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Synthesis of an anthraquinone-containing polymeric photosensitizer and its application in aerobic photooxidation of thioethers†

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Work on the synthesis of a polymeric photosensitizer and its application in the photooxidation of thioethers is reported herein. Firstly, the polymeric photosensitizer was designed and synthesized by the reaction of anthraquinone-2-carbonyl chloride (**AQ-2-COCl**) with poly(2-hydroxyethyl methacrylate) (**PHEMA**). Then, the visible light-induced photooxidation of thioethers under aerobic conditions was investigated. The results revealed that the reaction yielded sulfoxides highly chemoselectively in excellent yields with good substrate tolerance. Importantly, **AQ-PHEMA** could be easily recovered and reused more than 20 times without significant loss of the catalytic activity.
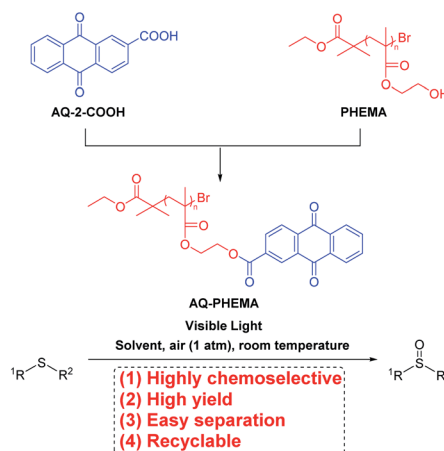
Introduction

Sulfoxides can be used as drugs[1] and preservatives[2] in daily life. They can also serve as important fragments in organic synthesis[3–5] and bioactive molecules.[6] Oxidation of thioethers into sulfoxides is the most direct method for the preparation of sulfoxides.[7–9] Some other methods for synthesizing sulfoxides were developed in the past few decades, such as organic catalytic oxidation,[10] hydrogen peroxide oxidation,[11,12] metal complex-catalyzed oxidation,[13,14] photooxidation,[15,16] *etc.* However, these methods normally require stoichiometric oxidants, which produce a large amount of environmentally harmful waste. At the same time, another issue of the above methods is controlling the selectivity for sulfoxide and over-oxidation to the sulfone by-product.[17] Although some catalytic systems exhibited high chemoselectivity with small molecular catalysts, from a practical application point of view, some of these catalysts could not be easily recovered after one catalytic cycle, or the catalyst was too expensive.[10,18] Considering the concept of "green chemistry", an environmentally friendly, highly catalytically efficient and highly selective oxidation of thioethers into sulfoxides is still urgently needed.

Visible light[19–32] is an economically green energy. Visible light-induced photocatalysis is a hot research topic[33–43] in organic synthesis. For example, Guo's group reported the

cyclopropanation of dibromomalonate derivatives and alkenes. This is the first report on the generation of carbanions under visible light photoredox catalysis.[44] Guo's group also reported the first activation of alkynes using a Lewis acid catalyst together with eosin Y as a small molecular photocatalyst.[45] Although small molecule photosensitizers[46–48] exhibit good catalytic properties in some reactions, their disadvantages, such as difficulty of separation and reuse as well as high cost, remain unsolved. Therefore, for the purpose of recycling the catalyst, polymeric photosensitizers which were designed and synthesized by linking photosensitive groups onto polymeric chains have drawn much attention from researchers.[49–55] Compared with small molecule photosensitizers, polymeric photosensitizers can be easily recycled, which not only reduces the cost, but also simplifies the process. Thus, they have been widely used in the fields of medicine, biology and hydrogels.[56–58]

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Scheme 1 The synthetic procedure of **AQ-PHEMA** and its application in the photooxidation of thioethers.
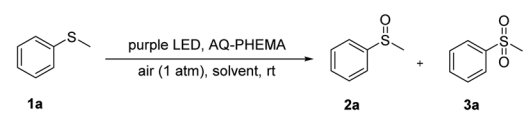
But the catalysts could not be easily recovered and reused. Thus, we wondered whether a small molecule photosensitizer could be attached to a polymer, forming a novel polymeric photocatalytic material. This catalytic material could be recycled and reused after catalyzing the photoreaction. With our continuing interest in the synthesis and application of **PHEMA**,[36] **AQ-2-COOH**[59–61] and **PHEMA**[36] were used to synthesize the designed polymeric photosensitizer **AQ-PHEMA** (Scheme 1) by immobilizing anthraquinone (AQ) onto **PHEMA**. In the next step, **AQ-PHEMA** (for synthesis and characterization of **AQ-PHEMA**, see ESI†) was tested as a photocatalyst in the visible light-induced photooxidation of thioethers under aerobic conditions. Finally, recycling experiments were carefully conducted.

Results and discussion

Optimization and scope investigation

In the beginning, methyl phenyl thioether (**1a**) was chosen as the model substrate for the investigation of **AQ-PHEMA**-catalyzed photooxidation. The initial attempt was carried out in cyclohexane under air atmosphere at room temperature. After 72 hours, the desired product methyl phenyl sulfoxide (**2a**) was formed in 21% NMR yield, with 29% of **1a** remaining unreacted and 2% of the over-oxidized by-product methyl phenyl sulfone (**3a**) being observed (entry 1, Table 1). Encouraged by this result, a survey of solvents was carried out (entries 2–10, Table 1). When toluene or THF was tested, the NMR yield of **2a** increased. But **3a** was also produced in a higher yield (entries 2 and 3, Table 1). Then, ethyl acetate, dichloromethane, acetone, and ether were tested. Although a small amount of **3a** was formed, the NMR yield of **2a** was remarkably increased (entries 4–7, Table 1). When CH_3CN or CH_3NO_2 was chosen as the solvent, **2a** was formed in an excellent yield with less than 5% **3a** generated (entries 8 and 9, Table 1). Fortunately, the reaction in CH_3OH gave a 99% NMR yield of **2a** with only 1% **3a** detected (entry 10, Table 1). Thus, CH_3OH was chosen as the optimal solvent for this reaction. Notably, **AQ-PHEMA** is insoluble in all the above tested solvents and can only be dispersed in the solvent, so it can be easily recovered by a simple filtration. Subsequently, modifications of the catalytic amount of **AQ-PHEMA** were conducted (entries 10–13, Table 1). The results showed that the catalytic amount of **AQ-PHEMA** could be reduced to 1 mol% (entry 12, Table 1). Next, control experiments were carried out and the results demonstrated that both the catalyst and light were necessary for this transformation (entries 14 and 15, Table 1). Furthermore, taking into account the thermal effect of the purple LED light, the reaction was carried out at 50 °C without light. The results confirmed that no reaction occurred at all (entry 16, Table 1). Next, the oxidation using AQ as catalyst was investigated. The reaction was completed in 9 hours with high chemoselectivity and excellent yield (entry 17, Table 1). However, AQ was difficult to recover due to its solubility in CH_3OH. Finally, to test whether the bromine atom derived from the initiator in the synthesis of **PHEMA** has some effect on the reaction, the oxidation using **PHEMA** as catalyst was investigated. No reaction took place (entry 18, Table 1). The above two

Table 1 Optimization of the reaction conditions[a]

Entry	Solvent	Catalyst (mol%)	Time (h)	1a	2a	3a
				NMR yield[b] (%)		
1	Cyclohexane	5	72	29	21	2
2	Toluene	5	57	0	30	16
3	THF	5	48	0	39	54
4	Ethyl acetate	5	49	0	50	19
5	DCM	5	72	0	51	3
6	Acetone	5	39	0	66	7
7	Et$_2$O	5	72	0	74	1
8	CH$_3$CN	5	36	0	95	5
9	CH$_3$NO$_2$	5	28	0	97	3
10	CH$_3$OH	5	16	0	99	1
11	CH$_3$OH	3	18	0	99	1
12	CH$_3$OH	1	24	0	99 (96)[c]	1
13	CH$_3$OH	0.5	24	48	44	6
14	CH$_3$OH	—	24	99	0	0
15[d]	CH$_3$OH	1	24	99	0	0
16[d,e]	CH$_3$OH	1	24	99	0	0
17[f]	CH$_3$OH	1	9	0	99	1
18[g]	CH$_3$OH	—	16	99	0	0

[a] The reaction was carried out using **1a** (1 mmol) and **AQ-PHEMA** in solvents (5 mL) irradiated by a purple LED under air atmosphere at rt. (Based on AQ anchored on **PHEMA**, the mass of 5 mol% **AQ-PHEMA** is 17 mg; the mass of 3 mol% **AQ-PHEMA** is 10 mg; the mass of 1 mol% **AQ-PHEMA** is 3 mg; and the mass of 0.5 mol% **AQ-PHEMA** is 2 mg.) [b] Yield determined by ^1H NMR analysis of the crude reaction mixture using CH_2Br_2 (1 mmol) as internal standard. [c] Isolated yield of **2a**. [d] The reaction was carried out without light. [e] The reaction was carried out at 50 °C. [f] The reaction was carried out using 1 mol% AQ as catalyst. [g] The reaction was carried out in the presence of 4 mg of **PHEMA**.

results clearly demonstrated that the bromine atom did not play an important role in this photocatalytic reaction and AQ was the key catalyst in this transformation. Thus, Condition A (1 mol% of **AQ-PHEMA**, CH_3OH, purple LED, air (1 atm), and room temperature) was considered as the optimized conditions for further studies.

With the optimized reaction conditions in hand, the scope of this photoreaction was explored (Table 2). Firstly, the electronic effect of the aryl group in methyl aryl thioether was examined. With strong electron donating groups, like methoxy, attached to the aryl ring, excellent yields were obtained for the *ortho*-, *meta*- and *para*-methoxyphenyl thioethers (**2b–d**). For weak electron donating groups, like methyl, the corresponding product (**2e**) could be generated in an excellent yield. Good reactivity was also observed with halogen-attached substrates (**2f–h**). Then, we tested substrates with strong electron withdrawing groups. The results showed that substrates with aldehyde (**2i**), nitrile (**2j**), methoxycarbonyl (**2k**) or trifluoromethyl (**2l**) worked very well. Notably, the naphthyl group was also tolerated under Condition A (**2m**). Next, the effect of different alkyl groups was examined. Reactants with ethyl, cyclopropyl and propynyl groups yielded

Table 2 Photooxidation of thioethers into sulfoxides under Condition A[a]

$${}^{1}R{-}S{-}R^{2} \xrightarrow[\text{air (1 atm), CH}_3\text{OH, rt}]{\text{purple LED, AQ-PHEMA (1 mol\%)}} {}^{1}R{-}\overset{\overset{\displaystyle O}{\|}}{S}{-}R^{2}$$

1 → **2**

2b, 24 h, 94%	**2c**, 24 h, 95%	**2d**, 22 h, 97%	**2e**, 22 h, 95%
2a, 24 h, 96%	**2f**, 25 h, 93%	**2g**, 25 h, 92%	**2h**, 27 h, 94%
2i, 23 h, 91%	**2j**, 27 h, 92%	**2k**, 24 h, 95%	**2l**, 26 h, 94%
2m, 28 h, 95%	**2n**, 35 h, 90%	**2o**, 34 h, 91%	**2p**, 27 h, 68%
2q, 30 h, 92%	**2r**, 24 h, 94%	**2s**, 25 h, 95%	**2t**, 29 h, 90%
2u, 32 h, 87%	**2v**, 33 h, 86%		

[a] All reactions were carried out using **1** (1 mmol) and **AQ-PHEMA** (1 mol%) in CH$_3$OH (5 mL) irradiated by a purple LED light at rt under air atmosphere. The isolated yield is reported.

the desired products (**2n–p**) in 90%, 91% and 68% isolated yield, respectively. The reactivity of diaryl thioethers was also investigated. Excellent chemoselectivity as well as excellent yields were observed (**2q–s**). Finally, reactions with dialiphatic thioethers were studied. Di-*n*-butyl thioether gave an excellent yield of **2t**, while tetrahydro-2*H*-thiopyran and tetrahydrothiophene led to slightly lower yields of **2u** and **2v**, respectively. The above results indicated that this reaction showed very good substrate scope and functional group tolerance.

Recycling experiments

To investigate the recyclability of **AQ-PHEMA** in this transformation, 4-methoxyphenyl methyl thioether (**1d**) was selected as the model substrate for the **AQ-PHEMA** recycling experiments under Condition A. **1d** could be completely consumed after 24 hours and the NMR yield of the product 4-methoxyphenyl methyl sulfoxide (**2d**) was 99% in the first cycle of the photocatalytic reaction. After the first cycle, the catalyst **AQ-PHEMA** could be easily separated and recovered by simple filtration and directly used for the second cycle. The following reaction cycles were performed using the same procedure (for the specific plan for the recycling experiments, see ESI†). The results showed that **AQ-PHEMA** could be reused more than 20 times without significant loss of the catalytic activity (Fig. 1).

At the end of the recycling experiments, the recovered **AQ-PHEMA** (after 23 cycles) was characterized by ^{1}H NMR and GPC. As shown in Fig. 2, no significant changes were observed in the ^{1}H NMR spectrum compared to the original **AQ-PHEMA**. The molecular weight $M_{n,GPC}$ and molecular distribution M_w/M_n of the recovered **AQ-PHEMA** (after 23 cycles) were very close to those of the original **AQ-PHEMA** (Fig. 3). These results clearly indicated that the structure of **AQ-PHEMA** did not change during the whole catalytic procedure.

Proposed mechanism

Based on the Guo group's outstanding work,[9] literature precedents[59–64] and the cyclic voltammogram of **AQ-PHEMA** under irradiation (see Fig. S2†), the following possible reaction
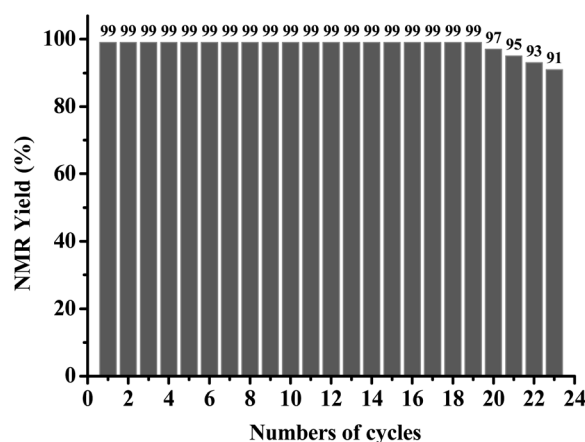

Fig. 1 Recycling experiments for the photocatalytic reaction of **1d**.
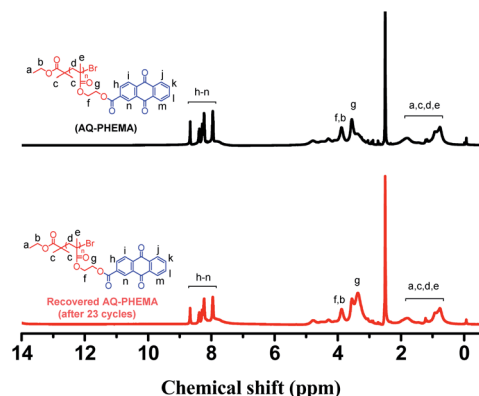
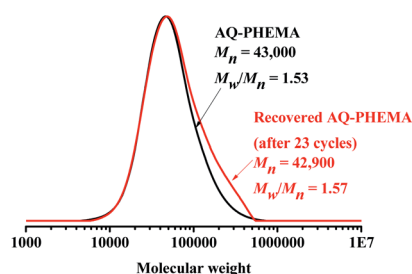Fig. 2 ^{1}H NMR spectra for **AQ-PHEMA** and the recovered **AQ-PHEMA** (after 23 cycles) in d_6-DMSO.

Fig. 3 The GPC traces of **AQ-PHEMA** and the recovered **AQ-PHEMA** (after 23 cycles).

mechanism was proposed as shown in Fig. 4. **AQ-PHEMA** was excited under visible light irradiation and subsequently sensitized oxygen to singlet oxygen which was more oxidative than normal triplet oxygen. Singlet oxygen could take an electron from the lone pair of electrons in sulfide **1** to form a sulfide
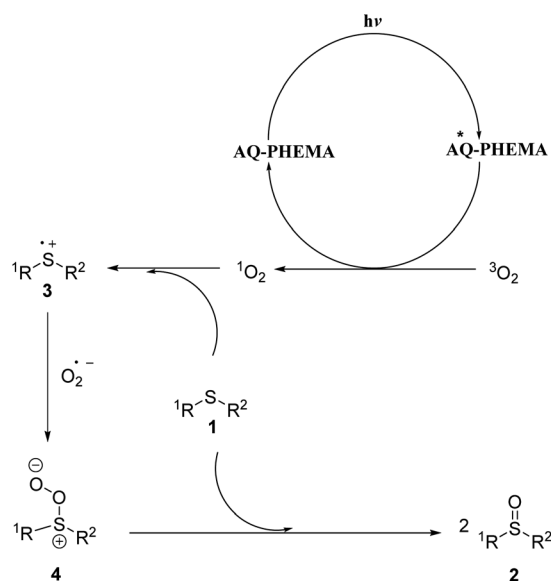
radical cation **3** and a superoxide radical anion, and then **3** further interacted with the superoxide radical anion to obtain intermediate **4**. **4** reacted with another molecule of thioether **1** to form the final sulfoxide product **2**.

Conclusions

In conclusion, we successfully synthesized the polymeric photosensitizer **AQ-PHEMA** by immobilizing the AQ functional group onto the precursor **PHEMA**. **AQ-PHEMA** could be used as a visible light sensitizer to catalyze the oxidation of thioethers into sulfoxides under aerobic conditions. The reaction exhibited high efficiency and chemoselectivity with extensive functional group tolerance. A possible mechanism was proposed. The **AQ-PHEMA** catalyst could be easily recovered and reused more than 20 times. The excellent photocatalytic properties, easy separation, and recyclability revealed the great potential of this catalyst in industrial applications and environment protection.

Conflicts of interest

There are no conflicts to declare.

Acknowledgements

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Fig. 4 A possible reaction mechanism.

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