

Aerobic Oxidation of Benzylic Alcohols with Solid Alkaline Metal Hydroxides¹

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Abstract—Solid alkaline metal hydroxides displayed high catalytic activity and full selectivity in the aerobic oxidation of benzylic alcohols in a non-polar medium. The activity of the solid bases, in decreasing order of reactivity, was KOH > NaOH ≫ LiOH. Water, which is the only by-product of the reaction, plays a crucial role in KOH deactivation by converting the crystal phase of KOH to KOH · H₂O, as confirmed by XRD measurements.

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INTRODUCTION

The oxidation of alcohols to their corresponding aldehydes and ketones is a fundamental reaction in organic synthesis [1–5]. The annual, worldwide production of carbonyl compounds is over 10⁷ tons, a significant amount of which is produced by the oxidation of alcohols [6]. Three oxidation methods are used to oxidize alcohol, including oxidation with stoichiometric amounts of hazardous inorganic compounds [1], catalytic dehydrogenation [7], and catalytic oxidative dehydrogenation [3–8].

The global trend toward green processes has promoted the use of catalysts in place of toxic reagents, and the resulting reaction exhibits improved activity and selectivity, thereby leading to a reduction in by-products. Three main catalytic oxidative dehydrogenation systems were reported in the literature: a coupled transfer dehydrogenation-hydrogenation reaction [8–10], in which unsaturated organic compounds are used as oxidants; oxidation using a peroxide, especially hydrogen peroxide, as the oxidant [3]; and aerobic oxidation, in which the oxidant is molecular oxygen [4–7]. Overall, the most environmentally friendly and promising alcohol oxidation method is aerobic oxidation.

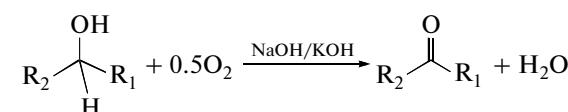
Traditionally, alcohol oxidations with homogeneous and heterogeneous catalysts and with different oxidants usually required the addition of inorganic bases, such as KOH, NaOH, and K₂CO₃, as co-catalysts [4–10]. The base is needed to activate the metal complex and/or to assist in proton dissociation from the hydroxyl group of the alcohol. Alcohol oxidations

with heterogeneous bases are common in transfer hydrogenation-dehydrogenation coupled reactions using ketone as the oxidant. These reactions are proposed to operate through the Meerwein–Ponndorf–Verley–Oppenauer mechanism, which entails a direct hydrogen transfer from a C–H of the alcohol to a carbonyl carbon via a cyclic mechanism. A common solid base catalyst is MgO, in whose presence the transfer hydrogenation can occur in either the gas or liquid phase [10, 11].

Although it was found that NaOH in its solid form has 5-fold more basic sites than the most common solid basic catalyst MgO [12] and uniform base strength distribution, its utilization as a solid base catalyst has been relatively ignored [13]. We recently characterized the basicity of solid alkaline hydroxides (AMH) with acid indicators and CO₂-TPD experiments [14]. The basicity strengths of KOH and NaOH were higher ($pK_a = 18.4–26.5$) than that of LiOH ($pK_a = 15.0–18.4$). CO₂-TPD experiments also confirmed the superior basicities of both NaOH and KOH. In addition, KOH was shown to have approximately 3.5-fold more basic sites and stronger basicity than NaOH.

The oxidation of alcohols with metal catalysts is frequently accompanied by the addition of soluble bases, including AMH, as co-catalysts [15–18], and solid bases are also often employed in catalytic alcohol oxidation systems [10, 11]. Solid AMH, however, were not reported as catalysts for aerobic alcohol oxidation. We recently reported the successful, liquid phase oxidation of 1-phenylethanol over solid AMH in the presence of different oxidants such as cyclohexanone, nitrobenzene, and molecular oxygen [14]. To investi-

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$R_1 = H$, alkyl
 $R_2 = \text{benzyl, alkyl}$

Scheme 1. Aerobic oxidation of alcohols.

gate the scope and limitations of using solid AMH as catalysts for the aerobic oxidation of alcohols, we studied the influence of different reaction conditions, such as solid base type, solvent type, and alcohol to AMH ratio, on the performance of solid AMH in the aerobic oxidation of alcohols (Scheme 1).

EXPERIMENTAL

Reaction Procedure

All chemicals were purchased from Aldrich. All the experiments were conducted using a glass autoclave (0.3 l, Büchi). In a typical reaction, the reactor was filled with solvent (usually toluene), alcohol, and solid alkaline hydroxide. Then it was heated to 80°C and pressurized to one atmosphere of oxygen and maintained at this pressure. Aerobic oxidation of 1-phenylethanol was typically performed by adding 2 g of 1-phenylethanol and 4 g of solid base, which was added as powder, to 120 ml of toluene under an oxygen atmosphere.

Analytical Procedure

Reaction conversion and product selectivity were determined by a Hewlett Packard 5890 Series II gas chromatograph equipped with FID detector and a packed, Varian column, with a WCOT fused silica (25 m \times 0.32 mm) coating CP-Chirasil Dex-CB, DF = 0.25 μm . Samples were withdrawn periodically from the reactor to determine reactant concentrations. In the GC procedure, helium was used as the carrier gas, with initial temperature: 100°C, final temperature: 130°C, initial time: 0 min, final time:

Table 1. The effect of solvent polarity on KOH performance in the aerobic oxidation of 1-phenylethanol^a

Entry	Solvent	Dielectric constant (25°C)	Yield, %
1	Toluene	2.379	62
2	Chlorobenzene	5.621	59
3	Tert Butyl Alcohol	12.47	23
4	DMF	38.32	3
5	Water	80	0

Note: ^a 2 g 1-phenylethanol, 2 g KOH, 80°C, 1 bar O₂, 1 h.

40 min, temperature rate: 10 K/min, and detector temperature: 250°C.

XRD Analysis

The phase composition of solid alkaline metal hydroxides was tested by X-ray diffraction (XRD). Wide-angle XRD (WAXS) patterns were collected on a Philips diffractometer PW 1050/70 (CuK_α radiation) with a diffracted beam graphite monochromator. Data were recorded at a 0.02° step size with a count time of 2 s for every step. The peak positions and the instrumental peak broadening (β) were determined by fitting each diffraction peak using APD computer software. Crystal diameter size was determined using the Scherrer equation $1 = K\lambda/[(B^2 - \beta^2)^{0.5} \cos(2\theta/2)]$, where $K = 1.000$, $\beta = 0.1^\circ$, $\lambda = 0.154$ nm, and B is the peak broadening at $2\theta = 31.16^\circ$; 38.08° ; 53.59° ; 55.32° ; 55.32° for NaOH and $2\theta = 23.41^\circ$; 24.86° ; 26.55° ; 28.4° ; 30.49° ; 32.475° ; 35.13° ; 36.4° ; 45.73° for KOH.

RESULT AND DISCUSSION

As previously stated, we reported that AMH in their solid form have high basic surface characters, making them suitable for use as catalysts for the oxidation of 1-phenylethanol with various oxidants. It was suggested that similar to the mechanism of transfer dehydrogenation-hydrogenation with transition metal complexes, the reactions over AMH initiate via the abstraction of the alcohol hydroxyl group's acidic proton by the base via the hydroxide ion on the surface of the AMH. These reactions form an alkoxide that can be stabilized by the metal cation, which acts as a Lewis acid. β -Elimination of the hydride can be then performed because the electron-withdrawing effect of the oxygen atom weakens the β -C–H bond relative to the other C–H bonds, and because resonance effects make the resulting carbonyl compound more stable than the alkoxide. Finally, the active sites can be regenerated by an oxidant that abstracts the proton and the hydride from the base [14].

Thus we initiated our investigation by studying how the polarity of the reaction solvent, as expressed by its dielectric constant, affected product yield, using KOH as the catalyst (Table 1). The results show that increasing the polarity of the solvent decreased the product yield, and in solvents that fully dissolve KOH, like DMF and water, no product was detected. The variable product yields can be explained by the change in base solubility in response to the different solvents. Increasing the polarity of the solvent caused base solubility to rise, resulting in free ions that were inactive in the oxidation reaction. The variability also implies that the reaction was not caused by any homogeneous species dissolved in the solvent.

Because toluene was found to be the best from among the tested solvents for the aerobic oxidation of

1-phenylethanol with KOH, it was also employed as the solvent in aerobic oxidations of representative aliphatic, alylic, and aromatic primary and secondary alcohols with KOH (Table 2). Only benzylic alcohols were efficiently oxidized over KOH, probably due to the electron-withdrawing effect of the aromatic ring that assists in the β -elimination of the hydride, which is the rate limiting step. In addition, the activity of the aerobic oxidation of benzyl alcohol (41% conversion in 1 h), a primary alcohol, was lower than that of 1-phenylethanol (94% conversion in 1 h), a secondary alcohol. Both reactions were run in the presence of 4 g of KOH and 2 g of substrate. The large conversion difference between the two alcohols probably results from the relatively higher stability of the secondary alcohols, which have two donating groups, while the primary alcohols only have one. All oxidation reactions exhibited full selectivities, and no over-oxidation was observed.

The higher conversion of 1-phenylethanol prompted its further testing, as a representative aromatic alcohol, with the three solid AMH representatives: KOH, NaOH, and LiOH in toluene (Fig. 1). Catalytic activities of the solid bases matched their respective base strengths: KOH > NaOH \gg LiOH [14]. In addition, the reaction with LiOH resulted in a negligible acetophenone yield while the reaction with KOH was much faster than that with NaOH, under similar conditions, and a high yield (~95%) was achieved after less than an hour. For example, using 2 g of 1-phenylethanol with 4 g of solid base resulted in a reaction yield of about 60% after 5 min with KOH and after 120 min with NaOH. However, in the reaction over KOH (Fig. 1), the maximum acetophenone yield achieved was approximately 95%, even when the reaction was continued for 45 h (not shown).

The effect of KOH and NaOH loading on the oxidation of 1-phenylethanol was also tested (Figs. 2 and

Table 2. Aerobic oxidation of different alcohols with KOH*

Entry	Alcohol	Yield, %
1	1-Phenylethanol	94
2	2-Methylbenzyl alcohol	50
3	Benzyl alcohol	48
4	Cinnamyl alcohol	7
5	Cyclohexanol	5
6	2-Octanol	4
7	2-Butanol	1

* 2 g alcohol, 4 g KOH, 80°C, 1 bar O₂, 1 h.

3, respectively). In general, an increase in the amount of either base boosted product yield, but this trend was much stronger with KOH. However, while the reactions with KOH stopped after less than an hour, those with NaOH continued. At low AMH loading (2 g), the initial yield with KOH was higher than that with NaOH, but because the reaction with KOH stopped after less than an hour and that with NaOH continued, after several hours its yield exceeded that of the KOH reaction.

Increasing the AMH (KOH, NaOH) to 1-phenylethanol ratio to more than 4 : 1 did not significantly change product yield. But when the concentration of 1-phenylethanol in the reaction mixture was increased and the amount of KOH was kept constant, product yield decreased proportionally (Fig. 2). The progress of the reactions over time was similar, however, indicating that the alcohol concentration does not change the reaction activity, and the reaction stopped after about 20 min.

Several tests were run to explore why the reaction over KOH stopped so quickly, despite its initially high activity. Two possible explanations emerged: some of

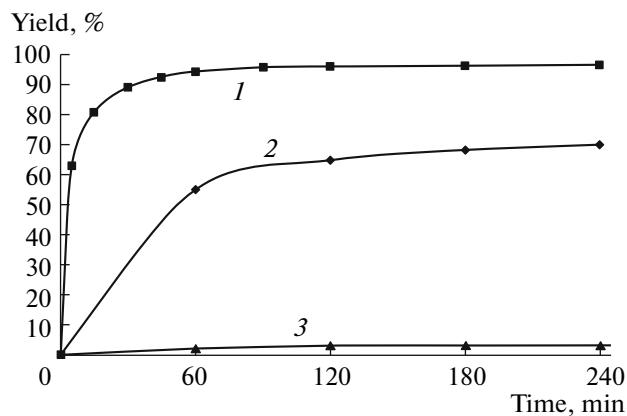


Fig. 1. Effect of solid base type on the aerobic oxidation of 1-phenylethanol (1, KOH; 2, NaOH; 3, LiOH). Reaction conditions: 2 g 1-phenylethanol, 4 g AMH, 80°C, 1 bar O₂.

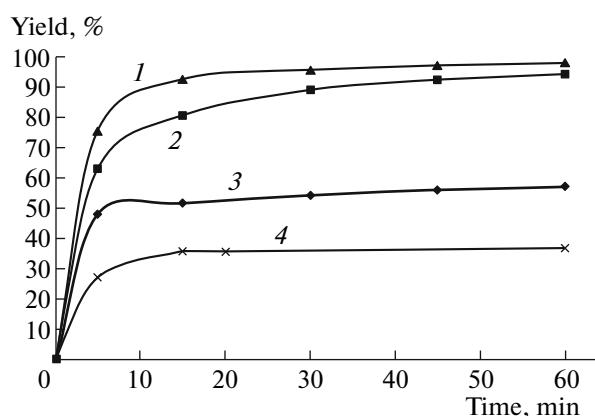


Fig. 2. Effect of KOH loading and 1-phenylethanol concentration on reaction progress in the aerobic oxidation of 1-phenylethanol (1, 8 g KOH, 2 g 1-phenylethanol; 2, 4 g KOH, 2 g 1-phenylethanol; 3, 2 g KOH, 2 g 1-phenylethanol; 4, 4 g KOH, 4 g 1-phenylethanol). Reaction conditions: 80°C, 1 bar O₂.

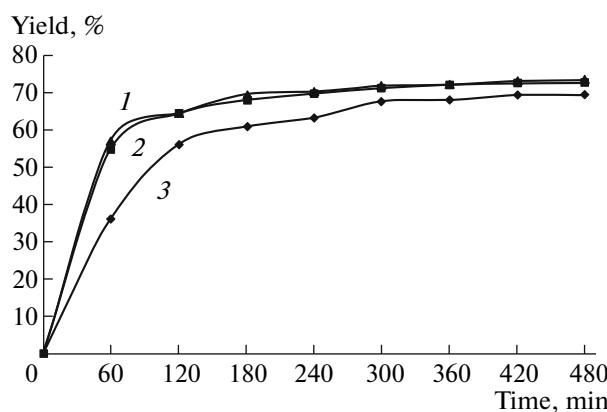


Fig. 3. Effect of NaOH loading on its performance in the aerobic oxidation of 1-phenylethanol (1, 8 g; 2, 4 g; 3, 2 g). Reaction conditions: 2 g 1-phenylethanol, 80°C, 1 bar O₂.

the acetophenone formed began functioning as an oxidant, abstracting hydrogen from the catalyst [14], thus promoting the reverse reaction to 1-phenylethanol, or the active sites on the catalyst were deactivated. But because the reaction stopped as it reached its equilibrium conversion, it should not be influenced by the amount of the catalyst (Fig. 2). Furthermore, the addition of the extra 2 g of 1-phenylethanol to the reaction mixture after 1 h did not change the total amount of acetophenone, which indicates that catalyst deactivation is the most likely reason that the reaction with KOH ended so quickly.

Catalyst deactivation may result from irreversible adsorption on the basic active sites or from alteration of their nature during the reaction. It was previously suggested that the reaction mechanism is initiated by dehydrogenation of the alcohol and adsorption on the catalyst surface of the proton and the hydride [14]. If that adsorption is irreversible, then it would block the active sites. However, although the conversion of 1-phenylethanol was augmented up to a certain loading in response to increased amounts of KOH (which consequently increased the number of active basic sites), it did not proportionally change the reaction yield (Fig. 1), indicating that deactivation is not caused by the active sites being blocked by irreversible adsorption of the proton and the hydride. Since the ketone formed can also adsorb to the catalyst surface, it may adsorb irreversibly, therefore blocking the active sites. Thus, 2 g of acetophenone were added to 2 g KOH in toluene, before the addition of 1-phenylethanol, and the reaction mixture was stirred under a nitrogen atmosphere for 1 h. Then 1-phenylethanol and oxygen were added to the reaction mixture and the reaction proceeded for 5 h. However, oxidation progress and the final conversion of 1-phenylethanol were identical to the case in which KOH was not treated with acetophenone. This indicates that acetophenone adsorption was reversible, and thus this

route for AMH deactivation can be eliminated. Moreover, constant equilibrium yield due to the reverse reaction of acetophenone, as in the case of dehydrogenation, is also excluded.

Deactivation of the active sites over KOH was studied further by examining the effect of oxygen molecules on the catalyst. Therefore, KOH (2 g) was stirred in toluene under an oxygen atmosphere for 1 h in the absence of the alcohol, at which time 1-phenylethanol was added. After adding 1-phenylethanol to the reaction mixture, the reaction rate was lower than it had been without previously treating KOH with oxygen (20% yield after 1 h vs. 60% when oxygen and 1-phenylethanol were added together). The maximum yields of both reactions, however, equalled 60%. It was therefore suggested that oxygen molecules only inhibit the reaction, most likely because they adsorbed to the active sites, but this adsorbed oxygen does not block the active sites. In addition, although the substrate can release the adsorbed oxygen from the solid base surface, thereby allowing the reaction to proceed, the reaction yield did not exceed 60%. Furthermore, increasing the oxygen pressure had little effect on the reaction rate, and the final yield did not change.

If neither acetophenone nor oxygen deactivates the active sites in KOH, the only by-product of the reaction, water, may be responsible. KOH and NaOH have 15 and (less than) 2 wt % of water, respectively, which can be either in hydrated form or adsorbed on the crystal surface. In addition, KOH easily adsorbed moisture from the air, thus becoming wetter and prompting the suggestion that water, which was generated during the reaction, adsorbed on the catalyst surface and changed its nature. Phase changes in the solids, therefore, were determined by XRD analysis of the two bases, KOH and NaOH, before and after the reaction (Fig. 4). Indeed, the phase analysis of KOH (Fig. 4a) clearly shows that it was changed during the reaction. The fresh base comprised 18% pure KOH while the rest was KOH · H₂O. The used sample, on the other hand, exhibited only trace amounts of pure KOH in the crystal structure and increased amounts of KOH · H₂O and other hydrated forms of KOH. But the use of pure mono-hydrated KOH in the aerobic oxidation of 1-phenylethanol yielded no acetophenone. In conclusion, the main reason for KOH deactivation was the transformation of KOH to KOH · H₂O, driven by the formation of water during the reaction. In addition, as the amounts of water and alcohol formed were equal (and comparable to the amount of KOH), the deactivation was very strong. In contrast, during the reaction with NaOH, there was no significant change in the amount of either pure or hydrated NaOH (Fig. 4b), lending additional support to the suggestion that NaOH is not deactivated.

The use of recycled AMH was also investigated. First, 1-phenylethanol was aerobically oxidized with both NaOH and KOH under typical conditions (2 g of solid base and 2 g of 1-phenylethanol in 120 ml tolu-

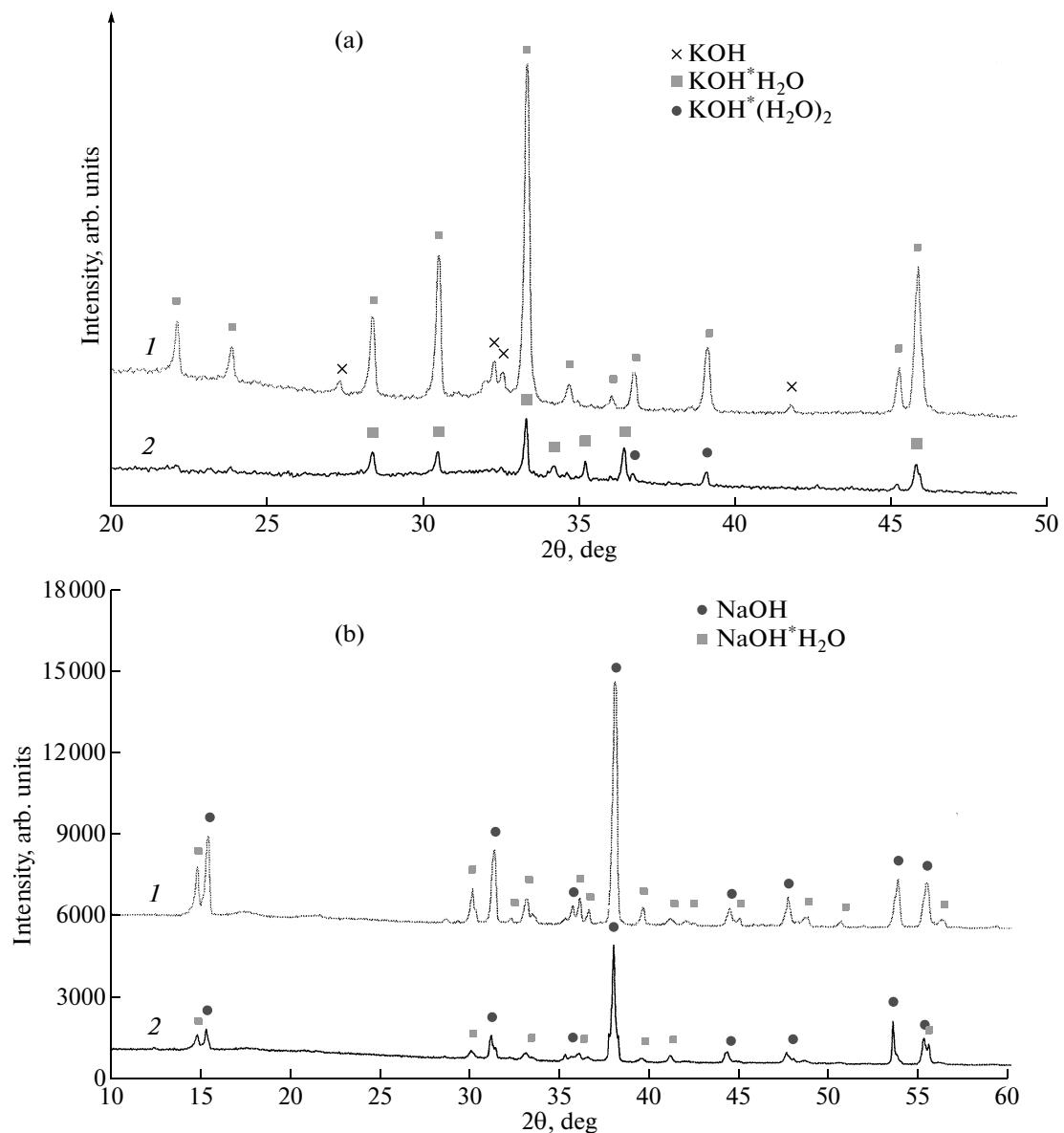


Fig. 4: (a) XRD measurements of KOH before (1) and after (2) 1-phenylethanol aerobic oxidation. (b) XRD measurements of NaOH before (1) and after (2) 1-phenylethanol aerobic oxidation.

ene). Stirring was stopped after reaching maximum yield (60% for KOH and 70% for NaOH), and the reaction mixture was allowed to sit until the solid had settled completely. The organic liquid was then decanted to separate the solvent from the solid and a fresh solution of 1-phenylethanol in toluene was added to the recycled solid. The reactor was again pressurized with 1 bar of oxygen and heated to 80°C. As expected, the run with recycled KOH showed negligible activity, even after 24 h, while the run with fresh KOH produced a 60% yield after 1 h. When NaOH was used as the catalyst, although the yield in the second run was lower than that in the first run (10 and 70%, correspondingly) after 5 h under similar conditions, the reaction continued and reached 70% con-

version after 24 h. These results support our conclusion that KOH was most likely deactivated because of a change (absent in the reaction with NaOH) that occurred in its hydrated form during the reaction. The lower activity of NaOH in the second run can be attributed to the adsorption of both water and oxygen from the first run, a process that may hinder the dehydrogenation of the fresh alcohol, as suggested above.

CONCLUSION

Solid AMH have been found to activate the aerobic oxidation of aromatic alcohols. Benzylic alcohols were oxidized at satisfactory rates over AMH with oxygen, but aliphatic alcohols showed poor oxidation yields.

Differences in the basicities of the various AMH were reflected in their performances in the oxidation reaction. For the aerobic oxidation of 1-phenylethanol over AMH, solid catalyst activity followed the order KOH > NaOH ≫ LiOH. It was found that the water by-product of aerobic oxidation plays a crucial role in KOH deactivation by converting the crystal phase of KOH to KOH · H₂O, as confirmed by XRD measurements. In contrast to KOH, NaOH did not show any signs of deactivation.

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