Direct Syntheses of Benzofuran-2(3*H*)-ones and Benzofuran-3(2*H*)-ones from 1-(2-Hydroxyphenyl)alkan-1-ones by CuBr₂ or CuCl₂

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New syntheses of benzofuran-2(3H)-ones and benzofuran-3(2H)-ones from 1-(2-hydroxyphenyl)alkan-1-ones via oxidative cyclization by CuBr₂ or CuCl₂ 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 CuBr₂ or CuCl₂ 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, ZnBr₂,⁴ Ag₂CO₃,^{5a} and AgBF₄^{5b} promote the 1,2-aryl shift of aromatic α -bromoketones. Thallium(III) nitrate⁶ and lead(IV) acetate⁷ 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 CuX₂-mediated reaction



Scheme 1.

Table	1.	Oxidative	reactions	OI	aromatic	α -naloketones



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



Scheme 3.

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 CuBr₂, 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 CuBr₂ 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 CuBr₂ 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-hydroxy-phenyl)alkan-1-ones with CuBr₂ or CuCl₂ is useful for the synthesis of benzofuran-2(3*H*)-ones and benzofuran-3(2*H*)-ones. Generally speaking, CuCl₂ is less reactive than CuBr₂ for the reactions described above. And CuCl₂ usually gave better results.

As typical procedures, the synthesis of 2a and 3a by the reaction of 1a with CuCl₂ is described as follows. An ethyleneglycol (5 mL) solution of 1a (0.36 g, 2.0 mmol) and CuCl₂ (0.80 g, 6.0 mmol) was stirred at 150 °C for 60 min. The mixture was



Scheme 5.

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.

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