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Cooperative Light-Activated lodine and Photoredox Catalysis for the Amination of Csp³–H Bonds

Peter Becker,^[a] Thomas Duhamel,^[a,c] Christopher J. Stein,^[b] Markus Reiher,*^[b] Kilian Muñiz*^[a,d]

Dedication ((optional))

Abstract: An unprecedented protocol for the cooperative interplay between molecular iodine and photoredox catalysis under dual light-activation for the intramolecular benzylic C—H amination is presented. Iodine serves as a catalyst for the formation of a new C—N bond by the activation of a remote Csp³–H bond (1,5-HAT process) under visible light irradiation, while the organic photoredox catalyst TPT effectively furnishes the re-oxidation of the molecular iodine catalyst. To explain the compatibility of the two involved photochemical steps, the key N—I bond activation was elucidated by computational methods. The new cooperative catalysis provides important implications for the combination of non-metallic main group catalysis with photocatalysis.

A fundamental goal in developing new catalytic processes is to establish environmentally benign and effective conditions. The activation of small organic molecules by photoredox catalytic systems under visible light has opened up a whole new field in catalysis leading to a plethora of effective transformations.^[1] Here, processes merging transition metal and photoredox catalysis are of exceptional value as the utilization of stoichiometric amounts of oxidizing reagents others than molecular oxygen is no longer required.^[2] Although this strategy has attracted the development of organic transformations including C-H bond activations using a number of metal catalysts,^[3] no strategies for combining photoredoxcatalyzed re-oxidation with iodine redox catalysis has been reported to date.^[4] Devising a practical methodology for the functionalization of non-activated Csp³-H bonds still represents a great challenge in modern organic synthesis. While the transition-metal catalyzed C-H bond transformation into new C-C and C-heteroatom bonds has been established over the past years, this strategy usually requires functional groups in close proximity to ensure regioselectivity and to overcome activation barriers.^[5] The modification of remote positions, however, further increases difficulties related to C-H bond activation concepts. Lately, our group developed the iodine catalyzed oxidative Hofmann-Löffler reaction of sulfonamides for the formation of pyrrolidines (Scheme 1).^[6a] In this process, an in situ formed N-I bond facilitates the formation of a nitrogen-centered amidyl radical,

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which induces a selective 1,5-HAT process^[7] to activate a remote Csp³–H bond for the subsequent C–N bond formation. Although of synthetic efficiency, the reaction requires stoichiometric amounts of hypervalent iodine reagents indicating a clear disadvantage. Rovis and Knowles independently reported a photoredox-based concept for the generation of amidyl radicals and subsequent activation of Csp³–H bonds by a 1,5-HAT process (Figure 1).^[8,9] They extended such processes by intermolecular radical interception with activated alkenes. Within this new C–C bond forming approach, however, an amination reaction is no longer feasible and the role of the amide is restricted to the generation of the requisite radicals.



Figure 1. Recent examples for the nitrogen-promoted application of 1,5-HAT processes for the functionalization of remote Csp³–H bonds.

To further improve the photochemical amidyl radical-promoted Csp³–H bond activation, we envisaged combining a 1,5-HAT process and a subsequent cyclization reaction to re-establish the original pathway to synthetically valuable pyrrolidines.

To foster such a reaction process, we pictured molecular iodine playing an essential role in the cyclization step of the envisaged process.^[10] In a cooperative catalysis with two individual photo-induced processes, the iodine catalyst would promote the pyrrolidine formation via activation of the N–H bond with a subsequent 1,5-HAT process, while the photoredox catalyst would furnish the reoxidation of the iodine after the extrusion by the cyclization event. Both catalysts, therefore, would be working cooperatively and demonstrate the first example of photoredox-catalyzed reoxidation of a molecular homogeneous iodine catalyst. Due to the consideration of metal-free processes using iodine instead of transition-metal catalysts and iodine's known ability to quench metal-to-ligand charge-transfer (MLCT) excited states of metal based photoredox catalysts,^[11] organic dyes were the preferred choice.^[12]

To this end, a solution of the model substrate **1a**, molecular iodine (10 mol%) and photoredox catalyst (5 mol%) in DCE under anhydrous or oxygen-free conditions was exposed to blue light (λ_{max} = 456 nm ± 12 nm) at room temperature. However, for all reactions with different organic dyes (Eosin Y, Fukuzumi's catalyst, and TPT, Figure 2) only trace amounts of the desired pyrrolidine **2a** were detected (Table 1, entry 1).

The first positive result was achieved when performing the reaction in unpurified solvent with $TPT^{[13]}$ as the photoredox catalyst of choice under air (20%, entry 2). A solvent mixture of

COMMUNICATION

DCE and HFIP^[14] dramatically improved the yield of **2a** to 84% (entry 3). When the TPT loading was reduced to 2 mol%, the yield dropped to 58% (entry 4).

 $\ensuremath{\text{Table 1.}}$ Screening of the conditions for the iodine/photoredox catalyzed process.

	e	IPT (x mol%) I ₂ (y mol%)	Me Me		
1a	Ph	HFIP/DCE, blue LED RT, 18 h), 2a	2a Ts	
No. ^[a]	х	у	Solvent	Yield [%]	
1 ^[b,c]	5	10	DCE	trace	
2 ^[c]	5	10	DCE	20	
3	5	10	HFIP/DCE	84	
4	2	10	HFIP/DCE	58	
5	2	5	HFIP/DCE	80	
6	1	5	HFIP/DCE	90	
7	1	2	HFIP/DCE	31 ^[d]	
8	0.5	5	HFIP/DCE	76 ^[d]	
9	-	5	HFIP/DCE	5 ^[d]	
10	1	-	HFIP/DCE	14 ^[d]	
11	1	5	HFIP/DCE	[e]	
12	1	5	HFIP/DCE	83 ^[f]	

[a] All reactions were stirred for 18 h under blue light irradiation in 3 mL of solvent (1:1) without external heating. Yields refer to isolated material after purification. [b] Reaction performed under anhydrous or oxygen-free conditions. [c] Eosin Y and Fukuzumi's catalyst (depicted in Figure 2) led to trace amounts of product. [d] Yields determined by NMR with 1,3,5-trimethoxybenzene as internal standard. [e] Reaction performed in absence of light. [f] Reaction performed at a 2 mmol scale, 22 h.



Figure 2. Organic dyes tested as photoredox catalysts.

However, a simultaneous reduction of the amount of iodine (5 mol%) led to similar yields (80%, entry 5), which indicates absorption of visible light by iodine at high concentrations. With only 5 mol% of iodine, the TPT loading was reduced to 1 mol% leading to 90% of **2a** (entry 6). A further reduction of iodine (2 mol%) led only to 31% yield (entry 7) accompanied by a large amount of side products stemming from over-oxidation. When 0.5 mol% TPT was used, still 76% of **2a** was formed (entry 8). These results indicate an important role of the I₂/TPT ratio to effectively cooperate in the catalytic reaction. To probe the necessity of both catalysts, control experiments were conducted. With iodine alone, the formation of 5% of **2a** was detected equivalent of only a stoichiometric reaction (entry 9). When TPT was added as single catalyst, 14% of pyrrolidine **2a** was formed accompanied by large amounts of decomposition products

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(entry 10). No pyrrolidine was formed in the absence of light demonstrating that the reaction is indeed light-driven (entry 11). At this point, it has to be stretched out that the intensity of the LED light-source was determined crucial.^[15] To finally demonstrate the robustness of the process, a 2 mmol scale was applied leading to 83% of **2a** under standard conditions with a slightly increased reaction time (entry 12).

Mechanistically, we propose a reaction sequence consisting of two individual light-induced catalytic reactions within several intertwined individual cycles (Figure 3). Raman spectroscopy was employed to identify the active molecular iodine catalyst. A rapid formation of hypoiodite^[16] in the wet reaction media from disproportionation of molecular iodine was observed, which explains the requirement for water traces to initiate the reaction.^[15] This catalyst state is in agreement to Ishihara's work on related hypoiodite catalysis.^[17] The concomitantly formed HI essentially participates in the final catalyst reoxidation event (cycle **A**).



Figure 3. Proposed mechanism for the dual light-induced cooperative iodine and photoredox catalyzed intramolecular amination of sulfonamides.

active hypoiodite catalyst initiates the organic The transformation via N-iodination of the substrate 1a to form the intermediate species I (cycle B).[18] Upon irradiation with visible light, the N-iodinated species I collapses to generate the amidyl radical species II. A subsequent 1,5-HAT process (III) within a radical chain reaction generates an alkyliodide species IV. Intramolecular isotope-labeling experiments^[19] revealed the hydrogen abstraction from II to III to be the rate-limiting step with a kinetic isotope effect of 2.3.^[15] The successful incorporation of iodine into the carbon framework precludes the requirement for intermolecular radical quenching.^[8a,b] It drives the reaction to the C-N bond formation, in which the sulfonamide attacks the intermediary C-I bond in an intramolecular substitution reaction to form the pyrrolidine 2a as the product. The extruded hydrogen iodide is then effectively reoxidized by TPT to molecular iodine in a single electron transfer process with molecular oxygen (cycle ${\bf C})^{[20]}$ This context characterizes the new photocatalytic iodine catalysis as an unprecedented iodine (-I/I) manifold and for the first time demonstrates that a catalytic functionalization of benzylic positions is possible without the involvement of iodine(III) oxidation states.

The conceptually important feature of the reaction consists in the compatibility of the dual role of light. First, there is its participation within the photoredox catalysis, which provides the

COMMUNICATION

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terminal oxidant for the overall catalysis. Secondly, it is involved in the homolytic cleavage of the N–I bond as the initial step within the C–H bond functionalization. In order to understand the molecular requirements for the elusive light-induced N–I bond cleavage at stage I, theory was employed.

The excitation energies for the ten lowest excited states of species I were calculated with time-dependent density functional theory (TDDFT) with the range-separated CAMY-B3LYP functional^[21] and environmental effects were included with a continuum solvation model. We accounted for the pronounced conformational freedom by carrying out TDDFT calculations on a closed (A) and an open structure (B), that were both optimized with DFT employing the PBE functional.^[22] The energy of both structures differs by less than 2.5 kcal/mol in favor of the open conformation. With an empirical dispersion correction,^[23] both energies are almost identical with the closed conformation being 0.15 kcal/mol lower in energy. A table with energies and oscillator strengths for all states and computational setups and more details on the methodology are included in the Supporting Information.^[16]



Figure 4. N–I anti-bonding LUMO of intermediate species I in a closed (A) and open (B) conformation. The orbitals were calculated with DFT employing the range-separated CAMY-B3LYP functional.

The seven lowest excited states correspond to excitations into the N-I anti-bonding lowest unoccupied molecular orbital (LUMO) and therefore weaken this bond and facilitate bond cleavage (Figure 4). Depending on the computational setup, the transition energies of these excitations cover a range of 100-130 nm with the lowest transition energy around 380 nm. Several effects shift the individual transition energies. One of them is the conformational freedom of I, which causes a shift of up to 15 nm for the open and closed structure considered in this study and other conformers might further extend that range. Another effect is the direct interaction of solvent molecules with I, that leads to a significant broadening of the individual bands due to a plethora of possible interactions. Furthermore, the error of TDDFT transition energies lies typically in the range of 0.2 eV, [24] which corresponds to about 30 nm in this wave length regime. These effects, and the fact that the long reaction times do not require a high efficiency of the photolytic reaction, explain the discrepancy of the calculated lowest energy transitions and the LED wave length. While we were mainly interested in identifying the character of the excitations that cause the photolytic reaction, we expect a higher efficiency of this reaction step for shorter wave lengths. It should be noted that both the inclusion of solvent

effects and the structural changes in both conformers have a pronounced effect on the oscillator strengths.

We confirmed that the lowest excited states have mainly LUMO character with complete active space self-consistent field calculations^[25] employing an active space consisting of 14 electrons in 16 orbitals, where the orbitals were selected with our automated active space selection protocol.^[26]

With this concise mechanistic explanation of the dual lightactivated iodine and photoredox catalyzed C–H amination and the theoretical understanding of the photolytical cleavage of the N–I bond in hand, we investigated the scope of the reaction process (Figure 5).



Figure 5. Scope of the intertwined iodine and photoredox catalyzed cyclization Conditions: I_2 (5 mol%), TPT (1 mol%), HFIP/DCE (3 mL), RT, blue light, 18 h. All C–N bonds formed in this process are highlighted in blue. Yields are generally stated as yields of isolated product obtained after purification by column chromatography; [a] two rotamers were observed by NMR; [b] isolated as 1:1 diasteromeric mixture; [c] isolated as a single diasteromer; [d] yield by ¹H NMR with 1,3,5-trimethoxybenzene as internal standard.

The process features an effective procedure to yield various 2arylpyrrolidines in good to excellent yields. A series of substrates with substituents in 4-position of the phenyl group are well tolerated (2a-e, 31-90% yield), with only the 4-chloro or 4bromo-substituted substrates leading to decreased yields due to over-oxidation (2d-e, 31-57% yield) by the photoredox catalyst. Also, substrates bearing 2- or 3-substituted arenes form pyrrolidines 2f-g in 60-90% yield demonstrating that steric factors only play a minor role. A possible Thorpe-Ingold-effect was shown to have little influence on the reaction since different substitution pattern in β -position of the amide were successfully tolerated (2h-j,m, 70-81%). Substrates with a phenyl backbone were subjected to the reaction conditions effectively yielding previously inaccessible isoindolines (2k-I, 73-94%). Different sulfonyl groups are also well tolerated in this process leading to 60-96% of the desired pyrrolidines 2n-r. For the first time benzamide and trifluoroacetamide derivatives are also

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applicable leading to the corresponding pyrrolidines **2s-t** in high yields (70-82%).^[27] In contrast to the previously described iodine(I/III) approach for the Hofmann-Löffler reaction, the intermediary benzyliodide of the iodine(-I/I) approach holds a weaker nucleofug requiring additional activation by the benzylic position to allow the internal substitution by the amide nucleophile.

In summary, we have introduced a novel concept of a dual lightactivated cooperative iodine- and photoredox catalysis and applied it to the intramolecular amination of remote sp³ C–H bonds. The iodine acts as the primary catalyst allowing the activation of the sp³ C–H bond by a light-induced homolytic cleavage of *in situ*-generated N–I bonds followed by a 1,5-HAT process. After recombination of the radicals and an intramolecular substitution, the molecular iodine catalyst is photoredox-catalytically reoxidized in a second light-induced process. The key step of the reaction, the cleavage of the intermediary N–I bond, has been rationalized by computational methods, while the presence of the active iodine species, hypoiodite, has been determined by Raman spectroscopy.

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Keywords: photoredox catalysis • iodine catalysis • 1,5-HAT process • cooperative catalysis • C–H bond amination

- a) M. H. Shaw, J. Twilton, D. W. C. MacMillan, J. Org. Chem. 2016, 81, 6898 – 6926; b) C. K. Prier, D. A. Rankic, D. W. C. MacMillan, Chem. Rev. 2013, 113, 5322.
- [2] For recent examples, see: Pd: a) S. R. Neufeldt, M. S. Sanford, Adv. Synth. Catal. 2012, 354, 3517; b) D. Kalyani, K. B. McMurtrey, S. R. Neufeldt, M. S. Sanford, J. Am. Chem. Soc. 2011, 133, 18566; Au: c) M. N. Hopkinson, B. Sahoo, F. Glorius, Adv. Synth. Catal. 2014, 356, 2794; d) X. Z. Shu, M. Zhang, Y. He, H. Frei, F. D. Toste, J. Am. Chem. Soc. 2014, 136, 5844; e) A. Tlahuext-Aca, M. N. Hopkinson, R. A. Garza-Sanchez, F. Glorius, Chem.-Eur. J. 2016, 22, 5909; Ni: f) J. C. Tellis, D. N. Primer, G. A. Molander, Science 2014, 345, 433; g) A. Noble, S. J. McCarver, D. W. C. MacMillan, J. Am. Chem. Soc. 2015, 137, 624; h) L. Chu, J. M. Lipshultz, D. W. C. MacMillan, Angew. Chem. 2015, 127, 8040; Angew. Chem. Int. Ed. 2015, 54, 7929; i) J. J. Murphy, P. Melchiorre, Nature 2015, 524, 297.
- For reviews on C–H bond functionalization in combination with photoredox catalysis, see: a) D. C. Fabry, M. Rueping, *Acc. Chem. Res.* 2016, *49*, 1969; b) Qin, L. Zhu, S. Luo, *Chem. Rev.* 2017, *117*, DOI: 10.1021/acs.chemrev.6b00657 and the references therein.
- [4] For synthetic applications of hypervalent iodine(III) reagents under photoredox catalysis, see: a) L. Wang, J. Liu, Eur. J. Org. Chem. 2016, 1813 and references therein; b) R. Sakamoto, T. Inada, S. Selmadurai, S. A. Moteki, K. Maruoka, Chem. Commun. 2016, 52, 3758.
- [5] a) M. Yan, J. C. Lo, J. T. Edwards, P. S. Baran, J. Am Chem. Soc.
 2016, 138, 12692; b) J. Yamaguchi, A. D. Yamaguchi, K. Itami, Angew.
 Chem. 2012, 124, 9092; Angew. Chem. Int. Ed. 2012, 51, 8960.

- [6] For recent reports on the Hofmann-Löffler reaction, see: a) C. Martínez, K. Muñiz, Angew. Chem. 2015, 127, 8405; Angew. Chem. Int. Ed. 2015, 54, 8287; b) C. Q. O'Broin, P. Fernández, C. Martínez, K. Muñiz, Org. Lett. 2016, 18, 436; c) E. A. Wappes, S. C. Fosu, T. C. Chopko, D. A. Nagib, Angew. Chem. 2016, 128, 10128; Angew. Chem Int. Ed. 2016, 55, 9974; d) N. R. Paz, D. Rodríguez-Sosa, H. Valdés, R. Marticorena, D. Melián, M. B. Copano, C. C. González, A. J. Herrera, Org. Lett. 2015, 17, 7564.
- For references regarding HAT processes, see: a) J. M. Mayer, Acc. Chem. Res. 2011, 44, 36; b) W. Liu, X. Huang, M.-J. Cheng, R. J. Nielsen, W. A. Goddard III, J. T. Groves, Science 2012, 337, 1322; c) J.
 L. Jeffrey, J. A. Terrett, D. W. C. MacMillan, Science 2015, 349, 1532.
- [8] a) J. C. K. Chu, T. Rovis, *Nature* 2016, 539, 272; b) G. J. Choi, Q. Zhu,
 D. C. Miller, C. J. Gu, R. R. Knowles, *Nature* 2016, 539, 268; c) X.-Q.
 Hu, J.-R. Chen, W.-J. Xiao, *Angew. Chem.* 2017, 129, 1988; *Angew. Chem. Int. Ed.* 2017, 56, 1960.
- [9] For alternative metal-mediated N-centered radical generation, see: a) T. Xiong, Q. Zhang, Chem. Soc. Rev. 2016, 45, 3069; b) J.-R. Chen, X.-Q. Hu, L.-Q. Lu, W.-J. Xiao, Chem. Soc. Rev. 2016, 45, 2044; c) L. Q. Nguyen, R. R. Knowles, ACS Catalysis 2016, 6, 2894.
- [10] For general concepts of iodine-catalyzed C-H/N-H coupling: a) P. Finkbeiner, B. Nachtsheim, *Synthesis* 2013, 45, 979; b) M. Uyanik, K. Ishihara, *ChemCatChem* 2012, 4, 177; c) J. Li, M. J. Lear, Y. Kawamoto, S. Umemiya, A. R. Wong, E. Kwon, I. Sato, Y. Hayashi, *Angew. Chem.* 2015, 127, 13178; *Angew. Chem. Int. Ed.* 2015, 54, 12986.
- [11] a) C. C. Clark, A. Marton, G. J. Meyer, *Inorg. Chem.* 2005, *44*, 3383; b)
 J. M. Gardner, M. Abrahamsson, B. H. Famum, G. J. Meyer, *J. Am. Chem. Soc.* 2009, *131*, 16206.
- a) N. A. Romero, D. A. Nicewicz, *Chem. Rev.* 2016, *116*, 10075; b) D.
 P. Hari, B. König, *Chem. Commun.* 2014, *50*, 6688; c) S. Fukuzumi, K.
 Ohkubo, *Org. Biomol. Chem.* 2014,*12*, 6059; d) M. Majek, A. J. von Wangelin, *Acc. Chem. Res.* 2016, *49*, 2316.
- [13] M. A. Miranda, H. García, Chem. Rev. 1994, 94, 1063.
- [14] The beneficial effect of HFIP might be aiding the protonation of the intermediary hypoiodite species and shifting the disproportionation equilibrium of the iodine species.
- [15] Please see supporting information for more experimental details.
- [16] In wet media molecular iodine *inter alia* disproportionates into iodide and hypoiodite (see supporting information for more details).
- [17] M. Uyanik, H. Hayashi, K. Ishihara, *Science* **2014**, *345*, 291.
- [18] This is in notable agreement with common stoichiometric Hofmann-Löffler reactions using the analogous hypobromite: a) A. W. Hofmann, Ber. Dtsch. Chem. Ges. 1883, 16, 558; b) K. Löffler, Ber. Dtsch. Chem. Ges. 1909, 42, 3427; c) M. E. Wolff, Chem. Rev. 1963, 63, 55.
- [19] E. J. Corey, W. R. Hertler, J. Am. Chem. Soc. 1960, 82, 1657.
- [20] We cannot completely rule out a potential participation of the reduced TPT in the N–I activation step. However, this would only permit a stoichiometric radical recombination from **III** to **IV**.
- [21] a) M. Seth, T. Ziegler, J. Chem. Theory Comput. 2012, 8, 901; b) Y. Akinaga, S. Ten-no, Chem. Phys. Lett. 2008, 462, 348.
- [22] a) J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* 1996, 77, 3865; b) J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* 1996, 77, 3865; c) J. P. Perdew, K. Burke, M. Ernzerhof, *Phys. Rev. Lett.* 1997, 78, 1396.
- [23] a) B. O. Roos, P. R. Taylor, P. E. Siegbahn, *Chem. Phys.* **1980**, *48*, 157; b) H.-J. Werner, P. J. Knowles, *J. Chem. Phys.* **1985**, *82*, 5053.
- [24] M. E. Casida, J. Mol. Struct. THEOCHEM 2009, 914, 3.
- [25] a) S. Grimme, J. Comput. Chem. 2004, 25, 1463. b) S. Grimme, J.
 Comput. Chem. 2006, 27, 1787. c) S. Grimme, J. Antony, S. Ehrlich, H.
 Krieg, J. Chem. Phys. 2010, 132, 154104.
- [26] a) C. J. Stein, M. Reiher, J. Chem. Theory Comput. 2016, 12, 1760; b)
 C. J. Stein, M. Reiher, Chimia 2017, 71, 170.
- [27] In agreement with our presented calculations, the previous limitation on sulfonamides^[6] is therefore not due to the potential role of this group as a photosensitizer. For a discussion of the nature of amides and their amidoyl radicals in Hofmann-Löffler reactions, see: D. Šakić, H. Zipse, *Adv. Synth. Catal.* **2016**, *358*, 3983.

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Entry for the Table of Contents

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More light, more possibilities! A dual light-activated intertwined iodine and photoredox-catalyzed process for the amination of remote sp³ C–H bond has been developed. While iodine promotes the activation of the sp³ C–H bond, the dye TPT efficiently acts as photoredox catalyst to regenerate the molecular iodine catalyst. The compatibility of the two processes is explained based on calculations.

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Page No. – Page No.