Visible-Light-Induced Desulfurative Coupling of Alkyl Benzothiazolyl Sulfides with Electron-Deficient Alkenes/Alkynes: Dual Role of Base-Activated Hantzsch Ester

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Abstract

Hantzsch ester is a widely used organic reductant. We describe a new use of this classical reductant in visible-light-induced desulfurative coupling of alkyl benzothiazolyl sulfides with electron-deficient alkenes/alkynes through activation with base additives. The $C(sp^3)$-S scission has been achieved in two independent ways, catalyst-free Hantzsch ester anion-mediated reaction and organo-photocatalysis. The synthetic utility is illustrated with several examples of the derivatization of natural products including monosaccharides. The mechanistic investigation has revealed that Hantzsch ester anion works as a photoreductant in the catalyst-free reaction, whereas it is included as a sacrificial reductant in the organo-photocatalysis.

Introduction

Hantzsch ester (**HEH**) is known as a readily accessible and bench-stable NAD(P)H model compound, and in organic synthesis field, it is generally used as a hydrogen source especially for metal-catalyzed and organocatalyzed transfer hydrogenations.[1] The utility of this compound and its analogous esters in photo-induced reactions has been focused in these decades, and they have been proved to serve as photo reductants,[2] sacrificial electron donors for photoredox catalysis,[3] and donors of EDA-complexes.[4] More recently, base-activated Hantzsch esters including deprotonated Hantzsch ester (Hantzsch ester anion, **HE⁻**) were reported as photo reductants for visible-light-induced dehalogenation[5] and desulfonylation.[6] Although limited in number, the carbon radicals generated by these highly reductive agents were applied to carbon-sulfur or carbon-carbon bond formation[5b,6b] including our desulfonylative reductive couplings (Figure 1a).[6a,6c]

The carbon-radical generation via carbon-sulfur bond cleavage under light irradiation has attracted intense interest from organic and bioorganic researchers because it allows site-selective transformation of bioactive molecules.[7] Considering the ease of handling and simplicity of activation, photoreductive cleavage of a $C(sp^3)$-S bond of heteroaryl sulfones[6a-c,8] seems to be reliable with the exception of a limited precedent of direct use of thiols.[9] Our research group reported Hantzsch ester activated by K_2CO_3 promotes carbon radical generation from alkyl benzothiazolyl sulfones under blue LED irradiation,[6a,6c] and this protocol was extended to radical *C*-glycosylation of 2-pyridyl glycosyl sulfones by the Koh's research group.[6b] Nambo,[8a,b,e] Dilman,[8c] and Chatterjee[8d] independently reported the complementary method based on photocatalysis, establishing bench-stable heteroaryl sulfones as alkyl radical precursors (Figure

1b). However, in terms of substrate preparation, it must be said that the oxidation of sulfides is a wasteful process. Against these backgrounds, we considered that the carbon-radical generation from alkyl heteroaryl sulfides replacing the one from alkyl heteroaryl sulfones should lead to expand the methodology for functionalization of bioactive molecules or their readily-accessible derivatives (Figure 1c).
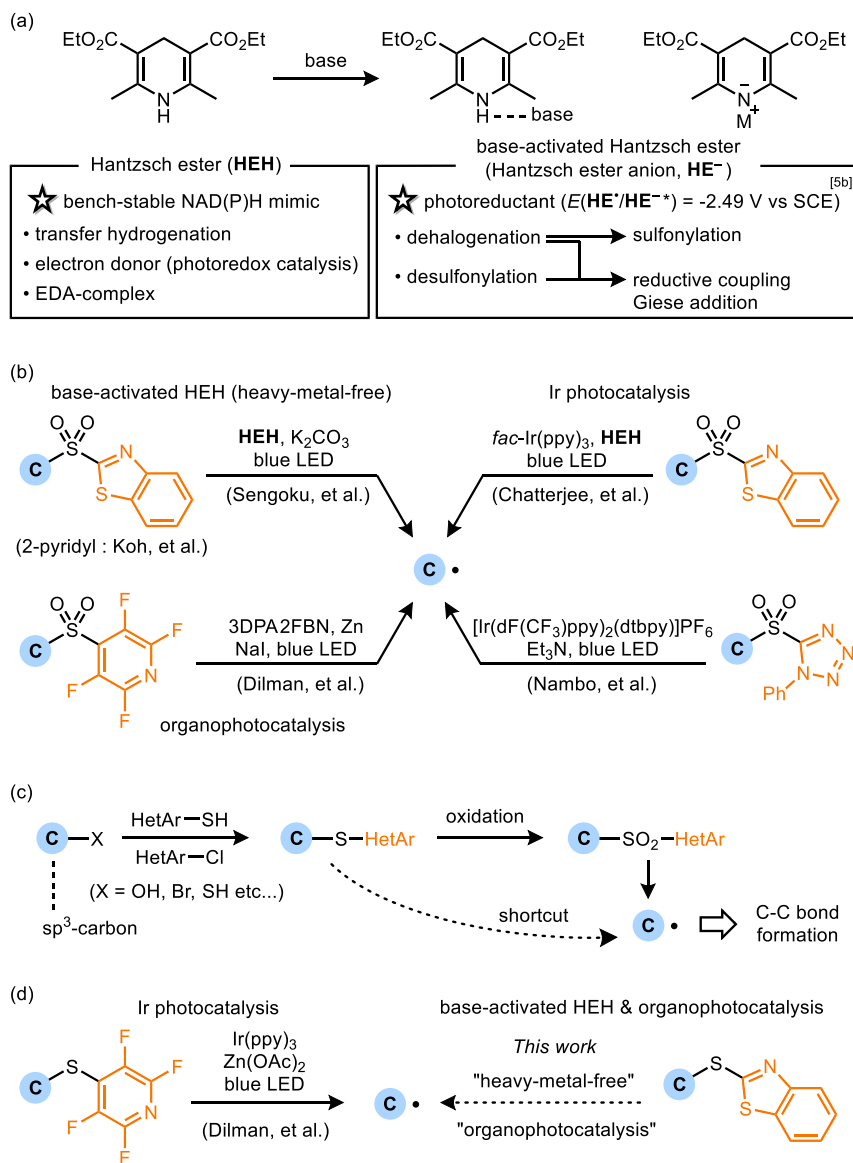

Figure 1. (a) Utility of Hantzsch ester and base-activated Hantzsch esters, (b) sp^3-carbon-radical generation from heteroaryl sulfones under visible light irradiation, (c) benefit of sp^3-carbon-radical generation via carbon-sulfur bond cleavage of sulfides, and (d) sp^3-carbon-radical generation from heteroaryl sulfides under visible light irradiation.

Visible-light-induced carbon-sulfur bond cleavage of alkyl heteroaryl sulfides has been reported by Dilman and co-workers.[10] Although only tetrafluoropyridyl sulfides were shown to be viable substrates, they succeeded in generating carbon radicals under iridium photocatalysis. According to their mechanistic investigations, the C(sp^3)-S scission occurs via a single electron transfer from photoexcited iridium catalyst. This mechanism encouraged us to apply our previous protocol using base-activated Hantzsch ester on reductive cleavage of alkyl benzothiazolyl sulfones to the transformation of the relevant sulfides (Figure

1d). Here, we report base-controlled dual role of Hantzsch ester in heavy-metal-free visible-light-induced desulfurative couplings. Hantzsch ester anion generated with Cs_2CO_3 led to the catalyst-free $C(sp^3)$-S bond cleavage of heteroaryl sulfides. Hantzsch ester also promoted alternative organo-photocatalytic reaction as a catalytic sacrificial reductant. The broad substrate scope of this photocatalytic method allowed *C*-glycosylation of glycosyl sulfides including a protective group-free derivative, which should be a new protocol shortcutting the carbohydrate synthesis.[11]
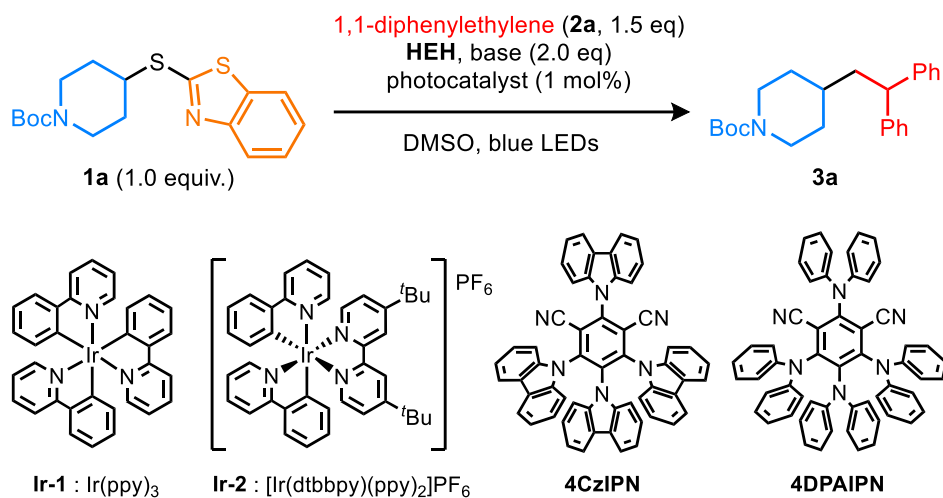
Results and Discussion

We initially investigated the $C(sp^3)$-S bond cleavage of **1a** using Hantzsch ester in the presence of base additives under blue-light irradiation (Table 1, for details, see Table S1 in the Supporting Information). The reactive intermediate was trapped with 1,1-diphenylethylene (**2a**), affording **3a**. The use of K_2CO_3 which was the optimum base additive for desulfonylative carbon-radical generation from alkyl benzothiazolyl sulfones[6a,6c] underwent the desired C–S scission to give **3a** in 10% yield along with the recovery of **1a** (entry 1). Among the homogeneous reaction conditions using organic bases, potassium *tert*-butoxide gave the relatively high yield of 78% (entry 2). However, these conditions were not acceptable because of the competitive substrate decomposition under the reaction conditions. On the other hand, under heterogeneous suspension conditions using inorganic bases, the product yield reached up to 94% by adding Cs_2CO_3 instead of K_2CO_3 (entry 3). The reactions in the absence of Cs_2CO_3, Hantzsch ester or blue LEDs resulted in no reaction, indicating that photoexcited base-activated Hantzsch ester induces the $C(sp^3)$-S bond cleavage. In addition, demonstrating the reaction using CsCl suggested that cesium cation is not contributing to electron transfer but would increase the solubility of carbonate anion (entries 4 and 5). The drastic improvement of the reaction efficiency should be attributed to the high population of base-activated Hantzsch ester which was observed at 475 nm on absorption spectra (Figures S2 and S3 in the Supporting Information).

Further screening of solvents and reagent amounts led to the establishment of a heavy-metal-free and catalyst-free $C(sp^3)$-S bond cleavage from benzothiazolyl sulfide (Tables S3 and S4 in the Supporting Information). However limited radical acceptors were viable because of the decomposition under the reaction conditions (details are described in Table 3). Then, we turned to expand the viability by applying reductive photocatalytic systems (for details, see Table S5 in the Supporting Information). When the reaction of **1a** and **2a** was carried out only with 1 mol% of $Ir(ppy)_3$ under blue-light irradiation, no C-S bond cleavage occurred. While the use of triethylamine as a sacrificial reductant resulted in no reaction, the reaction with Hantzsch ester gave the desired product in 8% yield. Notably, the reaction efficiency was significantly improved by adding Hantzsch ester and K_2CO_3, affording **3a** in 85% yield (Table 1, entry 6). Since **3a** was provided only in 10% yield through the reaction with Hantzsch ester and K_2CO_3 as described in entry 1, it can be said that the C-S bond cleavage is mainly ascribed to photoredox catalysis. Similar trends were observed with [Ir(dtbbpy)(ppy)$_2$]PF$_6$ (**Ir-2**), 1,2,3,5-tetrakis(carbazol-9-yl)-4,6-dicyanobenzene (**4CzIPN**) or 2,4,5,6-tetrakis(diphenylamino)isophthalonitrile (**4DPAIPN**), among them, **4DPAIPN** gave the highest yield of 98% (entries 7–9). More emphatically, the addition of γ-terpinene allowed Hantzsch ester to act as a catalytic reducing agent, and **3a** was obtained in 94% yield under these reaction conditions

(entry 10).

1,1-diphenylethylene (**2a**, 1.5 eq)
HEH, base (2.0 eq)
photocatalyst (1 mol%)
DMSO, blue LEDs

1a (1.0 equiv.) → **3a**

Ir-1 : Ir(ppy)₃   **Ir-2** : [Ir(dtbbpy)(ppy)₂]PF₆   **4CzIPN**   **4DPAIPN**

| Entry	**HEH** (eq)	base	photocatalyst	Time (h)	**3a** (%)
1[b]	2.0	K₂CO₃	–	24	10
2[c]	2.0	t-BuOK	–	14	78
3[b]	2.0	Cs₂CO₃	–	19	94
4[b,d]	2.0	DBU	–	24	11
5[b,d]	2.0	K₂CO₃	–	24	53
6[e]	1.3	K₂CO₃	**Ir-1**	24	85
7[e]	1.3	K₂CO₃	**Ir-2**	24	85
8[e]	1.3	K₂CO₃	**4CzIPN**	24	77
9[e]	1.3	K₂CO₃	**4DPAIPN**	24	98
10[e]	0.2	K₂CO₃	**4DPAIPN**	24	94
11[f]	1.3	K₂CO₃	**4DPAIPN**	24	71

[a] The full details are summarized in Tables S1–S6 in the Supporting Information. [b] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.150 mmol), **HEH** (0.200 mmol) and base (0.200 mmol) in DMSO (3.0 mL) under blue LED irradiation. [c] Improved reaction conditions after investigation of reagent amounts. For details, see Table S2 in the Supporting Information. [d] The reaction was performed in the presence of CsCl (4.0 equiv.). [e] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.150 mmol), photocatalyst (1 mol%), **HEH** (0.130 mmol) and K₂CO₃ (0.200 mmol) in DMSO (1.0 mL) under blue LED irradiation. [f] The reaction was performed on a 1.0 mmol (**1a**) scale.

On the screening of solvents for the **4DPAIPN**-catalyzed reaction, DMSO was found to be the most effective, but the reaction proceeded in a range of solvent such as THF, acetonitrile, dichloromethane, and toluene, in which Cs₂CO₃ and Hantzsch ester did not give the target product (Table S6 in the Supporting Information). The fact that **3a** was yielded in 88% yield even in methanol indicated that transformation of

non-protected carbohydrates would be feasible. Under the optimum reaction conditions, a reaction using 1.0 mmol of **1a** (260 mg) also worked well to yield **3a** in a 71% yield (Table 1, entry 11).

Next, the applicability of various aryl sulfides was investigated for the two optimum conditions (Condition A: **HEH**, Cs_2CO_3, Condition B: **4DPAIPN**, **HEH**, K_2CO_3). The results are summarized along with their reduction potentials in Table 2. Phenyl and pyridyl sulfides **1b,c** were unreactive, likely due to their low reduction potentials. Other heteroaryl sulfides **1d–f** which show higher reduction potentials rather than that of **1c** were found to be promising substrates under both reaction conditions, affording **3a** in 33–98% yields. Meanwhile, 2-benzoxazolyl sulfide **1g** gave 73% yield of **3a** under the condition B, whereas the condition A gave a trace amount of the product, indicating the superiority of the condition B in terms of reactivity.

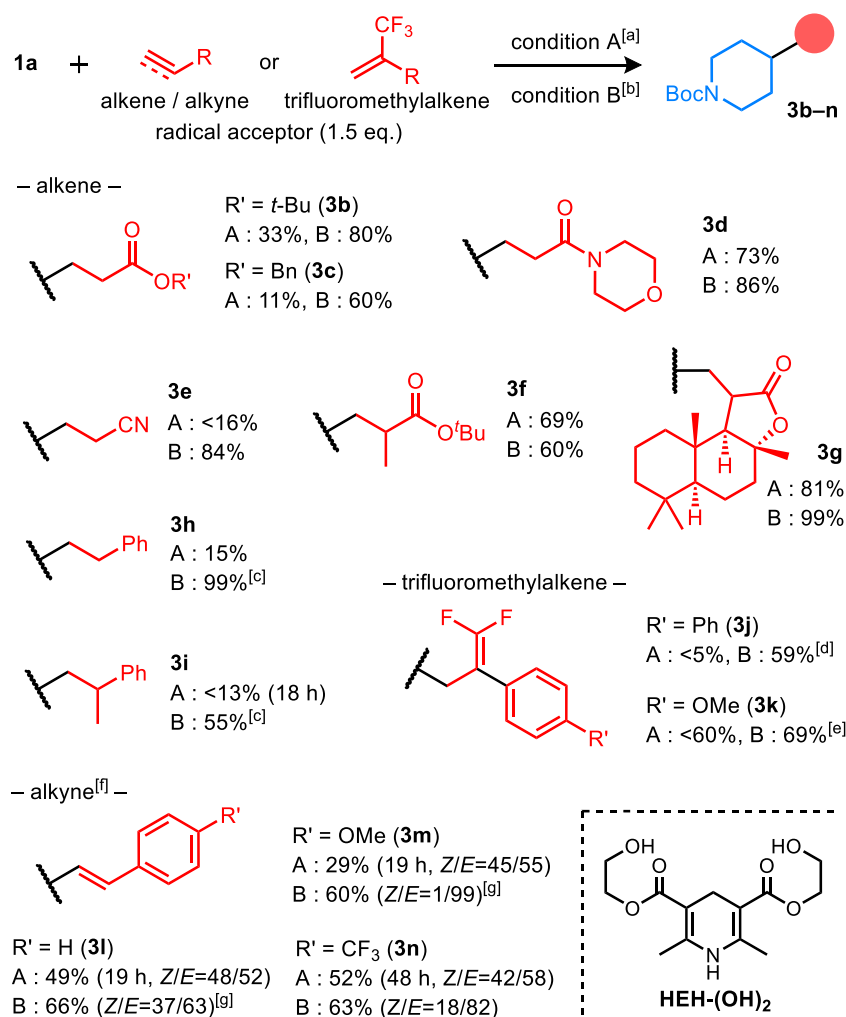**Table 2.** Screening of heteroaryl substituents for desulfurative coupling.
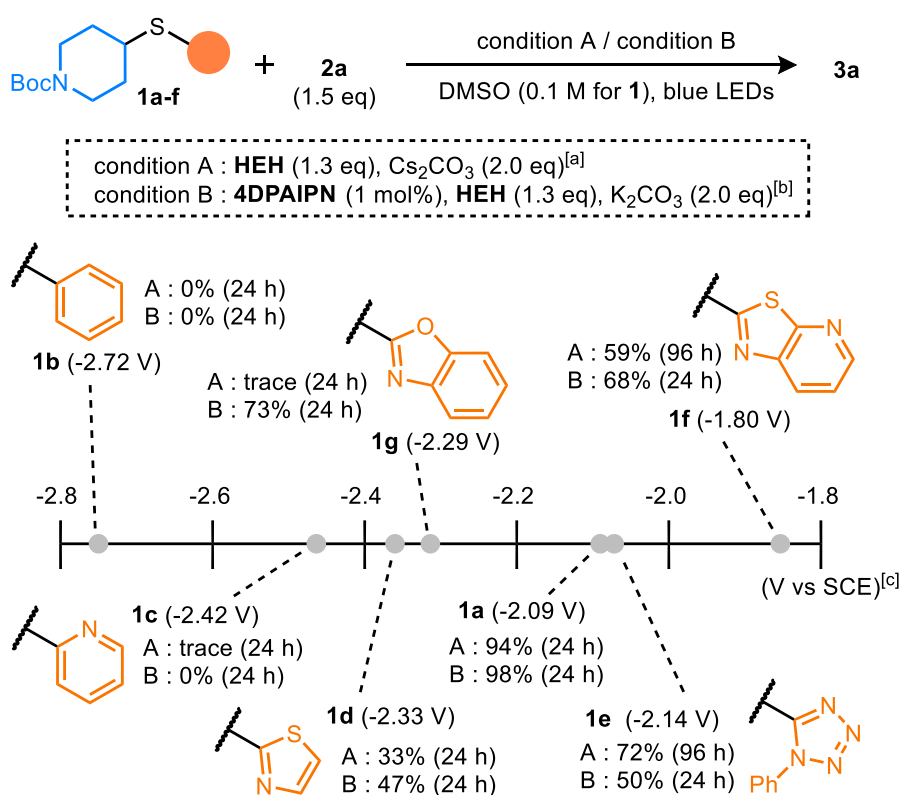
[a] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.150 mmol), **HEH** (0.130 mmol) and base (0.200 mmol) in DMSO (1.0 mL) under blue LED irradiation. [b] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.150 mmol), photocatalyst (1 mol%), **HEH** (0.130 mmol) and K_2CO_3 (0.200 mmol) in DMSO (1.0 mL) under blue LED irradiation. [c] The details are summarized in Figure S4 in the Supporting Information.

Three types of radical acceptors were tested to evaluate the generality of these protocols (Table 3). Electron deficient alkenes and trifluoroalkenes were applicable to the reaction using **HEH** and Cs_2CO_3, albeit the competitive photoreduction of the acceptors[5a] led to poor yields in several cases (**3b**: 33%, **3c**: 11%, **3e**: <16%, **3j**: <5%). Reductive coupling with arylacetylenes gave the desired products in 29–52% yields. In these cases, *N*-Boc piperidine was obtained as a major side-product, which would be produced

hydrogen atom transfer of radical intermediate.

**Table 3.** Screening of radical acceptors for desulfurative coupling.

– alkene –

R' = *t*-Bu (**3b**)
A : 33%, B : 80%

R' = Bn (**3c**)
A : 11%, B : 60%

3d
A : 73%
B : 86%

3e
A : <16%
B : 84%

3f
A : 69%
B : 60%

3g
A : 81%
B : 99%

3h
A : 15%
B : 99%[c]

– trifluoromethylalkene –

R' = Ph (**3j**)
A : <5%, B : 59%[d]

R' = OMe (**3k**)
A : <60%, B : 69%[e]

3i
A : <13% (18 h)
B : 55%[c]

– alkyne[f] –

R' = OMe (**3m**)
A : 29% (19 h, *Z/E*=45/55)
B : 60% (*Z/E*=1/99)[g]

R' = H (**3l**)
A : 49% (19 h, *Z/E*=48/52)
B : 66% (*Z/E*=37/63)[g]

R' = CF$_3$ (**3n**)
A : 52% (48 h, *Z/E*=42/58)
B : 63% (*Z/E*=18/82)

HEH-(OH)$_2$

[a] The reactions were carried out with **1a** (0.100 mmol), radical acceptor (0.150 mmol), **HEH** (0.130 mmol) and Cs$_2$CO$_3$ (0.200 mmol) in DMSO (1.0 mL) under blue LED irradiation. The reactions were performed for 24 h unless otherwise noted. [b] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.150 mmol), photocatalyst (0.001 mmol), **HEH** (1.3 mmol) and K$_2$CO$_3$ (0.200 mmol) in DMSO (1.0 mL) under blue LED irradiation for 24 h. [c] The reactions were carried out with 3.0 equivalents of alkenes. [d] The reactions were carried out with **1a** (0.200 mmol), **2a** (1.20 mmol), photocatalyst (0.002 mmol), **HEH-(OH)$_2$** (1.04 mmol) and K$_2$CO$_3$ (1.60 mmol) in DMSO (2.0 mL) [e] The reactions were carried out with **1a** (0.100 mmol), **2a** (0.600 mmol), photocatalyst (0.001 mmol), **HEH-(OH)$_2$** (0.521 mmol) and K$_2$CO$_3$ (0.808 mmol) in DMSO (1.0 mL) [f] The *Z/E* ratios were determined by ^{1}H NMR. [g] The products were obtained as an inseparable mixture with *N*-Boc piperidine (**3l**) or HEH (**3m**). The yields were calculated from ^{1}H NMR analysis. The desired products were isolated through a deprotection/reprotection sequence (**3l**: 54%, *Z/E*=24/76; **3m**: 36%, Z/E=1/99).

Organo-photocatalytic reactions with alkenes and arylacetylenes gave improved results (**3b–k**: 55–99% yields) compared to the respective reactions using Hantzsch ester and Cs$_2$CO$_3$, because low population of base-activated Hantzsch ester suppressed the undesired photo-reduction process. The reactions providing **3j** and **3k** were carried out with a highly polar Hantzsch ester derivative[12] **HEH-(OH)$_2$** because

they were obtained as an inseparable mixture with Hantzsch ester or its pyridine derivative. Reactions of arylacetylenes gave **3l**–**n** in 60–66% yields. The diastereoselectivity of the alkene products were increased up to 1/99 (*Z*/*E*). Deuteration experiment using Hantzsch ester-d_2 and Cs_2CO_3 gave **3n** with 89% deuterium incorporation, showing that vinyl radical intermediate abstracts the hydrogen from Hantzsch ester. On the other hand, reaction using **4DPAIPN**, Hantzsch ester-d_2 and K_2CO_3 gave **3n** with 13% deuterium incorporation (Figure S5 in the Supporting Information). These results suggests that protonation of vinyl anion, which would be generated by photocatalytic single electron reduction of vinyl radical along with *Z*/*E* isomerization, should be the major pathway rather than hydrogen abstraction of the radical intermediate under organo-photocatalytic conditions.
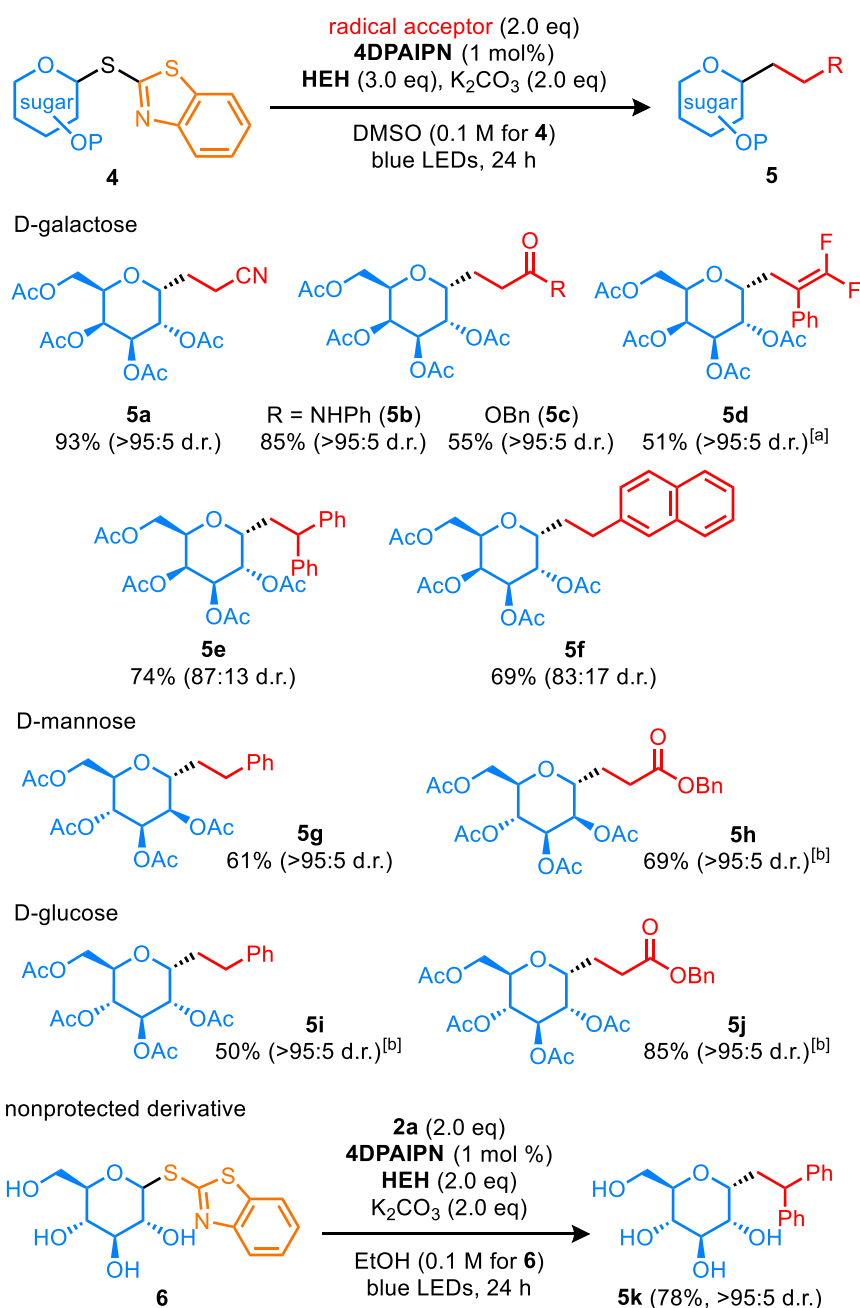
Table 4. Scope of benzothiazolylsulfides for carbon-radical generation.
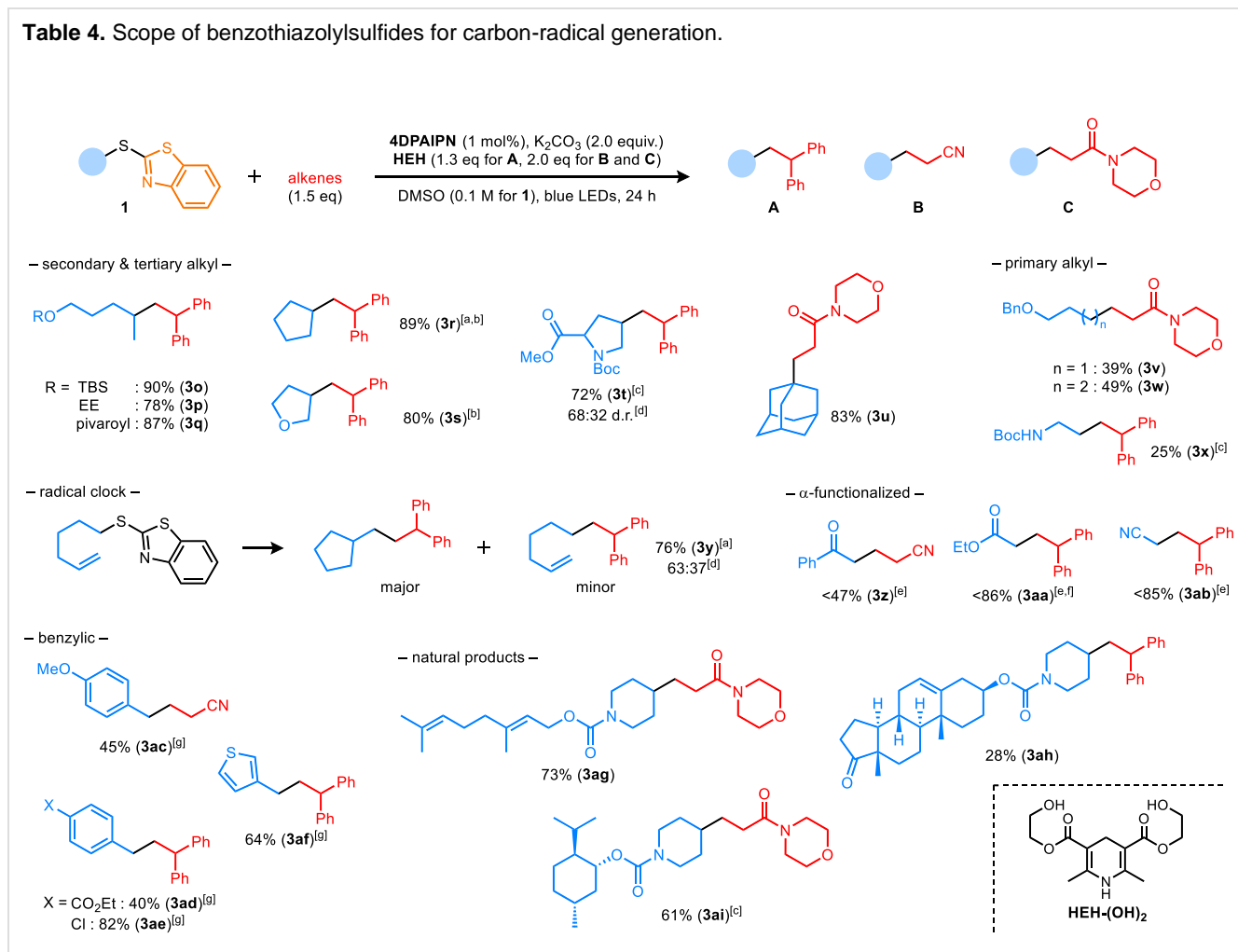
[a] The reaction was carried out with sulfide (0.300 mmol) and 1,1-diphenylethylene (0.200 mmol). [b] The reactions were carried out with 2.0 equivalents of **HEH**. [c] The reactions were carried out with **HEH-(OH)₂** instead of **HEH**. [d] The ratio was determined by ^{1}H NMR analysis. [e] The product was obtained as an inseparable mixture with structure unidentified side products. [f] The undesired product could be separated after hydrolysis. The corresponding carboxylic acid (**2aa'**) was obtained in 52% two-step yield. [g] The reactions were carried out with 10 equivalents of alkenes.

Then, we investigated the scope of alkyl groups on benzothiazolyl sulfides through the organo-photocatalytic reaction with 1,1-diphenylethylene (Table 4). Several sulfides were reacted with acrylonitrile

or 1-morpholinoprop-2-en-1-one as an alternative acceptor in view of purification. Secondary and tertiary alkyl benzothiazolyl sulfides including a furan and a pyrrolidine derivatives were excellent substrates, providing the corresponding adducts **3o**–**u** in 72–90% yields. Primary alkyl ones were also viable, albeit with less efficiency, probably because of poor stability of primary alkyl radicals (**3v**–**x**, 25–49% yields). As for the protecting groups, various functionalities such as *tert*-butyldimethylsilyl (**3o**), ethoxyethyl (EE, **3p**), pivaloyl (**3q**), and benzyl (**3v,w**) groups for a hydroxyl group as well as *N*-Boc group (**3x**) were tolerated under the standard reaction conditions. The radical clock substrate gave a 63:37 mixture of ring-closed and ring-opened products **3y** in 76% combined yield. Reactions toward keto, ester, cyano, phenyl and 3-thienyl derivatives at the α position also gave the desired adducts **3z**–**3af**. However, the relevant 4-pyridyl and *N*-Boc-3-indolyl derivatives gave no desired products, even though they were completely consumed after 24-hour reaction. The desulfurative transformation was applicable to structurally complex molecules prepared from geraniol, dehydroepiandrosterone, and menthol, affording **3ag**–**ai** in 28–73 yields.

As a further extension of this method, *C*-glycosylation using benzothiazolyl glycosyl sulfides were examined. Tetraacetates were chosen because of the ease of preparation, and the prepared sulfides were found to be stable for at least one month under ambient atmosphere. The reaction conditions were reevaluated for complete consumption of glycosyl benzothiazolyl sulfides (Table S7 in the Supporting Information). Under the optimized reaction conditions described in Table 5, variety of *C*-glycosides **5a**–**j** were produced in 50–93% yields with high α-isomer selectivity which is in line with the general trend of radical *C*-glycosylation.[13] Furthermore, this method allowed the transformation of nonprotected substrate **6** in ethanol, affording the corresponding adduct **5k** in 78% yield.

Table 5. Application to *C*-glycosylation using bench-stable sulfides.

D-galactose

5a
93% (>95:5 d.r.)

R = NHPh (**5b**)
85% (>95:5 d.r.)

OBn (**5c**)
55% (>95:5 d.r.)

5d
51% (>95:5 d.r.)[a]

5e
74% (87:13 d.r.)

5f
69% (83:17 d.r.)

D-mannose

5g
61% (>95:5 d.r.)

5h
69% (>95:5 d.r.)[b]

D-glucose

5i
50% (>95:5 d.r.)[b]

5j
85% (>95:5 d.r.)[b]

nonprotected derivative

2a (2.0 eq)
4DPAIPN (1 mol %)
HEH (2.0 eq)
K_2CO_3 (2.0 eq)

EtOH (0.1 M for **6**)
blue LEDs, 24 h

5k (78%, >95:5 d.r.)

[a] The reaction was carried out with 1.5 equivalents of **HEH** and 2 equivalents of K_2CO_3. [b] The reactions were carried out with 5.0 equivalents of alkenes.

Based on the obtained results in Table 1 and the previous reports,[5] it can be inferred that Hantzsch ester anion is in situ generated from Cs_2CO_3 and Hantzsch ester and acts as a photoreductant in the catalyst-free reaction. To prove this mechanism, we performed the reaction of **1a** and **2a** using pre-prepared Hantzsch ester anion. Isolation of Hantzsch ester anions generated from Hantzsch ester by treatment with various strong bases was unsuccessful because of their poor stability, but the desired reaction proceeded by directly adding **1a** and **2a** to the degassed THF solution of Hantzsch ester anion (**HE-K**) followed by

photoirradiation to afford **3a** in 68% yield (Figure 2a). Furthermore, Stern-Volmer experiments showed that **1a** quenched the fluorescence of Hantzsch ester-Cs_2CO_3 at the excitation wavelength of 465 nm and a linear correlation between these reagents was observed (Figure S6 in the Supporting Information). These results support that the $C(sp^3)$-S bond cleavage from benzothiazolyl sulfides proceeds through the electron transfer from the photoexcited Hantzsch ester anion to the sulfide substrate, and thus we proposed the reaction mechanism as shown in Figure 2b.
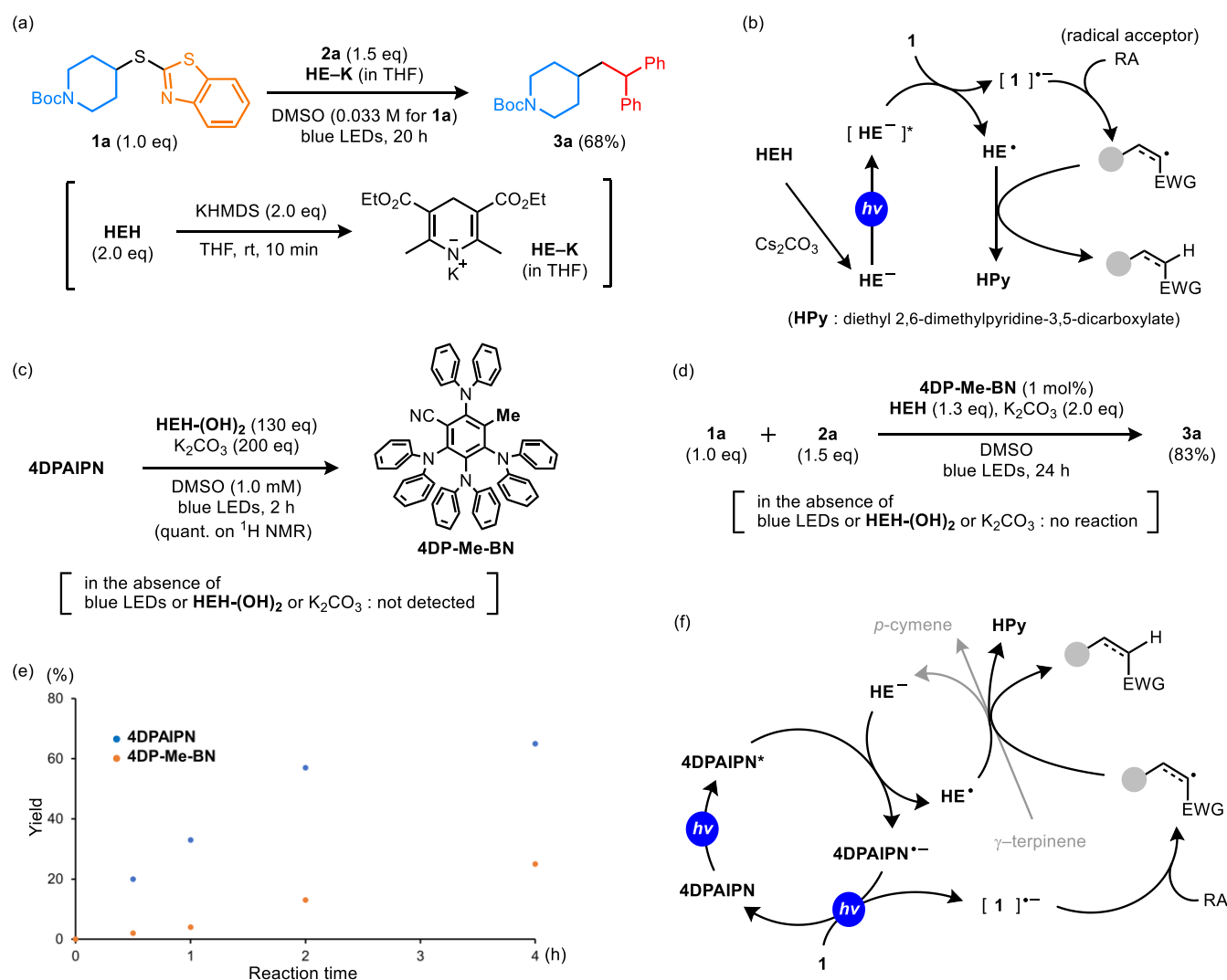

Figure 2. (a) Demonstration of the desulfurative coupling using in situ generated Hantzsch ester anion (**HE-K**), (b) plausible mechanism for Hantzsch ester anion-mediated desulfurative coupling, (c) photodegradation of **4DPAIPN**, (d) demonstration of the desulfurative coupling using **4DP-Me-BN** as a photocatalyst, (e) time-dependent reaction profile of organo-photocatalytic desulfurative coupling, and (d) plausible mechanism for **4DPAIPN**-catalyzed desulfurative coupling.

Meanwhile, organo-photocatalysis should mainly include $C(sp^3)$-S bond cleavage mediated by **4DPAIPN** rather than Hantzsch ester anion because the use of K_2CO_3 and **HEH** is not effective for degradation of benzothiazolyl sulfide as observed in Table 1. In consideration with the potentials of photoexcited **4DPAIPN** ($E(\text{PC}^{•+}/\text{PC}^*)$ = -1.52 V vs SCE)[14] and **4DPAIPN**$^{•-}$ ($E(\text{PC}/\text{PC}^{•-})$ = -1.65 V vs SCE), electron transfer to

benzothiazolyl sulfide (E(**1a/1a$^{\bullet-}$**) = -2.09 V vs SCE) from these species would not take place. The former was experimentally supported by Stern-Volmer experiments in Figure S7 in the Supporting Information. Therefore, we focused on the photodegradation reported by König[15b] and Kwon[15a]. In fact, we observed the generation of a fluorescent component on the TLC analysis during the reaction in many cases. The ^{1}H NMR spectrum of the products obtained from the degradation of **4DPAIPN** through the reaction in Figure 2c was identical with that of **4DP-Me-BN**, which was not generated in the absence of **HEH-(OH)$_2$**, K$_2$CO$_3$, or blue LEDs (Figure S8 in the Supporting Information). The photoinduced desulfurative coupling using **4DP-Me-BN** formed the radical adduct in 83% yield (Figure 2d). In this system, highly reductive **4DP-Me-BN$^{\bullet-}$** (E(PC/PC$^{\bullet-}$) = -2.05 V vs SCE)[15a] is likely to occur electron transfer to benzothiazolyl sulfide.

To confirm the involvement of **4DP-Me-BN** in the desulfurative coupling, we subsequently investigated a time-dependent reaction profile. As summarized in Figure 2e, the reaction profile obtained under standard reaction conditions using **4DPAIPN** is unexpectedly quite different with that obtained with **4DP-Me-BN**. Considering these results and the fact that the degradation of **4DPAIPN** was partial even after 18-hour reaction (Figure S9 in the Supporting Information), the **4DP-Me-BN**-promoted desulfurative process is unlikely to be a main process of the present transformation.

As another pathway, we considered the consecutive photo-induced electron transfer (ConPET) process including **4DPAIPN$^{\bullet-}$**.[16] To confirm this, we attempted to observe the generation of **4DPAIPN$^{\bullet-}$** on UV-Vis absorption spectrum of a mixture of **4DPAIPN**, **HEH**, and K$_2$CO$_3$ (Figure S10 in the Supporting Information). After one-minute irradiation of blue LEDs to the solution, an increase of absorbance at 530–700 nm was observed, which suggests that the geenration of **4DPAIPN$^{\bullet-}$**.[16c] The absorbance was decreased after adding **1a**. These results would indicate the possibility of the ConPET process of this transformation. Focused on the fact that the oxidation potential of Hantzsch ester (E(**HEH$^{\bullet+}$/HEH**) = +1.0 V vs SCE)[3b] is higher than that of excited **4DPAIPN** (E(PC*/PC$^{\bullet-}$) = +0.90 V vs SCE) and the C-S bond cleavage did not proceed under the conditions using **4DPAIPN** and **HEH** in the absence of K$_2$CO$_3$, slightly generated Hantzsch ester anion (E(**HE$^{\bullet}$/HE$^-$**) = -0.19 V vs SCE)[5c] are likely to work as a sacrificial reductant for the generation of **4DPAIPN$^{\bullet-}$**. Thus, we propose the plausible reaction mechanism presented in Figure 2f. γ-Terpinene is involved in the regeneration of **HEH** and in the hydrogenation of adducts.

Conclusion

In conclusion, we have developed visible-light-induced desulfurative coupling of alkyl benzothiazolyl sulfides with electron-deficient alkenes/alkynes. We have achieved two types of C(sp^3)-S scission using Hantzsch ester anion as a key reductant. Hantzsch ester anion prepared with Cs$_2$CO$_3$ worked as a photoreductant, leading to catalyst- and heavy-metal-free transformation. The alternative combination of Hantzsch ester and K$_2$CO$_3$ was proved to serve mainly as a sacrificial reducing agent in photoredox catalysis, but partly involved in photodegradation of **4DPAIPN** to **4DP-Me-BN**. The organo-photocatalytic transformation could be applied to a wide range of substrates including protective group-free thioglycoside. Direct radical generation from heteroaryl sulfides, which do not require transformation to the relevant sulfones or sulfonium salts, is expected to extend the options in the synthesis of multifunctional bioactive molecules.

Supporting Information

Experimental details and all relevant data (including NMR spectra and mechanical study data) related to this study are available in the Supporting Information file. The authors have cited additional references within the Supporting Information.[17–52]

Acknowledgements

References

[1] a) T. Li, Q. Zhou, F. Meng, W. Cui, Q. Li, J. Zhu, Y. Cao, *Eur. J. Org. C.* **2023**, *26*, e202300507; b) A. M. F. Phillips, A. J. L. Pombeiro, *Org. Biomol. Chem.* **2017**, *15*, 2307–2340; c) C. Zheng, S.-L. You, *Chem. Soc. Rev.* **2012**, *41*, 2498–2518; d) M. Rueping, J. Dufour, F. R. Schoepke, *Green Chem.* **2011**, *13*, 1084–1105.

[2] a) G. S. Yedase, S. Venugopal, P. Arya, V. R. Yatham, Asian J. Org. Chem. **2022**, *11*, e202200478; b) W. Huang, X. Cheng, *Synlett* **2017**, *28*, 148–158.

[3] a) Z. Zhang, J.-H. Ye, T. Ju, L.-L. Liao, H. Huang, Y.-Y. Gui, W.-J. Zhou, D.-G. Yu, *ACS Catal.* **2020**, *10*, 10871–10885; b) P.-Z. Wang, J.-R. Chen, W.-J. Xiao, *Org. Biomol. Chem.* **2019**, *17*, 6936–6951.

[4] a) X. Li, W. Si, Z. Liu, H. Qian, T. Wang, S. Leng, J. Sun, Y. Jiao, X. Zhang, *Org. Lett.* **2022**, *24*, 4070–4074; b) J. Wu, P. S. Grant, X. Li, A. Noble, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2019**, *58*, 5697–5701; c) J. Zhang, Y. Li, R. Xu, Y. Chen, *Angew. Chem. Int. Ed.* **2017**, *56*, 12619–12623.

[5] a) P. C. Gallage, M. G. McKee, S. P. Pitre, *Org. Lett.* **2024**, 26, 1975–1979; b) J. Xu, Y. Lan, B. Liu, *J. Org. Chem.* **2024**, *89*, 599–604; c) D.-L. Zhu, Q. Wu, H.-Y. Li, H.-X. Li, J.-P. Lang, *Chem. Eur. J.* **2020**, *26*, 3484–3488.

[6] a) T. Sengoku, H. Iwama, T. Shimotori, K. Fujimoto, T. Inuzuka, K. Matsune, H. Yoda, *J. Org. Chem.* **2023**, *88*, 12776–12782; b) Q. Wang, B. C. Lee, T. J. Tan, Y. Jiang, W. H. Ser, M. J. Koh, *Nat. Synth.* **2022**, *1*, 967–974; c) T. Sengoku, D. Ogawa, H. Iwama, T. Inuzuka, H. Yoda, *Chem. Commun.* **2021**, *57*, 9858–9861; d) M. D. Heredia, W. D. Guerra, S. M. Barolo, S. J. Fornasier, R. A. Rossi, M. E. Budén, *J. Org. Chem.* **2020**, *85*, 13481–13494.

[7] a) Z. Liu, Y. Okamoto, S. Sato, *ChemCatChem* **2024**, e202301424; b) T. A. King, J. M. Kandemir, S. J. Walsh, D. R. Spring, *Chem. Soc. Rev.* **2021**, *50*, 39–57.

[8] a) Y. Tahara, K. Ghosh, M. Nambo, *Can. J. Chem.* **2023**, *101*, 491–496; b) R. Ohkura, M. Ohtsuka, J. C.-H. Yim, M. Nambo, C. M. Crudden, *Synlett* **2023**, *34*, 81–85; c) A. G. Savchenko, M. O. Zubkov, V. A. Kokorekin, J. Hu, A. Dilman, *ChemCatChem* **2023**, *15*, e202300505; d) B. Paul, H. Paul, I. Chatterjee, *Synthesis* **2022**, *54*, 5409–5422; e) M. Nambo, K. Ghosh, J. C.-H. Yim, Y. Tahara, N. Inai, T. Yanai, C. M. Crudden, *ACS Catal.* **2022**, 9526–9532.

[9] a) R. Jing, W. C. Powell, K. J. Fisch, M. A. Walczak, *J. Am. Chem. Soc.* **2023**, 145, 22354–22360; b) R. C. Griffiths, F. R. Smith, D. Li, J. Wyatt, D. M. Rogers, J. E. Long, L. M. L. Cusin, P. J. Tighe, R. Layfield, J. D. Hirst, M. M. Müller, N. J. Mitchell, *Chem. Eur. J.* **2023**, *29*, e202202503; c) R. C. Griffiths, F. R. Smith, J. E. Long, D. Scott, H. E. L. Williams, N. J. Oldham, R. Layfield, N. J. Mitchell, *Angew. Chem. Int. Ed.* **2022**, *61*, e202110223.

[10] L. I. Panferova, M. O. Zubkov, V. A. Kokorekin, V. V. Levin, A. D. Dilman, *Angew. Chem. Int. Ed.* **2021**, *60*, 2849–2854.

[11] During the course of the manuscript preparation, an interesting way to generate glycosyl radicals from 2,3,5,6-tetrafluoropyridine-4-thioglycoside was published: Y. Jiang, Y. Wei, Q.-Y. Zhou, G.-Q. Sun, X.-P. Fu, N. Levin, Y. Zhang, W.-Q. Liu, N. Song, S. Mohammed, B. G. Davis, M. J. Koh, *Nature* **2024**, *631*, 319–327.

[12] Ya. R. Uldrikis, G. Ya. Dubur, I. V. Dipan, B. S. Chekavichus, *Chem. Heterocycl. Compd.* **1975**, *11*, 1070–1076.

[13] L.-Y. Xu, N.-L. Fan, X.-G. Hu, *Org. Biomol. Chem.* **2020**, *18*, 5095–5109.

[14] M. Garreau, F. Le Vaillant, J. Waser, *Angew. Chem. Int. Ed.* **2019**, *58*, 8182–8186.

[15] a) Y. Kwon, J. Lee, Y. Noh, D. Kim, Y. Lee, C. Yu, J. C. Roldao, S. Feng, J. Gierschner, R. Wannemacher, M. S. Kwon, *Nat. Commun.* **2023**, *14*, 92; b) S. Grotjahn, B. König, *Org. Lett.* **2021**, *23*, 3146–3150.

[16] a) F.-P. Huang, W.-J. Qin, X.-Y. Pan, K. Yang, K. Wang, Q.-H. Teng, *J. Org. Chem.* **2024**, 89, 4395–4405; b) W. Wei, C. Li, Y. Fan, X. Chen, X. Zhao, B. Qiao, Z. Jiang, *Angew. Chem. Int. Ed.* **2024**, *63*, e202406845; c) A. F. Chmiel, O. P. Williams, C. P. Chernowsky, C. S. Yeung, Z. K. Wickens, *J. Am. Chem. Soc.* **2021**, *143*, 10882–10889.