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Emodin as a novel organic photocatalyst for selective oxidation of sulfides under mild conditions†

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Herein, we have developed naturally-occurring **Emodin**, which is commercially available at low-cost, as a novel organic photocatalyst for the first time. **Emodin** was successfully employed in the selective oxidation of sulfides promoted by visible-light, delivering valuable sulfoxides with high efficiency. Mechanistic investigations suggested both single-electron transfer (SET) and energy transfer (EnT) pathways might be involved in the oxidation reaction.

Visible-light-promoted reactions have attracted great interest from chemists over the past decade for the usage of sunlight as the renewable energy source.[1] As a logical consequence, the development of novel photocatalysts plays an essential role in the field of photocatalysis.[2] Among them, organo-photocatalysts, such as Rose bengal,[3] Eosin Y,[4] 9,10-dicyanoanthracene (DCA),[5] *etc*, were more appealing due to the avoidance of toxic, expensive and environmentally unfriendly metals (Fig. 1).[6] However, the investigations of organic photocatalysts were restricted in a limited number of well-developed skeletons. Thus, it is worth further developing more varieties of organo-photocatalysts with versatile frameworks.

Meanwhile, nature generously provided plentiful natural products as high-efficient catalysts.[7] Recently, we have successfully exploited cercosporin[8] from plant pathogenic fungi *Cercospora* species as a novel photocatalyst in oxidation,[9] cycloaddition[10] and cross-coupling[11] reactions. Take it into consideration that **Emodin**[12] has the similar quinone skeleton with hydroxy groups and photostablity (see ESI†) as cercosporin, we rationalize naturally-occurring **Emodin** might have potential photophysical properties[13] as a novel photoredox catalyst, which has yet not been reported to the best of our knowledge (Scheme 1a).

On the other hand, selective oxidation is a kind of fundamental reactions along with significant challenges because of the over-oxidation and the hazardous oxidizing agents employed in the reactions.[14] With the growing environmental concerns, photocatalytic selective oxidation has been considered as an alternative method utilizing oxygen as green terminal oxidant and visible-light as renewable energy source.[15] Based on our continuous interest in developing novel photocatalysts from natural products and their applications in photoredox-catalyzed reactions, herein, we will report the first example of **Emodin**-catalyzed selective oxidation of sulfides with the promotion of visible-light (Scheme 1b).

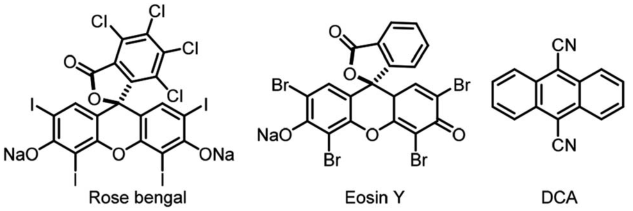
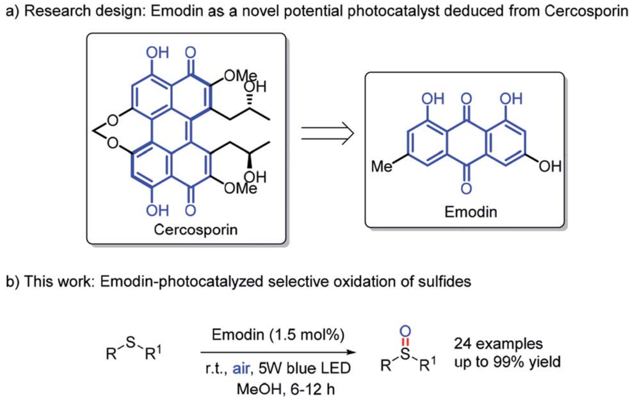


Fig. 1 Selected examples for organic photocatalysts.


a) Research design: Emodin as a novel potential photocatalyst deduced from Cercosporin

b) This work: Emodin-photocatalyzed selective oxidation of sulfides

Scheme 1 **Emodin**-catalyzed selective oxidation of sulfides.

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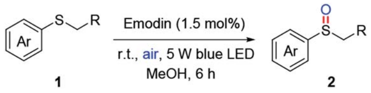
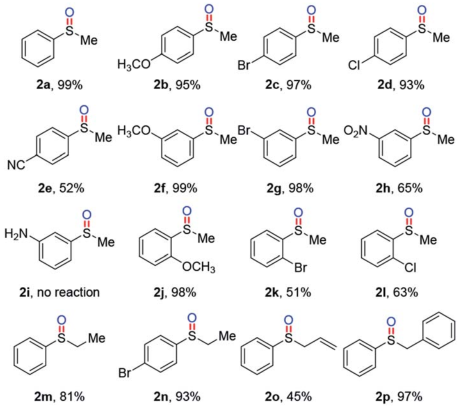
Table 1 Effect of reaction parameters[a]

Entry	Variation from the *standard conditions*	Yield[b] (%)
1	None	99
2	EtOH instead of MeOH	82
3	DMSO instead of MeOH	25
4	DMF instead of MeOH	41
5	Dioxane instead of MeOH	53
6	THF instead of MeOH	19
7	Toluene instead of MeOH	24
8	**Emodin** (2%) instead of **Emodin** (1.5%)	99
9	**Emodin** (1%) instead of **Emodin** (1.5%)	90
10	**Emodin** (0.5%) instead of **Emodin** (1.5%)	76
11	5 W CFL instead of 5 W blue LED	71
12	5 W green LED instead of 5 W blue LED	29
13	30 W blue LED instead of 5 W blue LED	58
14	Eosin Y instead of **Emodin**	93
15	Methylene blue instead of **Emodin**	51
16	Methyl orange instead of **Emodin**	None
17	Rhodamine B instead of **Emodin**	None

[a] Conducted with **1a** (0.25 mmol), **Emodin** (1.5 mol%) in methanol (2 mL) at room temperature under air atmosphere for 6 h. [b] Isolated yield.

Table 2 Substrate scope of aryl alkyl sulfides[a,b]

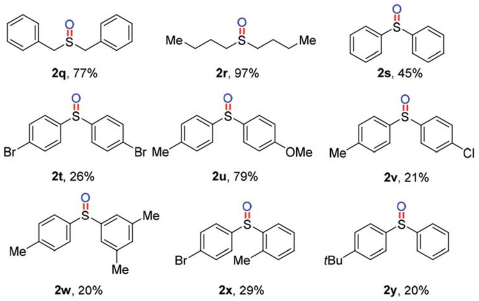




2a, 99%; **2b**, 95%; **2c**, 97%; **2d**, 93%; **2e**, 52%; **2f**, 99%; **2g**, 98%; **2h**, 65%; **2i**, no reaction; **2j**, 98%; **2k**, 51%; **2l**, 63%; **2m**, 81%; **2n**, 93%; **2o**, 45%; **2p**, 97%

[a] Conducted with **1** (0.25 mmol), **Emodin** (1.5 mol%) in methanol (2 mL) at room temperature under air atmosphere for 6–12 h. [b] Isolated yield.

Table 3 Substrate scope of other sulfides[a,b]



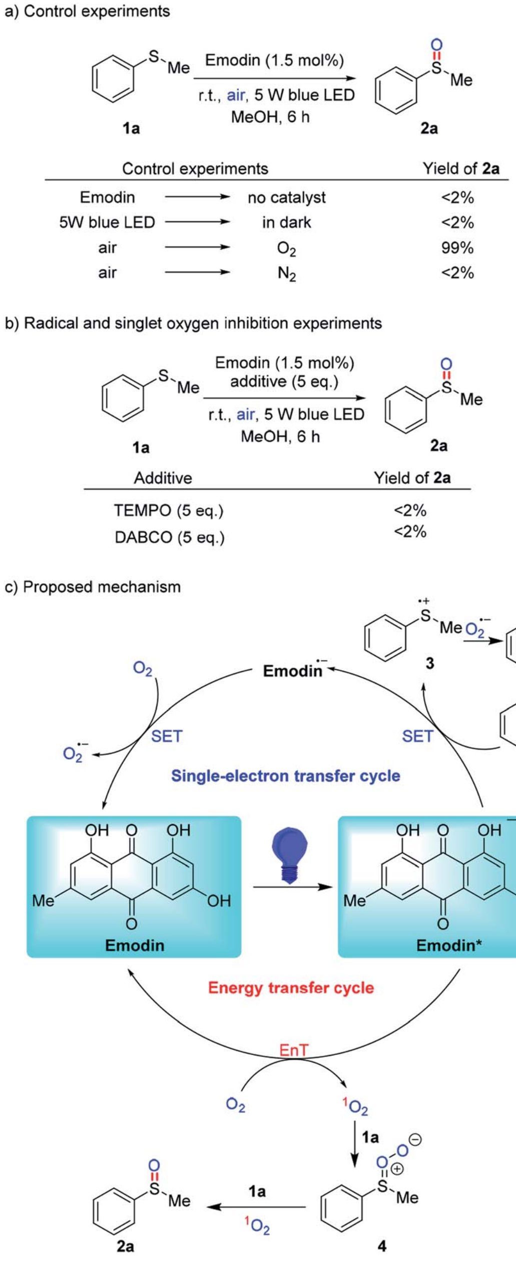
2q, 77%; **2r**, 97%; **2s**, 45%; **2t**, 26%; **2u**, 79%; **2v**, 21%; **2w**, 20%; **2x**, 29%; **2y**, 20%

[a] Conducted with **1** (0.25 mmol), **Emodin** (1.5 mol%) in methanol (2 mL) at room temperature under air atmosphere for 6–12 h. [b] Isolated yield.

After systematic reaction condition evaluations, the selective oxidation of thioanisole was successfully achieved in 99% yield with **Emodin** (1.5 mol%) as the photocatalyst in methanol at room temperature under air atmosphere (Table 1, entry 1). Solvents screening revealed that protonic solvents (MeOH and EtOH) showed better results than others like DMF, DMSO, dioxane, THF and toluene (Table 1, entries 2–7). Increasing the amount of **Emodin** had little influence on the reaction, while decreasing the amount to 1 and 0.5 mol% would decelerate the reaction (Table 1, entries 8–10). Additionally, in this selective oxidation process, 5 W blue LED was proved better light source than corresponding CFL and green LED (Table 1, entries 11–12), which shows that when the maximum absorption wavelength of the photocatalyst is consistent with the emission spectrum of the light source (see ESI†), the catalytic efficiency is the highest. Unexpectedly, a reduced result was obtained using 30 W blue LED, which probably resulted from the side-reactions induced by high energy of the light source (Table 1, entry 13). Other organic photocatatlysts were also tested, Eosin Y has the similar photocatalytic efficiency compared to **Emodin** (Table 1, entry 14), while the photocatalytic activities of other organic catalysts (methylene blue, methyl orange and Rhodamine B) were obviously lower than that of **Emodin** (Table 1, entries 15–17).

With the optimal reaction conditions, we next investigated the substrate scope of aryl alkyl sulfides, and the results were summarized in Table 2. Electron-donating group (–OMe) and halogen groups (–Br, –Cl) at the *para*-position of the benzene ring led to the oxidation products **2b–2d** in 93–99% yields; electron-withdrawing group (–CN) led to **2e** in moderate yield. Products **2f–2h** with *meta*-substitutions were produced in 65–99% yields. Unfortunately, substrate with unprotected amino group (**1i**) was an unsuccessful example in the reaction. When methoxy group was substituted at the *ortho*-position of the benzene ring, **2j** could be delivered in 98% yield; while **2k** and **2l** with bromine and chlorine atoms at the *ortho*-position showed poor efficiency probably due to the steric hindrance. Moreover, this oxidative reaction was tolerant of ethyl (**2m**, **2n**), allyl (**2o**) and benzyl (**2p**) sulfides.

Subsequently, other sulfides with two alkyl groups or two aryl groups were tested (Table 3). Benzyl sulfoxide **2q** and *n*-butyl



Control experiments			Yield of **2a**
Emodin	→	no catalyst	<2%
5W blue LED	→	in dark	<2%
air	→	O_2	99%
air	→	N_2	<2%

Additive	Yield of **2a**
TEMPO (5 eq.)	<2%
DABCO (5 eq.)	<2%

Scheme 2 Mechanistic insights.

sulfoxide **2r** were achieved in good to excellent yields (77–97%). What is more, symmetric (**1s**, **1t**) and unsymmetrical (**1u**–**1y**) diphenyl sulfides were also compatible in the oxidation reactions, producing corresponding diphenyl sulfoxides **2s**–**2y** in 20–79% yields.

Next, several control experiments were carried out to gain more insight into the mechanism of this novel **Emodin**-catalyzed oxidation reaction of sulfides. The reaction was completely inhibited without the catalyst or the light source; and the reaction was not affected when air was changed to oxygen, but failed if air was replaced by nitrogen, which revealing the roles of these factors (Scheme 2a). Furthermore, the radical and singlet oxygen inhibition experiments suggested that both $O_2^{\bullet -}$ and $^1O_2$ are responsible for the **Emodin**-catalyzed oxidation reaction of sulfides (Scheme 2b). According to the above-mentioned results and previous literature, we have proposed the reaction mechanism in Scheme 2c. First, the photocatalyst **Emodin** was excited with light irradiation to generate the excited species **Emodin***. In the SET cycle, reductive quenching occurred to produce sulfide radical cation **3** along with the radical anion **Emodin**$^{\bullet -}$. Subsequently, **Emodin**$^{\bullet -}$ was oxidized by oxygen to regenerate **Emodin** into the next catalytic cycle and achieve the reactive radical anion $O_2^{\bullet -}$, which further reacted with radical cation **3** to deliver methyl phenyl sulfoxide **2a**. While in the EnT cycle, singlet oxygen $^1O_2$ was produced to oxidize **1a** to the product **2a** *via* the intermediate **4**, and photocatalyst **Emodin** was regenerated simultaneously.

Conclusions

The natural product **Emodin** has been developed as a novel organic photocatalyst for the first time. **Emodin**-photocatalyzed selective oxidation reaction of sulfides with the promotion of visible-light proceeded in high efficiency and exhibited good functional group tolerance. Two possible mechanism including SET and Ent cycles were proposed according to the mechanistic investigations. Further investigations on **Emodin**-catalyzed photoredox reactions are currently underway in our laboratory.

Conflicts of interest

There are no conflicts to declare.

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