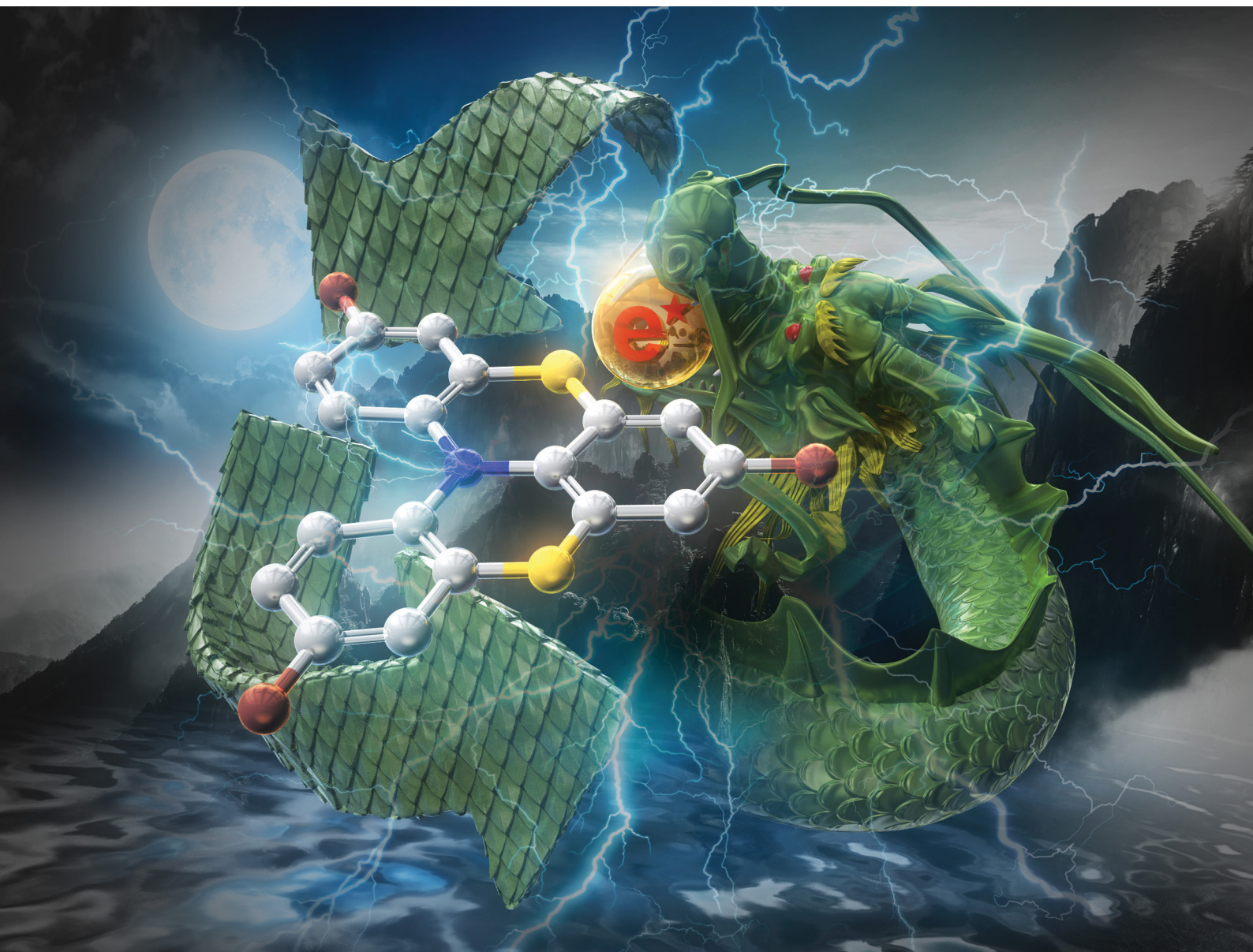


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Strongly reducing helical phenothiazines as recyclable
organophotoredox catalysts



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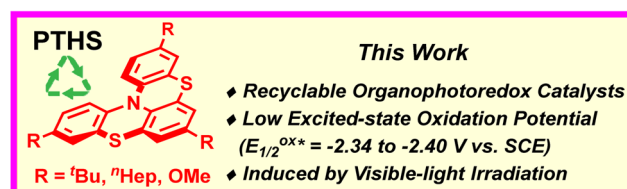
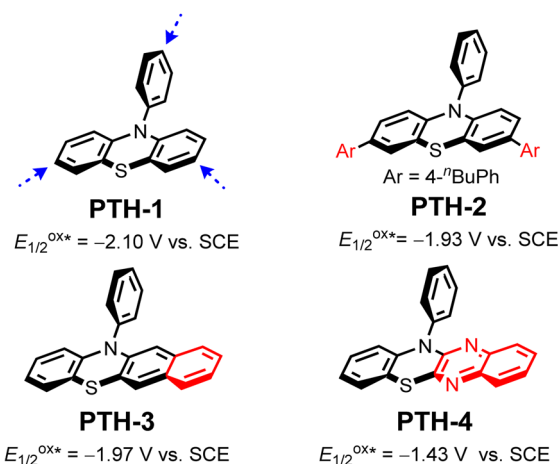
Recyclable phenothiazine organophotoredox catalysts (PTHS 1–3, $E_{1/2}^{ox*} = -2.34$ to -2.40 V vs. SCE) have been developed. When the recycling performance was evaluated, PTHS-1 could be recovered at least four times without loss of its catalytic activity. These recyclable organophotoredox catalysts represent a promising tool for sustainable organic synthesis.

Recycling photocatalysts has attracted much attention as a critical factor in emerging chemical technologies in terms of environmental concerns and economic benefits. While recycling heterogeneous photocatalysts such as semiconductors and polymers has been widely developed due to their easy separation and reusability, that of homogeneous photocatalysts such as metal-based polypyridyl complexes of ruthenium and iridium as well as organic dyes has received less attention.¹ Although there are some examples of recycling metal-based polypyridyl complexes,² recycling organophotocatalysts remains much less explored and is usually limited to the use of polymer methods.³ Recently, a nanofiltration process for the recovery of the 4CzIPN organophotocatalyst under continuous-flow conditions has been reported, albeit the recycling performance was not examined.⁴ Considering that organophotoredox catalysts are cost-effective and of low toxicity, the development of an approach for their recycling is highly desirable in the context of sustainable organic synthesis.

10-Aryl phenothiazines are widely used as photocatalysts for photoredox reactions and atom-transfer-radical-addition polymerizations in organic chemistry (Fig. 1; e.g., **PTH-1**).⁵ Due to their low excited-state oxidation potentials ($E_{1/2}^{ox*} \approx -2.10$ V vs. SCE), a number of 10-aryl-phenothiazine-catalyzed photoredox reactions

that proceed *via* oxidative quenching cycles have been developed.⁶ However, the high reactivity of the *p*-position relative to the nitrogen atom on 10-aryl phenothiazines renders these prone to reacting with electrophiles.⁷ Thus, several modified 10-aryl phenothiazine catalysts have recently been explored (Fig. 1; **PTH 2–4**).⁸ Despite these advances, the development of more stable and sustainable photoredox catalysts remains highly desirable.

To explore the recyclability of organophotoredox photocatalysts, we have designed and synthesized recyclable phenothiazine organophotoredox catalysts (Fig. 1; **PTHS**).⁹ The catalyst design is based on the following considerations: (i) in order to increase the stability of the catalyst and the reducing properties, bulky and electron-donating groups such as the ^tBu



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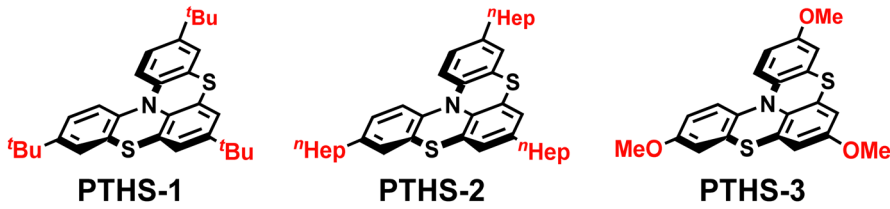
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† Electronic supplementary information (ESI) available. See DOI: <https://doi.org/10.1039/d4cc00904e>

Fig. 1 Representative phenothiazine catalysts.



Table 1 Synthesis and physical properties of the PTHS organophotoredox catalysts^a

					
Catalyst	$E_{1/2}(C^{*+}/C^{*})^a$ (V)	$E_{1/2}(C^{*+}/C)^b$ (V)	$E_{0,0}$ (eV)	Excitation λ_{max} (nm)	Emission λ_{max} (nm)
PTHS-1	−2.34	0.86	3.20	317	449
PTHS-2	−2.35	0.80	3.15	316	460
PTHS-3	−2.40	0.64	3.04	314	475

^a Excited-state oxidation potentials were estimated on the basis of the ground-state redox potentials and the intersection of the absorption and emission bands. ^b Determined by cyclic voltammetry in CH₂Cl₂ vs. SCE.¹

group are introduced at the *p*-position relative to the nitrogen atom on the phenothiazine catalysts;¹⁰ (ii) in order to absorb visible light and increase the stability of the radical intermediate, the phenothiazine catalysts are endowed with a thia-bridged helically shaped structure, which expands the π conjugation compared to 10-phenylphenothiazine (PTH-1).¹⁰

We initially synthesized a series of phenothiazine catalysts (PTHS 1–3) that were obtained in short steps and a moderate yield using commercially available starting materials to probe the relationship between their structure and physical properties (Table 1).^{11,12} Interestingly, we found that these catalysts have low excited-state oxidation potentials ($E_{1/2}^{ox*} = -2.34$ to -2.40 V vs. SCE) compared to other phenothiazine catalysts such as PTH 1–4. Therefore, PTHS 1–3 were expected to reduce various substrates *via* oxidative quenching cycles. In addition, the PTHS catalysts exhibit an absorption band in the visible spectrum, which indicates that they can be activated by visible light.

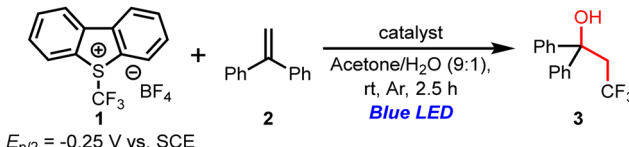
With these promising results in hand, we applied the PTHS catalysts to various types of photoredox reactions. First, we examined the three-component oxytrifluoromethylation of 1,1-diphenylethylene (2; Table 2).¹³ The reactions proceeded smoothly in the presence of a catalytic amount of PTHS 1–3 (1.0 mol%) to give the desired product (3) in a good yield. In

addition, a variety of alkenes can be applied to the reaction.¹¹ Blank experiments in the absence of a catalyst or light confirmed that the reaction requires a PTHS catalyst and irradiation with blue LEDs to proceed.¹¹ Since the PTHS catalysts have low excited-state oxidation potentials, the CF₃ radical was smoothly generated from Umemoto's reagent (1; $E_{p/2} = -0.25$ V vs. SCE)¹⁴ and then reacted with 2 to give the desired product (3). This organophotocatalytic reaction is significantly more cost-effective and sustainable than previously reported methods based on transition-metal catalysts.¹³

Next, we investigated a visible-light-mediated decarboxylative C(sp³)–O bond formation (Table 3). Nagao and Ohmiya have reported that PTH-3 catalyzes the decarboxylative coupling between aliphatic alcohol 5 and redox-active esters such as 4 ($E_{p/2} = -1.08$ V vs. SCE).^{8b} It thus seems feasible to speculate that the PTHS catalysts might also be applied to the decarboxylative C(sp³)–O bond formation from ester 4 to provide the corresponding ether (6) in a moderate yield.

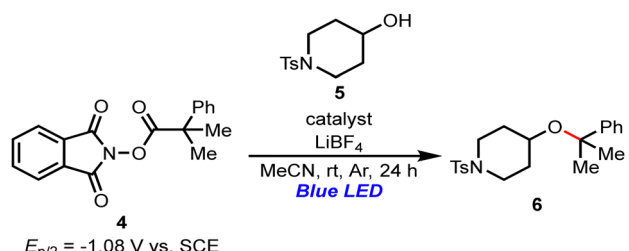
The results of the defluoroalkylation of 1,3-bis(trifluoromethyl)benzene (7) with unactivated alkenes are shown in Table 4.¹⁵ When 7 ($E_{p/2} = -2.07$ V vs. SCE) was treated with

Table 2 Three-component oxytrifluoromethylation of 1,1-diphenylethylene^a

 <p>$E_{p/2} = -0.25$ V vs. SCE</p>		
Entry	Catalyst	Yield (%)
1	PTHS-1	79
2	PTHS-2	72
3	PTHS-3	80

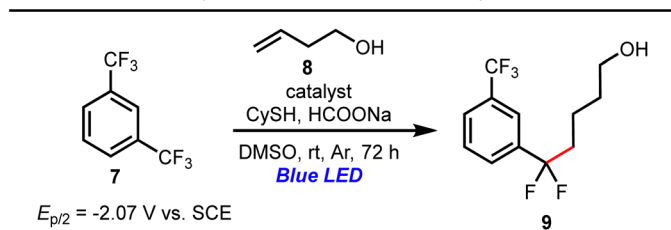
^a All reactions were carried out with 1 (0.105 mmol), 2 (0.1 mmol), and the catalyst (1.0 mol%) in acetone/H₂O (9:1, v/v) at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{max} = 425$ nm, 18 W).

Table 3 Decarboxylative C(sp³)–O bond formation^a

 <p>$E_{p/2} = -1.08$ V vs. SCE</p>		
Entry	Catalyst	Yield (%)
1	PTHS-1	60
2	PTHS-2	48
3	PTHS-3	40

^a All reactions were carried out with 4 (0.2 mmol), 5 (0.6 mmol), LiBF₄ (10 mol%), and the catalyst (10 mol%) in MeCN at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{max} = 425$ nm, 18 W).



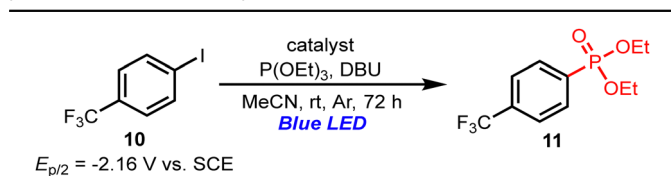
Table 4 Defluoroalkylation of 1,3-bis(trifluoromethyl)benzene^a

Entry	Catalyst	Yield (%)
1	PTHS-1	83
2	PTHS-2	47
3	PTHS-3	Trace
4	PTH-3	6

^a All reactions were carried out with **7** (0.1 mmol), **8** (0.3 mmol), cyclohexane thiol (10 mol%), sodium formate (0.3 mmol), and the catalyst (10 mol%) in DMSO at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{\max} = 425$ nm, 18 W).

3-buten-1-ol (**8**) in the presence of **PTHS-1** and **PTHS-2**, the reaction proceeded effectively to give **9** in a moderate to good yield (Table 4, entries 1 and 2). In contrast, **PTHS-3** furnished a trace amount of the product and unknown byproducts, and 1, 3-bis(trifluoromethyl)benzene was not recovered due to its low boiling point (Table 4, entry 3). **PTHS-3** has a low oxidation potential compared to **PTHS-1** and **2** (**PTHS-3**: $E_{1/2}(C^{\bullet+}/C) = 0.64$ V vs. SCE, **PTHS-1**: $E_{1/2}(C^{\bullet+}/C) = 0.86$ V vs. SCE, **PTHS-2**: $E_{1/2}(C^{\bullet+}/C) = 0.80$ V vs. SCE), suggesting that the oxidation of sodium formate would not proceed efficiently.¹⁵ Given that the excited-state oxidation potential of **PTH-3** is lower than the reduction potential of **7**, the reaction with **PTH-3** was also inefficient (Table 4, entry 4).

Subsequently, we investigated the photoredox cross-coupling reaction between 4-trifluoromethyliodobenzene (**10**) and triethylphosphite in the presence of the **PTHS** catalysts, which afforded aromatic phosphonate **11** in good yield (Table 5).¹⁶ Although **10** has a low reduction potential ($E_{p/2} = -2.16$ V vs. SCE),¹⁷ the single-electron transfer from the **PTHS** catalysts to **10** is energetically favorable due to the low excited-state oxidation potentials of the **PTHS** catalysts ($E_{1/2}^{ox*} = -2.34$ to -2.40 V vs. SCE). Moreover,

Table 5 Photoredox cross-coupling reaction of 4-trifluoromethyliodobenzene with triethylphosphite^a

Entry	Catalyst	Yield (%)
1	PTHS-1	77
2	PTHS-2	78
3	PTHS-3	78

^a All reactions were carried out with **10** (0.1 mmol), triethylphosphite (0.3 mmol), DBU (0.2 mmol), and the catalyst (10 mol%) in MeCN at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{\max} = 425$ nm, 18 W).

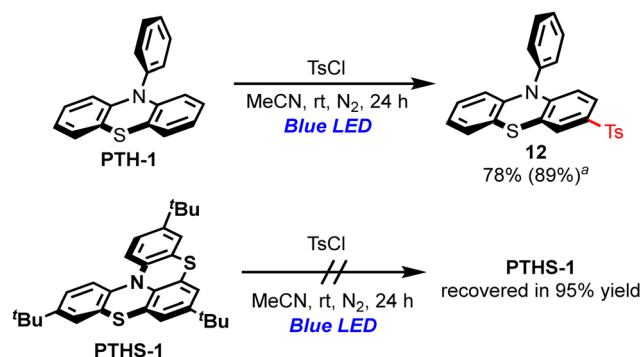
various aryl iodides can be suitable for the reactions to give the corresponding products in high yields.¹¹ Accordingly, the **PTHS** catalysts are suitable for photoredox reactions *via* oxidation-quenching cycles.

To examine the stability of the catalysts, we carried out the photochemical sulfonylation of **PTH-1** and **PTHS-1** (Scheme 1). When **PTH-1** was treated with tosyl chloride (TsCl) under irradiation with blue LEDs, monosulfonylated **12** was obtained in 78% yield due to the high reactivity of the *p*-position relative to the nitrogen atom in 10-aryl phenothiazines.^{8a} In contrast, **PTHS-1** was effectively recovered in 95% yield, proving that the presence of *t*Bu groups increases the catalyst stability. Therefore, **PTHS-1** is applicable to various photoredox reactions, which cannot be effectively achieved by hitherto reported phenothiazine catalysts.

The high stability of **PTHS-1** also prompted us to investigate its recycling performance (Table 6). After completion of the cross-coupling reaction of **10** with triethylphosphite, **PTHS-1** was collected *via* extraction with EtOAc and column chromatography, and the ability of recycled **PTHS-1** to catalyze the reaction was examined. **PTHS-1** could be effectively recovered at least four times without loss of its catalytic activity. In contrast, **PTH-1** suffered from an obvious loss of catalytic activity. Thus, **PTHS-1** is demonstrably a recyclable organophotocatalyst and suitable for sustainable synthetic methods.

Finally, when the reaction was performed on a gram scale, the desired product was obtained in 85% yield (1.20 g) with 96% recovery of **PTHS-1** (Scheme 2). Thus, **PTHS-1** is a highly active catalyst with high recoverability even when used on a gram scale.

In summary, we have developed strongly reducing and recyclable phenothiazine organophotoredox catalysts (**PTHS 1-3**) that can be activated by visible light. These catalysts exhibit relatively low excited-state oxidation potentials ($E_{1/2}^{ox*} = -2.34$ to -2.40 V vs. SCE). The **PTHS-1** can be recovered at least four times without loss of its catalytic activity in the cross-coupling reaction of 4-trifluoromethyliodobenzene ($E_{p/2} = -2.16$ V vs. SCE), highlighting its potential for



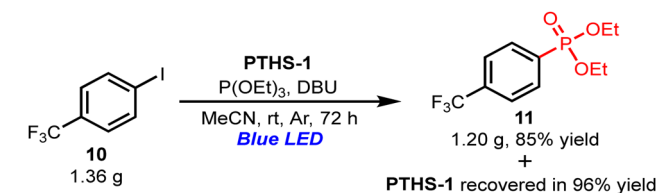
Scheme 1 Photochemical sulfonylation of phenothiazines. All reactions were carried out with phenothiazines (0.2 mmol) and tosyl chloride (TsCl; 0.2 mmol) in MeCN at room temperature for 24 h under an N₂ atmosphere and blue LED irradiation ($\lambda_{\max} = 425$ nm, 18 W). ^aPreviously reported product yield.^{7a}



Table 6 Recycling performance of phenothiazine catalysts^a

Run	1	2	3	4
PTHS-1 yield (%)	77	78	75	79
PTH-1 yield (%)	54	32	23	9

^a All reactions were carried out with **10** (0.1 mmol), triethylphosphite (0.3 mmol), DBU (0.2 mmol), and the catalyst (10 mol%) in MeCN at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{\text{max}} = 425 \text{ nm}$, 18 W).



Scheme 2 Gram-scale photoredox cross-coupling reaction of 4-iodo-1-(trifluoromethyl)benzene with triethylphosphite. The reaction was carried out with **10** (5.0 mmol), triethylphosphite (15.0 mmol), DBU (10.0 mmol), and **PTHS-1** (10 mol%) in MeCN at room temperature under an Ar atmosphere and blue LED irradiation ($\lambda_{\text{max}} = 425 \text{ nm}$, 18 W).

sustainable photocatalysis. These recyclable organophotoredox catalysts thus represent a promising tool for sustainable organic synthesis.

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Conflicts of interest

There are no conflicts to declare.

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