Pd/C and $NaBH_4$ in Basic Aqueous Alcohol: An Efficient System for an Environmentally Benign Oxidation of Alcohols

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Abstract: We report the oxidation of a wide range of alcohols using an environmentally benign and economical process. The use of Pd/C heterogeneous catalysts along with $NaBH_4$ in aqueous ethanol or methanol and either K_2CO_3 or KOH as base at room temperature under molecular oxygen or air give the corresponding oxidation products. This protocol is versatile since it is capable of oxidizing alcohols to its desired carbonyl or carboxyl counterpart. Room temperature reaction in aqueous system and recyclability of the catalyst are among the advantages of this manipulation. These advantages make the process safe and cheaper rendering it favorable from both economic and environmental viewpoints.

Key words: alcohols, oxidation, Pd/C heterogeneous catalysis, sodium borohydride, carbonyl compounds, carboxylic acids

The oxidation of an alcohol to its carbonyl counterpart is one of the fundamental and most widely used organic manipulations in synthetic chemistry both in academic and industrial points of view. There are a large number of methods developed for such a transformation and chemists continue to find ways to improve it. Traditionally, oxidations of alcohols make use of chromium based reagents, activated DMSO, hypervalent iodine compounds, $KMnO_4$, silver carbonate, among others.[1] These methods showed efficiency and versatility to some extent, however, it makes use of stoichiometric or excess amounts of heavy metal catalysts such as Cr and Mn while some of the oxidants used are expensive. For these reasons, these methods rendered an environmental treat and economical issue that makes it unviable for industrial applications. Thus, modifications and improvements to these existing methods were developed. For instance, several transition metals such as Co,[2] Cu,[3] Ru[4], and Se[5] either as complex or anchored in some solid support were introduced. Another transition metal gaining popularity is palladium. Conventionally, it is used in tandem with various oxidants or in complex forms using known or designed ligands while nowadays, immobilization in solid supports to make it nano in size is the trendiest.[6] Most of these Pd-catalyzed oxidations are homogeneous in nature while others employed high catalyst loading making such protocol impractical. In addition, some of these methods utilized high reaction temperature and wasteful organic solvents. Aside from variations in metal catalyst, another modification developed is the use of various co-oxidants. These include molecular oxygen,[7] aryl halide,[8] sodium hypochlorite,[9] hypervalent iodine,[10] α-bromosulfoxide,[11] and a lot more. Although using these co-oxidants gave well to excellent yield, using molecular oxygen remains to be the best choice. It is readily available and generates water as the only by-product. In view of this existing scenario on oxidation reactions, there is still a need to develop an ideal system for oxidation of alcohols. A heterogeneous catalyst driven aerobic oxidation in aqueous media and ambient temperature would be an excellent alternative. This shall offer safer and cheaper advantages rendering an economical and environmentally benign protocol.

Previously, we have reported the Pd/C-catalyzed oxidation using sodium borohydride as an efficient oxidation system for alcohols[12] and aldehydes[13] under aerobic conditions. In this paper, we provide a full account of our oxidation protocol including the possible reaction mechanism associated with it.

Our group has been dedicated to the development of heterogeneous catalyst protocol for various organic transformations, and oxidation of alcohols has been one of them. Our trust is to use environmentally benign and economical system by utilizing readily available materials and aqueous media at ambient temperature. Thus, we considered Pd/C as a heterogeneous catalyst for oxidation. To the best of our knowledge there was only one paper that introduced Pd/C oxidation reaction of alcohols, though it has limited scope.[14] Furthermore, we also considered the fact that in the presence of excess oxygen, overoxidation on the surface of the palladium catalyst might occur, which will eventually deactivate the metal catalyst.[15] To solve this dilemma, we considered sodium borohydride, a reducing agent, to reactivate the palladium surface. This idea sounds extraordinary, but it does work astoundingly. We found that 0.1 equivalent of $NaBH_4$ would be enough to facilitate the oxidation reaction. We also tried this reaction without $NaBH_4$, simply with Pd/C in MeOH or in aqueous MeOH in the presence of base; however, we only observed a trace amount of oxidation product monitored by TLC. Indeed, the use of $NaBH_4$ facilitates this oxidation reaction smoothly.

Using benzyl alcohol as test substrate, we examined various aqueous alcohols as solvent. As shown in Table 1,

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Table 1 Influence of Various Aqueous Alcohol Solvents for the Oxidation of Benzyl Alcohol to Benzaldehyde

Entry	Solvent	Time (min)	Yield (%)[a]
1	EtOH–H_2O	20	95
2	MeOH–H_2O	20	95
3	*i*-PrOH–H_2O	20	92

[a] Isolated yield using Pd/C (0.025 equiv), $NaBH_4$ (0.1 equiv), K_2CO_3 (3.0 equiv), and bubbling O_2 at r.t.

both aqueous ethanol and methanol gave favorable oxidation product.

Next, we investigated the effect of base and solvent on the same oxidation reaction as shown in Table 2. We found that K_2CO_3 (3.0 equiv) with aqueous ethanol gave benzaldehyde (entry 1) and prolonging the time decreased the yield of aldehyde to 74% accompanied by the formation of 21% carboxylic acid (entry 2). Changing the solvent to methanol gave only carboxylic acid at a longer reaction time (entry 3); but changing the base to KOH provided the same product at a slightly higher yield and at much shorter reaction time (entry 4). This simply indicates that methanol assisted the formation of carboxyl oxidation product. These findings make this protocol versatile for oxidation of alcohols. There could be a choice for the oxidation of alcohol either to carbonyl or to carboxyl functionality as product.

In addition, we also investigated the influence of catalyst loading in this oxidation protocol as shown in Table 3. It was apparent that 0.025 equivalent of Pd was enough to give favorable result. In fact, this loading value will eventually lead to a significantly reduced value because of the reusability of this catalyst.

We have previously reported the oxidation of benzylic and allylic alcohols.[12] The data shown in Table 4 were the optimized results using aqueous ethanol as solvent. Primary benzylic alcohols (entries 1–10) gave excellent yield except for those having highly electron-withdrawing substituents (entries 7, 8, and 10). For these entries (7, 8, and 10) aqueous methanol gave better yield compared to aqueous ethanol as solvent, which resulted in an even lower yield or trace amount of product. Presumably, the presence of an electron-withdrawing group influences the adsorption of the substrate on the surface of Pd due to the electronic effect. The use of methanol solvent somehow assisted the oxidation reaction resulting in a higher yield than using aqueous ethanol as solvent. Primary allylic alcohols also gave excellent results (entries 11 and 12), however, it required longer reaction time compared to primary benzylic alcohols. The same observation holds with secondary benzylic alcohols (entries 13 to 21) and secondary allylic alcohol (entry 22). It is noteworthy to mention that other functional groups were preserved in this system.

Table 2 Influence of Base and Solvent on the Oxidation of Benzyl Alcohol

Entry	Base	Solvent[a]	Time (h)	Yield (%)[b]	
				Benz-aldehyde	Carboxylic acid
1	K_2CO_3	EtOH–H_2O	0.33	95	–
2	K_2CO_3	EtOH–H_2O	24	74	21
3	K_2CO_3	MeOH–H_2O	12	–	91
4	KOH	MeOH–H_2O	2.5	–	93

[a] Ratio of alcohol to H_2O used: 1:2.
[b] Isolated yield using Pd/C (0.025 equiv), $NaBH_4$ (0.1 equiv), base (3.0 equiv), and bubbling O_2 at r.t.

Table 3 Influence of Catalyst Loading on the Oxidation of Benzyl Alcohol to Benzaldehyde

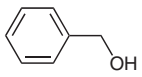
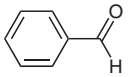
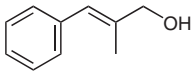
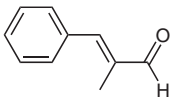
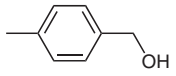
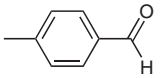
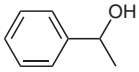
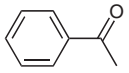
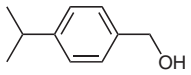
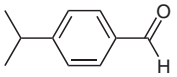
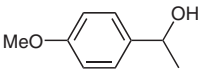
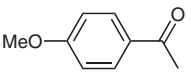
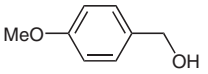
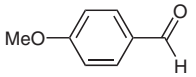
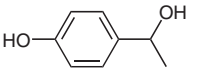
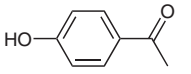
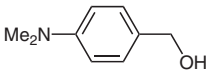
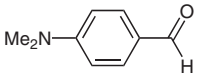
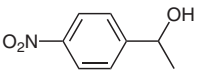
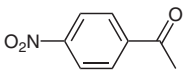
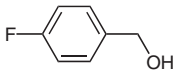
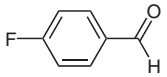
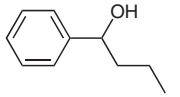
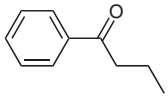
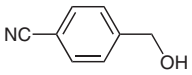
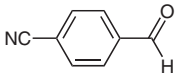
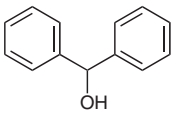
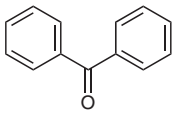
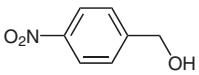
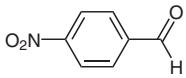
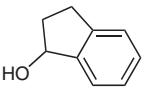
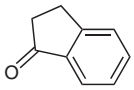
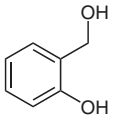
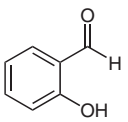
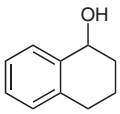
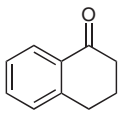
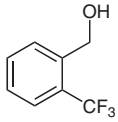
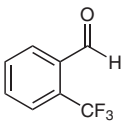
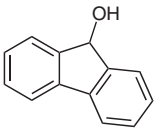
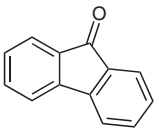
Entry	Pd/C (equiv)	Time (min)	Yield (%)[a]
1	0.005	60	85
2	0.01	60	87
3	0.02	30	87
4	0.025	20	95
5	0.03	20	95

[a] Isolated yield using $NaBH_4$ (0.1 equiv), K_2CO_3 (3.0 equiv), and bubbling O_2 at r.t.

Our system was also applicable for the oxidation of alcohols to carboxylic acids by simply changing the solvent and base to aqueous methanol and KOH, respectively, as aforementioned. A wide range of starting primary alcohols was considered as shown in Table 5 and all afforded the 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 15 and 17 hours, respectively afforded carboxylic acid as the sole product. It was expected that at longer reaction time the formed methyl ester was hydrolyzed in KOH solution to give potassium salt of the carboxylic acid. More substituted benzylic alcohols (entries 12 and 13), though they required longer reaction times, also gave reasonable yields of the products. It was again noteworthy to mention that this protocol was chemoselective since oxygen sensitive functional groups like alkene was preserved.

In the reaction of 1-phenylethane-1,2-diol (entry 22), shorter reaction time (9 h) afforded a mixture of benzoylformic acid (47%), 2-hydroxyacetophenone (43%), and methyl benzoylformate (9%). The formation of 2-hydroxyacetophenone implied that the benzylic alcohol moiety was oxidized faster than the aliphatic alcohol moiety however; prolonging the reaction time gave benzoylformic acid as the sole product. This result was further verified when we checked the reactivity of benzylic and aliphatic alcohol intermolecularly as shown in Scheme 1. Using K_2CO_3 as base gave 92% of compound **3** while

Table 4 Oxidation of Primary, Secondary Benzylic, and Allylic Alcohols

Entry	Starting alcohol	Time (h)	Product	Yield (%)[a]	Entry	Starting alcohol	Time (h)	Product	Yield (%)[a]
1		0.33		95	12		3		91
2		0.33		94	13		0.33		95
3		0.50		95	14		0.33		93
4		0.33		92	15[b]		2		91
5		1.50		93	16[b]		12		44
6		0.50		91	17		0.33		93
7[b]		12		73	18		0.50		94
8[b]		12		21	19		0.33		93
9		2		88	20		0.33		93
10[b]		3		35	21		1		90
11		3		91	22		24		87

[a] Isolated yield using Pd/C (0.025 equiv), $NaBH_4$ (0.1 equiv), K_2CO_3 (3.0 equiv) and bubbling O_2 in EtOH–H_2O (1:2) as solvent at r.t.
[b] Ratio of MeOH to H_2O used: 1:2.

97% of compound **2** was recovered after 20 minutes. Prolonging the time to 12 hours gave 73% of **4**, 58% of **6**, recovered 32% of **2**, and trace amounts of **3** and **5**. Changing the base to KOH gave 93% of **4**, 12% of **6**, recovered 85% of **2**, and no aldehyde products was observed after one hour. Indeed, benzylic alcohol was more reactive than aliphatic alcohol.

Scheme 1 Selectivity reaction between benzylic and aliphatic alcohols

Table 5 Oxidation of Various Primary Alcohols to Carboxylic Acids

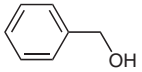
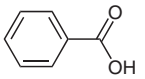
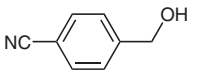
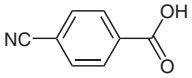
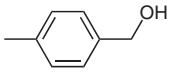
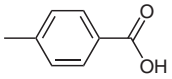
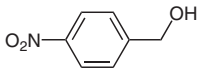
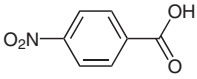
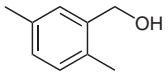
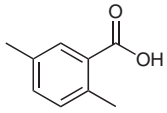
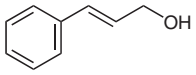
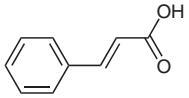
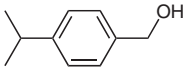
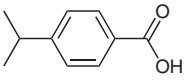
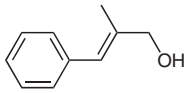
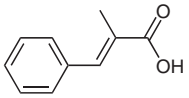
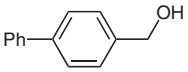
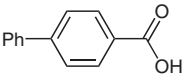
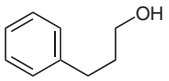
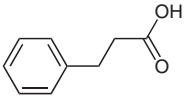
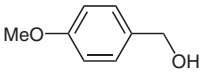
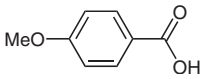
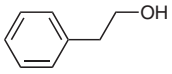
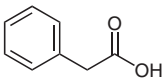
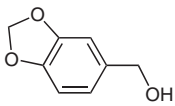
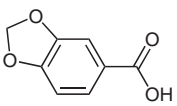
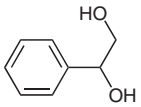
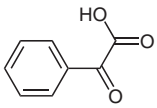
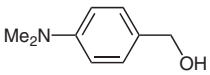
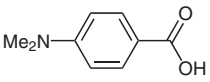
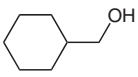
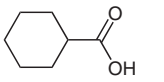
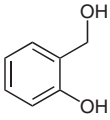
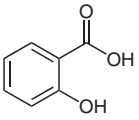
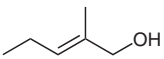
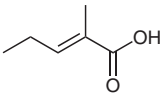
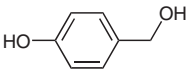
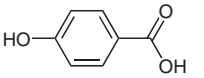
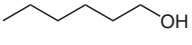
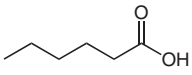
Entry	Starting alcohol	Time (h)	Product	Yield (%)[a]	Entry	Starting alcohol	Time (h)	Product	Yield (%)[a]
1		2.5		93	16		4		91
2		12		91	17		48		87
3		14		91	18		36		87
4		14		92	19		36		88
5		6		89	20		17		92
6		15		92	21		17		91
7		17		22	22		15		91
8		40		88	23		24		93
9		24		86	24		7		89
10		72		84	25		24		91
11		9		89	26		4		80
12[b]		48		89	27		50		90
13		72		81	28		19		92
14		4		90	29		24		87
15		12		90	30		7		87

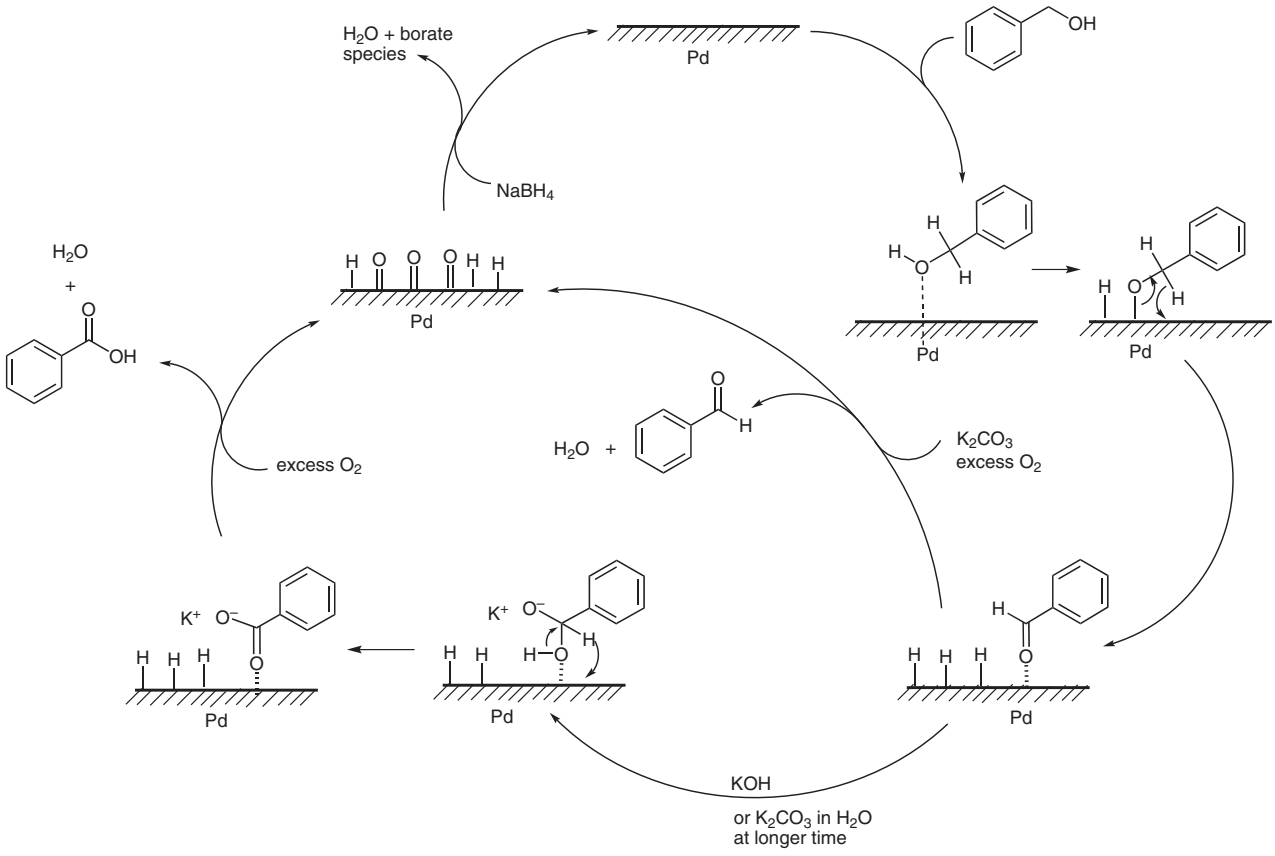
Table 6 Recycle Test of Pd/C Using Benzyl Alcohol

Run	Yield (%)	Run	Yield (%)
1	94	6	TLC monitored
2	93	7	TLC monitored
3	93	8	TLC monitored
4	92	9	TLC monitored
5	92	10	93

Moreover, nonactivated alkanols (entries 23 and 25) and heterocyclic alcohols (entries 26–30) also gave excellent oxidation product using this protocol. Furthermore, as an application, this could be a good alternative method for the preparation of *o*-vanillic acid (product of entry 12), a frequently used starting material for alibendol[16] synthesis. Usually *o*-vanillic acid was prepared from *o*-vanillin using harsh reaction conditions[17] and thus, our protocol is a valuable alternative. This one-pot oxidation of alcohol offered mild reaction conditions compared to known methods, which usually employed noxious reagents and high reaction temperatures.[18]

Reusability of the catalyst is the primary consideration in developing new catalyst. It is essential particularly in cost reduction and minimizing environmental treat leading to a sustainable process. To check the recyclability of our catalyst, several runs using benzyl alcohol were done. We simply filtered the Pd/C catalyst from the reaction mixture after 20 minutes of reaction, washed with plenty of water and ethanol, and then reused for the next run. As shown in Table 6, the yield from the 1st to the 5th run was almost the same, while from the 6th to the 9th runs, the reaction was simply monitored by TLC. The final test run (10th) was isolated obtaining the same yield of benzaldehyde. This series of experiments showed that the catalyst could be used continuously without loss of activity for the oxidation of alcohols.

It is widely accepted that metal-catalyzed oxidation of alcohol proceeded via coordination of the alcohol on the surface of the metal catalyst followed by β-hydride elimination to produce the carbonyl compound along with palladium hydride species, otherwise known as oxidative dehydrogenation.[6b,19] This was investigated by the group of Whitesides[20] using Pt metal and by Hronec et. al[14] using Pd metal. We concurred with this mechanistic pathway as shown in Scheme 2. The first step in the reaction was the adsorption of alcohol on the surface of the Pd via insertion of Pd atom into the O–H bond followed by β-hydride elimination to produce the carbonyl compound along with palladium populated with hydride species. The nature of base determined the path of the reaction. If K_2CO_3 was used it could readily release the carbonyl compound along with H_2O as by product. Prolonging the reaction time enabled the water to react further with aldehyde to form geminal diol, which eventually gets converted into carboxylic acid. This process readily occurs when the base



Scheme 2 Proposed mechanism for the oxidation of alcohols

used was KOH. On the other hand, some of the palladium hydride species was oxidized by the excess oxygen, which was either adsorbed on the surface or dissolved in the upper layer of the Pd lattice to produce certain amount of palladium oxide. In view of the fact that the metallic palladium and not the oxidic one was the active phase in aerobic alcohol oxidation[21] it was necessary to convert the palladium oxide present into metallic palladium to continue the catalytic cycle. Thus, we introduced $NaBH_4$ to reduce the metallic oxide and regenerate the palladium surface. We found that 0.10 equivalent of $NaBH_4$ was enough to regenerate the surface and continue its catalytic cycle. Sodium borohydride indeed helped in the reactivation of catalyst because without it the reaction will not proceed as abovementioned. In this system, no carbonyl reduction products were observed. This means that $NaBH_4$ reacted faster with the oxidized palladium surface than the carbonyl products. Furthermore, we also presumed that the alcohol solvents used (MeOH and EtOH) somewhat augment the reaction rate, especially methanol.

Herein, we have introduced a remarkable alternative for the oxidation of alcohols. Our protocol can be used to oxidize alcohols either to carbonyl or carboxyl counterpart by simply varying the base and solvent system. This protocol consisting of recyclable heterogeneous Pd/C catalyst in aqueous alcohol solvent and K_2CO_3 or KOH base in tandem with sodium borohydride under oxygen or air offered a cheaper and safer manipulation making it economical and environmentally benign process.

All starting materials and authentic samples of the products were commercially available and used without further purification. The spectra of the products were compared with that obtained from Aldrich, unless otherwise specified by a reference. ^{1}H NMR spectra were obtained using Mercury 300 and Bruker 300 MHz NMR spectrometers. Analytical TLC was conducted on aluminum backed silica gel plates (0.2 mm). Developed plates were visualized with UV light or with ninhydrin or cerium molybdate staining solutions. Column chromatography was performed using silica gel 60 (230–400 mesh).

Oxidation of Benzylic or Allylic Alcohols to Its Corresponding Carbonyl Compounds; General Procedure

$NaBH_4$ (0.010 g, 0.2774 mmol) was added slowly to a suspension of Pd/C (0.074 g, 0.069 mmol) in H_2O (13 mL), followed by K_2CO_3 (1.14g, 8.322 mmol). Then the starting material, benzylic or allylic alcohol (0.30 g for benzyl alcohol, 2.774 mmol) was introduced and finally EtOH or MeOH (7.0 mL) was added to the resulting suspension. The resulting reaction mixture was stirred vigorously at r.t. under O_2 balloon. Alternatively, O_2 gas was bubbled into the mixture through a long needle with the use of several balloons. The progress of the oxidation reaction was monitored by TLC (silica gel). After completion of the reaction, the mixture was neutralized with dil. HCl and the aqueous layer was extracted with EtOAc (3 × 20 mL). The organic layer was separated, dried ($MgSO_4$), and concentrated on a rotary evaporator. The residue was purified by flash silica gel column chromatography (EtOAc–*n*-hexane, 1:3–7) (Table 4).

Benzaldehyde (Table 4, Entry 1)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.02 (s, 1 H), 7.87 (d, *J* = 8.1 Hz, 2 H), 7.63–7.58 (br m, 1 H), 7.49–7.47 (br m, 1 H).

***p*-Tolualdehyde (Table 4, Entry 2)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.92 (s, 1 H), 7.76 (d, *J* = 7.8 Hz, 2 H), 7.31 (d, *J* = 7.8 Hz, 2 H), 2.31 (s, 3 H).

4-Isopropylbenzaldehyde (Table 4, Entry 3)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.96 (s, 1 H), 7.80 (d, *J* = 8.7 Hz, 2 H), 7.38 (d, *J* = 8.7 Hz, 2 H), 2.98 (m, 1 H), 1.27 (d, *J* = 6.9 Hz, 6 H).

4-Methoxybenzaldehyde (Table 4, Entry 4)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.88 (s, 1 H), 7.76 (d, *J* = 8.4 Hz, 2 H), 6.98 (d, *J* = 8.4 Hz, 2 H), 3.78 (s, 3 H).

4-*N*,*N*-Dimethylaminobenzaldehyde (Table 4, Entry 5)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.65 (s, 1 H), 7.57 (d, *J* = 8.1 Hz, 2 H), 6.67 (d, *J* = 9.0 Hz, 2 H), 3.08 (s, 6 H).

4-Fluorobenzaldehyde (Table 4, Entry 6)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.95 (s, 1 H), 7.92–7.87 (br m, 2 H), 7.22–7.17 (br m, 2 H).

4-Cyanobenzaldehyde (Table 4, Entry 7)[22]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.10 (s, 1 H), 7.99 (d, *J* = 8.1 Hz, 2 H), 7.85 (d, *J* = 8.4 Hz, 2 H).

4-Nitrobenzaldehyde (Table 4, Entry 8)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.15 (s, 1 H), 8.39 (d, *J* = 8.4 Hz, 2 H), 8.07 (d, *J* = 8.7 Hz, 2 H).

Salicylaldehyde (Table 4, Entry 9)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.02 (s, 1 H), 9.89 (s, 1 H), 7.57–7.53 (br m, 2 H), 7.02–6.98 (br m, 2 H).

2-α,α,α-Trifluoromethylbenzaldehyde (Table 4, Entry 10)[23]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.40 (s, 1 H), 8.14–8.11 (br m, 1 H), 7.80–7.68 (br m, 3 H).

***trans*-Cinnamaldehyde (Table 4, Entry 11)**

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.71 (d, *J* = 8.4 Hz, 1 H), 7.59–7.43 (m, 5 H), 6.76 (dd, *J* = 8.4, 6.9 Hz, 1 H), 6.70 (dd, *J* = 8.4, 6.9 Hz, 1 H).

α-Methyl *trans*-Cinnamaldehyde (Table 4, Entry 12)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 9.68 (s, 1 H), 7.56–7.38 (br m, 5 H), 7.24 (s, 1 H), 2.08 (s, 3 H).

Acetophenone (Table 4, Entry 13)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.94 (br m, 2 H), 7.56–7.46 (br m, 3 H), 2.60 (s, 3 H).

4-Methoxyacetophenone (Table 4, Entry 14)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.92 (d, *J* = 8.4 Hz, 2 H), 6.92 (d, *J* = 8.7 Hz, 2 H), 3.85 (s, 3 H), 2.54 (s, 3 H).

4-Hydroxyacetophenone (Table 4, Entry 15)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.07 (br s, 1 H), 7.92 (d, *J* = 8.4 Hz, 2 H), 6.96 (d, *J* = 8.7 Hz, 2 H), 2.59 (s, 3 H).

4-Nitroacetophenone (Table 4, Entry 16)[24]

^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.28 (d, *J* = 7.2 Hz, 2 H), 8.09 (d, *J* = 7.5 Hz, 2 H), 2.66 (s, 3 H).

Butyrophenone (Table 4, Entry 17)

^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.97–7.94 (br m, 2 H), 7.55–7.43 (br m, 3 H), 2.94 (t, *J* = 7.2 Hz, 2 H), 1.81–1.73 (m, 2 H), 1.00 (t, *J* = 7.5 Hz, 3 H).

Benzophenone (Table 4, Entry 18)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.83 (d, *J* = 7.5 Hz, 4 H), 7.59 (t, *J* = 7.5 Hz, 2 H), 7.49 (t, *J* = 7.5 Hz, 4 H).

1-Indanone (Table 4, Entry 19)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.75 (d, *J* = 7.8 Hz, 1 H), 7.56 (t, *J* = 7.2 Hz, 1 H), 7.48 (d, *J* = 6.9 Hz, 1 H), 7.39 (t, *J* = 7.8 Hz, 1 H), 3.14 (t, *J* = 5.4 Hz, 2 H), 2.68 (m, 2 H).

α-Tetralone (Table 4, Entry 20)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.02 (d, *J* = 7.8 Hz, 1 H), 7.45 (t, *J* = 7.2 Hz, 1 H), 7.31–7.22 (br m, 2 H), 2.95 (t, *J* = 5.7 Hz, 2 H), 2.64 (t, *J* = 6.3 Hz, 2 H), 2.12 (m, 2 H).

9-Fluorenone (Table 4, Entry 21)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.65 (d, *J* = 7.6 Hz, 2 H), 7.52–7.45 (br m, 4 H), 7.31–7.26 (br m, 2 H).

***trans*-4-Phenylbut-3-en-2-one (Table 4, Entry 22)**
^{1}H NMR (300 MHz, $CDCl_3$): δ = 7.55–7.53 (m, 2 H), 7.49 (s, 1 H), 7.41–7.39 (m, 2 H), 6.75 (s, 1 H), 6.69 (s, 1 H), 2.39 (s, 3 H).

Oxidation of Primary Alcohols to Carboxylic Acids; General Procedure
$NaBH_4$ (0.010g, 0.2774 mmol) was added slowly to a suspension of Pd/C (0.074 g, 0.069 mmol) in H_2O (13 mL), followed by KOH (0.467g, 8.322 mmol). Then, the starting primary alcohol (0.30 g for benzyl alcohol, 2.774 mmol) was added, followed by MeOH (7 mL). The reaction mixture was stirred vigorously under air at r.t. The progress of the oxidation was monitored by TLC (silica gel) and the reaction was stopped based on TLC monitoring. Upon completion of the reaction, the mixture was neutralized with dil. HCl. If the crude product was quite soluble in organic solvent, it was extracted with EtOAc (3 × 20 mL). The combined organic layers were dried ($MgSO_4$) and concentrated on a rotary evaporator. The residue was purified by flash silica gel column chromatography using EtOAc or appropriate EtOAc–hexane eluent system. If the solubility of crude product was poor in organic solvent, the residue was purified by preloaded silica gel column chromatography with appropriate MeOH–$CHCl_3$ eluent system (Table 5).

Benzoic Acid (Table 5, Entry 1)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.65 (br s, 1 H), 8.14 (d, *J* = 8.1 Hz, 2 H), 7.63–7.44 (br m, 3 H).

***p*-Toluic Acid (Table 5, Entry 2)**
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.60–10.80 (br s, 1 H), 8.01 (d, *J* = 8.1 Hz, 2 H), 7.28 (d, *J* = 8.4 Hz, 2 H), 2.43 (s, 3 H).

2,5-Dimethylbenzoic Acid (Table 5, Entry 3)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.55 (br s, 1 H), 7.60 (s, 1 H), 7.18 (d, *J* = 6.9 Hz, 1 H), 7.12 (d, *J* = 6.9 Hz, 1 H), 2.44 (s, 3 H), 2.26 (s, 3 H).

4-Isopropylbenzoic Acid (Table 5, Entry 4)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.06 (d, *J* = 8.7 Hz, 2 H), 7.33 (d, *J* = 8.4 Hz, 2 H), 2.99 (m, 1 H), 1.28 (d, *J* = 7.2 Hz, 6 H).

4-Phenylbenzoic Acid (Table 5, Entry 5)[25]
^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ = 7.99 (d, *J* = 8.4 Hz, 2 H), 7.68–7.61 (br m, 4 H), 7.45–7.40 (br m, 3 H).

4-Methoxybenzoic Acid (Table 5, Entry 6)[26]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.90–11.50 (br s, 1 H), 7.86 (d, *J* = 6.6 Hz, 2 H), 6.87 (d, *J* = 6.6 Hz, 2 H), 3.78 (s, 3 H).

Piperonylic Acid (Table 5, Entry 7)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.78 (br s, 1 H), 7.53 (d, *J* = 8.1 Hz, 1 H), 7.34 (s, 1 H), 6.98 (d, *J* = 8.4 Hz, 1 H), 6.11 (s, 2 H).

4-*N*,*N*-Dimethylaminobenzoic Acid (Table 5, Entry 8)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.10 (br s, 1 H), 7.75 (d, *J* = 8.7 Hz, 2 H), 6.70 (d, *J* = 8.7 Hz, 2 H), 2.99 (s, 6 H).

Salicylic Acid (Table 5, Entry 9)
^{1}H NMR (DMSO-d_6): δ = 11.01–11.90 (br s, 1 H), 7.81 (d, *J* = 7.8 Hz, 1 H), 7.53 (t, *J* = 6.9 Hz, 1 H), 6.98–6.91 (br m, 2 H).

4-Hydroxybenzoic Acid (Table 5, Entry 10)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.45 (br s, 1 H), 10.25 (br s, 1 H), 7.80 (d, *J* = 8.7 Hz, 2 H), 6.83 (d, *J* = 8.7 Hz, 2 H).

Isophthalic Acid (Table 5, Entry 11)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.49 (s, 1 H), 8.17 (d, *J* = 7.5 Hz, 2 H), 7.66 (t, *J* = 7.5 Hz, 1 H).

***o*-Vanillic Acid (Table 5, Entry 12)[27]**
^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.38 (d, *J* = 8.1 Hz, 1 H), 7.21 (d, *J* = 7.5 Hz, 1 H), 6.85 (t, *J* = 8.7 Hz, 2 H), 3.81 (s, 3 H).

Vanillic Acid (Table 5, Entry 13)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 7.46–7.44 (m, 2 H), 6.85 (d, *J* = 8.7 Hz, 1 H), 3.81 (s, 3 H).

4-Fluorobenzoic Acid (Table 5, Entry 14)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.70 (br s, 1 H), 7.93 (br m, 2 H), 7.10 (br m, 2 H).

2-α,α,α-Trifluoromethylbenzoic Acid (Table 5, Entry 15)[28]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 13.20 (br s, 1 H), 7.74–7.59 (br m, 4 H).

4-Cyanobenzoic Acid (Table 5, Entry 16)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 14.00–12.00 (br s, 1 H), 8.07 (d, *J* = 9.7 Hz, 2 H), 7.96 (d, *J* = 8.4 Hz, 2 H).

4-Nitrobenzoic Acid (Table 5, Entry 17)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 14.00–12.00 (br s, 1 H), 8.21 (d, *J* = 8.1 Hz, 2 H), 8.13 (d, *J* = 8.1 Hz, 2 H).

***trans*-Cinnamic Acid (Table 5, Entry 18)**
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.00–10.00 (br s, 1H), 7.81 (d, *J* = 15.9 Hz, 1 H), 7.56 (t, *J* = 3.6 Hz, 2 H), 7.42 (m, 3 H), 6.47 (d, *J* = 15.6 Hz, 1 H).

α-Methylcinnamic Acid (Table 5, Entry 19)
^{1}H NMR (300 MHz, $CDCl_3$ + DMSO-d_6): δ = 7.85 (s, 1 H), 7.46–7.33 (br m, 5 H), 2.15 (s, 3 H).

Hydrocinnamic Acid (Table 5, Entry 20)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 10.05 (br s, 1 H), 7.31–7.18 (br m, 5 H), 2.95 (t, *J* = 7.8 Hz, 2 H), 2.63 (t, *J* = 8.1 Hz, 2 H).

Phenylacetic Acid (Table 5, Entry 21)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.2 (br s, 1 H), 7.34–7.22 (br m, 5 H), 3.64 (s, 2 H).

Benzoylformic Acid (Table 5, Entry 22)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 8.38 (d, *J* = 8.4 Hz, 2 H), 7.72 (t, *J* = 7.5 Hz, 1 H), 7.54 (t, *J* = 7.8 Hz, 2 H).

Cyclohexanecarboxylic Acid (Table 5, Entry 23)[29]
^{1}H NMR (300 MHz, $CDCl_3$): δ = 11.76 (br s, 1 H), 2.11–1.15 (br m, 11 H).

2-Methylpent-2-enoic Acid (Table 5, Entry 24)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.16 (br s, 1 H), 6.65 (t, *J* = 7.2 Hz, 1 H), 2.15 (m, 2 H), 1.74 (s, 3 H) 1.00 (m, 3 H).

Hexanoic Acid (Table 5, Entry 25)
^{1}H NMR (300 MHz, $CDCl_3$): δ = 12.00–10.00 (br s, 1 H), 2.36 (t, *J* = 7.5 Hz, 2 H), 1.65 (quint, *J* = 7.5 Hz, 2 H), 1.37–1.31 (m, 4 H), 0.91 (t, *J* = 6.9 Hz, 3 H).

2-Furoic Acid (Table 5, Entry 26)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 13.0 (br s, 1 H, CO_2H), 8.30 (s, 1 H, H-1), 7.78 (s, 1 H, H-2), 6.77 (s, 1 H, H-3).

Pyrrole-2-carboxylic Acid (Table 5, Entry 27)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.20 (br s, 1 H), 11.69 (br s, 1H), 6.94 (s, 1 H), 6.71 (s, 1 H), 6.11 (s, 1 H).

4-Methylimidazole-5-carboxylic Acid (Table 5, Entry 28)[30]
^{1}H NMR (300 MHz, DMSO-d_6): δ = 12.78 (br s, 1 H,), 9.78 (s, 1 H, NH), 7.75 (br s, 1 H, CH), 2.42 (s, 3 H).

Isonicotonic Acid (Table 5, Entry 29)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 8.76 (d, *J* = 3.6 Hz, 2 H), 7.80 (d, *J* = 3.6 Hz, 2 H).

Pyridine-2-carboxylic Acid (Table 5, Entry 30)
^{1}H NMR (300 MHz, DMSO-d_6): δ = 13.20 (br s, 1 H), 8.72 (m, 1 H, ArH), 8.07–7.97 (m, 2 H, ArH), 7.66–7.61 (m, 1 H, ArH).

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