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Phenanthrene Synthesis by Eosin Y-Catalyzed, Visible Light-Induced [4+2] Benzannulation of Biaryldiazonium Salts with Alkynes

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Abstract: A metal-free, visible light-induced [4+2] benzannulation of biaryldiazonium salts with alkynes was developed. With eosin Y as photoredox catalyst, a variety of 9-substituted or 9,10-disubstituted phenanthrenes were obtained *via* a cascade radical addition and cyclization sequence.

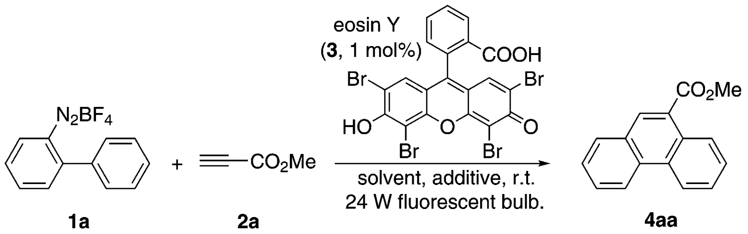
Keywords: alkynes; benzannulation; diazonium salts; phenanthrenes; visible light

Aryldiazonium salts are precursors that can efficiently generate aryl radicals *via* the homolytic dediazoniation of ArN_2^+.[1] The established dediazoniation methods include: (i) organic reduction at an electrode; (ii) radiation from solvated electrons generated in water; (iii) photo-induced electron transfer; (iv) reduction by metal cations; (v) induction using an anion; (vi) solvent-induced dediazoniation with the solvent serving as the electron donor.[2] Although the radical reaction by photochemical decomposition of diazonium salts is clean and cost-effecient,[3] there is often competition with the reaction in which the aryl cation is formed.[4] Moreover, the energy-consuming UV radiation is generally required for these photochemical transformations.[5] Visible-light in combination with a photoredox catalyst provides an environmentally friendly method to access free radical intermediates that can be used in various chemical reactions.[6] Diazonium salts act as oxidative quenchers in photoredox chemistry,[7] which was first applied by Deronzier in the visible light-mediated Pschorr reaction[8] and oxidation of benzyl alcohol.[9] A recent report by Sanford demonstrated a Pd-catalyzed room temperature C−H arylation reaction using aryldiazonium salts under visible light photoredox conditions.[10] In addition, organic dyes have also been used as inexpensive photocatalyts in visible light-induced C−H bond arylation of heteroarenes with aryldiazonium salts.[11]

Phenanthrenes are important organic compounds with wide range of applications in medicinal chemistry[12] and material sciences.[13] The classical method to synthesize phenanthrene derivatives is the photocyclization of stilbenes.[14] Cycloisomerization of arynes with unsaturated compounds,[15] the connection of two aromatic rings through cross-coupling followed by intramolecular cyclization[16] are also frequently utilized for the synthesis of phenanthrenes. Recently, the transition metal-catalyzed [4+2] benzannulation of biaryl compounds with alkynes, which allows the creation of a series of phenanthrenes through direct activation of C−H bonds, has attracted much attention.[17] The use of biaryldiazonium salts as substrates provides an alternative route for the synthesis of phenanthrenes *via* a radical reaction. In 1988, Zanardi and co-workers reported an intermolecular cycloaddition of biphenyldiazonium salts with mono-substituted acetylenes in pyridine,[18] in which the aryl radicals were generated through the decomposition of azo-type adducts of diazonium salts and pyridine.[19] Although the scope of this reaction was limited and yields of phenanthrenes were rather low due to the side reactions, this seminal work indicates that a cascade radical addition and cyclization is indeed possible for the synthesis of phenanthrenes. Herein we wish to report an eosin Y-catalyzed, visible light-induced [4+2] benzannulation between biaryldiazonium salts and alkynes, which allows the assembly of various 9-substituted and 9,10-disubstituted phenanthrenes under mild conditions.

Initially, a 1:1 mixture of biphenyldiazonium salt **1a** and methyl propiolate **2a** was irradiated with a 24-W fluorescent bulb for 12 h in the presence of 1 mol% of eosin Y (**3**) at room temperature. To our delight, it afforded the desired phenanthrene **4aa** in 25% yield (Table 1, entry 1). The use of an excess of **2a** resulted in higher yield and the best ratio of **1a** to **2a** is 1:5

Table 1. Optimization of the reaction conditions.[a]



Entry	Conditions	Yield[b]
1	**2a** (1 equiv.), MeCN	25%
2	**2a** (3 equiv.), MeCN	53%
3	**2a** (5 equiv.), MeCN	71%
4	**2a** (10 equiv.), MeCN	72%
5	**2a** (5 equiv.), DMSO	46%
6	**2a** (5 equiv.), DMF	31%
7	**2a** (5 equiv.), NMP	25%
8	**2a** (5 equiv.), dioxane	20%
9	**2a** (5 equiv.), THF	12%
10	**2a** (5 equiv.), toluene	6%
11	**2a** (5 equiv.), MeCN, NEt_3 (2 equiv.)	37%
12	**2a** (5 equiv.), MeCN, *t*-BuOLi (2 equiv.)	50%
13	**2a** (5 equiv.), MeCN, no light	Trace
14	**2a** (5 equiv.), MeCN, no catalyst	Trace
15[c]	**2a (3 equiv.), MeCN**	**74%**

[a] All the reactions were carried out with biphenyldiazonium salt **1a** (0.2 mmol), methyl propiolate **2a** and eosin Y (1 mol%) in 0.6 mL of solvent at room temperature with irradiation using a 24-W fluorescent bulb for 12 h.

[b] Yield was determined by ^1H NMR with $MeNO_2$ as internal standard.

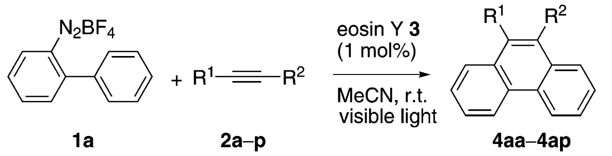
[c] **1a** was added in batches (0.04 mmol every hour).

(Table 1, entries 2–4). The benzannulation was found to proceed better in polar solvents, with MeCN giving the most desirable result (Table 1, entries 4–7). The observed low yields of the reactions in less polar solvents may be attributed to the poor solubility of the diazonium salts in these solvents (Table 1, entries 8–10). Diminished yields were obtained when NEt_3 and *t*-BuOLi were used, which was perhaps caused by the direct reaction of base with **1a**. In the control experiments, trace amounts of the products were detected in the absence of either light or the catalyst (Table 1, entries 13 and 14). Strikingly, the yield of **4aa** was increased to 74% by addition of diazonium salt **1a** gradually. Moreover, the amount of **2a** could be reduced to 3 equiv. using this method (Table 1, entry 15).

With the optimized reaction conditions in hand, the scope of this transformation was studied by using biphenyldiazonium salts **1a** and various alkynes. As shown in Table 2, the reaction proceeded smoothly with a series of terminal arylalkynes (Table 2, entries 2–10). Various functional groups including chloro, fluoro, ester, ketone, nitro and methoxy are tolerated under the chosen reaction conditions. A higher electron-withdrawing character of the substituents on the aromatic ring of the alkynes resulted in higher yields compared to substituents with a more electron-donating character. These results indicated that the addition of a radical to electron-deficient alkynes is more favourable. 2-Ethynylpyridine can also be used as a substrate in this reaction, affording the 9-(2-pyridyl) phenanthrene **4ak** in 51% yield (Table 2, entry 11). The [4+2] benzannulation between biphenyldiazonium salt **1a** and 4-phenyl-1-butyne gives the phenanthrene **4al** in 47% yield (Table 2, entry 12). Additionally, internal alkynes also reacted smoothly with **1a**, leading to the formation of the corresponding 9,10-disubstituted phenanthrenes in moderate yields (Table 2, entries 13–16). In the case of 1,4-diphenylbutadiyne, only one C≡C bond reacted, which afforded the phenylethynyl-substituted phenanthrene **4ap** in a yield of 59% (Table 2, entry 16).

In the next step, we chose methyl propiolate as the substrate for the benzannulation with various biaryldiazonium salts. As shown in Table 3, the reaction tolerates various functional groups including methyl, chloro, trifluoromethyl, phenyl and methoxy in the biphenyldiazonium salts (Table 3, entries 1–5). In addition, we did not find any dehalogenated product from the radical reactions involving a chlorine functionality (Table 3, entry 2). The reaction also worked smoothly when only one *ortho* hydrogen atom was available in the biaryldiazonium salts, however, the product was

Table 2. Reaction scope of alkynes.[a]



Entry	R^1	R^2	Product	Yield[b]
1	H	CO_2Me	**4aa**	67%
2	H	Ph	**4ab**	60%
3	H	*p*-Me-C_6H_4	**4ac**	55%
4	H	*m*-Me-C_6H_4	**4ad**	49%
5	H	*p*-OMe-C_6H_4	**4ae**	32%
6	H	*p*-Cl-C_6H_4	**4af**	63%
7	H	*p*-F-C_6H_4	**4ag**	81%
8[c]	H	*p*-CO_2Me-C_6H_4	**4ah**	71%
9[c]	H	*p*-$COCH_3$-C_6H_4	**4ai**	64%
10[c]	H	*p*-NO_2-C_6H_4	**4aj**	66%
11	H	2-pyridyl	**4ak**	51%
12	H	CH_2CH_2Ph	**4al**	47%
13	CO_2Et	CO_2Et	**4am**	57%
14	Ph	CO_2Et	**4an**	55%
15[c]	Ph	COPh	**4ao**	42%
16[c]	Ph	C≡CPh	**4ap**	59%

[a] All the reactions were carried out with biphenyl diazonium salt **1a** (0.3 mmol), alkynes (3 equiv,) and eosin Y (1 mol%) in 0.6 mL MeCN at room temperature with the irradiation of a 24-W fluorescent bulb for 12 h; **1a** was added in six portions (0.05 mmol per every hour).

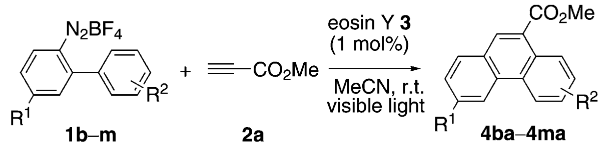
[b] Isolated yield.

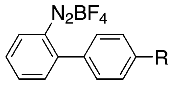
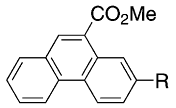
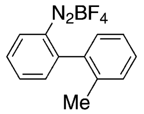
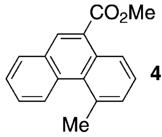
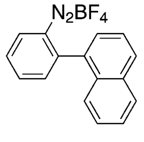
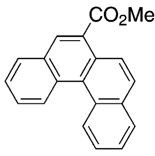
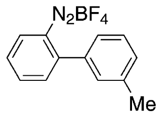
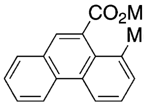
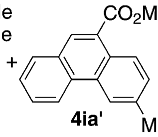
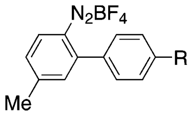
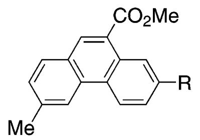
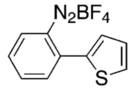
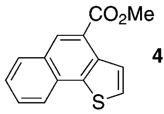
[c] 1.6 mL of MeCN were used.

obtained in a lower yield (Table 3, entries 6 and 7). When two non-equivalent *ortho*-hydrogen atoms were available, two regioisomers were obtained and the product with the least steric hindrance predominates (Table 3, entry 8). The biaryldiazonium salts **1j**, **1k**, **1l** underwent reaction with methyl propiolate to give the corresponding 9-substituted phenanthrenes **4ja**, **4ka**, **4la** in yields of 77%, 62% and 65% respectively. The structure of **4la** was confirmed by X-ray crystal diffraction.[20] Gratifyingly, we found that 2-(2-thienyl)-phenyldiazonium salt also reacts in this annulation reaction to generate a heteroaromatic system (Table 3, entry 12).

A plausible mechanism for this visible light-induced [4+2] benzannulation is described in Scheme 1. Firstly, photoexcitation of eosin Y by visible light generates excited eosin Y*. Then a biaryl radical is formed *via* single-electron-transfer (SET) from the diazonium salt **1** and concomitant oxidation of eosin Y* to eosin $Y^{\bullet +}$.[8–11] The addition of the biaryl radical to alkyne generates the vinyl radical **B**, followed by an intramolecular radical cyclization to give the cyclized radical intermediate **C**. A single-electron oxidation of **C** by the eosin Y radical cation regenerates the photocatalyst and forms the cation intermediate **D**. Lastly, deprotonation of **D** leads to the desired phenanthrene **4**.

Table 3. Reaction scope of biaryldiazonium salts.[a]



Entry	Diazonium salt	Product	Yield[b]
			
1	**1b**, R = Me	**4ba**	73%
2	**1c**, R = Cl	**4ca**	65%
3	**1d**, R = CF_3	**4da**	70%
4	**1e**, R = Ph	**4ea**	63%
5[c]	**1f**, R = OMe	**4fa**	57%
6	 **1g**	 **4ga**	41%
7	 **1h**	 **4ha**	25%
8[d]	 **1i**	 +  **4ia** **4ia'**	65% (1:3)
			
9	**1j**, R=H	**4ja**	77%
10	**1k**, R=Me	**4ka**	62%
11	**1l**, R=Cl	**4la**	65%
12	 **1m**	 **4ma**	49%

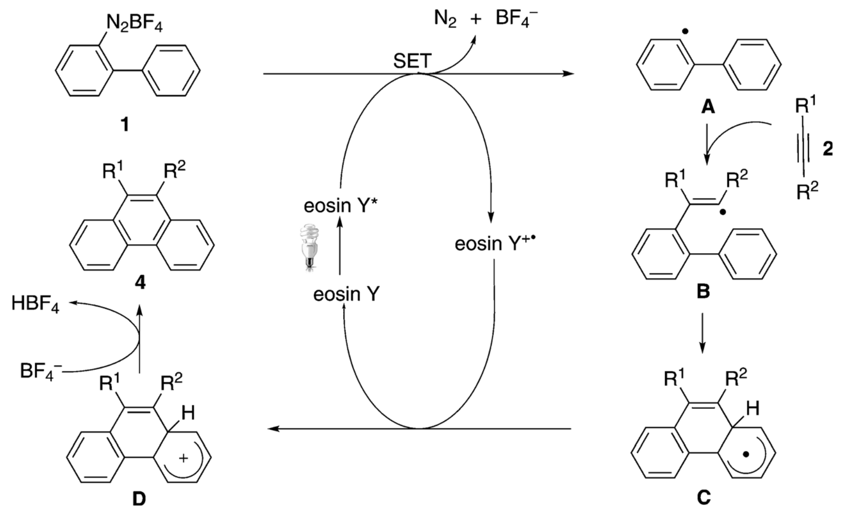
[a] *Reaction conditions:* biaryldiazonium salts **1** (0.3 mmol), methyl propiolate (3 equiv.) and eosin Y (1 mol%) in 0.6 mL MeCN at room temperature with the irradiation of a 24-W fluorescent bulb for 12 h; diazonium salt was added in six batches (0.05 mmol per every hour).

[b] Isolated yield.

[c] 10 equiv. of methyl propiolate were used.

[d] Total yields of **4ia** and **4ia'**, the ratio was calculated on the basis of the isolated yields of these two compounds.

In conclusion, we have developed an eosin Y-catalyzed, visible light-induced [4+2] benzannulation of biaryldiazonium salts with alkynes. A wide range of



Scheme 1. Plausible mechanism.

functional groups can be tolerated in the reaction conditions proposed. Various 9-substituted and 9,10-disubstituted phenanthrenes were assembled *via* cascade radical addition and cyclization. This study opens up possibilities for developing new reactions based on visible light-induced sequential radical reactions. Further investigations on this type of photo-reaction are ongoing in our lab and the results will be reported in due course.

Experimental Section

General Experimental Procedure for Visible Light-Induced [4+2] Benzannulation of Biaryldiazonium Salts with Alkynes

In a 10-mL snap vial were placed eosin Y (1 mol%, 2 mg), alkyne (0.9 mmol) and 0.1 mL of dry MeCN (1 mL of dry MeCN was used when alkynes are solid) under nitrogen. Then biphenyldiazonium salt **1** (0.3 mmol) was divided into six fractions, each fraction was dissolved in 0.1 mL of MeCN and every hour one fraction was added *via* syringe. During this period, the reaction tube was illuminated with a 24-W fluorescent bulb at room temperature. After 12 h of irradiation, the resulting mixture was filtered through a short path of silica gel, eluting with ethyl acetate. The volatile compounds were removed under vacuum and the residue was purified by column chromatography (SiO_2) with hexane/ethyl acetate.

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[20] See the Supporting Information for the crystallographic structure of compound **4la**. CCDC 897028 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.