

Dirhodium(II) Caprolactamate: An Exceptional Catalyst for Allylic Oxidation

Arthur J. Catino, Raymond E. Forslund, and Michael P. Doyle*

Department of Chemistry and Biochemistry, University of Maryland, College Park, Maryland 20742

Received August 3, 2004; E-mail: mdoyle3@umd.edu

Allylic oxidation holds a venerable position in organic synthesis. The regioselective functionalization of an allylic C–H bond with oxygen is a value-added operation yielding a wide range of synthetically useful products.^{1,2} Particularly important is the direct synthesis of enones and enediones from the oxidation of readily available alkenes.³ Traditional methods typically employ stoichiometric metal oxidants.⁴ Transition metal catalyzed processes in conjunction with a terminal oxidant offer a promising alternative, but limitations arise from high catalyst loading, lengthy reaction times, harsh conditions, and/or poor selectivity.⁵ Herein we describe a new allylic oxidation protocol using dirhodium catalysis that is mild and selective and operates with unprecedented turnover number and frequency.

Dirhodium(II) complexes, specifically $\text{Rh}_2(\text{OAc})_4$ and $\text{Rh}_2(\text{pfb})_4$ (Figure 1), have been reported to have limited activity for allylic

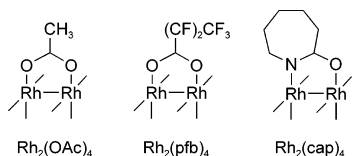
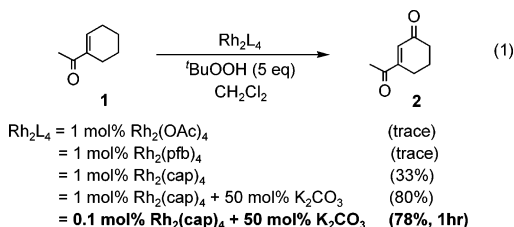


Figure 1. Dirhodium(II) catalysts.

oxidation of olefins with *tert*-butyl hydroperoxide (TBHP).⁶ With poor yields that preclude wide application, little has been done to address the activation of peroxide by dirhodium.^{7,8} Generally speaking, the most effective catalysts for allylic oxidation, as pointed out by Kochi, are those metals that readily undergo 1-electron redox processes, e.g., $\text{Fe}^{2+} \rightleftharpoons \text{Fe}^{3+}$, $\text{Cu}^{1+} \rightleftharpoons \text{Cu}^{2+}$, and $\text{Co}^{2+} \rightleftharpoons \text{Co}^{3+}$.⁹ With this in mind, we considered bench-stable and readily prepared dirhodium(II) caprolactamate ($\text{Rh}_2(\text{cap})_4$, *vide infra*).¹⁰ Cyclic voltammetry data for $\text{Rh}_2(\text{cap})_4$ obtained by Ren showed a reversible oxidation at 55 mV (in CH_3CN , vs Ag/AgCl) corresponding to the $\text{Rh}_2^{4+}/\text{Rh}_2^{5+}$ redox couple.¹¹ Moreover, $\text{Rh}_2(\text{cap})_4$ readily underwent a 1-electron oxidation ($E_{1/2} = 11$ mV), in contrast to $\text{Rh}_2(\text{OAc})_4$ and $\text{Rh}_2(\text{pfb})_4$ ($E_{1/2} = 1170$ and >1800 mV, respectively).¹² This striking data revealed that $\text{Rh}_2(\text{cap})_4$ could access and transverse the $\text{Rh}_2^{4+}/\text{Rh}_2^{5+}$ oxidation states and compelled us to examine its ability as a catalyst for allylic oxidation.

We initiated our study by examining the allylic oxidation of 1-acetylcyclohexene **1** (eq 1).¹³ As expected, 1 mol % $\text{Rh}_2(\text{OAc})_4$



or $\text{Rh}_2(\text{pfb})_4$ with anhydrous TBHP¹⁴ (5 equiv) in CH_2Cl_2 after 12 h yielded only trace amounts of enedione **2**. On the other hand, we

found that under the same conditions 1 mol % $\text{Rh}_2(\text{cap})_4$ provided **2** in 33% yield in only a few minutes.¹⁵ Considering literature precedence for the intermediacy of allylic *tert*-butyl peroxy ethers¹⁶ along with their facile conversion to carbonyl compounds with base,¹⁷ addition of K_2CO_3 (50 mol %) to the reaction mixture greatly improved yield to 80% without compromising reaction time.¹⁸ Upon further examination, we were able to reduce catalyst loading to only 0.1 mol % $\text{Rh}_2(\text{cap})_4$ (substrate/catalyst loading = 1000) producing enedione **2** in 78% yield in just 1 h. Further optimization showed a considerable dependence on the amount of terminal

Table 1. $\text{Rh}_2(\text{cap})_4$ -Catalyzed Allylic Oxidation of Olefins¹⁹

entry	olefin	product	$\text{Rh}_2(\text{cap})_4$ (mol%)	time (h)	yield (%) ^a
1			0.1	1	60 ^b
2			0.1	1	94
3			0.1	1	77
4			0.1	1	92
5 ^d			1.0	24	64
6			0.1	0.3	89 ^c
7			0.1	1	75
8			0.1	1	86
9			0.1	1	79
10 ^{d,e}			1	3	83
11 ^{d,e}			1	3	61

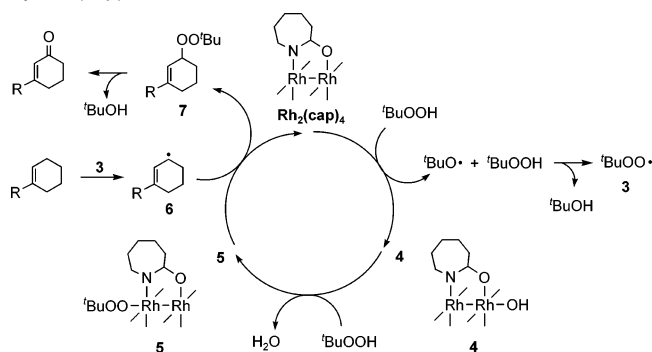
^a Isolated yield after chromatography. ^b Diminished yield due to product volatility. ^c Reaction performed on a 1.00-g scale. ^d Catalyst added in two portions (0.5 mol % catalyst and 5 equiv of TBHP at the start, and another 0.5 mol % catalyst and 5 equiv of TBHP midway through the indicated time). ^e Reaction performed at 40 °C.

oxidant, as product yield diminished with TBHP below three equivalents consistent with the stoichiometry of the reaction.¹⁸ Screening various solvents showed that CH₂Cl₂ was superior, and no reaction was observed in THF or acetonitrile.¹⁸

Using these optimized conditions, we examined the allylic oxidation of representative olefins (Table 1).¹⁹ Most olefins were rapidly converted to enones and enediones in 1 h with only 0.1 mol % Rh₂(cap)₄. Complete selectivity was observed in all cases, yielding only the products indicated. Noteworthy is the selectivity observed for 1-methylcyclohexene (entry 6) and 3-methylcyclohexene (entry 7), which were both converted to seudenone, an insect pheromone isolated from the Douglas-fir beetle.²⁰ Overall, the reaction is operationally simple to perform while being tolerant of air and atmospheric moisture.

Mechanistically, extensive investigations have shown that Rh₂(cap)₄ undergoes a 1-electron oxidation in the presence of TBHP to form a Rh₂⁵⁺ species tentatively assigned as **4**, which can be converted under the reaction conditions to dirhodium peroxyether complex **5** (Scheme 1). Evidence for this oxidative transformation includes a dramatic color change from light blue to deep red in CH₂Cl₂. The UV–visible spectrum of the catalyst upon addition of TBHP revealed a low-energy adsorption at 974 nm (δ – δ^* transitions) consistent with a mixed-valent dinuclear metal species.^{21,22} In addition, the product of the reaction of Rh₂(cap)₄ and TBHP was isolated and analyzed by ¹H NMR despite its paramagnetic nature and showed a new signal at 1.24 ppm.²³ We believe these data support the formation of dirhodium *tert*-butyl peroxyether complex **5**. Furthermore, evolution of oxygen during the course of the reaction was observed and is consistent with the formation of *tert*-butyl peroxy radical **3**, which is known to dimerize to di-*tert*-butyltetraoxide.²⁴ More importantly, though, **3** is capable of selective hydrogen atom abstraction to produce radical **6**.²⁵ Ligand transfer of the metal-bound peroxide to the carbon-centered radical forms the mixed peroxide **7** and regenerates the catalyst (as Rh₂⁴⁺). This proposed sequence thus constitutes a redox chain catalytic cycle.²⁶ Finally, rapid decomposition of **7**, which we have isolated as a product from the reaction, yields the enone or enedione as shown.²⁷

Scheme 1. Mechanistic Proposal for Allylic Oxidation Catalyzed by Rh₂(cap)₄



In summary, we have developed a novel catalytic allylic oxidation protocol based on dirhodium. The unique reactivity of Rh₂(cap)₄ emanates from its ability to undergo facile redox chemistry, namely Rh₂⁴⁺ ⇌ Rh₂⁵⁺. Further studies will be aimed at accessing the active oxidant and developing new applications including enantioselective processes that involve higher-valent dirhodium intermediates.

Acknowledgment. We are grateful to the NSF and the NIH (GM-46503) for their generous support. Special thanks to Prof. Tong Ren for alerting us to the comparative electrochemical data.

Supporting Information Available: Experimental procedures and additional information. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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- (15) Longer reaction times did not increase yield.
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- (19) Representative Procedure (0.1 mol % catalyst): A 25 mL flask equipped with a stirbar was charged with olefin (2.72 mmol, 100 mol %), CH₂Cl₂ (10 mL), K₂CO₃ (1.36 mmol, 50 mol %), and Rh₂(cap)₄ (0.0027 mmol, 0.1 mol %). The flask was sealed with a septum, allowing inclusion of air. An empty balloon was added to capture oxygen generated during the course of the reaction. To the mixture was added *tert*-butyl hydroperoxide (13.6 mmol, 5 equiv) in one portion via syringe from which the color of the solution immediately turned from light blue to deep red. Oxygen generation was observed inflating the balloon. After 1 h the solution was filtered over a short plug of silica gel to remove the catalyst. Column chromatography (SiO₂) yielded the analytically pure compound.
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- (23) Isolated as a deep-red solid after chromatography. Submitting this complex (0.1 mol %) to the oxidation of **1** gave **2** in 53% under identical reaction conditions. See Supporting Information. We were unable to obtain a well-defined EPR signal of the oxidized Rh₂⁵⁺ complex. Efforts are underway to obtain a crystal structure of this complex.
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- (27) We have isolated **7** (where R = Ph) from the oxidation of 1-phenylcyclohexene. Resubmitting **7** to the reaction resulted in quantitative conversion to the product shown in Table 1, entry 3. See Supporting Information for details.

JA045330O