Illuminating Inert Bonds: LMCT Catalysis at the Frontiers of Sustainable Chemistry

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Illuminating the Future of Sustainable Synthesis

The demand for sustainable synthesis compels chemistry to reinvent its strategies for molecular construction. Traditional approaches, often dependent on noble metals, high energy input, and hazardous reagents, face mounting limitations in light of environmental and economic concerns. In this context, visible-light photocatalysis has rapidly ascended as a transformative platform. By directly harnessing the energy of photons, it enables chemical transformations that are not only efficient and versatile but also inherently aligned with the principles of green chemistry.

Among the most compelling opportunities created by this approach is the selective functionalization of inert bonds—particularly C–H and C–C bonds. These bonds are omnipresent and form the very skeleton of organic molecules, yet their stability makes them resistant to direct transformation. Photocatalysis provides a unique solution by accessing highly reactive open-shell intermediates under mild conditions, offering pathways to convert simple hydrocarbons into complex and valuable products. [1, 2] This reactivity expands the synthetic toolbox, creating unprecedented opportunities for molecular design and feedstock valorization.

Yet, with opportunity comes challenge. The same radical pathways that enable access to unreactive bonds also confront us with fundamental questions of control—how to precisely govern transient intermediates, balance broad substrate scope with selectivity, and translate these advances into scalable processes. Addressing such challenges calls for strategies beyond currently employed noble metal photocatalysts, turning instead to earth-abundant metals as sustainable alternatives. These systems not only reduce costs and improve accessibility but also open new possibilities for regulating radical reactivity and tuning the interplay between light excitation and bond activation, thereby laying the foundation for more efficient and sustainable photocatalytic methods, as exemplified by recent advances with inexpensive metal catalysts.

Transforming Inert Bonds through LMCT Catalysis

In my lab, we established the LMCT catalysis platform that enables selective activation of inert $C(sp^3)$–H and $C(sp^3)$–$C(sp^3)$ bonds.(Fig 1.) This strategy operates through coordination of the substrate to a high-valent metal complex, photoexcitation of the LMCT band, and subsequent bond homolysis. Unlike conventional photoredox catalysis, which relies on single electron transfer from an excited or oxidized photocatalyst, LMCT catalysis embeds the oxidation step directly into the excitation event. As a result, oxidation occurs exclusively at the transiently coordinated functional group, while more easily oxidized functionalities remain untouched.

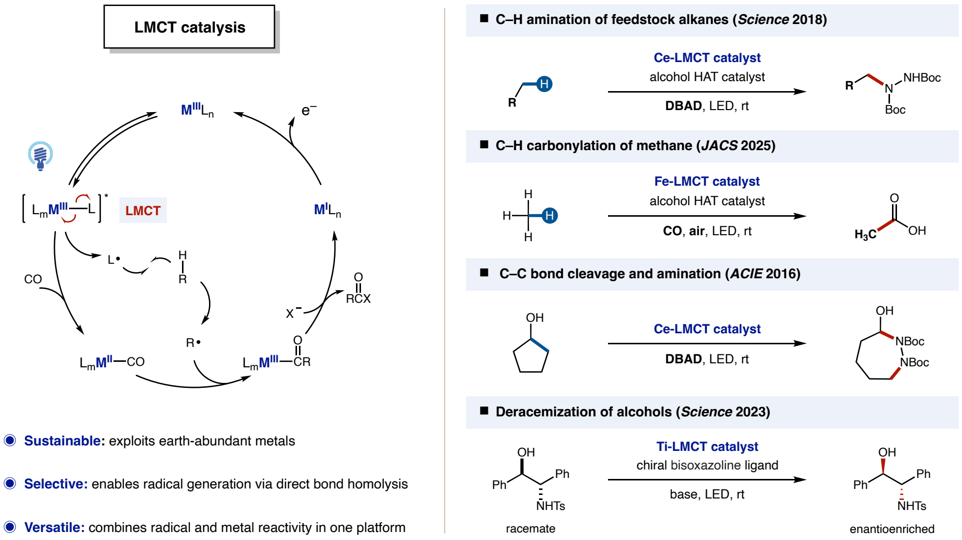

Fig. 1. LMCT catalysis for the selective functionalizations of the C–H and C–C bonds.

This unique selectivity allows us to accomplish open-shell activations that were previously inaccessible—such as the direct oxidation of alkoxides to alkoxy radicals. By simply irradiating the coordination complex of a substrate with a high valent metal such as Ce(IV), we generate alkoxy radicals in a straightforward and broadly applicable fashion under mild conditions. The beauty of the system lies in its simplicity: no specialized photocatalyst is required, and the substrate–metal coordination itself triggers photocatalytic activity. With this platform, we have harnessed alkoxy-radical-mediated HAT to selectively functionalize inert C–H bonds. For instance, we demonstrated highly selective amination, alkylation, and arylation of methane and other gaseous alkanes under ambient and extremely mild conditions [3,4]. The key lies in the controllable generation of alkoxy radicals that can efficiently abstract hydrogen from methane.

Building on this foundation, we developed an Fe-LMCT catalyzed aerobic carbonylation of methane [5]. Under LED irradiation at room temperature, a single iron catalyst orchestrates both the generation of methyl radicals and their selective capture. This dual control over radical initiation and trapping overcomes the notorious challenge of unselective aerobic oxidation, delivering unprecedented selectivity for carbonylation. Central to this success is the radical–metal synergy enabled by the photoinduced iron-

LMCT system, which we believe will continue to unlock new opportunities for open-shell transformations under mild conditions.

We further extended this paradigm to C–C bond activation through alkoxy radical β-scission [6]. Here, LMCT catalysis cleaves C–C bonds adjacent to hydroxyl groups, avoiding strain-release strategies typically required by transition-metal pathways. Selectivity is governed by the stability of the carbon-centered radical formed, which can then be trapped in diverse ways—for example, with amination reagents to forge C–N bonds. Beyond amination, the same radical intermediate drives alkylation, HAT reduction, oxidation, and cross-coupling—showcasing LMCT catalysis as a general strategy for skeletal modification.

More recently, we applied LMCT catalysis to stereochemical editing. We developed an LMCT-enabled deracemization platform that reversibly cleaves and reforms C–C bonds in cycloalkanols and amino alcohols [7]. Using a single chiral Ti catalyst—ligated with a chiral phosphoric acid or bisoxazoline ligand—we achieved efficient enantioselective deracemization, even for substrates with adjacent or fully substituted stereogenic centers. The process delivers enantioenriched alcohols with excellent selectivity, highlighting how LMCT catalysis can merge radical reactivity with stereocontrol through multiplicative stereoinduction.

Beyond Excitation: Outlook on LMCT Catalysis

LMCT catalysis has also been extended to a wide range of transformations, including decarboxylative functionalization [8, 9, 10], alkene activation [11, 12], and other valuable reactions. A key advantage lies in its reliance on earth-abundant metals, whose flexible valence states can engage in diverse elementary steps. Importantly, LMCT excitation and subsequent bond homolysis generate low-valent metal species that are often overlooked but can themselves function as active catalysts, mediating bond formation or classical organometallic steps. This dual reactivity highlights the potential of LMCT to merge radical pathways with transition-metal catalysis in innovative ways. Moreover, radical intermediates produced via LMCT can interact intimately with the metal center, and both radical and metal species can be tuned through ligand design and reaction conditions. Such compatibility allows LMCT catalysis to integrate smoothly into established catalytic cycles, thereby broadening the scope of sustainable synthesis.

Looking ahead, a central challenge is to control the reactivity of high-valent metal species in their LMCT excited states. Ligand design will be critical in modulating both radical and metal intermediates, while kinetic parameters—such as homolysis rates, radical lifetimes, and trapping efficiencies—must be understood in the context of excited-state potential energy surfaces. Advances in ultrafast spectroscopy and time-resolved techniques are beginning to reveal these transient dynamics, although capturing shortlived species remains difficult. Equally important is elucidating the interplay between radicals and metal fragments, where effects such as solvation, cage escape, and electronic repulsion strongly influence catalytic outcomes. Systematic exploration of these fundamental aspects will expand the utility of LMCT catalysis, consolidating its role as a versatile and sustainable platform for complex molecule synthesis and functional material development.

Acknowledgments

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