

Copper-triethanolamine complex as efficient and active catalyst for selective oxidation of alkylarenes to phenyl ketones by *tert*-butylhydroperoxide

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Received 7 July 2007; revised 22 October 2007; accepted 26 October 2007
Available online 30 October 2007

Abstract—Several types of alkylarenes were selectively oxidized to the corresponding α -phenyl ketones in moderate to good selectivities and conversions using *tert*-butylhydroperoxide in the presence of a tetranuclear copper-triethanolamine complex under mild reaction conditions.

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Selective oxidation of alkylarenes to aromatic ketones is one of the most important fundamental reactions, with respect to both academic and industrial purposes in the manufacture of various perfumes, drugs, and pharmaceuticals. The earlier processes, such as the oxidation reaction of the methylene group attached to the aromatic ring using stoichiometric quantities of oxidizing agents like KMnO_4 or $\text{K}_2\text{Cr}_2\text{O}_7$ and by Friedel–Crafts acylation reaction of aromatics with acid halide/anhydride using stoichiometric amounts of corrosive AlCl_3 as catalyst,^{1,2} for the production of aromatic ketones suffered from their corrosive and environmentally unfriendly nature. Recently there has been an increased interest in the development of clean and economical processes for the selective oxidation of alkylarenes to higher-value added phenyl ketones. In this line the catalytic systems heterogeneously and homogeneously in combination with environmentally benign oxidants like O_2 , H_2O_2 and *tert*-butylhydroperoxide (TBHP) are highly desirable systems to be tested and developed.^{3,4} It is known that copper species are widely present in nature and in many enzymes, some multinuclear copper complexes have been applied as catalyst for C–H oxidation in the presence of H_2O_2 and TBHP.⁵ Pomberio and his co-workers synthesized several copper(II)-triethanolamine complexes as catalysts for the oxidation of cyclo-

hexane and alkanes. The reactions showed potentially higher yields.⁶ In this Letter, we report the results obtained with copper(II)-triethanolamine complexes **1–4**, that is, dimeric $[\text{Cu}_2(\text{H}_2\text{tea})_2(\text{C}_6\text{H}_5\text{COO})_2] \cdot 2\text{H}_2\text{O}$ **1**, trimeric $[\text{Cu}_3(\text{H}_2\text{tea})_2(4\text{-OC}_6\text{H}_4\text{COO})_2(\text{H}_2\text{O})] \cdot 4\text{H}_2\text{O}$ **2**, tetrameric $[\text{O} \llcorner \text{Cu}_4(\text{tea})_4(\text{BOH})_4][\text{BF}_4]_2$ **3**, and polymeric $[\text{Cu}_2(\text{H}_2\text{tea})_2\{\mu\text{-C}_6\text{H}_4(\text{COO})_{2-1,4}\}]_n \cdot 2n\text{H}_2\text{O}$ **4**, for the selective oxidation of alkylarenes to the corresponding aromatic ketones using TBHP as oxidant under mild conditions. The results showed, in particular, that the alkylarenes like ethylbenzene and 1-bromo-4-*n*-alkylbenzenes could be converted to the corresponding α -phenyl ketones with selectivity higher than 90% in moderate to good conversions at 343 K by the tetranuclear complex **3**.

The Cu(II) atoms in complexes **1** and **4** are hexa-coordinated with triethanolamine ligand and carboxylate ligand (for **1**) or terephthalic acid ligand (for **4**), respectively. While the Cu(II) species in complexes **2** and **3** are penta-coordinated with triethanolamine ligand. Complex **3** is a cage structure composed of centro-symmetric subunits $[\text{O} \llcorner \text{Cu}_4(\text{tea})_4(\text{BOH})_4]$ and BF_4^- per unit, where an oxygen atom is embedded into the center of four Cu atoms and each Cu atom coordinates with one tetradentate triethanolamine ligand and the central oxygen atom. Moreover, four B–OH groups connect three oxygen atoms of different triethanolamine ligand.⁶ The geometries of complexes **1–4** are shown in Figure 1S (see Supplementary data).

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It has been reported that high catalytic activity and excellent selectivity in the oxidation of ethylbenzene to acetophenone were possibly obtained by using cobalt(III) complexes and Co/SBA-15 as catalysts in the presence of O₂ or air without the need of solvent.^{3b,7} But the reaction was carried out under pressure and higher temperatures. Other catalyst systems such as anthraquinone derivatives/*N*-hydroxyphthalimide/zeolite HY biomimetic system, complexes of Cu, Ti, and Fe, *o*-phenanthroline-mediated metal-free catalytic system, MnO₄⁻-exchanged MgAl hydrotalcite, NiAl hydrotalcite, Mn-MCM-41, Ba-, and V-containing compounds were also found to be active and efficient for the selective oxidation of ethylbenzene to acetophenone with dioxygen, TBHP, or H₂O₂ as oxidants.^{4,5,8} Table 1 lists the oxidation of ethylbenzene in the presence of different Cu compounds as the catalysts with TBHP under mild reaction conditions. All these Cu compounds afforded acetophenone as major product. Among them complex **3** exhibited the highest acetophenone yield, while complexes **1**, **2**, **4**, Cu(NO₃)₂, and CuCl₂ were less effective than **3** (see entries 1–4 and 15, 16). A controlled experiment without any copper compounds under identical conditions gave negligible conversion (entry 17). The influences of different parameters (the ratio of TBHP to ethylbenzene, temperature, and time profile) on the performance of **3** for the oxidation of ethylbenzene are also incorporated in Table 1. It was found that the ratio of TBHP to ethylbenzene could significantly

affect the conversion and acetophenone selectivity (entries 5–7). Higher conversion associated with higher selectivity was obtained when the ratio of TBHP to ethylbenzene was set at 3:1. When the reaction temperature was increased from 313 to 343 K, the conversion of ethylbenzene increased drastically from 9.2% to 63.7%, where the selectivity to main product acetophenone was also increased from 70.9% to 91.7% (entries 8–10). However, when the reaction temperature increased to 353 K, a considerable amount of unknown tar-like products was formed, probably due to extensive carbonization which occurred. By prolonging the reaction time from 1 to 7 h, both the conversion and acetophenone selectivity increased gradually and reached almost saturation by 7 h of reaction. No remarkable increase in the conversion and selectivity were obtained by further extending the reaction time to 10 h.

When using the protocol for the oxidation of other alkylarenes with complex **3**, the corresponding phenyl ketones were also formed as the major products with moderate to good selectivities (Table 2). However, a different reactivity was observed with the substrates having different side-chains and electron-withdrawing groups in the aromatic ring. In general, the longer is the side-chain, the lower is the selectivity to ketone. For instance, *n*-propylbenzene and *n*-butylbenzene were oxidized to propiophenone and butyrophenone with selectivities of 76.3% and 61.5% in conversions of

Table 1. Selective oxidation of ethylbenzene by several copper compounds using TBHP oxidant^a

CCc1ccccc1 $\xrightarrow[\text{313-343 K}]{\text{Copper complex, CH}_3\text{CN, TBHP}}$ CC(=O)c1ccccc1 (I) + CC(O)c1ccccc1 (II) + O=Cc1ccccc1 (III) + Others

Entry	Catalyst	<i>T</i> (K)	Time (h)	TBHP/substrate (molar ratio)	Conversion ^b (%)	Selectivity ^c (%)			Yield ^d (%)
						I	II	III	
1	1	333	7	2	48.7	68.5	11.2	2.1	32.9
2	2	333	7	2	44.7	59.7	4.5	1.9	26.7
3	3	333	7	2	61.7	82.6	5.1	1.3	51.0 (41.9)
4	4	333	7	2	30.7	39.1	8.1	2.3	12.0
5	3	333	7	0	2.3	35.7	6.3	16.3	0.8
6	3	333	7	1	29.8	43.6	6.8	2.2	13.0
7	3	333	7	3	66.3	90.2	3.6	0.6	59.8 (47.8)
8	3	313	7	2	9.2	70.9	7.2	1.1	6.5
9	3	323	7	2	45.7	75.6	5.6	1.7	34.5
10	3	343	7	2	63.7	91.7	3.7	1.8	58.4
11	3	343	1	2	37.0	96.8	1.6	0.5	35.8
12	3	343	3	2	47.8	93.4	2.2	1.3	44.6 (32.3)
13	3	343	4	2	50.0	94.0	2.5	1.0	47.0
14	3	343	5	2	54.3	93.2	1.8	1.6	50.6
15	Cu(NO ₃) ₂	333	7	2	51.2	72.3	2.2	3.2	37.0
16	CuCl ₂	333	7	2	28.5	53.8	6.7	0.7	15.3
17	—	333	7	2	1.7	99.0	0	0	1.7

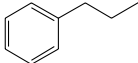
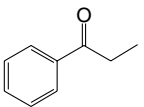
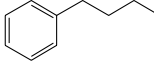
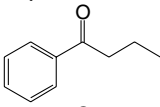
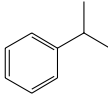
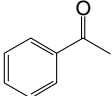
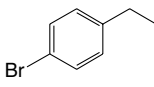
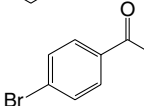
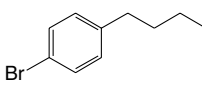
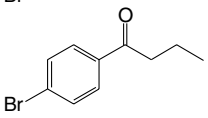
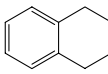
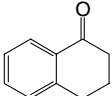

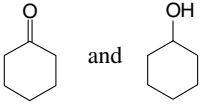
^a Ethylbenzene (6 mmol) and copper compound (0.015 mmol) in CH₃CN (5 mL).

^b Average conversion of two runs based on GC results (DM-Wax 30 m × 0.25 mm × 1.0 μm). The reaction mixture was analyzed twice, before and after treatment with PPh₃.^{8d,e} No differences from each other were obtained.

^c The other products (mainly benzoic acid) have not been incorporated for conciseness.

^d The data in parenthesis are the isolated yields of acetophenone.

Table 2. Oxidation of alkylarenes catalyzed by complex **3** using TBHP oxidant^a

Entry	Substrate	Major product	Time (h)	Conversion ^b (%)	Selectivity ^c (%)	Yield ^d (%)
1			5	63.1	76.3	48.1 (44.3)
2			5	52.6	61.5	32.3 (31.2)
3			3	46.8	42.8	20.0 (18.3)
4			10	79.2	93.8	74.3 (65.5)
5			10	55.8	92.3	51.5 (50.3)
6			3	72.7	65.8	47.8
7			7	52.1	45.6 and 23.4	23.8 (21.6) ^e

^a Substrate (6 mmol), complex **3** (0.015 mmol), and TBHP (12 mmol) in CH₃CN (5 mL) at 343 K.

^b Average conversion of two runs based on GC results.

^c The other products such as carboxylic and alcoholic species have not been incorporated for conciseness.

^d The data in parenthesis are the isolated yields of the corresponding major product.

^e The yield of cyclohexanone.

63.1% and 52.6% at 343 K for 5 h, respectively (entries 1 and 2). The 1-bromo-4-*n*-alkylarenes were converted to the corresponding phenyl ketones with selectivities above 90% (entries 4 and 5). A yield as high as 74.3% for 4'-bromoacetophenone can be obtained by the oxidation of 1-bromo-4-ethylbenzene at 343 K for 10 h (entry 4). The reaction mechanism of *iso*-propylbenzene to acetophenone by the protocol is not clear enough at present (entry 3), but it would undergo the cleavage of a C–C bond. When tetrahydronaphthalene was employed as a substrate, α -tetralone was obtained with 65.8% selectivity in a reaction conversion of 72.7% at 343 K for 3 h (entry 6). In the case of cyclohexane, a conversion of 52.1% was obtained at 343 K for 7 h, affording cyclohexanone and cyclohexanol as the major products with selectivities of 45.6% and 23.4%, respectively.

The oxidations from alkylarenes to ketones were conceivably passing through the aromatic alcohols as intermediates. We have used α -phenylethanol as a substrate and carried out the oxidation reaction under identical conditions. The results showed that the acetophenone was obtained in a yield higher than 99%.

In summary, we have reported that the tetranuclear copper-triethanolamine complex **3** catalyzed the oxidation of alkylarenes to phenyl ketones using TBHP as ox-

idant. The process exhibited advantages of mild reaction conditions and higher selectivities, providing a simple method to synthesize aromatic ketones starting from alkylarene substrates.

Acknowledgments

The authors gratefully acknowledge the financial supports from the NSFC (20473065 and 20433030), the Key Project of Fujian Province (2005HZ01-3) and the Research Fund for the Doctoral Program of Higher Education (20050384011) and the Key Project of Chinese Ministry of Education (106099).

Supplementary data

Supplementary data associated with this article can be found, in the online version, at doi:10.1016/j.tetlet.2007.10.135.

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