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Reaction of 2-Pentene-1,4-diones with Cyclic 1,3-Dicarbonyl Compounds in the Presence of BF_3 and the Related Reaction

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Abstract— The reaction of 2-pentene-1,4-diones as a building block with cyclic 1,3-dicarbonyl compounds gave furo[3,2-*b*]benzofuran-8(7*H*)-ones and/or 2-(acetyl-2-hydroxy-1-propenyl)-6,7-dihydrobenzofuran-4(5*H*)-ones in good yields. The obtained 2-(acetyl-2-hydroxy-1-propenyl)-6,7-dihydrobenzofuran-4(5*H*)-ones underwent the photocyclization to produce benzo[*b*]naphtho[1,2-*d*]furan-11(8*H*)-ones in quantitative yields.

Keywords: Lewis acid; heterocyclic compounds; furobenzofuranones; photocyclization; benzonaphthofurans

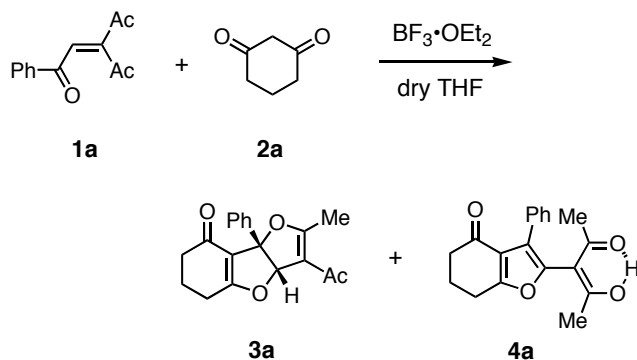
1. Introduction

Furans and their derivatives are widely present in nature and not only one of the most important heterocyclic compounds in organic chemistry, but also building blocks which are essential for the total synthesis of the complicated naturally occurring metabolites.¹ Polyfunctionalized furans are versatile and useful synthetic starting materials for the preparation of a variety of heterocyclic and acyclic compounds.² It is also well-known that furans are used in acid-catalyzed hydrolysis, autoxidation, Diels-Alder reaction, photocyclization, hydrogenation, substitution, and so on.³ Recently, Onitsuka et al. reported that endoperoxide intermediates obtained by the photosensitized oxygenation of furans were selectively transformed into 2-pentene-1,4-diones **1** and oxiranes by the hydrolysis.⁴ The enediones **1** were not stable in air due to an extremely electron-deficient alkene so that they were highly reactive. Since the acid-catalyzed cyclization of 1,4-diketones are well-known, the BF_3 -catalyzed cyclization of the enediones **1** was examined. In the presence of a weak nucleophile such as water, the BF_3 -catalyzed cyclization of enediones **1** gave bis(furyl)methanes together with small amounts of the reduction products. On the other hand, in the case of a strong nucleophile such as 1,3-diketone- BF_3 enolate complex, the reaction gave the trisubstituted furans under reflux conditions and the tetrasubstituted furans at 0 °C. Moreover, when the 2-pentene-1,4-diones **1** were allowed to react with acetoacetamides under high concentrated conditions in THF at 0 °C, 2,6-dioxabicyclo-

[3.3.0]octenes were obtained. The 2,6-Dioxabicyclo[3.3.0]-octene derivatives were found in nature as various metabolites and biologically active substances. The skeleton is important from the standpoint of a total synthesis of natural products.⁵ In this study, the reaction of 2-pentene-1,4-diones **1** as a building block developed by our laboratory with various cyclic 1,3-dicarbonyl compounds **2** in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ was examined. In addition, since the photoreaction of 2,6-dioxabicyclo[3.3.0]octenes in the presence of acid gave naphtho[2,1-*b*]furans along with a small amount of tetrasubstituted furans as the intermediate,⁶ the photoreaction of 6,7-dihydrobenzofurans prepared by the acid-catalyzed decomposition of the products was also investigated.

2. Results and Discussion

The reaction of 2-pentene-1,4-diones **1** with various cyclic 1,3-dicarbonyl compounds **2** was carried out in the presence of $\text{BF}_3 \cdot \text{OEt}_2$ in dry THF under various reaction conditions. The reaction of 3-acetyl-1-phenyl-2-pentene-1,4-dione (**1a**) with 1,3-cyclohexanedione (**2a**) at room temperature at the molar ratio of **1a**:**2a**: BF_3 = 1:10:1 gave



Scheme 1

Table 1. Reaction of **1a** with **2a** in the Presence of Boron Trifluoride^{a)}

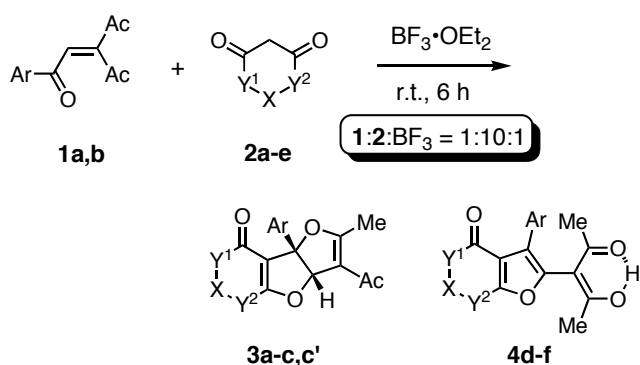
Entry	1a : 2a : BF_3	THF /mL	Temp/ °C	Time/ h	Product yield/%	
					3a	4a
1	1:10:1	0.5	0	12	71	trace
2	1:10:1	0.5	rt	12	90	9
3	1:10:1	0.5	rt	6	91	6
4	1:10:1	0.5	rt	3	82	-
5	1:10:1	0.5	reflux	6	-	52
6	1:10:1	1	rt	6	82	trace
7	1:10:1	5	rt	6	71	-
8	1:3:1	0.5	rt	6	79	trace
9	1:1:1	0.5	rt	6	31	trace
10	1:10:2	0.5	rt	6	80	9
11 ^{b)}	1:10:1	0.5	rt	6	86	5

a) The reaction of **1a** (0.5 mmol) with **2a** was carried out in the presence of $\text{BF}_3 \cdot \text{OEt}$ in dry THF.

b) $\text{BF}_3 \cdot \text{THF}$ was used.

3a,5,6,8b-tetrahydrofuro[3,2-*b*]benzofuran-8(7*H*)-one **3a** in a 91 % yield together with 6,7-dihydrobenzofuran-4(5*H*)-one **4a** as a by-product (Scheme 1 and Table 1).

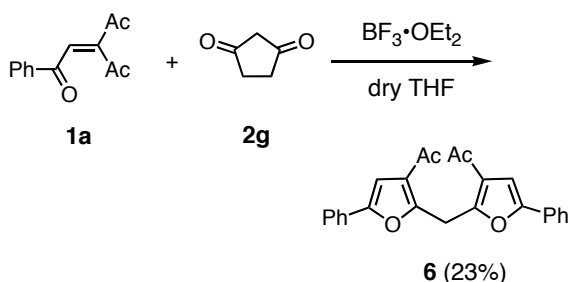
A similar reaction using other cyclic 1,3-dicarbonyl compounds such as dimedone (**2b**), 4,4-dimethyl-1,3-cyclohexanedione (**2c**), 1,3-dimethyl-barbituric acid (**2d**), 1,3-diethyl-2-thiobarbituric acid (**2e**) was next examined. As a result, tricyclic compounds **3b**, **3c**, **3c'**, and bicyclic compounds **4d**, **4e**, **4f** were obtained in good yields (84 %, 47 %, 30 %, 98 %, 54 %, and 67 %, respectively) (Scheme 2).



- 3a** : Ar = Ph, X = Y = CH₂ (91%)
3b : Ar = Ph, X = CMe₂, Y = CH₂ (84%)
3c : Ar = Ph, X = Y² = CH₂, Y¹ = CMe₂ (47%)
3c' : Ar = Ph, X = Y¹ = CH₂, Y² = CMe₂ (30%)
4d : Ar = Ph, X = CO, Y = NMe (98%)
4e : Ar = Ph, X = CS, Y = NEt (54%)
4f : Ar = 4-MeO-C₆H₄, X = Y = CH₂ (67%)

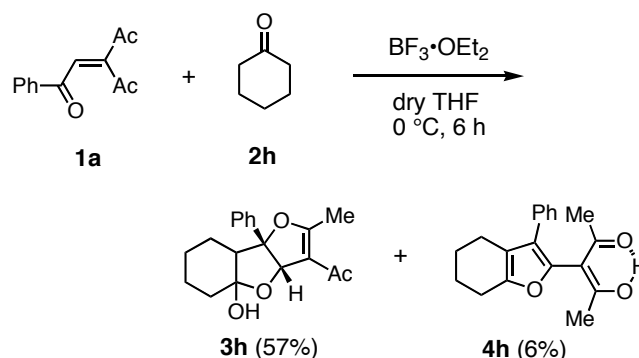
Scheme 2

However, the reaction of 2-pentene-1,4-dione **1a** with 1,3-cyclopentanedione (**2g**) only gave bis(furyl)-methane **6** in low yield. It was considered that since 1,3-cyclopentanedione (**2g**) is present as a keto form under ambient conditions and 1,3-cyclohexanedione (**2a**) as a enol form, 1,3-cyclopentanedione (**2g**) may be hard to react with 2-pentene-1,4-dione (**1a**) (Scheme 3).



Scheme 3

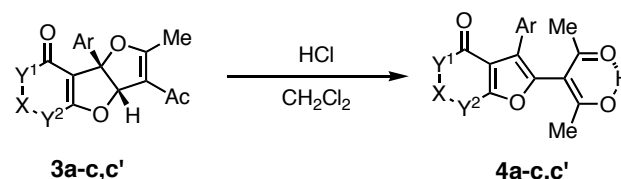
In order to apply the reaction, the reaction of cyclohexanone was also conducted under the same reaction conditions, giving tricyclic compound **3h** and bicyclic



Scheme 4

compound **4h** (Scheme 4).

Finally, we investigated the photoreaction of 6,7-dihydrobenzofuran-4(5*H*)-ones **4**. In order to prepare the 6,7-dihydrobenzofuran-4(5*H*)-ones **4**, the tricyclic compounds **3a-c,c'** were treated with concentrated hydrochloric acid in dichloromethane to produce the corresponding benzofuranones **4a-c,c'** (Scheme 5).



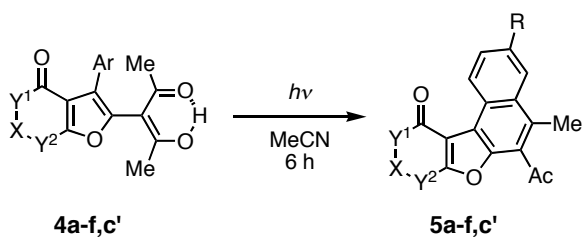
- 4a** : Ar = Ph, X = Y = CH₂ (85%)
4b : Ar = Ph, X = CMe₂, Y = CH₂ (85%)
4c : Ar = Ph, X = Y² = CH₂, Y¹ = CMe₂ (81%)
4c' : Ar = Ph, X = Y¹ = CH₂, Y² = CMe₂ (78%)

Scheme 5

With 6,7-dihydrobenzofuran-4(5*H*)-ones **4** in hand, the photoreaction of **4a-f,c'** was carried out in acetonitrile under an argon atmosphere at room temperature using a 100-W high-pressure mercury lamp in a quartz cell to give benzo[*b*]naphtho[1,2-*d*]furan derivatives **5** in good to quantitative yields (Scheme 6).

3. Conclusion

When the 2-pentene-1,4-diones **1a,b** were allowed to react with cyclic 1,3-dicarbonyl compounds **2a-e** and cyclohexanone **2h** in dry THF at room temperature at the molar ratio of **1:2:BF₃** = 1:10:1, the synthesis of the furo[3,2-*b*]benzofurans **3a-c',3h** and the benzofurans **4d-f**



5a : R = H, X = Y = CH ₂	(75%)
5b : R = H, X = CMe ₂ , Y = CH ₂	(94%)
5c : R = H, X = Y ² = CH ₂ , Y ¹ = CMe ₂	(77%)
5c' : R = H, X = Y ¹ = CH ₂ , Y ² = CMe ₂	(96%)
5d : R = H, X = CO, Y = NMe	(92%)
5e : R = H, X = CS, Y = NEt	(96%)
5f : R = OMe, X = Y = CH ₂	(66%)

Scheme 6

was achieved in high yields. In the case of 1,3-cyclopentanedione (**2g**), the bis(furyl)methane **6** was only produced. In addition, the photocyclization of the obtained benzofuran derivatives **4** resulted in the benzo[*b*]naphtho[1,2-*d*]furans **5** in excellent yield.

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