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A unified photoredox-catalysis strategy for C(sp³)-H hydroxylation and amidation using hypervalent iodine†

Guo-Xing Li,^a Cristian A. Morales-Rivera,^b Fang Gao,^a Yaxin Wang,^a Gang He,^a Peng Liu^{ID}*^b and Gong Chen^{ID}*^{ac}

We report a unified photoredox-catalysis strategy for both hydroxylation and amidation of tertiary and benzylic C–H bonds. Use of hydroxyl perfluorobenziodoxole (PFBI–OH) oxidant is critical for efficient tertiary C–H functionalization, likely due to the enhanced electrophilicity of the benziodoxole radical. Benzylic methylene C–H bonds can be hydroxylated or amidated using unmodified hydroxyl benziodoxole oxidant BI–OH under similar conditions. An ionic mechanism involving nucleophilic trapping of a carbocation intermediate by H₂O or CH₃CN cosolvent is presented.

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Introduction

Methods for efficient and selective alkyl C–H oxidation could streamline the synthesis of fine chemicals, natural products, and drug metabolites.^{1,2} Despite rapid advances in the development of metal-catalyzed reactions³ and reagents,⁴ synthetically useful C(sp³)-H oxygenation chemistry is still in great demand.^{5,6} Recently, radical reactions mediated by hypervalent iodine(III) reagents have emerged as viable means to oxygenate C(sp³)-H bonds under mild conditions.^{7–11} Ochiai first reported the oxidation of activated C(sp³)-H bonds of benzyl and allyl ethers to the corresponding esters using *t*-butylperoxy benziodoxole (BI–OO*t*Bu, **1**) via H-abstraction by benziodoxole radical BI• **2** (Scheme 1A).⁹ Maruoka elegantly demonstrated the use of acyclic iodane reagents **3** and **5** in the selective oxidation of unactivated methylene C–H bonds of simple alkanes to the corresponding ketones, effected by more reactive iodanyl radical intermediates **4** and **6**.¹⁰ Notably, Maruoka's oxygenation reactions proceed with a selectivity for secondary over tertiary C–H bonds. Herein, we report an efficient and broadly applicable photoredox-catalysis strategy for the selective hydroxylation of tertiary and benzylic C–H bonds using hydroxyl benziodoxoles as oxidant and H₂O as cosolvent and hydroxylation reagent. This reaction system can be easily modulated to

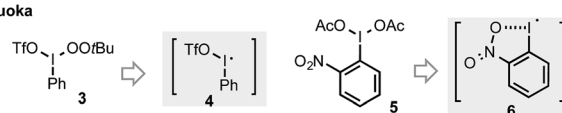
A) Radical C(sp³)-H oxygenation using hypervalent iodine



Ochiai



Maruoka



B) This work



Scheme 1 C(sp³)-H oxygenation and amination with hypervalent iodine(III).

^aState Key Laboratory and Institute of Elemento-Organic Chemistry, College of Chemistry, Collaborative Innovation Center of Chemical Science and Engineering (Tianjin), Nankai University, Tianjin 300071, China. E-mail: gongchen@nankai.edu.cn

^bDepartment of Chemistry, University of Pittsburgh, Pittsburgh, PA 15260, USA. E-mail: pengliu@pitt.edu

^cDepartment of Chemistry, The Pennsylvania State University, 104 Chemistry Building, University Park, PA 16802, USA. E-mail: guc11@psu.edu

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achieve tertiary and benzylic C–H amidation with high efficiency and selectivity using CH₃CN as co-solvent and amidation reagent.

Results and discussion

Previously, we discovered a visible light-promoted method for tertiary C–H azidation using Zhdankin reagent BI–N₃ **11** (see entry 1, Table 1), [Ru(bpy)₃]Cl₂ photosensitizer, and household compact fluorescent lamp (CFL) irradiation.^{12–14} We proposed a radical chain mechanism for this azidation reaction, beginning with formation of BI radical **2** *via* single electron reduction of **11** by a photoexcited Ru(II)* species. BI' **2** then selectively abstracts a H atom from the substrate (*e.g.* 4-methylpentyl benzoate **7**), forming tertiary alkyl radical intermediate, which reacts with **11** to give C–H azidation product and

regenerate radical **2**, propagating a radical chain reaction. Encouraged by these results, we questioned whether the reaction with the corresponding hydroxyl benziodoxole could offer C–H hydroxylation product under similar conditions.

As shown in Table 1, we commenced the investigation of tertiary C–H hydroxylation of **7** with BI–OH **13** under the irradiation of CFL (23 W) using [Ru(bpy)₃]Cl₂ as photocatalyst in hexafluoroisopropanol (HFIP) at 30 °C. Our previous work has shown that BI–OH **13** can be used to generate BI' **2** under similar conditions for a Minisci-type C–H alkylation reaction of *N*-heteroarenes with alkyl boronic acids.^{15,16} However, subjecting **7**, **13**, and [Ru(bpy)₃]Cl₂ to CFL irradiation produced only trace amount of the desired hydroxylation product **8**, with **7** largely unconsumed (entry 2). However, adding H₂O to the reaction increased the yield of **8** to 29% (entry 3). Our previous

Table 1 Tertiary C–H hydroxylation of **7** with hydroxyl benziodoxoles

Entry	Reagents (equiv.)	Solvents	Yield ^a (%) 8
1	BI–N ₃ 11 (2)	HFIP	<1 ^b
2	BI–OH 13 (2)	HFIP	<2
3	BI–OH 13 (2)	HFIP/H ₂ O (26/1)	29
4	4FBI–OH 14 (2)	HFIP/H ₂ O (26/1)	32
5	4CF ₃ BI–OH 15 (2)	HFIP/H ₂ O (26/1)	38
6	TFBI–OH 16 (2)	HFIP/H ₂ O (26/1)	46
7	PFBI–OH 17 (2)	HFIP/H ₂ O (26/1)	51
8	4MOBI–OH 18 (2)	HFIP/H ₂ O (26/1)	25
9	BI–OAc 12 (2)	HFIP/H ₂ O (26/1)	18
10	17 (2.5)	HFIP/H₂O (26/1)	64^c
11	17 (2.5)	HFIP/H ₂ O (10/1)	55
12	17 (2.5), O ₂ (1 atm)	HFIP/H ₂ O (26/1)	29
13	17 (2.5), Ir(ppy) ₃ (2.5 mol%)	HFIP/H ₂ O (26/1)	<2
14	17 (2.5), [Ru(bpz) ₃](PF ₆) ₂ (2.5 mol%)	HFIP/H ₂ O (26/1)	<2
15	17 (2.5), in darkness	HFIP/H ₂ O (26/1)	<2
16	17 (2.5), [Ru(bpy) ₃]Cl ₂ (1 mol%)	HFIP/H ₂ O (26/1)	40
17	17 (2.5)	HFIP	4
18	17 (2.5)	DMSO/H ₂ O (26/1)	<2
19	17 (2.5)	HFIP/CH ₃ CN (26/1) ^d	<2 (+10% of 10)
20	17 (2.5)	HFIP/CH₃CN (4/3)^d	<2 (+56% of 10)^e
21	13 (2.5)	HFIP/CH ₃ CN (4/3) ^d	<2 (+8% of 10)



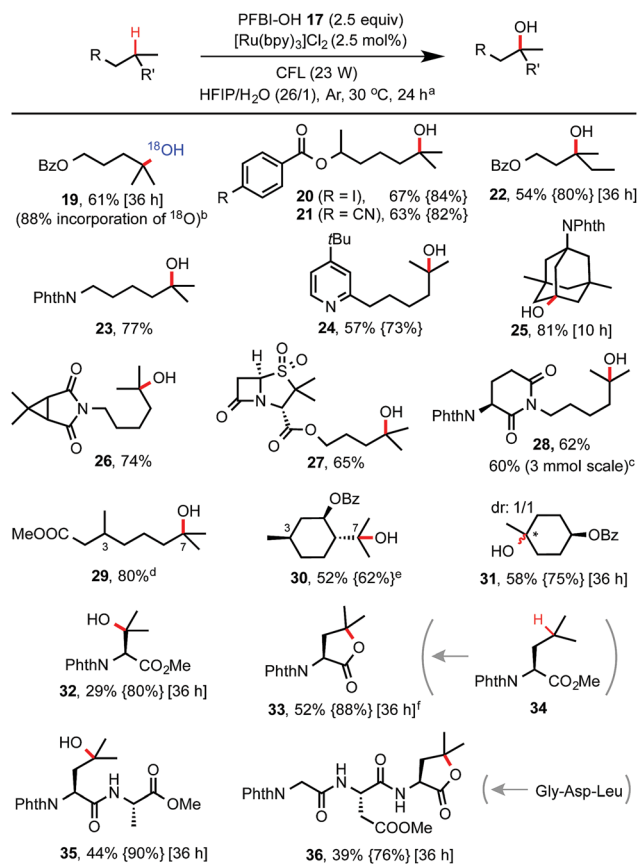
^a Isolated yield on a 0.2 mmol scale, *c* ~ 50 mM, ACS grade of HFIP was used. ^b 58% of **9** was obtained. ^c 8% of **7** was recovered. ^d Anhydrous HFIP and CH₃CN dried over 4 Å molecular sieves were used. ^e *c* ~ 30 mM, ~10% of **7** was recovered. See ESI for more screening results.



work has indicated that the spin density of Bl^\cdot is delocalized on both O and I atoms and that Bl^\cdot is more stable than benzoyloxy radical BzO^\cdot .¹⁵ The stability of Bl^\cdot may explain the observed weak reactivity for H-abstraction and the low conversion of **7**.^{17,18} We speculated that installation of electron-withdrawing groups on the aryl motif of Bl would increase its electrophilicity, and enhance its H-abstraction reactivity. As shown in entries 4–7, Bl-OH analogs **14–17** with different electron-withdrawing groups were prepared and evaluated (see ESI† for more details).¹⁹ We were pleased to find that these Bl-OH analogs provided improved results, and hydroxyl perfluorobenziodoxole (PFBI-OH, **17**) gave the best yield.^{20,21} A 64% isolated yield of **8** was obtained when 2.5 equiv. of **17** was used (entry 10). Regarding the optimization of this hydroxylation reaction, we note: (1) addition of H_2O is critical to obtain high yield (see entries 10 vs. 17). (2) **17** has high polarity and only dissolves well in polar solvents such as HFIP, DMSO, DMF; HFIP gives significantly better results than other solvent tested; (3) under O_2 atmosphere, the reaction gave significantly diminished yield (entry 12); (4) in the dark, the reaction gave no product (entry 15); (5) only trace amount (<3% yield) of methylene C–H hydroxylation side product was detected. Interestingly, when the reaction was performed in mixed HFIP/ CH_3CN solvents (4/3) under similar conditions we obtained 56% yield of the C–H aminated product **10** with excellent selectivity (entry 20).

With optimized conditions in hand, we investigated the substrate scope of this C–H hydroxylation reaction (Scheme 2). In general, the reaction proceeds with excellent selectivity for tertiary C–H bonds and in good yield. Common functional groups including CN, iodo, esters, amide, imide and pyridine moiety are tolerated. When reaction of **7** was performed in a mixture of HFIP and H_2^{18}O (97% ^{18}O), ^{18}O -labelled product **19** was obtained. C–H hydroxylation of sulbactam and thalidomide derivatives (see **27** and **28**) bearing β -lactam and imide groups proceeded in good yield. **28** was obtained in 60% yield on a gram scale. Both steric and electronic factors influence the reactivity of tertiary C–H bonds. For instance, tertiary C–H hydroxylation took place selectively at the more distal 3° carbon of **29**. Hydroxylation of the sterically hindered and electron-poor tertiary C–H bond of phthaloyl valine methyl ester gave **32** in moderate yield. In comparison, C–H hydroxylation of leucine methyl ester **34** provided lactone product **33** in 52% yield. Moreover, short peptide substrates (see **35** and **36**) can be C–H hydroxylated on the Leu residue with excellent selectivity under standard conditions.

While a number of methods for oxidation of benzylic methylene groups to ketones have been developed,²² practical methods for C–H hydroxylation of these methylene groups to benzyl alcohols are sparse.²³ As shown in Scheme 3, we subjected 4-ethylphenyliodide to our standard C–H hydroxylation conditions with PFBI-OH **17**, and obtained the alcohol product **37** in 40% yield along with 22% of ketone **37'** and other unidentified by-products. We were delighted to find that use of 2 equiv. of Bl-OH **13** under the same conditions gave **37** in 71% yield along with 8% of ketone. More ketone **37'** (24%) was obtained when 4 equiv. of Bl-OH was used for extended reaction

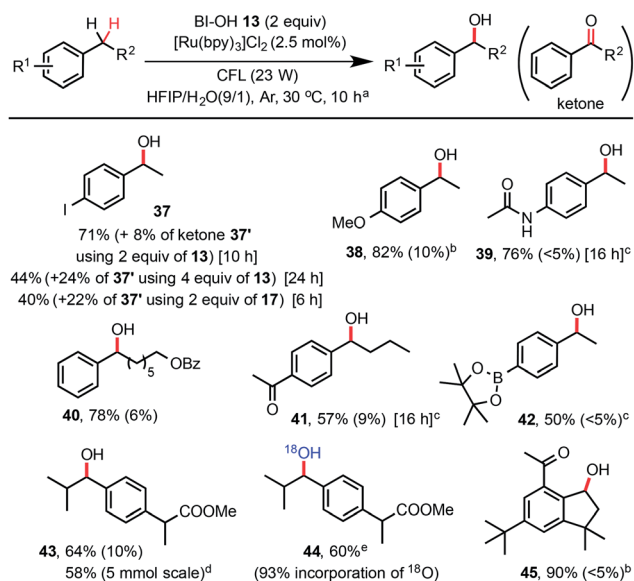


Scheme 2 Substrate scope of tertiary C–H hydroxylation with PFBI-OH **17**. (a) Isolated yield on 0.2 mmol scale under the standard conditions, $c \sim 50$ mM. For reaction with <85% conversion of starting material, yields based on recovered SM (BRSM) were given in braces. (b) H_2^{18}O (97% ^{18}O) was used. (c) 3 mmol scale, 46 h. (d) C_3 hydroxylation product <5%. (e) No C_3 hydroxylation product was detected. (f) No free OH product was obtained.

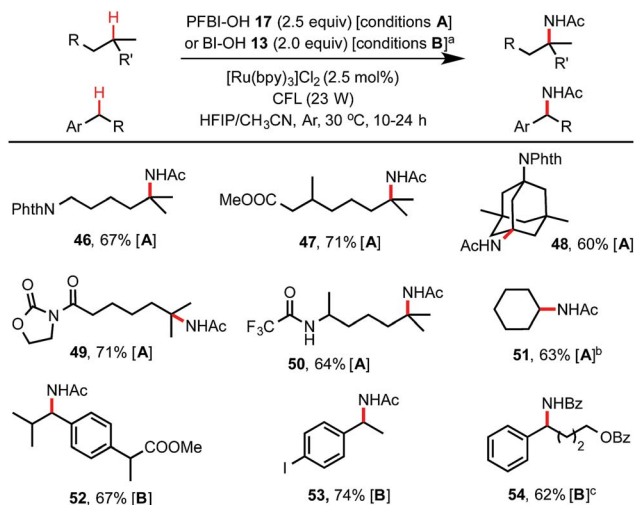
time (24 h). This Bl-OH mediated benzylic C–H hydroxylation exhibited excellent chemo-selectivity and broad substrate scope. The reaction tolerates functional groups such as iodo, ketone, amide, even pinacolyl boronate ester (see **42**). Electron-deficient arenes are less reactive and require the use of 4 equiv. of Bl-OH **13** (see **41**). Electron-rich substrates give good yield with 1.5 equiv. of Bl-OH (see **38**). Reaction of ibuprofen methyl ester gave **43** in 64% yield without the formation of tertiary C–H hydroxylated product. The same reaction in H_2^{18}O gave ^{18}O -labelled product **44**. Reaction of natural product celestolide gave product **45** in excellent yield.

As shown in Scheme 4, by simply switching to the HFIP/ CH_3CN solvents, this hydroxyl benziodoxole-mediated reaction system provides an excellent method for $\text{C}(\text{sp}^3)\text{-H}$ amidation, which remains a challenging transformation for C–H functionalization chemistry.^{24,25} Tertiary C–H amidation with PFBI-OH **17** and benzylic C–H amidation with Bl-OH **13** proceeded with yields and regio-selectivity similar to the corresponding C–H hydroxylations carried out in HFIP/ H_2O solvents. Unactivated methylene C–H bonds were generally unreactive with either **13** or **17**. However, cycloalkanes such as cyclohexane were efficiently amidated with **17** (see **51**), probably due to their





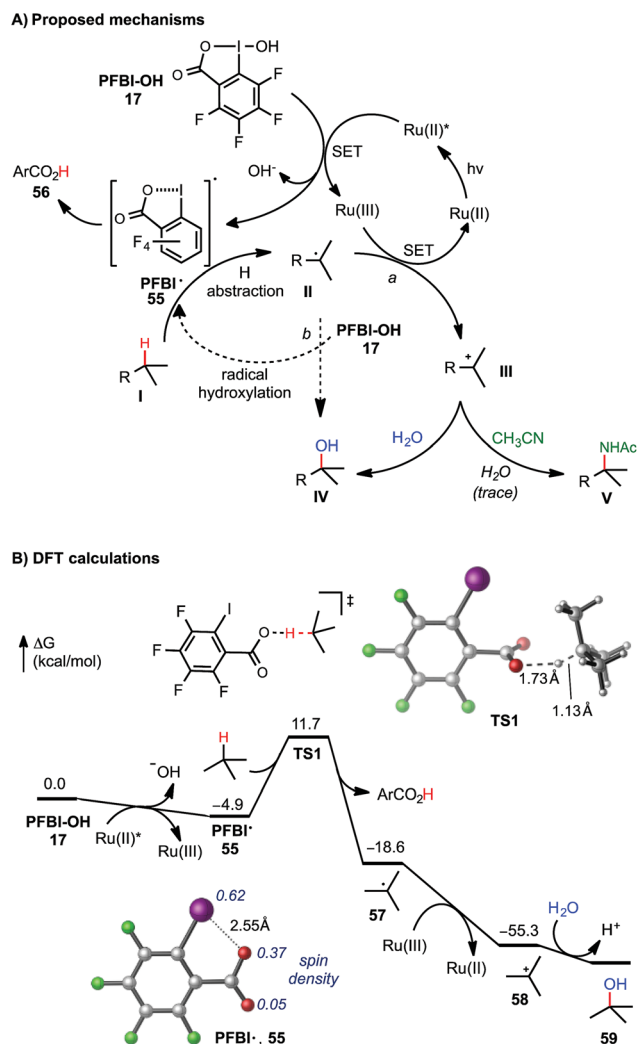
Scheme 3 Substrate scope of benzylic C–H hydroxylation with BI-OH 13. (a) Isolated yield on a 0.2 mmol scale under standard conditions, $c \sim 45$ mM, yield of ketone by-product was given in parentheses. (b) 1.5 equiv. of 13 was used. (c) 4 equiv. of 13 was used. (d) 5 mmol scale, 20 h. (e) H₂¹⁸O (97% ¹⁸O) was used.



Scheme 4 C(sp³)-H amidation with 13 or 17. (a) Conditions A for tertiary C–H amidation, HFIP/CH₃CN (4/3), $c \sim 30$ mM, 24 h; conditions B for benzylic C–H amidation, HFIP/CH₃CN (8/3), $c \sim 35$ mM, 10 h. Anhydrous HFIP and CH₃CN dried over 4 Å molecular sieves were used. Isolated yield on a 0.2 mmol scale. (b) 1 equiv. of cyclohexane was used, 0.5 mmol scale. (c) PhCN was used as cosolvent, HFIP/PhCN (8/5), $c \sim 30$ mM, 10 h.

slightly more activated C–H bonds and more favorable kinetics.^{25b} Product 54 carrying a benzamide group was obtained in good yield using HFIP/PhCN solvent under similar conditions. Generally, the competing C–H hydroxylation reactions were well suppressed (<2% yield) in HFIP/nitrile solvents.

As shown in Scheme 5A, two C–O bond forming mechanisms were initially considered for this C–H hydroxylation reaction:



Scheme 5 Mechanistic consideration of C(sp³)-H functionalization with PFBI-OH. DFT calculations were performed at the M06-2X/6-311++G(d,p)-SDD/SMD(HFIP)//M06-2X/6-31+G(d)-SDD level of theory. All energies are in kcal mol⁻¹. See ESI† for details of DFT calculations with BI-OH.

nucleophilic trapping of a carbocation intermediate with H₂O (pathway a) or a radical chain reaction with the hydroxyl benziodoxole reagents (pathway b).^{23c} In contrast to the large quantum yield Φ observed in our previously reported visible light-promoted C–H azidation reaction with BI-N₃ 11,¹² a small Φ (0.85, measured by Yoon's method²⁶) of the C–H hydroxylation reaction of 7 with PFBI-OH 17 suggested a non-radical chain mechanism (see ESI† for details). The dependence of the reactivity on the H₂O co-solvent and the formation of amidation product in the presence of CH₃CN product strongly support ionic pathway a. Stern–Volmer experiments confirmed that the excited state of photocatalyst [Ru(bpy)₃]Cl₂ can be quenched by the addition of PFBI-OH 17, while no obvious luminescence change of the photocatalyst was observed in the presence of substrate 7 (see ESI† for details).²⁷

The mechanism of tertiary C–H hydroxylation with PFBI-OH 17 likely begins with single electron transfer (SET) from photoexcited Ru(II)* to PFBI-OH 17, generating radical PFBI• 55.



Radical **55** abstracts a H atom from alkane substrate **I**, forming tertiary carbon radical **II**. **II** can be oxidized by the Ru(III) species, forming tertiary carbocation intermediate **III**, and regenerating the photocatalyst. Finally, tertiary carbocation intermediate **III** is attacked by H₂O to give hydroxylated product **IV**. Trapping of **III** by CH₃CN can give the amidated product **V** following a Ritter reaction-type mechanism.^{25b} We speculate that Bl-OH mediated benzylic C-H hydroxylation and amidation proceeds through a similar mechanism, involving cleavage of benzylic C-H bond with less electrophilic Bl' 2.

This mechanism is supported by density functional theory (DFT) calculations using *t*-butane as a model substrate (Scheme 5B). The initial SET reduction of PFBl-OH **17** to PFBl' **55** is significantly more exergonic than the SET with Bl-OH **13** to Bl' **2** ($\Delta G = -4.9$ kcal mol⁻¹ with PFBl-OH **15** vs. -0.9 kcal mol⁻¹ with Bl-OH **13**).^{28,29} With its spin density delocalized over the O and I atoms, PFBl' **55** undergoes facile H-abstraction of *t*-butane through an O-centered transition state (**TS1**) with a ΔG^\ddagger of 16.6 kcal mol⁻¹ to give *t*Bu'.³⁰ This H-abstraction process is promoted by the electron-deficient perfluoroaryl group. The corresponding H-abstraction with Bl' **2** requires a noticeably higher barrier of 18.2 kcal mol⁻¹ (see ESI†). The subsequent oxidation of *t*Bu' by Ru(III) to *t*butyl cation is highly exothermic. Finally, the *t*butyl cation is trapped with H₂O, providing *t*BuOH. Taken together, the DFT calculations indicated the perfluorinated analogue PFBl-OH promotes both the initial SET reduction and the H-abstraction steps in the catalytic cycle of the tertiary C-H hydroxylation.

Conclusions

In summary, we have developed a unified photoredox-catalysis strategy for both C(sp³)-H hydroxylation and amidation using hydroxyl benziodoxole oxidant. This strategy allows the selective functionalization of tertiary and benzylic methylene C-H bonds under mild conditions. These reactions exhibit excellent substrate scope, and offer an efficient and convenient method for late-stage derivatization of complex substrates. Distinct from the radical chain mechanism invoked for our previous tertiary C-H azidation reaction with azido benziodoxole, we propose a new product-forming pathway: photoredox catalyzed formation of a carbocation intermediate, followed by nucleophilic trapping with H₂O or nitrile cosolvent. Further expansion of the nucleophile scope and the functionalization of unactivated methylene C-H bonds using this reaction system are currently under investigation.

Conflicts of interest

There are no conflicts to declare.

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Notes and references

- (a) T. Newhouse and P. S. Baran, *Angew. Chem., Int. Ed.*, 2011, **50**, 3362; (b) M. C. White, *Science*, 2012, **335**, 807; (c) J. Genovino, D. Sames, L. G. Hamann and B. B. Touré, *Angew. Chem., Int. Ed.*, 2016, **55**, 14218.
- (a) P. A. Wender, M. K. Hilinski and A. V. W. Mayweg, *Org. Lett.*, 2005, **7**, 79; (b) K. Chen and P. S. Baran, *Nature*, 2009, **459**, 824; (c) E. M. Stang and M. C. White, *Nat. Chem.*, 2009, **1**, 547.
- For selected metal-catalyzed C(sp³)-H oxygenation reactions, see: (a) M. S. Chen and M. C. White, *Science*, 2007, **318**, 783; (b) Y.-H. Zhang and J.-Q. Yu, *J. Am. Chem. Soc.*, 2009, **131**, 14654; (c) M. Zhou, N. D. Schley and R. H. Crabtree, *J. Am. Chem. Soc.*, 2010, **132**, 12550; (d) E. McNeill and J. Du Bois, *J. Am. Chem. Soc.*, 2010, **132**, 10202; (e) M. Lee and M. S. Sanford, *J. Am. Chem. Soc.*, 2015, **137**, 12796.
- For selected C-H hydroxylation with dioxiranes and oxaziridines, see: (a) D. Yang, M.-K. Wong, X.-C. Wang and Y.-C. Tang, *J. Am. Chem. Soc.*, 1998, **120**, 6611; (b) B. H. Brodsky and J. Du Bois, *J. Am. Chem. Soc.*, 2005, **127**, 15391; (c) K. Chen, J. M. Richter and P. S. Baran, *J. Am. Chem. Soc.*, 2008, **130**, 7247; (d) N. D. Litvinas, B. H. Brodsky and J. Du Bois, *Angew. Chem., Int. Ed.*, 2009, **48**, 4513; (e) S. Kasuya, S. Kamijo and M. Inoue, *Org. Lett.*, 2009, **11**, 3630; (f) A. M. Adams and J. Du Bois, *Chem. Sci.*, 2014, **5**, 656.
- For other selected methods for C(sp³)-H oxygenation: (a) X. Li, X. Che, G.-H. Chen, J. Zhang, J.-L. Yan, Y.-F. Zhang, L.-S. Zhang, C.-P. Hsu, Y. Q. Gao and Z.-J. Shi, *Org. Lett.*, 2016, **18**, 1234; (b) J. Ozawa, M. Tashiro, J. Ni, K. Oisaki and M. Kanai, *Chem. Sci.*, 2016, **7**, 1904.
- For a photoredox-catalyzed sulfonate-directed C(sp³)-H hydroxylation, see: A. Hollister, E. S. Conner, M. L. Spell, K. Deveaux, L. Maneval, M. W. Beal and J. R. Ragains, *Angew. Chem., Int. Ed.*, 2015, **54**, 7837.
- For selected reviews on hypervalent iodine, see: (a) Hypervalent Iodine Chemistry-Modern Developments in Organic Synthesis, *Topics in Current Chemistry*, ed. T. Wirth, M. Ochiai, V. V. Zhdankin, G. F. Koser, H. Tohma and Y. Kita, Springer, Berlin, 2003; (b) T. Wirth, *Angew. Chem., Int. Ed.*, 2005, **44**, 3656; (c) V. V. Zhdankin and P. J. Stang, *Chem. Rev.*, 2008, **108**, 5299; (d) T. Dohi and Y. Kita, *Chem. Commun.*, 2009, **16**, 2073; (e) Y. Li, D. P. Hari, M. V. Vita and J. Waser, *Angew. Chem., Int. Ed.*, 2016, **55**, 4436.
- (a) R. Samanta, K. Matcha and A. P. Antonchick, *Eur. J. Org. Chem.*, 2013, 5769; (b) T. Dohi and Y. Kita, *ChemCatChem*, 2014, **6**, 76; (c) L. Bering and A. P. Antonchick, *Chem. Sci.*, 2017, **8**, 452.
- M. Ochiai, T. Ito, H. Takahashi, A. Nakanishi, M. Toyonari, T. Sueda, S. Goto and M. Shiro, *J. Am. Chem. Soc.*, 1996, **118**, 7716.



- 10 (a) S. A. Moteki, A. Usui, T. Zhang, C. R. S. Alvarado and K. Marouka, *Angew. Chem., Int. Ed.*, 2013, **52**, 8657; (b) S. A. Moteki, S. Selvakumar, T. Zhang, A. Usui and K. Marouka, *Asian J. Org. Chem.*, 2014, **3**, 932.
- 11 Y. Zhao and Y. Y. Yeung, *Org. Lett.*, 2010, **12**, 2128. A carbonyl-directed methylene C–H oxygenation using $\text{PhI}(\text{OAc})_2$ and $t\text{BuOOH}$, yielding ketones, is described.
- 12 Y. Wang, G.-X. Li, G. Yang, G. He and G. Chen, *Chem. Sci.*, 2016, **7**, 2679.
- 13 (a) V. V. Zhdankin, A. P. Krasutsky, C. J. Kuehl, A. J. Simonsen, J. K. Woodward, B. Mismash and J. T. Bolz, *J. Am. Chem. Soc.*, 1996, **118**, 5192; (b) A. Sharma and J. F. Hartwig, *Nature*, 2015, **517**, 600.
- 14 For selected reviews on photoredox catalysis reactions: (a) J. M. R. Narayanam and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2011, **40**, 102; (b) T. P. Yoon, M. A. Ischay and J. N. Du, *Nat. Chem.*, 2010, **2**, 527; (c) C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322; (d) J. Xie, H. Jin, P. Xu and C. Zhu, *Tetrahedron Lett.*, 2014, **55**, 36.
- 15 G.-X. Li, C. A. Morales-Rivera, Y. Wang, F. Gao, G. He, P. Liu and G. Chen, *Chem. Sci.*, 2016, **7**, 6407.
- 16 For use of BI–OH in photoredox-promoted reactions: (a) H. Huang, G. Zhang, L. Gong, S. Zhang and Y. Chen, *J. Am. Chem. Soc.*, 2014, **136**, 2280; (b) H. Tan, H. Li, W. Ji and L. Wang, *Angew. Chem., Int. Ed.*, 2015, **54**, 8374; (c) K. Jia, F. Zhang, H. Huang and Y. Chen, *J. Am. Chem. Soc.*, 2016, **138**, 1514.
- 17 (a) J. Barluenga, E. Campos-Gomez, D. Rodriguez, F. Gonzalez-Bobes and J. M. Gonzalez, *Angew. Chem., Int. Ed.*, 2005, **44**, 5851; (b) Ref. 9 and 13a.
- 18 The relatively weak H-abstraction reactivity of BI^\cdot is less consequential in the C–H azidation reaction because the reaction proceeds *via* a radical chain pathway.
- 19 M. Linuma, K. Moriyama and H. Togo, *Eur. J. Org. Chem.*, 2014, 772.
- 20 For the original report of PFBI–OH 17, see: R. D. Richardson, J. M. Zayed, S. Altermann, D. Smith and T. Wirth, *Angew. Chem., Int. Ed.*, 2007, **46**, 6529. PFBI–OH can be readily prepared on the gram scale in 2 steps from a cheap precursor (2,3,4,5-tetrafluorobenzoic acid, <\$250 per kg) without column purification. It is a stable solid which can be stored in dark for 2 months and conveniently handled under air on the bench top.
- 21 For a recent use of PFBI–OH 17 in photoredox-mediated reaction, see: K. Jia, Y. Pan and Y. Chen, *Angew. Chem., Int. Ed.*, 2017, **56**, 2478.
- 22 For recent examples of benzylic C–H oxygenation to form ketones: (a) T. Dohi, N. Takenaga, A. Goto, H. Fujioka and Y. Kita, *J. Org. Chem.*, 2008, **73**, 7365; (b) J.-B. Xia, K. W. Cormier and C. Chen, *Chem. Sci.*, 2012, **3**, 2240.
- 23 For recent examples of benzylic methylene C–H oxygenation to install NHPI, ONO_2 , or OTFA groups, see: (a) J. M. Lee, E. J. Park, S. H. Cho and S. Chang, *J. Am. Chem. Soc.*, 2008, **130**, 7824; (b) S. Kamijo, Y. Amaoka and M. Inoue, *Tetrahedron Lett.*, 2011, **52**, 4654; (c) R. Sakamoto, T. Inada, S. Selvakumar, S. A. Moteki and K. Marouka, *Chem. Commun.*, 2016, **52**, 3758.
- 24 For selected reviews on C–H amination: (a) F. Collet, C. Lescot and P. Dauban, *Chem. Soc. Rev.*, 2011, **40**, 1926; (b) J. L. Roizen, M. E. Harvey and J. Du Bois, *Acc. Chem. Res.*, 2012, **45**, 911.
- 25 For selected example of intermolecular $\text{C}(\text{sp}^3)\text{--H}$ amination: (a) X.-Q. Yu, J.-S. Huang, X.-G. Zhou and C.-M. Che, *Org. Lett.*, 2000, **2**, 2233; (b) Q. Michaudel, D. Thevenet and P. S. Baran, *J. Am. Chem. Soc.*, 2012, **134**, 2547; (c) J. L. Roizen, D. N. Zalatan and J. Du Bois, *Angew. Chem., Int. Ed.*, 2013, **52**, 11343; (d) K. Kiyokawa, T. Kosaka, T. Kojima and S. Minakata, *Angew. Chem., Int. Ed.*, 2015, **54**, 13719; (e) G. Pandey and R. Laha, *Angew. Chem., Int. Ed.*, 2015, **54**, 14875; (f) K. Kiyokawa, K. Takemoto and S. Minakata, *Chem. Commun.*, 2016, **52**, 13082.
- 26 For a leading reference characterizing chain processes in visible light photoredox catalysis based on the measurements of quantum yield Φ : M. A. Crismesia and T. P. Yoon, *Chem. Sci.*, 2015, **6**, 5426. A reaction with $\Phi \gg 1$ could only be consistent with a product-forming chain mechanism.
- 27 N. J. Turro, *Modern Molecular Photochemistry*, Benjamin/Cummings, Menlo Park, CA, 1978.
- 28 (a) M. J. Frisch, *et al.*, *DFT calculations were performed using Gaussian 09, Revision D.01*, Gaussian, Inc., Wallingford CT, 2009. Geometries were optimized at the M06-2X/6-31+G(d)-SDD level of theory in the gas phase. Single point energies were calculated at the M06-2X/6-311++G(d,p)-SDD level with the SMD solvation model in HFIP. See ESI† for computational details. For recent computational studies on photoredox mediated C–C bond formation reactions, see: (b) O. Gutierrez, J. C. Tellis, D. N. Primer, G. A. Molander and M. C. Kozlowski, *J. Am. Chem. Soc.*, 2015, **137**, 4896; (c) T. B. Demissie, K. Ruud and J. H. Hansen, *Organometallics*, 2015, **34**, 4218.
- 29 The experimental redox potentials of $E_{\text{Ru}(\text{bpy})_3^{3+/2+}}^0$ (-0.81 V vs. SCE in MeCN) and $E_{\text{Ru}(\text{bpy})_3^{3+/2+}}^0$ ($+1.29$ V vs. SCE in MeCN) were used in the computation of the SET reaction energies with $\text{Ru}(\text{ii})^*$ and $\text{Ru}(\text{iii})$. See: (a) C. R. Bock, T. J. Meyer and D. G. Whitten, *J. Am. Chem. Soc.*, 1975, **97**, 2909. For DFT calculations of redox potentials, see: ref. 16 and (b) P. Winget, C. J. Cramer and D. G. Truhlar, *Theor. Chem. Acc.*, 2004, **112**, 217; (c) A. A. Isse, C. Y. Lin, M. L. Coote and A. Gennaro, *J. Phys. Chem. B*, 2011, **115**, 678; (d) H. G. Roth, N. A. Romero and D. A. Nicewicz, *Synlett*, 2016, **27**, 714.
- 30 Our DFT calculation shows that the I-centered H-abstraction pathway from 55 yields a highly unstable hydriodane and is much less favourable (see ESI† for details).

