Environmentally Benign Oxidation Reaction of Benzylic and Allylic Alcohols to Carbonyl Compounds Using Pd/C with Sodium Borohydride

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Abstract: Pd/C catalyst in aqueous alcohol with molecular oxygen, sodium borohydride, and potassium carbonate efficiently oxidized benzylic and allylic alcohols. The use of a reducing reagent, sodium borohydride, for the reactivation of active sites of the Pd surface proved to be remarkable. The utilization of room temperature reaction condition and aqueous alcohol solvent as well as the recyclability of Pd/C makes this manipulation very interesting from an economic and environmental perspective.

Key word: palladium, oxidations, alcohols, sodium borohydride, oxygen

The oxidation of alcohols to aldehydes and ketones is one of the most important organic manipulations in organic synthesis.[1] There are versatile methods for such conversion like using metal-based oxidants (chromium reagents, manganese reagents, ruthenium reagents, etc.), dimethyl sulfoxide reagents, halogen-based oxidants, Oppenauer and related oxidants, electrochemical and photochemical oxidations, and other miscellaneous oxidation methods.[2] In addition to these methods, the use of heterogeneous or immobilized metal catalyst under aerobic condition has been extensively reported due to the possibility of recycling the catalyst and the environment friendliness of the system.[3] Several research works related to the aerobic and catalytic oxidation of alcohols by heterogeneous or immobilized Pd-catalyst system have been widely developed.[3a–d,3h–k,4] Since molecular oxygen is readily available and soluble in common organic solvents,[5] it is ideal to use as an environmentally benign reoxidant for Pd-catalyst. However, heterogeneous or immobilized Pd-catalyzed aerobic oxidations usually require high reaction temperatures (> 80 °C).[4] Recently, Sigman and co-workers reported the first example of a Pd-catalyzed aerobic oxidation of alcohols at room temperature.[6] They used homogeneous Pd(II) catalyst [3 mol% of $Pd(OAc)_2$] with triethylamine as an additive in 15% tetrahydrofuran–toluene solution. Finding appropriate reaction methods such as lowering reaction temperature and using readily available heterogeneous or immobilized Pd catalyst for aerobic alcohol oxidation seemed to be very challenging. Here we report a remarkable method for benzylic and allylic alcohol oxidation to the corresponding carbonyl compound using Pd/C catalyst in the presence of sodium borohydride under oxygen.

To date, it is mostly accepted that the oxidation of primary alcohol to the corresponding aldehyde follows dehydrogenation mechanism as shown below in Equation 1.[7] Since this oxidation reaction proceeds under an oxygen atmosphere, the adsorbed co-product, hydrogen, is oxidized with molecular oxygen to afford freshly active sites on the surface of the catalyst.

$$\mathrm{R{-}CH_2{-}OH_{ad}} \longleftrightarrow \mathrm{R{-}CH_2{-}O_{ad}} \quad + \quad \mathrm{H_{ad}}$$
$$\mathrm{R{-}CH_2{-}O_{ad}} \longleftrightarrow \mathrm{R{-}CH{=}O_{ad}} \quad + \quad \mathrm{H_{ad}}$$

Equation 1

'Over-oxidation' of the active sites on the surface of the catalyst due to very high concentration of oxygen has been commonly known to deactivate the metal catalyst.[8] We extraordinarily chose a reducing reagent, sodium borohydride, which is readily available and relatively stable in protic solvents, to reactivate the over-oxidized palladium surface under molecular oxygen. The use of sodium borohydride posed several considerations including its reaction rate and reducing power. It must react with the over-oxidized palladium surface faster than the reaction product (aldehyde or ketone) would do and its reactivity with respect to time should be checked in the presence of a protic solvent, especially an aqueous system. To verify these factors sodium borohydride was dissolved in water and was kept for 24 hours at room temperature followed by addition of benzaldehyde. Benzaldehyde was completely reduced to benzyl alcohol within 20 minutes. To generalize this method we thoroughly investigated the appropriate reaction conditions, such as the solvent system (H_2O, aq EtOH, THF, aq THF, DMSO, aq MeCN, etc.), the additive (AcOH, Et_3N, K_2CO_3, etc.), and the reaction temperature. Optimization of the reaction conditions for the oxidation of benzyl alcohol and 1-phenylethanol (Scheme 1) as test compounds gave aqueous ethanol as the best solvent system and potassium carbonate as the most appropriate additive. Furthermore, the use of Pd/C catalyst with sodium borohydride boosted the reaction rate as shown in Table 1.

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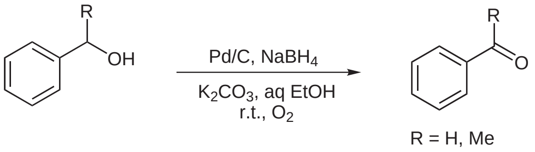
Table 1 The Optimization of Benzyl Alcohol and 1-Phenylethanol Oxidation[a]

Entry	Pd/C[b] (equiv)	$NaBH_4$ (equiv)	K_2CO_3 (equiv)	Time	R	Yield (%)[c]
1	0.1	–	–	24 h	H	71
2	0.1	–	3.0	20 h	H	73
3	0.1	1.0	–	30 min	H	92
4	0.01	0.1	3.0	1 h	H	87
5	0.025	0.1	3.0	20 min	H	95
6	0.1	1.0	–	20 min	Me	91
7	0.01	1.0	–	30 min	Me	87
8	0.025	0.1	3.0	20 min	Me	95

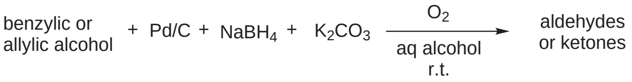
[a] Aqueous EtOH (H_2O–EtOH = 2:1) was used.
[b] Pd/C (10 wt%) was used.
[c] Yields refer to isolated products.



Scheme 1

Entries 5 and 8 in Table 1 reveal that the use of Pd/C (0.025 equiv), sodium borohydride (0.1 equiv), and potassium carbonate (3.0 equiv) at room temperature under an oxygen atmosphere afforded the best yield for the oxidation. Sodium borohydride (entries 3–8) plays a very significant role in this reaction. Furthermore, the results imply that the reaction of sodium borohydride with the over-oxidized palladium surface is faster than that of the reaction product, benzaldehyde or acetophenone. This clearly illustrates the remarkable ability of sodium borohydride to facilitate the oxidation of benzylic alcohols with heterogeneous Pd/C catalyst under molecular oxygen. The recyclability of Pd/C catalyst has been also tested with benzyl alcohol. Pd/C was directly filtered from the reaction mixture, washed with sufficient water and ethanol, and was reused for the next cycle. In the first to the fifth cycles, the reaction product, benzaldehyde was isolated in excellent yields (95%, 93%, 93%, 92%, 92% yields, respectively). Oxidation reaction in the sixth to the ninth cycles was monitored by thin layer chromatography, and the reaction always completed within 20 minutes. Benzaldehyde was isolated in 93% yield at the tenth trial. This means that the Pd/C catalyst can be used continuously for this oxidation reaction.

To validate this protocol we applied it to various benzylic and allyic alcohols in aqueous methanol, ethanol, and isopropanol solvents (Scheme 2).[9]



Scheme 2

Table 2 The Oxidation of Various Benzylic and Allylic Alcohols

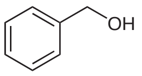
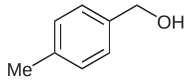
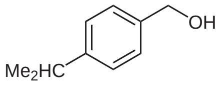
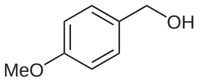
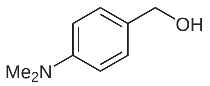
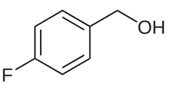
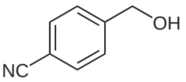
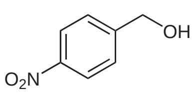
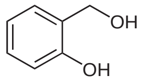
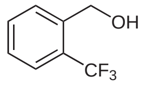
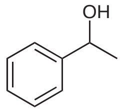
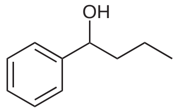
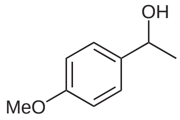
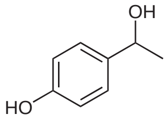
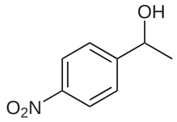
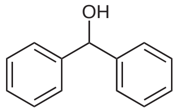
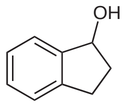
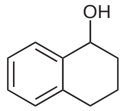
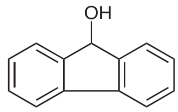
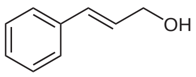
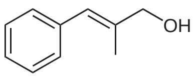
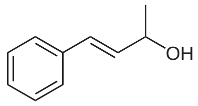
Entry	Starting alcohol	Alcohol (co-solvent)[a]	Time	Yield (%)[b]
1		MeOH EtOH *i*-PrOH	20 min 20 min 20 min	95 95 92
2		MeOH EtOH *i*-PrOH	20 min 20 min 20 min	92 94 95
3		MeOH EtOH *i*-PrOH	30 min 30 min 20 min	90 94 95
4		MeOH EtOH *i*-PrOH	20 min 20 min 20 min	90 92 92
5		MeOH EtOH *i*-PrOH	2 h 1.5 h 30 min	91 93 93
6		MeOH EtOH *i*-PrOH	30 min 30 min 30 min	91 91 90
7		MeOH EtOH *i*-PrOH	12 h 12 h 12 h	73 30 53

Table 2 The Oxidation of Various Benzylic and Allylic Alcohols (continued)

Entry	Starting alcohol	Alcohol (co-solvent)[a]	Time	Yield (%)[b]
8		MeOH	12 h	21
		EtOH	12 h	trace
		i-PrOH	12 h	trace
9		MeOH	2 h	91
		EtOH	2 h	88
		i-PrOH	2 h	86
10[c]		MeOH	3 h	35
		EtOH	3 h	26
		i-PrOH	3 h	NR
11		MeOH	20 min	94
		EtOH	20 min	95
		i-PrOH	20 min	92
12		MeOH	20 min	92
		EtOH	20 min	93
		i-PrOH	20 min	95
13		MeOH	20 min	93
		EtOH	20 min	93
		i-PrOH	20 min	95
14		MeOH	2 h	91
		EtOH	2 h	70
		i-PrOH	2 h	70
15		MeOH	12 h	44
		EtOH	12 h	21
		i-PrOH	12 h	20
16		MeOH	30 min	93
		EtOH	30 min	94
		i-PrOH	30 min	95
17		MeOH	20 min	90
		EtOH	20 min	93
		i-PrOH	20 min	91
18		MeOH	20 min	90
		EtOH	20 min	93
		i-PrOH	20 min	93
19		MeOH	1 h	91
		EtOH	1 h	90
		i-PrOH	1 h	90
20		MeOH	3 h	87
		EtOH	3 h	91
		i-PrOH	3 h	89
21		MeOH	3 h	90
		EtOH	3 h	91
		i-PrOH	3 h	93
22		MeOH	1 d	87
		EtOH	1 d	75
		i-PrOH	1 d	69

[a] Aqueous EtOH (H_2O–EtOH = 2:1) was used.

[b] Yields refer to isolated products.

[c] Prolonging the reaction time (> 12 h) showed no improvement in the yield (TLC monitoring).

The progress of the oxidation reaction was monitored via silica gel thin-layer chromatography. As shown in Table 2, every aqueous alcoholic co-solvent afforded good to excellent results. An electron-withdrawing substituent (entries 7, 8, 10, and 15) on the phenyl group afforded poorer reaction yield than the others. Presumably, benzylic alcohols involving phenyl groups with electron-withdrawing substituent are less adsorbed on the Pd surface due to the electronic effect. Compared to benzylic alcohols, the allylic alcohols needed longer reaction time and gave slightly lower yields. ^{1}H NMR data of all the products are comparable with the commercially available compounds.

In conclusion, we have achieved a remarkable method for the oxidation of various benzylic and allylic alcohols to the corresponding aldehydes and ketones using Pd/C catalyst in aqueous alcohol with molecular oxygen, sodium borohydride, and potassium carbonate. The use of a reducing reagent, sodium borohydride, for the reactivation of the active sites on the Pd surface proved to be remarkable. We have also investigated the oxidation of primary alcohol to carboxylic acid using open-air conditions. The oxidation reaction undergoes smoothly and presumably this will also be true for the oxidation of alcohols to aldehydes. These result will be reported in the due course. The utilization of room temperature reaction condition and aqueous alcohol solvent as well as the recyclability of Pd/C makes this manipulation very interesting from an economic and environmental perspective.

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(9) **General Procedure for the Oxidation of Benzylic or Allylic Alcohols**: A catalytic amount of Pd/C (0.025 equiv) was added to H_2O (2 volume). $NaBH_4$ (0.1 equiv) was slowly added to this suspension followed by K_2CO_3 (3.0 equiv). After addition of the starting materials, benzylic or allylic alcohol (1.0 equiv) was added to the resulting suspension followed by addition of MeOH, EtOH, or *i*-PrOH (1 volume) at r.t. The resulting reaction mixture was stirred vigorously under an oxygen atmosphere (maintained with a balloon). Alternatively, oxygen gas was bubbled into the reaction mixture through a long needle with the use of several balloons. The progress of the oxidation reaction was monitored by silica gel TLC. The resulting reaction mixture was neutralized with a dilute HCl solution and the aqueous layer was extracted with sufficient EtOAc. The organic layer was separated, dried over anhyd $MgSO_4$, and concentrated via rotary evaporation. The residue was purified by silica gel flash column chromatography (EtOAc–*n*-hexane = 1:3–1:7). Reactions were typically run on a 2–3-mmol scale.