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External Oxidant-Free Oxidative Cross-Coupling: A Photoredox Cobalt-Catalyzed Aromatic C-H Thiolation for Constructing C-S Bonds

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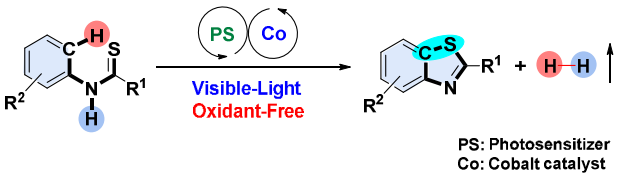
ABSTRACT: An external oxidant-free oxidative coupling for aromatic C–H thiolation by visible-light photoredox cobalt-catalysis has been developed. Various substrates could afford benzothiazoles in good to excellent yields, and only H_2 is generated as a side product. When catalytic TBAOH was used as the base, not only 2-aryl but also 2-alkylbenzothiazoles could be obtained through this novel dehydrogenative coupling reaction. This method could be scaled up and applied to the synthesis of biologically active molecules bearing benzothiazole structural scaffolds (potent antitumor agents). Furthermore, the unexpected oxidation byproducts amides, which are often generated in oxidative cyclization of thiobenzanilides, can be completely avoided. Mechanistic studies showed that the H_2 originates from the substrates. And the kinetic studies indicate that the interaction between the cobalt catalyst and proton might be involved in the rate-limiting process.

INTRODUCTION

Construction of carbon-heteroatom bonds is a fundamental research area in chemical science, since the introduction of heteroatoms is important to the functional properties of organic compounds. Cross-coupling is perhaps the most powerful tool for constructing carbon-heteroatom bonds.[1] However, in the classic cross-coupling between a nucleophile and an electrophile, significant amounts of undesirable byproducts are usually produced.[2] The recent developed oxidative cross-coupling between C–H and heteroatom–H nucleophiles has advanced the construction of C–heteroatom bonds towards sustainable synthesis.[3] However, oxidants and proton acceptors have to be applied as the sacrificial reagents, which lead to some wasteful by-products or oxidation side reactions.

Therefore, it would be appealing to develop oxidative cross-couplings between C–H and heteroatom-H nucleophiles for constructing C–heteroatom bonds under oxidant-free and proton-acceptor-free conditions.[4] However, there are only a few examples where this mechanistic paradigm has been applied to the construction of C–C,[5] S–S,[6] C–N[7] and C–P[8] bond formations from their corresponding C–H and X–H (X = C, N, P, S) nucleophiles. As one of the most important carbon-heteroatom bonds in organic chemistry, C–S bonds are frequently found in important pharmaceuticals and biologically active natural compounds.[9] To the best of our knowledge, there is no report on C–S bond formation from C–H thiolation under oxidant-free condition with generation of H_2. Especially, up to now, no examples have been reported to realize intramolecular cross-coupling under oxidant-free conditions. Herein, we report our progress on aromatic C–H thiolation with liberation of H_2 by visible-light photocatalysis (Scheme 1). The products of this transformation are benzothiazoles, a class of structurally important scaffolds that have drawn much attention on developing synthetic methods for accessing such ubiquitous structural units.[10]



Scheme 1. Oxidant-free Aromatic C-H Thiolation to Construct C-S Bonds

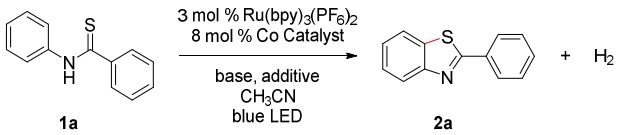
Among such synthetic methods, the intramolecular cyclization of thiobenzanilide derivatives is an significant approach to form benzothiazoles, such as transition-metal-catalyzed cyclization of *o*-halothiobenzanilides[10b,10c] and direct oxidative C-H functionalization of thiobenzanilides.[10e-i] Despite these advances, it is sometimes difficult to keep away from tiring pre-functionalization and unexpected byproducts. For example, the conversion from thiobenzanilides to benzothiazoles might face the problem of oxidation byproducts, amides, resulting from the use of oxidants. In this article, we report the development of a novel external oxidant-free photoredox cobalt catalyzed C-H functionalization reaction, in which the generation of benzamides was successfully avoided.

RESULT AND DISCUSSION

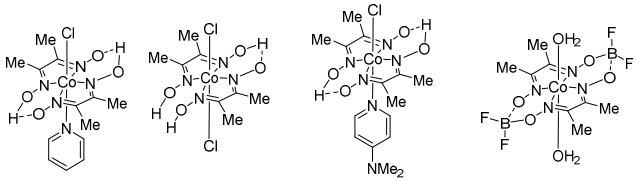
Initially Exploration and the Impact of the Proton-reducing Catalyst. We initially explored the intramolecular oxidative cyclization of *N*-phenylbenzothioamide **1a** under external oxidant-free conditions. The transformation could be achieved smoothly with the combination of a photosensitizer and a proton reducing catalyst under weak alkaline conditions, and H_2 was detected as the only byproduct (for details, see Supporting Information, Table S1). It is noteworthy that the chemo-selectivity of this transformation was excellent without the generation of benzamides. After the initial screening, the irradiation of 3 mol % $Ru(bpy)_3(PF_6)_2$, 8 mol % $Co^{III}(dmgH)_2PyCl$ (dmgH = dimethylglyoximate) and 1.2 equiv of base, sodium carbonate, in CH_3CN could give 75% yield of **2a** (Table 1, entry 1). In the presence of photosensitizer and

base, a range of cobaloximes as the proton reducing catalysts (Table 1, Co catalyst A–D) were capable of catalyzing the desired reaction, with $[Co^{III}(dmgH)_2(4\text{-}NMe_2\text{-}C_5H_4N)Cl]$ leading to the highest yield of H_2 generation and chemical yield (Table 1, entry 3).

Table 1. Optimization of the Reaction Conditions [a]



entry	Co catalyst	base	additive	yield (%)[b]	H_2 (%)[c]
1[d]	**A**	Na_2CO_3	–	75	25
2[d]	**B**	Na_2CO_3	–	55	9
3[d]	**C**	Na_2CO_3	–	99	69
4[d]	**D**	Na_2CO_3	–	0	0
5	**C**	Na_2CO_3	–	99	70
6	**C**	K_2CO_3	–	94	38
7	**C**	Cs_2CO_3	–	36	5
8	**C**	NaOAc	–	0	0
9	**C**	DBU	–	0	0
10	**C**	DMAP	–	0	0
11	**C**	Na-Gly	–	99	79
12[e]	**C**	Na-Gly	DMAP	99	99
13[e, f]	**C**	Na-Gly	DMAP	99	99



$[Co^{III}(dmgH)_2PyCl]$ **Catalyst A** | $[Co^{II}(dmgH)_2Cl_2]$ **Catalyst B** | $[Co^{III}(dmgH)_2(4\text{-}Me_2N\text{-}C_5H_4N)Cl]$ **Catalyst C** | $[Co^{II}(dmgBF_2)_2(H_2O)_2]$ **Catalyst D**

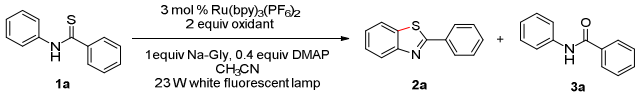
[a] Conditions: **1a** (0.20 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), Co catalyst (8 mol %) and base (1.0 equiv) were added in CH_3CN (2 mL) under an argon atmosphere, and irradiation of 3W blue LEDs for 12 h at rt. [b] Isolated yields were showed. [c] Determined by GC-TCD using pure methane as an internal standard. [d] 1.2 equiv of base was used. [e] 0.4 equiv of additive was added. [f] 23W white fluorescent light was used; DMAP = 4-dimethylaminopyridine.

Impact of the Base. The key of this transformation was the careful selection of an appropriate base, which would meet three criteria: (a) a pK_b low enough to abstract a proton from substrates, (b) a mild conjugate acid to act as a hydrogen atom donor, which could achieve the protonation process of the proton reducing catalysts, (c) redox inertia (would not act as an electron donor). On reducing the amount of base to one equivalent (entry 5), or even 0.6 equivalent (see Supporting Information, Table S1), the yield of **2a** was still excellent with efficient evolution of H_2. Further examinations of base were conducted (Table 1, entries 5–11), which revealed a strong dependence on the reaction pH. A relatively weak base (pKa = 9–12), such as carbonate or sodium glycinate was effective, while a stronger base or weaker one was not suitable for this transformation. When the carbonates were chosen as the base, high yield of benzothiazole product could be obtained, while low yield of H_2 was detected (Table 1 entries 1–7). It might be due to that some CO_2 could be *in-situ* generated, and the low yield of H_2 relative to benzothiazole might result from the reduction of CO_2.[11] Therefore, sodium glycinate was used instead of Na_2CO_3 (Table 1, entry 11). Further improvement in efficiency of H_2 evolution was achieved through the addition of 0.4 equivalent of DMAP (entry 12, 99% yield and 99% H_2 generation). DMAP might act as a weak organic base, whose more acidic conjugate acid could promote the protonation of cobalt catalyst. In addition, when the light source was replaced by white fluorescent lamp, the reaction still had a good efficiency (Table 1, entry 13).

Control experiments without the addition of either photosensitizer, proton reducing catalyst, base or the irradiation of visible light clearly demonstrated that visible-light and all components are essential in the catalytic system (for details, see Supporting Information, Table S2, entries 1–5). No H_2 evolution was observed when the substrate **1a** was absent in the mixture (Table S2, entry 6), which indicated that the substrate might act as the electron donor in the reaction.

Comparison with Photoredox Catalyzed Oxidative Conditions. In the comparison with the photoredox catalyzed oxidative conditions, it was found that the presence of oxidants, such as O_2,[10g] $K_2S_2O_8$ and H_2O_2, would increase the generation of oxidation byproduct *N*-phenylbenzamide **3a** (Table 2, entries 2–5). By contrast, under the external oxidant-free conditions, the desired coupling products **2a** could be afforded with high selectivity.

Table 2. Comparison with Photoredox Catalyzed Oxidative Conditions [a]



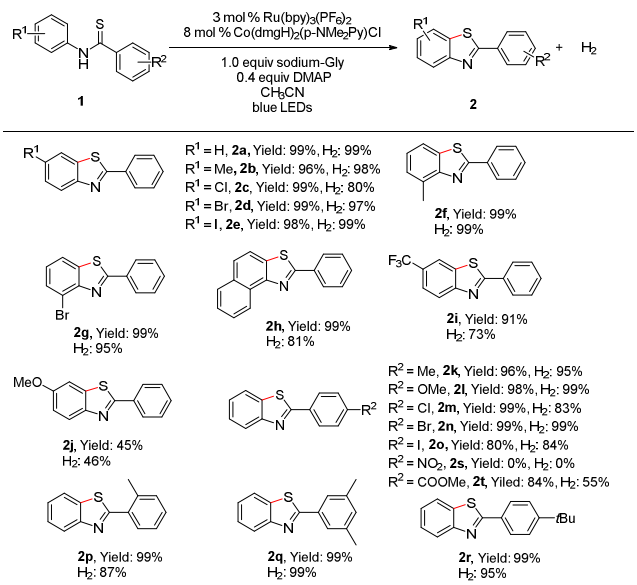
entry	oxidant	yield (%)[b]	
		2a	**3a**
1[c]	-	99	0
2[d]	O_2	7	49
3	$K_2S_2O_8$	26	38
4	H_2O_2	16	17

[a] Reaction conditions: **1a** (0.35 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol%), oxidant (2 equiv), sodium-Gly (1.0 equiv) and DMAP (0.4 equiv) were added in CH_3CN (2 mL) under irradiation of 23W white fluorescent lamp for 12 h at rt. [b] Yield was determined by GC analysis. [c] $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %) was used in place of oxidant. [d] 1 atm O_2 was used.

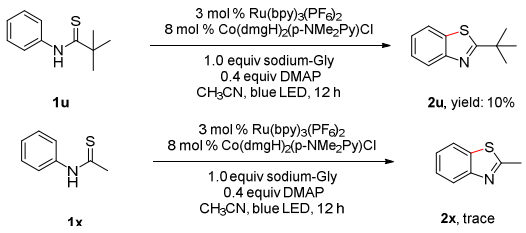
The Scope of Intramolecular External Oxidant-free Oxidative Cyclization of Thiobenzanilides. We next explored the scope and generality of this oxidant-free cyclization protocol using the optimized conditions (condition A, Table 1, entry 12). As shown in Scheme 2, a range of *N*-phenylbenzothioamides, with either electron-rich or electron-poor substituents on the *ortho* or *para* position of *N*-aryl ring, were viable in this transformation (Scheme 2, **2a–2j**). Notably, halogen substituents including Cl, Br, I could be well tolerated under the standard reaction conditions (Scheme 2, **2c–2e**) and displayed high activity with an equivalent amount of H_2 generation, providing more chances for further functionalization or modification of these molecules. However, strong electron-donating group (–OMe) or strong electron-withdrawing groups ($-CF_3$) on *N*-aryl ring decreased the reactivity (Scheme 2, **2i**, **2j**). In addition, the *meta* substitution on *N*-aryl ring of thioanilides would afford a mixture of products with C-H functionalization on *ortho* and *para* position by using this method (for details, see Supporting information, Figure S15). The reaction of *N*-naphthalene substituted benzothioamide could also give an excellent yield for the cyclization product (Scheme 2, **2h**, 99%). Substituent diversity of 2-aryl group was also explored by using this photoredox catalytic system (Scheme 2, **2k–2r**). Both electron-rich and electron-poor substituents on 2-aryl group reacted smoothly to give the corresponding benzothiazoles in high yields (Scheme 2, **2l** and **2t**). From the reactions of various substrates with substituents at *ortho, meta* or *para* position of aromatic ring, the corresponding 2-arylbenzothiazoles were obtained in generally excellent yields (Scheme 2, **2k**, **2p** and **2q**). In addition, halo

substituents in 2-aryl group were also tolerated (Scheme 2, **2m**, **2n** and **2o**). Then we further applied this optimized reaction conditions for the synthesis of 2-alkylbenzothiazoles. When 2-aryl groups were replaced by alkyl groups such as *tert*-butyl or methyl, however, low yields were obtained, presumably as a result of their higher pKa, which makes them harder to deprotonate (Scheme 3).

Scheme 2. Substrate Scope of the Synthesis of Substituted 2-Arylbenzothiazoles[a]



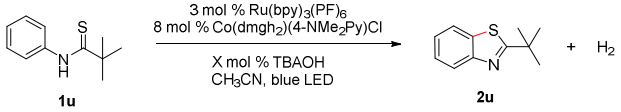
[a] Reaction conditions A: **1** (0.20 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %), sodium-Gly (1.0 equiv) and DMAP (0.4 equiv) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs, for 12 h at rt; H_2 was detected by GC-TCD using pure methane as an internal standard; and isolated yields of benzothiazoles were shown.



Scheme 3. Oxidative Cyclization for the Synthesis of 2-Alkylbenzothiazoles[a]

Therefore, a stronger base like tetrabutylammonium hydroxide was used instead of sodium glycinate. Interestingly, the concentration of proton seemed to have an important influence on the efficiency of reaction (Table 3). Due to the low concentration of proton, the use of 1 equiv of TBAOH as the external base provided the corresponding benzothiazole **2u** from 2,2-dimethyl-*N*-phenylpropanethioamide **1u** in poor yield (Table 3, entry 1). However, employing the catalytic amount of TBAOH as the base, the yield of **2u** was significantly increased (Table 3, entries 2–3). Especially, when 10 mol % TBAOH was used, the corresponding 2-alkylbenzothiazole **2u** and generation of H_2 were achieved in yield 99% and 86%, respectively (Table 3, entry 3). But further decrease of the base loading would inhibit the efficiency of reaction (Table 3, entry 4).

Table 3. The Influence of the Base Loading[a]

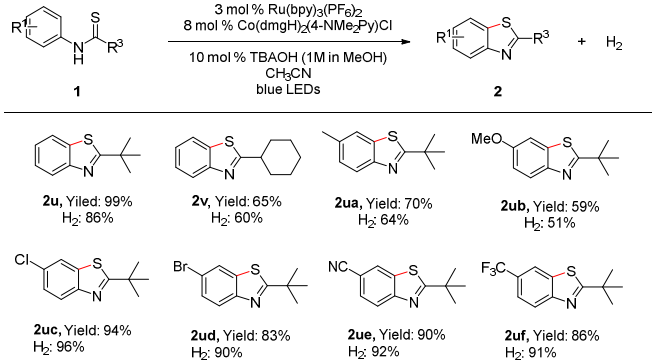


entry	X	yield (%)[b]	H_2 (%)[c]
1	100	trace	trace
2	30	38	21
3	10	99	86
4	5	0	0

[a] Conditions: **1u** (0.20 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %) and TBAOH (1M in MeOH) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs for 12 h at rt. [b] Isolated yields were showed; [c] Determined by GC-TCD by using pure methane as an internal standard.

With this optimized condition in hand (condition B), we examined the scope of alkyl substituted thioamide derivatives for the synthesis of corresponding 2-alkylbenzothiazoles (Scheme 4). Alkyl group such as *tert*-butyl (**2u**) and cyclohexyl (**2v**) groups could be compatible with this external oxidant-free condition, and the desired products were isolated in good to excellent yields. Unfortunately, only trace amount of 2-methylbenzothiazole (**2x**) could be observed in this catalytic system. Then, we also studied the influence of the substituents on the *N*-aromatic ring of substrates. Both electron-donating and electron-withdrawing substituents, such as methyl (**2ua**), methoxyl (**2ub**) cyano (**2ue**) and trifluoromethyl (**2uf**) groups, all gave good to excellent chemical yields with the H_2 evolution. Electron-withdrawing group on the benzene ring promote this transformation by making deprotonation of the corresponding substrate more easily (**2uc**-**2uf**). In addition, this reaction can be applied to the substrates bearing halogen atoms such as Cl (**2uc**), Br (**2ud**), which provided the possibility for further functionalization.

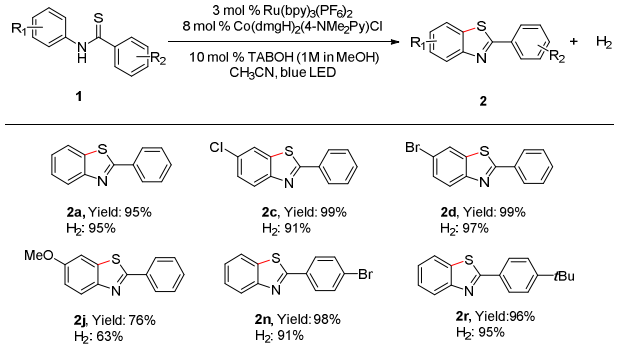
Scheme 4. Substrate Scope of the Synthesis of Substituted 2-Alkylbenzothiazoles[a]



[a] Conditions B: **1u**, **1ua–f**, and **1v** (0.20 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %) and 10 mol % TBAOH (1M in MeOH) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs for 12h at rt; H_2 was detected by GC-TCD using pure methane as an internal standard; and isolated yields of benzothiazoles were shown.

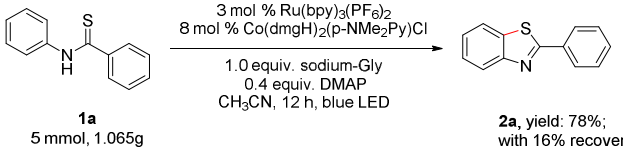
To further demonstrate the usefulness of this catalytic protocol (condition B), the application of this method in synthesis of 2-arylbenzothiazoles was also investigated (Scheme 5). Under condition B, 2-aryl substituted benzothiazole derivatives could also be afforded in good to excellent yields.

Scheme 5. Substrate Scope of the Synthesis of Substituted 2-Arylbenzothiazoles Using Condition B[a]

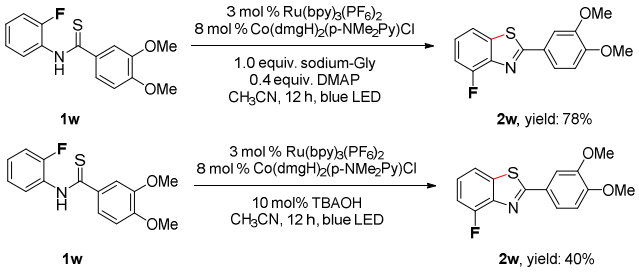


[a] Conditions B: **1** (0.20 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %) and 10 mol % TBAOH (1M in MeOH) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs for 12 h at rt; H_2 was detected by GC-TCD using pure methane as an internal standard; and isolated yields of benzothiazoles were shown.

Application of the Reaction to the Synthesis of Biologically Active Molecules. It is worth noting that the reaction can be effectively scaled up with good efficiency. For example, the oxidative cyclization of *N*-phenylbenzothioamide **1a** is operationally simple and amenable to gram-scale synthesis in 78% yield with 16% recovery of starting material (Scheme 6). Moreover, due to the high selectivity and efficiency, this visible-light-mediated cobalt catalyzed coupling strategy offers promising synthetic routes for the construction of a library of medicinal compounds having benzothiazole structural scaffolds. For instance, the 4-fluoro-2-(3,4-dimethoxyphenyl)benzothiazoles (**2w**) is a potent antitumor agent and showed good inhibitory potency against the human cancer cells.[12] By using condition A, **2w** could be constructed with good chemo-selectivity and efficiency (Scheme 7, condition A: 78%). However, a lower yield was observed under condition B (Scheme 7, condition B: 40%).



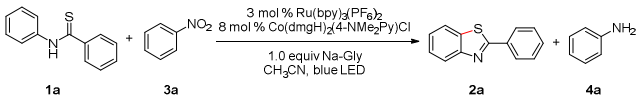
Scheme 6. Gram Scale Reaction of the Synthesis of 2-Arylbenzothiazoles



Scheme 7. Application of the Reaction in the Synthesis of Antitumor Agent

***In-situ* Hydrogenation of Nitroarenes.** In order to further utilize the generated H_2, we tried to combine this external oxidant-free oxidative coupling reaction to hydrogenation directly in one-pot. Under condition A, the *in-situ* hydrogenation of nitroarenes could be achieved in excellent yields without use of any sacrificial oxidant and reductant (Table 4, entry 1). Meanwhile, the control experiments were conducted. Both the conversion of coupling product and the yield of hydrogenation product would decrease in the absence of photosensitizer or cobalt catalyst (Table 4, entries 2-3), which showed that the generated Co-H intermediate might be crucial.[13] In addition, the reaction can proceed smoothly without adding DMAP (Table 4, entry 5).

Table 4. *In-situ* Hydrogenation of Nitroarenes [a]

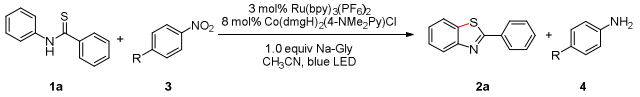


entry	PS	catalyst C	base	additive	yield (%)[b]	
					2a	**4a**
1	+	+	+	+	>99	87
2	-	+	+	+	11	10
3	+	-	+	+	36	34
4	+	+	-	+	0	0
5	+	+	+	-	>99	>99

[a] Reaction conditions: **1a** (0.35 mmol), **3a** (0.1 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %), sodium-Gly (1.0 equiv) and DMAP (0.4 equiv) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs 24 h at rt. [b] Yield was determined by GC-FID analysis. PS: photosensitizer.

Then, the generality of nitroarenes of this *in-situ* hydrogenation reaction was explored under this condition (Table 5). Various substituted nitrobenzenes could be reduced to the corresponding anilines by the *in-situ* generated reductants. Only the nitro group was reduced, while other easily reducible groups like bromo or carbonyl substituents in the nitrobenzenes would not change.

Table 5. The Generality of *In-situ* Hydrogenation of Nitroarenes[a]



entry	R	yield (%)[b]	
		2a	**4**
1	H(**3a**)	>99	99
2	Me(**3b**)	>99	95
3	OMe(**3c**)	>99	>99
4	COMe(**3d**)	99	92
5	Br(**3e**)	40	12

[a] Reaction conditions: **1a** (0.35 mmol), **3** (0.1 mmol), $Ru(bpy)_3(PF_6)_2$ (3 mol %), $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ (8 mol %) and sodium-Gly (1.0 equiv) were added in CH_3CN (2 mL) under an argon atmosphere and irradiation of 3W blue LEDs for 24 h at rt. [b] Yield was determined by GC-FID analysis.

Elucidation of the Mechanism. From the profile of the reaction with the light off/on over time, it was observed that the transformation progressed smoothly under irradiation with visible-light, but no further conversion was observed when the light source was removed (Figure 1). This result showed that the continuous irradiation of visible light is indispensable, and also indicated that the reaction proceeds through a photoredox catalytic pathway rather than radical chain propagation.

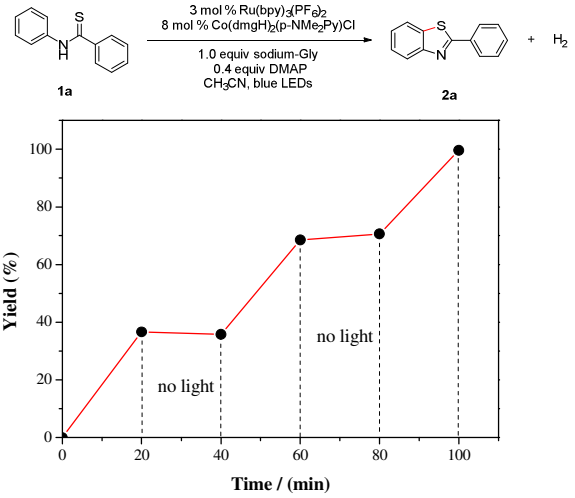


Figure 1. Profile of the reaction with the light off/on over time; yields were determined by GC analysis.

Furthermore, a series of emission quenching experiments were performed to acquire further insight into the photoredox catalytic cycle (Figure 2). As shown, the experiments revealed that sodium *N*-phenylbenzimidothioate and $Co^{III}(dmgH)_2(4\text{-}NMe_2Py)Cl$ both could quench the excited state of $Ru(bpy)_3(PF_6)_2$ (Figure 2). However, the quenching rate constant of sodium *N*-phenylbenzimidothioate is much bigger than the cobalt complex. In addition, DMAP or substrate **1a** could not be an emission quencher of $Ru(bpy)_3^{2+}$. These results suggest that the reaction might undergo an efficiently reductive quenching mechanism, in which **1a** might deprotonate firstly and then be oxidized by the excited state of photosensitizer.

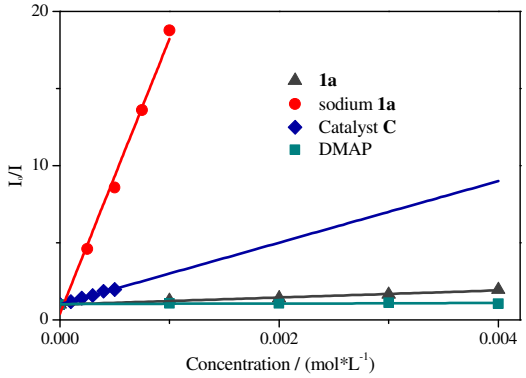
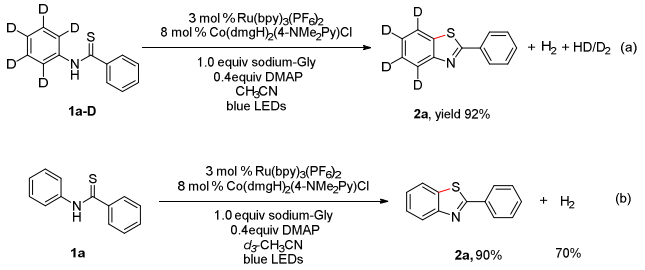


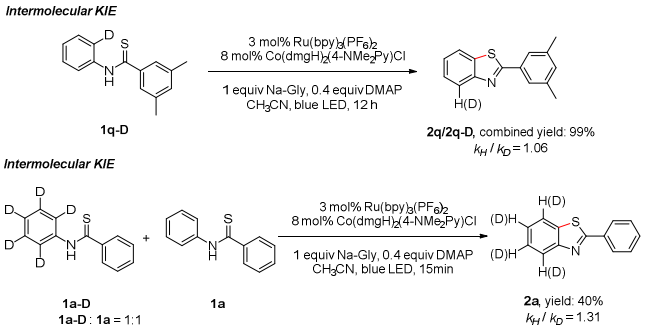
Figure 2. $Ru(bpy)_3(PF_6)_2$ emission quenching with *N*-phenylbenzothioamide, sodium *N*-phenylbenzimidothioate, $Co(dmgH)_2(4\text{-}NMe_2Py)Cl$ and DMAP; I_0 and I represent the intensities of the emission in the absence and presence of the quencher.

In order to find out the source of H_2, experiments with deuterated substrate were carried out. As shown in Scheme 8, D_2 or HD would be formed as the byproducts, when *N*-phenylbenzothioamide **1a** was replaced by a deuterated substrate **1a-D** (Scheme 8, a). However, when d_3-CH_3CN was used as solvent, only H_2 would be found (Scheme 8, b). In previous reports, water was frequently used as co-solvent and it was believed to be important in mediating the proton exchange processes.[5c] However, in this reaction, we realized the cross-coupling with hydrogen evolution reactions in organic solvent. And these results indicated that the released H_2 directly originates from the substrates.



Scheme 8. Deuterium Experiments for Reactions.

Intra- and intermolecular kinetic isotope effects (KIE, k_H / k_D) were obtained by using deuterated substrates (Scheme 9). No significant intramolecular kinetic isotope effect was observed (KIE value was 1.06, for details, see Supporting Information). Then parallel reactions were further performed with **1a** and **1a-D** to determine if cleavage of the aromatic C–H bond is the turnover-limiting step of the reaction. The reaction of the same amount of substrate **1a** and deuterated substrate **1a-D** under the standard conditions for 15 min provided a mixture of the products deuterium-**2a** (**2a-D**) and **2a** in 40% combined yields, in which the ratio of **2a** : **2a-D** was 1.31 (Scheme 9). Both of the observed intra- and intermolecular KIE values revealed that the C–H bond cleavage might not be the rate-determining step.



Scheme 9. Kinetic Isotope Effects of the Reaction.

Subsequently, to further investigate the mechanism in detail, the kinetic experiments were conducted using *in-situ* IR under condition B. Through *in-situ* IR (Figure 3), 2-phenylbenzothiazole **2a** was detected and accumulated at the same rate as the consumption of *N*-phenylbenzothioamide **1a**. Under the irradiation of blue LEDs, **1a** was converted completely only in one hour.

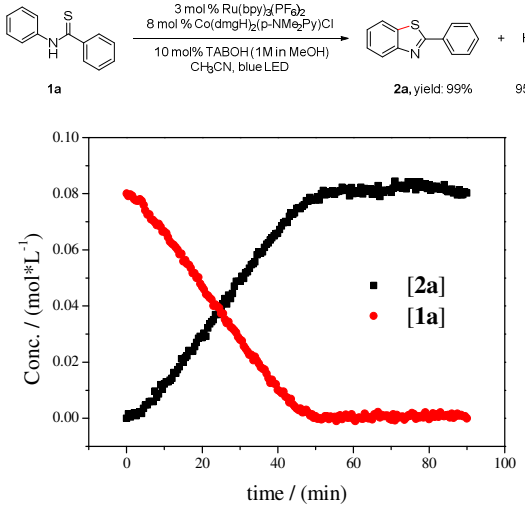


Figure 3. The kinetic profile of the reaction by *in-situ* IR.

Kinetic Studies by *in-situ* IR. Using *in-situ* IR, some kinetic studies were performed to determine the order of reaction components in this external oxidant-free coupling reaction. In the presence of 10 mol % TBAOH as the catalytic base, initial rates were monitored upon changing the concentration of substrate (**1a**), photosensitizer and cobalt catalyst, respectively (Figure 4). The initial reaction rate was almost invariant when using different concentrations of the substrate (**1a**) or photosensitizer (Figure 4, A and B). These results revealed that the reaction rate was independent on the concentration of substrate and photosensitizer, and consumption of substrate or photoredox catalytic cycle might not be involved in the rate-limiting step. Then, further kinetic investigation for the relationship between reaction rate and the concentration of $Co(dmgH)_2(4\text{-}NMe_2py)Cl$ was conducted (Figure 4, C). It was found that the initial reaction rate changed using different concentration of cobalt catalyst. Shown in the Figure 4 (D), the double-log-plot of reaction rate against the concentration of cobalt catalyst exhibited approximately a linear relationship, and the slope is about 1.076, which suggested a first-order dependence on catalyst concentration in this range of concentration of Co catalyst. All of above mentioned results suggested that the interaction between the proton-reducing catalyst and dissociated proton might be a slow step throughout the reaction, but consumption of substrate and photoredox catalytic cycle might be relative fast steps.

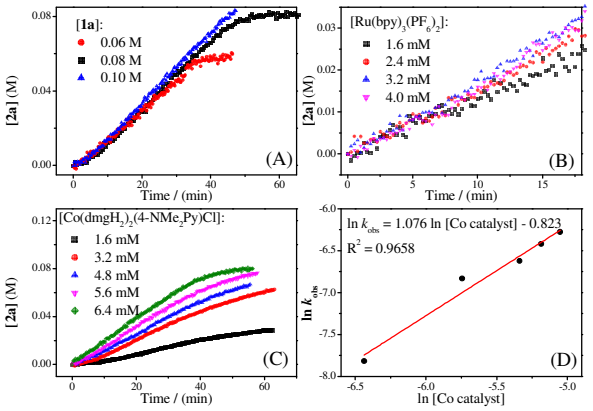
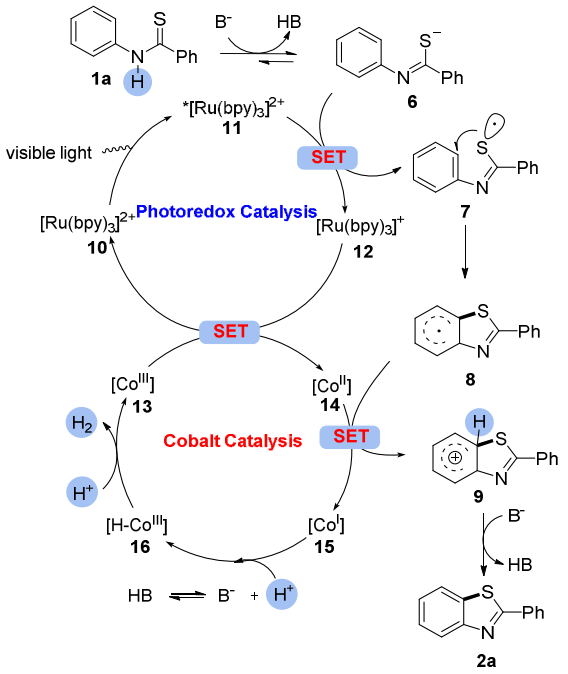


Figure 4. Kinetic studies of the external oxidant-free oxidative coupling for aromatic C–H thiolation

Base on the above experimental mechanistic data and the mechanistic insights of the previous cases, a plausible pathway for this oxidant-free aromatic C–H thiolation process is proposed. Specifically, both electron transfer and proton transfer were postulated through the synergistic combination of photoredox catalysis and cobalt catalysis. The specific mechanistic details are outlined in Scheme 10.



Scheme 10. Proposed Mechanism.

Initially, $Ru(bpy)_3^{2+}$ (**10**) is excited by visible light to provide a long-lived excited state(1100 ns),[14] $*Ru(bpy)_3^{2+}$ (**11**), which can be readily reduced or oxidized by substrate quenchers. While $*Ru(bpy)_3^{2+}$ is a strong oxidant ($E_{1/2\ red}$ [$*Ru(bpy)_3^{2+}$/ $Ru(bpy)^{3+}$] = +0.77 V vs SCE),[15] its capacity for single electron transfer (SET) with *N*-phenylbenzothioamide **1a** would be unfavourable (cyclic voltammetry experiments were carried out, see Supporting Information). However, an anion intermediate resulting from the acid-base equilibrium emerged with a dramatically decreased oxidation peak potential under alkaline conditions. Therefore the single electron transfer (SET) from an anion intermediate of thioamide **6** to excited state of photosensitizer would be feasible to produce $Ru(bpy)_3^{+}$ and a sulfur centeted radical **7**. Given that $Ru(bpy)_3^{+}$ has been shown to be a potent reductant ($E_{1/2\ red}$ [$Ru(bpy)_3^{+}$/ $Ru(bpy)_3^{2+}$] = -1.33 V vs SCE),[15d] single-electron transfer (SET) to the catalyst [Co^{III}] **13** would rapidly give [Co^{II}] **14** while itself being regenerated to $Ru(bpy)_3^{2+}$ to complete the photoredox cycle ($E_{1/2\ red}$ Co^{III}/Co^{II} = -0.83 V vs SCE)[16]. On the other hand, the addition of the sulfur radical **7** to the benzene ring produces the reactive aryl radical **8**. Thereafter, radical **8** release an electron to [Co^{II}] **14** ($E_{1/2\ red}$ Co^{II}/Co^{I} = -1.08 V vs SCE)[16] to generate a cation **9**, which would release a proton and rearomatize to provide benzothiazole (**2a**). And the [Co^{I}] species (**15**) can be protonated to form [Co^{III}–H] species (**16**) by the conjugate acid of base. Then this hydride could react with another proton to release H_2 and regenerate [Co^{III}] species (**13**).[17]

CONCLUSIONS

We have developed an external oxidant-free C–H functionalization/C–S bond formation reaction to form the benzothiazoles. Stoichiometric oxidation reagents can be avoided and dihydrogen is the only byproduct of the reaction. Notably, this reaction exhibits a wide range of functional-groups tolerance with high activity. The base might act as a vital role of proton mediator. Especially, 2-alkylbenzothioazoles could be afforded in good to excellent yields when catalytic TBAOH was used as the base. These catalytic systems can be scaled up in gram scale and applied in the pharmaceutical synthesis. Meanwhile, the combination of the oxidant-free coupling reaction and hydrogenation of nitrobenzenes could be achieved in one-pot. A detailed mechanistic survey, including deuterium experiments, KIE and *in-situ* IR ki-

netic studies had been presented, which indicated that H_2 is generated directly from the substrates and the interaction between the cobalt catalyst and proton is the rate-limiting process. The transformation holds significant potential for the applications to a series of organic reactions.

ASSOCIATED CONTENT

Supporting Information

The experimental procedure, characterization data, and copies of ^1H and ^{13}C NMR spectra. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interests.

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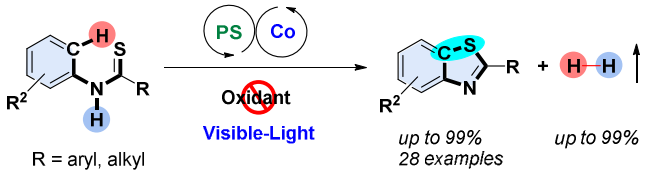
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Co
Oxidant
Visible-Light
R = aryl, alkyl
up to 99%
28 examples
up to 99%