Homogeneous Catalysis

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Switchable Catalysis

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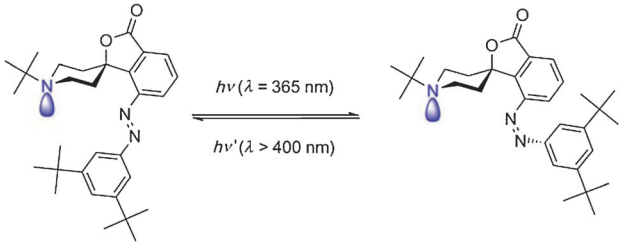
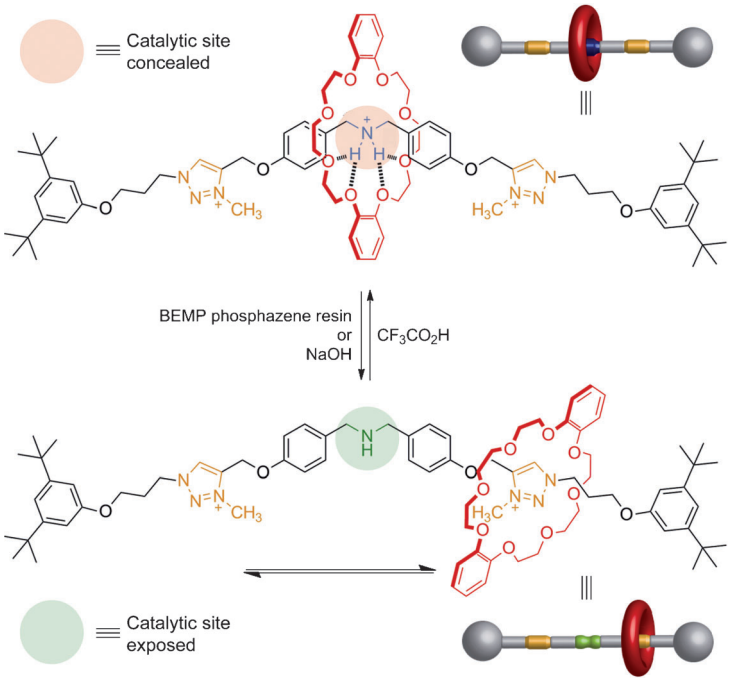
In the living cell, uncountable reactions occur in parallel. To ensure that all these processes proceed without interfering with one another, these operations must be controlled, their function must be switchable, and the switching must be reversible.[1] But "function by switching" is not only crucial for life, it is also important for materials. What kind of input can be used for switching, what kind of function can be switched?

The physical properties of molecules, for instance optical or magnetic properties, can be switched by external stimuli. But also chemical reactivity can be turned on and off. The external signals may be of physical nature, for instance irradiation, or of chemical nature. The simplest chemical input is a change of the pH value but also supramolecular interactions such as hydrogen bonding and ligand-to-metal complexation may be the stimuli for reversible switching.



Scheme 1. Photoswitchable piperidine base.[4]

While the switching of optical has been possible for quite some time—with the chemical calculator (moleculator) being one prominent example[2]—the switchable control of chemical reactivity, and specifically catalysis, has only recently gained momentum.[3] In 2008, Hecht and co-workers[4] described a tertiary piperidine base that bears an azo residue (Scheme 1). When switched by irradiation, the *E* azo group isomerizes into the *Z* isomer resulting in increased exposure of the basic nitrogen atom. Upon irradiation with light of a longer wavelength, the piperidine nitrogen atom is shielded again. The organic base is switchable by light.



Scheme 2. A rotaxane with an amine unit and two triazolium ions in the axis can be switched by protonation.[5]

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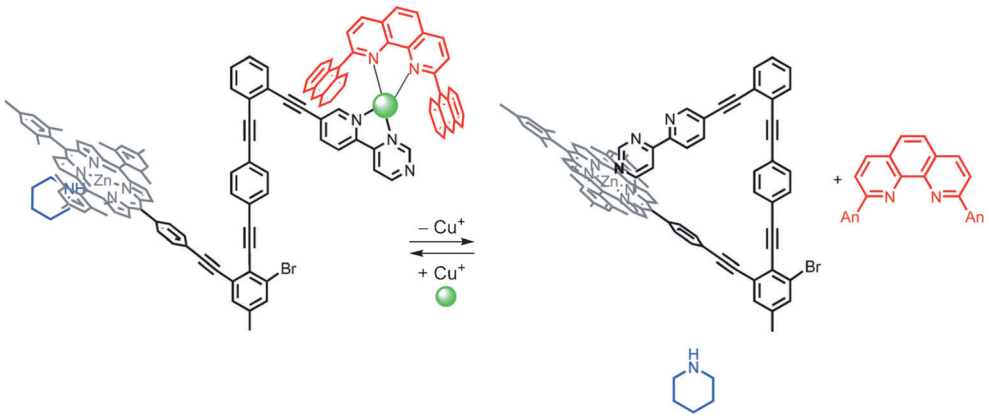
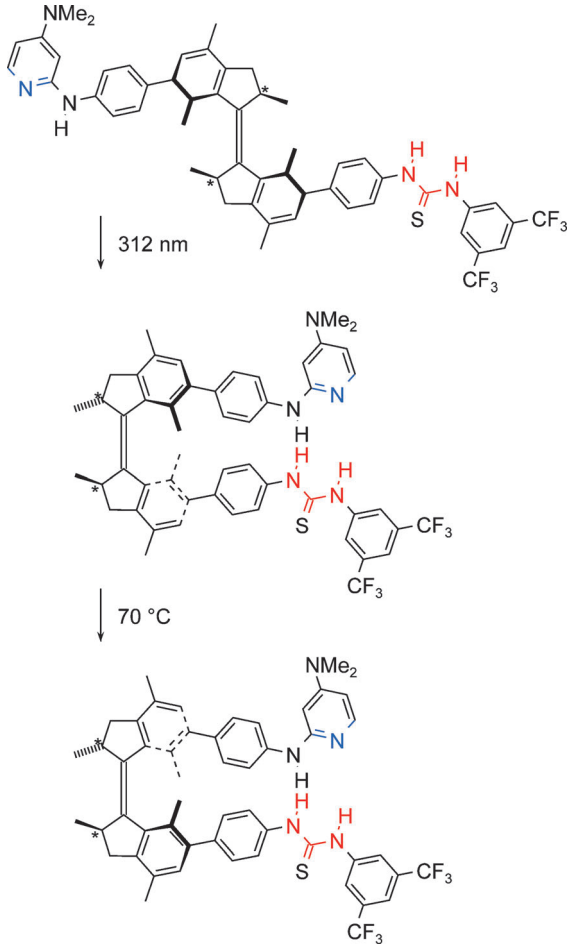


Scheme 3. The coordination of a 4-aza-2,2′-bipyridine tether to a zinc porphyrin can be switched on and off by removal or addition of copper(I) ions (An = anthracene). In the four-coordinate state, the zinc ion scavenges piperidine from the solution and thus piperidine organocatalysis is not possible.[6]

In addition to being bases, secondary amines can be used as nucleophilic catalysts and both imine and enamine organocatalysis is possible. Leigh et al.[5] reported on a rotaxane with a secondary amine in its axis (Scheme 2). When protonated, the ammonium ion becomes the recognition site for the crown ether ring of the rotaxane. The ring is bound at this site and the protonated amine is shielded. The axis also contains two triazolium sites. When the pH is increased to deprotonate the ammonium ion, the ring is no longer bound there but at one of the heteroaromatic ions. Thus by change of pH, the ammonium ion is switched into a secondary amine which is capable of acting as an organocatalyst. The conjugate addition of a thiol to an enal such as cinnamonaldehyde (see Scheme 5) was catalyzed efficiently (83% yield) by the unprotonated rotaxane, while no reaction was observed when the amine was protonated and shielded by the ring. Control experiments with the axis alone showed that the shielding and stabilization of the protonated ammonium ion by the ring in the rotaxane is crucial for the off/on function.

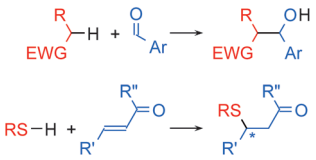
A second example of switchable organocatalysis has been described recently by Schmittel and co-workers.[6] They prepared a zinc porphyrin complex in which the coordination number at the zinc ion can be switched from five to four (Scheme 3). Here, the stimulus is the addition of another transition-metal ion, a copper(I) ion bound to a shielded 1,10-phenanthroline. Without copper, the fifth coordination site of the zinc atom is occupied intramolecularly by a pyrimidine tether. By design, the pyrimidine itself is part of a 4-aza-2,2′-bipyridyl system. The two not yet complexing nitrogen atoms can bind to added copper in a chelating fashion. Then, steric repulsion leads to a decomplexation of the tether from the zinc porphyrin, and the fifth binding site at the zinc atom is liberated. Back-switching is possible by removal of the copper(I) ions and this is possible by adding cyclam as a stronger copper complexing ligand. The authors exploit the switchability of the fifth coordination site to control the binding of piperidine. In the presence of copper, the tether is removed from the zinc center and piperidine is bound at the fifth coordination site. When copper is removed, piperidine is liberated. It was shown that a piperidine-catalyzed Knoevenagel reaction (see Scheme 5) can be switched off and on by the addition and removal of copper(I) to this system.



Scheme 4. From top to bottom: the (*P*,*P*)-*trans* stereoisomer of a unidirectional molecular motor with catalytic activity [the chiral centers always remain (*R*,*R*); the ethene bond is drawn with an extended length for clarity reasons]. Upon irradiation, switching occurs and the (*M*,*M*)-*cis* isomer forms. Now the two catalytic centers are close to one another and catalysis is enhanced. Thermal isomerization gives a second catalytically active isomer, (*P*,*P*)-*cis*.[7]

Bifunctional organocatalysis has also been switched. Feringa and Wang[7] connected a tertiary amine as a Brønsted base and a thiourea as a twofold hydrogen bond donor to the framework of their unidirectional molecular motor (Scheme 4). The switching part is a chiral tetrasubstituted C–C double bond which can be isomerized from *trans* to *cis* and vice versa. Additional helical chirality leads to four stereochemical states of the motor. These states are accessible by successive irradiation with light of different wavelengths and heating. It could be shown that the different stereoisomers not only showed different catalytic activity, the enantioselectivity of the organocatalytic addition of a thiol to an enone (see Scheme 5) could be switched from 1:1 [(*P*,*P*)-*trans*] to 3:1 [(*M*,*M*)-*cis*] or 1:3 [(*P*,*P*)-*cis*].

These recent advances in the field of switchable molecules should encourage future research on "function by switching". The organocatalysts can be switched on and off at will; the reactions that can be switched in this way at present are shown in Scheme 5. The switching signals may vary: light, pH, or another chemical species. By a combination of several catalysts and different input signals, the goal of influencing several catalytic processes selectively in parallel (orthogonal!) should become possible.



Scheme 5. Organocatalyzed reactions that can be switched on and off. Top: aldol type additions of C–H acids (EWG = electron-withdrawing group) to carbonyl compounds (with catalysts from Scheme 1 and 3). Bottom: Michael additions of thiols to unsaturated carbonyl compounds (with catalysts from Scheme 2 and Scheme 4).

Furthermore, the switchable porphyrin complexes have the potential of switchable catalytic activity and/or selectivity through the action of the transition-metal ion in the complex itself. A recent example of a switchable metal catalyst has been described by Mirkin et al.,[8] who used an aluminum salen complex for the ring-opening polymerization of ε-caprolactam; in this case the catalytic activity was switched by yet another chemical input: chloride ions.

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