

Letter

Bromine Radical Catalysis by Energy Transfer Photosensitization

Dian-Feng Chen, Cameron Chrisman, and Garret M. Miyake

ACS Catal., **Just Accepted Manuscript** • DOI: 10.1021/acscatal.0c00281 • Publication Date (Web): 30 Jan 2020

Downloaded from pubs.acs.org on January 31, 2020

Just Accepted

"Just Accepted" manuscripts have been peer-reviewed and accepted for publication. They are posted online prior to technical editing, formatting for publication and author proofing. The American Chemical Society provides "Just Accepted" as a service to the research community to expedite the dissemination of scientific material as soon as possible after acceptance. "Just Accepted" manuscripts appear in full in PDF format accompanied by an HTML abstract. "Just Accepted" manuscripts have been fully peer reviewed, but should not be considered the official version of record. They are citable by the Digital Object Identifier (DOI®). "Just Accepted" is an optional service offered to authors. Therefore, the "Just Accepted" Web site may not include all articles that will be published in the journal. After a manuscript is technically edited and formatted, it will be removed from the "Just Accepted" Web site and published as an ASAP article. Note that technical editing may introduce minor changes to the manuscript text and/or graphics which could affect content, and all legal disclaimers and ethical guidelines that apply to the journal pertain. ACS cannot be held responsible for errors or consequences arising from the use of information contained in these "Just Accepted" manuscripts.

Bromine Radical Catalysis by Energy Transfer Photosensitization

Dian-Feng Chen, Cameron H. Chrisman, and Garret M. Miyake*

Department of Chemistry, Colorado State University, Fort Collins, Colorado 80523, United States

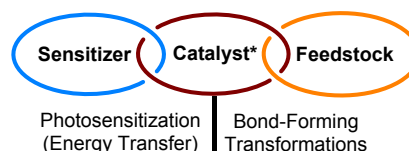
KEYWORDS: Catalysis, Bromine Radical, Photocatalysis, Energy Transfer, Cycloaddition.

ABSTRACT: We report here a mild, safe, and user-friendly bromine radical catalysis system that enables efficient [3+2] cycloaddition of diversely substituted vinyl- and ethynylcyclopropanes with a broad range of alkenes, including drug-like molecules and pharmaceuticals. Key to the success is the use of photosensitizing triplet state β -fragmentation of a judiciously selected pre-catalyst, cinnamyl bromide, to generate bromine radicals in a controlled manner using ppm-level photocatalyst (i.e. 4CzIPN) loading.

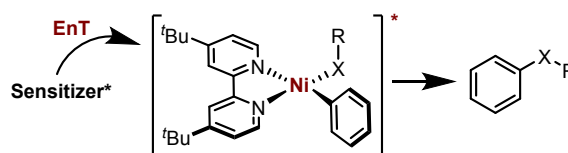
Excited-state molecules, compared to the ground state, possess distinct electronic configurations, which alter the spin-multiplicity and bond strength, thus exhibiting unique chemical properties and reactivity.¹ Although direct photoexcitation is straightforward to access excited-state reactivity, the majority of organic molecules require ultraviolet (UV) light irradiation and quartz reaction vessels that challenges practicality, selectivity, and functional group tolerance.² Recently, visible-light photocatalysis has emerged as a sustainable and powerful tool to access excited-state reactivity under mild conditions, enabling numerous bond-forming reactions.³ Most examples have utilized single electron-transfer (ET) mechanisms, i.e. photoredox catalysis,⁴ while transformations proceeding through energy transfer (EnT) catalysis, i.e. photosensitization,⁵ are relatively underdeveloped. EnT catalysis is unique in that it largely relies on the relative triplet energies of the photocatalyst (PC) and the substrates. Upon photosensitization, the partial diradical character of a substrate may significantly lower the kinetic barriers toward otherwise disfavored transformations, such as [2+2] photocycloadditions,⁶ photoisomerization of alkenes,⁷ and others.⁸

For billions of years nature has utilized EnT to convert solar energy into chemical energy (Figure 1a).⁹ This synergy has inspired synthetic chemists to develop excited-state organometallic catalysis via photosensitization as a novel activation pathway.¹⁰⁻¹¹ The paradigm of such catalysis is triplet excited-state Ni^{II} complex-catalyzed C-C and C-X (X = O, N) cross coupling reactions, (Figure 1b).¹¹ Another elegant example employed two-center photocatalysis for the generation and trapping of (hetero)aryl radicals.¹² Specifically, $\text{Ru}(\text{bpy})_2\text{Cl}_2$ was used to absorb visible light and transfer the energy to pyrene, enabling the efficient single-electron reduction of (hetero)aryl halides and triflates (Figure 1c). Although the concept of photosensitization-initiated catalysis has been established as a robust strategy with great synthetic potential, the excited-state activation mode and further application in discovering valuable and unique bond-forming reactions are still in their infancy.

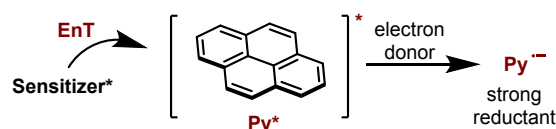
(a) Photosynthetic Process in Nature



(b) Excited-State Organometallics via EnT



(c) Photosensitization-Initiated Photoredox Catalysis



(d) This Work: Bromine Radical Catalysis by Photosensitization

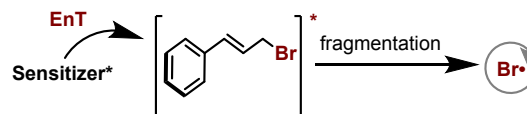


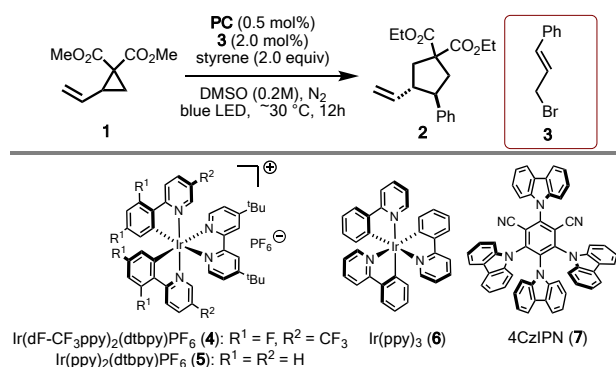
Figure 1. Photosensitization-Initiated Excited-State Catalysis

Heteroatom-centered radicals, e.g., bromine radicals, are vigorously involved in fundamental bromination reactions providing invaluable Br-containing compounds for further build-up of molecular complexity and diversity.¹³ One of the intriguing features of the bromine radical is that it can reversibly add to carbon-carbon π -bonds (via addition and elimination).¹⁴ Exploiting this reversibility, we envisioned a bromine radical catalysis system for the activation of alkenes or alkynes. To the best of our knowledge, such a catalysis still remains unknown. The immediate challenges to realize this bromine radical catalysis is the need for mild and controlled

generation of bromine radicals. Two classical strategies to deliver a bromine radical includes (i) photolysis of molecular bromine (Br_2), a highly toxic, corrosive, and volatile liquid,¹⁵ and (ii) thermolysis of N-bromosuccinimide (NBS), meanwhile generating reactive succinimide radicals that can abstract hydrogen atoms from weak C-H bonds (e.g. allylic C-H bonds).¹⁶ The resulting carbon radical, after hydrogen atom abstraction (HAT), may terminate the bromine radical. In light of the [2+2] photocycloaddition of styrene derivatives,^{8a} we hypothesized that, upon photosensitization, the partial diradical character of an excited state styrene derivative, e.g., cinnamyl bromide, would allow β -fragmentation to liberate a bromine radical that may be intercepted for catalysis (Figure 1d).¹⁷

[3+2] cycloaddition of vinyl cyclopropanes and alkenes is a typical reaction to evaluate the addition/elimination radical replay reactivity. It is important to note that such a cycloaddition has been well-established through classical thiyl¹⁸ and tin¹⁹ radical catalysis. However, several limitations still remain. First, commonly used precursors of tin or thiyl radicals are highly toxic and smelly tin hydride, thiols or disulfides. Second, harsh conditions for radical initiation, such as high temperature or UV light irradiation, which exhibits negative impact on practicality. Here, we report a method for mildly controlling bromine radicals through parts-per-million (ppm) level EnT photocatalysis, which enables efficient cycloaddition of vinyl- and ethynylcyclopropane and alkenes with excellent functional group tolerance.

Table 1. Optimization of Conditions for Visible Light-Gated Bromine Radical-Catalyzed [3+2] Cycloaddition of Vinylcyclopropane **1 and Styrene^a**



Entry	PC	E_T (kcal/mol)	[Br]	Yield (%) ^b
1	4	61	3	95
2	5	49	3	11
3	6	55	3	0
4	7	58	3	93
5 ^c	7	58	3	0
6	-	-	3	0
7	7	58	-	0
8 ^{d,e}	7	58	3	93
9 ^{d,f}	7	58	3	92(88) ^g
10 ^{d,h}	7	58	3	30

^aAll reactions were performed on 0.2 mmol scale. Regardless of reaction conditions, d.r. was 70:30. ^bDetermined by ¹H

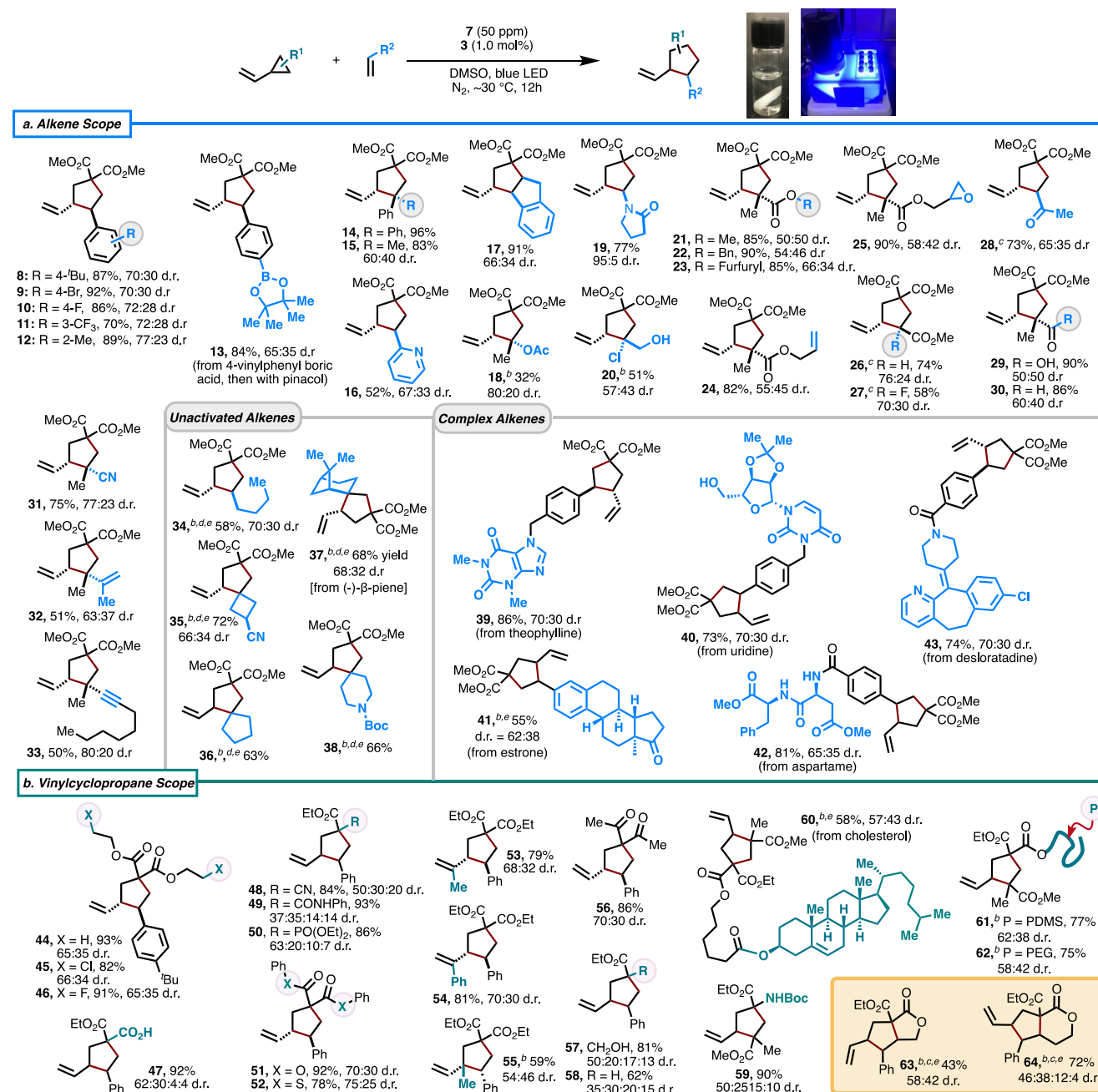
NMR using trimethoxybenzene as an internal standard. ^cNo light. ^d1.0 mol% **3** was used. ^e0.1 mol% 4CzIPN was used. ^f50 ppm 4CzIPN was used. ^gIsolated yield. ^h10 ppm 4CzIPN was used.

Initial hypothesis validation began with investigation of the reaction between 1,1-dimethoxycarboxyl-2-vinylcyclopropane (**1**) and styrene as the substrates in DMSO, and 34 W blue LED as the light source (Table 1). Inspired by MacMillan's photoredox strategy to form bromine radicals,²⁰ catalyst combinations of **4** with various bromide salts in different solvents were evaluated (Table S1). Unfortunately, none of these experiments resulted in any conversion after 12 h. We then turned our attention to the strategy of photosensitization to generate bromine radicals. Due to the possibility of recombination of the bromine and carbon radicals, the use of substoichiometric quantities of **3** should favor high conversion. Gratifyingly, the [3+2] cycloaddition of **1** (1.0 equiv) and styrene (2.0 equiv) proceeded in the presence of **4** (0.5 mol%) and **3** (2.0 mmol%) to yield the cyclopentane product **2** in 95% NMR yield (Table 1, entry 1). The subsequent examination of popular photocatalysts (PCs) revealed a correlation between reaction efficiency and the PCs triplet energy (E_T). More specifically, reactions utilizing PCs with higher E_T resulted in higher yields, which is consistent with the photoinduced EnT mechanism (entries 1–2 and 4). The donor-acceptor fluorophore 4CzIPN (**7**)²¹ provides comparable yield to the precious iridium-based photocatalyst **4**. We chose **7** for further optimization. Importantly, no conversion was observed in the absence of light, PC or **3** (entries 6–8). Moreover, attempts on lower catalysts loading were successful that 0.005 mol% (50 ppm) of **7** and 1.0 mol% of **3** enabled the formation of **2**, as a 70:30 (trans/cis) mixture of diastereomers, in 88% isolated yield (entry 10), highlighting the robustness of this photocatalytic system.

With optimal conditions in hand, we investigated the substrate scope (Table 2). Generally, a broad range of vinylcyclopropanes and alkenes is amenable to this protocol, affording vinylcyclopentane products in moderate to excellent yields and with diastereomeric ratios (d.r.) ranging from 50:50 to 95:5. Reactions of **1** with styrenes bearing substituents on the phenyl ring or at α -position, including alkyl and aryl groups, proceed well to give products **8–15** in good to excellent yields (70–96% yield). Notably, boric acid is tolerated (**13**, 84% yield after a subsequent reaction with pinacol), providing opportunities for late-stage functionalization through cross-coupling reactions. 2-vinyl pyridine and 1*H*-indene readily participate in this transformation (**16**, 48% yield; **17**, 91% yield). Electron-rich alkenes also engage in reactivity to afford products (**18–20**, 32–77% yield). It is noteworthy that the cycloaddition of **1** with N-vinylpyrrolidone exhibited excellent diastereoselectivity (d.r. = 95:5). With a diverse set of electron-deficient alkenes, we demonstrate excellent functional group tolerance of fluorine, epoxide, ketone, carboxylic acid, aldehyde and nitrile (**21–31**, 58–90% yield). Cycloadditions of diene and enyne substrates affords corresponding products in moderate yields (**32**, 51% yield; **33**, 50% yield). Although a higher loading of **7** (500 ppm) was used, good yields were maintained across a range of unactivated alkenes (**34–38**, 58–72% yield). In the reaction of (-)- β -piene, the bridged bicyclic motif is retained (**37**), suggesting that the ring-forming step in this cycloaddition is fast.

To demonstrate the utility of this new protocol, we selected several complex molecules of diverse biological activities for

Table 2. Scope of Visible Light-Gated Bromine Radical-Catalyzed [3+2] Cycloaddition of Vinylcyclopropanes and Alkenes^a



^aConditions: vinylcyclopropane (0.20 mmol), alkene (0.40 mmol), 7 (50 ppm), 3 (1.0 mol%), DMSO (0.2 M), 30 °C, 34 W blue LED, 12h. ^b2.0 mol% 3 was used. ^c0.1 M in DMSO. ^d0.4 M in DMSO. ^e500 ppm of 7 was used.

late-stage functionalization. 4-vinylbenzylated theophylline, a phosphodiesterase inhibitor,²² and uridine, one of the standard nucleosides, were efficient substrates (39–43, 73–86% yield). Due to solubility issue in DMSO, an estrone derivative affords product 41 in only moderate yield (55%). Aspartame, a dipeptide sweetener, is converted into 42 in 81% yield. Gratifyingly, this [3+2] cycloaddition is effective for 4-vinyl benzoylated desloratadine (43, 74% yield), a popular tricyclic antihistamine.

We next explored the vinylcyclopropane scope (Table 2b). Diverse substituents on either the malonate motif (44–46,

82–93% yield), vinyl group (53–54, 79–81% yield), or cyclopropane scaffold (55, 59% yield) are tolerated. This cycloaddition is also amenable to a range of electron-deficient patterns bearing various functionalities, such as carboxylic acid (47, 92% yield), amide (49, 93% yield), phosphonate (50, 86% yield), alcohol (57, 86% yield) and carbamate (59, 90% yield), delivering corresponding products in good to excellent yield (47–52, 56–59, 62–93% yield). Reaction of a substrate containing hydrophobic cholesterol motif is challenging in DMSO and provides 60 in 58% yield. Vinylcyclopropanes bearing tethered polydimethylsiloxane (PDMS) or polyethylene glycol (PEG) efficiently react with methyl

methacrylate (MMA) to afford products **61** and **62** in 77% and 75% yield, respectively. Moreover, well-designed substrates with pendant alkenyl functionality possibly engage in

intramolecular reactivity to access advanced bicyclic scaffolds. This concept is demon-

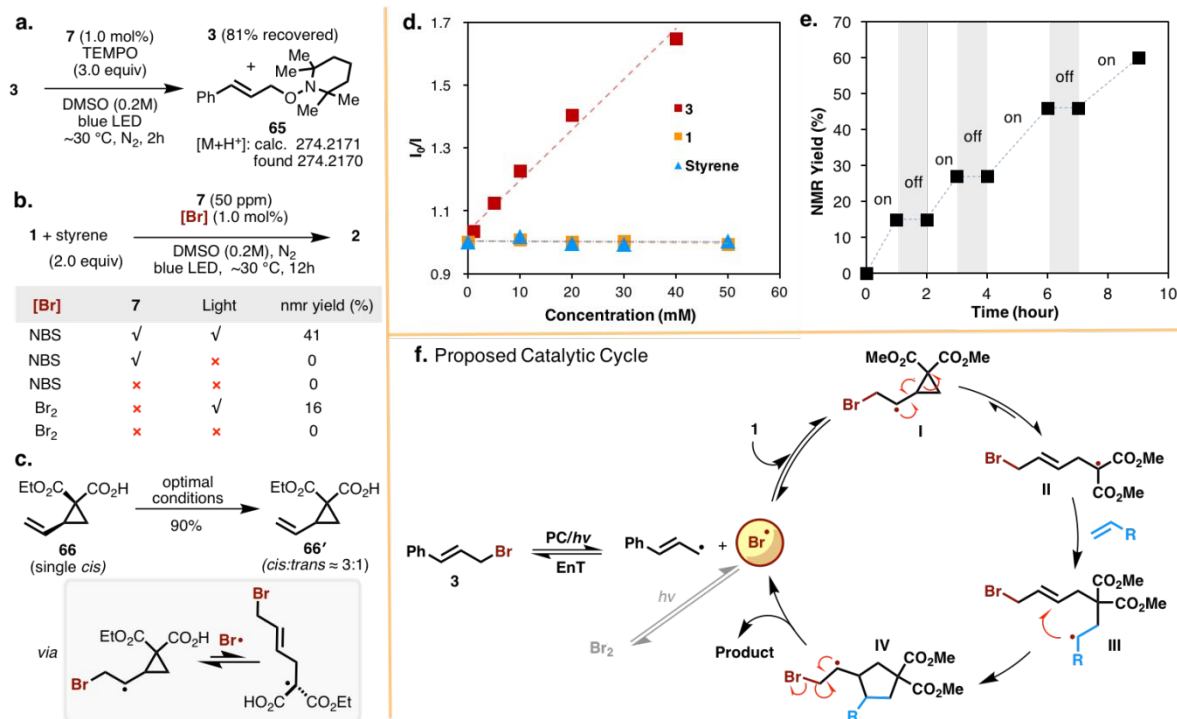
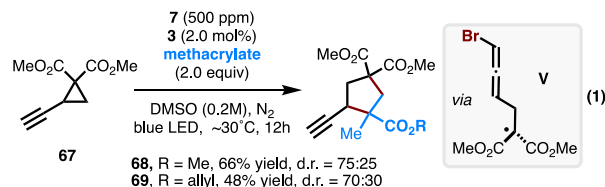


Figure 2. Mechanistic studies (a. TEMPO trapping experiment, b. Examination of alternative precatalysts, c. Radical epimerization experiment, d. Stern-Volmer quenching experiment, e. "On/off" experiment) and proposed catalytic cycle (f).

-strated in the successful synthesis of γ - and δ -lactones **63** (43% yield) and **64** (72% yield).

For the reaction mechanism, a Stern-Volmer quenching experiment reveals the feasible interaction between **7** and **3** (Figure 2d). However, the single-electron oxidation pathway to generate bromine radicals is thermodynamically unfavorable ($[E_{1/2}^{\text{red}}(7^*/7^-)] = +1.37$ vs SCE, $[E_{1/2}^{\text{ox}}(3/3^{++})] = 2.01$ V vs SCE, see Figure S5), suggesting that previously proposed photosensitization via EnT is likely the dominant pathway. Several control experiments were performed to gain insight into this reaction mechanism. First, radical trapping using TEMPO supports the formation of cinnamyl carbon radical (Figure 2a). However, the bromine radical-TEMPO adduct was not detected, presumably due to stability issues. Second, reactivity of other precatalysts, such as NBS and Br₂, was investigated (Figure 2b). Photosensitization of NBS or direct photolysis of Br₂ provides similar catalytic reactivity, but in much lower yields (41% and 16% yield, respectively), evidencing the key role of bromine radical in this transformation. Third, epimerization of **66** under optimal conditions strongly supports the radical mechanism (Figure 2c). Furthermore, temporal "on/off" control on the reaction (Figure 2e) showcases the light-controlled feature of this bromine radical catalysis. Accordingly, we proposed a catalytic cycle as shown in Figure 2f. Upon visible light irradiation, PC **7** is capable of sensitizing triplet-state fragmentation of **3** to release a bromine radical. Addition of the bromine radical to the vinyl group of **1** gives a transient radical species **I**, which undergoes a fast but reversible ring-opening process to furnish intermediate **II**. A subsequent radical addition of **II** to alkenes, followed by a ring-closure reaction, affords intermediate **IV**. In this step, the spin center

shifts to the position for β -elimination, giving the final product, meanwhile regenerating bromine radical to enter into next catalytic cycles. Efficient radical-radical coupling of bromine radical and cinnamyl carbon radical leads to the dormant precatalyst (**3**), which is evidenced by the high-yielding recovery of **3** in TEMPO trapping experiment (81%, Figure 2b). Possibly, Br₂, formed through recombination of two bromine radicals, may be another dormant species within this photosystem.



Lastly, we examined the performance of bromine radicals in the activation of C-C triple bonds. Under optimal conditions, in situ generated bromine radicals add to alkyne group of ethynylcyclopropane **67**, followed by a similar ring-opening reaction, to give the key allenyl intermediate **V** (eq. 1). Trapping of **V** with methacrylates successfully afford ethynylcyclopentanes **68** and **69** in 66% and 48% yield, respectively. Continued efforts to functionalize more challenging molecules (such as alkanes via HAT) utilizing this mild bromine radical catalysis are underway.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website. Experimental procedures, analytical data, and NMR spectra.

AUTHOR INFORMATION

Corresponding Author

*garret.miyake@colostate.edu

ORCID

Dian-Feng Chen: 0000-0003-1821-9783

Garret M. Miyake: 0000-0003-2451-7090

Notes

The authors declare no competing financial interest.

ACKNOWLEDGMENT

Research reported in this publication was supported by Colorado State University and the National Institute of General Medical Sciences of the National Institutes of Health under Award Number R35GM119702. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

REFERENCES

- (1) Hammond, G. S.; Turro, N. J. *Organic Photochemistry. Science*, **1963**, *142*, 1541–1553.
- (2) Hoffmann, N. Photochemical Reactions as Key Steps in Organic Synthesis. *Chem. Rev.* **2008**, *108*, 1052–1103.
- (3) Schultz, D. M.; Yoon, T. P. Solar Synthesis: Prospects in Visible Light Photocatalysis. *Science*, **2014**, *343*, 1239176.
- (4) 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*, 5322–5363.
- (5) (a) Strieth-Kalthoff, F.; James, M. J.; Teders, M.; Pitzer, L.; Glorius, F. Energy Transfer Catalysis Mediated by Visible Light: Principles, Applications, Directions. *Chem. Soc. Rev.* **2018**, *47*, 7190–7202; (b) Zhou, Q.-Q.; Zou, Y.-Q.; Lu, L.-Q.; Xiao, W.-J. Visible-Light-Induced Organic Photochemical Reactions Through Energy-Transfer Pathways. *Angew. Chem., Int. Ed.* **2019**, *58*, 1586–1604.
- (6) For selected examples: (a) Ikezawa, H.; Kutal, C.; Yasufuku, K.; Yamazaki, H. Direct and Sensitized Valence Photoisomerization of a Substituted Norbornadiene. Examination of the Disparity between Singlet- and Triplet-state Reactivities. *J. Am. Chem. Soc.* **1986**, *108*, 1589–1594; (b) Zou, Y.-Q.; Duan, S.-W.; Meng, X.-G.; Hu, X.-Q.; Gao, S.; Chen, J.-R.; Xiao, W.-J. Visible Light Induced Intermolecular [2+2]-Cycloaddition Reactions of 3-Ylideneoxindoles through Energy Transfer Pathway. *Tetrahedron* **2012**, *68*, 6914–6919; (c) Lu, Z.; Yoon, T. P. Visible Light Photocatalysis of [2+2] Styrene Cycloadditions by Energy Transfer. *Angew. Chem., Int. Ed.* **2012**, *51*, 10329–10332; (d) Lei, T.; Zhou, C.; Huang, M.-Y.; Zhao, L.-M.; Yang, B.; Ye, C.; Xiao, H.; Meng, Q.-Y.; Ramamurthy, V.; Tung, C.-H.; Wu, L.-Z. General and Efficient Intermolecular [2+2] Photodimerization of Chalcones and Cinnamic Acid Derivatives in Solution through Visible-Light Catalysis. *Angew. Chem., Int. Ed.* **2017**, *56*, 15407–15410; (e) Zhao, J.; Brosmer, J. L.; Tang, Q.; Yang, Z.; Houk, K. N.; Diaconescu, P. L.; Kwon, O. Intramolecular Crossed [2+2] Photocycloaddition through Visible Light-Induced Energy Transfer. *J. Am. Chem. Soc.* **2017**, *139*, 9807–9810; (f) Hörmann, F. M.; Chung, T. S.; Rodriguez, E.; Jakob, M.; Bach, T. Evidence for Triplet Sensitization in the Visible-Light-Induced [2+2] Photocycloaddition of Eniminium Ions. *Angew. Chem., Int. Ed.* **2018**, *57*, 827–831; (g) Zhu, M.; Zheng, C.; Zhang, X.; You, S.-L. Synthesis of Cyclobutane-Fused Angular Tetracyclic Spiroindolines via Visible-Light-Promoted Intramolecular Dearomatization of Indole Derivatives. *J. Am. Chem. Soc.* **2019**, *141*, 2636–2644. For selected examples of enantioselective [2+2] photocycloaddition, see: (h) Alonso, R.; Bach, T. A Chiral Thioxanthone as an Organocatalyst for Enantioselective [2+2] Photocycloaddition Reactions Induced by Visible Light. *Angew. Chem., Int. Ed.* **2014**, *53*, 4368–4371; (i) Blum, T. R.; Miller, Z. D.; Bates, D. M.; Guzei, I. A.; Yoon, T. P. Enantioselective Photochemistry through Lewis Acid-Catalyzed Triplet Energy Transfer. *Science* **2016**, *354*, 1391–1395; (j) Tröster, A.; Alonso, R.; Bauer, A.; Bach, T. Enantioselective Intermolecular [2+2] Photocycloaddition Reactions of 2(1H)-Quinolones Induced by Visible Light Irradiation. *J. Am. Chem. Soc.* **2016**, *138*, 7808–7811; (k) Skubi, K. L.; Kidd, J. B.; Jung, H.; Guzei, I. A.; Baik, M.-H.; Yoon, T. P. Enantioselective Excited-State Photoreactions Controlled by a Chiral Hydrogen-Bonding Iridium Sensitizer. *J. Am. Chem. Soc.* **2017**, *139*, 17186–17192; (l) Daub, M. E.; Jung, H.; Lee, B. J.; Won, J.; Baik, M.-H.; Yoon, T. P. Enantioselective [2+2] Cycloadditions of Cinnamate Esters: Generalizing Lewis Acid Catalysis of Triplet Energy Transfer. *J. Am. Chem. Soc.* **2019**, *141*, 9543–9547.
- (7) For selected examples, see: (a) Hammond, G. S.; Turro, N. J.; Leermakers, P. A. The Mechanisms of Photoreactions in Solution. IX. Energy Transfer from the Triplet States of Aldehydes and Ketones to Unsaturated Compounds. *J. Phys. Chem.* **1962**, *66*, 1144–1147; (b) Singh, K.; Staig, S. J.; Weaver, J. D. Facile Synthesis of Z-Alkenes via Uphill Catalysis. *J. Am. Chem. Soc.* **2014**, *136*, 5275–5278; (c) Metternich, J. B.; Gilmour, R. A Bio-Inspired, Catalytic E → Z Isomerization of Activated Olefins. *J. Am. Chem. Soc.* **2015**, *137*, 11254–11257; (d) Metternich, J. B.; Gilmour, R. One Photocatalyst, n Activation Modes Strategy for Cascade Catalysis: Emulating Coumarin Biosynthesis with (–)-Riboflavin. *J. Am. Chem. Soc.* **2016**, *138*, 1040–1045; (e) Singh, K.; Fennell, C. J.; Coutasias, E. A.; Latifi, R.; Hartson, S.; Weaver, J. D. Light Harvesting for Rapid and Selective Reactions: Click Chemistry with Strain-Loadable Alkenes. *Chem*, **2018**, *4*, 124–137.
- (8) For selected examples, see: (a) Farney, E. P.; Yoon, T. P. Visible-Light Sensitization of Vinyl Azides by Transition-Metal Photocatalysis. *Angew. Chem., Int. Ed.* **2014**, *53*, 793–797; (b) Brachet, E.; Ghosh, T.; Ghosh, I.; König, B. Visible Light C–H Amidation of Heteroarenes with Benzoyl Azides. *Chem. Sci.* **2015**, *6*, 987–992; (c) Scholz, S. O.; Farney, E. P.; Kim, S.; Bates, D. M.; Yoon, T. P. Spin-Selective Generation of Triplet Nitrenes: Olefin Aziridination through Visible-Light Photosensitization of Azidoformates. *Angew. Chem., Int. Ed.* **2016**, *55*, 2239–2242; (d) Münster, N.; Parker, N. A.; van Dijk, L.; Paton, R. S.; Smith, M. D. Visible Light Photocatalysis of 6π Heterocyclization. *Angew. Chem., Int. Ed.* **2017**, *56*, 9468–9472; (e) Teders, M.; Henkel, C.; Anhäuser, L.; Strieth-Kalthoff, F.; Gómez-Suárez, A.; Kleinmans, R.; Kahnt, A.; Rentmeister, A.; Guldi, D. M.; Glorius, F. The Energy-Transfer-Enabled Biocompatible Disulfide-Ene Reaction. *Nat. Chem.* **2018**, *10*, 981–988.
- (9) Mirkovic, T.; Ostroumov, E. E.; Anna, J. M.; VanGrondelle, R.; Govindjee, Scholes, G. D. Light Absorption and Energy Transfer in the Antenna Complexes of Photosynthetic Organisms. *Chem. Rev.* **2017**, *117*, 249–293.
- (10) Yoo, W.-J.; Tsukamoto, T.; Kobayashi, S. Visible Light-Mediated Ullmann-Type C–N Coupling Reactions of Carbazole Derivatives and Aryl Iodides. *Org. Lett.* **2015**, *17*, 3640–3642.
- (11) (a) Heitz, D. R.; Tellis, J. C.; Molander, G. A. Photochemical Nickel-Catalyzed C–H Arylation: Synthetic Scope and Mechanistic Investigations. *J. Am. Chem. Soc.* **2016**, *138*, 12715–12718; (b) Welin, E. R.; Le, C.; Arias-Rotondo, D. M.; McCusker, J. K.; MacMillan, D. W. C. Photosensitized, Energy Transfer-Mediated Organometallic Catalysis through Electronically Excited Nickel(II). *Science* **2017**, *355*, 380–385; (c) Kim, T.; McCarver, S. J.; Lee, C.; MacMillan, D. W. C. Sulfonamidation of Aryl and Heteroaryl Halides through Photosensitized Nickel Catalysis. *Angew. Chem., Int. Ed.* **2018**, *57*, 3488–3492. (d) Kudisch, M.; Lim, C.H.; Thordarson, P.; Miyake, G. M. Energy Transfer to Ni-Amine Complexes in Dual Catalytic, Light-Driven C–N Cross-Coupling Reactions. *J. Am. Chem. Soc.* **2019**, *141*, 19479–19486.
- (12) Ghosh, I.; Shaikh, R. S.; König, B. Sensitization-Initiated Electron Transfer for Photoredox Catalysis. *Angew. Chem., Int. Ed.* **2017**, *56*, 8544–8549.
- (13) Saikia, I.; Jyoti, A.; Phukan, B. Use of Bromine and Bromo-Organic Compounds in Organic Synthesis. *Chem. Rev.* **2016**, *116*, 6837–7042.
- (14) Studer, A.; Curran, D. P. Catalysis of radical reactions: a radical chemistry perspective. *Angew. Chem., Int. Ed.* **2016**, *55*, 58–102.

(15) Goehring, R. R. Bromine. *e-EROS Encyclopedia of Reagents for Organic Synthesis*. **2001**, DOI: 10.1002/047084289X.rb256.

(16) Virgil, S. C.; Jenkins, P. R.; Wilson, A. J.; Romero, M. D. G. N-Bromosuccinimide. *e-EROS Encyclopedia of Reagents for Organic Synthesis*. **2006**, DOI: 10.1002/047084289X.rb318.pub2.

(17) The photoisomerization of 2-phenylallyl chloride was previously observed, which arose from the generation and recombination of a radical pair. See: Xu, B.; Tambar, U. K. Remote Allylation of Unactivated C(sp³)-H Bonds Triggered by Photogenerated Amidyl Radicals. *ACS Catal.* **2019**, *5*, 4627–4631.

(18) (a) Miura, K.; Fugami, K.; Oshima, K.; Utimoto, K. Synthesis of Vinylcyclopentanes from Vinylcyclopropanes and Alkenes Promoted by Benzenethiyl Radical. *Tetrahedron Lett.* **1988**, *29*, 5135–5138; (b) Feldman, K. S.; Berven, H. M.; Weinred, P. H. 2,2-Dihalovinylcyclopropanes as Highly Diastereoselective Three-Atom Addends in Phenylthio Radical Mediated Vinylcyclopentane Synthesis. *J. Am. Chem. Soc.* **1993**, *115*, 11364–11365; (c) Hashimoto, T.; Kawamata, Y.; Maruoka, K. An Organic Thiyl Radical Catalyst for Enantioselective Cyclization. *Nat. Chem.* **2014**, *6*, 702–705; (d) Hashimoto, T.; Takino, K.; Hato, K.; Maruoka, K. A

Bulky Thiyl - Radical Catalyst for the [3+2] Cyclization of N-Tosyl Vinylaziridines and Alkenes. *Angew. Chem., Int. Ed.* **2016**, *55*, 8081–8035.

(19) Zhang, H.; Curran, D. P. A Short Total Synthesis of (±)-Epimelosine and (±)-Melosine Enabled by a Cascade Radical Annulation of a Divinylcyclopropane. *J. Am. Chem. Soc.* **2011**, *133*, 10376–10378.

(20) Zhang, P.; Le, 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*, 8084–8087.

(21) Luo, J.; Zhang, J. Donor-acceptor fluorophores for visible-light promoted organic synthesis: photoredox/Ni dual catalytic C(sp³)-C(sp²) cross-coupling. *ACS Catal.* **2016**, *6*, 873–877.

(22) Boswell-Smith, V.; Cazzola, M.; Page, C. P. Are phosphodiesterase 4 inhibitors just more theophylline? *J. Allergy Clin. Immunol.* **2006**, *117*, 1237–1243.

Table of Contents Image for

Bromine Radical Catalysis by Energy Transfer Photosensitization

Dian-Feng Chen, Cameron H. Chrisman, and Garret M. Miyake*

Department of Chemistry, Colorado State University, Ft Collins, Colorado 80523, United States

