

Dirhodium-Catalyzed Phenol and Aniline Oxidations with T-HYDRO. Substrate Scope and Mechanism of Oxidation

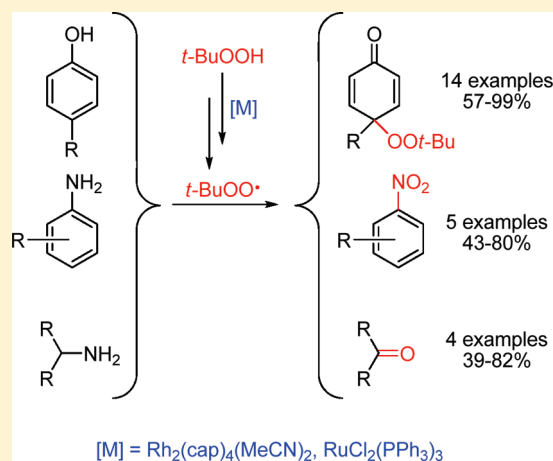
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S Supporting Information

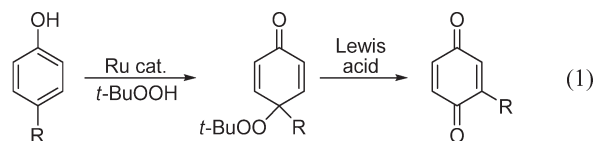
ABSTRACT: Dirhodium caprolactamate, $\text{Rh}_2(\text{cap})_4$, is a very efficient catalyst for the generation of the *tert*-butylperoxy radical from *tert*-butyl hydroperoxide, and the *tert*-butylperoxy radical is a highly effective oxidant for phenols and anilines. These reactions are performed with 70% aqueous *tert*-butyl hydroperoxide using dirhodium caprolactamate in amounts as low as 0.01 mol % to oxidize *para*-substituted phenols to 4-(*tert*-butyldioxy)cyclohexadienones. Although these transformations have normally been performed in halocarbon solvents, there is a significant rate enhancement when $\text{Rh}_2(\text{cap})_4$ -catalyzed phenol oxidations are performed in toluene or chlorobenzene. Electron-rich and electron-poor phenolic substrates undergo selective oxidation in good to excellent yields, but steric influences from bulky *para* substituents force oxidation onto the *ortho* position resulting in *ortho*-quinones. Comparative results with $\text{RuCl}_2(\text{PPh}_3)_3$ and CuI are provided, and mechanistic comparisons are made between these catalysts that are based on diastereoselectivity (reactions with estrone), regioselectivity (reactions with *p*-*tert*-butylphenol), and chemoselectivity in the formation of 4-(*tert*-butyldioxy)cyclohexadienones. The data obtained are consistent with hydrogen atom abstraction by the *tert*-butylperoxy radical followed by radical combination between the phenoxy radical and the *tert*-butylperoxy radical. Under similar reaction conditions, *para*-substituted anilines are oxidized to nitroarenes in good yield, presumably through the corresponding nitrosoarene, and primary amines are oxidized to carbonyl compounds by TBHP in the presence of catalytic amounts of $\text{Rh}_2(\text{cap})_4$.



INTRODUCTION

The oxidation of phenols is important for its role in biochemical processes¹ as well as for the synthetic versatility of the process and their derived products.² Detailed mechanistic studies have captured essential elements of the transformation that converts phenols to phenoxy radicals.³ The outcome of the oxidative process is dependent on the substrate and oxidant and can result in coupling^{4,5} or quinol/quinone-derived products.² In 1996, Murahashi and co-workers investigated the oxidation of phenols by *tert*-butyl hydroperoxide in anhydrous benzene using $\text{RuCl}_2(\text{PPh}_3)_3$ as the catalyst and found good yields of 4-(*tert*-butyldioxy)cyclohexadienones that in selected cases underwent Lewis acid promoted rearrangement to quinone (eq 1).⁶ Recently, this methodology has been applied to a synthesis of vitamins K_1 and K_3 .⁷ The uses of *tert*-butyl hydroperoxide in dirhodium caprolactamate [$\text{Rh}_2(\text{cap})_4$]-catalyzed oxidations has been of interest to us since we discovered the advantages of this combination for allylic oxidation of cyclic olefins.⁸ In that initial effort, as with the Murahashi phenol oxidation, we employed anhydrous *tert*-butyl hydroperoxide, but subsequent examination of the reaction and reaction conditions^{9,10} showed us that the less expensive T-HYDRO

(70% *tert*-butyl hydroperoxide in water) was equally, if not more, effective as an oxidant when catalyzed by dirhodium caprolactamate; $\text{Rh}_2(\text{cap})_4$ undergoes only limited hydrolysis during the course of the reaction.



The low oxidation potential of $\text{Rh}_2(\text{cap})_4$ has made this catalyst eminently suitable as a catalyst for cleavage of the peroxide bond of *tert*-butyl hydroperoxide with the resulting *tert*-butoxy radical undergoing rapid hydrogen atom abstraction from *tert*-butyl hydroperoxide to form the *tert*-butyl peroxy radical that is the selective oxidant for allylic oxidation,⁸⁻¹⁰ as well as benzylic oxidation,¹¹ propargylic oxidation,¹² and oxidations of tertiary and secondary amines.^{13,14} Less well appreciated

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Scheme 1. $\text{Rh}_2(\text{cap})_4$ -Catalyzed Conversion of *tert*-Butyl Hydroperoxide to the *tert*-Butylperoxy Radical

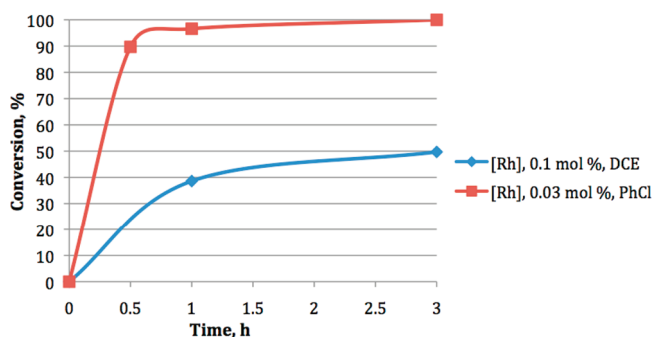
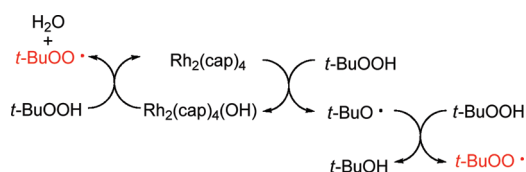


Figure 1. Percent conversion versus time for $\text{Rh}_2(\text{cap})_4$ -catalyzed oxidation of **1** by T-HYDRO (4.0 equiv) at 40 °C in DCE and PhCl.

is the oxidation of *tert*-butyl hydroperoxide by oxidized dirhodium caprolactamate that produces the *tert*-butyl peroxy radical directly.¹⁰ This turnover (Scheme 1) serves as a pump that produces a flux of the *tert*-butyl peroxy radical for oxidation, and the effectiveness of other catalysts for oxidations by *tert*-butyl hydroperoxide can be measured against this turnover.¹⁰ Although reports of catalytic oxidations by *tert*-butyl hydroperoxide often propose different mechanisms for oxidations, the viability of the process lies in the reaction conditions and outcomes (turnover number and rate, product yield, catalyst loading, and required amount of oxidant). In this paper, these factors have been thoroughly investigated for oxidations of phenols by *tert*-butyl hydroperoxide with dirhodium caprolactamate in comparison with other transition-metal catalysts.

RESULTS AND DISCUSSION

Phenol Oxidation. The challenges for phenol oxidation by *tert*-butyl hydroperoxide include effective reaction with economical and safe T-HYDRO, high product selectivity and yield, low catalyst loading, and mild conditions; these were set as baseline conditions for reactions catalyzed by $\text{Rh}_2(\text{cap})_4$. To compare catalytic systems and optimize purification conditions we used 2,6-di-*tert*-butyl-4-methylphenol (**1**) as the substrate with reactions taking place under gentle heating in 1,2-dichloroethane (DCE) and catalyzed by $\text{Rh}_2(\text{cap})_4$, $\text{RuCl}_2(\text{PPh}_3)_3$, or Cu^{I} salts which were all soluble in the reaction media. We began our evaluation with 4 equiv of T-HYDRO (eq 2). Previously, DCE was found to be optimal for allylic oxidation with T-HYDRO catalyzed by $\text{Rh}_2(\text{cap})_4$.^{8–10} Under these conditions, the ruthenium catalyst gave complete conversion within 3 h at a loading of 0.1 mol %, in contrast to 48 h for dirhodium caprolactamate and copper iodide. In screening other solvents for phenolic oxidation, the rate for catalytic oxidation of this phenol in aromatic hydrocarbon solvents was observed to be significantly increased

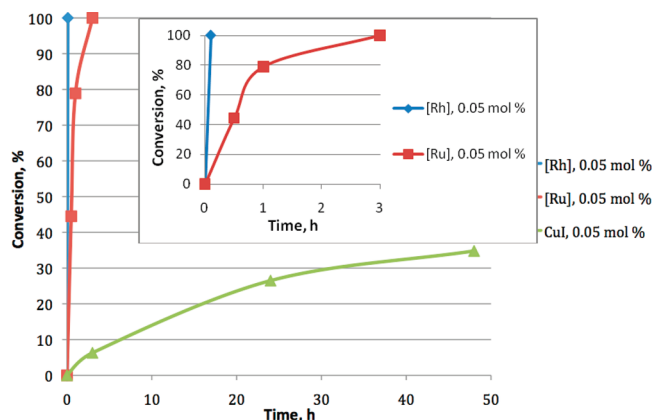
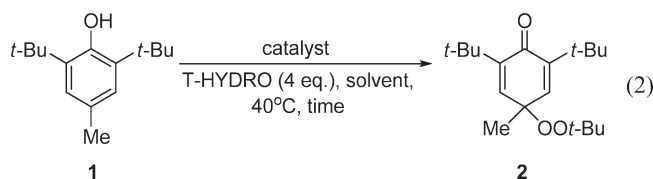


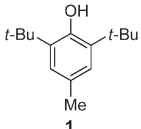
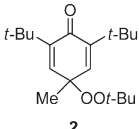
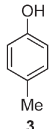
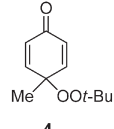
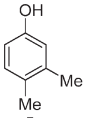
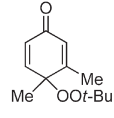
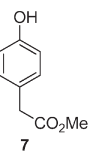
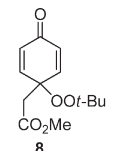
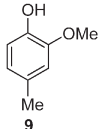
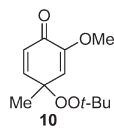
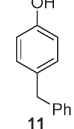
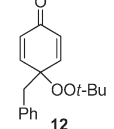
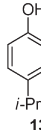
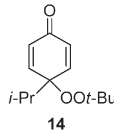
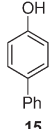
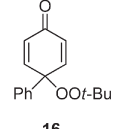
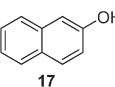
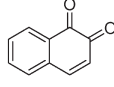
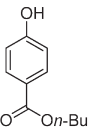
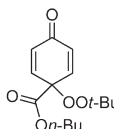
Figure 2. Comparative time courses for the oxidation of **1** by T-HYDRO (4.0 equiv) in PhCl catalyzed by 0.05 mol % of $\text{Rh}_2(\text{cap})_4$, $\text{RuCl}_2(\text{PPh}_3)_3$, or CuI at 40 °C.

over that in dichloromethane or dichloroethane.¹⁵ The progress for the $\text{Rh}_2(\text{cap})_4$ -catalyzed oxidation of **1** in chlorobenzene exemplifies this rate increase (Figure 1), but this enhancement is not observed with either $\text{RuCl}_2(\text{PPh}_3)_3$ or CuI. The reaction time for the $\text{Rh}_2(\text{cap})_4$ -catalyzed oxidation was lowered from 48 h in DCE to just 10 min in chlorobenzene with only 0.05 mol % of catalyst loading, and the same rate enhancement and product outcome was obtained for reactions performed in toluene. With only 0.01 mol % of $\text{Rh}_2(\text{cap})_4$ in chlorobenzene, complete conversion occurred in 48 h. Lowering the number of molar equivalents of T-HYDRO from 4 to 2 resulted in incomplete conversion, presumably due to competing dimerization of *tert*-butyl peroxy radicals with subsequent formation of *tert*-butyl peroxide and molecular oxygen.¹⁶ Use of CuBr and CuCl gave results that demonstrated their low catalytic activity relative to CuI, and reaction rates were measurably faster with $\text{Rh}_2(\text{cap})_4$ than with either $\text{RuCl}_2(\text{PPh}_3)_3$ or CuI (Figure 2).



Application of $\text{Rh}_2(\text{cap})_4$ -catalyzed T-HYDRO oxidations to representative phenols is reported in Table 1. Reactions were performed at 40 °C in the indicated solvent. Use of 2,6-di-*tert*-butyl-4-methylphenol (BHT) provided standard conditions from which optimal conditions for oxidations, catalyzed by various metallic reagents, could be assessed. *Para*-Substituted phenols gave the expected dienone products in very high yields; *p*-quinones are produced from phenols without *para* substituents.¹⁷ For reactions with the volatile phenols, DCE was preferred as the solvent in order to optimize product isolation through the use of a lower boiling solvent; otherwise, toluene was the preferred solvent. In some cases, an increase in T-HYDRO from 4 to 10 equiv was necessary to significantly improve yields (entries 5, 6, and 8). For comparison, Murahashi's use of anhydrous TBHP in benzene (4.0 equiv) with 0.3 mol % of $\text{RuCl}_2(\text{PPh}_3)_3$ at room temperature produced **4** in 85% yield, **6** in 77% yield, **8** in 82% yield, **12** in 78% yield, **14** in 86% yield, and

Table 1. Catalytic *tert*-Butyl Hydroperoxide Oxidation of *Para*-Substituted Phenols and 2-Naphthol

entry	phenol	catalyst	catalyst loading, mol %	equiv. of T-HYDRO	solvent	product	isolated yield ^{a,b}
1	 1	Rh ₂ (cap) ₄	1.0	4	DCE	 2	99
		Rh ₂ (cap) ₄	0.03	4	PhMe		98
		CuI	0.1	4	PhMe		97 ^c
		RuCl ₂ (PPh ₃) ₃	0.05	4	PhMe		94
2	 3	Rh ₂ (cap) ₄	1.0	10	DCE	 4	82
3	 5	Rh ₂ (cap) ₄	1.0	10	DCE	 6	88
4	 7	Rh ₂ (cap) ₄	1.0	10	DCE	 8	87
5	 9	Rh ₂ (cap) ₄	1.0	4	DCE	 10	71
		Rh ₂ (cap) ₄	1.0	10	DCE		90
6	 11	Rh ₂ (cap) ₄	1.0	4	DCE	 12	72
		Rh ₂ (cap) ₄	1.0	10	DCE		91
7	 13	Rh ₂ (cap) ₄	1.0	4	DCE	 14	35
		Rh ₂ (cap) ₄	1.0	10	DCE		58
8	 15	Rh ₂ (cap) ₄	0.05	8	PhMe	 16	57 ^d
9	 17	Rh ₂ (cap) ₄	0.05	4	PhMe	 18	57 ^{e,f}
10	 19	Rh ₂ (cap) ₄	2.0	10	PhCl	 20	66

^aYield after column chromatography. ^bReaction time was 45 min in DCE and 3 h in toluene. ^cThe reaction time was 24 h. ^dFour equiv of T-HYDRO was added at once at 0 °C at the beginning of the reaction followed after 1 h by another 4 equiv of T-HYDRO, and then the reaction was allowed to warm to room temperature. ^eA solution of 2-naphthol was added dropwise to a solution of Rh₂(cap)₄ and T-HYDRO. ^fYield was determined by ¹H NMR using compound 2 as an internal standard.

Table 2. Oxidation of Phenols Bearing Bulky Para Substituents with 4 equiv of T-HYDRO in Toluene

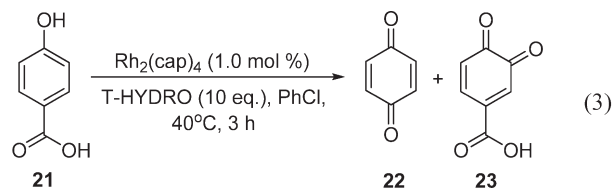
entry	phenol	catalyst	loading, mol %	ratio of <i>o</i> -/ <i>p</i> -oxidation products	yield, %
1	13	Rh ₂ (cap) ₄	0.05	27:73 ^a	51 ^b
		Rh ₂ (cap) ₄	0.05	39:61	53 ^c
2	25	CuI	1.0	0:100 ^a	24 ^{a,d}
		RuCl ₂ (PPh ₃) ₃	0.1	43:57 ^a	46 ^a

^a Determined by ¹H NMR with **2** as an internal standard. ^b Yield of **14** after chromatographic purification. ^c Combined yield of **26** and **27** after chromatographic purification. ^d Reported yield is for 37% conversion.

16 in 91% yield.⁶ The use of up to 10 equiv of T-HYDRO to produce yields comparable to those of Murahashi may be related to the higher flux of *tert*-butylperoxy radicals produced in the Rh₂(cap)₄-catalyzed reactions, but the general outcome of reactions catalyzed by either RuCl₂(PPh₃)₃ or by Rh₂(cap)₄ is the same.

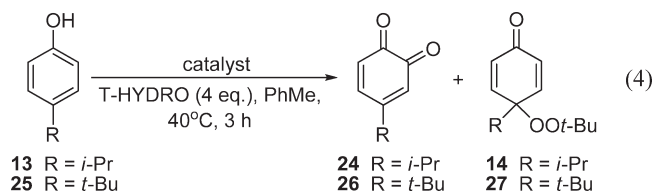
Although isolated product yields are usually high, and the dienone is generally stable to the reaction conditions, the peroxidation process has limitations. The product from oxidation of **15** (entry 8) undergoes slow decomposition; keeping pure **16** in a DCE solution at 40 °C overnight resulted in complete consumption of peroxide to unknown products. However, lowering the reaction temperature minimized decomposition of **16**. 2-Naphthol was found to be susceptible to probable dimerization⁴ or polymerization; however, maintaining an excess of oxidant by adding the substrate solution dropwise to a mixture of Rh₂(cap)₄ and T-HYDRO in toluene afforded a good yield of 1,2-naphthoquinone.

Phenols bearing electron-withdrawing groups such as carbonyl and carboxylate in the *para*-position underwent oxidation in chlorobenzene using 1–2 mol % of dirhodium caprolactamate. In the absence of a labile hydrogen on the position adjacent to carbonyl group, as with the common antifungal preservative in cosmetic products¹⁸ butyl paraben (entry 10), the peroxide product is successfully isolated in good yield. However, oxidation of *p*-hydroxybenzoic acid resulted in the formation of *p*-benzoquinone as a major product along with a minor *ortho* oxidation product (**23**) that was detected by ¹H NMR and GC/MS (eq 3).¹⁹ This decarboxylation process is intriguing in its induction by oxidation that occurs through hydrogen transfer from a remote functional group.

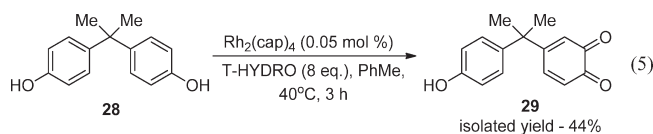


Phenolic oxidation ordinarily occurs with functionalization of its *para* position (Table 1, entries 1–8, 10). This result is consistent with the greater spin density at the *para* position in phenolic radicals.²⁰ However, bulky substituents in the *para* position provide sufficient steric hindrance to alter the regioselectivity of trapping by the *tert*-butylperoxy group (eq 4). Functionalization at the *ortho* position increases with the size of the *para* substituent, as is evident from comparison of phenols with isopropyl and *tert*-butyl substituents (Table 2). Similar outcomes were obtained with the use of Rh₂(cap)₄ and RuCl₂(PPh₃)₃ (entry 2), suggesting the similarity in reaction pathways between these two catalysts. However, use of CuI with **25** resulted in the sole formation of mixed peroxide **27**, albeit in

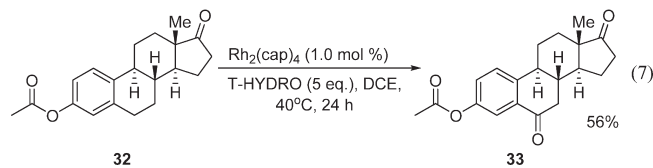
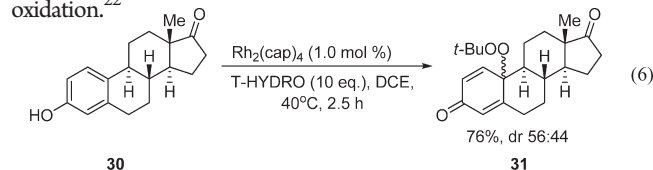
low yield, without evidence for **26**. *Ortho* oxidation of *para*-substituted phenols has been reported to be a selective process for TBHP oxidation by a silica gel supported complex of 1,4,7-trimethyl-1,4,7-triazacyclononane that results in ruthenium–catecholate complexes.²¹



Oxidation of bisphenol A (BPA) reveals another dimension of selectivity. This compound undergoes oxidation of just one phenol ring to produce *ortho*-quinone **29** in 44% yield along with minor amounts of unidentified products. This selectivity presumably arises from steric hindrance to trapping by the *tert*-butylperoxy group at the position *para* to the hydroxy group. The greater solubility of **29** in the aqueous layer than in the organic layer provides protection of **29** from further oxidation that is exemplified by a complex product mixture, as occurs with longer reaction times or subjecting isolated **29** to oxidation under the same conditions. We speculate that oxidation occurs in the organic layer, especially in aromatic solvents, but also in DCE, and not in the aqueous layer. As a result, BPA undergoes oxidation of one phenolic ring in the organic phase or at the aqueous–organic interface, and this product migrates to the aqueous layer where **29** is preserved from subsequent oxidation.

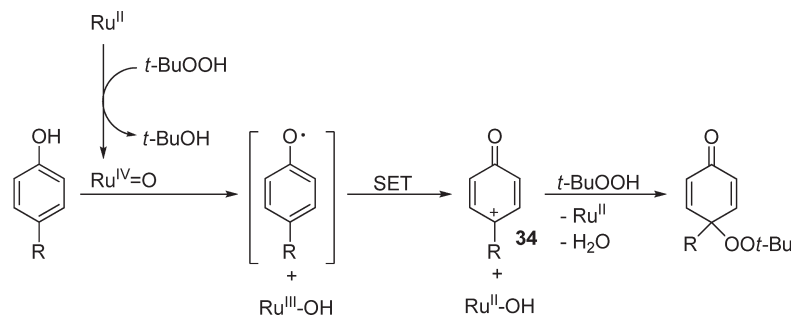


Investigations of the peroxidation of estrone provided an opportunity to evaluate selectivity in product formation and through this study to better understand the mechanism of oxidation. Murahashi has reported that the oxidation of estrone **30** catalyzed by RuCl₂(PPh₃)₃ yielded dienone **31** in 89% yield with a diastereomeric ratio 56:44. We found an identical diastereomer ratio when the oxidation of estrone by T-HYDRO is catalyzed by Rh₂(cap)₄ indicating the same intermediates for both catalysts (eq 6). An essential role of the phenolic O–H bond for peroxidation is indicated in the result from oxidation of acetylated estrone **32** (eq 67), and the methodology for this functionalization is superior to the alternative chromium trioxide oxidation.²²

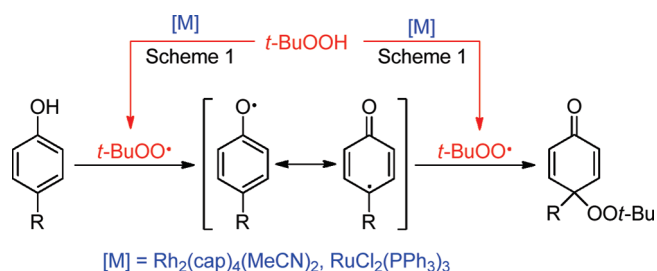


Our group has reported that dirhodium-catalyzed TBHP decomposition occurs by a radical pathway that is consistent

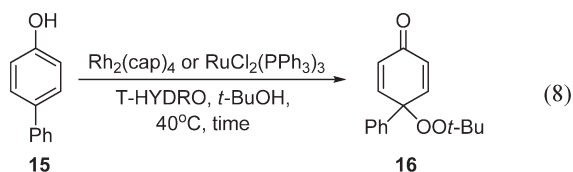
Scheme 2. Proposed Phenol Oxidation through Hydrogen Atom Abstraction Followed by Single Electron Transfer (SET)



Scheme 3. Mechanism of Transition-Metal-Catalyzed Phenolic Oxidation with TBHP

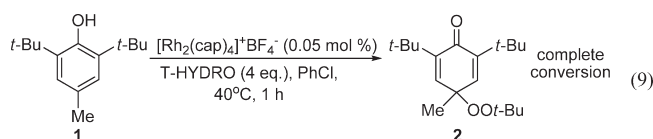


with results for allylic,^{8–10} benzylic,¹¹ and propargylic oxidations¹² and oxidations of secondary amines¹³ (Scheme 1),¹⁰ and a similar free radical mechanism was expected for phenolic oxidation. However, Murahashi, using anhydrous TBHP, has stated that phenolic oxidation occurs through an oxo–ruthenium complex resulting in the formation of a dienyl cation **34** that forms the observed peroxidation product by recombination with *tert*-butyl hydroperoxide (Scheme 2).^{6,23} We discounted this mechanism because use of T-HYDRO provides excellent yields of mixed peroxides **2**, **6**, **8**, **10**, and **12** (Table 1, entries 1, 3, 4, 5, and 6) and did not produce the corresponding hydroxy derivative that would be expected from a reaction pathway that involved **34** with either $\text{Rh}_2(\text{cap})_4$ or $\text{RuCl}_2(\text{PPh}_3)_3$. In addition, we performed the catalytic oxidation of **15** in nucleophilic media that would allow trapping by *tert*-butyl alcohol or water if **34** was involved (eq 8). For the $\text{Rh}_2(\text{cap})_4$ - and $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed oxidations by T-HYDRO the only isolated product was the mixed peroxide **16** which is consistent with the radical mechanism being operative with both catalysts.



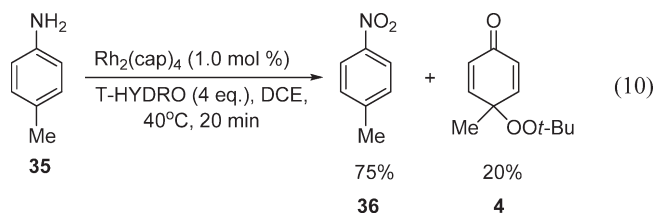
To further understand the mechanism for peroxide decomposition catalyzed by $\text{Rh}_2(\text{cap})_4$ that is proposed in Scheme 1, the completion time for oxidation of **1** with T-HYDRO catalyzed by the oxidized form of dirhodium caprolactamate is identical to that from the same reaction catalyzed by neutral dirhodium caprolactamate (eq 9). These data are consistent with the

involvement of $[\text{Rh}_2(\text{cap})_4]^+$ species in the catalytic cycle that is presented in Scheme 1.



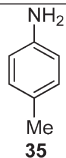
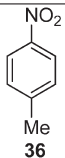

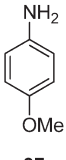
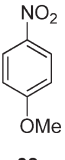
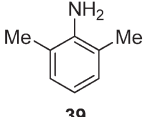
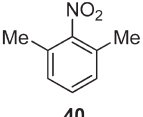
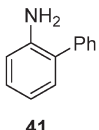
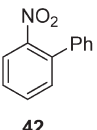
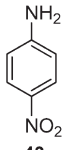
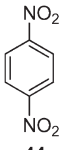
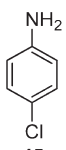
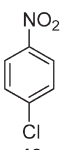
In summary, $\text{Rh}_2(\text{cap})_4$ is a highly efficient catalyst for the peroxidation of phenols, especially when the oxidation is performed in aromatic hydrocarbon solvents. Product ratios from the oxidation of estrone **30** by TBHP and those from reactions at the ortho and para positions of phenol **25** with catalytic amounts of $\text{Rh}_2(\text{cap})_4$ and $\text{RuCl}_2(\text{PPh}_3)_3$, as well as the absence of products from nucleophilic trapping of a cationic intermediate, suggest operation of the *tert*-butylperoxy radical generation mechanism (Scheme 1) coupled with recombination (Scheme 3) for phenolic oxidations by TBHP catalyzed by $\text{Rh}_2(\text{cap})_4$, $\text{RuCl}_2(\text{PPh}_3)_3$, and possibly CuI. Abstraction of the phenolic hydrogen by the *tert*-butylperoxy radical is followed by trapping of the phenolic radical by another *tert*-butylperoxy radical (Scheme 3). Efficiency in these processes is determined by the flux of the *tert*-butylperoxy radical generated according to Scheme 1.

Aniline Oxidation. The dirhodium caprolactamate/T-HYDRO catalytic oxidative system oxidizes aniline substrates preferentially to nitro compounds (Table 3) rather than to dienimines that by hydrolysis would result in dienones. *p*-Toluidine is oxidized to *p*-nitrotoluene in good yield, but with detectable amounts of dienone **4** (eq 10). TBHP was equally efficient in a 5 M anhydrous solution in decane and in a 70% aqueous solution (entry 1). Nitro compounds were readily obtained from anilines bearing strong or weak electron-donating substituents (entries 1–3). The presence of an aromatic ring in the ortho position (entry 4), or a strongly electron-withdrawing group in the para position (entries 5 and 6), significantly decreases product yield. Expectedly, electron-withdrawing substituents lower the reaction rate and make possible selective oxidation of just one amino group in *p*-phenylenediamine.



Monitoring the oxidation of aniline **35** with GC/MS revealed the presence of an intermediate with a $M + 14$ mass that is, most likely, the corresponding nitroso compound. Detection of

Table 3. Rh₂(cap)₄-Catalyzed Aniline Oxidation

entry	aniline	method ^a	product	isolated yield, %
1	 35	A	 36	79
		B	 36	75
2	 37	A	 38	60
3	 39	A	 40	80
4	 41	B	 42	43
5	 43	A	 44	16
6	 45	A	 46	51

^a Method A: Rh₂(cap)₄ (0.1 mol %), DCM (0.27 M), TBHP in decane (4 equiv), NaHCO₃ (0.5 equiv), rt, 16 h. Method B: Rh₂(cap)₄ (1.0 mol %), DCE (0.5 M), T-HYDRO (4 equiv), 40 °C, 20 min.

dienone **4** in the reaction mixture from oxidation of **35** indicates that, similar to phenolic oxidation, aniline oxidation includes hydrogen atom abstraction from an amino group followed by trapping by the peroxy radical at nitrogen or at the 4-position. A mechanism for aniline oxidation to nitroarenes in which a nitrosobenzene intermediate was speculated has been proposed for TBHP oxidation of anilines catalyzed by cobalt Schiff base complexes, but the initial hydrogen abstraction from the N–H bond is proposed to occur with *tert*-butoxy radicals rather than *tert*-butyl peroxy radicals.²⁴

In contrast to reactions of secondary amines that form imines¹³ and with tertiary amines that form iminium ions,¹⁴ dirhodium-catalyzed TBHP oxidations of aliphatic primary amines result in the oxidative removal of the amino group in moderate to good yields (Table 4). The reaction has greater efficiency for amines whose adjacent C–H bond has a lower bond dissociation energy (e.g., entry 2), but other modes of

hydrogen atom abstraction (e.g., entry 4) are presumably occurring.

EXPERIMENTAL SECTION

General Information. All reactions were performed under atmospheric conditions unless the conditions are specified. Infrared spectra were recorded on a FT/IR spectrometer. ¹H NMR spectra were recorded on 400 and 600 MHz spectrometers equipped with a BBI probe. Tetramethylsilane (TMS) (0.00 ppm) was used as an internal standard for all spectra. Data are reported as follows: chemical shift (in ppm, δ), integration, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, sept = septet, br = broad, m = multiplet), and coupling constants (in Hz). ¹³C NMR spectra were recorded on a 125 MHz spectrometer equipped with a TXI probe and operated with complete proton decoupling. Chemical shifts are reported in ppm utilizing CDCl₃ peak as a reference (77.0 ppm). Thin-layer chromatography was performed

Table 4. Rh₂(cap)₄-Catalyzed TBHP Oxidation of Primary Amines

Entry	Reactant ^a	Product	Yield, %
1			39 ^b
2			82
3			41
4			55

^a Reactions were performed on 1.34 mmol scale using 4.0 equiv of TBHP in decane and 1.0 mol % Rh₂(cap)₄ in DCM (0.27 M) for 16 h. ^b Two equiv of TBHP was used.

on silica gel coated on a glass plates (250 μm, F-254), and spots were visualized with 254 nm ultraviolet light. Flash chromatography used silica gel (32–63 μm), neutral alumina (50–200 μm), or Florisil (100–200 μm) as a stationary phase. High-resolution mass spectra (HRMS) were acquired on a ESI-TOF spectrometer. Rh₂(cap)₄ was prepared according to the literature procedure.²⁵

All previously unreported products were characterized by ¹H and ¹³C NMR and HRMS. Spectra of peroxides **2**, **4**, **6**, **8**, **12**, **14**, **24**, and **31** are in agreement with published information.⁶ Spectra of carbonyl compounds **16**,²⁶ **33**,²⁷ **48**,²⁸ **50**,²⁹ and **52**²⁹ and nitro arenes **36**,³⁰ **38**,³¹ **40**,³⁰ **42**,³² **44**,³³ and **46**³⁰ are identical to reported spectra.

General Procedure for Transition-Metal Complex Catalyzed Phenolic Oxidation in DCE or Toluene. The phenol derivative (2.0 mmol for oxidation in DCE; 3.0 mmol for oxidation in toluene), a catalyst, and a solvent (4.0 mL of DCE; 6.0 mL of toluene) were placed in a 6-dram screw-cap vial containing a magnetic stirring bar. The suspension containing a small amount of undissolved Rh₂(cap)₄ was heated to 40 °C in an oil bath at 250 rpm, and T-HYDRO was added all at once via syringe. The reaction mixture was loosely capped to allow release of built-up pressure and stirred at 40 °C. Then the reaction mixture was transferred to a 100-mL round-bottom flask and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, DCM/AcOEt/hexane). Fractions containing the product were combined, and the solvent was evaporated under reduced pressure. A fraction of the peroxide products were dried under high vacuum for 20 min (0.09 Torr, room temperature).

4-(tert-Butylperoxy)-2-methoxy-4-methylcyclohexa-2,5-dien-1-one (10): colorless oil; ¹H NMR (500 MHz, CDCl₃) δ 6.91 (dd, *J* = 10.1, 2.7 Hz, 1 H), 6.23 (d, *J* = 10.1 Hz, 1 H), 5.77 (d, *J* = 2.6 Hz, 1 H), 3.70 (s, 3 H), 1.45 (s, 4 H), 1.20 (s, 9 H); ¹³C NMR (125 MHz, CDCl₃) δ 181.0, 151.4, 150.7, 127.7, 117.5, 79.8, 77.8, 54.8, 26.3, 24.2; *R*_f = 0.32 (hexane/AcOEt (10:1)); HR-MS (ESI) calcd for C₁₂H₁₉O₄ 227.12834, found 227.12928 (M + H); IR (thin film) cm⁻¹ 2980, 1678, 1646, 1619, 1455.

n-Butyl 1-(tert-butylperoxy)-4-oxocyclohexa-2,5-diene-1-carboxylate (20): pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 7.08

(d, *J* = 10.1 Hz, 2 H), 6.36 (d, *J* = 10.0 Hz, 2 H), 4.20 (t, *J* = 6.5 Hz, 2 H), 1.70–1.60 (m, 2 H), 1.43–1.34 (m, 2 H), 1.25 (s, 9 H), 0.93 (t, *J* = 7.4 Hz, 3 H); ¹³C NMR (125 MHz, CDCl₃) δ 184.9, 167.0, 142.7, 130.8, 81.4, 79.3, 66.3, 30.4, 26.3, 18.9, 13.6; *R*_f = 0.40 (hexane/AcOEt/DCM 10:1:1); HR-MS (ESI) calcd for C₁₅H₂₃O₅ 283.15455, found 283.15216 (M + H).

4-tert-Butylbenzo-1,2-quinone (26): brown oil; ¹H NMR (400 MHz, CDCl₃) δ 7.19 (dd, *J* = 10.4, 2.4 Hz, 1 H), 6.40 (d, *J* = 10.4 Hz, 1 H), 6.29 (d, *J* = 2.2 Hz, 1 H), 1.24 (s, 9 H). ¹³C NMR (125 MHz, DMSO) δ 180.3, 180.2, 162.1, 140.0, 129.4, 123.8, 35.6, 27.8; *R*_f = 0.28 (hexane/AcOEt/DCM (4:1:1)); HR-MS (ESI) calcd for C₁₀H₁₃O₂ 165.09155, found 165.09168 (M + H).

4-tert-Butyl-4-(tert-butylperoxy)cyclohexa-2,5-dien-1-one (27): pale yellow oil; ¹H NMR (500 MHz, CDCl₃) δ 7.03 (d, *J* = 10.4 Hz, 2 H), 6.31 (d, *J* = 10.4 Hz, 2 H), 1.22 (s, 9 H), 1.03 (s, 9 H); ¹³C NMR (125 MHz, DMSO) δ 185.5, 150.5, 130.6, 82.6, 80.1, 40.0, 26.4, 26.0; *R*_f = 0.26 (hexane/AcOEt/DCM (8:1:1)); HR-MS (ESI) calcd for C₁₄H₂₂O₃ 238.15689, found 238.15372 (M⁺).

4-[1-(4-Hydroxyphenyl)-1-methylethyl]benzo-1,2-quinone (29): dark brown oil; ¹H NMR (500 MHz, CDCl₃) δ 7.16 (d, *J* = 8.6 Hz, 2 H), 6.87 (m, *J* = 8.8 Hz, 2 H), 6.65 (dd, *J* = 10.3, 2.4 Hz, 1 H), 6.50 (d, *J* = 2.1 Hz, 1 H), 6.22 (d, *J* = 10.3 Hz, 1 H), 5.28 (s, 1 H), 1.54 (s, 6 H); ¹³C NMR (150 MHz, CDCl₃) δ 180.4 (2 C), 161.4, 154.8, 141.5, 136.1, 129.0, 127.8, 123.8, 115.9, 43.0, 27.3; *R*_f = 0.48 (hexane/AcOEt/DCM (8:1:1)); HR-MS (ESI) calcd for C₁₅H₁₅O₃ 243.10212, found 243.10110 (M + H).

Procedure for Kinetic Measurements of Transition-Metal-Catalyzed Oxidations of 2,6-Di-tert-Butyl-4-methylphenol (1) by T-HYDRO. Phenol **1** (13.63 mmol, 3.00 g), catalyst, and solvent (27.0 mL) were placed in a 125-mL Erlenmeyer flask containing a magnetic stirring bar. The suspension containing a small amount of undissolved catalyst was heated to 40 °C on a stirrer-hot plate, and T-HYDRO was added all at once via syringe. Immediately after T-HYDRO addition, the mixture became cloudy due to formation of an aqueous layer, and the color of the mixture became red for Rh₂(cap)₄-

catalyzed, dark green for $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed, or yellow for Cu salt-catalyzed reaction after 4 h. The catalyst precipitate was completely dissolved within 1 min after T-HYDRO addition. The flask was equipped with a septum containing a needle to release any built-up pressure and was stirred at 40 °C. After the specified time, a small aliquot (about 0.10 mL) of the organic layer was taken out, and the solvent was rapidly evaporated under high vacuum for 5 min (0.09 Torr, room temperature). The residue was dissolved in CDCl_3 and analyzed by ^1H NMR spectroscopy. Percent conversion was measured as ratio of integral values of alkene protons of product 2 (s, 6.56 ppm) to aromatic protons of 1 (s, 6.98 ppm).

Oxidation of 4-Phenylphenol (15) in Toluene. 4-Phenylphenol 15 (3.0 mmol, 510 mg), $\text{Rh}_2(\text{cap})_4(\text{MeCN})_2$ (1.5 μmol , 1.1 mg) or $\text{RuCl}_2(\text{PPh}_3)_3$ (3.0 μmol , 2.9 mg), and toluene (6.0 mL) were placed in 6-dram screw-cap vial containing a magnetic stirring bar. The mixture was sonicated to ensure maximal dissolution of the phenol in a resulting suspension. The resulting mixture with partially undissolved phenol was placed in an ice bath and stirred for about 3 min to allow the temperature to equilibrate to 0 °C. T-HYDRO (12.0 mmol, 1.66 mL, 4.0 equiv) was added via syringe dropwise over the period of 1 min with intensive stirring. After 1 h of stirring at 250 rpm at 0 °C, another 4.0 equiv of T-HYDRO was added via syringe all at once. The vial was removed from the ice bath, and the reaction mixture was allowed to warm to room temperature. The mixture was stirred at 250 rpm for 3 h at room temperature. The mixture was transferred to 100-mL round-bottom flask and concentrated on a rotary evaporator (20 Torr, room temperature). The residue was dissolved in DCM, and the residue was purified by column chromatography (neutral alumina, 18 mm diameter, 18 cm height, $\text{EtOAc}/\text{DCM}/\text{hexane}$ (1:1:16, 250 mL)). Fractions containing the product 16 were combined, and the solvent was evaporated on a rotary evaporator (60 Torr, room temperature); in the case of product with a large molecular mass the residue was further dried under high vacuum for 20 min (0.09 Torr, room temperature) to yield 441 mg (57%) and 278 mg (36%) of mixed peroxide 16 as a pale yellow oil for $\text{Rh}_2(\text{cap})_4$ - and $\text{RuCl}_2(\text{PPh}_3)_3$ -catalyzed reactions, respectively: ^1H NMR (500 MHz, CDCl_3) δ 7.42–7.33 (m, 5 H), 7.01 (m, $J = 10.2$ Hz, 2H), 6.33 (d, $J = 10.2$ Hz, 2H), 1.29 (s, 9 H); ^{13}C NMR (125 MHz, CDCl_3) δ 185.9, 150.0, 136.9, 128.9, 128.8, 125.8, 80.6, 79.6, 26.5; $R_f = 0.31$ ($\text{hexane}/\text{AcOEt}$ (10:1)); HR-MS (ESI) calcd for $\text{C}_{16}\text{H}_{19}\text{O}_3$ 259.13342, found 259.13258 (M + H).

Oxidation of 4-Phenylphenol (15) in *tert*-Butyl Alcohol. 4-Phenylphenol 15 (1.0 mmol, 170 mg), $\text{Rh}_2(\text{cap})_4(\text{MeCN})_2$ (10.0 μmol , 7.4 mg) or $\text{RuCl}_2(\text{PPh}_3)_3$ (20.0 μmol , 19.2 mg), and *tert*-butyl alcohol (5.0 mL) were placed in 6-dram screw-cap vial containing a magnetic stirring bar. The mixture was sonicated to facilitate a complete dissolution of the phenol. The resulting mixture was placed in an oil bath and warmed to 40 °C. T-HYDRO (10.0 mmol, 1.38 mL, 10 equiv) was added via syringe all at once, and the reaction was stirred at 40 °C. The reaction mixture was transferred to 100-mL round-bottom flask and concentrated on a rotary evaporator (20 Torr, room temperature). The residue was dissolved in DCM, and the residue was purified by column chromatography (neutral alumina, 18 mm diameter, 18 cm height, $\text{EtOAc}/\text{DCM}/\text{hexane}$ (1:1:16, 250 mL)). Fractions containing 16 were combined, and the solvent was evaporated on a rotary evaporator (60 Torr, room temperature). The residue was further dried under high vacuum for 20 min (0.09 Torr, room temperature) to yield 433 mg (56%) and 124 mg (16%) mixed peroxide 16 as a pale yellow oil for $\text{Rh}_2(\text{cap})_4$ and $\text{RuCl}_2(\text{PPh}_3)_3$ catalyzed reactions, respectively.

Oxidation of 2-Naphthol (17). $\text{Rh}_2(\text{cap})_4(\text{MeCN})_2$ (0.50 μmol , 1.1 mg) and toluene (10.0 mL) were placed in a 50-mL Erlenmeyer flask, and the suspension was warmed to 40 °C. T-HYDRO (12.0 mmol, 1.66 mL, 4.0 equiv) was added via syringe dropwise followed immediately by dropwise addition over 5 min of a solution of 2-naphthol 17 (3.0 mmol, 432 mg) and peroxide 2 (1.0 mmol, 308 mg) that was used as

an internal standard in toluene (20.0 mL). After completion of the addition, the reaction mixture was stirred for 20 min at 40 °C, and then a small aliquot (about 0.10 mL) of the organic layer was removed and the solvent was evaporated under high vacuum over 5 min (0.09 Torr, room temperature). The residue was dissolved in CDCl_3 and analyzed by ^1H NMR spectroscopy. The percent yield was determined from the integral values of internal standard 2 (s, 6.56 ppm) and alkene proton of 18 (d, 6.44 ppm): ^1H NMR (600 MHz, CDCl_3) δ 8.11 (d, $J = 7.6$ Hz, 1 H), 7.66 (t, $J = 7.5$ Hz, 1 H), 7.52 (t, $J = 7.6$ Hz, 1 H), 7.46 (d, $J = 10.1$ Hz, 1 H), 7.38 (d, $J = 7.5$ Hz, 1 H), 6.44 (d, $J = 10.1$ Hz, 1 H); ^{13}C NMR (150 MHz, CDCl_3) δ 180.9, 178.9, 145.3, 135.8, 134.8, 131.6, 130.8, 130.2, 129.8, 127.9; $R_f = 0.16$ ($\text{hexane}/\text{AcOEt}/\text{DCM}$ (8:1:1)).

General Procedure for $\text{Rh}_2(\text{cap})_4$ -Catalyzed Oxidation of Anilines with 5 M TBHP in Decane or with T-HYDRO. The substituted aniline (2.0 mmol), $\text{Rh}_2(\text{cap})_4(\text{MeCN})_2$ (14.8 mg, 0.020 mmol), and DCE (4.0 mL) were placed in a 4-dram screw-cap vial containing a magnetic stirring bar. The suspension was heated to 40 °C in an oil bath, and 5 M TBHP solution in decane (1.6 mL, 8.0 mmol, 4.0 equiv) or T-HYDRO (1.1 mL, 8.0 mmol, 4.0 equiv) was added all at once via syringe. The reaction solution/mixture was loosely capped to release any built-up pressure and stirred for 20 min at 40 °C. Then the reaction mixture was transferred to a 100-mL round-bottom flask and concentrated under reduced pressure, and the residue was purified by column chromatography (silica gel, $\text{DCM}/\text{AcOEt}/\text{hexane}$). Fractions containing the product were combined, and the solvent was evaporated under reduced pressure followed by additional drying under high vacuum for 20 min (0.09 Torr, room temperature).

■ ASSOCIATED CONTENT

Supporting Information. Kinetic data and product characterization (^1H and ^{13}C spectra) of new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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