

# Palladium-mediated aerobic oxidation of organic substrates: the role of metal versus hydrogen peroxide

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## Abstract

Palladium species catalyze the aerobic oxidation of a variety of organic substrates. The reoxidation of palladium(0) to palladium(II) by dioxygen, a necessary step in these catalytic oxidations, results in the simultaneous formation of free peroxide. However, the continued catalytic generation of peroxide requires the rereduction of palladium(II) to palladium(0). This can be achieved by alkenes and alcohols which are then converted to carbonyl compounds. In these cases, no sacrificial coreductant is necessary and the peroxide appears to play no significant part in the oxidation of these substrates. On the other hand, palladium(II) does not readily oxidize primary or aromatic C–H bonds thereby preventing its reduction by them. Thus, a sacrificial coreductant is required to reduce palladium(II), and carbon monoxide and dihydrogen can fulfill this role. The peroxide generated in these cases is subsequently used to effect the oxidation of the alkane and arene either by palladium(II) or by a second catalyst.

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*Keywords:* Catalyst; Oxidation; Palladium; Hydrogen peroxide; Benzene; Phenol; Vanadium; Iron

## 1. Introduction

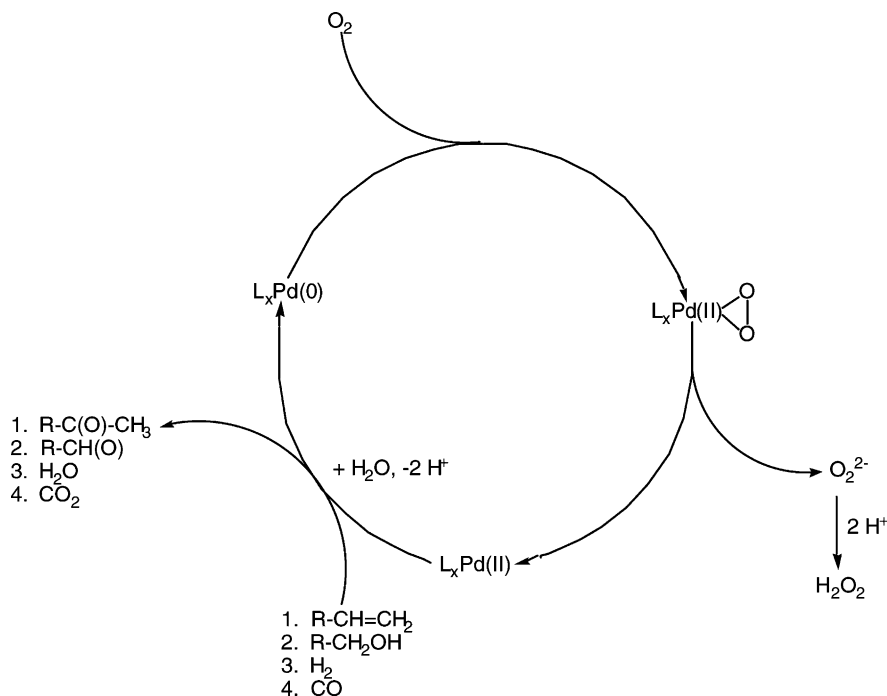
Various palladium species mediate the aerobic oxidation of organic substrates [1]. Some of the more important examples are the conversion of alkenes to aldehydes or ketones (Wacker process) [2], the oxidation of alcohols to carbonyl compounds [3–7], the hydroxylation and further oxidation of primary C–H bonds [8–10], and the deep oxidation of toxic organics [11]. In alkene and alcohol oxidations, the oxidant responsible for substrate oxidation is the palladium(II) ion which is then reduced to a palladium(0) species. The latter is subsequently reoxidized to palladium(II) by dioxygen. Copper compounds

have sometimes been employed to aid this reoxidation step [2]. What has sometimes been overlooked is that the two-electron oxidation of palladium(0) to palladium(II) by dioxygen simultaneously generates a second, potentially powerful, oxidant: free peroxide ( $O_2^{2-}$  or  $H_2O_2$ ) (see Scheme 1). What role does the peroxide play in these oxidations? Can it be used for oxidations not catalyzed by palladium(II)? A related question is why a sacrificial coreductant (e.g. dihydrogen or carbon monoxide) is required for the oxidation of strong primary C–H bonds [8–11] but not for “easy” oxidations involving alkenes and alcohols [1–7]. Herein we present our perspective on these issues.

## 2. Results and discussions

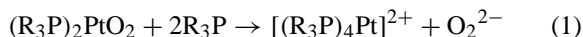
The formation of free peroxide in the oxidation of palladium(0) or platinum(0) to the corresponding

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Scheme 1.

divalent compounds by dioxygen is, by now, well documented by us and others. A plausible mechanism for this is as shown in Scheme 1. The first step involves the formation of a metal-peroxo complex. The coordinated peroxide can then be displaced from the metal by the addition of a ligand, e.g. Eq. (1), [12]. More commonly, in acidic solutions, it is protonated to form hydrogen peroxide [13,14].

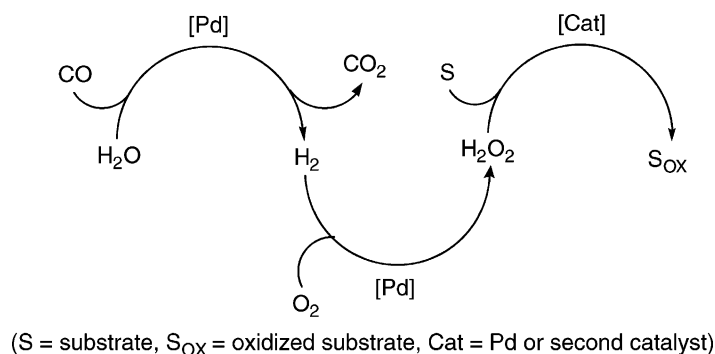


What is the fate of the free peroxide? One suggestion is that the (hydrogen) peroxide is rapidly disproportionated to water and dioxygen by the metal species present and takes no further part in the oxidations. For example, during olefin oxidation with palladium diacetate and hydrogen peroxide, decomposition of the oxidant was observed [15]. This effect was more pronounced in the absence of the substrate.

Despite the previous report regarding rapid metal-catalyzed peroxide disproportionation, examples exist where hydrogen peroxide has been shown to not only form in the reaction but also to remain in solution for a measurable period of time. One example

involves the aerobic oxidation of alcohols by a combination of palladium acetate and pyridine [6]. In this case, it has been suggested that the peroxide may actually compete with the substrate for binding to the metal center and, therefore, its removal by decomposition (e.g. by molecular sieves) promotes substrate oxidation. We have also demonstrated the formation of hydrogen peroxide in the aerobic oxidation of alkanes by metallic palladium in the presence of carbon monoxide (Scheme 2) [16]. Additionally, several patents and papers report the palladium-catalyzed generation of hydrogen peroxide in relatively high concentrations in the absence of an oxidizable substrate [17,18]. These reactions involve the use of dioxygen and either carbon monoxide or dihydrogen. Both metallic palladium, as well as discrete palladium compounds, have been employed as catalysts for the reaction.

Furthermore, we have recently completed work showing the persistence of palladium-generated hydrogen peroxide in solution. This oxidant remains in solution long enough to interact with another catalyst (e.g. vanadium or iron). Thus, hydrogen peroxide, generated in situ by metallic palladium-catalyzed



Scheme 2.

Table 1  
Yields for several vanadium and iron catalysts for benzene oxidation<sup>a</sup>

Entry number	Hydroxylation catalyst	Turnovers per h <sup>b</sup>	Phenol (mmol)	Benzoquinone (mmol)
1	None	–	0.003	–
2	V(acetylacetonate) <sub>3</sub>	70	0.449	–
3	V(O)(acetylacetonate) <sub>2</sub>	68	0.438	–
4	V(O)(acetylacetonate) <sub>2</sub> <sup>c</sup>	0	0.000	–
5	VO(O <sub>2</sub> )(2-picoline)(H <sub>2</sub> O) <sub>2</sub>	55	0.355	–
6	Tris(dibenzoylmethanato)Fe(III)	41	0.263	0.050
8	Fe(II) acetate	28	0.179	0.033
9	Fe(acetylacetonate) <sub>3</sub>	59	0.378	0.040
10	Fe(II) chloride-4H <sub>2</sub> O	39	0.247	0.049

<sup>a</sup> Reactions were performed using the catalyst noted (3.2 μmol), 5% Pd on Al<sub>2</sub>O<sub>3</sub> (20.0 mg), benzene (2 ml), and glacial acetic acid (2.5 ml). The reactions were performed in glass liners in 300 ml stainless steel autoclaves with H<sub>2</sub> (100 psi), N<sub>2</sub> (1000 psi), and O<sub>2</sub> (100 psi) at 65 °C for 2 h. Values listed are the average of at least two runs.

<sup>b</sup> Phenol (mmol)/catalyst (mmol) (V or Fe) per h.

<sup>c</sup> Catalyst (0.16 mmol) with no palladium, dihydrogen, or dioxygen present.

reaction of dioxygen with either carbon monoxide or dihydrogen, can be employed to carry out catalytic oxidations using a second catalyst. For example, Tables 1 and 2 show results on the oxidation of benzene and

cyclohexane. Table 1, entries 1 and 2 show that very little oxidation occurs in the absence of the second, hydroxylation catalyst (vanadium species). Control experiments show that vanadium(acetylacetonate)<sub>3</sub>

Table 2  
Yields for selected cyclohexane oxidation catalysts<sup>a</sup>

Entry number	Hydroxylation catalyst	Turnovers per h <sup>b</sup>	Cyclohexanol (mmol)	Cyclohexanone (mmol)
1	Tris(dibenzoylmethanato)Fe(III)	17	0.066	0.0214
2	Fe(II) acetate	32	0.125	0.0400
3	V(O)(acetylacetonate) <sub>2</sub>	25	0.0787	0.0400
4	V(acetylacetonate) <sub>3</sub>	38	0.138	0.0519

<sup>a</sup> Reactions were performed using the catalyst noted (3.2 μmol), 5% Pd on Al<sub>2</sub>O<sub>3</sub> (20.0 mg), cyclohexane (1.5 ml), and propionic acid (3 ml). The reactions were performed in glass liners in 300 ml stainless steel autoclaves with H<sub>2</sub> (100 psi), N<sub>2</sub> (1000 psi), and O<sub>2</sub> (100 psi) at 36 °C for 2 h. Values listed are the average of at least four runs.

<sup>b</sup> [Cyclohexanol (mmol) + 2 × (cyclohexanone (mmol))]/catalyst (mmol) (Fe or V) per h.

will catalyze the hydroxylation of benzene by hydrogen peroxide, even in the absence of metallic palladium, dihydrogen and dioxygen. Furthermore, no oxidation occurs when the vanadium hydroxylation catalyst is used without some source of hydrogen peroxide (Table 1, entry 4). Thus, metallic palladium is active in the formation of hydrogen peroxide, which in turn generates an active catalytic species from the vanadium complex.

It is possible to adjust the ratio of the hydrogen peroxide generating catalyst (palladium) to the hydroxylation catalyst (vanadium or iron) such that the first reaction becomes rate-limiting. Under these conditions, the yield of oxidized organic product increases linearly with increasing amount of metallic palladium. Other lines of evidence also suggest that hydrogen peroxide formation is the slow step under these conditions. As Fig. 1 shows, the energy of activation is

similar regardless of the hydroxylation catalyst or the substrate. Thus, the values obtained are 5.4, 5.9, and 5.1 kcal/mol for the hydroxylation of benzene with V(acetylacetonate)<sub>3</sub>, the hydroxylation of benzene with tris(dibenzoylmethanato)iron(III), and the hydroxylation of cyclohexane with V(acetylacetonate)<sub>3</sub>, respectively. The linear fit observed for cyclohexane oxidation is poorer at higher temperatures; at lower temperatures (data not shown) the fit is comparable to the other two reactions. The activation energy values do not change significantly when the stirring rate is changed, indicating that gas diffusion is not the rate-limiting step [19]. Furthermore, the values are close to that calculated from a report of gas-phase benzene to phenol oxidation by a palladium–copper composite catalyst, carried out around 200 °C, in the presence of dihydrogen and dioxygen: 6.1 kcal/mol [20]. Given the very different nature of the two

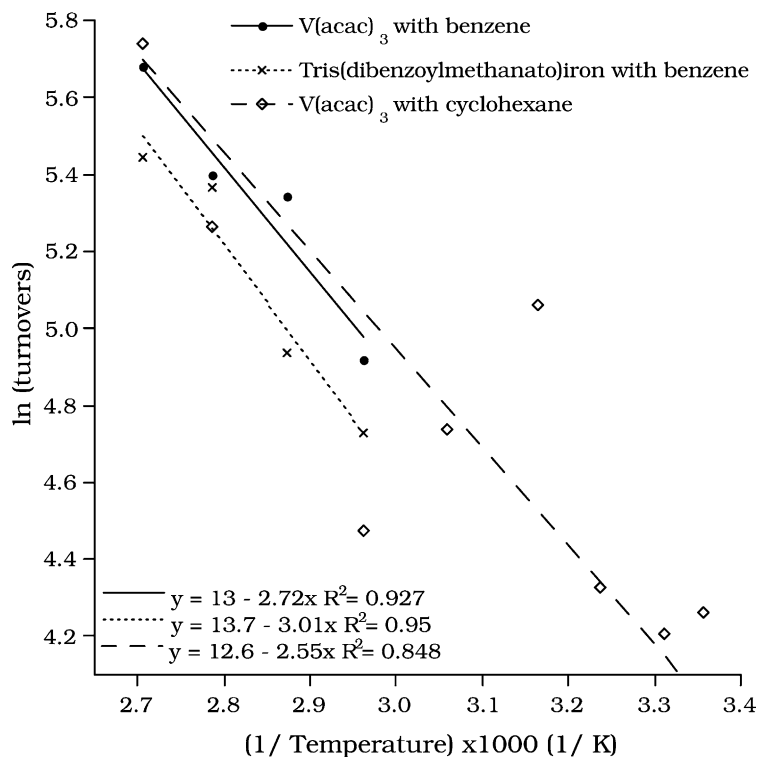


Fig. 1. Arrhenius plots for two catalysts and two substrates: for reactions with benzene, benzene (2 ml) was allowed to react with V(acetylacetonate)<sub>3</sub> (3.2 μmol) or tris(dibenzoylmethanato)iron (3.2 μmol), 5% Pd on Al<sub>2</sub>O<sub>3</sub> (20.0 mg) in glacial acetic acid (2.5 ml). For the reactions with cyclohexane, cyclohexane (1.5 ml) was allowed to react with V(acetylacetonate)<sub>3</sub> (3.2 μmol), and 5% Pd on Al<sub>2</sub>O<sub>3</sub> (20.0 mg) in propionic acid (3 ml). Reactions were run in glass liners in 300 ml stainless steel autoclaves under an atmosphere consisting of H<sub>2</sub> (100 psi), N<sub>2</sub> (1000 psi), and O<sub>2</sub> (100 psi) for 2 h. Reactions were repeated at least three times and the data here is an average.

substrate oxidations (even the C–H bond dissociation energies are quite different), the simplest explanation for the observed similarity is that the slow step is the formation of hydrogen peroxide.

There are other examples of the use of in situ generated hydrogen peroxide in catalytic oxidations. We have used metallic palladium alone for the deep oxidation of toxic organic compounds [11] and in combination with copper chloride for hydroxylation of primary C–H bonds, including those of alkanes [8–10]. In each case, a coreductant, carbon monoxide or dihydrogen, is required. Recent publications from other groups on catalytic oxidation of hydrocarbons also call for either carbon monoxide or dihydrogen as the coreductant [21]. These include alkene epoxidation and aromatic hydroxylation. Although not always specifically proposed, the in situ formation of hydrogen peroxide appears likely in every case.

An important question that needs to be addressed is why a coreductant is required for the hydroxylation of strong primary and aromatic C–H bonds but not for “easy” oxidations involving alkenes and alcohols. Clearly, the aerobic oxidation of palladium(0) to palladium(II) also produces hydrogen peroxide and does not need a coreductant. However, the continued catalytic generation of hydrogen peroxide requires the rereduction of palladium(II) to palladium(0) (see Scheme 1). This can be achieved by alkenes and alcohols which are then converted to carbonyl compounds. In these cases, no sacrificial coreductant is necessary and the hydrogen peroxide appears to play no significant part in the oxidation of these substrates. On the other hand, palladium(II) does not readily oxidize primary or aromatic C–H bonds thereby preventing its reduction by them. Thus, a sacrificial coreductant is required to reduce palladium(II). Carbon monoxide and dihydrogen fulfill this role, being oxidized to carbon dioxide and water, respectively. The hydrogen peroxide generated in these cases is subsequently used to effect the oxidation of the alkane and arene either by palladium(II) or by a second catalyst.

It is clear from the previous discussion that the aerobic oxidation of palladium(0) results in the formation of hydrogen peroxide, both in the presence and absence of a sacrificial coreductant. Furthermore, the hydrogen peroxide produced can be used for substrate oxidation using a second catalyst. This allows oxida-

tions that are not catalyzed by palladium(II) species (e.g. aliphatic and aromatic hydroxylations and alkene epoxidation) to occur. More importantly, by using palladium as a “hydrogen peroxide generator,” most oxidation procedures that use hydrogen peroxide as the oxidant can, in principle, be converted to one that utilizes dioxygen! Of course, a coreductant, carbon monoxide or dihydrogen, will be required. However, from an economic standpoint, hydrogen peroxide is significantly ( $\geq 5$  times) more expensive than either carbon monoxide or dihydrogen. The practical advantage of using an in situ hydrogen peroxide generator is that the transportation, storage and handling problems associated with hydrogen peroxide are eliminated, and the amount of water in the oxidation system is minimized.

### 3. Experimental

#### 3.1. General procedures

*Caution: Due care must be taken when dealing with gas mixtures under pressure. Special attention must be paid to gas flammability limits [22].* All reactions were performed in 300 ml Parr stainless steel autoclaves. Analyses were done on a HP-5890 series II FID/TCD gas chromatograph with a 3396 Integrator. Reactions with benzene used a J + W DB-5, 30 m, i.d. = 0.53 mm column with splitless injection technique and *o*-dichlorobenzene internal standard. Cyclohexane reactions were analyzed with an Alltech EC-1000, 30 m, i.d. = 0.25 mm column and utilized a 100:1 split ratio. *m*-Xylene was used as an internal standard. Reaction products were confirmed using comparison to known compounds and further confirmed using GC–MS.

#### 3.2. Materials

Glacial acetic acid and benzene were obtained from EM science. Pd supported on Al<sub>2</sub>O<sub>3</sub> (5%) and V(O)(acetylacetonate)<sub>2</sub> were obtained from Strem Chemical. Tris(dibenzoylmethanato)iron was purchased from TCI Chemical. VO(O<sub>2</sub>)(2-picolinate)(H<sub>2</sub>O)<sub>2</sub> was synthesized according to the literature methods [23]. All other materials used were purchased from Aldrich. All chemicals were used as received.

### 3.3. General reaction conditions

V(acetylacetonate)<sub>3</sub> (1.1 mg, 3.2 μmol) and 5% Pd on Al<sub>2</sub>O<sub>3</sub> (20.0 mg) were weighed into ca. 25 ml constricted neck glass liner. To this, a small magnetic stir bar was added along with 2 ml of benzene and 2.5 ml of glacial acetic acid. In the case of cyclohexane oxidation, cyclohexane (1.5 ml) and propionic acid (3 ml) were employed. The mixture was sealed in the autoclave and flushed thoroughly with hydrogen. It was then charged with H<sub>2</sub> (100 psi), N<sub>2</sub> (1000 psi), and O<sub>2</sub> (100 psi) in that order and placed in a temperature regulated oil bath for 2 h. Internal autoclave temperatures were determined using an autoclave equipped with a temperature sensor. At the end of the reaction, the autoclave was cooled in ice, slowly degassed, and the contents filtered through a 2 μm filter to remove the supported palladium catalyst. After internal standard addition, the liquid was analyzed with GC. Reactions were repeated and the results reported are the average of at least two experiments.

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