Chemical Science

ROYAL SOCIETY OF CHEMISTRY

EDGE ARTICLE

View Article Online
View Journal | View Issue

Cite this: *Chem. Sci.*, 2022, **13**, 13466

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

Received 5th October 2022
Accepted 31st October 2022

DOI: 10.1039/d2sc05521j

rsc.li/chemical-science

Alkylboronic acids as alkylating agents: photoredox-catalyzed alkylation reactions assisted by K_3PO_4†

Fuyang Yue, Henan Ma, Hongjian Song,* Yuxiu Liu, Jianyang Dong* and Qingmin Wang*

Despite the ubiquity of alkylboronic acids in organic synthesis, their utility as alkyl radical precursors in visible-light-induced photocatalytic reactions is limited by their high oxidation potentials. In this study, we demonstrated that an inorganophosphorus compound can modulate the oxidation potentials of alkylboronic acids so that they can act as alkyl radical precursors. We propose a mechanism based on the results of fluorescence quenching experiments, electrochemical experiments, ^{11}B and ^{31}P NMR spectroscopy, and other techniques. In addition, we describe a simple and reliable alkylation method that has good functional group tolerance and can be used for direct C–B chlorination, cyanation, vinylation, alkynylation, and allylation, as well as late-stage functionalization of derivatized drug molecules. Notably, alkylboronic acids can be selectively activated in the presence of a boronic pinacol ester.

Introduction

Alkyl radicals (R˙), which are among the most fundamental intermediates in organic chemistry, can be generated from feedstock chemicals such as alkanes, alkenes, amines, carboxylic acids, alcohols, ketones, aldehydes and their derivatives and can be used for various synthetic transformations.[1–14] The reactivity of alkyl radicals is complementary to that of other alkyl intermediates, such as carbanions, carbocations, and carbenes; and taken together, these intermediates offer flexible synthetic routes to structurally complex, C(sp3)-rich scaffolds. Traditionally, alkyl radicals were rarely used in reaction design because they are usually generated by means of energy-intensive or complicated procedures. In addition, their reactivity is difficult to control, which can lead to the formation of byproducts.[15] However, over the past 10 years, as a result of pioneering work by the groups of MacMillan, Stephenson, Yoon, and others, visible-light-induced free radical reactions have emerged as useful tools for accomplishing synthetic transformations under mild, environmentally benign conditions.[16–25] Unlike traditional methods for generating alkyl radicals, visible-light-induced photocatalysis can produce low concentrations of free radicals. Although photochemical approaches have been employed to accomplish economical, scalable, and unique transformations, chemists have continued to search for novel alkyl radical precursors and methods for production of alkyl radicals.[26–31]

We reasoned that organoboron species might be useful for this purpose. Organoborons have long been recognized as valuable synthetic intermediates and have recently become more accessible as highly functionalized building blocks because of the development of flexible synthetic approaches from various functional groups.[32,33] Visible-light-induced photoredox reactions involving alkyl radicals generated from organoboron species have been shown to be an important tool for the preparation of high-value organic compounds.[32–38] Since the pioneering work reported by the Molander[37] and Akita[38] groups, trifluoroborates, which are synthesized from boronic esters or boronic acids, have been widely used for various organic transformations, mainly because of their low oxidation potentials [~1.2 V *vs.* the saturated calomel electrode (SCE)] and bench stability. In recent years, other boric acid derivatives, such as borate esters, borooctene, and their metal salts (*e.g.*, lithium alkyl borates based on boron ferrocene), have also been explored to enrich their applications (Fig. 1A).[39–54]

Although organoboron species have been widely used as sources of alkyl radicals, boronic acids are more suitable precursors because they are widely available from commercial and synthetic sources. In addition, they have a vacant p orbital centered on the B atom, which facilitates the formation reversible-lattice bonds with O or N nucleophiles.[55–57] Although the number of applications of boron-containing molecules in the fields of medicine (*e.g.*, tavaborole and crisaborole),

State Key Laboratory of Elemento-Organic Chemistry, Research Institute of Elemento-Organic Chemistry, College of Chemistry, Frontiers Science Center for New Organic Matter, Nankai University, Tianjin 300071, People's Republic of China. E-mail: wangqm@nankai.edu.cn; songhongjian@nankai.edu.cn; jydong@mail.nankai.edu.cn

† Electronic supplementary information (ESI) available. See DOI: https://doi.org/10.1039/d2sc05521j

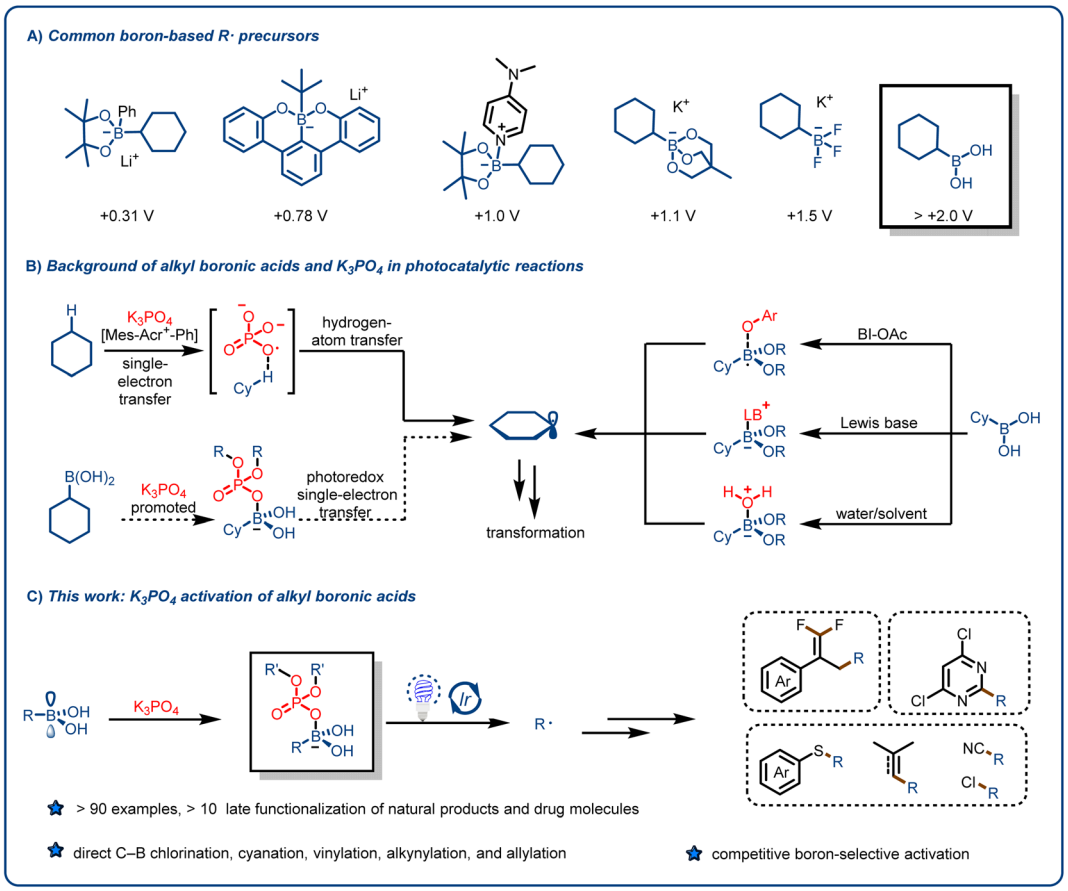


Fig. 1 From inspiration to reaction design. (A) Typical boronic acid derivatives used as alkyl radical sources, along with their oxidation potentials (*vs.* SCE). (B) Background of alkyl boronic acids and K_3PO_4 in photocatalytic reactions. BI-OAc = acetoxybenziodoxole. (C) Activation of alkylboronic acids by K_3PO_4.

materials chemistry, and biomedical engineering has increased substantially in the past decade, maintaining their high commercial availability,[39–54] only a few studies have focused on the use of boronic acids as alkyl radical precursors, primarily because of the high oxidation potentials of boronic acids (>2.0 V *vs.* SCE).[39–48] To overcome this challenge, Chen's group activated boronic acids with a mild oxidant (acetoxybenziodoxole) to generate alkyl radical intermediates (Fig. 1B, right),[55] but the use of the oxidant limits the applications of this method. Ley and coworkers[40] reported the formation of Lewis base adducts of boronic acids, and this mode of activation increased the range of applications of boronic acids and their derivatives (Fig. 1B, right). However, rapid protonation of the carbanion intermediates formed by Giese-type addition limits the opportunity for intramolecular elimination reactions that proceed *via* polar crossing. The groups of Bloom[42] and Sharma[56] recently demonstrated the generation of alkyl radicals by means of proton-coupled electron transfer or direct oxidation of boronic acids using water or dimethylformamide as both a solvent and an activating agent (Fig. 1B, right). Chen's group[57] reported a method whereby the reaction substrate activates the alkylboronic acids. It is clear from the above-described literature that boronic acids can be used to form various types of C–C and C–heteroatom bonds.

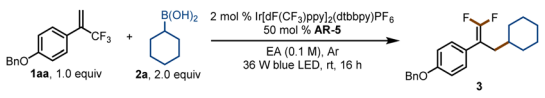
We speculated that we could unlock the full potential of alkylboronic acids as radical precursors and overcome their limitations by introducing a simple reagent such as an organophosphorus compound. These compounds not only have important biological functions but also are widely used in biomedicine, the agrochemical industry, agriculture, materials science, and other fields.[58–70] Moreover, Alexanian *et al.* found that K_3PO_4 can act as hydrogen-atom-transfer reagents in a highly oxidizing photocatalytic system: specifically, an oxygen-centered radical generated from a phosphate salt can abstract hydrogen atoms from unactivated aliphatic C–H bonds[71] (Fig. 1B, left top). Inspired by this work, we hypothesized that the interaction between a suitable activation reagent and the vacant p orbital of a boronic acid would reduce the oxidation potential of the acid and thus result in the release of an alkyl radical under mild photocatalytic conditions (Fig. 1B, left

bottom). Herein, we report that our hypothesis was confirmed, and that we were able to develop a widely applicable method for the formation of alkyl radicals from various alkylboronic acids and participation of the generated radicals in functionalization reactions of electron-deficient olefins and other compounds (Fig. 1C).

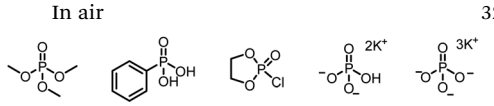
Results and discussion

For our initial experiments, we chose 1-(benzyloxy)-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**1aa**) and cyclohexylboronic acid (**2a**) as model substrates (Table 1). A mixture of the substrates in dry ethyl acetate ([**1aa**] = 0.1 M) containing Ir[dF(CF$_3$)ppy]$_2$(dtbbpy)PF$_6$ (2 mol%) as a photocatalyst and K$_3$PO$_4$ (**AR-5**, 0.5 equiv.) as an activation reagent was irradiated with a 36 W blue LED at room temperature under argon for 16 h. To our delight, the desired defluorinative alkylation product **3** was obtained in 82% yield (entry 1). Various other activation reagents were then tested. **AR-4** gave a slightly lower yield of **3** (70%, entry 2), but all the other tested activation reagents gave yields of <50% (entry 3). Decreasing the amount of **AR-5** decreased the yield of **3** considerably (entry 4), but increasing the amount improved the yield (entries 5–7). The control experiments proved that the photocatalyst, the activation reagent, light, and an oxygen-free atmosphere were essential for the transformation (entries 8–11; see the ESI† for details). Thus, the optimal conditions identified for this defluorinative alkylation involved the use of [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ as a photocatalyst and K$_3$PO$_4$ as an activation reagent in dry ethyl acetate.

Table 1 Optimization of conditions for defluorinative alkylation of 1-(benzyloxy)-4-(3,3,3-trifluoroprop-1-en-2-yl)benzene (**1aa**) with cyclohexylboronic acid (**2a**)[a]



Entry	Deviation from standard conditions	Yield (%)[b]
1	None	82 (80[c])
2	**AR-4** as the activation reagent	70
3	**AR-1–AR-3** as the activation reagent	<50
4	0.2 equiv. of **AR-5**	34
5	1.0 equiv. of **AR-5**	95
6	1.5 equiv. of **AR-5**	94
7	2.0 equiv. of **AR-5**	97
8	No photocatalyst	NR
9	No activation reagent	NR
10	No light	NR
11	In air	32



[a] Standard conditions: **1aa** (0.2 mmol), **2a** (0.4 mmol), photocatalyst (0.004 mmol), activation reagent (0.1 mmol), ethyl acetate (EA, 2 mL), Ar, 36 W blue LED, rt, 16 h. [b] Yields were determined by ^{19}F NMR spectroscopy with fluorobenzene as an internal standard. NR = no reaction. [c] Isolated yield.

To gain insight into the mechanism underlying the observed reactivity, we performed UV-vis spectroscopy and a fluorescence quenching experiment and prepared a Stern–Volmer plot (Fig. 2A). UV-vis spectroscopy confirmed our assumption that the proposed transient intermediate acted as a reductive quencher for excited-state [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$. Although the boronic acid and K$_3$PO$_4$ alone did not quench the photocatalyst, when we mixed the two reagents together, obvious quenching of the photocatalyst was observed (see the ESI† for more details). Next, we carried out a light/dark experiment (Fig. 2B), which showed that when there was no light, the reaction ceased; this result indicates that any chain-propagation process was short-lived and that light was essential for product formation. We carried out electrochemical analyses of each reaction component with Ag/AgNO$_3$ as a reference electrode. We detected a new, low-potential oxidation peak; and the cyclic voltammetry results suggested that coordination between the activation reagent and boronic acid lowered the oxidation potential of the acid (Fig. 2C). As a result, the K$_3$PO$_4$-activated acid could undergo efficient single-electron oxidation by excited-state [Ir(dF(CF$_3$)ppy)$_2$(dtbbpy)]PF$_6$ ($E_{1/2}$ = +1.21 V *vs.* SCE in MeCN). These preliminary observations were reinforced by NMR spectroscopy (Fig. 2D). When we added the activation reagent to cyclohexylboronic acid, the signal for the boron atom showed an obvious upfield shift (the spectrum was recorded in D$_2$O). In addition, we found that mixing the activation reagent with boronic acid resulted in a slight downfield shift in the ^{31}P NMR spectrum of the former. Finally, we found that reaction was prevented by radical scavengers (Fig. 2E), and radical-trapping product 1-(cyclohexyloxy)-2,2,6,6-tetramethylpiperidine or (2-cyclohexylethene-1,1-diyl) dibenzene was detected by high-resolution mass spectrometry. This experiment clearly indicates that the reaction proceeded through a free radical pathway.

In light of these observations, we propose the mechanism illustrated in Fig. 2F. First, the photocatalyst is excited by blue light, and the resulting excited state is quenched by complex **A** to form an alkyl radical. The radical adds to the α-trifluoromethyl arylalkene to afford a CF$_3$-substituted styrene carbon radical. This radical undergoes single-electron reduction by the reduced photocatalyst to form a carbanion, which undergoes an E1cb elimination reaction to afford the desired product.

With the optimized conditions in hand, and convincing evidence for the proposed mechanism, we set out to study the scope of the reaction with respect to alkylboronic acid (Fig. 3). The conditions were broadly applicable for defluorinative alkylation reactions of **1aa** and showed outstanding selectivity and functional group compatibility. Various primary boronic acids, including halogenated long-chain alkylboronic acids and an iodine-substituted aromatic alkylboronic acid, were suitable substrates; the desired products (**4–9**) were obtained in 72–82% yields. Two secondary boronic acids gave **10** and **11** in 87% and 85% yields, respectively, which were slightly higher than the

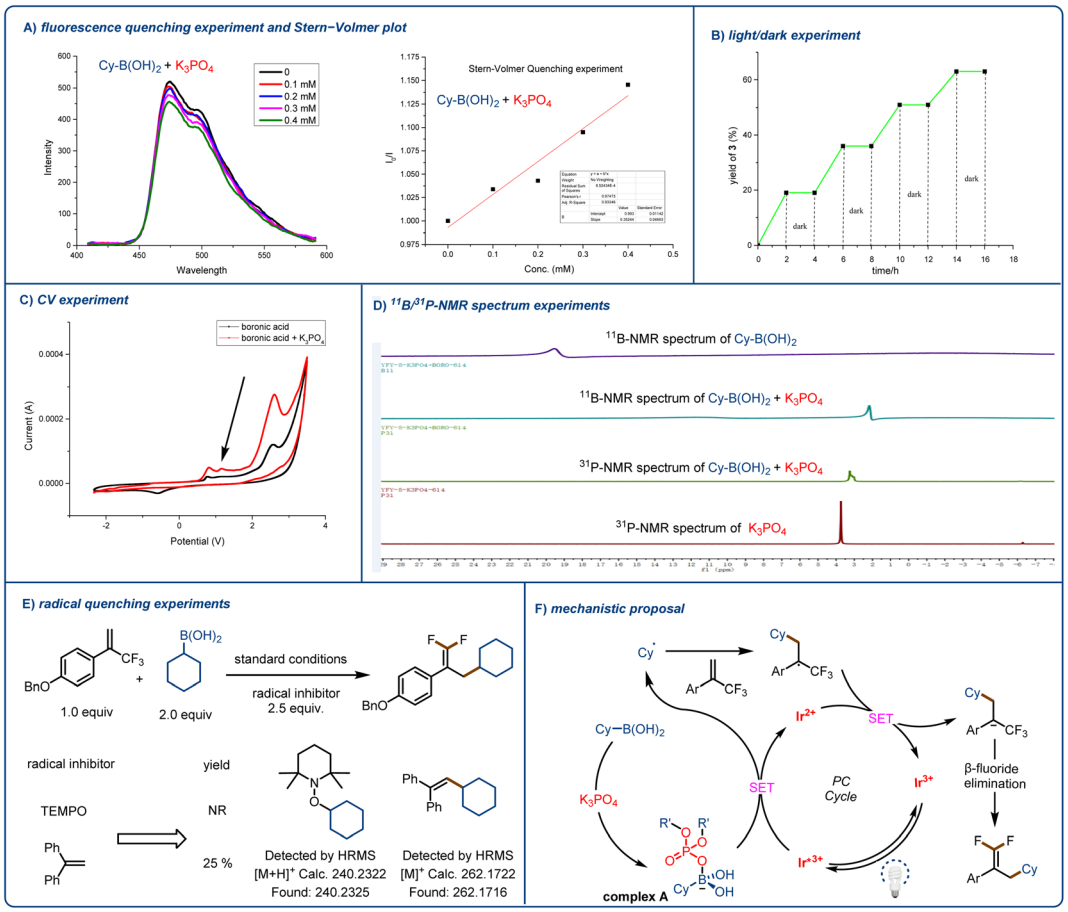


Fig. 2 Mechanistic experiments. (A) Fluorescence quenching experiment and Stern–Volmer plot confirming that the excited state of the photocatalyst was quenched by the cyclohexylboronic acid–K_3PO_4 complex. (B) Light/dark experiment. (C) Cyclic voltammograms showing lowering of the cyclohexylboronic acid oxidation potential by K_3PO_4. (D) ^{11}B NMR and ^{31}P NMR spectra in D_2O (0.5 mL). (E) Radical quenching experiments. (F) Proposed mechanism, R′ = cyclohexylboronic acid.

yields obtained with primary alkylboronic acids. Secondary alkylboronic acids bearing five- and six-membered rings, including bulky, sterically demanding groups, gave **3** and **12–15** in excellent yields. In addition, we were pleased to find that a tertiary alkylboronic acid gave desired products **16** and **17** in good yield (75% and 82%).

Next, we explored the scope with respect to the α-trifluoromethyl arylalkene. We found that arylalkenes with a *para* electron-donating group afforded the corresponding products **18** and **19** in 72% and 78% yields, respectively. However, when the *para* substituent was a substituted aryl ring, the yields were somewhat lower (**20–24**, 57–68%). The position of a phenyl group on the arylalkene had little effect on the yield; products **25–27** were obtained in 85–88% yields. α-Trifluoromethyl arylalkenes bearing an electron-withdrawing group gave somewhat lower yields (**28–32**). Substrates containing functionality that is useful for further synthetic manipulations, such as a pyridine ring (**33**, 54%), a quinoline ring (**34**, 52%), or a naphthalene ring (**35**, 72%; **36**, 60%), were well tolerated. Disubstituted arylalkenes gave **37–42** in moderate yields, and a trisubstituted arylalkene was tolerated as well (**43**, 77%). Interestingly, when the substrate had a strongly electron-withdrawing substituent, pairs of products were obtained (**44–46**). We speculated that in these reactions, the carbanion intermediate was stabilized by the electron-withdrawing group, which made elimination of a fluoride ion more difficult.

Finally, we explored the use of sulfur-containing radical acceptors for this activation mode (Fig. 4). Sulfur-containing motifs are present in chiral ligands, catalysts, bioactive molecules, and natural products and are used in asymmetric catalysis; and the formation of $C(sp^3)$–S bonds has long been of interest to chemists.[72–75] We began by exploring the use of SOMO-philes **1b** (SOMO = singly occupied molecular orbital) as radical acceptors. After optimizing the reaction conditions, we found that sulfide **47** could be obtained in 80% yield from *S*-phenyl benzenethiol-sulfonate and cyclohexylboronic acid (**2a**). *S*-Phenyl benzenethiol-sulfonates with an electron-donating (**48** and **49**) or electron-withdrawing (**50–52**)

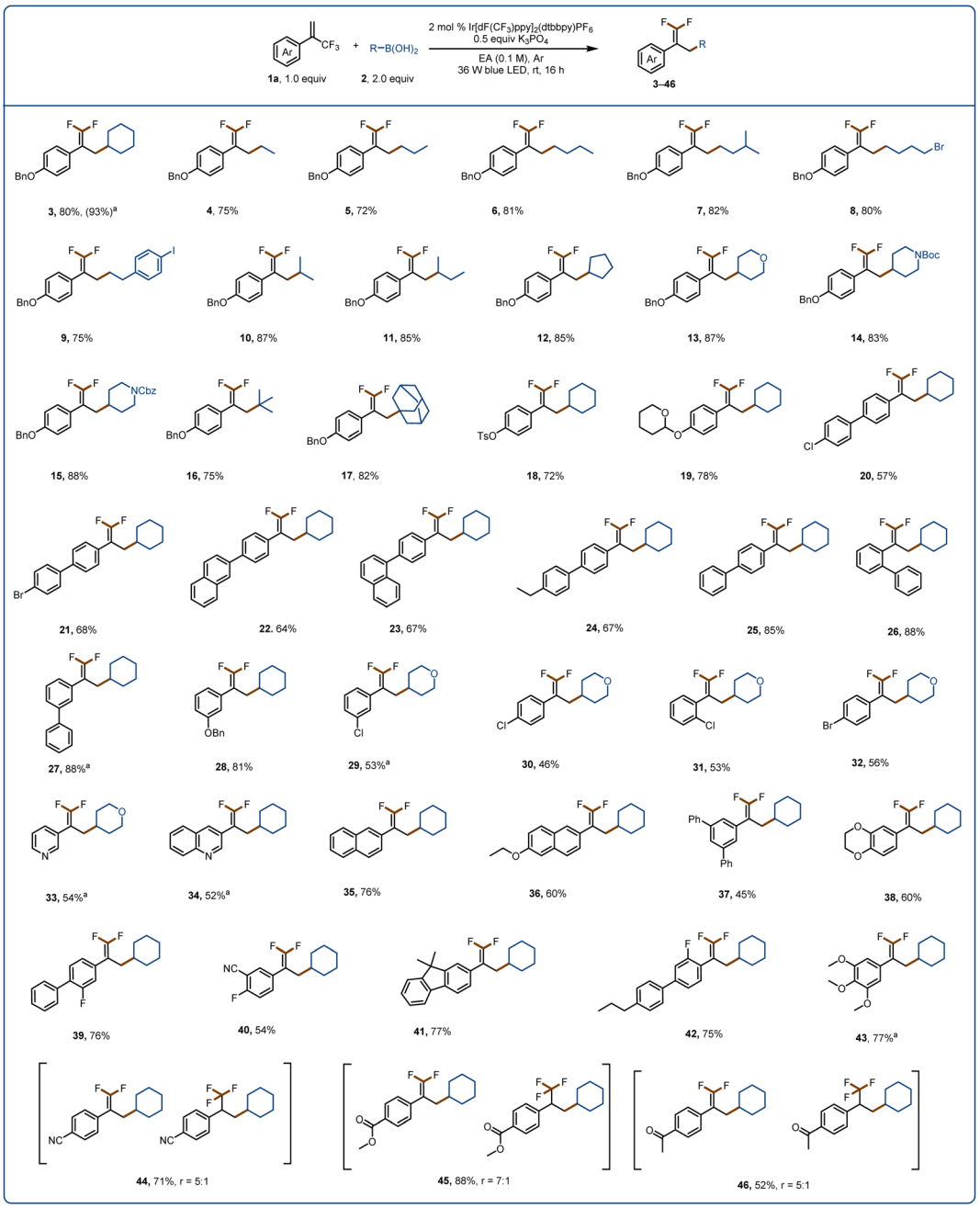


Fig. 3 Substrate scope of the defluorinative alkylation reaction. Reaction conditions, unless otherwise noted: **1** (0.2 mmol), 2 (0.4 mmol), K_3PO_4 (0.1 mmol, 0.5 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2 mol%), ethyl acetate (EA, 2.0 mL), Ar, 36 W blue LED, rt, 16 h. [a]K_3PO_4 (0.2 mmol, 1.0 equiv.).

substituent provided the corresponding products in moderate yields. When the substituent was in the *meta* or *ortho* position, the yield decreased (**53–58**). A disubstituted benzenethiol-sulfonate and a pyridyl benzenethiol-sulfonate were also suitable, affording the desired products **59** (62%) and **60** (42%), respectively. We also found that various primary and secondary alkylboronic acids reacted with *S*-phenyl benzenethiol-sulfonate to provide the corresponding sulfides (**61–66**) in 66–80% yields. We tested SOMO-philes **1c** and **1d**, which allowed us to achieve the products of direct C–B chlorination (**67**), cyanation (**68**), vinylation (**69–76**), alkynylation (**77**), and allylation (**78**). Finally, when we used heteroaryl sulfone **1e** as the radical acceptor, alkylation products **79–81** were obtained in moderate yields.

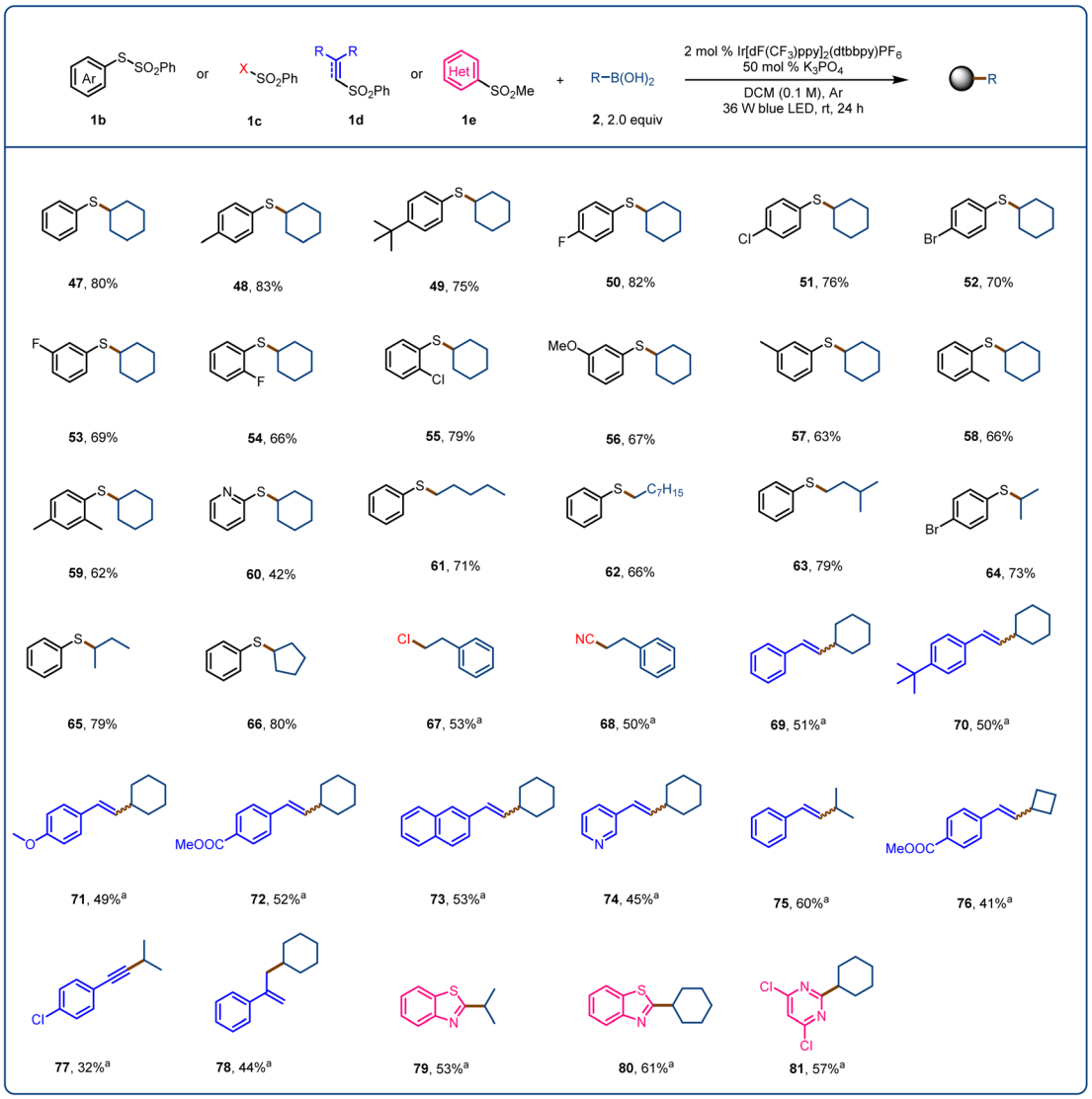


Fig. 4 Scope with respect to the radical acceptor. Reaction conditions, unless otherwise noted: **1** (0.2 mmol), **2** (0.4 mmol), K_3PO_4 (0.1 mmol, 0.5 equiv.), $Ir[dF(CF_3)ppy]_2(dtbbpy)PF_6$ (2 mol%), dichloromethane (DCM, 2.0 mL), Ar, 36 W blue LEDs, rt, 24 h. [a]K_3PO_4 (0.2 mmol, 1.0 equiv.).

The broad substrate scope and promising functional group compatibility of these reactions encouraged us to evaluate their utility for late-stage modification of natural products, pharmaceuticals, and other bioactive molecules (Fig. 5A). Because of their lipophilicity, metabolic stability, binding selectivity, and bioabsorption characteristics, organofluorine motifs are widely used in polymers and pharmaceuticals.[76] Such motifs are useful for overcoming a major challenge in drug discovery and development, that is, the need to replace metabolically reactive groups without affecting biological activity.[70–82] With this in mind, we performed late-stage defluorinative alkylation of various bioactive molecules to obtain products **82–90**. In addition, we were pleased to find that ketoprofen-, ibuprofen-, and L-menthol-derived alkenylation products (**91–93**) could be obtained in good yields. Moreover, we performed a gram–scale reaction of **94** to give 1.1 g (62% yield) of **21** (Fig. 5B). The bromine substituent allowed us to convert **21** to **96** in high yield *via* a Suzuki reaction, underscoring the synthetic utility of the defluorinative alkylation method. When the benzene ring of the α-trifluoromethyl arylalkene had a strongly electron-withdrawing carbomethoxy (**97**) or ketone (**98**) group, we could obtain products **99** and **100**, respectively, by increasing the reaction temperature, prolonging the reaction time, and increasing the amount of the activation reagent (which also acted as a base). Because of the importance of selective activation in the presence of other boron-based species, we tested our method with a boronic pinacol ester (**101**) and found that it was not activated by K_3PO_4 (Fig. 5D). In addition, only the boronic acid was activated when a boronic pinacol ester (**102**)

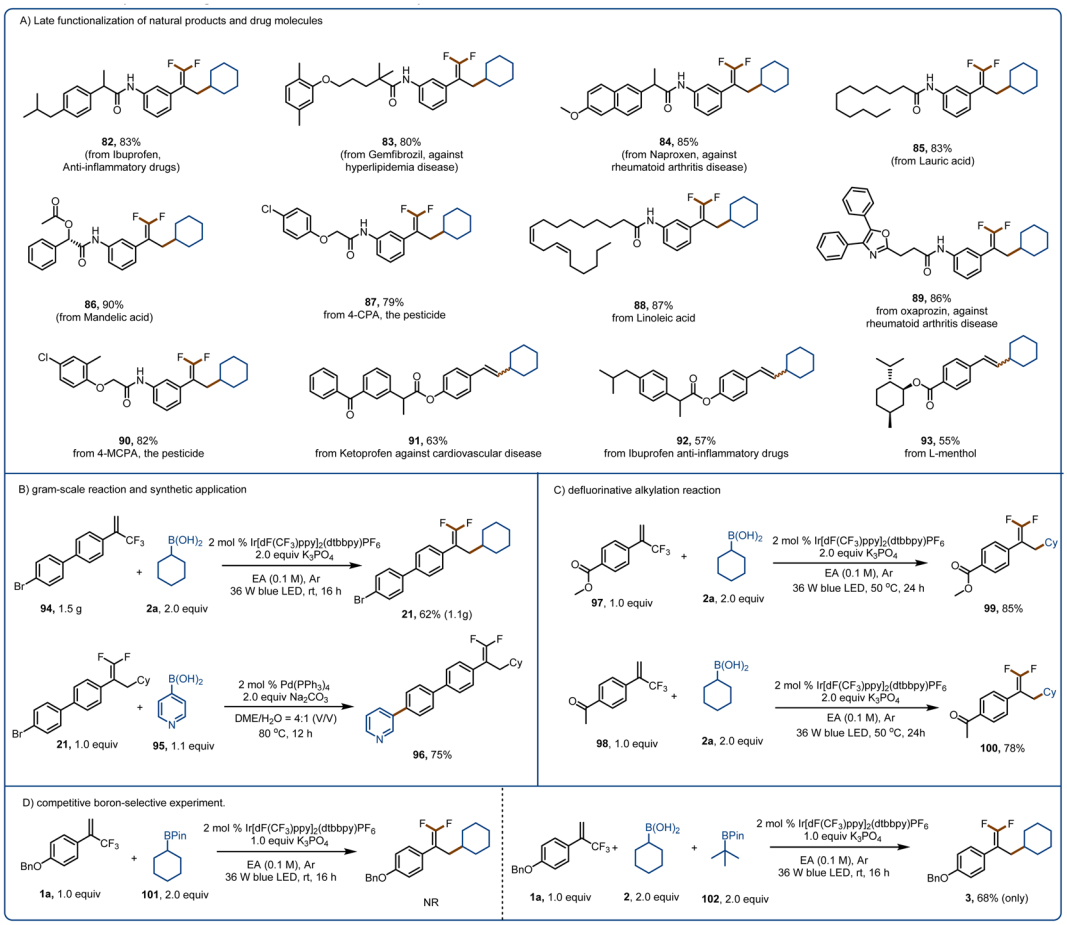


Fig. 5 Late-stage functionalization of bioactive molecules and synthetic applications of the defluorinative alkylation method. (A) Late-stage functionalization of natural products and drugs. (B) Gram-scale reaction and synthetic applications. (C) Defluorinative alkylation reactions of substrates with electron-withdrawing substituents. (D) Competitive experiment to assess boron selectivity.

and a boronic acid (**2a**) were present in the same reaction mixture.

Conclusions

In conclusion, we have demonstrated that activation by an inorganophosphorus compound can lower the oxidation potentials of alkylboronic acids. In addition, we found that boronic acids can be selectively activated in the presence of a boronic ester, indicating that our method may find utility for building complex molecular scaffolds. We carried out late-stage functionalization of some natural products and drugs. On the basis of the findings reported herein, we believe that our approach will facilitate the efficient use of boronic acids as alkyl radical sources in the evolving field of photoredox catalysis.

Date availability

The ESI† includes all experimental details, including optimization of the synthetic method, synthesis and characterization of all starting materials and products reported in this study, and mechanistic studies. NMR spectra of all products reported are included as well.

Author contributions

F. Y. conceived the chemistry and designed the experiments under the guidance of Professor Q. W., Dr H. S. and Dr J. D.; F. Y., H. M. and Y. L. conducted the experiments or analyzed the data. F. Y. wrote the manuscript. All authors have given approval to the final version of the manuscript.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

We are grateful to the National Natural Science Foundation of China (21732002 and 22077071) and Frontiers Science Center for New Organic Matter, Nankai University (63181206) for generous financial support for our programs.

Notes and references

1 D. Ravelli, S. Protti and M. Fagnoni, *Chem. Rev.*, 2016, **116**, 9850–9913.
2 K. L. Skubi, T. R. Blum and T. P. Yoon, *Chem. Rev.*, 2016, **116**, 10035–10074.
3 C. K. Prier, D. A. Rankic and D. W. C. MacMillan, *Chem. Rev.*, 2013, **113**, 5322–5363.
4 W. Ding, L. Lu, Q. Zhou, Y. Wei, J. Chen and W.-J. Xiao, *J. Am. Chem. Soc.*, 2017, **139**, 63–66.
5 X.-Y. Yu, J.-R. Chen and W.-J. Xiao, *Chem. Rev.*, 2021, **121**, 506–561.
6 X. Wu and C. Zhu, *Acc. Chem. Res.*, 2020, **53**, 1620–1636.
7 K. J. Romero, M. S. Galliher, D. A. Pratt and C. R. J. Stephenson, *Chem. Soc. Rev.*, 2018, **47**, 7851–7866.
8 L. Buzzetti, A. Prieto, S. R. Roy and P. Melchiorre, *Angew. Chem., Int. Ed.*, 2017, **56**, 15039–15043.
9 R. A. Garza-Sanchez, A. Tlahuext-Aca, G. Tavakoli and F. Glorius, *ACS Catal.*, 2017, **7**, 4057–4061.
10 P. Liu, W. Liu and C.-J. Li, *J. Am. Chem. Soc.*, 2017, **139**, 14315–14321.
11 W. Liu, P. Liu, L. Lv and C.-J. Li, *Angew. Chem., Int. Ed.*, 2018, **57**, 13499–13503.
12 R. S. J. Proctor, H. J. Davis and R. J. Phipps, *Science*, 2018, **360**, 419–422.
13 D. Zheng and A. Studer, *Angew. Chem., Int. Ed.*, 2019, **131**, 15950–15954.
14 Z. Zuo and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2014, **136**, 5257–5260.
15 C. Huang, J. Li and C.-J. Li, *Chem. Sci.*, 2022, **13**, 5465–5504.
16 D. Nicewicz and D. W. C. MacMillan, *Science*, 2008, **322**, 77–80.
17 D. A. Nagib, M. E. Scott and D. W. C. MacMillan, *J. Am. Chem. Soc.*, 2009, **131**, 10875–10877.
18 M. A. Ischay, M. E. Anzovino, J. Du and T. P. Yoon, *J. Am. Chem. Soc.*, 2008, **130**, 12886–12887.
19 J. M. R. Narayanam, J. W. Tucker and C. R. J. Stephenson, *J. Am. Chem. Soc.*, 2009, **131**, 8756–8757.
20 S. Li and Z. Xie, *J. Am. Chem. Soc.*, 2022, **144**, 7960–7965.
21 Y. Yin, Y. Dai, H. Jia, J. Li, L. Bu, B. Qiao, X. Zhao and Z. Jiang, *J. Am. Chem. Soc.*, 2018, **140**, 6083–6087.
22 A. Hu, J. Guo, H. Pan and Z. Zuo, *Science*, 2018, **361**, 668–672.
23 M. Silvi, C. Sandford and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2017, **139**, 5736–5739.
24 A. Bunescu, Y. Abdelhamid and M. J. Gaunt, *Nature*, 2021, **598**, 597–603.
25 T. Constantin, M. Zanini, A. Regni, N. S Sheikh, F. Juliá and D. Leonori, *Science*, 2020, **367**, 1021–1026.
26 J. D. Bell and J. A. Murphy, *Chem. Soc. Rev.*, 2021, **90**, 9540–9685.
27 A. Y. Chan, I. B. Perry, N. B. Bissonnette, B. F. Buksh, G. A. Edwards, L. I. Frye, O. L. Garry, M. N. Lavagnino, B. X. Li, Y. Liang, E. Mao, A. Millet, J. V. Oakley, N. L. Reed, H. A. Sakai, C. P. Seath and D. W. C. MacMillan, *Chem. Rev.*, 2022, **122**, 1485–1542.
28 S. Crespi and M. Fagnoni, *Chem. Rev.*, 2020, **120**, 9790–9833.
29 L. Capaldo, D. Ravelli and M. Fagnoni, *Chem. Rev.*, 2022, **122**, 1875–1924.
30 (*a*) J. Chen, X. Hu, L. Lu and W. Xiao, *Acc. Chem. Res.*, 2016, **49**, 1911–1923; (*b*) J. Xie, J. Yu, M. Rudolph, F. Rominger and A. S. K. Hashmi, *Angew. Chem., Int. Ed.*, 2016, **55**, 9416–9421; (*c*) W. Xing, J. Wang, M. Fu and Y. Fu, *Chin. J. Chem.*, 2022, **40**, 323–328; (*d*) L. Xi, *Chin. J. Chem.*, 2020, **38**, 897–898.
31 H. Cao, X. Tang, H. Tang, Y. Yuan and J. Wu, *Chem. Catal.*, 2021, **1**, 523–598.
32 G. Duret, R. Quinlan, P. Bisseret and N. Blanchard, *Chem. Sci.*, 2015, **6**, 5366–5382.
33 K. Duan, X. Yan, Y. Liu and Z. Li, *Adv. Synth. Catal.*, 2018, **360**, 2781–2795.
34 J. Chen, X. Hu, L. Lua and W. Xiao, *Chem. Soc. Rev.*, 2016, **45**, 2044–2056.
35 M. Li, Y. Wei, J. Liu, H. Chen, L. Lu and W. Xiao, *J. Am. Chem. Soc.*, 2017, **139**, 14707–14713.
36 B. Lu, M. Xu, X. Qi, M. Jiang, W. Xiao and J. Chen, *J. Am. Chem. Soc.*, 2022, **144**, 14923–14935.
37 J. C. Tellis, D. N. Primer and G. A. Molander, *Science*, 2014, **345**, 433–436.
38 Y. Yasu, T. Koike and M. Akita, *Adv. Synth. Catal.*, 2012, **354**, 3414–3420.
39 C. Shu, A. Noble and V. K. Aggarwal, *Angew. Chem., Int. Ed.*, 2019, **58**, 3870–3874.
40 F. Lima, U. K. Sharma, L. Grunenberg, D. Saha, S. Johannsen, J. Sedelmeier, E. V. Van der Eycken and S. V. Ley, *Angew. Chem., Int. Ed.*, 2017, **56**, 15136–15140.
41 Y. Iwata, Y. Tanaka, S. Kubosaki, T. Morita and Y. Yoshimi, *Chem. Commun.*, 2018, **54**, 1257–1260.
42 M. Chilamari, J. R. Immel and S. Bloom, *ACS Catal.*, 2020, **10**, 12727–12737.
43 I. B. Seiple, S. Su, R. A. Rodriguez, R. Gianatassio, Y. Fujiwara, A. L. Sobel and P. S. Baran, *J. Am. Chem. Soc.*, 2010, **132**, 13194–13196.
44 L. Zhang and Z.-Q. Liu, *Org. Lett.*, 2017, **19**, 6594–6597.
45 Y. Sato, K. Nakamura, Y. Sumida, D. Hashizume, T. Hosoya and H. Ohmiya, *J. Am. Chem. Soc.*, 2020, **142**, 9938–9943.
46 A. Fawcett, J. Pradeilles, Y. Wang, T. Mutsuga, E. L. Myers and V. K. Aggarwal, *Science*, 2017, **357**, 283–286.
47 Y. Cheng, C. Mück-Lichtenfeld and A. Studer, *J. Am. Chem. Soc.*, 2018, **140**, 6221–6225.
48 H. Huang, K. Jia and Y. Chen, *Angew. Chem., Int. Ed.*, 2015, **54**, 1881–1884.
49 H. Huang, G. Zhang, L. Gong, S. Zhang and Y. Chen, *J. Am. Chem. Soc.*, 2014, **136**, 2280–2283.
50 H. Huo, K. Harms and E. Meggers, *J. Am. Chem. Soc.*, 2016, **138**, 6936–6939.
51 E. E. Stache, T. Rovis and A. G. Doyle, *Angew. Chem., Int. Ed.*, 2017, **56**, 3679–3683.
52 F. Lima, M. A. Kabeshov, D. N. Tran, C. Battilocchio, J. Sedelmeier, G. Sedelmeier, B. Schenkel and S. V. Ley, *Angew. Chem., Int. Ed.*, 2016, **55**, 14085–14089.
53 D. Kaiser, A. Noble, V. Fasano and V. K. Aggarwal, *J. Am. Chem. Soc.*, 2019, **141**, 14104–14109.
54 D. Shi, C. Xia and C. Liu, *CCS Chem.*, 2021, **3**, 1718–1728.

55 G.-X. Li, C. A. Morales-Rivera, Y. Wang, F. Gao, G. He, P. Liu and G. Chen, *Chem. Sci.*, 2016, **7**, 6407–6412.
56 P. Ranjan, S. Pillitteri, G. Coppola, M. Oliva, E. V. Van der Eycken and U. K. Sharma, *ACS Catal.*, 2021, **11**, 10862–10870.
57 S. Xie, D. Li, H. Huang, F. Zhang and Y. Chen, *J. Am. Chem. Soc.*, 2019, **141**, 16237–16242.
58 A. Suzuki, *Angew. Chem., Int. Ed.*, 2011, **50**, 6722–6737.
59 D. G. Hall, *Boronic Acids: Preparation and Applications in Organic Synthesis and Medicine*, WileyVCH, Weinheim, 2007.
60 A. H. Dardir, P. R. Melvin, R. M. Davis, N. Hazari and M. Mohadjer Beromi, *J. Org. Chem.*, 2018, **83**, 469–477.
61 M. J. West, J. W. B. Fyfe, J. C. Vantourout and A. J. B. Watson, *Chem. Rev.*, 2019, **119**, 12491–12523.
62 B. C. Das, P. Thapa, R. Karki, C. Schinke, S. Das, S. Kambhampati, S. K. Banerjee, P. Van Veldhuizen, A. Verma, L. M. Weiss and T. Evans, *Med. Chem.*, 2013, **5**, 653–676.
63 Y. Shoji, Y. Ikabata, Q. Wang, D. Nemoto, A. Sakamoto, N. Tanaka, J. Seino, H. Nakai and T. Fukushima, *J. Am. Chem. Soc.*, 2017, **139**, 2728–2733.
64 V. D. Nguyen, V. T. Nguyen, S. Jin, H. T. Dang and O. V. Larionov, *Tetrahedron*, 2019, **75**, 584–602.
65 U. Pradere, E. C. Garnier-Amblard, S. J. Coats, F. Amblard and R. F. Schinazi, *Chem. Rev.*, 2014, **114**, 9154–9218.
66 M. D. Sørensenet, L. K. A. Blæhr, M. K. Christensen, T. Høyer, S. Latini, P. V. Hjarnaa and F. Björkling, *Bioorg. Med. Chem.*, 2003, **11**, 5461–5484.
67 M. Sawaet, T. Kiyoi, K. Kurokawa, H. Kumihara, M. Yamamoto, T. Miyasaka, Y. Ito, R. Hirayama, T. Inoue, Y. Kirii, E. Nishiwaki, H. Ohmoto, Y. Maeda, E. Ishibushi, Y. Inoue, K. Yoshino and H. Kondo, *J. Med. Chem.*, 2002, **45**, 919–929.
68 A. Babbset, *et al.*, *Tetrahedron*, 2020, **76**, 130819–130827.
69 A. Nocentiniet, V. Alterio, S. Bua, L. Micheli, D. Esposito, M. Buonanno, G. Bartolucci, S. M. Osman, Z. A. ALOthman, R. Cirilli, M. Pierini, S. M. Monti, L. D. C. Mannelli, P. Gratteri, C. Ghelardini, G. D. Simone and C. T. Supuran, *J. Med. Chem.*, 2020, **63**, 5185–5200.
70 M. Dutartre, J. Bayardon and S. Jugé, *Chem. Soc. Rev.*, 2016, **45**, 5771–5794.
71 K. A. Margrey, W. L. Czaplyski, D. A. Nicewicz and E. J. Alexanian, *J. Am. Chem. Soc.*, 2018, **140**, 4213–4217.
72 P. Johannesson, G. Lindeberg, A. Johansson, G. V. Nikiforovich, A. Gogoll, B. Synnergren, M. Le Grèves, F. Nyberg, A. Karlén and A. Hallberg, *J. Med. Chem.*, 2002, **45**, 1767–1777.
73 N. Wang, P. Saidhareddy and X. Jiang, *Nat. Prod. Rep.*, 2020, **37**, 246–275.
74 S. Ni, L. Zhang, W. Zhang, H. Mei, J. Han and Y. Pan, *J. Org. Chem.*, 2016, **81**, 9470–9475.
75 Y. Wang, L. Deng, X. Wang, Z. Wu, Y. Wang and Y. Pan, *ACS Catal.*, 2019, **9**, 1630–1634.
76 J. Fried and E. Sabo, *J. Am. Chem. Soc.*, 1954, **76**, 1455–1456.
77 M. Inoue, Y. Sumii and N. Shibata, *ACS Omega*, 2020, **5**, 10633–10640.
78 C. Alonso, E. M. de Marigorta, G. Rubiales and F. Palacios, *Chem. Rev.*, 2015, **115**, 1847–1935.
79 T. Furuya, A. S. Kamlet and T. Ritter, *Nature*, 2011, **473**, 470–477.
80 J. Hu, W. Zhang and F. Wang, *Chem. Commun.*, 2009, 7465–7478.
81 H. Xiao, Z. Zhang, Y. Fang, L. Zhu and C. Li, *Chem. Soc. Rev.*, 2021, **50**, 6308–6319.
82 G. Tarantino and C. Hammond, *Green Chem.*, 2020, **22**, 5195–5209.