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Photo-induced aromatic assembly of benzocycloalka[1,2-*b*]furan and spiro[furan-2(3*H*),1'-benzocycloalkane] derivatives

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Abstract—The photo-induced benzannulation of benzocycloalka[1,2-*b*]furans produced hydrohelicene-type compounds in good yields. A similar photoreaction of the spiro[furan-2(3*H*),1'-benzocycloalkane]s afforded dihydrophenalene derivatives in moderate yields. Benzo[*kl*]xanthene was also formed by a similar photoreaction of spiro[furan-2(3*H*),9'-xanthene]. The reaction pathway was elucidated by the ¹H NMR spectrum of the reaction mixture and the alternative synthesis of the intermediate. © 2005 Elsevier Ltd. All rights reserved.

There are many reports of the photochemical reaction of furan derivatives.¹ Recently, we reported that the irradiation of 3-acetyl-5,5-diaryl-2-methyl-4,5-dihydrofurans using a high-pressure mercury lamp gave naphthalene derivatives in quantitative yields (Scheme 1).² It could be construed that this photoreaction presumably proceeded through the photoactivation of the α , β -unsaturated carbonyl group, followed by an intramolecular cyclization, and successive aromatization. In addition, the photo-induced benzannulation was accelerated by an acid catalyst, such as hydrochloric acid. In light of the importance of the aromatic assembly in organic synthesis, we applied the reaction to benzocycloalka[1,2-*b*]-furans and spirofurans, with the aim of constructing the polycyclic aromatic framework. Moreover, the other





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objective was to clarify the reaction pathway of the photochemical reaction by the isolation of the intermediates. Herein, we briefly present these results.

Benzocyclopenta[1,2-b]furan $(1a)^3$ (0.2 mmol) was irradiated for 6 h in acetonitrile (9 mL) containing 2 M hydrochloric acid (1 mL) under an argon atmosphere at room temperature using a 100 W high-pressure mercury lamp, giving 6-acetyl-5-methyl-7*H*-benzo[*c*]fluorene (**2a**) in good yield (Scheme 2 and Table 1, entry 1).^{4,5}



Scheme 2.

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Table 1. Acid-catalyzed photoreaction of benzocycloalka[1,2-*b*]furan derivatives $1a-e^a$

Entry	Benzocycloalkafuran	Time (h)	Recovery (%)	Product (yield/%) ^b
1	1a (<i>n</i> = 1)	6	11	2a (76)
2	1b $(n = 2)$	6	13	2b (61)
3	1c $(n = 3)$	3	16	2c (45)
4	1d (<i>n</i> = 1)	6	18	2d (52)
5	1e $(n = 2)$	5 days	48	i.m. ^c

^a The photoreaction of benzocycloalkafuran **1** (0.2 mmol) was carried out at 23 °C in acetonitrile (9 mL) containing 2 M hydrochloric acid (1 mL) using a 100 W high-pressure mercury lamp.

^b The yield based on the benzocycloalkafuran 1 used.

^c An intractable mixture was obtained without the recovery of **1e**, and the desired **2e** was not isolated.



Scheme 3.

Although the starting 1a was recovered after irradiation (11% recovery), prolonged irradiation did not effectively improve the yield. The photoreaction of other benzocycloalka[1,2-b]furan derivatives 1b-e³ was next examined under similar reaction conditions and the corresponding benzannulated angular products 2b-d were obtained except for the reaction of 1e (Scheme 2 and Table 1). Surprisingly, the naphthalene-substituted tetrahydronaphtho[1,2-b]furan le resisted the photoreaction even for a 5-day UV exposure and, ultimately, the desired dihydro [5] helicene 2e was not isolated (entry 5), presumably due to the steric hindrance between the naphthalene ring and the dihydronaphthalene ring. However, a similar reaction of structurally crowded dihydrofuran such as 1f gave 4-(1-naphthyl)phenanthrene 2f in 94% yield (Scheme 3).

We next examined a similar photoreaction of spirofurans $3a-j^3$ Spiro[furan-2(3*H*),1'-benzocyclohexane] (3a) (0.2 mmol) was irradiated for 1–6 h in acetonitrile (9 mL) containing 2 M hydrochloric acid (1 mL) under an argon atmosphere at room temperature, giving 5-acetyl-6-methyl-2,3-dihydrophenalene (4a) (Scheme 4 and Table 2, entries 1-4).^{4,6} The spirofuran 3a was transformed by the UV irradiation for approximately 3 h into 4a (entry 3). Prolonged irradiation did not change the product distribution (entries 4) similar to the photoreaction of 1a. Therefore, the product 4a might be stable against UV light and 3 h should be enough to complete the photoreaction of the spirofuran 3a. The use of a triplet photosensitizer, such as benzophenone, did not influence the photoreaction at all. Other spiro[furan-2(3H),1'-benzocycloalkane] derivatives **3b**-j³ were next examined under similar reaction conditions (Scheme 4 and Table 2). Although the irradiation of 3b gave the





Table 2. Acid-catalyzed photoreaction of spiro[furan-2(3*H*),1'-ben-zocycloalkane] derivatives 3a-j^a

Entry	Spirofuran	Time (h)	Recovery (%)	Product (yield/%) ^b	
1	3a	1	20	4a (15)	
2	3a	2	7	4a (25)	
3	3a	3	4	4a (31)	
4	3a	6	1	4a (31)	
5	3b	3	5	4b (62)	
6	3c	4	0	4c (44)	
7	3d	18	14	4d (trace)	4d ' (4)
8	3e	12	12	4e (trace)	4d ' (4)
9	3f	6	4	i.m. ^c	
10	3g	3	20	3h (36)	
11	3h	3	40	3g (21)	
12	3i	6	0	4i (12)	
13	3j	24	0	4j (trace)	4j' (trace)

^a The photoreaction of spirofuran **3** (0.2 mmol) was carried out at 23 °C in acetonitrile (9 mL) containing 2 M hydrochloric acid (1 mL) using a 100 W high-pressure mercury lamp.

^b The yield based on the spirofuran 3 used.

 $^{\rm c}$ An intractable mixture was obtained and the desired 4f was not isolated.

corresponding dihydrophenalene **4b** in good yield (entry 5), other spirofurans afforded the benzannulation products in moderate to poor yields (entries 6–8, 12, and 13). Longer reaction times were required to consume the spirofuran esters **3d** and **3e**. However, a small amount of the unusual 6-hydroxydihydrophenalene **4d**' was only isolated along with a trace amount of the desired dihydrophenalene esters **4d** and **4e** (entries 7 and 8). The structure of **4d**' was elucidated by a spectroscopic method and finally X-ray crystallography.⁷ Presumably, the

photodegradation of the ester group might complicate the reaction. Spiro[furan-2(3H),1'-(2',3'-dihydroindene)] 3f was decomposed under the photoreaction conditions, and no products were isolated (entry 9). Very interestingly, the irradiation of 3g for 3 h gave 3h in 36% yield along with the unchanged 3g (20% recovered) (entry 10). On the other hand, a similar irradiation of 3h afforded 3g in 21% yield together with the unchanged 3h (40%) recovered) (entry 11).8 These results indicated that the spirofuran was opened once by the UV irradiation, and recyclized to give the corresponding isomeric spirofuran. That is to say, it supported the assumption that the intermediate formed from 3g and 3h should be the same compound. In addition, it appears that the spirofuran 3h is more stable than 3g under the same conditions, therefore, the equilibrium of the photoisomerization lies with the spirofuran 3h (3g:3h =1:1.8–1.9). In fact, the result was also supported by the PM3 calculation.⁹ 2-Acetyl-3-methyl-1-phenyl-7-oxa-7H-benz[de]anthracene (4i) was also obtained by the photoreaction of 4-acetyl-5-methyl-3-phenylspiro[furan-2(3H),9'-xanthene] (3i) (entry 12). However, the yield of 4i was lower than that of the other photoreaction products 4a-c. Presumably, it might be difficult to cyclize the bulky intermediate. The single crystals of 3i and 4i were measured by X-ray diffraction and the exact structures were determined.⁷ In comparison with these data, it was apparent that the UV irradiation caused a rearrangement of the dihydrofuran ring of 3i into the new aromatic ring of 4i. The result of the reaction of the spiro[furan, xanthene] ester 3j was similar to that of esters 3d and 3e (entry 13).

In order to examine the photoreaction pathway, the ¹H NMR spectrum of the reaction mixture of **3a** was taken just after the 1 h irradiation. As a result, it showed the presence of an enol hydrogen ($\delta = 16.5$ ppm) derived from the corresponding furan ring-opened intermediates (*E*)-**A** and (*Z*)-**B** (Scheme 5). Although the intermediate





Scheme 6.

(E)-A is ca. 3 kcal/mol more stable than (Z)-B based on the PM3 calculation, the intermediate (Z)-B would be cyclized by the acid-catalyzed photoreaction, followed by aromatization accompanying dehydration to give 4a. On the contrary, in the case of 3b ($R^1 = Me$, $R^2 = Ac$, $R^3 = Ph$), the intermediate corresponding to **B** ($\mathbb{R}^3 = \mathbb{Ph}$) should be favorable for the intermediate, such as $A(R^3 = Ph)$, due to the steric repulsion between the R^3 phenyl group and the tetrahydronaphthalene ring,¹⁰ which allowed **4b** to be preferentially produced. Unfortunately, the intermediates, such as A and B, could not be isolated from the reaction mixture, but the corresponding ring-opened dihydronaphthalene 5 was alternatively obtained in 73% yield by the acid-catalyzed decomposition of 1b (Scheme 5).^{3,11} The photoreaction of 5 gave 2b in a better yield (81%) than that of the direct irradiation of 1b (61%) and, furthermore, the reaction time required only 3 h (compared with Table 1, entry 2). Naturally, stirring 5 under similar reaction conditions without UV irradiation did not give any products. Therefore, it strongly supported the supposition that the furan ring-opened products, such as A, B, or 5, must be the intermediate in the photoreaction. In addition, the UV irradiation is essential for the acceleration of both the ring-opening and recyclization step.² In fact, the results of the photoreaction of 7 and 7' could also be explained by the supposition, that is, both naphthalenes 8 and 8' were obtained in a ratio of 3:7 during a similar ring-opened intermediate C (Scheme 6).

It was concluded that the photoreaction of the benzocycloalka[1,2-b]furans 1 and spirofurans 3 in the presence of acid resulted in the hydrohelicene 2 and dihydrophenalene derivatives 4, respectively. The reaction pathway was also explained by the photo-induced cleavage of the carbon–oxygen bond of the furan ring assisted by acid, giving the intermediate, such as (Z)-**B**, which would be intramolecularly cyclized by the photoexcitation, accompanied by the dehydration to provide the final aromatic aggregates. In this connection, the dehydrogenation of **2b** was carried out using DDQ in dry benzene for 3 days to give the [4]helicene **6** having an acetyl and a methyl functionality in 80% yield (Scheme 5).¹²

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Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet. 2005.08.134.

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- 4. The benzocyclopenta[1,2-*b*]furan (1a) or spirofuran 3a (0.2 mmol) was added to a mixture of acetonitrile (9 mL) and 2 M hydrochloric acid (1 mL) in a 10 mL quartz irradiation tube previously purged with argon for a period of 1 min. The tube was sealed with a glass stopper. The solution was then irradiated by a 100 W high-pressure

mercury lamp (Eikohsha EHB-WI-100 lamp) for 6 h using a merry-go-round apparatus. After the irradiation, the mixture was extracted with dichloromethane and the obtained products were separated by silica gel TLC (Wakogel B-10) with diethyl ether-hexane (2:8 v/v) as the developing solvent. The analytical sample was further purified by recrystallization from ethanol.

- 5. 6-Acetyl-5-methyl-7*H*-benzo[*c*]fluorene (**2a**): $R_{\rm f} = 0.76$ (7:3 diethyl ether–hexane); yellow prisms (from ethanol), mp 104.0–105.0 °C; IR (neat) v 1703 (C=O); ¹H NMR (CDCl₃) δ 8.61 (1H, d, J = 8.45 Hz, arom H), 8.19 (1H, d, J = 7.89 Hz, arom H), 7.98 (1H, d, J = 8.45 Hz, arom H), 7.58–7.13 (5H, m, arom H), 3.73 (2H, s, CH₂), 2.54 (3H, s, CH₃), 2.52 (3H, s, COCH₃); ¹³C NMR (CDCl₃) δ 207.1 (C=O), 143.6, 142.0, 137.4, 136.8, 135.3, 132.3, 129.6, 128.0 (arom C), 126.9, 126.8, 125.9, 125.6, 125.2, 124.7, 124.2, 122.7 (arom CH), 36.4 (C-7), 32.3 (COCH₃), 16.4 (CH₃); Anal. Calcd for C₂₀H₁₆O: C, 88.20; H, 5.92. Found: C, 88.40; H, 5.92.
- 6. 5-Acetyl-6-methyl-2,3-dihydrophenalene (4a): $R_{\rm f} = 0.37$ (2:8 diethyl ether–hexane); colorless prisms (from ethanol), mp 55.5–56.0 °C; IR (CHCl₃) v 1685 (C=O); ¹H NMR (CDCl₃) δ 7.97 (1H, d, J = 8.64 Hz, arom H), 7.46 (1H, dd, J = 8.64, 6.98 Hz, arom H), 7.32–7.27 (2H, m, arom H), 3.10 (4H, dd, J = 11.94, 5.88 Hz, CH₂ × 2), 2.72 (3H, s, CH₃), 2.63 (3H, s, COCH₃), 2.12–2.02 (2H, m, CH₂); ¹³C NMR (CDCl₃) δ 204.8 (C=O), 136.8, 136.7, 134.4, 133.2, 130.9, 130.8 (arom C), 126.1, 125.4, 123.3, 121.8 (arom CH), 31.5 (C-3), 31.4 (C-1), 31.0 (COCH₃), 23.1 (C-2), 15.8 (CH₃); MS m/z (rel intensity), 224 (M⁺, 63), 210 (17), 209 (100), 181 (39), 165 (48), 152 (18), 76 (13), 43 (17). Anal. Calcd for C₁₆H₁₆O: C, 85.68; H, 7.19. Found: C, 85.58; H, 7.30.
- The X-ray crystallographic data of 3i, 4d', and 4i have been deposited as supplementary publication numbers CCDC249342, CCDC251416, and CCDC251415, respectively. Copies of the data can be obtained, free of charge, on application to CCDC, 12 Union Road, Cambridge, CB2 1EZ, UK [fax: +44(0) 1223 336033 or e-mail: deposit@ccdc.cam.ac.uk].
- 8. The blank experiment of **3h** was conducted in the same reaction media for 36 h in the dark to afford **3g** in only 9% yield.
- 9. The heats of formations for 3g and 3h were revealed to be -21.7 and -22.7 kcal/mol, respectively, based on the PM3 calculations. The PM3 calculations were performed by CAChe Work System version 4.9.3.
- 10. The ring-opened intermediate corresponding to **B** $(\mathbf{R}^3 = \mathbf{Ph})$ from **3b** was ca. 12 kcal/mol more stable than the intermediate, such as **A** $(\mathbf{R}^3 = \mathbf{Ph})$, according to the PM3 calculation.
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