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Environmentally benign oxidation reaction of aldehydes to their corresponding carboxylic acids using Pd/C with $NaBH_4$ and KOH

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Abstract—Pd/C catalyst in aqueous methanol with sodium borohydride and potassium hydroxide under the air efficiently oxidized aldehydes to their corresponding carboxylic acids at room temperature. The utilization of room temperature reaction, aqueous methanol solvent, and the open-air conditions make this manipulation very interesting for economic and environmental perspectives.

The oxidation of aldehydes to their corresponding carboxylic acids is one of the most common organic reactions in organic chemistry.[1] In addition to numerous versatile methods for the oxidation of aldehydes, more convenient methods such as Baeyer–Villiger oxidation,[2] Cannizzaro reaction,[3] and metal catalyzed oxidation[4] have been reported. Recently, we have investigated the remarkable oxidation reaction of benzylic and allylic alcohols to their corresponding aldehydes and ketones with Pd/C, sodium borohydride, and potassium carbonate under oxygen.[5] In this reaction, it was realized that the use of sodium borohydride boosted the reaction. Furthermore, we have observed that prolonging the reaction (oxidation of benzyl alcohol) time to 12 h while stirring in aqueous methanol (H_2O/methanol = 2:1, v/v) produced benzoic acid in 91% yield. Having obtained these results, we want to investigate the oxidation of aldehydes to their corresponding carboxylic acids by using the same reaction conditions.

When we initiated this oxidation of aldehydes, we changed the base to potassium hydroxide (1.0 molar amount) to shorten the reaction time. As expected, the oxidation of benzaldehyde was completed within 1.5 h. The amount of base also affects the reaction yield; the use of 3.0 molar amount of potassium hydroxide gave the best yield (91%) in this reaction.

It is mostly considered that the oxidation of benzaldehyde to benzoic acid by novel metal catalyst with hydroxide base in aqueous solution follows either the hydration of benzaldehyde to a geminal diol and the subsequent dehydrogenation on metal catalyst (Eq. 1) or the disproportionation of benzaldehyde under basic conditions (Cannizzaro reaction, Eq. 2) as shown below.[6] Since aromatic and aliphatic aldehydes with no α hydrogen are known to follow the Cannizzaro reaction when treated with sodium hydroxide or other strong bases, we need to check this possibility under the same reaction conditions (Pd/C catalyst in the presence of potassium hydroxide and sodium borohydride).

Initially, we examined the reaction of benzaldehyde with potassium hydroxide in aqueous methanol (H_2O/methanol = 2:1, v/v) at room temperature in the air. Even

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Keywords: Pd/C; Oxidation reaction; Aldehydes; Carboxylic acids; $NaBH_4$; KOH; Under the air.

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$$\begin{tikzcd} \mathrm{Ph{-}CHO_{ad}} + \mathrm{H_2O} \arrow[r, phantom, "\rightleftharpoons"] & \mathrm{Ph{-}CH(OH)_{2,ad}} \arrow[r, phantom, "\rightleftharpoons"] & \mathrm{Ph{-}COOH_{ad}} + 2\mathrm{H_{ad}} \arrow[d, "^{-}\mathrm{OH}"] \\ & & \mathrm{Ph{-}CO\bar{O}} + \mathrm{H_2O} \end{tikzcd} \tag{1}$$

$$2\mathrm{Ph{-}CHO} + {}^{-}\mathrm{OH} \rightarrow \mathrm{Ph{-}COO^{-}} + \mathrm{Ph{-}CH_2OH} \tag{2}$$

after vigorous stirring for 2 h, the oxidation did not proceed at all. We added 0.025 molar amount of Pd/C to the reaction mixture to investigate the effect of palladium catalyst on the reaction. Monitoring for 2 h by silica-gel thin layer chromatography showed primarily the unreacted starting material, benzaldehyde, and a detectable amount of potassium benzoate. During the monitoring, formation of benzyl alcohol was not observed, which indicates that the oxidation might not be related to Cannizzaro reaction pathway (disproportionation). However, similar to our previous observation,[5] the addition of 0.1 molar amount of sodium borohydride completes the reaction within 1.5 h. It was presumed that the reaction proceeded via the hydration of benzaldehyde to a geminal diol and subsequently dehydrogenation on metal catalyst. Moreover, once more we have proven that the use of sodium borohydride was remarkable for the oxidation reaction.

From the aforementioned reaction conditions, we further investigate the oxidation of various aldehydes in aqueous methanol solvent (Scheme 1).[7]

The progress of the oxidation reaction was monitored by silica-gel thin layer chromatography. Upon completion, the reaction mixture was neutralized with 0.1 M aqueous HCl solution and the product was separated by silica-gel column chromatography using an appropriate eluent system. ^{1}H NMR data of all the products are comparable with the commercialized compounds. As shown in Table 1, all of the aldehydes afforded their corresponding carboxylic acids in excellent yield. In the case of entries 6 and 7, trace amount of methyl ester was obtained along with carboxylic acid as a major product in shorter reaction time. However, prolonging the reaction time to 5 and 4 h, respectively, afforded carboxylic acid as the sole product. It was presumed that the formed methyl ester was hydrolyzed in KOH solution to give potassium salt of the carboxylic acid. The effect of electron donating group and electron withdrawing group on the benzaldehyde substrates cannot be generalized with respect to reaction time. Among the benzaldehydes involving electron donating substituents (resonance donors; entries 6–10), the cases of entries 8, 9, and 10 took longer reaction time than the other cases. Also, the more substituted phenyl groups (entries 11 and 12) took longer reaction time. In the case of *p*-chloro- and *p*-bromobenzaldehyde, dehalogenation was also observed along with the oxidation product (entries 18 and 19). When we tried the oxidation of *o*-iodobenzyl alcohol as an initial study of this oxidation reaction, we only obtained a deiodinated product, benzaldehyde. Compared to the oxidation of aromatic aldehydes, the oxidation of aliphatic aldehydes slowly proceeded (entries 24–29). Aldol reaction of aliphatic aldehydes might occur, which competes with the oxidation reaction, thus it took longer time to complete.

Our protocol provides a milder and facile methodology for oxidation reaction that is useful for organic synthesis. For instance, *o*-vanillic acid (the product of entry 11) is frequently used as starting material for the synthesis of Alibendol,[8] an antispasmodic, choleretic, and cholekinetic active pharmaceutical ingredient. It can be prepared from *o*-vanillin by several methods such as using Pd/C with B_2O_3, Pt/C with $Bi_3(SO_4)_3$, $NaClO_2$ with H_2O_2, and Ag_2O.[9] Most of these methods are carried out in harsh reaction conditions and thus, our methodology is a valuable alternative.

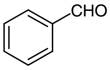
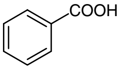
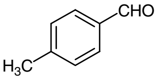
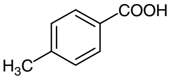
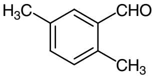
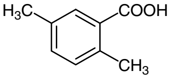
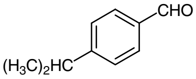
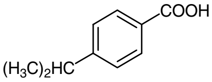
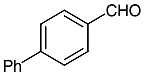
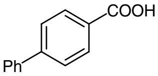
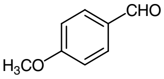
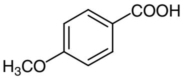
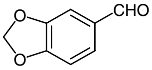
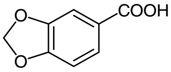
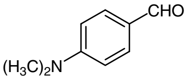
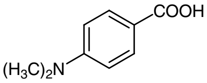
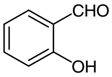
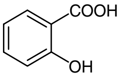
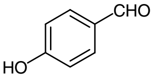
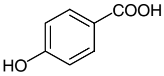
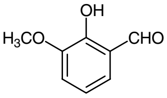
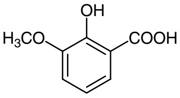
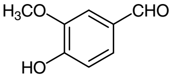
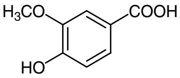
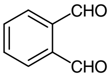
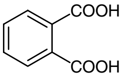
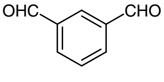
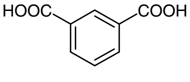
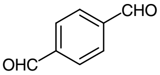
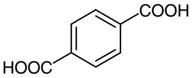
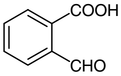
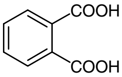
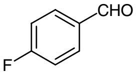
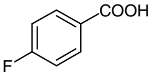
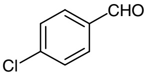
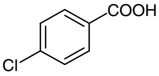
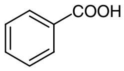
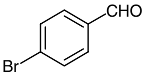
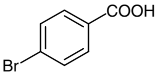
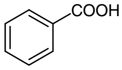
Since we have tested the reusability of Pd/C catalyst in the oxidation of benzyl alcohol,[5] it is believed that Pd/C catalyst can be used continuously for this oxidation reaction as well. Furthermore, we previously reported the use of aqueous ethanol or isopropanol solvent for the oxidation of benzylic and allylic alcohols.[5] Thus, for this oxidation reaction it is expected that these environmentally safer solvents may also be used in lieu of methanol.

In conclusion, we have achieved a remarkable method for the oxidation of various aldehydes to their corresponding carboxylic acids using Pd/C catalyst, sodium borohydride, and potassium hydroxide in aqueous methanol under air. The utilization of room temperature reaction, aqueous methanol solvent, and the open-air conditions make this manipulation very interesting for economic and environmental perspectives.

$$\underset{(1.0)}{\text{Aldehyde}} + \underset{(0.025)}{\text{Pd/C}} + \underset{(0.1)}{\mathrm{NaBH_4}} + \underset{(3.0)}{\text{KOH}} \xrightarrow[\substack{\mathrm{H_2O}\text{: methanol} \\ (2{:}1,\ v/v)}]{\text{air, room temp.}} \xrightarrow[\text{neutralization}]{\text{HCl}} \text{Carboxylic Acid}$$

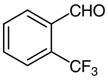
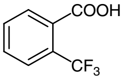
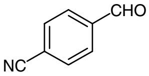
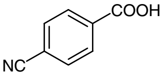
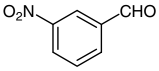
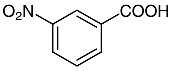
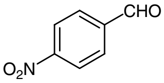
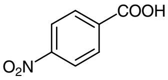
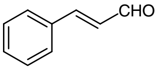
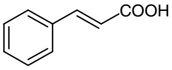
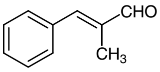
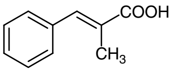
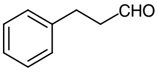
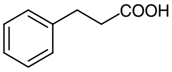
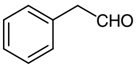
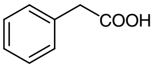
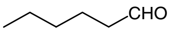
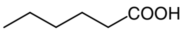
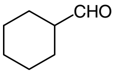
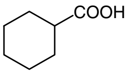
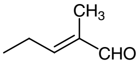
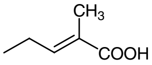
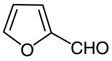
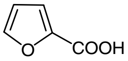
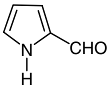
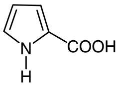
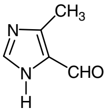
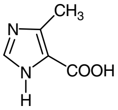
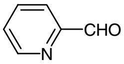
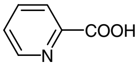
Scheme 1.

Table 1. The oxidation of various aldehydes under the air with vigorous stirring

Entry	Starting aldehyde	Reaction time (h)	Product	Yield[a] (%)
1		1.5		91
2		1.5		91
3		6		90
4		12		93
5		2		92
6		5		91
7		4		90
8		36		89
9		24		91
10		72		85
11[b]		48		89
12		24		89
13		7		90
14		6		88
15		7		90
16		3		86
17		3		88
18		3	, 	78, 16
19		4	, 	45, 45

(*continued on next page*)

Table 1 (*continued*)

Entry	Starting aldehyde	Reaction time (h)	Product	Yield[a] (%)
20		3		88
21		3		90
22		7		85
23		8		86
24		24		91
25		24		91
26		17		87
27		17		86
28		24		91
29		24		93
30		3		87
31		3		84
32		37		92
33		13		91
34		4		89

[a] Yields refer to isolated products.

[b] Pd/C (0.1 molar amount), $NaBH_4$ (1.1 molar amount), and KOH (4.0 molar amount) are used.

Acknowledgments

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7. *General procedure for the oxidation of aldehydes*: A catalytic amount of Pd/C (0.025 molar amount) was added in H_2O (2 vol). Sodium borohydride (0.1 molar amount) was slowly added to this suspension followed by KOH (3.0 molar amount). After addition of the starting material, aldehyde (1.0 molar amount), to the resulting suspension addition of methanol (1 vol) follows. The resulting reaction mixture was vigorously stirred under the air at room temperature. The progress of the oxidation reaction was monitored by silica-gel thin layer chromatography. After completion of the reaction, the resulting mixture was neutralized with 0.1 M aqueous HCl solution. If the crude product is quite soluble in organic solvent, it was extracted with sufficient ethyl acetate. The combined organic layer was separated, dried over anhydrous $MgSO_4$, and concentrated via rotary-evaporation. The residue was purified by flash silica-gel column chromatography with ethyl acetate or appropriate ethyl acetate/hexane eluent system. If the solubility of crude product is poor in organic solvent, the residue was purified by pre-loaded silica-gel column chromatography with appropriate methanol/chloroform eluent system.
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