Tetrahedron Letters 49 (2008) 5336–5338

Contents lists available at ScienceDirect

Tetrahedron Letters

journal homepage: www.elsevier.com/locate/tetlet

Cesium hydroxide-promoted aerobic oxidation of *sec*-aromatic alcohols

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ARTICLE INFO

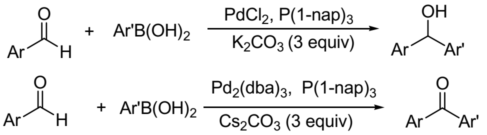
Article history:
Received 13 February 2008
Revised 10 June 2008
Accepted 13 June 2008
Available online 18 June 2008

Keywords:
Diarylketone
Cesium hydroxide
Aerobic oxidation
sec-Aromatic alcohol
Aryl ketones

ABSTRACT

A CsOH-promoted aerobic oxidation of *sec*-aromatic alcohols has been developed, using air as a free and clean oxidant, and providing aryl ketones in good to excellent yields.

The oxidation of *sec*-alcohols into ketones is one of the most important functional group transformation reactions in organic chemistry. In the past decades, much attention has been paid to develop efficient methods for this transformation.[1] Many stoichiometric oxidants, such as chromium(VI) and manganese reagents, were employed.[2] Considering environmental and economic demands, developing relative clean and efficient methods has been a highly desired goal in organic synthesis. Molecular oxygen usually plays an important role in the oxidation reaction.[3] Lately, many examples of using copper,[4] palladium[5] and ruthenium[6] catalysts for such kind of oxidation reactions using molecular oxygen or air have been reported. Very recently, the efficient non-equivalent for activation of molecular oxygen and its application in aerobic alcohol oxidation described by Hu is of great interest due to the obviation of transition metal.[7]

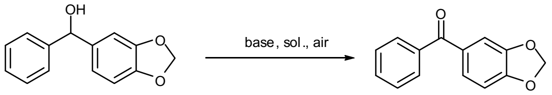


(1)

In our previous work, we found that the combination of K_2CO_3, $PdCl_2$ and $P(1\text{-nap})_3$ in THF could efficiently catalyze the reaction of aryl aldehydes with aryl boronic acids, providing the carbinol derivatives in good yield. During the researching process, we found that aryl ketones were formed. Interestingly, the employment of Cs_2CO_3 instead of K_2CO_3 provides the aryl ketones in moderate to good yields under air (Eq. 1).[8] The desired products were at least partly oxidized from the corresponding secondary alcohol, which was formed in situ by the addition of organoboronic acids to aldehydes. Herein, we wish to explore the feasibility of catalytic amount of base-promoted aerobic oxidation of *sec*-aryl alcohol.

Initially, we studied the aerobic oxidation of benzo[*d*][1,3]dioxol-5-yl(phenyl)methanol in the presence of a series of bases in the common organic solvents. The results are summarized in Table 1. At first, weak bases such as CsF, K_2CO_3 and Cs_2CO_3 were tested in the transformation. Much to our disappointment, these weak bases

Table 1
Screen of the base in aerobic oxidation of carbinol[a]



Entry	Base	Equiv	Solvent	Yield[b] (%)
1	KOH	0.4	Toluene	84
2	KOH	0.2	Toluene	26
3[b]	CsOH	0.2	Toluene	82
4	NaOH	0.2	Toluene	77
5	CsF	0.2	Toluene	<5
6	K_2CO_3	0.2	Toluene	<5
7	Cs_2CO_3	0.2	Toluene	<5
7	$K_3PO_4{\cdot}3H_2O$	0.2	Toluene	<5
8	CsOH	0.2	THF	10
9	CsOH	0.2	CH_3CN	11
10	CsOH	0.2	Dioxane	<5
11	CsOH	0.2	EtOH	<5

[a] All reactions were run under air in the presence of indicated amounts of base in indicated solvents under refluxing for 24 h.
[b] Isolated yield.

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0040-4039/$ - see front matter © 2008 Published by Elsevier Ltd.
doi:10.1016/j.tetlet.2008.06.061

were totally ineffective. So we employed several strong bases to test the activity. In the presence of 0.4 equiv KOH, 84% of the product was isolated. However, the yield dramatically decreased to 26% in the presence of 0.2 equiv of KOH. Surprisingly, 82% and 77% products were formed in the presence of 0.2 equiv of CsOH and NaOH, respectively. Solvents also played important roles in the oxidation reaction. Among the tested common organic solvents, toluene was the best. At last, the optimal reaction condition was to use 0.2 equiv of CsOH in toluene under air.

With the optimized reaction conditions in hand, a series of substrates were subjected to broaden the substrates scope (Fig. 1). The electronic effect of the substitution groups on the aryl ring was not obvious in the reaction. The carbinol derivatives possessing both electron-withdrawing groups and electron-donating groups ran smoothly, and provided corresponding aryl ketones in good to excellent yields. The hindrance in the *ortho*-position of the aryl group had little effects on the yield such as **2j** and **2k** were isolated in 97% and 82% yields, respectively. The hetero-carbinol derivatives such as **1m**, **1n**, **1o** were also good substrates in the reaction. 1-(Naphthalen-1-yl)ethanol **1p** and 1-(*p*-phenyl)phenylethanol **1q** also ran smoothly, and the products were isolated in moderate yields. Interestingly, **1l** could proceed smoothly to deliver the product **2l** in 70% isolated yield. 2-Hydroxy-1,2-di-tolylethanone was also a good reaction partner and **2r** was formed in 74% yield. However, alkyl alcohols, such as cyclohexanol did not work under this condition. The reaction could run under N_2, and 84% yield of benzophenone was isolated in the presence of 1.0 equiv of CsOH.

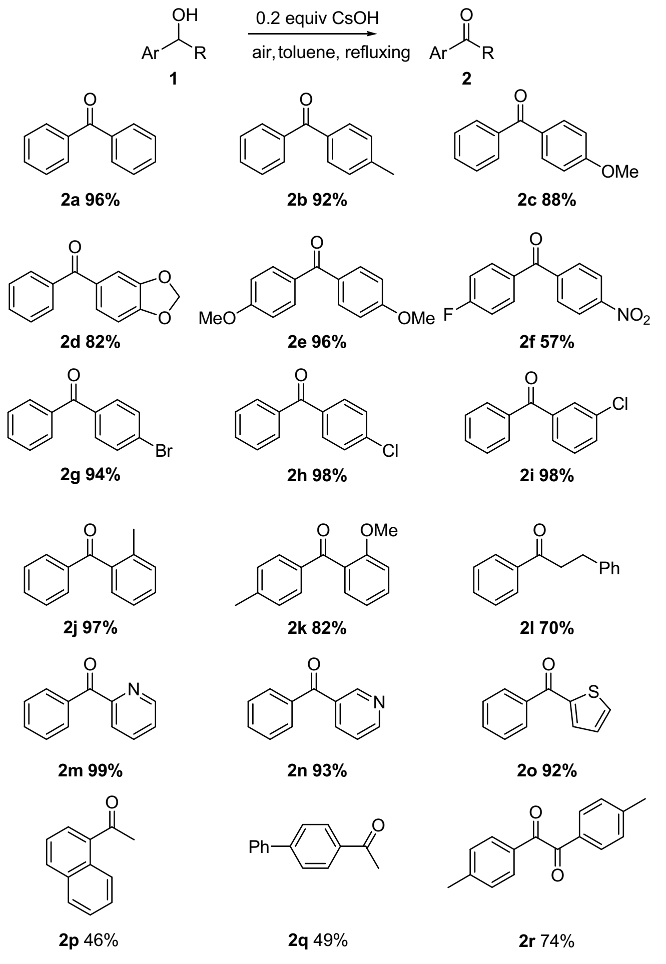

Figure 1. Cesium hydroxide-promoted aerobic oxidation of *sec*-aromatic alcohols. Reagents and conditions: carbinol (0.5 mmol), CsOH (15 mg, 0.1 mmol), toulene (3 mL), under air at 110 °C for 24 h. Isolated yield.

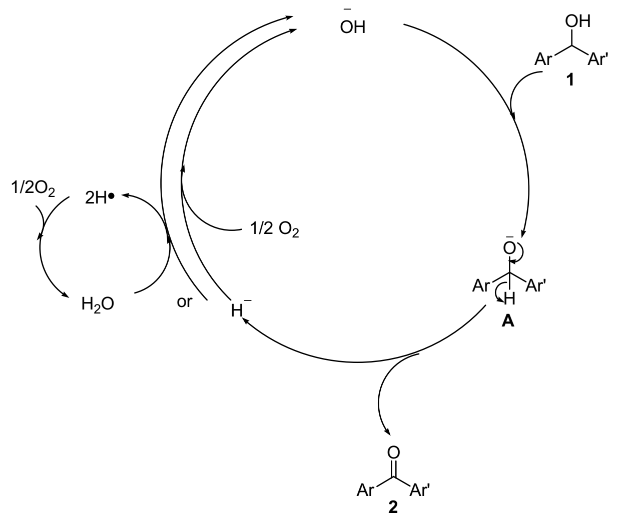

Figure 2. Plausible mechanism.

A plausible mechanism was proposed, as shown in Figure 2.

The catalytic cycle might contain three steps: (1) carbinol could undergo deprotonation to form intermediate **A**; (2) intermediate **A** could extrude a H^- to form the oxidation product;[9] (3) the formed H^- either could react with O_2 to form OH^- or could undergo direct hydrolysis to form OH^- and 2 mol of atomic hydrogens, which could react with O_2 to form H_2O. A radical pathway could not be ruled out either.

In conclusion, a CsOH-promoted aerobic oxidation of *sec*-aromatic alcohols has been developed, providing corresponding ketones in good to excellent yields. Both the use of air as a free and environment-friendly oxidant and the obviation of transition-metal catalyst all consist of the charming characters in this procedure.[10]

Acknowledgement

We thank the National Natural Science Foundation of China (No. 20504023) for financial support.

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2008.06.061.

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10. *General procedure:* Under air, a reaction tube was charged with CsOH (14.9 mg, 20 mol %), *sec*-aromatic alcohol (0.5 mmol) and toluene (3 mL). The mixture was heated under air at 110 °C for 24 h, then cooled to room temperature. The mixture was concentrated in vacuo and the residue was purified by flash column chromatography on a silica gel to give the desired product.