

UC Irvine

UC Irvine Previously Published Works

Title

An Enlightening Reactor

Permalink

<https://escholarship.org/uc/item/5z63f5q6>

Journal

ACS Central Science, 3(6)

ISSN

2374-7943

Authors

Kim, Daniel K
Dong, Vy M

Publication Date

2017-06-28

DOI

10.1021/acscentsci.7b00218

Copyright Information

This work is made available under the terms of a Creative Commons Attribution License, available at <https://creativecommons.org/licenses/by/4.0/>

Peer reviewed

An Enlightening Reactor

Daniel K. Kim and Vy M. Dong

Department of Chemistry, University of California, Irvine, California 92697, United States

A photoreactor from a collaboration between the MacMillan Lab and Merck could provide a widespread tool for synthetic chemists in the photoredox space.

In recent years, the reaction vessel by which chemists perform organic reactions has undergone major changes. No longer limited to round-bottom flasks, we can perform experiments in microwave ovens, flow reactors,^{1–3} and 96-well plates.^{4,5} Each of these technologies has enabled breakthroughs in organic synthesis not easily achieved using conventional flasks. In the rapid development of photoredox technology, a gap in physical technology has led to a wide range of protocols that use different light sources.⁶ A standard, affordable reactor that is easy to use would accelerate the use of photoredox methodology. To address this, a collaboration between Merck researchers and the MacMillan laboratory at Princeton has produced an integrated photoreactor built with a modular design (Figure 1).⁷

The simple and elegant design allows for efficient catalysis of photoredox reactions. A sampling of top pharmaceutical photoredox coupling reactions were tested with the new integrated photoreactor. In general, the small-scale photoreactor could be employed broadly. The new photoreactor enables rate accelerations between 2 to 20 times when evaluating various photoredox transformations using a 360° light source. The designer photoreactor could also precisely control the LED output power, a parameter previously challenging to control.

The silyl-mediated cross-electrophilic cross-coupling reaction was sensitive to the buildup of hydrobromic acid at the maximum LED output level (Figure 2).⁸ However, by precisely controlling the power level, the scientists could balance reaction rates, which resulted in a 6-fold improvement in reaction time. In the future, the development of a photoreactor that can hold multiple reaction vials will enable accelerated discoveries for new technologies in fragment-based coupling reactions.

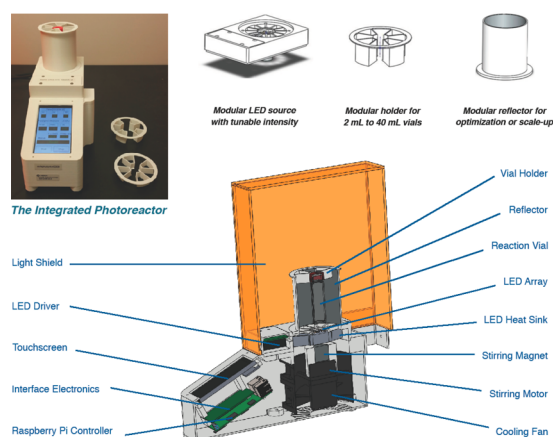


Figure 1. A simple modular design for an LED powered photoreactor. Reprinted with permission from ref 7. Copyright 2017 American Chemical Society.

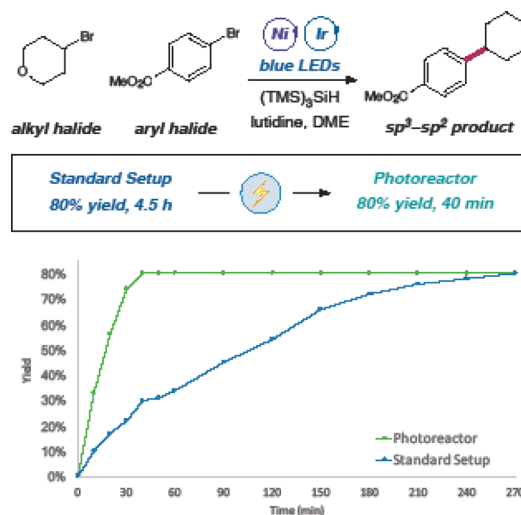


Figure 2. Balancing optimal output LED power for enhanced reactivity. Reprinted with permission from ref 7. Copyright 2017 American Chemical Society.

Most importantly, these integrated photoreactors were implemented across 10 different medicinal chemistry groups at 4 different Merck research sites. This led to the successful standardization of LED protocols used across the sites. Synergistic partnerships between academia and industry

Published: June 9, 2017

The new photoreactor enables rate accelerations between 2 to 20 times when evaluating various photoredox transformations using a 360° light source.

often present opportunities to pool ideas and resources to solve synthetic challenges.⁹ The advent of the integrated photoreactor should improve the ability to translate protocols from academia to industry due to its modularity and ease of use. This integrated photoreactor will augment the translation of protocols from academia to industry and light a path for developing the molecules of tomorrow.

Author information

E-mail: dongv@uci.edu.

ORCID 

Vy M. Dong: [0000-0002-8099-1048](https://orcid.org/0000-0002-8099-1048)

REFERENCES

- (1) Wegner, J.; Ceylan, S.; Kirschning, A. Ten Key Issues in Modern Flow Chemistry. *Chem. Commun.* **2011**, *47*, 4583.
- (2) Tucker, J. W.; Zhang, Y.; Jamison, T. F.; Stephenson, C. R. J. Visible-Light Photoredox Catalysis in Flow. *Angew. Chem., Int. Ed.* **2012**, *51*, 4144.
- (3) Andrews, R. S.; Becker, J. J.; Gagné, M. R. A Photoflow Reactor for the Continuous Photoredox-Mediated Synthesis of C-Glycoamino Acids and C-Glycolipids. *Angew. Chem., Int. Ed.* **2012**, *51*, 4140.
- (4) Corcoran, E. B.; Pirmot, M. T.; Lin, S.; Dreher, S. D.; DiRocco, D. A.; Davies, I. W.; Buchwald, S. L.; MacMillan, D. W. C. Aryl Amination Using Ligand-Free Ni(II) Salts and Photoredox Catalysis. *Science* **2016**, *353*, 279.
- (5) McNally, A.; Prier, C. K.; MacMillan, D. W. C. Discovery of an α -Amino C–H Arylation Reaction Using the Strategy of Accelerated Serendipity. *Science* **2011**, *334*, 1114.
- (6) Prier, C. K.; Rankic, D. A.; MacMillan, D. W. C. Visible Light Photoredox Catalysis with Transition Metal Complexes: Applications in Organic Synthesis. *Chem. Rev.* **2013**, *113*, 5322.
- (7) Le, C. C.; Wismer, M. K.; Shi, Z.-C.; Zhang, R.; Conway, D. V.; Li, G.; Vachal, P.; Davies, I. W.; MacMillan, D. W. C. A General Small-Scale Reactor To Enable Standardization and Acceleration of Photocatalytic Reactions. *ACS Cent. Sci.* **2017**, DOI: [10.1021/acscentsci.7b00159](https://doi.org/10.1021/acscentsci.7b00159).
- (8) Zhang, P.; Le, C. C.; MacMillan, D. W. C. Silyl Radical Activation of Alkyl Halides in Metallaphotoredox Catalysis: A Unique Pathway for Cross-Electrophile Coupling. *J. Am. Chem. Soc.* **2016**, *138*, 8084.
- (9) Michaudel, Q.; Ishihara, Y.; Baran, P. S. Academia–Industry Symbiosis in Organic Chemistry. *Acc. Chem. Res.* **2015**, *48*, 712.