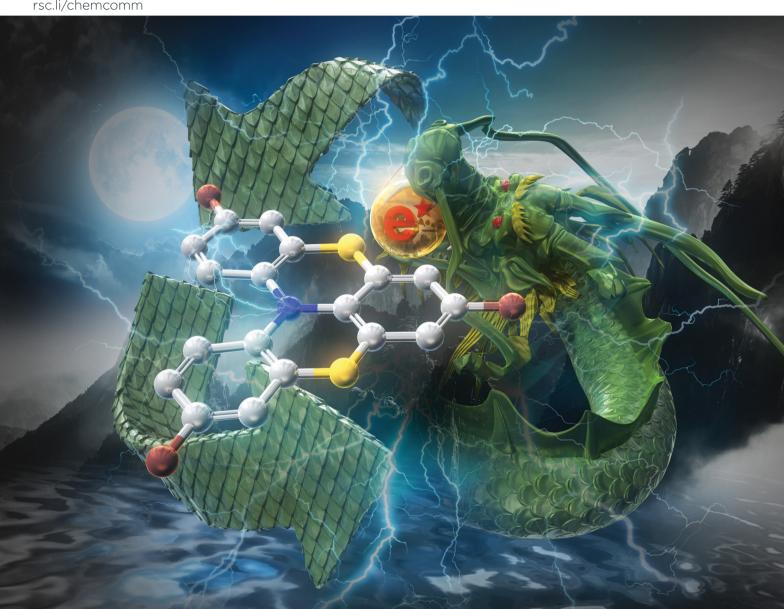
Volume 60 Number 36 4 May 2024 Pages 4735-4862

ChemComm

Chemical Communications

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ISSN 1359-7345



COMMUNICATION

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ChemComm



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View Article Online



Cite this: Chem. Commun., 2024, 60, 4765

Received 26th February 2024, Accepted 15th March 2024

DOI: 10.1039/d4cc00904e

rsc.li/chemcomm

Strongly reducing helical phenothiazines as recyclable organophotoredox catalysts†

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Recyclable phenothiazine organophotoredox catalysts (PTHS 1-3, $E_{1/2}^{\text{ox}*}$ = -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 recvcling 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 costeffective 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). Due to their low excited-state oxidation potentials ($E_{1/2}^{\text{ox}*} \approx -2.10 \text{ V } \nu \text{s. SCE}$), 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). 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

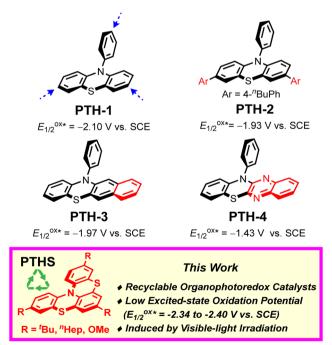


Fig. 1 Representative phenothiazine catalysts

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

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

Catalyst	$E_{1/2}(C^{\bullet^+}/C^*)^a(V)$	$E_{1/2}(C^{\bullet+}/C)^b(V)$	$E_{0,0}$ (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 $CH_2Cl_2 \nu s$. 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 ($E_{1/2}^{\text{ox}*} = -2.34 \text{ to } -2.40 \text{ V}$ 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

 $\begin{tabular}{lll} \textbf{Table 2} & Three-component oxytrifluoromethylation of 1,1-diphenylethylene$^a \end{tabular}$

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/ H_2O (9:1, v/v) at room temperature under an Ar atmosphere and blue LED irradiation (λ_{max} = 425 nm, 18 W).

addition, a variety of alkenes can be applied to the reaction. 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. Since the **PTHS** catalysts have low excited-state oxidation potentials, the CF₃ radical was smoothly generated from Umemoto's reagent (1; $E_{\rm p/2} = -0.25~{\rm V}~vs.~{\rm SCE})^{14}$ 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. Since the PTHS catalysts and irradiation was smoothly generated from Umemoto's reagent (1; $E_{\rm p/2} = -0.25~{\rm V}~vs.~{\rm SCE})^{14}$ 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.

Next, we investigated a visible-light-mediated decarboxylative $C(sp^3)$ -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 $(E_{p/2} = -1.08 \text{ V vs. SCE})$. It thus seems feasible to speculate that the **PTHS** catalysts might also be applied to the decarboxylative $C(sp^3)$ -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 ($E_{\rm D/2}=-2.07~{\rm V}$ vs. SCE) was treated with

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

TsN
$$\frac{O}{S}$$
 OH

TsN $\frac{O}{S}$ OH

Catalyst

LiBF₄

MeCN, rt, Ar, 24 h

Blue LED

 $\frac{A}{E_{D/2}} = -1.08 \text{ V vs. SCE}$

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 ($\lambda_{\rm max}$ = 425 nm, 18 W).

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

Entry	Catalyst	Yield (%)
1	PTHS-1	83
2	PTHS-2	47
3	PTHS-3	Trace
4	РТН-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 ($\lambda_{\text{max}} = 425 \text{ nm}$, 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**: $E_{1/2}(C^{\bullet +}/C) = 0.80 \text{ V } \nu s. \text{ SCE}$, 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 ($E_{\rm p/2} = -2.16 \,\rm V$ vs. SCE), ¹⁷ the singleelectron transfer from the PTHS catalysts to 10 is energetically favorable due to the low excited-state oxidation potentials of the **PTHS** catalysts ($E_{1/2}^{\text{ox}*} = -2.34 \text{ to } -2.40 \text{ V}$ vs. SCE). Moreover,

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

catalyst
$$P(OEt)_3, DBU$$

$$MeCN, rt, Ar, 72 h$$

$$Blue LED$$

$$E_{p/2} = -2.16 \text{ V vs. SCE}$$

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

^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 $(\lambda_{\text{max}} = 425 \text{ nm}, 18 \text{ W}).$

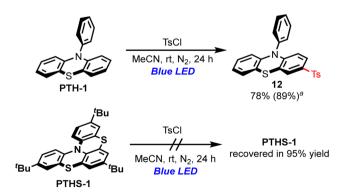
various aryl iodides can be suitable for the reactions to give the corresponding products in high yields. 11 Accordingly, the PTHS catalysts are suitable for photoredox reactions via oxidationquenching cycles.

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, monosulfonvlated 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 ^tBu 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 $(E_{1/2}^{\text{ox}*} = -2.34 \text{ to } -2.40 \text{ V } \text{vs. SCE})$. The **PTHS-1** can be recovered at least four times without loss of its catalytic activity in the cross-coupling reaction of 4-trifluoromethyliodobenzene ($E_{\rm p/2}$ = -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 N_2 atmosphere and blue LED irradiation (λ_{max} = 425 nm, 18 W). ^a Previously reported product yield.7a

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Table 6 Recycling performance of phenothiazine catalysts^a

^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 $(\lambda_{\text{max}} = 425 \text{ nm}, 18 \text{ W}).$

Scheme 2 Gram-scale photoredox cross-coupling reaction of 4-trifluoromethylbenzene 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 (λ_{max} = 425 nm, 18 W).

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

This work was supported by JKA and its promotion funds from KEIRIN RACE, Murata Science Foundation, and Wesco Scientific Promotion Foundation. We appreciate the assistance of the Division of Instrumental Analysis at Okayama University with NMR spectroscopy and high-resolution mass spectrometry.

Conflicts of interest

There are no conflicts to declare.

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