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Letter

Light-Mediated Sulfur–Boron Exchange

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character of the fluorinated pyridine fragment plays an important role in generating alkyl radicals.

B oronic acids and esters play an important role in organic chemistry as versatile building blocks,¹ which are used in Suzuki coupling² as well as in transition-metal-free processes.³ Development of approaches for their synthesis still constitutes a subject of intensive investigations. Besides classical hydroboration and organolithium (or organomagnesium) methods, direct C-H borylation reactions mediated by transition metals have been extensively evaluated.⁴ Another inherently wide approach toward boronic derivatives involves conversion of carbon-heteroatom bonds (where heteroatom means O, S, N, and halogen).⁵ In these reactions, activation of the C-Het bond typically proceeds via a metal-based oxidative addition event, and this is mainly applied to C(sp²)-Het substrates such as aromatics and alkenes.⁶

primary, secondary, and tertiary sulfides. The electron depleting

The advent of light-mediated reactions has sparked the development of free radical reactions.⁷ Indeed, generation of alkyl radicals via photoredox-type cleavage of sp³ C–Het bonds followed by trapping with a diboron reagent has offered a novel path toward boronic esters⁸ (Scheme 1). Alternatively, alkyl radicals formed via decarboxylation of derivatives of carboxylic acids were also borylated.⁹ A key issue in these reactions is the ability of a diboron reagent in combination with an amide solvent under irradiation to initiate the radical processes.^{9a} This principle was exploited for borylation of other substrates such as pyridinium salts,¹⁰ alkyl halides,¹¹ and *N*-hydroxyphthalimide derivatives.^{9,12,13} It was also noted that the radical initiation step of these reactions can proceed without any photocatalyst.

Recently, we introduced a tetrafluoropyridinylthio (PyfS) group as a fragment for generation of alkyl radicals via the photoredox pathway.¹⁴ Importantly, compounds with this group can be accessed by a variety of methods including C–H activation, group transfer reaction, and thiol–ene radical addition, as well as by classical nucleophilic substitution reactions (either by introducing PyfS anion or from thiols and pentafluoropyridine). Given the electron depleting nature of the fluorinated pyridine fragment, we reasoned that this group would be amenable to interaction with diboron reagents upon





irradiation. Herein, we report that PyfS-compound 1 can be converted into boronic esters via light-mediated reaction. It should be noted that transformation of sulfides to boronic esters has previously been performed either via prior conversion of the C–S bond into carbanionic species¹⁵ or by transition-metal-catalyzed reactions.¹⁶ Photoredox borylation of aromatic sulfonium salts has also been reported to afford aromatic boronic esters.¹⁷ Taking into account that sulfides 1

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can be accessed from alkanes, 14c our method constitutes an alternative for direct radical C–H borylation. 18

Cyclohexyl sulfide 1a was selected as a model substrate and its reaction with bis(catecholato)diboron was evaluated (Table 1). The reaction was best performed in the presence of an

Table 1. Optimization Studies

SPy	B ₂ Cat ₂ (2 equiv) 3DPA2FBN (1.3%) ff DMF, 400 nm, 6 h	Ph ₂ N NPh ₂
└── 1a	then pinacol, NEt ₃ , 6 h	NPh ₂
	~ 2a	3DPA2FBN
number	deviation from optimized condition	yield of 2a , ^{<i>a</i>} %
1	-	82
2	No catalyst	80
3	DMA as solvent	45
4	DMSO as solvent	-
5	MeCN as solvent	-
7	MeOH as solvent	-
8	No catalyst, MeCN as solvent	-
9	Ir(ppy) ₃ as photocatalyst	67 ^b
10	Ru(bpy) ₃ (PF ₆) ₂ as photocatalyst	17^{b}
11	4CzIPN as photocatalyst	62 ^b
12	Blue LED	59 ^b
13	Blue LED, no catalyst	42^{b}
14	No light	-
15	B ₂ Pin ₂ as reagent	-
16	B ₂ Npg ₂ as reagent	-
^{<i>a</i>} Isolated y	rield. ^b Determined by GC analysis.	

organic photocatalyst $(3DPA2FBN)^{19}$ in *N*,*N*-dimethylformamide as the solvent under irradiation with 400 nm light. Subsequent treatment of the mixture with pinacol and triethylamine led to boronic ester **2a**. Of special note is that in the absence of the photocatalyst, the product was formed with similar yield. However, while carrying out variation of substrates, we observed that the use of the photocatalyst gave consistently better yields. With Ir and Ru based catalysts, as well as with blue LED irradiation, inferior yields were observed. Diboron reagents having pinacolate (B₂Pin₂) or neopentyl glycolate (B₂Npg₂) were ineffective.

A series of PyfS-compounds 1 were obtained via different protocols such as double bond thiol addition, C-H activation, atom transfer reaction, nucleophilic substitution of alkyl halide with the thiolate, and interaction of a free thiol with pentafluoropyridine. Under optimized conditions, these sulfides were converted into boronic esters 2 (Scheme 2). The reaction typically works well with primary and secondary sulfides. Benzylic substrate, which generates less reactive benzylic radical, also afforded the target boronic ester 2j. The ester group is tolerated (product 20), while a substrate bearing the acetoxy group located at the γ -position with respect to the sulfide provided moderate yield of the expected product (compound 2p), which may be associated with inductive effect of the acetoxy group. When 1,3-disulfide was subjected to standard conditions, the substitution of the second PyS-group was slow, requiring 2 days for the formation of product 2q. Rewardingly, tertiary sulfides furnished corresponding boronic esters, though with moderate yields, presumably due to facile oxidation of intermediate tertiary radicals to carbocations (compounds 2r-u). The reaction

Scheme 2. Synthesis of Boronic Esters 2^{a}



^aIsolated yield. ^bIn the absence of the catalyst. ^cReaction time 48 h.

performed on a gram scale (1.06 g of 1a) afforded the product in 85% isolated yield. α, α -Difluorinated sulfide (4-PhC₆H₄CH₂CF₂SPyf) derived from difluorostyrene^{14a} was also evaluated. Though the starting sulfide was consumed, treatment of the reaction mixture with either pinacol/triethyl ammine or potassium hydrogen difluoride did not afford the product.

Concerning the mechanism, the reaction may proceed via either catalyst-free or catalytic pathways (Scheme 3). In the former case, the diboron reagent and DMF are expected to form the EDA complex. Subsequent irradiation triggers the electron transfer from the electron-rich boryl fragment to the electron-poor PyfS-group leading to a radical anion and a DMF-complexed diboron radical cation. Fragmentation of the sulfide radical anion generates the alkyl radical and the thiolate, which can take the boryl group leading to the boryl radical species A. Formation of the carbon-boron bond may occur by attack of the alkyl radical at the diboron reagent, in a manner proposed by Aggarwal.^{9a} Species A is a good electron donor and can give an electron to the sulfide to regenerate the radical. In a catalytic pathway, the photoredox step generates the radical, which then attacks at the diboron reagent. At the final step, species A is oxidized by the photocatalyst followed by trapping with the sulfide anion.

The radical character of the process was supported by an experiment with TEMPO, which inhibited the product

Scheme 3. Proposed Mechanism

Catalyst-free pathway

(a) Intitiation



Catalytic pathway



Product formation step



formation. However, distinguishing between the catalytic and noncatalytic pathways is difficult, and two mechanisms can be operative. Measurement of UV–vis absorption spectra of the mixture of sulfide 1a and B_2Cat_2 in DMF did not show any additional bands (see Supporting Information for details). The redox potentials of the excited state of the photocatalyst and of the sulfides are close (3DPA2FBN, $E(PC^*/PC^+) - 1.60 V_j^{19}$ sulfide 1a, $-1.84 V_j^{14c}$ vs SCE), and oxidative quenching would be possible. The role of pinacol/triethylamine is to convert the primary borylation product (RBCat) into the final product RBPin (2) via transesterification reaction (Scheme 3, bottom equation).

In summary, a method for the light-promoted conversion of sulfides into boronic esters is described. The electron withdrawing nature of the tetrafluoropyridinylthio group, which is prone to EDA formation and single electron reductions, is believed to be the key feature responsible for the reaction efficiency.

ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge at https://pubs.acs.org/doi/10.1021/acs.orglett.1c01080.

Experimental procedures, compound characterization data, copies of NMR spectra for all compounds (PDF)

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Author Contributions

The manuscript was written through contributions of all authors. All authors have given approval to the final version of the manuscript.

Notes

The authors declare no competing financial interest.

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