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Selective synthesis of secondary amines by Pt nanowire catalyzed reductive amination of aldehydes and ketones with ammonia†

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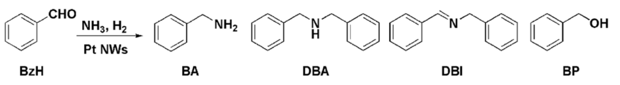
The process of the reductive amination of aldehydes or ketones in the presence of ammonia using unsupported ultra-thin Pt nanowires has been developed. This catalytic system shows high activity and selectivity under mild reaction conditions.

Dibenzylamine (DBA) is an important compound with widespread applications in rubber compounding, corrosion inhibitors, pharmaceutical intermediates and lithium amide chemistry.[1] Various methods have been developed for the synthesis of DBAs including the reductive amination of aldehydes with ammonia or primary amines;[2] selective amine cross-coupling *via* a "borrowing hydrogen" pathway;[3] *N*-alkylation of amines with alcohols;[4] transfer hydrogenation reactions of nitriles by alcohols[5] and direct hydrogenation of nitriles.[6] The reductive amination of aldehydes with ammonia is the most practical and valuable approach and results in the formation of benzylamines (BAs), DBAs or tribenzylamines (TBAs). The main challenge of this process is to increase the selectivity of the end products. Gross *et al.*[7] reported that a homogeneous Rh-catalyst can be used in the synthesis of BAs *via* the reductive amination of carbonyl compounds with aqueous ammonia. However, the process requires high hydrogen pressure (65 bar) and temperature (135 °C). RANEY® Ni was commonly used as a heterogeneous catalyst for the reductive amination of aldehydes in the presence of ammonia in early literature.[8] Disadvantages of this process include the high hydrogen pressure (20–100 bar) required as well as the relatively low activity and selectivity achieved and its environmental problems. Supported noble metal catalysts can also be used in this process with a higher yield and selectivity being obtained under mild reaction conditions. Heinen *et al.* used a Pd/C catalyst for the effective preparation of DBA under 40 bar hydrogen pressure.[9] Gomez *et al.* compared the catalytic activity of RANEY® Ni, RANEY® Co, Ru/C, Pd/C, Rh/C Pt/C and PtO_2 in the reductive amination of benzaldehyde with ammonia and found that Ru showed the highest catalytic activity under 40 bar hydrogen pressure.[10] All these catalysts are active and selective in the reductive amination of benzaldehyde with ammonia; however, they always require high hydrogen pressure in the reaction. This is not favourable in industrial applications as it is energy intensive and can be unsafe. A sustainable environmentally and industrially friendly process for the highly selective reductive amination of aldehydes with ammonia is thus of great fundamental as well as practical interest.

With the development of nanotechnology, nanowires (NWs) have been found to be more highly active catalysts in many reactions compared with nanoparticles.[11] Pt has seldom been reported in reductive amination as it may be deactivated by the adsorption of amines.[12] However, Pt NWs show outstanding catalytic activity in C–N coupling reactions; we obtained DBA using benzaldehyde and BA as substrates[13] and synthesized *N*-substituted isoindolinones from 2-carboxybenzaldehyde and amines.[14] Inspired by these results, we herein report a facile and efficient approach to synthesize DBA and its derivatives (DBAs) using a Pt NW catalyst by one-pot reductive amination of aldehydes with ammonia under mild reaction conditions.

The ultra-thin Pt nanowire (Pt NW) catalyst was prepared through acidic etching of FePt NWs.[15] No Fe was detected by inductively coupled plasma (ICP) analysis indicating that Fe was removed from the FePt NWs. TEM images indicated that the NW diameter is approximately 1.5 nm and several micrometres in length (Fig. S1, ESI†). This NW catalyst will precipitate within a few minutes in a solvent when quiescent and is therefore easy to recycle upon completion of the reaction.

Initially, the reductive amination of benzaldehyde (BzH) was conducted with aqueous ammonia under 1 bar hydrogen as aqueous ammonia is the most economical N source. BA, DBA and dibenzylimine (DBI) were detected in the reaction (Scheme 1). In addition, benzyl alcohol (BP) which is obtained by direct hydrogenation of BzH was also detected. The solvent was first optimized and DBA was the main product when Pt NWs were used as the catalyst (Table 1, entries 1–8). Compared with these solvents, ethanol was found to be the best solvent yielding 93.3% DBA (entry 3). Water, which is clearly a green solvent, can also be



Scheme 1 Reductive amination of benzaldehydes with ammonia.

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† Electronic supplementary information (ESI) available: Full details of the synthesis and characterization of the Pt nanowires as well as details of the reaction and compound characterization data. See DOI: 10.1039/c2cc34461k

Table 1 Optimization of reaction conditions[a]

Entry	Solvent	*T* (°C)	Conv[b]. (%)	Selectivity[b] (%) BA	DBA	DBI	BP
1	Methanol	40	100	1.1	84	14	0.9
2	Water	80	100	16.9	76.3	5.9	0.9
3	Ethanol	80	100	2.2	93.3	3.3	1.2
4	*n*-Heptane	80	100	5.6	88	2.7	3.7
5	Toluene	80	100	4.1	82.2	10.8	5.9
6	*o*-Xylene	80	100	20.3	68.3	4	7.4
7	*m*-Xylene	80	100	17.5	63.7	8.9	9.9
8	*p*-Xylene	80	100	11.9	75.5	4.6	8.0
9	Dioxane	80	100	11.7	30.4	8.4	49.5
10	Ethanol	40	100	3.5	82.5	14	0
11	Ethanol	60	100	6.9	86.3	5.1	1.7
12[c]	Ethanol	80	100	3	80.3	5.3	10.2
13[d]	Ethanol	80	100	14.3	59.2	6	20.6

[a] Reaction conditions: BzH (1.0 mmol), 25% aqueous ammonia (2 equiv.) and solvent (2 mL) at 1 bar H_2 with 0.005 mmol Pt NW catalyst for 12 h. [b] GC yield. [c] Pt NR catalyst (D = 2.5 nm, L = 10–20 nm). [d] Pt NP catalyst (D = 3.7 nm).

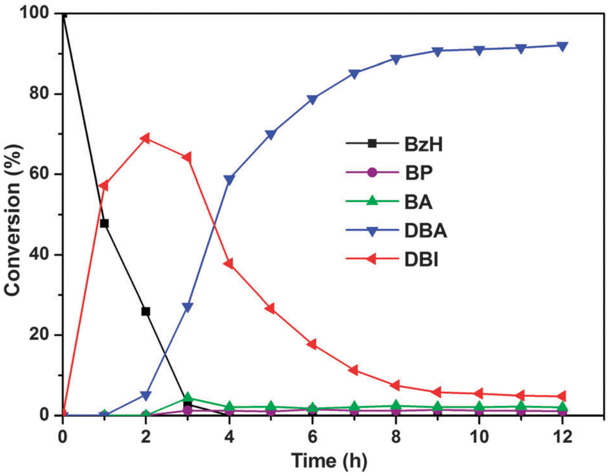


Fig. 1 Time–conversion plot for reductive amination of BzH with ammonia.

used as the solvent in this reaction yielding 76.3% DBA in 12 hours at 80 °C (entry 2). When xylene was used as the solvent, the yield of BA increased to 11–20% (entries 6–8) and the selectivity of DBA decreased to 63–76%. When 1,4-dioxane was used as the solvent, BzH was reduced easily and 49.5% BP (by-product) resulted which is not favourable for DBA formation (entry 9).

The activity of the Pt NW catalyst at different temperatures was also investigated using ethanol as solvent (entries 3, 10 and 11). At low temperature (40 °C), the selectivity of DBA was 82.5%. This selectivity increased to 86.3% when the temperature increased to 60 °C. A higher DBA yield can be obtained at 80 °C. Increasing the reaction temperature increases the selectivity to DBA and decreases the selectivity to DBI. This is in agreement with a previous result where DBA is obtained by the hydrogenation of DBI (intermediate).[16]

In order to compare the catalytic activity and selectivity of Pt NWs, Pt nanorods (NRs) and nanoparticles (NPs)[17] were also used as catalysts in this reaction. The DBA yields are 80.3 and 59.2% in NR and NP systems, respectively. The selectivity of BP increased to 10.2% in the NR system and 20.6% in the NP system which adversely affects DBA formation.

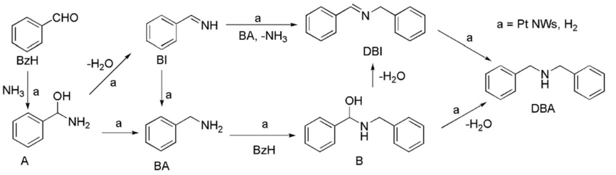
The molar ratio of BzH and ammonia is another factor which will influence the reaction selectivity. Without ammonia use, BP was the major product (Table 2, entry 1). When ammonia was added, DBA was obtained as the main product. However, a higher ammonia concentration decreases the selectivity of DBA and increases the selectivity of BA and DBI (entries 2–7). This is not favourable for DBA formation and the higher ammonia concentration decreases the catalyst reaction activity.[18]

Table 2 Reductive amination for different molar ratios of BzH to ammonia[a]

Entry	Ammonia (equiv.)	Conv.[b] (%)	Selectivity[b] (%) BA	DBA	DBI	BP
1	0	100	—	—	—	> 99
2	0.5	100	2.3	55.1	3.9	38.7
3	1	100	2.0	84.3	5.1	8.6
4	2	100	2.2	93.3	3.3	1.2
5	3	100	5.9	87.2	4.1	2.8
6	4	100	9.4	81.7	7.4	1.5
7	5	100	10.2	78.5	10.1	1.2
8	10	100	11.7	74.7	12.4	1.2

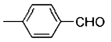
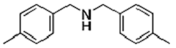
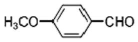
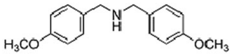
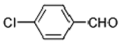
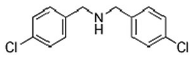
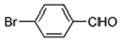
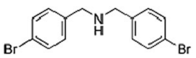
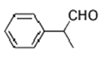
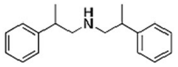
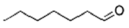
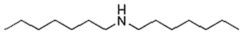
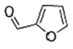
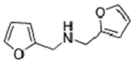
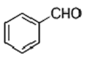
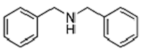
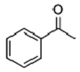
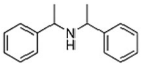
[a] Reaction conditions: BzH (1.0 mmol), 25% aqueous ammonia and ethanol (2 mL) at 80 °C, 1 bar H_2 with 0.005 mmol Pt NW catalyst for 12 h. [b] GC yield.

To elucidate the reaction mechanism, a time–conversion analysis based on GC-yield (Fig. 1) was carried out. The reaction can be divided into two parts: (1) BzH was converted rapidly to DBI in the presence of ammonia in the first three hours; (2) DBA was obtained by the reduction of DBI in the following nine hours. DBI is the reaction intermediate and the reduction of DBI is the rate-determining step. Many research groups have proposed the mechanism for the reductive amination of benzaldehyde with ammonia.[16] BA and DBA are obtained by the hydrogenation of imines or direct hydrogenolysis of carbinolamines (Scheme 2) and Pt NWs have shown excellent activity in the latter step in our previous work.[13] Carbinolamines (A) cannot be obtained as they are unstable in the reaction and dehydrate rapidly to BA or benzylimine (BI) which is subsequently reduced to BA. When BA is obtained in the presence of BzH, a new carbinolamine (B) will be formed and dehydrated rapidly to DBA or DBI. In this catalytic system, DBI can be reduced to DBA with the assistance of Pt NWs. BA can also react with BI to form DBI through a deamination reaction.[3] In all these reactions, DBI is the only intermediate which is stable and can be detected. This is in agreement with our time-conversion results from GC. Besides the reactions presented above, trace BP was obtained by direct hydrogenation of BzH which is the competing reaction to obtaining the carbinolamines (A). TBA may also be produced from the reaction of DBA with BzH; however, no TBA was detected by GC when Pt NWs were used as the catalyst and DBA was the main product.



Scheme 2 Reaction mechanism for reductive amination of BzH with ammonia.

Table 3 Pt NW catalysed reductive amination of different aldehydes with aqueous ammonia under H_2 (1 bar) atmosphere^a

Entry	R-CHO	Product	Conv.^{b} (%)	Selectivity^b (%)
1			100	93.2(92)
2			100	77.8(73)
3			100	93.1(90)
4			100	87.8(85)
5			100	96.9(96)
6			100	71.3(65)
7^c			90.9	76.8(71)
8^d			100	90.2(90)
9^d			80	70.0(67)

^{a} Reaction conditions: aldehyde (1.0 mmol), 25% aqueous ammonia (2 equiv.) and ethanol (2 mL) at 80 °C ,1 bar H_2 with the 0.005 mmol Pt NW catalyst for 24 h. ^{b} GC yield. ^{c} 40 °C. ^{d} CH_3COONH_4 (1 mmol) was used instead of ammonia. The values in the parentheses are the yield of isolated products.

In this reaction, the Pt NW catalyst can be separated by simple centrifugation or precipitation easily. The catalytic activity is maintained and the catalyst can be reused up to 6 times (Fig. S5, ESI†). The Pt NWs are relatively stable (Fig. S6, ESI†) and no Pt leaching was detected by ICP.

With the optimized reaction conditions for the preparation of DBA, the Pt NW catalyst was tested with a series of aldehydes (aromatic and aliphatic aldehydes) in the presence of ammonia (Table 3). Irrespective of the electronic nature of the substituent, we obtained good to excellent yields of DBAs from the aromatic aldehydes (entries 1–4). Aliphatic aldehydes (linear or α-branched) can also react with ammonia and the corresponding DBAs will be obtained with good yields (entries 5–6). When furan-2-carbaldehyde was used, 76.8% of the corresponding DBA was obtained (entry 7). Using ammonium acetate instead of ammonia in the presence of BzH, a yield of 90.2% DBA can be obtained (entry 8). Acetophenone, which shows no activity in aqueous ammonia, was successfully converted to the corresponding DBA with a yield of 56% when ammonium acetate was used as the ammonia source (entry 9). Unsymmetrical DBAs can also be obtained with this catalytic system in good yield (33–63%) (Table S1, ESI†).

In conclusion, a facile and efficient process for the synthesis of DBAs through direct reductive amination of aldehydes has been developed using the unsupported Pt NW catalyst under mild reaction conditions. The Pt NW catalyst exhibited excellent activity and selectivity in reductive amination using ammonia or ammonium acetate as the substrate and can be recycled easily. We envision that the Pt catalyst will be an important type of catalyst for the industrial synthesis of amines.

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