[13] Electrical potentials greater than −800 mV can damage the monolayer and make the substrate susceptible to nonspecific adhesion, thereby preventing detachment of cells when soluble peptide is added.
[14] To show that the electrical potential did not affect normal cell behavior, a potential of −700 mV was applied for 4 minutes to cells adhered to the surface shown in Scheme 1 A. As expected, this short electrical pulse did not affect cell morphology, and cells continued to grow and divide normally.
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Bionic Catalyst Design: A Photochemical Approach to Artificial Enzyme Function

Günther Knör*[a]

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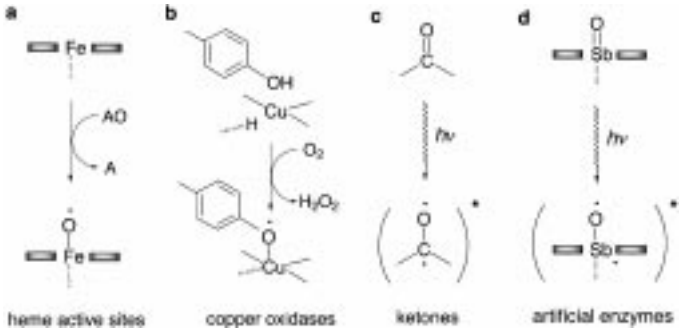
Successful imitation of the environmentally benign processes mediated by natural biopolymers remains a difficult challenge for future green-chemistry technologies. Among the most important industrial and synthetic goals that rely on the exploitation of sustainable resources are the controlled activation of atmospheric dioxygen[1, 2] and the ecological conversion of alcohols into carbonyl compounds.[3] Several native enzymes catalyze the transformation of primary alcohols under aerobic conditions, producing aldehydes and hydrogen peroxide. To mimic the regulation mechanisms and the selective chemistry of enzymes in the absence of a protein environment, the novel strategy of bionic photocatalysis tries to impose light-induced electronic, energetic, and geometric changes on artificial substrate recognition sites.[4] As an example of this bio-inspired catalyst design leading to photocatalytic artificial enzymes (photozymes), a robust synthetic oxidoreductase for the photo-assisted two-electron oxidation of alcohols and the catalytic accumulation of hydrogen peroxide is presented. It is concluded that photochemical modeling of enzymatic key functions has the potential to offer new pathways for a pollution-free production of industrial chemicals driven by solar energy under ambient conditions.

[a] *Dr. G. Knör*
Universität Regensburg
Institut für Anorganische Chemie
93040 Regensburg (Germany)
Fax: (+49) 941-943-4488
E-mail: guenther.knoer@chemie.uni-regensburg.de

Free radicals are agressive species that tend to cause irreversible degradation of biological tissue and synthetic materials. Therefore, the survival of living cells and chemical sytems with a dynamic function critically depends on the control mechanisms for reactive radical intermediates. Nevertheless, there is an increasing number of reports on biocatalytic transformations involving protein radicals,[5] and there are substantial efforts to understand and mimic these processes for synthetic applications.[6–8] In many cases hydrogen atom abstraction from the substrate (S) is considered as one of the mechanistic key steps catalyzed by radical enzymes (E) as shown in Equation (1):

$$E^{\bullet} + S{-}H \longrightarrow E{-}H + S^{\bullet} \quad (1)$$

Scheme 1 illustrates some of the design principles that have been followed for the construction of a simple photon-driven functional model of native oxidoreductase enzymes that are capable of catalyzing H-atom transfer processes. The synthetic



Scheme 1. *How are molecules activated for hydrogen atom transfer chemistry? Different ways to induce the desired catalytic reactivity at a given site are shown. The common link is a species with unpaired spin density at an oxygen atom accessible to the substrate. a) Formation of the so-called compound I intermediates[9] in heme-enzyme mechanisms (AO = oxygen atom donor). b) Coordination of a protein-bound tyrosyl radical cofactor in the active form[10] of the copper-containing enzyme galactose oxidase. c) The radical character of $n \rightarrow \pi^*$-excited states of carbonyl compounds, which enables a photochemical hydrogen abstraction[11, 12] without multiple turnovers. d) Photocatalytic enzyme counterparts (photozymes) combine and modify the most efficient strategies described.*

photocatalyst SbO(tpp)OH reported here (Scheme 1 d) consists of an antimony metal center with a terminal oxo group ($Sb^{V}{=}O$) which can mediate hydrogen abstraction, a macrocyclic ligand (tpp = *meso*-tetraphenylporphyrin) acting as the light-harvesting and radical-stabilizing subunit, and a further axial ligand (OH^-) to form a coordinatively saturated compound. The monoprotonated catalyst precursors[13] of the type $[Sb(tpp)(OH)_2]^+ X^-$ are rather stable coordination compounds that can be stored for several years in the dark without decomposition.

As an example of a catalytic substrate transformation that is considered to involve hydrogen abstraction as the rate-determining mechanistic step,[5, 10] the two-electron oxidation of primary alcohols to aldehydes with dioxygen acting as the electron acceptor was chosen [Eq. (2)]:

$$RCH_2OH + O_2 \longrightarrow RCHO + H_2O_2 \quad (2)$$

Antimony porphyrins with hydrogen-bond-forming axial ligands are capable of binding alcohols in their secondary coordination sphere,[14] which results in a favorable substrate preorientation in the microenvironment of their active site (Figure 1). Hydrogen bonds are known to modulate the electronic coupling between radicals and high-valent metal-oxo

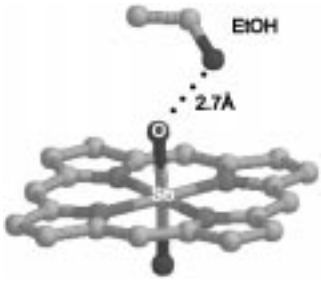


Figure 1. *A glance at the artificial enzyme–substrate complex. Ethanol is already preorganized in the second coordination sphere of the dark-adapted catalyst by hydrogen bonding. Coordinates are taken from the X-ray crystal structure of the antimony(v) octaethylporphyrin derivative,[14] substituents and hydrogen atoms are omitted for clarity.*

units,[15] and one might expect that the attachment to a hydrogen-bond-accepting moiety should make an alcohol substrate easier to oxidize. This kind of alcohol recognition function also introduces some substrate selectivity to avoid a competitive catalytic transformation of the desired aldehyde reaction product, which should not form hydrogen bonds with a terminal oxo fragment.

While no significant thermal reaction of the catalyst with methanol or ethanol was observed in neutral aerated solution, addition of base and irradiation with visible light were found to be sufficient cofactors to activate the compound for immediate substrate conversion (Figure 2). The process has a pH optimum in alkaline solution, which clearly coincides with the formation of the deprotonated SbO(tpp)OH form of the catalyst containing an Sb = O metal-oxo functionality (Figure 2a) according to Equation (3):

$$[Sb(tpp)(OH)_2]^+ + OH^- \longrightarrow SbO(tpp)OH + H_2O \quad (3)$$

Obviously the oxyl-radical-type reactivity of the terminal oxo ligand required for hydrogen atom transfer (Scheme 1) is only present in the excited state of the catalyst molecule. Therefore, both pH and light intensity variations (Figure 2b) can be applied as simple regulation mechanisms for the catalytic conversion of alcohol substrates.

The formation of aldehydes as permanent oxidation products is accompanied by the accumulation of equimolar amounts of hydrogen peroxide according to Equation (2). The quantum yield of product formation is determined as $\phi = 0.02$ for monochromatic irradiation with 546-nm light. At the same time, a photocatalyst degradation quantum yield of $\phi \leq 3 \times 10^{-5}$ can be estimated from the degree of bleaching of the porphyrin absorption bands. Assuming complete deactivation of the catalytic system when more than 99% of the porphyrin complex

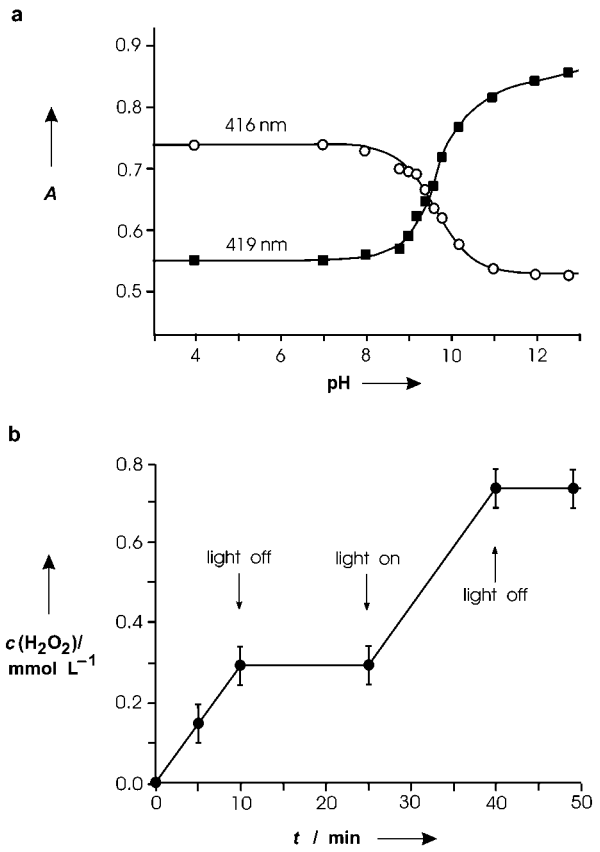


Figure 2. *Control and regulation of the catalytic activity. a) Spectrophotometric titration curves in aqueous buffer solution demonstrate the interconversion of $[Sb(tpp)(OH)_2]^+$ (open circles) and the metal-oxo form SbO(tpp)OH, (filled squares) with $pK_a = 9.7 \pm 0.1$ at 25 °C. Note that phenoles such as tyrosine show similar pK_a values. b) Accumulation of hydrogen peroxide during monochromatic irradiation of 8.0×10^{-5} M SbO(tpp)OH at 546 nm (5.6 mW cm^{-2}, 25 °C, 1 atm air pressure) in a 2:1 mixture of ethanol and 0.1 M NaOH. Equimolar amounts of acetaldehyde and H_2O_2 are detected after t = 50 min. The photoassisted substrate conversion is completely switched off in dark periods, which corresponds to a convenient reversible noncompetitive inhibition of the catalysis.*

are destroyed, this value corresponds to an average turnover number (TON) of $\geq$4000 cycles of each catalyst molecule before degradation. Under typical reaction conditions (Figure 2b) the amount of products formed is proportional to the total number of photons absorbed and the substrate transformation according to Equation (2) also proceeds when polychromatic lamp light or sunlight are applied as an irradiation source. Even diffuse daylight is sufficient to maintain a slow catalytic reaction.

The efficiency of the photochemically driven substrate conversion can be compared with other natural and artificial systems that are capable of catalyzing the oxidation of alcohols under mild conditions (Table 1). With the exception of alcohol oxidase, a native flavoprotein specialized for ethanol and methanol transformation, the specific activity of SbO(tpp)OH can very well compete with that of other enzymes and the best synthetic model systems known so far.

Scheme 2 illustrates a proposed mechanism for the homogeneous photocatalytic substrate conversion process according to the overall stoichiometry given in Equation (2). The redox cycle

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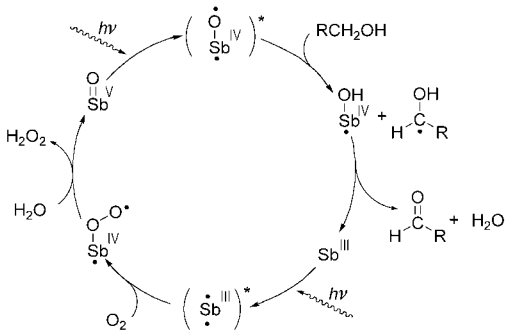
Table 1. *Comparison of different homogeneous catalysts for the aerobic oxidation of ethanol to acetaldehyde under ambient conditions.[a]*

Catalyst system (source)	Characteristics	k_{cat} [s^{-1}]	Spec. activity [$\mu mol\,mg^{-1}\,min^{-1}$][b]	Ref.
alcohol oxidase (*Poria contigua*)[c]	flavoprotein (FAD, no metal)	200	19.43	[17]
galactose oxidase (*Fusarium spp.*)	copper enzyme (tyrosyl radical)	0.02[d]	0.02	[18]
cytochrome P450 (human CYP2E1)	heme protein (iron porphyrin)	0.21[e]	–[e]	[19]
OEC of PS II (green plants)[f]	manganese cluster (tyrosyl radical)	0.38	0.47	[20]
$[Cu(L^4)]PF_6$ (synthetic)[g]	metal complex (phenoxyl radical)	0.03[d]	2.31	[21]
SbO(tpp)OH, *hν* (synthetic)	metalloporphyrin (546-nm light)[h]	0.01[d]	0.46	this work
SbO(tpp)OH, *hν* (synthetic)	metalloporphyrin (sunlight)[i]	0.05[d]	3.34	this work

[a] At 25 °C unless otherwise stated; note that the rates are a function of the irradiance in the photon-driven systems. [b] Specific activity in units per milligram of catalyst. [c] At 30 °C; the enzyme consists of eight FAD-containing subunits. [d] Identical to the turnover frequency (TOF). [e] At 37 °C; molecular weight not available. [f] Oxygen-evolving complex of photosystem II reaction center; specific activity per milligram of chlorophyll. [g] At 22 °C, $(L^4)^{-1}$ = monoanion of *N*-(3,5-di-*tert*-butyl-2-hydroxyphenyl)-*N*′-(3,5-di-*tert*-butyl-2-phenoxyl)-1,2-diiminoquinone. [h] Monochromatic irradiation, 5.6 $mW\,cm^{-2}$. [i] Calculated for polychromatic solar irradiation at sea level (air mass AM = 2.0)[22] with a threshold wavelength of 600 nm corresponding to 40.6 $mW\,cm^{-2}$.



Scheme 2. *Proposed mechanism for the photocatalytic oxidation of primary alcohols by dioxygen. Irradiation of the antimony(v) oxo species is followed by hydrogen abstraction from the substrate, electron transfer, and subsequent release of aldehyde and water. The reduced antimony(iii) form of the catalyst is photochemically reoxidized in the presence of dioxygen[16] to regenerate the active antimony(v) species and hydrogen peroxide. During steady-state irradiation, the photostationary mixture almost exclusively contains the oxidized form of the catalyst, which suggests that hydrogen atom transfer is the rate-determining step of the cycle.*

consists of two coupled photochemical reactions. Upon visible light irradiation the oxidized catalyst relaxes to an excited state with partial charge transfer (CT) character (mixed ligand-to-metal/ligand-to-ligand CT), in which an oxyl-radical-type axial electron distribution is achieved and the second unpaired spin is delocalized between the central atom and the stabilizing porphyrin ligand (not shown). This species attacks the primary alcohol substrate by a hydrogen abstraction step which is followed by an electron transfer to release the aldehyde product and the low-valent form of the catalyst. The antimony(iii) complex is photochemically reoxidized via a metal-centered sp-excited state (s^1p^1 electronic configuration) that undergoes spin pairing with dioxygen and release of peroxide to regenerate the high-valent starting compound. This second part of the catalytic cycle has been investigated in more detail before.[16] At very high levels of product accumulation a slow competing thermal oxidation of the low-valent form of the catalyst by hydrogen peroxide is possible,[16] which should lead to an increasing self-inhibition of the system when the permanent products are not removed from the reaction mixture.

The present results demonstrate that bionic design principles, together with the exploitation of light as a source of information and thermodynamic driving force, can lead to efficient catalysts with artificial enzymatic function (photozymes). Convenient regulation and activation by photons under mild reaction conditions makes this novel approach very attractive for the development of benign solar chemical processes.

Experimental Section

The reduced antimony(iii) and the oxidized antimony(v) forms of the photocatalyst were prepared as described elsewhere.[13, 16] The neutral metal-oxo species[23] SbO(tpp)OH was generated in situ by deprotonation with aqueous sodium hydroxide. The pK_a value for this reaction was determined spectrophotometrically in thermostated aqueous buffer solutions. All other experiments were performed at 298 K under aerobic conditions in the presence of large excess amounts of the corresponding alcohols (methanol, ethanol) to ensure substrate saturation conditions at various light intensities (typically alcohol/water = 2:1, 0.1 mM catalyst, pH 12.5).

Electronic spectra were recorded with an Uvikon 860 double-beam spectrophotometer. Continuous monochromatic photolysis (546 nm) was carried out with a Hanovia Xe/Hg 977 B-1 (1 kW) lamp equipped with a Schoeffel GM 250-1 monochromator. Quantum yields of product formation were determined with a calibrated Polytec pyroelectric radiometer (RkP-345 detector). Polychromatic irradiation experiments were performed by direct exposure of samples to sunlight in Pyrex vessels. The accumulation of aldehydes was followed by a specific colorimetric assay[24] in a commercially available version (Merck). Hydrogen peroxide was determined quantitatively by the peroxidase-catalyzed oxidation of 4-aminophenazone in the presence of chromotropic acid.[25]

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