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## COMMUNICATION

# Highly Efficient Aerobic Oxidation of Various Amines Using Pd₃Pb Intermetallic Compound Catalysts

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**Intermetallic Pd₃Pb supported on Al₂O₃ can act as a highly efficient heterogeneous catalyst for the oxidation of various amines including primary, secondary, aromatic, aliphatic, and cyclic amines.**

The oxidation of amines to imines is an important chemical transformation because of the versatile application of imines as intermediates in the synthesis of medicines or biologically active nitrogen-containing organic molecules.[1] Several oxidation procedures that involve stoichiometric oxidants such as 2-iodoxybenzoic acid[2] or *N-tert*-butylphenylsulfinimidoyl chloride[3] have been reported. However, the establishment of an efficient heterogeneous catalytic system that uses molecular oxygen as a sole oxidant is desired in view of the principles of green chemistry.[4] In this context, several aerobic oxidation systems based on supported transition metal catalysts have been reported. Ru-based catalysts such as Ru/hydroxyapatite[5] and Ru/Al₂O₃[6] are known to be effective for nitrile synthesis from primary amines. However, they exhibit much lower catalytic activity toward imine formation from secondary amines. Nanoparticulate Au catalysts such as Au/CeO₂,[7] Au/TiO₂,[8] and Au/C[9] have recently been reported to serve as active catalysts for imine synthesis. The substrate scope, however, has been limited to benzylamine derivatives and indoline, i.e., activated amines. Moreover, a decrease in selectivity occurs due to undesired C–N bond cleavage. The replacement of Au with a less expensive metal is also desirable for practical use. Although several photocatalytic systems for the oxidation of amines to imines have also been reported,[10] drawbacks to these systems remain, including their low catalytic activity, low selectivity, and/or limited substrate scope. To this point, no heterogeneous catalyst for imine synthesis that provides high catalytic activity, high selectivity, and wide substrate scope has been reported in the literature. Recently, attention has been increasingly focused on the use of intermetallic compounds as catalyst materials. Intermetallics often have specific crystal structures and hence provide highly ordered surface atom arrangements. Several unique catalytic properties of intermetallics compared with those of pure metals and solid solution alloys have been revealed due to such specific structures.[11] For example, we previously reported that Pd-based intermetallic compounds supported on silica, such as Pd₃Pb/SiO₂ and Pd₃Bi/SiO₂, exhibit much higher catalytic activities toward the oxidative acetoxylation of 1,3-butadiene than monometallic Pd/SiO₂.[12] During the course of our attempt to develop Pd-based oxidation chemistry, we observed that Pd₃Pb exhibits high catalytic activity and selectivity in amine

oxidation. Herein, we report a novel and highly efficient heterogeneous catalytic system based on Pd₃Pb for the oxidation of a variety of amines including primary, secondary, aromatic, aliphatic, and cyclic ones.

A series of Pd-based intermetallic compounds supported on silica (Pd$_x$M$_y$/SiO₂; M = Bi, Fe, Ga, In, Pb, Sb, Sn, and Zn) were prepared by conventional impregnation followed by H₂ reduction at 400–800°C (see Supporting Information for the experimental details). Formation of the desired intermetallic phase was confirmed by X-ray diffraction (XRD; Fig. S1). The catalytic performance of these intermetallic compounds and that of monometallic Pd were compared in the oxidation of dibenzylamine to *N*-benzylidenebenzylamine, as shown in Fig. 1. Only a 4% conversion was obtained with Pd/SiO₂ after 5 h of reaction, whereas most of the intermetallic compounds gave higher yields.
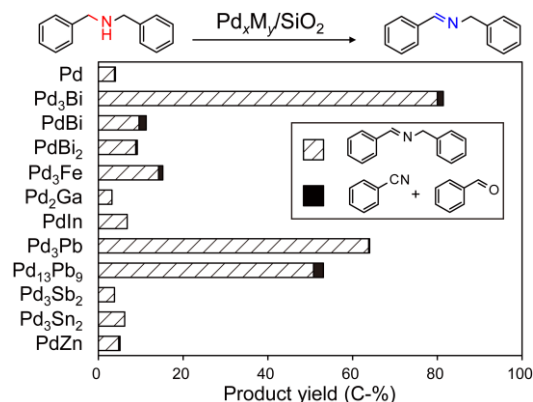


Fig. 1. Aerobic oxidation of dibenzylamine over various Pd-based intermetallic compounds and Pd supported on silica. Reaction conditions: amine, 1.0 mmol; catalyst, 100 mg (Pd: 2.8 mol%); solvent, 5 ml (*p*-xylene); atmosphere, 5% O₂/Ar; temperature, 110°C; time, 5 h.

Notably, Pd₃Bi/SiO₂, Pb₃Pb/SiO₂, and Pd₁₃Pb₉/SiO₂ showed much higher catalytic activities (82, 64, and 53% conversion, respectively) compared to the other catalysts (< 15%). Small amounts of benzonitrile and benzaldehyde, which resulted from C–N bond cleavage, were detected with both Pd₃Bi/SiO₂ and Pd₁₃Pb₉/SiO₂. The formation of such byproducts was scarcely observed when Pb₃Pb/SiO₂ was employed (> 99 C-% selectivity). The most active catalyst (Pd₃Bi/SiO₂) and the most selective catalyst (Pb₃Pb/SiO₂) were then employed to oxidize *N*-isopropyl-benzylamine (Fig. S2).

The Pb$_3$Pb/SiO$_2$ catalyst gave the corresponding dehydrogenated imine, *N*-benzylideneisopropylamine, in 95 C-% yield after 5 h of reaction. In contrast, when Pb$_3$Bi/SiO$_2$ was employed, substantial catalyst deactivation occurred at 50% conversion. Thus, Pd$_3$Pb was the most promising intermetallic phase for amine oxidation.

We subsequently optimized the catalyst support for Pd$_3$Pb. In general, catalyst supports used for intermetallics have been limited to silica or carbon, which results in weak metal–support interaction because strong metal–support interaction tends to inhibit intermixing of the component metal elements. Very recently, however, we established an innovative methodology to prepare single-phase intermetallic nanoparticles on support materials that exhibit strong interactions, such as alumina.[13] In this study, Pd$_3$Pb supported on a series of oxide supports such as TiO$_2$, Al$_2$O$_3$, and MgO were prepared by impregnation followed by H$_2$ reduction at 450, 600, and 600°C, respectively, so that the obtained particles were uniform in size. XRD patterns of these samples confirmed that the desired Pd$_3$Pb phase was formed with high phase purity and similar crystallite sizes (16–19 nm) on each support (Fig. S3). Fig. 2a shows the turnover frequencies (TOFs) obtained during the oxidation of dibenzylamine over Pd$_3$Pb and monometallic Pd supported on the various supports. In the case of Pd$_3$Pb, a steep increase in TOF was
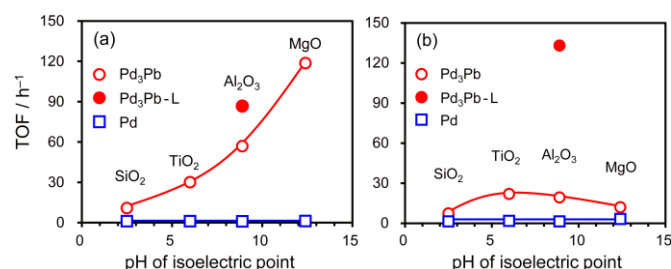


Fig. 2. Correlation between the TOF obtained in the oxidation of a) dibenzylamine and b) benzylamine using supported Pd$_3$Pb and Pd catalysts and the pH of the isoelectric point of the catalyst support. Reaction conditions: amine, 0.5 mmol; catalyst, 50 mg (Pd: 2.8 mol%); solvent, 5 ml (p-xylene); atmosphere, 5% O$_2$/Ar; temperature, 110°C.

observed as the basicity of the support increased. The most basic support, MgO, gave a TOF of 119 h$^{-1}$. Notably, however, no change in the TOF was observed among the monometallic Pd catalysts. Therefore, Pd$_3$Pb/MgO exhibited a TOF that was 100 times higher than that of Pd/MgO. These results suggest that the presence of both the intermetallic phase and basic sites on the support are essential for achieving a large increase in catalytic activity. In our previous study, we also successfully prepared nanosized Pd$_3$Pb supported on alumina via LiBH$_4$ reduction at 80°C (particle size, 3–5 nm; described as Pd$_3$Pb/Al$_2$O$_3$-L).[13] This catalyst afforded a higher TOF (87 h$^{-1}$) than that of the H$_2$-reduced catalyst (57 h$^{-1}$). We subsequently performed a similar catalytic test using benzylamine as a substrate (Fig. 2b). As with most of the heterogeneous amine oxidation catalytic systems, *N*-benzylidene-benzylamine was the main product. Monometallic Pd catalysts showed very low TOF values that, as with the case of dibenzylamine oxidation, exhibited no dependence on the basicity of the support. In the case of Pd$_3$Pb, however, a volcano-type relationship with TiO$_2$ at the top was observed between TOF and the basicity of the support. Furthermore, a remarkable increase in TOF was achieved when the particle size was reduced: 19 h$^{-1}$ (Pd$_3$Pb/Al$_2$O$_3$) → 133 h$^{-1}$ (Pd$_3$Pb/Al$_2$O$_3$-L). On the basis of these results, we concluded that Pd$_3$Pb/Al$_2$O$_3$-L was the most promising catalyst for amine oxidation.

The substrate scope of Pd$_3$Pb/Al$_2$O$_3$-L in amine oxidation was investigated using various amines including primary, secondary, aromatic, aliphatic, and cyclic amines, as shown in Table 1.

**Table 1.** Oxidation of various amines using Pd$_3$Pb/Al$_2$O$_3$-L.[a]



| entry | substrate | product | time /h | conv. (%) | sel. (C-%)[b] |
|---|---|---|---|---|---|
| 1 | R = H | R = H | 1 | 100 | 76 (21) |
| 2 | R = Me | R = Me | 1 | 100 | 82 (15) |
| 3 | R = Cl | R = Cl | 3 | 85 | 74 (26) |
| 4 | | | 1 | 96 | 90 (10) |
| 5 | | | 2 | 94 | 77 (8) |
| 6 | R' = Me | R' = Me | 1 | 100 | 85 |
| 7 | R' = Et | R' = Et | 1 | 98 | 90 |
| 8 | R' = *i*Pr | R' = *i*Pr | 1.5 | 94 | 94 |
| 9 | R' = *t*Bu | R' = *t*Bu | 1 | 95 | 96 |
| 10 | R' = Bn | R' = Bn | 1.5 | 99 | 97 |
| 11[c] | R' = Ph | R' = Ph | 5 | 94 | 94 |
| 12[d] | | | 3 | 90 | 86 |
| 13[d] | | | 4 | 81 | 80 |
| 14 | | | 3.5 | 90 | >99 |
| 15 | | | 0.3 | 100 | >99 |
| 16 | reuse 1 | | 0.3 | 99 | >99 |
| 17 | reuse 2 | | 0.3 | 97 | >99 |

[a] Reaction conditions are shown in the caption of Fig. 2. [b] The numbers in parentheses indicate selectivity to corresponding nitrile. [c] Catalyst, Pd$_3$Pb/MgO; temperature, 120°C. [d] Catalyst, 100 mg; temperature, 130°C.

Benzylamine and *p*-methylbenzylamine were converted into the corresponding dimerized imines with small amounts of nitriles in 1 h (entries 1 and 2). A longer reaction time (3 h) was needed to obtain a good yield with *p*-chloro-substituted amine (entry 3). Total selectivity toward the oxidation products (imine and nitrile) was close to 100 C-% in each case. In addition, oxidation of the aliphatic primary amines, butylamine and isobutylamine, gave the corresponding imines in high yields within 1 and 2 h, respectively (entries 4 and 5). A series of aromatic secondary amines (*N*-alkylbenzylamines; R′ = Me, Et, *i*Pr, *t*Bu, and Bn, entries 6–10) were converted into dehydrogenated imines in excellent yields in 1 or 1.5 h. In this series, as the steric hindrance around the N atoms decreased (*t*Bu → *i*Pr → Et → Me), the selectivity slightly decreased by the formation of benzaldehyde and *N*-benzylidenebenzylamine, which probably resulted from C–N bond cleavage. This result may reflect the fact that an undesired C–N bond cleavage becomes slightly allowed in a sterically unhindered environment. However, emphasis should be placed on the fact that selectivities greater than 90 C-% were maintained even at almost complete conversions. The obtained yield in each case (entries 6–10) is the highest value ever reported.[7b, 9, 10b, 14] Surprisingly, however, the oxidation of *N*-phenylbenzylamine did not proceed at all over Pd$_3$Pb/Al$_2$O$_3$-L (data not shown). This reaction was effectively catalyzed by Pd$_3$Pb/MgO (entry 11). Furthermore, the aliphatic secondary amines, dibutylamine and diisobutylamine, were converted into the corresponding dehydrogenated imines with good yields within a few hours (entries 12 and 13). To the best of our knowledge, this work represents the first report of the successful aerobic oxidation of

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aliphatic secondary amines using a heterogeneous catalyst. The oxidation of cyclic amines such as 1,2,3,4-tetrahydroquinoline and indoline gave aromatized quinolone and indole, respectively, with excellent yields (entries 14 and 15). Particularly, in the latter case, the reaction occurred quantitatively in only 0.3 h, which also afforded higher TOF (119 h$^{-1}$) than those of Ru (18 h$^{-1}$)[6] and Au (92 h$^{-1}$)[7b] catalysts. The catalyst used in indoline oxidation was easily separated from the reaction mixture by simple decantation and was reused at least twice, with the catalytic activity being almost maintained (entries 16 and 17). Thus, Pd$_3$Pb/Al$_2$O$_3$-L exhibited not only excellent catalytic activity and selectivity but also wide substrate scope and reusability.

We then investigated the reason for the great enhancement in catalytic activity by the formation of the Pd$_3$Pb intermetallic phase. Analogous to the well-studied oxidation of alcohols over supported Pd catalysts,[15] the aerobic oxidation of amine appears to proceed via a two-step dehydrogenation and oxygenation of the hydrogen to form a water molecule. A possible reaction mechanism for the oxidation of a secondary amine over Pd$_3$Pb/SiO$_2$ is shown in Scheme 1a: 1) adsorption of the amine (N–H activation), 2) C–H activation, 3) desorption of the imine, and 4) removal of the hydrogen atoms by oxygen. A kinetic study of the oxidation of dibenzylamine over Pd$_3$Pb/SiO$_2$ revealed a first-order relationship with amine concentration ([A] = 0.10–0.28 M) and a zero-order dependence of the reaction rate on the partial pressure of oxygen ($P_{O_2}$: 2.0–10 kPa). Moreover, a primary kinetic isotope effect was observed with $N$-deuterated dibenzylamine ($k_H/k_D$ = 2.2). These results strongly indicate that the dissociative adsorption of dibenzylamine (step 1) is the rate-determining step over Pd$_3$Pb/SiO$_2$. A similar kinetic study for Pd/SiO$_2$ showed that the reaction orders with [A] and $P_{O_2}$ were both close to zero. Furthermore, no kinetic isotope effect was observed ($k_H/k_D$ = 1.0) with deuteration at the benzylic positions (dibenzylamine-$\alpha,\alpha,\alpha,\alpha$-$d_4$) where C–H activation occurred (step 2). These results imply that the rate-determining step over Pd/SiO$_2$ is the desorption of imine (step 3).
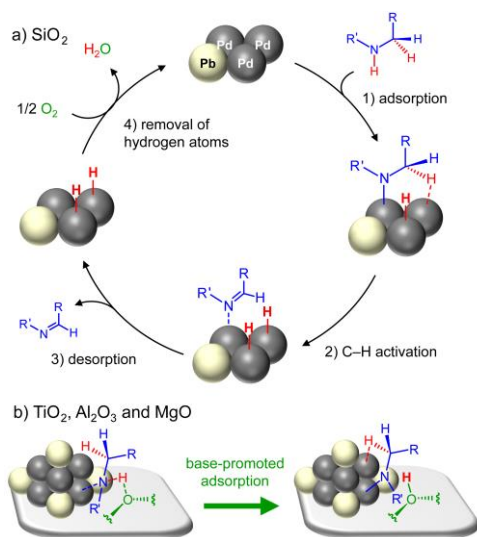


Scheme 1. Possible reaction mechanisms of oxidation of secondary amines over Pd$_3$Pb supported on a) SiO$_2$ and b) TiO$_2$, Al$_2$O$_3$, and MgO. A portion of the atomic arrangement on the Pd$_3$Pb {111} facets is illustrated.

On the basis of the obtained results, we concluded that the higher catalytic activity of Pd$_3$Pb/SiO$_2$ compared to that of Pd/SiO$_2$ was due to promotion of the desorption rate; i.e., the intermetallic Pd$_3$Pb phase or the Pb atoms themselves provide favorable desorption sites. In the chemistry of alcohol oxidation, the addition of Pb or Bi to Pt-group metals is known to improve their catalytic activity or selectivity.[15,16] A number of explanations to these positive effects have been advocated and are still under debate.[15-17] However, the effect revealed in the present study, i.e., promotion of desorption, is completely different from those previously proposed for alcohol oxidation. Thus, the findings in the present study provide not only a highly efficient catalytic system but also an entirely novel insight into Pd-based oxidation chemistry.

The ability of the basicity of the support to enhance the catalytic activity can be attributed to the acceleration of amide formation facilitated by basic sites adjacent to the Pd$_3$Pb particles (Scheme 1b). Such base-mediated deprotonation is common in alcohol oxidation over Pt-group metals and over Au catalysts.[15] In the case of amine oxidation over Pd/SiO$_2$, however, such a promotion effect does not appear because the reaction rate is limited at the desorption step. Thus, the intermetallic Pd$_3$Pb phase is also necessary to exert the base-promotion effect during amine oxidation.

In conclusion, intermetallic Pd$_3$Pb exhibits catalytic activity that is remarkably higher than that of a monometallic Pd catalyst in the oxidation of amines to imines. Nanoparticulate Pd$_3$Pb supported on Al$_2$O$_3$ can act as a highly efficient heterogeneous catalyst for the oxidation of various amines. The obtained catalytic activities, selectivities, and substrate scope are superior to those of existing heterogeneous catalysts. The enhanced catalytic activity of Pd$_3$Pb is attributed to its ability to promote imine desorption.

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