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Copper(II)-catalyzed C–H oxidation of alkylbenzenes and cyclohexane with hydrogen peroxide

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Abstract—Copper(II) complex 1 efficiently catalyses the oxidation of alkylbenzenes and cyclohexane into the corresponding ketones in moderate to high yields in the presence of 30% H₂O₂. This protocol is simple, clean and generates water as the only by-product.

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Transition-metal-catalyzed oxidation of organic compounds with atom efficient oxidants such as O_2 or H_2O_2 is rapidly gaining importance as a viable alternative to the environmentally hazardous metal promoted stoichiometric oxidations.^{1,2} Recent studies have shown that transition metals in combination with various oxidizing agents convert a wide range of hydrocarbons to the corresponding oxidized products.³ These oxidations are modeled on certain enzymes that perform the oxidation of hydrocarbons in natural systems.⁴ In spite of many studies, there are very few which use H₂O₂ as a source of oxygen in the C-H oxidation of alkanes.⁵ More recently, we have reported the oxidation of alcohols to carbonyl compounds with a cobalt(II) complex in the presence of 30% H₂O₂ in high yields.⁶ This protocol functions in the absence of additive and generates water as the only by-product. Herein, we wish to report the oxidation of alkylbenzenes and cyclohexane to the corresponding ketones with copper(II) complex 1 in the presence of 30% H₂O₂ in moderate to high yields (Scheme 1).⁷

The oxidation of diphenylmethane was first examined as a standard substrate with 30% H₂O₂ in the presence of a catalytic amount of **1** in acetonitrile under ambient conditions (Table 1).⁸ As expected the oxidation took place to afford a 1:1 mixture of diphenylmethanol and benzophenone in 34% yield in the presence of a **1** and 10 equiv. of 30% H₂O₂ in 16 h. Alternatively, the reaction can be driven to the formation of benzophe-

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Scheme 1.

Table 1. Copper(II)-catalyzed benzylic oxidation of diphenylmethane to benzophenone with 30% H₂O₂^a

Entry	Catalyst (0.1 mol%)	Time (h)	Conv. ^b (%)	Selectivity ^b (%)
1 ^{c,d}	1	16	18	>99
2	1	5	87	>99
3	None	16	_	_
4	$Cu(OAc)_2$	5	8	>99
5	Cu ^{II} salen	5	58	>99

^a A solution of the catalyst (0.1 mol%), diphenylmethane (2 mmol), 30% H₂O₂ (2.26 mL, 20 mmol) and acetonitrile (2 mL) was stirred under atmospheric oxygen at ca. 80°C.

^b Determined by GC.

^c Reaction was performed at ambient temperature.

^d Diphenylmethanol (16%) obtained.

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none in 87% yield by heating the reaction mixture at 80°C for 5 h (entry 2). A control experiment without catalyst 1 using the same reaction conditions showed no oxidation. $Cu(OAc)_2$ and Cu^{II} salen were also examined as catalysts for this reaction, however, they were less effective compared to 1 and afforded benzophenone in 8 and 58% yields, respectively (entries 4 and 5).

To evaluate the scope of the reaction, the oxidations of ethylbenzene, butylbenzene, ethyl phenylacetate, tetralin and cyclohexane were further studied (Table 2). As above, all the substrates consistently underwent oxidation selectively to the corresponding ketones in high yields. The substrates, butylbenzene, ethylbenzene and ethyl phenylacetate, were oxidized to the respective ketones in 82-88% yields (entries 1–3). Similarly, cyclohexane underwent oxidation to cyclohexanone in 18% yield and tetralin was converted to α -tetralone in 89% yield (entries 5 and 4). It is noteworthy to mention that no oxidation was observed in the aromatic ring of the

Table 2. Oxidation of alkylbenzenes and cyclohexane to the corresponding ketones with catalyst 1 in the presence of $30\% H_2O_2^a$



^aA solution of the catalyst 1 (0.1 mol%), substrate (2 mmol), 30% H_2O_2 (2.26 mL, 20 mmol) and acetonitrile (2 mL) was stirred at ca. 80 °C for 5 h. ^bDetermined by GC. ^cAll the compounds were characterized by comparing their analytical data (¹H NMR, IR and MS) with the analyses of authentic samples. ^d4 mmol of the substrate used. ^eReaction was carried out for 10 h.



Figure 1. Progress of the oxidation of ethylbenzene to acetophenone with complex 1 and 30% H₂O₂.

alkyl benzenes. Likewise, in the case of butylbenzene, the oxidation took place selectively at the benzylic C–H bond and no oxidation was observed in the remaining C–H bonds. The profile of the oxidation of ethylbenzene to acetophenone is shown in Figure 1.

In conclusion, we have described a simple, clean and efficient catalytic oxidation procedure that allows the transformation of alkylbenzenes and cyclohexane into the corresponding ketones in moderate to high yields.

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- 7. The reaction of salicylaldehyde (122 mg, 1 mmol) with ethylenediamine (30 mg, 0.5 mmol) in methanol (5 mL) afforded salen-H₂ as a lemon yellow powder in 81% (217 mg), which was further reacted with NaBH₄ (32 mg) in methanol (5 mL) for 2 h at ambient temperature. Removal of the solvent on a rotary evaporator followed by treatment with water afforded salen-H₄ as a colorless powder in 72% (162 mg) yield. ¹H NMR (CDCl₃, 90 MHz) δ

6.7–7.2 (m, 8H), 3.9 (s, 4H), 2.85 (s, 4H); IR (KBr) 3288, 2909, 2868, 2827, 1608, 1565, 1398, 1260, 999 cm⁻¹. Anal. calcd for $C_{16}H_{20}N_2O_2$: C, 70.56; H, 7.40; N, 10.29. Found: C, 70.42; H, 7.39; N, 10.31. The salen-H₄ (150 mg, 0.55 mmol) was then reacted with Cu(OAc)₂ (200 mg, 1 mmol) in methanol (10 mL) at 50°C for 2.5 h under a nitrogen atmosphere. Evaporation of the solvent on a rotary evaporator gave a powder which was purified on silica gel (60–120 mesh) column chromatography using EtOAc and MeOH (15:5) as eluent to afford complex 1 as a green powder in 70% yield: UV–vis (CH₃CN) λ_{max} 328, 584 nm; FAB MS: m/z 334 (M⁺).

8. A homogeneous solution of the alkane (2 mmol), complex 1 (0.1 mol%) and 30% H_2O_2 (2.26 mL, 20 mmol) was stirred in acetonitrile (2 mL) at ca. 80°C for the appropriate time (see Table 2). The reaction mixture was then cooled to room temperature and dimethyl sulphide (50 µl) was added. After GC analysis of the reaction mixture, the aqueous solution was removed on a rotary evaporator and the residue was treated with diethyl ether (15 mL). The organic solution was washed with saturated brine. Drying (Na₂SO₄) and evaporation of the solvent on rotary evaporator afforded a residue which was passed through a short pad of silica gel using ethyl acetate and hexane as eluent to afford the analytically pure products.