Chemical Science



EDGE ARTICLE

View Article Online
View Journal | View Issue



Cite this: Chem. Sci., 2025, 16, 1411

dll publication charges for this article have been paid for by the Royal Society of Chemistry

Received 25th October 2024 Accepted 11th December 2024

DOI: 10.1039/d4sc07243j

rsc.li/chemical-science

Synthesis of fluorine-containing bicyclo[4.1.1] octenes *via* photocatalyzed defluorinative (4 + 3) annulation of bicyclo[1.1.0] butanes with *gem*-difluoroalkenes†

Kuan Zhang,^a Zhengyang Gao,^a Yan Xia,^a Pengfei Li,^{ab} Pin Gao, ^b Xin-Hua Duan ^a and Li-Na Guo ^b*

Although bicyclo[4.1.1] systems are privileged scaffolds in many natural products and drug molecules, efficient synthetic approaches to these systems remain underdeveloped. In this work, we disclose a photoredox-catalyzed defluorinative (4 + 3) annulation of bicyclo[1.1.0]butanes with gemdifluoroalkenes, which provides practical and straightforward access to the fluorine-containing bicyclo [4.1.1]octenes. Our protocol is characterized by mild conditions, broad substrate scope, excellent functional group tolerance and good to excellent yields. Notably, the ease and variety of product derivatizations further enrich the diversity and complexity of the fluorine-containing bicyclo[4.1.1] systems.

Introduction

In the realm of drug development, the concept of "escaping flatland" is gaining prominence, as sp³-hybridized bioisosteres such as bicyclo[1.1.1]pentanes (BCPs), bicyclo[2.1.1]hexanes (BCHs), and bicyclo[3.1.1]heptanes (BCHeps) can improve the pharmacokinetic properties of drug candidates by replacing benzene rings. Additionally, Grygorenko has reported that bicyclo[n.1.1] bridged cycloalkane derivatives (n > 3) are potential bioisosteres of disubstituted benzene rings. Among these, the bicyclo[4.1.1] systems are particularly significant scaffolds found in natural products and drug molecules (Scheme 1a and 1b).1 However, efficient synthetic strategies to access these scaffolds remain a challenge and are underdeveloped. Intramolecular cyclization represents an efficient strategy for the construction of bicyclic[4.1.1] systems (Scheme 1c). Oku and coworkers² reported the synthesis of oxa-bicyclo[4.1.1]octanes (oxa-BCOs) by thermally-driven [2 + 2] cycloaddition. Bach and co-workers3 disclosed a photocatalyzed [2 + 2] cycloaddition to access these oxa-BCOs. Recently, Xu's group4 reported a SmI₂mediated reductive radical 1,6-addition strategy for constructing bicyclo[4.1.1]octane (BCO) scaffolds. Grygorenko and co-

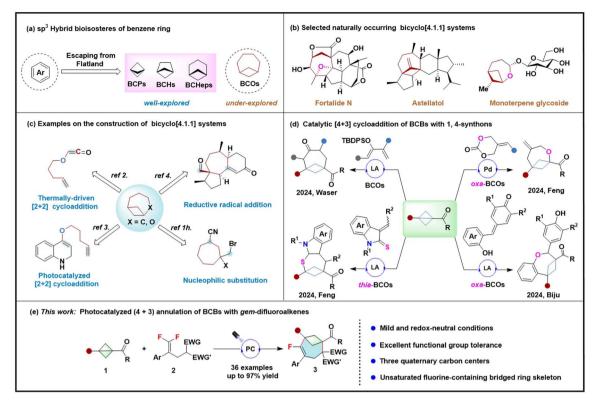
Bicyclo[1.1.0]butanes (BCBs) are the smallest fused carbocycles, possessing a strain energy of 267 kJ mol⁻¹.5 Consequently, they are highly reactive and valuable synthons in many chemical transformations that involve the release of ring strain.6 Since Blanchard's pioneering work on the thermally induced [3 + 2] cycloaddition of BCBs with olefins, the cycloadditions of BCBs have garnered significant interests from chemists.⁷ A variety of [3 + 2] and [3 + 3] cycloadditions of BCBs have been developed through visible light-mediated energy transfer,8 visible light photoredox catalysis,9 transition metal catalysis,10 boron radical catalysis11 and Lewis acid catalysis,12 providing efficient strategies for the synthesis of bicyclo[2.1.1] and bicyclo[3.1.1] systems. However, there have been only a few reports on the construction of bicyclo[4.1.1] systems (Scheme 1d).13 Waser and co-workers demonstrated a Lewis acidcatalyzed [4 + 3] cycloaddition of BCBs with dienol ethers to afford the BCOs. 13a Feng and co-workers reported a Lewis acidcatalyzed [4 + 3] cycloaddition of BCBs with 3benzylideneindoline-2-thiones to give the thia-BCOs.13b They also reported the palladium-catalyzed decarboxylative [4 + 3] cycloaddition of BCBs with 2-alkylidenetrimethylene carbonates to yield the oxa-BCOs.13c Biju and co-workers presented a Lewis acid-catalyzed (4 + 3) annulation of BCBs with para-quinone methides to give the oxa-BCOs.13d Despite these fascinating

workers¹ reported an intramolecular nucleophilic substitution strategy for the BCO backbones. However, the requirement for complex substrates and the lack of generality have limited the applicability of this monomolecular reaction strategy. Given the significance of bicyclo[4.1.1] systems, there is still an urgent and ongoing need to develop universal and rapid synthetic methods for obtaining complex BCOs.

^{*}Department of Chemistry, School of Chemistry, Xi'an Key Laboratory of Sustainable Energy Material Chemistry, Engineering Research Center of Energy Storage Materials and Devices, Ministry of Education, Xi'an Jiaotong University, Xi'an 710049, China. E-mail: guoln81@xjtu.edu.cn

^bFrontier Institute of Science and Technology, State Key Laboratory for Mechanical Behavior of Materials, Xi'an Jiaotong University, Xi'an 710049, China

[†] Electronic supplementary information (ESI) available. CCDC 2382103 and 2382195. For ESI and crystallographic data in CIF or other electronic format see DOI: https://doi.org/10.1039/d4sc07243j



Scheme 1 Importance and synthetic strategies of the bicyclo[n.1.1] systems.

achievements, the synthesis of unsaturated bicyclo[4.1.1] octenes has never been reported. Therefore, there is a significant need to explore new catalytic systems and unsaturated π systems for the annulation reactions of BCBs, which could greatly enrich the structural diversity of bicyclo[n.1.1] systems.

Due to the unique properties of the fluorine atom, organic fluorides represent an attractive class of candidates in the pharmaceutical, agrochemical and material sciences. It has been documented that 15-20% of the newly marketed drugs are organic fluorinated compounds.14 Thus, the incorporation of the fluorine atom into the bridged ring skeletons is an important but challenging task. In this context, the groups of Ma and Mykhailiuk separately reported a [3 + 1] cycloaddition of BCBs with difluorocarbenes, providing an intriguing strategy for the synthesis of 2,2-difluorobicyclo[1.1.1]pentanes However, the construction of the fluorinated bicyclo[n.1.1]alkanes ($n \ge 2$) remains undeveloped. gem-Difluoroalkenes, as readily accessible fluorine-containing building blocks, have shown excellent performance in the construction of complex fluorinated compounds.16 We wonder whether gem-difluoroalkenes can serve as 4C synthons in the annulation reactions of BCBs to construct fluorine-containing bicyclo[4.1.1] systems (Scheme 1e). In this study, we report a visible light photoredox defluorinative (4 + 3) annulation of BCBs with gem-difluoroalkenes, which results in the formation of monofluorinated bicyclo[4.1.1]octenes. This protocol is characterized by readily available starting materials, mild reaction conditions and excellent functional group tolerance, providing a facile

approach to the bicyclo[4.1.1]octenes featuring one fluorine atom and three quaternary carbon centers.

Results and discussion

Initially, BCB 1a and gem-difluoroalkene 2a were chosen as model substrates to determine the optimal reaction conditions (Table 1). Fortunately, the (4 + 3) annulation of 1a with 2a proceeded efficiently using Ru(bpy)3Cl2 as photocatalyst and Cs₂CO₃ as base in CH₃CN under 30 W blue LEDs irradiation for 12 h, yielding the desired monofluorinated bicyclo [4.1.1] octene 3aa in 72% NMR yield (entry 1). Other organic and Ir-based photocatalysts were also tested for this transformation, with Ru(bpy)₃Cl₂ still being the best (entries 2 and 3). Solvent screening showed that CH3CN was still the optimal solvent (entries 4 and 5). Screening of inorganic and organic bases showed that K₂CO₃ and K₃PO₄ were also effective, but both gave relatively lower yields than Cs₂CO₃ (entries 6 and 7). Satisfyingly, increasing the amount of 2a and Cs2CO3 to 1.5 equiv. improved the yield of 3aa to 80% (entry 8). Extending the reaction time from 12 h to 18 h further improved the yield of 3aa up to 88% (entry 9). Reducing the catalyst loading to 1 mol% still gave a comparable yield of 3aa (entry 10). Finally, control experiments indicated that the photocatalyst, base and visible light irradiation were all essential for this conversion (entry 11).

With the optimal conditions in hand, the generality and limitations of the BCBs 1 were first evaluated using the *gem*-difluoroalkene 2a as a model substrate (Table 2). A variety of 1,3-disubstituted BCBs 1 bearing an ester group reacted efficiently

Table 1 Optimization of reaction conditions^a

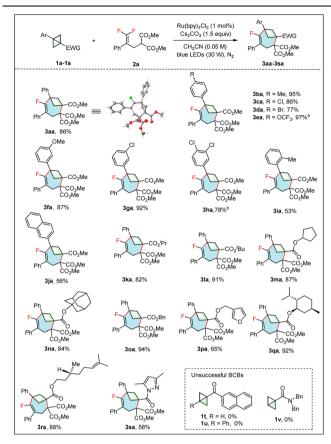
Edge Article

| Entry | Variation from standard conditions | Yield |
|-------|--|----------------------|
| 1 | None | 72 |
| 2 | 4CzIPN, [Acr ⁺ -Mes]ClO ₄ ⁻ | 60, trace |
| 3 | Ir[dF(CF ₃)ppy ₂ (dtbbpy)]PF ₆ | 68 |
| 4 | Acetone or DCE as solvent | 58, 37 |
| 5 | THF or toluene as solvent | 36, 65 |
| 6 | K ₂ CO ₃ or K ₃ PO ₄ as base | 36, 34 |
| 7 | Et ₃ N as base | Trace |
| 8 | 1.5 equiv. of 2a and Cs ₂ CO ₃ | 80 |
| 9 | 18 h | 88 |
| 10 | 1 mol% Ru(bpy) ₃ Cl ₂ | 89 (86) ^b |
| 11 | No PC or no base or no hv | 0 |

 $[^]a$ Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2a** (0.24 mmol, 1.2 equiv.), PC (2 mol%), Cs₂CO₃ (0.2 mmol, 1.0 equiv.), in CH₃CN (0.05 M), blue LEDs (30 W), rt, for 12 h, under N₂. Yields were determined by 1 H NMR using 1,3,5-trimethoxybenzene as an internal standard. b Isolated yield.

with gem-difluoroalkene 2a to yield the desired fluorinated products 3aa-3pa in good to excellent yields. Among these, the structure of 3aa was further confirmed by single crystal X-ray diffraction. Meanwhile, we carried out a crystallographic analysis of the ORTEP diagram for 3aa and provided the values of the geometrical parameters $(r, \theta, \varphi_1, \varphi_2)$ associated with the exit vectors. As noted by Grygorenko and coworkers, 1h all these values fall within the β region of the exit vector plot, and therefore, can be considered as bioisosteres of meta-disubstituted benzene (Fig. 1). The electronic effect on the benzene ring didn't show any significant influence on the reaction efficiency. BCBs with electron-withdrawing or -donating groups at the para- and meta-positions of the benzene ring all reacted well to afford the desired products 3aa-3ha in excellent yields. Functional groups, such as Br (3da) and OCF3 (3ea) were fully compatible with this reaction. The BCB with an ortho-Me group on the benzene ring gave a relatively lower yield (3ia, 53% vs. 3ba, 95%), probably due to steric hindrance. The 2-naphthyl substituted BCB 1j also worked efficiently and gave a moderate yield of 3ja. In addition to the methyl ester, BCBs containing various ester groups, including alkyl esters (1k and 1l), cycloalkyl esters (1m and 1n), benzyl ester (1o) and furan-2-ylmethyl ester (1p) all gave the corresponding products 3ka-3pa in 65-94% yields. The steric hindrance of the ester group did not affect the reaction efficiency. Remarkably, the BCBs obtained from complex natural alcohols such as menthol and citronellol were also applicable to this reaction, giving products 3qa and 3ra in 92% and 88% yields, respectively. The BCB containing an amide group (1s) was also a viable substrate, giving the product 3sa in 58% yield. Unfortunately, the substituted BCBs containing a carbonyl (1t and 1u) or amide group (1v) did not yield the expected products.

Table 2 Scope of BCBs^a



^a Reaction conditions: 1 (0.2 mmol, 1.0 equiv.), 2a (0.3 mmol, 1.5 equiv.), Ru(bpy)₃Cl₂ (1 mol%), Cs₂CO₃ (0.3 mmol, 1.5 equiv.), CH₃CN (0.05 M), under N₂. Isolated yield. n. r. = no reaction. ^b Using Ir $[dF(CF_3)ppy_2(dtbbpy)]PF_6$ instead of Ru(bpy)₃Cl₂.

The scope of *gem*-difluoroalkenes 2 was then investigated using 1a as a model substrate (Table 3). A number of aryl *gem*-difluoroalkenes containing electron-donating and -withdrawing groups on the benzene ring were well engaged in this annulation reaction, giving the desired products 3ab-3an in good to excellent yields. Functional groups, such as OMe (3ae and 3ak), TMS (3af), Br (3ai) and acetyl (3al) all survived well in this transformation, providing opportunities for further product

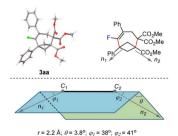
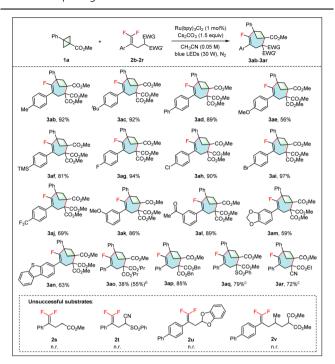


Fig. 1 The corresponding values of the geometrical parameters associated with the exit vectors n_1 and n_2 of **3aa**; geometrical definition of exit vectors and associated parameters.

Table 3 Scope of gem-difluoroalkenes

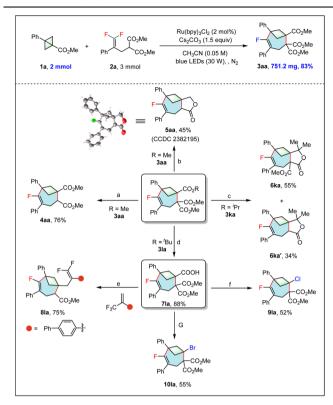


^a Reaction conditions: **1a** (0.2 mmol, 1.0 equiv.), **2** (0.3 mmol, 1.5 equiv.), Ru(bpy)₃Cl₂ (1 mol%), Cs₂CO₃ (0.3 mmol, 1.5 equiv.), CH₃CN (0.05 M), under N₂. Isolated yield. n. r. = no reaction. ^b Recovery of **1a** was given in parentheses. ^c Using K₂CO₃ instead of Cs₂CO₃.

modification. The gem-difluoroalkene with a dibenzo [b,d]thiophen-3-yl group was also amenable, yielding the product 3an in 63% yield. In addition, the gem-difluoroalkene with two isopropyl ester groups also worked, but gave the product 3ao in only 38% yield due to the low conversion. Satisfactorily, the gemdifluoroalkene with two benzyl ester groups gave the target product 3ap in 85% yield. As anticipated, the gem-difluoroalkene with one ester group (2s) didn't engage in this annulation reaction, probably due to the polarity mismatch. Replacement of one ester group with a sulfonyl (2q) or cyano (2r) group also successfully led to the corresponding products 3aq and 3ar in good yields. However, no reaction was observed when both ester groups were replaced by cyano and sulfonyl groups (2t). The gem-difluoroalkene with a 1,3-benzodioxole substituent $(2\mathbf{u})$ also failed to undergo this (4+3) annulation reaction due to the polarity mismatch. Unfortunately, the gem-difluoroalkene 2v, with an extended carbon chain, was incompatible with the reaction.

To demonstrate the potential application of this reaction, large-scale synthesis and derivatizations of products were carried out (Table 4). When the reaction was scaled up to 2.0 mmol, the monofluorinated bicyclo[4.1.1]octene 3aa was obtained in 83% isolated yield. Treatment of 3aa with LiCl and $\rm H_2O$ at 140 °C afforded the decarboxylated product 4aa in 76% yield. Reduction of 3aa with LiAlH₄ followed by treatment of the crude product with PTSA and cyclohexanone led to an unexpected product 5aa in 45% yield. When 3ka was treated with 2.5

Table 4 Scale-up synthesis and derivatizations^a

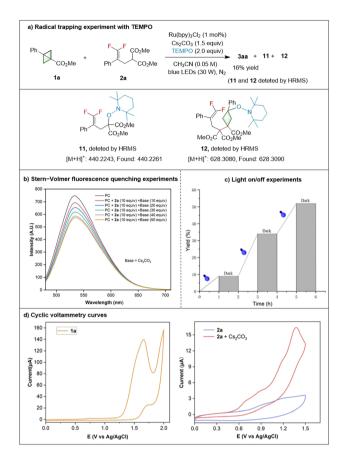


^a Reaction conditions: (a) LiCl (1.0 equiv.), H_2O (1.0 equiv.), DMSO, 140 °C; (b) LiAlH₄ (5.0 equiv.), THF, 0 °C, then cyclohexanone (1.0 equiv.), PTSA (20 mol%), toluene, reflux; (c) MeMgBr (2.5 equiv.), THF, rt; (d) TFA (5.0 equiv.), DCM, rt; (e) 4CzIPN (2 mol%), C_2CO_3 (1.0 equiv.), DMSO, blue LEDs (30 W); (f) NCS (2.1 equiv.), Fe(OAc)₂ (10 mol%), 4,4'-dimethoxy-2,2'-bipyridine (10 mol%), 2,4,6-collidine (1.8 equiv.), C_3CO_3 (10 mol%), 4,4'-dimethoxy-2,2'-bipyridine (10 mol%), 2,4,6-collidine (1.8 equiv.), C_3CO_3 (10 mol%), 2,4,6-collidine (10 m

equiv. of MeMgBr, two different lactones **6ka** and **6ka**' were formed in 55% and 34% yields respectively. The *tert*-butyl ester group in **3la** could be hydrolyzed using TFA to yield the product **7la** in an 88% yield. The acid **7la** could be reacted with α -CF₃ alkene under photoredox catalysis to give the *gem*-difluoroalkene **8la** in a 75% yield through a decarboxylation/radical addition/ β -fluorine elimination cascade. Notably, the decarboxylative halogenations of **7la** could also be achieved *via* an iron-catalyzed LMCT strategy, leading to the formation of the chloride **9la** and bromide **10la** in yields of 52% and 55%, respectively.

To shed light on the mechanism of this annulation reaction, some control experiments were carried out (Scheme 2). Firstly, when 2.0 equiv. of TEMPO, a well-known radical scavenger, was added to the system, the model reaction was significantly inhibited, with the yield reduced from 89% to 16%. In addition, alkyl-TEMPO adducts **11** and **12** were detected by HRMS, indicating that the reaction proceeded *via* a radical pathway. A series of fluorescence quenching experiments were then carried out using 4CzIPN as the photosensitizer. ¹⁷ It was found that the

Edge Article Chemical Science



Scheme 2 Mechanism studies.

4CzIPN* can be efficiently quenched by the anionic **2a**, suggesting that an excited state charge transfer occurred between the 4CzIPN* and the anionic **2a**. The light on/off experiments showed that continuous visible light irradiation was essential for this conversion. Finally, cyclic voltammetry (CV) experiments were conducted. BCB **1a** exhibited an oxidation peak at +1.4 V *versus* the saturated calomel electrode (SCE), which is considered beyond the reach of the Ru(bpy)₃Cl₂ excited state at +0.77 V *versus* SCE. The oxidation potential of compound **2a** was effectively lowered from 0.69 V to 0.56 V *versus* SCE in the presence of a base. These findings suggest that the oxidation of **2a** by the Ru(bpy)₃Cl₂ excited state is thermodynamically favorable.

Based on the above results, a plausible pathway is proposed in Scheme 3. First, the ground state $Ru(\pi)$ is irradiated with visible light to form the excited state $Ru(\pi)^*$. A SET event then occurs between the $Ru(\pi)^*$ and the deprotonated 2a to form the electrophilic radical intermediate I and $Ru(\pi)$. Intermediate I then undergoes regionselective addition to BCB 1a to give the alkyl radical intermediate II. Intermediate II undergoes intramolecular radical addition to give the benzyl radical intermediate III, which is reduced by $Ru(\pi)$ to give the carbanion intermediate IV and regenerate the $Ru(\pi)$ species. Finally, β -fluorine elimination takes place to give the target product 3aa.

Scheme 3 Proposed mechanism.

Conclusions

In summary, we have developed a photoredox (4 + 3) annulation of bicyclo[1.1.0]butanes (BCBs) with *gem*-difluoroalkenes that provides a facile approach to the all-carbon bicyclo[4.1.1] octenes with one fluorine atom and three quaternary carbon centers. This protocol features readily available starting materials, mild conditions, excellent functional group tolerance and good to excellent yields. Remarkably, the ease of large-scale synthesis and derivatizations highlights its potential application in organic synthesis. The incorporation of fluorine atom may further modify the physicochemical properties of this all-carbon bicyclo[4.1.1] system and would be valuable for the development of new drugs.

Data availability

The authors confirm that the data supporting the findings of this study are available within the ESI.†

Author contributions

K. Z. performed all the experiments and prepared the manuscript and ESI.† Z. G. and Y. X. performed the preparation of raw materials. P. L., P. G., X.-H. D. and L.-N. G. directed this project and revised the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

Financial support from the National Natural Science Foundation of China (No. 22171220, 21971201) and the Fundamental Research Funds of the Central Universities (No. xtr072022003) is greatly appreciated. We also thank Mr Zhang, Miss Feng, and Miss Bai at the Instrument Analysis Center of Xi'an Jiaotong University for their assistance with NMR and HRMS analysis.

Notes and references

- 1 (a) R. Gianatassio, J. M. Lopchuk, J. Wang, C.-M. Pan, L. R. Malins, L. Prieto, T. A. Brandt, M. R. Collins, G. M. Gallego, N. W. Sach, J. E. Spangler, H. Zhu, J. Zhu and P. S. Baran, Science, 2016, 351, 241-246; (b) X. Ma and L. N. Pham, Asian J. Org. Chem., 2020, 9, 8-22; (c) J. M. Anderson, N. D. Measom, J. A. Murphy and D. L. Poole, Angew. Chem., Int. Ed., 2021, 60, 24754-24769; (d) M. M. D. Pramanik, H. Qian, W.-J. Xiao and J.-R. Chen, Org. Chem. Front., 2020, 7, 2531-2537; (e) A. Denisenko, P. Garbuz, S. V. Shishkina, N. M. Voloshchuk and P. K. Mykhailiuk, Angew. Chem., Int. Ed., 2020, 59, 20515-20521; (f) R. Kleinmans, S. Dutta, K. Ozols, H. Shao, F. Schäfer, R. E. Thielemann, H. T. Chan, C. G. Daniliuc, K. N. Houk and F. Glorius, J. Am. Chem. Soc., 2023, 145, 12324-12332; (g) T. Iida, J. Kanazawa, T. Matsunaga, K. Miyamoto, K. Hirano and M. Uchiyama, J. Am. Chem. 2022, **144**, 21848–21852; (h) V. V. Semeno, V. O. Vasylchenko, I. M. Fesun, L. Y. Ruzhylo, M. O. Kipriianov, K. P. Melnykov, A. Skreminskyi, R. Iminov, P. Mykhailiuk, B. V. Vashchenko and O. O. Grygorenko, Chem. Eur. J., 2024, 30, e202303859; (i) Q. Wang, J. Han and B. Bao, J. Food Biochem., 2017, 41, e12320; (j) Z.-P. Ge, B. Zhou, F. M. Zimbres, R. S. Haney, Q.-F. Liu, Y. Wu, M. B. Cassera, J.-X. Zhao and J.-M. Yue, Org. Biomol. Chem., 2022, 20, 9000-9009.
- 2 A. Oku, Y. Sawada, M. Schroeder, I. Higashikubo, T. Yoshida and S. Ohki, *J. Org. Chem.*, 2004, **69**, 1331–1336.
- (a) C. Mülle, A. Bauer, M. M. Maturi, M. C. Cuquerella,
 M. A. Miranda and T. Bach, J. Am. Chem. Soc., 2011, 133,
 16689–16697; (b) K. A. B. Austin, E. Herdtweck and
 T. Bach, Angew. Chem., Int. Ed., 2011, 50, 8416–8419.
- 4 N. Zhao, S. Yin, S. Xie, H. Yan, P. Ren, G. Chen, G. Chen and J. Xu, *Angew. Chem.*, *Int. Ed.*, 2018, 57, 3386–3390.
- 5 R. J. Meier, *ChemEngineering*, 2021, 5, 24-44.
- 6 For reviews on BCBs, see: (a) J. Turkowska, J. Durkaab and D. Gryko, Chem. Commun., 2020, 56, 5718–5734; (b)
 C. B. Kelly, J. A. Milligan, L. J. Tilley and T. M. Sodano, Chem. Sci., 2022, 13, 11721–11737; (c) P. Bellotti and F. Glorius, J. Am. Chem. Soc., 2023, 145, 20716–20732; (d)
 Q.-Q. Hu, J. Chen, Y. Yang, H. Yang and L. Zhou, Tetrahedron Chem., 2024, 9, 100070.
- 7 A. Cairncross and E. P. Blanchard, J. Am. Chem. Soc., 1966, 88, 496–504.
- 8 (*a*) R. Kleinmans, T. Pinkert, S. Dutta, T. O. Paulisch, H. Keum, C. G. Daniliuc and F. Glorius, *Nature*, 2022, **605**, 477–482; (*b*) R. Guo, Y.-C. Chang, L. Herter, C. Salome, S. E. Braley, T. C. Fessard and M. K. Brown, *J. Am. Chem. Soc.*, 2022, **144**, 7988–7994; (*c*) T. V. T. Nguyen, A. Bossonnet, M. D. Wodrich and J. Waser, *J. Am. Chem. Soc.*, 2023, **145**, 25411–25421.
- 9 (a) Y. Zheng, W. Huang, R. K. Dhungana, A. Granados, S. Keess, M. Makvandi and G. A. Molander, *J. Am. Chem. Soc.*, 2022, 144, 23685–23690; (b) J. L. Tyler, F. Schäfer,

- H. Shao, C. Stein, A. Wong, C. G. Daniliuc, K. N. Houk and F. Glorius, *J. Am. Chem. Soc.*, 2024, **146**, 16237–16247.
- 10 (a) S. Agasti, F. Beltran, E. Pye, N. Kaltsoyannis, G. Crisenza and D. J. Procter, Nat. Chem., 2023, 15, 535-541; (b) J. Zhou, Y. Xiao, L. He, X.-Y. Gao, X.-C. Yang, W.-B. Wu, G. Wang, J. Zhang and J.-J. Feng, J. Am. Chem. Soc., 2024, 146, 19621-19628; (c) Z. Lin, H. Ren, X. Lin, X. Yu and J. Zheng, J. Am. Chem. Soc., 2024, 146, 18565-18575; (d) H. Wang, R. Gao and X. Li, J. Am. Chem. Soc., 2024, 146, 21069-21077.
- 11 (a) M. Xu, Z. Wang, Z. Sun, Y. Ouyang, Z. Ding, T. Yu, L. Xu and P. Li, Angew. Chem., Int. Ed., 2022, 61, e202214507; (b)
 Y. Liu, S. Lin, Y. Li, J.-H. Xue, Q. Li and H. Wang, ACS Catal., 2023, 13, 5096-5103; (c) T. Yu, J. Yang, Z. Wang, Z. Ding, M. Xu, J. Wen, L. Xu and P. Li, J. Am. Chem. Soc., 2023, 145, 4304-4310.
- 12 (a) K. Dhake, K. J. Woelk, J. Becica, A. Un, S. E. Jenny and D. C. Leitch, Angew. Chem., Int. Ed., 2022, 61, e202204719; (b) Y. Liang, F. Paulus, C. G. Daniliuc and F. Glorius, Angew. Chem., Int. Ed., 2023, 62, e202305043; (c) N. Radhoff, C. G. Daniliuc and A. Studer, Angew. Chem., Int. Ed., 2023, 62, e202304771; (d) D. Ni, S. H, X. Tian, Y. Y, Z. Li and L. Deng, Angew. Chem., Int. Ed., 2023, 62, e202308606; (e) L. Tang, Y. Xiao, F. Wu, J.-L. Zhou, T.-T. Xu and J.-J. Feng, Angew. Chem., Int. Ed., 2023, 62, e202310066; (f) K. Zhang, S. Tian, W. Li, X. Yang, X.-H. Duan, L.-N. Guo and P. Li, Org. Lett., 2024, 26, 5482–5487; (g) Q.-Q. Hu, L.-Y. Wang, X.-H. Chen, Z.-X. Geng, J. Chen and L. Zhou, Angew. Chem., Int. Ed., 2024, 63, e202405781; (h) D. Sarkar, S. Deswal, R. C. Das and A. T. Biju, Chem. Sci., 2024, 15, 16243–16249.
- 13 (a) S. Nicolai and J. Waser, Chem. Sci., 2024, 15, 10823–10829; (b) J.-J. Wang, L. Tang, Y. Xiao, W.-B. Wu, G. Wang and J.-J. Feng, Angew. Chem., Int. Ed., 2024, 63, e202405222; (c) X.-Y. Gao, L. Tang, X. Zhang and J.-J. Feng, Chem. Sci., 2024, 15, 13942–13948; (d) S. Deswal, A. Guin and A. T. Biju, Angew. Chem., Int. Ed., 2024, e202408610.
- 14 (a) S. Ali and J. Zhou, Eur. J. Med. Chem., 2023, 256, 115476–115487; (b) Q. Wang, Y. Bian, G. Dhawanc, W. Zhang, A. Sorochinskye, A. Makaremf, V. Soloshonokg and J. Han, Chin. Chem. Lett., 2024, 35, 109780–109781.
- (a) X. Ma, D. L. Sloman, Y. Han and D. J. Bennett, *Org. Lett.*,
 2019, 21, 7199–7203; (b) R. M. Bychek, V. Hutskalova,
 Y. P. Bas, O. A. Zaporozhets, S. Zozulya, V. V. Levterov and
 P. K. Mykhailiuk, *J. Org. Chem.*, 2019, 84, 15106–15117.
- 16 (a) K. Chen, W. Chen, F. Chen, H. Zhang, H. Xu, Z. Zhou and W. Yi, Org. Chem. Front., 2021, 8, 4452–4458; (b) Z. Li, Y. Zhang, Y. Zhang, X. He and X. Shen, Angew. Chem., Int. Ed., 2023, 62, e202303218; (c) L. Yang, Z. Tao, H.-D. Xu, M.-H. Shen and H. Chu, Org. Lett., 2024, 26, 5782–5787.
- 17 When performing fluorescence quenching with Ru(bpy)₃Cl₂, the separate addition of base has an impact on the luminescence curve of Ru(bpy)₃Cl₂. Consequently, we chose 4CzIPN as the photosensitizer for fluorescence quenching experiment.