

ORGANIC DYES AS PHOTOREDOX CATALYSTS

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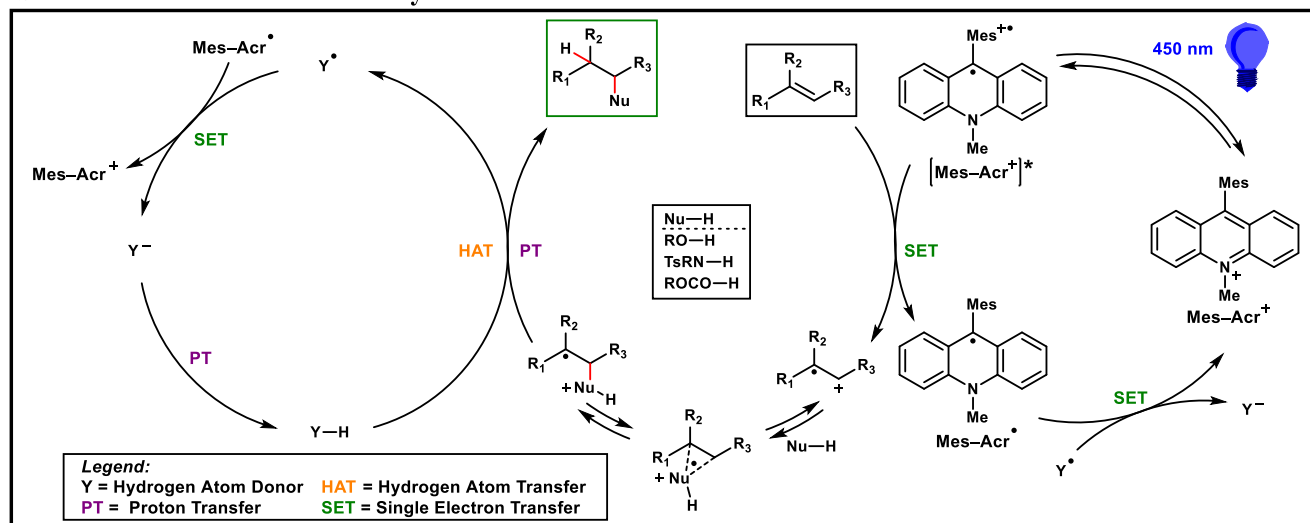
INTRODUCTION

The essential role that single-electron transfer (SET) reactions play in biological processes has inspired the development of synthetic methods to access radicals. While many methods require harsh conditions or toxic metals, photoredox catalysis has emerged as a mild means to afford single electron chemistry. Transition metal complexes are most widely used as photoredox catalysts; however, certain organic dyes serve as inexpensive and metal-free alternatives.¹ The 9-mesityl-10-methylacridinium ion (Mes-Acr⁺) is an exceptional catalyst capable of redox chemistry inaccessible to common transition metal photoredox catalysts. Among the reactions catalyzed by Mes-Acr⁺ are anti-Markovnikov hydrofunctionalizations,² cycloadditions,^{3,4} and arene functionalizations.⁵

ANTI-MARKOVNIKOV HYDROFUNCTIONALIZATIONS

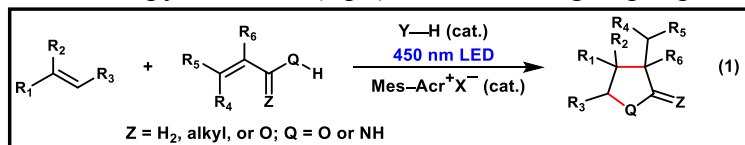
The Nicewicz group applied Mes-Acr⁺ as a photoredox catalyst for the intramolecular anti-Markovnikov hydroetherification and hydroamination of olefins to form cyclic ethers and amines, respectively.¹ Intermolecular reactions with amines,^{2a} carboxylic acids,¹ and mineral acids^{2b} are also possible under similar conditions. The olefin undergoes oxidation to a cation radical followed by nucleophilic attack to regioselectively form the more stable radical. Deprotonation and hydrogen atom transfer (HAT) then generate the product (Scheme 1). Anti-Markovnikov hydrotrifluoromethylation of alkenes was achieved using sodium trifluoromethylsulfinate as a trifluoromethyl radical source. Notably, Ru(bpy)₃ was ineffective as a catalyst for the hydrofunctionalization reactions. These studies served as an initial demonstration of the mild conditions, functional group tolerance, and oxidizing power of Mes-Acr⁺ as a photoredox catalyst.

Scheme 1. Anti-Markovnikov Hydrofunctionalization of Alkenes



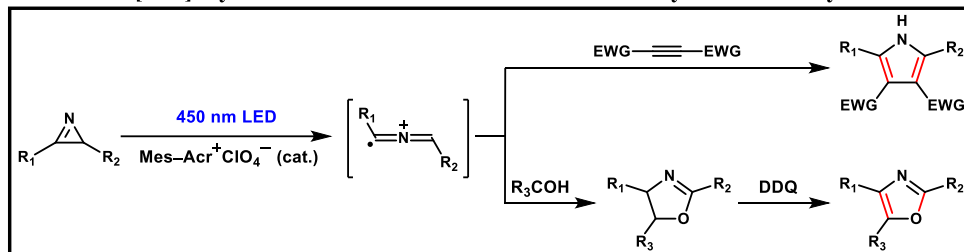
CYCLOADDITIONS

The cation-radical generated from alkene oxidation undergoes polar radical crossover cycloadditions (PRCC) with alkenyl nucleophiles. The reaction was developed for the synthesis of highly substituted tetrahydrofurans,¹ lactones,^{3a,3b} lactams, and pyrrolidines (eq 1).^{3c} The Xiao group reported the oxidation of 2*H*-azirines to afford cation radicals that undergo [3+2] cycloaddition with alkynes⁴ and aldehydes^{4b} (Scheme 2).



The method was applied to the syntheses of an HMG-CoA reductase inhibitor and a cyclooxygenase-2 inhibitor.

Scheme 2. [3+2] Cycloadditions from 2*H*-Azirines and Alkynes or Aldehydes



ARENE FUNCTIONALIZATIONS

The Nicewicz group recently showed that Mes-Acr⁺ and derivatives catalyze the direct C-H amination of electron rich arenes with nitrogen heterocyclic nucleophiles.⁵ The value of this method in drug design and natural product synthesis was demonstrated in the late stage derivatization of biologically active molecules. Anilines were synthesized in a similar fashion using ammonium carbamate as an ammonia equivalent.

CONCLUSION

Photoredox catalysis provides a mild approach to single-electron chemistry. Transition metal complexes are most commonly used as catalysts, but organic dyes are often more powerful excited state oxidants that afford functionalization of challenging substrates. The unique properties of photoexcited Mes-Acr⁺ have led to its recent development as a catalyst for several valuable transformations.

REFERENCES

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