

# Bifunctional Solid Catalyst for the One-Pot Selective N-Monoalkylation of Amines with Alcohols

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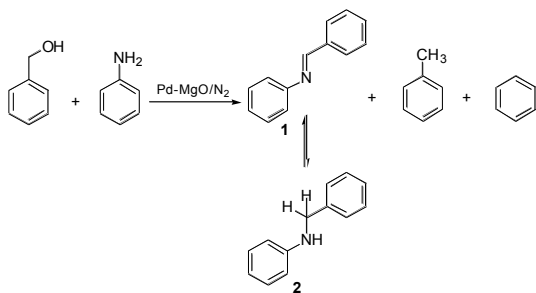
**Abstract:** It has been found that a bifunctional metal Pd/base (MgO) catalyst performs the selective monoalkylation of amines with alcohols. The reaction goes through a series of consecutive steps in a cascade mode. The controlling step of the process is the hydride transfer from the metal to the imine. By changing the crystallite size of the Pd it is demonstrated that this is a structure sensitive reaction, while the competing process leading to subproducts are not. The high efficiency of the catalytic system has allowed to extent the process to the one-pot synthesis of piperazines.

## Introduction

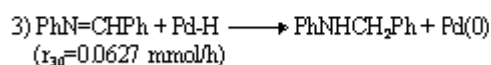
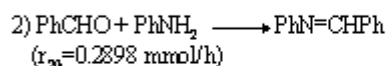
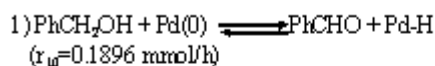
Monoalkylation of amines with alcohols is a reaction that produces C-N bonds yielding substituted amines [1]. It has been reported that Ru(II) and Ir (I) complexes are able to catalyze the direct alkylation of amines and sulfonamides by alcohols under transfer hydrogenation conditions [2,3]. However, these reactions usually require an excess of a soluble base and the valuable catalysts are difficult to recover. We will show here that by using a heterogeneous bifunctional solid catalyst of Pd on MgO, is possible to catalyze the monoalkylation of amines through a series of consecutive reactions in a cascade mode with high selectivity through the borrowing hydrogen methodology.

## Results and Discussion

For proving the concept we have used the reaction between benzylic alcohol and aniline. Thus, when benzylic alcohol was allowed to react with aniline in trifluorotoluene at 180°C with Pd-MgO as catalyst, the products obtained were the imine benzylidene-phenyl-amine **1** and the benzylphenylamine **2**. These products account for 92% of the converted material, the rest of the products being toluene and benzene (see Scheme 1, entry 1, table 1).



Scheme 1. Product distribution obtained in the N-alkylation reaction of aniline with benzyl alcohol catalyzed by Pd/MgO (0.8% Pd) at 180 °C.



Scheme 2. Initial reaction rates (r) calculated for the sequential transformation between benzyl alcohol and aniline catalyzed by Pd/MgO (0.8% Pd) at 180 °C.

We have measured the initial reaction rates for each one of the reactions occurring in a sequential mode on Pd-MgO (0.8% Pd) (see Scheme 2). The results obtained clearly show that the slowest reaction step is, indeed, the hydrogenation of the imine by the surface hydrides.

Table 1. N-Alkylation of anilines with benzyl alcohol catalyzed with diverse bifunctional solid catalysts.[a]

Entry	Catalyst	C[%] <sup>[b]</sup>	Yield [%] <sup>[c]</sup>				t [h]	TON <sup>[d]</sup>
			1	2	benzene	toluene		
1	Pd/MgO (0.8%)	99	13	79	traces	7	0.25	192
2	Pd/C (5%)	91	23	28	3	16	2.3	198
3 <sup>[f]</sup>	Pd/MgO (0.8%)	96	12	84	0	0	6	97 <sup>[e]</sup>
4	Pd/Ht (0.55%)	100	11	49	5	34	2	182
5	Pd/HAP (55%)	100	39	26	3	31	2	167
6	Au/MgO (1.0%)	93	49	38	3	2	5	156
7	Pt/MgO (1.0%)	98	21	61	6	11	1	145

[a] Reaction conditions: benzyl alcohol (1 mmol), aniline (3 mmol), n-dodecane (0.1 mmol), catalyst (0.0075 mmol Pd, Pt, or Au), trifluorotoluene (1 mL), T=180 8C. [b] Conversions were determined by GC on the basis of benzyl alcohol consumption. [c] Determined by GC. [d] Turnover number calculated as mmol of converted alcohol/mmol of catalyst (total Pd content). [e] Turnover number calculated as mmol of converted alcohol/mmol of surface Pd atoms. [f] After two uses.

When the initial reaction rate per metal surface atom (turnover frequency, TOF) is plotted versus the average crystallite size for Pd (see Figure 1), it can be seen that the initial reaction rates for the formation of the amine (product 2) as well as the formation of benzaldehyde increase exponentially as the Pd crystallite size decreases.

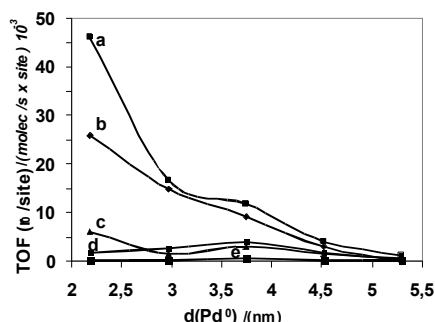


Figure 1. Plots showing the initial reaction rates ( $r_0$ ) per surface atom as a function of metal particle size ( $d$ ) for a) the hydrogenation transfer reaction to afford 2; b) dehydrogenation of benzyl alcohol to afford benzaldehyde; c) condensation reaction to give 1; d) hydrogenolysis reaction to give toluene; and e) decarbonylation reaction to afford benzene.

This result clearly indicates that both reactions, i.e., the hydride transfer reaction to the imine as well as dehydrogenation of the alcohol, are structure sensitive reactions [4]. On the other hand, since the initial reaction rate per metal surface atom remains constant with particle size for the competing reactions, giving toluene and benzene, one can increase the selectivity to product 2 by preparing catalysts with smaller Pd crystallite sizes. Moreover, the solid can be recovered and reused up to three times with a slight loss of activity on recycle.

We show that this system can be applied to build organic molecules of industrial interest such as piperazines.

## References

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