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Palladium-Catalyzed Allylic Oxidation of Cyclohexenes Using Molecular Oxygen as Oxidant

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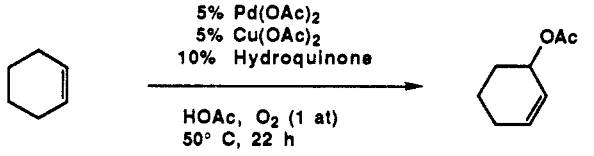
Summary: Cyclohexene and some related alkenes are readily converted into allyl acetates by catalytic amounts of palladium acetate and a reoxidation system consisting of molecular oxygen and either hydroquinone and a second transition metal acetate or cobalt(II) Schiff's base complexes such as 7 and 8.

Methods for selective oxidation of alkenes by transition-metal catalysts have been studied extensively during the last decade.[1] We have recently been able to develop an efficient palladium-catalyzed procedure for allylic acetoxylation of alkenes.[2] In this procedure, the palladium catalyst is continuously reoxidized by a combination of manganese dioxide and a catalytic amount of benzoquinone, which probably acts both as a reoxidant and ligand to palladium.[3] For some time we have tried to develop an alternative process which uses molecular oxygen in place of manganese dioxide. The reoxidation of the reduced form of benzoquinone appeared to be the crucial point of our system. We therefore focused our attention on catalysts for oxidation of hydroquinone to benzoquinone by molecular oxygen. Several such systems are known, but suffer from serious disadvantages such as low efficiency and rapid decomposition.[1l,4] Copper(II) chloride has been used both as stoichiometric oxidant in acetoxylation[5] and as catalytic oxidant in the Wacker process.[1a-c] However, it has been shown that chloride ions interfere in acetoxylation reactions.[3,5] In this paper we report on a successful system using copper acetate. We also present a "compact" system where the quinoid moiety is incorporated into the reoxidation catalyst. In a typical experiment, palladium acetate (0.25 mmol), copper(II) acetate (0.25 mmol), and hydroquinone (0.5 mmol) were dissolved in 25 mL of acetic acid. After evacuation, the atmosphere was changed to oxygen (1 atm), and cyclohexene (4.9 mmol) was added. The reaction mixture was heated for 22 h at 50 °C to give better than 85% yield of cyclohexenyl acetate[6] (1) (Scheme I).

Scheme I



1 >85%

Copper acetate could be replaced by manganese(III) or cobalt(II) acetate. Although these are less efficient than copper acetate, the result suggests that a number of other metal salts can probably also be used as cooxidants together with oxygen (Figure 1). In the absence of palladium acetate, no product is obtained. Leaving out copper acetate leads to the formation of only 5-10% of 1 together with more than 20% benzene. If hydroquinone is left out, the reaction still proceeds but now at a much lower rate and benzene (7-11%) is formed. Also the induction period is longer than when hydroquinone is added. When benzoquinone is used in place of hydroquinone, the reaction is unaffected except that the induction period disappears. Experiments with 5 and 15 mol % hydroquinone added show that the reaction rate increases with increasing amount of hydroquinone. Increasing the amount of copper acetate from 5 to 15 mol % does not appreciably change the reaction rate, nor does an increase of the O_2 pressure (5 atm) noticeably change the rate (Figure 2).[7]

An exploratory study of some other cycloalkenes was also carried out. 1-Methyl-, 3-methyl-, and 4-methylcyclohexene all gave mixtures of allylic acetates (total conversion of starting materials) in accordance with earlier results,[2] 2 (37%) and 3 (63%) from 1-methylcyclohexene, 2 (49%), 4 (24%), and 5 (27%) from 3-methylcyclohexene, and 4 (26%), 5 (19%), and 6 (55%) from 4-methylcyclohexene (Figure 3).

A palladium mirror was generally formed on the walls of the reaction vessel when copper(II) and other metal acetates were used as oxidants. Interestingly, a decrease in the initial concentration of palladium leads to an approximately proportional decrease in the rate. Since the formation of a precipitate must deplete the reaction mixture of catalyst, we also studied ways to keep palladium in solution. Triphenylphosphine is inefficient since it is rapidly oxidized to triphenylphosphine oxide. A stable palladium(0) complex such as Pd(DBA)$_2$[8] was not useful due to dehydrogenation of cyclohexene to benzene. However, it occurred to us that a compact reoxidation

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(6) The reaction was monitored by GLC using undecane (100 μL) as internal standard. Cyclohexenyl acetate (1) was also prepared on a larger scale. Thus palladium(II) acetate (1 mmol, 224 mg), copper(II) acetate (1 mmol, 200 mg), and hydroquinone (2 mmol, 220 mg) were dissolved in glacial acetic acid (50 mL). After changing atmosphere to oxygen and adding cyclohexene (20 mmol, 2.0 mL), the mixture was stirred for 18 h at 50 °C. Water (75 mL) was added, and the mixture was extracted with petroleum ether/ether (4 × 50 mL, 1:1). The combined organic phases were washed with sodium hydroxide (3 × 50 mL, 2 M) and water (50 mL) and dried (magnesium sulfate). After filtration and evaporation of solvents, distillation gave 2.2 g of cyclohexenyl acetate (80%) as a colorless oil.

(7) If air is used instead of oxygen, the reaction is extremely slow. Dehydrogenation of cyclohexene occurs instead, and benzene is formed.

(8) DBA = dibenzylideneacetone.

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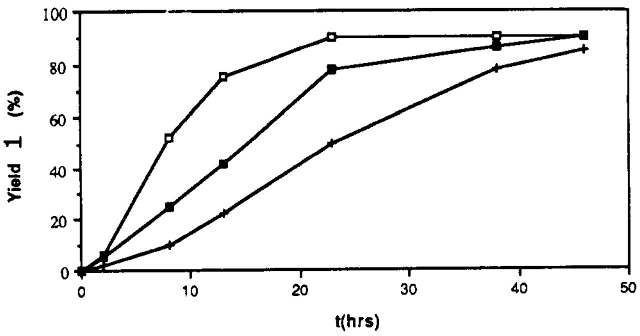


Figure 1. Formation of cyclohexenyl acetate catalyzed by palladium acetate, hydroquinone/molecular oxygen, and (□) copper, (■) manganese, or (+) cobalt acetate.

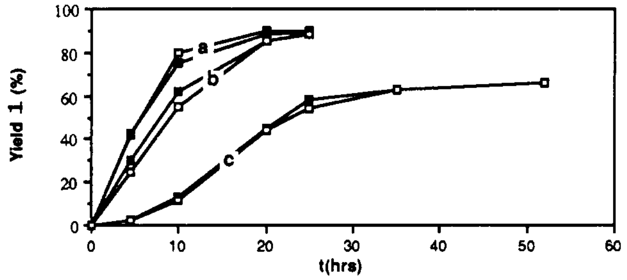


Figure 2. Effect of copper acetate and hydroquinone concentration on the formation of cyclohexenyl acetate. (a) 15% (b) 5%, and (c) 0% of hydroquinone. (■) 15% and (□) 5% of copper acetate.

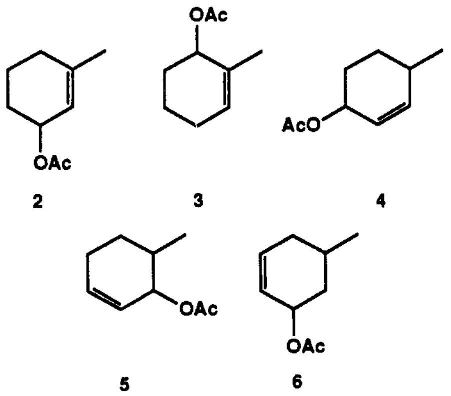
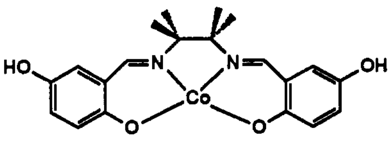
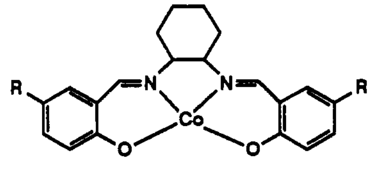


Figure 3.



7



8 R = OH

9 R = H

system, which incorporates the quinone and the cooxidant in one molecule, might be superior to the mixture of metal acetate and hydroquinone. This may also be an advantage in systems where free benzoquinone tends to undergo competing reactions such as Diels–Alder addition.[3] We therefore prepared a Salen[9] type complex 7 in situ by mixing the ligand[10] (5 mol %) with an equivalent amount of cobalt(II) acetate (5 mol %) and then performed acetoxylation as described above but leaving out hydroquinone.

The acetoxylation was somewhat slower than for the copper acetate/hydroquinone system, but about 90% yield of cyclohexenyl acetate was obtained after 40 h. The related compound 8 (5 mol %) gave 68% yield. If the hydroxyl group in 8 was replaced by hydrogen as in 9, only small amounts of cyclohexenyl acetate (19%) were formed together with substantial amounts of benzene from dehydrogenation of cyclohexene, and in this case palladium(0) was also precipitated as a mirror. If instead a mixture of 9 (5 mol %) and hydroquinone (10 mol %) was used, the product cyclohexenyl acetate was again formed in good yield (80%).[7,11] Our results thus show that efficient palladium-catalyzed acetoxylation of cyclohexene can be achieved, using oxygen as oxidant, if a mixture of hydroquinone or benzoquinone and a transition metal acetate is used as cooxidant. Exploratory experiments also suggest that this mixture can be replaced by a compact cooxidant such as 7 which incorporates the quinone moiety and is reminiscent of biological electron transfer systems. This type of oxidation system appears potentially useful for all types of oxidation reactions where a quinone moiety is essential, and the concept is being studied further in our laboratories.

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Supplementary Material Available: The preparation of the ligands 7–9 together with ^{1}H NMR data (1 page). Ordering information is given on any current masthead page.

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(9) Salen: *N,N'*-bis(salicylidene)ethyleneamine.

(10) The ligands were fully characterized by elemental analyses (C, H) and NMR spectra.

(11) Similar conditions have been used for diacetoxylation of 1,3-dienes, ref 11.

The Intramolecular Salt Effect[1]

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Summary: Ionic groups and salt bridges in the active sites of enzymes are thought to have important effects upon substrate reactivity. This paper describes the evaluation of an ion pair as an intramolecular effector of reaction rate for an addition reaction, the reaction of benzylic primary amines with methyl propynoate.