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New protocol of copper-catalyzed oxidative C(CO)—C bond cleavage of aryl and aliphatic ketones to organic acids using O_2 as the terminal oxidant

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ABSTRACT

Catalytic oxidation of C—C bond is a key technology to transform petroleum-based as well as sustainable biomass feedstock into more valuable oxygenates. We herein describe a convenient and useful oxidation strategy of converting ketones into carboxylic acids using homogeneous copper catalyst without additives and with O_2 as the terminal oxidant. A wide range of aryl and aliphatic ketones as well as β–O–4 lignin models were selectively oxidized to acids via C—C bond cleavage. Mechanism studies by EPR and in situ NMR elucidate the principles of Cu/O_2 reactivity that involves C—H bond and O_2 activation via a peroxide species. This provides an important foundation for expanding the scope of useful aerobic oxidation reactions using copper catalysts.

1. Introduction

The selective oxidation of C—C bonds and the use of O_2 as a stoichiometric oxidant represent two prominent challenges in catalysis [1]. Copper has demonstrated excellent activity in aerobically oxidative functionalization of C—C bonds, especially for direct transformation of ketones recently. For example, ketone α-C—C bond conversion renders the synthesis of versatile functionalized compounds, such as aldehydes [2,3], amides [4–6], nitriles [7–9], and esters [10–12]. On the other hand, direct C—C bond oxidative cleavage of ketones to carboxylic acids has not been reported using copper catalyst under additive-free conditions.

Direct conversion of ketone to acid using O_2 as the terminal oxidant is an attractive and challenging pathway. Precedents of ketones to acids conversion either use electron-rich ketone substrates featuring electron-transfer to catalytic sites or require additives to activate inert ketone C—C bond or use non-green oxidants [13–15]. For instance, hypervalent iodine compound, or sequential reaction with urea and H_2O_2 in ionic liquids was used for the conversion of aryl ketones to acids [16–18]. Only two metal catalysts (Rh and Mn) have been reported for ketone oxidation in acetic acid [19–22]. A recent example reports a metal-free approach but requires the mixture of ozone and trifluoroacetic acid [23]. An excellent work by Pochampalli and co-workers reports the conversion of aryl/alkyl/vinyl ketones to aromatic acids, but NH_2OH is indispensable to activate ketones via oxime intermediates [24]. Therefore, a direct, efficient catalytic system that can convert ketones to acids in high selectivity using O_2 as the oxidant needs to be developed, which involves the cleavage of robust C—C bond.

The activation of O_2 and oxidation of C—H bond are usually the most important procedures during the Cu-catalyzed oxidation and oxygenation reactions [25–33]. In general, base additives are essential to promote hydrogen abstraction. Besides, organic ligands are usually indispensable for generating active copper complex cores with O_2. Therefore, it is difficult to achieve the direct C—C cleavage with single copper catalyst. Meanwhile, excellent works and mechanistic insights have proposed metal-free transformation of diarylethanones to arylmethanoic acids promoted by base [34], or copper catalyzed ketone transformations to esters and amides [4,6,10–12,35]. And for simple aryl methyl ketones to carboxylic acids through C—C cleavage, there is no systematic report about the applications and mechanism of this transformation catalyzed by copper with O_2.

We here demonstrate the Cu-catalyzed C(CO)—C bond cleavage without any base additive or additional complex ligand (Scheme 1). As a continuation of our previous work on cleavage of C—C bond at interfacial CuO-Cu_2O sites [36,37], we here report an unexpected and remarkably active and selective C—C cleavage by $Cu(NO_3)_2$

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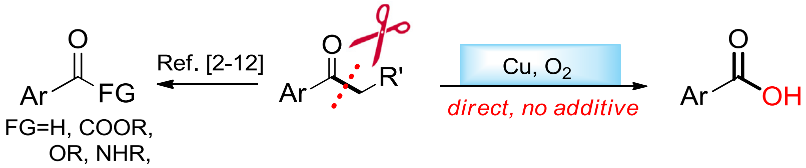

Scheme 1. The Cu-catalyzed C(CO)–C(α) bond cleavage of ketones.

catalyst, which is easily reached in laboratory, cheap to use in industry and safe to handle. The copper catalyst is highly effective for the oxidative cleavage of aryl ketones, aliphatic ketones as well as sustainable lignin β-O-4 ketones to acids in acetonitrile. Mechanistic studies show that ketone is activated by $Cu(NO_3)_2$ catalyst via a single electron transfer process, with the following multiple-step oxidation and C—C cleavage on copper site giving the final acid.

2. Experimental

2.1. Materials

All reagents were of analytical-reagent grade purchased from Aladdin, Alfa, and J&K Chemicals, and were used without further purification.

2.2. Experimental procedures

2.2.1. The oxidation of acetophenone and substituted aryl ketones

The catalytic reactions were performed in a 15-mL autoclave reactor with an internal Teflon insert. Typically, 0.5 mmol of ketone, 0.1 mmol of copper salt and 2 mL of solvent were added into the reactor. Then, the reactor was charged with 0.6 MPa O_2 and heated to 120 °C under magnetic stirring. After cooling to the room temperature, the reaction mixture was diluted with 4 mL methanol before analysis. The products were identified and quantified using gas chromatography-mass spectrometry (GC–MS) and an Agilent 7890A/5975C instrument equipped with an HP-5 MS column (30 m in length, 0.25 mm in diameter). p-Xylene was used as the internal standard.

2.2.2. The oxidation of *β*–O–4 and *β*–1 lignin model ketones procedure for preparation of 2-phenoxy-1-phenylethanone (***4a***)

2-Phenoxy-1-phenylethanone was prepared by the literature procedures [38,39]. A 350 mL pressure bottle was charged with phenol (6.9 g, 73 mmol) and K_2CO_3 (10.4 g, 75 mmol) in acetone (150 mL) in Ar atmosphere and stirred at room temperature (RT) for 30 min. To this solution, 2-bromoacetophenone (14.0 g, 70 mmol) was added, and the resulting suspension was stirred at RT for 16 h, after which the suspension was filtered and concentrated *in cacuo*. The solid was dissolved in ethyl acetate and washed with NaOH aqueous (5%, 30 mL) and water (30 mL). The organic phase was dried over anhydrous Na_2SO_4. The crude product was recrystallized from ethanol to give 2-phenoxy-1-phenylethanone as a white solid in 87% yield. Spectral data were in accordance with those previously reported. For the other methoxyl substituted 2-phenoxy-1-phenylethanone, the preparation procedure is the same as described above, except for using different stating materials.

The procedure and product detection methods for the oxidation reactions were unchanged, while the amount of substrate was reduced to 0.1 mmol, with the molar ratio of catalysts and substrates consistent with the optimized conditions.

2.2.3. The oxidation of aliphatic methyl ketones

The procedures and amounts of materials were the same as depicted above. After reactions, the mixture was diluted with 0.005 M H_2SO_4 aqueous solution to certain volume. The products were identified and quantified using High Performance Liquid Chromatography (HPLC) of an Agilent 1260 Infinity System equipped with an Hi-plex H column (8 um, 300 $*$ 7.7 mm), using external standard method with RID and UV (210 nm) detectors.

For the oxidation of acetone, 2-pentanone and 2-heptanone, the product yield was quantified using HPLC (data shown in Scheme S1).

$$\text{Yield of acid} = \frac{\text{moles of certain carboxylic acid product}}{\text{moles of substrate}}$$

$$\text{YC} = \text{Yield of carbon} = \frac{\text{moles of carbon atoms in acid product}}{\text{total moles of carbon atoms in substrate}}$$

TYC means the total yield of carbon for all the carboxylic acid products.

2.3. The analytical procedure

2.3.1. The detection of reaction compounds

For aryl ketones, the carboxylic acid products were esterified to the methyl esters before analysis using GC–MS. After cooling to room temperature, excess amount of absolute methanol and catalytic amount of H_2SO_4 were added and refluxed for 6 h, and then the esterified sample was analyzed and quantified using GC–MS and GC. The typical GC traces of the product analysis (oxidation of acetophenone for 3 h) are shown in Figs. S1 and S2. As for the isolated yield, after the autoclave was cooled, aqueous HCl solution (0.1 M) was added into the system. The precipitated solids were washed with cold water for three times and then vacuum dried for 10 h at 50 °C. If no obvious solid appeared after acidification, the mixture was extracted with ethyl acetate (3 × 20 mL) and the combined organic layers were rotary evaporated to remove ethyl acetate. Solid products obtained were vacuum dried for 10 h at 60 °C.

2.3.2. Spectroscopic measurements

Electron paramagnetic resonance (EPR) spectra were taken on a Bruker spectrometer in the X-band at 77 K with a field modulation of 100 kHz. The microwave frequency was maintained at 9.4 GHz. The prepared solutions of indicated components were taken out into a small capillary tube and preserved in liquid nitrogen for low temperature EPR examination.

Gas products analysis was conducted in a U-type quartz tube connected to a Mass spectrometer (GSD320 Thermostar). ^1H NMR and ^{13}C NMR spectra of isolated products were recorded with a Bruker 400 M spectrometer while the NMR spectra of mixtures for intermediates during reaction were recorded on Bruker 700 M spectrometer.

2.3.3. Cyclic voltammetry

ACHI 650D Bipotentiostat (Shanghai Chenhua) was used for the electrochemical measurements in a conventional three-electrode