetic molecules and structures as well as microfabricated devices [1–5]. From the design and control of structure derive selectivity, information storage and utilization, and other features that render the function effective or viable.

Examination of the operating protocols of complex biological entities, those from the level of cells up to mammals, clearly reveals another feature of design and control, namely that *the genesis (synthesis, self assembly, etc.) of an operating unit is often linked to its function and visa versa*. Such entities have an ability to sense the damage that is an inevitable consequence of functioning and repair this damage. Fig. 1 illustrates some general points. Here a catalyst (e.g. an enzyme) damaged by a particular process, Eq. (1), is indirectly 'repaired' (its function regenerated) via complex cellular machinery that facilitate several processes (i.e. disassembly, discarding of damaged units, and reassembly with undamaged units) that are collectively represented by Eq. (3) in Fig. 1. In contrast, the less sophisticated (molecular) entities in Nature, such as an enzyme itself alone, as well as

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virtually all man-made catalysts (and dynamically functioning devices in general) do not possess the machinery analogous to Eq. (3). Nor are they capable of direct repair (Eq. (2)) so damage to the enzyme or device leads irreversibly to loss of function or death.

The goal of this research is to design catalysts with an ability to sense damage during operation and counteract this damage, or effectively repair the damage. While this could, in principle, be done in an indirect multistep manner as in cells, Eq. (3), we seek a more direct manner here, one involving direct counteracting (repairing) reaction(s), Eq. (2). One can term, albeit somewhat fancifully, a catalyst that has an ability to sense damage and effect repair, as one with a crude 'intelligence' with regard to its own integrity. Such 'smart' catalysts are more appropriately viewed as 'smart' catalytic systems as the ability to facilitate the repair, Eq. (2) in Fig. 1, involves the complete thermodynamic system — all reactants, products, solvent, catalyst, and other components. The impetus for the development of such 'smart' catalyst systems is two-fold: to design better more resilient catalysts, and to stimulate the evaluation of synthetic catalysts in the broadest biomimetic context. In conjunction with this, we seek to clarify relationships between the control and other features of biocatalysts (devised and implemented through natural selection and evolution) and those of man-made catalysts (devised through human ingenuity and need).

2. Concept

Three simple aspects are implicit in the design of a smart catalytic system, illustrated in Eqs. (4) and (5).

catalyst precursor units   catalyst
(structural components)

$$(4)$$
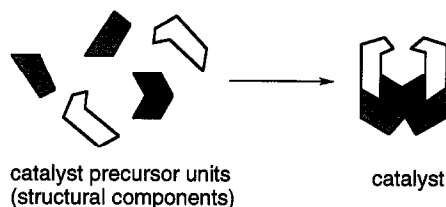
$$A + B \xrightarrow{\text{catalyst}} C + D \qquad (5)$$

First, the synthesis of the catalyst, Eq. (4), and its catalysis, Eq. (5), should take place at the same time and in the same place. If this is the case then one particular type of damage due to the catalysis (Eq. (5)), namely that involving degradation of the catalyst into its original synthetic components (the reverse of Eq. (4)),
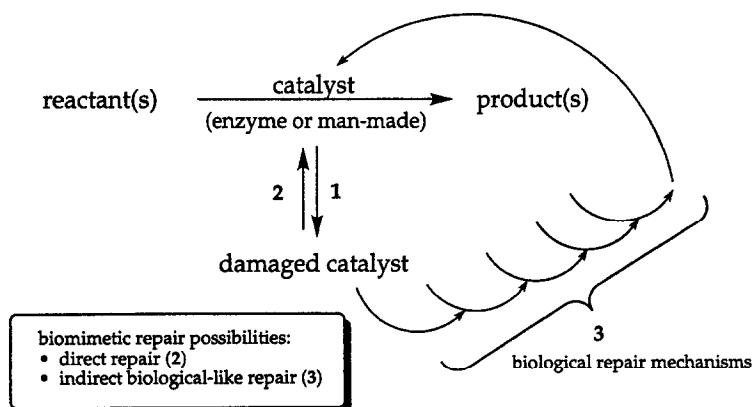

reactant(s) $\xrightarrow[\text{(enzyme or man-made)}]{\text{catalyst}}$ product(s)

2 ↕ 1

damaged catalyst

biomimetic repair possibilities:
• direct repair (2)
• indirect biological-like repair (3)

3
biological repair mechanisms

Fig. 1. General features of catalyst function, damage and repair.

should be 'sensed' and counteracted. That is, Eq. (4) will proceed, again, from left to right effectively repairing this damage. Second, catalyst synthesis should be engineered to take place under all conditions of catalysis and different conversions of the substrate (% reaction). Catalyst self assembly under initial conditions for example says nothing about catalyst self assembly under the final conditions as these two sets of conditions are different. Thus catalyst self assembly needs to be evaluated under initial, intermediate, and final conditions. Importantly, the above equations and conditions do not simply involve a self assembling catalyst system that is in equilibrium with its components nor a catalyst that is thermodynamically stable. Few if any catalysts, including enzymes, are thermodynamically stable under turnover conditions. The conditions above assure that the catalyst is kinetically capable of forming under turnover conditions and that the final resting place is in a reasonably deep kinetic minimum. Third, damage and repair of the fully formed catalyst under operating conditions needs to be documented. This is far from simple. In an initial effort published earlier this year we reported the total self assembly of a multicomponent homogeneous polyoxometalate cluster under the same conditions where it functions as a selective catalyst [6]. The catalytic reaction in this case was epoxidation catalyzed by a d-electron transition metal (Co^{II})-substituted polyoxometalate [7–13]. The work reported here is a more utilitarian system in which a d^0 V^V-substituted polyoxomolybdate [14–18], $H_4PVMo_{11}O_{40}$, illustrated in Fig. 2, forms under conditions where it also catalyzes the dehydrogenation and aromatization of a terpene, α-terpinene, to p-cymene.

3. Experimental section

3.1. Materials and instrumentation

All chemicals were commercially available reagent grade and were used as received. V_2O_5 was sonicated for 6 hrs before use. Acetonitrile was Burdick and Jackson glass-distilled grade. The α-terpinene (Sigma) with a purity of 89% by gas chromatography (GC) contained 5% p-cymene and other unidentified impurities. tert-Butyl hydroperoxide (TBHP) was a 90% aqueous solution from Aldrich. Gas chromatographic analyses were performed using a Hewlett-Packard 6890 instrument equipped with a flame ionization detector (FID) and a cross-linked 5% phenyl methyl silicone capillary column using nitrogen as the carrier gas. Cumene was used as an internal standard to quantify the reaction. ^{51}V NMR spectra were recorded on a GE GN-500 spectrometer and chemical shifts were referenced to 100% $VOCl_3$ as an external standard.
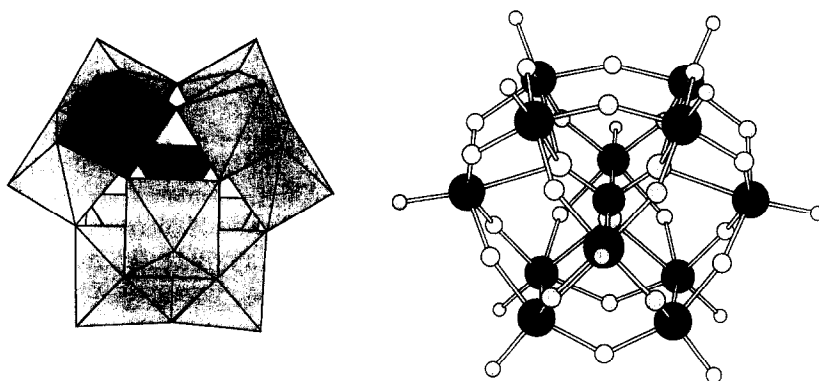

Fig. 2. Structure of $H_4PVMo_{11}O_{40}$ in polyhedral (left) and ball-and-stick (right) illustrations. The P^V atom (PO_4 tetrahedron) resides in the central tetrahedral cavity and the V^V atom (VO_6 octahedron) resides in the upper left hand corner in both illustrations.

The concentrations of $H_4PVMo_{11}O_{40}$ were calculated by reference to a $K_8H_1P_2V_3W_{15}O_{62}$ solution of known concentration in a capillary insert. The reaction temperature was maintained at $25 \pm 1°C$ using a Dataplate 720 series digital hot plate/stirrer.

3.2. Kinetics of the formation of the catalyst

The solution containing the $H_4PVMo_{11}O_{40}$ in the process of forming was obtained by reacting the molybdenum precursor with a known amount of V_2O_5. This reaction was followed by ^{51}V NMR. To make the molybdenum precursor, 29.6 g of MoO_3 was added to 600 mL H_2O containing 3.03 g 85% H_3PO_4. The mixture was refluxed overnight to dissolve the solid. A few drops of H_2O_2 were added to oxidize the reduced molybdenum species if the solution was slightly green. After cooling, the solution was filtered to remove any remaining solid and concentrated to about 200 mL using a rotary evaporator and then transferred to a 250 mL volumetric flask and diluted to 250 mL. To make $H_4PVMo_{11}O_{40}$, 0.7108 g V_2O_5 was added to 130 mL of the above molybdenum precursor solution, and the mixture was stirred at 800 rpm. Aliquots were taken out, centrifuged and the ^{51}V NMR spectra were recorded within 10 min.

3.3. Kinetics of oxidative dehydrogenation of α-terpinene

In a typical reaction, 3.00 mL of acetonitrile containing 40 μL of α-terpinene (2.19×10^{-4} mol) was placed in a Schlenk flask fitted with a magnetic stirring bar and rubber septum. Each reaction was degassed and placed under argon. A solution of 31 μL (2.79×10^{-4} mol) of TBHP in 2.00 mL of acetonitrile and 0.50 mL of the catalyst solution in the process of formation were added simultaneously to initiate the reaction. The reaction was stirred at 800 rpm. Aliquots were taken out at the appropriate intervals and quenched by an acetonitrile solution of

tert-butylammonium borohydride before GC analyses.

4. Results and discussion

Conditions have been found under which the polyoxometalate, $H_4PVMo_{11}O_{40}$, forms from its precursor species, Eq. (6), while it functions as an effective catalyst for the dehydrogenation of α-terpinene, Eq. (7). The reactions shown in Eqs. (6) and (7) were selected because the formation of $H_4PVMo_{11}O_{40}$ (Eq. (6)) is relatively slow and the dehydrogenation of α-terpinene (Eq. (7)) is a fairly fast. This, in turn, facilitates a detailed study of both the catalyst self assembly, Eq. (6), and the catalysis, Eq. (7). The oxidative dehydrogenation of α-terpinene by O_2 catalyzed by $H_5PV_2Mo_{10}O_{40}$ has been studied and the data supporting a two-step mechanism are quite strong [19]. TBHP was used in place of O_2 as a terminal oxidant in this study because the reaction rate is increased fifty-fold. The catalytic reaction was found to be pH sensitive and special attention was made to make sure the pH of the solution with the forming catalyst remained almost constant.

$$\left. \begin{array}{l} H_3PO_4 + MoO_3 \rightarrow \text{Molybdenum precursor} \\ \text{Molybdenum precursor} + V_2O_5 \rightarrow H_4PVMo_{11}O_{40} \end{array} \right\}$$

$$(6)$$

α-terpinene   TBHP   p-cymene   TBA
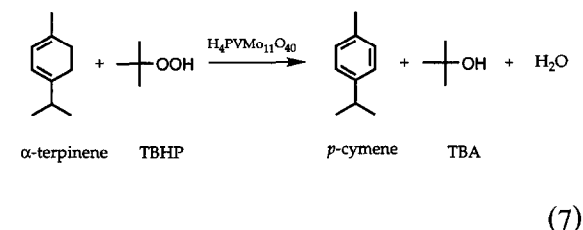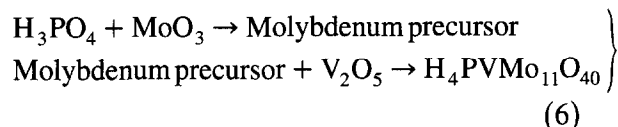
$$(7)$$

Fig. 3 correlates the rate of Eq. (6) with the initial rates of catalytic dehydrogenation, Eq. (7). It is noted that the concentration of $H_4PVMo_{11}O_{40}$ increases linearly with time and is the only vanadium-containing species formed in solution when the conversion is less than
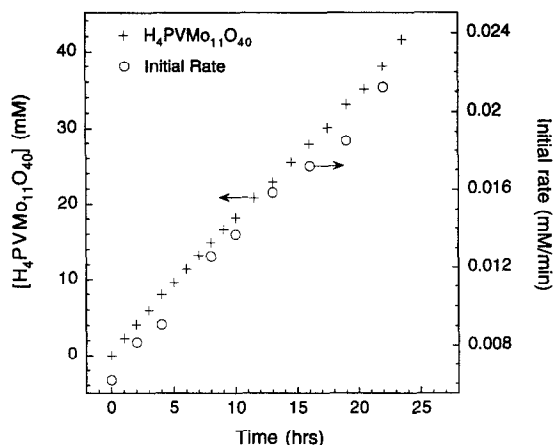
Fig. 3. Kinetic profile showing the correlation between the formation of the catalyst, $H_4PVMo_{11}O_{40}$, (Eq. (6)) and its catalytic reactivity in the oxidative dehydrogenation of α-terpinene by TBHP (Eq. (7)) as a function of time.

70% (based on the limiting reagent V_2O_5). The catalytic profile of the forming catalyst (i.e. the initial rate for oxidative dehydrogenation of α-terpinene) has a similar linear relationship with time. The correlation of catalyst self assembly, Eq. (6), with catalyst function, Eq. (7) establishes two important points: First, it proves that the active catalyst (the species facilitating dehydrogenation in this case) is indeed the final self assembled complex, $H_4PVMo_{11}O_{40}$. In effect, the catalytic chemistry, Eq. (7), provides a kinetic 'resolution' of or kinetically defines the true catalyst. Second, the smooth correlation argues against a catalytic system in a state of chemical instability (a dissipative state). Catalytic domains can reside in such far-from-equilibrium states [20] and in such states their properties are not always predictable. The system here is kinetically well behaved and while not at equilibrium, it is not far from equilibrium.

One caveat in these experiments is that the medium is not identical in Eqs. (6) and (7). The multicomponent catalyst self assembly, Eq. (6), is conducted in water, while the catalysis, Eq. (7), is conducted in an acetonitrile solution containing water. One control experiment involved running Eq. (6) in a 50:50 by volume mixture of water and acetonitrile. While the rate for Eq. (6)

was more than three times slower than in 100% water, the reaction, nonetheless, proceeded well.

Two additional control experiments were conducted. One involved reaction of α-terpinene and TBHP only; the other involved reaction of α-terpinene and TBHP with the molybdenum precursor. In the first control experiment, the reaction rate was dependent on the concentration of the substrate, while in the catalyzed reaction, the rate was independent of the concentration of the substrate. Clearly the control reaction without the catalyst proceeds via a different mechanism. When the concentration of the catalyst was low, in the early stage of the reaction (the first 5 min), the rate of α-terpinene direct oxidation by TBHP was on the same magnitude as the rate of α-terpinene oxidation catalyzed by $H_4PVMo_{11}O_{40}$. However, the rate of catalyzed oxidation dominated the total reaction at later reaction times. The second control experiment, the oxidation of α-terpinene by TBHP with the molybdenum precursor, was at least three times slower than that of $H_4PVMo_{11}O_{40}$ and was used as the time $t = 0$ point in the Fig. 3.

In conclusion, the coupling of the kinetics of the catalyst self-assembly and its activity in the oxidative dehydrogenation of α-terpinene provide evidence that Eqs. (6) and (7) constitute another example of a catalyst system with a 'dynamic stability'. Fragmentation of the catalyst into its initial synthetic precursors during catalysis either by chemical or physical means will be reversed spontaneously as a driving force and a kinetic facility must exist for its regeneration. In other words, the system has a built-in mechanism to heal itself if damaged by fragmentation into its original synthetic precursors.

Studies are in progress to optimize parameters so that Eqs. (6) and (7) can take place under final reaction conditions (depleted substrate and accumulated products). Conditions are also being sought where the catalyst can be demonstrably damaged and subsequently exhibit repair while exhibiting catalytic turnover. The rational

search for conditions under which Eqs. (6) and (7) could take place simultaneously proved to be less than straightforward; the identification of conditions that will allow damage and repair to be quantified during catalysis will be an even greater challenge.

Acknowledgements

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