

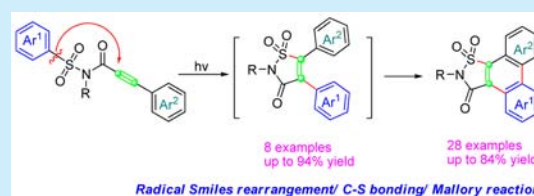
UV Light Induced Direct Synthesis of Phenanthrene Derivatives from a Linear 3-Aryl-*N*-(arylsulfonyl) Propiolamides

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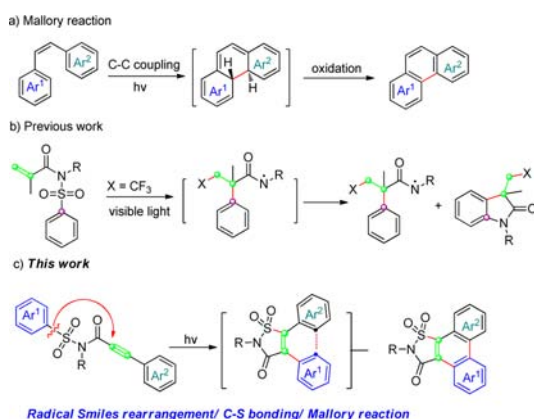
S Supporting Information

ABSTRACT: A novel photochemical approach for the synthesis of phenanthrene derivatives from linear 3-aryl-*N*-(arylsulfonyl) propiolamides via a tandem radical Smiles rearrangement/C–S bonding/Mallory reaction is disclosed. The control experiment results and isolation of the key intermediates give further insight into the reaction mechanism. Gram scale reaction using a flow reactor demonstrated the synthetic potential applications of our protocol.



Among the UV light-induced cyclization reactions, the oxidative photocyclization of stilbene is of great interest owing to its preminent reactivity in photochemistry.¹ Moreover, stilbene derivatives that contain heteroatoms or large conjugated systems on aryl moieties could also undergo the same reaction to give corresponding products. This typical reaction is known as the Mallory reaction² and has been extensively investigated for the synthesis of polycyclic aromatic hydrocarbons (PAHs) and other exceptional molecular structures^{3,4} (Scheme 1a). Relevant

Scheme 1. Previous Work and Our Discovery



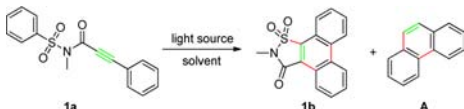
reaction mechanisms have been widely studied⁵ and clearly declared: upon irradiation, the intermediate *trans*-4a,4b-dihydrophenanthrene was formed, which then could be oxidized to phenanthrenes or transformed into other different products through elimination or rearrangement. Despite enormous achievements in photochemistry over the past years,^{3,4,6} stilbenes utilized in the Mallory reaction still, in most cases, require advance preparation. Furthermore, compounds comprising a less active C≡C bond were rarely reported to participate in this classical reaction.⁷

Recently, our group reported a visible-light induced cascade reaction initiated by CF₃ radical addition to the C–C double bond of *N*-(arylsulfonyl)acrylamides and afforded two products: α -arylamines and oxindoles (Scheme 1b).⁸ Inspired by this strategy, we synthesized a derivative compound, 3-aryl-*N*-(arylsulfonyl) propiolamide, by replacement of the unsaturated C=C bond with C≡C bond that directly tethered to an aromatic ring. Unfortunately, no expected amine or oxindole products were detected when it was subjected to the similar reaction conditions. However, when the substrate was exposed to UV light, we serendipitously discovered a new approach to efficient synthesis of various phenanthrene derivatives from linear, easily made *N*-(arylsulfonyl)propiolamides via a radical Smiles rearrangement⁹/C–S bonding/Mallory reaction cascade (Scheme 1c). Herein we present what we have achieved regarding this unique and interesting new reaction.

Our initial discovery was made by subjecting *N*-methyl-3-phenyl-*N*-(phenylsulfonyl) propiolamide **1a** to the irradiation of a high-pressure mercury lamp with a Pyrex filter in acetonitrile (5 mM) under air. After 4 h, compound **1b** was isolated as a major product in 60% yield along with 15% of phenanthrene **A** as a side product (Table 1, entry 1), in which the structures were characterized by 1D and 2D NMR spectra. It is of interest to point out that the isothiazolone S,S-dioxide framework contained in the product **1b** is quite a popular element in many chemically bioactive motifs (Figure 1).¹⁰ For example, saccharin is best-known as the oldest sweetener,¹¹ whose scaffold has drawn much attention in medicinal chemistry and has been identified as a key pharmacophore of biologically active compounds.¹⁰ In addition, modified saccharin compounds have demonstrated extensive application in enzyme inhibitors (Figure 1).^{10b,12} However, the traditional methods to construct the five-member structure are rare and tedious,^{10b,13} thus limiting their utility in synthesis. Therefore, we were intrigued to optimize the reaction conditions.

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Table 1. Optimization of the Conditions toward the Synthesis of **1b**^a


entry	solvent	light source	time (h)	yield (%) ^b	
				1b	A
1	MeCN	HP mercury lamp	4.0	60	15
2	MeCN	MP mercury lamp	2.5	70	10
3	MeCN	300 nm	1.5	73	<5
4	MeCN	350 nm	18	48	10
5	MeCN	180 nm	1.5	72	<5
6	MeCN ^c	300 nm	1.5	73	<5
7	MeCN ^d	300 nm	1.5	53	30
8	benzene	300 nm	2.0	67	13
9	CH ₂ Cl ₂	300 nm	2.0	69	10
10	THF	300 nm	3.0	55	25
11	toluene	300 nm	2.0	71	<5
12	MeOH	300 nm	3.5	40	12

^aReaction conditions: **1a** (0.2 mmol), solvent (anhydrous 40 mL), under air atmosphere. ^bIsolated yield. ^cUnder O₂ atmosphere. ^dUnder N₂ atmosphere.

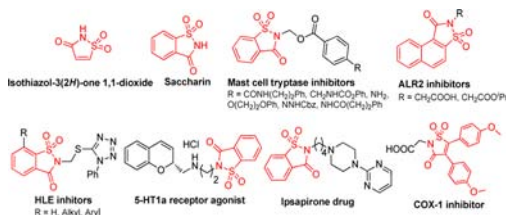
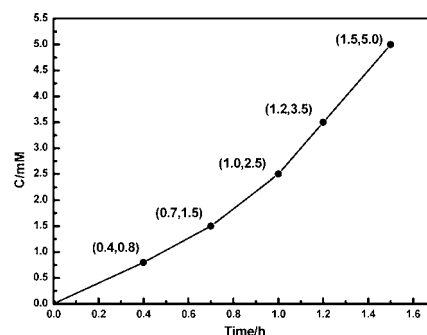
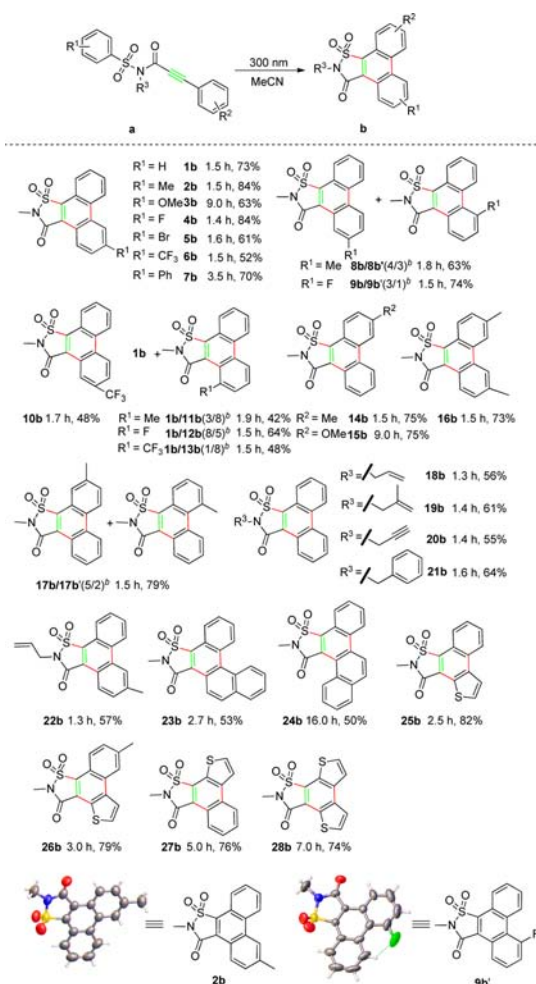


Figure 1. Representative bioactive isothiazolone 1,1-dioxide derivatives.

Screening of the light source revealed that 300 nm wavelength light afforded the best yield (Table 1, entries 1–5). Based on the optimal light source, a set of solvents were then examined, and acetonitrile was found to be the ideal medium (Table 1, entries 3, 8–12). Notably, the presence of oxygen could significantly affect the yield of the desired product. For example, when the reaction was performed under an air or oxygen atmosphere, the yield was higher than in the case of a nitrogen atmosphere (Table 1, entries 3, 6–7). In addition, we found that the reaction required a longer time to complete when the concentration of substrate **1a** was higher; the relationship between the substrate concentration and reaction time for **1a** to be completely consumed is displayed with a concentration–time curve, as shown in Figure 2, which revealed that the reaction time was in direct proportion to the substrate concentration.

With the optimal reaction conditions in hand, we then prepared a series of *N*-tosylpropionamides and submitted them to the standard conditions; the results are listed in Scheme 2.

As shown in Scheme 2, both electron-donating and -withdrawing substituents were well tolerated under the reaction conditions. For example, the *p*-methyl, *p*-methoxyl, *p*-halo, *p*-CF₃, and *p*-phenyl substituted substrates could be smoothly converted into corresponding products in moderate to high yields (Scheme 2, 2b–7b). As a bonus, one of the products **2b** was suitable for single X-ray diffraction analysis (Scheme 2). Notably, the reaction was sensitive to the position of the substituent, e.g., the *m*-substituted substrate **8a**, affording regioisomers of **8b** and **8b'** in an approximate ratio of 4:3,

Figure 2. Concentration–time curve of **1a**.Scheme 2. Reaction Scope toward the Synthesis of Compound **b**^a

^aReaction conditions: **a** (0.2 mmol), MeCN (anhydrous 40 mL) under air atmosphere; isolated yields are shown. ^bThe ratio is determined by GC.

while the F-substituted substrate **9a** afforded the regioisomers of **9b** and **9b'** in a ratio of 3:1. However, the reaction of the *m*-CF₃ substituted substrate **10a** showed high regioselectivity with **10b** as the single isomeric product, which might be attributed to a strong steric effect of the CF₃ group. It is noteworthy that the *o*-substituted substrate could produce both an unsubstituted product **1b** by elimination of the *o*-substituent and a desired *ortho*-substituted product (Scheme 2, 11b–13b), in which the formation of **1b** was in agreement with the classical Mallory

isolation of the key intermediates involved in the reaction process added more credence to the proposed mechanism. Finally, the gram scale reaction using a flow reactor further demonstrated the synthetically potential applications.

■ ASSOCIATED CONTENT

Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.6b00878.

Crystallographic file for **2b** (CIF)

Crystallographic file for **9b'** (CIF)

Experimental procedures and ^1H and ^{13}C NMR spectra for all compounds (PDF)

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Notes

The authors declare no competing financial interest.

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