Direct Syntheses of Benzofuran-2(3*H*)-ones and Benzofuran-3(2*H*)-ones from 1-(2-Hydroxyphenyl)alkan-1-ones by $CuBr_2$ or $CuCl_2$

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New syntheses of benzofuran-2(3*H*)-ones and benzofuran-3(2*H*)-ones from 1-(2-hydroxyphenyl)alkan-1-ones via oxidative cyclization by $CuBr_2$ or $CuCl_2$ are described. A new synthesis of 1*H*-isochromene-1,4(3*H*)-diones via similar procedures is also described.

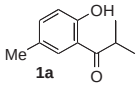
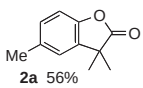
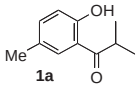
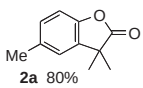
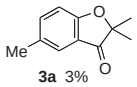
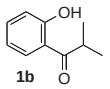
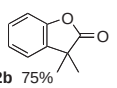
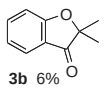
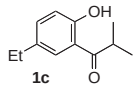
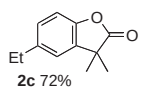
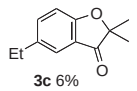
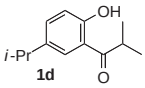
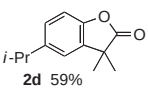
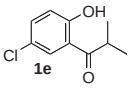
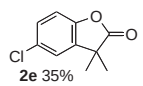
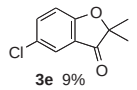
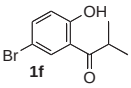
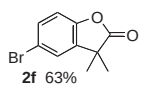
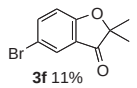
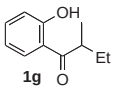
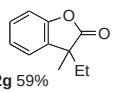
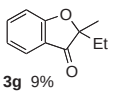
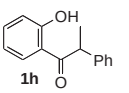
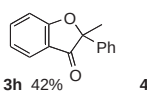
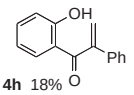
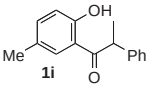
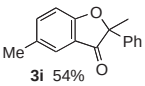
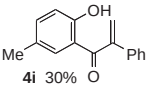
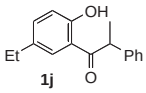
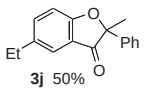
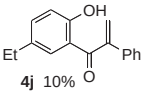
Oxidative reactions using $CuBr_2$ are useful in organic synthesis.[1] The reaction with aromatic ketone in $CHCl_3$–AcOEt is an especially useful method for chemoselective α-bromination.[2] In this paper, we report new types of reactions of aromatic ketones with $CuBr_2$ or $CuCl_2$.

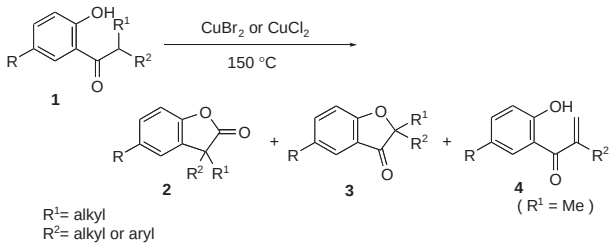
When 1-(2-hydroxyphenyl)alkan-1-ones (**1**) were treated with $CuBr_2$ or $CuCl_2$ in ethylene glycol (EG) or di(ethyleneglycol) dimethyl ether (2-methoxyethyl ether: MEE) at 150 °C, oxidative cyclization occurred to give benzofuran-2(3*H*)-ones (**2**), benzofuran-3(2*H*)-ones (**3**), and α-methyleneketone (**4**)[3] (Scheme 1). The ratio of **2**, **3**, and **4** depends on the structure of **1** and the reaction conditions. Results are summarized in Table 1.

When both R^1 and R^2 are alkyl groups, **2** was obtained as a major product, and in most cases a small amount of **3** was also obtained. The reaction, which produced **2**, proceeded with a migration of the aryl group (1,2-aryl shift). On the other hand, when the R^2 is phenyl group, 1,2-aryl shift did not occur to yield **3** and a small amount of **4**. Similar examples of the 1,2-aryl shift of acetophenone derivatives have already been reported. For example, $ZnBr_2$,[4] Ag_2CO_3,[5a] and $AgBF_4$[5b] promote the 1,2-aryl shift of aromatic α-bromoketones. Thallium(III) nitrate[6] and lead(IV) acetate[7] promote the oxidative 1,2-aryl shift of acetophenone. Because of the similarity to our results, the photoalcoholysis of aromatic α-haloketones by Tomioka et al.[8] is quite interesting. When aromatic α-haloketones were irradiated with 300-W high-pressure Hg lamp, three different types of reactions occured: (1) 1,2-aryl shift, (2) cyclization without 1,2-aryl shift, and (3) elimination to give α-methyleneketone;[8] all also occurred in our experiments. This suggests that the photoalcoholysis of aromatic α-haloketones and our CuX_2-mediated reaction proceed in somehow similar mechanisms. Tomioka suggested that an intermediate of the photoalcoholysis was a keto cation, which is generated via an electron transfer between keto radical and Br•. The mechanism of CuX_2-mediated reaction can also be explained in this context. The tentative mechanism is as follows (Scheme 2).

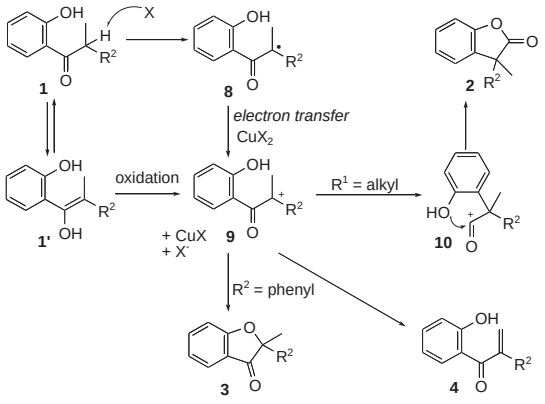
Initially, halogen radical X• generated from CuX_2 (or X_2 generated from CuX_2) abstract the *a*-hydrogen of **1** to give radical **8**. Single electron transfer from **8** to CuX_2 gives keto cation **9**, CuX, and X^-. An oxidation of enol **1′** is also plausible route to

Table 1. Oxidative reactions of aromatic α-haloketones

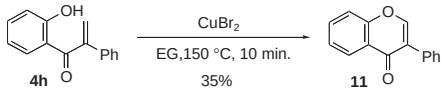
Substrate (**1**)	CuX_2 (equiv.) Solvent Conditions	Products Isolated yield/%	
 **1a**	$CuBr_2$ (2) EG 150 °C, 10 min.	 **2a** 56%	
 **1a**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2a** 80%	 **3a** 3%
 **1b**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2b** 75%	 **3b** 6%
 **1c**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2c** 72%	 **3c** 6%
 **1d**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2d** 59%	
 **1e**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2e** 35%	 **3e** 9%
 **1f**	$CuCl_2$ (3) EG 180 °C, 30 min.	 **2f** 63%	 **3f** 11%
 **1g**	$CuCl_2$ (3) EG 150 °C, 60 min.	 **2g** 59%	 **3g** 9%
 **1h**	$CuBr_2$ (2) MEE 150 °C, 10 min.	 **3h** 42%	 **4h** 18%
 **1i**	$CuBr_2$ (2) MEE 150 °C, 10 min.	 **3i** 54%	 **4i** 30%
 **1j**	$CuBr_2$ (2) MEE 150 °C, 10 min.	 **3j** 50%	 **4j** 10%



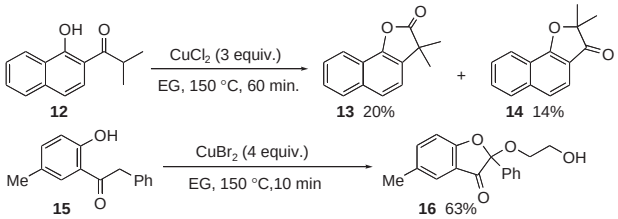
Scheme 1.



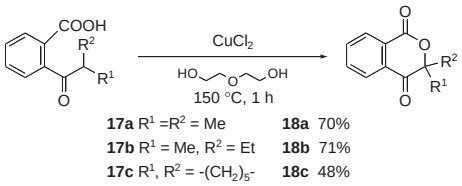
Scheme 2.



Scheme 3.



Scheme 4.



Scheme 5.

9. When both R^1 and R^2 are alkyl groups, the keto cation **9** is not stable and isomerise to the more stable acyl cation **10** presumably through an arenium ion intermediate. The following intramolecular nucleophilic attack of hydroxy group gives **2**. When R^2 is phenyl group, the cation **9** is stabilized by the phenyl group, and the 1,2-aryl shift lose a driving force, and the following reactions proceed without migration of the aryl group. The intramolecular nucleophilic attack of an oxygen atom of the hydroxy group produces **3**, and E1-type elimination produces **4**.

Note that the α-methylene ketone **4** is not an intermediate in this reaction. When **4h** was treated with $CuBr_2$, isoflavone (**11**) was obtained as a main product, but not **3h** (Scheme 3).

Naphthalene derivative **12** also reacted with $CuCl_2$ under similar conditions to give **13** and **14** (Scheme 4). However, probably due to the difficulty of the migration of the naphthyl group, the yield of lactone **13** is lower than the examples of acetophenone derivatives **1a**–**1g**. When R′ is a hydrogen, the reaction with 2 equiv. of $CuBr_2$ usually gave a mixture of unidentified products, probably because of further oxidative reactions. However, benzylketone **15** was gave acetal **16** in 63% yield by the reaction with 4 equiv. of $CuBr_2$ in EG (Scheme 4).

Similarly, 2-carboxy acetophenones **17** reacted with $CuCl_2$ under similar conditions to yield 1*H*-isochromene-1,4(3*H*)-diones **18** (Scheme 5). In these cases, 1,2-aryl shift was not observed. The cationic migration of the aryl group was suppressed, probably reflecting the electron-withdrawing effect of the carboxy group.

In conclusion, oxidative cyclization of 1-(2-hydroxyphenyl)alkan-1-ones with $CuBr_2$ or $CuCl_2$ is useful for the synthesis of benzofuran-2(3*H*)-ones and benzofuran-3(2*H*)-ones. Generally speaking, $CuCl_2$ is less reactive than $CuBr_2$ for the reactions described above. And $CuCl_2$ usually gave better results.

As typical procedures, the synthesis of **2a** and **3a** by the reaction of **1a** with $CuCl_2$ is described as follows. An ethyleneglycol (5 mL) solution of **1a** (0.36 g, 2.0 mmol) and $CuCl_2$ (0.80 g, 6.0 mmol) was stirred at 150 °C for 60 min. The mixture was poured into water (20 mL), and extracted with ethyl acetate. After usual work-up, it was purified by column chromatography on silica gel to give **2a** (0.28 g, 1.6 mmol) in 80% yield and **3a** (0.010 g, 0.056 mmol) in 3% yield.

References and Notes

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