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Visible light enabled [4+2] annulation reactions for anthracenone-furans from 2,3-dibromonaphthoquinone and phenylbenzofurans†

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A facile visible light promoted approach to anthracenone-furans from readily available 2,3-dibromonaphthoquinones and phenylbenzofurans *via* a formal Diels Alder reaction is reported. This reaction involves wavelength-selective agitation of 4CzIPN, energy transfer to quinones, recombination of 1,6-biradicals and elimination to give anthracenone-furans in good to excellent yields in one pot.

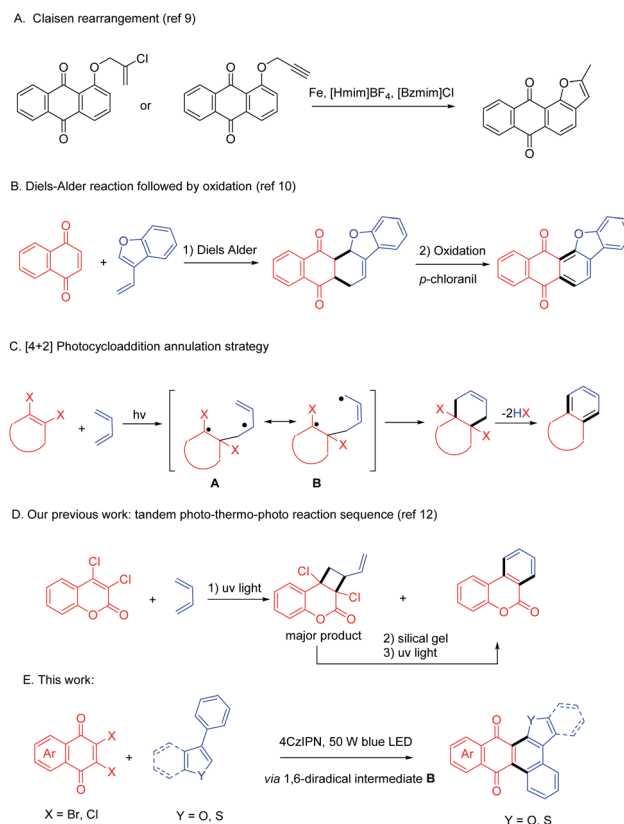
Introduction

Polycyclic compounds such as anthraquinones exhibit remarkable bioactivities¹ such as antimicrobial and antiviral,² anticancer,³ anti-inflammatory,^{1c,4} and so on. Anthraquinones can also serve as textile dyes,⁵ semiconductors in organic electronic devices⁶ and colorimetric reagents⁷ for their prominent photophysical properties. Functionalization of anthraquinones is an efficient way to access more versatile materials. For example, a fused polycyclic compound containing both anthraquinone and furan motifs, *i.e.*, anthracenone-furan, has been proved to be potentially useful in biological applications.⁸ However, lack of efficient synthetic methods impedes further application of this versatile scaffold, which urges synthetic chemists to develop new approaches.

To synthesize anthracenone-furan using a furannulation strategy, Aghapour⁹ reported a reductive Claisen rearrangement reaction of propargyloxanthraquinones or 2'-chloroprop-2'-enyloxanthraquinones in ionic liquids (Scheme 1, path A). Another synthetic approach to access this important scaffold is benzannulation approach through Diels Alder reaction of naphthoquinone and vinyl benzofuran followed by oxidation to give aromatized product (Scheme 1, path B).¹⁰ They are both efficient and selective syntheses. Unfortunately, both of them require the pre-synthesis of anthraquinone or vinyl furans so that the reaction scope is limited. Additionally, harsh reaction conditions such as high reacting temperatures are often required for DA reactions and stoichiometric oxidant is a prerequisite to oxidize the cyclohexene intermediate.

Photocycloaddition is well known as a powerful synthetic method to afford polycyclic products under mild conditions,¹¹ which has been applied to synthesize complicated molecules

including natural products. We thus designed a photoinduced benzannulation strategy from easily available cyclic dihaloethylene and 1,3-dienes (Scheme 1, path C). The benzannulated product can be obtained *via* [4 + 2] photocycloaddition and elimination of two HX. This method successfully excludes both the harsh conditions in [4 + 2] cycloaddition and the use of oxidant in the aromatizing procedure. However, [4 + 2]



Scheme 1 Synthetic approaches to anthracenone-furans.

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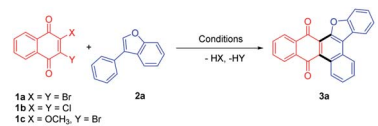
photocycloaddition is often accompanied with pervasive [2 + 2] cycloaddition *via* a 1,4-biradical intermediate **A**. For example, we have reported a facile one-pot photo-thermal-photo reaction sequence to synthesize dibenzopyranone (Scheme 1, path D).¹² Initially, dibenzopyranone was given as a minor product after direct UV irradiation, so that the subsequent thermal-photo reaction sequence was required to transform the predominated cyclobutane. Recently Huang and Nicewicz¹³ reported an elegant visible light mediated [4 + 2] cycloaddition of styrenes in the presence of PhSSPh, which acts as a HAT cocatalyst and converts the chemo-selectivity from [2 + 2] to [4 + 2]. In an alternative way, we hypothesized that the extension of the aromatic system would do favor to stabilize the 1, 6-diradical **B** and give more thermally stable [4 + 2] cycloadduct as preferred product. Another issue for photocycloaddition strategy is that annulated products with enlarged conjugation system often absorb light much stronger than substrates, which prohibited the excitation of substrates, usually leading to an incomplete transformation.¹⁴ In the past decade, photocycloaddition *via* photoredox catalysis has been achieved a huge progress using visible light photocatalyst (VLPC).¹⁵ Inspired by the successful visible light driving [4 + 2] reactions,¹⁶ we altered the direct agitation method to photosensitizing strategy and tried to excite substrates by energy transfer from selective agitated VLPC under blue LED irradiation. Herein, we report a visible light enabled [4 + 2] photocycloaddition of 2,3-dihalo quinones (**1**) and phenylbenzofurans (**2**, **4**) mediated by organo-photocatalyst to give polycyclic anthracenone-furans (**3**, **5**) in one pot (Scheme 1, path E).

Results and discussion

Initially, the visible light mediated reaction of 2,3-dibromoquinone (**1a**) and 3-phenylbenzofuran (**2a**) was studied. To our delight, anthracenone-furan **3a** was yielded as the only isolatable product in all the investigated conditions. Selected results are summarized in Table 1 (for more details, please see Table S1 in the ESI†).

Irradiation of **1a** and **2a** in the absence of VLPC gave annulated **3a** in 51% yield under two 24 W blue LEDs for 168 h (entry 1, Table 1). Several VLPCs such as Thioxanthene-9-one (TXO), Rose Bengal (RB), Butanedione (BD) and 4CzIPN were chosen to promote this reaction (entries 2–6). Among them, 4CzIPN was the most efficient, which gave **3a** in 88% yield after 49 h irradiation. It is supposed to be owing to both suitable absorption wavelength ($\lambda_{\text{max}} = 471 \text{ nm}$) and high triplet energy ($E^T = 2.68 \text{ eV}$)¹⁷ to be selectively excited and promote the cycloaddition *via* energy transfer. TXO possess a similar triplet energy ($E^T = 2.8 \text{ eV}$) with a shorter absorption wavelength ($\lambda_{\text{max}} = 360 \text{ nm}$)¹⁸, which gave **3a** in 79% yield, slightly lower than 4CzIPN. Meanwhile, RB¹⁸ ($\lambda_{\text{max}} = 549 \text{ nm}$, $E^T = 1.8 \text{ eV}$) gave **3a** in 60% yield. Butanedione¹⁹ ($\lambda_{\text{max}} = 430 \text{ nm}$, $E^T = 2.44 \text{ eV}$) gave **3a** in 54% yield. It evidently shows that organo-photocatalyst with higher triplet energy gives better yields of **3a**. Therefore, this reaction presumably proceeds through a triplet energy transfer mechanism.²⁰ The assessment of solvent reveals the reaction can be

Table 1 Condition screening for annulation reaction^a



Entry	VLPC, 5%	Solvent	Time, h	Yield ^b , %
1	No PC	Benzene	168	51
2	TXO	Benzene	53	75
3	Rose Bengal, 2%	Benzene	65	60
4	Butanedione, 30%	Benzene	75	54
5	4CzIPN	Benzene	49	88
6	4CzIPN, 2%	Benzene	51	79
7	4CzIPN	DCE	56	52
8	4CzIPN	Dioxane	39	57
9	4CzIPN	MeCN	48	19
10 ^c	4CzIPN	Benzene	38	87
11 ^d	4CzIPN	Benzene	10	92
12 ^e	4CzIPN	Benzene	156	NR
13 ^{d,f}	4CzIPN	Benzene	11	61
14 ^{d,g}	4CzIPN	Benzene	7	76

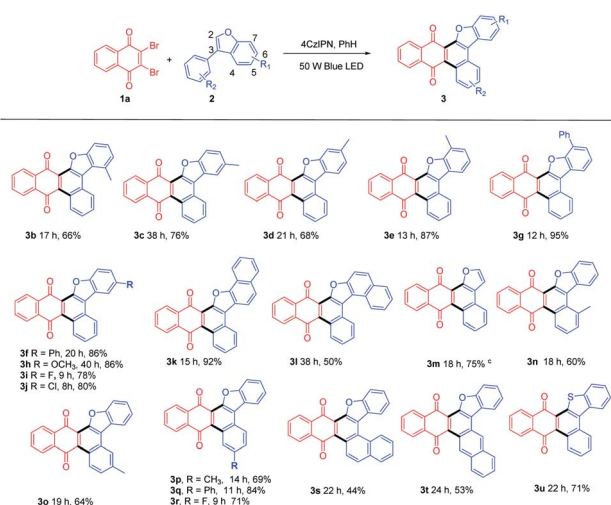
^a Reagents and conditions: 0.1 mmol **1a** (31.5 mg), 0.13 mmol **2a** (25.2 mg) and 0.005 mmol VLPC in 10 mL distilled benzene was ultrasonicated and purged with N₂ for 10 minutes and then irradiated under 24 W blue LED. TXO: Thioxanthene-9-one. 4CzIPN: 2,4,5,6-tetrakis(carbazol-9-yl)-1,3-dicyanobenzene. ^b Isolated yield. ^c Pyridine (2.2 eq.) was added. ^d 50 W blue LED was used as light source. ^e NO light, under reflux. ^f 2,3-Dichloronaphthoquinone (**1b**) was used instead of **1a**. ^g 2-Bromo-3-methoxynaphthoquinone (**1c**) was used instead of **1a**.

carried out in polar solvent such as DCE or 1,4-dioxane, but **3a** was given in low yields (52–57%, entries 7–8). When the reaction was carried out in MeCN, **3a** was given in poor yield (19%). Some complicated byproducts were formed, which might be due to side reactions triggered by electron transfer in high polar solvent. Extra addition of pyridine to remove the generated HBr did shorten the reaction time for several hours, but showed no improvement in yield (entry 10). Finally, the reaction mixture was irradiated under a 50 W blue LED for 10 h in the presence of 5% 4CzIPN to give **3a** in 92% yield (entry 11). Control experiment of refluxing in PhH for 156 h in dark gave no product (entry 12), which confirmed the visible light irradiation as a prerequisite. It should also be noted that **1a** could be replaced by 2,3-dichloronaphthoquinone (**1b**) or 2-bromo-3-methoxynaphthoquinone (**1c**), which gave **3a** in lower yields (entries 13–14).

With this optimized condition in hand, we performed the reactions of **1a** with a scope of 3-phenylbenzofurans (**2**) with substituents on both benzofuran ring (R₁) and substituted phenyl ring (R₂). The results were summarized in Table 2.

Both electron-donating (Me (**3b–3e**, **3n–3p**), Ph (**3f**, **3g**, **3q**), OCH₃ (**3h**)) and electron-withdrawing (F(**3i**, **3r**), Cl(**3j**)) substituted benzofurans, either at R₁ or R₂ position could afford annulated anthracenone-furans (**3b–3j**, **3n–3r**) in good to excellent yields (60–95%), which exhibited a good tolerance to the electronic characters of substituents. 3-Phenylnaphtho[1,2-*b*]

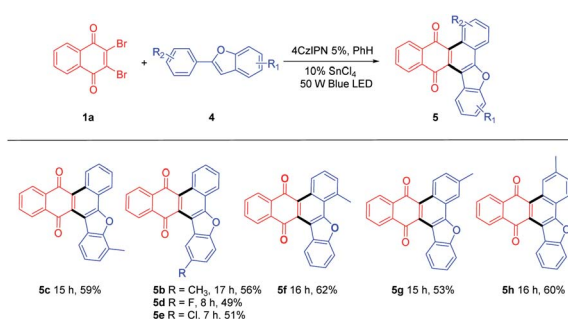


Table 2 Scope of 3-phenylbenzofurans (2)^{a,b}

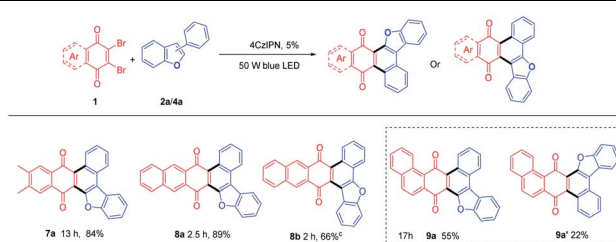
^a Reagents and conditions: 0.1 mmol **1a**, 0.13 mmol **2** and 0.005 mmol 4CzIPN in 10 mL distilled benzene was ultrasonicated and purged with N₂ for 10 minutes and then irradiated under 50 W blue LED. ^b Isolated yield. ^c 10% SnCl₄ was added.

furan (**2k**) gave anthracenone-furan **3k** in excellent yield (92%) as well. While 1-phenylnaphtho[2,1-*b*]furan (**2l**) or naphthylbenzofurans (**2s**, **2t**) gave anthracenone-furans (**3l**, **3s**, **3t**) in moderate yields (44–53%) with longer reaction times needed to complete transformation. This is in accordance with the 3-phenylbenzothiophene (**2u**), which gave **3u** with 71% yield after 22 h irradiation. It could be attributed to stronger competitive absorption of annulated product vs. photosensitizers (Table S3†).

For further extension of reaction scope, irradiation of **1a** with 2-phenylbenzofuran (**4a**) gave both annulated **5a** (46%) and oxetane **6a** (17%) (Scheme 2). Oxetane was reported to be the major product in photoreaction of 1,4-naphthoquinone and **4a** via the Paternò-Büchi reaction.²¹ Oxetane **6a** can undergo retro PB reaction slowly to give **1a** and **4a**, which are converted to **5a** upon irradiation. Several Lewis acid cocatalysts were used to efficiently decompose **6a** (Table S2†). At last, when irradiated in the presence of 10% SnCl₄ under 50 W blue LED, the reaction was accomplished in 8 h and **5a** was given as the only product in 69% yield. With this condition in hand, several 2-phenylbenzofurans (**4**) were investigated as listed in Table 3. There was no significant difference observed in the yields of annulated products from 2-phenylbenzofurans substituted with electron-donating or withdrawing substituents (49–62%). Notably, this Lewis acid mediation strategy also can be applied to 3-phenylfuran to afford **3m** in 75% yield (Table 2).

Scheme 2 Synthesis of anthracenone-furan **5a**.Table 3 Scope of 2-phenylbenzofurans (4)^{a,b}

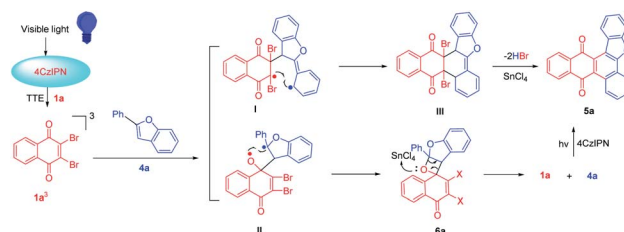
^a Reagents and conditions: 0.1 mmol **1a**, 0.13 mmol **2** and 0.005 mmol 4CzIPN in 10 mL distilled benzene was ultrasonicated and purged with N₂ for 10 minutes and then irradiated under 50 W blue LED. ^b Isolated yield.

Table 4 The Scope of quinones^{a,b}

^a Reagents and conditions: 0.1 mmol **1a**, 0.13 mmol **4** and 0.005 mmol 4CzIPN in 10 mL distilled benzene was ultrasonicated and purged with N₂ for 10 minutes and then irradiated under 50 W blue LED. ^b Isolated yield. ^c 10% SnCl₄ was added.

Some other dibromoquinones (**1d–1f**) were also studied. 2,3-Dibromo-6,7-dimethylnaphthalene-1,4-dione (**1d**) gave **7a** in 84% yield. 2,3-Dibromoanthracene-1,4-dione (**1e**) could react with **2a** or **4a** to yield **8a** (87%) or **8b** (66%) smoothly (Table 4). For the reaction of 2,3-dibromophenanthrene-1,4-dione (**1f**), the annulated regio-isomers **9a/9a'** were obtained in 55% or 22% yields. These examples exhibited the successful application of this approach to rather large polycyclic systems.

The plausible mechanism of this reaction can be interpreted as shown in Scheme 3 with the reaction of **1a** and **4a** as an example. The selective absorption of blue light by the 4CzIPN photosensitizer can drive the reaction through triplet-triplet



Scheme 3 Proposed mechanism.



energy transfer to excite dibromo naphthoquinone **1a** to $^3\mathbf{1a}^*$. The triplet $^3\mathbf{1a}^*$ reacts with **4a** to form 1,6-biradical intermediate **I** or 1,4-biradical **II**. Upon the following ISC and radical recombination, intermediate **I** gives cyclohexene **III**, which can be converted to **5a** after elimination of two HBr with the assistance of SnCl_4 . The intermediate **II** can give oxetane **6a** as a transient intermediate, which undergoes *retro*-PB reaction promoted by SnCl_4 to starting materials that are converted to **5a** upon photosensitizing.

Conclusions

In conclusion, we developed an efficient one-pot visible light promoted reaction to give the versatile anthracenone-furans from readily available starting materials with good to excellent yields. Using blue light and 4CzIPN as the driving force guarantees annulation reaction not only cleaner but also a precise agitation of VLPC leading to an efficient and complete conversion of quinones. Stannic chloride (SnCl_4) accelerates the decomposition of oxetane side product to restart $[4 + 2]$ annulation reaction and improves the overall yields of annulated products. It can be applied to benzothiophenes or other dibromoquinones to afford polycyclic molecules with up to seven fused rings. We believe this method will benefit both the pharmaceutical and material chemistry by providing an alternative efficient platform to polyaromatic heterocyclic compounds.

Conflicts of interest

The authors declare no competing financial interest.

Acknowledgements

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