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Synthesis of Benzoaryl-5-yl(2-hydroxyphenyl)methanones via Photoinduced Rearrangement of (*E*)-3-Arylvinyl-4*H*-chromen-4-ones

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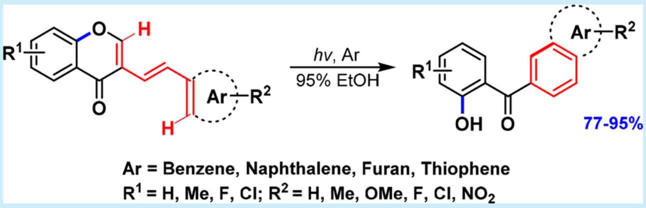
Supporting Information



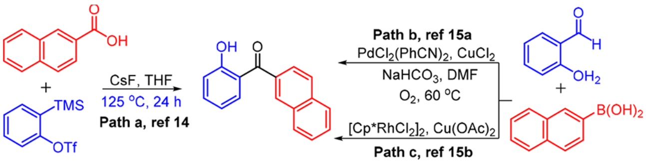
ABSTRACT: A concise and efficient photoinduced rearrangement of (*E*)-3-arylvinyl-4*H*-chromen-4-ones for the synthesis of benzoaryl-5-yl(2-hydroxyphenyl)methanones is described. Benzoaryl-5-yl-(2-hydroxyphenyl)methanones were obtained in 77−95% yields via the irradiation of (*E*)-3-arylvinylchromones in the 95% EtOH with a high-pressure mercury lamp at room temperature under Ar atmosphere. The reported method provides a novel procedure for the synthesis of *α*,*α*′-diaryl ketone derivatives without addition of any transition metals and oxidants or other additives. A plausible mechanism was proposed, and the rearrangement product was characterized by NMR, HRMS, and X-ray.

Light, as a clean, convenient energy, usually needs short reaction time with high atom efficiency in many reactions.[1] After the photon was absorbed by the substrates, electrons transit from the ground state to the excited state, and as a result, the structure and properties of the molecule were changed. Since there is no requirement for additional additives or reagents for the photochemical reaction, it demonstrates the meaning of green chemistry.[2] Nowadays, photochemical reaction has been used as a practical synthetic method in various areas of organic chemistry, such as total synthesis,[3] asymmetric synthesis[4] and metal catalysis,[5] green organic synthesis,[6] photolabile protecting groups,[7] and so on.[8] Photoinduced rearrangement is a common phenomenon in photochemistry.[9] Rearrangement of diarylethenes, which usually involves photoinduced cyclization, sigmatropic hydrogen shift, opening of an aromatic ring, and formation of rearrangement products, is one of the typical photoinduced rearrangements and has been recently reviewed.[10]

Due to its biological activity, *α*,*α*′-diaryl ketone skeleton was usually considered a biologically active moiety in pharmaceutical chemistry.[11] The *ortho*-hydroxyl-substituted diaryl ketone moiety has been found in some natural products,[12] and potential biological activity was observed as well.[13] However, only a few methods have been reported, and either elevated temperature[14] or transition-metal catalyst[15] was required for the reaction to proceed smoothly.

Treatment of *β*-naphthoic acid with 2-(trimethylsilyl)phenyl trifluoromethanesulfonate in the presence of cesium fluoride at 125 °C for 24 h gave the corresponding product in 44% yield via the rearrangement of a four-membered ring intermediate (Scheme 1, path a).[14] Alternatively, Pd-catalyzed direct arylation of salicylaldehyde with 2-naphthaleneboronic acid in DMF under O_2 atmosphere afforded (2-hydroxyphenyl)(naphthalen-2-yl)-methanone in 65% yield (path b).[15a] Later on, $[Cp^*RhCl_2]_2$ was successfully applied to the same substrates with slightly elevated temperature to give *ortho*-hydroxyl-substituted diaryl ketone product in better yield 98% (path c).[15b]

Scheme 1. Reported Synthesis of (2-Hydroxyphenyl)(naphthalen-2-yl)-methanone



In our group, various complicated fused-polyheterocyclics, e.g., 2*H*-phenanthro[9,10-*c*]pyrazoles,[16] dibenzo [*f*,*h*][1,2,4]-triazolo[3,4-*b*]quinazolines,[17] 7a-phenyl-1a,7a-dihydrobenzo-pyrano[2,3-*b*]azirin-7-ones,[18] polybenzoquinazolines,[19] benzo-[*c*]furo[2,3-*a*]xanthenone,[20] 14*H*-dibenzo[*a*,*c*]-xanthen-14-one,[21] benzo[*e*]-chromeno[2,3-*g*]indol-13(1*H*)-one,[22] and C5-modified pyrimidine and pyrimidine nucleoside derivatives[23] were synthesized via photochemical process. In 1996, Silva et al. reported that the photo-oxidative cyclization of (*E*)-2-styryl-chromones at ambient temperature for 30−50 days in the open air gave 12*H*-benzo[*a*]xanthene-12-ones in moderate yields (Scheme 2).[24] In this Letter, interestingly, when (*E*)-3-styryl-chromone **1a** was irradiated by UV light, the rearrangement product (2-hydroxyphenyl)(naphthalen-2-yl)methanone **2a** was obtained. We demonstrated a simple and efficient protocol for the synthesis of benzoaryl-5-yl-(2-hydroxyphenyl)methanones **2** via the photoinduced rearrangement of (*E*)-3-arylvinyl-chromenes **1** with irradiation by a high-pressure mercury lamp at room temperature under Ar atmosphere (Scheme 3).

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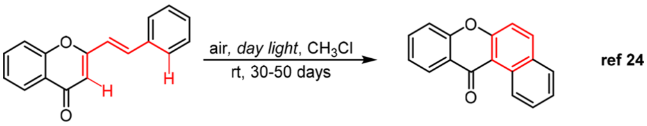
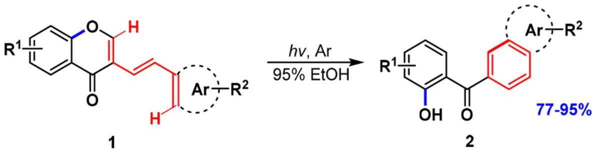
Org. Lett. XXXX, XXX, XXX−XXX

Scheme 2. Synthesis of 12*H*-benzo[*a*]xanthen-12-one by Photochemical Reaction of (*E*)-2-Styryl-4*H*-chromen-4-one

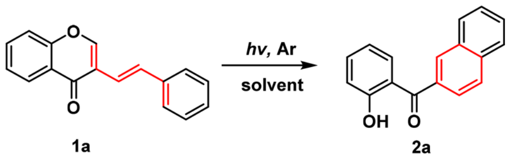


Scheme 3. Synthesis of Benzoaryl-5-yl(2-hydroxyphenyl)methanones 2 via the Photoinduced Rearrangement of (*E*)-3-Arylvinyl-4*H*-chromen-4-ones 1



Ar = Benzene, Naphthalene, Furan, Thiophene
R^1 = H, Me, F, Cl; R^2 = H, Me, OMe, F, Cl, NO_2

Table 1. Optimization of the Reaction Conditions[a]

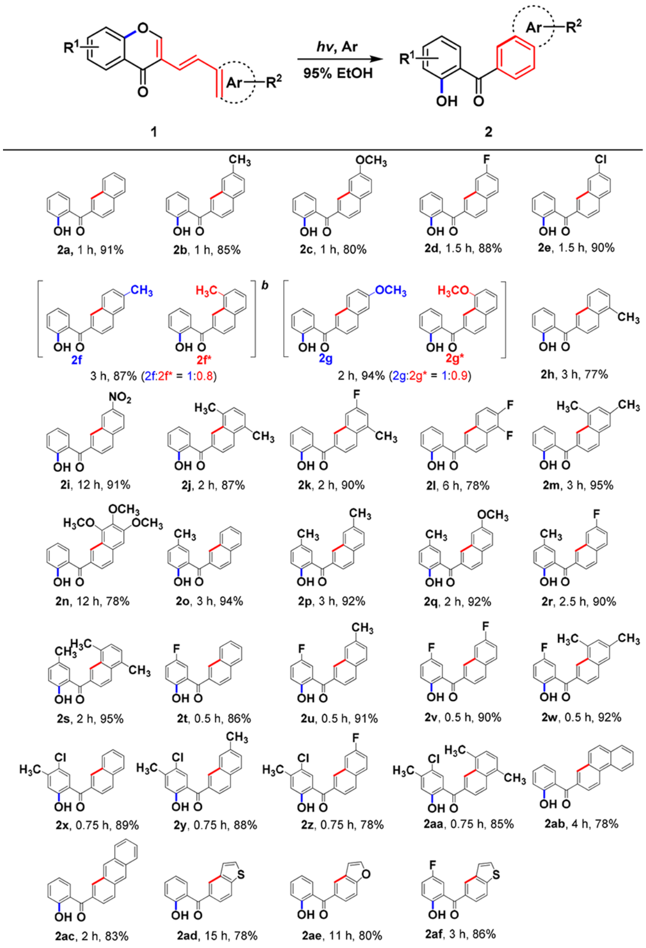


entry	solvent	atmosphere	concn (mM)	time (h)[b]	yield (%)[c]
1	ACE	Ar	5	12	40
2	DCM	Ar	5	4	64
3	ACN	Ar	5	6	53
4	EtOH	Ar	5	1	83
5	MeOH	Ar	5	1	80
6	EtOH/H_2O (5:1)	Ar	5	1	70
7	EtOH/H_2O (7:1)	Ar	5	1	84
8	95% EtOH	Ar	5	1	91
9	95% EtOH	Ar	3	1	80
10	95% EtOH	Ar	7	1	81[d]
11	95% EtOH	air	5	1	83

[a]Irradiation of **1a** (0.25 mmol) in various solvents (50 mL, 5 mM) with high-pressure mercury lamp (500 W) at room temperature. [b]Reaction time was determined by complete consumption of **1a**. [c]Isolated yields. [d]5% **1a** was left by ^{1}H NMR determination.

The substrate (*E*)-3-styryl-chromone **1a** was synthesized on the basis of the literature report.[25] The photoinduced rearrangement of **1a** was performed at ambient temperature under the UV irradiation with Ar atmosphere (Table 1). Initially, irradiation of **1a** in acetone with a high-pressure mercury lamp (500 W) at room temperature for 12 h yielded (2-hydroxyphenyl)(naphthalen-2-yl)methanone **2a** in 40% yield (Table 1, entry 1). Yields of **2a** increased slightly in dichloromethane or acetonitrile (53−64%) with shorter reaction time 4−6 h, (entries 2−3). It is surprising to find out that protic solvents could significantly improve the rearrangement efficiency to give **2a** in over 80% within 1 h (entries 4−5). Inspired by the interesting result, a significant amount of water was added to alcohol. However, the corresponding product **2a** was obtained in either lower yield (entry 6) or comparable yield with extended reaction time (entry 7). Interestingly, the yield of **2a** was successfully boosted to 91% by limiting the added water to 5% (95% ethanol, entry 8). Notably, lower or higher reaction concentration or open air condition decreased the yields of **2a** (entries 9−11). Thus, the irradiation of **1a** (5 mM) in 95% EtOH at ambient temperature under Ar atmosphere for 1 h was determined to be the optional conditions.

Scheme 4. Scope of the Reaction[a]



[a]Irradiation of **1a** (5 mM) in 95% EtOH (50 mL) with high-pressure mercury lamp (500 W) at room temperature under Ar atmosphere. The ratios of **2f**/**2f*** and **2g**/**2g*** were determined by ^{1}H NMR.

With the optimized condition determined, the scope of and generality for rearrangement of (*E*)-3-arylvinyl-4*H*-chromen-4-ones **1** were subsequently explored (Scheme 4). Thus, a wide range of substrates **1** with different functional groups were subjected to the optimal condition to give corresponding rearrangement products **2** in moderate to high yields (77−95%). Although slightly longer reaction time was required, higher yields of **2** were obtained for the substrates bearing an electron withdrawing group (EWG) at the para-position of the phenyl group compared to those with an electron donating group (EDG) (**2b**−**2e**, **2i**). The presence of *m*-Me or *m*-OMe in the substrates led to the formation of **2** in a mixture of two regioisomers with the ratio of ∼5:4 (**2f**−**2g**), which could probably be explained by the steric hindrance. Various di- and trisubstituted substrates have also been explored (**2j**−**2n**).

The effect of the various substituents on the chromen-4-one ring was also investigated. Although the presence of EWG significantly shortened reaction time compared to those bearing EDG, the rearrangement products were still obtained in excellent yields (Scheme 4, **2o**−**2aa**). Replacement of phenyl with naphthalene and heteroaromatics require extended reaction time to give **2** in desired yields, especially for **2ad** and **2ae**. In summary, a wide range of functional groups (halogen and NO_2) could be successfully tolerated, which provide possibility for further modification.

The structure of **2** was established via ^{1}H NMR, ^{13}C NMR, HRMS, IR, and X-ray structure of **2h**. The molecular structure of **2h** was depicted in Figure 1.[26] The *ortho*-hydroxyl-substituted diaryl ketone moiety of **2h** included three benzene rings [A (C1−C6), B (C8−C10, C15−C17), and C (C10−C15)]. An intramolecular O−H···O hydrogen bond was observed, and the bond length was 2.593 Å. The dihedral angle of the benzene ring (A) and naphthalene ring (BC) was 45.9°. It was worthy to note that the $\pi-\pi$ stacking was not observed in the X-ray structure of **2h**.

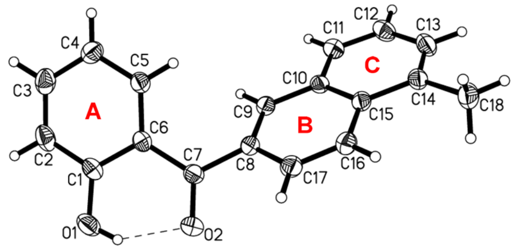


Figure 1. ORTEP (30%) diagram of compound **2h**.

The UV absorption spectra of **1a** and **2a** are shown in Figure 2. Due to the formation of a carbonyl group and expansion of aromatic rings, the typical $\pi \rightarrow \pi^*$ absorption was observed at 292 nm (ε = 28200 $L \cdot mol^{-1} \cdot cm^{-1}$) and 312 nm ($\varepsilon$ = 23200 $L \cdot mol^{-1} \cdot cm^{-1}$) in **1a**, which were nearly in accordance with the excited 297 and 313 nm light of a high-pressure mercury lamp. The absorption of **2a** was 267, 301, and 350 nm.

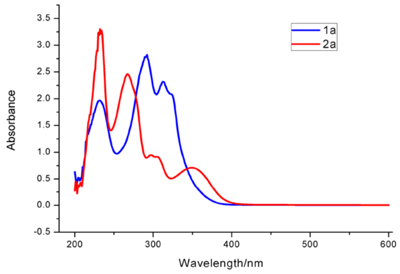
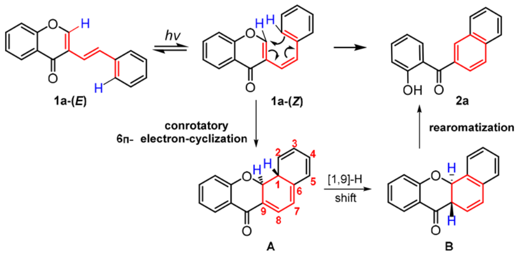


Figure 2. UV absorption spectra of **1a** and **2a** in ethanol.

On the basis of experimental data and literature reports,[9,10,27] a plausible mechanism for the formation of **2a** was proposed and presented in Scheme 5. It is believed that irradiation of **1a**-(E) with a high-pressure mercury lamp led to the formation of **1a**-(Z) via photoisomerization, followed by a 6π-electron-cyclization to give intermediate A. This is a typical well-known cyclization for diarylethenes and has been recently well reviewed.[28] Due to the presence of hydrogens at C1/C2, the rearomatization of the core (naphthalene ring) was proposed to proceed via sigmatropic rearrangement along with the C1−O bond cleavage.[27b] Thus, intermediate B was proposed to be generated via a thermal suprafacial [1,9]-H shift. It was believed that the presence of a carbonyl group[27b] significantly facilitates the rearrangement process. As a result of proton migration and the opening of the heterocyclic pyran ring, rearrangement product **2a** was isolated as the only product via the restoration of aromaticity. The presence of an intramolecular hydrogen bond between the hydroxyl group and the carbonyl group might further stabilize **2a**. To the best of our knowledge, only few similar examples for the described rearrangement were reported.[9,27,29]

Scheme 5. Proposed Mechanism for Rearrangement of 1a



In summary, we have successfully investigated the photochemical property of (E)-3-arylvinyl-4H-chromen-4-ones, which provided access to the rearrangement product benzoaryl-5-yl(2-hydroxyphenyl)methanones in high yields under Ar atmosphere with the irradiation of a high-pressure mercury lamp at room temperature. The advantages of the demonstrated method include (a) excellent functional group tolerance, (b) nontoxic solvent (95% EtOH), (c) no requirement of transition metal/additives, (d) good to excellent yields, and (e) high atom efficiency. The rearrangement is believed to proceed via trans−cis photoisomerization, electron-cyclization, [1,9]-sigmatropic shift, and rearomatization, which led to the pyran ring-opening to give a more stable product.[27a]

■ ASSOCIATED CONTENT

S Supporting Information

The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.orglett.7b03007.

Experimental procedures and detailed characterization data of all new compounds (PDF)

X-ray data of **2h** (CIF)

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Notes

The authors declare no competing financial interest.

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