An Efficient Oxidation of 2,6-di-tert-Butylphenol to 3,3',5,5'-tetra-tert-Butyl-4,4'-Diphenoquinone Catalyzed by Lewis Acid System in the Presence of Molecular Oxygen

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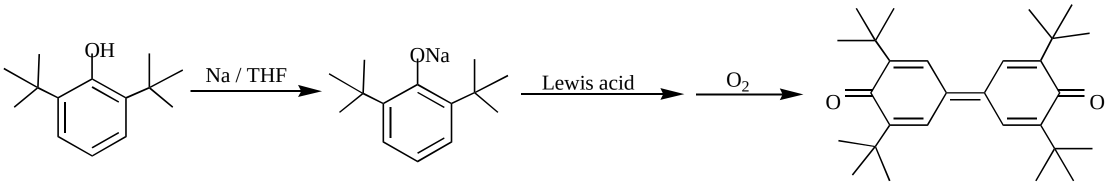
Abstract: An efficient and simple method for the preparation of 3,3',5,5'-tetra-tert-butyl-4,4'-diphenoquinone (TBDPQ) is reported using Lewis Acid as an effective catalyst in the presence of molecular oxygen from 2,6-di-tert-butylphenol (DBP). The present methodology offers several advantages, such as excellent yields, accessible and inexpensive catalysts, easy work-up and green conditions. The oxidation reaction was found to proceed in two steps and the oxidation kinetics for $FeCl_3$ system was examined in detail.

Keywords: 2,6-di-tert-butylphenol, catalysis, diphenoquinone, Lewis Acid, mechanism, oxidation, oxidation kinetics.

INTRODUCTION

3,3',5,5'-tetra-tert-butyl-4,4'-diphenoquinone (TBDPQ) is a valuable raw material for highly functionalized photosensitizers [1, 2]. TBDPQ can be conventionally synthesized by the oxidative coupling of 2,6-di-tert-butylphenol (DBP) using stoichiometric inorganic oxidants [3], that produces copious amounts of wastes. With ever-growing environmental issues of chemical processes, much attention has been paid to the use of molecular oxygen as a "green" oxidant to achieve TBDPQ. Up to now, considerable efforts have been dedicated to improve the performance of the reaction. Several Cu-containing enzymes and some Cu, Co and Mn complexes have been utilized as catalysts for this oxidation [4-14]. Some of these methods, however, suffer from drawbacks, which include unsatisfactory yields, high temperature, long reaction times and use of toxic, not available or costly catalysts. Therefore, there is a need to develop more efficient and simple method for the preparation of TBDPQ. Lewis acids are distinguished by a number of practical advantages, such as the ease of accessibility, inexpensive metals, and the high durability of the catalysts [15, 16]. These advantages led us to explore their further applications as catalysts. We report here a clean and simple synthesis of TBDPQ from the oxidative C-C coupling reaction of DBP under O_2 atmosphere using alkali-promoted various Lewis acids as catalysts (Scheme **1**).



Scheme 1. Two-steps synthetic route to TBDPQ.

EXPERIMENTAL

In the catalysis stage, manipulations were performed under argon using the standard Schlenk techniques. THF and toluene were distilled from sodium benzophenone ketyl before use. In the oxidation stage, the reaction was performed under O_2. The oxidation product TBDPQ was characterized by Elemental analysis, IR, ^{1}H NMR and X-Ray diffraction. Carbon and hydrogen analyses were performed by direct combustion with a Carlo-Erba EA-1110 instrument. The IR spectra were recorded with a Nicolet-550 FT-IR spectrometer as KBr pellets. ^{1}H NMR spectra were recorded in $CDCl_3$ on an INOVA-400MHz.

Synthesis of Na-Phenolate

A Schlenk flask was charged with Na (2.5 g, 110 mmol), THF (250 mL) and a stir bar. In this solution was added DBP (20.6 g, 100.0 mmol) at room temperature under argon, then the reaction immediately gave H_2 and Na-phenolate. The precipitate was removed by centrifugation.

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Table 1. Aerobic Oxidation of 2,6-di-tert-butylphenol (DBP) Catalyzed by Various Lewis Acids[a].

Entry	Catalyst	[Cat.]/ [Na-phenolate]	Temper (°C)	Yield[b] (%)
1	$CaCl_2$	1:5	20	80.8
2	$AlCl_3$	1:5	20	73.7
3	$ZnCl_2$	1:5	20	73.5
4	$FeCl_3$	1:3	20	100
5	$FeCl_3$	1:5	20	87.1
6[c]	$FeCl_3$	1:5	20	35.2
7	$FeCl_3$	1:8	20	78.5
8	$FeCl_3$	1:10	20	63.8
9	$FeCl_3$	1:20	20	34.7
10	$FeCl_3$	1:5	0	50.2
11	$FeCl_3$	1:5	10	67.8
12	$FeCl_3$	1:5	40	67.3
13	$FeCl_3$	1:5	50	54.3
14[d]	$FeCl_3$	1:5	20	trace
15[f]	---	1:5	20	trace
16[g]	$FeCl_3$	1:3	20	100 (Reuse-1)
17[g]	$FeCl_3$	1:3	20	100 (Reuse-2)
18[g]	$FeCl_3$	1:3	20	93.5 (Reuse-3)
19[g]	$FeCl_3$	1:3	20	93.2 (Reuse-4)
20[g]	$FeCl_3$	1:3	20	94.0 (Reuse-5)

[a] Conditions: THF as solvent, Catalysis time = 120 min, Oxidation time = 120 min.
[b] Yield is based on isolated products after completion of the reaction.
[c] Toluene as solvent.
[d] The oxidation of the alkali-free DBP is under the same conditions of run 5.
[f] The oxidation reaction without catalyst ($FeCl_3$) is under the same conditions of run 5.
[g] Reuse-1〜Reuse-5.

Synthesis of TBDPQ

To a slurry of $FeCl_3$ (0.32 g, 2.0 mmol) in THF (10 mL) was slowly added was a solution of Na-phenolate (30.5 ml, 10.0 mmol) in THF. This solution was stirred for 120 min (catalysis stage) at room temperature under argon. And the mixture was stirred at room temperature for another 120 min (oxidation stage) under an O_2 atmosphere. The precipitate was removed by centrifugation. Then the solvent was completely removed in a vacuum, and hexane was added to extract the product. Red crystals were obtained from a concentrated hexane solution and gave 1.69 g of TBDPQ (82.7% yield). Elemental analysis (%) calcd. for $C_{28}H_{40}O_2$ (408.62 g mol^{-1}): C 82.30, H 9.87; Found: C 82.42, H 9.72. IR (KBr pellet, cm^{-1}): 2956 (m), 1604 (s), 1568 (m), 1455 (m), 1089 (m), 894 (m), 818 (w), 512 (m). δ_H (400 MHz, $CDCl_3$): 7.73 (s, 4H, Ar-H), 1.39 (s, 36H, $-C(CH_3)_3$).

Catalyst Reuse

Reuse of catalyst $FeCl_3$ was performed as follows: oxidation of **TBDPQ** was carried out under standard reaction conditions of Table **1**. After the completion of the first run, the initial amount of Na-phenolate was again fed into reaction mixture with removal of the product.

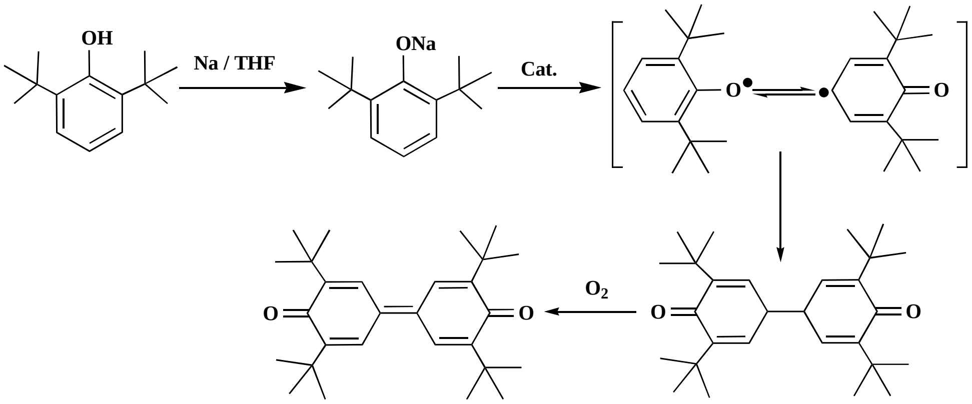
X-ray Structure Determination of TBDPQ

Suitable single crystals of TBDPQ were sealed in a thin-walled glass capillary respectively for determining the single-crystal structure. Crystal data: $C_{28}H_{40}O_2$, Mr = 408.60, triclinic, p-1, a (Å) = 6.0569(4), b (Å) = 10.3440(9), c (Å) = 10.4338(9), α (deg)= 81.441(7), β (deg)=76.459(6), γ (deg)=81.163(7), Z = 1, F(000) = 224, D_{calc} (Mg m^{-3})= 1.088, Abscoeff (mm^{-1}) = 0.066, T (K) = 193(2), $R1$ = 0.0430, $wR2$ = 0.1146. Single-crystal X-ray diffraction data for TBDPQ were recorded on a Bruker CCD Area Detector diffractometer by using the ω/φ scan technique with MoKα radiation (λ = 0.71073 Å). Absorption corrections were applied by using multiscan techniques [17]. The structure was solved and refined by direct methods with SHELXS-97 [18]. All nonhydrogen atoms were refined with anisotropic temperature parameters, hydrogen atoms were refined as rigid groups. CCDC-757801 contains the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre *via* www.ccdc.cam.ac.uk/data_request/cif.

Table 2. Comparison of the Results of $FeCl_3$ in the Aerobic Oxidation of 2,6-di-tert-butylphenol (DBP) with those of other Catalysts Reported in the Literature.

Entry	Catalyst	Conditions	Temper (°C)	Yield (%)
1	$FeCl_3$	[Cat.]/[phenolate] = 1:10, 4h	20	63.8[a]
2	$Na/Mg\text{-}Al\text{-}CO_3$	[Cat.]/[phenolate] = 1:5,10h	130	5[21]
3	$Na/Cu\text{-}Mg\text{-}Al\text{-}CO_3$	[Cat.]/[phenolate] = 1:5,10h	130	61[21]
4	Cu/Na MCM-41	Cat.= 0.2g, phenolate = 0.5mmol, 24h	40	5.6[4]
5	Cu/Na MCM-41 +CH_3COOK	Cat.= 0.2g, phenolate = 0.5mmol, 24h	40	14.9[4]
6	Cu shiff base complex immobilized on silica	Cat.= 10 mmol, phenolate = 1mmol, H_2O_2 = 1.5 mmol, 24h	-50	12[22]
7	four new pyrazole-Ligand + $2Cu(NO_3)$	Cat.= 3.33 mmol, phenolate = 0.2 mmol	25	<20[5]

a. this work



Scheme 2. The catalytic mechanism of DBP oxidation using the alkali promoted Lewis acid.

RESULTS AND DISCUSSION

In continuation of our interest toward the exploitation of Lewis Acid as a cheap, easily available and eco-friendly catalyst for the development of new synthetic methodologies in organic synthesis, we now report a simple and efficient synthesis of TBDPQ. The oxidation of Na-phenolate species was carried out using various Lewis acids as catalysts under an O_2 atmosphere, which is summarized in Table **1**. Notably, these simple Lewis acids were found to be highly active catalysts for the oxidative coupling of DBP·Na to TBDPQ in high activity at 20°C. The oxidation products obtained in the present study were identified as TBDPQ. No monomeric oxidation product such as benzoquinone derivatives was detected under the present reaction conditions. For example, when the mole ratio of [Cat.]/[Na-phenolate] is 1:5, the conversion reaches to 87.1% for $FeCl_3$; 80.8% for $CaCl_2$; 73.7% for $AlCl_3$ and 73.5% for $ZnCl_2$ (Table **1**, entries 1-4 and 6). Activity order of these Lewis acids is $ZnCl_2 \approx AlCl_3 < CaCl_2 < FeCl_3$ [19, 20]. $FeCl_3$ acts as an effective catalyst with respect to reaction temperature, times and yields, compared with other catalysts known to facilitate this transformation (Table **2**).

The reaction catalyzed by $FeCl_3$ was examined in detail because of the best catalytic activity. The influence of the molar ratio of [$FeCl_3$] to [Na-phenolate] on the yields of the oxidation products was investigated. As shown in Table **1**, the increase in the catalyst concentration leads to the increasing of oxidation conversion (Table **1**, entries 4, 5 and 7-9). To examine the influence of the reaction temperature on the activity, these reactivities of $FeCl_3$ from 0 °C to 50 °C were measured. The results indicate that the conversion increases with an increasing of temperature from 0°C to 20°C while decreases with temperature from 20°C to 50°C (Table **1**, entries 5 and 10-13). The reaction in THF yields higher conversion than that in toluene (Table **1**, entries 5-6). Further, the oxidations in the fifth run using the spent $FeCl_3$ catalyst even gave similar TBDPQ yields (Table **1**, entries 16-20). The Fe^{III} can act as a recyclable catalyst, it is attributed to resultant Fe^{II} which is reoxidized to Fe^{III} by O_2.

To further investigate the mechanism, the result obtained with the alkali-free DBP catalyzed by $FeCl_3$ is also included. In the case of the alkali-free DBP, the yield of TBDPQ was quite low under the same conditions (Table **1** entry 14), and the result is similar to that catalyzed by the Cu complex [4]. It is also noticed that the oxidative coupling of DBP·Na without $FeCl_3$ shows no activity at all under the same conditions (Table **1** entry 15). Therefore, we proposed a catalytic mechanism of this DBP oxidation using the alkali promoted Lewis acid as shown in Scheme **2**. We supposed that the corresponding phenoxy radical was formed *via* one-electron

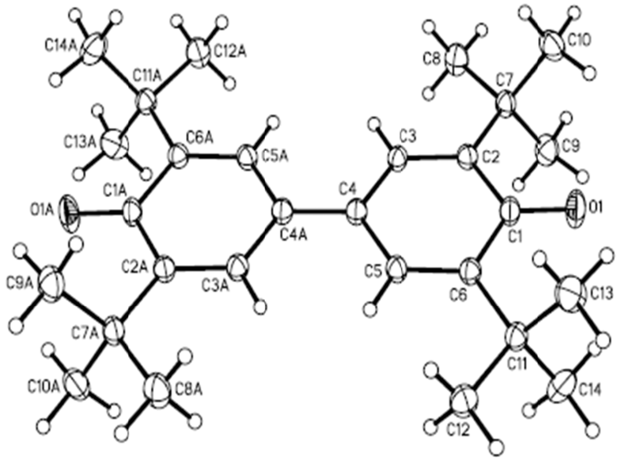


Fig. (1). Molecular structure of TBDPQ.

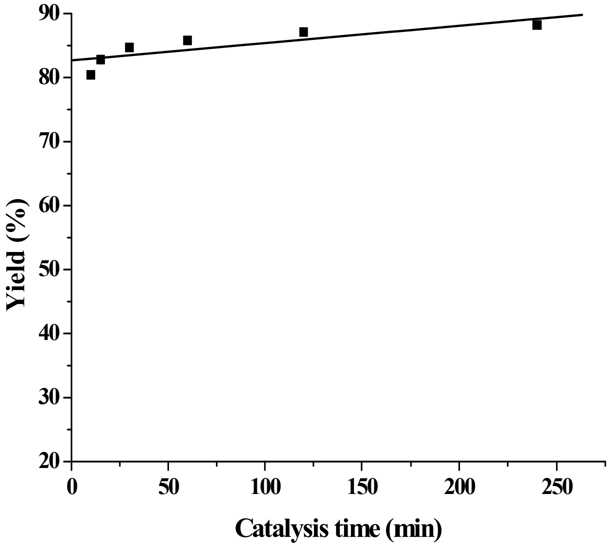


Fig. (2). Plot of the conversion versus catalysis time with $FeCl_3$ in THF at 20 °C, oxidation time = 120 min, $[FeCl_3]/[Na\text{-phenolate}] = 1:5$.

transfer from the phenolate anion to Lewis acid catalyst. A dimmer arose through C–C coupling of the phenoxy radicals and could be easy rearranged to more stable tautomer with two hydroxyl groups. Then this dimmer was further oxidated to TBDPQ by O_2. From this mechanism, the oxidation reaction catalyzed by Lewis acid in the presence of O_2 was found to proceed in two steps. In the catalysis stage, the reaction was rapid, likely due to the fast formation of free radicals catalyzed by Lewis acid. Then, the reaction proceeded at a relatively slow rate in the oxidation stage. For validating it, the oxidation kinetics for $FeCl_3$ system was examined at 20 °C and the results are depicted in Figs. **2** and **3**. In the catalysis stage, the conversion remains almost unchanged after the short induction period (Fig. **2**). The conversion increases rapidly in the first 60 minutes of the oxidation stage while it is hardly influenced in the latter oxidation time (Fig. **3**).

CONCLUSIONS

We have developed a convenient Lewis Acid-catalyzed synthetic protocol for TBDPQ in the presence of molecular oxygen from DBP. The Lewis acid catalysts were expanded to several commonly used metal halides, and the catalytic performance of these catalysts was compared. Our preliminary results illustrated that $FeCl_3$ was the most effective and reusable catalyst and provided higher yields in short reaction times at relatively low temperatures when compared to some of the other existing methods. The significant advantages of this methodology are excellent yields, short reaction times, elimination of dangerous and harmful inorganic wastes, simple work-up procedure and no chromatographic separation is necessary to get the spectra-pure compounds. Further application of the catalytic system to other reactions is in progress.

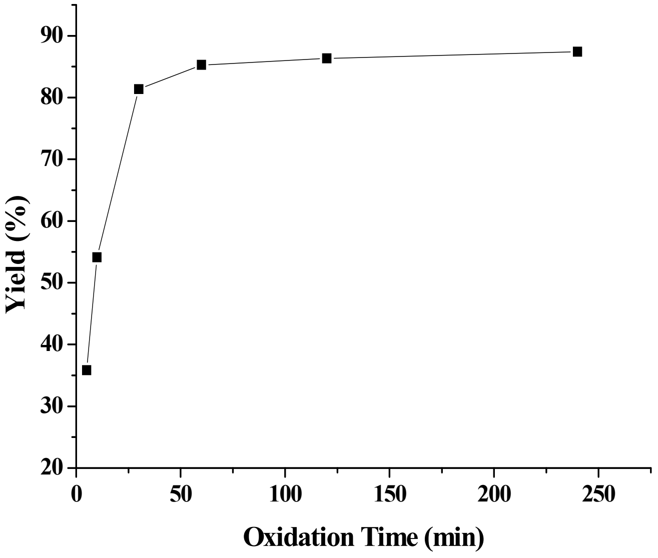


Fig. (3). Plot of the conversion versus oxidation time with $FeCl_3$ in THF at 20 °C, catalysis time = 30 min, $[FeCl_3]/[Na\text{-phenolate}] = 1:5$.

CONFLICT OF INTEREST

The author(s) confirm that this article content has no conflicts of interest.

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