Angewandte Chemie International Edition

Photochemistry

DOI: 10.1002/anie.201307206

# Homogeneous Visible-Light Photoredox Catalysis**

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*Dedicated to Professor Xiyan Lu on the occasion of his 85th birthday*

alkylation · green chemistry · homogeneous catalysis · photochemistry · synthetic methods

Exploring conceptually new catalytic modes for chemo- and regioselective activation of small molecules and chemical bonds is a key feature of modern chemistry.[1] In this regard, metal catalysis,[2] organocatalysis,[3] as well as biocatalysis[4] have fascinated chemists for decades. Fundamental chemical transformations based on these three kinds of catalytic modes have been well established over the past century. These catalytic methods have also been widely applied to chemical industry for the synthesis of numerous useful compounds and materials. Despite advances, the search for sustainable and green methods for the preparation of fine chemicals is a highly desirable goal.[5] During the last five years, homogeneous photoredox catalysis[6] using visible light has emerged as a novel activation mode to advance these goals because of the inherent green chemistry features of visible light, including nonpollution and abundance. Currently, visible-light photoredox catalysis is regarded as a flourishing research field thanks to the effectiveness of $[Ru(bpy)_3]^{2+}$ and similar metal polypyridyl complexes as well as organic dyes.

Two distinctive pathways, reductive and oxidative quenching, are frequently introduced to describe the mechanism of visible-light photoredox catalysis. The former means the reductive quencher such as a tertiary amine reduces the excited-state photocatalyst to the low oxidation ground-state species and the latter is the oxidative quencher. For example, methyl viologen oxidizes the excited state photocatalyst to the corresponding high oxidation ground-state species. Seminal works by the groups of MacMillan and others[6] have explored features of processes involving these two kinds of single-electron-transfer (SET) pathways. Despite the obvious appeal of this methodology, visible-light photoredox catalysis also suffers from several challenging problems. In most cases only one reactant is activated in the quenching cycles, and extra oxidants or reductants, which are eventually sacrificed, need to be added to complete the catalytic cycle. Accordingly, the design of a new strategy involving simultaneous activation of two or more reaction partners in a single photoredox catalytic cycle, designated as “killing two birds with one stone” by us in this highlight, is in high demand (Scheme 1).

In 1992, a similar strategy was used by the Kisch group in heterogeneous photocatalytic addition reactions between cyclic enol ethers and 1,2-diazenes.[7] The reaction was driven by electron ($e^-$) and hole ($h^+$) pairs which were generated in the presence of either ZnS or CdS under irradiation of visible or ultraviolet light (Scheme 2). The photogenerated electron reduced the 1,2-diazene **1** to the nitrogen-centered radical **4**, and in the meantime the positively charged hole oxidized the enol ether **2** to the radical intermediate **5**. The coupling of **4** and **5** then afforded the corresponding product **3**. However, the photocorrosion of the semiconductor photocatalyst as well as the reaction efficiency and chemoselectivity have often limited the broad applications of this methodology in synthetic chemistry. Therefore, the introduction of this concept into homogeneous visible-light photoredox catalysis will provide a robust and useful platform for new reaction designs

A major breakthrough in the realm of homogeneous visible-light photoredox catalysis was disclosed by the group of MacMillan, and it elegantly highlighted this strategy. In 2011, MacMillan and co-workers described the visible-light induced C−H arylation of various tertiary amines with benzylic amines by means of an accelerated serendipity method (Scheme 3).[8] The reaction is initiated by an oxidative quenching between the excited state $[Ir(ppy)_3]^*$ and 1,4-dicyanobenzene (DCB) in light of their oxidation or reduction potential, thus generating the radical anion **9**. The resultant high oxidation, ground-state species $[Ir^{IV}(ppy)_3]$ interacted subsequently with the other amine **6** by a single-electron transfer to give the amine radical cation **10** with the release of $[Ir(ppy)_3]$ to complete the catalytic cycle. The α-amine radical **11** was generated from the intermediate **10** with the aid of NaOAc by deprotonation. The next step is the radical–radical coupling process of **9** and **11** with subsequent release of $CN^-$ to give the benzylic amine product **8**. The significance of this transformation is that the two coupling partners, amine and 1,4-DCB, were activated simultaneously. Remarkably, no extra oxidative or reductive reagent was introduced in this reaction. This attractive strategy might provide important insights into visible-light photoredox catalysis and help us to design new types of reactions in a more green and sustainable manner.

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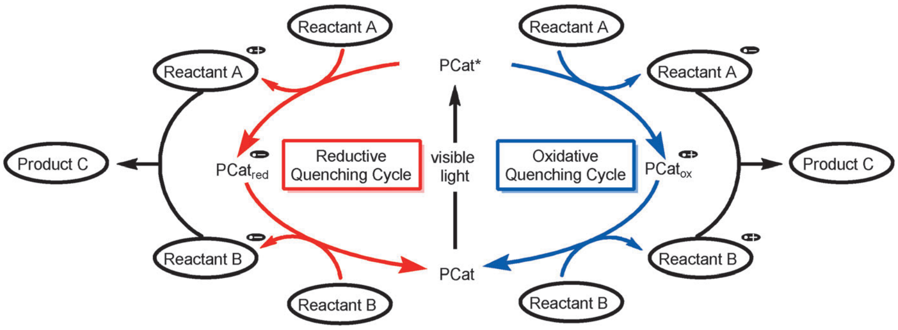
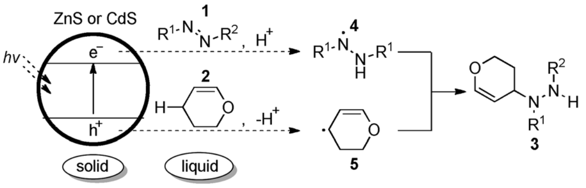
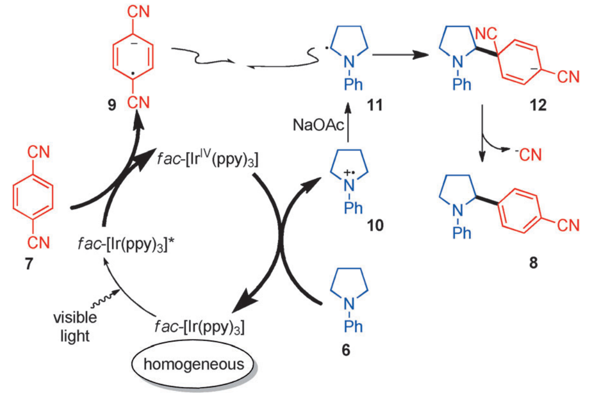
[**] Financial support by the National Science Foundation of China (NO. 21232003) and the National Basic Research Program of China (2011CB808603) are gratefully acknowledged. Y.-Q.Z. thanks the Excellent Doctorial Dissertation Cultivation Grant from Central China Normal University (CCNU13T04094).



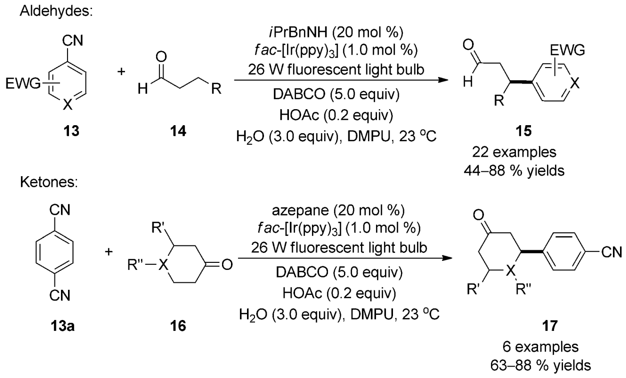
**Scheme 1.** Concept of "killing two birds with one stone" in visible-light photoredox catalysis. PCat = photocatalyst.



**Scheme 2.** Heterogeneous photocatalytic addition reactions in the presence of semiconductor catalyst ZnS or CdS.



**Scheme 3.** Proposed mechanism of visible-light induced α-amino C—H arylation. ppy = 2-phenylpyridine.



**Scheme 4.** Visible-light induced β-arylation of aldehydes and ketones. DABCO = 1,4-diazabicyclo[2.2.2]octane, DMPU = 1,3-dimethyl-3,4,5,6-tetrahydro-2(1*H*)-pyrimidinone, EWG = electron-withdrawing group.

In addition, the group of MacMillan successfully combined visible-light photoredox catalysis and organocatalysis to realize the enantioselective intermolecular α-alkylation of aldehydes in 2008.[9] Importantly, they have now expanded this synergistic strategy to target β-functionalized carbonyls. In this context, they have developed a conceptually new approach to β-arylation of saturated aldehydes and ketones using an interesting visible-light-induced mode in combination with organocatalysis.[10] This methodology tolerates a wide range of carbonyls, and various aldehydes and ketones coupled with either cyanobenzene or cyanoheteroaromatics under the optimized reaction conditions to afford the corresponding products in moderate to good yields (Scheme 4). To examine the enantioselective variant of this reaction, a cinchona-derived amine was introduced as the organocatalyst, and the enantioenriched product was obtained in 82% yield, albeit with moderate enantiomeric excess (50%). Aldehydes or ketones were first activated by the amine and the resulting emamine intermediate, together with the coupling partner cyanobenzene, participated in the photoredox cycle simultaneously.

In conclusion, recent advances in homogeneous, visible-light photoredox catalysis are highlighted with a focus on the activation of the two reaction partners simultaneously under reaction conditions which do not require a quenching reagent. One of the substrates serves as an oxidant and the other serves as a reductant to complete the catalytic cycle. The activation mode wherein two reaction partners are activated in one catalytic system make this protocol quite attractive, and it provides an atom-economic and environmentally benign way to synthesize useful building blocks and products. We believe that this "killing two birds with one stone" strategy will help chemists to design more and more interesting, useful, and sustainable reactions in the near future.

Received: August 16, 2013

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